Development of Lewis Acid Catalyzed Methods for Carbonyl-Olefin Metathesis, Enantiodivergent Total Synthesis of Lingzhiol and Studies Towards the Divergent Synthesis of *ent*-Kaurenes

by

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Dedication

To my family, friends, and all the members in the Schindler lab who have helped me over the last six years.

Acknowledgements

The work presented in this dissertation is a compilation of contributions. Collaborators on projects are acknowledged at the beginning of each chapter.

Most importantly, I want to thank Prof. Corinna Schindler for taking me on as one of her first graduate students and helping to personally train me in organic chemistry and synthesis while providing me with the opportunities to learn about building a new lab group, recruit students and develop new projects. I am grateful for her continued support through various challenges and continuing to support me in the months following the defense of this dissertation.

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Abstract

The development of new methods for forming carbon-carbon bonds is an important area of research in synthetic organic chemistry. Accomplishing the direct formation of new C-C bonds between a carbonyl and olefin starting material is a powerful transformation, enabling the synthesis of new olefin-containing molecules, especially for molecules containing small rings. Recently, the Schindler group has developed an operationally simple, mild, and environmentally benign strategy for carbonyl-olefin metathesis reactions relying on iron(III) as a Lewis acid. Rather than relying on stoichiometric alkylidenes as reagents, the Lewis acid catalyst induces oxetane formation and subsequent fragmentation, enabling catalyst turnover and producing acetone or aromatic aldehydes as waste products.

This dissertation describes the application and extension of this method to a variety of new systems. Polycyclic aromatic hydrocarbons, important in material science and polymer chemistry, have been prepared under these conditions. Alkyl ketones, previously found to be problematic substrates, can undergo the carbonyl-olefin metathesis reaction in systems when iron(III) is able to form singly bridged homo-dimers that lead to much greater carbonyl activation than their monomeric counterparts. Finally, carbonyl-olefin metathesis is demonstrated in transannular systems. Ten membered rings derived from biologically important steroid molecules are shown to undergo divergent reactivity when treated with different Lewis acid catalysts.

Total synthesis of terpene natural products is also an important and active area of research in synthesis as means of delivering useful quantities of biologically important, naturally occurring molecules as well as a driving force for the discovery and development of new methods.

The tetracyclic meroterpenoid lingzhiol has potential reno-protective biologically activity and is a small but synthetically interesting natural product. This dissertation describes the completion of an enantioselective total synthesis of this compound. In the course of these studies, a metal-mediated reversal of enantioselectivity was discovered. This enables the enantioselective synthesis of both enantiomers.

Finally, *ent*-kaurene diterpenoid natural products are a large class of complex natural products that are found in various traditional East Asian medicines. Over 600 compounds of this class are known and their biological activity has made them targets for synthetic chemistry over the last 60 years. Most of the existing synthetic strategies enable preparation of only one to three ent-kaurene compounds. Here is described studies toward a divergent synthetic strategy relying on synthesis of a common intermediate, which can be elaborated to numerous *ent*-kaurenes.

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Chapter 1 Introduction – Carbonyl-Olefin Metathesis

1.1 History

Carbonyl-olefin metathesis is valuable transformation in synthetic organic chemistry, enabling the direct carbon-carbon bond formation between a carbonyl and an alkene

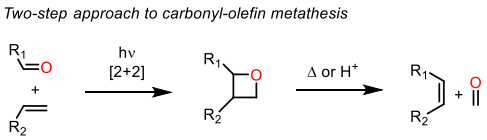

Figure 1-1 Photocycloaddition followed by fragmentation as a two step approach to carbonyl-olefin metathesis

functional group.[1] Carbonyl-olefin metathesis reactions directly forges these bonds, enabling rapid access to cyclic olefins without requiring functional group interconversions or redox manipulations. The earliest approach to carbonyl-olefin metathesis reactions involves a two-step oxetane formation by photocycloaddition followed by acid- or heat-mediated fragmentation (Figure 1-1).

1.2 Olefin-Olefin Metathesis

A remarkable advance in carbon-carbon bond forming reactions enabled by ruthenium and molybdenum alkylidene catalysts was awarded the Nobel Prize in 2005 for revolutionizing various areas of chemistry, including fine chemical synthesis, natural product synthesis and polymerization.[2] This area of research is well-established, highly active and rapidly expanding, and extensively reviewed.[3] Recent developments in catalytic carbonyl-olefin metathesis reactions have mirrored the development of olefin-olefin metathesis reactions, including ring-closing[4], ring-opening[5], and intermolecular

carbonyl-olefin metathesis reactions[6]. Importantly, no transannular olefin-olefin metathesis reactions are known, in contrast to the carbonyl-olefin metathesis reactions presented in Chapter 4.

1.3 Challenges in Catalytical Carbonyl-Olefin Metathesis

Extension of the alkylidene-mediated olefin-olefin metathesis mechanism to carbonyl-olefin metathesis was reported by Grubbs and Fu in an important advance.[7] By

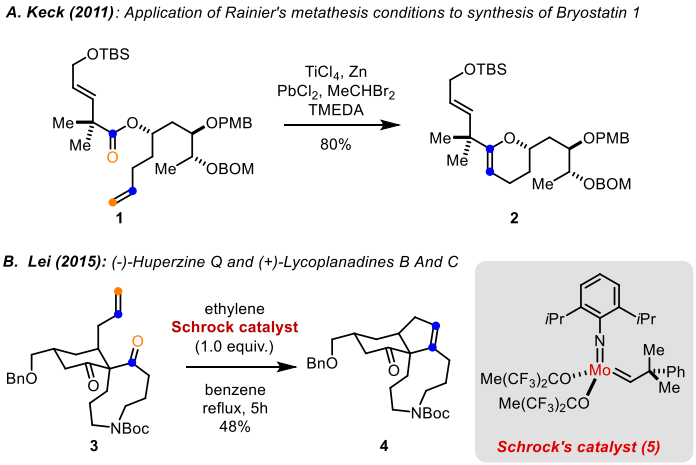

Figure 1-2 Select examples applying carbonyl-olefin metathesis in synthesis

using Schrock's catalyst (**5**) as a stoichiometric reagent, they were able to accomplish the direct formation of a carbon-carbon double bond from an olefin and carbonyl. Efforts to develop catalytic protocols based on this design principle have proven unsuccessful in because the metal-oxo byproducts are highly inert and cannot be reduced to re-enter the catalytic cycle. More cost-effective titanium-based protocol has also been developed by Rainier and coworkers but suffers from the same challenge and no catalytic protocol has been disclosed.[8] Tungsten alkylidene mediated ring-closing carbonyl-olefin metathesis reactions have also been disclosed.[9] The value of these methods has been demonstrated in various total synthesis efforts (Figure 1-2), including Lei's synthesis of Huperzine Q and Lycoplanadines[10], Keck's approach to Bryostatin 1[11], and more[12].

1.4 Lewis Acid-Mediated Carbonyl-Olefin Metathesis

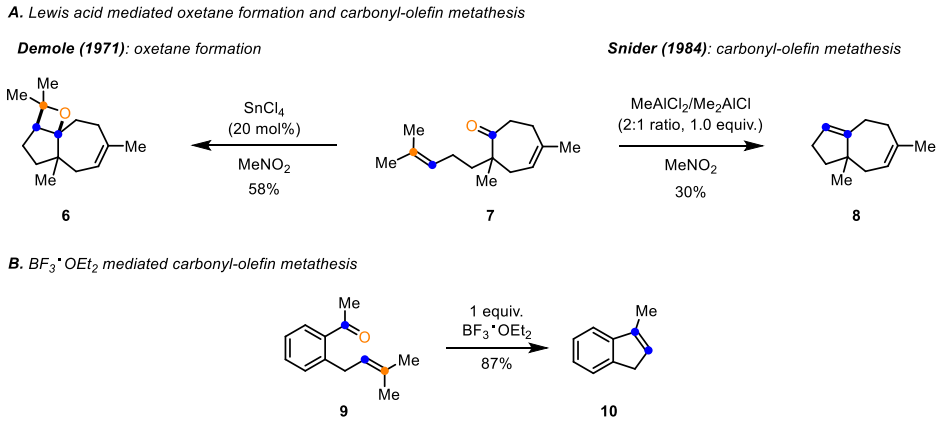

Figure 1-3 Stoichiometric Lewis acid mediated carbonyl-olefin metathesis reactions

Several isolated examples have been reported in the literature describing carbonyl-olefin metathesis reactions relying on stoichiometric Lewis acids. Demole and coworkers have shown that oxetane **6** can be formed when treating cycloheptene **7** with $SnCl_4$[13], while carbonyl-olefin metathesis product **8** was formed in low yield when the same substrate was subjected to mixtures of alkylaluminum Lewis acids (Figure 1-3A)[14]. Schmaltz and co-workers observed that a small scope of prenyl ketones could be cyclized with stoichiometric BF_3•OEt_2 (Figure 1-3B)[15], while transannular metathesis[16] was observed in a single case with excess BF_3•OEt_2. An early example of Lewis acid catalyzed carbonyl-olefin metathesis was shown by Franzén using catalytic trityl cation, affording intermolecular carbonyl-olefin metathesis products in low yields.[17]

1.5 Catalytic Methods in Carbonyl-Olefin Metathesis

Lambert and coworkers[18] described the first catalytic method for carbonyl olefin metathesis. This approach, catalyzed by hydrazine **11**, relies on the strain release of cyclopropene substrates to couple them with aldehydes (Figure 1-4A).

Our research group has recently reported a new general method for catalytic

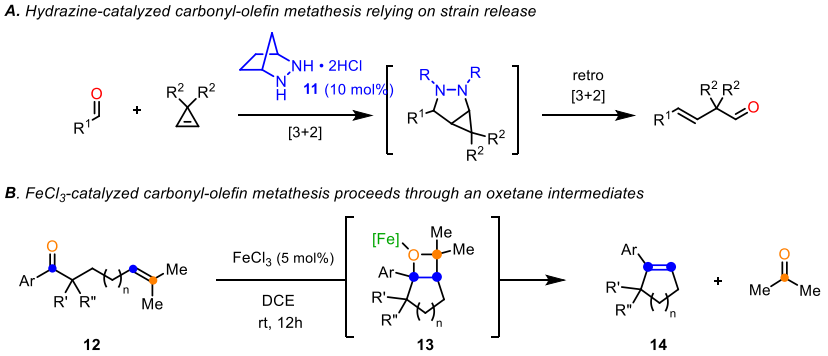

Figure 1-4 Catalytic methods in carbonyl-olefin metathesis relying on A) hydrazine catalysts and B) Lewis acidic $FeCl_3$

carbonyl-olefin metathesis of aryl ketones relying on $FeCl_3$ as a Lewis acid catalyst (Figure 1-4B).[4a] This method proceeds under mild conditions and detailed mechanistic studies have been undertaken.[19] Rather than forming an unreactive metal-oxo byproduct, the Lewis acid induces a concerted, asynchronous [2 + 2] cycloaddition to form activated oxetane **13**, which then undergoes fragmentation to provide the desired product and a waste carbonyl (typically acetone or benzaldehyde). This method has been extended to a variety of systems, including intermolecular reactions[20], amine-containing substrates[4b], alkyl ketones[4c], polycyclic aromatic hydrocarbons[21], and transannular systems[6]. The development of several of these methods is detailed in this dissertation.

1.6 Additional Recent Catalytic Methods for Carbonyl-Olefin Metathesis

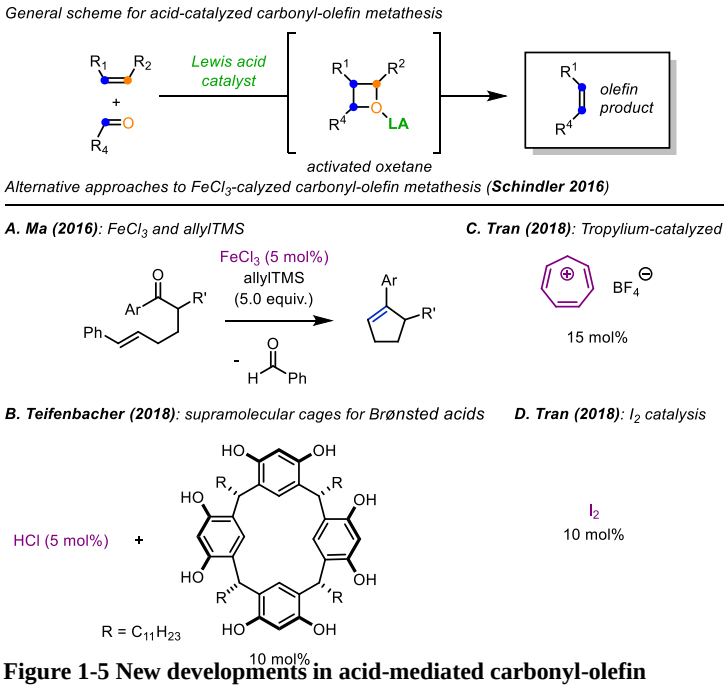

Figure 1-5 New developments in acid-mediated carbonyl-olefin metathesis reactions

Since our initial report of $FeCl_3$-catalyzed carbonyl-olefin metathesis, various other groups have become active in this area of research (Figure 1-5). Ma and coworkers have also investigated $FeCl_3$-catalyzed carbonyl-olefin metathesis reactions of styrenyl olefins in which the benzaldehyde byproduct is sequestered by allylTMS[22], while Tran has reported various carbonyl-olefin metathesis reactions catalyzed by tropylium cation[23] and molecular iodine.[24] Tiefenbacher and coworkers have reported that macromolecular cages and HCl are also capable of catalyzing these reactions.[25] With increasing interest in this area in recent years and continued investigations from our group, we expect this field to continue to be a versatile and robust area of research in synthetic chemistry.

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Chapter 2 $FeCl_3$-Catalyzed Carbonyl Olefin Metathesis for the Synthesis of Polycyclic Aromatic Hydrocarbons

The work described in this chapter has been published and is adapted with permission from: McAtee, C. S.; **Riehl, P. S.**; Polycyclic Aromatic Hydrocarbons via Iron(III)-Catalyzed Carbonyl-Olefin Metathesis. *J. Am. Chem. Soc*. **2017**, *139*, 2960-2963.

2.1 Synthetic Approaches Towards Polycyclic Aromatic Hydrocarbons

Polycyclic aromatic hydrocarbons (PAHs)[1] are an important class of organic compounds comprised of phenanthrenes, pyrenes, picenes, chrysenes and others. Important optical[2], electronic[3], and chelating[4] properties make these compounds desirable synthetic targets, with important applications in materials science[4,5] asymmetric catalysis[6], total synthesis[7], and molecular recognition[8]. Previously established synthetic approaches to these compounds include the McMurray coupling[9,10] relying on low-valent titanium reagents (Figure 2-1A), or oxidative photocyclization of stilbenes[11]. These reactions are limited by their reliance on harsh reaction conditions and competing intermolecular substrate dimerization[12]. More recent advances have relied on Diels-Alder cycloadditions[13], radical cyclizations[14], or precious metal-catalyzed cycloisomerizations[15]. Finally, rhodium-catalyzed dimerization of bis(N-tosylhydrazones)[16] **2** (Figure 2-1A) and ruthenium alkylidene-catalyzed olefin-olefin metathesis[17] of bis(alkenes) **4** represent mild approaches for synthesis of polycyclic aromatic hydrocarbons (Figure 2-1A). Our

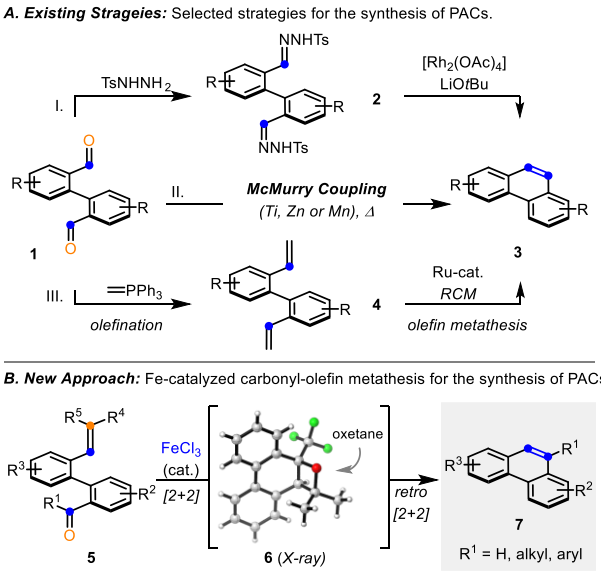
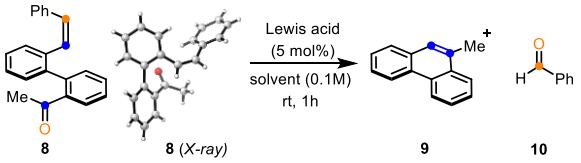


Figure 2-1 A. Existing approaches to PAHs B. Carbonyl-Olefin metathesis approach

laboratory has recently reported an $FeCl_3$-catalyzed carbonyl-olefin metathesis reaction that proceeds efficiently under mild reaction conditions at ambient temperatures. This method enables formation of a new olefin product through direct reaction between olefin and carbonyl starting materials initiated by Lewis acid activation of the carbonyl fragment. Herein is described the application of this strategy for the mild and general synthesis of a wide array of PAHs. Importantly, both ketones and aldehydes are competent carbonyl coupling partners. This reaction proceeds through intermediate oxetanes **6** to afford good to excellent yields of the metathesis products (Figure 2-1B). A variety of Lewis acids were previously shown to promote the carbonyl-olefin metathesis reaction[18,19], but the unique combination of Lewis acidity[20] and oxophilicity[21] was shown to be optimal. Presented here is the application of this method to the synthesis of PAHs.

2.2 Reaction Optimization

Table 2-1 Evaluation of Lewis Acids for Synthesis of PAHs by Carbonyl-Olefin Metathesis



8 **8** (*X-ray*) **9** **10**

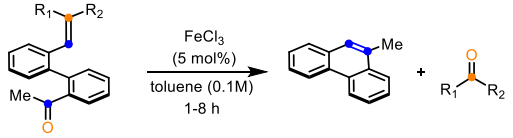
entry	Lewis acid	solvent	yield **9** (%)	conversion (%)
1	$TiCl_4$	DCE	3	7
2	$SnCl_4$	DCE	0	6
3	$FeCl_2$	DCE	0	2
4	$Cu(OTf)_2$	DCE	0	0
5	$ZnCl_2$	DCE	22	26
6	$BF_3{\cdot}Et_2O$	DCE	31	35
7	$AlCl_3$	DCE	93	100
8	$GaCl_3$	DCE	88	100
9	$FeCl_3$	DCE	97	100
10	$FeCl_3$	DCE (0.01M)	95	100
11	$FeCl_3$	toluene	99	100
12	$FeCl_3$	DMF	0	0
13	$FeCl_3$	1,4-dioxane (0.1M)	0	6
14	HCl	DCE	0	0
15	*p*TsOH	DCE	0	0

Biaryl ketone **8** was selected for reaction optimization, and upon treatment with various Lewis acids ($TiCl_4$, $SnCl_4$, $FeCl_2$, $Cu(OTf)_2$, $ZnCl_2$), little or no product formation was observed. Stronger Lewis acids $GaCl_3$ and $AlCl_3$ fully consumed the starting material **8** and afforded 88% and 93% yields of product **9** respectively. In contrast to previous work in this area, $BF_3{\bullet}OEt_2$ led to low yields of metathesis product **9**.[22] 5 mol% $FeCl_3$ in dichloroethane or toluene were identified as optimal reaction conditions leading to 97% and 99% yield of product, respectively (entries 9 and 11, Table 1). The yield of product was slightly diminished under more dilute conditions (entry 10, Table 2-1). Coordinating solvents (1,4 dioxane, DMF, entries 12 and 13, Table 2-1) led to no formation of phenanthrene product **9** due to deactivation of the Lewis acid catalyst. Additionally, Brønsted acids HCl[23] and *p*TsOH in dichloroethane afforded no conversion of starting material (entries 14 and 15, Table 2-1).

We next evaluated various biaryl olefin substitutions for their ability to undergo the carbonyl-olefin metathesis reaction (Table 2-2). Electron-rich, electron-poor and

unsubstituted styrenes were competent partners for the carbonyl-olefin metathesis reaction (entries 1-6, Table 2-2). However, all but unsubstituted styrene **11** and prenyl-substituted **17** required elevated temperatures (50 °C) to achieve full conversion. Both *E*- and *Z*-isomers of *para*-methylstyrenes **12** and **13** reacted in similarly high yields of

Table 2-2 Alkene Evaluation for Formation of 9



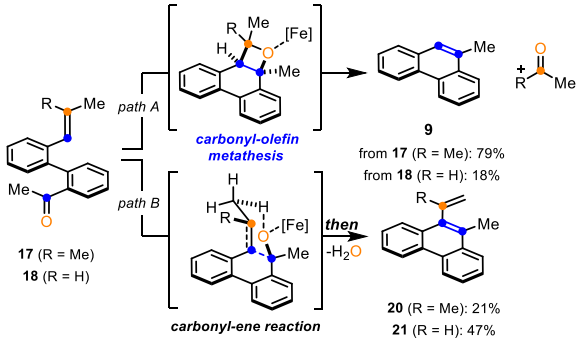
11-19 **9**

entry	alkene	yield (%)	entry	alkene	yield (%)
1	**11**[a]	90	5	**15**[b]	80
2	**12**[b]	82	6	**16**[b]	84
3	**13**[b]	89	7	**17**	79
4	**14**[b]	86	8	**18**[b]: R= Me	11
			9	**19**[b]: R= H	n.r.

Conditions: biaryl (0.13 mmol), $FeCl_3$ (5 mol%) in toluene (0.1 M); [a] mixture of *E/Z* (2:1) isomers; [b] reaction heated to 50°C.

82% and 89% respectively, indicating an indiscriminate reaction mechanism and enabling the use of *E*/*Z* mixtures of substrates. Benzaldehyde byproducts were observed during the course of the reaction but did not inhibit the formation of the resultant metathesis products. Prenylated substrate **17** afforded lower yield (79%, entry 7, Table 2-2) of desired product **9** than the styrenyl substrates, and crotyl substrate **18** resulted in dramatically diminished yields of 18%. Finally, no reaction was observed when treating the terminal alkene **19** under the optimal reaction conditions. Diminished yields in reaction of prenyl- and crotyl-containing substrates **17** and **18** were found to be a result of a competing $FeCl_3$-catalyzed carbonyl-ene reaction to form **20** and **21** in 21% and 47%

yield respectively under the optimal reaction conditions (Figure 2-2). The findings stand it contrast to previous work in our group on $FeCl_3$-catalyzed ring-closing carbonyl-olefin metathesis reactions[18], which found prenyl-derived substrates were superior to the analogous styrenes.



Conditions: biaryl (0.13 mmol), $FeCl_3$ (5 mol%) in dichloroethane (0.1M), rt, 1h; [a)] yield determined by ^1H NMR analysis with 1,3,5-trimethoxybenzene as internal standard.

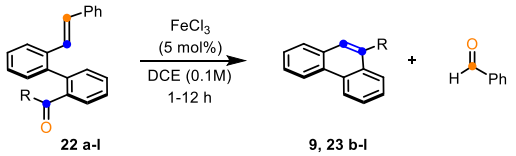
Figure 2-2 Competing carbonyl-olefin metathesis and carbonyl-ene reactions

2.3 Carbonyl Substitution

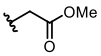
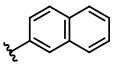
The optimized reaction conditions for $FeCl_3$-catalyzed carbonyl-olefin metathesis were found to be effective for a variety of carbonyl substituents. While aldehydes were previously found to be unreactive for this transformation, **22b** was found to smoothly undergo the reaction to afford metathesis product **23b** in 75% yield under the optimized conditions.

In addition to aldehyde and methyl ketone substrates, sterically demanding substrates containing isopropyl (**22c**) and *tert*-butyl (**22d**) groups were reacted to form the alkylated phenanthrene products in 79% and 55% yield, respectively, although the latter

Table 2-3 Evaluation of Carbonyl Substituents



22 a-l 9, 23 b-l

entry	substrate		yield (%)	entry	substrate		yield (%)
1		**22a**	99	7		**22g**[a]	50
2		**22b**	75	8		**22h**	72
3		**22c**	79	9		**22i**[a]	52
4		**22d**[a]	55	10		**22j**	N.R.
5		**22e**	67	11		**22k**	N.R.
6		**22f**	53	12		**22l**	N.R.

Conditions: biaryl (0.13 mmol), $FeCl_3$ (5 mol%) in dichloroethane (0.1M), rt, 1-12h;
[a] reaction heated to 50ºC.

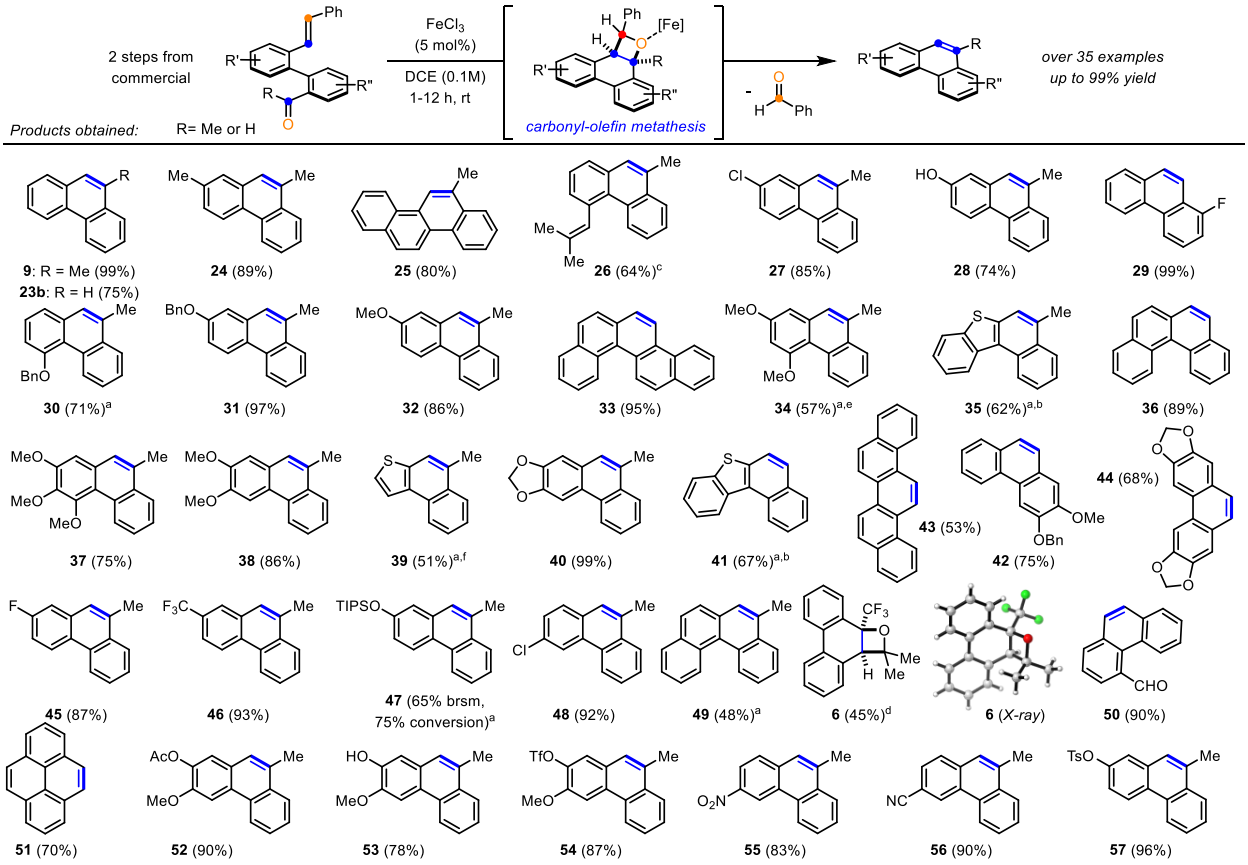
required heating for the reaction to proceed efficiently (entries 3 and 4, Table 2-3). Phenyl and naphthyl substituted carbonyls (**22e** and **22f**) also proceeded efficiently (entries 5 and 6, Table 3). Biaryl enone **22g** was also a competent substrate (at elevated temperatures) for the reaction to afford **23g** in 50% yield, bearing an exocyclic olefin as a functional handle for further reactivities (entry 7, Table 2-3). Additionally, β-ketoester **22h** lead to metathesis product **23h** in moderate yield of 72%, while trifluoromethyl ketone **22i** was also a viable substrate, affording 52% yield of phenanthrene product **23i** (entries 8 and 9, Table 2-3). Finally, carboxylic acids **22j** and their ester (**22k**) and amide (**22l**) derivatives were unreactive, affording only recovered starting material (entries 10-12, Table 2-3).

2.4 Substrate Scope

A wide variety of substituted PAH frameworks were accessible under the optimized reaction conditions. When subjecting the biaryl substrates to these conditions, the desired PAH products were obtained along with benzaldehyde as the byproduct. Electron-poor phenanthrenes bearing halogen (**27**, **29**, **45**), trifluoromethyl (**46**), nitro (**55**), and nitrile

(**56**) substituents were formed in high yields exceeding 85% (Table 2-4). Electron-rich phenanthrenes bearing methoxy (**32**, **38**, **42**) and benzyl ether (**30**, **31**, **42**) functionalities

Table 2-4 Scope of $FeCl_3$-Catalyzed Carbonyl-Olefin Metathesis for PAH Synthesis



Conditions: biaryl (0.13 mmol), $FeCl_3$ (5 mol%), in DCE (0.1M), rt, 1-12 h; [a] reaction heated to 50°C; [b] reaction was run with 20 mol% catalyst loading; [c] starting material is bis-prenylated biaryl ketone (see Supporting Information for details); [d] substrate is the prenylated analog of **22i**; reaction was run in toluene as solvent; [e] starting material is reisolated; [f] substrate decomposition was observed at the elevated reaction temperatures.

were also formed in excellent yield (Table 2-4). However, *ortho*-methoxy substituents lead to diminished yields of 75% and 57% yield (**34** and **37**, Table 2-4). Dioxole-substituted phenanthrenes **40** and **44** were formed in 99% and 68% yield when treated with $FeCl_3$. Additionally, sulfur-containing PAHs (**35**, **39**, and **41**) are also accessible by carbonyl-olefin metathesis. Earlier approaches to such structural motifs require harsh reaction conditions and suffer from competing reaction pathways leading to low yields.[24] Unprotected phenols and aldehydes were well-tolerated under the reaction conditions to afford **28** and **50** in 74% and 90% yield, respectively. Larger polycyclic aromatic

hydrocarbons including methylchrysene **25** and benzo(*c*)phenanthrene **36** were accessible using this carbonyl-olefin metathesis strategy in 80% and 89% yield, respectively (Table 2-4).

2.5 Isolation of an Oxetane

The $FeCl_3$-catalyzed carbonyl-olefin metathesis reaction is understood based on various experimental and computational studies to proceed by concerted, asynchronous [2+2] cycloaddition to afford an oxetane, which then fragments by a retro-[2+2] mechanism to afford the metathesis product and a waste carbonyl[18]. Interestingly, in our early studies with prenylated substrates, the prenyl analog of trifluoromethyl ketone **22i** did not afford any metathesis product **23i** when treated under the optimal reaction conditions. Instead, 45% yield of oxetane **6** was isolated and the structure was confirmed by X-ray crystallography (Table 2-4). This finding supports our hypothesis that this reaction proceeds through oxetane intermediates.

2.6 Bis(Carbonyl-Olefin Metathesis) Reaction

Higher-order polycyclic aromatic compounds have substantial impact in material science and polymer chemistry.[25] In order to demonstrate the potential utility of this method in polymer chemistry, triaryl diketone **58** was prepared and subjected to the

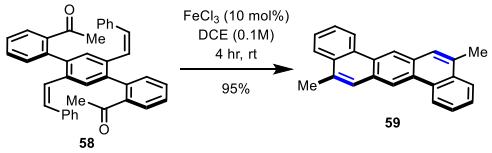


Figure 2-3 Bis(carbonyl-olefin) metathesis for synthesis of higher order PAHs

optimized conditions for carbonyl-olefin metathesis. As a result, dibenz[*a*,*h*]antracene **59** was formed in excellent yield of 95%.

2.7 Conclusions

This work has detailed the development of a mild, operationally simple, and highly selective method for the preparation of polycyclic aromatic hydrocarbons. The reaction tolerates a broad array of alkene and carbonyl coupling partners and enables the preparation of diversely functionalized polycyclic aromatic hydrocarbons, including higher order PAHs. The isolation and unambiguous characterization of an oxetane **6** supports the mechanistic hypothesis that oxetanes are reactive intermediates in the $FeCl_3$-catalyzed carbonyl-olefin metathesis reaction.

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Chapter 3 $FeCl_3$-Catalyzed Carbonyl-Olefin Metathesis of Alkyl Ketones via a Superelectrophilic Iron(III) Homodimers

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3.1 Carbonyl-Olefin Metathesis

Carbonyl-olefin metathesis reactions are an important class of carbon-carbon bond formation reactions that have recently experienced significant advances. They are highly valuable for their ability to directly form new carbon-carbon bonds between carbonyl and olefin functional groups. Early examples of this type of reaction have relied on the formation of oxetane followed by a second fragmentation step.[1] Employing stoichiometric molybdenum alkylidenes as reagents represents an important advance in this area.[2] The first catalytic method for carbonyl-olefin metathesis employs bicyclic hydrazine catalysts and relies on strain release to enable the reaction to proceed.[3] Most recently, Lewis-acid catalyzed protocols have been developed as a viable method for carbonyl-olefin metathesis.[4,5,6] Binding to a Lewis acid catalyst, such as $FeCl_3$, activates the carbonyl functionality to perform a [2+2]-cycloaddition to form an oxetane intermediate that subsequently undergoes retro-[2+2]-cycloaddition that leads to the desired olefin product along with a waste carbonyl (such as acetone or benzaldehyde). Successful

Lewis acid catalyzed protocols have been developed for both intramolecular and intermolecular carbonyl-olefin metathesis reactions.[7,8] However, the current approaches are all limited to aryl carbonyl substrates while the corresponding alkyl carbonyls remains elusive[4-8]. The work presented here describes the extension of this method to alkyl ketones and corresponding mechanistic investigations that suggest singly bridged $FeCl_3$ homodimers are the active catalytic species leading to superelectrophilic activation of the carbonyl.

3.2 Initial Investigations

Initial efforts in our laboratory to develop an $FeCl_3$-catalyzed carbonyl-olefin metathesis reaction were highly successful when employing aryl ketone **1** as substrate to afford **2** as metathesis product in 99% yield (Figure 3-1).[5a] The corresponding alkyl ketone **4** afforded no conversion to the desired metathesis product **5**. Earlier mechanistic work

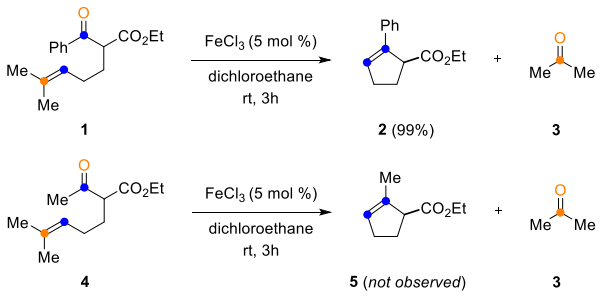


Figure 3-1 Alkyl vs. aryl ketones in $FeCl_3$-catalyzed carbonyl-olefin metathesis reactions

in our group identified three challenges associated with alkyl ketone substrates. 1) Aryl substrates bind more favorably (2.4 kcal/mol) to $FeCl_3$ than the acetone byproduct of the carbonyl-olefin metathesis reaction (Figure 3-2). However, alkyl ketones **7** bind less strongly to $FeCl_3$, requiring stronger Lewis acids to activate these substrates. Additionally, competitive binding of the Lewis acid to the acetone byproduct **3** is more significant and catalyst inhibition is a potential problem. 2) Our group's mechanistic investigations

identified the aromatic ring of the aryl ketones to be required for transition state stabilization by redistributing electron density and lowering the HOMO of **8** to reduce the barrier towards oxetane formation.[5c] 3) Recent work in TfOH-catalyzed oxygen atom transfer has shown that competing oxetane fragmentation pathways exist, leading to products different from the desired carbonyl-olefin metathesis product.[9] Specifically, α-

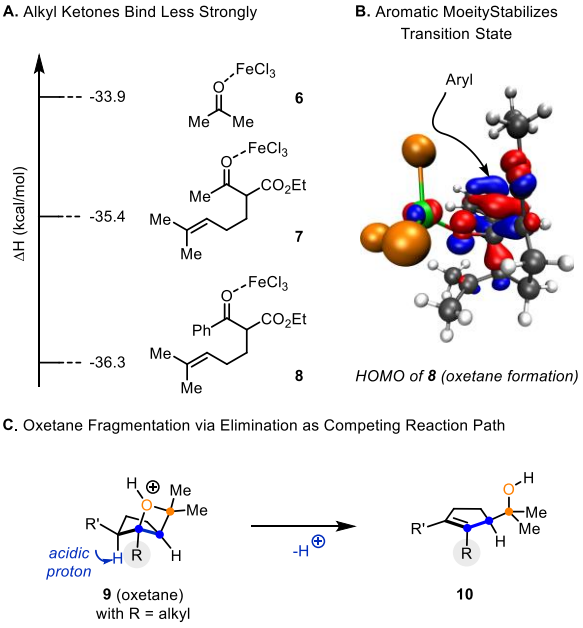


Figure 3-2 Challenges for carbonyl-olefin metathesis of alkyl ketones

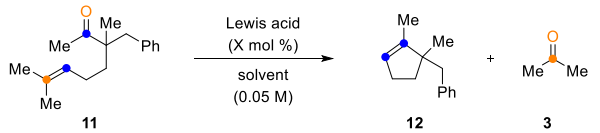
protons to the carbonyl functionality can lead to a distinct oxetane fragmentation pathway resulting in the formation of unsaturated alcohols **10** (Figure 3-2).[10] Based on these challenges, we hypothesized that the alkyl ketone substrates would require a much stronger Lewis acid than $FeCl_3$. We also sought to optimize the reaction on a new substrate **11** bearing an α-quaternary center to avoid the possible competing oxetane fragmentation pathways (Table 3-1).

3.3 Reaction Optimization

We first sought to evaluate the carbonyl-olefin metathesis reaction of alkyl ketones with different Lewis acids using α-quaternary ketone substrate **11**. Stronger Lewis acids

than $FeCl_3$ were first evaluated. Substoichiometric amounts of strongly Lewis acidic $AlCl_3$ resulted in no formation of the desired metathesis product **12** (entry 1, Table 3-1). Stoichiometric ethylaluminum sesquichloride (EASC) afforded the formation of **12** in 30% yield with no recovered starting material (entry 6, Table 3-1). Control reactions employing weaker Lewis acids including $SnCl_4$ and $GaCl_3$ afforded the desired product **12** in low yields of 30% and 21% respectively, along with significant decomposition of the starting material (entries 3 and 5, Table 3-1). BF_3•OEt_2 afforded similarly low yields while $TiCl_4$ afforded no cyclopentene product **12** (entries 2 and 4, Table 3-1). Based on these results, we investigated the ability of various loadings of $FeCl_3$ to catalyze this transformation. Surprisingly, formation of metathesis product **12** was observed in 44% yield after only 15 minutes (entry 7, Table 3-1). This yield was increased to 68% by doubling the catalyst loading to 10 mol% (entry 8, Table 3-1). Optimal reaction time was found to be 3 hours, after which time 74% yield of product was observed (78% conversion, entry 9, Table 3-1). Further attempts to optimize this reaction showed that the yield decreased to 37% when employing DCM as solvent in place of DCE (entry 10, Table 3-1). Furthermore, no reaction was observed with toluene as solvent (entry 11, Table 3-1). These results both starkly with our previous studies into $FeCl_3$-catalyzed carbonyl-olefin metathesis reactions of aryl ketones which generally tolerates chlorinated hydrocarbons and aromatic solvents.[5a,c] Finally, substoichiometric Brønsted acids including HCl, TfOH, and H_2SO_4

Table 3-1 Lewis Acid Optimization for Alkyl Carbonyl-Olefin Metathesis



11 12 3

entry	Lewis acid	mol %	solvent	time (h)	yield **12** (%)	conv. (%)
1	$AlCl_3$	5	DCE	24	0	0
2	$TiCl_4$	5	DCE	24	0	36
3	$GaCl_3$	5	DCE	16	21	82*
4	$BF_3{\cdot}OEt_2$	5	DCE	24	24	51
5	$SnCl_4$	5	DCE	24	30	70*
6	EASC	100	DCE	16	30	100*
7	$FeCl_3$	5	DCE	15 min	44	48
8	$FeCl_3$	10	DCE	15 min	68	70
9	$FeCl_3$	10	DCE	15 min	74	78
10	$FeCl_3$	5	DCM	3	37	40
11	$FeCl_3$	5	toluene	24	0	25
12	HCl	5	DCE	24	0	7
13	TfOH	5	DCE	24	0	3
14	H_2SO_4	5	DCE	24	0	93*

Conditions: All reactions were performed using 0.16 mmol of ketone **11** and Lewis acid in solvent (0.05 M) at 23 °C. EASC = ethyl aluminum sesquichloride.*Substrate decomposition was observed.

failed to afford the desired carbonyl-olefin metathesis product **12** (entries 12-14, Table 3-1).

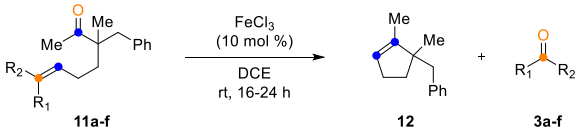
Interestingly, the results obtained indicating $FeCl_3$ was the optimal Lewis acid catalyst did not corroborate our previous theoretical investigations based on enthalpies for Lewis acid activation that predict the need for a stronger Lewis acid to effectively activate alkyl ketones.

3.4 Olefin Substitution

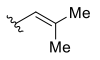
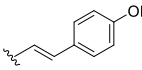
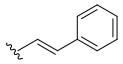
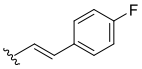
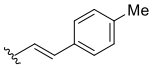
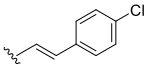
We next varied the substituents on the olefin functionality for this $FeCl_3$-catalyzed carbonyl-olefin metathesis reaction. Prenyl-substituted ketone **11b** resulted in the formation of metathesis product **12** in 74% yield (entry 1, Table 3-2). Initial studies found that the corresponding styrenyl-substituted ketones **11b**-**11f** showed little to no reactivity when subjected to initial reaction conditions. Subsequent investigations concluded that this poor reactivity can be attributed to product inhibition caused by the benzaldehyde byproducts. We therefore sought to investigate additives capable of sequestering the

corresponding aldehydes[5f] and ultimately found that allyltrimethylsilane enabled catalytic

Table 3-2 Effect of Olefin Substituent on Carbonyl-Olefin Metathesis of Alkyl Ketones



11a-f 12 3a-f

entry	olefin	yield (%)	entry	olefin	yield (%)
1	 11a	74%	4	 11d	5%[a]
2	 11b	77%[a]	5	 11e	30%[a]
3	 11c	78%[a]	6	 11f	25%[a]

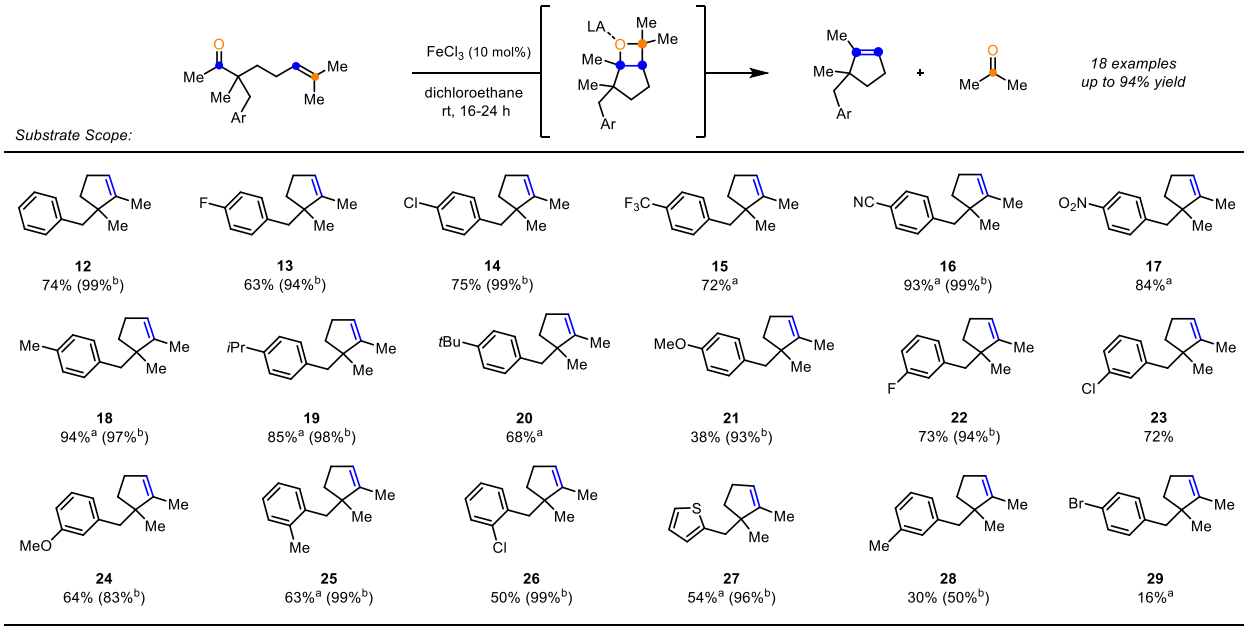
Conditions: All reactions were performed using 0.5 mmol of ketone **11a-f** and 0.05 mmol of $FeCl_3$ in dichloroethane as solvent (0.05 M) at 23 °C for 16-24 h. [a]Addition of 5.0 equiv. of allyltrimethylsilane.

carbonyl-olefin metathesis to proceed in these systems. In the presence of the allyltrimethylsilane additive, these styrenyl ketones afford cyclopentene product **12** in up to 78% yield (Table 3-2).

3.5 Substrate Scope

The optimal conditions for carbonyl-olefin metathesis of alkyl ketones proved to be efficient for a variety of substrates incorporating various substituents and functional groups (Table 3-3 and 3-4). Substrates with electron-poor aryl residues in the β-position were well tolerated, affording 63-93% yields of the desired cyclopentene products (**13**-**17**, Table 3-3). Electron-rich β-arylated substrates also afford the metathesis products in up to 94% yield (**18**-**21**, Table 3-3). Substrates bearing methyl or chloro substituents in the *ortho*-position led to diminished yields of 63% and 50% respectively (**25** and **26**), while *meta*-substituted substrates provided good yields from 64% to 76% (**22**-**24**, Table 3-3). A thiophene-containing substrate was also tolerated, affording **27** in 54% yield. In addition to methyl ketones, ethyl and isobutyl ketones reacted under the optimal conditions,

Table 3-3 Substrate Scope: Aryl Substitutions



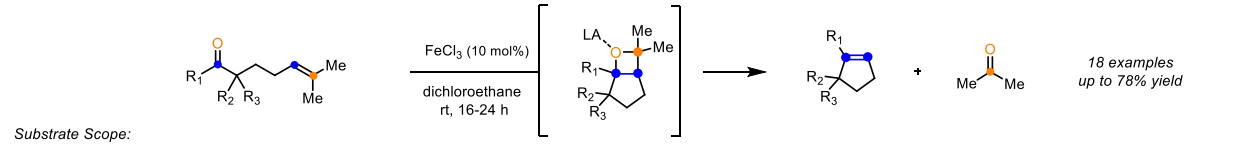
Conditions: All reactions were performed using 10 mol % of Lewis acid, $FeCl_3$, in DCE (0.05M) at 23 °C for 16-24 h or [a]80 °C for 3 h. [b]Yields are based on recovered starting material. [c]50 mol % $FeCl_3$ in DCE (0.05M) at 0 °C to 23 °C.

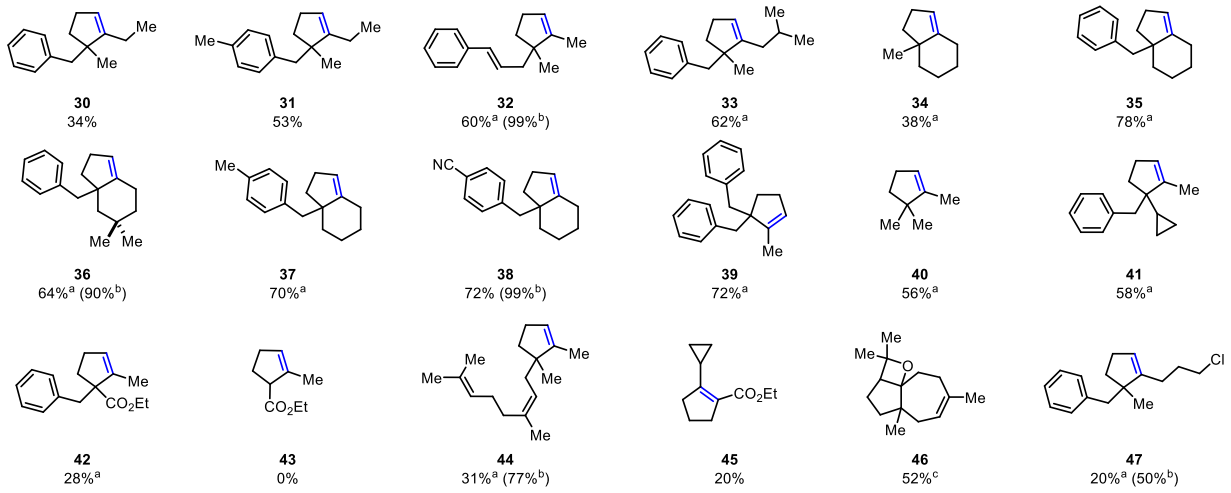
although in lower yields of 34-62%, presumably due to the increased steric bulk near the carbonyl reactive site (**30**, **33**, Table 3-4).

Substrates bearing additional olefin substituents, including cinnamyl and geranyl, proved to be reactive and afforded the corresponding products **32** and **44** in 60% and 31% yield, respectively. Various substituents in the carbonyl α-position were tolerated under the reaction conditions. Cyclopentene **40** with two alkyl groups was obtained in 56% yield, while cyclopropyl derivative **41** was isolated in 58% yield. β-ketoester substrates (**42**-**44**, Table 3-4) provided low or no yields of metathesis products. Cyclohexanone derivatives reacted efficiently under the optimized conditions to afford bicyclic products in yields up to 78% (**34**-**38**, Table 3-4). A cycloheptyl ketone substrate

did not result in the formation of the desired metathesis product, but instead oxetane **46**[11] was isolated in 52% yield.

Table 3-4 Substrate Scope: Functional Group Tolerance





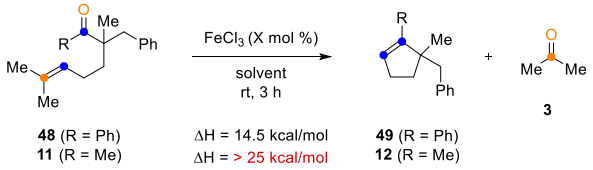
30 34%
31 53%
32 60%[a] (99%[b])
33 62%[a]
34 38%[a]
35 78%[a]
36 64%[a] (90%[b])
37 70%[a]
38 72% (99%[b])
39 72%[a]
40 56%[a]
41 58%[a]
42 28%[a]
43 0%
44 31%[a] (77%[b])
45 20%
46 52%[c]
47 20%[a] (50%[b])

Conditions: All reactions were performed using 10 mol % of Lewis acid, $FeCl_3$, in DCE (0.05M) at 23 °C for 16-24 h or [a]80 °C for 3 h. [b]Yields are based on recovered starting material. [c]50 mol % $FeCl_3$ in DCE (0.05M) at 0 °C to 23 °C.

3.6 Kinetic Studies

During the development of this method, we noted that alkyl ketone substrates reacted differently than aryl ketones in three key ways (Figure 3-3). 1) $FeCl_3$-catalyzed carbonyl-olefin metathesis of alkyl ketone **11** proceeded in the highest yield (74%) in dichloroethane, while the yield dropped dramatically in dichloromethane and no product was formed when employing toluene as solvent. The corresponding aryl ketone **48** reacted effectively in all three solvents, providing 65% to 99% yield. 2) Higher catalyst loading (10 mol% vs. 5 mol%) was shown to result in higher yields of desired carbonyl-olefin metathesis product **12** in the alkyl ketone system while aryl ketones reacted smoothly with as little as 1 mol% $FeCl_3$. 3) Gas-phase calculations of the reaction pathway

Table 3-5 Different Reactivity of $FeCl_3$-Catalyzed Carbonyl-Olefin Metathesis for Aryl vs. Alkyl Ketones



48 (R = Ph)
11 (R = Me)

ΔH = 14.5 kcal/mol
ΔH = > 25 kcal/mol

49 (R = Ph)
12 (R = Me)

entry	R	$FeCl_3$ (X mol %)	solvent	yield **49** or **12** (%)
1	Ph	5	toluene	65
2	Ph	5	dichloromethane	78
3	Ph	5	dichloroethane	99
4	Me	10	toluene	0
5	Me	10	dichloromethane	37
6	Me	10	dichloroethane	74

for $FeCl_3$ catalyzed carbonyl-olefin metathesis of alkyl ketone **11** showed that the activation barriers for the reaction were too high for the reaction to proceed under ambient conditions (>25 kcal/mol). The analogous barriers for the corresponding aryl ketones was found to be significantly lower (14.5 kcal/mol).

Intrigued by the unexpectedly high reactivity of $FeCl_3$ and unique solvent dependence of the reaction, we carried out kinetic studies to obtain further insight into the controlling features of this transformation. Previous investigations into the mechanism of carbonyl-olefin metathesis reactions of aryl ketone **1** revealed a zero-order rate dependence on substrate and a first-order dependence on $FeCl_3$.[5c] This indicated that $FeCl_3$-bound substrate complex **50** is the resting state of the catalyst and that a classic activation mode of the aryl ketone – in which monomeric $FeCl_3$ binds the ketone – is operative in this mechanism (Figure 3-4C). α-quaternary aryl ketone substrate **11** was also found to have first-order rate dependence on the $FeCl_3$ catalyst concentration and zero-order dependence on substrate. Kinetic studies on the analogous alkyl ketone **11** also demonstrated zero-order dependence on substrate, consistent with a catalyst resting state of monomeric $FeCl_3$ bound to substrate (**52**, Figure 3-4C). However, the reaction of

alkyl ketone **11** was found to proceed with second order kinetics with respect to $FeCl_3$ (Figure 3-4B), suggesting that a different mode of activation was operational for alkyl

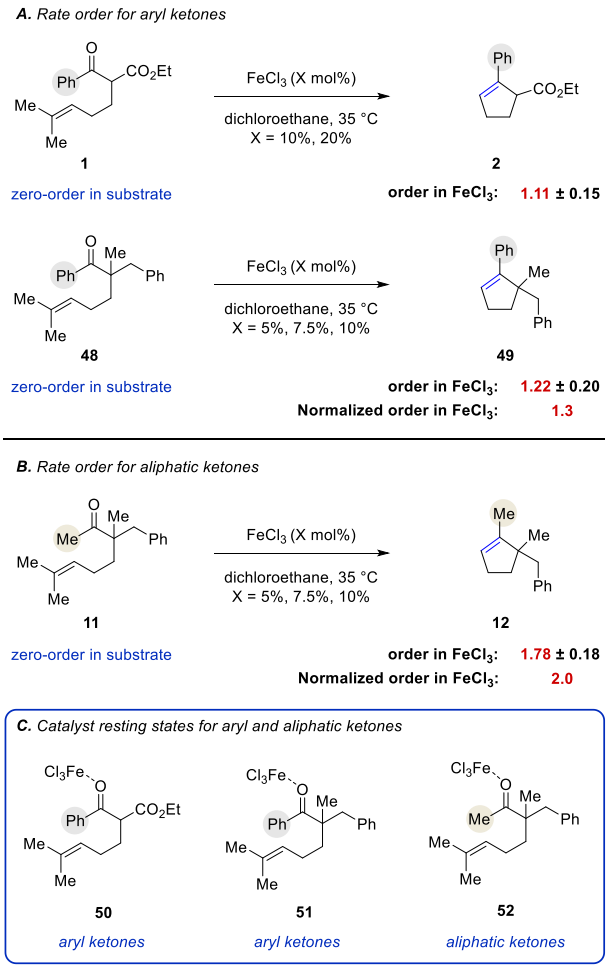


Figure 3-3 Kinetic investigations in carbonyl-olefin metathesis of various ketone substrates

ketones than for aryl substrates.[12,13] These results support a hypothesis that two equivalents of the $FeCl_3$ catalyst are involved in the rate-determining step of the carbonyl-olefin metathesis reaction of alkyl ketones, while only one equivalent of $FeCl_3$ is involved in the reaction of aryl ketone analogs.

3.7 Possible Alternative Lewis Acid Activation Modes

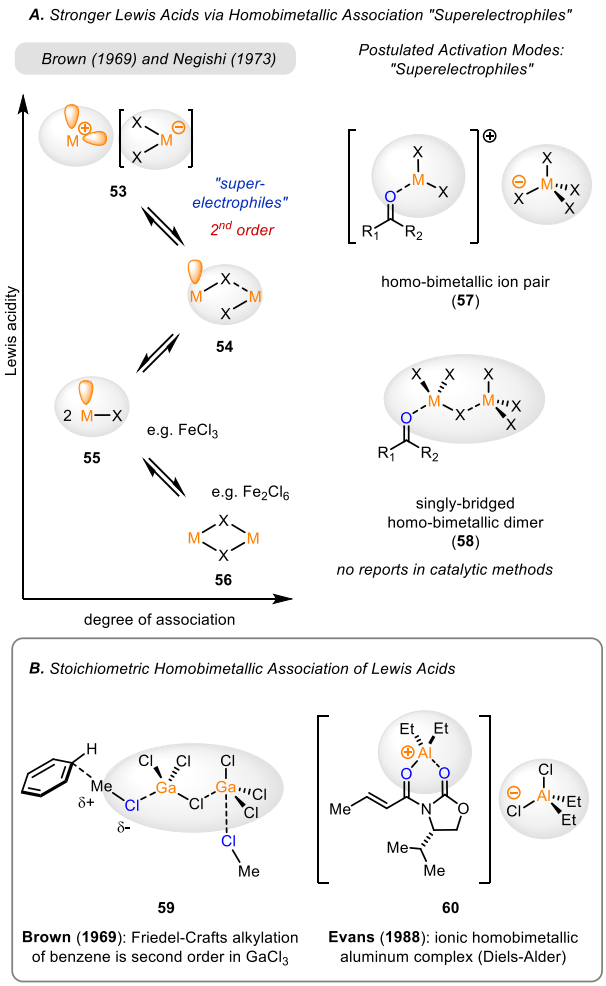


Figure 3-4 Various modes of Lewis acid activation of ketones

Several Lewis acid mediated activation modes for carbonyls have been previously postulated in addition to the standard monomeric activation. One such mode is the association of two monomeric Lewis acids to form single bridged dimers **54** (Figure 3-5A) that are stronger Lewis acids than their monomeric counterparts. This strategy has been described as "highly desirable" [14] as a reaction design principle as early as the 1960s to take advantage of the inherent tendency of such Lewis acids to associate into "superelectrophiles". Polarization of single bridged dimers of type **54** could induce ionization into the doubly electron-poor ion pairs **53**. Both species **53** and **54** fall into Olah's definition of superelectrophiles by exhibiting higher reactivity than their

corresponding monomeric species **55**.[15] Hetereobimetallic superelectrophiles resulting from the association of two different metals have been demonstrated as important advances in organometallic chemistry,[16] but the homobimetallic analog is considered rare and has remained unexplored in catalysis.[17] Isolated reports of homobimetallic Lewis acids as stoichiometric reagents have been postulated. Brown and coworkers observed second-order rate dependence in $GaCl_3$-promoted Friedel-Crafts alkylation, which led to a hypothesis that superelectrophilic gallium-dimers were the active species (**59**, Figure 3-5B), but singly-bridged homodimers **59** could not be distinguished from ion pairs.[18] Evans and coworkers suggested that carbonyl activation by homobimetallic aluminum ion pairs **60** in stoichiometric Et_2AlCl-mediated Diels-Alder reactions (Figure 3-5B).[19,20,21]

We considered these two distinct activation modes for alkyl ketones in the carbonyl-olefin metathesis reaction described here: singly-bridged $FeCl_3$ dimers (**61**) or ion pairs (**62**) (Figure 3-6). The neutral reaction pathway begins with the first equivalent of $FeCl_3$ binding the ketone of substrate **11** to reach the resting state **52**. The second equivalent of $FeCl_3$ then binds to the first through a chloride, forming singly bridged homobimetallic dimer **61** (Figure 3-6), which induces substantial polarization in the substrate to activate the ketone for carbonyl-olefin metathesis. Alternatively, homobimetallic dimer **61** can be polarized with participation from the dichloroethane solvent to ion pair **62**, which is similarly capable of activating the carbonyl for the desired reaction.

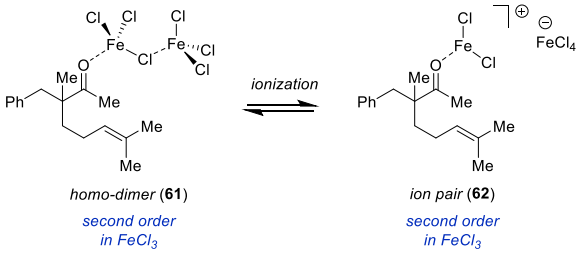


Figure 3-5 Two possible superelectrophilic activation modes for alkyl ketones

3.8 Spectroscopic Investigations

To gain additional support for the hypothesis that $FeCl_3$ superelectrophiles are operational in this reaction and to differentiated between singly bridged and ion pairs as catalytic species, we conducted various spectroscopic measurements of the alkyl ketone substrate and $FeCl_3$. Reduced ketone **63** was employed in these studies to stop the relatively fast metathesis reaction from interfering with the measurements. We first conducted infrared experiments to relate Lewis acid strength to carbonyl activation based on the change in observed absorption frequency.[22,23] The carbonyl signal of substrate **63** in DCE solution was measured at 1700 cm^{-1}, and upon treatment with one equivalent of $FeCl_3$, a new signal at 1642 cm^{-1} was observed, consistent with coordination of $FeCl_3$ to form complex **64** (Figure 3-7B). Addition of a second equivalent of $FeCl_3$ resulted in appearance of another signal with a lower absorption frequency at 1615 cm^{-1}, suggesting further carbonyl activation through a stronger Lewis acid. Both the singly bridged homodimer of $FeCl_3$ (**65**) and the ion pair (**66**) are expected to lead to lower carbonyl absorption frequencies upon coordination. The measured changes in absorption

frequencies are consistent with the calculated shifts in absorption frequencies for the singly-bridged homodimer (Figure 3-7B).

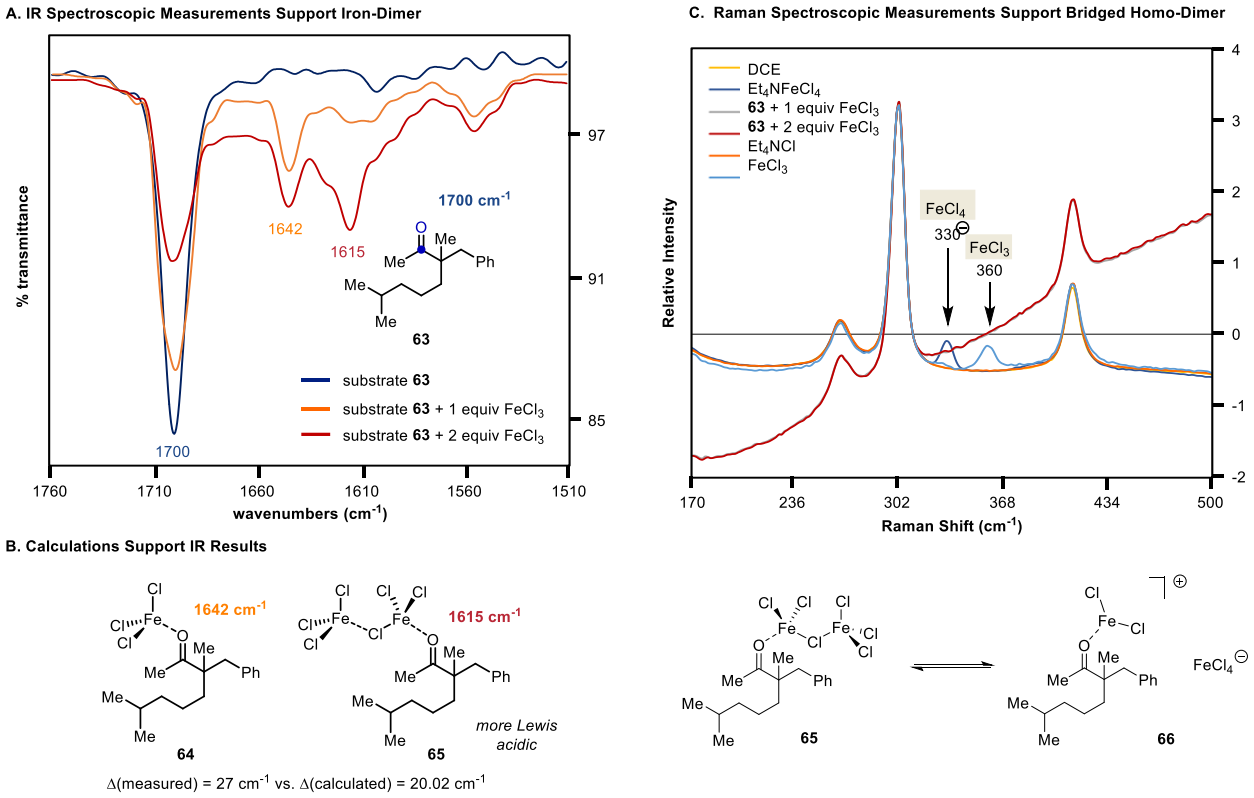


Figure 3-6 IR and Raman spectroscopic measurements of alkyl ketone 63 with $FeCl_3$

Raman spectroscopic measurements indicated no formation of $FeCl_4^-$ anion (330 cm^{-1})[24,25] upon addition of $FeCl_3$ to alkyl ketone **63** in dichloroethane (Figure 3-7C). Additionally, electron paramagnetic resonance (EPR) experiments were carried out to further investigate the catalyst resting state and distinguish between singly bridged homodimers and ion pairs as the active catalytic species. Samples containing increasing ratios of alkyl ketone **63** to $FeCl_3$ in DCE were prepared and the EPR spectra were acquired at 4 K (Figure 3-8). High spin EPR spectra with g=4.29 were obtained for all ratios of **63** with $FeCl_3$ as expected for iron(III) species. The increase in concentration of **63** relative to $FeCl_3$ leads to an increase in signal intensity in the EPR spectrum, consistent with iron(III)-bound complex **65** as the major species in solution, as this

complex has an unpaired spin and as a result has a measurable EPR signal. The singly-

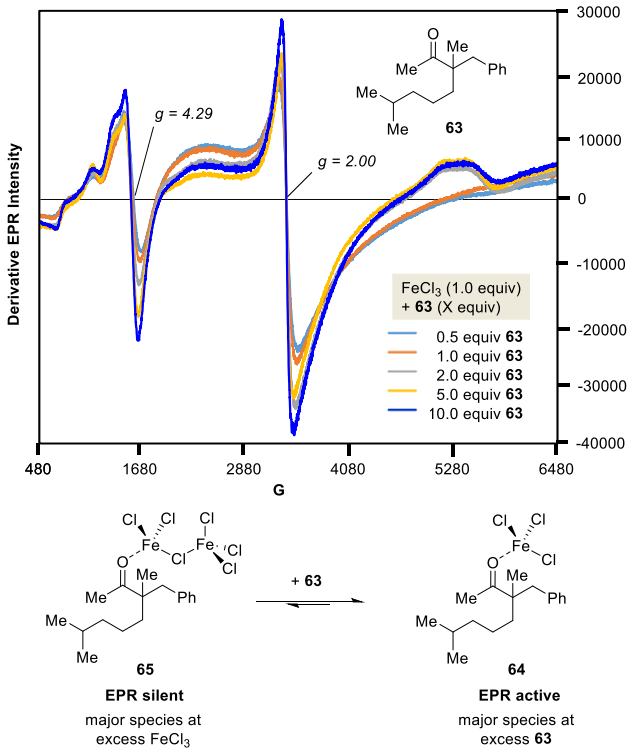


Figure 3-7 EPR spectroscopic measurements of 63 with $FeCl_3$ (4 K)

bridged homo-dimer is expected to be favored when an excess of $FeCl_3$ is present relative to **63** in solution, and because the dimeric species is EPR silent, the diminished EPR signal at higher $FeCl_3$ concentrations relative to **63** is consistent with the presence of singly bridged iron(III) homo-dimers. Importantly, no signal is observed for the EPR active $FeCl_4^-$ anion[26], providing additional support for the neutral reaction pathway.

3.9 Lewis Acid Mixtures as Stronger Catalysts

Taken together, our mechanistic investigations support a mechanism proceeding through the Lewis acid activation of the carbonyl by a homobimetallic $FeCl_3$ species. We examined the possibility that stronger Lewis acids could be generated by generating more reactive dimer species. To this end, the composition of mixtures of $GaCl_3$ and $GaBr_3$ has been studied by Cerny and coworkers, who were able to show that halogen exchange

occurs between these species and the major species in nonpolar solutions are $Ga_2Cl_3Br_3$

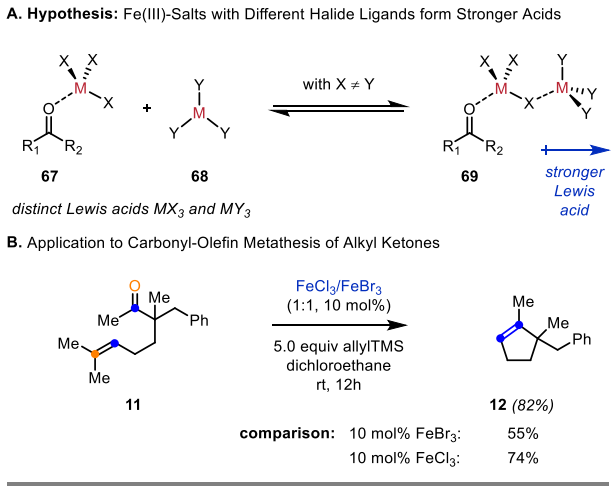


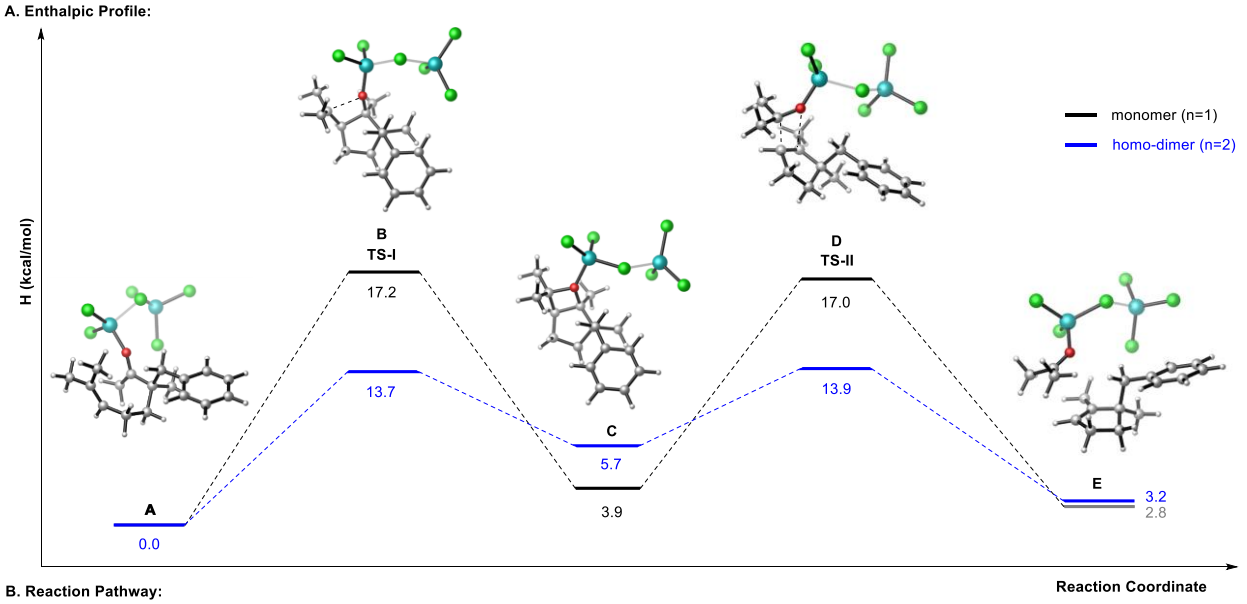
Figure 3-8 Mixtures of Lewis acids to generate stronger catalysts *in situ*

and $Ga_2Cl_4Br_2$.[27] We hypothesized that combining distinct Lewis acids $FeCl_3$ and $FeBr_3$ would lead to a similar halogen exchange and form stronger Lewis acid superelectrophiles *in situ*, improving the yield of the carbonyl-olefin metathesis reaction of alkyl ketones (Figure 3-9). Upon treating ketone substrate **11** with 10 mol% of an equimolar mixture of $FeCl_3$ and $FeBr_3$, the cyclopentene product was formed in slightly higher yield (82%) than obtained with 10 mol% $FeCl_3$ alone (74%). This result is consistent with the hypothesis that two different iron(III) Lewis acids can be combined to form stronger Lewis acid catalysts leading to higher reactivity.

3.10 Computational Investigation of Mechanism

Quantum chemical simulations were performed to further probe the mechanism of the carbonyl-olefin metathesis reaction of alkyl ketones.[28,29] The simulations employed density functional theory at the B97-D level of theory with implicit solvation (see appendix 3 for additional details). The most favorable computed reaction pathway for both monomeric $FeCl_3$ and singly-bridged homodimers is shown in Figure 3-10. Both pathways proceed by an initial concerted, asynchronous ring-closing (**B**) followed by ring-opening

(**D**) steps through intermediate oxetane (**C**), which were also the key steps in the carbonyl-



activation mode	A*	B (TS-I)*	C*	D (TS-II)*	E*
monomer (n=1)	0.0	17.2	3.9	17.0	2.8
homo-dimer (n=2)	0.0	13.7	5.7	13.9	3.2

*values refer to enthalpies H in kcal/mol.

Figure 3-9 Computed enthalpic profile of two possible carbonyl activation mechanisms for $FeCl_3$-catalyzed alkyl carbonyl-olefin metathesis

olefin metathesis reaction of aryl ketones. The overall barrier is shown to be 3.5 kcal/mol lower when the carbonyl is activated by a singly-bridged $FeCl_3$ homodimer. This most favored computationally-detected pathway shows a Lewis acid activation of a Lewis acid-Lewis base complex, leading to an ultimately stronger Lewis acid activating the carbonyl for reaction. The Fe-O bond is shortened in comparison to the monomeric complex while the Fe-Cl bond of the Cl-Fe-Cl bridge is lengthened, leading to a charge transfer from the first iron atom into the second. In the monomer case, 0.33 units of charge are withdrawn from the carbonyl substrate, while in the homo-dimer 0.45 units of charge are withdrawn. This increase in activation of the carbonyl is necessary in the alkyl case but not for the

aryl analogs, which are able to delocalize the charge through conjugation with the arene. These simulations are consistent with the kinetic studies and spectroscopic results obtained in this system and further support the hypothesis that bridged homo-dimers of $FeCl_3$ lead to increase activation of the carbonyl and enable the carbonyl-olefin metathesis of alkyl ketones.

3.11 Summary of Mechanism

With these combined results, we propose that $FeCl_3$-catalyzed carbonyl-olefin metathesis of alkyl ketones proceeds by a different activation mode than for aryl ketones. Aryl ketones are activated by a monomeric binding of $FeCl_3$ through catalyst resting state **70**[30,31], leading to sufficient activation of the carbonyl to undergo the metathesis reaction. The observed first-order kinetics with respect to $FeCl_3$ are consistent with this mechanistic proposal, and computational studies identified the aryl substituent as an essential

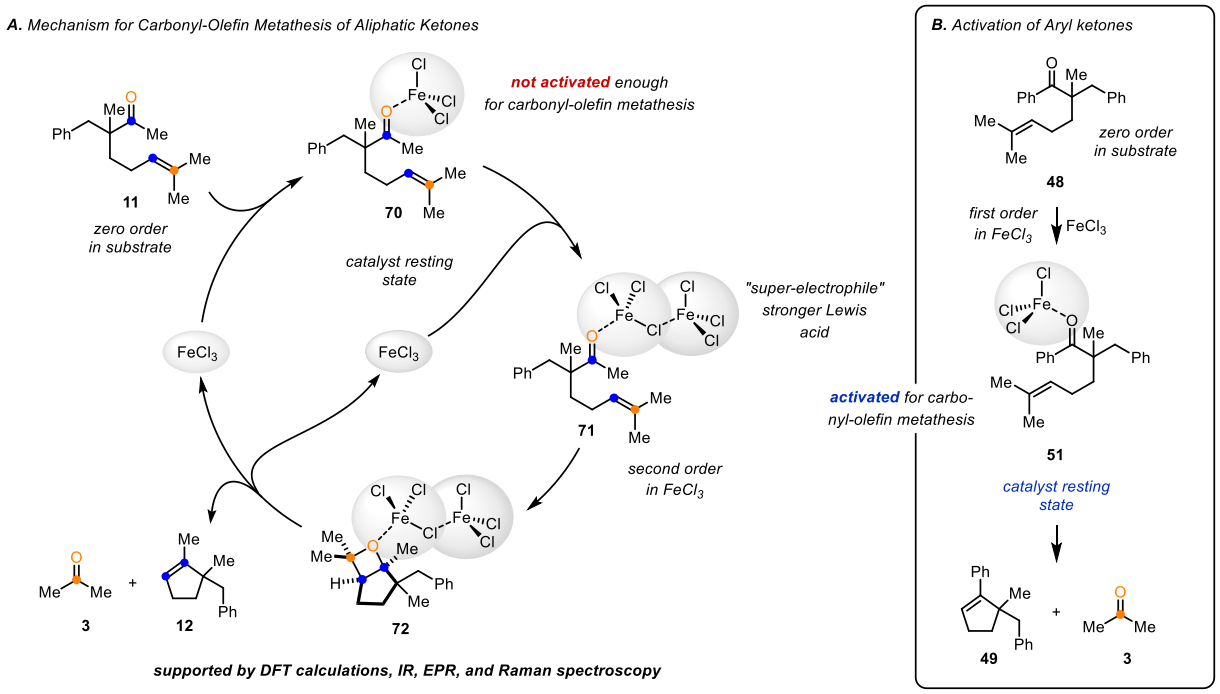


Figure 3-10 Overview of mechanism for $FeCl_3$-catalyzed carbonyl-olefin metathesis of alkyl ketones

structural component for stabilization of the transition state by delocalization of electron

density, thus enabling the formation of an intermediate oxetane. The corresponding alkyl ketones lack this mechanism of stabilization and therefore remain unreactive until a second equivalent of $FeCl_3$ binds to the first, forming a more potent Lewis acid catalyst and further activating the carbonyl for reactivity through a lower-energy transition state (Figure 3-11). As a result, intermediate oxetane **72** can form, which subsequently fragments and leads to the desired metathesis product **12** and acetone **3** as a byproduct.

3.12 Conclusions

Bimetallic association mechanisms of Lewis acid activation have been suggested as a potential strategy for generating stronger Lewis acids as early as 60 years ago. Heterobimetallic versions of this principle have been shown in the literature, but the corresponding homobimetallic association mode was dismissed as "of little or no synthetic consequence".[17] Our studies in carbonyl-olefin metathesis have demonstrated that Lewis acid activation by homodimeric Lewis acids can be a desirable activation mode enabling otherwise inaccessible transformations in organic synthesis. Specifically, the *in situ* generation of $FeCl_3$ homodimers has extended the scope of the Lewis acid catalyzed carbonyl-olefin metathesis reaction to include alkyl ketone substrates.

3.13 References

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6) For a review on Lewis acid-catalyzed carbonyl-olefin metathesis reactions, see: Ludwig, J.R.; Schindler, C.S. *Synlett* **2017**, *28*, 1501-1509.

7) For approaches relying on carbocation-based Lewis acids as catalysts in carbonyl-olefin metathesis, see: (a) Bah, J.; Franzén, J.; Naidu, V.R. *Eur. J. Org. Chem.* **2015**, *8*, 1834-1839; (b) Tran, U.P.N.; Oss, G.; Pace, D.P.; Ho, J.; Nguyen, T.V. *Chem. Sci.* **2018**, *9*, 5145-5151.

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Chapter 4 Catalytic, Transannular $FeCl_3$-Catalyzed Carbonyl-Olefin Metathesis Reactions

The work described in this chapter has been made available as a pre-print: **Riehl, P.S.**; Nasrallah, D.J.; Schindler, C.S. *ChemRxiv* **2019**, DOI: 10.26434/chemrxiv.8341070.v3 and has been accepted for publication in *Chemical Science*.

4.1 Established Classes of Carbonyl-Olefin Metathesis Reactions

Carbonyl-olefin metathesis reactions are a desirably class of strategies for direct

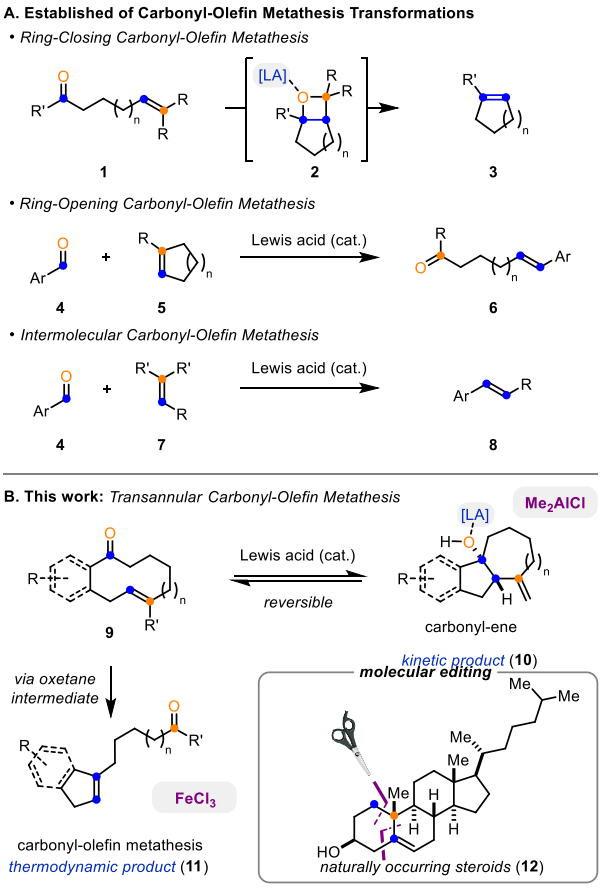


Figure 4-1 Types of carbonyl-olefin metathesis

carbon-carbon bond formation from carbonyl and olefin functional groups.[1] Recent

advances in this area of chemistry have resulted in the development of several distinct classes of carbonyl-olefin metathesis reactions – largely mirroring the earlier developments in olefin-olefin metathesis chemistry – including ring-closing[2] (**3**), ring-opening[3] (**6**) and intermolecular[4] (**8**) carbonyl-olefin metathesis reactions (Figure 4-1).[5] The extension of this method into transannular systems represents a mechanistically distinct, fourth reactivity mode that lacks an analog in olefin-olefin metathesis literature. Specifically, the mechanism of the transannular carbonyl-olefin metathesis reactions involves a competing but reversible carbonyl-ene[6] pathway, where the carbonyl-olefin metathesis product is ultimately the thermodynamically favored product.

4.2 Divergent Pathways and Molecular Editing

Our studies show that the different pathways for reaction between transannular carbonyl and olefin functionalities can be favored selectively based on choice of Lewis acid catalyst. The transannular carbonyl-olefin metathesis reaction is a ring contraction that leads to a new and distinct carbocyclic framework. As a result, these reactions are valuable tools for the selective molecular editing of biologically important natural products, allowing rapid access to structurally distinct scaffolds in a single transformation. The concept of molecular editing “whereby one could selectively insert, delete or exchange atoms in highly elaborated molecules”[7] has been identified as an important area of opportunity to explore new chemical space and potentially be highly impactful in the innovative development of new pharmaceuticals. Important advances have already been made in insertion and deletion of atoms in complex molecules by C-H activation strategies[8], approaches allowing for selective exchange of atoms remain rare and represent a challenge in current synthetic chemistry.[9] The newly developed transannular

carbonyl-olefin metathesis reaction, as applied to natural product derived scaffolds[10], can contribute to this emerging area of research. Importantly, the ability of different Lewis acids to afford distinct products enable a rapid and divergent molecular editing strategy for steroid-derived scaffolds by selecting for either a carbonyl-ene reaction or a carbonyl-olefin metathesis reaction.

4.3 Evaluation of Lewis Acids

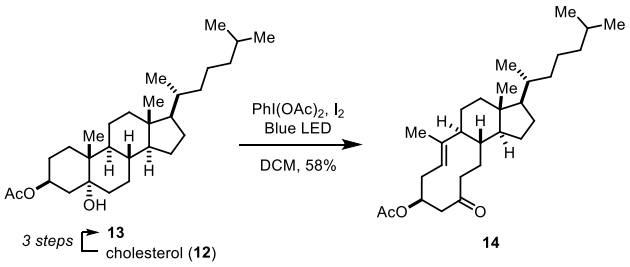
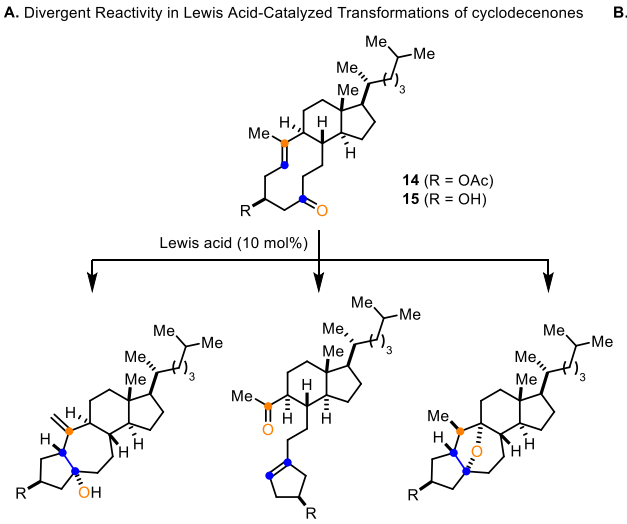


Figure 4-2 Synthesis of cyclodecenone 14

To study the transannular carbonyl-olefin metathesis reaction in detail, we require efficient synthetic access to functionalized cholesterol-derived cyclodecenone **14**.[11] We developed a short 4-step sequence to convert naturally occurring steroids to highly functionalized cyclodecenone systems (Figure 4-2).[12] This sequence began with epoxidation of cholesterol, followed by reduction and acetylation to provide acetate **13**. Suárez oxidation[13] with (diacetoxyiodo)benzene and iodine led to 58% isolated yield of **14** by an alkoxy radical fragmentation.

We then evaluated the ability of various Lewis acids to promote transannular metathesis reactions between the carbonyl and olefin functionalities of **14**. Upon treatment with $Sc(OTf)_3$ as catalyst, the desired metathesis product was isolated in 33% yield along with two additional reaction products, which were identified as the carbonyl-ene product **16** (15% yield) and tetrahydrofuran **19** (20% yield) (entry 1, Figure 4-3). However, when treated with catalytic BF_3•OEt_2, the carbonyl-ene product was not



entry	Lewis acid	mol%	R	yield **A** (%)	yield **B** (%)	yield **C** (%)
1	$Sc(OTf)_3$	10	OAc	15	33	20
2	$BF_3{\cdot}Et_2O$	10	OAc	-	30	23
3	$BF_3{\cdot}Et_2O$	100	OAc	-	11	25
4	$GaCl_3$	10	OAc	-	3	-
5	$SnCl_4$	10	OAc	-	22	44
6	$SnCl_4$	10	OH	-	65	-
7	$FeCl_3$	10	OAc	-	39	31
8	$FeCl_3$	10	OH	-	75	-
9	$TiCl_4$	10	OAc	-	-	43
10	Me_2AlCl[a]	100	OAc	85	-	-

Conditions: Substrate **14** or **15** (0.11 mmol), Lewis acid (10 mol%) in DCE (0.05M) at room temperature. [a]Reaction performed at 0 °C.

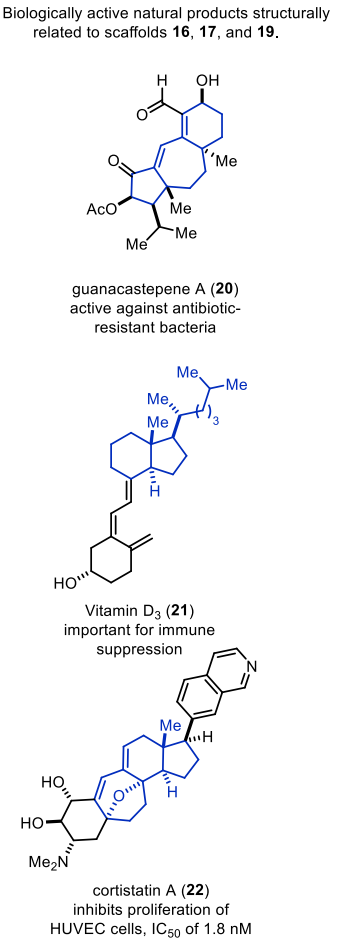


Figure 4-3 Reaction optimization for transannular carbonyl-olefin metathesis

detected and the metathesis product and tetrahydrofuran **19** were isolated in 30% and 23% yield respectively (entry 2, Figure 4-3A). Stoichiometric $BF_3{\bullet}OEt_2$[14] also resulted in isolation of these products, albeit in diminished yields of 11% and 25%, respectively (entry 3, Figure 4-3A). $GaCl_3$ has previously been identified as an optimal catalyst for intermolecular ring-opening carbonyl-olefin metathesis reactions, but it failed to promote the transannular carbonyl-olefin metathesis reaction in this system (entry 4, Figure 4-3A). $SnCl_4$ resulted in higher reactivity, providing 22% yield of metathesis product **17** and 44% yield of tetrahydrofuran **19** (entry 5, Figure 4-3A). When cyclodecenone substrate **15** bearing a free alcohol in place of an acetate was subjected to these conditions, metathesis product **18** was formed 65% yield as the exclusive product (entry 6, Figure 4-

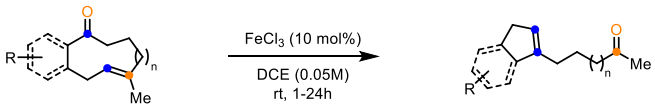
3A). The increase in selectivity with free alcohol **15** led us to evaluate additional Lewis acid catalysts. Subjecting acetate **14** to $FeCl_3$ afforded a mixture of the carbonyl-olefin metathesis product **17** and tetrahydrofuran **19** in moderate yields of 39% and 31% respectively (entry 7, Figure 4-3A). The free alcohol-containing carbonyl-olefin metathesis product **17** could be isolated in high yield of 75% as the sole reaction product when treating alcohol **15** with $FeCl_3$ (entry 8, Figure 4-3A).

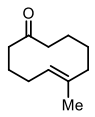
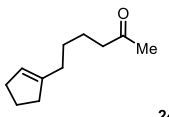
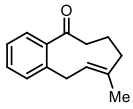
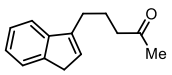
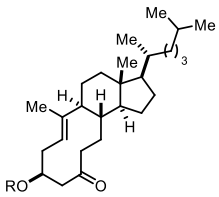
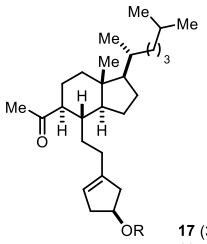
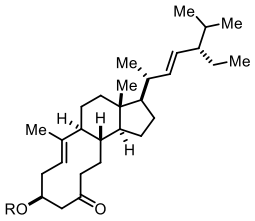
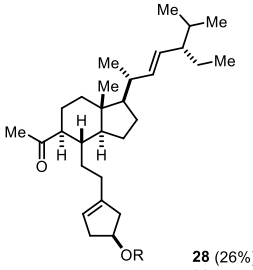
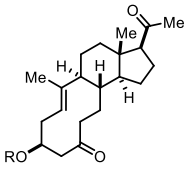
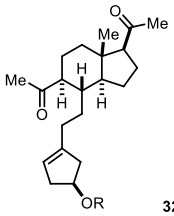
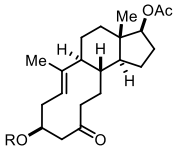
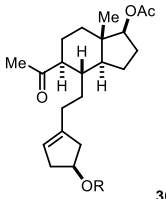
Additional investigations found that specific Lewis acids are capable of selectively forming the carbonyl-ene product **16** or tetrahydrofuran **19**. Specifically, treatment of **14** with $TiCl_4$ gave rise to exclusive formation of tetrahydrofuran **19** in 43% yield while Me_2AlCl afforded the corresponding carbonyl-ene product **16** in 85% yield (entries 9 and 10, Figure 4-3A). These results suggest the appropriate choice of Lewis acid enables selective access to one of three distinctive frameworks, representing a powerful approach to divergent molecular editing by Lewis acid mediated transannular reactions between a carbonyl and an olefin. The three different products isolated closely resemble known biologically important natural products guanacastepene A (**20**)[15], vitamin D_3 (**21**)[16], and cortistatin A (**22**)[17] (Figure 4-3B).

4.4 Reaction Scope

The optimal reaction conditions for Lewis acid catalyzed transannular carbonyl-olefin metathesis relying on $FeCl_3$ were demonstrated to be general for various 9- and 10-membered ring systems (Figure 4-4). Unfunctionalized medium-sized rings were viable substrates and afforded moderate to good yields of metathesis products. Specifically, cyclodecenone **23** and cyclononenone **25** formed the desired metathesis products **24** and **26** in 42% and 64% yield, respectively. To evaluate the potential of this

Table 4-1 Scope of FeCl3-Catalyzed Carbonyl-Olefin Metathesis



entry	substrate	product	entry	substrate	product
1	 **23**	 **24** (42%)	2	 **25**	 **26** (64%)
3 R = Ac 4 R = H	 **14** **15**	 **17** (39%) **18** (75%)	5 R = Ac 6 R = H	 **27** **29**	 **28** (26%) **30** (51%)
7 R = TBS 8 R = H	 **31** **33**	 **32** (69%) **34** (84%)	9 R = Ac 10 R = H	 **35** **37**	 **36** (46%) **38** (44%)

Conditions: Substrate (0.11 mmol), $FeCl_3$ (10 mol%) in DCE (0.05M) at room temperature.

reaction for molecular editing in natural product derived systems, the cyclodecenones derived from several naturally occurring steroids were investigated. Cholesterol, stigmasterol, pregnenolone, and dehydroepiandrosterone derived cyclodecenones were readily available through our synthetic strategy (Figure 4-4). Acetate **14** gave 39% yield of the carbonyl-olefin metathesis product while the corresponding alcohol **15** led to increased yield of 75%. Stigmasterol-derived cyclodecenones **27** and **29** afforded 26% and 51% yield, respectively, when treated with $FeCl_3$ (entries 5 and 6, Figure 4-4). TBS ether **31** obtained from pregnenolone provided 69% yield of metathesis product and the free alcohol **33** reacted to give 84% yield (entries 7 and 8, Figure 4-4). Dehdyroepiandrosterone-derived **35** and **37** led to metathesis products **36** and **38** in 44% and 46% yield, respectively (entries 9 and 10, Figure 4-4).

4.5 Mechanistic Studies

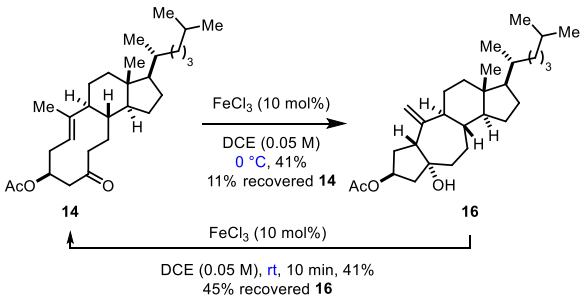


Figure 4-4 Reversibility of the $FeCl_3$-catalyzed transannular carbonyl-ene reaction

We conducted additional experiments to probe the mechanism of the FeCl3-catalyzed transannular carbonyl-olefin metathesis reaction, beginning with experiments on temperature dependence. When treated with $FeCl_3$ at 0 °C, cyclodecalenone **14** did not afford metathesis product **17**, tetrahydrofuran **19**, or possible oxetane intermediate **39**; instead, carbonyl-ene product **16** was isolated in 41% yield along with 11% recovered starting material (Figure 4-5). When carbonyl-ene product **16** was subjected to the optimized reaction conditions (10 mol% $FeCl_3$ in DCE at room temperature) for ten minutes, reversion to cyclodecenone **14** was observed in 45% yield along with 41% of recovered **16**, indicating that $FeCl_3$ can catalyze both the carbonyl-ene reaction of **14** as well as the retro carbonyl-ene reaction. This stands in stark contrast to previous observations in $GaCl_3$-catalyzed ring-opening carbonyl-olefin metathesis in which competing carbonyl-ene products undergo irreversible pathways that are responsible for the diminished yields of metathesis products.[3]

4.6 Computational Investigation of Mechanism

To further investigate the mechanism of the transannular carbonyl-olefin metathesis reaction as distinct from ring-closing, ring-opening, and intermolecular

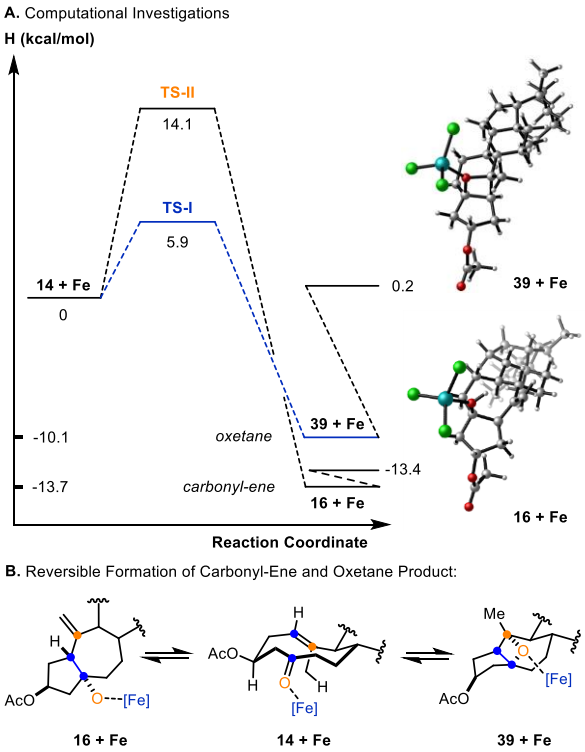


Figure 4-5 Computed energies comparing carbonyl-ene and oxetane-forming pathways

carbonyl-olefin metathesis reactions, we conducted computational investigations (unrestricted B97-D density functional and 6-31G* basis set).[18] Our studies showed that cyclodecenone **14**[19] can under go either of two reversible reactions upon binding to $FeCl_3$ (**14** + Fe, Figure 4-6) leading to oxetane formation via asynchronous concerted [2+2]-cycloaddition that proceeds with an enthalpic barrier of 5.9 kcal/mol (**39** + Fe, via TS-I Figure 4-6) or carbonyl-ene reaction that proceeds with a barrier of 14.1 kcal/mol (**16** + Fe via TS-II, Figure 4-6) above the substrate complex (**14** + Fe, Figure 4-6). In addition, our previous experimental results have shown that carbonyl-ene product **16** is stable and isolable while oxetane **39** could not be isolated. The computed relative enthalpies of the uncoordinated oxetane (+0.2 kcal/mol), which is 13.6 kcal/mol higher than computed energy of uncoordinated carbonyl-ene product are consistent with these observations. Computational investigations into the fragmentation of oxetane **39** revealed two possible

paths for fragmentations; 1) an asynchronous, concerted retro-[2+2] cycloaddition proceeds with a barrier of 15.1 kcal/mol to form metathesis product (**17** + Fe, Figure 4-7). 2) Oxetane **39** can alternatively fragment upon elimination to result in cycloheptene (**40** + Fe), which proceeds with a barrier of 17.9 kcal/mol, which represents an unprecedented mode of Lewis acid-catalyzed oxetane fragmentation.[20] Intramolecular addition of the resulting tertiary alcohol to the alkene moiety results in formation of furan byproduct

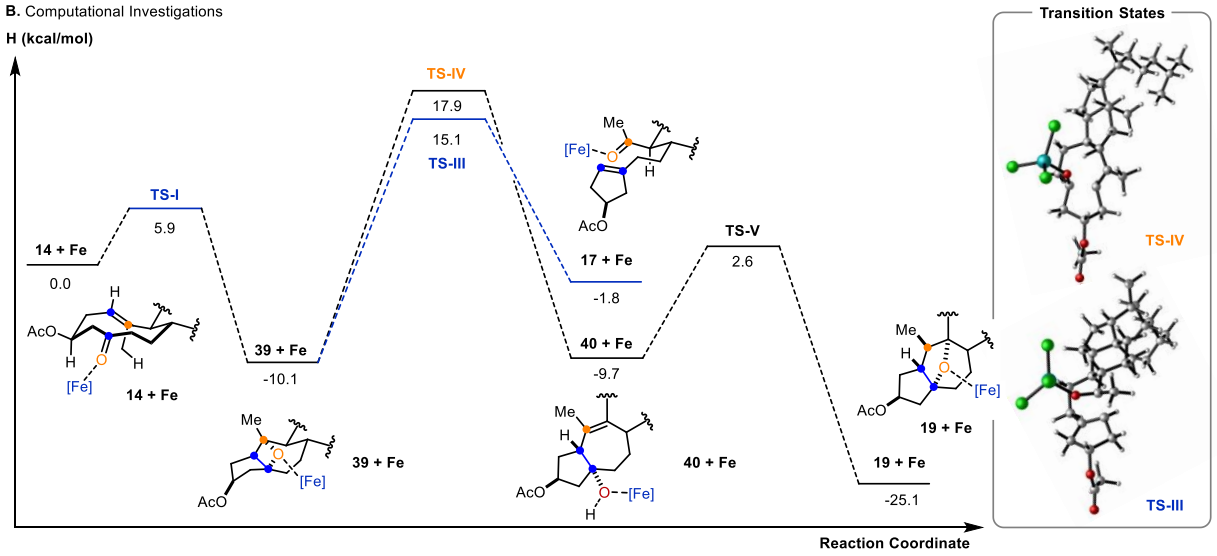


Figure 4-6 Computed reaction coordinate for transannular carbonyl-olefin metathesis and furan formation

observed under $FeCl_3$-catalysis (**19** + Fe, Figure 4-7).

These investigations suggest oxetane fragmentation is the rate-limiting step of both transannular carbonyl-olefin metathesis and furan formation. These results are consistent with our experimental results that indicated temperatures greater than 0 °C are required to afford carbonyl-olefin metathesis product **17** (TS-III, 15.1 kcal/mol) or furan **19** (TS-IV, 17.9 kcal/mol) (Figure 4-7).

4.7 Summary of Mechanistic Hypothesis

Based on the combined experimental and computational, we propose a mechanism for $FeCl_3$-catalyzed transannular carbonyl-olefin metathesis that differs from

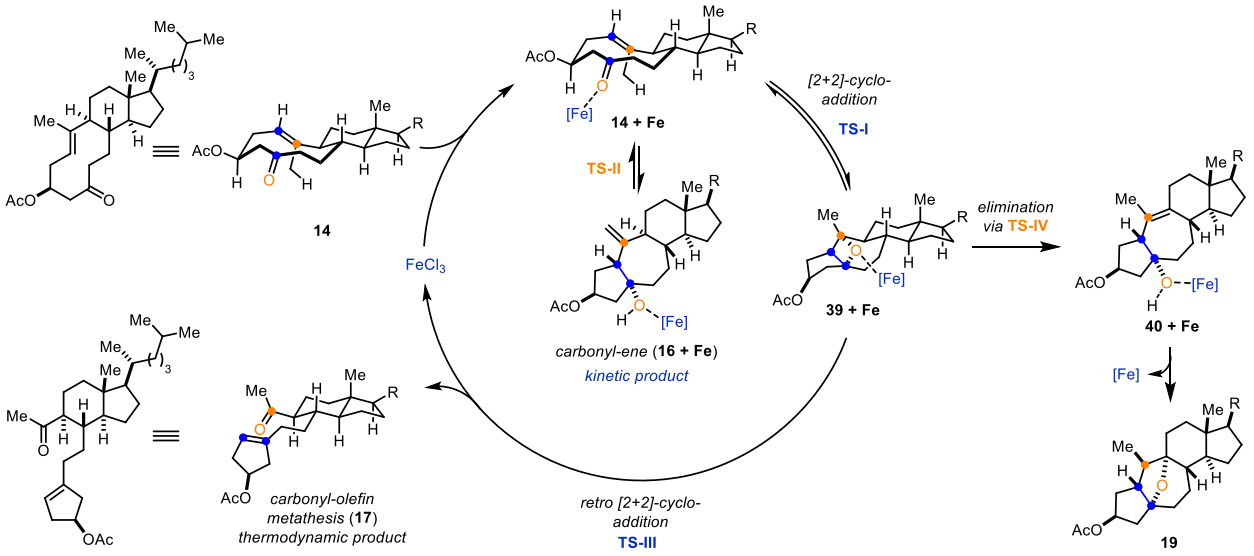
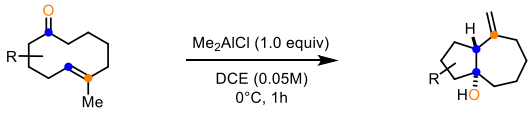
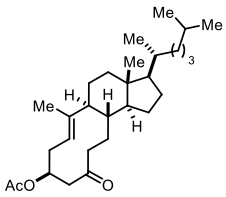
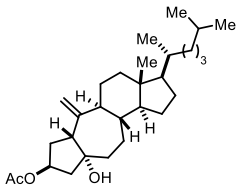
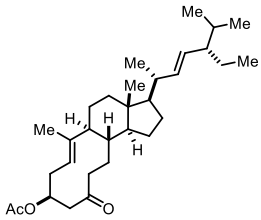
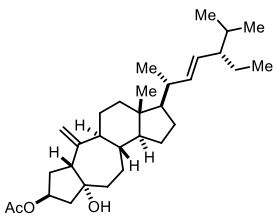
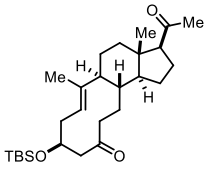
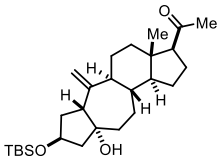
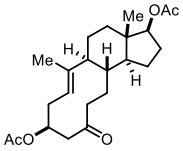
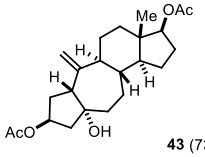


Figure 4-7 Mechanism for transannular carbonyl-olefin metathesis and competing pathways

the mechanisms for ring-opening, ring-closing, and intermolecular carbonyl-olefin metathesis reactions (Figure 4-17). Activation of the carbonyl moiety in substrate **14** with Lewis acid leads to either of two reversible transformations. A reversible carbonyl-ene reaction forms kinetic product **16** while reversible asynchronous, concerted [2+2] cycloaddition results in oxetane **39**. Importantly, the carbonyl-ene product **16** can be isolated at lower temperatures under otherwise identical conditions. The $FeCl_3$-coordinated oxetane can subsequently undergo one of two distinct fragmentation pathways. Asynchronous, concerted retro-[2+2] leads to the expected carbonyl-olefin metathesis product **17**, while unanticipated $FeCl_3$-catalyzed fragmentation leads to elimination to afford a cycloheptene intermediate that undergoes intramolecular hydroalkoxylation to tetrahydrofuran product **19**. Importantly, other Lewis acids can select between these competing reaction paths. Specifically, when substrate **14** is treated with Me_2AlCl as Lewis acid, the carbonyl-ene product **16** is isolated as the exclusive product in high yield. Furthermore, treatment of **14** with $TiCl_4$ affords tetrahydrofuran product **19**

Table 4-2 Susbstrate scope of Me_2AlCl-Mediated Transannular Carbonyl-Ene Reaction



entry	substrate	product	entry	substrate	product
1		**14**  **16** (85%)	2		**27**  **41** (76%)
3		**31**  **42** (73%)	4		**35**  **43** (73%)*

Conditions: Substrate (0.11 mmol), Me_2AlCl (10 mol%) in DCE (0.05M) at 0°C for 1h. *reaction carried out on 0.056 mmol scale at room temperature.

as the sole product, suggesting that this catalyst favors the elimination of oxetane intermediate **39**.

We also observed that substituents in the 2-position relative to the carbonyl had a significant impact on the yield and selective of the carbonyl-olefin metathesis reaction. Our initial hypothesis that hydroxyl functionality in this position led to bidentate binding of substrate to the $FeCl_3$ catalyst found no support in computational modeling studies. Our revised hypothesis is that the pendant acetate transiently binds $FeCl_3$ in a bindentate manner in the $FeCl_3$-oxetane complex **39** + Fe. Elongation of the C-O bond of the oxetane leads to disruption of the retro-[2+2] pathway, inhibiting the carbonyl-olefin metathesis reaction and enabling formation of the tetrahydrofuran byproduct **19**.

4.8 Substrate Scope of Me_2AlCl-Mediated Carbonyl-Ene Reaction

The final portion of our investigation focused on the evaluation of generality of the Me_2AlCl-mediated carbonyl-ene reaction.[21] Various steroid-derived cyclodecenones were treated with stoichiometric Me_2AlCl to form the desired carbonyl-ene products.

Cyclodecenone **14** resulted in tetracycle **16** in 85% yield, while stigmasterol-derived **27** afforded 76% yield of carbonyl-ene product **41** (entries 1 and 2, Figure 4-9). Similarly, carbonyl-ene products were formed exclusively when treating pregnenolone- and dehydroepiandrosterone-derived cyclodecenones **31** and **35** in 73% and 59% yield, respectively (entries 3 and 4, Figure 4-9).

4.9 Conclusions

Transannular carbonyl-olefin metathesis reactions have been studied as a fourth, similar, but distinct class of Lewis acid catalyzed carbonyl-olefin metathesis reactions. The competing carbonyl-ene and [2+2] cycloaddition pathways have been investigated experimentally and computationally. The competing but reversible carbonyl-ene pathway can be favored with Me_2AlCl but with $FeCl_3$, this pathway is reversible, and the thermodynamically favored metathesis product is ultimately formed. Importantly, both the carbonyl-olefin metathesis reaction and carbonyl-ene reaction have been demonstrated in steroid-derived cyclodecenone, indicating their utility for molecular editing of complex scaffolds.

4.10 Reference

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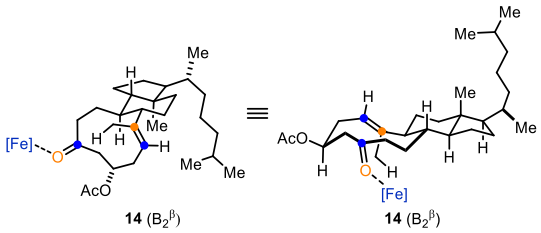
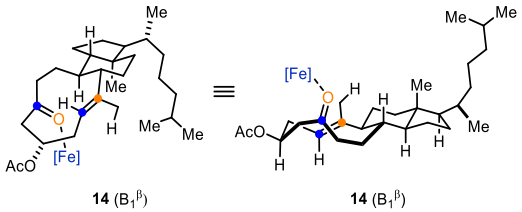


14 (B_2^{β}) **14** (B_2^{β})

In comparison, conformation **44** was found to lead to the preferential formation of diastereomeric product epi-**16** that is not observed experimentally under our optimal reaction conditions. See Supporting Information for details.



14 (B_1^{β}) **14** (B_1^{β})

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Chapter 5 Natural Product Total Synthesis: Lingzhiol and *ent*-Kaurenes

5.1 Importance of Total Synthesis

The development of new synthetic methods is a critical area of research in synthetic organic chemistry. Of similar importance is the rapid, efficient, scalable and enantioselective synthesis of new compounds. Natural products are an excellent source of inspiration for synthetic chemists. Being prepared by the enzymatic machinery of living cells, they often have complex functionality that present challenges for synthetic chemists. Importantly, because they are prepared in nature, these compounds often have desirable pharmacological properties such as solubility and bioavailability and have potential as biologically active molecules.[1] Some famous examples of medicines that are natural products or inspired by natural products are illustrated in Figure 1.

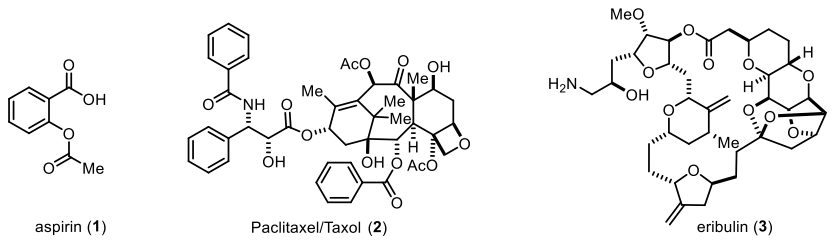

Figure 5-1 Representatitive Drugs from Natural Products

In addition to serving as potentially important medicinal compounds and as a testing ground for the utility of new synthetic methods, total synthesis can serve as both a driving force inspiring the design and development of new methods by presenting a challenge that existing methods cannot overcome. Alternatively, unexpected outcomes in complex systems can lead to serendipitous discovery of new reactivity. [2]

5.2 Biologically Active Terpene Natural Products

Terpene compounds are among the most ubiquitous in nature and encompass an enormous area of chemical space, with many different geometric arrangements and oxidation patterns across dozens of classes of compounds.[3]

The following chapters discuss total synthesis efforts aimed at both the meroterpenoid lingzhiol and a general class of diterpenoids, the ent-kaurenes. History and biological activity of these compounds is addressed at the outset of each respective chapter.

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Chapter 6 Total Synthesis of Lingzhiol and Discovery of a Metal-Controlled Reversal of Enantioselectivity

The work presented in this chapter is in preparation for publication and has been done in collaboration with Alistair Richardson (chemistry Ph.D. candidate, Schindler group) and Tatsuhiro Sakamoto (visiting scholar, Schindler group).

6.1 Introduction and Biological Activity

Lingzhiol (**1**) is a tetracyclic, rotary-door shaped meroterpenoid natural product isolated from *Ganoderma lucidum*, a well-known mushroom with various uses in

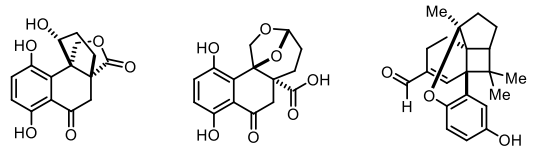


Figure 6-1 Meroterpenoid natural products from *Ganoderma* species

traditional East Asian medicine.[1] Several other meroterpenoids from this genus have been isolated and are related to lingzhiol both with respect to structure and putative biological activity (Figure 6-1).[2] Upon isolation in 2013, Yan and coworkers carried out biological activity studies and identified that both (+)- and (–)-lingzhiol inhibited generation of collagen IV, fibronectin, and reactive oxygen species (ROS). Importantly, the selective inhibition of phosphorylation of Smad3, a signaling protein that upon phosphorylation is

implicated in renal fibrosis. Another signaling protein (Smad2) has reno-protective properties and lingzhiol does not inhibit the phosphorylation of this protein.[3]

The biosynthetic origin of lingzhiol has not been elucidated, but two proposals are described in the literature. The first involves various cyclization and oxidation steps from another natural product, fornicin A (Figure 6-2A). The second proposal involves cyclization of a geranylated hydroquinone, followed by oxidation and semipinacol rearrangement (Figure 6-2B).

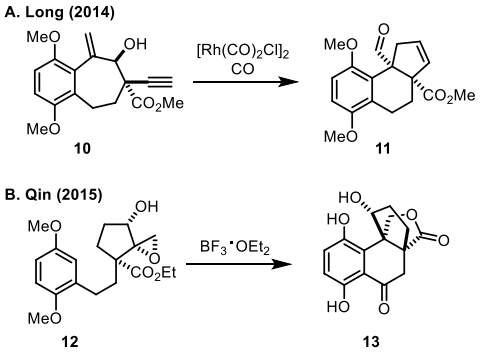


Figure 6-3 Previous approaches to the total synthesis of lingzhiol

In the short time since its structure was reported, seven syntheses of lingzhiol have been described (including three enantioselective syntheses). The first of these syntheses relied on a rhodium-catalyzed [3+2] cycloaddition to afford (–)-lingzhiol in 17 steps (Figure 6-3A).[4] The Chen group reported a racemic synthetic approach relying on an epoxy-arene cyclization strategy (Figure 6-3B)[5,6] and were later able to develop an enantioselective

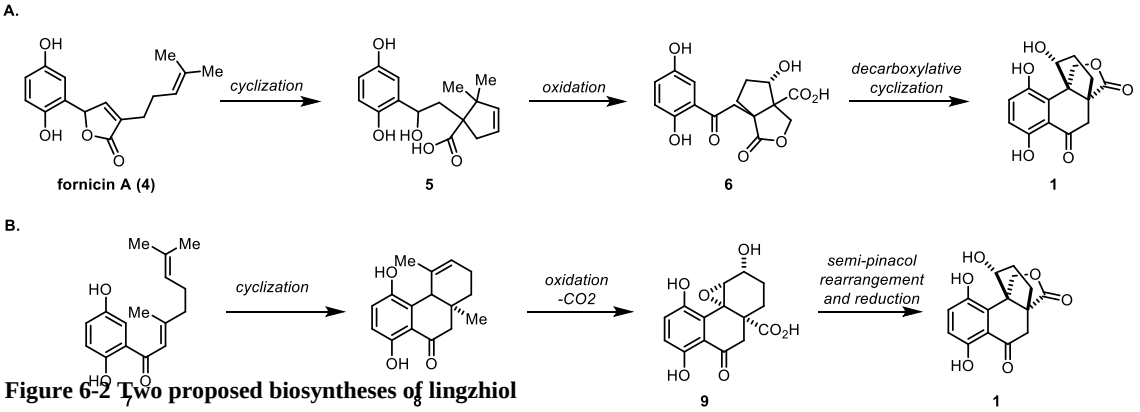


Figure 6-2 Two proposed biosyntheses of lingzhiol

variant.[7] Additional strategies relying on titanocene-catalyzed radical cyclization[8] and semi-pinacol rearrangement have also been reported.[9,10]

6.2 Retrosynthetic Analysis

We envisioned that the lingzhiol core structure **14** could be quickly constructed by a one-pot reductive semipinacol/lactonization cascade reaction mediated by Et_3Al (Figure 6-4)[11]. The requisite epoxy alcohol **16** was expected to be readily accessible from tricyclic enone **17**, which could be prepared from known[12] β-keto ester of tetralone **18**.

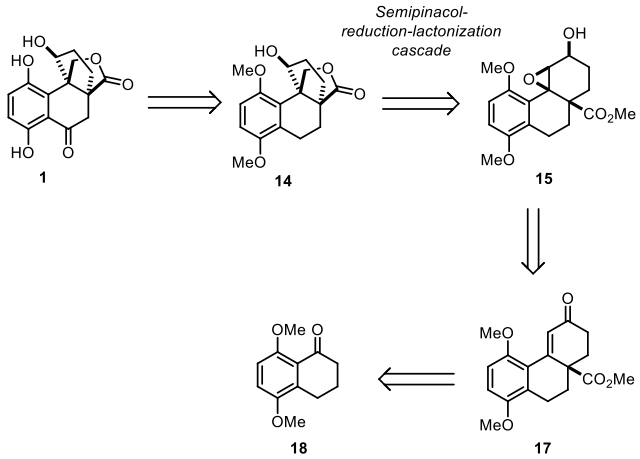


Figure 6-4 Retrosynthetic analysis of lingzhiol

We envisioned that elaboration of lingzhiol core **14** to the natural product **1** would be possible by direct benzylic oxidation followed by BBr_3-mediated methoxy deprotection, previously shown to be effective at revealing the hydroquinone moiety of lingzhiol.

6.3 Model Studies

Our studies commenced with the unsubstituted model alcohol **18**, which was readily oxidized to the desired epoxide **21**. Treatment with triethylaluminum in THF

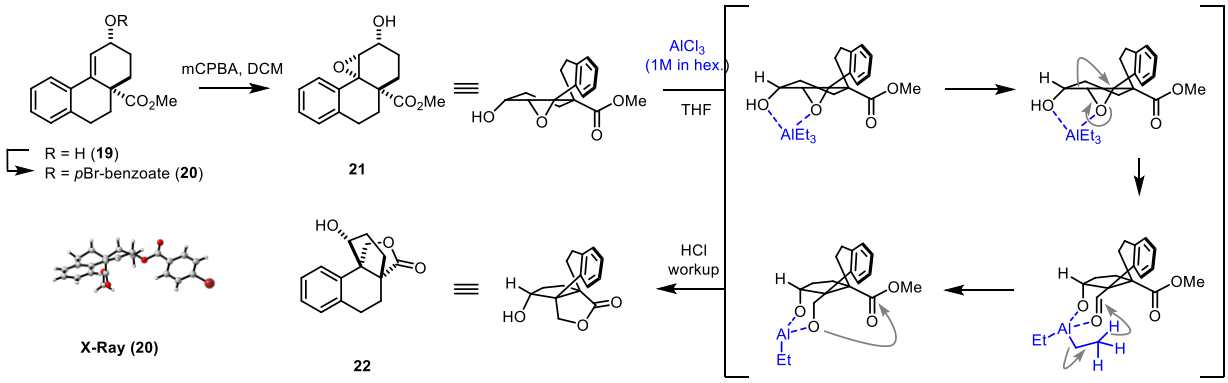
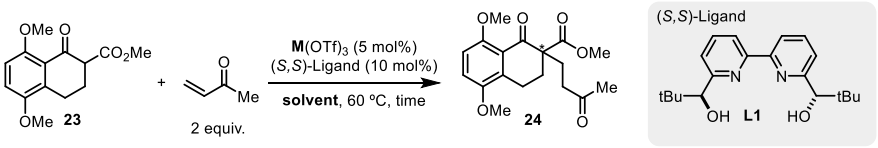


Figure 6-5 Model studies demonstrate the viability of a reductive semipinacol cascade

enabled successful isolation of tetracycle **22**, indicating the viability of our retrosynthetic strategy (Figure 6-5).

6.4 Discovery of Metal-Controlled Reversal of Enantioselectivity

Table 6-1 Optimization of Conditions for Metal-Catalyzed Michael Addition



entry	M	solvent	reaction time	yield	ee
1	Sc^{3+}	DCE	96 h	31%	–90% ee
		benzene	96 h	trace	
2	Y^{3+}	DCE	18 h	92%	71% ee
		benzene	18 h	91%	91% ee
3	Dy^{3+}	DCE	17 h	88%	76% ee
		benzene	17 h	83%	90% ee
4	La^{3+}	DCE	14 h	93%	–60% ee
		benzene	14 h	97%	–43% ee
5	Y^{3+}	benzene (0.04 M, 80 °C)	16 h	99%	95% ee

We then turned our attention to the substituted tetralone necessary to employ this approach to lingzhiol. We sought to adapt a known scandium-catalyzed enantioselective conjugate addition reaction[13] relying on chiral bipyridine ligand **L1** to synthesize enantiomerically enriched Michael adduct **24**, which would set the absolute stereochemistry for the entire synthesis. Conjugate addition of β-keto ester to methyl vinyl

ketone under the optimal conditions reported by Ogawa and coworkers afforded the desired product in excellent enantiomeric excess, but only in low yield (30%) after extended reaction times of 96 hours. Extensive optimization efforts are summarized in Table 6-1. When lanthanide triflates were used in place of $Sc(OTf)_3$, reaction times were dramatically shortened and high yields were isolated. The optimal conditions relied on 5 mol% $Y(OTf)_3$ and 10 mol% chiral bipyridine ligand in benzene (0.04 M) at 80 °C. These conditions enabled isolation of **24** in 99% yield and 95% ee after 16 hours. Remarkably, this compound had the opposite absolute configuration when compared to the product initially isolated from the scandium-catalyzed reaction, despite using the *same enantiomer* of chiral ligand **L1**.

This is highly useful in the synthesis of lingzhiol, as both enantiomers were isolated from the natural source and both were separately shown to exhibit the reported biological activity.[1]

6.5 Non-Linear Effect Study for Sc- and Y-Catalyzed Conjugate Addition

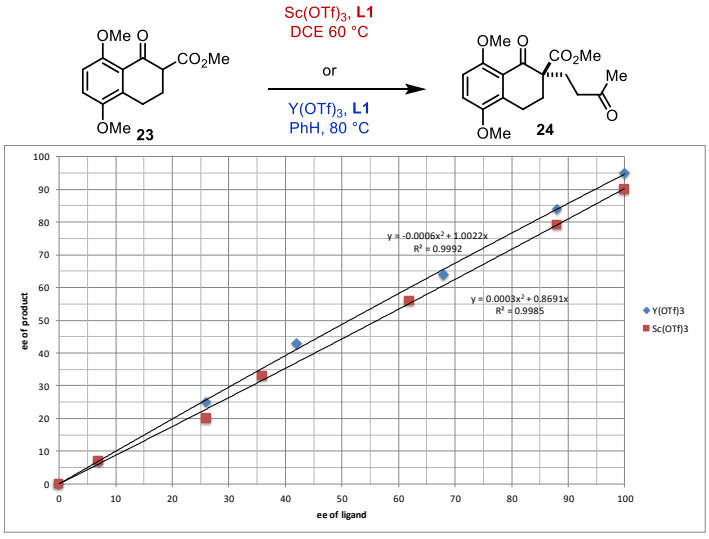


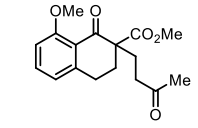
Figure 6-6 Non-linear effect study shows no non-linear effect

Our initial hypothesis to explain the reversal of enantioselectivity when replacing scandium with yttrium was that a higher-order metal-ligand complex was forming in the yttrium case due to the larger ionic radius of the metal center. To look for a non-linear effect[14] of this sort, we prepared mixtures of ligand with varying ee, and measured the resulting ee of the product in both the scandium and yttrium catalyzed systems. The resulting plots of ligand ee vs. product ee were linear for both yttrium and scandium (Figure 6-6), suggesting that a 1:1 metal to ligand ratio was the active catalyst for both catalytic systems.

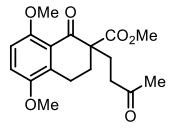
6.6 Lewis Basic *ortho*-Substituents Lead to High ee in Yttrium-Catalyzed Conjugate Addition Reactions

Table 6-2 Evaluation of Electron Rich Substrates for Michael Reaction

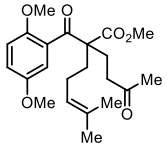
ortho-methoxy functionality appears crucial for high ee in $Y(OTf)_3$ catalyzed reaction to afford high ee



$Y(OTf)_3$: 94%, 90% ee (18 h)
$Sc(OTf)_3$: 15%, –85% ee (96 h)

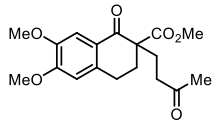


$Y(OTf)_3$: 99%, 95% ee (16 h)
$Sc(OTf)_3$: 31%, -90% ee (96 h)

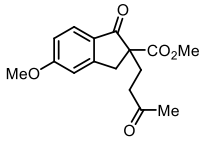


$Y(OTf)_3$: 12%, 67% ee (96 h)
$Sc(OTf)_3$: No reaction (96 h)

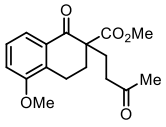
other methoxy-containing substrates only afford high ee with $Sc(OTf)_3$ and not $Y(OTf)_3$



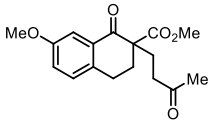
$Y(OTf)_3$: 92%, 14% ee (18 h)
$Sc(OTf)_3$: 29%, –90% ee (96 h)



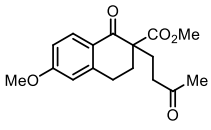
$Y(OTf)_3$: 99%, 24% ee (18 h)
$Sc(OTf)_3$: 93%, –94% ee (18 h)



$Y(OTf)_3$: 94%, 13% ee (18 h)
$Sc(OTf)_3$: 89%, 97% ee



$Y(OTf)_3$: 94%, 17% ee (18 h)
$Sc(OTf)_3$: 46%, 90% ee



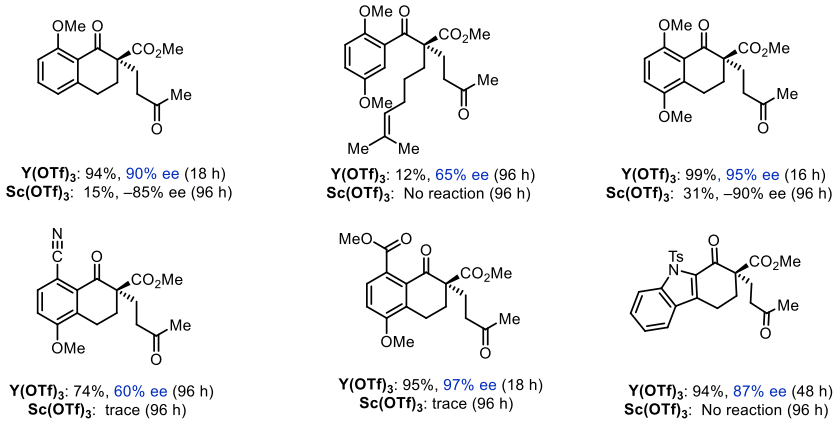
$Y(OTf)_3$: 93%, 16% ee (18 h)
$Sc(OTf)_3$: 18%, 39% ee (48 hr)

To probe the controlling features of this transformation, we prepared an array of tetralone-derived β-keto ester substrates. Our first hypothesis was that highly electron rich substrates formed tightly bound metal-substrate complexes with the yttrium catalyst,

leading to high enantioselectivities. However, various electron-rich substrates were found to afford poor ee under the optimal conditions for $Y(OTf)_3$ (Table 6-2).

Noting that only *ortho*-methoxy substituted substrates provided highly enantioenriched products, we prepared several *ortho*-substituted β-keto esters and found that those containing coordinating functional groups gave moderate to high ee's, while an uncoordinating ethyl group afforded near-racemic product (Table 6-3). This observation, coupled with the substantial difference in ionic radius between scandium and yttrium,[15] lead to a new mechanistic model: the substrates engage the smaller scandium metal center in a two-point binding fashion. In the larger yttrium case, the Lewis basic ortho-substituent also binds the metal, resulting in a complete "flipping" of the substrate and leading to a complete reversal of facial selectivity (Figure 6-7).

Table 6-3 Evaluation of ortho-Substituted Substrates for Michael Addition



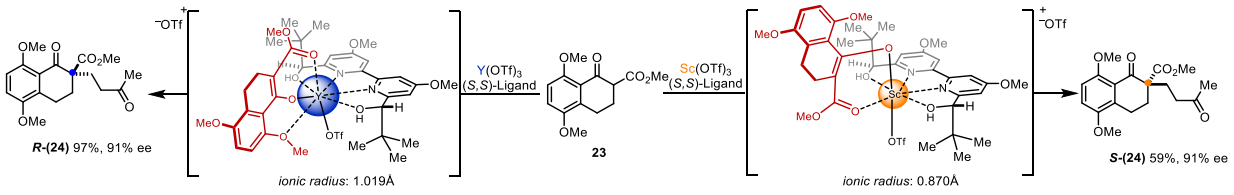
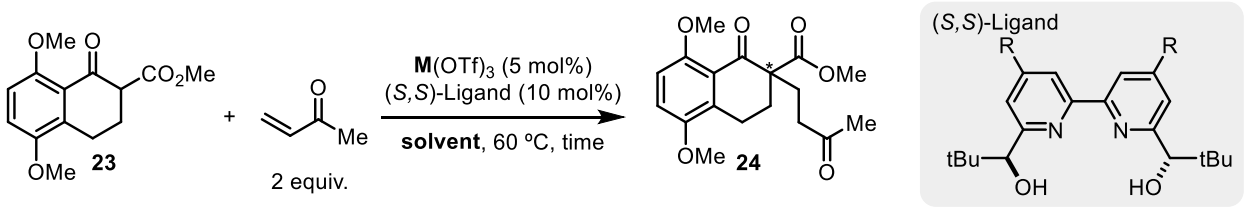


Figure 6-7 Proposed model for orgin of reversal of enantioselective between Sc and Y

6.7 Ligand Optimization

While the observed reversal of enantioselectivity maintains high ee for both the $Sc(OTf)_3$ and $Y(OTf)_3$, the yield in the $Sc(OTf)_3$ system could not be improved above 30% after 96 hours. The mechanism of the metal-catalyzed conjugate addition of β-keto esters proceeds through a metal enolate,[14] which we hypothesized is poorly nucleophilic, leading to sluggish reactivity to form **24**. To enhance this reactivity, we prepared more electron-rich bipyridine ligand **L2** and tested its reactivity in this system. Table 6-4 summarizes the comparative results between ligands **L1** and **L2** under both optimized $Sc(OTf)_3$ and

Table 6-4 Ligand Optimization



entry	M	solvent	temp (°C)	R	time (hr)	yield	ee
1	Sc^{3+}	DCE	60	H	96	31%	–90%
2		DCE		OMe	96	59%	–91%
3	Y^{3+}	benzene	80	H	14	99%	93%
4		benzene		OMe	4	97%	91%

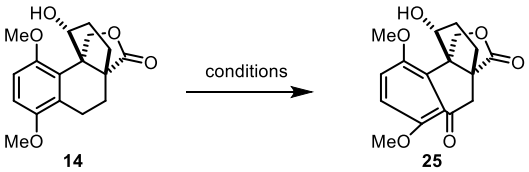
$Y(OTf)_3$ reaction conditions. More electron rich ligand **L2** leads to a nearly double isolated yield of Michael adduct **24** (30% with **L1**, 59% with **L2**) without any loss of ee. Similarly, employing ligand **L2** under the optimized conditions for $Y(OTf)_3$ again affords high yields and excellent enantioselectivity in diminished reaction time of 4 hours.

6.8 Completion of the Total Synthesis of Lingzhiol

Having extensively optimized for highly enantioselective and synthetically useful conditions to prepare both (*R*)- and (*S*)-**24**, we then sought to elaborate these chiral adducts to lingzhiol (Figure 6-8). Sodium methoxide mediated aldol condensation

smoothly afforded enone **17**, which was then reduced to allylic alcohol **25** with (*S*)-CBS catalyst and borane. Treatment with *m*CPBA was expected to form epoxy-alcohol **15**, but instead the sole product was aldehyde **27**, resulting from spontaneous semi-pinacol rearrangement of the epoxide. Epoxide **15** could not be isolated, even when employing coordinating solvents or adding base to the reaction mixture. Although the one-pot

Table 6-5 Evaluation of Benzylic Oxidation Conditions



14 **25**

entry	conditions	yield (%)
1	Rh_2cap_4, T-HYDRO	6
2	Rh_2cap_4, TBHP	38 (76 BRSM)
3	$RuCl_3$, TBHP	N.D.
4	NBS/H_2O then MnO_2	N.D.
5	$Co(OAc)_2$, NHPI, O_2, HFIP	N.D.
6	$Pd(OH)_2$, TBHP	N.D.
7	oxone, KBr	N.D.

reductive semi-pinacol approach proposed in our retrosynthetic approach was no longer possible, reduction of aldehyde **27** with $NaBH_4$ proceeded efficiently to provide lingzhiol core **16**, whose structure was unambiguously confirmed by X-ray crystallography.

Installation of the benzylic ketone in the presence of an unprotected secondary alcohol presented a final challenge for the completion of the total synthesis. While

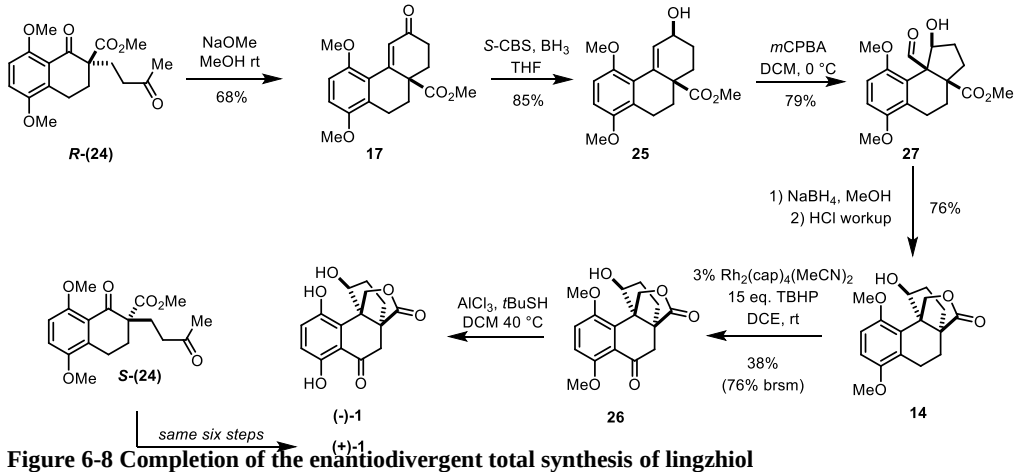


Figure 6-8 Completion of the enantiodivergent total synthesis of lingzhiol

protection of the alcohol followed by harsh benzylic oxidation conditions and subsequent deprotection is precendented,[6,9] it represents an inefficient approach.[16] Other syntheses report a two-step oxidation procedure relying on benzylic bromination with NBS followed by selective MnO2-mediated oxidation. In our hands and others[9], this approach proved unsuccessful. As such, we sought to employ radical oxidation conditions that would selectively target the weak benzylic C-H bond without oxidizing the secondary alcohol. Various reported oxidation conditions[17] were evaluated (Table 6-5), but only the dirhodium catalyzed benzylic oxidation reported by Doyle[18] enabled isolation of oxidation product **26** in 43% yield (76% BRSM).

BBr_3-mediated demethylation has previously been reported as the final step in the synthesis of lingzhiol. In our hands, this reagent resulted only in reisolation of the starting material or mono-demethylation. Employing alternative demethylation conditions relying on $AlCl_3$ and *tert*-butyl thiol effectively furnished lingzhiol. This sequence afforded (–)-lingzhiol in a total of only eight steps from commercially available starting material in 13% overall yield and 93% ee. The same sequence from *S*-**(24)** afforded (+)-lingzhiol in 10% overall yield and 95% ee.

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Chapter 7 Studies Toward the Total Synthesis of *ent*-Kaurene Diterpenoids via a Divergent Approach from a Common Intermediate.

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7.1 History and Biosynthesis

Plant terpene natural products are one of the largest class of natural products and are derived from a common biosynthetic pathway involving isoprene units.[1] These compounds are divided into a variety of different classes based on their size and degree

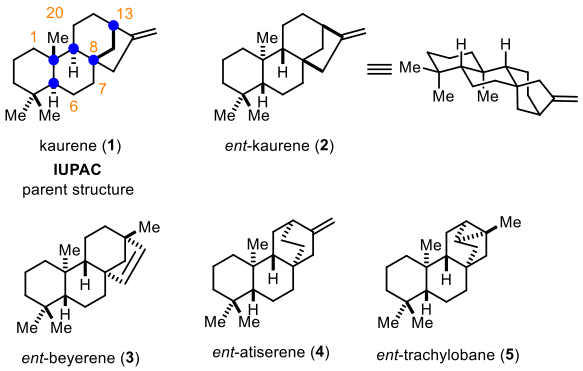


Figure 7-1 *ent*-Kaurene parent structure and related natural product classes

of cyclization. *ent*-Kaurene natural products represent an important class of tetracyclic diterpenoids (C_{20}), along with *ent*-beyerenes (**3**), *ent*-atiserines (**4**), and *ent*-trachylobanes

(**5**).[2] The kaurene carbocyclic structure (**1**) has been defined by IUPAC[3], but most isolated natural products have the opposite stereochemical configuration and are therefore labeled as *ent*-kaurenes (**2**; Figure 1). Over 600 *ent*-kaurenes have been isolated from the over 150 flowering plants from the genus *Isodon*. These plants are typically found in southeast Asia and have been used to treat cancer and various inflammation-related illnesses in traditional Chines medicine.[4] These compounds are also structurally related to the steviol glycosides isolated from *Stevia rebaudiana* and commonly used as sweeteners, particularly in recent years in the United States.

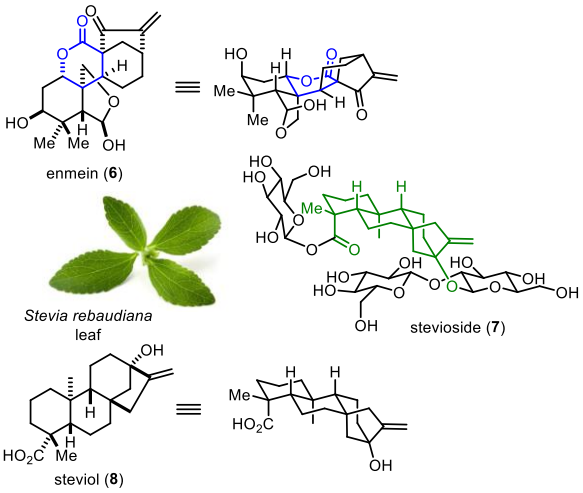


Figure 7-2 Historically important *ent*-kaurenes

Efforts to isolate and characterize *ent*-kaurenes date as early as 1901[5], and the first investigations into their biological activities began in 1910[6]. Figure 2 shows the structures of enmein (**6**) and steviol (**8**), the two *ent*-kaurenes whose structures were of most interest during these early investigations. While enmein was isolated in 1958, the structure was not unambiguously determined until 1966 as a result of the collaboration of three research groups in Japan.[7]

The tetracyclic compounds of the *ent*-kaurene family have their biosynthetic origin from geranylgeranyl pyrophosphate (**9**), which undergoes cyclization to form *ent*-copalyl

pyrophosphate (**10**, Figure 3).[8] **10** is cyclized further by *ent*-kaurene synthase to **11**, which undergoes a Wagner-Meerwein rearrangement to carbocation **13**, affording the hydrocarbon core of the *ent*-kaurenes upon deprotonation. Oxidation, typically by P450 enzymes, leads to many natural products including steviol (**8**) as well as gibberellins (which are not classified as *ent*-kaurenes or addressed in this dissertation).[9] This biosynthetic pathway is also intimately related to the pathways for the syntheses of *ent*-beyerene (**3**), *ent*-trachylobane (**5**), and *ent*-atiserine (**4**).[10]

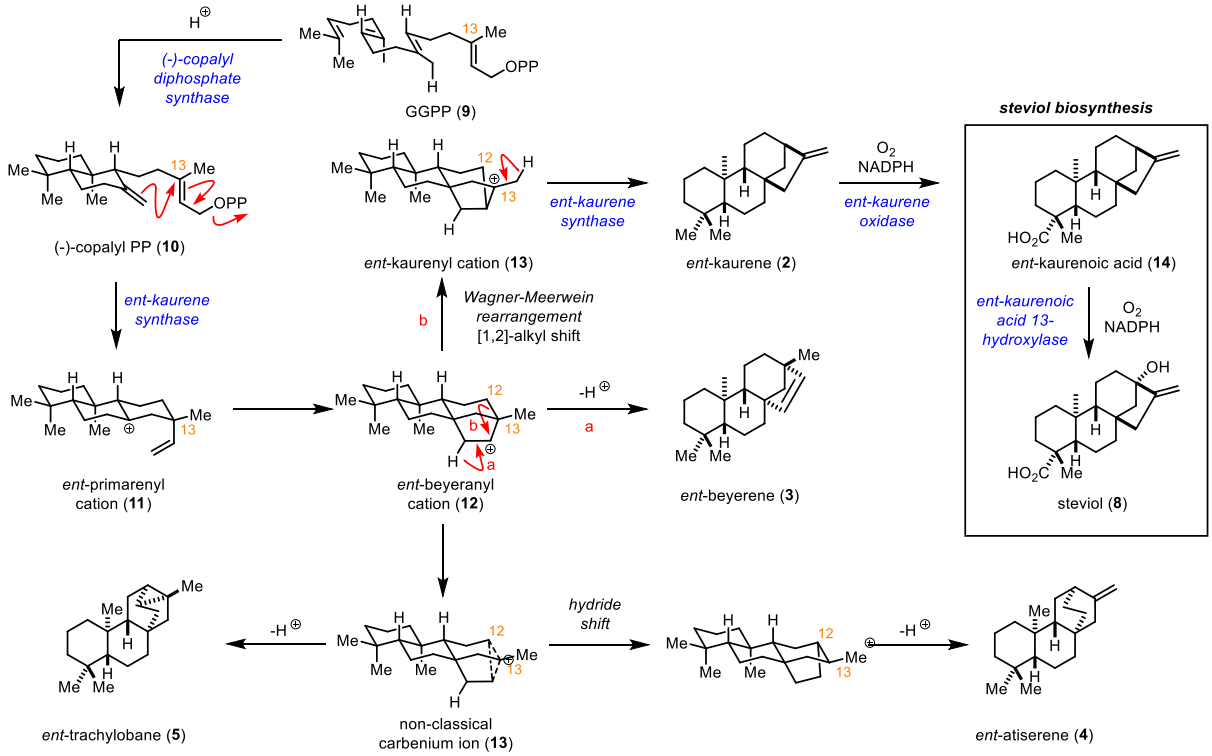
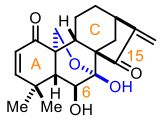


Figure 7-3 Biosynthesis of *ent*-kaurenes and related natural products

7.2 Biological Activity

The *ent*-kaurenes have been implicated as the biologically active components of *Isodon* plant species that have been used in traditional Asian medicines for treatment of various ailments including bacterial infections, inflammatory diseases, and cancer.



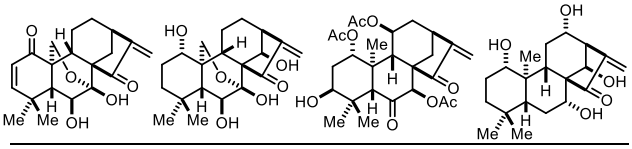
eriocalyxin B (**15**)

Categories	Name	MIC/μg·mL^{-1}
Gram-positive bacteria	*Staphylococcus aureus*	31
	Stpahylococcus epidermidis	62
	Streptococcus sanguis	62
Gram-negative bacteria	*Escherichia coli*	500
	Enterobacter gergoviae	2000
Microzyme	*Candida albicans*	62
Epiphyte	*Zygosaccharomyces bailii*	63

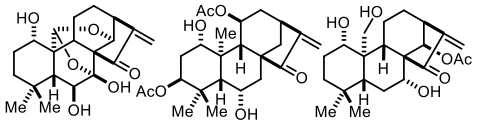
Figure 7-4 Antibacerial activity of eriocalyxin B

Early studies concluded that the electrophilic exocyclic enone moiety was integral for the activity of certain ent-kaurenes against Gram-positive bacteria.[11] This structure activity relationship is of substantial interest to our group and is one of the factors inspiring our synthesis of these compounds. Eriocalyxin B (**15**) has two electrophilic Michael acceptor groups and has been shown to have particularly high activity as an antibacterial agent (Figure 4).[12]

Antitumor activity of certain *ent*-kaurenes such as enmein (**6**) have been reported as early as 1961.[13] The Michael acceptor functionality was again implicated in this activity by binding thiol residues in cysteines in cancer-cell enzymes, leading to cell death. Selective binding to these enzymes is a result of the structure and specific oxidation. Significant debate exists in the literature as to the mechanisms by which these



eriocalyxin B (**15**)	oridonin (**16**)	adenanthin (**17**)	excisanin (**18**)
decrease of telomerase activity	*decrease of telomerase activity*	*peroxiredoxin inhibition*	*inhibition of AKT*
activation of p53	*activation of p53*		
inhibition of NF-κB (non-competitive binding)	*inhibition of AKT*		
	inhibition of NF-κB		



ponicidin (**19**)	inflexinol (**20**)	kamebakaurin (**21**)
able to bind and cleave DNA	*covalent modification of p50*	*interacts with both p65 and p50*
	decreases translocation of p65 and p50	

Figure 7-5 Representative biological activities of various *ent*-kaurenes

compounds inhibit cancer cell growth. Various pathways, including telomerase[14], p53 activation[15], phosphatidyl-inositol 3-kinase/protein kinase B[16], epidermal growth factor receptor signaling[17], and AMP-activated protein kinase inhibition[18] have all been implicated in the anti-tumor activity of various *ent*-kaurene natural products (Figure 5). Importantly, these compounds are also hypothesized to have anti-cancer activities originating from their ability to inhibit the NF-kB transcription factor, which is implicated in a large majority of cancers and is of particular interest to our research group.[19]

7.3 Previous Syntheses

Because of their biological activities and their structural complexity, these compounds have been popular targets for synthetic organic chemists for many decades. The first synthesis of kaurene was successfully completed and disclosed by the Ireland research group in the 1960's (Figure 6). Since then, many syntheses and efforts towards *ent*-kaurene natural products have been described in racemic and enantioselective approaches. A landmark synthesis in this area is the Reisman group's approach to three different ent-kaurenes from a common intermediate and relying on SmI_2-mediated reductive cyclization reactions (Figure 7).[20] A detailed review from our group describes

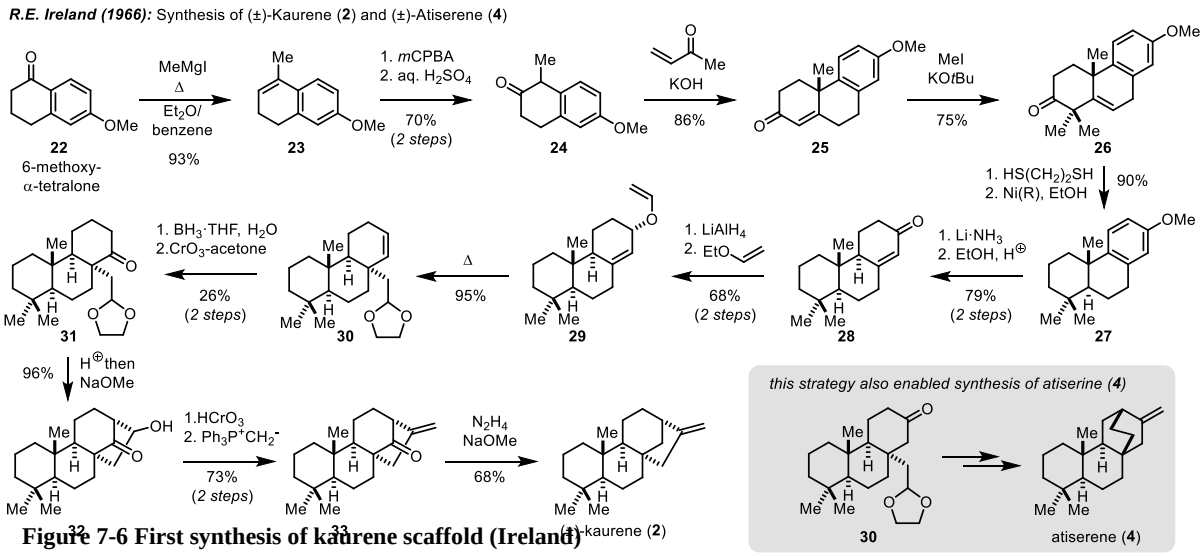


Figure 7-6 First synthesis of kaurene scaffold (Ireland)

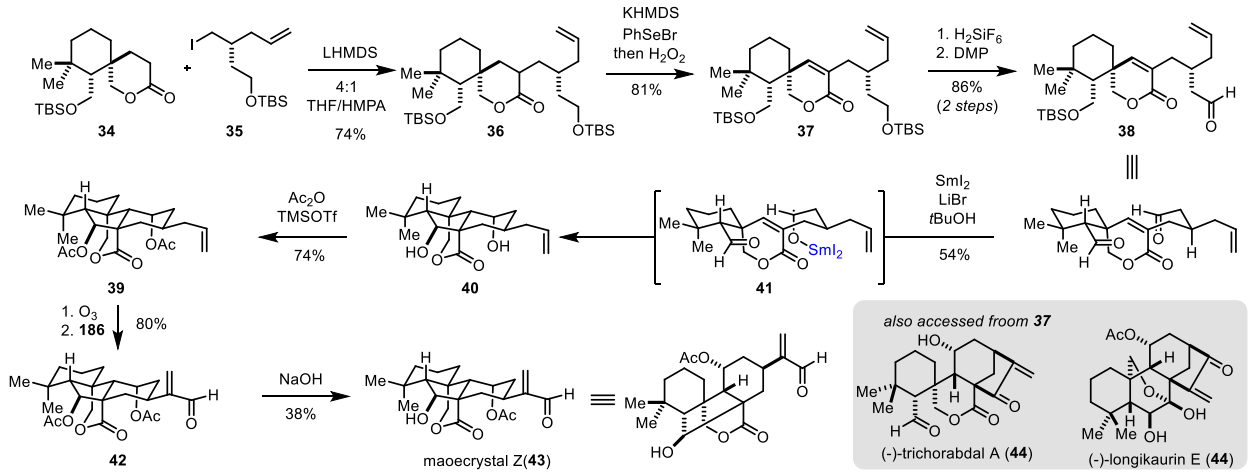


Figure 7-7 Reisman's approach to three members of this class of natural products

many of these approaches through 2015.[21] Since then, these compounds have remained active targets for synthesis. For example, Lee and coworkers disclosed a synthetic approach to eriocalyxin B (**15**), neolaxiflorin L (**52**) and xerophilusin I (**51**) in 2018 (Figure 8).[22] However, this synthesis resulted in racemic compounds, and while three natural products are reported, they differ only in oxidation state of one ring of the tetracyclic compound.

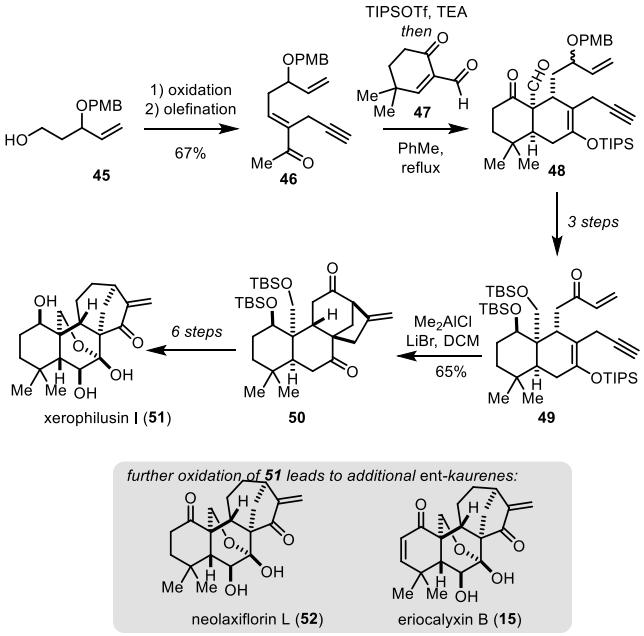


Figure 7-8 Recent synthetic approach to eriocalyxin B

7.4 Retrosynthetic Analysis: Divergent Approach Via a Common Intermediate

In our approach to the synthesis of *ent*-kaurenes, we envisioned that common intermediate **56** could be constructed by esterification of two fragments **58** and **59**

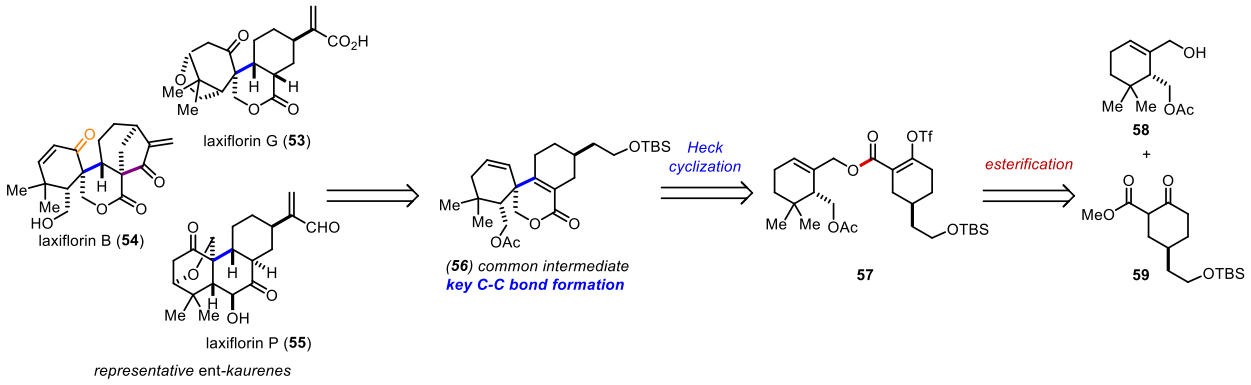


Figure 7-9 Retrosynthesis of a common intermediate to this family

followed by an intramolecular Heck reaction to afford the key carbon-carbon bond (Figure 9). **58** was expected to be available from commercially available geranic acid **66**, while **59** was expected to be prepared from 1,4-cyclohexanedione mono-ethylene ketal **73**, which is also readily available on large scale. Known asymmetric reactions were expected to be adaptable to prepare these two fragments in asymmetric fashion, enabling the preparation of tricyclic intermediate **57** in enantioenriched fashion.

7.5 Heck Reaction in Model System

Literature examples forming six-membered rings are sparse[23], and no examples of six-membered ring involving allylic esters are reported. However, the Thomson group reported the application of a Heck reaction between an aryl bromide and a trisubstituted olefin as a key step (Figure 10A) in their synthesis of *ent*-kaurene natural product and popular synthetic target maeocrystal V.[24] Encouraged by this result, we prepared model vinyl bromide **62** and investigated the palladium-catalyzed Heck reaction to form tricyclic lactone **65** using $Pd(PPh_3)_4$. We found that competitive insertion of palladium into the

allylic position afforded diene **63**, while insertion into the vinyl bromide followed by proto-

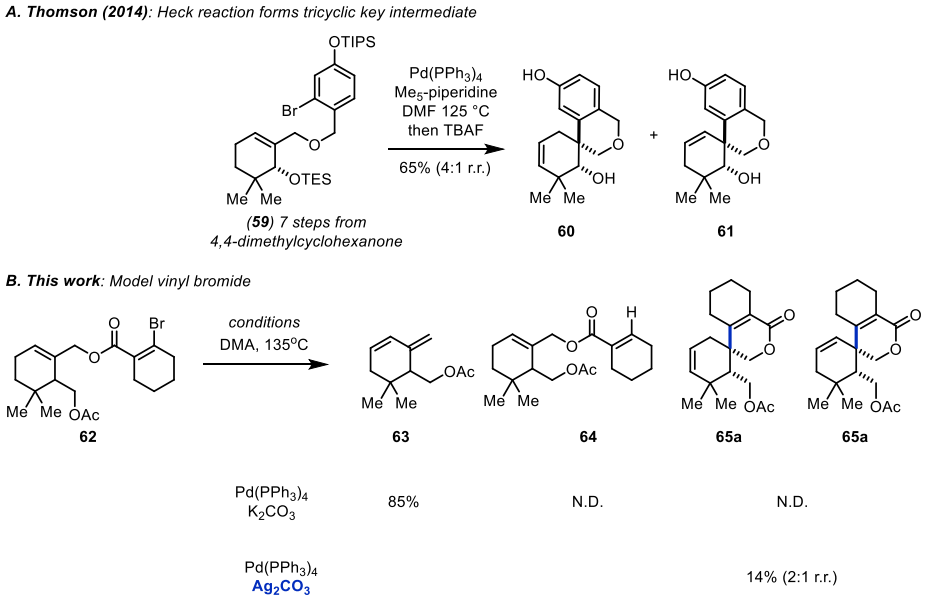


Figure 7-10 Heck reaction model studies

demetallation afforded reduction product **64**. Productive migratory insertion leading to the key carbon-carbon bond formation was found to be possible when switching the base to silver carbonate in place of potassium carbonate. As a result, the desired tricycle **65** could be isolated in 14% yield as a 2:1 mixture of olefin isomers.

7.6 Fragment Synthesis: Allylic Alcohol from Geranic Acid

The acid-mediated cyclization of geranic acid **66** to afford cyclogeranic acid **67** is well known,[25] and the installation of the desired stereocenter in high enantiomeric excess has been studied extensively by Fehr.[26] We found that acid-mediated cyclization with phosphoric acid effectively afforded the desired endocyclic isomer of cyclogeranic acid **67a** along with undesired exocyclic isomer **67b** in up to 82% yield as an 8:1 mixture (Figure 11B). By subjecting this compound to the optimized conditions for TfOH-catalyzed cyclization between carbonyls and trisubstituted olefins reported by our laboratory[27], we were able to isolate high yields of endocyclic isomer **67a** as the sole reaction product.

Thioesterification to **69**, deprotonation with *n*BuLi and re-protonation with chiral ephedrine-derived acid **70** under Fehr's conditions followed by reduction with $LiAlH_4$ gave cyclogeraniol in high over 90% ee. Acetylation of the primary alcohol proceeded smoothly to give acetate **71** in 80% yield over two steps after distillation.

Installation of the allylic alcohol functionality (Figure 11C) provided a significant challenge for completing fragment **58**. Allylic oxidation strategies relying on selenium dioxide[28], palladium C-H activation[29], NBS[30], and I_2[31] all failed to install C-H oxidation of the methyl group in appreciable yield. Instead, treatment with *tert*-butyl hypochlorite as an electrophilic chlorine source[32] afforded secondary allylic chloride **72**, which could be oxidized with silver(II) oxide to afford a 4:1 mixture of allylic alcohols **58a** and **58b** in 15-30% yield over two steps, with elimination to diene **63** accounting for the mass balance.

While this strategy enabled access to the desired allylic alcohol, the low yield and moderate selectivity remained a challenge. As a result, we investigated a three-step protocol, again beginning with chlorination of **71**. Subsequent S_N2' reaction with sodium

formate and TBAI afforded an allylic formate that could be selectively cleaved in the presence of the acetate protecting group by treatment with methanolic triethylamine, smoothly furnishing desired allylic alcohol **58** in 48% yield over three steps.

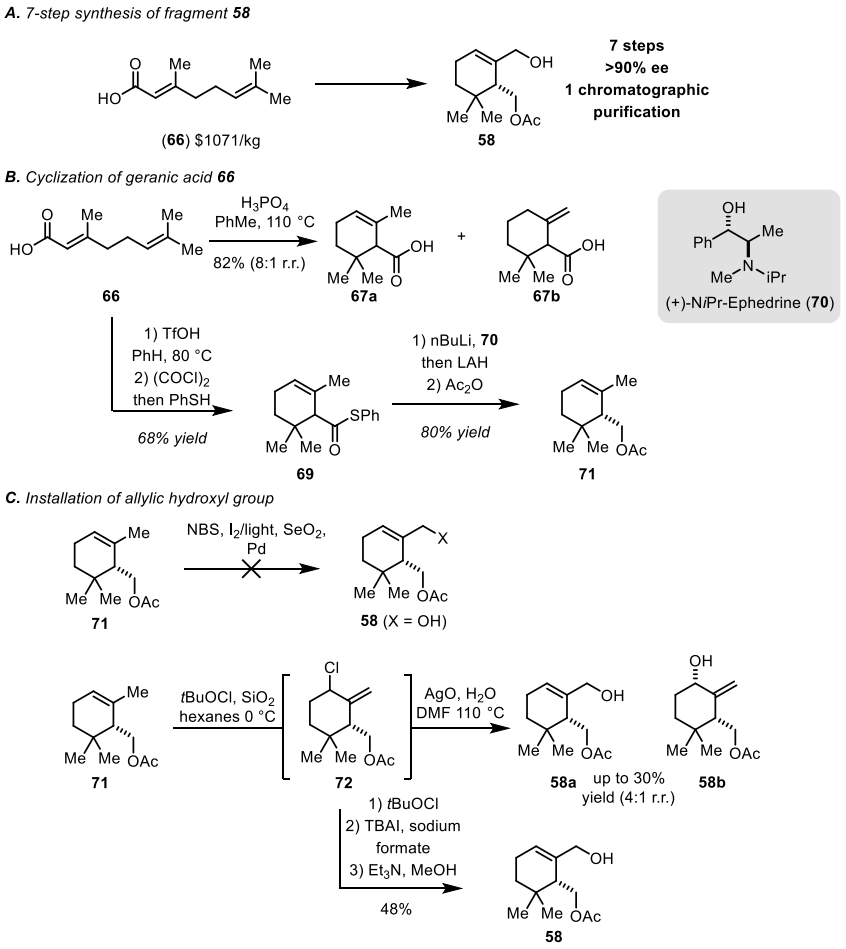


Figure 7-11 Forward synthesis of fragment 58

7.7 Fragment Synthesis: β-Keto Ester from 1,4-Cyclohexanedione Ketal

The elaboration of 1,4-cyclohexanedione monoethylene ketal **73** to known[33] symmetrical TBS-protected primary alcohol **74** was adapted from literature protocols to provide greater than 100 grams in a 5-step sequence. The asymmetric carboxylation of this was achieved by adapting a procedure reported by Koga and coworkers.[34] This two-step sequence (Figure 12) commenced with a desymmetrizing deprotonation at -100 °C using chiral base **75** followed by trapping of the enolate with TMSCl. The silyl enol ether

76 is then lithiated with methyllithium-lithium bromide complex followed by carboxylation with Mander's reagent, enabling efficient access to β-keto ester **59** in 82% ee (measured

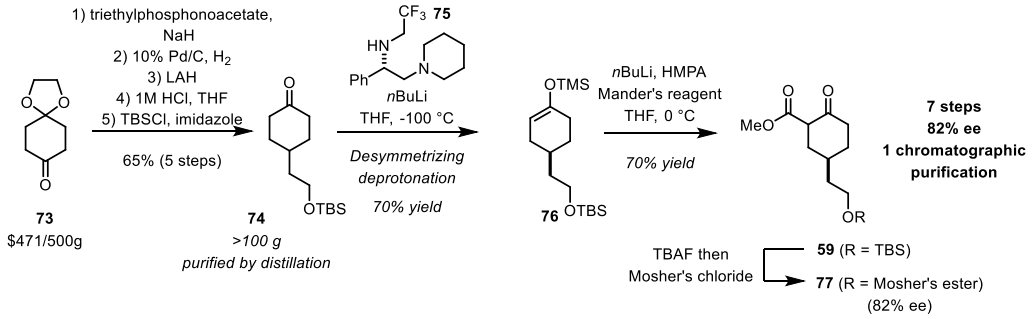


Figure 7-12 Forward synthesis of fragment 59

by ^{19}F NMR of the analogous Mosher ester **77**).

7.8 Heck Reaction Affords Common Intermediate

The methyl ester of **59** is readily transesterified with allylic alcohol **58** by DMAP catalysis[35], combining the two fragments and affording **78**. Treatment with Tf_2O and DIPEA provides triflate **79** in up to 90% yield (Figure 13).

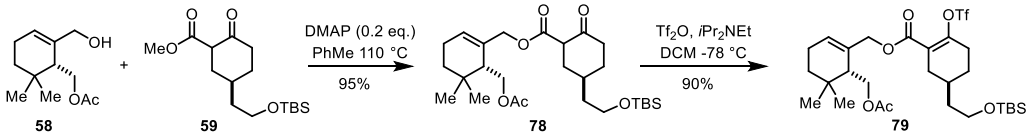


Figure 7-13 Transesterification and triflation

Adapting the conditions for the model Heck reaction of **62** to **65** (Chapter 7.5) surprisingly did not translate to the fully elaborated natural product system in **79**, instead affording poorly reproducible yields of 1-35% of triflate reduction product rather than cyclized Heck product **58**.

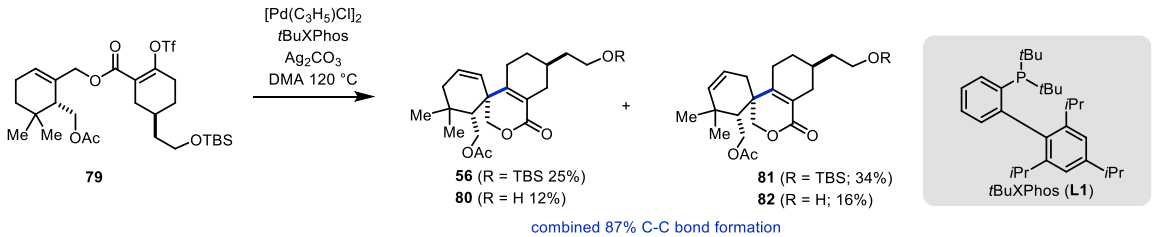


Figure 7-14 Forward synthesis: highest yielding Heck reaction

We then evaluated many conditions for this reaction in collaboration with Merck and found that high temperatures were crucial for this reaction to proceed and DMA was the optimal solvent. *t*BuXPhos ligand **L1** and allylpalladium chloride dimer were identified as an optimal catalyst system for this reaction affording a mixture of four tricyclic products, all of which have the key carbon-carbon bond in 87% combined yield of carbon-carbon bond forming products (Figure 14).

7.9 Elaboration to *ent*-Kaurene Natural Products

With effective conditions to forge the key carbon-carbon bond of **58** by a Pd-catalyzed Heck reaction in hand, our attention is now focused on elaboration of this compound to various *ent*-kaurene natural products. This work is still in progress, and the planned elaboration of compound **58** (and **80**-**82**) to representative *ent*-kaurenes is described in Figure 15. Established collaborations are also in place to enable biological evaluations as anti-cancer therapeutics upon completion of the syntheses.

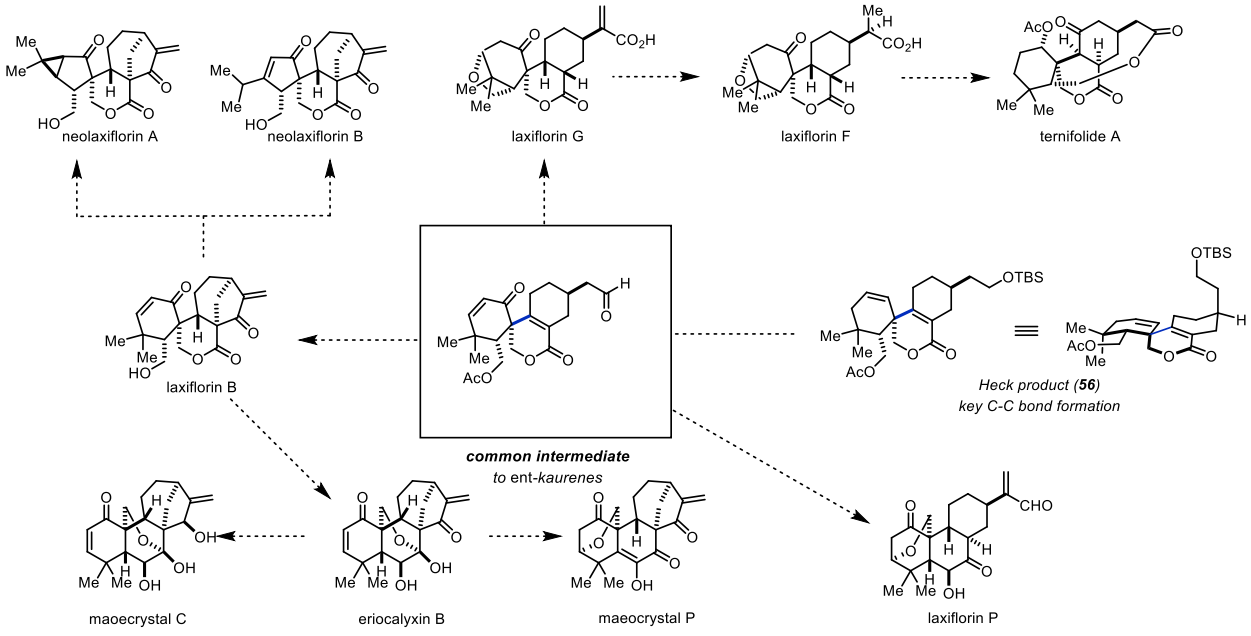


Figure 7-15 Elaboration of Heck product 58 to *ent*-kaurenes

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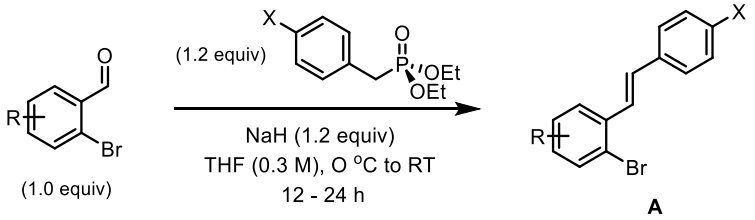
Appendices

Appendix 1

Synthesis of Polycyclic Aromatic Hydrocarbons by COM – Experimental Details

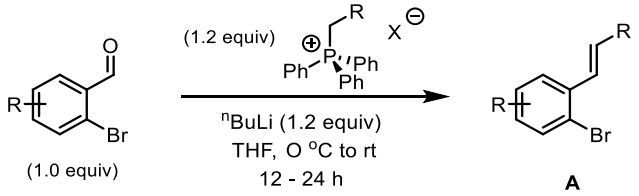
General olefination procedure A for substrate precursors (A):



X= H, Cl, F, Me, OMe

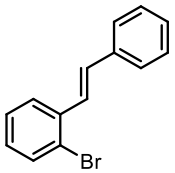
A 50 mL round bottom flask equipped with a magnetic stir bar was charged with diethyl benzylphosphonate (1.1 equiv) and dry THF (0.3 M). The solution was cooled to 0 °C with an ice bath followed by NaH addition (1.2 equiv). After stirring for 30 min at 0 °C the starting aryl aldehyde (1 equiv) was slowly added. The reaction was allowed to warm to room temperature and stirred until judged complete by TLC analysis (12-24 h). The reaction mixture was then cooled to 0 °C and quenched with aqueous ammonium chloride (n mL). The biphasic solution was extracted with ethyl acetate (3 × n mL). The combined organic phases were washed with brine (n mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified *via* flash column chromatography eluting with a mixture of hexanes and ethyl acetate to give the pure stilbene derivative (**A**).

General olefination procedure B for substrate precursors (A):

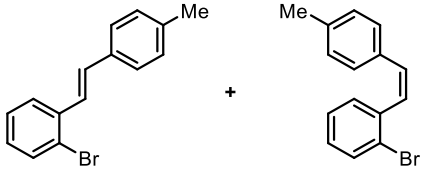


X= Br, I

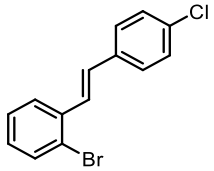
A 50 mL round bottom flask equipped with a magnetic stir bar was charged with Wittig salt (1.1 equiv) and dry THF (0.3 M). The solution was cooled to 0 °C with an ice bath followed by ^{n}BuLi addition (1.2 equiv). After stirring for 30 min at 0 °C the starting aryl aldehyde (1 equiv) was slowly added. The reaction was allowed to warm to room temperature and stirred until judged complete by TLC analysis (12-24 h). The reaction mixture was then cooled to 0 °C and quenched with aqueous ammonium chloride (n mL). The biphasic solution was extracted with ethyl acetate (3 × n mL). The combined organic phases were washed with brine (n mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified *via* flash column chromatography eluting with a mixture of hexanes and ethyl acetate to give the pure olefin (**A**).



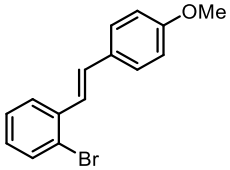
(*E*)-1-bromo-2-styrylbenzene (A1): General olefination procedure **A** was followed employing 2-bromobenzaldehyde (54 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 12.71 g (91%) of **A1** as a clear oil. Spectroscopic data matched reported literature data.[1] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.8 Hz, 1H), 7.63 – 7.51 (m, 3H), 7.47 (d, *J* = 16.2 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.35 – 7.27 (m,2H), 7.12 (t, *J* = 7.6 Hz, 1H), 7.05 (d, *J* = 16.2 Hz, 1H).



(*E*)-1-bromo-2-(4-methylstyryl)benzene + (*Z*)-1-bromo-2-(4-methylstyryl)benzene (*E*-A2 & ***Z*-A2):** General olefination procedure **A** was followed employing (2.72 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 218 mg (30%) of ***E*-A2** and 120 mg (16%) of ***Z*-A2** as a clear oil. Spectroscopic data matched reported literature data.[2] Spectral data for ***E*-A2. ^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 16.2 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 7.9 Hz, 2H), 7.12 – 7.10 (m, 1H), 7.02 (d, *J* = 16.2 Hz, 1H), 2.38 (s, 3H). Spectral data for ***Z*-A2**. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.21 (dd, *J* = 7.1, 2.1 Hz, 1H), 7.12 – 7.07 (m, 2H), 7.04 (d, *J* = 8.1 Hz, 2H), 6.99 (d, *J* = 8.1 Hz, 2H), 6.65 (d, *J* = 12.1 Hz, 1H), 6.56 (d, *J* = 12.1 Hz, 1H), 2.29 (s, 3H).

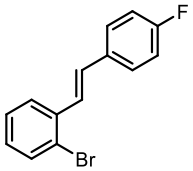


(*E*)-1-bromo-2-(4-chlorostyryl)benzene (A3): General olefination procedure **A** was followed (2.72 mmol scale). Purification by flash column chromatography eluting with hexanes/EtOAc provided 425 mg (56%) of **A3** as a white powder. Spectroscopic data matched reported literature data.[3] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.8 Hz, 1H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.42 (s, 1H), 7.33 (m, 3H), 7.15 – 7.11 (m, 1H), 6.98 (d, *J* = 16.2 Hz, 1H).

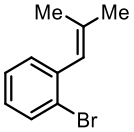


(*E*)-1-bromo-2-(4-methoxystyryl)benzene (A4): General olefination procedure **A** was followed (2.72 mmol scale). Purification by flash column chromatography eluting with hexanes/EtOAc

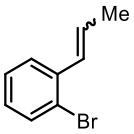
provided 245 mg (31%) of **A4** as a white solid. Spectroscopic data matched reported literature data.[3] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.8 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 8.6 Hz, 2H), 7.36 – 7.27 (m, 2H), 7.11 – 7.07 (m, 1H), 7.00 (d, *J* = 16.2 Hz, 1H), 6.92 (d, *J* = 8.7 Hz, 1H), 3.84 (s, 3H).



(*E*)-1-bromo-2-(4-fluorostyryl)benzene (A5): General olefination procedure **A** was followed (2.72 mmol scale). Purification by flash column chromatography eluting with hexanes/EtOAc provided 245 mg (53%) of **A5** as a clear oil. Spectroscopic data matched reported literature data.[3] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.7 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.54 (dd, *J* = 8.4, 5.5 Hz, 2H), 7.39 (d, *J* = 16.2 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.09 (t, *J* = 8.6 Hz, 2H), 7.01 (d, *J* = 16.2 Hz, 1H).

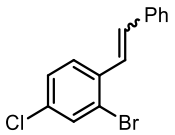


1-bromo-2-(2-methylprop-1-en-1-yl)benzene (A6): General olefination procedure **B** was followed employing 2-bromobenzaldehyde (12.4 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 2295 mg (89%) of **A6** as a clear oil. Spectroscopic data matched reported literature data.[4] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.59 – 7.56 (m, 1H), 7.30 – 7.23 (m, 2H), 7.10 – 7.06 (m, 1H), 6.27 (s, 1H), 1.96 (s, 3H), 1.77 (s, 3H).

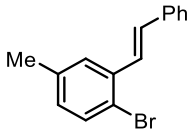


1-bromo-2-(prop-1-en-1-yl)benzene (A7): General olefination procedure **B** was followed employing ethyl triphenylphosphonium bromide (5.43 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 756 mg (71%) of **A7** as a *E/Z* (3:1) mixture, as a clear oil. Spectroscopic data matched reported literature data.[5]

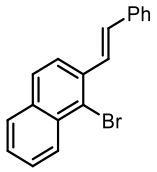
1-bromo-2-vinylbenzene (A8): General olefination procedure **B** was followed employing 2-bromobenzaldehyde (7.07 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 890 mg (69%) of **A8** as a clear oil. Spectroscopic data matched reported literature data.[6] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.9 Hz, 2H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.12 (t, *J* = 7.7 Hz, 1H), 7.06 (dd, *J* = 17.4, 11.0 Hz, 1H), 5.71 (d, *J* = 17.4 Hz, 1H), 5.37 (d, *J* = 10.9 Hz, 1H).



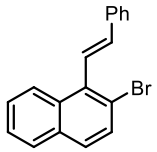
1-bromo-4-chloro-2-styrylbenzene (A9): General olefination procedure **A** was followed employing 2-bromo-5-chlorobenzaldehyde (2.62 mmol scale). Purification by flash column chromatography eluting with hexanes/EtOAc provided 395 mg (52%) of **A9** as an inseparable mixture of alkene isomers (3.88:1) as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$;) δ 7.58 – 7.51 (m, 3H), 7.43 – 7.35 (m, 4H), 7.32 (t, *J* = 7.3 Hz, 1H), 7.04 (d, *J* = 16.2 Hz, 1H), 6.88 – 6.84 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 138.66, 136.51, 134.04, 132.63, 128.88, 128.79, 128.60, 128.46, 128.32, 126.97, 126.49, 126.25. **IR** (cm^{-1}): 2155.7, 1413.1, 1340.7, 1321.5, 1251.0, 1107.8, 1079.4, 1023.3, 954.9, 822.7, 803.5, 752.0, 684.7. **HRMS**: Calculated for $C_{14}H_{10}BrCl^{+}$ ($[M]^{+}$): 291.9654 Found: 291.9659.



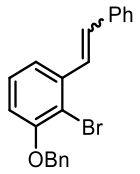
(*E*)-1-bromo-4-methyl-2-styrylbenzene (A10): General olefination procedure **A** was followed employing 2-bromo-5-methylbenzaldehyde (2.39 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 486 mg (74%) of **A10** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.56 (t, *J* = 8.2 Hz, 1H), 7.48 – 7.34 (m, 1H), 7.32 – 7.24 (m, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 16.2 Hz, 1H), 2.34 (s, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.34, 137.38, 1034.38, 133.65, 130.66, 128.92, 128.68, 128.08, 127.53, 126.94, 126.54, 124.15, 21.03. **IR** (cm^{-1}): 3045.3, 1594.0, 1492.9, 1483.5, 1448.1, 1228.2, 1037.9, 965.2, 954.5, 811.6, 751.6, 705.3, 689.9. **HRMS**: Calculated for $C_{15}H_{13}Br^{+}$ ($[M]^{+}$): 272.0201 Found: 272.0201.



(*E*)-1-bromo-2-styrylnaphthalene (A11): General olefination procedure **A** was followed employing 1-bromo-2-naphthaldehyde (3.25 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 624 mg (62%) of **A11** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.5 Hz, 1H), 7.85 – 7.77 (m, 4H), 7.62 (d, *J* = 5.1 Hz, 2H), 7.60 – 7.58 (m, 1H), 7.53 – 7.49 (m, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.18 (d, *J* = 16.2 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 137.36, 134.91, 134.11, 132.99, 132.35, 129.01, 128.80, 128.38, 128.29, 127.98, 127.97, 127.86, 127.12, 126.76, 124.41, 124.15. **IR** (cm^{-1}): 3052.1, 1548.8, 1492.1, 1445.4, 1330.4, 1264.9, 1234.5, 958.3, 865.3, 804.5, 767.9, 738.5, 668.0, 657.0. **HRMS**: Calculated for $C_{18}H_{13}Br^{+}$ ($[M]^{+}$): 308.0201 Found: 308.0196.



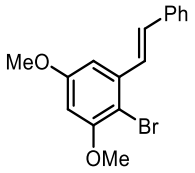
(*E*)-2-bromo-1-styrylnaphthalene (A12): General olefination procedure **A** was followed employing 2-bromo-1-naphthaldehyde[7] (2.98 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 818 mg (89%) of **A12** as a white powder. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.28 – 8.23 (m, 1H), 7.86 – 7.81 (m, 1H), 7.69 – 7.59 (m, 4H), 7.54 – 7.47 (m, 2H), 7.43 (m, 2H), 7.35 (m, 2H), 6.89 (d, *J* = 16.6 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 137.10, 136.90, 135.67, 133.07, 133.02, 130.18, 129.00, 128.72, 128.57, 128.39, 127.08, 126.89, 126.39, 126.25, 126.17, 121.82. **IR** (cm^{-1}): 3050.8, 2919.6, 1561.5, 1499.1, 1449.2, 1378.3, 1114.5, 967.9, 891.1, 820.5, 801.7, 744.6, 724.2, 687.9. **HRMS**: Calculated for $C_{18}H_{13}Br^+$ ($[M]^+$): 308.0201 Found: 308.0196.



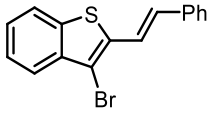
1-(benzyloxy)-2-bromo-3-styrylbenzene (A13): General olefination procedure **A** was followed employing 3-(benzyloxy)-2-bromobenzaldehyde[8] (1.0 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 156 mg (43%) of **A13** as an inseperable *E/Z* mixture (3.3:1), as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$; for major *E* isomer) δ 7.61 – 7.56 (m, 1H), 7.51 (dd, *J* = 17.6, 11.1 Hz, 2H), 7.46 – 7.28 (m, 4H), 7.27 – 7.22 (m, 1H), 7.21 – 7.12 (m, 3H), 7.10 – 6.98 (m, 1H), 6.90 – 6.77 (m, 2H), 6.75 – 6.61 (m, 1H), 5.19 (s, *J* = 8.7 Hz, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$; for the *E/Z* mixture) δ 155.30, 139.91, 138.93, 137.05, 136.59, 136.58, 136.38, 131.71, 131.20, 129.73, 129.05, 128.73, 128.58, 128.09, 128.06, 127.92, 127.85, 127.75, 127.53, 127.26, 127.03, 126.99, 126.87, 123.21, 119.23, 114.54, 113.96, 112.37, 112.05, 70.95, 70.88.

IR (cm^{-1}): 3024.3, 1588.2, 1561.4, 1494.5, 1446.0, 1425.9, 1378.1, 1289.7, 1267.4, 1054.9, 1026.8, 906.2, 772.9, 729.0, 691.5. **HRMS**: Calculated for $C_{21}H_{18}BrO^+$ ($[M + H^=]^+$): 365.0536 Found: 365.0532.

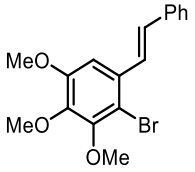
(*E*)-4-(benzyloxy)-1-bromo-2-styrylbenzene (A14): General olefination procedure **A** was followed employing 5-(benzyloxy)-2-bromobenzaldehyde[9] (2.84 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 1.04 g (67%) of **A14** as a white solid. **^{1}H** NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.4 Hz, 2H), 7.50 – 7.25 (m, 11H), 6.99 (d, *J* = 16.2 Hz, 1H), 6.78 (dd, *J* = 8.8, 3.0 Hz, 1H), 5.10 (s, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 158.40, 138.13, 137.12, 136.77, 133.82, 131.80, 128.96, 128.89, 128.38, 128.36, 127.74, 127.66, 127.09, 116.00, 115.41, 113.22, 70.57. **IR** (cm^{-1}): 1584.4, 1474.5, 1461.8, 1405.5, 1380.9, 12229.4, 1206.6, 1173.6, 1115.9, 1003.5, 955.8, 833.6, 823.0, 771.8, 739.7, 695.2, 657.9. **HRMS**: Calculated for $C_{21}H_{18}BrO^+$ ($[M + H^=]^+$): 365.0536 Found: 365.0532.



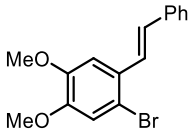
(*E*)-2-bromo-1,5-dimethoxy-3-styrylbenzene (A15): General olefination procedure **A** was followed employing 2-bromo-3,5-dimethoxybenzaldehyde[10] (3.60 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 1.15 g (64%) of **A15** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.60-7.51 (m, 3H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.32 – 7.27 (m,1H), 7.02 (d, *J* = 16.1 Hz, 1H), 6.82 (d, *J* = 2.7 Hz, 1H), 6.45 (d, *J* = 2.6 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 159.81, 157.09, 138.93, 137.15, 131.84, 128.94, 128.31, 128.19, 127.08, 105.34, 102.89, 99.29, 56.59, 55.81. **IR** (cm^{-1}): 1580.5, 1446.0, 1414.7, 1349.9, 1282.6, 1204.5, 1165.4, 1070.5, 1019.7, 955.5, 822.8, 801.9, 750.1, 702.0, 688.7, 604.6. **HRMS**: Calculated for $C_{16}H_{16}BrO_2^+$: 319.0328 Found: 319.0332.



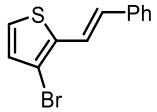
(*E*)-3-bromo-2-styrylbenzo[b]thiophene (A16): General olefination procedure **A** was followed employing 3-bromobenzo[b]thiophene-2-carbaldehyde (1.74 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 212 mg (67%) of **A16** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.9 Hz, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 2H), 7.51 (d, *J* = 16.1 Hz, 1H), 7.45 – 7.35 (m, 4H), 7.32 (t, *J* = 7.3 Hz, 1H), 7.10 (d, *J* = 16.1 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 139.04, 137.45, 136.69, 136.58, 132.91, 129.05, 128.72, 127.08, 126.23, 125.46, 123.25, 122.50, 120.81, 108.77. **IR** (cm^{-1}): 3023.3, 1488.7, 1430.0, 1318.0, 1295.4, 1253.9, 942.8, 921.8, 746.8, 721.8, 687.6. **HRMS**: Calculated for $C_{21}H_{18}BrO^+$ ($[M]^+$): 313.9765 Found: 313.9760.



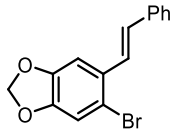
(*E*)-2-bromo-3,4,5-trimethoxy-1-styrylbenzene (A17): General olefination procedure **A** was followed employing 2-bromo-3,4,5-trimethoxybenzaldehyde[11] (3.64 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 1.27 g (51%) of **A17** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.6 Hz, 2H), 7.47 (d, *J* = 16.1 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.01 (s, 1H), 6.94 (d, *J* = 16.1 Hz, 1H), 3.94 (s, 3H), 3.92 (s, 6H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 153.03, 151.20, 143.13, 137.20, 133.06, 130.94, 128.96, 128.22, 127.91, 126.97, 111.38, 105.45, 61.44, 61.17, 56.44. **IR** (cm^{-1}): 1479.0, 1447.6, 1422.3, 1388.8, 1345.6, 1238.2, 1207.8, 1166.3, 1104.4, 1050.5, 1005.8, 987.7, 957.8, 927.8, 862.4, 816.4, 752.4, 694.9. **HRMS**: Calculated for $C_{17}H_{18}BrO_3^+$: 349.0434 Found: 349.0437.



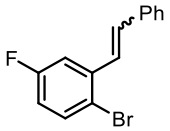
(*E*)-1-bromo-4,5-dimethoxy-2-styrylbenzene (A18): General olefination procedure **A** was followed employing 2-bromo-4,5-dimethoxybenzaldehyde (2.09 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 601 mg (90%) of **A18** as a white solid. Spectroscopic data matched reported literature data.[12] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.5 Hz, 2H), 7.38 (m, 3H), 7.29 (d, *J* = 7.2 Hz, 1H), 7.16 (s, 1H), 7.05 (s, 1H), 6.93 (d, *J* = 16.2 Hz, 1H), 3.95 (s, 3H), 3.90 (s, 3H).



(*E*)-3-bromo-2-styrylthiophene (A19): General olefination procedure **A** was followed (3.85 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 652 mg (64%) of **A19** as a pale yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 6.0 Hz, 1H), 7.17 (d, *J* = 5.3 Hz, 1H), 6.99 (d, *J* = 4.3 Hz, 1H), 6.97 (d, *J* = 6.5 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 137.43, 136.84, 131.01, 130.51, 128.98, 128.30, 126.80, 124.13, 120.31, 111.13. **IR** (cm^{-1}): 3103.2, 3023.1, 1504.2, 1487.7, 1429.8, 1146.7, 952.6, 882.9, 838.1, 751.3, 707.3, 688.2. **HRMS**: Calculated for $C_{12}H_9BrS^+$ ($[M]^+$): 263.9603 Found: 263.9608.

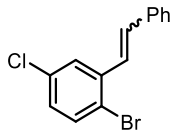


(*E*)-5-bromo-6-styrylbenzo[d][1,3]dioxole (A20): General olefination procedure **A** was followed employing 6-bromobenzo[d][1,3]dioxole-5-carbaldehyde (2.95 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 728 mg (82%) of **A20** as a white solid. Spectroscopic data matched reported literature data .[13] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.5 Hz, 2H), 7.38 (m, 2H), 7.31 – 7.24 (m, 2H), 7.15 (s, 1H), 7.04 (s, 1H), 6.89 (d, *J* = 16.1 Hz, 1H), 6.00 (s, 2H).



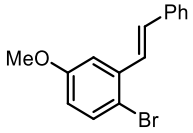
1-bromo-4-fluoro-2-styrylbenzene (A21): General olefination procedure **A** was followed employing 2-bromo-5-fluorobenzaldehyde (2.4 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 365 mg (55%) of **A21** as an inseparable mixture of alkene isomers (6.25:1) as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$; for major *E* isomer) δ 77.61 (d, *J* = 2.4 Hz, 1H), 77.53 (d, *J* = 7.6 Hz, 2H), 77.48 (d, *J* = 8.5 Hz, 1H), 77.36 (dd, *J* =

15.3, 7.1 Hz, 3H), 77.29 (t, *J* = 7.3 Hz, 1H), 77.07 (dd, *J* = 8.6, 2.5 Hz, 1H), 77.01 (d, *J* = 16.2 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$ for major *E* isomer) δ 162.11 (d, *J*= 245.0), 138.7 (d, J= 8.7), 136.51, 134.17 (d, *J*= 8.7), 132.54, 128.79 128.43, 126.96, 126.57 (d, *J*= 2.5), 115.95 (d, *J*= 23.0), 113.24 (*J*= 23.5). **IR** (cm^{-1}): 3024.0, 1599.1, 1571.3, 1457.9, 1410.0, 1255.6, 1159.6, 1027.7, 956.7, 746.6, 695.5, 596.0. **HRMS**: Calculated for $C_{14}H_{10}BrF^+$ ($[M]^+$): 275.9950 Found: 275.9949.

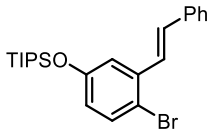


2-bromo-4-chloro-1-styrylbenzene (A22): General olefination procedure **A** was followed employing 2-bromo-4-chlorobenzaldehyde (2.39 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 357 mg (52%) as an inseparable mixture of alkene isomers (3.86:1) of **A22** as clear crystals. **^{1}H NMR** (500 MHz, $CDCl_3$; for the mixture of isomers) δ 7.64 (d, *J* = 2.4 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 2.05H), 7.53 – 7.48 (m, 1.11H), 7.38 (m, 3.08H), 7.32 (t, *J* = 7.3 Hz, 1.07H), 7.26 – 7.19 (m, 0.79H), 7.14 (m, 0.75H), 7.11 – 7.08 (m, 1.11H), 7.04 (d, *J* = 16.2 Hz, 1.28H), 6.72 (d, *J* = 12.1 Hz, 0.31H), 6.53 (d, *J* = 12.1 Hz, 0.31H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 136.93, 135.98, 133.78, 132.82, 132.17, 129.01, 128.53, 128.09, 127.50, 127.09, 126.51, 124.35. **IR** (cm^{-1}): 3058.2, 1600.4, 1495.6, 1412.0, 1319.7, 1277.8, 1249.3, 1151.6, 1107.4, 1078.1, 1221.3, 954.4, 922.2, 822.2, 751.6, 709.9, 684.1. **HRMS**: Calculated for $C_{14}H_{10}BrCl^+$ ($[M]^+$): 291.9654 found: 291.9659.

1-bromo-2-styryl-4-(trifluoromethyl)benzene (A23): General olefination procedure **A** was followed employing 2-bromo-5-(trifluoromethyl)benzaldehyde (2.39 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 249 mg (32%) of **A23** as an inseparable mixture of alkene isomers (6.25:1) as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$; for major *E* isomer) δ 7.89 (s, 1H), 7.73 – 7.69 (m, 1H), 7.58 (d, *J* = 7.5 Hz, 2H), 7.45 (d, *J* = 16.2 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.37 – 7.31 (m, 2H), 7.14 – 7.09 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$; for major *E* isomer) δ 138.01, 136.37, 133.65, 133.16, 130.15 (q, *J*= 33.7), 128.83, 128.60, 127.01, 126.11, 124.95 (q, *J*= 3.7), 123.38 (q, *J*= 3.7). **IR** (cm^{-1}): 3058.2, 1631.2, 1600.4, 1495.6, 1412.0, 1319.7, 1277.8, 1249.3, 1151.6, 1107.4, 954.4, 751.6. **HRMS**: Calculated for $C_{15}H_{10}BrF_3^+$ ($[M]^+$): 325.9918 found: 325.9925

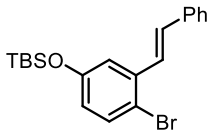


(*E*)-1-bromo-4-methoxy-2-styrylbenzene (A24): General olefination procedure **A** was followed employing 2-bromo-5-methoxybenzaldehyde (2.39 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 549 mg (80%) of **A24** as a white solid. Spectroscopic data matched reported literature data.[14] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.7 Hz, 2H), 7.49 – 7.36 (m, 4H), 7.30 (t, *J* = 7.3 Hz, 1H), 7.20 (d, *J* = 2.9 Hz, 1H), 7.02 (d, *J* = 16.2 Hz, 1H), 6.72 (dd, *J* = 8.8, 2.9 Hz, 1H), 3.85 (s, 3H

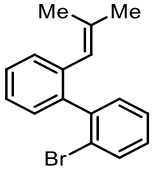


(*E*)-(4-bromo-3-styrylphenoxy)triisopropylsilane (A25): To a 50 mL round bottom flask equipped with a magnetic stir bar were added 2-bromo-5-hydroxy-benzaldehyde (500 mg, 2.49 mmol) and DMF (20 mL) at room temperature. To this reaction mixture was added imidazole (423 mg, 6.22 mmol) and triisopropylsilyl chloride (575 mg, 2.98 mmol). After 3 h, water was added and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (1 × 10 mL), dried over $MgSO_4$ and concentrated under reduced pressure to yield the crude 2-bromo-5-((triisopropylsilyl)oxy)benzaldehyde (844 mg). The aldehyde was used without further purification.

General olefination procedure **A** was followed employing 2-bromo-5-((triisopropylsilyl)oxy)benzaldehyde (1.69 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 325 mg (45%) of **A25** as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.6 Hz, 2H), 7.44 – 7.36 (m, 4H), 7.30 (t, *J* = 7.3 Hz, 1H), 7.20 (d, *J* = 2.8 Hz, 1H), 6.97 (d, *J* = 16.2 Hz, 1H), 6.69 (dd, *J* = 8.7, 2.8 Hz, 1H), 1.35 – 1.24 (m, 3H), 1.14 (d, *J* = 7.4 Hz, 18H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.79, 138.05, 137.17, 133.71, 131.45, 128.93, 128.28, 127.80, 127.07, 120.96, 118.05, 115.44, 18.15, 12.88. **IR** (cm^{-1}): 2942.9, 2865.3, 1586.6, 1461.3, 1403.9, 1291.0, 1173.6, 994.6, 958.6, 880.8, 826.4, 750.6, 720.2, 686.0, 434.1. **HRMS**: Calculated for $C_{23}H_{31}BrOSi^+$ ($[M]^+$): 430.1328 found: 430.1326.

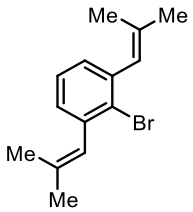


(*E*)-(4-bromo-3-styrylphenoxy)(tert-butyl)dimethylsilane (A26): General olefination procedure A was followed employing 2-bromo-5-((tert-butyldimethylsilyl)oxy)benzaldehyde[15] (1.90 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 385 mg (52%) of **A26** as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.6 Hz, 2H), 7.40 (m, 4H), 7.29 (t, *J* = 7.3 Hz, 1H), 7.13 (s, *J* = 2.1 Hz, 1H), 6.97 (d, *J* = 16.2 Hz, 1H), 6.64 (d, *J* = 8.6 Hz, 1H), 1.01 (s, 9H), 0.23 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.40, 138.18, 137.17, 133.77, 131.57, 128.94, 128.30, 127.74, 127.08, 121.21, 118.34, 115.87, 25.91, 18.46, -4.15. **IR** (cm^{-1}): 2927.6, 2856.0, 1586.6, 1560.2, 1461.7, 1289.8, 1253.2, 1172.3, 993.4, 958.5, 860.6, 836.0, 779.8, 750.1. **HRMS**: Calculated for $C_{20}H_{25}BrOSi^+$ ($[M]^+$): 388.0858 found: 388.0864.

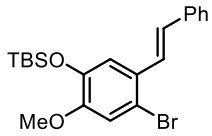


2-bromo-2'-(2-methylprop-1-en-1-yl)-1,1'-biphenyl (A27): General olefination procedure **A** was followed employing 2'-bromo-[1,1'-biphenyl]-2-carbaldehyde[16] (2.68 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 414 mg (54%) of **A27** as a clear oil **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.38 – 7.27 (m, 5H), 7.23

– 7.11 (m, 3H), 5.87 (s, 1H), 1.75 (s, *J* = 0.6 Hz, 3H), 1.71 (s, *J* = 1.0 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 142.42, 140.54, 137.34, 135.61, 132.46, 131.37, 129.63, 129.53, 128.46, 127.35, 126.81, 125.80, 123.82, 123.80, 26.20, 19.42. **IR** (cm^{-1}): 2907.1, 1462.9, 1440.1, 1375.1, 1223.9, 1003.6, 827.6, 748.1, 699.7, 661.6, 617.1. **HRMS**: Calculated for $C_{16}H_{15}Br^+$ ($[M]^+$): 286.0357 found: 286.0359



2-bromo-1,3-bis(2-methylprop-1-en-1-yl)benzene (A28): General olefination procedure **B** was followed employing 2-bromoisophthalaldehyde (0.8 mmol) and isopropyltriphenylphosphonium iodide (2.2 equiv) Purification by flash column chromatography eluting with hexanes/EtOAc provided 157 mg (74%) of **A28** as a clear oil **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 – 7.16 (m, 1H), 7.07 (d, *J* = 7.6 Hz, 2H), 6.27 (s, 2H), 1.93 (s, *J* = 1.4 Hz, 6H), 1.74 (s, *J* = 1.3 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.01, 135.89, 128.76, 126.21, 125.86, 125.56, 26.07, 19.34. **IR** (cm^{-1}): 2922.0, 1977.4, 1494.8, 1375.9, 1184.6, 1020.9, 905.1, 727.0. **HRMS**: Calculated for $C_{14}H_{17}Br^+$ ($[M]^+$): 264.0514 found: 264.0512.

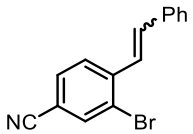


(*E*)-(4-bromo-2-methoxy-5-styrylphenoxy)(tert-butyl)dimethylsilane (A29): To a 100 mL round bottom flask equipped with a magnetic stir bar were added 2-bromo-5-hydroxy-4-methoxy-benzaldehyde (1500 mg, 6.49 mmol) and DCM (40 mL) at room temperature. To this reaction mixture was added imidazole (884 mg, 13.0 mmol) and TBSCl (1468 mg, 9.74 mmol). After 5 h, water was added and the mixture was extracted with DCM (3 × 20 mL). The combined organic layers were washed with brine (1 × 20 mL), dried over $MgSO_4$ and concentrated under reduced pressure to yield the crude 2-bromo-5-[tert-butyl(dimethyl)silyl]oxy-4-methoxy-benzaldehyde. Purification by flash column chromatography eluting with hexanes/EtOAc provided 1592 mg (71%) of 2-bromo-5-[tert-butyl(dimethyl)silyl]oxy-4-methoxy-benzaldehyde as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.15 (s, 1H), 7.39 (s, 1H), 7.04 (s, 1H), 3.89 (s, 3H), 0.99 (s, 9H), 0.16 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 190.96, 156.94, 145.20, 126.98, 120.71, 120.62, 116.24, 56.16, 25.81, 18.62, -4.42. **IR** (cm^{-1}): 2929.0, 2856.3, 1683.2, 1587.6, 1498.5, 1438.0, 1275.7, 1251.6, 1213.8, 1155.4, 1026.3, 855.0, 836.4, 780.8. **HRMS**: Calculated for $C_{14}H_{21}O_3BrSi^+$ ($[M + H^+]^+$): 345.0516 found: 345.0516.

(*E*)-(4-bromo-2-methoxy-5-styrylphenoxy)(tert-butyl)dimethylsilane was prepared according to general olefination procedure **A** employing 2-bromo-5-[tert-butyl(dimethyl)silyl]oxy-4-methoxy-benzaldehyde (4.05 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 1100 mg (65%) of **A29** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.6 Hz, 2H), 7.36 (m, 3H), 7.28 – 7.24 (m, 1H), 7.16 (s, 1H), 7.03 (s, 1H), 6.86 (d, *J* = 16.1 Hz, 1H), 3.82 (s, 3H), 1.02 (s, 9H), 0.18 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 151.51, 144.87, 137.50, 129.77, 129.59, 128.88, 127.88, 127.34, 126.83, 118.49, 116.25, 115.77, 55.88, 25.94, 18.70, -4.37. **IR** (cm^{-1}): 2955.1, 2925.7, 2853.4, 1592.7, 1499.9, 1436.4, 1389.1, 1272.9,

1249.7, 1167.8, 1032.4, 956.6, 862.4, 832.1, 783.1, 794.3. **HRMS**: Calculated for $C_{21}H_{27}O_2BrSi^+$ ($[M]^+$): 418.0964 found: 418.0955.

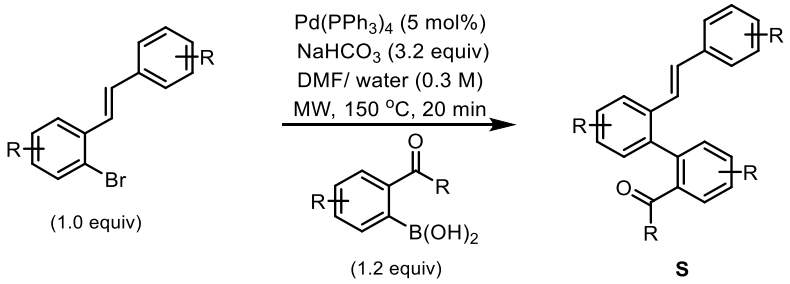
2-bromo-4-nitro-1-styrylbenzene (A30): General olefination procedure **B** was followed employing 2-bromo-4-nitrobenzaldehyde (2.17 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 485 mg (73%) as an inseparable mixture of alkene isomers (2.0:1.0) of **A30** as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$; for *E*/*Z* mixture) δ 8.50 (m, 1.12H), 8.19 (dd, *J* = 8.7, 2.2 Hz, 0.33H), 7.94 (dd, *J* = 8.6, 2.2 Hz, 0.91H), 7.84 (d, *J* = 8.7 Hz, 0.36H), 7.61 (d, *J* = 7.3 Hz, 0.78H), 7.50 (d, *J* = 16.2 Hz, 0.50H), 7.44 (t, *J* = 7.4 Hz, 0.73H), 7.38 (t, *J* = 7.3 Hz, 0.39H), 7.33 (d, *J* = 8.6 Hz, 0.95H), 7.26 – 7.21 (m, 3.30H), 7.13 (m, 1.92H), 6.89 (d, *J* = 12.1 Hz, 1H), 6.63 (d, *J* = 12.1 Hz, 0.96H).**^{13}C NMR** (125 MHz, cdcl$_3$; for *E*/*Z* mixture) δ 147.16, 146.96, 145.13, 143.77, 136.20, 135.81, 135.55, 134.54, 131.56, 129.45, 129.16, 128.73, 128.67, 128.36, 128.23, 127.90, 127.54, 126.83, 125.66, 124.36, 123.90, 122.76, 122.12.**IR** (cm^{-1}): 3022.7, 2853.5, 1625.9, 1579.7, 1515.1, 1492.4, 1339.5, 1265.9, 1113.9, 1035.8, 892.4, 863.2, 771.0, 726.5, 695.4. **HRMS**: Calculated for $C_{14}H_{10}BrNO_2^+$ ($[M]^+$): 302.9895 found: 302.9898.



3-bromo-4-styrylbenzonitrile (A31): General olefination procedure **A** was followed employing 3-bromo-4-formylbenzonitrile[17] (3.33 mmol). Purification by flash column chromatography afforded 200 mg (21% yield) of an *E/Z* mixture (1.5:1.0) of the title compound as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$, for *E/Z* mixture) δ 7.93 (d, *J* = 1.6 Hz, 1.5H), 7.72 (d, *J* = 8.3 Hz, 0.8H), 7.71 (d, *J* = 8.3 Hz, 1.5H), 7.57 (d, *J* = 7.5 Hz, 3.2H), 7.41 (t, *J* = 6.7 Hz, 25H), 7.39 – 7.32 (m, 4.7H), 7.24 – 7.20 (m, 2.6H), 7.11 – 7.06 (m,3.4H), 6.81 (d, *J* = 12.0 Hz, 1H), 6.54 (d, *J* = 12.1 Hz, 1H). **^{13}C NMR** (176 MHz, $CDCl_3$, for *E/Z* mixture) δ 139.77, 138.93, 136.26, 135.37, 134.35, 134.30, 134.09, 134.00, 133.71, 131.55, 131.23, 130.23, 129.67, 129.14, 129.08, 129.06, 128.99, 128.73, 128.31, 127.45, 127.29, 125.50, 118.30, 118.11, 112.06, 111.39. **IR** (cm^{-1}): 2229.4, 1467.2, 1222.9, 1156.4, 818.0, 754.5, 688.0, 607.3. **HRMS**: calculated for $C_{15}H_{10}BrN^+$ ($[M^+]$): 282.9997 Found: 282.9986.

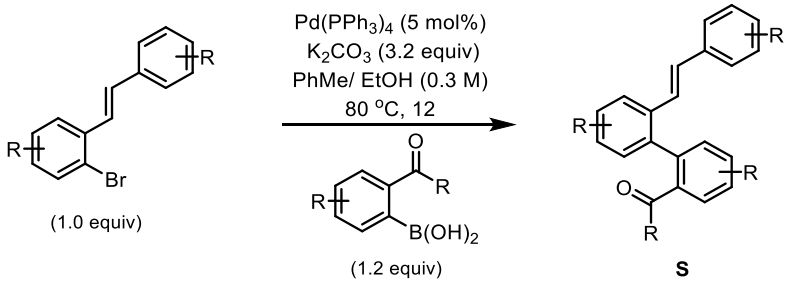
b. Synthesis of biaryl metathesis substrates

General cross-coupling procedure A for metathesis substrates (S):

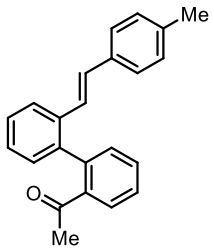


Procedure adopted from van der Eycken et al.[18] To a Chemglass microwave vial equipped with a magnetic stir bar were added 2-bromo-aryl styrene (1.0 equiv), $NaHCO_3$ (3.2 equiv), aryl boronic acid (1.2 equiv), and $Pd(PPh_3)_4$ (5 mol%). A solution of DMF/ water (0.3 M; 1:1) was then added and the vial sealed. The vial was heated under microwave irradiation (150 °C, 20 min) at atmospheric pressure. After the reaction was allowed to cool to room temperature, it was diluted with ethyl acetate (n mL) and washed with water (3 × n mL) and brine (1 × n mL). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified *via* flash column chromatography eluting with a mixture of hexanes and ethyl acetate to give the pure coupled product (**S**).

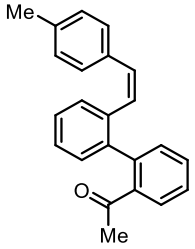
General cross-coupling procedure B for metathesis substrates (S):



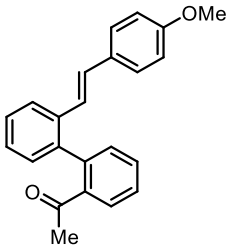
To a Chemglass reaction tube equipped with a magnetic stir bar were added aryl bromide (1.0 equiv), K_sCO_3 (3.2 equiv), aryl boronic acid (1.2 equiv), and $Pd(PPh_3)_4$ (5 mol%). A solution of toluene/ ethanol (0.3 M; 1:1) was then added and the vial sealed. The reaction was heated to 80 °C for 12 h. After the reaction was allowed to cool to room temperature, it was diluted with ethyl acetate (15 mL) and washed with water (3 × n mL) and brine (1 × n mL). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified *via* flash column chromatography eluting with a mixture of hexanes and ethyl acetate to give the pure cross coupled product (**S**).



(*E*)-1-(2'-(4-methylstyryl)-[1,1'-biphenyl]-2-yl)ethan-1-one (12): Prepared according to general cross coupling procedure **A** between ***E*-A2** (0.55 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 109 mg (64% yield) of **12** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.7 Hz, 1H), 7.71 (d, *J* = 6.9 Hz, 1H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.20 (t, *J* = 8.7 Hz, 3H), 7.09 (d, *J* = 7.6 Hz, 2H), 7.00 (d, *J* = 16.2 Hz, 1H), 6.83 (d, *J* = 16.2 Hz, 1H), 2.32 (s, 3H), 2.00 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.93, 141.08, 140.03, 139.88, 137.88, 136.00, 134.73, 131.72, 131.03, 130.62, 130.52, 129.57, 128.48, 128.44, 127.82, 127.59, 126.72, 125.72, 125.65, 29.94, 21.47. **HRMS**: calculated for $C_{23}H_{20}ONa^+$ ([M + Na^+]$^+$): 335.1406 Found 335.1404.

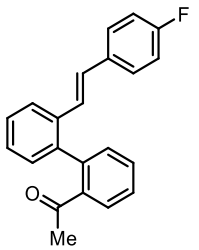


(*Z*)-1-(2'-(4-methylstyryl)-[1,1'-biphenyl]-2-yl)ethan-1-one (13): Prepared according to general cross coupling procedure **A** between ***Z*-A2** (0.40 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 61 mg (49% yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.6 Hz, 1H), 7.48 – 7.38 (m, 2H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.27 (s, *J* = 4.7 Hz, 2H), 7.23 – 7.15 (m, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.41 (d, *J* = 12.3 Hz, 1H), 6.16 (d, *J* = 12.2 Hz, 1H), 2.31 (s, 3H), 2.12 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.84, 140.64, 140.14, 137.31, 136.08, 133.99, 131.54, 130.95, 130.88, 130.21, 129.70, 129.55, 129.12, 128.98, 128.44, 128.12, 127.64, 127.60, 126.70, 29.66, 21.47. **IR** (cm^{-1}): 3059.2, 3015.0, 2922.2, 1688.6, 1594.0, 1509.1, 1437.4, 1354.1, 1267.7, 1246.3, 908.5, 822.9, 761.0, 729.6. **HRMS**: calculated for $C_{23}H_{20}ONa^+$ ([M + Na^+]$^+$): 335.1406 Found 335.1404.

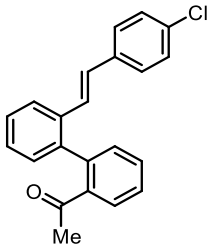


(*E*)-1-(2'-(4-methoxystyryl)-[1,1'-biphenyl]-2-yl)ethan-1-one (14): Prepared according to general cross coupling procedure **A** between **A4** (0.52 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 123 mg (72%

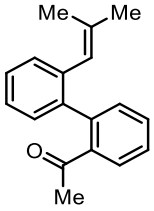
yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.9 Hz, 1H), 7.70 (d, *J* = 7.7 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.32 – 7.27 (m, 2H), 7.27 – 7.23 (m, 2H), 7.19 (d, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 16.2 Hz, 1H), 6.83 (d, *J* = 8.6 Hz, 2H), 6.74 (d, *J* = 16.2 Hz, 1H), 3.79 (s, 3H), 1.99 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.99, 159.58, 141.10, 139.92, 139.87, 136.11, 131.68, 131.03, 130.49, 130.33, 130.16, 128.47, 128.41, 128.02, 127.79, 127.40, 125.45, 124.55, 114.30, 55.51, 29.93. **HRMS**: calculated for $C_{23}H_{24}O_2N^+$ ([M + NH_4^+]$^+$): 346.1802 Found 346.1801.



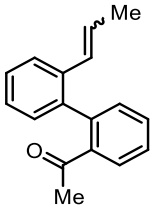
(*E*)-1-(2'-(4-fluorostyryl)-[1,1'-biphenyl]-2-yl)ethan-1-one (15): Prepared according to general cross coupling procedure **A** between **A5** (0.54 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 121 mg (71% yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.9 Hz, 1H), 7.71 (d, *J* = 7.7 Hz, 1H), 7.54 (t, *J* = 7.3 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.35 – 7.30 (m, 2H), 7.29 – 7.24 (m, 3H), 7.21 (d, *J* = 7.5 Hz, 1H), 6.99 – 6.95 (m, 2H), 6.77 (d, *J* = 16.2 Hz, 1H), 1.99 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.63, 162.33 (d, *J*= 247.4), 140.85, 139.91, 139.48, 135.47, 133.43 (d, *J*= 3.2), 131.39, 130.86, 130.24, 129.17, 128.28, 128.22, 128.08, 128.02, 127.63 (d, *J*= 11.0), 126.21 (d, *J*= 2.0), 125.36, 115.64, 115.47, 29.66. **IR** (cm^{-1}): 3053.1, 1673.7, 1596.6, 1509.1, 1463.6, 1270.8, 1229.4, 1158.9, 973.8, 823.9, 759.7. **HRMS**: calculated for $C_{22}H_{17}OFNa^+$ ([M + Na^+]$^+$): 339.1161 Found 339.1159.



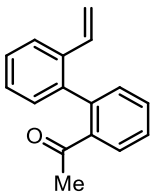
(*E*)-1-(2'-(4-chlorostyryl)-[1,1'-biphenyl]-2-yl)ethan-1-one (16): Prepared according to general cross coupling procedure **A** between **A3** (0.34 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 53 mg (47% yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.8 Hz, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.54 (t, *J* = 6.9 Hz, 1H), 7.48 (t, *J* = 7.0 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.33 (m, 3H), 7.24 – 7.20 (m, 4H), 6.96 (d, *J* = 16.2 Hz, 1H), 6.82 (d, *J* = 16.2 Hz, 1H), 2.00 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.79, 141.07, 140.27, 139.64, 135.98, 135.54, 133.51, 131.64, 131.11, 130.49, 129.31, 129.01, 128.53, 128.47, 128.01, 127.96, 127.93, 127.30, 125.68, 29.89. **IR** (cm^{-1}): 3054.0, 2249.2, 1683.6, 1491.5, 1354.4, 1245.4, 1088.2, 905.7, 812.3, 726.2, 430.0. **HRMS**: calculated for $C_{22}H_{21}OClN^+$ ([M + NH_4^+]$^+$): 350.1306 Found 350.1305.



1-(2'-(2-methylprop-1-en-1-yl)-[1,1'-biphenyl]-2-yl)ethan-1-one (17): Prepared according to general cross coupling procedure **B** between **A6** (2.15 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 335 mg (62% yield) of the title compound as a clear oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.7 Hz, 1H), 7.51 – 7.46 (m, 1H), 7.39 (td, *J* = 7.6, 1.1 Hz, 1H), 7.37 – 7.33 (m, 1H), 7.31 – 7.26 (m, 2H), 7.26 – 7.21 (m, 2H), 5.79 (s, 1H), 1.97 (s, 3H), 1.75 (s, 3H), 1.72 (s, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 202.47, 140.81, 140.60, 140.55, 137.19, 136.43, 131.33, 130.91, 130.12, 129.81, 128.13, 127.64, 127.44, 126.71, 124.44, 29.56, 26.46, 19.37. **IR** (cm^{-1}): 2972.3, 2907.9, 1682.9, 1593.5, 1436.2, 1375.8, 1351.9, 1263.1, 1243.9, 1233.4, 952.9, 830.8, 750.2, 593.4. **HRMS**: calculated for $C_{18}H_{18}ONa^+$ ($[M + Na^+]^+$): 250.1358 Found 250.1354.

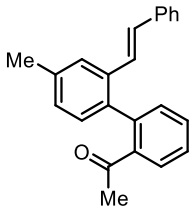


1-(2'-(prop-1-en-1-yl)-[1,1'-biphenyl]-2-yl)ethan-1-one (18): Prepared according to general cross coupling procedure **A** between **A7** (0.76 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 105 mg (58% yield) of the title compound as a clear oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.68 (dd, *J* = 10.1, 5.0 Hz, 1H), 7.65 (dd, *J* = 7.7, 1.2 Hz, 0.5H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.51 (td, *J* = 7.4, 1.2 Hz, 1H), 7.50 – 7.47 (m, 0.5H), 7.43 (td, *J* = 7.6, 1.2 Hz, 1H), 7.41 (td, *J* = 7.6, 1.2 Hz, 0.5H), 7.39 – 7.36 (m, 1H), 7.34 (td, *J* = 7.7, 1.3 Hz, 1H), 7.32 – 7.29 (m, 0.5H), 7.28 – 7.22 (m, 3H), 7.14 (dd, *J* = 7.6, 1.1 Hz, 1H), 6.18 – 6.10 (m, 2H), 6.05 (dd, *J* = 11.5, 1.8 Hz, 0.5H), 5.67 (dq, *J* = 11.6, 7.1 Hz, 0.5H), 1.98 (s, 1.5H), 1.95 (s, 3H), 1.80 (dd, *J* = 7.1, 1.8 Hz, 3H), 1.75 (d, *J* = 4.8 Hz, 6H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 203.18, 202.85, 141.04, 140.79, 140.77, 140.43, 140.22, 139.20, 136.60, 136.00, 131.58, 131.39, 131.06, 131.01, 130.30, 130.04, 129.88, 129.09, 129.02, 128.45, 128.41, 128.34, 128.09, 127.95, 127.72, 127.71, 127.68, 127.21, 127.07, 125.76, 29.94, 29.78, 18.97, 14.58. **IR (cm^{-1}):** 3018.0, 2362.3, 1681.9, 1593.2, 1468.3, 1435.6, 1352.5, 1263.7, 1232.9, 964.2, 749.8, 593.8. **HRMS**: calculated for $C_{17}H_{17}O^+$ ($[M + H^+]^+$): 237.1274 Found 237.1278.

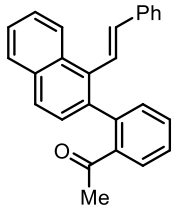


1-(2'-vinyl-[1,1'-biphenyl]-2-yl)ethan-1-one (19): Prepared according to general cross coupling procedure **A** between **A8** (0.82 mmol) and 2-acetylphenylboronic acid. Purification by flash

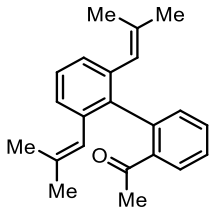
column chromatography eluting with hexanes/EtOAc afforded 42 mg (23% yield) of the title compound as a clear oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.51 (td, *J* = 7.5, 1.3 Hz, 1H), 7.44 (tt, *J* = 7.7, 3.9 Hz, 1H), 7.39 (dt, *J* = 7.5, 3.6 Hz, 1H), 7.31 (td, *J* = 7.5, 1.1 Hz, 1H), 7.29 – 7.25 (m, 1H), 7.17 (dd, *J* = 7.6, 1.2 Hz, 1H), 6.49 (dd, *J* = 17.5, 11.0 Hz, 1H), 5.68 (dd, *J* = 17.4, 0.7 Hz, 1H), 5.17 (dd, *J* = 11.0, 0.8 Hz, 1H), 1.97 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 203.03, 140.89, 139.89, 139.78, 136.22, 134.93, 131.51, 131.00, 130.24, 128.43, 128.42, 127.93, 127.80, 125.60, 115.90, 29.90. **IR** (cm^{-1}): 3067.3, 2251.0, 1683.6, 1417.3, 1355.0, 1268.8, 1245.3, 907.4, 762.7, 726.7, 647.7, 459.0. **HRMS**: calculated for $C_{25}H_{28}ON^+$ ($[M + H^+]^+$): 223.1117 Found 223.1121.



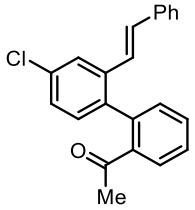
(*E*)-1-(4'-methyl-2'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one (S2): Prepared according to general cross coupling procedure **A** between **A10** (0.55 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 155 mg (90% yield) of the title compound as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.7 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.30 (m, 5H), 7.25 – 7.17 (m, 2H), 7.03 – 6.95 (m, 2H), 6.86 (d, *J* = 16.2 Hz, 1H), 2.38 (s, 3H), 2.00 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.83, 140.81, 139.85, 139.69, 137.45, 137.41, 132.77, 131.44, 130.89, 130.76, 129.45, 129.11, 128.57, 128.16, 127.53, 127.49, 126.44, 126.34, 125.37, 29.73, 21.13. **IR** (cm^{-1}): 3021.1, 1680.3, 1594.6, 1353.5, 1266.4, 965.7, 812.8, 757.2, 730.6, 690.3, 595.0. **HRMS**: calculated for $C_{23}H_{24}ON^+$ ($[M + NH_4^+]^+$): 330.1852 Found 300.1856.



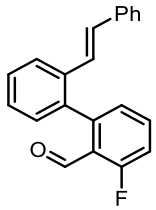
(*E*)-1-(2-(1-styrylnaphthalen-2-yl)phenyl)ethan-1-one (S3): Prepared according to general cross coupling procedure **B** between **A12** (0.97 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 154 mg (46% yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.37 – 8.29 (m, 1H), 7.94 – 7.89 (m, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 7.7 Hz, 1H), 7.56 – 7.49 (m, 3H), 7.40 (m, 3H), 7.34 – 7.29 (m, 4H), 7.28 – 7.22 (m, 1H), 7.17 (d, *J* = 16.6 Hz, 1H), 6.60 (d, *J* = 16.6 Hz, 1H), 2.06 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.30, 141.22, 140.55, 137.62, 137.51, 136.82, 133.57, 133.54, 131.97, 131.88, 131.12, 128.84, 128.67, 128.50, 128.07, 127.99, 127.67, 127.53, 126.75, 126.55, 126.22, 126.04, 125.42, 29.75. **IR** (cm^{-1}): 3054.7, 1682.3, 1594.2, 1484.5, 1354.1, 1264.2, 1247.5, 969.2, 820.1, 732.6, 692.8, 597.0. **HRMS**: calculated for $C_{26}H_{24}ON^+$ ($[M + NH_4^+]^+$): 366.1852 Found 366.1857.



1-(2',6'-bis(2-methylprop-1-en-1-yl)-[1,1'-biphenyl]-2-yl)ethan-1-one (S4): Prepared according to general cross coupling procedure **B** between **A28** (0.97 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 154 mg (46% yield) of the title compound as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.7 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 2H), 7.07 (d, *J* = 7.5 Hz, 1H), 5.67 (s, 2H), 1.93 (s, 3H), 1.75 (s, 6H), 1.66 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.37, 140.38, 139.87, 139.59, 137.34, 135.38, 131.61, 130.91, 128.32, 128.19, 127.23, 126.82, 124.97, 29.13, 26.40, 19.41. **IR** (cm^{-1}): 2970.5, 2913.6, 2853.1, 1682.7, 1441.3, 1419.9, 1375.2, 1351.8, 1278.0, 1246.7, 847.0, 758.0, 730.9. **HRMS**: calculated for $C_{22}H_{28}ON^+$ ($[M + NH_4^+]^+$): 322.2165 Found 322.2165

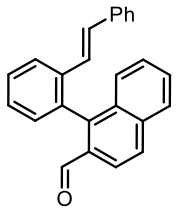


(*E*)-1-(4'-chloro-2'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one (S5): Prepared according to general cross coupling procedure **A** between **A22** (0.51 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 132 mg (78% yield) of the title compound as clear crystals. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.72 (m, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.28 (m, 6H), 7.23 (m, 1H), 7.13 (d, *J* = 8.2 Hz, 1H), 7.02 (d, *J* = 16.2 Hz, 1H), 6.77 (d, *J* = 16.2 Hz, 1H), 2.09 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.21, 140.74, 138.71, 138.65, 137.52, 136.99, 134.38, 131.80, 131.70, 131.58, 131.27, 128.90, 128.62, 128.30, 128.19, 127.65, 126.91, 125.58, 125.47, 29.87. **IR** (cm^{-1}): 1687.6, 1595.8, 1468.8, 1354.6, 1264.0, 1094.4, 964.3, 909.7, 823.0, 731.0, 702.6, 595.2. **HRMS**: calculated for $C_{22}H_{21}OClN^+$ ($[M + NH_4^+]^+$): 350.1306 Found 350.1311

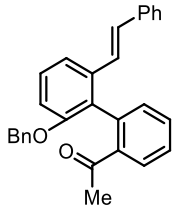


(*E*)-3-fluoro-2'-styryl-[1,1'-biphenyl]-2-carbaldehyde (S6): Prepared according to general cross coupling procedure **A** between 2-bromo-6-fluorobenzaldehyde (0.74 mmol) and (*E*)-(2-styrylphenyl)boronic acid.. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 153 mg (69% yield) of the title compound as a pale yellow oil.**^{1}H NMR** (700 MHz, $CDCl_3$) δ 9.91 (s, 1H), 7.63 – 7.59 (m, 1H), 7.47 (ddd, *J* = 8.0, 7.5, 0.8 Hz, 1H), 7.35

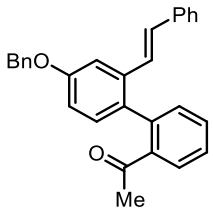
(td, *J* = 7.5, 1.1 Hz, 1H), 7.32 – 7.27 (m, 4H), 7.25 – 7.20 (m, 3H), 7.17 – 7.14 (m, 1H), 7.04 (d, *J* = 16.2 Hz, 1H), 6.78 (d, *J* = 16.2 Hz, 1H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 188.90, 162.45 (d, *J*= 263.5), 145.63, 137.01, 136.36 (d, J= 2.1), 136.20, 134.54 (d, *J*= 10.3), 131.09, 130.49, 128.78, 128.64, 127.90, 127.41 (d, *J*= 3.6), 127.35, 126.61, 125.94, 125.53, 123.17 (d, *J*= 6.8), 116.19 (d, *J*= 21.3). **IR** (cm^{-1}): 3023.3, 2851.2, 1696.2, 1603.6, 1238.7, 1189.8, 962.0, 913.9, 798.5, 756.5, 735.3, 689.6. **HRMS**: calculated for $C_{21}H_{15}OFNa^+$ ([M + Na^+]$^+$): 325.0999 Found 325.1003.



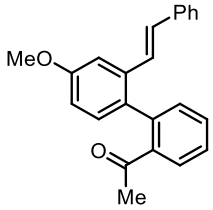
(*E*)-1-(2-styrylphenyl)-2-naphthaldehyde (S7): Prepared according to general cross coupling procedure **B** between 1-bromo-2-naphthaldehyde (1.28 mmol) and (*E*)-(2-styrylphenyl)boronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 322 mg (75% yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.82 (s, 1H), 8.10 (d, *J* = 8.6 Hz, 1H), 7.97 (m, 2H), 7.91 (d, *J* = 7.9 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.55 (m, 2H), 7.43 (dd, *J* = 18.1, 7.6 Hz, 2H), 7.30 (d, *J* = 7.5 Hz, 1H), 7.18 – 7.12 (m, 2H), 7.08 (d, *J* = 7.4 Hz, 2H), 7.03 (d, *J* = 16.2 Hz, 1H), 6.51 (d, *J* = 16.2 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 192.53, 145.19, 137.52, 136.83, 136.12, 134.09, 132.46, 131.70, 131.57, 130.80, 128.95, 128.91, 128.63, 128.46, 128.28, 127.76, 127.66, 127.24, 127.12, 126.52, 125.83, 125.20, 122.09. **IR** (cm^{-1}): 3057.1, 1688.0, 1594.3, 1493.6, 1429.1, 1379.3, 1330.2, 1264.0, 1239.8, 961.8, 821.6, 732.1, 691.0. **HRMS**: calculated for $C_{25}H_{22}ON^+$ ([M + NH_4^+]$^+$): 357.1250 Found 357.1256.



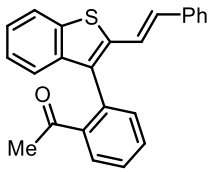
(*E*)-1-(2'-(benzyloxy)-6'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one (S8): Prepared according to general cross coupling procedure **A** between **A13** (0..41 mmol) and 2-acetylphenylboronic acid.. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 62 mg (37% yield) of the title compound as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.7 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 7.9 Hz, 1H), 7.33 (t, *J* = 7.8 Hz, 1H), 7.30 – 7.17 (m, 9H), 7.12 (d, *J* = 7.3 Hz, 2H), 7.00 (dd, *J* = 16.2, 1.8 Hz, 1H), 6.91 (d, *J* = 8.1 Hz, 1H), 6.76 (dd, *J* = 16.2, 2.3 Hz, 1H), 5.00 (s, 2H), 2.09 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.55, 155.74, 140.78, 137.50, 137.41, 137.27, 135.83, 132.53, 131.23, 130.54, 130.28, 128.93, 128.77, 128.53, 128.43, 127.81, 127.71, 127.68, 126.95, 126.76, 118.52, 111.87, 70.46, 29.19. **IR** (cm^{-1}): 3024.3, 1683.0, 1596.4, 1569.1, 1451.0, 1263.4, 1057.4, 960.0, 786.9, 731.8, 692.0, 599.2. **HRMS**: calculated for $C_{29}H_{28}O_2N^+$ ([M + NH_4^+]$^+$): 422.2115 Found 422.2119.



(*E*)-1-(4'-(benzyloxy)-2'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one (S9): Prepared according to general cross coupling procedure **A** between **A14** (2 x 211 mg, 0.58 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 63 mg (combined) (13% yield) of the title compound as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.6 Hz, 1H), 7.60 – 7.19 (m, 14H), 7.12 (d, *J* = 8.4 Hz, 1H), 7.04 – 6.91 (m, 2H), 6.86 (d, *J* = 16.2 Hz, 1H), 5.17 (s, 2H), 2.00 (s, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 203.32, 159.01, 141.42, 139.40, 137.33, 137.04, 136.99, 133.10, 131.98, 131.71, 130.95, 130.87, 128.87, 128.85, 128.38, 128.34, 128.02, 127.86, 127.67, 126.83, 126.62, 114.39, 111.83, 70.43, 30.02. **IR** (cm^{-1}): 1681.8, 1597.4, 1499.5, 1466.1, 1279.0, 1229.9, 1026.4, 996.6, 963.0, 756.3, 728.6. **HRMS**: calculated for $C_{29}H_{28}O_2N^+$ ([M + NH_4^+]$^+$): 422.2115 Found: 422.2118.

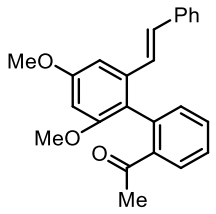


(*E*)-1-(4'-methoxy-2'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one (S10): Prepared according to general cross coupling procedure **A** between **A24** (150 mg, 0.52 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 128 mg (75% yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.7 Hz, 1H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.35 – 7.27 (m, 6H), 7.22 (t, *J* = 6.9 Hz, 1H), 7.12 (d, *J* = 8.4 Hz, 1H), 7.01 (d, *J* = 7.8 Hz, 1H), 6.89 (dd, *J* = 15.6, 9.4 Hz, 2H), 3.91 (s, 3H), 2.00 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 203.34, 159.79, 141.43, 139.45, 137.35, 136.97, 132.86, 132.01, 131.71, 130.94, 130.80, 128.86, 128.37, 128.01, 127.65, 126.84, 126.72, 113.70, 110.69, 55.62, 30.02. **IR** (cm^{-1}): 2833.2, 1683.7, 1603.1, 1473.8, 1281.5, 1243.7, 1212.0, 1165.8, 1048.1, 971.0, 882.9, 809.2, 758.3, 728.1, 695.7, 596.6. **HRMS**: calculated for $C_{23}H_{24}O_2N^+$ ([M + NH_4^+]$^+$): 346.1802 Found 346.1807..

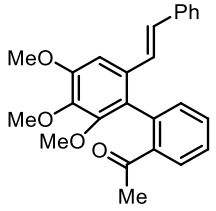


(*E*)-1-(2-(2-styrylbenzo[b]thiophen-3-yl)phenyl)ethan-1-one (S11): Prepared according to general cross coupling procedure **A** between **A16** (100 mg, 0.32 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 98 mg (87% yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.8

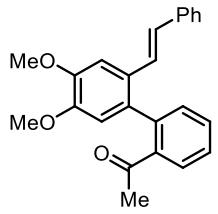
Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 7.1 Hz, 3H), 7.31 (m, 4H), 7.23 (d, *J* = 7.3 Hz, 1H), 7.05 (d, *J* = 16.0 Hz, 1H), 6.98 (d, *J* = 16.0 Hz, 1H), 1.97 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 202.64, 141.91, 140.73, 139.81, 138.00, 136.70, 134.49, 133.42, 132.37, 132.10, 131.68, 129.05, 128.92, 128.69, 128.41, 126.93, 125.70, 125.17, 122.93, 122.50, 120.61, 29.36. **IR (cm^{-1}):** 1681.9, 1351.9, 1431.0, 1351.9, 1273.8, 1236.3, 948.9, 765.0, 752.0, 732.4, 689.5, 472.2. **HRMS**: calculated for $C_{24}H_{22}ONS^+$ ([M + NH_4^+]$^+$): 372.1417 Found 372.1422.



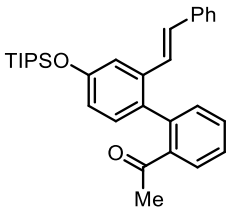
(*E*)-1-(2',4'-dimethoxy-6'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one (S12): Prepared according to General Cross Coupling Procedure A between **A15** (185 mg, 0.58 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 103 mg (50% yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.6 Hz, 1H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.27 (s, 1H), 7.23 – 7.14 (m, 2H), 6.99 (d, *J* = 16.2 Hz, 1H), 6.91 (d, *J* = 2.0 Hz, 1H), 6.75 (d, *J* = 16.2 Hz, 1H), 6.48 (d, *J* = 2.0 Hz, 1H), 3.93 (s, 3H), 3.69 (s, 3H), 2.10 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 202.20, 160.57, 157.84, 141.48, 137.76, 137.39, 135.32, 133.00, 131.06, 130.53, 128.81, 128.19, 127.91, 127.59, 127.18, 126.81, 122.48, 101.52, 98.34, 55.82, 55.64, 29.22. **IR** (cm^{-1}): 1683.8, 1597.2, 1575.8, 1456.8, 1349.1, 1276.5, 1245.3, 1199.6, 1154.4, 1079.2, 1059.3, 960.3, 757.4, 736.8, 691.7. **HRMS**: calculated for $C_{24}H_{23}O_3^+$ ([M + H^+]$^+$): 359.1642 Found: 359.1650.



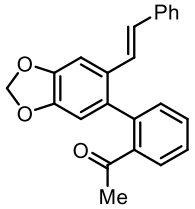
(*E*)-1-(2',3',4'-trimethoxy-6'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one (S13): Prepared according to General cross coupling procedure **A** between **A17** (150 mg, 0.43 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 70 mg (42% yield) of the title compound as a white solid. **^{1}H NMR** (700 MHz, $CDCll_3$) δ 7.78 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.53 (td, *J* = 7.5, 1.3 Hz, 1H), 7.47 (td, *J* = 7.6, 1.1 Hz, 1H), 7.30 – 7.23 (m, 5H), 7.20 (td, *J* = 5.8, 3.0 Hz, 1H), 7.05 (s, 1H), 6.89 (d, *J* = 16.1 Hz, 1H), 6.69 (d, *J* = 16.2 Hz, 1H), 3.99 (s, 3H), 3.92 (s, 3H), 3.57 (s, 3H), 2.18 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.69, 153.45, 151.06, 142.23, 140.99, 137.45, 135.28, 132.74, 131.59, 131.03, 129.58, 128.82, 128.44, 127.78, 127.74, 126.94, 126.66, 104.29, 61.27, 60.74, 56.24, 29.22. **IR** (cm^{-1}): 1687.8, 1591.3, 1475.8, 1400.5, 1345.5, 1235.2, 1094.3, 1003.1, 960.0, 753.0, 693.9. **HRMS**: calculated for $C_{25}H_{22}O_4Na$ ([M + Na^+]$^+$): 411.1567 Found: 411.1572.



(*E*)-1-(4',5'-dimethoxy-2'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one (S14): Prepared according to general cross coupling procedure **A** between **A18** (150 mg, 0.47 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 121 mg (72% yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.4 Hz, 1H), 7.54 – 7.51 (m, 1H), 7.46 (t, *J* = 7.2 Hz, 1H), 7.35 – 7.24 (m, 6H), 7.20 (t, *J* = 6.9 Hz, 1H), 6.93 (d, *J* = 16.2 Hz, 1H), 6.85 (d, *J* = 16.2 Hz, 1H), 6.69 (d, *J* = 2.7 Hz, 1H), 4.02 (s, 3H), 3.87 (s, 3H), 2.01 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 203.49, 149.24, 148.95, 141.52, 139.36, 137.62, 132.94, 131.90, 130.92, 128.84, 128.65, 128.39, 128.32, 127.83, 127.67, 126.58, 126.47, 113.30, 108.02, 56.28, 56.23, 30.00. **IR** (cm^{-1}): 3010.6, 1692.2, 1513.4, 1470.9, 1239.2, 1207.5, 1140.6, 1023.1, 947.6, 879.2, 831.6, 763.9, 751.9, 695.2. **HRMS**: calculated for $C_{24}H_{26}O_3N^+$ ($[M + NH_4^+]^+$): 376.1807 Found 376.1899.

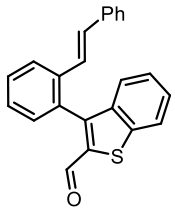


(*E*)-1-(2'-styryl-4'-((triisopropylsilyl)oxy)-[1,1'-biphenyl]-2-yl)ethan-1-one (S15): Prepared according to general cross coupling procedure **A** between **A25** (150 mg, 0.34 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 97 mg (59% yield) of the title compound as a clear oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.7 Hz, 1H), 7.49 (t, *J* = 7.4, 1H), 7.42 (t, *J* = 7.5, 1H), 7.35 – 7.23 (m, 7H), 7.20 (m, 1H), 7.03 (d, *J* = 8.3 Hz, 1H), 6.99 – 6.91 (m, 1H), 6.88 – 6.81 (m, 2H), 1.92 (s, 3H), 1.37 – 1.23 (m, 3H), 1.14 (d, *J* = 7.3 Hz, 18H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 203.70, 156.47, 141.60, 139.47, 137.35, 136.96, 134.03, 133.84, 133.07, 131.89, 131.73, 130.86, 130.56, 128.90, 128.83, 128.72, 128.65, 128.35, 127.97, 127.62, 126.84, 126.66, 119.66, 116.79, 30.02, 18.18, 12.93. **IR (**cm^{-1}): 2943.9, 2866.2, 1682.0, 1596.9, 1467.2, 1282.1, 1212.1, 994.9, 906.3, 881.8, 728.5, 689.4. **HRMS:** calculated for $C_{31}H_{42}O_2NSi^+$ ($[M + NH_4^+]^+$): 488.2979 Found 488.2983.

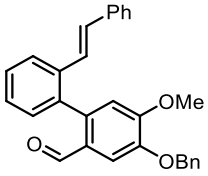


(*E*)-1-(2-(6-styrylbenzo[d][1,3]dioxol-5-yl)phenyl)ethan-1-one (S16): Prepared according to general cross coupling procedure **A** between **A20** (200 mg, 0.66 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 72 mg (32% yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.71 (d, *J* =

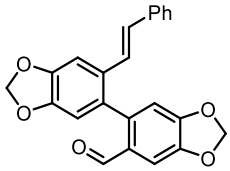
7.6 Hz, 1H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.29 (m, 6H), 7.25 – 7.16 (m, 1H), 6.90 (d, *J* = 16.1 Hz, 1H), 6.77 (d, *J* = 16.2 Hz, 1H), 6.70 (s, 1H), 6.06 (s, 2H), 2.10 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.84, 148.24, 147.49, 141.27, 139.46, 137.54, 134.34, 131.88, 131.09, 130.02, 128.84, 128.82, 128.40, 127.89, 127.69, 126.60, 126.38, 110.33, 105.16, 101.66, 29.95. **IR** (cm^{-1}): 2889.6, 1681.7, 1474.4, 1234.7, 1206.7, 1037.8, 966.7, 935.8, 756.0, 725.0, 696.4, 590.7. **HRMS**: calculated for $C_{23}H_{22}O_3N^+$ ($[M + NH_4^+]^+$): 360.1594 Found 360.1598



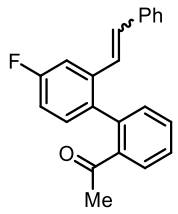
(E)-3-(2-styrylphenyl)benzo[b]thiophene-2-carbaldehyde (S17): Prepared according to general cross coupling procedure **B** between 3-bromobenzothiophene-2-carbaldehyde (1.24 mmol) and (*E*)-(2-styrylphenyl)boronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 285 mg (67% yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.97 (d, *J* = 8.2 Hz, 1H), 7.92 (d, *J* = 7.9 Hz, 1H), 7.60 – 7.50 (m, 3H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.38 (dd, *J* = 14.9, 7.6 Hz, 2H), 7.24 – 7.16 (m, 5H), 7.10 (d, *J* = 16.2 Hz, 1H), 6.78 (d, *J* = 16.2 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 185.95, 146.65, 141.94, 139.92, 139.72, 137.58, 137.02, 131.74, 131.36, 131.31, 129.67, 128.80, 128.68, 128.14, 127.70, 126.80, 126.00, 125.95, 125.93, 125.53, 123.49. **IR** (cm^{-1}): 3025.1, 1661.9, 1520.2, 1346.8, 1264.3, 1208.4, 1168.7, 961.8, 905.7, 761.2, 726.7, 689.8, 664.2, 611.2. **HRMS**: calculated for $C_{23}H_{16}OSNa^+$ ($[M + Na^+]^+$): 363.0814 Found 363.0819.



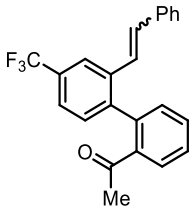
(*E*)-4-(benzyloxy)-5-methoxy-2'-styryl-[1,1'-biphenyl]-2-carbaldehyde (S18): Prepared according to general cross coupling procedure **B** between 5-(benzyloxy)-2-bromo-4-methoxybenzaldehyde[19] (300 mg, 0.93 mmol) and (*E*)-(2-styrylphenyl)boronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 162 mg (41% yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.59 (s, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.63 (s, 1H), 7.52 (d, *J* = 7.4 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 2H), 7.28 (m, 4H), 7.24 – 7.19 (m, 1H), 7.04 (d, *J* = 16.2 Hz, 1H), 6.82 (m, 2H), 5.33 – 5.11 (m, 2H), 3.91 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 190.98, 154.12, 148.24, 140.21, 137.29, 137.07, 136.61, 136.53, 131.45, 130.92, 128.87, 128.79, 128.37, 128.06, 127.89, 127.84, 127.40, 126.80, 126.55, 125.56, 113.77, 110.51, 71.12, 56.52. **IR** (cm^{-1}): 1671.5, 1588.0, 1506.0, 1346.7, 1277.6, 1236.2, 1134.6, 1013.9, 756.1, 746.0, 736.1, 691.6. **HRMS**: calculated for $C_{29}H_{28}O_3N^+$ ($[M + NH_4^+]^+$): 438.2064 Found 438.2067.



(*E*)-6'-styryl-[5,5'-bibenzo[d][1,3]dioxole]-6-carbaldehyde (S19): Prepared according to general cross coupling procedure **A** between **A20** (150 mg, 0.50 mmol) and (6-formylbenzo[d][1,3]dioxol-5-yl)boronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 98 mg (53% yield) of the title compound as a white powder. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.57 (s, 1H), 7.47 – 7.46 (s, 1H), 7.31 – 7.17 (m, 6H), 6.90 (d, *J* = 16.1 Hz, 2H), 6.76 – 6.65 (m, 3H), 6.12 (d, *J* = 15.4 Hz, 2H), 6.05 (s, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 190.53, 152.37, 148.54, 148.22, 147.32, 141.84, 137.35, 131.37, 130.54, 130.00, 129.35, 128.82, 127.86, 126.69, 126.10, 111.21, 110.98, 106.21, 105.00, 102.40, 101.78. **IR** (cm^{-1}): 2848.0, 1681.7, 1609.3, 1497.5, 1473.2, 1421.6, 1346.5, 1243.8, 1208.0, 1036.4, 928.0, 874.1, 756.2, 691.9. **HRMS**: calculated for $C_{23}H_{16}O_5Na^+$ ([M + Na^+]$^+$): 395.0890 Found 395.0894.

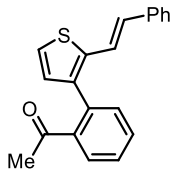


1-(4'-fluoro-2'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one (S20): Prepared according to general cross coupling procedure **A** between **A21** (150 mg, 0..54 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 81 mg (48% yield) as an *E/Z* mixture (3.33:1) of the title compound as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$; for major *E* isomer) δ 7.72 (d, *J* = 7.6 Hz, 1H), 7.54 (m,1H), 7.47 (m, 2H), 7.33 – 7.26 (m, 4H), 7.26 – 7.20 (m, 2H), 7.16 (m, 2H), 7.02 (m, 2H), 6.81 (d, *J* = 16.2 Hz, 1H), 2.06 (s, *J* = 4.4 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$; for major *E* isomer) δ 202.51, 162.93 (d, *J*= 245.0), 141.05, 138.82, 137.91 (d, *J*=7.5), 136.99, 132.02, 131.95, 131.88, 131.72, 131.19, 128.92, 128.56, 128.32, 128.09, 126.94, 125.75, 114.76 (d, *J*= 21.2), 112.06 (d, *J*= 22.5) 29.91. **IR (**cm^{-1}): 3056.2, 1685.7, 1602.9, 1578.3, 1498.3, 1468.4, 1354.0, 1264.4, 1196.4, 1158.5, 961.6, 757.3, 731.2. **HRMS**: calculated for $C_{22}H_{21}OFN^+$ ([M + NH_4^+]$^+$): 334.1632 Found 334.1604.

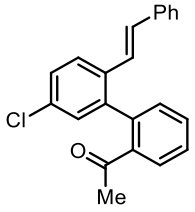


1-(2'-styryl-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)ethan-1-one (S21): Prepared according to general cross coupling procedure **A** between **A23** (200 mg, 0.66 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 72 mg (32% yield) as an *E/Z* mixture (3.33:1.0) of the title compound as a white solid. **^{1}H NMR (**700 MHz, $CDCl_3$; for *E/Z* mixture) δ 7.99 (s, 1H), 7.78 (dt, *J* = 10.1, 0.96H), 7.76 – 7.72 (m, 0.28H),

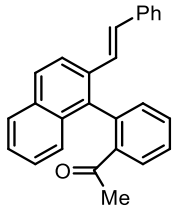
7.61 – 7.56 (m, 1.89H), 7.55 – 7.51 (m, 1.45H), 7.51 – 7.44 (m, 0.60H), 7.32 (m, 5.89H), 7.27 – 7.16 (m, 2.62H), 7.07 (d, *J* = 16.2 Hz, 1H), 6.82 (d, *J* = 16.2 Hz, 0.30H), 6.51 (d, *J* = 12.2 Hz, 0.28H), 6.15 (d, *J* = 12.2 Hz, 1H), 2.32 (s, 0.79H), 2.17 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$, for *E* isomer) δ 201.21, 143.60, 139.97, 138.54, 136.69, 136.36, 131.99, 131.32, 131.29, 130.41, 128.70, 128.57, 128.24, 128.16, 126.70, 125.26, 124.15 (q, *J*= 271.2 Hz), 123.83 (q, *J*= 8.6 Hz), 122.29 (q, *J*= 3.7 Hz), 29.36. **IR** (cm^{-1}): 3057.9, 2360.1, 1687.7, 1324.3, 1244.8, 1160.8, 1112.2, 1081.7, 968.0, 771.7, 757.1, 735.8, 692.2. **HRMS**: calculated for $C_{23}H_{21}OF_3N^+$ ([M + NH_4^+]$^+$): 384.1570 Found 384.1575



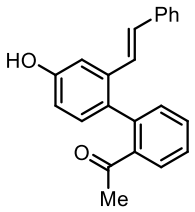
(*E*)-1-(2-(2-styrylthiophen-3-yl)phenyl)ethan-1-one (S22): Prepared according to General cross coupling procedure **A** between **A19** (150 mg, 0.57 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 98 mg (57% yield) of the title compound as a pale yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.7 Hz, 1H), 7.55 (t, *J* = 7.0 Hz, 1H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.35 (d, *J* = 7.9 Hz, 3H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.23 (t, *J* = 6.2 Hz, 2H), 6.97 – 6.92 (m, 3H), 2.08 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 203.72, 141.55, 139.20, 139.11, 136.99, 134.72, 131.45, 131.17, 130.42, 130.03, 128.89, 128.47, 128.14, 128.01, 126.66, 123.87, 120.30, 29.79. **IR** (cm^{-1}): 3102.9, 3026.1, 1670.0, 1593.1, 1443.2, 1350.7, 1279.8, 1268.2, 1233.7, 951.8, 768.2, 733.9, 713.3, 683.9, 665.9. **HRMS**: calculated for $C_{20}H_{17}OS^+$ ([M + H^+]$^+$): 305.0995 Found 305.0992.



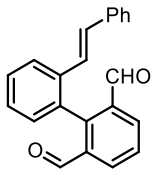
(*E*)-1-(5'-chloro-2'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one (S23): Prepared according to general cross coupling procedure **A** between **A9** (150 mg, 0.51 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 103 mg (63% yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.6 Hz, 1H), 7.69 (d, *J* = 8.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.53 – 7.49 (m, 1H), 7.39 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.33 – 7.26 (m, 5H), 7.26 – 7.19 (m, 2H), 6.99 (d, *J* = 16.2 Hz, 1H), 6.76 (d, *J* = 16.2 Hz, 1H), 2.13 (s, 3H).**^{13}C NMR** (175 MHz, $CDCl_3$) δ 201.75, 141.83, 140.45, 138.58, 137.18, 134.48, 133.28, 131.58, 131.40, 131.09, 129.99, 128.87, 128.68, 128.47, 128.33, 128.11, 126.88, 126.79, 125.57, 29.74. **IR** (cm^{-1}): 3058.2, 1687.1, 1494.8, 1464.8, 1354.1, 1264.1, 1097.0, 963.4, 813.4, 758.6, 731.8, 690.4. **HRMS**: calculated for $C_{22}H_{21}OClN^+$ ([M + NH_4^+]$^+$): 350.1306 Found 350.1308.



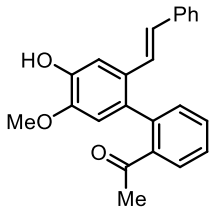
(*E*)-1-(2-(2-styrylnaphthalen-1-yl)phenyl)ethan-1-one (S24): Prepared according to general cross coupling procedure **A** between **A11** (200 mg, 0.65 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 89 mg (40% yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.92 (q, *J* = 8.8 Hz, 3H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.33 – 7.27 (m, 6H), 7.23 – 7.19 (m, 1H), 7.15 (d, *J* = 16.3 Hz, 1H), 6.87 (d, *J* = 16.3 Hz, 1H), 1.85 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 201.67, 141.26, 137.70, 137.51, 137.15, 133.16, 133.06, 132.99, 132.53, 131.69, 130.61, 129.00, 128.84, 128.62, 128.31, 128.23, 127.95, 126.99, 126.95, 126.80, 126.48, 126.17, 122.97, 29.56. **IR** (cm^{-1}): 3056.9, 1680.9, 1594.1, 1353.5, 1273.7, 1244.7, 958.3, 811.2, 760.7, 739.7, 791.1, 596.1. **HRMS**: calculated for $C_{26}H_{24}ON^+$ ($[M + NH_4^+]^+$): 366.1852 Found 366.1857.



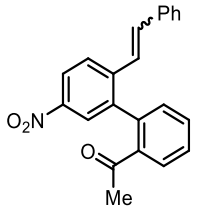
(*E*)-1-(4'-hydroxy-2'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one (S25): Prepared according to general cross coupling procedure **A** between **A26** (150 mg, 0.35mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 71 mg (66% yield) of the title compound as a pale white solid. The *tert*-butyldimethylsilyl ether was cleaved under the reaction conditions. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.1 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.30 (m, 5H), 7.22 (m, 2H), 7.06 (d, *J* = 8.2 Hz, 1H), 6.99 (d, *J* = 16.2 Hz, 1H), 6.84 (d, *J* = 16.2 Hz, 1H), 6.79 (dd, *J* = 8.2, 2.1 Hz, 1H), 5.16 (s, 1H), 2.02 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 203.70, 155.85, 141.39, 139.39, 137.28, 137.24, 132.91, 132.03, 131.90, 131.02, 130.94, 128.87, 128.37, 128.06, 127.69, 126.85, 126.38, 115.20, 112.09, 30.03. **IR** (cm^{-1}): 3207.0, 1679.1, 1572.4, 1475.5, 1305.9, 1213.9, 963.3, 833.6, 773.6, 759.9, 728.2, 696.0. **HRMS**: calculated for $C_{22}H_{22}O_2N^+$ ($[M + NH_4^+]^+$): 332.1645 Found 332.1648.



(*E*)-2'-styryl-[1,1'-biphenyl]-2,6-dicarbaldehyde (S26): Prepared according to general cross coupling procedure **B** between 2-bromoisophthalaldehyde (300 mg, 1.41 mmol) and (*E*)-(2-styrylphenyl)boronic acid 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 89 mg (40% yield) of the title compound as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 9.74 (s, *J* = 0.6 Hz, 1H), 8.30 (d, *J* = 7.7 Hz, 2H), 7.85 (d, *J* = 7.9 Hz, 1H), 7.72 (t, *J* = 7.7 Hz, 1H), 7.55 (td, *J* = 7.8, 0.7 Hz, 1H), 7.41 (td, *J* = 7.5, 1.1 Hz, 1H), 7.30 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.25 (d, *J* = 7.1 Hz, 2H), 7.23 – 7.19 (m, 3H), 7.04 (d, *J* = 16.1 Hz, 1H), 6.61 (d, *J* = 16.1 Hz, 1H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 190.92, 147.16, 137.77, 136.75, 135.15, 132.94, 132.48, 131.69, 131.40, 129.86, 129.00, 128.85, 128.42, 127.65, 126.87, 125.91, 125.34. **IR** (cm^{-1}): 3061.7, 2868.2, 1678.0, 1449.2, 1386.1, 1232.3, 963.8, 921.3, 794.4, 763.0, 746.5, 691.4. **HRMS**: calculated for. $C_{22}H_{20}O_2N^+$ ($[M + NH_4^+]^+$): 330.1489 Found 330.1493.

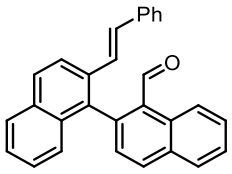


(*E*)-1-(4'-hydroxy-5'-methoxy-2'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one (S27): Prepared according to general cross coupling procedure **A** between **A29** (150 mg, 0.35 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 107 mg (87% yield) of the title compound as a pale white solid. The *tert*-butyldimethylsilyl ether was cleaved under the reaction conditions. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.7 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.36 (s, 1H), 7.32 – 7.26 (m, 5H), 7.19 (t, *J* = 6.9 Hz, 1H), 6.93 (d, *J* = 16.1 Hz, 1H), 6.82 (d, *J* = 16.1 Hz, 1H), 6.65 (s, 1H), 5.66 (s, 1H), 3.87 (s, 3H), 2.01 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 203.75, 146.46, 145.88, 141.59, 139.37, 137.62, 132.30, 131.95, 130.85, 129.18, 129.07, 128.80, 128.25, 127.77, 127.63, 126.62, 126.03, 112.71, 111.31, 56.31, 30.05. **IR** (cm^{-1}): 3535.8, 1677.3, 1594.1, 1509.6, 1278.0, 1238.4, 1141.7, 905.2, 724.1, 647.3. **HRMS**: calculated for $C_{23}H_{20}O_3Na$ ($[M + Na^+]^+$): 367.1305, found: 367.1302.

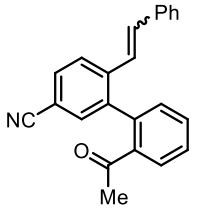


1-(5'-nitro-2'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one (S28): Prepared according to general cross coupling procedure **A** between **A30** (100 mg, 0.33 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 71 mg (63% yield) of the title compound as a pale yellow foam and an *E/Z* mixture (1.62:1.0). **^{1}H NMR** (700 MHz, $CDCl_3$, for *E/Z* mixture) δ 8.23 (dd, *J* = 8.7, 2.2 Hz, 1H), 8.09 (dd, *J* = 12.3, 2.3 Hz, 1.41H), 7.97 (dd, *J* = 8.6, 2.3 Hz, 0.63H), 7.84 (t, *J* = 12.4, 2H), 7.81 – 7.78 (m, 0.61H), 7.61 (tt, *J* = 7.0, 3.5 Hz, 1H), 7.59 – 7.48 (m, 2.36H), 7.40 (d, *J* = 8.6 Hz, 0.72H), 7.34 – 7.17 (m, 9.95H), 7.13 (d, *J* = 16.2 Hz, 1.15H), 6.76 (d, *J* = 16.3 Hz, 1.11H), 6.56 (d, *J* = 12.3 Hz, 0.72H), 6.10 (d, *J* = 12.3

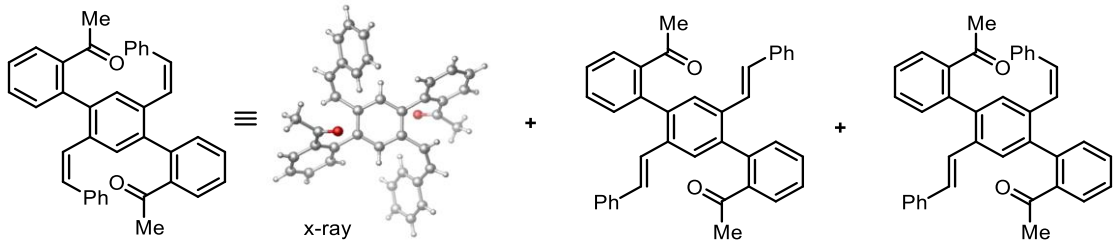
Hz, 0.68H), 2.43 (s, 1.86H), 2.28 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$, for *E/Z* mixture) δ 200.38, 200.34, 146.87, 146.66, 142.95, 142.87, 142.39, 141.78, 139.37, 139.01, 138.46, 138.13, 136.52, 135.92, 134.36, 133.69, 131.97, 131.90, 131.76, 131.46, 130.19, 129.18, 128.99, 128.95, 128.90, 128.82, 128.70, 128.59, 128.23, 127.35, 127.15, 126.04, 124.93, 124.89, 124.66, 123.00, 122.05, 29.26, 28.74. **IR** (cm^{-1}): 2954.2, 1733.9, 1688.2, 1516.9, 1343.4, 1283.6, 1246.5, 1232.9, 1044.2, 943.8, 759.0, 707.5. **HRMS**: Calculated for $C_{22}H_{17}O_3N^+$ ($[M]^+$): 343.1208 found: 343.1205.



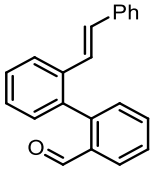
(*E*)-2-styryl-[1,2'-binaphthalene]-1'-carbaldehyde (S29): Prepared according to general cross coupling procedure **A** between 2-bromo-1-naphthaldehyde (150 mg, 0.64 mmol) and (*E*)-(2-styrylnaphthalen-1-yl)boronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 103 mg (42% yield) of **S29** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.95 (s, 1H), 9.40 (d, *J* = 8.6 Hz, 1H), 8.20 (d, *J* = 8.3 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.97 (q, *J* = 8.8 Hz, 2H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.78 – 7.75 (m, 1H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.45 (m, 2H), 7.35 – 7.31 (m, 1H), 7.29 (d, *J* = 6.9 Hz, 1H), 7.23 – 7.15 (m, 7H), 6.83 (d, *J* = 16.2 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 194.59, 146.04, 137.20, 135.00, 134.41, 134.00, 133.81, 133.68, 132.85, 131.32, 130.85, 130.17, 129.75, 129.65, 129.07, 128.87, 128.81, 128.72, 128.30, 128.11, 127.34, 127.29, 126.88, 126.80, 126.59, 126.44, 126.38, 122.87. **IR** (cm^{-1}): 2858.1, 2361.9, 1678.2, 1590.9, 1558.1, 1505.4, 1429.6, 1180.0, 1147.6, 1059.2, 966.5, 817.6, 745.7. **HRMS**: calculated for $C_{29}H_{24}ON^+$ ($[M + NH_4^+]^+$): 402.1852 Found 402.1853.



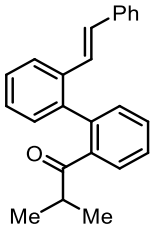
2'-acetyl-6-styryl-[1,1'-biphenyl]-3-carbonitrile (S30): Prepared according to general cross coupling procedure **A** between 3-bromo-4-styrylbenzonitrile (**A31**) (130 mg, 0.46 mmol) and 2-acetylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 79 mg (53% yield) of an *E/Z* mixture (3.0:1.0) of the title compound as a yellow-white solid**. ^{1}H NMR** (500 MHz, $CDCl_3$, for *E/Z* mixture) δ 7.99 (s, 1H), 7.81 – 7.73 (m, 1.3H), 7.63 – 7.45 (m, 4.2H), 7.35 – 7.20 (m, 9.3H), 7.17 (t, *J* = 6.7 Hz, 1H), 7.02 (d, *J* = 16.2 Hz, 1.1H), 6.71 (d, *J* = 16.2 Hz, 1.1H), 6.50 (d, *J* = 12.2 Hz, 0.4H), 6.04 (d, *J* = 12.2 Hz, 0.4H). **^{13}C NMR** (126 MHz, $CDCl_3$, for *E/Z* mixture) δ 200.79, 200.64, 145.15, `139.60, 138.51, 137.16, 136.64, 133.05, 132.84, 131.75, 131.70, 131.36, 131.08, 130.82, 130.78, 130.54, 130.50, 129.38, 129.02, 128.97, 128.83, 128.76, 128.73, 128.60, 128.50, 128.25, 126.97, 126.93, 124.72, 119.01, 112.15, 29.32, 28.80. **IR** (cm^{-1}): 2223.6, 1682.8, 1245.6, 973.0, 894.6, 827.8, 777.6, 756.4, 732.4, 695.7, 606.7. **HRMS**: calculated for $C_{23}H_{18}NO$ ($[M+H^+]^+$): 324.1383 Found: 324.1381.



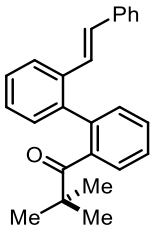
1,1'-(2',5'-distyryl-[1,1':4',1''-terphenyl]-2,2''-diyl)bis(ethan-1-one) (58): Prepared according to general cross coupling procedure **A** between ((2,5-dibromo-1,4-phenylene)bis(ethene-2,1-diyl))dibenzene[20] (100 mg, 0.23 mmol), 2-acetylphenylboronic acid (93 mg, 0.57 mmol), $Pd(PPh_3)_4$ (26 mg, 10 mol%), $NaHCO_3$ (115 mg, 1.36 mmol) and DMF/H_2O (1:1; 0.1 M). Purification by flash column chromatography eluting with hexanes/EtOAc afforded 39 mg (33% yield) of an inseperable *Z/Z', E/E'* and *E/Z'* mixture as a yellow-white solid**.** This isomeric mixture was used in the title reaction without further resolution. **^{1}H NMR** (700 MHz, $CDCl_3$, for *Z/Z', E/E' and E/Z' mixture*) δ 7.79 (d, *J* = 11.2 Hz, 0.49H), 7.73 (m, 1.42H), 7.69 (d, *J* = 7.3 Hz, 0.76H), 7.67 – 7.58 (m, 2.66H), 7.58 – 7.51 (m, 1.03H), 7.50 – 7.33 (m, 7.62H), 7.33 – 7.15 (m, 16.90H), 7.02 (m, 2.76H), 6.94 – 6.87 (m, 0.64H), 6.75 (m, *J* = 19.2 Hz, 0.66H), 6.43 (d, *J* = 12.1 Hz, 1.75H), 6.26 (d, *J* = 12.2 Hz, 0.57H), 6.18 (d, *J* = 12.2 Hz, 1.72H), 2.31 (s, 6H), 2.18 (s, 0.84H), 2.14 (s, 1.24H). **^{13}C NMR** (175 MHz, $CDCl_3$, *Z/Z', E/E'* and *E/Z'* mixture) δ 202.66, 201.67 (broad), 141.22, 140.88, 140.30, 140.15, 139.73 (broad), 139.24, 137.32, 136.96 (broad), 136.83, 135.38, 135.34, 135.30, 135.27 (overlap), 135.23, 135.14, 135.06, 134.91, 132.36, 132.30, 132.01, 131.58 (overlap), 131.51 (overlap), 131.30, 131.22, 131.08, 130.86, 130.72 (overlap), 130.69, 130.47, 129.85, 129.07 (broad), 128.86, 128.81, 128.68, 128.54 (overlap), 128.43 (overlap), 128.30 (overlap), 128.27, 128.24, 128.21, 128.18, 128.15, 128.09, 127.95 (overlap), 127.46 (overlap), 127.28 (overlap), 126.85, 126.80, 125.84, 125.63, 30.13 (broad), 30.01 (overlap), 29.93 (overlap), 29.77. **IR** (cm^{-1}): 3052.7, 1688.1, 1595.2, 1354.2, 1264.0, 963.6, 923.6, 762.3, 732.1, 697.0. **HRMS**: calculated for $C_{38}H_{34}NO_2^+$ ($[M+NH_4^+]^+$): 536.2584 Found: 536.2575.



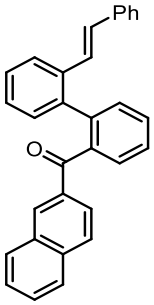
(*E*)-2'-styryl-[1,1'-biphenyl]-2-carbaldehyde (22b): Prepared according to general cross coupling procedure **A** between **A1** (6 x 150 mg) and 2-formylphenylboronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 500 mg (51% yield) of the title compound as a clear oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.08 – 8.06 (m, 1H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.49 – 7.45 (m, 1H), 7.40 – 7.34 (m, 3H), 7.30 – 7.25 (m, 7H), 7.21 (ddd, *J* = 8.6, 5.7, 3.3 Hz, 1H), 7.03 (d, *J* = 16.2 Hz, 1H), 6.78 (d, *J* = 16.2 Hz, 1H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 192.26, 144.81, 137.27, 136.84, 134.55, 133.81, 131.67, 131.27, 131.16, 128.85, 128.83, 128.35, 128.05, 127.53, 127.48, 126.80, 126.47, 125.68. **IR** (cm^{-1}): 1686.9, 1596.6, 1498.7, 1466.8, 1279.2, 1264.8, 1230.4, 1204.8, 1171.3, 999.9, 962.8, 756.4, 729.4, 690.9. **HRMS**: calculated for $C_{21}H_{17}O^+$ ($[M + H^+]^+$): 307.1090 Found: 307.1099.



(*E*)-2-methyl-1-(2'-styryl-[1,1'-biphenyl]-2-yl)propan-1-one (22c): Prepared according to general cross coupling procedure **A** between 1-(2-bromophenyl)-2-methylpropan-1-one[21] (131 mg) and (*E*)-(2-styrylphenyl)boronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 90 mg (48% yield) of the title compound as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.9 Hz, 1H), 7.55 (t, *J* = 14.4 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.36 – 7.27 (m, 6H), 7.22 (t, *J* = 7.2 Hz, 1H), 7.15 (d, *J* = 7.6 Hz, 1H), 7.05 (d, *J* = 16.2 Hz, 1H), 6.94 (d, *J* = 16.2 Hz, 1H), 2.62 – 2.49 (m, 1H), 0.89 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (17 MHz, $CDCl_3$) δ 210.94, 141.27, 139.81, 138.87, 137.59, 135.70, 131.74, 130.79, 130.33, 130.16, 128.83, 128.40, 128.32, 127.87, 127.79, 127.60, 126.90, 126.82, 125.70, 39.72, 19.37, 18.31. **IR** (cm^{-1}): 1735.0, 1685.8, 1594.4, 1495.4, 1465.0, 1379.9, 1212.2, 977.7, 760.3, 734.9, 690.1. **HRMS**: calculated for $C_{24}H_{26}ON^+$ ([M + NH_4^+]$^+$):: 344.2009 Found: 344.2015.



(*E*)-2,2-dimethyl-1-(2'-styryl-[1,1'-biphenyl]-2-yl)propan-1-one (22d): Prepared according to general cross coupling procedure **A** between 1-(2-bromophenyl)-2,2-dimethylpropan-1-one[22] (150 mg) and (*E*)-(2-styrylphenyl)boronic acid.. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 92 mg (43% yield) of the title compound as a white solid. **^{1}H NMR** (401 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.8 Hz, 1H), 7.44 – 7.17 (m, 14H), 7.03 (d, *J* = 8.3 Hz, 2H), 0.93 (s, 9H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 215.51, 142.18, 139.33, 137.73, 136.64, 135.96, 131.95, 131.85, 129.86, 128.84, 128.31, 128.19, 127.78, 127.48, 127.27, 127.11, 126.80, 125.87, 125.62, 44.93, 27.61. **IR** (cm^{-1}): 1683.9, 1235.5, 963.6, 759.1, 690.5. **HRMS**: calculated for $C_{25}H_{28}ON^+$ ([M + NH_4^+]$^+$): 358.2165 Found: 358.2169.

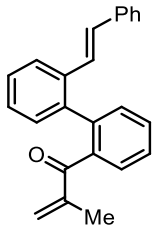


(*E*)-naphthalen-2-yl(2'-styryl-[1,1'-biphenyl]-2-yl)methanone (22f): To a 50 mL round bottom flask equipped with a magnetic stir bar was added a solution of 2-bromonaphthalene (1455 mg, 7.03 mmol) and 20 mL of THF. To this solution was added magnesium shavings (158 mg, 6.49

mmol) and a crystal of I_2. The mixture was allowed to stir at rt for 1 h. Next, the mixture was cooled to 0 ^oC with an ice-bath and at which time 2-bromobenzaldehyde (1000 mg, 5.40 mmol) in a solution of THF (5 mL) was added. The reaction mixture was allowed to sir at 0 ^oC and slowly warmed to rt. When judged complete by TLC analysis, the reaction was quenched with NH_4Cl (aq.) (20 mL) and extracted with Et_2O (3 x 20 mL). The combined organic layers were washed with brine (1 x 20 mL), dried over $MgSO_4$, and concentrated in *vacuo* to yield the crude alcohol (1002 mg). This was used in the next step without further purification.

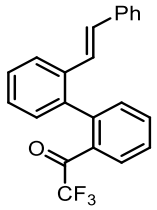
To a 50 mL round bottom flask was added the crude alcohol (1000 mg) and 15 mL of DMSO. Next, IBX (1341 mg, 4.79 mmol) was added to the reaction solution at rt and allowed to stir for 3 h. The reaction was quenched with water (20 mL) and stirred for an addition 1 h. Next the reaction was filtered and extracted with EtOAc (3 x 20 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in *vacuo.* The crude ketone was purified by flash column chromotagraphy with hexanes/EtOAc to afford 756 mg (44% over two steps) of (2-bromophenyl)(naphthalen-2-yl)methanone as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 8.02 (dd, *J* = 8.6, 1.5 Hz, 1H), 7.94 (s, 1H), 7.90 (m, 3H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.50 – 7.34 (m, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 196.08, 141.08, 136.13, 133.75, 133.48, 133.32, 132.64, 131.39, 129.99, 129.30, 129.15, 128.88, 128.08, 127.46, 127.07, 125.00, 119.89. **IR** (cm^{-1}): 3057.8, 1660.1, 1430.1, 1290.7, 1232.9, 1200.2, 1112.4, 919.3, 850.3, 926.8, 778.5, 754.0, 735.5, 689.1. **HRMS**: calculated for $C_{17}H_{11}OBrNa^+$ ([M + Na^+]$^+$): 332.9885 Found 332.9884.

(*E*)-naphthalen-2-yl(2'-styryl-[1,1'-biphenyl]-2-yl)methanone was prepared according to general cross coupling procedure **A** between (2-bromophenyl)(naphthalen-2-yl)methanone (150 mg, 0.48 mmol) and (*E*)-(2-styrylphenyl)boronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 93 mg (47% yield) of **22f** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.77 – 7.71 (m, 2H), 7.68 – 7.60 (m, 3H), 7.58 – 7.43 (m, 5H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.25 (m, 4H), 7.22 – 7.16 (m, 2H), 7.16 – 7.09 (m, 2H), 7.05 (d, *J* = 16.2 Hz, 1H), 6.78 (d, *J* = 16.2 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 197.83, 140.54, 140.08, 139.44, 137.70, 135.70, 135.43, 134.90, 132.48, 132.14, 131.74, 130.82, 130.55, 130.34, 129.71, 129.36, 128.74, 128.38, 128.11, 127.99, 127.77, 127.38, 127.35, 127.32, 126.73, 126.52, 125.58, 125.08. **IR** (cm^{-1}): 3051.7, 1660.8, 1623.2, 1291.7, 1117.7, 964.3, 919.4, 781.2, 759.6, 748.8, 732.0, 695.3. **HRMS**: calculated for $C_{31}H_{23}O^+$ ([M + H^+]$^+$): 411.1743 Found 411.1751.

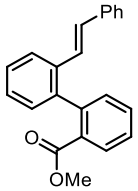


(*E*)-2-methyl-1-(2'-styryl-[1,1'-biphenyl]-2-yl)prop-2-en-1-one (22g): Prepared according to general cross coupling procedure **A** between 1-(2-bromophenyl)-2-methylprop-2-en-1-one (150 mg, 0.66 mmol) and (*E*)-(2-styrylphenyl)boronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 127 mg (59% yield) of the title compound as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.8 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.46 (t, *J* = 7.2 Hz, 1H), 7.37 – 7.28 (m, 6H), 7.24 (q, *J* = 7.6 Hz, 2H), 7.11 (d, *J* = 7.5 Hz, 1H), 7.02

(d, *J* = 16.2 Hz, 1H), 6.93 (d, *J* = 16.2 Hz, 1H), 5.55 (s, 1H), 5.39 (s, 1H), 1.68 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 200.34, 145.28, 140.32, 139.64, 139.62, 137.67, 135.58, 131.53, 130.94, 130.03, 129.70, 128.78, 128.57, 128.08, 127.91, 127.77, 127.35, 127.32, 127.29, 126.73, 125.56, 17.41. **IR** (cm^{-1}): 3055.8, 1657.2, 1494.5, 1435.7, 1327.9, 1264.3, 1196.0, 1015.2, 963.2, 906.2, 760.5, 732.5, 690.4. **HRMS**: calculated for $C_{24}H_{24}ON^+$ ($[M + NH_4^+]^+$): 342.1852 Found 342.1860.

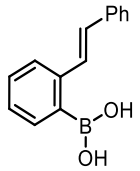


(*E*)-2,2,2-trifluoro-1-(2'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one (22i): Prepared according to general cross coupling procedure **A** between 1-(2-bromophenyl)-2,2,2-trifluoroethan-1-onemethanone (200 mg, 0.79 mmol) and (*E*)-(2-styrylphenyl)boronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 115 mg (41% yield) of the title compound as a clear oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.9 Hz, 1H), 7.73 – 7.64 (m, 2H), 7.54 (td, *J* = 7.7, 1.2 Hz, 1H), 7.45 – 7.37 (m, 2H), 7.32 (td, *J* = 7.5, 1.1 Hz, 1H), 7.29 – 7.23 (m, 4H), 7.23 – 7.18 (m, 1H), 7.15 (dd, *J* = 7.6, 1.0 Hz, 1H), 6.96 (d, *J* = 16.2 Hz, 1H), 6.73 (d, *J* = 16.2 Hz, 1H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 183.12 (q, *J*= 35),142.72, 138.62, 137.17, 135.59, 133.18, 132.44, 131.77, 130.94, 129.61, 128.99, 128.97, 128.50, 128.29, 127.66, 127.58, 127.51, 126.53, 126.19, 125.73, 115.94 (q, *J*= 292). **IR** (cm^{-1}): 3024.4, 1725.4, 1594.7, 1494.9, 1199.5, 1182.5, 1140.8, 962.1, 933.9, 757.8, 736.0, 689.8, 661.0. **HRMS**: calculated for $C_{22}H_{16}OF_3^+$ ($[M + H^+]^+$): 353.1148 Found 353.1149.

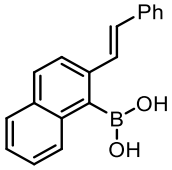


Methyl (*E*)-2'-styryl-[1,1'-biphenyl]-2-carboxylate (22j): Prepared according to general cross coupling procedure **A** between methyl 2-bromobenzoate (6 x 258 mg) and (*E*)-(2-styrylphenyl)boronic acid. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 652 mg (29% yield) of the title compound as a thick clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.96 (d, *J* = 7.8 Hz, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.34 – 7.26 (m, 6H), 7.19 (m, 2H), 7.00 (d, *J* = 16.2 Hz, 1H), 6.81 (d, *J* = 16.2 Hz, 1H), 3.54 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$):δ 168.09, 141.91, 140.83, 137.69, 135.55, 131.89, 131.67, 131.51, 130.12, 129.86, 129.62, 128.75, 127.84, 127.68, 127.63, 127.33, 127.15, 126.72, 125.07, 52.16. **IR** (cm^{-1}): 1727.4, 1596.8, 1430.3, 1250.6, 1124.6, 1082.1, 961.0, 749.1, 7124, 690.1 **HRMS**: calculated for $C_{22}H_{19}O_2^+$($[M + H^+]^+$): 315.1380 Found: 315.1380.

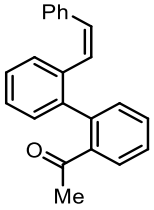
c. Miscellaneous procedures



(*E*)-(2-styrylphenyl)boronic acid: Prepared according to the reported literature procedure:[23] (*E*)-1-bromo-2-styrylbenzene **(A1)** (3.0 g, 11.6 mmol) was dissolved in THF (60 mL) and cooled to -78 °C. Next,. *n*BuLi (2.5 M in hexane, 7.0 mL, 17.4 mmol) was added dropwise and the reaction mixture was stirred for 30 minutes before triisopropoxyborate (4.0 mL, 17.4 mmol) was added slowly. The reaction mixture was allowed to warm to rt with stirring overnight. The reaction mixture was quenched with 1M HCl and allowed to stir for 1 hour before being concentrated by rotary evaporator and extracted with two portions of DCM (3 x 30 mL). The combined organic layers were dried over Na_2SO_4 and concentrated by rotary evaporator. The solid product was dried under high vacuum and used without further purification.

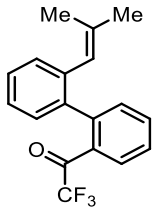


(*E*)-(2-styrylnaphthalen-1-yl)boronic acid: (*E*)-1-bromo-2-styrylnaphthalene **(A11)** (300 mg, 0.97 mmol) was dissolved in THF (9 mL) and cooled to -78 °C. Next, *n*BuLi (2.5 M in hexane, 0.47 mL, 1.07 mmol) was added dropwise and the reaction mixture was stirred for 30 minutes before triisopropoxyborate (0.34 mL, 1.46 mmol) was added slowly. The reaction mixture was allowed to warm to rt with stirring overnight. The reaction mixture was quenched with 1M HCl and allowed to stir for 1 hour before being concentrated by rotary evaporator and extracted with two portions of DCM (3 x 5 mL). The combined organic layers were dried over Na_2SO_4 and concentrated by rotary evaporator. The orange semi-solid product was dried under high vacuum and used without further purification.

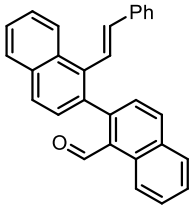


(*Z*)-1-(2'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one (8): General olefination procedure **B** was followed employing 2'acetyl-[1,1'-biphenyl]-2-carbaldehyde[26] (9.37 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc provided 1485 mg (53%) of **8** and its alkene isomer (E:Z; 2.2:1) as a clear oil. Recrystallization from hexanes afforded exclusively the *Z* alkene (**8**). Spectroscopic data for *E/Z* mixture prior to recrystallization: **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.9 Hz, 1H), 7.71 (d, *J* = 7.7 Hz, 1H), 7.65 (d, *J* = 7.5 Hz, 0.5H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.45 – 7.39 (m, 1.5H), 7.30 (m, 9.5H), 7.23 – 7.15 (m, 4H), 7.02 (d, *J* = 16.2 Hz, 1H), 6.88 (d, *J* = 16.2 Hz, 1H), 6.45 (d, *J* = 12.2 Hz, 0.5H), 6.22 (d, *J* = 12.2 Hz, 0.5H), 2.14 (d, *J* = 0.5 Hz, 1.5H), 2.00 (d, *J* = 0.4 Hz, 3H).**^{13}C NMR** (175 MHz, $CDCl_3$) δ 202.88, 202.75, 141.04, 140.61, 140.17, 140.10, 139.79, 137.47, 136.94, 135.87, 135.80, 131.69, 131.53, 131.04, 130.91, 130.64, 130.52, 130.22, 129.71, 129.24, 129.21, 129.05, 128.84, 128.75, 128.49, 128.46, 128.41, 128.15, 127.92, 127.87, 127.77, 127.70, 127.65, 127.45, 126.79, 126.68, 125.71, 29.93, 29.66. **IR** (cm^{-1}): 1684.6, 1593.5, 1494.4, 1467.9, 1453.8, 1352.4, 1244.0, 1073.6, 1003.7,

962.2, 757.2, 732.5, 690.4. Spectroscopic data for **8**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 6.7 Hz, 1H), 7.43 (pd, *J* = 7.4, 1.6 Hz, 2H), 7.32 (dd, *J* = 10.3, 4.3 Hz, 1H), 7.29 – 7.14 (m, 9H), 6.45 (d, *J* = 12.3 Hz, 1H), 6.22 (d, *J* = 12.3 Hz, 1H), 2.14 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 202.77, 140.72, 140.60, 140.10, 136.94, 135.87, 131.54, 131.03, 130.91, 130.22, 129.71, 129.21, 129.05, 128.41, 128.15, 127.70, 127.66, 127.45, 29.67. **IR** (cm^{-1}): 3014.2, 1688.4, 1591.9, 1473.5, 1444.4, 1350.8, 1245.4, 965.9, 776.0, 762.5, 703.8, 692.9, 596.0. **HRMS**: calculated for $C_{22}H_{18}O^+$ ($[M]^+$): 298.1358 Found 298.1365.

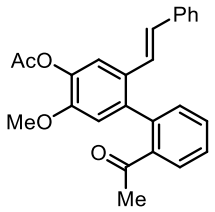


2,2,2-trifluoro-1-(2'-(2-methylprop-1-en-1-yl)-[1,1'-biphenyl]-2-yl)ethan-1-one (S31): A 25 mL round bottom flask containing a stirred solution of 2-bromo-2'-(2-methylprop-1-en-1-yl)-1,1'-biphenyl **(A27**, 350 mg, 1.22 mmol) in THF (10 mL)**,** was cooled to -78 °C. At which time, ^{n}BuLi (2.5 M in hexanes, 0.54 mL, 1.34 mmol) was slowly added. This solution was allowed to stir for 30 min. Next, ethyl trifluoroacetate (0.26 mL, 2.19 mmol) was added. The resultant mixture was allowed to slowly warm to room temperature over 3 h. The reaction mixture was quenched with NH_4Cl^+ (aq) (10 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification was accomplished employing flash column chromatography with hexanes/EtOAc to afford 156 mg (42%) of **S31** as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.9 Hz, 1H), 7.66 (td, *J* = 7.6, 1.2 Hz, 1H), 7.48 (td, *J* = 7.8, 1.1 Hz, 1H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.36 – 7.30 (m, 2H), 7.27 – 7.20 (m, 2H), 5.68 (s, 1H), 1.71 (s, 3H), 1.67 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 181.89 (q, *J*= 34.6), 143.35, 139.05, 137.45, 136.13, 133.29, 132.00, 131.44, 129.98, 129.09, 128.39, 128.38, 127.38, 127.07, 126.79, 123.75, 116.10 (q, *J*= 292.9). **IR** (cm^{-1}): 3072.0, 1454.2, 1435.9, 1229.8, 1162.6, 1138.1, 1115.3, 1056.5, 1016.2, 927.8, 736.3, 694.6, 647.8. **HRMS**: calculated for $C_{18}H_{19}OF_3N^+$ ($[M + NH_4^+]^+$): 322.1413 Found 322.1414.

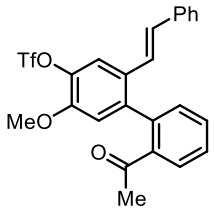


(*E*)-1'-styryl-[2,2'-binaphthalene]-1-carbaldehyde (S32): Sodium hydride (60% dispersion in mineral oil, 31mg, 0.77 mmol) was suspended in THF (6 mL) and cooled on an ice bath. Diethyl benzylphosphonate (0.134 mL, 0.64 mmol) was added via syringe and stirred for 30 minutes. [2,2'-binaphthalene]-1,1'-dicarbaldehyde[25] was added as a solid and the reaction mixture was allowed to warm to rt over 1 h. The reaction mixture was then heated to 50 °C for 6 hours. The mixture was allowed to cool to room temperature and quenched with water, then neutralized with saturated aqueous ammonium chloride. The aqueous layer was extracted twice with ethyl acetate and the combined organic layers were washed with brine and dried over Na_2SO_4. The resulting crude product was purified by silica gel column chromatography eluting with hexanes/EtOAc to afford

136 mg (27%) of the title compound as a foamy yellow solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 10.22 (s, 1H), 9.30 (d, *J* = 8.6 Hz, 1H), 8.35 (dd, *J* = 6.1, 3.5 Hz, 1H), 8.05 (d, *J* = 8.3 Hz, 1H), 7.96 (dd, *J* = 6.1, 3.4 Hz, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.87 (d, *J* = 8.3 Hz, 1H), 7.70 – 7.66 (m, 1H), 7.62 – 7.56 (m, 3H), 7.48 (d, *J* = 8.3 Hz, 1H), 7.45 (d, *J* = 8.3 Hz, 1H), 7.25 – 7.16 (m, 6H), 6.65 (d, *J* = 16.5 Hz, 1H).**^{13}C NMR** (176 MHz, $CDCl_3$) δ 194.59, 149.05, 137.57, 137.20, 135.13, 134.97, 134.16, 133.78, 133.28, 131.89, 130.71, 129.48, 129.29, 128.88, 128.78, 128.72, 128.53, 128.12, 127.34, 127.20, 127.01, 126.71, 126.62, 126.17, 126.06, 125.29. **IR** (cm^{-1}): 3048.5, 1680.9,1590.0, 1503.3, 1429.8, 1264.0, 1175.8, 1057.3, 964.5, 819.8, 733.7. **HRMS**: calculated for $C_{29}H_{20}O^+$ ($[M]^+$):: 384.1514 Found: 384.1518. .

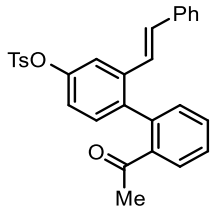


(*E*)-2'-acetyl-5-methoxy-2-styryl-[1,1'-biphenyl]-4-yl acetate (S34): To a 10 mL flame-dried round bottom flask was added **S27** (100 mg, 0.29 mmol) along with DCM (2 mL) under an atmosphere of nitrogen. After cooling the resultant mixture to 0 °C, DMAP (0.35 mg, 2.9 μmol), Ac_2O (41.2 μL, 0.47 mmol) and TEA (60.5 μL, 0.44 mmol) were successively added. The reaction mixture was slowly allowed to warm to room temperature. After 8 h, the reaction was quenched with NH_4Cl^+ (aq) (5 mL) and extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification was accomplished employing flash column chromatography with hexanes/EtOAc to afford 109 mg (97%) of **S34** as a clear foam. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.6 Hz, 1H), 7.56 (td, *J* = 7.5, 1.3 Hz, 1H), 7.53 – 7.46 (m, 2H), 7.35 (d, *J* = 7.5 Hz, 1H), 7.33 – 7.27 (m, 4H), 7.21 (dq, *J* = 8.6, 4.3 Hz, 1H), 6.92 (d, *J* = 16.2 Hz, 1H), 6.79 (m, 2H), 3.83 (s, 3H), 2.39 (s, 3H), 2.06 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.98, 169.07, 150.57, 141.19, 139.99, 138.85, 138.51, 137.40, 131.58, 131.02, 129.48, 128.82, 128.78, 128.34, 128.11, 127.73, 126.59, 125.38, 119.94, 114.25, 56.25, 29.98, 20.88. **IR** (cm^{-1}): 3053.8, 2056.0, 1759.6, 1685.6, 1506.0, 1438.2, 1205.0, 1133.4, 1022.1, 961.9, 732.2. **HRMS**: calculated for $C_{25}H_{26}O_4N$ ($[M + NH_4^+]^+$): 404.1856, found: 404.1856.

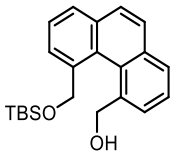


(*E*)-2'-acetyl-5-methoxy-2-styryl-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate (S35): To a 10 mL flame-dried round bottom flask was added **S27** (100 mg, 0.29 mmol) along with DCM (4 mL) under an atmosphere of nitrogen. After cooling the resultant mixture to 0 °C, Tf_2O (58. μL, 0.35 mmol) and TEA (88 μL, 0.58 mmol) were successively added. The reaction mixture was slowly allowed to warm to room temperature. After 4 h, the reaction was quenched with NH_4Cl^+ (aq) (5 mL) and extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over

$MgSO_4$ and concentrated under reduced pressure. Purification was accomplished employing flash column chromatography with hexanes/EtOAc to afford 97 mg (70%) of **S35** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 1H), 7.60 – 7.55 (m, 2H), 7.52 (m, 1H), 7.34 – 7.30 (m, 1H), 7.29 (d, *J* = 4.3 Hz, 4H), 7.25 – 7.20 (m, 1H), 6.88 (d, *J* = 16.2 Hz, 1H), 6.85 (s, 1H), 6.70 (d, *J* = 16.2 Hz, 1H), 3.90 (s, 3H), 2.13 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.91, 150.42, 141.12, 140.59, 138.75, 138.23, 136.99, 131.47, 131.38, 130.62, 129.35, 128.89, 128.64, 128.57, 128.15, 126.75, 124.74, 119.55, 114.84, 119.01 (q, *J* = 318.8), 56.62, 29.69. **IR (**cm^{-1}**):** 3032.2, 1688.9, 1609.7, 1503.3, 1419.3, 1320.0, 1240.0, 1204.5, 1136.6, 1101.0, 856.2, 756.2, 734.5. **HRMS**: calculated for $C_{24}H_{23}O_5NF_3S$ ($[M + NH_4^+]^+$): 494.1244, found: 494.1244.

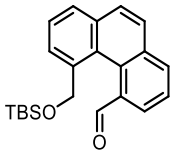


(*E*)-2'-acetyl-2-styryl-[1,1'-biphenyl]-4-yl 4-methylbenzenesulfonate (S36): To a 10 mL flame-dried round bottom flask was added **S25** (120 mg, 0.38 mmol) along with DCM (4 mL) under an atmosphere of nitrogen. After cooling the resultant mixture to 0 ^oC, TsCl (87 mg, 0.38 mmol) and TEA (0.16 mL, 1.15 mmol) were successively added. The reaction mixture was slowly allowed to warm to room temperature. After 12 h, the reaction was quenched with NH_4Cl^+ (aq) (5 mL) and extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification was accomplished employing flash column chromatography with hexanes/EtOAc to afford 85 mg (48%) of **S36** as a pale yellow foam. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.78 (d, *J* = 6.9 Hz, 2H), 7.70 (d, *J* = 7.7 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.36 (m, 3H), 7.31 – 7.21 (m, 6H), 7.09 (d, *J* = 8.3, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 6.81 (d, *J* = 16.2 Hz, 1H), 6.71 (d, *J* = 16.2 Hz, 1H), 2.46 (s, 3H), 1.98 (s, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 202.08, 149.78, 145.74, 140.84, 138.99, 138.49, 137.62, 136.86, 132.55, 132.06, 131.59, 131.53, 131.25, 130.02, 128.92, 128.63, 128.38, 128.27, 126.89, 125.36, 121.34, 119.42, 29.80, 21.98. **IR (**cm^{-1}): 2959.5, 1687.5, 1448.5, 1428.9, 1284.2, 1232.5, 1178.1, 1092.1, 943.9, 880.6, 707.6. **HRMS**: calculated for $C_{29}H_{28}O_4NS^+$ ($[M + NH_4^+]^+$): 486.1734, found: 486.1730.

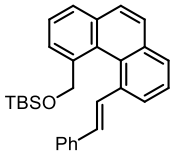


(5-(((tert-butyldimethylsilyl)oxy)methyl)phenanthren-4-yl)methanol (S37i-a): Phenanthrene-4,5-diyldimethanol[26] (893 mg, 3.75 mmol) was dissolved in DMF (4 mL). TBSCl (678 mg, 4.5 mmol) and imidazole (765 mg, 11.2 mmol) were added and the reaction mixture was stirred overnight. The reaction was diluted with water and diethyl ether. The layers were separated and the aqueous layer was washed with two portions of ether. The combined organic layers were

washed with brine and dried over $MgSO_4$, then concentrated by rotary evaporator. The product was purified by silica gel column chromatography eluting with hexanes/ethyl acetate to afford 281 mg (21% yield) of the title product as a clear oil. This reaction was carried out twice and the combined product was used in the next step. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.89 – 7.73 (m, 4H), 7.69 – 7.54 (m, 4H), 5.06 (d, *J* = 12.1 Hz, 1H), 4.99 (d, *J* = 12.1 Hz, 1H), 4.86 (d, *J* = 12.2 Hz, 1H), 4.75 (d, *J* = 12.1 Hz, 1H), 0.76 (s, 9H), -0.22 (s, 3H), -0.33 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 139.62, 139.33, 133.54, 127.89, 127.71, 127.65, 127.15, 127.04, 126.96, 126.88, 126.86, 126.72, 126.56, 63.82, 63.54, 25.96, 18.34, -5.29, -5.37**. IR** (cm^{-1}): 2926.2, 2884.4, 2854.1, 1469.7, 1251.3, 1164.4, 1101.7, 1066.3, 1004.1, 955.6, 889.6, 824.3, 772.6, 723.7, 673.8. **HRMS**: calculated for $C_{22}H_{28}O_2SiNa^+$ ($[M+Na^+]^+$): 375.1751 Found: 375.1753.

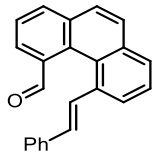


5-(((tert-butyldimethylsilyl)oxy)methyl)phenanthrene-4-carbaldehyde (S37i-b): (5-(((tert-butyldimethylsilyl)oxy)methyl)phenanthren-4-yl)methanol (**S37i-a**) (514 mg, 1.50 mmol), tetrapropylammonium perruthenate (26 mg, 0.07 mmol) and N-methylmorpholine N-oxide (256 mg, 2.1 mmol) were combined and dissolved in DCM (15 mL). The reaction mixture was stirred at room temperature until judged complete by TLC. The reaction mixture was filtered through a plug of silica eluting with DCM and the solvent was removed by rotary evaporator. The crude product was purified by silica gel column chromatography eluting with hexanes/ethyl acetate, affording 416 mg (81% yield) of product as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.93 (s, 1H), 8.22 (d, *J* = 7.3 Hz, 1H), 8.11 (d, *J* = 7.7 Hz, 1H), 7.94 (d, *J* = 7.4 Hz, 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.79 – 7.65 (m, 4H), 5.03 (br d, *J* = 79.4 Hz, 2H), 0.75 (s, 9H), -0.12 – -0.37 (br m, 6H). **^{13}C NMR** (176 MHz, $CDCl_3$): δ 191.83, 140.94, 135.38, 134.14, 133.84, 133.09, 129.91, 128.38, 128.29, 128.10, 127.20, 126.79, 126.55, 126.48, 126.00, 63.50, 25.95, 18.35, -5.33. **IR** (cm^{-1}): 1685.4, 1469.9, 1249.6, 1219.7, 1074.3, 832.0, 774.1, 723.9. **HRMS**: calculated for $C_{22}H_{26}O_2SiNa^+$ ($[M+Na^+]^+$): 373.1594 Found: 373.1596.

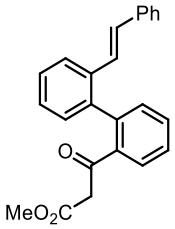


(*E*)-tert-butyldimethyl((5-styrylphenanthren-4-yl)methoxy)silane (S37i-c): NaH (1.33 g, 5.85 mmol) was added to a solution of diethyl benzylphosphonate (1.33 g, 5.85 mmol) in DMF (5 mL) at 0 °C and allowed to stir for 30 min, at which time a solution of 5-(((tert-butyldimethylsilyl)oxy)methyl)phenanthrene-4-carbaldehyde (**S37i-b**) (410 mg, 1.17 mmol) in DMF (3 mL) was added slowly. The reaction mixture was allowed to warm to room temperature and stirred for 2 h, before cooling to 0 °C and quenching with water. The aqueous layer was washed with three portions of ethyl acetate and the combined organic layers were washed with brine and dried over Na_2SO_4. The crude product was purified by silica gel column chromatography eluting with hexanes/ethyl acetate to afford 374 mg (75% yield) of the title compound as a clear oil. **^{1}H**

NMR (500 MHz, $CDCl_3$): δ 7.92 (d, *J* = 7.5 Hz, 1H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.79 (dd, *J* = 12.7, 7.7 Hz, 2H), 7.71 – 7.55 (m, 4H), 7.45 (d, *J* = 7.8 Hz, 2H), 7.33 (dd, *J* = 19.3, 11.8 Hz, 3H), 7.25 (m, *J* = 13.4 Hz, 2H), 7.05 (d, *J* = 16.4 Hz, 1H), 5.05 (d, *J* = 12.9 Hz, 1H), 4.75 (d, *J* = 13.0 Hz, 1H), 0.66 (s, 9H), -0.33 (s, 3H), -0.45 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 140.29, 137.72, 137.01, 134.48, 133.32, 130.41, 129.11, 128.98, 128.80, 128.30, 127.85, 127.34, 127.32, 126.99, 126.81, 126.62, 126.57, 126.40, 124.25, 64.70, 25.98, 18.39, -5.43, -5.47. **IR** (cm^{-1}): 1470.0, 1251.4, 1070.4, 973.1, 834.0, 775.1, 755.4, 721.6, 960.0, 667.7. **HRMS**: Calculated for $C_{25}H_{23}OSi^+$ ($[M-C_4H_9]^+$): 367.1518 Found: 367.1518

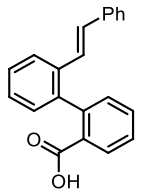


(*E*)-5-styrylphenanthrene-4-carbaldehyde (S37): (*E*)-tert-butyldimethyl((5-styrylphenanthren-4-yl)methoxy)silane (**S37i-d**) (360 mg, 0.85 mmol) was dissolved in THF (8.5 mL) and cooled to 0 °C before a solution of TBAF (1M in THF, 2.2 mL, 2.20 mmol) was added slowly. The reaction mixture was allowed to warm to room temperature and stirred for 3 h, at which time the reaction mixture was diluted with water and diethyl ether. The layers were separated and the organic layer was washed with saturated aqueous ammonium chloride and brine and dried over $MgSO_4$. The solvent was removed by rotary evaporator and the crude material was dissolved in DMSO (3 mL) and IBX (285 mg, 1.01 mmol) was added and the reaction mixture was stirred at room temperature for 4 h. The mixture was diluted with water and diethyl ether and filtered through a pad of celite. The layers were separated and the aqueous layer was extracted with two more portions of ether. The combined organic layers were washed with brine and dried over $MgSO_4$ and concentrated by rotary evaporator. The crude product was purified by silica gel column chromatography to afford 106 mg (41% yield) of the title compound as a yellow-white foam. **^{1}H NMR** (401 MHz, $CDCl_3$): δ 10.04 (s, 1H), 8.21 (d, *J* = 7.4 Hz, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.90 (dd, *J* = 15.6, 7.5 Hz, 2H), 7.84 – 7.63 (m, 5H), 7.44 (d, *J* = 7.5 Hz, 2H), 7.40 – 7.33 (m, 3H), 7.29 (d, *J* = 7.4 Hz, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$): δ 189.13, 138.51, 137.43, 135.70, 134.71, 133.95, 132.82, 132.67, 129.97, 128.94, 128.70, 128.32, 128.06, 127.99, 127.57, 127.37, 127.03, 126.89, 126.82, 126.81, 126.27. **IR** (cm^{-1}): 1725.7, 1684.3, 1447.6, 1275.5, 1213.9, 1133.5, 1018.3, 969.2, 907.5, 831.5, 761.3, 719.3, 690.1, 646.2. **HRMS**: calculated for $C_{23}H_{17}O^+$ ($[M+H^+]^+$): 309.1274 Found: 309.1270.

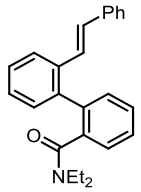


Methyl (*E*)-3-oxo-3-(2'-styryl-[1,1'-biphenyl]-2-yl)propanoate (22h): Sodium hydride (60% dispersion in mineral oil, 181 mg, 4.5 mmol) was suspended in dimethyl carbonate (10 mL) and a solution of **11** (450 mg, 1.5 mmol) in dimethyl carbonate (5 mL) was added dropwise at room temperature. The reaction mixture was then heated to reflux and monitored until complete by TLC

analysis. Purification by flash column chromatography eluting with hexanes/EtOAc afforded 174 mg (33% yield) as a mixture of keto/enol tautomers. NMR spectra in $CDCl_3$ appeared as a mixture of keto/enol tautomers. **^{1}H NMR** (500 MHz, DMSO) δ 7.83 (t, *J* = 8.0 Hz, 2H), 7.65 (t, *J* = 7.1 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.38 – 7.26 (m, 5H), 7.16 (dd, *J* = 29.9, 22.6 Hz, 3H), 6.73 (d, *J* = 16.3 Hz, 1H), 3.70 (d, *J* = 16.6 Hz, 1H), 3.58 – 3.52 (m, 1H), 3.48 (s, 2H). **^{13}C NMR** (126 MHz, DMSO) δ 196.16, 167.31, 139.41, 139.38, 138.30, 136.91, 134.96, 131.67, 131.61, 129.95, 129.84, 128.74, 128.70, 128.09, 127.91, 127.74, 127.48, 126.26, 126.20, 125.93, 125.37, 51.74, 47.48. **IR** (cm^{-1}): 1741.0, 1692.7, 1616.5, 1593.4, 1470.7, 1436.2, 1388.6, 1319.3, 1273.1, 1241.4, 1092.8, 1073.1, 983.4, 962.8, 823.9. **HRMS**: calculated for $C_{24}H_{24}O_3N^+$: 374.1751 Found: 374.1755.



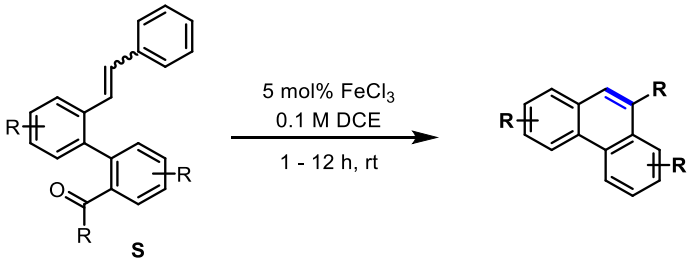
(*E*)-2'-styryl-[1,1'-biphenyl]-2-carboxylic acid (22k): Potassium trimethylsilanoate (1.16g, 9.1 mmol) was dissolved in THF (10 mL) and transferred to a solution of ester **22j** (570 mg, 1.83 mmol) in THF (8 mL) and the mixture was stirred overnight at rt. The solvent was then stripped by rotary evaporator and the crude mixture was taken up in diethyl ether and extracted with two portions of aqueous sodium hydroxide (1M). The combined aqueous layers were then acidified to pH 1 with concentrated HCl and extracted with four portions of diethyl ether. The combined organic layers were dried over MgSO4 and concentrated by rotary evaporator to afford 545 mg (83% yield) of the title compound as a white solid. **^{1}H** NMR (700 MHz, $CDCl_3$): δ 8.03 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.58 (td, *J* = 7.5, 1.3 Hz, 1H), 7.47 (td, *J* = 7.8, 1.1 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.32 – 7.23 (m, 6H), 7.19 (ddd, *J* = 8.5, 5.8, 2.8 Hz, 1H), 7.16 (dd, *J* = 7.5, 0.9 Hz, 1H), 6.95 (d, *J* = 16.2 Hz, 1H), 6.79 (d, *J* = 16.2 Hz, 1H). **^{13}C NMR** (176 MHz, $CDCl_3$): δ 171.54, 142.60, 140.50, 137.69, 135.58, 132.41, 132.20, 131.02, 130.12, 129.95, 129.60, 128.73, 127.91, 127.68, 127.67, 127.30, 127.05, 126.74, 125.26. **IR** (cm^{-1}): 2534.3, 1691.0, 1570.9, 1470.9, 1405.9, 1293.6, 1276.9, 1145.9, 965.9, 805.0, 767.8, 754.8, 691.8, 659.6 **HRMS**: calculated for $C_{21}H_{16}O_2Na^+$ ($[M+Na^+]^+$): 323.1043 Found: 323.1043.



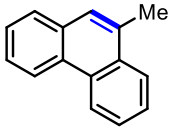
(E)-N,N-diethyl-2'-styryl-[1,1'-biphenyl]-2-carboxamide (22l): (*E*)-2'-styryl-[1,1'-biphenyl]-2-carboxylic acid (**22k**) (250 mg, 0.83 mmol) was treated with thionyl chloride (0.60 mL, 8.3 mmol) and heated to reflux for 3 h, at which time the reaction mixture was allowed to cool and volatiles were removed by rotary evaporator. The resulting crude material was dissolved in DCM (10 mL) and diethylamine (0.17 mL, 1.66 mmol) was added. The reaction mixture was stirred until judged complete by TLC. The solvent was removed by rotary evaporator and the crude material was purified directly by silica gel column chromatography eluting with hexanes/EtOAc to afford 296

mg (61% yield) of the title compound as a thick yellow oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.8 Hz, 1H), 7.43 (s, 3H), 7.38 – 7.13 (m, 9H), 7.05 (m, 2H), 3.73 (s, 1H), 2.94 (m, 2H), 2.63 (br s, 1H), 0.96 (br s, 1H), 0.86 – 0.65 (m, 5H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.15, 137.70, 131.55, 129.79, 128.84, 128.19, 127.88, 126.72, 125.35, 42.71, 38.16, 13.90, 12.08. **IR** (cm^{-1}): 1623.3, 1494.1, 1424.4, 1379.3, 1362.2, 1312.3, 1287.7, 1220.0, 1085.8, 962.3, 910.7, 760.0, 729.4, 690.8. **HRMS**: calculated for $C_{25}H^{26}NO$ ($[M+H^+]^+$): 356.2009 Found: 356.2012.

6. Synthesis of metathesis products



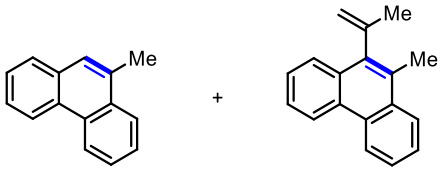
General procedure for Carbonyl-Olefin Metathesis:
A flame-dried 1–dram vial was charged with $FeCl_3$ (1 mg, 0.13 mmol) and DCE (1.3 mL) PhMe was used as solvent when indicated. The solution was stirred at room temperature. To this mixture was added starting ketone **S** (0.13 mmol), and the resultant mixture was stirred for the indicated time at room temperature, unless otherwise specified. Upon completion (as determined by TLC analysis), the reaction mixture was passed through a short silica plug eluting with DCM (25 mL). The filtrate was concentrated under reduced pressure, and the crude material was purified using column chromatography, with the indicated eluent to give the pure metathesis adducts.



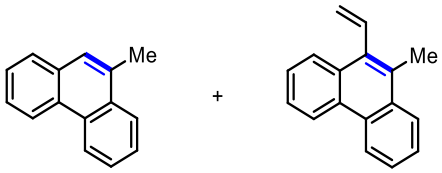
9-methylphenanthrene (9): The cyclization of **8** was performed on 0.13 mmol scale with a total reaction time of 1 h. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 25 mg (99%) of **9** as a white solid. Spectroscopic data matched reported literature data.[24] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.73 (d, *J* = 7.8 Hz, 1H), 8.66 (d, *J* = 7.9 Hz, 1H), 8.07 (d, *J* = 7.7 Hz, 1H), 7.81 (d, *J* = 7.6 Hz, 1H), 7.71 – 7.62 (m, 2H), 7.62 – 7.53 (m, 3H), 2.75 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 132.46, 132.06, 132.00, 130.36, 129.65, 127.80, 126.71, 126.55, 126.49, 126.19, 125.78, 124.64, 122.98, 122.43, 20.02.

9-methylphenanthrene (9): The cyclization of **11** was performed on 0.13 mmol scale in PhMe as solvent, with a total reaction time of 24 h. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 22.5 mg (90%) of **9** as a white solid.
9-methylphenanthrene (9): The cyclization of **12** was performed on 0.13 mmol scale in PhMe as solvent, with a total reaction time of 8 h at 50 °C. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 20.5 mg (82%) of **9** as a white solid.
9-methylphenanthrene (9): The cyclization of **13** was performed on 0.13 mmol scale in PhMe as solvent, with a total reaction time of 8 h at 50 °C. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 22.2 mg (89%) of **9** as a white solid.

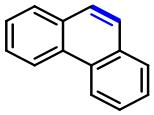
9-methylphenanthrene (9): The cyclization of **14** was performed on 0.13 mmol scale in PhMe as solvent, with a total reaction time of 6 h at 50 °C. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 21.4 mg (86%) of **9** as a white solid.
9-methylphenanthrene (9): The cyclization of **15** was performed on 0.13 mmol scale in PhMe as solvent, with a total reaction time of 6 h 50 °C. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 20.0 mg (80%) of **9** as a white solid.
9-methylphenanthrene (9): The cyclization of **16** was performed on 0.13 mmol scale in PhMe as solvent, with a total reaction time of 6 h 50 °C. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 21.0 mg (84%) of **9** as a white solid.



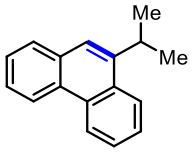
9-methylphenanthrene + 9-methyl-10-(prop-1-en-2-yl)phenanthrene[27] **(9 + 20):** The cyclization of **17** was performed on 0.13 mmol scale in PhMe as solvent, with a total reaction time of 1 h at rt . Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 26 mg of **9** (19.8 mg, 79%) and **9b** (6.2 mg, 21%) as an inseparable mixture (1.0:0.26; ratio by NMR analysis), as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$; as a mixture of **9** and **9b**) δ 8.73 (d, *J* = 11.4 Hz, 1.10H), 8.70 (d, *J* = 8.9 Hz, 0.34H), 8.66 (d, *J* = 8.0 Hz, 0.94H), 8.15 – 8.10 (m, 0.25H), 8.10 – 8.04 (m, 0.92H), 8.01 (d, *J* = 7.8 Hz, 0.25H), 7.81 (d, *J* = 7.4 Hz, 0.98H), 7.66 (m, 2.24H), 7.62 – 7.52 (m, 3.04H), 5.57 (s, 0.26H), 5.00 (s, 0.28H), 2.74 (s, 3H), 2.69 (s, 0.69H), 2.14 (s, 0.57H). **^{13}C NMR** (125 MHz, $CDCl_3$; as a mixture of **9** and **9b**) δ 144.46, 138.48, 132.48, 132.09, 132.02, 131.98, 130.46, 130.38, 129.68, 129.61, 129.53, 128.86, 128.68, 128.56, 128.30, 127.82, 127.58, 126.73, 126.63, 126.57, 126.51, 126.21, 125.90, 125.80, 125.60, 124.89, 124.66, 123.00, 122.77, 122.53, 122.45, 116.71, 24.86, 20.04, 16.49.



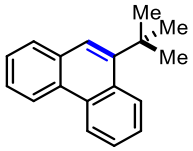
9-methylphenanthrene + 9-methyl-10-vinylphenanthrene (9 + 21): The cyclization of **18** was performed on 0.12 mmol scale in PhMe as solvent, with a total reaction time of 6 h at 50 °C . Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 19 mg of **9** (4.5 mg, 18%) and **9c** (13.3 mg, 47%) as an inseparable mixture (0.4:1.0; ratio by NMR analysis), as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$; as a mixture of **9** and **9c**) δ 8.72 (m, 2.19H), 8.67 (d, *J* = 7.9 Hz, 0.36H), 8.14 (m, 1.74H), 8.08 (d, *J* = 7.6 Hz, 0.36H), 7.82 (d, *J* = 7.5 Hz, 0.45H), 7.72 – 7.63 (m, 2.38H), 7.63 – 7.53 (m, 2.39H), 7.13 (dt, *J* = 25.0, 12.5 Hz, 1.05H), 5.85 (d, *J* = 11.4 Hz, 1H), 5.42 (d, *J* = 17.9 Hz, 0.97H), 2.76 (s, 3.82H). **^{13}C NMR** (125 MHz, $CDCl_3$; as a mixture of **9** and **9c**) δ 135.75, 133.93, 132.69, 132.30, 132.23, 131.35, 130.59, 129.93, 129.89, 129.55, 129.36, 129.29, 129.22, 128.04, 126.94, 126.88, 126.79, 126.73, 126.62, 126.46, 126.42, 126.26, 126.01, 125.90, 125.32, 124.87, 123.21, 122.98, 122.77, 122.66, 121.79, 20.25, 17.17.



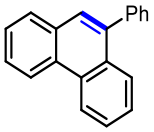
Phenanthrene (23b): The cyclization of **22b** was performed on 0.13 mmol scale (37 mg) with a total reaction time of 4 h. Purification by flash column chromatography eluting with hexanes/EtOAc provided 18 mg (75%) of **23b** as a white solid. Spectroscopic data matched that reported.[28] **^{1}H NMR** (401 MHz, $CDCl_3$) δ 8.70 (d, *J* = 8.2 Hz, 2H), 7.90 (d, *J* = 7.8 Hz, 2H), 7.75 (s, 2H), 7.67 (t, *J* = 7.5 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 132.26, 130.52, 128.78, 127.13, 126.77, 122.87.



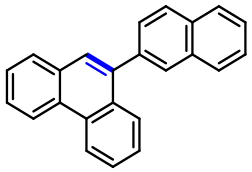
9-Isopropylphenanthrene (23c): The cyclization of **22c** was performed on 0.13 mmol scale with a total reaction time of 4 h. Purification by flash column chromatography eluting with hexanes/EtOAc provided 23 mg (79%) of **23c** as a colorless oil.[29] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.81 – 8.71 (m, 1H), 8.69 – 8.62 (m, 1H), 8.21 (m, 1H), 7.91 – 7.80 (m, 1H), 7.74 – 7.46 (m, 5H), 3.82 – 3.69 (m, 1H), 1.49 (s, 3H), 1.47 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 142.80, 132.19, 131.12, 130.96, 129.59, 128.51, 126.75, 126.66, 126.16, 126.12, 124.17, 123.52, 122.59, 122.42, 28.83, 23.55.



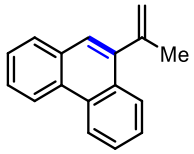
9-(*tert*-butyl)phenanthrene (23d): The cyclization of **22d** was performed on 0.13 mmol scale with a total reaction time of 12 h at 50 °C. Purification by flash column chromatography eluting with hexanes/EtOAc provided 16.4 mg (55%) of **23d** as a white solid. Spectroscopic data matched that reported.[30] **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.82 – 8.77 (m, 1H), 8.64 (d, *J* = 8.1 Hz, 1H), 8.54 (dd, *J* = 7.3, 1.4 Hz, 1H), 7.86 (d, *J* = 7.7 Hz, 1H), 7.76 (s, 1H), 7.61 (m, 4H), 1.70 (s, 9H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 144.19, 132.01, 131.87, 131.06, 129.86, 128.89, 127.88, 126.78, 126.44, 125.58, 125.52, 124.31, 123.87, 122.40, 36.15, 32.06.



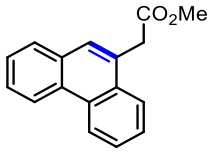
9-Phenylphenanthrene (23e): The cyclization of **22e** was performed on 0.13 mmol scale (47 mg) with a total reaction time of 24 h. Purification by flash column chromatography eluting with hexanes/EtOAc provided 22 mg (67%) of **23e** as a white solid. Spectroscopic data matched that reported.[31] **^{1}H NMR** (401 MHz, $CDCl_3$) δ 8.79 (d, *J* = 8.3 Hz, 1H), 8.74 (d, *J* = 8.2 Hz, 1H), 7.92 (t, *J* = 8.7 Hz, 2H), 7.79 – 7.38 (m, 10H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 141.02, 139.00, 131.78, 131.36, 130.84, 130.28, 130.17, 128.88, 128.52, 127.72, 127.58, 127.15, 127.06, 126.80, 126.71, 126.66, 123.11, 122.75.



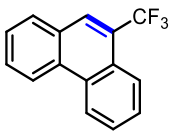
9-(naphthalen-2-yl)phenanthrene (23f): The cyclization of **22f** was performed on 0.13 mmol scale with a total reaction time of 24 h. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 21 mg (53%) of **23f** as a white solid. Spectroscopic data matched reported literature data.[32] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.81 (d, *J* = 8.3 Hz, 1H), 8.76 (d, *J* = 8.2 Hz, 1H), 8.03 (s, 1H), 8.00 – 7.89 (m, 5H), 7.79 (s, 1H), 7.69 (m, 3H), 7.64 (t, *J* = 7.3 Hz, 1H), 7.60 – 7.50 (m, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 138.92, 138.60, 133.70, 132.89, 131.82, 131.46, 130.89, 130.26, 128.92, 128.91, 128.65, 128.29, 128.08, 128.00, 127.88, 127.24, 127.11, 126.87, 126.78, 126.73, 126.56, 126.31, 123.16, 122.79.



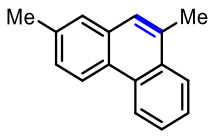
9-(prop-1-en-2-yl)phenanthrene (23g): The cyclization of **22g** was performed on 0.13 mmol scale with a total reaction time of 12 h at 50°C. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 14 mg (50%) of **23g** as a yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.73 (d, *J* = 8.2 Hz, 1H), 8.68 (d, *J* = 8.1 Hz, 1H), 8.09 (d, *J* = 8.1 Hz, 1H), 7.86 (d, *J* = 7.7 Hz, 1H), 7.69 – 7.55 (m, 5H), 5.44 (s, 1H), 5.15 (s, 1H), 2.25 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 145.25, 141.05, 131.89, 130.49, 130.02, 128.65, 126.90, 126.67, 126.66, 126.54, 126.52, 125.14, 123.14, 122.69, 116.33, 25.25. **IR** (cm^{-1}): 3072.8, 2923.1, 1492.8, 1449.3, 1372.0, 1258.0, 1040.0, 905.3, 767.6. **HRMS**: calculated for $C_{17}H_{14}$ $[M]^+$: 218.1096, found: 218.1096.



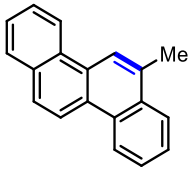
Methyl 2-(phenanthren-9-yl)acetate (23h): The cyclization of **22h** was performed on 0.13 mmol scale (49 mg) with a total reaction time of 24 h. Purification by flash column chromatography eluting with hexanes/EtOAc provided 24 mg (72%) of **23h** as a pale yellow solid. Spectroscopic data matched that reported.[33] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.77 – 8.72 (m, 1H), 8.67 (d, *J* = 8.2 Hz, 1H), 8.07 – 8.01 (m, 1H), 7.88 – 7.83 (m, 1H), 7.72 – 7.54 (m, 55H), 4.13 (s, 2H), 3.70 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 172.26, 131.76, 131.29, 130.95, 130.45, 129.19, 129.12, 128.60, 127.13, 126.98, 126.91, 126.73, 124.62, 123.44, 122.73, 52.44, 39.86.



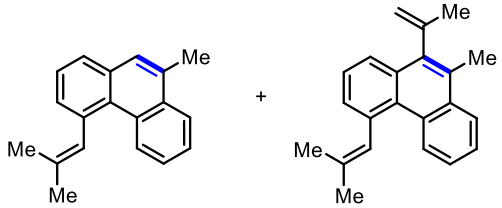
9-(trifluoromethyl)phenanthrene (23i): The cyclization of **22i** was performed on 0.13 mmol scale (47 mg) with a total reaction time of 1 h at 50 °C. Purification by flash column chromatography eluting with hexanes/EtOAc provided 16.5 mg (52%) of **23i** as a white solid. Spectroscopic data matched that reported.[34] **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.77 (d, *J* = 8.2 Hz, 1H), 8.71 (d, *J* = 8.3 Hz, 1H), 8.25 (d, *J* = 8.2 Hz, 1H), 8.19 (s, 1H), 7.97 (t, *J* = 9.5 Hz, 1H), 7.78 (t, *J* = 7.1 Hz, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.68 (t, *J* = 7.0 Hz, 1H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 132.02, 131.20, 130.14, 129.68, 129.21, 127.69, 127.58, 127.55, 127.27 (q, J= 6.3 Hz), 127.04, 125.41 (q, J= 2.7 Hz) , 124.89 (q, J= 29.8), 123.40, 122.91.



2,9-dimethylphenanthrene (24): The cyclization of **S2** was performed on 0.13 mmol scale with a total reaction time of 1 h. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 24 mg (89%) of **24** as a white solid. Spectroscopic data matched reported literature data.[35] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.79 – 8.67 (m, 1H), 8.46 (s, 1H), 8.11 – 8.01 (m, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.70 – 7.60 (m, 2H), 7.56 (s, 1H), 7.39 (dd, *J* = 24.8, 8.0 Hz, 1H), 2.73, 3H), 2.63 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 135.60, 132.43, 131.60, 130.36, 130.16, 129.92, 128.50, 127.89, 126.77, 126.57, 126.19, 124.84, 123.18, 122.44, 22.31, 20.19.

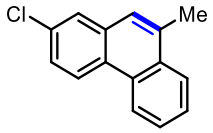


6-methylchrysene (25): The cyclization of **S3** was performed on 0.15 mmol scale with a total reaction time of 1 h. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 29 mg (80%) of **25** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.81 (dd, *J* = 14.7, 8.3 Hz, 2H), 8.71 (d, *J* = 9.1 Hz, 1H), 8.58 (s, 1H), 8.21 – 8.12 (m, 1H), 8.03 – 7.90 (m, 2H), 7.71 (qdd, *J* = 6.8, 6.2, 1.4 Hz, 3H), 7.66 – 7.56 (m, 1H), 2.91 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 133.38, 132.49, 132.17, 130.87, 130.42, 128.74, 127.53, 126.73, 126.68, 126.56, 126.51, 126.46, 124.93, 123.79, 123.32, 121.75, 121.36, 20.85. **IR** (cm^{-1}): 2923.8, 1596.5, 1513.9, 1483.1, 1438.3, 1399.6, 1244.5, 1156.1, 1035.6, 873.9, 823.3, 755.2. **HRMS**: calculated for $C_{19}H_{14}$ $[M]^+$: 242.1096 found: 242.1095..

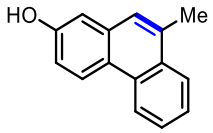


9-methyl-4-(2-methylprop-1-en-1-yl)phenanthrene + 9-methyl-4-(2-methylprop-1-en-1-yl)-10-(prop-1-en-2-yl)phenanthrene (26 + 26b): The cyclization of **S4** was performed on 0.12 mmol scale with a total reaction time of 1 h. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 28 mg of **26** (18 mg, 64%) and **26b** (10 mg, 30%) as an

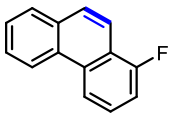
inseparable mixture (1:0.69; ratio by NMR analysis), as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$; as a mixture of **26** and **26b**) δ 9.28 (d, *J* = 8.4 Hz, 1H), 9.24 (d, *J* = 8.5 Hz, 0.57H), 8.13 (d, *J* = 8.2 Hz, 0.66H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 8.1 Hz, 0.64H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.66 – 7.55 (m, 3.62H), 7.52 (m, 1.76H), 7.37 (t, *J* = 8.3 Hz, 1.66H), 6.83 (s, 1H), 6.81 (s, 0.55H), 5.57 (s, 0.63H), 5.01 (s, 0.62H), 2.73 (s, 3H), 2.69 (s, 1.52H), 2.15 (s, 1.64H), 2.10 (s, *J* = 3.6 Hz, 4.43H), 1.88 (s, 1.60H), 1.83 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$; as a mixture of **26** and **26b**) δ 145.22, 139.09, 136.66, 136.55, 133.45, 133.28, 133.14, 132.80, 132.37, 132.35, 132.00, 131.80, 131.10, 130.45, 130.20, 130.02, 129.92, 128.81, 128.75, 128.31, 127.94, 127.67, 127.14, 126.26, 126.11, 125.89, 125.71, 125.49, 125.30, 124.81, 124.53, 124.41, 116.94, 26.14, 26.09, 25.17, 20.22, 19.88, 19.80, 16.85. **HRMS (26)**: calculated for $C_{19}H_{18}$ ([M]$^{+}$): 246.1409, found: 246.1405. **HRMS (26b)**: calculated for $C_{19}H_{18}$ ([M]$^{+}$): 286.1722, found: 286.1721.



2-chloro-9-methylphenanthrene (27): The cyclization of **S5** was performed on 0.13 mmol scale with a total reaction time of 1 h. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 25 mg (85%) of **27** as a white solid. Spectroscopic data matched reported literature data.[35] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.65 (dd, *J* = 9.7, 7.0 Hz, 1H), 8.55 (dd, *J* = 8.8, 2.3 Hz, 1H), 8.05 (d, *J* = 7.6 Hz, 1H), 7.81 – 7.74 (m, 1H), 7.72 – 7.62 (m, 2H), 7.52 (d, *J* = 8.8 Hz, 1H), 7.46 (d, *J* = 15.8 Hz, 1H), 2.74 (d, *J* = 7.7 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 134.24, 133.26, 132.52, 132.15, 130.15, 128.21, 127.01, 126.93, 126.84, 126.42, 125.85, 125.00, 124.35, 123.13.

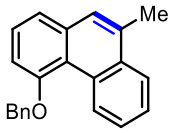


9-methylphenanthren-2-ol (28): The cyclization of **S25** was performed on 0.13 mmol scale with a total reaction time of 12 h. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 24 mg (75%) of **28** as a yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.2 Hz, 1H), 8.54 (d, *J* = 8.5 Hz, 1H), 8.02 (d, *J* = 8.1 Hz, 1H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.46 (s, 1H), 7.17 – 7.13 (m, 2H), 4.95 (b, 1H), 2.72 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 154.13, 133.51, 133.42, 131.03, 130.48, 126.36, 125.89, 125.59, 124.68, 124.43, 124.14, 122.42, 115.76, 111.06, 20.06.

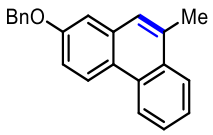


1-fluorophenanthrene (29): The cyclization of **S6** was performed on 0.13 mmol scale with a total reaction time of 1 h. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 26 mg (99%) of **29** as a pale yellow solid. Spectroscopic data matched reported literature data.[36] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 8.2 Hz, 1H), 8.47 (d, *J* = 8.4 Hz, 1H), 8.04 (d, *J* = 9.1 Hz, 1H), 7.92 (d, *J* = 9.0 Hz, 1H), 7.81 (d, *J* = 9.1 Hz, 1H), 7.71 – 7.54 (m, 3H), 7.29 (m, 1H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 159.28 (d, *J* = 250.1 Hz), 132.15 (d, *J* = 4.4 Hz), 132.08, 129.64 (d, *J* = 2.6 Hz), 128.78, 127.37 (d, *J* = 1.8 Hz), 127.10, 127.0, 126.47 (d, *J* = 8.7

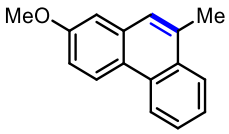
Hz), 123.01, 121.56 (d, *J* = 15.4 Hz), 118.51 (d, *J* = 7.0 Hz), 118.39 (d, *J* = 3.9 Hz), 111.01 (d, *J* = 20.4 Hz).



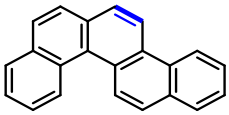
4-(benzyloxy)-9-methylphenanthrene (30): The cyclization of **S8** was performed on 0.13 mmol scale with a total reaction time of 12 h. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 24 mg (71%) of **30** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.83 (t, *J* = 12.2 Hz, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.65 – 7.52 (m, 5H), 7.50 – 7.42 (m, 4H), 7.38 (t, *J* = 7.3 Hz, 1H), 7.17 (dd, *J* = 5.9, 3.1 Hz, 1H), 5.40 (s, *J* = 11.4 Hz, 2H), 2.74 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 157.57, 137.00, 134.59, 133.07, 132.59, 130.47, 129.03, 128.65, 128.00, 127.66, 127.23, 126.45, 125.98, 125.80, 123.97, 121.25, 120.30, 109.39, 71.24, 20.15. **IR** (cm^{-1}): 2921.0, 1567.5, 1441.5, 1301.0, 1241.4, 1229.9, 1055.6, 880.7, 744.7, 757.7, 715.8, 691.5. **HRMS**: calculated for $C_{22}H_{19}O$ ($[M + H^+]^+$): 299.1436, found: 299.1430.



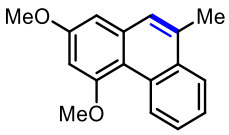
2-(benzyloxy)-9-methylphenanthrene (31): The cyclization of **S9** was performed on 0.13 mmol scale with a total reaction time of 12 h. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 38 mg (97%) of **31** as a yellow-white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.62 (d, *J* = 8.2 Hz, 1H), 8.56 (d, *J* = 8.9 Hz, 1H), 8.03 (d, *J* = 8.2 Hz, 1H), 7.66 – 7.61 (m, 1H), 7.60 – 7.54 (m, 1H), 7.51 (m, *J* = 8.2 Hz, 3H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.36 (d, *J* = 7.4 Hz, 1H), 7.30 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.27 (d, *J* = 2.6 Hz, 1H), 5.23 (s, 2H), 2.73 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 157.73, 137.19, 133.57, 133.41, 131.29, 130.71, 128.84, 128.23, 127.79, 126.58, 126.53, 125.78, 124.88, 124.39, 124.38, 122.74, 116.88, 109.52, 70.34, 20.28. **IR** (cm^{-1}): 1600.2, 1492.1, 1447.3, 1382.6, 1363.1, 1305.8, 1228.0, 1181.0, 1020.4, 995.7, 887.6, 827.8, 777.5, 7449, 720.7, 694.1. **HRMS**: Calculated for $C_{22}H_{19}O^+$ ($[M + H^+]^+$): 299.1430 Found: 299.1433.



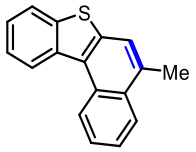
2-methoxy-9-methylphenanthrene (32): The cyclization of **S10** was performed on 0.13 mmol scale with a total reaction time of 12 h. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 25 mg (86%) of **32** as a white solid. Spectroscopic data matched reported literature data.[35] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.62 (dd, *J* = 8.2, 0.5 Hz, 1H), 8.55 (d, *J* = 9.0 Hz, 1H), 8.02 (dt, *J* = 10.1, 5.0 Hz, 1H), 7.66 – 7.61 (m, 1H), 7.61 – 7.55 (m, 1H), 7.52 (s, 1H), 7.23 (dd, *J* = 9.0, 2.7 Hz, 1H), 7.19 (d, *J* = 2.6 Hz, 1H), 3.96 (s, 1H), 2.73 (d, *J* = 0.6 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 158.55, 133.62, 133.40, 131.26, 130.75, 126.59, 126.52, 125.73, 124.88, 124.33, 124.23, 122.72, 116.41, 108.21, 55.60, 20.28.



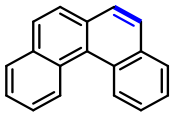
benzo[c]chrysene (33): The cyclization of **S29** was performed on 0.13 mmol scale with a total reaction time of 12 h. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 35 mg (96%) of **33** as a white solid. Spectroscopic data matched reported literature data.[37] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.07 (t, *J* = 8.3 Hz, 2H), 8.89 – 8.80 (m, 2H), 8.09 – 8.00 (m, 3H), 7.97 (d, *J* = 9.2 Hz, 1H), 7.94 – 7.86 (m, 2H), 7.77 – 7.62 (m, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 133.85, 131.83, 131.24, 130.77, 130.43, 130.27, 128.74, 128.71, 128.39, 128.27, 127.75, 127.26, 126.87, 126.85, 126.80, 126.64, 126.44, 126.31, 126.16, 123.57, 122.08.



2,4-dimethoxy-9-methylphenanthrene (34): The cyclization of **S12** was performed on 0.13 mmol scale with a total reaction time of 12 h at 50 °C. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 19 mg (57%) of **34** as a white solid. Starting material was not fully consumed in the reaction. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 9.61 (d, *J* = 8.6 Hz, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.62 (t, *J* = 7.7 Hz, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.50 (s, 1H), 6.85 (s, 1H), 6.74 (s, 1H), 4.10 (d, *J* = 1.5 Hz, 3H), 3.96 (d, *J* = 1.6 Hz, 3H), 2.71 (s, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 160.03, 158.39, 135.61, 133.85, 131.77, 130.92, 128.11, 127.29, 126.31, 125.07, 124.25, 115.16, 101.04, 98.95, 55.94, 55.58, 20.39. **IR** (cm^{-1}): 1613.2, 1572.0, 1449.7, 1345.8, 1325.2, 1208.3, 1158.8, 1104.8, 1062.2, 1004.8, 890.9, 802.5, 753.4, 717.9, 626.2. **HRMS**: Calculated for $C_{17}H_{17}O_2^+$ ($[M + H^+]^+$) : 253.1223 Found: 253.1224.

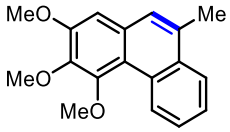


5-methylbenzo[b]naphtho[1,2-d]thiophene (35): The cyclization of **S11** was performed on 0.13 mmol scale with a total reaction time of 4 h at 50 °C and 20 mol% $FeCl_3$. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 20 mg (62%) of **35** as a pale yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.05 (d, *J* = 8.5 Hz, 1H), 8.83 (d, *J* = 8.3 Hz, 1H), 8.18 (d, *J* = 8.3 Hz, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.79 (s, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 2.82 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 139.56, 138.74, 137.08, 134.26, 131.51, 131.03, 128.01, 126.99, 125.67, 125.07, 125.01, 124.99, 124.63, 123.89, 123.42, 121.78, 20.44. **IR** (cm^{-1}): 2920.2, 1594.0, 1510.6, 1461.3, 1373.9, 1235.6, 1211.7, 1163.8, 886.0, 745.4. **HRMS**: calculated for $C_{17}H_{12}S$ $[M]^+$: 248.0660 found: 248.0662.

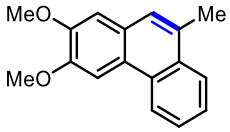


benzo[c]phenanthrene (36): The cyclization of **S7** was performed on 0.14 mmol scale with a total reaction time of 1 h. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 29 mg (89%) of **36** as a white solid. Spectroscopic data matched reported literature

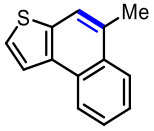
data.[38] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.16 (d, *J* = 8.5 Hz, 2H), 8.04 (d, *J* = 7.9 Hz, 2H), 7.92 (d, *J* = 8.5 Hz, 2H), 7.84 (d, *J* = 8.5 Hz, 2H), 7.72 – 7.68 (m, 2H), 7.64 (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 133.49, 130.97, 130.30, 128.52, 127.89, 127.45, 127.33, 126.83, 126.10, 125.83.



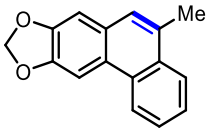
2,3,4-Trimethoxy-9-methylphenanthrene (37): The cyclization of **S13** was performed on 0.13 mmol scale (51 mg) with heating to 50°C for a total reaction time of 12 h. Purification by flash column chromatography eluting with hexanes/EtOAc provided 32 mg (87%) of **37** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.62 – 9.53 (m, 1H), 8.08 – 7.99 (m, 1H), 7.68 – 7.55 (m, 2H), 7.47 (s, 1H), 7.03 (s, 1H), 4.03 (s, 3H), 4.01 (s, 6H), 2.70 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 152.70, 152.61, 142.49, 132.52, 131.89, 130.35, 130.28, 127.21, 126.87, 126.56, 125.69, 124.43, 118.31, 104.79, 61.52, 60.47, 56.06, 20.30. **IR** (cm^{-1}): 1598.3, 1493.4, 1449.7, 1399.5, 1356.0, 1248.0, 1140.7, 1089.1, 1000.6, 890.2, 760.1, 750.5, 701.4. **HRMS**: Calculated for $C_{18}H_{19}O_3^+$: 283.1329 Found: 283.1329.



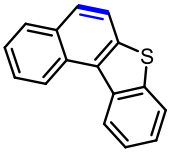
2,3-dimethoxy-9-methylphenanthrene (38): The cyclization of **S14** was performed on 0.13 mmol scale with a total reaction time of 12 h. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 28 mg (86%) of **38** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.56 (d, *J* = 7.9 Hz, 1H), 8.07 – 8.01 (m, 1H), 7.99 (s, 1H), 7.67 – 7.61 (m, 1H), 7.61 – 7.56 (m, 1H), 7.50 (s, 1H), 7.18 (s, 1H), 4.11 (s, 3H), 4.04 (s, 3H), 2.72 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 149.57, 148.98, 131.48, 130.94, 130.10, 127.33, 126.14, 126.06, 125.70, 125.00, 124.25, 122.72, 107.96, 103.53, 56.22, 56.11, 20.11. **IR** (cm^{-1}): 2935.6, 1604.6, 1504.5, 1463.5, 1437.4, 1391.4, 1251.0, 1216.2, 1193.9, 1154.7, 1021.6, 752.1. **HRMS**: calculated for $C_{17}H_{17}O_2$ ($[M + H^+]^+$): 253.1223, found: 253.1224.



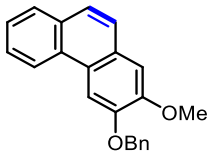
5-methylnaphtho[2,1-b]thiophene (39): The cyclization of **S22** was performed on 0.13 mmol scale with a total reaction time of 12 h 50 °C. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 13 mg (51%) of **39** as a white solid. Starting material decomposition was observed at elevated reaction temperatures Spectroscopic data matched reported literature data.[39] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.38 – 8.33 (m, 1H), 8.10 – 8.05 (m, 1H), 7.98 – 7.93 (m, 1H), 7.75 (s, 1H), 7.65 – 7.60 (m, 1H), 7.60 – 7.55 (m, 1H), 7.50 (d, *J* = 5.4 Hz, 1H), 2.77 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 137.48, 135.01, 131.42, 130.71, 129.58, 126.34, 125.36, 125.08, 124.71, 124.29, 122.19, 121.02, 20.25.



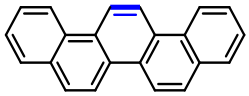
5-methylphenanthro[2,3-d][1,3]dioxole (40): The cyclization of **S16** was performed on 0.13 mmol scale with a total reaction time of 1 h. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 31 mg (99%) of **40** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.53 – 8.47 (m, 1H), 8.05 – 8.01 (m, 1H), 8.00 (s, 1H), 7.66 – 7.55 (m, 2H), 7.47 (s, 1H), 7.15 (s, 1H), 6.09 (s, 2H), 2.71 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 147.71, 147.68, 131.49, 131.01, 130.40, 128.58, 126.63, 126.13, 125.85, 125.79, 124.92, 122.98, 105.36, 101.39, 101.04, 20.04. **IR** (cm^{-1}): 2902.5, 1482.0, 1451.9, 1395.9, 1225.8, 1180.6, 1036.5, 938.4, 881.8, 847.4, 758.2, 701.0. **HRMS**: calculated for $C_{16}H_{13}O_2$ ($[M + H^+]^+$): 237.0910, found: 237.0910.



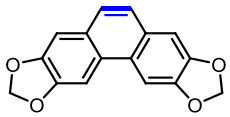
benzo[b]naphtho[1,2-d]thiophene (41): The cyclization of **S17** was performed on 0.13 mmol scale with a total reaction time of 6 h at 50 °C and 20 mol% $FeCl_3$. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 21 mg (67%) of **41** as a pale yellow solid. Spectroscopic data matched reported literature data.[40] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.02 (d, *J* = 8.5 Hz, 1H), 8.87 (d, *J* = 8.3 Hz, 1H), 8.03 (dd, *J* = 11.6, 8.3 Hz, 2H), 7.91 (q, *J* = 8.7 Hz, 2H), 7.75 (t, *J* = 7.7 Hz, 1H), 7.63 – 7.58 (m, 2H), 7.51 (t, *J* = 7.5 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 139.72, 138.60, 136.70, 131.92, 130.64, 129.44, 129.03, 127.84, 127.13, 125.21, 124.89, 124.80, 124.71, 123.20, 123.18, 121.07.



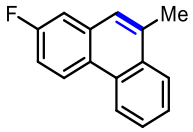
3-(benzyloxy)-2-methoxyphenanthrene (42): The cyclization of **S18** was performed on 0.13 mmol scale with a total reaction time of 12 h. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 31 mg (75%) of **42** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.54 (d, *J* = 8.3 Hz, 1H), 8.04 (s, *J* = 5.3 Hz, 1H), 7.86 (t, *J* = 8.3 Hz, 1H), 7.62 (m, 2H), 7.56 – 7.50 (m, 1H), 7.43 – 7.37 (m, 1H), 7.33 (dd, *J* = 13.5, 6.1 Hz, 1H), 7.29 (s, 1H), 5.32 (s, 1H), 4.12 (d, *J* = 3.6 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 150.05, 148.71, 137.05, 131.60, 129.91, 128.87, 128.85, 128.17, 127.57, 127.26, 126.38, 126.20, 125.80, 125.35, 122.38, 110.86, 103.95, 71.08, 56.34. **IR** (cm^{-1}): 2930.4, 1602.1, 1506.5, 1467.2, 1379.8, 1265.1, 1216.8, 1156.0, 1012.3, 855.1, 739.8, 695.6. **HRMS**: calculated for $C_{22}H_{19}O_2$ ($[M + NH_4^+]^+$): 332.1645, found: 332.1644.



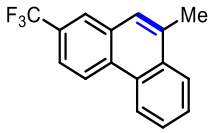
Picene (43): The cyclization of **S32** was performed on 0.13 mmol scale with a total reaction time of 12 h. Purification by preparative thin layer chromatography eluting with hexanes/EtOAc (4:1) provided 19 mg (53%) of **43** as a pale brown solid. Picene **43** is very insoluble in organic solvents. Spectroscopic data matched reported literature data.[41] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.97 (s, 2H), 8.87 (d, *J* = 8.4 Hz, 2H), 8.80 (d, *J* = 9.2 Hz, 2H), 8.03 (t, *J* = 9.0 Hz, 3H), 7.75 (t, *J* = 7.1 Hz, 2H), 7.67 (t, *J* = 7.3 Hz, 3H).



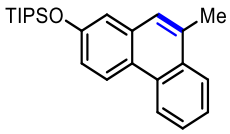
phenanthro[2,3-d:6,7-d']bis([1,3]dioxole) (44): The cyclization of **S19** was performed on 0.11 mmol scale with a total reaction time of 12 h. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 20 mg (68%) of **44** as a white solid. Spectroscopic data matched reported literature data.[42] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.50 (s, 1H), 7.18 (s, 1H), 6.08 (s, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 148.17, 147.20, 127.96, 126.56, 124.99, 105.70, 101.43, 100.66.



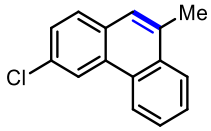
2-fluoro-9-methylphenanthrene (45): The cyclization of **S20** was performed on 0.14 mmol scale with a total reaction time of 12 h. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 26 mg (87%) of **45** as a white solid. Spectroscopic data matched reported literature data.[35] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.62 (dd, *J* = 14.5, 6.7 Hz, 1H), 8.06 (d, *J* = 8.1 Hz, 1H), 7.66 (qd, *J* = 13.6, 6.9 Hz, 1H), 7.55 – 7.48 (m, 1H), 7.49 – 7.39 (m, 1H), 7.32 (tt, *J* = 16.1, 8.1 Hz, 1H), 2.74 (s, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.63 (d, *J* = 245.8 Hz), 134.25, 133.62 (d, *J* = 8.7 Hz), 131.75, 130.38, 126.55, 126.48, 126.20 (d, *J* = 3.6 Hz), 125.02, 125.0 (d, *J*= 8.7), 123.02, 114.87 (d, *J* = 23.7 Hz), 112.03 (d, *J* = 20.3 Hz), 20.27.



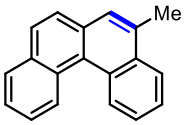
9-methyl-2-(trifluoromethyl)phenanthrene (46): The cyclization of **S21** was performed on 0.13 mmol scale with a total reaction time of 12 h. Purification by flash column chromatography eluting with hexanes/EtOAc (12:1) provided 31 mg (93%) of **46** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.73 (m, 3H), 8.13 – 8.06 (m, 2H), 7.78 (dd, *J* = 8.7, 1.4 Hz, 1H), 7.75 – 7.68 (m, 2H), 7.63 (s, 1H), 2.76 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 134.22, 132.74, 131.67, 131.29, 129.62, 128.32 (q, *J* = 32.2 Hz), 127.61, 126.76, 126.43, 125.07 (q, *J* = 4.2 Hz), 124.85, 124.45 (q, *J*= 271.3), 123.40, 123.31, 121.60 (q, *J* = 3.2 Hz). **IR** (cm^{-1}): 2923.3, 1361.7, 1331.8, 1279.8, 1200.6, 1165.7, 1114.1, 1075.8, 906.2, 825.4, 754.8, 723.6, 706.0. **HRMS**: Calculated for $C_{16}H_{11}F_3^+$ ($[M]^+$): 260.0813 found: 260.0813.



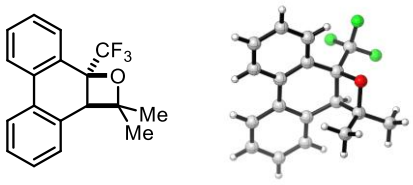
triisopropyl((9-methylphenanthren-2-yl)oxy)silane (47): The cyclization of **S15** was performed on 0.13 mmol scale with a total reaction time of 6 h at 50 °C. Purification by flash column chromatography eluting with hexanes/EtOAc (19:1) provided 15 mg (65% brsm) of **47** as a white solid and 10 mg of recovered **S15** (75% conv). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.61 (d, *J* = 8.2 Hz, 1H), 8.51 (d, *J* = 8.9 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 2.3 Hz, 1H), 7.19 (dd, *J* = 8.8, 2.4 Hz, 1H), 2.71 (s, 3H), 1.33 (h, *J* = 7.4 Hz, 3H), 1.15 (d, *J* = 7.5 Hz, 18H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.01, 133.68, 133.10, 131.34, 130.75, 126.48, 125.75, 124.86, 124.49, 124.15, 122.75, 120.49, 116.19, 20.26, 18.21, 12.98. **IR** (cm^{-1}): 2943.0, 2866.7, 1611.6, 1491.8, 1462.6, 1450.2, 1308.0, 1251.9, 1175.7, 967.9, 884.1, 858.6, 737.8. **HRMS**: Calculated for $C_{24}H_{32}OSi^+$ ($[M]^+$): 364.2222 found: 364.2230.



3-chloro-9-methylphenanthrene (48): The cyclization of **S23** was performed on 0.13 mmol scale with a total reaction time of 12 h. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 24 mg (92%) of **48** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.65 – 8.62 (m, 1H), 8.61 (d, *J* = 1.5 Hz, 1H), 8.08 – 8.04 (m, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.70 – 7.65 (m, 2H), 7.55 (s, 1H), 7.51 (dd, *J* = 8.4, 2.0 Hz, 1H), 2.73 (s, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 133.16, 132.50, 131.93, 130.97, 130.48, 129.62, 129.41, 127.37, 127.28, 126.73, 126.24, 124.96, 123.27, 122.41, 20.24. **IR** (cm^{-1}): 1750.7, 1594.9, 1491.1, 1445.6, 1429.2, 1410.0, 1371.0, 1214.3, 1160.8, 1093.6, 1065.2, 1019.4, 944.8, 870.6, 803.9, 743.7, 715.7, 684.1. **HRMS**: calculated for $C_{15}H_{11}Cl$ $[M]^+$: 226.0549 found: 226.0546.

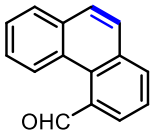


5-methylbenzo[c]phenanthrene (49): The cyclization of **S24** was performed on 0.12 mmol scale with a total reaction time of 12 h at 50 °C. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 14 mg (48%) of **49** as a yellow solid. Spectroscopic data matched reported literature data.[35] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.14 (d, *J* = 8.3 Hz, 1H), 9.08 (d, *J* = 8.5 Hz, 1H), 8.19 (d, *J* = 7.6 Hz, 1H), 8.01 (d, *J* = 7.9 Hz, 1H), 7.88 (d, *J* = 8.5 Hz, 1H), 7.77 (d, *J* = 8.5 Hz, 1H), 7.73 – 7.64 (m, 4H), 7.60 (t, *J* = 7.4 Hz, 1H), 2.82 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 133.45, 133.28, 130.99, 130.67, 130.43, 128.74, 128.60, 128.07, 127.70, 127.33, 126.66, 126.56, 126.29, 126.01, 125.86, 125.65, 124.64, 19.98.

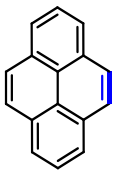


x-ray

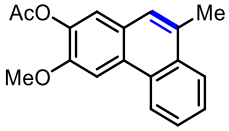
(2aR,10bS)-2,2-dimethyl-10b-(trifluoromethyl)-2a,10b-dihydro-2H-phenanthro[9,10-b]oxete (6): The cyclization of **S31** was performed on 0.13 mmol scale in PhMe with a total reaction time of 4 h. Purification by preparative thin layer chromatography eluting with hexanes/EtOAc (9:1) provided 17.8 mg (45%) of **6** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 7.9, 2.3 Hz, 2H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.48 (t, *J* = 7.0 Hz, 1H), 7.37 (t, *J* = 7.9 Hz, 2H), 7.29 (d, *J* = 7.4 Hz, 1H), 7.03 (d, *J* = 7.3 Hz, 1H), 4.34 (s, 1H), 1.66 (s, 3H), 1.02 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 132.78, 131.92, 130.34, 130.24, 129.72, 129.09, 128.93, 128.89, 128.68, 128.67, 123.71, 123.51, 88.47, 46.43, 30.76, 24.98. **IR** (cm^{-1}): 2924.2, 2851.2, 1449.9, 1303.9, 1259.8, 1227.9, 1154.4, 1019.4, 974.2, 940.1, 844.2, 774.4, 757.7, 738.5, 731.0. Unable to observe the trifluoromethyl quartet after 3000 scans. **HRMS**: calculated for $C_{17}H_{14}$ $[M]^+$: 304.1075 found: 304.1080.



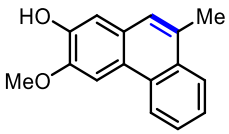
phenanthrene-4-carbaldehyde (50): The cyclization of **S26** was performed on 0.13 mmol scale with a total reaction time of 12 h. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 27 mg (90%) of **50** as a pale yellow solid. Spectroscopic data matched reported literature data.[40] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.69 (s, 1H), 8.14 – 8.07 (m, 3H), 8.00 (d, *J* = 7.1 Hz, 1H), 7.86 (d, *J* = 8.8 Hz, 1H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.75 – 7.68 (m, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.33, 135.53, 133.73, 133.46, 133.39, 130.68, 129.33, 128.87, 128.47, 128.20, 127.83, 127.03, 126.81, 126.33.



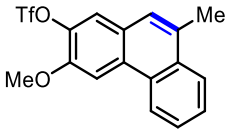
pyrene (51): The cyclization of **S37** was performed on 0.13 mmol scale with a total reaction time of 30 minutes. Purification by flash column chromatography eluting with hexanes/EtOAc provided 18 mg (70%) of **51** as an off-white solid. Spectroscopic data matched reported literature data.[44] **^{1}H NMR** (700 MHz, $CDCl_3$): δ 8.19 (d, *J* = 7.5 Hz, 2H), 8.09 (s, 2H), 8.02 (t, *J* = 7.5 Hz, 1H). **^{13}C NMR** (176 MHz, $CDCl_3$): δ 131.34, 127.61, 126.08, 125.16, 124.87.



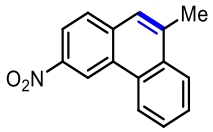
3-methoxy-9-methylphenanthren-2-yl acetate (52): The cyclization of **S34** was performed on 0.13 mmol scale with a total reaction time of 4 h. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 33 mg (90%) of **52** as a pale yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.62 – 8.57 (m, 1H), 8.08 (s, 1H), 8.07 – 8.03 (m, 1H), 7.67 – 7.62 (m, 2H), 7.47 (s, 2H), 4.06 (s, 3H), 2.71 (s, 3H), 2.40 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.42, 150.19, 140.31, 132.33, 131.22, 129.87, 128.82, 126.80, 126.68, 126.22, 126.05, 125.06, 123.16, 121.00, 104.54, 56.26, 20.99, 20.10. **IR** (cm^{-1}): 2938.3, 1761.7, 1620.9, 1607.1, 1503.6, 1463.4, 1440.0, 1366.9, 1254.9, 1211.1, 1195.4, 1135.2, 1027.7, 908.7, 754.2, 734.2, 624.9. **HRMS**: calculated for $C_{18}H_{17}O_3$ ($[M + H^+]^+$): 281.1172, found: 281.1172.



3-methoxy-9-methylphenanthren-2-ol (53): The cyclization of **S27** was performed on 0.13 mmol scale with a total reaction time of 12 h. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 24 mg (78%) of **53** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.54 (d, *J* = 8.1 Hz, 1H), 8.03 (d, *J* = 8.1 Hz, 1H), 7.98 (s, 1H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.46 (s, 1H), 7.28 (s, 1H), 5.90 (s, 1H), 4.12 (s, 3H), 2.71 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.81, 145.95, 131.42, 131.04, 130.24, 127.87, 126.14, 126.03, 125.62, 125.04, 124.04, 122.58, 111.05, 102.79, 56.25, 20.12. **IR** (cm^{-1}): 3396.0, 2932.2, 1529.5, 1503.2, 1438.0, 1246.4, 1216.6, 1157.6, 1029.4, 840.1, 750.0. **HRMS**: calculated for $C_{16}H_{15}O_2$ ($[M + H^+]^+$): 239.1067, found: 239.1064.

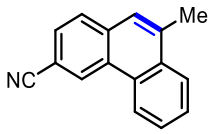


3-methoxy-9-methylphenanthren-2-yl trifluoromethanesulfonate (54): The cyclization of **S35** was performed on 0.13 mmol scale with a total reaction time of 2 h. Purification by flash column chromatography eluting with hexanes/EtOAc (10:1) provided 42 mg (87%) of **54** as a pale yellow solid **^{1}H NMR** (500 MHz, $cdcl_3$) δ 8.60 – 8.56 (m, 1H), 8.11 (s, 1H), 8.08 – 8.02 (m, 1H), 7.71 – 7.66 (m, 2H), 7.64 (m, 1H), 7.48 (s, 1H), 4.12 (s, 3H), 2.71 (s, 3H). ^{13}C NMR (125 MHz, $cdcl_3$) δ 149.40, 138.68, 132.45, 132.10, 129.92, 129.11, 127.26, 126.39, 126.13, 125.48, 124.95, 123.10, 120.66, 118.82 (q, *J*= 318.8), 105.13, 56.29, 19.84. **IR** (cm^{-1}): 2930.0, 1622.4, 1506.0, 1418.7, 1246.1, 1201.3, 1139.0, 1101.3, 1026.3, 968.0, 862.4, 755.5. **HRMS**: Calculated for $C_{17}H_{13}O_4F_3S^+$ ($[M]^+$): 370.0487 found: 370.0486.

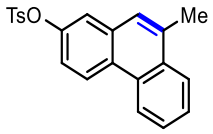


9-methyl-3-nitrophenanthrene (55): The cyclization of **S28** was performed on 0.13 mmol scale with a total reaction time of 12 h. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 26 mg (93%) of **55** as a pale yellow solid. **^{1}H NMR** (500 MHz,

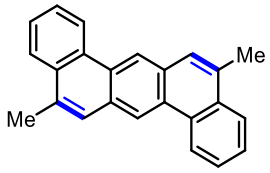
$CDCl_3$) δ 9.54 (s, 1H), 8.76 (d, *J* = 7.5 Hz, 1H), 8.34 (dd, *J* = 8.7, 2.2 Hz, 1H), 8.12 (d, *J* = 7.5 Hz, 1H), 7.89 (d, *J* = 8.7 Hz, 1H), 7.76 (pd, *J* = 7.0, 1.5 Hz, 2H), 7.64 (s, 1H), 2.79 (s, *J* = 0.7 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 145.64, 137.86, 135.93, 132.55, 130.53, 129.40, 129.05, 128.17, 127.75, 125.99, 125.29, 123.49, 120.72, 119.26, 20.57. **IR** (cm^{-1}): 3085.7, 1609.8, 1503.9, 1333.3, 1302.0, 1100.1, 889.2, 872.3, 750.0, 741.9, 710.4. **HRMS**: Calculated for $C_{15}H_{11}NO_2^+$ ($[M]^+$): 237.0790 found: 237.0786.



9-methylphenanthrene-2-carbonitrile (56): The cyclization of **S30** was performed on a 0.13 mmol scale with a total reaction time of 25 h. Purification by flash column chromatography eluting with hexanes/EtOAc provided 25 mg (90%) of **56** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.72 (d, *J* = 8.0 Hz, 2H), 8.16 (s, 1H), 8.11 (dd, *J* = 7.1, 1.9 Hz, 1H), 7.80 – 7.70 (m, 3H), 7.59 (s, 1H), 2.77 (s, 3H). ^{13}C NMR (176 MHz, $CDCsl_3$) δ 135.17, 133.26, 133.05, 132.41, 131.66, 129.58, 128.44, 127.46, 127.28, 125.90, 125.19, 123.80, 123.79, 119.55, 110.03, 20.32. **^{13}C NMR** (176 MHz, $CDCl_3$) δ 135.17, 133.26, 133.05, 132.41, 131.66, 129.58, 128.44, 127.46, 127.28, 125.90, 125.19, 123.80, 123.79, 119.55, 110.03, 20.32. **IR** (cm^{-1}): 2225.4, 1487.6, 1438.5, 1407.9, 1245.7, 1212.6, 1155.9, 892.0, 860.3, 825.1, 775.7, 751.3, 717.9, 622.7, 606.9. **HRMS**: calculated for $C_{16}H_{11}N$ ($[M+H^+]^+$): 218.0964 Found: 218.0960.



9-methylphenanthren-2-yl 4-methylbenzenesulfonate (57): The cyclization of **S36** was performed on 0.13 mmol scale with a total reaction time of 4 h. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 45 mg (96%) of **57** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.64 – 8.57 (m, 1H), 8.53 (d, *J* = 9.0 Hz, 1H), 8.07 – 8.01 (m, 1H), 7.74 (d, *J* = 8.1 Hz, 2H), 7.69 – 7.62 (m, 2H), 7.45 (d, *J* = 2.2 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 2H), 7.18 (dd, *J* = 9.0, 2.3 Hz, 1H), 2.71 (s, 3H), 2.44 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 148.20, 145.53, 134.28, 132.91, 132.63, 132.21, 130.00, 129.96, 128.78, 128.49, 127.13, 126.89, 126.28, 125.00, 124.46, 123.24, 120.41, 120.33, 21.92, 20.23. **IR** (cm^{-1}): 3065.9, 2925.3, 1611.2, 1597.2, 1491.1, 1448.8, 1368.6, 1189.6, 1177.0, 1091.5, 947.4, 829.6, 737.2. **HRMS**: calculated for $C_{22}H_{22}O_3NS^+$ ($[M + NH_4^+]^+$): 380.1315 found: 380.1312.

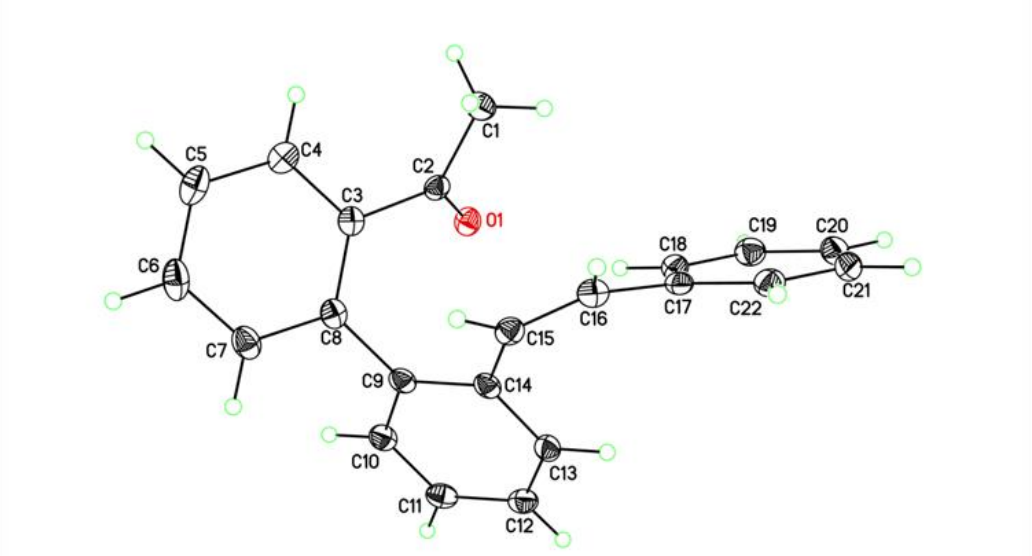


5,12-dimethylbenzo[k]tetraphene (59): The cyclization of **58** was performed on 0.075 mmol scale with a total reaction time of 4 h and 10 mol% $FeCl_3$. Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided 21 mg (90%) of **59** as a pale yellow

solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 9.03 (s, 2H), 8.89 (d, *J* = 7.9 Hz, 2H), 8.08 (d, *J* = 7.9 Hz, 2H), 7.79 (s, 2H), 7.73 (t, *J* = 7.4 Hz, 2H), 7.69 (t, *J* = 6.6 Hz, 2H), 2.78 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 132.55, 132.49, 130.59, 130.56, 129.04, 127.40, 127.10, 126.62, 124.97, 123.39, 121.31, 20.46. **IR** (cm^{-1}): 2920.0, 1628.1, 1438.4, 1273.5, 1028.7, 897.9, 859.4, 755.5, 700.5. **HRMS**: Calculated for $C_{24}H_{18}^{+}$ ($[M]^{+}$): 306.1409 found: 306.1401.

7. X-Ray Crystallographic Data

Structure Determination of (*Z*)-1-(2'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one (9) (CCDC 1505968)



Colorless block-like crystals of **(*Z*)-1-(2'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one** were grown from a hexane/ethyl acetate solution of the compound at 22 deg. C. A crystal of dimensions 0.16 x 0.16 x 0.14 mm was mounted on a Rigaku AFC10K Saturn 944+ CCD-based X-ray diffractometer equipped with a low temperature device and Micromax-007HF Cu-target micro-focus rotating anode (λ = 1.54187 A) operated at 1.2 kW power (40 kV, 30 mA). The X-ray intensities were measured at 85(1) K with the detector placed at a distance 42.00 mm from the crystal. A total of 2028 images were collected with an oscillation width of 1.0° in ω. The exposure

times were 1 sec. for the low angle images, 5 sec. for high angle. The integration of the data yielded a total of 12297 reflections to a maximum 2θ value of 136.43° of which 2831 were independent and 2729 were greater than 2σ(I). The final cell constants (Table 1) were based on the xyz centroids 5758 reflections above 10σ(I). Analysis of the data showed negligible decay during data collection; the data were processed with CrystalClear 2.0 and corrected for absorption. The structure was solved and refined with the Bruker SHELXTL (version 2014/6) software package, using the space group P1bar with Z = 2 for the formula $C_{22}H_{18}O$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0446 and wR2 = 0.1039 [based on I > 2sigma(I)], R1 = 0.0454 and wR2 = 0.1045 for all data. Additional details are presented in Table 1 and are given as Supporting Information in a CIF file. Acknowledgement is made for funding from NSF grant CHE-0840456 for X-ray instrumentation.

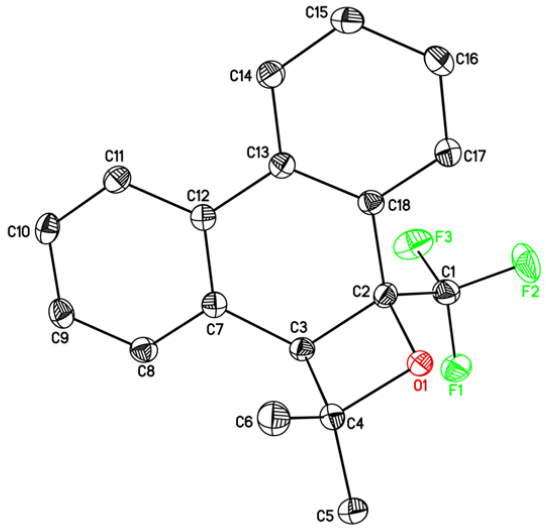
Sheldrick, G.M. SHELXTL, v. 2014/6; Bruker Analytical X-ray, Madison, WI, 2014.

CrystalClear Expert 2.0 r16, Rigaku Americas and Rigaku Corporation (2014), Rigaku Americas, 9009, TX, USA 77381-5209, Rigaku Tokyo, 196-8666, Japan.

Crystal data and structure refinement for **(*Z*)-1-(2'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one**

Identification code	**(*Z*)-1-(2'-styryl-[1,1'-biphenyl]-2-yl)ethan-1-one**
Empirical formula	C22 H18 O
Formula weight	298.36
Temperature	85(2) K
Wavelength	1.54178 A
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 7.85230(10) A alpha = 77.261(5) deg. b = 9.3906(2) A beta = 84.541(6) deg. c = 11.5779(8) A gamma = 71.939(5) deg.
Volume	791.35(6) A^3
Z, Calculated density	2, 1.252 Mg/m^3
Absorption coefficient	0.580 mm^-1
F(000)	316
Crystal size	0.160 x 0.160 x 0.140 mm
Theta range for data collection	3.916 to 68.215 deg.
Limiting indices	-9<=h<=9, -11<=k<=11, -13<=l<=13
Reflections collected / unique	12297 / 2831 [R(int) = 0.0465]
Completeness to theta = 67.679	97.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.925 and 0.843
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2831 / 0 / 210
Goodness-of-fit on F^2	1.122
Final R indices [I>2sigma(I)]	R1 = 0.0446, wR2 = 0.1039
R indices (all data)	R1 = 0.0454, wR2 = 0.1045
Extinction coefficient	0.077(3)
Largest diff. peak and hole	0.239 and -0.296 e.A^-3

Structure Determination of 2,2-dimethyl-10b-(trifluoromethyl)-2a,10b-dihydro-2H-phenanthro[9,10-b]oxete (6)



(CCDC 1505967)

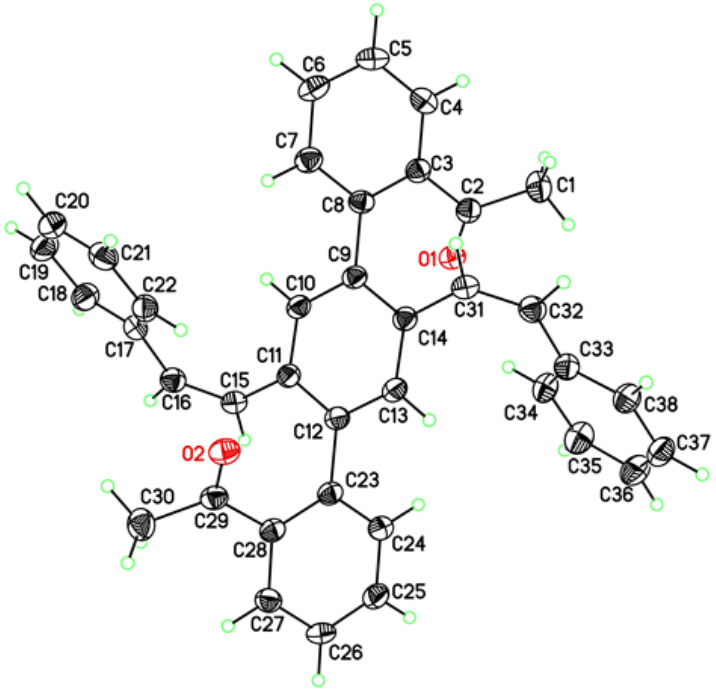
Colorless plates of **2,2-dimethyl-10b-(trifluoromethyl)-2a,10b-dihydro-2H-phenanthro[9,10-b]oxete** were grown from a dichloromethane solution of the compound at 22 deg. C. A crystal of dimensions 0.17 x 0.12 x 0.04 mm was mounted on a Rigaku AFC10K Saturn 944+ CCD-based X-ray diffractometer equipped with a low temperature device and Micromax-007HF Cu-target micro-focus rotating anode (λ = 1.54187 A) operated at 1.2 kW power (40 kV, 30 mA). The X-ray intensities were measured at 85(1) K with the detector placed at a distance 42.00 mm from the crystal. A total of 2028 images were collected with an oscillation width of 1.0° in ω. The exposure times were 1 sec. for the low angle images, 4 sec. for high angle. Rigaku d*trek images were exported to CrysAlisPro for processing and corrected for absorption. The integration of the data yielded a total of 21527 reflections to a maximum 2θ value of 138.38° of which 2617 were independent and 2584 were greater than $2\sigma(I)$. The final cell constants (Table 1) were based on the xyz centroids 17451 reflections above $10\sigma(I)$. Analysis of the data showed negligible decay during data collection; the data were processed with CrystalClear 2.0 and corrected for absorption. The structure was solved and refined with the Bruker SHELXTL (version 2014/6) software package, using the space group P2(1)/n with Z = 4 for the formula $C_{18}H_{15}OF_3$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0478 and wR2 = 0.1172 [based on I > 2sigma(I)], R1 = 0.0480 and wR2 = 0.1175 for all data. Additional details are presented in Table 1 and are given as Supporting Information in a CIF file. Acknowledgement is made for funding from NSF grant CHE-0840456 for X-ray instrumentation.
Sheldrick, G.M. SHELXTL, v. 2014/6; Bruker Analytical X-ray, Madison, WI, 2014.

CrystalClear Expert 2.0 r16, Rigaku Americas and Rigaku Corporation (2014), Rigaku Americas, 9009, TX, USA 77381-5209, Rigaku Tokyo, 196-8666, Japan.

CrysAlisPro 1.171.38.41 (Rigaku Oxford Diffraction, 2015).
Crystal data and structure refinement for **2,2-dimethyl-10b-(trifluoromethyl)-2a,10b-dihydro-2H-phenanthro[9,10-b]oxete**

Identification code	**2,2-dimethyl-10b-(trifluoromethyl)-2a,10b-dihydro-2H-phenanthro[9,10-b]oxete**
Empirical formula	C18 H15 F3 O
Formula weight	304.30
Temperature	85(2) K
Wavelength	1.54184 A
Crystal system, space group	Monoclinic, P2(1)/n
Unit cell dimensions	a = 7.88370(10) A alpha = 90 deg. b = 12.60220(10) A beta = 95.2380(10) deg. c = 14.49740(10) A gamma = 90 deg.
Volume	1434.33(2) A^3
Z, Calculated density	4, 1.409 Mg/m^3
Absorption coefficient	0.955 mm^-1
F(000)	632
Crystal size	0.170 x 0.120 x 0.040 mm
Theta range for data collection	4.658 to 69.189 deg.
Limiting indices	-9<=h<=9, -15<=k<=15, -17<=l<=17
Reflections collected / unique	21527 / 2617 [R(int) = 0.0536]
Completeness to theta = 67.684	98.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.91522
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2617 / 0 / 202
Goodness-of-fit on F^2	1.136
Final R indices [I>2sigma(I)]	R1 = 0.0478, wR2 = 0.1172
R indices (all data)	R1 = 0.0480, wR2 = 0.1175
Extinction coefficient	0.0278(14)
Largest diff. peak and hole	0.326 and -0.401 e.A^-3

Structure Determination for **1,1'-(2',5'-di((*Z*)-styryl)-[1,1':4',1''-terphenyl]-2,2''-diyl)bis(ethan-1-one)**



(CCDC 1530039)

Colorless block-like crystals of **1,1'-(2',5'-di((*Z*)-styryl)-[1,1':4',1''-terphenyl]-2,2''-diyl)bis(ethan-1-one)** were grown from a dichloromethane/hexane solution of the compound at 22 deg. C. A crystal of dimensions 0.21 x 0.11 x 0.10 mm was mounted on a Rigaku AFC10K Saturn 944+ CCD-based X-ray diffractometer equipped with a low temperature device and Micromax-007HF Cu-target micro-focus rotating anode (λ = 1.54187 A) operated at 1.2 kW power (40 kV, 30 mA). The X-ray intensities were measured at 85(1) K with the detector placed at a distance 42.00 mm from the crystal. A total of 2028 images were collected with an oscillation width of 1.0° in ω. The exposure times were 1 sec. for the low angle images, 5 sec. for high angle. Rigaku d*trek images were exported to CrysAlisPro for processing and corrected for absorption. The integration of the data yielded a total of 41858 reflections to a maximum 2θ value of 138.66° of which 5089 were independent and 4803 were greater than 2σ(I). The final cell constants (Table 1) were based on the xyz centroids 21176 reflections above 10σ(I). Analysis of the data showed negligible decay during data collection. The structure was solved and refined with the Bruker SHELXTL (version 2014/6) software package, using the space group P2(1)/n with Z = 4 for the formula $C_{38}H_{30}O_2$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0597 and wR2 = 0.1647 [based on I > 2sigma(I)], R1 = 0.0615 and wR2 = 0.1673 for all data. Additional details are presented in Table 1 and are given as Supporting Information in a CIF file. Acknowledgement is made for funding from NSF grant CHE-0840456 for X-ray instrumentation.

Sheldrick, G.M. SHELXTL, v. 2014/6; Bruker Analytical X-ray, Madison, WI, 2014.

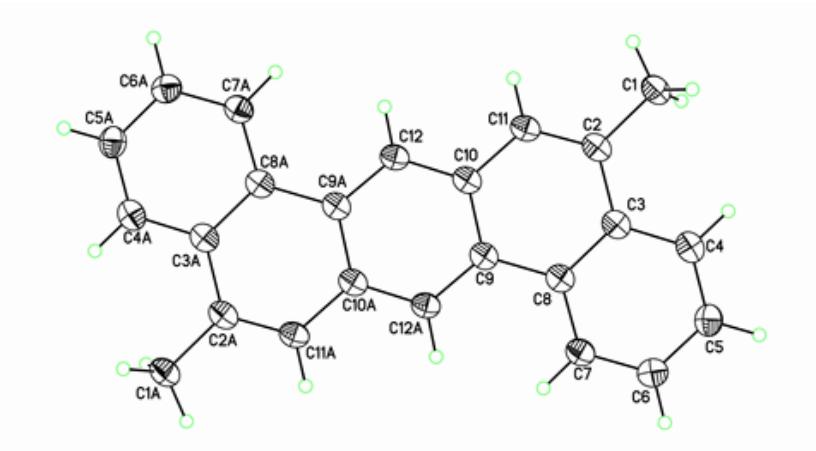
CrystalClear Expert 2.0 r16, Rigaku Americas and Rigaku Corporation (2014), Rigaku Americas, 9009, TX, USA 77381-5209, Rigaku Tokyo, 196-8666, Japan.

CrysAlisPro 1.171.38.41 (Rigaku Oxford Diffraction, 2015).

Crystal data and structure refinement for **1,1''-(2',5'-di((*Z*)-styryl)-[1,1':4',1''-terphenyl]-2,2''-diyl)bis(ethan-1-one)**

Identification code	**1,1''-(2',5'-di((*Z*)-styryl)-[1,1':4',1''-terphenyl]-2,2''-diyl)bis(ethan-1-one)**
Empirical formula	C38 H30 O2
Formula weight	518.62
Temperature	85(2) K
Wavelength	1.54184 A
Crystal system, space group	Monoclinic, P2(1)/n
Unit cell dimensions	a = 10.62617(10) A alpha = 90 deg. b = 19.11003(16) A beta = 90.5435(8) deg. c = 13.49063(11) A gamma = 90 deg.
Volume	2739.37(4) A^3
Z, Calculated density	4, 1.257 Mg/m^3
Absorption coefficient	0.590 mm^-1
F(000)	1096
Crystal size	0.210 x 0.110 x 0.100 mm
Theta range for data collection	4.011 to 69.330 deg.
Limiting indices	-12<=h<=12, -23<=k<=22, -16<=l<=16
Reflections collected / unique	41858 / 5089 [R(int) = 0.0539]
Completeness to theta = 67.684	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.84698
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5089 / 0 / 364
Goodness-of-fit on F^2	1.035
Final R indices [I>2sigma(I)]	R1 = 0.0597, wR2 = 0.1647
R indices (all data)	R1 = 0.0615, wR2 = 0.1673
Extinction coefficient	0.0013(3)
Largest diff. peak and hole	0.581 and -0.346 e.A^-3

Structure Determination for **5,12-dimethylbenzo[k]tetraphene**



(CCDC 1530358)

Yellow plates of **5,12-dimethylbenzo[k]tetraphene** were grown from a dichloromethane/hexane solution of the compound at 22 deg. C. A crystal of dimensions 0.17 x 0.11 x 0.11 mm was mounted on a Rigaku AFC10K Saturn 944+ CCD-based X-ray diffractometer equipped with a low temperature device and Micromax-007HF Cu-target micro-focus rotating anode (λ = 1.54187 A) operated at 1.2 kW power (40 kV, 30 mA). The X-ray intensities were measured at 85(1) K with the detector placed at a distance 42.00 mm from the crystal. A total of 2028 images were collected with an oscillation width of 1.0° in ω. The exposure times were 1 sec. for the low angle images, 4 sec. for high angle. Rigaku d*trek images were exported to CrysAlisPro for processing and corrected for absorption. The integration of the data yielded a total of 22025 reflections to a maximum 2θ value of 138.26° of which 1452 were independent and 1420 were greater than 2σ(I). The final cell constants (Table 1) were based on the xyz centroids 14219 reflections above 10σ(I). Analysis of the data showed negligible decay during data collection. The structure was solved and refined with the Bruker SHELXTL (version 2014/6) software package, using the space group Pbca with Z = 4 for the formula $C_{24}H_{18}$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. The molecule lies on an inversion center of the crystal lattice. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0399 and wR2 = 0.0975 [based on I > 2sigma(I)], R1 = 0.0404 and wR2 = 0.0979 for all data. Additional details are presented in Table 1 and are given as Supporting Information in a CIF file. Acknowledgement is made for funding from NSF grant CHE-0840456 for X-ray instrumentation.

Sheldrick, G.M. SHELXTL, v. 2014/6; Bruker Analytical X-ray, Madison, WI, 2014.

CrystalClear Expert 2.0 r16, Rigaku Americas and Rigaku Corporation (2014), Rigaku Americas, 9009, TX, USA 77381-5209, Rigaku Tokyo, 196-8666, Japan.

CrysAlisPro 1.171.38.41 (Rigaku Oxford Diffraction, 2015).

Crystal data and structure refinement for **5,12-dimethylbenzo[k]tetraphene**

Identification code	ccm530
Empirical formula	C24 H18
Formula weight	306.38
Temperature	85(2) K
Wavelength	1.54184 A
Crystal system, space group	Orthorhombic, Pbca
Unit cell dimensions	a = 13.92565(12) A alpha = 90 deg. b = 6.76441(5) A beta = 90 deg. c = 16.55751(12) A gamma = 90 deg.
Volume	1559.70(2) A^3
Z, Calculated density	4, 1.305 Mg/m^3
Absorption coefficient	0.556 mm^-1
F(000)	648
Crystal size	0.170 x 0.110 x 0.110 mm
Theta range for data collection	5.343 to 69.132 deg.
Limiting indices	-16<=h<=16, -8<=k<=8, -20<=l<=20
Reflections collected / unique	22025 / 1452 [R(int) = 0.0537]
Completeness to theta = 67.684	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.88200
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1452 / 0 / 111
Goodness-of-fit on F^2	1.122
Final R indices [I>2sigma(I)]	R1 = 0.0399, wR2 = 0.0975
R indices (all data)	R1 = 0.0404, wR2 = 0.0979
Extinction coefficient	0.0197(14)
Largest diff. peak and hole	0.226 and -0.285 e.A^-3

Appendix 2

Carbonyl-Olefin Metathesis of Alkyl Ketones – Experimental Details

FT-IR Experiments

Transmission IR spectra were recorded on a Nicolet iS10 FT-IR Spectrometer using 0.25 mm path length KBr solution cell.

IR measurements of compound 29 with A) no additive, B) 1 equiv $FeCl_3$ and 3) 2 equiv $FeCl_3$.

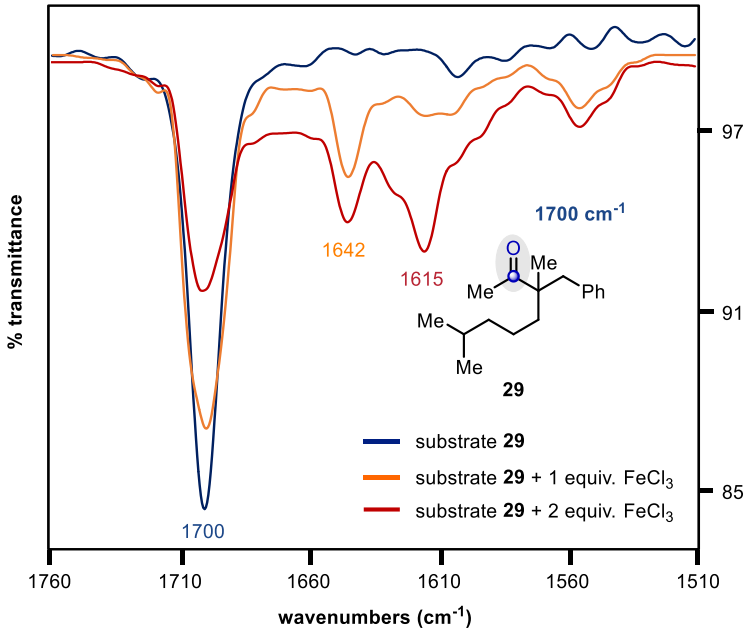


Figure A2-1: IR Spectra of 29 with $FeCl_3$

Compound 29 + no additive: To a 1 dram vial was added **29** (5.0 mg, 0.02 mmol) along with 2 mL of DCE. Then, 100 µL of this solution was transferred *via* syringe into a transmission IR solution cell and the IR spectrum was immediately recorded.

Compound 29 + 1 equiv $FeCl_3$: To a 1 dram vial was added **29** (5.0 mg, 0.02 mmol) along with 1 mL of DCE. The resultant solution was then added to a mixture of $FeCl_3$ (3.3 mg, 0.02 mmol) in DCE (1 mL). Then, 100 µL of this homogenous solution was transferred *via* syringe into a transmission IR solution cell and the IR spectrum was immediately recorded.

Compound 29 + 2 equiv $FeCl_3$: To a 1 dram vial was added **29** (5.0 mg, 0.02 mmol) along with 1 mL of DCE. The resultant solution was then added to a mixture of $FeCl_3$ (6.6 mg, 0.04 mmol) in DCE (1 mL). Then, 100 µL of this homogenous solution was transferred *via* syringe into a transmission IR solution cell and the IR spectrum was immediately recorded.

IR measurements of compound 29 with A) no additive, B) 0.5 equiv $FeCl_3$ + 0.5 equiv $FeBr_3$ and 3) 1 equiv $FeCl_3$ + 1 equiv $FeBr_3$.

EPR Experiments

Electronic Paramagnetic Resonance Spectroscopy were performed on a Bruker X-band EMX spectrometer equipped with an Oxford instruments liquid helium cryostat. Samples were all prepared as 50 μM (with respect to $FeCl_3$) solutions in degassed 1, 2-dichloroethane (freeze-pump-thaw) and were frozen in liquid nitrogen. All samples were acquired using ~20 mW microwave power and 100 kHz field modulation with amplitude set to 5 G. Raw data were worked up using the program SpinCount (version 2.2.40), written by Prof. Michael Hendrich, Carnegie Mellon University.

When increasing the concentration of reduced substrate **29** relative to $FeCl_3$, a stock solution of 1:1 $FeCl_3$:**29** was prepared and filtered through a cotton plug to remove any heterogeneous $FeCl_3$ before additional equivalents of **29** were added to the samples. This same stock solution was used for all samples. This ensures that any changes in the signals observed are a result of changing equilibrium between $FeCl_3$ and **29** in solution.

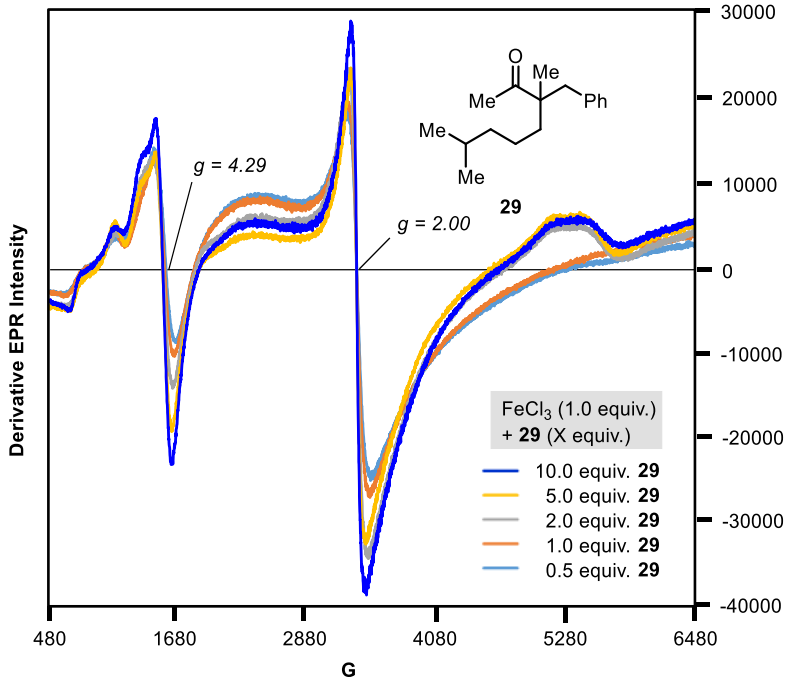


Figure A2-2: EPR Spectra of 29 and FeCl3.

High-spin EPR spectra with g = 4.29 are obtained for all ratios of **29** to $FeCl_3$, consistent with a Fe^{3+} species. Addition of an excess of aliphatic ketone **29** displays an increase in signal strength, indicating that iron coordinated-complex **30** is the major species in solution. We propose that an equilibrium exists between carbonyl-coordinated $FeCl_3$ species **30** and **31**. While $FeCl_3$-dimer species **31** is EPR-silent, the $FeCl_3$-monomer species **30** is EPR-active and displays an increasingly more intense signal with the addition of **29**, indicating that **30** is the major species in solution.

Raman Experiments

Conventional Raman spectra were collected using a Renishaw inVia Raman microscope equipped with a Leica microscope, RenCam CCD detector, 532 nm Kr+ laser, 1800 lines/nm grating, and 50 μm slit. Spectra were collected in extended scan mode in the range of 3600-100 cm^{-1} and then analyzed using the Wire 3.1 software package.

Solutions of the following were prepared (with 10 mL DCE) and transferred to 1 dram vials and directly submitted to Raman spectroscopic experimentation:

- $FeCl_3$ (8.228 mg, 0.051 mmol)
- 1 equiv $FeCl_3$ (8.228 mg, 0.051 mmol) + Reduced Substrate **29** (12.50 mg, 0.051 mmol)
- 2 equiv $FeCl_3$ (16.460 mg, 0.101 mmol) + Reduced Substrate **29** (12.50 mg, 0.051 mmol)
- Et_4NFeCl_4 (16.63 mg, 0.051 mmol)
- Et_4NCl (8.407 mg, 0.051 mmol)
- DCE
- 0.5 equiv $FeCl_3$ (8.228 mg, 0.051 mmol) + 0.5 equiv $FeBr_3$ (15.073 mg, 0.051 mmol)
- 0.5 equiv $FeCl_3$ (4.114 mg, 0.026 mmol) + 0.5 equiv $FeBr_3$ (7.537 mg, 0.026 mmol) + Reduced Substrate **29** (12.50 mg, 0.051 mmol)

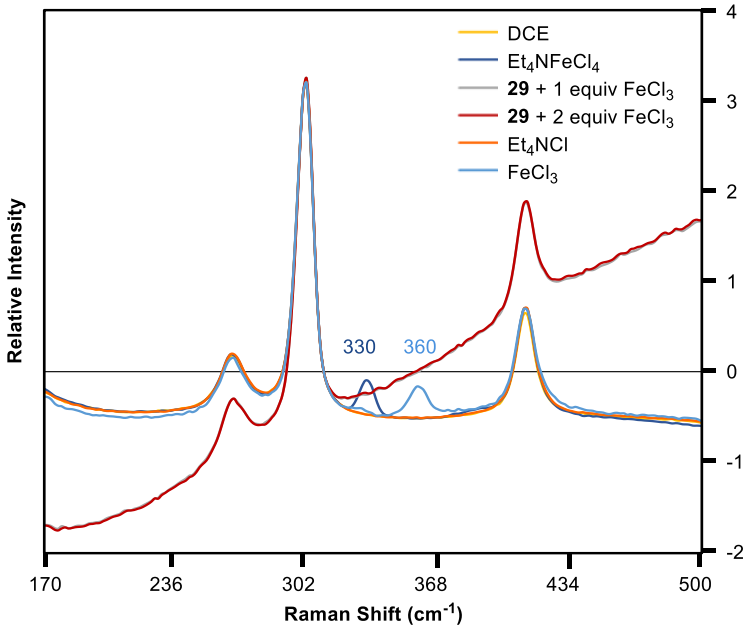


Figure A2-3: Raman Spectra of 29 and $FeCl_3$.

Raman spectroscopic experiments display prominent shifts for $FeCl_3$ and $FeCl_4^-$ in DCE at 360 and 330 cm^{-1}, respectively. The addition of substrate **29**, at 1 and 0.5 equivalents, does not afford a shift correlating to $FeCl_4^-$, but displays some fluorescence, due to presence of organic substrate, skewing measured spectra. Control spectra were taken for Et_4NCl, counterion of $FeCl_4$-, and DCE, the solvent, and both do not interfere with characteristic $FeCl_4^-$ shift.

Kinetic Experiments[159]

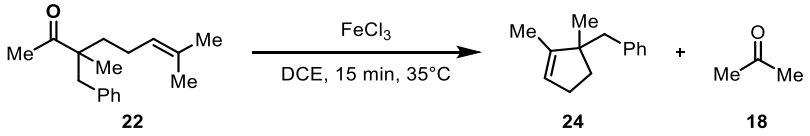
Procedure for Kinetic Analysis:

A 10 mL RBF was flame-dried and was charged with FeCl3 (0.99 mg, 0.025 equiv, 0.99 mg, 0.05 equiv or 1.99 mg, 0.10 equiv) under inert atmosphere and a small stir bar. The flask was sealed with a rubber septa and transferred to a fume hood where it was flushed with N2 gas. The flask was heated to 35°C and anhydrous 1,2-dichloroethane (DCE) was added (4.00 mL for 2.5 mol%, or 2.00 mL for 5 and 10 mol%). The reaction mixture was stirred for 15 minutes at 35°C, at which point the reaction was clear and pale yellow in color. The substrate (60 mg, 0.246 mmol for 2.5 mol% or 30 mg, 0.123 mmol for 5 and 10 mol%) was added in 1 mL or 0.5 mL of DCE and approx. 25-50 μL of the reaction was immediately withdrawn for the zero timepoint and was charged into a separate vial, of which 10 μL was immediately removed and inserted into a GC vial with a 2:1 mixture of acetonitrile and methanol to quench the reaction. This process of withdrawing an aliquot and then adding 10 μL of the reaction mixture to prepared GC vials was repeated every minute for 15 minutes in total. Dodecane was used as the internal standard.
GC vial preparation for quenching: Sample GC vials were prepared by adding 465 μL of a 2:1 mixture of acetonitrile and methanol and 25 μL of a 5mM solution of dodecane in acetonitrile. When an aliquot is withdrawn from the reaction mixture, 10 μL is added to the prepared GC vial and shaken immediately to efficiently quench $FeCl_3$ in the reaction mixture. Samples were analyzed via gas chromatography (GC) on a Shimadzu GC-2010 Plus system using a Shimadzu SHRXI-5MS column.

Rate Order:
The rate order for $FeCl_3$ in the aliphatic carbonyl-olefin metathesis reaction of substrate **22** were determined using the following equation, where *y* = order and *m* = slope.

$$\ln\left(\frac{m_{10\ mol\%}}{m_{5\ mol\%}}\right) = y \ln\left(\frac{concentration_{10\ mol\%}}{concentration_{5\ mol\%}}\right)$$

Kinetic Studies:
Effect of catalyst loading.
The effect of $FeCl_3$ concentration upon reaction rate was determined. Analysis of the reaction rate of 5 mol% and 10 mol% of $FeCl_3$ confirmed the reaction is 1.8±0.09 order in $FeCl_3$. Analysis of the reaction rate of 2.5 mol% and 5 mol% of $FeCl_3$ confirmed the reaction is 1.7±0.06 order in $FeCl_3$.



22 24 18

[159] Baxter, R.D., Sale, D., Engle, K.M., Yu, J., Blackmond, D.G. Mechanistic Rationalization of Unusual Kinetics in Pd-Catalyzed C-H Olefination. *J. Am. Chem. Soc.* **134**, 4600-4606 (2012).

Table A2-1. Raw Data for kinetic analysis of $FeCl_3$ in aliphatic carbonyl-olefin metathesis reaction.

$FeCl_3$ Loading	10 mol%	5 mol%	2.5 mol%	$FeCl_3$ Loading	10 mol%	5 mol%	2.5 mol%
Time (s)	**22** (M)	**22** (M)	**22** (M)	Time (s)	**22** (M)	**22** (M)	**22** (M)
0	0.00083	0.00092	0.00104	0	0.00083		
60	0.00075	0.00085	0.00103	60	0.00075		
120	0.00068	0.00079	0.00102	120	0.00068	0.00079	
180	0.00060	0.00077	0.00101	180	0.00060	0.00077	0.00101
240	0.00052	0.00075	0.00100	240	0.00052	0.00075	0.00100
300	0.00049	0.00073	0.00100	300	0.00049	0.00073	0.00100
360	0.00043	0.00070	0.00099	360	0.00043	0.00070	0.00099
420	0.00040	0.00067	0.00099	420		0.00067	0.00099
480	0.00038	0.00066	0.00098	480		0.00066	0.00098
540	0.00035	0.00065	0.00098	540		0.00065	0.00098
600	0.00033	0.00063	0.00097	600		0.00063	0.00097
660	0.00031	0.00061	0.00096	660		0.00061	0.00096
720	0.00030	0.00060	0.00096	720		0.00060	0.00096
780	0.00029	0.00058	0.00095	780		0.00058	0.00095
840	0.00029	0.00058	0.00093	840			
900	0.00028	0.00056	0.00092	900			

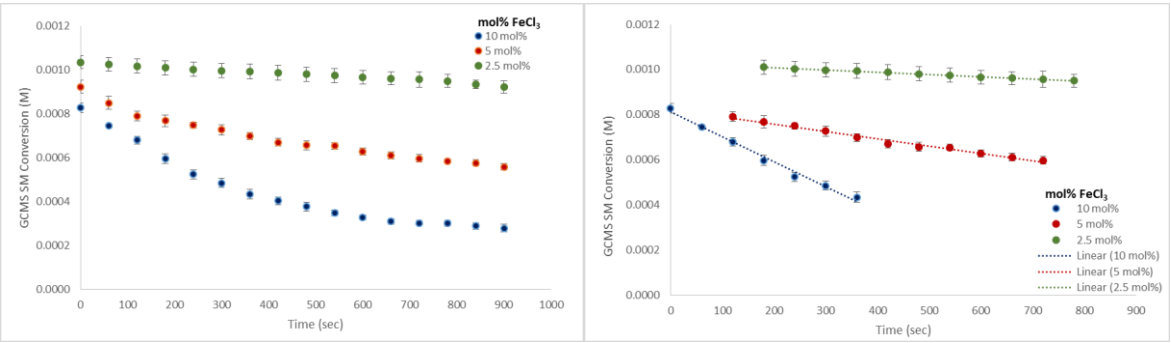


Figure A2-4. Concentration variation of $FeCl_3$ on the aliphatic carbonyl-olefin metathesis reaction over 15 minutes (left) and the linear portions for initial rate analysis (right).

Table A2-2. Trendline data for the linear portion of the reaction.

$FeCl_3$ Loading	10 mol%	5 mol%	2.5 mol%
Slope	-1.11e-06 ± 5.41e-08	-3.16e-07 ± 1.22e-08	-9.99e-08 ± 1.78e-09
y-intercept	8.13e-04 ± 1.17e-05	8.20e-04 ± 6.05e-06	1.03e-03 ± 9.20e-07
R^2	0.98820556	0.98528223	0.9971475

Computational Experiments

Experimental Details

Geometry optimizations were performed using the UB97-D density functional[160], and the double-ζ, polarized basis set, 6-31G*[161] as implemented in the Q-Chem 4.0 program package[162]. The spin multiplicity was fixed at 6 (hextet) when one equivalent of iron was present, and 11 when two

equivalents were present. The CPCM model[163] was used in single point computations to correct for solvent effects in 1, 2-dichloroethane. Frequency computations gave thermodynamic corrections in the rigid rotor, harmonic oscillator approximation at 298 K. In these corrections, low frequencies were reassigned to 50 cm^{-1} due to their high anharmonicity, which has no effect on enthalpies because the low frequency limit of H for a harmonic oscillator is equal to kT, and is not a function of frequency.

Reaction path optimization was performed via the Growing String Method[164,165,166] (GSM), using double and single-ended strategies. GSM performs minimum energy reaction path optimization and exact transition state searches. GSM strings were considered converged when the RMS gradient on the transition state node fell below 0.0005 Hartree/Å. Note that because GSM performs a minimum energy path search that contains the transition state, this calculation serves as a replacement for the intrinsic reaction coordinate (IRC) path, which is simply a minimum energy path in mass-weighted coordinates. This procedure provides strong evidence that the reported transition states connect to the string endpoints[14]. After the initial GSM computation, transition states were reoptimized using the default transition state optimizer in Q-Chem to provide refined energetics and structures.

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XYZ Structures

Iron Dimer Reactant Complex
50

C	-0.75815511	-5.45680815	3.75045108
C	-0.01563746	-5.47782856	2.55900791
C	0.01087425	-4.34908356	1.72720254
C	-0.70742142	-3.18454954	2.06448693
C	-1.43621567	-3.17224656	3.26915256
C	-1.46544584	-4.29788724	4.10623282
C	-0.68375289	-1.98131072	1.14328987
C	-1.80665654	-1.98145123	0.05532350
C	-1.67372096	-3.24616105	-0.85637883
C	-1.61190592	-0.81429222	-0.90431439
O	-0.51512941	-0.17992274	-0.86619125
Fe	0.61851475	1.00330113	-1.89955060
Cl	1.22260874	2.65028481	-0.61558579
C	-2.54678672	-0.57503904	-2.05571195
C	-3.22748177	-2.00445954	0.68530774
C	-3.56959587	-0.76308772	1.54775186
C	-3.53060035	0.48720156	0.71870114
C	-2.62267703	1.49448679	0.77184103
C	-1.49375450	1.58052892	1.76833527
Cl	2.48312994	-0.32431933	-2.24759134
Cl	-0.30544022	1.64709373	-3.74336726
C	-2.65831257	2.60231644	-0.25156793
H	-3.53482727	-1.01525492	-1.88713474
H	-2.09174667	-1.03838263	-2.94819710
H	-2.62927436	0.50096222	-2.25331896
H	-3.28611526	-2.91282179	1.30351226
H	-3.98005994	-2.11379031	-0.11121570
H	-0.77024128	-1.05465213	1.72593172
H	0.28510053	-1.94220663	0.62603179
H	-0.69156954	-3.28411529	-1.34779584
H	-1.78724847	-4.13151893	-0.21578221
H	-2.45460145	-3.26209999	-1.63004423
H	-4.58124551	-0.91541883	1.96252093
H	-2.87855695	-0.70464730	2.39816190
H	-4.30202129	0.54990428	-0.05666910
H	-3.50211540	2.49230868	-0.94899118
H	-1.71696992	2.61305603	-0.82965831
H	-2.72291664	3.59096687	0.23403649
H	-1.38622151	2.61466350	2.13367911
H	-1.62779720	0.91964734	2.63574680
H	-0.53906229	1.32121378	1.28110713
H	-1.97431913	-2.26863128	3.56213489
H	0.59871909	-4.36301412	0.80671301
H	0.55039832	-6.36896452	2.28063626
H	-2.03330462	-4.26566396	5.03828866
H	-0.77584343	-6.33287234	4.40157991
Fe	2.12489365	-1.66767717	-4.24515826
Cl	2.43396080	-0.36132761	-5.94318865
Cl	3.58073713	-3.26915415	-4.04692936
Cl	0.04773716	-2.37329694	-4.00710709

Fe Dimer First TS
50

C	-0.34438251	-5.46949949	3.42705877
C	0.29407851	-5.39787941	2.17874107
C	0.18266503	-4.24091269	1.39397806
C	-0.57410287	-3.13950494	1.83945949
C	-1.19511005	-3.21669885	3.10243933
C	-1.08646880	-4.37188311	3.89094151
C	-0.71814845	-1.90278420	0.97855280
C	-1.95041986	-1.93123520	0.00918184
C	-1.75680809	-3.05011798	-1.03008871
C	-2.11927978	-0.50572321	-0.66573768
O	-0.91772855	0.25591457	-0.65950349
Fe	0.32169631	1.07123965	-1.72128393
Cl	1.13695672	2.73508762	-0.47906791
C	-2.73100555	-0.53458619	-2.06048110
C	-3.28047119	-2.10490811	0.77514811
C	-3.52119335	-0.74983095	1.46864999
C	-3.17157565	0.27284170	0.37428254
C	-2.38191057	1.47662255	0.64064952
C	-1.49922798	1.67555610	1.80702989
Cl	2.15335485	-0.36118989	-2.03395127
Cl	-0.53542860	1.85396319	-3.57100066
C	-2.53425401	2.63357540	-0.27596843
H	-3.67009100	-1.10621299	-2.05633197
H	-2.02554531	-1.01313236	-2.75429621
H	-2.92004424	0.48415881	-2.42553561
H	-3.23976096	-2.94602509	1.48008121
H	-4.08971811	-2.30450799	0.05329729
H	-0.78276455	-1.01742532	1.62544837
H	0.18027150	-1.76942485	0.35959072
H	-0.86569557	-2.87882783	-1.64831169
H	-1.62539246	-4.00467317	-0.50188222
H	-2.62843031	-3.14271739	-1.69378962
H	-4.55518109	-0.61598747	1.81927675
H	-2.85746469	-0.65938083	2.33802594
H	-4.05446058	0.53734867	-0.22435057
H	-2.88386002	2.33515359	-1.27184287
H	-1.61516602	3.23318594	-0.33785623
H	-3.32393995	3.26994764	0.17490345
H	-1.80125801	2.61068796	2.31375624
H	-1.48326902	0.84539734	2.51828581
H	-0.48079839	1.87432491	1.42223420
H	-1.75988894	-2.35811838	3.47700561
H	0.69322004	-4.18450722	0.43160656
H	0.88757229	-6.23956340	1.81627017
H	-1.57260611	-4.41140189	4.86829218
H	-0.25580580	-6.36938748	4.03906829
Fe	1.86598096	-2.26888879	-3.47135431
Cl	3.52703408	-2.23663160	-4.86558382
Cl	1.88123712	-4.00650521	-2.13269898
Cl	-0.09082747	-1.98818014	-4.42204147

Fe Dimer Oxetane Intermediate

50

C -0.304415 -5.476787 3.421441
C 0.293353 -5.396699 2.152742
C 0.144322 -4.238418 1.377042
C -0.609023 -3.145731 1.850711
C -1.186341 -3.230847 3.133638
C -1.040524 -4.387351 3.913345
C -0.790965 -1.908326 1.000420
C -2.045069 -1.947274 0.060072
C -1.901295 -3.115008 -0.930800
C -2.279337 -0.556367 -0.633813
O -1.145939 0.463917 -0.407220
Fe 0.370521 0.993933 -1.529667
Cl 1.399773 2.568414 -0.436276
C -2.647873 -0.588122 -2.100323
C -3.355070 -2.048648 0.893779
C -3.574662 -0.633353 1.477630
C -3.200271 0.280962 0.291494
C -2.093195 1.368946 0.394567
C -1.478389 1.712015 1.740470
Cl 1.707245 -0.873037 -1.579747
Cl -0.255867 1.592813 -3.508838
C -2.390657 2.620693 -0.424180
H -3.552622 -1.204081 -2.213606
H -1.858756 -1.039275 -2.714650
H -2.862744 0.421181 -2.473603
H -3.284748 -2.834803 1.657991
H -4.190472 -2.307587 0.220368
H -0.853011 -1.028934 1.652188
H 0.092710 -1.771548 0.366270
H -1.005459 -3.001506 -1.557596
H -1.813161 -4.057196 -0.372331
H -2.773897 -3.195998 -1.594108
H -4.604932 -0.465019 1.821259
H -2.908501 -0.473002 2.335718
H -4.094222 0.658756 -0.224441
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H -1.496756 3.254913 -0.516910
H -3.171042 3.198746 0.095907
H -2.182542 2.354642 2.291969
H -1.259225 0.829286 2.353133
H -0.544415 2.272880 1.591012
H -1.745162 -2.377161 3.527143
H 0.621674 -4.174834 0.396688
H 0.882085 -6.232184 1.769269
H -1.493811 -4.434634 4.906370
H -0.187924 -6.377689 4.027521
Fe 1.892780 -2.208184 -3.634399
Cl 3.200367 -1.066391 -4.926787
Cl 2.714192 -4.056752 -2.822464
Cl -0.154917 -2.437336 -4.371306

Fe Dimer Second TS
50

C 0.31134251 -5.47195207 2.72551616
C 0.24359319 -5.58496211 1.32745702
C -0.21025384 -4.50718558 0.55462577
C -0.59130103 -3.29767558 1.17064166
C -0.51158359 -3.19189177 2.57435467
C -0.06426837 -4.27064979 3.34896021
C -1.04630343 -2.12400115 0.34283691
C -2.62127856 -2.14512722 0.04629637
C -2.99063882 -3.38596581 -0.77905408
C -2.92004131 -0.83616096 -0.61587540
O -0.65731498 1.05586842 0.31227340
Fe 0.88074982 1.14462464 -0.74735856
Cl 1.99308599 2.89445698 -0.06496320
C -2.85852892 -0.64380133 -2.08055751
C -3.41701549 -2.01008292 1.37221988
C -3.29674537 -0.50795131 1.72314183
C -3.19966160 0.17602386 0.34520808
C -1.88627591 1.57952575 0.30269958
C -2.21452242 2.31863371 1.60479697
Cl 2.06392916 -0.82670497 -0.30678359
Cl 0.47818180 1.15937958 -2.89673523
C -2.21977209 2.40999637 -0.93982837
H -3.27919207 -1.51312646 -2.60740435
H -1.79241023 -0.60946076 -2.38774039
H -3.34490852 0.28016743 -2.41427226
H -3.02384583 -2.68001743 2.14863150
H -4.47021915 -2.27791144 1.18590322
H -0.79510076 -1.19020068 0.85687090
H -0.54078327 -2.12359227 -0.62785546
H -2.38052663 -3.45389672 -1.69149575
H -2.80459390 -4.28559779 -0.17630383
H -4.05690863 -3.36225476 -1.05588514
H -4.13725700 -0.12883205 2.32033792
H -2.37543402 -0.33558973 2.30035727
H -4.00291065 0.86618592 0.06526718
H -1.98192641 1.87637112 -1.86531956
H -1.59095577 3.31517282 -0.90369777
H -3.27387237 2.72332914 -0.94126126
H -3.27953962 2.58602405 1.65846062
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H -0.23477302 -4.58606982 -0.53304608
H 0.56040077 -6.50585791 0.83499993
H 0.00413866 -4.17016513 4.43405652
H 0.66953336 -6.31062634 3.32561155
Fe 2.23697026 -2.29426789 -2.22911778
Cl 3.60948154 -1.34594758 -3.61203097
Cl 3.01168966 -4.12795525 -1.33736170
Cl 0.22457791 -2.64587378 -3.09057035

Fe Dimer Product
50

C 0.317427 -5.380992 2.757863
C 0.424184 -5.349788 1.358125

C -0.084604 -4.261207 0.637205
C -0.706432 -3.185278 1.302179
C -0.795172 -3.222206 2.708579
C -0.291533 -4.311126 3.433605
C -1.264482 -2.015553 0.527031
C -2.766971 -2.175130 0.074732
C -2.930973 -3.428147 -0.802519
C -3.164784 -0.884516 -0.641764
O -0.491433 0.984750 -0.219039
Fe 0.959899 1.235591 -1.498105
Cl 1.705687 3.191298 -0.884833
C -2.848280 -0.643561 -2.083797
C -3.728118 -2.161586 1.298675
C -4.004713 -0.657833 1.577418
C -3.798322 -0.038292 0.209688
C -1.435968 1.711687 0.195479
C -1.657730 1.811253 1.674172
Cl 2.446495 -0.422223 -0.935889
Cl 0.241457 1.207041 -3.533214
C -2.091730 2.685754 -0.739352
H -3.371921 -1.383087 -2.712103
H -1.775076 -0.778477 -2.296872
H -3.152116 0.360904 -2.413223
H -3.321502 -2.709195 2.159328
H -4.672822 -2.644703 1.001123
H -1.194750 -1.105282 1.141163
H -0.660561 -1.849226 -0.376018
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H -3.974368 -3.523433 -1.145982
H -5.012920 -0.471854 1.982536
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H -0.363402 -4.320185 4.523196
H 0.717135 -6.227250 3.319958
Fe 2.427323 -2.354417 -2.436861
Cl 3.654446 -1.773639 -4.127182
Cl 3.256517 -3.949731 -1.212517
Cl 0.316092 -2.683357 -2.939880

General Information

General Laboratory Procedures.
All moisture-sensitive reactions were performed under an atmosphere of nitrogen in flame-dried round bottom flasks or glass vials fitted with rubber septa and/or septa equipped screw caps. Stainless steel syringes were used to transfer air or moisture-sensitive liquids. Flash chromatography was performed using silica gel SiliaFlash® 40-63 micron (230-400 mesh) from Silicycle.

Materials and Instrumentation.

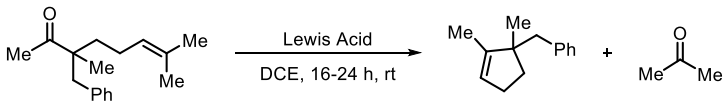
All chemicals were purchased from Sigma-Aldrich, VWR, Oakwood or Acros and were used as received unless otherwise stated. Tetrahydrofuran was dried by being passed through columns of activated alumina. Proton Nuclear Magnetic Resonance NMR (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Varian Unity Plus 400, Varian MR400, Varian vnmrs 500, Varian Inova 500, Varian Mercury 500, and Varian vnmrs 700 spectrometers. Chemical shifts for protons are reported in parts per million and are references to the NMR solvent peak ($CDCl_3$: δ_H 7.27). Chemical shifts for carbons are reported in parts per million and are referenced to the carbon resonances of the NMR solvent (CDCl3: δ_C 77.0). Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants in Hertz (Hz). Gas chromatography (GC) was conducted on a Shimadzu GC-2010 Plus system using a Shimadzu SHRXI-5MS column. Mass spectroscopic (MS) data was recorded at the Mass Spectrometry Facility at the Department of Chemistry of the University of Michigan in Ann Arbor, MI on an

Agilent Q-TOF HPLC-MS with ESI high resolution mass spectrometer. Infrared (IR) spectra were obtained using either an Avatar 360 FT-IR or Perkin Elmer Spectrum BX FT-IR spectrometer. IR data are represented as frequency of absorption (cm^{-1}).

Abbreviations used: DMP **= 1,1,1-Tris(acetyloxy)-1,1-dihydro-1,2-benziodoxol-3-(1H)-one,** EtOAc = ethyl acetate, DMF = N,N'-dimethylformamide, DCM = dichloromethane, DCE = 1,2-dichloroethane, HCl = hydrogen chloride, IBX = 2-Iodoxybenzoic acid, $NaHCO_3$ = sodium bicarbonate, MeOH = methanol, THF = tetrahydrofuran, Na_2SO_4 = sodium sulfate, $MgSO_4$ = magnesium sulfate, DMSO = dimethyl sulfoxide, IBX = 2-iodoxybenzoic acid, DMS = dimethyl sulfoxide, LDA = lithium diisopropylamine, DIBAL-H = Diisobutylaluminium hydride, TMSCN = trimethylsilyl cyanide, AllylTMS = allyltrimethylsilane, BnBr = benzyl bromide, TBSCl = tert-butyldimethylsilyl chloride, *n*-BuLi = n-butyllithium, TLC = thin layer chromatography.

Optimization

Table A2-3. Lewis Acid Evaluation

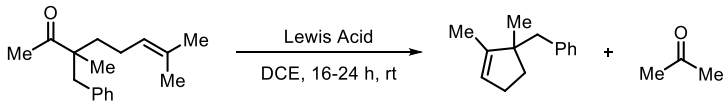


22 **24** **18**

entry	Lewis Acid	mol%	Temp. (°C)	solvent	yield **24** (%)	conversion (%)
1	$FeCl_3$	5	22	DCE (0.05M)	74	75
2	$GaCl_3$	5	22	DCE (0.05M)	21	82
3	$Fe(OTf)_3$	5	22	DCE (0.05M)	0	0
4	$Sc(OTf)_3$	5	22	DCE (0.05M)	6	16
5	$SnCl_4$	5	22	DCE (0.05M)	30	70
6	$BF_3•OEt_2$	5	22	DCE (0.05M)	24	51
7	$AlCl_3$	5	22	DCE (0.05M)	4	3
8	$TiCl_4$	5	22	DCE (0.05M)	0	36
9	$FeCl_3$ + AcOH	5	22	DCE (0.05M)	57	59
10	BCl_3	5	22	DCE (0.05M)	0	14
11	$FeBr_3$	5	22	DCE (0.05M)	55	70
12	$FeCl_2$	5	22	DCE (0.05M)	0	5
13	$FeSO_4•7H_2O$	5	22	DCE (0.05M)	0	0
14	$RuCl_3$	5	22	DCE (0.05M)	0	16
15	$Fe(acac)_3$	5	22	DCE (0.05M)	0	0
16	*p*TsOH	5	22	DCE (0.05M)	0	1
17	$AsCl_3$	5	22	DCE (0.05M)	0	4
18	FeF_3	5	22	DCE (0.05M)	0	1
19	$Fe(oxalate)_2•2H_2O$	5	22	DCE (0.05M)	0	44
20	H_2SO_4	5	22	DCE (0.05M)	6	93
21	HCl	5	22	DCE (0.05M)	3	7
22	$InCl_3$	5	22	DCE (0.05M)	6	27
23	$SbCl_3$	5	22	DCE (0.05M)	0	0
24	TfOH	5	22	DCE (0.05M)	0	3
25	$Yb(OTf)_3$	5	22	DCE (0.05M)	0	10
26	$ZnBr_2$	5	22	DCE (0.05M)	0	50
27	$ZnCl_2$	5	22	DCE (0.05M)	0	5
28	EASC	100	22	DCE (0.05M)	30	100

Conditions: All reactions were performed using 0.16 mmol ketone **22**, 0.008 mmol Lewis acid at room temperature for 16-24 h. Yield determined by ^{1}H NMR using naphthalene as an internal standard. EASC = ethyl aluminum sesquichloride.

Table A2-4. Catalyst Loading Evaluation

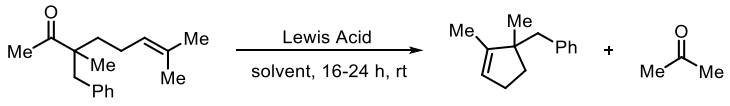


22 **24** **18**

entry	Lewis Acid	mol%	Temp. (°C)	solvent	yield **24** (%)	conversion (%)
28	$FeCl_3$	1	22	DCE (0.05M)	0	5
1	$FeCl_3$	5	22	DCE (0.05M)	74	75
29	$FeCl_3$	10	22	DCE (0.05M)	74	78
30	$FeCl_3$	20	22	DCE (0.05M)	54	67
31	$FeCl_3$	50	22	DCE (0.05M)	23	70
32	$FeCl_3$	100	22	DCE (0.05M)	0	100

Conditions: All reactions were performed using 0.16 mmol ketone **22**, 0.008 mmol Lewis acid at room temperature for 16-24 h. Yield determined by ^{1}H NMR using naphthalene as an internal standard.

Table A2-5. Solvent Evaluation

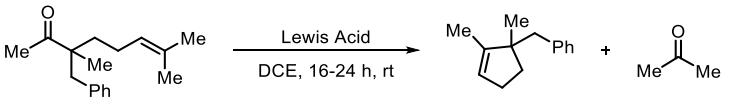


22 **24** **18**

entry	Lewis Acid	mol%	Temp. (°C)	solvent	yield **24** (%)	conversion (%)
1	$FeCl_3$	5	22	DCE (0.05M)	74	75
40	$FeCl_3$	5	22	DCM (0.05M)	37	40
41	$FeCl_3$	5	22	Toluene (0.05M)	0	25
42	$FeCl_3$	5	22	Benzene (0.05M)	0	50
43	$FeCl_3$	5	22	F-Toluene (0.05M)	0	30
44	$FeCl_3$	5	22	Hexanes (0.05M)	0	16

Conditions: All reactions were performed using 0.16 mmol ketone **22**, 0.008 mmol Lewis acid at room temperature for 16-24 h. Yield determined by ^{1}H NMR using naphthalene as an internal standard.

Table A2-6. Concentration Evaluation

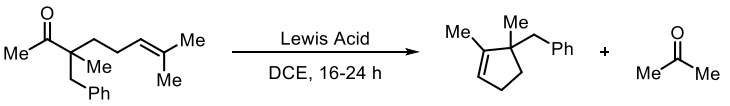


22 **24** **18**

entry	Lewis Acid	mol%	Temp. (°C)	solvent	yield **XX** (%)	conversion (%)
33	$FeCl_3$	5	22	DCE (1.00M)	61	60
34	$FeCl_3$	5	22	DCE (0.10M)	64	65
1	$FeCl_3$	5	22	DCE (0.05M)	74	75
35	$FeCl_3$	5	22	DCE (0.01M)	73	76
36	$FeCl_3$`	10	22	DCE (1.00M)	70	72
37	$FeCl_3$	10	22	DCE (0.10M)	73	70
38	$FeCl_3$	10	22	DCE (0.05M)	74	78
39	$FeCl_3$	10	22	DCE (0.01M)	77	80

Conditions: All reactions were performed using 0.16 mmol ketone **22**, 0.008 mmol Lewis acid at room temperature for 16-24 h. Yield determined by ^{1}H NMR using naphthalene as an internal standard.

Table A2-7. Temperature Evaluation

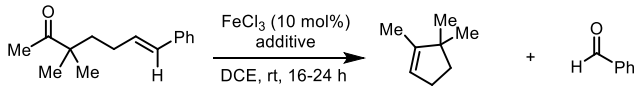


22 **24** **18**

entry	Lewis Acid	mol%	Temp. (°C)	solvent	yield **24** (%)	conversion (%)
1	$FeCl_3$	5	22	DCE (0.05M)	74	75
45	$FeCl_3$	5	40	DCE (0.05M)	44	62
46	$FeCl_3$	5	60	DCE (0.05M)	53	69
47	$FeCl_3$	5	80	DCE (0.05M)	59	78

Conditions: All reactions were performed using 0.16 mmol ketone **22**, 0.008 mmol Lewis acid at room temperature for 16-24 h. Yield determined by ^{1}H NMR using naphthalene as an internal standard.

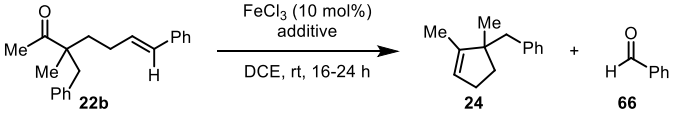
Table A2-8 and 2-9. Extensive Additive Evaluations



65 49 66

entry	additive	equiv.	yield **64** (%)	Conversion (%)
1	AllylTMS	0.5	1.3	26
2	AllylTMS	1.0	11.6	30
3	AllylTMS	2.0	12.4	39
4	AllylTMS	3.0	14.5	42
5	AllylTMS	5.0	18.9	51
6	TMSOTf	3.0	1.7	58
7	Anisole	3.0	0	79
8	1,3,5-trimethoxybenzene	3.0	0	30
9	Triethylsilane	3.0	8	45
10	TMSCN	3.0	10	82
11	Vinyl Acetate	3.0	4	13
12	Molecular Sieves	--	20	19
13	$NaHSO_3$	3.0	0	0

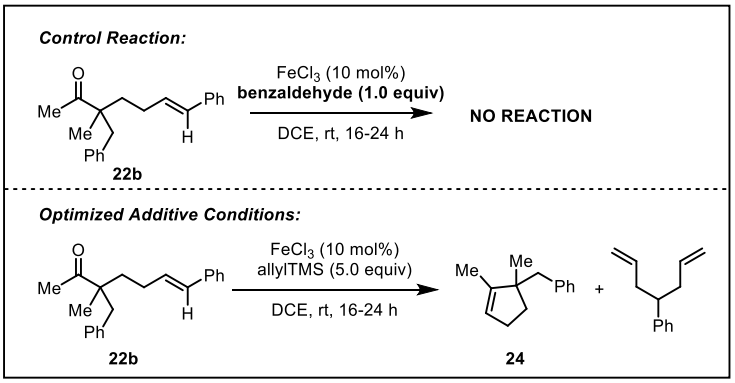
Conditions: All reactions were performed using 0.06 mmol of **65** and 10 mol% Lewis acid in DCE (0.05M). Yields are reported as GC yields.



22b 24 66

entry	additive	equiv.	yield **24** (%)
1	AllylTMS	5.0	69
2	Triethylsilane	3.0	9
3	TMSCN	3.0	12
4	Vinyl Acetate	3.0	6
5	Molecular Sieves	--	9
6	$NaHSO_3$	3.0	0

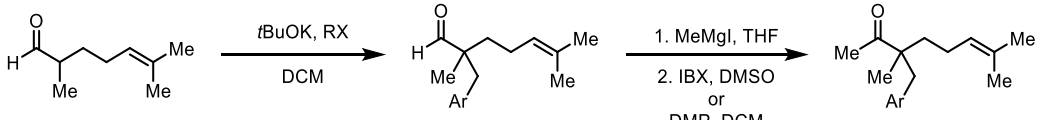
Conditions: All reactions were performed using 0.06 mmol of **22** and 10 mol%$FeCl_3$ in DCE (0.05M). NMR yields with naphthalene as internal standard.



Experimental Procedures

Synthesis of metathesis substrates.

General procedures for synthesis of substrates.



melonal **a** **S**

General procedure A: Arylation/alkylation of melonal to form a intermediates.

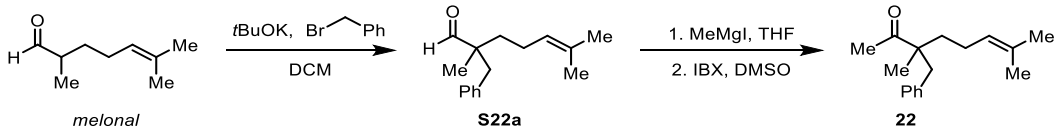
A round bottom flask equipped with a magnetic stir bar was charged with 2,6-dimethyl-5-heptenal (1.0equiv) and dry DCM (0.2M). The solution was cooled to 0°C with an ice bath and then KO*t*Bu (1.3 equiv) was added and the mixture was allowed to stir for 15 minutes at 0°C. Aryl/alkyl halide (1.3 equiv) was then added slowly via syringe. The reaction was allowed to warm to room temperature as it was stirred for 3-24 hours. When TLC showed full conversion, the reaction was quenched with sat. aq. NH_4Cl and after 15 minutes of stirring was extracted with DCM (3 x 50

mL). The organic layer was washed with brine and then dried over Na_2SO_4, filtered and concentrated under reduced pressure to remove all volatile components. The crude product was purified *via* column chromatography eluting with the hexanes/EtOAc (9:1) to give the pure arylated ketone **a**.

General procedure B: Grignard addition to intermediates a.
A round bottom flask equipped with a magnetic stir bar was charged with **a** (1.0 equiv) and dry THF (0.2M). The solution was cooled to 0°C with an ice bath and alkylmagnesium halide (1.5 equiv) was added slowly via syringe. The reaction mixture was allowed to warm to room temperature and was stirred for 3-24 hours. After TLC showed full conversion, the reaction was quenched with addition of sat. aq. NH_4Cl. After stirring for 30 minutes, the reaction was extracted with EtOAc (3 x 50 mL). The organic phase was washed with brine and dried over Na_2SO_4, filtered and concentrated under reduced pressure to remove all volatile components. The crude product was purified *via* column chromatography eluting with the indicated solvent to give the mixture of diastereomers of alkylated ketone **b.**

General procedure C1: Oxidation of intermediates b.
A round bottom flask equipped with a magnetic stir bar was charged with **b** (1.0 equiv) and dry DMSO (0.2M). IBX was added (1.2 equiv) slowly to the reaction mixture at room temperature. The reaction mixture was stirred for 2-4 hours. The reaction was quenched with addition of water. After stirring for 45 minutes, the reaction was extracted with EtOAc (3 x 50 mL). The organic phase was washed with brine and dried over Na_2SO_4, filtered concentrated under reduced pressure to remove all volatile components. The crude product was purified *via* column chromatography eluting with the hexanes/EtOAc (9:1) to give the pure ketone substrate.

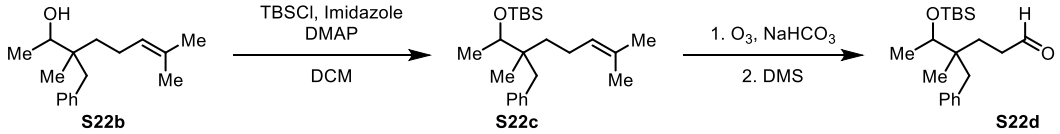
General Procedure C2: Oxidation of intermediates b.
Alternate oxidation was performed with **b** (1.0 equiv) in dry DCM (0.2M) and DMP (1.0 equiv) was added at room temperature and the reaction was allowed to stir for 1-2 hours before it was quenched with water and then filtered and the organic layer was extracted with EtOAc and washed with brine before drying over Na_2SO_4.



melonal **S22a** **22**

2-benzyl-2,6-dimethylhept-5-enal (S22a): General procedure A was followed employing melonal (10.7 mmol) and benzyl bromide (13.9 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S22a** 1.88 g (76%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 9.58 (s, 1H), 7.25 (m, 5H), 5.05 (m, 1H), 2.88 (d, J = 13.6 Hz, 1H), 2.73 (d, J = 13.6 Hz, 1H), 1.95 (m, 2H), 1.68 (s, 3H), 1.59 (s, 3H), 1.48 (m, 2H), 1.02 (s, 3H).
3-benzyl-3,7-dimethyloct-6-en-2-ol (S22b): General procedure B was followed employing **S22a** (8.16 mmol) and 3.0M MeMgI (12.24 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S22b** 1.51 g (75%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.24 (m, 5H), 5.11 (m, 1H), 3.67 (m, 1H), 2.70 (m, 2H), 2.04 (m, 2H), 1.70 (s, 3H), 1.64 (s, 3H), 1.22 (m, 2H), 1.20 (d, J = 11.7 Hz, 3H), 0.87 (s, 3H).

3-benzyl-3,7-dimethyloct-6-en-2-one (22): General procedure C1 was followed employing **S22b** (3.09 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **22** 1.31 g (88%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.27-7.20 (m, 3H), 7.11-7.08 (m, 2H), 5.06 (m, 1H), 2.96 (d, *J* = 13.5 Hz, 1H), 2.71 (d, *J* = 13.5 Hz, 1H), 2.10 (s, 3H), 1.95-1.87 (m, 2H), 1.74 (ddd, *J* = 13.6, 12.0, 5.0 Hz, 1H), 1.68 (s, 3H), 1.59 (s, 3H), 1.44 (ddd, *J* = 13.6, 11.8, 5.3 Hz, 1H), 1.10 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.5, 137.6, 130.8, 130.3, 128.0, 126.4, 123.8, 52.2, 44.3, 38.7, 26.6, 25.7, 23.3, 20.7, 17.7; ν_{max} (FTIR)/cm^{-1}: 2970, 2924, 2854, 1702, 1454, 1354, 1154, 1090, 754, 704; *m/z* (ESI+) HRMS [M+H] $C_{17}H_{24}O^+$: formula found. 245.1800 cald. 245.1897.



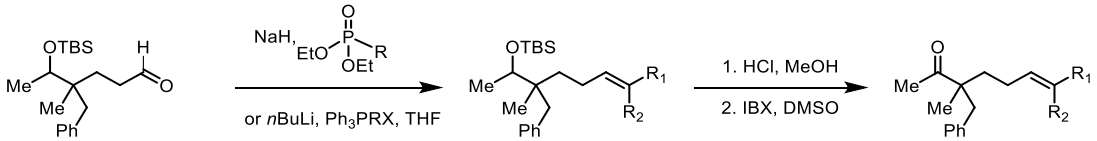
S22b S22c S22d

4-benzyl-5-((tert-butyldimethylsilyl)oxy)-4-methylhexanal (S22c): Protection: A round bottom flask equipped with a magnetic stir bar was charged with 3-benzyl-3,7-dimethyloct-6-en-2-ol (2.0 g, 8.12 mmol, 1.0 equiv) **S22b** and dry DCM (40 mL, 0.2M). Imidazole (2.76 g, 40.6 mmol, 5.0 equiv), TBSCl (1.83 g, 12.1 mmol, 1.5 equiv) and DMAP (5 mg, 0.041 mmol, 0.005 equiv) were added at room temperature and the reactions was allowed to stir for 6-8 hours. The reaction was quenched with the addition of water and after stirring for 10 minutes, was extracted with DCM (3 x 50 mL). The organic layer was washed with 1M HCl (40 mL), sat. aq. $NaHCO_3$ (40 mL) and brine (40 mL) and then dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography eluting with hexanes/EtOAc (12:1) to give 2.63 g (90%) of the desired product as diastereomers, as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.25 (m, 2H), 7.19 (m, 1H), 7.15 (m, 2H), 5.03 (m, 1H), 3.73 (m, 1H), 2.65 (m, 2H), 1.96 (m, 2H), 1.68 (s, 3H), 1.60 (m, 3H), 1.29 (m, 2H), 1.15 (m, 3H), 0.93 (m, 9H), 0.08 (m, 6H).

Ozonolysis: A round bottom flask was equipped with a magnetic stir bar and a solution of **S22c** (1.0 equiv) and DCM (0.2M). The flask was cooled to -78°C and ozone was bubbled through the solution until it maintained a blue color. N_2 gas was then bubbled through until solution as clear again and dimethyl sulfide (1.6 equiv) was added and the solution was allowed to warm to room temperature overnight. The reaction mixture was then concentrated and then filtered through a silica plug with DCM as the eluent and concentrated before it was further reacted crude, **S22d**.

General procedure D: Olefination, deprotection and oxidation of substrates 22b-f.

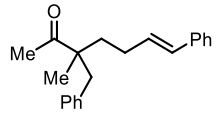
D1: HWE Olefination, D2: Wittig Olefination



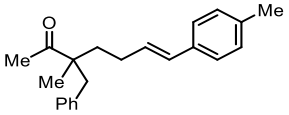
S22d 22b-f

HWE Olefination: A round bottom flask equipped with a magnetic stir bar was charged with a suspension of NaH (1.1 equiv) in dry THF (0.5M) and cooled to 0°C with an ice bath before the appropriate phosphonate (1.0 equiv) was added and the reaction was stirred for 1 hour while warming to room temperature. The reaction was then cooled to 0°C with an ice bath and 4-benzyl-5-((tert-butyldimethylsilyl)oxy)-4-methylhexanal (1.0 equiv) was added dropwise. The reaction was allowed to warm to room temperature and stirred for 6-12 hours before quenching with the addition of ice water, extraction with EtOAc (3 x 50 mL) and washing with brine (50 mL) before it was dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the desired

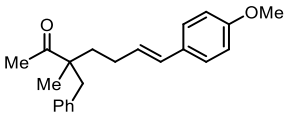
product as an oil which was further reacted crude. **Wittig Olefination:** A round bottom flask equipped with a magnetic stir bar was charged with a suspension of appropriate Wittig salt (1.3 equiv) in dry THF (0.3M) and cooled to 0°C with an ice bath before *n*-BuLi (2.5M in hexanes, 1.5 equiv) was added and the mixture was stirred for 1 hour at 0°C. 4-benzyl-5-((tert-butyldimethylsilyl)oxy)-4-methylhexanal (1.0 equiv) in dry THF (0.4M) was then added slowly. The reaction was allowed to warm to room temperature and stirred for 6-12 hours. The reaction was quenched with the addition of sat. aq. NH_4Cl (40 mL) and then extracted with EtOAc (3 x 50 mL) and washed with brine (50 mL) and dried over Na_2SO_4 filtered and concentrated under reduced pressure and then dissolved in DCM and eluted through a silica plug to remove triphenylphosphine oxide and concentrated under reduced pressure to give the desired product as an oil which was further reacted crude. **Deprotection:** The crude material was dissolved in HCl in methanol (1.5 M) and the reaction was stirred under N_2 gas at room temperature overnight. The reaction was quenched by the addition of water and extraction with diethyl ether (3 x 40 mL). The organic phase was washed with brine (40 mL) and then dried over $MgSO_4$, filtered and concentrated under reduced pressure to give an oil which was used crude in further reactions. **Oxidation:** The crude material after deprotection was dissolved in dry DMSO (0.5M) and IBX (1.0 equiv) was added and the reaction was stirred at room temperature for 2-4 hours. The reaction was quenched by addition of water and then after stirring for 45 minutes, was filtered through Celite® with EtOAc as eluent followed by the separation of phases and extraction with EtOAc (2 x 50 mL) and then the organic phase was washed with brine (40 mL) and dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography eluting with hexanes/EtOAc (12:1) to give the ketone substrate **22b-f**.



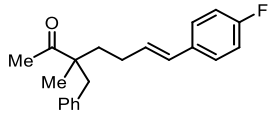
(E)-3-benzyl-3-methyl-7-phenylhept-6-en-2-one (22b): General procedure D1 was followed employing **S22d** (10.46 mmol) and diethylphenyl phosphonate (10.46 mmol). After three steps, **22b** was produced 611 mg (20%). ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.36 – 7.27 (m, 6H), 7.22 (ddd, *J* = 15.7, 10.1, 4.2 Hz, 2H), 7.13 – 7.09 (m, 2H), 6.38 (d, *J* = 15.8 Hz, 1H), 6.16 (dt, *J* = 15.8, 6.9 Hz, 1H), 2.98 (d, *J* = 13.5 Hz, 1H), 2.74 (d, *J* = 13.5 Hz, 1H), 2.21 – 2.09 (m, 5H), 1.92 (ddd, *J* = 13.7, 11.8, 5.0 Hz, 1H), 1.62 – 1.56 (m, 1H), 1.16 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.4, 137.5, 137.4, 130.3, 130.2, 130.0, 128.5, 128.1, 127.0, 126.5, 125.9, 52.1, 44.5, 38.1, 28.3 26.8, 20.8; ν_{max} (FTIR)/cm^{-1}: 2933, 2830, 1980, 1955, 1699, 1450, 1406, 1226, 1103, 852; *m/z* (ESI+) HRMS [M+Na] $C_{21}H_{24}O^+$: formula found 215.1729, cald. 215.1719.



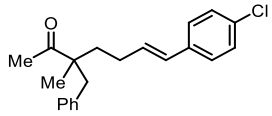
(E)-3-benzyl-3-methyl-7-(p-tolyl)hept-6-en-2-one (22c): General procedure D1 was followed employing **S22d** (2.99 mmol) and diethyl (4-methylbenzyl)phosphonate (2.99 mmol). After three steps, **22c** was produced 348 mg (38%). ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.26 (s, 2H), 7.22 (dd, *J* = 7.6, 5.6 Hz, 3H), 7.13 – 7.08 (m, 4H), 6.35 (d, *J* = 15.8 Hz, 1H), 6.13 – 6.06 (m, 1H), 2.97 (d, *J* = 13.5 Hz, 1H), 2.73 (d, *J* = 13.5 Hz, 1H), 2.34 (d, *J* = 12.6 Hz, 3H), 2.17 – 2.07 (m, 5H), 1.90 (ddd, *J* = 13.7, 11.8, 5.0 Hz, 1H), 1.59 – 1.54 (m, 1H), 1.14 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.5, 137.4, 136.7, 134.7, 130.3, 130.0, 129.2, 128.9, 128.1, 126.4, 125.8, 52.1, 44.5, 38.2, 28.3, 26.8, 21.1, 20.7; ν_{max} (FTIR)/cm^{-1}: 2930, 2925, 2828, 1952, 1706, 1448, 1399, 1220, 1114, 742; *m/z* (ESI+) HRMS [M+NH_4] $C_{22}H_{26}O^+$: formula found. 324.2324 cald. 324.2322.



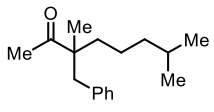
(E)-3-benzyl-7-(4-methoxyphenyl)-3-methylhept-6-en-2-one (22d): General procedure D2 was followed employing **S22d** (4.48 mmol) and (4-methoxybenzyl)triphenylphosphonium bromide (6.73 mmol). After three steps, **22d** was produced 837 mg (58%). ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.25 – 7.16 (m, 4H), 7.09 (d, *J* = 7.3 Hz, 1H), 7.04 (d, *J* = 7.3 Hz, 1H), 6.87 (d, *J* = 8.6 Hz, 1H), 6.84 (s, 1H), 6.33 (dd, *J* = 25.6, 13.7 Hz, 1H), 6.00 (dt, *J* = 15.7, 6.8 Hz, 1H), 3.80 (s, 2H), 2.95 (dd, *J* = 15.8, 13.6 Hz, 1H), 2.71 (dd, *J* = 21.8, 13.5 Hz, 1H), 2.28 – 2.12 (m, 2H), 2.10 – 2.06 (m, 2H), 1.90 – 1.84 (m, 1H), 1.57 – 1.55 (m, 1H), 1.13 (s, 2H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.5, 158.8, 137.4, 130.3, 129.8, 128.1, 127.0, 126.4, 113.9, 113.6, 55.3, 52.2, 44.5, 38.6, 28.3, 26.8, 20.8; ν_{max} (FTIR)/cm^{-1}: 2935, 2827, 1980, 1932, 1703, 1456, 1399, 1220, 1105, 836; *m/z* (ESI+) HRMS [M+] $C_{22}H_{26}O_2^+$: formula found 322.4356, cald. 322.4476.



(E)-3-benzyl-7-(4-fluorophenyl)-3-methylhept-6-en-2-one (22e): General procedure D1 was followed employing **S22d** (4.48 mmol) and diethyl (4-fluorobenzyl)phosphonate (4.48 mmol). After three steps, **22e** was produced 597 mg (43%). ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.30 – 7.18 (m, 5H), 7.10 (d, *J* = 7.3 Hz, 2H), 7.03 – 6.95 (m, 2H), 6.33 (d, *J* = 15.8 Hz, 1H), 6.06 (dt, *J* = 15.7, 6.8 Hz, 1H), 2.96 (d, *J* = 13.5 Hz, 1H), 2.73 (d, *J* = 13.5 Hz, 1H), 2.22 – 2.05 (m, 5H), 1.94 – 1.87 (m, 1H), 1.56 (ddd, *J* = 13.7, 11.8, 5.1 Hz, 1H), 1.15 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.1, 161.7 (d, *J* = 246.0 Hz), 137.1, 133.6 (d, *J* = 3.2), 130.0, 129.7 (d, *J* = 2.1 Hz), 128.0 (d, *J* = 3.6 Hz), 127.3 (d, *J* = 7.8 Hz), 126.3, 115.4 (d, *J* = 21.6 Hz), 51.9, 44.3, 37.8, 28.0, 26.6, 20.5; ν_{max} (FTIR)/cm^{-1}: 2938, 2828, 1978, 1944, 1698, 1448, 1408, 1226, 1102, 1022; *m/z* (ESI+) HRMS [M+Na] $C_{21}H_{23}FO^+$: formula found.333.1632 cald. 333.1625.



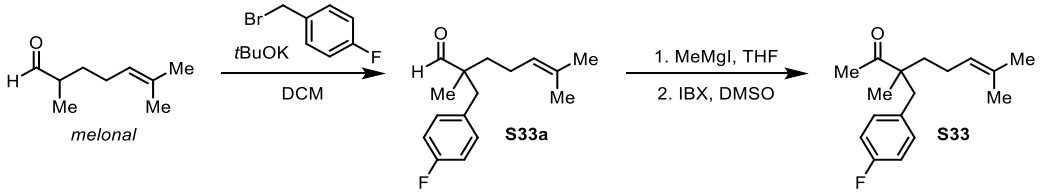
(E)-3-benzyl-7-(4-chlorophenyl)-3-methylhept-6-en-2-one (22f): General procedure D1 was followed employing **S22d** (4.48 mmol) and diethyl (4-chlorobenzyl)phosphonate (4.48 mmol). After three steps, **22f** was produced 351 mg (24%). ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.32 – 7.19 (m, 7H), 7.11 (d, *J* = 7.2 Hz, 2H), 6.34 (d, *J* = 15.8 Hz, 1H), 6.15 (dt, *J* = 15.7, 6.9 Hz, 1H), 2.98 (d, *J* = 13.5 Hz, 1H), 2.75 (d, *J* = 13.5 Hz, 1H), 2.22 – 2.09 (m, 5H), 1.92 (ddd, *J* = 13.7, 11.9, 5.0 Hz, 1H), 1.59 – 1.55 (m, 1H), 1.17 (s, 3H); ^{13}C NMR (135 MHz, DCl_3) δ_C 206.9, 137.3, 136.0, 132.5, 130.8, 130.2, 129.0, 128.6, 128.1, 127.1, 126.5, 52.0, 44.5, 37.9, 28.3, 26.8, 20.8; ν_{max} (FTIR)/cm^{-1}: 2938, 2922, 2826, 1977, 1700, 1443, 1398, 1220, 1102, 798; *m/z* (ESI+) HRMS [M+Na] $C_{21}H_{23}ClO^+$: formula found. 349.1336 cald. 349.1330.



29

3-benzyl-3,7-dimethyloctan-2-one (29): To a flame-dried 100 mL round-bottom flask equipped with a magnetic stir bar was added Pd/C (549 mg, 0.258 mmol, 5% w/w). A stream of MeOH (25 mL) was then added slowly down the side of the flask. Next, the suspension was sparged with a

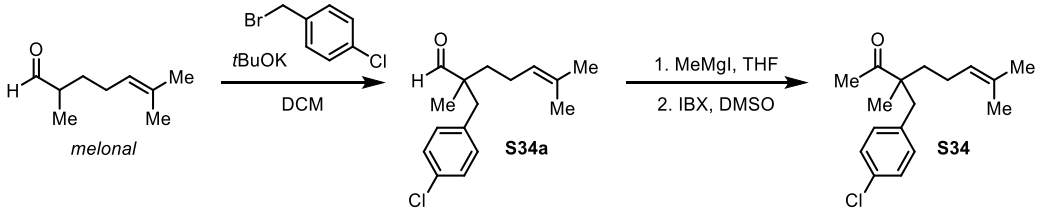
balloon of H_2 gas for 30 min. At this time, sparging was ceased and a solution consisting of methyl ketone **22** (900 mg, 3.68 mmol) and MeOH (5 mL) was added dropwise to the reaction mixture. The flask was equipped with a balloon of H2 and allowed to stir at room. After 2 h, there was complete consumption of starting material by TLC analysis. The reaction was then filtered through a Celite® plug eluting with DCM (40 mL). The eluent was concentrated under reduced pressure and the resultant crude residue was purified via flash column chromatography over silica (1% to 15% EtOAc in hexanes) to afford the reduced methyl ketone **29** 781 mg (86%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.28-7.18 (m, 3H), 7.08 (d, J = 7.1 Hz, 2H), 2.95 (d, J = 13.5 Hz, 1H), 2.70 (d, J = 13.5 Hz, 1H), 2.09 (s, 3H), 1.66 (dd, J = 17.6, 8.4 Hz, 1H), 1.53 (dd, J = 13.1, 6.6 Hz, 1H), 1.42-1.34 (m, 1H), 1.31-1.10 (m, 4H), 1.08 (s, 3H), 0.88 (t, J = 7.8 Hz, 6H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.8, 137.8, 130.2, 128.0, 126.3, 52.3, 44.2, 39.6, 39.0, 27.8, 26.6, 22.59, 22.58, 22.4, 20.8; ν_{max} (FTIR)/cm^{-1}: 2952, 2868, 1702, 1466, 1384, 1354, 1127, 753, 734, 701; *m/z* (ESI+) HRMS [M+H] $C_{17}H_{27}O^+$: formula found 247.2062, cald. 247.2056.



2-(4-fluorobenzyl)-2,6-dimethylhept-5-enal (S33a): General procedure A was followed employing melonal (14.3 mmol) and 1-(bromomethyl)-4-fluorobenzene (18.5 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S33a** 3.54 g (85%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 9.56 (s, 1H), 7.06-6.85 (m, 4H), 5.05 (t, J =7.0 Hz, 1H), 2.86 (d, J = 13.8 Hz, 1H), 2.70 (d, J = 13.8 Hz, 1H), 2.02-1.87 (m, 2H), 1.68 (s, 3H), 1.64-1.55 (m, 4H), 1.01 (s, 3H).

3-(4-fluorobenzyl)-3,7-dimethyloct-6-en-2-ol (S33b): General procedure B was followed employing **S33a** (1.2 mmol) and 3.0M MeMgI (1.8 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S33b** 319 mg (56%) as the diastereomers, as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.15 (m, 2H), 6.96 (m, 2H), 5.08 (m, 1H), 3.65 (m, 1H), 2.64 (m, 2H), 2.05 (m, 2H), 1.70 (s, 3H), 1.63 (s, 3H), 1.27 (m, 2H), 1.21 (d, J = 6.4 Hz, 3H), 0.85 (m, 3H).

3-(4-fluorobenzyl)-3,7-dimethyloct-6-en-2-one (S33): General procedure C1 was followed employing **S33b** (0.68 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S33** 178 mg (88%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.07-7.00 (m, 2H), 6.98-3.89 (m, 2H), 5.04 (t, J = 7.0 Hz, 1H), 2.93 (d, J = 13.6 Hz, 1H), 2.65 (d, J = 13.6 Hz, 1H), 2.08 (s, 3H), 1.95-1.82 (m, 2H), 1.76-1.66 (m, 4H), 1.58 (s, 3H), 1.42 (ddd, J = 13.7, 11.5, 5.6 Hz, 1H), 1.09 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.4, 161.6 (d, J = 244.5 Hz), 133.3 (d, J = 3.3 Hz), 132.1, 131.6 (d, J = 7.8 Hz), 123.7, 114.8 (J = 21.1 Hz), 52.2, 43.2, 38.7, 26.6, 25.6, 23.3, 20.7, 17.7; ν_{max} (FTIR)/cm^{-1}: 2966, 2926, 2856, 1700, 1508, 1354, 1222, 1158, 1100, 824; *m/z* (ESI+) HRMS [M+H] $C_{17}H_{23}FO^+$: formula found. 262.1735 cald. 262.1733.

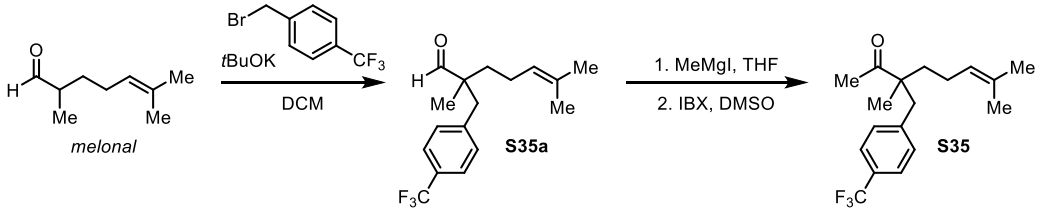


2-(4-chlorobenzyl)-2,6-dimethylhept-5-enal (S34a): General procedure A was followed employing melonal (14.3 mmol) and 1-(bromomethyl)-4-chlorobenzene (18.5 mmol). Purification

by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S34a** 3.78 g (49%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 9.55 (s, 1H), 7.27-7.19 (m, 2H), 7.03 (dd, *J* = 8.8, 2.1 Hz, 2H), 5.06-5.00 (m, 1H), 2.86 (d, *J* = 13.7 Hz, 1H), 2.69 (d, J = 13.7 Hz, 1H), 2.00-1.87 (m, 2H), 1.68 (s, 3H), 1.64-1.55 (m, 4H), 1.45 (ddd, *J* = 14.0, 11.0, 5.9 Hz, 1H), 1.01 (s, 3H).

3-(4-chlorobenzyl)-3,7-dimethyloct-6-en-2-ol (S43b): General procedure B was followed employing **S34a** (1.13 mmol) and 3.0M MeMgI (1.47 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S34b** 318 mg (73%) as the diastereomers, as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.29 (m, 2H), 7.17 (m, 2H), 5.12 (m, 1H), 3.68 (m, 1H), 2.07 (m, 2H), 1.74 (s, 3H), 1.67 (s, 3H), 1.34 (m, 2H), 1.22 (d, *J* = 6.2 Hz, 6H), 0.88 (s, 3H).

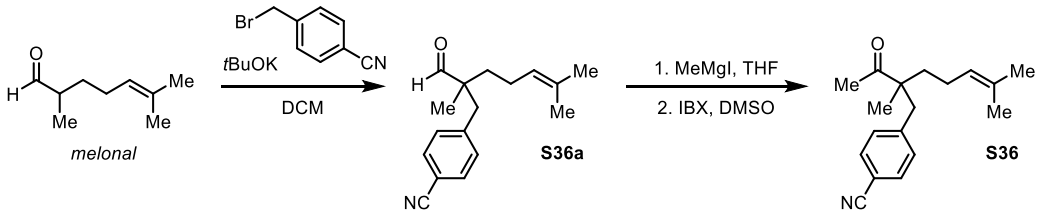
3-(4-chlorobenzyl)-3,7-dimethyloct-6-en-2-one(S34): General procedure C1 was followed employing **S34b** (0.79 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S34** 217 mg (97%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.24-7.19 (m, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 5.05 (m, 1H), 2.93 (d, *J* = 13.5 Hz, 1H), 2.64 (d, *J* = 13.5 Hz, 1H), 2.10 (s, 3H), 1.92-1.82 (m, 2H), 1.71-1.67 (m, 3H), 1.58 (s, 3H), 1.42 (ddd, *J* = 13.8, 11.5, 5.6 Hz, 1H), 1.09 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.3, 1.6.3, 132.4, 132.3, 131.7, 128.3, 123.8, 52.3, 43.4, 38.9, 26.7, 25.8, 23.4, 21.0, 17.8; ν_{max} (FTIR)/cm^{-1}: 2972, 2914, 2850, 1702, 1490, 1354, 1152, 1092, 1016, 824; *m/z* (ESI+) HRMS [M+H] $C_{17}H_{23}ClO^+$: formula found. 278.1429 cald. 278.1437.



2,6-dimethyl-2-(4-(trifluoromethyl)benzyl)hept-5-enal (S35a): General procedure A was followed employing melonal (14.3 mmol) and 1-(bromomethyl)-4-(trifluoromethyl)benzene (18.5 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S35a** 4.26 g (65%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 9.56 (s, 1H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 7.8 Hz, 2H), 5.05 (t, *J* = 6.5 Hz, 1H), 2.95 (d, *J* = 13.6 Hz, 1H), 2.78 (d, *J* = 13.6 Hz, 1H), 2.01-1.92 (m, 2H), 1.69-1.58 (m, 7H), 1.47 (ddd, *J* = 14.1, 10.3, 6.7 Hz, 1H), 1.02 (s, 3H).

3,7-dimethyl-3-(4-(trifluoromethyl)benzyl)oct-6-en-2-ol (S35b): General procedure B was followed employing **S35a** (8.4 mmol) and 3.0M MeMgI (12.6 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S35b** 2.63 g (81%) as the diastereomers, as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.53 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 5.05 (t, *J* = 6.8, 1H), 3.66 (q, *J* = 6.4 Hz, 1H), 2.76 (dd, *J* = 27.5, 13.1 Hz, 2H), 2.02 (m, 2H), 1.69 (s, 3H), 1.62 (s, 3H), 1.2 (d, *J* = 6.2 Hz, 3H), 1.19 (m, 2H), 0.86 (s, 3H).

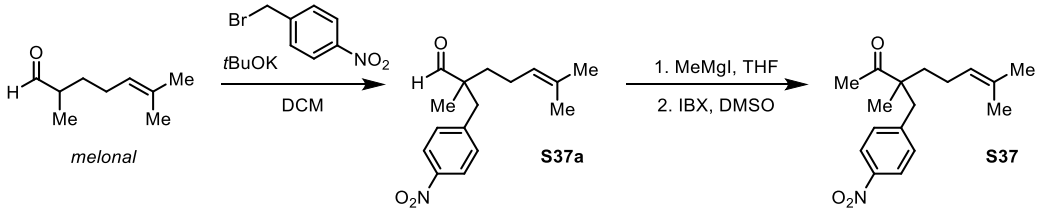
3,7-dimethyl-3-(4-(trifluoromethyl)benzyl)oct-6-en-2-one (S35): General procedure C1 was followed employing **S35b** (0.9 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S35** 238 mg (85%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.52 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 2H), 5.05 (t, *J* = 7.0 Hz, 1H), 3.05 (d, *J* = 13.4 Hz, 1H), 2.73 (d, *J* = 13.4 Hz, 1H), 2.12 (s, 3H), 1.96-1.86 (m, 2H), 1.74-1.67 (m, 4H), 1.60 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 212.9, 164.2, 142.0, 132.3, 130.6, 124.9 (q, *J* = 3.7), 124.8, 123.5, 52.1, 43.4, 38.8, 26.5, 25.6, 23.2, 20.9, 17.7; ν_{max} (FTIR)/cm^{-1}: 2968, 2926, 2858, 1702, 1324, 1130, 1114, 1068, 1018, 852; *m/z* (ESI+) HRMS [M+H] $C_{18}H_{23}F_3O^+$: formula found. 312.1706 cald. 312.1701.



4-(2-formyl-2,6-dimethylhept-5-en-1-yl)benzonitrile (S36a): General procedure A was followed employing melonal (7.13 mmol) and 4-(bromomethyl)benzonitrile (9.27 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S36a** 1.70 g (93%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 9.54 (s, 1H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 5.04 (t, *J* = 6.9 Hz, 1H), 2.97 (d, *J* = 13.7 Hz, 1H), 2.77 (d, *J* = 13.6 Hz, 1H), 1.96 (dt, *J* = 13.2, 6.7 Hz, 2H), 1.68 (s, 3H), 1.63 – 1.57 (m, 4H), 1.49 – 1.44 (m, 1H), 1.02 (s, 3H).

4-(2-(1-hydroxyethyl)-2,6-dimethylhept-5-en-1-yl)benzonitrile (S36b): General procedure B was followed employing **S36a** (7.13 mmol) and 3.0M MeMgI (10.70 mmol). The product was used crude in the following step.

4-(2-acetyl-2,6-dimethylhept-5-en-1-yl)benzonitrile (S36): General procedure C1 was followed employing **S36b** (3.76 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S36** 930 mg (92%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.38 (d, *J* = 8.3 Hz, 2H), 6.97 (d, *J* = 8.3 Hz, 2H), 5.05 (t, *J* = 7.0 Hz, 1H), 2.93 (d, *J* = 13.5 Hz, 1H), 2.64 (d, *J* = 13.5 Hz, 1H), 2.10 (s, 3H), 1.89 (dt, *J* = 17.2, 8.8 Hz, 2H), 1.74 – 1.65 (m, 4H), 1.59 (s, 3H), 1.43 (ddd, *J* = 13.8, 11.4, 5.7 Hz, 1H), 1.09 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 212.6, 143.6, 132.4, 131.8, 131.1, 123.3, 118.9, 110.3, 52.1, 43.5, 38.9, 26.5, 25.7, 23.2, 21.1, 17.7; ν_{max} (FTIR)/cm^{-1}: 2968, 2924, 2855, 1700, 1487, 1404, 1353, 1152, 1011, 982; *m/z* (ESI+) HRMS [M+] $C_{18}H_{23}NO^+$: formula found. 270.1914, cald. 270.1914.

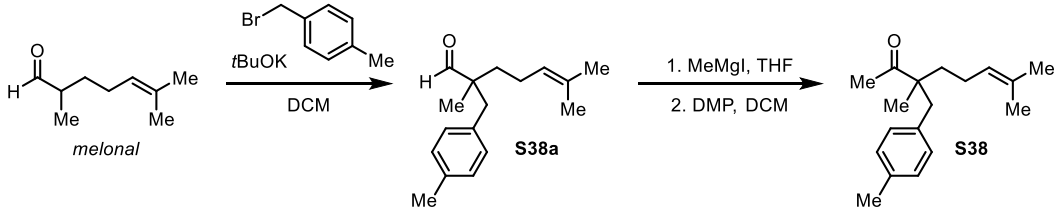


2,6-dimethyl-2-(4-nitrobenzyl)hept-5-enal (S37a): General procedure A was followed employing melonal (14.26 mmol) and 1-(bromomethyl)-4-nitrobenzene (18.54 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S37a** 2.50 g (64%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 9.55 (s, 1H), 8.14 (d, *J* = 8.7 Hz, 2H), 7.28 (d, *J* = 7.4 Hz, 3H), 5.04 (t, *J* = 7.0 Hz, 1H), 3.02 (d, *J* = 13.5 Hz, 1H), 2.82 (d, *J* = 13.5 Hz, 1H), 1.97 (d, *J* = 7.5 Hz, 2H), 1.69 (s, 3H), 1.64 – 1.59 (m, 4H), 1.52 – 1.45 (m, 1H), 1.04 (s, 3H).

3,7-dimethyl-3-(4-nitrobenzyl)oct-6-en-2-ol (S37b): General procedure B was followed employing **S37a** (11.87 mmol) and 3.0M MeMgI (35.60 mmol). The product was used crude in the following step.

3,7-dimethyl-3-(4-nitrobenzyl)oct-6-en-2-oneone (S37): General procedure C1 was followed employing **S37b** (0.24 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S37** 20.5 mg (30%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 8.01 – 7.77 (m, 2H), 7.06 (d, *J* = 6.1 Hz, 2H), 5.04 (t, *J* = 6.9 Hz, 1H), 3.04 (d, *J* = 13.3 Hz, 1H), 2.70 (d, *J* = 13.3 Hz, 1H), 2.58 (s, 3H), 2.12 (s, 3H), 1.90 (d, *J* = 8.2 Hz, 2H), 1.68 (s, 4H), 1.59 (s, 3H), 1.47 (dd, *J* = 8.0, 4.8 Hz, 1H), 1.11 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 212.6, 144.1, 134.6, 132.4, 128.7, 124.5, 123.4, 52.1, 43.0, 38.9, 26.4, 25.7, 23.2, 21.2, 17.7; ν_{max} (FTIR)/cm^{-1}:

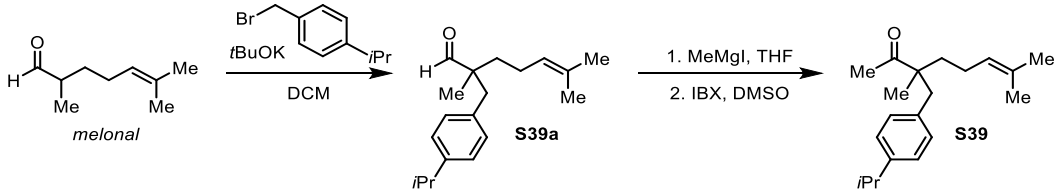
2969, 2924, 2853, 2360, 2339, 1702, 1610, 1518, 1343, 835; *m/z* (ESI+) HRMS [M+] $C_{17}H_{23}NO_3^+$: formula found. 290.1811, cald. 290.1711.



2,6-dimethyl-2-(4-methylbenzyl)hept-5-enal (S38a): General procedure A was followed employing melonal (3.07 mmol) and 1-(bromomethyl)-4-methylbenzene (3.99 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S38a** 630 mg (84%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 9.57 (s, 1H), 7.08 (d, *J* = 7.6 Hz, 2H), 6.98 (d, *J* = 7.3 Hz, 2H), 5.05 (t, *J* = 6.7 Hz, 1H), 2.84 (d, *J* = 13.8 Hz, 1H), 2.69 (d, *J* = 13.7 Hz, 1H), 2.32 (s, 3H), 2.00-1.86 (m, 2H), 1.68 (s, 3H), 1.66-1.57 (m, 4H), 1.50-1.41 (m, 2H), 1.01 (s, 3H).

3,7-dimethyl-3-(4-methylbenzyl)oct-6-en-2-ol (S38b): General procedure B was followed employing **S38a** (3.07 mmol) and 3.0M MeMgI (4.61 mmol). Product used crude in the next reaction.

3,7-dimethyl-3-(4-methylbenzyl)oct-6-en-2-one (S38): General procedure C2 was followed employing **S38b** (2.15 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S38** 400 mg (72%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.07 (d, *J* = 7.6 Hz, 2H), 6.98 (d, *J* = 7.6 Hz, 2H), 5.06 (t, *J* = 6.6 Hz, 1H), 2.91 (d, *J* =13.5 Hz, 1H), 2.67 (d, *J* = 13.5 Hz, 1H), 2.32 (s, 3H), 2.10 (s, 3H), 1.97-1.79 (2H, m), 1.78-1.63 (m, 4H), 1.59 (s, 3H), 1.43 (td, *J* = 12.7, 5.2 Hz, 1H), 1.09 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.6, 135.9, 134.4, 131.2, 130.1, 128.8, 123.9, 52.3, 43.9, 38.6, 26.6, 25.7, 23.3, 21.0, 20.6, 17.7; ν_{max} (FTIR)/cm^{-1}: 2966, 2916, 2848, 1702, 1515, 1446, 1357, 1353, 1117, 1114; *m/z* (ESI+) HRMS [M+H] $C_{18}H_{26}O^+$: formula found. 259.2054, cald. 259.2056.

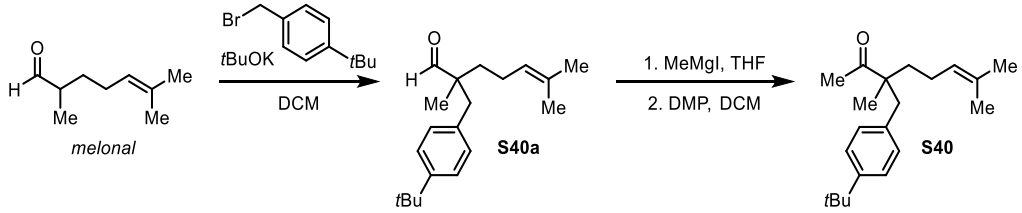


2-(4-isopropylbenzyl)-2,6-dimethylhept-5-enal (S39a): General procedure A was followed employing melonal (5.6 mmol) and 1-(bromomethyl)-4-isopropylbenzene (7.2 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S39a** 1.52 g (49%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 9.58 (s, 1H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.0 Hz, 2H), 5.06 (t, *J* = 7.0 Hz, 1H), 2.93-2.81 (m, 3H), 2.70 (d, *J* = 13.7 Hz, 1H), 2.03-1.86 (m, 2H), 1.68 (s, 3H), 1.66-1.57 (m, 4H), 1.53-1.43 (m, 1H), 1.24 (d, *J* = 6.9 Hz, 6H), 1.02 (s, 3H).

3-(4-isopropylbenzyl)-3,7-dimethyloct-6-en-2-ol (S39a): General procedure B was followed employing **S39a** (1.1 mmol) and 3.0M MeMgI (1.7 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S39b** 318 mg (65%) as the diastereomers, as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.13 (m, 4H), 5.09 (m, 1H), 3.67 (m, 1H), 2.89 (m, 1H), 2.68 (m, 2H), 2.06 (m, 2H), 1.70 (s, 3H), 1.63 (s, 3H), 1.29 (m, 2H), 1.26 (d, *J* = 7.0 Hz, 6H), 0.87 (s, 3H).

3-(4-isopropylbenzyl)-3,7-dimethyloct-6-en-2-one (S39): General procedure C1 was followed employing **S39b** (0.7 mmol). Purification by flash column chromatography eluting with

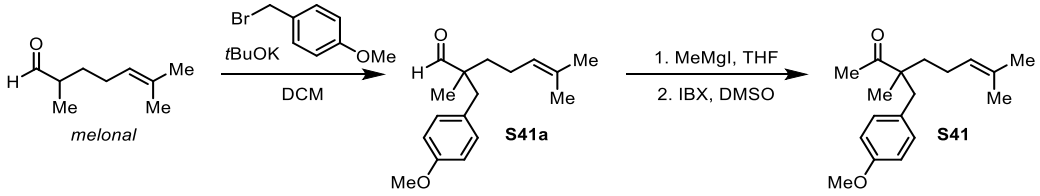
hexanes/EtOAc (3:2) provided **S39** 204 mg (73%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.11 (d, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 8.0 Hz, 2H), 5.05 (t, *J* = 7.0 Hz, 1H), 2.93-2.83 (m, 2H), 2.67 (d, *J* = 13.5 Hz, 1H), 2.10 (s, 3H), 1.96-1.81 (m, 2H), 1.76-1.67 (m, 4H), 1.58 (s, 3H), 1.43 (ddd, *J* = 13.7, 11.8, 5.4 Hz, 2H), 1.23 (d, *J* = 6.9 Hz, 6H), 1.08 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.7, 146.9, 134.8, 130.1, 130.0, 126.1, 123.9, 52.3, 43.9, 38.6, 33.6, 26.5, 25.7 24.0, 23.3, 20.6, 17.7; ν_{max} (FTIR)/cm^{-1}: 2960, 2918, 2856, 1702, 1512, 1462, 1358, 1354, 1112, 822; *m/z* (ESI+) HRMS [M+H] $C_{20}H_{30}O^+$: formula found. 287.2364 cald. 287.2369.



2-(4-(tert-butyl)benzyl)-2,6-dimethylhept-5-enal (S40a): General procedure A was followed employing melonal (6.27 mmol) and 1-(bromomethyl)-4-(tert-butyl)benzene (8.15 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S40a** 1.5 g (84%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 9.58 (s, 1H), 7.28 (d, *J* = 8.9 Hz, 2H), 7.02 (d, *J* = 8.2 Hz, 2H), 5.06 (m, 1H), 2.77 (dd, *J* = 60.1, 13.7 Hz, 2H) 2.06 – 1.93 (m, 4H), 1.30 (s, 9H), 1.00 (s, 3H).

3-(4-(tert-butyl)benzyl)-3,7-dimethyloct-6-en-2-ol (S40b): General procedure B was followed employing **S40a** (4.81 mmol) and 3.0M MeMgI (7.21 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S40b** 838 mg (58%) as the diastereomers, as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.29 (d, *J* = 8.2 Hz, 2H), 7.12 (dd, *J* = 8.2, 1.8 Hz, 2H), 5.10 (dt, *J* = 14.3, 7.1 Hz, 1H), 3.66 (dq, *J* = 12.8, 6.4 Hz, 1H), 2.79-2.45 (m, 2H), 2.09-1.80 (m, 4H), 1.77-1.67 (m, 4H), 1.63 (s, 3H), 1.33-1.30 (m, 11H), 1.19 (dd, *J* = 10.8, 6.4 Hz, 1H), 0.91-0.82 (m, 3H).

3-(4-(tert-butyl)benzyl)-3,7-dimethyloct-6-en-2-one (S40): General procedure C2 was followed employing **S40b** (3.66 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S40** 880 mg (80%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.27 (d, *J* = 8.1 Hz, 2H), 7.02 (d, *J* = 8.1 Hz, 2H), 5.07 (t, *J* = 6.9 Hz, 1H), 2.91 (d, *J* = 13.6 Hz, 1H), 2.39 (d, *J* = 13.6 Hz, 1H), 2.12 (s, 3H), 1.93-1.83 (m, 2H), 1.77-1.71 (m, 1H), 1.69 (s, 3H), 1.59 (s, 3H), 1.45 (ddd, *J* = 13.4, 11.9, 5.4 Hz, 1H), 1.32 (s, 9H), 1.10 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.6, 149.1, 134.4, 131.9, 129.9, 124.9, 123.9, 52.3, 43.8, 38.6, 34.4, 31.4, 26.5, 25.7, 23.4, 20.7, 17.7; ν_{max} (FTIR)/cm^{-1}: 2963, 2361, 2338, 1700, 1652, 1506, 1361, 1269, 1108, 835; *m/z* (ESI+) HRMS [M+H] $C_{21}H_{32}O^+$: formula found. 301.2527, cald. 301.2526.

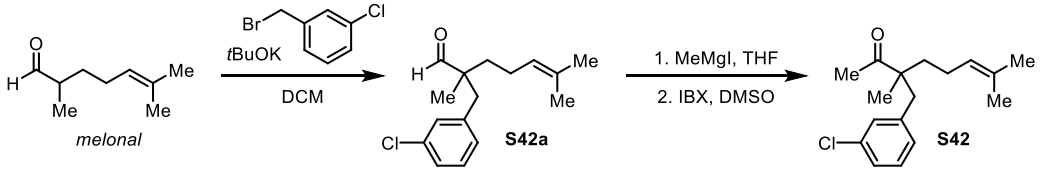


2-(4-methoxybenzyl)-2,6-dimethylhept-5-enal (S41a): General procedure A was followed employing melonal (5.71 mmol) and 1-(bromomethyl)-4-methoxybenzene (7.42 mmol). Product was used crude in following reaction.

3-(4-methoxybenzyl)-3,7-dimethyloct-6-en-2-ol (S41b): General procedure B was followed employing **S41a** (4.4 mmol) and 3.0M MeMgI (6.6 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S41b** 792 mg (66%) as the diastereomers, as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H (7.11 (dd, *J* = 8.6 2.8 Hz, 2H), 6.83

(d, *J* = 8.6 Hz, 2H), 5.13-5.05 (m, 1H), 3.8 (s, 3H), 3.69-3.61 (m, 1H), 2.72-2.50 (m, 2H), 2.06-1.97 (m, 2H), 1.69 (d, *J* = 4.3 Hz, 3H), 1.63 (d, *J* = 2.8 Hz, 3H), 1.34-1.09 (m, 6H), 0.83 (d, *J* = 18.2 Hz, 3H).

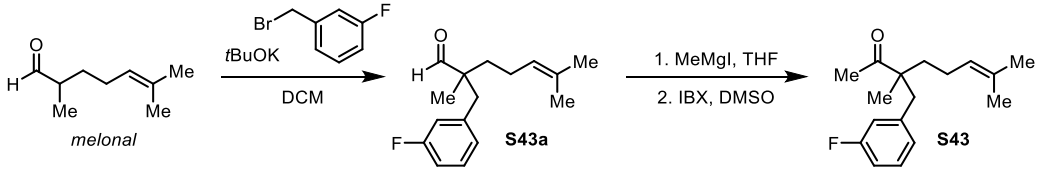
3-(4-methoxybenzyl)-3,7-dimethyloct-6-en-2-one (S41): General procedure C1 was followed employing **S41b** (3.91 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S41** 700 mg (65%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.00 (d, *J* = 8.4 Hz, 2H), 6.80 (d, *J* = 8.4 Hz, 2H), 5.06 (t, *J* = 6.6 Hz, 1H), 3.79 (s, 3H), 2.89 (d, *J* = 13.6 Hz, 2H), 2.64 (d, *J* = 13.7 Hz, 2H), 2.09 (s, 3H), 1.94-82 (m, 2H), 1.77-1.67 (m, 4H), 1.59 (s, 3H), 1.45-1.39 (m, 2H), 1.09 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.7, 158.2, 131.9, 131.1, 129.6, 123.9, 113.4, 55.2, 52.3, 43.5, 38.6, 26.6, 25.6, 23.3, 20.6, 17.6; ν_{max} (FTIR)/cm^{-1}: 2962, 2914, 2856, 1700, 1610, 1512, 1460, 1246, 1038, 820; *m/z* (ESI+) HRMS [M+H] $C_{18}H_{26}O_2^+$: formula found 274.1934, cald. 274.1933.



2-(3-chlorobenzyl)-2,6-dimethylhept-5-enal (S42a): General procedure A was followed employing melonal (14.26 mmol) and 1-(bromomethyl)-3-chlorobenzene (18.54 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S42a** 1.85 g (49%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 9.55 (s, 1H), 7.07 (m, 4H), 5.05 (m, 1H), 2.78 (m, 2H), 1.94 (m, 2H), 1.68 (s, 3H), 1.59 (s, 3H), 1.54 (m, 2H), 1.03 (s, 3H).

3-(3-chlorobenzyl)-3,7-dimethyloct-6-en-2-ol (S42b): General procedure B was followed employing **S42a** (2.89 mmol) and 3.0M MeMgI (4.34 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S42b** 811 mg (36%) as the diastereomers, as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.16 (m, 3H), 7.09 (m, 1H), 5.10 (m, 1H), 3.63 (m, 1H), 2.65 (m, 2H), 2.03 (m, 2H), 1.71 (s, 3H), 1.64 (s, 3H), 1.28 (m, 2H), 1.19 (m, 3H), 0.82 (s, 3H).

3-(3-chlorobenzyl)-3,7-dimethyloct-6-en-2-one (S42): General procedure C1 was followed employing **S42b** (1.05 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S42** 292 mg (40%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.19 (dd, *J* = 4.8, 1.2 Hz, 2H), 7.10 (s, 1H), 7.00 – 6.93 (m, 1H), 5.05 (t, *J* = 7.1 Hz, 1H), 2.95 (d, *J* = 13.5 Hz, 1H), 2.66 (d, *J* = 13.5 Hz, 1H), 2.11 (s, 3H), 1.89 (td, *J* = 12.7, 6.6 Hz, 2H), 1.73 – 1.66 (m, 4H), 1.60 (s, 3H), 1.45 (ddd, *J* = 13.8, 11.0, 6.1 Hz, 1H), 1.10 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.0, 139.8, 133.8, 132.2, 130.3, 129.3, 128.5, 126.6, 123.6, 52.1, 43.4, 38.7, 26.5, 25.7, 23.3, 20.9, 17.7; ν_{max} (FTIR)/cm^{-1}: 2968, 2926, 2848, 1702, 1596, 1572, 1428, 1354, 1084, 782; *m/z* (ESI+) HRMS [M+Na] $C_{17}H_{23}ClO^+$: formula found. 301.1335 cald. 301.1330.

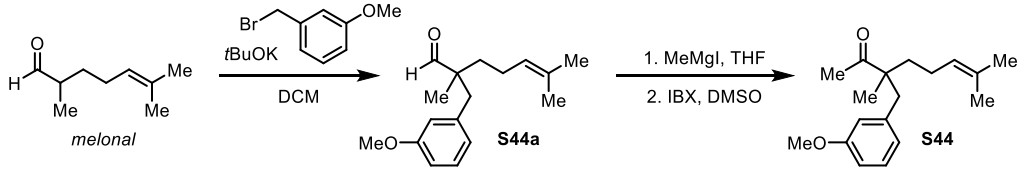


2-(3-fluorobenzyl)-2,6-dimethylhept-5-enal (S43a): General procedure A was followed employing melonal (14.26 mmol) and 1-(bromomethyl)-3-fluorobenzene (18.54 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S43a** 2.67 g (75%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 9.56 (s, 1H), 7.23 (dd, *J* = 14.1, 7.9 Hz, 1H), 6.95-6.80 (m, 3H), 5.05 (t, *J* = 7.0 Hz, 1H), 2.89 (d, *J* = 13.7 Hz, 1H), 2.72 (d, *J* = 13.7

Hz, 1H), 2.18 (s, 3H), 1.98-1.86 (m, 2H), 1.68 (s, 3H), 1.66-1.58 (m, 4H), 1.54 (ddd, *J* = 14.0, 10.6, 6.2 Hz, 1H), 1.03 (s, 3H).

3-(3-fluorobenzyl)-3,7-dimethyloct-6-en-2-ol (S43b): General procedure B was followed employing **S43a** (9.85 mmol) and 3.0M MeMgI (14.78 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S43b** 1.61 g (62%) as the diastereomers, as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.23 (dd, *J* = 14.7, 7.5 Hz, 1H), 7.00-6.87 (m, 3H), 5.15-4.98 (m, 1H), 3.72-3.59 (m, 1H), 2.83-2.51 (m, 2H), 2.09-1.99 (m, 2H), 1.72-1.61 (m, 6H), 1.39-1.19 (m, 5H), 1.15-1.03 (m, 6H), 0.87 (s, 3H).

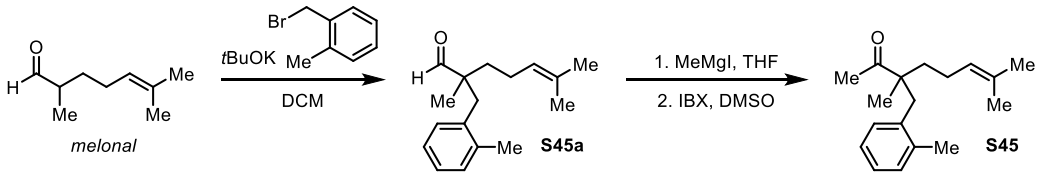
3-(3-fluorobenzyl)-3,7-dimethyloct-6-en-2-one (S43): General procedure C1 was followed employing **S43b** (4.11 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S43** 861 mg (80%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.22 (dd, *J* = 14.2, 7.8 Hz, 1H), 6.95-6.78 (m, 3H), 5.05 (t, *J* = 7.0 Hz, 1H), 2.97 (d, *J* = 13.5 Hz, 1H), 2.68 (d, *J* = 13.5 Hz, 1H), 2.11 (s, 3H), 1.95-1.84 (m, 2H), 1.75-1.68 (m, 4H), 1.59 (s, 3H), 1.50-1.41 (m, 1H), 1.10 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.1, 166.5 (d, *J* = 245.3 Hz), 140.3 (d, *J* = 7.2 Hz), 132.2, 129.4 (d, *J* = 8.3 Hz), 126.0 (d, *J* = 2.8 Hz), 123.6, 117.1 (d, *J* = 20.9 Hz), 113.3 (d, *J* = 21.0 Hz), 52.1, 43.6, 38.8, 26.5, 25.6, 23.3, 20.9, 17.7; ν_{max} (FTIR)/cm^{-1}: 2972, 2928, 2856, 1702, 1586, 1446, 1354, 1252, 1144 786; *m/z* (ESI+) HRMS [M+H] $C_{17}H_{23}FO^{+}$: formula found. 262.1725 cald. 262.1733.



2-(3-methoxybenzyl)-2,6-dimethylhept-5-enal (S44a): General procedure A was followed employing melonal (8.91 mmol) and 1-(bromomethyl)-3-methoxybenzene (11.59 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S44a** 2.32 g (48%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 9.57 (s, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.80-6.59 (m, 3H), 5.05 (t, *J* = 6.4 Hz, 1H), 3.79 (s, 3H), 2.86 (d, *J* = 13.6 Hz, 1H), 2.70 (d, *J* = 13.6 Hz, 1H), 1.99-1.84 (m, 2H), 1.70-1.58 (m, 7H), 1.53-1.44 (m, 1H), 1.03 (s, 3H).

3-(3-methoxybenzyl)-3,7-dimethyloct-6-en-2-ol (S44b): General procedure B was followed employing **S44a** (1.54 mmol) and 3.0M MeMgI (2.30 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S44b** 425 mg (60%) as the diastereomers, as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.19 (m, 1H), 6.77 (m, 3H), 5.10 (m, 1H), 3.80 (s, 3H), 3.69 (m, 1H), 2.70 (m, 2H), 2.06 (m, 2H), 1.69 (s, 3H), 1.63 (s, 3H), 1.35-1.10 (m, 6H), 0.88 (s, 3H).

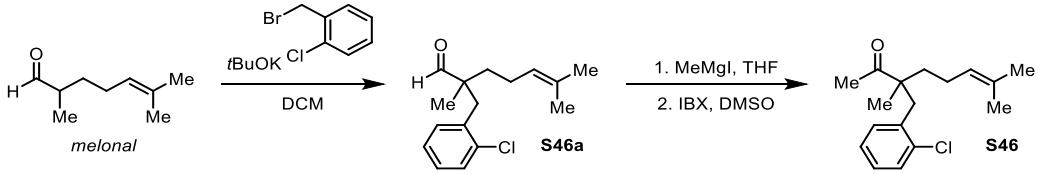
3-(3-methoxybenzyl)-3,7-dimethyloct-6-en-2-one (S44): General procedure C1 was followed employing **S44b** (0.88 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S44** 240 mg (86%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.17 (t, *J* = 7.9 Hz, 1H), 6.75 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.61-6.59 (m, 2H), 5.05 (t, *J* = 7.0 Hz, 1H), 3.78 (s, 3H), 2.93 (d, *J* = 13.4 Hz, 1H), 2.66 (d, *J* = 13.4 Hz, 1H), 2.10 (s, 3H), 1.95-1.83 (m, 2H), 1.77-1.66 (m, 4H), 1.58 (s, 3H), 1.44 (ddd, *J* = 13.6, 11.6, 5.5 Hz, 1H), 1.11 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.5, 159.3, 139.2, 132.0, 128.9, 123.8, 122.7, 116.2, 111.5, 55.1, 52.2, 44.2, 38.8, 26.6, 25.6, 23.3, 20.8, 17.7; ν_{max} (FTIR)/cm^{-1}: 2936, 2926, 2854, 1698, 1582, 1454, 1262, 1046, 784; *m/z* (ESI+) HRMS [M+H] $C_{18}H_{26}O_2^{+}$: formula found. 275.2002 cald. 275.2006.



2,6-dimethyl-2-(2-methylbenzyl)hept-5-enal (S45a): General procedure A was followed employing melonal (14.26 mmol) and 1-(bromomethyl)-2-methylbenzene (18.54 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S45a** 1.66 g (47%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 9.57 (s, 1H), 7.16 – 7.07 (m, 3H), 7.05 – 7.00 (m, 1H), 5.07 (ddd, *J* = 7.0, 4.2, 1.3 Hz, 1H), 2.92 (d, *J* = 14.1 Hz, 1H), 2.79 (d, *J* = 14.1 Hz, 1H), 2.30 (s, 3H), 1.94 (dtd, *J* = 18.9, 13.3, 6.9 Hz, 2H), 1.78 – 1.71 (m, 1H), 1.69 (s, 3H), 1.59 (s, 3H), 1.55 – 1.48 (m, 1H), 1.04 (s, 3H).

3,7-dimethyl-3-(2-methylbenzyl)oct-6-en-2-ol (S45b): General procedure B was followed employing **S45a** (6.14 mmol) and 3.0M MeMgI (9.21 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S45b** 1.31 g (82%) as the diastereomers, as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.22 – 7.09 (m, 4H), 5.16 – 5.01 (m, 1H), 3.88 – 3.71 (m, 1H), 2.88 – 2.58 (m, 2H), 2.37 (s, 3H), 2.03 (dq, *J* = 15.7, 8.0 Hz, 2H), 1.91 – 1.59 (m, 7H), 1.38 (ddd, *J* = 24.2, 10.6, 5.5 Hz, 3H), 1.23 (dd, *J* = 12.6, 6.4 Hz, 3H), 0.84 (d, *J* = 10.2 Hz, 3H).

3,7-dimethyl-3-(2-methylbenzyl)oct-6-en-2-one (S45): General procedure C1 was followed employing **S45b** (5.04 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S45** 1.17 g (90%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.17 – 7.06 (m, 3H), 7.02 – 6.98 (m, 1H), 5.09 – 5.04 (m, 1H), 2.96 (d, *J* = 14.2 Hz, 1H), 2.80 (d, *J* = 14.2 Hz, 1H), 2.30 (s, 3H), 2.10 (s, 3H), 1.97 – 1.80 (m, 3H), 1.69 (s, 3H), 1.59 (s, 3H), 1.51 – 1.43 (m, 1H), 1.11 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 214.0, 137.0, 136.1, 130.5, 130.4, 126.4, 125.6, 123.9, 52.7, 40.5, 39.2, 26.8, 23.4, 20.1, 17.6; ν_{max} (FTIR)/cm^{-1}: 2966, 2924, 2856, 1702, 1450, 1376, 1354, 1150, 1114, 742; *m/z* (ESI+) HRMS [M+H] $C_{18}H_{26}O^+$: formula found. 259.2053 cald. 259.2056.

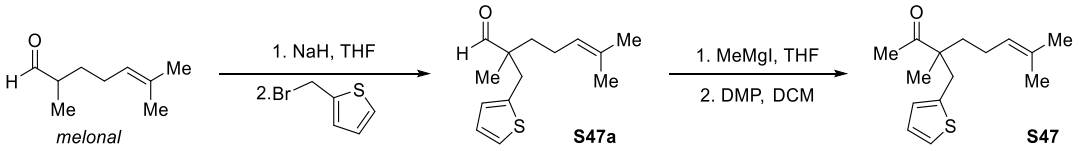


2-(2-chlorobenzyl)-2,6-dimethylhept-5-enal (S46a): General procedure A was followed employing melonal (14.26 mmol) and 1-(bromomethyl)-2-chlorobenzene (18.54 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S46a** 2.08 g (54%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 9.61 (s, 1H), 7.35 (dt, *J* = 7.1, 3.0 Hz, 1H), 7.20 – 7.12 (m, 3H), 5.07 (t, *J* = 7.0 Hz, 1H), 3.09 (d, *J* = 13.9 Hz, 1H), 2.96 (d, *J* = 13.9 Hz, 1H), 2.04 – 1.86 (m, 2H), 1.78 – 1.68 (m, 4H), 1.59 – 1.50 (m, 4H), 1.05 (s, 3H).

3-(2-chlorobenzyl)-3,7-dimethyloct-6-en-2-ol (S46b): General procedure B was followed employing **S46a** (6.61 mmol) and 3.0M MeMgI (10.18 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S46b** 1.43 g (77%) as the diastereomers, as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.42 - 7.26 (m, 2H), 7.21 – 7.11 (m, 2H), 5.18 – 5.00 (m, 1H), 3.85 – 3.68 (m, 1H), 2.99 – 2.81 (m, 2H), 2.06 – 1.84 (m, 2H), 1.70 – 1.52 (m, 5H), 1.43 (ddd, *J* = 13.9, 13.4, 4.5 Hz, 2H), 1.29 – 1.11 (m, 4H), 0.87 (d, *J* = 9.1 Hz, 3H).

3-(2-chlorobenzyl)-3,7-dimethyloct-6-en-2-one (S46): General procedure C1 was followed employing **S46b** (4.59 mmol). Purification by flash column chromatography eluting with

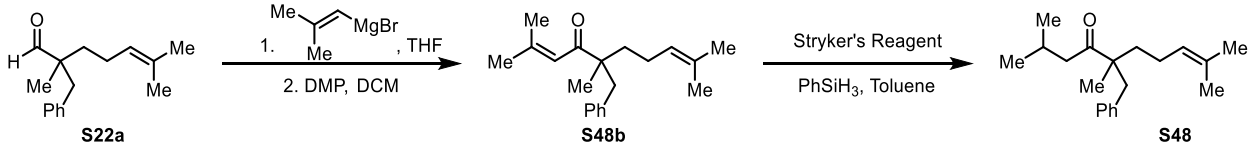
hexanes/EtOAc (3:2) provided **S46** 1.06 g (83%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.35 (dd, *J* = 5.7, 3.5 Hz, 1H), 7.14 (ddd, *J* = 13.4, 8.3, 4.8 Hz, 3H), 5.07 (t, *J* = 6.5 Hz, 1H), 3.10 (d, *J* = 13.9 Hz, 1H), 3.01 (d, *J* = 13.9 Hz, 1H), 2.16 (s, 3H), 1.95 – 1.78 (m, 3H), 1.68 (s, 3H), 1.59 (s, 3H), 1.54 – 1.45 (m, 1H), 1.13 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.4, 135.8, 135.2, 132.1, 131.8, 129.7, 127.7, 126.5, 123.8, 52.8, 39.8, 39.0, 26.5, 25.7, 23.3, 20.0, 17.7; ν_{max} (FTIR)/cm^{-1}: 2968, 2928, 2858, 1702, 1446, 1440, 1354, 1088, 1040, 754; *m/z* (ESI+) HRMS [M+H] $C_{17}H_{23}ClO^+$: formula found. 279.1516 cald. 279.1510.



2,6-dimethyl-2-(thiophen-2-ylmethyl)hept-5-enal (S47a): General procedure A was followed employing melonal **(**5.50 mmol) and 2-(bromomethyl)thiophene (7.15 mmol). The product was used crude in following step.

3,7-dimethyl-3-(thiophen-2-ylmethyl)oct-6-en-2-ol (S47b): General procedure B was followed employing **S47a** (5.50 mmol) and 3.0M MeMgI (6.05 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S47b** 850 mg (61%) as the diastereomers, as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.15 (d, 1H, *J* = 5.1), 6.95 (dd, 1H, *J* = 5.0, 3.5), 6.83 (d, 1H, *J* = 2.8), 5.16-5.06 (m, 1H), 3.68 (m, 1H), 2.90 (m, 2H), 2.03 (m, 2H), 1.71 (m, 3H), 1.63 (m, 3H), 1.57-1.46 (m, 2H), 0.93-0.86 (m, 3H).

3,7-dimethyl-3-(thiophen-2-ylmethyl)oct-6-en-2-one (S47): General procedure C2 was followed employing **S47b** (3.37 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S47** 650 mg (77%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.15 (d, *J* = 5.1 Hz, 1H), 6.96 – 6.88 (m, 1H), 6.78 (d, *J* = 3.0 Hz, 1H), 5.08 (t, *J* = 6.3 Hz, 1H), 3.21 (d, *J* = 14.7 Hz, 1H), 2.96 (d, *J* = 14.7 Hz, 1H), 2.16 (s, 3H), 1.93 (dd, *J* = 15.9, 7.6 Hz, 2H), 1.77 – 1.68 (m, 4H), 1.62 (s, 3H), 1.52 (d, *J* = 8.5 Hz, 1H), 1.19 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.0, 139.6, 132.2, 126.9, 126.6, 124.0, 123.6, 52.1, 38.5, 37.4, 26.2, 25.7, 23.2, 21.3, 17.7; ν_{max} (FTIR)/cm^{-1}: 2967, 2916, 2361, 2338, 1700, 1558, 1506, 1352, 1152, 1032; *m/z* (ESI+) HRMS [M+] $C_{15}H_{22}OS^+$: formula found. 250.1379, cald. 250.1391.

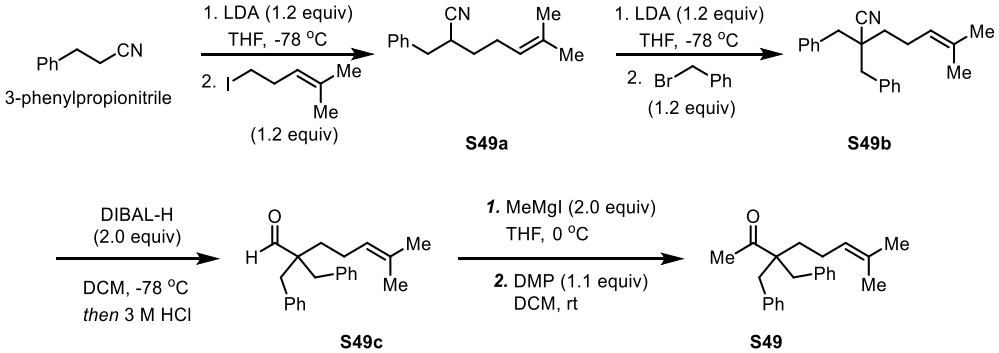


5-benzyl-2,5,9-trimethyldeca-2,8-dien-4-ol (S48a): General procedure B was followed employing **S22a** (3.47 mmol) and 0.5M 2-methyl-2-propenylbromide (5.21 mmol). Purification by silica plug with dichloromethane as the eluent provided **S48a** as a clear oil that was directly used in the following step.

5-benzyl-2,5,9-trimethyldeca-2,8-dien-4-one (S48b): General procedure C2 was followed employing **S48a** (1.10 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S48b** 200 mg (64%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.24 (t, J = 7.6 Hz, 2H), 7.19 (t, J = 7.3 Hz, 1H), 7.08 (d, J = 7.7 Hz, 2H), 6.39 (d, J = 1.0 Hz, 1H), 5.06 (t, J = 6.5 Hz, 1H), 2.98 (d, J = 13.6 Hz, 1H), 2.72 (d, J = 13.6 Hz, 1H), 2.14 (s, 3H), 1.93 (s, 3H), 1.91 – 1.81 (m, 2H), 1.77 – 1.72 (m, 1H), 1.67 (s, 3H), 1.56 (s, 3H), 1.42 (td, J = 13.0, 5.0 Hz, 1H), 1.05 (s, 3H).

5-benzyl-2,5,9-trimethyldec-8-en-4-one (S48): S48 formed from **S48b** (0.70 mmol) according to reported procedure[167] to provide **S48** 80 mg (40%) as clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H

7.27 – 7.16 (m, 3H), 7.09 (d, *J* = 7.0 Hz, 2H), 5.05 (t, *J* = 7.0 Hz, 1H), 2.96 (d, *J* = 13.4 Hz, 1H), 2.67 (d, *J* = 13.4 Hz, 1H), 2.20 (dd, *J* = 45.4, 30.1 Hz, 3H), 1.88 (d, *J* = 7.2 Hz, 2H), 1.74 – 1.65 (m, 4H), 1.59 (s, 3H), 1.45 – 1.36 (m, 1H), 1.10 (s, 3H), 0.89 (dd, *J* = 11.9, 6.5 Hz, 6H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 214.7, 137.9, 131.8, 130.5, 127.9, 126.2, 124.0, 51.7, 47.5, 44.1, 38.8, 25.7, 23.6, 23.3, 22.8, 20.8, 17.7; ν_{max} (FTIR)/cm^{-1}: 2956, 2866, 1700, 1452, 1377, 1120, 1025, 996, 842, 702; *m/z* (ESI+) HRMS [M+H] $C_{20}H_{30}O^+$: formula found. 287.2363, cald. 287.2369.



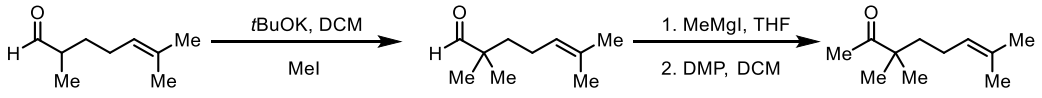
2-benzyl-6-methylhept-5-enenitrile (S49a): A flame-dried, 200 mL round bottom flask equipped with a magnetic stir bar, was topped with a rubber septa and a nitrogen inlet. The flask was then charged with diisopropylamine (2.6 mL, 18.3 mmol) and THF (55 mL). This solution was then cooled to -78 °C followed by slow addition of *n*-BuLi (7.3 mL, 18.3 mmol, 2.5 M in hexanes). After 5 min of stirring, 3-phenylpropionitrile (2.0 mL, 15.2 mmol) was added dropwise via syringe at -78°C, which was left to stir for an additional 30 min at this temperature. Next, 5-iodo-2-methylpent-2-ene[168] (3.80 g, 18.3 mmol) was added in one portion. The reaction solution was warmed to room temperature and allowed to stir overnight. With consumption of starting material determined by TLC, the reaction was quenched with sat. NH_4Cl (aq.) and poured into a separatory funnel. The mixture was extracted with Et_2O (3 × 30 mL). The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure. The crude oil was purified via flash column chromatography over silica (1% to 15% EtOAc in hexanes) to afford the **S49a** in 2.80 g (86%) as a clear oil. ^{1}H NMR (700 MHz, $CDCl_3$) δ_H 7.33 (t, *J* = 7.5 Hz, 2H), 7.29 – 7.26 (m, 1H), 7.24 (d, *J* = 7.7 Hz, 2H), 5.04 (t, *J* = 7.1 Hz, 1H), 2.91 (dd, *J* = 13.7, 8.4 Hz, 1H), 2.86 (dd, *J* = 13.8, 6.2 Hz, 1H), 2.78 (tt, *J* = 9.1, 5.7 Hz, 1H), 2.24 (td, *J* = 14.1, 6.8 Hz, 1H), 2.17 (td, *J* = 15.4, 7.9 Hz, 1H), 1.71 – 1.65 (m, 4H), 1.64 – 1.58 (m, 4H).

2,2-dibenzyl-6-methylhept-5-enenitrile (S49b): A flame-dried, 50 mL round bottom flask equipped with a magnetic stir bar, was topped with a rubber septa and a nitrogen inlet. The flask was then charged with diisopropylamine (0.50 mL, 3.52 mmol) and THF (15 mL). This solution was then cooled to -78 °C followed by slow addition of *n*-BuLi (1.41 mL, 3.52 mmol, 2.5 M in hexanes). After 5 min of stirring, 2-benzyl-6-methylhept-5-enenitrile (**S49a**) (500 mg, 2.34 mmol) was added dropwise *via* syringe at -78 °C, which was left to stir for an additional 30 min at this temperature. Next, benzyl bromide (0.56 mL, 4.69 mmol) was added in one portion. The reaction solution was warmed to room temperature and allowed to stir overnight. With consumption of starting material (determined by TLC), the reaction was quenched with sat. NH_4Cl (aq.) and poured into a separatory funnel. The mixture was extracted with Et_2O (3 × 20 mL). The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure. The crude oil was purified *via* flash column chromatography over silica (1% to 15% EtOAc in hexanes) to afford **S49b** 600 mg (84%) as a clear oil which solidifies upon cooling. ^{1}H NMR (700 MHz, $CDCl_3$) δ_H 7.35 – 7.32 (m, 4H), 7.29 (m, 6H), 5.00 (t, *J* = 6.7 Hz, 1H), 2.89 – 2.87 (d, J= 13.7,

2H), 2.85 (d, *J* = 13.7 Hz, 1H), 2.20 (dd, *J* = 16.3, 7.4 Hz, 2H), 1.66 (s, 3H), 1.59 (s, 3H), 1.54 – 1.50 (m, 2H).

2,2-dibenzyl-6-methylhept-5-enal (S49c): To a flame dried 50 mL round bottom flask flushed under an inert atmosphere was added 2,2-dibenzyl-6-methylhept-5-enenitrile (600 mg, 1.98 mmol) and DCM (10 mL). The solution was cooled to -78 °C followed by slow addition of DIBAL-H (3.95 mL, 3.95 mmol, 1 M in hexanes) via syringe. This temperature was maintained for 2 h and then warmed to 0°C with an ice bath. With consumption of starting material (determined by TLC) the reaction was quenched with 3 M HCl (5 mL) and stirred for an addition 1 h. The biphasic mixture was poured into a separatory funnel along with water (10 mL). The solution was extracted with DCM (3 × 15 mL). The combined organics were washed with brine, dried over Na2SO4 and concentrated under reduced pressure. The crude aldehyde was purified via flash column chromatography over silica (1% to 15% EtOAc in hexanes) to afford **S49c** 350 mg (58%) as a clear oil. ^{1}H NMR (500 MHz, CDCl3) δ_H 9.63 (s, 1H), 7.29 – 7.26 (m, 4H), 7.22 (t, J = 7.2 Hz, 2H), 7.11 (d, J = 7.3 Hz, 4H), 5.00 (t, J = 7.0 Hz, 1H), 2.97 (d, J = 14.1 Hz, 2H), 2.83 (d, J = 14.1 Hz, 2H), 2.07 (dd, J = 16.3, 7.4 Hz, 2H), 1.65 (s, 3H), 1.56 (s, 3H), 1.52 (m, 2H).

3,3-dibenzyl-7-methyloct-6-en-2-one (S49): To a flame-dried, 25 mL round-bottom flask equipped with a magnetic stir bar was added 2,2-dibenzyl-6-methylhept-5-enal **S49c** (300 mg, 0.98 mmol) and THF (5 mL). This solution was then cooled to 0 °C with an ice bath. Next, MeMgI (0.49 mL, 1.47 mmol, 3.0 M in Et_2O) was added slowly *via* syringe and the resultant mixture was allowed to warm to room temperature. When the aldehyde was consumed (determined by TLC) the solution was recooled to 0°C and subsequently quenched with dropwise addition of sat. NH_4Cl (aq.). The mixture was poured into a separatory funnel and extracted with Et_2O (3 × 15 mL). The combined organics were washed with brine, dried over $MgSO_4$, and concentrated. The crude oil was used in the next step without further purification. To an oven-dried, 10 mL round-bottom flask equipped with a magnetic stir, was dissolved the crude alcohol in DCM (10 mL). To this solution was added DMP (448 mg, 1.06 mmol). After stirring at room temperature for 2 h, water (20 mL) was added and the reaction was extracted with DCM (3 × 15 mL). The combined organics were dried with Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified *via* flash column chromatography over silica (0.5% to 12% EtOAc in hexanes) to afford **S49** 166 mg (54%) over two steps as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.27 – 7.23 (m, 4H), 7.22 – 7.18 (m, 2H), 7.10 – 7.05 (m, 4H), 5.05 – 5.00 (m, 1H), 3.06 (d, *J* = 14.3 Hz, 2H), 2.88 (d, *J* = 14.3 Hz, 2H), 2.10 (dd, *J* = 16.3, 7.5 Hz, 2H), 1.95 (s, 3H), 1.67 (s, 3H), 1.59 (s, 3H), 1.58 – 1.54 (m, 2H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 214.0, 137.5, 131.9, 129.9, 128.2, 126.4, 123.5, 56.3, 40.9, 32.6, 28.1, 25.7, 22.8, 17.7;ν_{max} (FTIR)/cm^{-1}: 3061.3, 2927.4, 1699.5, 1496.2, 1453.8, 1352.9, 1183.2, 1152.3, 747.7, 701.4; *m/z* (ESI+) HRMS [M+H] $C_{23}H_{28}O^+$: formula found 321.2215, cald. 321.2213.

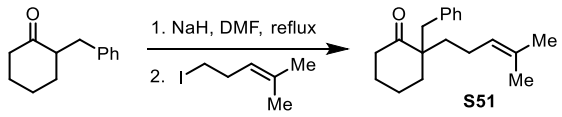


2,2,6-trimethylhept-5-enal (S50a): General procedure A was followed employing melonal (11.23 mmol) and iodomethane (14.60 mmol). Purification by silica plug with DCM as the eluent provided **S50a** as a clear oil that was directly used in the next step.

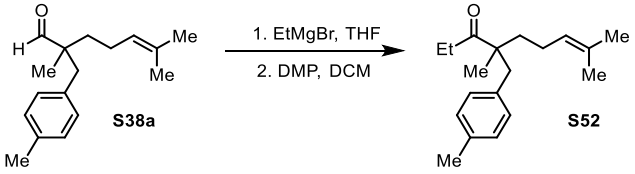
3,3,7-trimethyloct-6-en-2-ol (S50b): General procedure B was followed employing **S50a** (11.23 mmol) and 3.0M MeMgI (16.85 mmol). The product was used crude in following step.

3,3,7-trimethyloct-6-en-2-one (S50): General procedure C2 was followed employing **S50b** (11.16 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2)

provided **S50** 1.70 g (90%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 5.07 (t, *J* = 6.9 Hz, 1H), 2.12 (s, 3H), 1.85 (dd, *J* = 16.3, 7.4 Hz, 2H), 1.68 (s, 3H), 1.58 (s, 3H), 1.54 – 1.50 (m, 1H), 1.13 (s, 6H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.9, 131.9, 124.0, 47.8, 40.1, 25.6, 25.0, 24.3, 23.5, 17.6; ν_{max} (FTIR)/cm^{-1}: 2967, 2928, 2361, 2337, 1702, 1652, 1558, 1456, 1353, 1118; *m/z* (ESI+) HRMS [M+] $C_{11}H_{20}O^+$: formula found. 168.1512, cald. 168.1514.

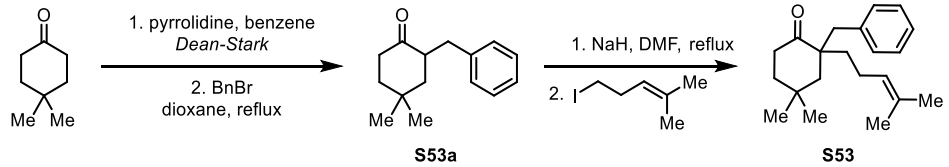


2-benzyl-2-(4-methylpent-3-en-1-yl)cyclohexan-1-one (S51): A 100 mL flame dried flask equipped with a stir bar and reflux condenser was charged with sodium hydride (3.38 mmol, 1.5 equiv, 60% dispersion) and dry DMF (20 mL, 0.12M) and cooled to 0 °C under nitrogen. 2-benzylcyclohexan-1-one (2.54 mmol, 1.0 equiv.) was added to the solution dropwise *via* syringe. The reaction was left stirring at 0°C for 30 min. and was then heated to 80 °C. 5-iodo-2-methylpent-2-ene (3.68 mmol, 1.5 equiv.) was added dropwise *via* syringe. The reaction was monitored by TLC until completion (3 h). The organic layer was extracted with ethyl acetate (150 mL) and washed with water (3x70 mL), sat. aq. NH_4Cl (50 mL), aq. $NaHCO_3$ (50 mL), and brine (1x50 mL). The organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. Purification flash column chromatography eluting with hexanes/EtOAc (7:2) provided **S51** 180 mg (27%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.26 (dd, *J* = 11.6, 3.8 Hz, 2H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.12 (d, *J* = 7.7 Hz, 2H), 5.05 (t, *J* = 6.5 Hz, 1H), 2.93 (d, *J* = 13.9 Hz, 1H), 2.90 (d, *J* = 13.9 Hz, 1H), 2.13 – 2.06 (m, 1H), 1.93 (dd, *J* = 7.7, 5.8 Hz, 1H), 1.79 – 1.63 (m, 10H), 1.61 (s, 3H), 1.42 (td, *J* = 13.1, 4.7 Hz, 1H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 214.9, 138.0, 131.9, 130.7, 127.9, 126.1, 123.8, 52.4, 40.2, 39.5, 36.3, 34.6, 27.0, 25.7, 22.5, 20.8, 17.7; ν_{max} (FTIR)/cm^{-1}: 3026, 2926, 2858, 1701, 1603, 1495, 1452, 1124, 1031, 735; *m/z* (ESI+) HRMS [M+H] $C_{19}H_{26}O^+$: formula found 271.2053, cald. 271.2056.

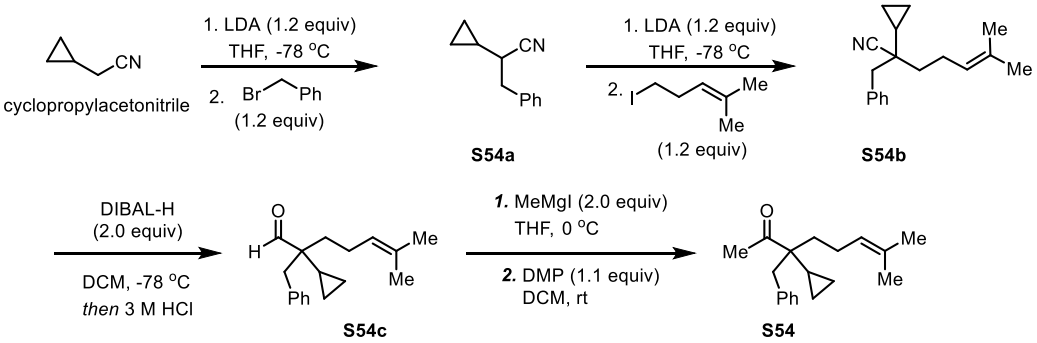


4,8-dimethyl-4-(4-methylbenzyl)non-7-en-3-ol (S52a): General procedure B was followed employing **S38b** (5.73 mmol) and 3.0M EtMgBr (8.60 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S52a** 1.10 g (70%) as the diastereomers, as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.18 – 6.95 (m, 4H), 5.13 – 5.04 (m, 1H), 3.32 – 3.24 (m, 1H), 2.76 – 2.50 (m, 2H), 2.33 (s, 3H), 2.08 – 1.91 (m, 2H), 1.71 – 1.61 (m, 6H), 1.38 – 1.30 (m, 3H), 1.03 – 0.99 (m, 2H), 0.94 – 0.84 (m, 6H).

4,8-dimethyl-4-(4-methylbenzyl)non-7-en-3-one (S52): General procedure C2 was followed employing **S52a** (4.01 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S52** 840 mg (77%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.05 (d, *J* = 7.8 Hz, 2H), 6.94 (d, *J* = 8.0 Hz, 2H), 5.04 (t, *J* = 6.9 Hz, 1H), 2.91 (d, *J* = 13.4 Hz, 1H), 2.62 (d, *J* = 13.4 Hz, 1H), 2.48 – 2.38 (m, 1H), 2.34 – 2.22 (m, 4H), 1.89 – 1.71 (m, 3H), 1.67 (s, 3H), 1.57 (s, 3H), 1.45 – 1.34 (m, 1H), 1.10 (s, 3H), 0.99 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 216.0, 135.8, 134.6, 131.8, 130.1, 128.7, 124.0, 51.9, 44.5, 39.0, 31.8, 25.7, 23.4, 21.0, 20.5, 17.6, 7.8; ν_{max} (FTIR)/cm^{-1}: 2969, 2929, 2361, 2336, 1700, 1652, 1558, 1475, 1032, 816; *m/z* (ESI+) HRMS [M+H] $C_{19}H_{28}O^+$: formula found 273.2211, cald. 273.2213.



2-benzyl-4,4-dimethyl-2-(4-methylpent-3-en-1-yl)cyclohexan-1-one (S53): S53 synthesized in the same manner as **S56**. For alkylation reaction employing 5-iodo-2-methylpent-2-ene (2.31 mmol) provided **S53** 150 mg (22%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.25 (d, J = 7.5 Hz, 2H), 7.21 (d, J = 7.2 Hz, 1H), 7.11 (d, J = 7.1 Hz, 2H), 5.04 (t, J = 7.0 Hz, 1H), 2.92 (d, J = 13.6 Hz, 1H), 2.85 (d, J = 13.6 Hz, 1H), 2.53 – 2.45 (m, 1H), 2.34 (ddd, J = 13.1, 7.4, 4.5 Hz, 1H), 2.04 (dd, J = 12.5, 6.4 Hz, 1H), 1.90 – 1.79 (m, 1H), 1.70 (d, J = 17.8 Hz, 6H), 1.61 – 1.55 (m, 6H), 1.09 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 216.1, 138.0, 131.9, 130.8, 127.9, 126.2, 123.8, 51.7, 46.7, 42.4, 37.6, 37.3, 36.3, 31.1, 29.7, 25.7, 22.9, 17.7, 14.1; ν_{max} (FTIR)/cm^{-1}: 2957, 2898, 2253, 2050, 1880, 1737, 1630, 1494, 1366, 1169; *m/z* (ESI+) HRMS [M+H] $C_{21}H_{30}O^{+}$: formula found 299.2365, cald. 299.2369.



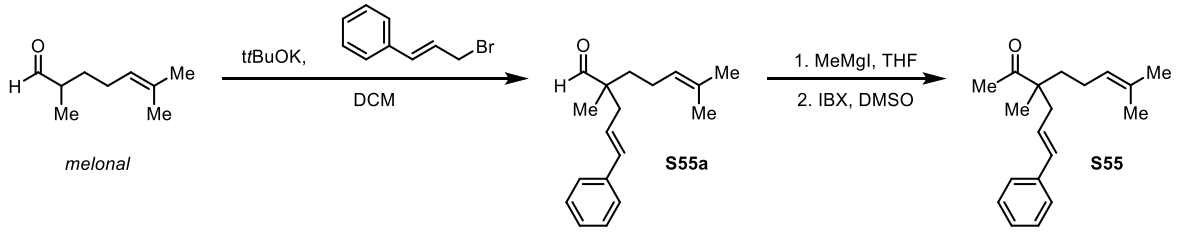
2-cyclopropyl-3-phenylpropanenitrile (S54a): A flame-dried, 200 mL round bottom flask equipped with a magnetic stir bar, was topped with a rubber septa and a nitrogen inlet. The flask was then charged with diisopropylamine (1.9 mL, 13.6 mmol) and THF (50 mL). This solution was then cooled to -78 °C followed by slow addition of *n*-BuLi (5.4 mL, 13.6 mmol, 2.5 M in hexanes). After 5 min of stirring, cyclopropylacetonitrile (1.0 g, 12.3 mmol) was added dropwise *via* syringe at -78°C, which was left to stir for an additional 30 min at this temperature. Next, benzyl bromide (1.61 mL, 13.6 mmol) was added in one portion. The reaction solution was warmed to room temperature and allowed to stir overnight. With consumption of starting material (determined by TLC), the reaction was quenched with sat. NH_4Cl (aq.) and poured into a separatory funnel. The mixture was extracted with Et_2O (3 × 40 mL). The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure. The crude oil was purified *via* flash column chromatography over silica (1% to 15% EtOAc in hexanes) to afford **S54a** 1.48 g (70%) as a clear liquid. Spectroscopic data was in accordance with previously reported literature data[169].

2-benzyl-2-cyclopropyl-6-methylhept-5-enenitrile (S54b): A flame-dried, 100 mL round bottom flask equipped with a magnetic stir bar, was topped with a rubber septa and a nitrogen inlet. The flask was then charged with diisopropylamine (0.99 mL, 7.01 mmol) and THF (35 mL). This solution was then cooled to -78 °C followed by slow addition of *n*-BuLi (2.8 mL, 7.01 mmol, 2.5 M in hexanes). After 5 min of stirring, 2-cyclopropyl-3-phenyl-propanenitrile (1.0 g, 5.84 mmol) was added dropwise *via* syringe at -78°C, which was left to stir for an additional 30 min at this temperature. Next, 5-iodo-2-methylpent-2-ene (1.47 g, 7.01 mmol) was added in one portion. The reaction solution was warmed to room temperature and allowed to stir overnight. With

consumption of starting material (determined by TLC), the reaction was quenched with sat. NH_4Cl (aq.) and poured into a separatory funnel. The mixture was extracted with Et_2O (3 × 20 mL). The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure. The crude oil was purified *via* flash column chromatography over silica (1% to 15% EtOAc in hexanes) to afford **S54b** 1.27 g (86%) as a clear liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.38 – 7.20 (m, 5H), 5.06 (t, *J* = 7.0 Hz, 1H), 3.02 – 2.96 (m, 2H), 2.31 (ddd, *J* = 17.2, 11.2, 5.1 Hz, 1H), 2.17 (ddd, *J* = 17.3, 11.2, 5.1 Hz, 1H), 1.78 – 1.49 (m, 8H), 0.74 (ddd, *J* = 20.1, 13.6, 7.6 Hz, 1H), 0.57 (dd, *J* = 14.7, 6.9 Hz, 2H), 0.51 – 0.40 (m, 1H), 0.39 – 0.25 (m, 1H).

2-benzyl-2-cyclopropyl-6-methylhept-5-enal (S54c): To a flame dried 50 mL round bottom flask flushed under an inert atmosphere was added 2-benzyl-2-cyclopropyl-6-methyl-hept-5-enenitrile (1.0 g, 3.95 mmol) and DCM (10 mL). The solution was cooled to -78 °C followed by slow addition of DIBAL-H (7.9 mL, 7.89 mmol, 1.0M in hexanes) *via* syringe. This temperature was maintained for 2 h and then warmed to 0 °C with an ice bath. With consumption of starting material (determined by TLC) the reaction was quenched with 3.0M HCl (5 mL) and stirred for an addition 1 h. The biphasic mixture was poured into a separatory funnel along with water (10 mL). The solution was extracted with DCM (3 × 15 mL). The combined organics were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude aldehyde was purified *via* flash column chromatography over silica (1% to 15% EtOAc in hexanes) to afford **S54c** 600 mg (59%) as a clear liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 9.51 (s, 1H), 7.28 – 7.23 (m, 2H), 7.23 – 7.16 (m, 3H), 5.09 – 5.02 (m, 1H), 2.88 (d, *J* = 13.7 Hz, 1H), 2.82 (d, *J* = 13.7 Hz, 1H), 2.17 – 2.07 (m, 1H), 2.04 – 1.94 (m, 1H), 1.67 (s, 3H), 1.59 (s, 3H), 1.40 (dt, *J* = 14.2, 7.1 Hz, 2H), 0.71 (ddd, *J* = 17.2, 8.5, 5.9 Hz, 1H), 0.50 – 0.33 (m, 4H).

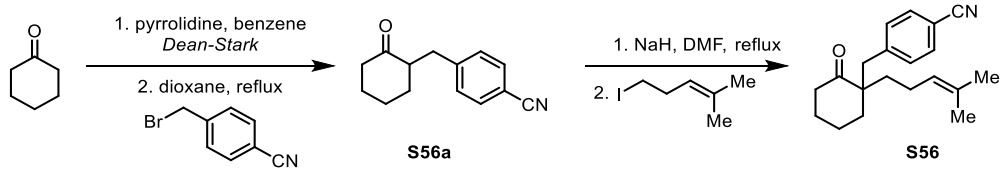
3-benzyl-3-cyclopropyl-7-methyloct-6-en-2-one (S54): To a flame-dried, 25 mL round-bottom flask equipped with a magnetic stir bar was added 2-benzyl-2-cyclopropyl-6-methyl-hept-5-enal (400 mg, 1.56 mmol) and THF (7 mL). This solution was then cooled to 0 °C with an ice bath. Next, MeMgI (0.78 mL, 2.34 mmol, 3.0M in Et_2O) was added slowly *via* syringe and the resultant mixture was allowed to warm to room temperature. When the aldehyde was consumed (determined by TLC) the solution was recooled to 0 °C and subsequently quenched with dropwise addition of sat. NH_4Cl (aq.). The mixture was poured into a separatory funnel and extracted with Et_2O (3 × 15 mL). The combined organics were washed with brine, dried over $MgSO_4$, and concentrated. The crude oil was used in the next step without further purification. To an oven-dried, 10 mL round-bottom flask equipped with a magnetic stir, was dissolved the crude alcohol in DCM (8 mL). To this solution was added DMP (728 mg, 1.72 mmol). After stirring at room temperature for 2 h, water (20 mL) was added and the reaction was extracted with DCM (3 × 15 mL). The combined organics were dried with Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified *via* flash column chromatography over silica (0.5% to 12% EtOAc in hexanes) to afford **S54** 285 mg (68%) as a clear oil. (285 mg, 1.05 mmol, clear oil). ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.23 (m, 2H), 7.20 – 7.16 (m, 3H), 5.02 (t, *J* = 6.7 Hz, 1H), 3.07 (d, *J* = 13.6 Hz, 1H), 2.66 (d, *J* = 13.6 Hz, 1H), 2.20 (s, 3H), 2.05 (td, *J* = 15.5, 7.7 Hz, 1H), 1.83 (td, *J* = 15.6, 7.8 Hz, 1H), 1.67 (s, 3H), 1.58 (s, *J* = 7.7 Hz, 3H), 1.20 (dd, *J* = 16.2, 7.2 Hz, 2H), 0.77 – 0.71 (m, 1H), 0.54 (tt, *J* = 9.0, 4.4 Hz, 1H), 0.51 – 0.46 (m, 1H), 0.42 (ddd, *J* = 14.5, 9.1, 5.4 Hz, 1H), 0.32 (dq, *J* = 10.9, 5.5 Hz, 1H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 212.2, 138.3, 131.9, 130.6, 127.7, 126.0, 123.9, 53.4, 39.5, 31.2, 27.1, 25.6, 22.7, 17.6, 17.1, 2.0, 1.9;ν_{max} (FTIR)/cm^{-1}: 2924.1, 1700.9, 1494.7, 1452.5, 1152.2, 1021.9, 829.4, 755.1, 700.4; *m/z* (ESI+) HRMS [M+H] $C_{19}H_{27}O^+$: formula found 271.2057, cald. 271.2056.



2-cinnamyl-2,6-dimethylhept-5-enal (S55a): General procedure A was followed employing melonal (7.13 mmol) and (E)-(3-bromoprop-1-en-1-yl)benzenenitrobenzene (9.27 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S55a** 1.20 g (66%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 9.53 (s, 1H), 7.38 – 7.28 (m, 4H), 7.25 – 7.19 (m, 1H), 6.44 (d, *J* = 15.7 Hz, 1H), 6.11 (dt, *J* = 15.5, 7.6 Hz, 1H), 5.07 (dd, *J* = 7.9, 6.5 Hz, 1H), 2.53 – 2.33 (m, 2H), 2.00 – 1.85 (m, 2H), 1.68 (s, 3H), 1.66 – 1.56 (m, 4H), 1.32 - 1.23 (m, 1H), 1.11 (s, 3H).

3-cinnamyl-3,7-dimethyloct-6-en-2-ol (S55b): General procedure B was followed employing **S55a** (7.13 mmol) and 3.0M MeMgI (10.70 mmol). The product was used crude in the following step.

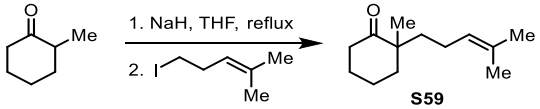
3-cinnamyl-3,7-dimethyloct-6-en-2-one (S55): General procedure C1 was followed employing **S55b** (4.41 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S55** 900 mg (76%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.30 (t, *J* = 6.7 Hz, 3H), 7.25 (d, *J* = 6.4 Hz, 1H), 7.19 (t, *J* = 7.0 Hz, 1H), 6.39 (d, *J* = 15.7 Hz, 1H), 6.10 – 6.01 (m, 1H), 5.05 (t, *J* = 6.8 Hz, 1H), 2.48 (dd, *J* = 14.0, 7.2 Hz, 1H), 2.35 (dd, *J* = 14.0, 7.8 Hz, 1H), 2.13 (s, 3H), 1.86 (ddd, *J* = 18.0, 11.8, 6.5 Hz, 2H), 1.72 – 1.62 (m, 4H), 1.58 – 1.48 (m, 4H), 1.15 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.0, 137.3, 133.1, 132.1, 128.5, 127.2, 126.1, 125.6, 123.8, 51.6, 41.3, 33.5, 25.6, 23.2, 21.1, 17.6; ν_{max} (FTIR)/cm^{-1}: 2967, 2914, 2362, 2336, 1700, 1653, 1558, 1457, 967, 733; *m/z* (ESI+) HRMS [M+H] $C_{19}H_{26}O^+$: formula found. 271.2054, cald. 217.2056.



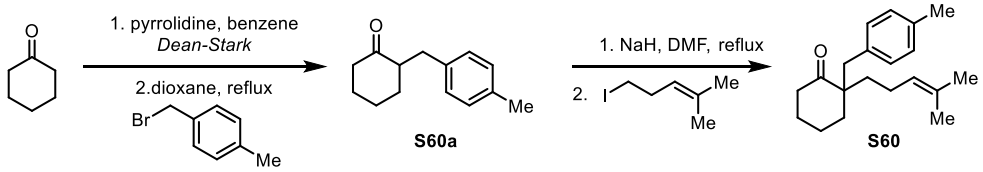
4-((1-(4-methylpent-3-en-1-yl)-2-oxocyclohexyl)methyl)benzonitrile (S56): S56a intermediate was synthesized according to reported literature procedure[170] and was consistent with reported spectroscopic data. **S56a** was then further reacted in the same manner as substrate **S51** and for alkylation reaction, employing 5-iodo-2-methylpent-2-ene (3.52 mmol) provided **S56** 183 mg (18%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.55 (d, *J* = 7.5 Hz, 2H), 7.25 (d, *J* = 7.7 Hz, 2H), 5.03 (t, *J* = 6.8 Hz, 1H), 3.07 (d, *J* = 13.7 Hz, 1H), 2.86 (d, *J* = 13.7 Hz, 1H), 2.51 – 2.43 (m, 1H), 2.39 – 2.34 (m, 1H), 2.09 – 2.03 (m, 1H), 1.95 (s, 1H), 1.80 – 1.57 (m, 12H), 1.37 (dd, *J* = 15.3, 10.6 Hz, 1H);^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.9, 144.2, 132.4, 131.7, 131.5, 123.7, 119.0, 110.1, 52.7, 40.3, 39.3, 36.3, 35.2, 26.9, 25.7, 22.4, 20.7, 17.7; ν_{max} (FTIR)/cm^{-1}: 2931, 2861, 2226, 1701, 1606, 1503, 1376, 1178, 954, 831; *m/z* (ESI+) HRMS [M+H] $C_{20}H_{25}NO^+$: formula found 296.2000, cald. 296.2009.

2-benzyl-1-cyclopropyl-2,6-dimethylhept-5-en-1-ol (S58a): General procedure B was followed employing **S22a** (3.26 mmol) and 0.5M cyclopropylmagnesium bromide (4.88 mmol). Purification by silica plug with dichloromethane as the eluent provided **S58a** as a clear oil that was directly used in the next step. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.29 – 7.15 (m, 5H), 5.09 (dt, *J* = 29.3, 6.5 Hz, 1H), 2.94 – 2.54 (m, 3H), 2.06 – 1.84 (m, 2H), 1.66 (dd, *J* = 30.7, 9.9 Hz, 6H), 1.28 – 1.06 (m, 3H), 0.90 (s, 3H), 0.64 – 0.47 (m, 2H), 0.25 (dddd, *J* = 27.7, 13.6, 9.2, 4.6 Hz, 2H).

2-benzyl-1-cyclopropyl-2,6-dimethylhept-5-en-1-one (S58): General procedure C2 was followed employing **S58a** (3.26 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S58** 500 mg (57%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.27 – 7.18 (m, 3H), 7.12 (d, *J* = 7.2 Hz, 2H), 5.09 (t, *J* = 6.9 Hz, 1H), 3.05 (d, *J* = 13.6 Hz, 1H), 2.79 (d, *J* = 13.6 Hz, 1H), 2.22 (ddd, *J* = 12.3, 7.9, 4.6 Hz, 1H), 1.89 (dtd, *J* = 17.1, 12.2, 5.3 Hz, 3H), 1.69 (s, 3H), 1.59 (s, 3H), 1.56 – 1.49 (m, 1H), 1.10 (s, 3H), 1.08 – 0.97 (m, 2H), 0.89 (ddd, *J* = 13.2, 8.2, 4.6 Hz, 2H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 214.3, 137.7, 131.8, 130.4, 127.9, 126.3, 124.0, 52.4, 44.3, 38.7, 25.7, 23.5, 20.4, 17.6, 16.8, 11.8, 11.4; ν_{max} (FTIR)/cm^{-1}: 2968, 2917, 2361, 2340, 1684, 1506, 1456, 1377, 1048, 700; *m/z* (ESI+) HRMS [M+H] $C_{19}H_{26}O^+$: formula found. 271.2056, cald. 271.2056.

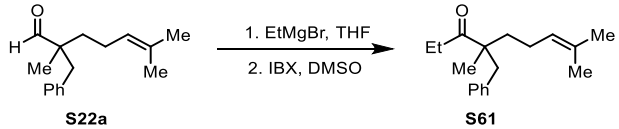


2-methyl-2-(4-methylpent-3-en-1-yl)cyclohexan-1-one (S59): A 100 mL flame dried flask equipped with a stir bar and reflux condenser was charged with sodium hydride (15.0 mmol, 1.7 equiv., 60% dispersion) and dry THF (45mL, 0.33M) and cooled to 0 °C under nitrogen. 2-methylcyclohexanone (8.92 mmol, 1.0 equiv.) was added to the solution dropwise *via* syringe. The reaction was left stirring at 0 °C for 30 min. and was then heated to 80°C. 5-iodo-2-methylpent-2-ene (13.37 mmol, 1.5 equiv.) was added dropwise *via* syringe. The reaction was monitored by TLC, until completion (2h). The organic layer was extracted with ethyl acetate (150 mL) and washed with water (3x70mL), sat. aq. NH_4Cl (50mL), aq. $NaHCO_3$ (50mL), and brine (1x50mL). The organic layer was dried with sodium sulfate and concentrated under reduced pressure. The product was isolated by flash chromatography (2:8, DCM:hexanes) to afford **S59** 583 mg (25%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 5.08 (t, *J* = 6.4 Hz, 1H), 2.48 – 2.32 (m, 2H), 1.99 – 1.87 (m, 2H), 1.85 – 1.66 (m, 9H), 1.61 – 1.54 (m, 4H), 1.46 – 1.38 (m, 1H), 1.07 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 216.0, 131.9, 124.1, 48.6, 39.5, 38.8, 37.7, 27.6, 25.7, 22.5, 22.5, 21.1, 17.6; ν_{max} (FTIR)/cm^{-1}:2930, 2903, 1703, 1700, 1448, 1375, 1122, 986, 827, 742; *m/z* (ESI+) HRMS [M+] $C_{13}H_{22}O^+$: formula found 195.1725, cald. 195.1743.



2-(4-methylbenzyl)-2-(4-methylpent-3-en-1-yl)cyclohexan-1-one (S60): S60a intermediate was synthesized according to reported literature procedure[19] and was consistent with reported spectroscopic data. **S56a** was then further reacted in the same manner as substrate **S51** and for alkylation reaction, employing 5-iodo-2-methylpent-2-ene (3.52 mmol) provided **S60** 245 mg (23%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.06 (d, *J* = 7.8 Hz, 2H), 6.99 (d, *J* = 7.8 Hz, 2H), 5.04 (t, *J* = 6.9 Hz, 1H), 2.89 (d, *J* = 13.9 Hz, 1H), 2.84 (d, *J* = 13.9 Hz, 1H), 2.42 (ddd, *J* = 30.2, 12.4, 7.5 Hz, 2H), 2.31 (s, 3H), 2.09 – 2.04 (m, 1H), 1.91 (dd, *J* = 9.3, 3.8 Hz, 1H), 1.78 – 1.60 (m, 12H), 1.42 (dd, *J* = 12.7, 4.7 Hz, 1H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 215.0, 135.6,

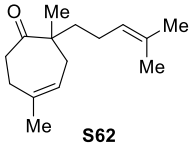
134.8, 131.9, 130.5, 128.6, 123.9, 52.4, 39.7, 39.5, 36.3, 34.6, 27.0, 25.7, 22.5, 21.0, 20.8, 17.7; ν_{max} (FTIR)/cm^{-1}: 3027, 2930, 2860, 1701, 1603, 1495, 1452, 1124, 954, 753; *m/z* (ESI+) HRMS [M+H] $C_{20}H_{28}O^+$: formula found 285.2211, cald. 285.2213.



S22a **S61**

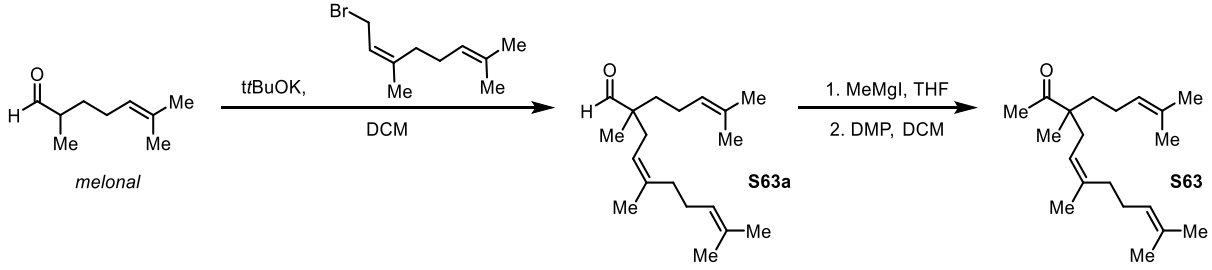
4-benzyl-4,8-dimethylnon-7-en-3-ol (S61a): General procedure B was followed employing **S22a** (4.34 mmol) and 3.0M EtMgBr (6.51 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S61a** 635 mg (56%) as the diastereomers, as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.29 (m, 2H), 7.21 (m, 3H), 5.10 (m, 1H), 3.29 (t, 1H, *J* = 11.7), 2.69 (m, 2H), 2.03 (m, 2H), 1.70 (s, 3H), 1.64 (s, 3H), 1.32 (m, 4H), 1.04 (m, 3H), 0.88 (s, 3H).

4-benzyl-4,8-dimethylnon-7-en-3-one (S61): General procedure C1 was followed employing **S61a** (2.44 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S61** 507 mg (80%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.25 (dt, *J* = 13.7, 6.8 Hz, 3H), 7.09 (d, *J* = 7.0 Hz, 2H), 5.07 (dd, *J* = 9.8, 4.0 Hz, 1H), 2.99 (d, *J* = 13.3 Hz, 1H), 2.69 (d, *J* = 13.3 Hz, 1H), 2.53 – 2.39 (m, 1H), 2.35 – 2.18 (m, 1H), 1.94 – 1.75 (m, 3H), 1.70 (s, 3H), 1.61 (s, 3H), 1.49 – 1.38 (m, 1H), 1.14 (s, 3H), 1.02 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 215.8, 137.7, 131.8, 130.2, 127.9, 126.3, 123.9, 51.8, 44.8, 39.0, 31.8, 25.6, 23.4, 20.5, 17.6, 7.7; ν_{max} (FTIR)/cm^{-1}: 2968, 2926, 2850, 1702, 1454, 1378, 1032, 918, 908, 702; *m/z* (ESI+) HRMS [M+] $C_{18}H_{26}O^+$: formula found. 258.1901, cald. 258.1984.



S62

2,5-dimethyl-2-(4-methylpent-3-en-1-yl)cyclohept-4-en-1-one (S62): **S62** was synthesized according to literature precedent and matches spectroscopic data.[171] ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 5.56-5.38 (m, 1H), 5.04 (ddd, *J* = 7.1, 5.7, 1.4 Hz, 1H), 2.94 (ddd, *J* = 11.4, 10.3, 5.6 Hz, 1H), 2.57-2.38 (m, 2H), 2.38-2.19 (m, 2H), 2.03 (dd, *J* = 15.2, 7.5 Hz, 1H), 1.93-1.78 (m, 2H), 1.74-1.63 (m, 6H), 1.57 (s, 2H), 1.53-1.41 (m, 2H), 1.07 (m, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 216.8, 136.8, 131.8, 124.1, 121.5, 53.7, 38.9, 37.8, 34.9, 31.9, 25.6, 25.2, 22.9, 22.0, 17.6.

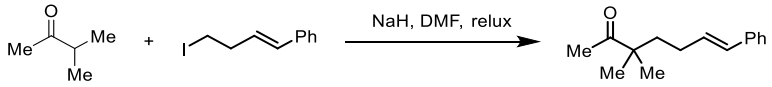


melonal **S63a** **S63**

(Z)-2,5,9-trimethyl-2-(4-methylpent-3-en-1-yl)deca-4,8-dienal (S63a): General procedure A was followed employing melonal (14.3 mmol) and geranyl bromide (17.1 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (9:1) provided **S63a** 2.07 g (53%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 9.46 (s, *J* = 9.8 Hz, 1H), 5.05 (m, 3H), 2.17 (m, 2H), 2.04 (m, 4H), 1.95 – 1.79 (m, 2H), 1.73 – 1.64 (m, 6H), 1.63 – 1.52 (m, 9H), 1.52 – 1.39 (m, 1H), 1.02 (s, 3H).

(Z)-3,6,10-trimethyl-3-(4-methylpent-3-en-1-yl)undeca-5,9-dien-2-ol (S63b): General procedure B was followed employing **S63a** (14.3 mmol) and 3.0M MeMgI (21.45 mmol). The product was used crude in the following step.

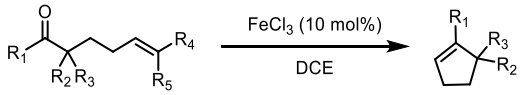
(Z)-3,6,10-trimethyl-3-(4-methylpent-3-en-1-yl)undeca-5,9-dien-2-one (S63): General procedure C2 was followed employing **S63b** (2.89 mmol). Purification by flash column chromatography eluting with hexanes/EtOAc (3:2) provided **S63** 750 mg (90%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 5.06 (m, 2H), 5.00 (m, 1H), 2.23 (m, 2H), 2.11 (s, 3H), 2.03 (dt, 2H, J = 29.8, 7.2 Hz), 1.83 (m, 2H), 1.68 (s, 6H), 1.61 (m, 10H), 1.47 (m, 1H), 1.09 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.7, 137.8, 131.9, 131.4, 124.2, 124.0, 119.4, 51.7, 39.9, 38.5, 36.4, 26.5, 25.68, 25.65, 25.58, 23.2, 20.5, 17.7, 17.6, 16.2; ν_{max} (FTIR)/cm^{-1}: 2966, 2916, 1733, 1700, 1652, 1558, 1456, 1375, 1032, 828; *m/z* (ESI+) HRMS [M+H] $C_{20}H_{34}O^+$: formula found. 291.2680, cald. 291.2682.



65

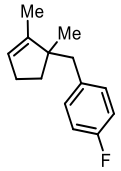
(E)-3,3-dimethyl-7-phenylhept-6-en-2-one (65): Synthesis of **65** according to literature precedent.[172] ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.31 (dt, 4H, J = 15.2, 7.7 Hz), 7.20 (t, 1H, J = 7.1 Hz), 6.39 (d, 1H, J = 15.8 Hz), 6.22-6.14 (m, 1H), 2.15 (s, 3H), 2.11 (dd, 2H, J = 15.8, 7.8 Hz), 1.74-1.68 (m, 2H), 1.17 (s, 6H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 213.8, 137.6, 130.2, 130.1, 128.5, 127.0, 125.9, 47.7, 39.5, 28.4, 26.7, 25.2, 24.4; ν_{max} (FTIR)/cm^{-1}: 2969, 2921, 2854, 2848, 1702, 1454, 1254, 1095, 764, 712; *m/z* (ESI+) HRMS [M+] $C_{15}H_{20}O^+$: formula found. 234.1853, cald. 234.1852.

General Procedure for the Carbonyl-Olefin Metathesis.

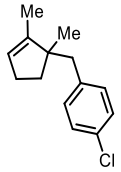


A flame-dried round bottom flask was charged with ketone substrate (1.0 equiv) at room temperature. To the flask was added $FeCl_3$ (0.10 equiv) in DCE (0.05M), and the resulting mixture was stirred for 16-24 hours at room temperature. Reaction was also run at reflux (80 °C) for 3 hours, when indicated. Upon completion (as determined by TLC analysis), the reaction mixture was passed through a short silica plug eluting with DCM (50 mL). The filtrate was concentrated under reduced pressure and the crude material was purified using column chromatography with the indicated eluent to give the pure metathesis adducts.

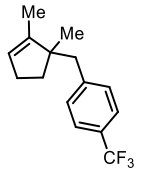
((1,2-dimethylcyclopent-2-en-1-yl)methyl)benzene (24): The cyclization of **22** (0.818 mmol) was performed according to general procedure for metathesis and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **24** 113 mg (74%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.26 – 7.15 (m, 5H), 5.28 (s, 1H), 2.61 (d, J = 13.2 Hz, 1H), 2.58 (d, J = 13.2 Hz, 1H), 2.02 – 1.94 (m, 2H), 1.74 – 1.70 (m, 4H), 1.49 – 1.45 (m, 1H), 1.05 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 145.9, 139.7, 130.2, 127.6, 125.7, 124.9, 50.2, 44.7, 36.7, 29.2, 25.4, 12.7; ν_{max} (FTIR)/cm^{-1}: 2928, 2864, 1976, 1716, 1492, 1454, 1376, 1090, 1016, 702; *m/z* (ESI+) HRMS [M+H] $C_{14}H_{18}^+$: formula found 186.1413, cald. 186.1409.



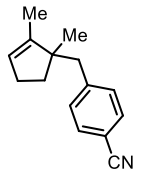
1-((1,2-dimethylcyclopent-2-en-1-yl)methyl)-4-fluorobenzene (33): The cyclization of **S33** (0.23 mmol) was performed according to general procedure for metathesis and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **33** 29.5 mg (63%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.11 – 7.06 (m, 2H), 6.95 – 6.89 (m, 2H), 5.28 (s, 1H), 2.58 (d, *J* = 13.4 Hz, 1H), 2.54 (d, *J* = 13.4 Hz, 1H), 2.01 – 1.96 (m, 1H), 1.90 (ddd, *J* = 12.2, 8.5, 3.9 Hz, 1H), 1.69 – 1.65 (m, 4H), 1.49 – 1.45 (m, 1H), 1.05 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 162.1, 145.4, 135.3, 131.4 (d, *J* = 7.8 Hz), 125.2, 114.3 (d, *J* = 20.9 Hz), 50.2, 43.8, 36.6, 29.2, 25.5, 12.7; ν_{max} (FTIR)/cm^{-1}: 2956, 2928, 2856, 1606, 1508, 1456, 1220, 1156, 1018, 826; *m/z* (ESI+) HRMS [M+H] $C_{14}H_{17}F^+$: formula found. 204.1320 cald. 204.1314.



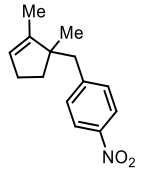
1-chloro-4-((1,2-dimethylcyclopent-2-en-1-yl)methyl)benzene (34): The cyclization of **S34** (0.22 mmol) was performed according to general procedure for metathesis and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **34** 36 mg (75%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.21 (d, *J* = 8.4 Hz, 2H), 7.07 (d, *J* = 8.4 Hz, 2H), 5.28 (s, 1H), 2.57 (d, *J* = 13.3 Hz, 1H), 2.54 (d, *J* = 13.3 Hz, 1H), 2.02 – 1.97 (m, 1H), 1.91 – 1.87 (m, 1H), 1.70 – 1.66 (m, 4H), 1.55 (s, 3H), 1.48 (ddd, *J* = 12.5, 8.9, 6.9 Hz, 1H), 1.05 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 145.3, 138.1, 131.6, 131.4, 127.7, 125.3, 50.2, 44.0, 36.6, 29.2, 25.5, 12.7; ν_{max} (FTIR)/cm^{-1}: 2930, 2922, 2852, 1700, 1490, 1454, 1090, 1016, 838, 804; *m/z* (ESI+) HRMS [M+H] $C_{14}H_{17}Cl^+$: formula found. 220.0983 cald. 220.1019.



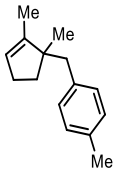
1-((1,2-dimethylcyclopent-2-en-1-yl)methyl)-4-(trifluoromethyl)benzene (35): The cyclization of **S35** (0.19 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **35** 35 mg (72%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.50 (d, *J* = 7.5 Hz, 2H), 7.25 (d, *J* = 7.6 Hz, 2H), 5.30 (s, 1H), 2.66 (d, *J* = 13.1 Hz, 1H), 2.63 (d, *J* = 13.1 Hz, 1H), 2.04 – 1.98 (m, 1H), 1.93 – 1.89 (m, 1H), 1.71 – 1.64 (m, 4H), 1.52 – 1.47 (m, 1H), 1.07 (d, *J* = 1.7 Hz, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 145.2, 143.8, 130.3, 125.6, 125.4, 124.6, 124.5, 50.3, 44.5, 36.6, 29.2, 25.6, 12.6; ν_{max} (FTIR)/cm^{-1}: 2956, 2932, 2856, 1616, 1418, 1322, 1160, 1120, 1066, 852; *m/z* (ESI+) HRMS [M+H] $C_{15}H_{17}F_3^+$: formula found 254.1284, cald. 254.1282.



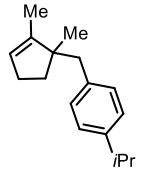
4-((1,2-dimethylcyclopent-2-en-1-yl)methyl)benzonitrile (36): The cyclization of **S36** (0.19 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **36** 36.5 mg (93%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.36 (d, *J* = 8.2 Hz, 2H), 7.01 (d, *J* = 8.1 Hz, 2H), 5.28 (s, 1H), 2.55 (d, *J* = 13.2 Hz, 1H), 2.52 (d, *J* = 13.2 Hz, 1H), 2.01 – 1.96 (m, 1H), 1.91 – 1.87 (m, 1H), 1.69 – 1.66 (m, 4H), 1.50 – 1.45 (m, 1H), 1.04 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 145.3, 138.6, 131.8, 131.0, 130.6, 125.3, 119.7, 50.1, 44.1, 36.6, 29.2, 25.5, 12.7; ν_{max} (FTIR)/cm^{-1}: 2952, 2925, 2849, 1486, 1453, 1377, 1071, 1011, 839, 799; *m/z* (ESI+) HRMS [M+] $C_{15}H_{17}N^+$: formula found 210.0998, cald. 210.1211.



1-((1,2-dimethylcyclopent-2-en-1-yl)methyl)-4-nitrobenzene (37): The cyclization of **S37** (0.07 mmol) was performed according to general procedure for metathesis and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **37** 14.3 mg (84%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.90 (d, *J* = 8.1 Hz, 5H), 7.10 (d, *J* = 8.2 Hz, 6H), 5.31 (s, 3H), 2.60 (s, 7H), 2.01 (d, *J* = 14.1 Hz, 4H), 1.90 (dd, *J* = 10.0, 5.2 Hz, 4H), 1.71 (s, 13H), 1.52 – 1.48 (m, 3H), 1.07 (d, *J* = 1.2 Hz, 10H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 146.0, 145.0, 134.4, 128.5, 125.5, 124.2, 50.4, 44.37, 36.7, 29.3, 25.6, 12.6; ν_{max} (FTIR)/cm^{-1}: 2955, 2928, 2851, 1609, 1514, 1450, 1340, 1276, 1034, 836; *m/z* (ESI+) HRMS [M+] $C_{14}H_{17}NO_2^+$: formula found 231.1001, cald. 231.1259.

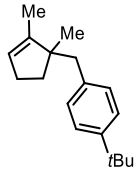


1-((1,2-dimethylcyclopent-2-en-1-yl)methyl)-4-methylbenzene (38): The cyclization of **S38** (0.23 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **38** 44 mg (94%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.08 – 7.02 (m, 4H), 5.28 (d, *J* = 1.3 Hz, 1H), 2.55 (s, 2H), 2.33 (s, 3H), 1.99 (dddd, *J* = 19.7, 12.6, 6.4, 3.1 Hz, 2H), 1.80 – 1.73 (m, 1H), 1.72 – 1.69 (m, 3H), 1.49 – 1.42 (m, 1H), 1.04 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 146.1, 136.6, 135.1, 130.1, 128.3, 124.7, 50.2, 44.2, 36.7, 29.2, 25.3, 21.0, 12.7; ν_{max} (FTIR)/cm^{-1}:2923, 2360, 2336, 1716, 1652, 1506, 1456, 1375, 1020, 810; *m/z* (ESI+) HRMS [M+] $C_{15}H_{20}^+$: formula found 200.1574, cald. 200.1565.

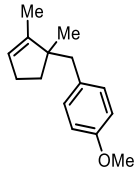


1-((1,2-dimethylcyclopent-2-en-1-yl)methyl)-4-isopropylbenzene (39): The cyclization of **S39** (0.21 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **39** 41 mg (85%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.11 (d, *J* = 8.1 Hz, 2H), 7.07 (d, *J* = 8.1 Hz, 2H), 5.28 (d, *J* = 1.4 Hz, 1H), 2.88 (dt, *J* = 13.8, 6.9 Hz, 1H), 2.56 (s, 2H), 2.04 – 1.93 (m,

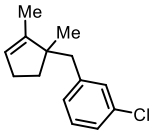
2H), 1.78 (dddd, *J* = 12.7, 10.2, 5.3, 2.2 Hz, 1H), 1.70 (dd, *J* = 5.2, 3.5 Hz, 3H), 1.48 – 1.42 (m, 1H), 1.25 (d, *J* = 6.9 Hz, 6H), 1.04 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 146.2, 146.1, 137.0, 130.1, 125.6, 124.7, 50.2, 44.2, 36.7, 33.6, 29.2, 25.3, 24.1, 24.0, 12.7; ν_{max} (FTIR)/cm^{-1}: 2952, 2922, 2864, 1512, 1458, 1360, 1100, 906, 822, 730; *m/z* (ESI+) HRMS [M+H] $C_{17}H_{24}^+$: formula found. 228.1880 cald. 228.1878.



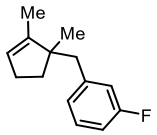
1-(tert-butyl)-4-((1,2-dimethylcyclopent-2-en-1-yl)methyl)benzene (40): The cyclization of **S40** (0.23 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **40** 38 mg (68%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.27 (d, 2H, *J* 8.0), 7.09 (d, 2H, *J* = 8.0), 5.30 (s, 1H), 2.57 (s, 2H), 2.08-1.94 (m, 2H), 1.87-1.74 (m, 1H), 1.71 (s, 3H), 1.50-1.42 (m, H), 1.33 (s, 9H), 1.05 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 148.4, 146.2, 136.6, 129.8, 124.7, 124.5, 50.1, 44.0, 36.7, 34.3, 31.4, 29.2, 25.6, 12.7; ν_{max} (FTIR)/cm^{-1}: 2964, 2864, 2363, 2339, 1700, 1652, 1558, 1458, 1354, 827; *m/z* (ESI+) HRMS [M+] $C_{18}H_{26}^+$: formula found 242.2026, cald. 242.2035.



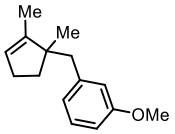
1-((1,2-dimethylcyclopent-2-en-1-yl)methyl)-4-methoxybenzene (41): The cyclization of **S41** (0.18 mmol) was performed according to general procedure for metathesis and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **41** 15 mg (38%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.05 (d, *J* = 8.5 Hz, 2H), 6.79 (d, *J* = 8.5 Hz, 2H), 5.26 (s, 1H), 3.79 (s, 3H), 2.52 (d, *J* = 1.8 Hz, 2H), 2.01 – 1.88 (m, 2H), 1.77 – 1.67 (m, 4H), 1.49 – 1.40 (m, 1H), 1.02 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 157.8, 145.9, 131.8, 131.0, 124.8, 113.0, 55.2, 50.2, 43.7, 36.7, 29.2, 25.4, 12.7; ν_{max} (FTIR)/cm^{-1}: 2918, 2850, 23662, 2338, 2192, 2016, 1652, 1512, 1456, 1248, 804; *m/z* (ESI+) HRMS [M+H] $C_{15}H_{20}O^+$: formula found 216.1512, cald. 216.1514.



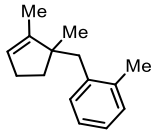
1-chloro-3-((1,2-dimethylcyclopent-2-en-1-yl)methyl)benzene (42): The cyclization of **S42** (0.22 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **42** 34 mg (72%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.17 (d, *J* = 5.3 Hz, 2H), 7.13 (s, 1H), 7.04 – 7.01 (m, 1H), 5.30 (s, 1H), 2.55 (t, *J* = 8.1 Hz, 2H), 2.05 – 1.98 (m, 1H), 1.92 (ddd, *J* = 12.3, 8.1, 3.8 Hz, 1H), 1.76 – 1.71 (m, 1H), 1.70 (s, 3H), 1.52 – 1.46 (m, 1H), 1.05 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 145.4, 141.8, 133.3, 130.1, 128.8, 128.3, 125.9, 125.2, 50.2, 44.3, 36.7, 29.2, 25.5, 12.6; ν_{max} (FTIR)/cm^{-1}: 2954, 2926, 2848, 1594, 1572, 1456, 1428, 1206, 1080, 780; *m/z* (ESI+) HRMS [M+H] $C_{14}H_{17}Cl^+$: formula found 220.1022, cald. 220.1019.



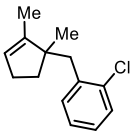
1-((1,2-dimethylcyclopent-2-en-1-yl)methyl)-3-fluorobenzene (43): The cyclization of **S43** (0.23 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **43** 34 mg (73%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.20 – 7.17 (m, 1H), 6.92 – 6.82 (m, 3H), 5.29 (d, *J* = 1.0 Hz, 1H), 2.59 (d, *J* = 13.2 Hz, 1H), 2.57 (s, 1H), 2.03 – 1.98 (m, 1H), 1.91 (ddd, *J* = 12.3, 8.2, 3.8 Hz, 1H), 1.74 – 1.70 (m, 1H), 1.68 (d, *J* = 1.7 Hz, 3H), 1.48 (ddd, *J* = 12.7, 8.9, 6.9 Hz, 1H), 1.04 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 162.4 (d, *J* = 244.3 Hz), 145.4, 142.3 (d, *J* = 7.1 Hz), 128.8 (d, *J* = 8.3 Hz), 125.9 (d, *J* = 2.7 Hz), 125.2, 116.8 (d, *J* = 20.7 Hz), 112.6 (d, *J* = 21.0 Hz), 50.2, 44.4, 36.7, 29.2, 25.5, 12.6; ν_{max} (FTIR)/cm^{-1}: 2954, 2930, 2852, 1734, 1612, 1584, 1488, 1446, 1252, 872; *m/z* (ESI+) HRMS [M+H] $C_{14}H_{17}F^+$: formula found 204.1320, cald. 204.1314.



1-((1,2-dimethylcyclopent-2-en-1-yl)methyl)-3-methoxybenzene (44): The cyclization of **S44** (0.36 mmol) was performed according to general procedure for metathesis and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **44** 50.5 mg (64%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.22 – 7.14 (m, 1H), 6.74 (dd, *J* = 15.4, 12.7 Hz, 3H), 5.30 (s, 1H), 3.81 (s, 3H), 2.56 (d, *J* = 13.9 Hz, 2H), 2.08 – 1.91 (m, 2H), 1.85 – 1.77 (m, 1H), 1.70 (d, *J* = 1.7 Hz, 3H), 1.48 (dd, *J* = 11.2, 8.1 Hz, 1H), 1.05 (d, *J* = 5.7 Hz, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 159.0, 146.0, 141.3, 128.4, 124.9, 122.8, 116.1, 110.9, 55.1, 50.2, 44.7, 36.8, 29.2, 25.4, 12.7; ν_{max} (FTIR)/cm^{-1}: 2923, 2361, 2339, 1699, 1558, 1488, 1436, 1261, 1152, 1050; *m/z* (ESI+) HRMS [M+] $C_{15}H_{20}O^+$: formula found. 216.1508, cald. 216.1514.

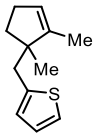


1-((1,2-dimethylcyclopent-2-en-1-yl)methyl)-2-methylbenzene (45): The cyclization of **S45** (0.23 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **45** 25 mg (63%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.14 – 7.09 (m, 4H), 5.33 (d, *J* = 1.1 Hz, 1H), 2.78 (d, *J* = 13.7 Hz, 1H), 2.54 (d, *J* = 13.7 Hz, 1H), 2.35 (s, 3H), 2.10 – 2.04 (m, 1H), 1.92 (ddd, *J* = 7.1, 4.4, 2.0 Hz, 2H), 1.68 (d, *J* = 1.6 Hz, 3H), 1.52 – 1.46 (m, 1H), 1.08 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 146.7, 138.2, 136.9, 130.7, 130.1, 125.7, 125.1, 124.7, 50.7, 39.9, 37.2, 29.3.25.4, 20.4, 12.9; ν_{max} (FTIR)/cm^{-1}: 2950, 2930, 2826, 2042, 1492, 1460, 1368, 1360, 1100, 742; *m/z* (ESI+) HRMS [M+H] $C_{15}H_{20}^+$: formula found 200.1565, cald. 200.1565.

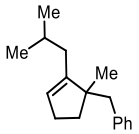


1-chloro-2-((1,2-dimethylcyclopent-2-en-1-yl)methyl)benzene (46): The cyclization of **S46** (0.22 mmol) was performed according to general procedure for metathesis and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **46** 24 mg (50%) as a

clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.36 – 7.32 (m, 1H), 7.14 (ddd, *J* = 9.3, 7.3, 2.2 Hz, 3H), 5.33 (s, 1H), 2.98 (d, *J* = 13.5 Hz, 1H), 2.63 (d, *J* = 13.5 Hz, 1H), 2.07 – 2.00 (m, 2H), 1.85 – 1.77 (m, 1H), 1.73 (d, *J* = 1.6 Hz, 3H), 1.47 (dt, *J* = 12.1, 7.9 Hz, 1H), 1.09 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 145.9, 137.5, 135.0, 132.0, 129.3, 127.1, 125.9, 125.2, 50.9, 43.4, 40.0, 36.7, 29.4, 25.5, 12.7; ν_{max} (FTIR)/cm^{-1}: 2954, 2932, 2862, 1732, 1442, 1360, 1096, 1036, 742, 682; *m/z* (ESI+) HRMS [M+H] $C_{14}H_{17}Cl^+$: formula found 220.1022, cald. 220.1019.



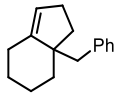
2-((1,2-dimethylcyclopent-2-en-1-yl)methyl)thiophene (47): The cyclization of **S47** (0.24 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **47** 24.7 mg (54%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.12 (d, *J* = 5.1 Hz, 1H), 6.94 – 6.92 (m, 1H), 6.78 (d, *J* = 3.3 Hz, 1H), 5.32 (s, 1H), 2.85 (d, *J* = 14.5 Hz, 1H), 2.82 (d, *J* = 14.5 Hz, 1H), 2.13 – 2.09 (m, 1H), 2.03 – 1.98 (m, 1H), 1.95 (ddd, *J* = 14.7, 6.6, 4.0 Hz, 1H), 1.69 (s, 3H), 1.60 – 1.57 (m, 1H), 1.08 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 145.4, 141.8, 126.3, 126.1, 125.3, 123.4, 50.2, 39.1, 36.6, 29.3, 25.2, 12.6; ν_{max} (FTIR)/cm^{-1}: 2926, 2361, 2338, 1733, 1652, 1506, 1456, 1374, 906, 731; *m/z* (ESI+) HRMS [M+H] $C_{12}H_{16}S^+$: formula found. 193.1255, cald. 193.1006.



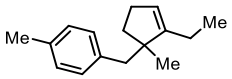
((2-isobutyl-1-methylcyclopent-2-en-1-yl)methyl)benzene (48): The cyclization of **S48** (0.07 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **48** 11 mg (62%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.26 – 7.15 (m, 5H), 5.30 (s, 1H), 2.58 (d, *J* = 4.1 Hz, 2H), 2.10 – 2.05 (m, 1H), 1.98 – 1.86 (m, 5H), 1.43 (dd, *J* = 7.7, 4.7 Hz, 1H), 1.02 (s, 3H), 0.99 – 0.96 (m, 6H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 149.1, 139.7, 130.3, 127.3, 126.7, 125.7, 123.7, 50.6, 44.9, 36.9, 36.5, 29.4, 26.7, 25.3, 23.2, 23.0; ν_{max} (FTIR)/cm^{-1}: 2951, 2865, 1493, 1451, 1368, 1173, 1081, 983, 827, 698; *m/z* (ESI+) HRMS [M+] $C_{17}H_{24}^+$: formula found. 228.1878, cald. 228.1878.

((2-methylcyclopent-2-ene-1,1-diyl)bis(methylene))dibenzene (49) The cyclization of **S49** (0.13 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **49** 25 mg (72%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.24 (m, 4H), 7.21 (d, *J* = 6.7 Hz, 2H), 7.16 (m, 4H), 5.29 (s, 1H), 2.78 (d, *J* = 13.3 Hz, 2H), 2.72 (d, *J* = 13.3 Hz, 2H), 1.87 (s, 3H), 1.81 – 1.76 (m, 2H), 1.41 (t, *J* = 7.0 Hz, 2H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 142.5, 139.2, 130.3, 127.9, 127.6, 125.7, 55.2, 44.1, 32.6, 29.7, 13.3; ν_{max} (FTIR)/cm^{-1}: 3026.7, 2918.8, 2849.5, 1494.4, 1452.5, 1377.0, 1079.0, 1030.4, 749.9, 698.2; *m/z* (ESI+) HRMS [M+] $C_{20}H_{22}^+$: formula found 262.1715, cald. 262.1722.

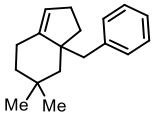
1,5,5-trimethylcyclopent-1-ene (50): The cyclization of **S50** (0.31 mmol) was performed according to general procedure for metathesis with the additive and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **50** 25.9 mg (56%) as a clear oil. Spectroscopic data is consistent with reported data.[173]



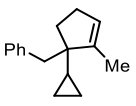
7a-benzyl-2,4,5,6,7,7a-hexahydro-1H-indene (51): The cyclization of **S51** (0.17 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **51** 27.6 mg (78%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.24 (t, *J* = 7.5 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.16 (d, *J* = 7.3 Hz, 2H), 5.23 (s, 1H), 2.78 (d, *J* = 13.2 Hz, 1H), 2.63 (d, *J* = 13.2 Hz, 1H), 2.43 – 2.40 (m, 1H), 2.23 (ddd, *J* = 13.7, 9.2, 4.7 Hz, 1H), 2.06 (dd, *J* = 12.8, 8.1 Hz, 1H), 1.97 (dd, *J* = 14.8, 10.6 Hz, 1H), 1.90 (dd, *J* = 20.9, 13.1 Hz, 2H), 1.76 – 1.70 (m, 1H), 1.65 – 1.58 (m, 2H), 1.38 (dt, *J* = 12.7, 9.5 Hz, 1H), 1.29 (tdd, *J* = 13.1, 9.0, 4.1 Hz, 1H), 1.22 (td, *J* = 13.4, 3.9 Hz, 1H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 147.5, 139.8, 130.3, 127.5, 125.6, 122.0, 50.3, 40.5, 40.2, 37.2, 29.6, 27.8, 26.7, 22.7; ν_{max} (FTIR)/cm^{-1}: 3026, 2925, 2850, 1491, 1452, 1050, 1030, 995, 820, 699; *m/z* (ESI+) HRMS [M+] $C_{16}H_{20}^+$: formula found 212.1571, cald. 212.1565.



1-((2-ethyl-1-methylcyclopent-2-en-1-yl)methyl)-4-methylbenzene (52): The cyclization of **S52** (0.37 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **52** 21 mg (53%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.04 (dd, *J* = 11.9, 6.7 Hz, 4H), 5.29 (s, 1H), 2.55 (s, 2H), 2.32 (s, 3H), 2.01 (d, *J* = 5.6 Hz, 2H), 1.97 – 1.92 (m, 1H), 1.79 (dd, *J* = 12.3, 5.1 Hz, 1H), 1.47 – 1.38 (m, 2H), 1.13 (t, *J* = 7.3 Hz, 3H), 1.03 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 152.2, 136.6, 135.1, 130.1, 128.3, 122.0, 50.5, 44.5, 29.3, 25.5, 21.0, 19.6, 12.2; ν_{max} (FTIR)/cm^{-1}: 2955, 2361, 2336, 1699, 1558, 1456, 1374, 1021, 810, 667; *m/z* (ESI+) HRMS [M+H] $C_{16}H_{22}^+$: formula found. 214.1732, cald. 214.1722.

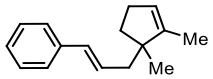


7a-benzyl-6,6-dimethyl-2,4,5,6,7,7a-hexahydro-1H-indene (53): The cyclization of **S53** (0.17 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **53** 26 mg (64%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.19 (dq, *J* = 14.6, 6.9 Hz, 5H), 5.25 (s, 1H), 2.98 (d, *J* = 13.3 Hz, 1H), 2.58 (d, *J* = 13.4 Hz, 1H), 2.35 (dd, *J* = 9.7, 6.5 Hz, 2H), 2.07 (dd, *J* = 12.7, 5.2 Hz, 1H), 1.85 (dd, *J* = 23.6, 9.7 Hz, 2H), 1.57 (d, *J* = 12.2 Hz, 1H), 1.39 (ddd, *J* = 14.5, 11.6, 7.3 Hz, 2H), 1.31 – 1.26 (m, 2H), 1.20 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 147.6, 139.9, 130.4, 127.4, 125.6, 122.7, 53.9, 43.4, 40.7, 40.2, 34.9, 31.7, 30.0, 27.6, 23.5; ν_{max} (FTIR)/cm^{-1}: 3083, 3027, 2049, 1658, 1494, 1452, 1385, 1363, 1043, 827; *m/z* (ESI+) HRMS [M+] $C_{18}H_{24}^+$: formula found 240.1871, cald. 240.1878.

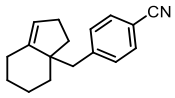


((1-cyclopropyl-2-methylcyclopent-2-en-1-yl)methyl)benzene (54): The cyclization of **S54** (0.13 mmol) was performed according to general procedure for metathesis at reflux for 3 hours

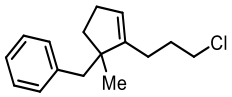
and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **54** 16 mg (58%) as a clear oil. ^1H NMR (400 MHz; $CDCl_3$) δ_H 7.21 (t, *J* = 7.3 Hz, 2H), 7.17 (t, *J* = 8.2 Hz, 3H), 5.25 (s, 1H), 2.69 (d, *J* = 13.3 Hz, 1H), 2.66 (d, *J* = 13.2 Hz, 1H), 1.89 – 1.82 (m, 1H), 1.76 (s, 3H), 1.56 – 1.44 (m, 2H), 1.14 – 1.06 (m, 1H), 0.98 – 0.91 (m, 1H), 0.36 (dq, *J* = 13.4, 4.4 Hz, 1H), 0.31 – 0.24 (m, 1H), 0.18 – 0.07 (m, 2H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 144.6, 139.4, 130.3, 127.3, 125.6, 125.4, 53.2, 43.9, 29.4, 29.2, 17.8, 13.2, 1.5, -0.3; ν_{max} (FTIR)/cm^{-1}: 3003.3, 2924.7, 2850.2, 1494.9, 1452.94, 1079.6, 1015.5, 756.7, 700.5; *m/z* (ESI+) HRMS [M+] $C_{16}H_{20}^+$: formula found 212.1656, cald. 212.1360.



(E)-(3-(1,2-dimethylcyclopent-2-en-1-yl)prop-1-en-1-yl)benzene (55): The cyclization of S**55** (0.22 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **55** 28.6 mg (60%) as a clear oil. ^1H NMR (400 MHz; $CDCl_3$) δ_H 7.35 (d, *J* = 7.5 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.20 (t, *J* = 7.2 Hz, 1H), 6.40 (d, *J* = 15.7 Hz, 1H), 6.20 – 6.14 (m, 1H), 5.32 (s, 1H), 2.29 – 2.11 (m, 5H), 1.93 (ddd, *J* = 13.6, 8.4, 5.6 Hz, 1H), 1.66 (d, *J* = 1.2 Hz, 3H), 1.63 – 1.59 (m, 1H), 1.06 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 145.9, 138.0, 131.6, 128.4, 128.3, 126.8, 126.0, 124.3, 49.5, 42.8, 36.7, 29.4, 25.4, 12.5; ν_{max} (FTIR)/cm^{-1}: 2954, 2912, 2044, 1772, 1654, 1440, 1276, 1158, 1090, 964; *m/z* (ESI+) HRMS [M+] $C_{16}H_{20}^+$: formula found. 212.1575, cald. 212.1565.

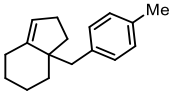


4-((2,3,4,5,6,7-hexahydro-3aH-inden-3a-yl)methyl)benzonitrile (56): The cyclization of **S56** (0.17 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **56** 29 mg (72%) as a clear oil. ^1H NMR (400 MHz; $CDCl_3$) δ_H 7.52 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 5.24 (s, 1H), 2.90 (s, 1H), 2.61 (d, *J* = 13.1 Hz, 1H), 2.44 (d, *J* = 13.7 Hz, 1H), 2.19 (t, *J* = 13.7 Hz, 1H), 1.96 – 1.93 (m, 2H), 1.89 (d, *J* = 13.1 Hz, 2H), 1.69 – 1.66 (m, 2H), 1.47 – 1.39 (m, 2H), 1.32 – 1.27 (m, 2H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 146.4, 145.7, 131.3, 130.9, 123.0, 119.6, 109.6, 50.6, 41.2, 40.9, 37.2, 29.6, 27.7, 26.7, 22.7; ν_{max} (FTIR)/cm^{-1}: 2931, 2861, 2226, 1700, 1606, 1504, 1445, 1414, 1125, 857; *m/z* (ESI+) HRMS [M+H] $C_{17}H_{19}N^+$: formula found 238.1567, cald. 238.1590.

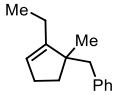


((2-(2-chloroethyl)-1-methylcyclopent-2-en-1-yl)methyl)benzene (58): The cyclization of **S58** (0.22 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **58** 10.9 mg (20%) as a clear oil. ^1H NMR (400 MHz; $CDCl_3$) δ_H 7.24 (d, *J* = 7.5 Hz, 2H), 7.20 (d, *J* = 7.3 Hz, 1H), 7.12 (d, *J* = 7.2 Hz, 2H), 5.04 – 4.98 (m, 1H), 3.51 (t, *J* = 7.2 Hz, 2H), 2.61 (q, *J* = 13.1 Hz, 2H), 2.47 (q, *J* = 7.2 Hz, 2H), 2.34 (ddd, *J* = 24.1, 17.0, 9.1 Hz, 2H), 1.76 – 1.70 (m, 1H), 1.66 – 1.59 (m, 2H), 1.36 (dt, *J* = 12.2, 7.4 Hz, 1H), 1.02 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 153.3, 139.4, 130.6, 127.5, 125.8, 115.5, 46.8, 46.3, 44.3, 39.2, 33.0, 29.6, 26.5, 22.0; ν_{max} (FTIR)/cm^{-1} : 2953, 2362, 2337, 1734, 1652, 1558, 1456, 1373, 1238, 908; *m/z* (ESI+) HRMS [M+] $C_{16}H_{21}Cl^+$: formula found 248.1335, cald. 248.1332.

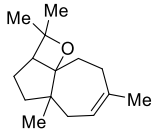
7a-methyl-2,4,5,6,7,7a-hexahydro-1H-indene (59): The cyclization of **S59** (0.26 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **59** 13.2 mg (38%) as a clear oil. Spectroscopic data is consistent with reported data.[174]



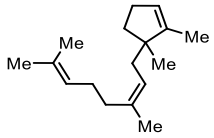
7a-(4-methylbenzyl)-2,4,5,6,7,7a-hexahydro-1H-indene (60): The cyclization of **S60** (0.09 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **60** 14.5 mg (70%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.05 (s, 4H), 5.22 (s, 1H), 2.71 (d, J = 13.3 Hz, 1H), 2.61 (d, J = 13.3 Hz, 1H), 2.41 (d, J = 13.9 Hz, 1H), 2.32 (s, 3H), 2.22 (t, J = 11.6 Hz, 1H), 2.05 (dd, J = 12.8, 8.1 Hz, 1H), 1.98 (dd, J = 14.7, 10.7 Hz, 1H), 1.89 (t, J = 13.0 Hz, 2H), 1.75 – 1.65 (m, 3H), 1.39 – 1.35 (m, 1H), 1.30 – 1.25 (m, 1H), 1.19 (dd, J = 13.4, 9.4 Hz, 1H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 147.8, 136.6, 135.0, 130.2, 128.3, 121.7, 50.3, 40.1, 40.0, 37.2, 29.6, 27.8, 26.7, 22.7, 21.0; ν_{max} (FTIR)/cm^{-1}: 2924, 2851, 2360, 2339, 1513, 1450, 1281, 1022, 849, 737; *m/z* (ESI+) HRMS [M+] $C_{17}H_{22}^+$: formula found 226.1719, cald. 226.1722.



((2-ethyl-1-methylcyclopent-2-en-1-yl)methyl)benzenefluorobenzene (61): The cyclization of **S61** (0.58 mmol) was performed according to general procedure for metathesis and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **61** 39 mg (34%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 7.24 – 7.17 (m, 3H), 7.13 (d, J = 6.7 Hz, 2H), 5.29 (d, J = 2.0 Hz, 1H), 2.59 (s, 2H), 2.04 – 1.93 (m, 4H), 1.49 – 1.39 (m, 2H), 1.14 (t, J = 7.3 Hz, 3H), 1.05 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 152.0, 139.7, 130.2, 127.5, 125.7, 122.2, 50.5, 45.0, 37.2, 29.2, 25.6, 19.6, 12.2; ν_{max} (FTIR)/cm^{-1}: 2964, 2361, 2337, 1716, 1699, 1558, 1456, 1374, 1057, 759; *m/z* (ESI+) HRMS [M+H] $C_{15}H_{20}^+$: formula found. 201.1656, cald. 201.1525.



2,2,4a,7-tetramethyl-2,2a,3,4,4a,5,8,9-octahydroazuleno[8a,1-b]oxete (62): S62 (2.27 mmol) was dissolved in 45 mL of DCE and $FeCl_3$ (1.14 mmol) was added at 0°C. The reaction was allowed to warm to room temperature and monitored by TLC. The reaction was quenched with elution through a silica plug, eluting with DCM and purification by flash column chromatography eluting with hexanes/EtOAc (5:1) provided **62** 254 mg (52%) as a clear oil. Spectroscopic data is consistent with literature precedent.[21] ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 5.36 (d, J = 5.9 Hz, 1H), 2.20-2.16 (m, 1H), 2.13-1.90 (m, 4H), 1.86-1.74 (m, 2H), 1.68 (s, 3H), 1.60-1.54 (m, 4H), 1.31 (s, 3H), 1.25 (s, 3H), 1.07 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 134.2, 119.9, 86.6, 78.0, 52.0, 47.8, 34.1, 30.9, 30.1, 29.6, 29.5, 26.0, 23.1, 22.5, 15.2.



(Z)-5-(3,7-dimethylocta-2,6-dien-1-yl)-1,5-dimethylcyclopent-1-ene (63): The cyclization of **S63** (0.22 mmol) was performed according to general procedure for metathesis at reflux for 3 hours and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **63** 16 mg (31%) as a clear oil. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 5.28 (d, *J* = 1.5 Hz, 1H), 5.14 – 5.06 (m, 2H), 2.19 – 2.13 (m, 2H), 2.09 – 1.98 (m, 5H), 1.80 (dd, *J* = 9.5, 3.3 Hz, 1H), 1.69 (d, *J* = 4.9 Hz, 3H), 1.64 – 1.58 (m, 8H), 1.56 – 1.50 (m, 2H), 1.00 (s, 3H); ^{13}C NMR (135 MHz, $CDCl_3$) δ_C 146.6, 135.9, 131.2, 124.4, 123.7, 121.8, 49.6, 40.0, 37.1, 36.6, 24.9, 26.7, 25.7, 25.0, 17.7, 16.2, 12.5; ν_{max} (FTIR)/cm^{-1}: 2915, 2850, 1652, 1558, 1472, 1409, 1381, 1104, 877, 715; *m/z* (ESI+) HRMS [M+H] $C_{17}H_{28}^+$: formula found. 232.2100, cald. 232.2191.

General procedure for carbonyl-olefin metathesis of substrates 22a-f with additive:
A flame-dried round bottom flask was charged with ketone substrate (1.0 equiv.) at room temperature. To the flask was added $FeCl_3$ (0.10 equiv.) in DCE (0.05M) followed by allyltrimethylsilane (5 equiv.) and the resulting mixture was stirred for 16-24 hours at room temperature. Upon completion (as determined by TLC analysis), the reaction mixture was passed through a short silica plug eluting with DCM (50 mL). The filtrate was concentrated under reduced pressure, and the crude material was purified using column chromatography, with the indicated eluent to give the pure metathesis product.

((1,2-dimethylcyclopent-2-en-1-yl)methyl)benzene (24): The cyclization of ketone substrate was performed according to general procedure for metathesis with the additive and purification by flash column chromatography eluting with pentane/Et_2O (12:1) provided **24** as a clear oil. Characterization for **24** listed above. Following listing provides scales and yields for each substrate that produces **24** as the metathesis product: **22b** (0.20 mmol) provides 28 mg (77%), **22c** (0.12 mmol) provides 18 mg (78%), **22d** (0.11 mmol) provides 1.0 mg (4%) **22e** (0.33 mmol) provides 18 mg (30%), **22f** (0.25 mmol) provides 13.5 mg (25%).

Appendix 3

Transannular Carbonyl-Olefin Metathesis – Experimental Details

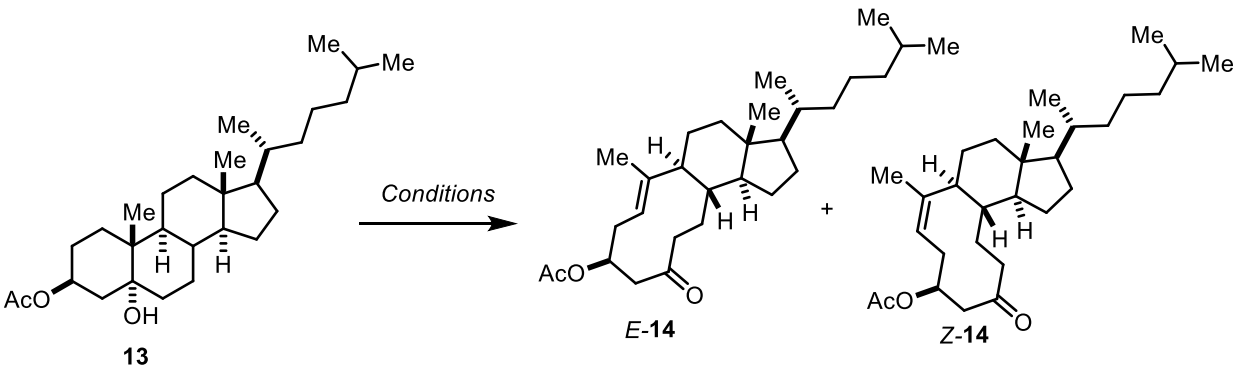
1. Evaluation of Reaction Conditions

a. Optimization of Ring Opening of Tertiary Alcohols

General procedure for ring opening of tertiary alcohol 13: **13**[1] (100 mg, 0.22 mmol) and PIDA (71 mg, 0.22 mmol) were dissolved in DCM (7 mL) and the solution was sparged with nitrogen for ten minutes. The flask was opened and iodine (57 mg, 0.22 mmol) was added and the septum quickly replaced. The reaction mixture was stirred under nitrogen atmosphere and irradiated with blue LEDs for 3 hours, at which time the mixture was diluted with DCM and poured into a separatory funnel containing saturated sodium bicarbonate and saturated sodium thiosulfate solutions. The layers were separated and the aqueous phase was washed with two additional portions of DCM. The combined organic layers were dried over Na_2SO_4 and concentrated by rotary evaporator before being purified by flash column chromatography eluting with hexanes/Et_2O to afford first *Z*-**14** followed *E*-**14**. The results are summarized in Table SI-1.

[1] Mihailović, M. L.; Lorenc, L.; Pavlović, V.; Kalvoda, J. *Tetrahedron* **1977**, *33*, 441.

Table A3-1: Optimization of ring opening for cyclodecenone preparation.



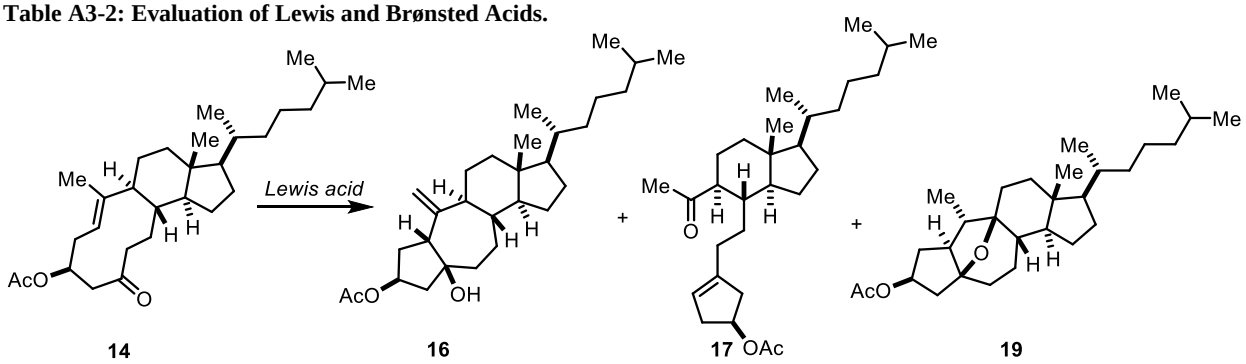
entry	oxidant	solvent	light source	yield *E* (%)	yield *Z* (%)
1[a]	HgO	CCl_4	floodlamp	14-23	not measured
2[b]	PIDA	CCl_4	floodlamp	36	5
3	PIDA	cyclohexane	N/A (110°C)	9	25
4	PIDA	cyclohexane	blue LED	13	38
5	PIDA	CCl_4	blue LED	31	20
6	PIDA	benzene	blue LED	44	8
7	PIDA	DCM	blue LED	45	-[c]
8	PIDA	MeCN	blue LED	-	-
9	PIDA (1eq)	DCM	blue LED	58	9
10[d]	PIDA (1eq)	DCM	blue LED	62	3

Conditions: substrate (0.22 mmol), oxidant (0.67 mmol, 3 equiv.), I_2 (0.25 mmol, 1.1 equiv.) in solvent listed (0.03 M), rt, irradiated 3 hr with light listed. [a]2.1 mmol scale, 3.1 equiv. HgO, 2.7 equiv. I_2, reaction performed in cold water chilled vessel, 1.5 hr. [b]14.8 mmol scale, 3 equiv. PIDA, 3 equiv. I_2, 0.16 M, perfomed in cold water chilled flask, 1.5 hr. [c]Z isomer observed by TLC but not crude NMR, was not isolated from column chromatography. [d]Reaction mixture sparged w/ N_2 before irradiation.

b. Evaluation of Various Lewis and Brønsted Acids

General procedure for evaluating Lewis and Brønsted acids: **14** (50 mg, 0.11 mmol, 1 equiv.) was dissolved in DCE (2.20 mL, 0.05M) and Lewis or Bronsted acid (0.011 mmol, 0.1 equiv.) was added at room temperature and the reaction mixture was allowed to stir for 24 hours before being passed through a plug of silica gel eluting with DCM. The crude reaction mixture was purified by flash column chromatography eluting with hexanes/Et_2O to afford products **16**, **17**, and/or **19** in the yields described in Table 2. Any deviations from this procedure are described in Table SI-2.

Table A3-2: Evaluation of Lewis and Brønsted Acids.



14 **16** **17** **19**

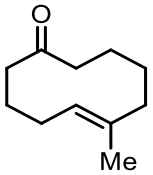
		isolated yields			
Entry	Lewis Acid	**16**	**17**	**19**	Rec. **14**
1	$Sc(OTf)_3$	15	33	20	-
2	$FeCl_3$	-	39	31	-
3	$FeCl_3$[a]	-	33	27	-
4	$FeCl_3$[b]	-	32	31	-
4	$FeCl_3$[c]	61	-	-	-
5	$AlCl_3$	-	27	27	-
6	$TiCl_4$	-	-	43	-
7	$SnCl_4$	-	22	44	-
8	$BF_3{\cdot}OEt_2$	-	30	23	-
9	$BF_3{\cdot}OEt_2$[d]	-	11	25	-
10	$GaCl_3$	-	3	-	-
11	$Y(OTf)_3$	22	-	-	18
12	Me_2AlCl	16	-	-	14
13	Me_2AlCl[e]	85	-	-	-
14	$SnCl_2{\cdot}2H_2O$	46	-	-	19
15	TfOH	-	18	16	-

Conditions: Substrate (0.11 mmol), Lewis acid listed (10 mol%), DCE (0.05M), rt, 24 hours. Deviations from standard conditions: [a]0°C. [b]80°C, 10 hours. [c]0°C, 30 minutes [d]100 mol% $BF_3{\cdot}OEt_2$, 5 hours. [e]100 mol% Me_2AlCl, 0°C, 1 hour.

2. Compound Preparation

a. Preparation of Substrates

i. Model Cycloalkenones

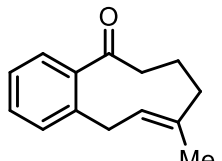


23

(*E*)-6-methylcyclodec-5-en-1-one (23): 2-methyl-1,2-divinylcyclohexan-1-ol[2] (1.37 g, 8.26 mmol) was dissolved in THF (25 mL) and cooled on an ice bath. Freshly rinsed and dried potassium hydride (387 mg, 9.91 mmol) was added portion-wise via spatula. The reaction mixture was removed from the ice bath, equipped with a reflux condenser and heated to reflux

[2] Holt, D. R. *Tet. Lett.* **1981**, *22*, 2243.

for one hour. The reaction mixture was cooled and poured onto a saturated solution of ammonium chloride and ice. The reaction mixture was extracted with three portions of diethyl ether. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated by rotary evaporator. The crude material was purified by flash column chromatography eluting with hexanes/diethyl ether to afford 343 mg (25% yield) of the title compound[3] as a clear, slightly yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.96 (d, *J* = 7.1 Hz, 1H), 2.37 (s, 2H), 2.09 (dd, *J* = 18.0, 12.4 Hz, 7H), 1.82 (d, *J* = 16.9 Hz, 2H), 1.71 (s, 3H), 1.53 (dd, *J* = 40.3, 16.8 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 212.78, 134.84, 129.41, 43.69, 42.68, 40.44, 28.61, 28.56, 25.43, 22.67, 16.21. **IR** (cm^{-1}): 2924.19, 2857.74, 1701.95, 1493.97, 1355.91, 1170.16, 1096.20, 960.88, 879.62, 849.26 **HRMS**: calculated for $C_{11}H_{18}O^+$ (M^+): 166.1358 found: 166.1360.

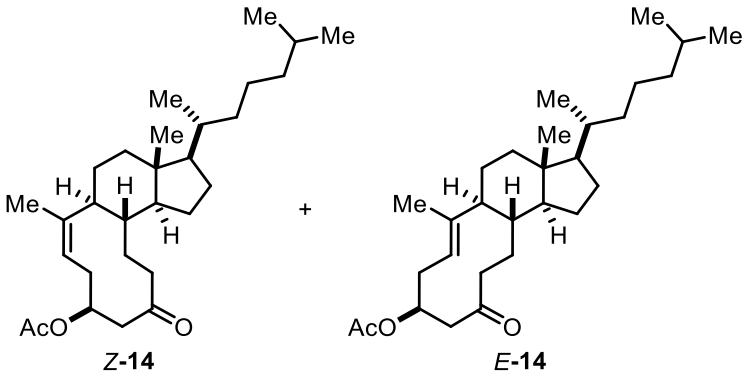


25

(*E*)-9-methyl-6,7,8,11-tetrahydro-5H-benzo[9]annulen-5-one (25): 2-chloroindanone[4] (1.00 g, 6.00 mmol) was dissolved in THF (20 mL) and cooled on an ice water bath and isopropenylmagnesium bromide (0.5 M in THF, 36.0 mL, 18.0 mmol) was slowly added. The reaction mixture was stirred at 0 °C until judged complete by TLC and quenched with a saturated aqueous solution of ammonium chloride. The aqueous layer was extracted with two portions of ethyl acetate, dried over Na_2SO_4 and concentrated by rotary evaporator. The crude material taken up in THF (20 mL) and cooled on an ice bath and vinylmagnesium bromide (1.0 M in THF, 36.0 mL, 36.0 mmol) was added slowly. The reaction mixture was heated to reflux for 6 hours and cooled to 0 °C and quenched with a saturated aqueous solution of ammonium chloride, extracted into ethyl acetate, dried over Na_2SO_4 and concentrated by rotary evaporator. The crude material was again taken up in THF (80 mL) and cooled on an ice bath. 18-crown-6 (1.90 g, 7.20 mmol) was added as a solid followed by hexane-washed KH (282 mg, 7.20 mmol). The reaction mixture was heated to reflux for 30 minutes before cooling back to 0 °C and quenching with saturated aqueous ammonium chloride solution. The reaction mixture was extracted into ethyl acetate, dried over Na_2SO_4 and concentrated by rotary evaporator. The crude material was purified by flash chromatography eluting with hexanes/EtOAc to afford 403 mg (17% yield over 3 steps) of the title compound as an orange solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.25 – 7.16 (m, 3H), 7.00 (d, *J* = 7.4 Hz, 1H), 5.38 (d, *J* = 11.0 Hz, 1H), 3.63 (dd, *J* = 14.8, 12.2 Hz, 1H), 3.11 (d, *J* = 14.7 Hz, 1H), 2.55 – 2.45 (m, 3H), 2.23 – 2.15 (m, 1H), 1.92 (dt, *J* = 10.4, 6.0 Hz, 2H), 1.54 (s, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 207.60, 146.12, 141.89, 138.89, 129.75, 128.12, 126.61, 126.11, 123.84, 42.27, 39.60, 33.77, 27.89, 16.53. **IR** (cm^{-1}): 2926.12, 1675.29, 1436.99, 1420.00, 1340.10, 1232.41, 1206.85, 1174.85, 1111.38, 1049.96, 991.35, 972.98, 958.03, 913.50, 891.26, 897.44, 809.02. **HRMS**: calculated for $C_{14}H_{17}O^+$ ($[M+H]^+$): 201.1274 found: 201.1271.

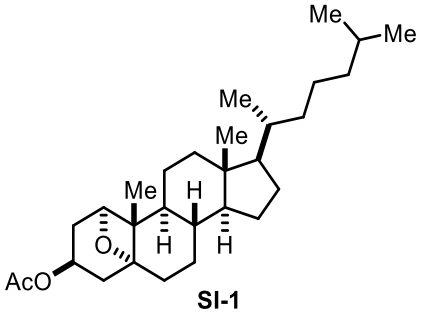
ii. Cholesterol-Derived

[3] Clive, D. J. L.; Russel, C. G; Suri, S. C. *J. Org. Chem.* **1982**, *47*, 1632.
[4] Mei, Y.; Bentley, P. A.; Du, J. *Tet. Lett.* **2008**, *49*, 3802.



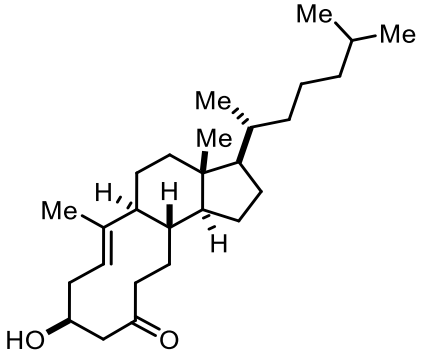
Z-**14** *E*-**14**

(3*R*,3*aR*,5a*S*,9*S*,13a*R*,13b*S*,*E*)-3a,6-dimethyl-3-(6-methylheptan-2-yl)-11-oxo-2,3,3*a*,4,5,5*a*,8,9,10,11,12,13,13*a*,13*b*-tetradecahydro-1H-cyclodeca[e]inden-9-yl acetate (14): **13**[1] (100 mg, 0.22 mmol) and PIDA (71 mg, 0.22 mmol) were dissolved in DCM (7 mL) and the solution was sparged with nitrogen for ten minutes. The flask was opened and iodine (57 mg, 0.22 mmol) was added and the septum quickly replaced. The reaction mixture was stirred under nitrogen atmosphere and irradiated with blue LEDs for 2 hours, at which time the mixture was diluted with DCM and poured into a separatory funnel containing saturated sodium bicarbonate and saturated sodium thiosulfate solutions. The layers were separated and the aqueous phase was washed with two additional portions of DCM. The combined organic layers were dried over Na_2SO_4 and concentrated by rotary evaporator before being purified by flash column chromatography eluting with hexanes/Et_2O to afford first 3 mg (3% yield) of undesired product *Z*-**14** followed by 62 mg (62% yield) of desired product *E*-**14** as a white solid. This reaction was scaled to 700 mg (1.54 mmol) scale (1.1 eq. PIDA, 1.8 eq. I_2, 37 mL DCM) and afforded 414 mg (59% yield) of *E*-**14** (any *Z*-**14** was discarded). Data for *Z*-**14**: **^{1}H NMR** (401 MHz, $CDCl_3$δ 5.46 – 5.37 (m, 1H), 5.23 (dd, *J* = 11.7, 5.0 Hz, 1H), 3.18 (dd, *J* = 16.2, 11.1 Hz, 1H), 2.65 – 2.51 (m, 1H), 2.35 (dd, *J* = 16.2, 4.8 Hz, 2H), 2.25 (dd, *J* = 12.0, 5.4 Hz, 1H), 2.13 – 1.82 (m, 8H), 1.74 – 1.48 (m, 8H), 1.41 – 0.83 (m, 22H), 0.69 (s, 3H). **IR** (cm^{-1}): 2944.09, 2862.26, 1733.14, 1679.69, 1440.08, 1372.73, 1186.01, 1028.73, 953.78, 908.74, 873.36. **HRMS**: calculated for $C_{29}H_{48}O_3^+$ ($[M+H^+]^+$): 445.3676 Found: 445.3679. **^{13}C NMR** (176 MHz, $CDCl_3$) δ 212.91, 170.44, 143.20, 119.83, 70.68, 55.91, 50.20, 42.94, 41.73, 41.06, 40.27, 39.69, 39.43, 36.54, 36.25, 35.80, 28.40, 28.19, 28.09, 27.29, 25.91, 24.16, 23.78, 22.97, 22.74, 21.49, 19.16, 18.80, 12.04. Data for *E*-**14**: **^{1}H NMR** (401 MHz, $CDCl_3$) δ 5.42 – 5.31 (m, 2H), 4.87 – 4.77 (m, 2H), 2.44 (ddd, *J* = 40.5, 26.0, 19.3 Hz, 11H), 2.09 – 0.84 (m, 70H), 0.71 (d, *J* = 10.9 Hz, 6H).**^{13}C NMR** (176 MHz, $CDCl_3$) δ 206.39, 170.00, 140.88, 123.36, 74.62, 56.44, 56.19, 54.87, 47.77, 42.86, 42.83, 39.64, 39.43, 38.26, 36.23, 35.92, 34.06, 28.16, 27.98, 27.67, 26.73, 25.50, 23.98, 22.97, 22.71, 21.40, 18.84, 13.29, 12.09. **IR** (cm^{-1}): 2945.31, 2926.35, 2865.10, 1727.69, 1700.83, 1434.60, 1419.17, 1365.78, 1236.82, 1200.37, 1118.57, 1032.10, 938.88, 907.06, 890.94. **HRMS**: calculated for $C_{29}H_{48}O_3^+$ ($[M+H^+]^+$): 445.3676 Found: 445.3674. Note: The *E*-cyclodecenone compound is not conformationally rigid in $CDCl_3$ and a minor conformer could be detected in the ^{1}H NMR (not reported above). The ^{1}H NMR spectrum was also acquired in d_6-DMSO, in which a single conformer was more preferred **^{1}H NMR** (700 MHz, DMSO) δ 5.18 (d, *J* = 11.1 Hz, 1H), 4.64 (d, *J* = 9.1 Hz, 1H), 2.55 (t, *J* = 12.5 Hz, 1H), 2.42 – 2.21 (m, 5H), 1.99 (s, 3H), 1.86 (d, *J* = 13.7 Hz, 1H), 1.72 (s, 4H), 1.55 (ddd, *J* = 29.9, 19.5, 5.7 Hz, 6H), 1.41 – 0.81 (m, 23H), 0.68 (s, 3H).



SI-1

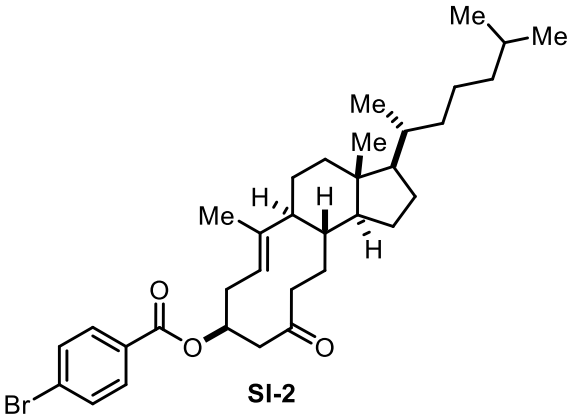
(1*S*,3*S*,5*R*,8*S*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-(6-methylheptan-2-yl)hexadecahydro-1,5-epoxycyclopenta[a]phenanthren-3-yl acetate (SI-1): 10 (250 mg, 0.56 mmol) was dissolved in 200 mL acetone and irradiated with an immersed Hanovia 450W medium-pressure UV lamp equipped with an isopropanol-cooled quartz cooling filter. When the starting material was judged consumed by TLC, the reaction mixture was concentrated and purified by flash column chromatography eluting with benzene/Et_2O to afford 28 mg (11% yield) of a clear oil. ^{1}H NMR (700 MHz, C_6D_6) δ 5.55 (ddd, *J* = 15.5, 9.7, 5.9 Hz, 1H), 3.81 (d, *J* = 5.7 Hz, 1H), 2.71 – 2.65 (m, 1H), 2.47 (dd, *J* = 14.5, 9.7 Hz, 1H), 2.03 (dd, *J* = 13.5, 4.3 Hz, 1H), 1.93 – 1.80 (m, 2H), 1.73 (d, *J* = 10.4 Hz, 3H), 1.52 (m, 11H), 1.31 – 1.08 (m, 8H), 1.07 – 0.83 (m, 13H), 0.74 (s, 3H), 0.66 (d, *J* = 8.9 Hz, 3H). ^{13}C NMR (176 MHz, C_6D_6) δ 169.64, 87.79, 82.83, 67.06, 56.55, 56.38, 47.40, 45.66, 42.80, 40.27, 39.97, 39.25, 36.67, 36.28, 34.50, 31.91, 31.45, 28.61, 28.46, 28.33, 24.73, 24.42, 23.47, 23.08, 22.82, 20.88, 19.14, 12.17, 11.83. **IR** (cm^{-1}): 2930.42, 2867.62, 1741.26, 1466.53, 1369.79, 1239.97, 1022.38 **HRMS**: calculated for $C_{29}H_{48}O_3Na^+$ ($[M+Na^+]^+$): 445.3673 found: 445.3675.



15

(3*R*,3*aR*,5*aS*,9*S*,13*aR*,13*bS*,E)-9-hydroxy-3a,6-dimethyl-3-(6-methylheptan-2-yl)-1,2,3,3*a*,4,5,5*a*,8,9,10,12,13,13*a*,13*b*-tetradecahydro-11H-cyclodeca[e]inden-11-one (15): **14** (407 mg, 0.92 mmol) was dissolved in DCM (3 mL) and KOH (1M in MeOH, 2.8 mL, 2.8 mmol) was added by syringe. The mixture was quenched with 1M aqueous HCl (1 mL), then diluted with water and DCM. The layers were separated and the aqueous layer washed with two additional portions of DCM. The combined organic layers were dried over Na_2SO_4 before being concentrated by rotary evaporator and purified by flash column chromatography eluting with hexanes/EtOAc to afford 369 mg (86% yield) of the title compound as a white solid. **^{1}H NMR** (700 MHz, DMSO) δ 4.89 (d, *J* = 5.3 Hz, 1H), 4.66 (dd, *J* = 10.5, 5.6 Hz, 1H), 4.04 (s, 1H), 2.37 (dd, *J* = 23.1, 10.0 Hz, 2H), 2.25 – 2.12 (m, 4H), 1.88 – 1.83 (m, 1H), 1.80 – 1.74 (m, 1H), 1.69 (s, 3H), 1.67 – 1.60 (m, 2H), 1.56 – 1.44 (m, 4H), 1.38 – 1.29 (m, 4H), 1.23 – 1.17 (m, 1H), 1.16 – 1.02 (m, 7H), 0.97 (dt, *J* = 17.9, 8.7 Hz, 2H), 0.88 (d, *J* = 6.4 Hz, 3H), 0.84 (dd, *J* = 6.5, 3.5

Hz, 6H), 0.67 (s, 3H).**^{13}C NMR** (176 MHz, DMSO) δ 206.91, 138.43, 124.06, 71.74, 55.75, 55.72, 54.46, 51.26, 42.16, 41.78, 38.87, 38.84, 37.42, 37.35, 35.54, 35.07, 27.32, 27.29, 27.10, 26.14, 24.83, 23.16, 22.52, 22.27, 18.44, 12.69, 11.65. **IR** (cm^{-1}): 2927.72, 2866.38, 1695.45, 1678.29, 144.52, 1383.09, 1366.17, 1273.65, 1253.95, 1168.74, 1113.34, 1086.47, 1052.40, 1026.05, 965.02, 920.39, 884.67. **HRMS**: calculated for $C_{27}H_{47}O_2^+$ ($[M+H^+]^+$): 403.3571 found: 403.3572.

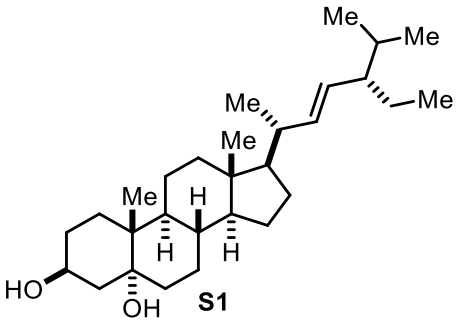


SI-2

(3*R*,3*aR*,5*aS*,9*S*,13*aR*,13*bS*,*E*)-3a,6-dimethyl-3-(6-methylheptan-2-yl)-11-oxo-2,3,3*a*,4,5,5*a*,8,9,10,11,12,13,13*a*,13*b*-tetradecahydro-1H-cyclodeca[e]inden-9-yl 4-bromobenzoate (**S-2**)[5]: **15** (25 mg, 0.062 mmol) was dissolved in DCM (0.2 mL) and pyridine (0.015 mL, 0.19 mmol), 4-bromobenzoyl chloride (16 mg, 0.075 mmol) and a spatula tip of DMAP were added. The reaction mixture was stirred at room temperature until judged complete by TLC. The reaction mixture was diluted with DCM and poured onto saturated aqueous ammonium chloride. The layers were separated and the aqueous layer was washed with two additional portions of DCM. The combined organic layers were dried over Na_2SO_4 and concentrated by rotary evaporator, then purified by flash column chromatography eluting with hexanes/EtOAc to afford 8 mg (22% yield) of product. Recrystallization by slow evaporation of diethyl ether afforded crystals that were analyzed by X-ray crystallography (see Part 5 for details). **^{1}H NMR** (700 MHz, $CDCl_3$δ 7.89 (d, *J* = 7.6 Hz, 2H), 7.58 (d, *J* = 7.8 Hz, 2H), 5.61 (s, 1H), 4.89 (d, *J* = 11.5 Hz, 1H), 2.70 – 2.43 (m, 5H), 2.31 – 2.25 (m, 1H), 1.93 (d, *J* = 12.1 Hz, 1H), 1.85 – 1.66 (m, 8H), 1.52 – 1.49 (m, 1H), 1.43 – 1.30 (m, 4H), 1.25 (d, *J* = 12.4 Hz, 3H), 1.13 (ddd, *J* = 28.5, 25.9, 11.5 Hz, 6H), 1.03 – 0.97 (m, 1H), 0.89 (dd, *J* = 29.8, 4.7 Hz, 9H), 0.71 (s, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 206.19, 164.83, 141.13, 131.92, 131.82, 131.26, 129.48, 128.17, 123.21, 75.51, 56.45, 56.23, 54.88, 47.81, 42.91, 42.85, 39.65, 39.44, 38.30, 36.24, 35.92, 34.13, 28.17, 27.99, 27.69, 26.77, 25.52, 23.99, 22.98, 22.72, 18.85, 13.38, 12.11. **IR** (cm^{-1}): 1722.40, 1271.80, 1168.30, f1117.72, 1013.00, 974.24 **HRMS**: calculated for $C_{34}H_{49}BrO_3^+$ ($[M+H^+]^+$): 585.2938 found: 585.2937.

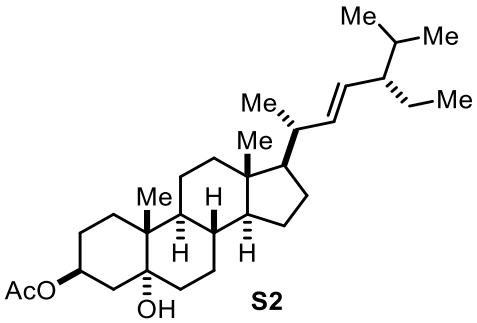
iii. Stigmasterol-Derived

[5] Mihailović, M. L.; Lorenc, L.; Popov, N.; Kalvoda, J. *Helv. Chim. Acta.* **1971**, *54*, 2281.



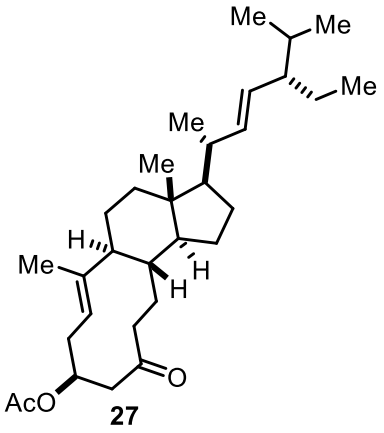
S1

(3*S*,5*R*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-17-((5*S, E*)-5-ethyl-6-methylhept-3-en-2-yl)-10,13-dimethylhexadecahydro-5H-cyclopenta[a]phenanthrene-3,5-diol (S1): Stigmasterol (3.0 g, 7.27 mmol) was dissolved in DCM (90 mL) and water (150 mL) and sodium carbonate (1.54 g, 14.5 mmol) were added. The mixture was cooled on an ice bath and *m*CPBA (~75% purity, 2.84 g, 12.4 mmol) was added as a solid. The reaction mixture was stirred at 0°C until judged complete by TLC, then quenched with a saturated aqueous solution of sodium thiosulfate. The layers were separated and the aqueous layer was washed with two additional portions of DCM. The combined organic layers were dried over Na_2SO_4, filtered through a pad of silica gel eluting with DCM, and concentrated by rotary evaporator. The crude material was then dissolved in THF (90 mL) and cooled on an ice bath. $LiAlH_4$ (552 mg, 14.5 mmol) was then added portionwise over several minutes. The reaction mixture was warmed to room temperature and then heated to reflux overnight. The mixture was again cooled on an ice bath and saturated aqueous sodium potassium tartrate was added dropwise. When gas evolution ceased, the reaction mixture was diluted with additional saturated aqueous sodium potassium tartrate and EtOAc. The mixture was stirred until the two phases began to separate. The layers were separated and the aqueous layer washed with two additional portions of EtOAc. The combined organic layers were dried over Na_2SO_4, filtered and concentrated by rotary evaporator. The crude material was purified by flash column chromatography eluting with hexanes/EtOAc to afford 1.27 g (41% yield) of the title compound as a white solid. **^{1}H NMR** (700 MHz, CDCl3) δ 5.14 (dd, *J* = 15.2, 8.7 Hz, 1H), 5.04 – 4.99 (m, 1H), 4.09 (dt, *J* = 15.9, 5.3 Hz, 1H), 2.07 – 1.77 (m, 4H), 1.74 – 1.59 (m, 4H), 1.54 – 1.38 (m, 9H), 1.32 – 0.97 (m, 18H), 0.87 – 0.75 (m, 9H), 0.69 – 0.63 (m, 3H).**^{13}C NMR** (176 MHz, $CDCl_3$) δ 138.46, 129.41, 75.50, 67.52, 56.45, 56.14, 51.38, 46.11, 44.06, 42.76, 40.68, 40.07, 38.97, 34.88, 34.56, 32.04, 31.05, 30.96, 29.09, 26.10, 25.56, 24.33, 21.50, 21.33, 21.25, 19.14, 16.41, 12.48, 12.41. **IR** (cm^{-1}): 3398.01, 2863.00, 1415.04, 1380.20, 1369.05, 1325.89, 1293.27, 1081.13, 1039.28, 969.22, 937.14, 918.88, 870.22, 823.04, 777.60, 730.76, 684.02, 665.09. **HRMS**: calculated for $C_{29}H_{50}O_2Na^+$ ($[M+Na^+]^+$): 453.3703 Found: 453.3700.



S2

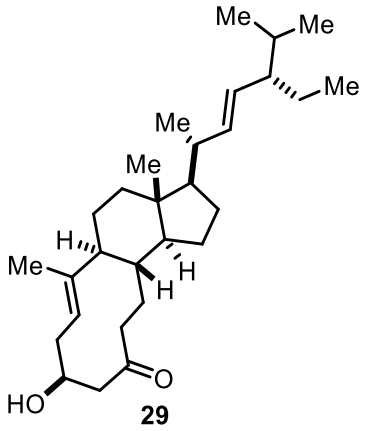
(3*S*,5*R*,8S,9*S*,10*R*,13*R*,14*S*,17*R*)-17-((5*S*,*E*)-5-ethyl-6-methylhept-3-en-2-yl)-5-hydroxy-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-3-yl acetate (S2): **S1** (1.26 g, 2.93 mmol) was dissolved in DCM (10 mL) and treated with DMAP (18 mg, 0.15 mmol) followed by pyridine (0.71 mL, 8.78 mmol) and acetic anhydride (0.33 mL, 3.51 mmol). The reaction mixture was stirred until judged complete by TLC and then quenched with saturated aqueous sodium bicarbonate solution and diluted with DCM. The reaction mixture was poured into a separatory funnel and the layers were separated. The aqueous layer was washed with DCM and the combined organic layers were washed with 1M aqueous HCl and brine, then dried over Na_2SO_4, concentrated and purified by flash column chromatography eluting with hexanes/EtOAc to afford 1.21 g (88% yield) of the title compound as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.20 – 5.12 (m, 2H), 5.01 (dd, *J* = 15.1, 8.7 Hz, 1H), 2.02 (d, *J* = 8.1 Hz, 4H), 1.95 (d, *J* = 12.6 Hz, 1H), 1.90 – 1.85 (m, 1H), 1.73 – 1.66 (m, 4H), 1.64 – 1.06 (m, 21H), 1.05 – 0.98 (m, 7H), 0.88 – 0.75 (m, 9H), 0.67 (s, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 170.75, 138.48, 129.41, 75.16, 71.00, 56.34, 56.13, 51.38, 45.80, 42.74, 40.69, 40.24, 40.01, 38.97, 34.91, 34.65, 32.04, 30.67, 29.09, 26.95, 26.06, 25.56, 24.33, 21.62, 21.42, 21.34, 21.24, 19.15, 16.26, 12.47, 12.40. **IR** (cm^{-1}): 2936.70, 2866.00, 1731.58, 1703.26, 1381.55, 1364.49, 1278.84, 1268.02, 1253.42, 1026.73, 1004.61. **HRMS**: calculated for $C_{31}H_{52}O_3Na^+$ ($[M+Na^+]^+$): 495.3809 Found: 495.3810.



27

(3*R*,3*aR*,5*aS*,9*S*,13*aR*,13*bS*,*E*)-3-((5*S*,*E*)-5-ethyl-6-methylhept-3-en-2-yl)-3*a*,6-dimethyl-11-oxo-2,3,3a,4,5,5a,8,9,10,11,12,13,13a,13b-tetradecahydro-1H-cyclodeca[e]inden-9-yl acetate (27): **S2** (500 mg, 1.06 mmol) and PIDA (375 mg, 1.16 mmol) were dissolved in DCM (33 mL) and sparged with N_2 for 10 minutes and I_2 (295 mg, 1.16 mmol) was added and the septum was quickly replaced. The reaction mixture was stirred while being irradiated with blue LED for 2 hours. The reaction mixture was poured into a separatory funnel containing saturated aqueous sodium bicarbonate and saturated aqueous sodium thiosulfate and diluted with DCM. The layers were separated and the aqueous layer was washed with an additional portion of DCM. The combined organic layers were dried over Na_2SO_4, concentrated and purified by flash column chromatography eluting with hexanes/Et_2O to afford 218 mg (44% yield) of **27** as a white solid. ^{1}H NMR (500 MHz, DMSO) δ 5.15 (dd, *J* = 15.1, 8.5 Hz, 2H), 5.02 (dd, *J* = 14.9, 8.7 Hz, 1H), 4.64 (d, *J* = 8.6 Hz, 1H), 2.54 (d, *J* = 12.3 Hz, 2H), 2.31 (ddd, *J* = 43.1, 25.2, 9.5 Hz, 5H), 2.05 – 1.93 (m, 4H), 1.84 (d, *J* = 10.1 Hz, 1H), 1.76 – 1.34 (m, 13H), 1.25 – 1.11 (m, 5H), 1.01 (dd, *J* = 29.0, 11.4 Hz, 5H), 0.85 – 0.68 (m, 11H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 206.38, 169.99, 140.84, 138.31, 129.55, 123.42, 74.62, 56.24, 56.23, 54.98, 51.37, 47.79, 42.87, 42.72, 40.65, 39.33, 38.26, 34.08, 32.04, 28.62, 27.67, 26.73, 25.57, 25.55, 21.42, 21.41, 21.25, 19.15, 13.30,

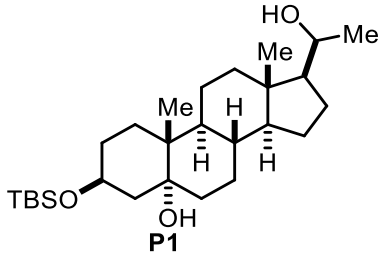
12.40, 12.31. **IR** (cm^{-1}): 2933.19, 2867.48, 1735.35, 1726.57, 1699.90, 14530.19, 1366.29, 1265.38, 1236.88, 1085.38, 1033.74, 986.82, 939.42. **HRMS**: calculated for $C_{31}H_{51}O_3^+$ ($[M+H^+]^+$): 471.3833 Found: 471.3834.



29

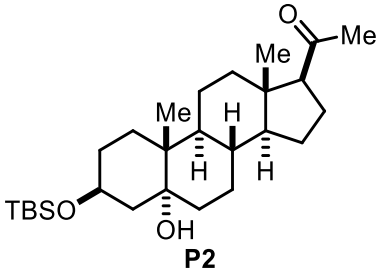
(3*R*,3*aR*,5*aS*,9*S*,13*aR*,13*bS*,*E*)-3-((5*S*,*E*)-5-ethyl-6-methylhept-3-en-2-yl)-9-hydroxy-3*a*,6-dimethyl-1,2,3,3a,4,5,5a,8,9,10,12,13,13a,13b-tetradecahydro-11H-cyclodeca[e]inden-11-one (39): **27** (60 mg, 0.13 mmol) was dissolved in DCM (0.5 mL) and a solution of KOH (1M in MeOH, 0.38 mL, 0.38 mmol) was added and the reaction mixture was allowed to stir at room temperature until judged complete by TLC. The reaction mixture was diluted with DCM and quenched with aqueous 1M HCl and poured into a separatory funnel. The layers were separated and the aqueous layer was washed with two additional portions of DCM. The combined organic layers were dried over Na_2SO_4, concentrated by rotary evaporator and purified by flash column chromatography to afford 53 mg (97% yield) of the title compound as a white solid. **^{1}H NMR** (700 MHz, DMSO) δ 5.15 (dd, *J* = 15.2, 8.6 Hz, 1H), 5.02 (dd, *J* = 15.1, 8.8 Hz, 1H), 4.89 (d, *J* = 5.3 Hz, 1H), 4.69 – 4.64 (m, 1H), 4.05 (d, *J* = 4.5 Hz, 1H), 2.37 (dd, *J* = 23.0, 10.1 Hz, 2H), 2.18 (ddd, *J* = 20.4, 19.6, 8.4 Hz, 4H), 2.02 (d, *J* = 6.7 Hz, 1H), 1.83 (d, *J* = 10.1 Hz, 2H), 1.69 (s, 2H), 1.67 – 1.59 (m, 3H), 1.56 – 1.47 (m, 4H), 1.42 – 1.30 (m, 3H), 1.23 – 1.12 (m, 5H), 1.06 – 0.96 (m, 5H), 0.82 (d, *J* = 6.2 Hz, 3H), 0.77 (dd, *J* = 9.6, 5.0 Hz, 6H), 0.69 (s, 3H). **^{13}C NMR** (176 MHz, DMSO) δ 207.16, 138.60, 137.96, 128.83, 124.08, 71.82, 55.81, 55.49, 54.60, 51.31, 50.58, 42.10, 41.83, 39.92, 38.72, 37.47, 37.36, 31.31, 28.11, 27.13, 26.21, 24.91, 24.85, 21.12, 20.93, 18.84, 12.82, 12.10, 11.92. **IR** (cm^{-1}): 2933.98, 2912.13, 2867.95, 1741.33, 1712.81, 1690.44, 1467.27, 1456.03, 1439.24, 1374.62, 1361.20, 1292.71, 1272.79, 1232.19, 1062.65, 1037.52, 1007.88, 950.17, 299.94, 918.34. **HRMS**: calculated for $C_{29}H_{49}O_2^+$ ($[M+H^+]^+$): 429.3727 Found: 437.3723.

iv. Pregnenolone-Derived



P1

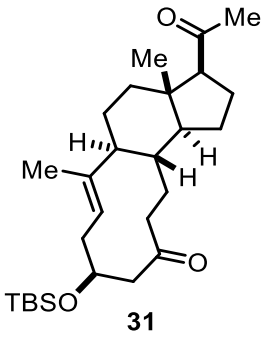
(3*S*,5*R*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-((*tert*-butyldimethylsilyl)oxy)-17-((S)-1-hydroxyethyl)-10,13-dimethylhexadecahydro-5H-cyclopenta[a]phenanthren-5-ol (P1): Pregnenolone (10 g, 31.6 mmol) was dissolved in DCM (200 mL) and *m*CPBA (~75% purity, 8.72 g, 37.9 mmol) was added as a solid. The reaction mixture was stirred overnight, then diluted with DCM and poured onto a mixture of saturated aqueous solutions of sodium bicarbonate and sodium thiosulfate. The layers were separated and the aqueous layer was extracted with two additional portions of DCM. The combined organic layers were dried over Na_2SO_4, filtered and concentrated by rotary evaporator. The crude material was taken up in an additional 200 mL of DCM and TBSCl (9.53 g, 63.2 mmol) was added followed by imidazole (6.45 g, 94.8 mmol). The reaction mixture was stirred at room temperature until judged complete by TLC, at which point the mixture was diluted with DCM and poured onto a solution of saturated aqueous ammonium chloride. The aqueous layer was washed with two additional portions of DCM and the combined organic layers were dried over Na_2SO_4, filtered and concentrated by rotary evaporator. The crude material was dissolved in 200 mL of THF and added by dropwise addition funnel to a suspension of $LiAlH_4$ (2.40 g, 63.2 mmol) in THF (100 mL). Upon completion of addition, the reaction mixture was heated to reflux for 24 hours. The reaction mixture was cooled on an ice bath and saturated aqueous sodium potassium tartrate was added slowly dropwise until gas evolution ceased. The mixture was then diluted with additional aqueous sodium potassium tartrate solution and ethyl acetate and stirred until the layers separated. The mixture was then poured into a separatory funnel and the layers were separated. The aqueous layer was washed with two additional portions of ethyl acetate. The combined organic layers were washed with saturated aqueous sodium chloride and dried over Na_2SO_4. After filtration and concentration under reduced pressure, the crude material was purified by flash column chromatography eluting with hexanes/EtOAc to afford 8.27 g (58% yield, 3 steps) of the title compound as a white solid. The stereochemistry of the secondary alcohol is not assigned as it is oxidized in the following step**.** **^{1}H NMR** (401 MHz, $CDCl_3$) δ 4.12 – 3.99 (m, 1H), 3.77 – 3.66 (m, 1H), 2.04 (d, *J* = 9.8 Hz, 1H), 1.78 – 1.02 (m, 26H), 0.99 (s, 3H), 0.88 (s, 9H), 0.74 (s, 3H), 0.05 (s, 6H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 75.61, 70.73, 68.15, 58.70, 55.83, 46.13, 44.67, 42.82, 40.30, 38.98, 34.75, 34.55, 31.40, 31.08, 26.15, 26.11 (3C), 25.80, 24.51, 23.79, 21.39, 18.39, 16.47, 12.79, -4.34, -4.45. **IR (cm^{-1}):** 2927.90, 2853.63, 1461.94, 1447.66, 1376.78, 1248.08, 1165.59, 1117.75, 1094.79, 1067.44, 1005.74, 693.47, 937.17, 903.93, 869.42, 836.11. **HRMS**: Calculated for $C_{27}H_{50}O_3SiNa^+$ ([M+Na^+]$^+$): 473.3421 Found: 473.3421.



P2

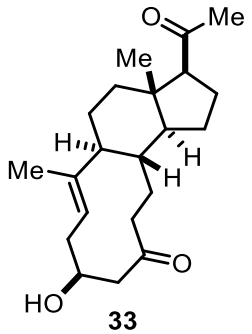
1-((3*S*,5*R*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-((*tert*-butyldimethylsilyl)oxy)-5-hydroxy-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)ethan-1-one (P2): Alcohol **P1** (3.38 g, 7.5 mmol) was suspended in DMSO (50 mL) and IBX was added as a solid. The reaction mixture was heated to 50°C and stirred until judged complete by TLC. The mixture was cooled on an ice bath and quenched with saturated aqueous sodium thiosulfate solution and diluted with ethyl acetate. After stirring until two layers were evident, the layers were separated and the aqueous layer was extracted with two additional portions of ethyl acetate. The combined

organic layers were washed with saturated sodium chloride and dried over Na_2SO_4, filtered and concentrated by rotary evaporator. The crude material was purified by flash column chromatography to afford 1.78 g (53% yield) of the desired product. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 4.05 (td, *J* = 10.6, 5.5 Hz, 1H), 2.53 (t, *J* = 9.0 Hz, 1H), 2.16 (d, *J* = 11.1 Hz, 1H), 2.11 (s, 3H), 2.01 (d, *J* = 12.3 Hz, 1H), 1.76 – 1.61 (m, 5H), 1.55 – 1.38 (m, 8H), 1.35 – 1.17 (m, 6H), 1.08 (s, 2H), 0.98 (s, 3H), 0.88 (s, 9H), 0.61 (d, *J* = 13.1 Hz, 3H), 0.05 (d, *J* = 7.1 Hz, 6H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 209.75, 75.55, 68.09, 63.93, 56.57, 45.91, 44.75, 44.51, 39.28, 38.95, 34.91, 34.56, 31.68, 31.38, 31.08, 26.10 (3C), 26.03, 24.46, 22.96, 21.51, 18.38, 16.42, 13.67, -4.34, -4.45. **IR** (cm^{-1}): 2930.09, 2889.95, 2852.49, 1684.86, 1470.75, 1446.86, 1384.10, 1358.47, 1251.72, 1186.21, 1117.24, 1098.23, 1076.54, 1006.54, 851.57, 835.92. **HRMS**: Calculated for $C_{27}H_{48}O_3SiNa^+$ ($[M+Na^+]^+$): 471.3265 Found: 471.3260.



31

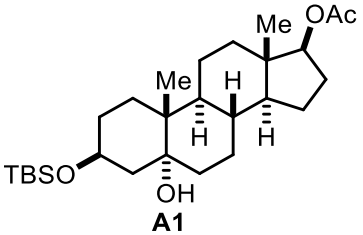
(3*S*,3*aS*,5*aS*,9*S*,13*aR*,13bS,E)-3-acetyl-9-((tert-butyldimethylsilyl)oxy)-3a,6-dimethyl-1,2,3,3a,4,5,5a,8,9,10,12,13,13a,13b-tetradecahydro-11H-cyclodeca[e]inden-11-one (31): **P2** (1.00 g, 2.23 mmol) and phenyliodine (III) diacetate (790 mg, 2.45 mmol) were dissolved in DCM and sparged with nitrogen gas for 10 minutes before the septum was quickly removed and I_2 (566 mg, 2.23 mmol) was added and the septum quickly replaced. The reaction mixture was irradiated with blue LEDs for 2 hours. The reaction mixture was poured onto saturated aqueous sodium thiosulfate and saturated aqueous sodium bicarbonate and diluted with DCM. After shaking until the purple color disappeared, the layers were separated and the aqueous layer was washed with two additional portions of DCM. The combined organic layers were dried over Na_2SO_4, filtered and concentrated by rotary evaporator before being purified by flash column chromatography eluting with hexanes/EtOAc to afford 806 mg (81% yield) of product as a white solid. **^{1}H NMR** (500 MHz, DMSO) δ 4.68 (d, *J* = 9.8 Hz, 1H), 4.24 (s, 1H), 2.59 (t, *J* = 9.2 Hz, 1H), 2.40 (dd, *J* = 29.6, 18.4 Hz, 2H), 2.20 (dd, *J* = 24.1, 14.4 Hz, 3H), 2.08 – 1.82 (m, 5H), 1.76 – 1.31 (m, 11H), 1.19 (dd, *J* = 27.1, 12.8 Hz, 4H), 0.87 (d, *J* = 9.9 Hz, 9H), 0.56 (s, 3H), 0.08 (d, *J* = 13.5 Hz, 6H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 209.66, 207.74, 139.26, 124.85, 73.85, 64.05, 56.17, 55.26, 52.15, 44.36, 42.70, 38.69, 38.62, 38.02, 31.82, 27.70, 26.70, 26.06 (3C), 25.71, 22.79, 18.36, 13.53, 13.36, -4.50, -4.66. **IR** (cm^{-1}): 2732.79, 2855.00, 1706.24, 1693.20, 1470.08, 1359.63, 1249.54, 1231.80, 1075.66 1039.85, 935.41, 899.21, 862.10. **HRMS**: Calculated for $C_{27}H_{46}O_3SiNa^+$ ($[M+Na^+]^+$): 469.3108 Found: 469.3110.



33

(3*S*,3*aS*,5*aS*,9*S*,13*aR*,13*bS*,*E*)-3-acetyl-9-hydroxy-3a,6-dimethyl-1,2,3,3*a*,4,5,5*a*,8,9,10,12,13,13*a*,13*b*-tetradecahydro-11H-cyclodeca[e]inden-11-one (33): **31** (720 mg, 1.61 mmol) was dissolved in THF (16 mL) and cooled on an ice bath. TBAF (1M in THF, 3.22 mL, 3.22 mmol) was added slowly via syringe and the reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was concentrated and directly purified by silica gel column chromatography to afford 462 mg (86% yield) of the desired product as a white solid. **^{1}H NMR** (700 MHz, DMSO) δ 4.91 (d, *J* = 15.2 Hz, 1H), 4.73 – 4.61 (m, 1H), 4.05 (s, 1H), 2.58 (dd, *J* = 21.9, 13.1 Hz, 1H), 2.37 (t, *J* = 12.4 Hz, 2H), 2.31 – 2.11 (m, 4H), 2.05 (s, 3H), 1.99 (dd, *J* = 21.0, 10.4 Hz, 1H), 1.89 (d, *J* = 11.2 Hz, 1H), 1.77 – 1.33 (m, 11H), 1.25 – 1.09 (m, 3H), 0.56 (s, 3H). **^{13}C NMR** (176 MHz, DMSO) δ 208.57, 207.24, 138.41, 124.31, 71.85, 62.76, 55.66, 54.48, 51.33, 43.49, 41.80, 37.55, 37.50, 37.31, 31.28, 27.13, 26.26, 25.05, 21.98, 13.05, 12.86 **IR** (cm^{-1}): 2934.46, 2854.53, 1692.91, 1677.88, 1427.72, 1381.84, 1354.73, 1249.84, 1102.68, 1036.37, 887.23, 863.22, 833.32, 799.36, 774.64, 636.80 **HRMS**: Calculated for $C_{21}H_{32}O_3Na^+$ ($[M+Na^+]^+$): 355.2244 Found: 355.2247.

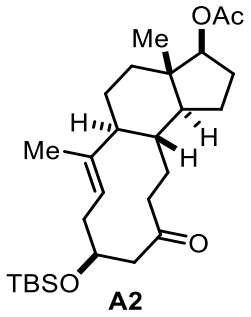
v. Androsterone-Derived (from Pregnenolone-Derived Intermediate)



A1

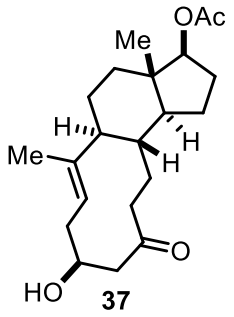
(3*S*,5*R*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-((*tert*-butyldimethylsilyl)oxy)-5-hydroxy-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl acetate (A1): 1-((3S,5R,8S,9S,10R,13S,14S,17S)-3-((tert-butyldimethylsilyl)oxy)-5-hydroxy-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)ethan-1-one (500 mg, 1.11 mmol) was dissolved in DCM (10 mL) and treated with *m*CPBA (1.03 g, 4.46 mmol) and allowed to stir at room temperature for 48 hours, at which point an additional portion of *m*CPBA (1.03 g, 4.46 mmol) was added and the reaction mixture was stirred for an additional 48 hours. The reaction was then poured onto a saturated solution of sodium thiosulfate and sodium bicarbonate and diluted with DCM. The layers were separated and the aqueous layer was washed with DCM. The combined organic layers were dried over Na_2SO_4 and concentrated by rotary evaporator before being purified by flash column chromatography to afford 200 mg (39% yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.59 (t, *J* = 8.5 Hz, 1H), 4.05 (td, *J* = 10.4, 5.1 Hz, 1H), 2.21 – 2.10 (m, 1H), 2.03 (s, 3H), 1.76 – 1.07 (m, 21H), 0.99 (s, 3H), 0.88 (s, 9H), 0.76 (d, *J* = 10.9 Hz, 3H), 0.05 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.35, 82.95,

75.54, 68.09, 50.65, 46.03, 44.73, 42.91, 39.02, 37.13, 34.72, 34.49, 31.38, 31.09, 27.72, 26.11 (3C), 25.66, 23.60, 21.34, 20.97, 18.39, 16.44, 12.34, -4.35, -4.45. **IR** (cm^{-1}): 2932.40, 2854.78, 1722.44, 1369.33, 1246.02, 1094.91, 1062.42, 1037.95, 1022.18, 1006.57, 871.14, 832.18. **HRMS**: Calculated for $C_{27}H_{48}O_4SiNa^+$ ([M+Na^+]$^+$): 487.3214 Found: 487.3214.



A2

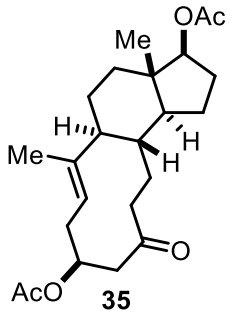
(3*S*,3*aS*,5*aS*,9*S*,13*aR*,13*bS*,*E*)-9-((*tert*-butyldimethylsilyl)oxy)-3a,6-dimethyl-11-oxo-2,3,3a,4,5,5a,8,9,10,11,12,13,13a,13b-tetradecahydro-1H-cyclodeca[e]inden-3-yl acetate (A2): **A1** (95 mg, 0.20 mmol) and phenyliodine(III) diacetate (200 mg, 0.43 mmol) were dissolved in DCM (6.5 mL) and sparged with N_2 for 10 minutes before I_2 (67 mg, 1.3 mmol) was added and the septum quickly replaced. The reaction mixture was irradiated with blue LEDs for 2 hours, at which time it was poured onto a mixture of saturated aqueous sodium thiosulfate and saturated aqueous sodium bicarbonate and diluted with DCM. The layers were separated and the aqueous layer was washed with two additional portions of DCM. The combined organic layers were dried over Na_2SO_4 and concentrated by rotary evaporator before purification by flash column chromatography eluting with hexanes/EtOAc to afford 140 mg (70% yield) of the title compound as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.85 – 4.76 (m, 1H), 4.59 (t, *J* = 8.5 Hz, 1H), 4.42 – 4.32 (m, 1H), 2.51 – 2.12 (m, 7H), 2.03 (s, 3H), 1.79 – 1.70 (m, 4H), 1.69 – 1.56 (m, 5H), 1.47 (ddd, *J* = 21.8, 14.6, 6.2 Hz, 2H), 1.36 – 1.22 (m, 2H), 1.18 (t, *J* = 12.1 Hz, 1H), 1.08 (td, *J* = 11.5, 7.4 Hz, 1H), 0.89 (s, 9H), 0.82 (s, 3H), 0.09 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 207.64, 171.24, 139.22, 124.69, 82.89, 73.79, 56.27, 52.11, 49.31, 42.77, 42.58, 38.63, 37.78, 36.45, 27.28, 27.17, 26.19, 26.00 (3C), 24.64, 21.31, 18.29, 13.33, 12.15, -4.56, -4.73. **IR** (cm-1): 2947.65, 2926.38, 2856.28, 1734.59, 1699.19, 1357.96, 1240.14, 1080.69, 1058.69, 1025.87, 936.20, 898.72, 832.69. HRMS: Calculated for $C_{27}H_{46}O_4Si^+$ ([M+Na^+]$^+$): 485.3058 Found: 485.3060.



37

(3*S*,3*aS*,5*aS*,9*S*,13*aR*,13*bS*,*E*)-9-hydroxy-3a,6-dimethyl-11-oxo-2,3,3a,4,5,5a,8,9,10,11,12,13,13a,13b-tetradecahydro-1H-cyclodeca[e]inden-3-yl acetate (37): **A2** (140 mg, 0.30 mmol) was dissolved in THF (3 mL) and cooled on an ice bath. A solution of TBAF (1M in THF, 0.61 mL, 0.61 mmol) was added slowly and the reaction mixture was allowed to warm to room temperature overnight. The reaction mixture was directly

concentrated by rotary evaporator and purified by flash column chromatography eluting with hexanes/EtOAc to afford 98 mg (93% yield) of the title product as a white solid. **^{1}H NMR** (700 MHz, DMSO) δ 4.92 (s, 1H), 4.67 (s, 1H), 4.52 (t, *J* = 8.3 Hz, 1H), 4.05 (s, 1H), 2.37 (t, *J* = 10.8 Hz, 2H), 2.19 (ddd, *J* = 31.1, 21.0, 11.0 Hz, 4H), 2.03 (d, *J* = 4.6 Hz, 1H), 1.98 (s, 3H), 1.69 (s, 4H), 1.64 – 1.36 (m, 7H), 1.27 (dd, *J* = 10.8, 5.6 Hz, 2H), 1.14 (dd, *J* = 21.9, 12.5 Hz, 2H), 1.09 – 0.93 (m, 2H), 0.78 (s, 3H). **^{13}C NMR** (176 MHz, DMSO) δ 207.28, 170.28, 138.38, 124.27, 81.94, 71.84, 55.75, 51.33, 48.62, 42.22, 41.74, 37.51, 37.12, 35.84, 26.77, 26.69, 25.76, 24.04, 20.88, 12.89, 11.90. **IR** (cm^{-1}): 2925.60, 2857.16, 1374.43, 1712.46, 1699.16, 1441.59, 1357.31, 1243.09, 1199.06, 1081.14, 1056.02, 950.20, 935.80. **HRMS**: Calculated for $C_{21}H_{32}O_4Na^+$ $[M+Na^+]^+$: 371.2193 Found 371.2197



35

(3*S*,3a*S*,5a*S*,9*S*,13a*R*,13b*S*,*E*)-3a,6-dimethyl-11-oxo-2,3,3a,4,5,5a,8,9,10,11,12,13,13a,13b-tetradecahydro-1H-cyclodeca[e]indene-3,9-diyl diacetate (35): **37** (88 mg, 0.25 mmol) was dissolved in DCM (1 mL) and treated with acetic anhydride (36 μL, 0.379 mmol) and pyridine (0.10 mL, 1.26 mmol) as well as a spatula tip of DMAP. The reaction was stirred until judged complete by TLC and quenched with saturated aqueous sodium bicarbonate and diluted with DCM. The layers were separated and the aqueous layer was extracted with two additional portions of DCM. The combined organic layers were then washed successively with 1M HCl and brine, then dried over Na_2SO_4 and concentrated by rotary evaporator. The crude product was purified by flash column chromatography eluting with hexanes/EtOAc to afford 60 mg (61% yield) of the title compound as an off white, powdery solid. **^{1}H NMR** (700 MHz, DMSO) δ 5.18 – 5.11 (m, 1H), 4.70 – 4.62 (m, 1H), 4.52 (t, *J* = 8.5 Hz, 1H), 2.57 (dd, *J* = 22.8, 10.0 Hz, 1H), 2.42 – 2.22 (m, 4H), 2.06 – 1.96 (m, 7H), 1.75 – 1.40 (m, 11H), 1.35 – 1.23 (m, 2H), 1.23 – 1.11 (m, 2H), 1.07 (td, *J* = 11.6, 7.4 Hz, 1H), 0.83 – 0.75 (m, 3H). **^{13}C NMR** (176 MHz, $cdcl_3$) δ 206.14, 171.21, 169.95, 140.18, 123.84, 82.84, 74.51, 56.13, 49.24, 47.75, 42.75, 42.64, 37.97, 36.38, 34.06, 27.26, 27.10, 26.24, 24.63, 21.37, 21.29, 13.29, 12.14 **IR** (cm^{-1}): 1731.47, 1699.70, 1372.08, 1237.94, 1089.74, 1025.77, 939.78, 880.21. **HRMS**: Calculated for $C_{23}H_{34}O_5Na^+$ $[M+Na^+]^+$: 413.2298 Found: 413.2302.

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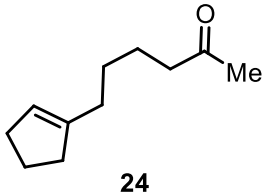
b. Lewis Acid Reactions

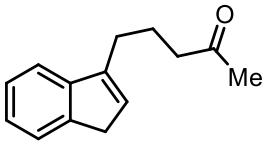
i. $FeCl_3$-Catalyzed Carbonyl-Olefin Metathesis

General procedure A for $FeCl_3$-catalyzed carbonyl-olefin metathesis: Cyclodecenone substrate (1 equiv.) was dissolved in DCE (0.05M) and $FeCl_3$ (0.1 equiv.) was added and the reaction mixture was stirred at room temperature until judged complete by TLC or for 24 hours. The crude reaction mixture was filtered through a plug of silica gel eluting with DCM to afford the crude products, which were purified by flash column chromatography.



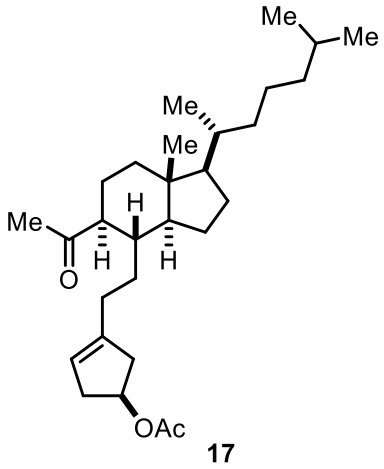
24

6-(cyclopent-1-en-1-yl)hexan-2-one (24): **23** (39 mg, 0.24 mmol) was subjected to the general metathesis procedure with $FeCl_3$ (3.8 mg) at room temperature for 1 hour to afford 42% yield by NMR vs. dimethyl terephthalate as an internal standard. An analytical sample was obtained by flash column chromatography eluting with hexanes/diethyl ether. **^{1}H NMR** (401 MHz, $CDCl_3$) δ 5.32 (s, 1H), 2.43 (t, *J* = 7.3 Hz, 2H), 2.28 (dd, *J* = 9.9, 4.6 Hz, 2H), 2.20 (d, *J* = 6.8 Hz, 2H), 2.13 (s, 3H), 2.07 (t, *J* = 7.0 Hz, 2H), 1.89 – 1.78 (m, 2H), 1.58 (dd, *J* = 15.2, 7.6 Hz, 2H), 1.48 – 1.38 (m, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 209.52, 144.56, 123.68, 43.88, 35.20, 32.62, 31.10, 30.10, 27.48, 23.87, 23.63. **IR** (cm^{-1}): 2930.45, 2849.67, 1709.14, 1408.14, 1358.15, 1162.14, 1030.83, 970.30.



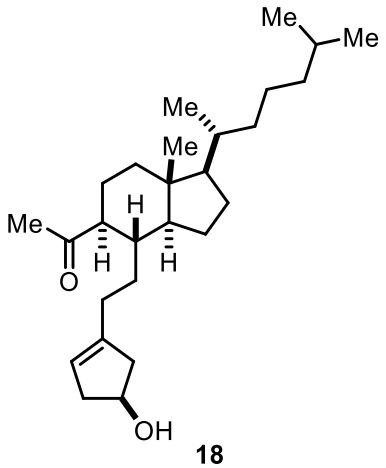
26

5-(1H-inden-3-yl)pentan-2-one (26): Prepared by subjecting **25** (50 mg, 0.25 mmol) to general procedure A. The crude product was purified by flash column chromatography eluting with hexanes/EtOAc to afford 32 mg (64% yield) of the title compound. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.4 Hz, 1H), 7.37 (d, *J* = 7.5 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 1H), 7.20 (td, *J* = 7.4, 0.9 Hz, 1H), 6.22 (s, 1H), 3.33 (d, *J* = 1.8 Hz, 2H), 2.57 (ddd, *J* = 7.6, 3.4, 1.6 Hz, 2H), 2.53 (t, *J* = 7.3 Hz, 2H), 2.14 (s, 3H), 2.01 – 1.95 (m, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 209.01, 145.35, 144.61, 143.76, 128.44, 126.17, 124.72, 123.90, 119.11, 43.37, 37.87, 30.16, 27.13, 22.08. **IR** (cm^{-1}): 2884.40, 1711.72, 1456.48, 1398.19, 1354.93, 1156.18. **HRMS**: calculated for $C_{14}H_{17}O$ ($[M+H^+]^+$): 201.1274 Found: 201.1273



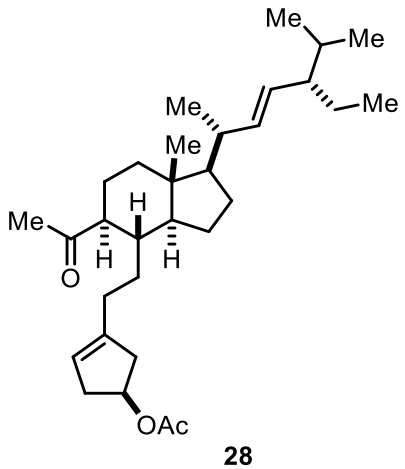
17

(1*S*)-3-(2-((1*R*,3*aS*,4*S*,5*S*,7a*R*)-5-acetyl-7a-methyl-1-(6-methylheptan-2-yl)octahydro-1H-inden-4-yl)ethyl)cyclopent-3-en-1-yl acetate (17): Prepared by subjecting substrate **14** (50 mg, 0.11 mmol) to general procedure A. The crude product was purified by silica gel column chromatography eluting with hexanes/Et_2O to afford 16 mg (31% yield) of furan **19** followed by 20 mg (39% yield) of the title compound **17**. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.35 – 5.27 (m, 1H), 5.24 (s, 1H), 2.67 (ddd, *J* = 24.1, 17.3, 6.1 Hz, 2H), 2.35 – 2.19 (m, 3H), 2.15 (s, 3H), 2.06 – 1.96 (m, 5H), 1.88 – 1.78 (m, 2H), 1.72 – 1.47 (m, 5H), 1.43 – 1.24 (m, 6H), 1.21 – 1.06 (m, 7H), 1.04 – 0.96 (m, 1H), 0.94 – 0.79 (m, 9H), 0.73 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 213.56, 171.28, 142.71, 120.47, 74.83, 56.80, 56.29, 53.03, 43.03, 42.37, 39.79, 39.70, 39.53, 36.71, 36.33, 35.91, 30.17, 29.30, 28.24, 28.06, 26.96, 26.42, 24.86, 23.99, 23.04, 22.78, 21.60, 18.92, 12.03. **IR** (cm^{-1}): 2929.48, 2866.74, 1736.06, 1707.86, 1364.74, 1026.23, 608.43. **HRMS**: calculated for $C_{29}H_{48}O_3$ ($[M+H^+]^+$): 445.3676 Found: 445.3675.



18

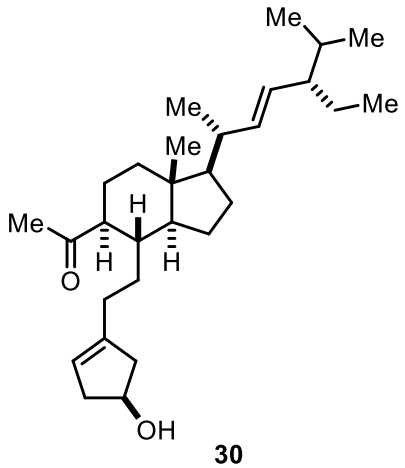
1-((1R,3aS,4S,5S,7aR)-4-(2-((S)-4-hydroxycyclopent-1-en-1-yl)ethyl)-7a-methyl-1-(6-methylheptan-2-yl)octahydro-1H-inden-5-yl)ethan-1-one (18): Prepared by subjecting substrate **15** (39 mg, 0.096 mmol) to general procedure A. The crude product was purified by silica gel column chromatography eluting with hexanes/EtOAc to afford 29 mg (75% yield) of the title compound as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.24 (s, 1H), 4.46 (s, 1H), 2.68 – 2.51 (m, 2H), 2.34 – 2.20 (m, 2), 2.16 (d, *J* = 12.7 Hz, 4H), 2.06 – 1.90 (m, 3H), 1.83 (dd, *J* = 10.2, 5.6 Hz, 2H), 1.73 – 1.58 (m, 3H), 1.51 (dd, *J* = 13.1, 6.5 Hz, 2H), 1.44 – 1.23 (m, 6H), 1.23 – 1.06 (m, 7H), 1.03 – 0.97 (m, 1H), 0.94 – 0.82 (m, 9H), 0.71 (d, *J* = 14.6 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 213.61, 142.68, 120.42, 72.28, 56.73, 56.23, 52.98, 45.52, 42.97, 39.64, 39.47, 36.65, 36.27, 35.85, 30.24, 29.21, 28.18, 28.00, 27.06, 26.35, 24.81, 23.93, 22.97, 22.71, 18.86, 11.97. **IR** (cm^{-1}): 2928.98, 2866.97, 1702.43, 1456.60, 1365.03, 1045.50, 955.33, 907.63, 839.04, 730.18. **HRMS**: Calculated for $C_{27}H_{47}O_2^+$ ($[M+H^+]^+$): 403.3571 Found: 403.3577.



28

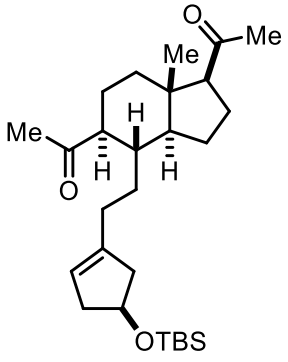
(1*S*)-3-(2-((1*R*,3*aS*,4*S*,5*S*,7*aR*)-5-acetyl-1-((5*S*,*E*)-5-ethyl-6-methylhept-3-en-2-yl)-7a-methyloctahydro-1H-inden-4-yl)ethyl)cyclopent-3-en-1-yl acetate (28): Prepared by subjecting substrate **27** (30 mg, 0.0064 mmol) to general procedure A. The crude product was purified by silica gel column chromatography eluting with hexanes/EtOAc to afford 8 mg (26% yield) of the title compound as a white solid. **^{1}H** NMR (700 MHz, $CDCl_3$) δ 5.30 (s, 1H), 5.23 (s, 1H), 5.14 (dd, *J* = 15.1, 8.7 Hz, 1H), 5.02 (dd, *J* = 15.0, 8.6 Hz, 1H), 2.70 (dd, *J* = 17.1, 6.0 Hz, 1H), 2.62 (dd, *J* = 17.2, 6.7 Hz, 1H), 2.27 (ddd, *J* = 44.5, 36.0, 17.8 Hz, 3H), 2.16 (d, *J* = 16.6

Hz, 3H), 2.08 – 1.93 (m, 7H), 1.82 (s, 1H), 1.75 – 1.65 (m, 2H), 1.63 – 1.50 (m, 5H), 1.45 – 1.32 (m, 3H), 1.29 – 1.24 (m, 1H), 1.22 – 1.11 (m, 5H), 1.01 (d, *J* = 6.5 Hz, 3H), 0.84 (d, *J* = 6.0 Hz, 3H), 0.80 (dd, *J* = 10.9, 6.5 Hz, 5H), 0.77 – 0.71 (m, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 213.45, 171.20, 142.61, 138.13, 129.72, 120.42, 74.76, 56.74, 56.04, 53.10, 51.40, 42.84, 42.28, 40.56, 39.71, 39.35, 36.62, 32.02, 30.12, 29.26, 28.70, 26.90, 26.32, 25.56, 24.88, 21.53, 21.34, 21.26, 19.12, 12.41, 12.15. **IR** (cm^{-1}): 2931.45, 2871.15, 1734.96, 1724.26, 1456.59, 1436.44, 1375.31, 1362.16, 1239.16, 1034.49, 1021.04, 969.19, 954.71, 944.93, 924.28, 906.74, 877.40. **HRMS**: Calculated for $C_{31}H_{50}O_3Na^+$ ($[M+Na^+]^+$): 493.3652 Found: 493.3659.



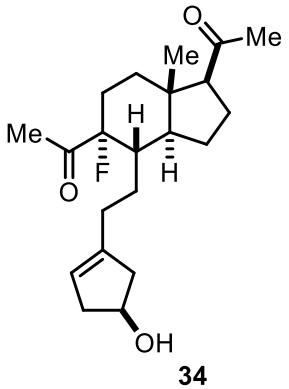
30

1-((1*R*,3*aS*,4*S*,5*S*,7*aR*)-1-((5*S*,*E*)-5-ethyl-6-methylhept-3-en-2-yl)-4-(2-((*S*)-4-hydroxycyclopent-1-en-1-yl)ethyl)-7a-methyloctahydro-1H-inden-5-yl)ethan-1-one (30): Prepared by subjecting substrate **29** (26 mg, 0.061 mmol) to general procedure A at room temperature for 3 hours. The crude product was purified by silica gel column chromatography eluting with hexanes/EtOAc to afford 13 mg (51% yield) of the title compound as a clear oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.23 (s, 1H), 5.14 (dd, *J* = 14.7, 8.8 Hz, 1H), 5.05 – 4.99 (m, 1H), 4.46 (s, 1H), 2.62 (d, *J* = 16.5 Hz, 1H), 2.55 (d, *J* = 16.6 Hz, 1H), 2.33 – 2.21 (m, 2H), 2.14 (d, *J* = 8.7 Hz, 4H), 2.08 – 1.92 (m, 4H), 1.80 (d, *J* = 26.9 Hz, 1H), 1.63 (ddd, *J* = 63.2, 33.2, 15.4 Hz, 7H), 1.46 – 1.10 (m, 10H), 1.01 (d, *J* = 5.8 Hz, 3H), 0.86 – 0.72 (m, 11H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 213.60, 142.63, 138.14, 129.69, 120.44, 72.25, 56.70, 56.02, 53.08, 51.38, 45.46, 42.93, 42.82, 40.56, 39.34, 36.61, 32.01, 30.23, 29.24, 28.69, 27.04, 26.31, 25.55, 24.88, 21.34, 21.25, 19.11, 12.41, 12.15. **IR** (cm^{-1}): 2952.76, 2927.85, 2876.55, 1704.07, 1366.32, 1047.42, 838.80, 735.80. **HRMS**: Calculated for $C_{29}H_{49}O_2^+$ ($[M+H^+]^+$): 429.3727 Found: 429.3732.



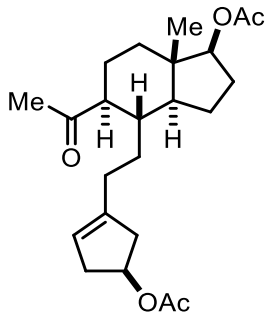
32

1,1'-((1*S*,3*aS*,4*S*,5*S*,7*aS*)-4-(2-((*S*)-4-((tert-butyldimethylsilyl)oxy)cyclopent-1-en-1-yl)ethyl)-7*a*-methyloctahydro-1H-indene-1,5-diyl)bis(ethan-1-one) (32): The reaction of **31** (30 mg, 0.067 mmol) was performed according general procedure A for 15 minutes and purification by flash column chromatography eluting with hexanes/EtOAc provided 21 mg (69% yield) of **32** as a clear wax followed by 4 mg (16% yield; see below for data) of **34**. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.19 (s, 1H), 4.53 – 4.45 (m, 1H), 2.53 (dd, *J* = 19.3, 10.0 Hz, 2H), 2.44 (dd, *J* = 15.6, 7.2 Hz, 1H), 2.32 (td, *J* = 12.0, 4.3 Hz, 1H), 2.25 – 2.14 (m, 5H), 2.12 (s, 4H), 2.05 (d, *J* = 12.4 Hz, 1H), 1.95 (s, 2H), 1.86 – 1.56 (m, 4H), 1.47 – 1.24 (m, 5H), 0.87 (d, *J* = 13.2 Hz, 9H), 0.69 (s, 3), 0.03 (d, *J* = 19.9 Hz, 6H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 212.79, 209.26, 142.14, 120.80, 72.94, 63.59, 56.49, 53.35, 45.30, 44.37, 42.78, 38.52, 36.73, 31.63, 30.19, 29.39, 27.43, 26.18, 26.12 (3C), 25.06, 22.84, 18.43, 13.34, -4.54, -4.56. **IR** (cm^{-1}): 2927.63, 2854.57, 1703.86, 1471.65, 1358.87, 1254.71, 1099.43, 1072.25, 908.89, 835.54 **HRMS**: Calculated for $C_{27}H_{46}O_3SiNa^+$ $[M+Na^+]^+$: 469.3108 Found: 469.3111.



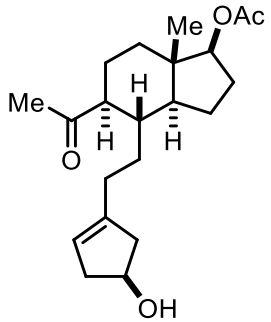
34

1,1'-((1*S*,3*aS*,4*S*,5*R*,7*aS*)-5-fluoro-4-(2-((*S*)-4-hydroxycyclopent-1-en-1-yl)ethyl)-7*a*-methyloctahydro-1H-indene-1,5-diyl)bis(ethan-1-one) (34): The reaction of **33** (31 mg, 0.093 mmol) was performed according to general procedure A at room temperature for 3 hours and purified by flash column chromatography eluting with hexanes/EtOAc to provide 26 mg of **34** (84%). **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.26 (s, 1H), 4.49 (d, *J* = 5.8 Hz, 1H), 2.70 – 2.61 (m, 1H), 2.56 (dt, *J* = 18.5, 7.6 Hz, 2H), 2.34 (td, *J* = 12.0, 4.3 Hz, 1H), 2.27 (d, *J* = 16.8 Hz, 1H), 2.23 – 1.95 (m, 10H), 1.89 – 1.82 (m, 1H), 1.82 – 1.65 (m, 3H), 1.64 – 1.55 (m, 3H), 1.49 – 1.24 (m, 5H), 0.70 (s, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 212.71, 209.13, 142.16, 120.49, 72.02, 63.37, 56.31, 53.17, 45.28, 44.20, 42.77, 38.31, 36.47, 31.48, 30.13, 29.22, 27.08, 25.99, 24.90, 22.64, 13.16. Two signals coincidentally overlap; all 27 can be seen in the C_6D_6 spectrum: **^{13}C NMR** (176 MHz, C_6D_6) δ 210.86, 142.81, 120.88, 72.02, 56.53, 56.45, 53.20, 45.61, 43.21, 43.08, 39.95, 39.68, 36.77, 36.65, 36.11, 30.62, 28.90, 28.47, 28.25, 27.52, 26.39, 25.03, 24.38, 23.06, 22.81, 19.03, 11.95. **IR** (cm^{-1}): 2923.67, 1699.09, 1421.99, 1354.59, 1231.48, 1174.89, 1046.29, 949.37, 918.72, 838.74, 729.40, 646.38. **HRMS**: Calculated for $C_{21}H_{33}O_3^+$ $[M+H^+]^+$: 333.2424 Found: 333.2431.



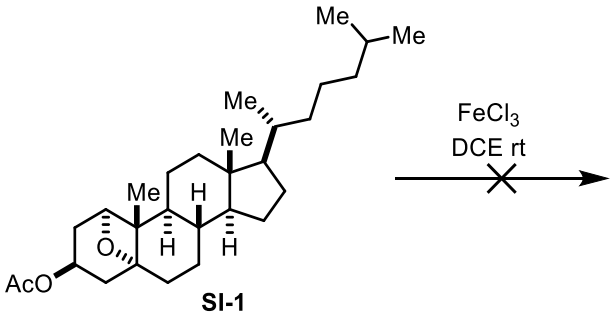
36

(*S*)-3-(2-((1*S*,3*aS*,4*S*,5*S*,7*a**S*)-1-acetoxy-5-acetyl-7*a*-methyloctahydro-1H-inden-4-yl)ethyl)cyclopent-3-en-1-yl acetate (36)**: The reaction of **35** (18.7 mg, 0.048 mmol) was performed according to general procedure A at room temperature for 24 hours and purified by flash column chromatography eluting with hexanes/EtOAc to provide 9 mg of **36** (46%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.31 (s, 1H), 5.25 (s, 1H), 4.62 (t, *J* = 8.3 Hz, 1H), 2.76 – 2.58 (m, 2H), 2.38 – 2.13 (m, 6H), 2.01 (dd, *J* = 17.2, 10.2 Hz, 7H), 1.88 (t, *J* = 11.0 Hz, 1H), 1.74 (dd, *J* = 34.5, 17.2 Hz, 3H), 1.61 – 1.47 (m, 4H), 1.47 – 1.28 (m, 3H), 1.28 – 1.14 (m, 2H), 0.83 (d, *J* = 15.1 Hz, 3H**). ^{13}C NMR** (126 MHz, $CDCl_3$) δ 212.74, 171.30, 171.17, 142.30, 120.67, 82.51, 74.71, 56.54, 47.73, 43.05, 42.27, 39.71, 36.56, 36.46, 29.91, 29.70, 27.29, 27.22, 25.89, 24.25, 21.50, 21.29, 12.03. **IR** (cm^{-1}): 1729.56, 1707.54, 1732.33, 1023.31, 733.29. **HRMS**: Calculated for $C_{23}H_{34}O_5Na^+$ $[M+H^+]^+$: 413.2298 Found:413.2300.



38

(1*S*,3*aS*,4*S*,5*S*,7*a**S*)-5-acetyl-4-(2-((*S*)-4-hydroxycyclopent-1-en-1-yl)ethyl)-7*a*-methyloctahydro-1H-inden-1-yl acetate (38)**: The reaction of **37** (20 mg, 0.057 mmol) was performed according to general procedure A at room temperature for 3 hours and purified by flash column chromatography eluting with hexanes/EtOAc to provide 9 mg of **38** (44%). **^{1}H NMR** (700 MHz, $CDCl_3$**)** δ 5.25 (s, 1H), 4.62 (t, *J* = 8.3 Hz,12H), 4.48 (s, 1H), 2.64 (d, *J* = 16.4 Hz, 1H), 2.55 (d, *J* = 14.6 Hz, 1H), 2.34 – 2.21 (m, 2H), 2.15 (d, *J* = 16.5 Hz, 4H), 2.02 (d, *J* = 35.6 Hz, 5H), 1.89 (s, 1H), 1.81 – 1.66 (m, 3H), 1.61 – 1.47 (m, 4H), 1.47 – 1.31 (m, 3H), 1.21 (d, *J* = 12.1 Hz,24H), 0.84 (d, *J* = 20.2 Hz, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 212.92, 171.33, 142.33, 120.66, 82.52, 72.20, 56.48, 47.69, 45.45, 43.03, 42.94, 36.53, 36.42, 30.01, 29.70, 27.34, 27.28, 25.88, 24.25, 21.31, 12.03. **IR** (cm^{-1}): 2922.74, 1731.67, 1706.10, 1452.62, 1359.87, 1044.89, 1021.12, 959.55, 916.03, 839.28. **HRMS**: Calculated for $C_{21}H_{33}O_4^+$ $[M+H^+]^+$: 349.2373 Found: 349.2377.

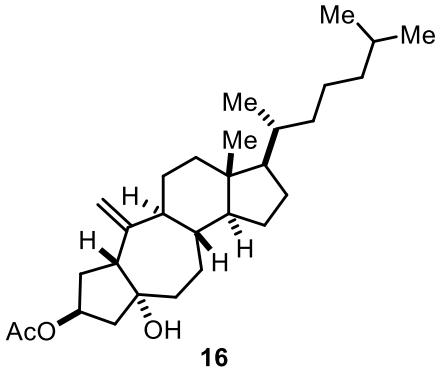


SI-1

Note: subjecting the isolated oxetane **SI-1** to the optimized conditions for FeCl3-catalyzed carbonyl-olefin metathesis afforded only a complex mixture.

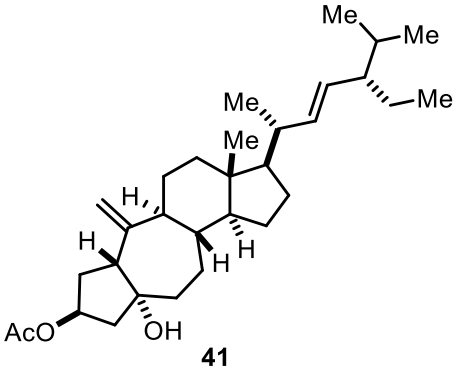
ii. Me_2AlCl-Mediated Carbonyl-Ene Reaction

General procedure B for Me_2AlCl-mediated carbonyl-ene reaction: Cyclodecenone substrate (1 equiv.) was dissolved in DCE (0.05M) and cooled to 0°C on an ice bath. Me_2AlCl (1M in hexanes, 1 equiv.) was added and the reaction mixture was stirred at this temperature for 1 hour. The reaction mixture was diluted with DCM, quenched with aqueous 1M HCl and extracted with two additional portions of DCM. The combined organic layers were dried over Na_2SO_4 and concentrated by rotary evaporator before purification by flash column chromatography.



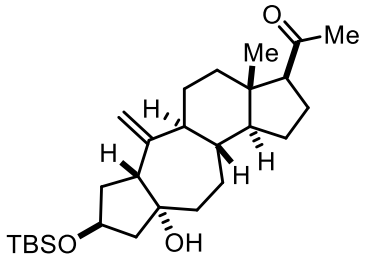
16

(3*R*,3*aR*,5*aS*,6*aR*,8*S*,9*aR*,11*aR*,11*bS*)-9a-hydroxy-3a-methyl-6-methylene-3-(6-methylheptan-2-yl)hexadecahydro-1H-indeno[5,4-f]azulen-8-yl acetate (16): The reaction of **14** (50 mg, 0.11 mmol) was performed according to general procedure B and purified by flash column chromatography eluting with hexanes/EtOAc to afford 42 mg (85% yield) of **16** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.25 – 5.19 (m, 1H), 5.14 (s, 1H), 5.00 (s, 1H), 2.99 (dd, *J* = 12.7, 6.4 Hz, 1H), 2.52 (dd, *J* = 15.0, 7.4 Hz, 1H), 2.31 (td, *J* = 13.4, 6.7 Hz, 1H), 2.13 (s, 1H), 2.08 – 1.78 (m, 7H), 1.76 – 1.60 (m, 4H), 1.54 – 1.08 (m, 16H), 1.03 – 0.82 (m, 11H), 0.73 (s, 3H**). ^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.92, 151.24, 114.21, 78.46, 74.45, 56.63, 55.24, 55.13, 48.90, 47.90, 43.23, 42.81, 40.82, 40.57, 39.66, 36.24, 35.92, 35.52, 33.36, 28.16, 28.15, 26.09, 24.64, 23.98, 22.97, 22.71, 21.58, 18.76, 12.51. **IR** (cm^{-1}): 2931.29, 2864.17, 11726.61, 1690.03, 1466.46, 1375.83, 1362.19, 1289.27, 1199.76, 1052.85, 1026.63, 1012.80, 968.70, 894.1. **HRMS**: calculated for $C_{29}H_{49}O_3^+$ $[M+H^+]^+$: 445.3676 Found: 445.3682.



41

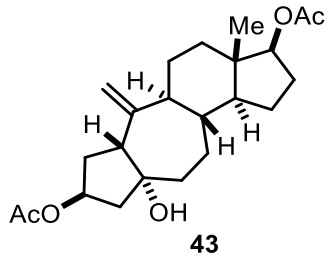
(3*R*,3*aR*,5*aS*,6*aR*,8*S*,9*aR*,11*aR*,11*bS*)-3-((5*S*,*E*)-5-ethyl-6-methylhept-3-en-2-yl)-9*a*-hydroxy-3*a*-methyl-6-methylenehexadecahydro-1H-indeno[5,4-f]azulen-8-yl acetate (41): The reaction of **27** (25 mg, 0.053 mmol) was performed according to general procedure B and purified by flash column chromatography eluting with hexanes/EtOAc to afford 19 mg (76% yield) of the title compound as white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.22 (s, 1H), 5.18 – 5.09 (m, 2H), 5.02 (dd, *J* = 16.1, 9.7 Hz, 2H), 2.99 (dd, *J* = 12.4, 6.2 Hz, 1H), 2.52 (dd, *J* = 14.8, 7.3 Hz, 1H), 2.31 (td, *J* = 13.4, 7.0 Hz, 1H), 2.14 (s, 1H), 2.10 – 1.87 (m, 7H), 1.67 (ddd, *J* = 47.5, 25.2, 14.9 Hz, 5H), 1.57 – 1.36 (m, 7H), 1.37 – 1.05 (m, 7H), 0.97 (dd, *J* = 52.1, 7.9 Hz, 4H), 0.88 – 0.67 (m, 11H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 170.93, 151.17, 138.26, 129.56, 114.25, 78.45, 74.43, 56.39, 55.32, 55.13, 51.37, 48.87, 47.88, 43.10, 42.79, 40.77, 40.63, 40.40, 35.51, 33.31, 32.02, 28.78, 26.06, 25.54, 24.68, 21.59, 21.31, 21.25, 19.14, 12.69, 12.41. **IR** (cm^{-1}): 2929.22, 2871.42, 1735.48, 1724.56, 1456.61, 1375.56, 1362.03, 1239.47, 1035.08, 1021.20, 969.50, 954.80, 924.47, 907.01, 877.71. **HRMS**: Calculated for $C_{31}H_{50}O_3Na^+$ $[M+Na^+]^+$: 493.3652 Found: 493.3666.



42

1-((3*S*,3*aS*,5*aS*,6*aR*,8*S*,9*aR*,11*aR*,11*bS*)-8-((tert-butyldimethylsilyl)oxy)-9*a*-hydroxy-3*a*-methyl-6-methylenehexadecahydro-1H-indeno[5,4-f]azulen-3-yl)ethan-1-one (42): The reaction of **31** (30 mg, 0.067 mmol) was performed according to general procedure B and purified by flash column chromatography to eluting with hexanes/EtOAc to afford 22 mg (73% yield) of the title compound as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.14 (s, 1H), 5.01 (s, 1H), 4.40 (d, *J* = 5.9 Hz, 1H), 3.12 (dd, *J* = 12.2, 6.9 Hz, 1H), 2.56 (t, *J* = 9.3 Hz, 1H), 2.36 (dd, *J* = 14.2, 6.8 Hz, 1H), 2.22 – 2.14 (m, 2H), 2.11 (d, *J* = 5.7 Hz, 3H), 2.02 – 1.93 (m, 3H), 1.80 – 1.75 (m, 1H), 1.70 – 1.63 (m, 3H), 1.61 – 1.51 (m, 4H), 1.46 (ddt, *J* = 17.2, 10.4, 4.9 Hz, 3H), 1.38 – 1.32 (m, 1H), 1.31 – 1.25 (m, 1H), 1.02 – 0.95 (m, 1H), 0.88 (s, 9H), 0.68 (s, 3H), 0.04 (s, 6H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 209.52, 151.66, 113.93, 71.34, 64.08, 55.56, 55.13, 52.50, 47.44, 44.65, 42.88, 40.75, 39.57, 38.83, 33.07, 31.61, 26.16, 26.08 (3C), 26.00, 24.79, 22.79, 18.33, 13.77, -4.54, -4.56. **IR** (cm^{-1}): 295.72, 2853.16, 1696.88, 1356.62, 1249.83, 1227.18,

1199.23, 1051.18, 966.68, 832.98, 877.97 **HRMS**: Calculated for $C_{27}H_{46}O_3Na^+[M^+Na^+]^+$: 469.3108 Found: 469.3160.

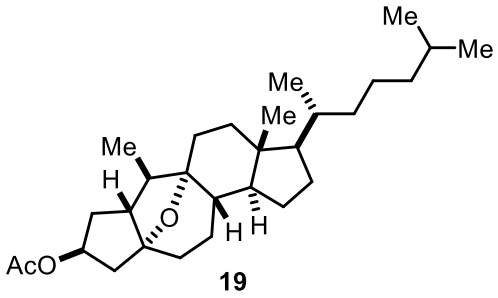


43

(3*S*,3*aS*,5*aS*,6*aR*,8*S*,9*aR*,11*aR*,11*bS*)-9*a*-hydroxy-3*a*-methyl-6-methylenehexadecahydro-1H-indeno[5,4-f]azulene-3,8-diyl diacetate (43): The reaction of **35** (20 mg, 0.051 mmol) was performed according to general procedure B and purified by flash column chromatography to eluting with hexanes/EtOAc to afford 12 mg (59% yield) of the title compound as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.23 (s, 1H), 5.16 (s, 1H), 5.02 (s, 1H), 4.63 (t, *J* = 8.4 Hz, 1H), 2.97 (dd, *J* = 12.6, 6.3 Hz, 1H), 2.54 (dd, *J* = 14.9, 7.4 Hz, 1H), 2.32 (td, *J* = 13.4, 7.1 Hz, 1H), 2.24 – 2.10 (m, 2H), 2.03 (dd, *J* = 18.2, 10.1 Hz, 7H), 1.95 (t, *J* = 9.8 Hz, 1H), 1.67 (ddd, *J* = 39.2, 29.1, 15.0 Hz, 5H), 1.54 – 1.43 (m, 5H), 1.34 (dt, *J* = 24.8, 9.3 Hz, 2H), 1.26 – 1.21 (m, 1H), 1.00 – 0.92 (m, 1H), 0.91 – 0.81 (m, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 171.26, 170.89, 150.55, 114.68, 82.71, 78.39, 74.37, 54.99, 49.56, 48.86, 47.92, 43.24, 42.68, 40.54, 37.34, 35.52, 32.72, 27.44, 25.46, 23.89, 21.58, 21.33, 12.53. **IR** (cm^{-1}): 2932.01, 1728.02, 1374.31, 1358.76, 1233.81, 1200.43, 1098.29, 1075.01, 1039.84, 1018.48, 980.48, 969.19, 908.95, 868.63, 827.89. **HRMS**: Calculated for $C_{23}H_{34}O_5Na^+[M+Na^+]^+$: 413.2298 Found: 413.2318.

iii. $TiCl_4$-Catalyzed Tetrahydrofuran Formation

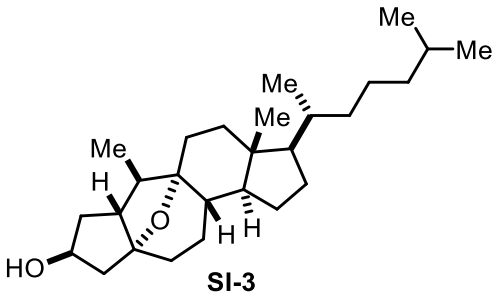
General procedure C for $TiCl_4$-catalyzed tetrahydrofuran formation: Cyclodecenone substrate (1 equiv.) was dissolved in DCE (0.05M) and a freshly prepared solution of $TiCl_4$ (1M in toluene, 0.1 equiv.) was added and the reaction mixture was stirred at room temperature for 24 hours.



19

(3*R*,3*aR*,5*aS*,6*R*,6*aR*,8*S*,9*aR*,11*aS*,11*bS*)-3*a*,6-dimethyl-3-(6-methylheptan-2-yl)tetradecahydro-6H-5*a*,9*a*-epoxyindeno[5,4-f]azulen-8-yl acetate (19): Compound **12** (50 mg; 0.11 mmol) was subjected to general procedure C and purified by flash column chromatography eluting with hexanes/EtOAc to afford 22 mg (43% yield) of the title compound. Unambiguous structural determination was achieved by X-ray crystallographic analysis of the deacetylated product **SI-3** (see below). **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.33 – 5.26 (m, 1H), 2.18 (dd, *J* = 13.8, 5.6 Hz, 1H), 2.10 (d, *J* = 9.1 Hz, 1H), 2.00 (s, 2H), 1.97 – 1.89 (m, 2H), 1.89 – 1.42 (m, 13H), 1.39 – 1.19 (m, 9H), 1.16 – 1.07 (m, 3H), 1.01 (dd, *J* = 20.0, 8.5 Hz, 4H), 0.91 – 0.82 (m, 9H), 0.63 (s, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 170.81, 90.03, 86.47, 77.57, 56.11,

53.47, 51.70, 46.78, 43.42, 42.17, 39.73, 39.69, 36.59, 36.22, 35.82, 33.43, 32.74, 30.56, 28.19, 28.16, 24.50, 23.80, 22.96, 22.73, 21.83, 21.46, 18.77, 13.33, 10.76. **IR** (cm^{-1}): 2933.08, 2912.57, 2866.52, 1741.12, 1467.21, 1456.21, 1439.22, 1374.42, 1360.66, 1232.22, 1062.64, 1037.56, 1007.71, 950.33, 930.14. **HRMS**: Calculated for $C_{29}H_{49}O_3^+[M+H^+]^+$: 445.3676 Found: 445.3672.



SI-3

(3*R*,3*aR*,5*aS*,6*R*,6*aR*,8*S*,9*aR*,11*aS*,11*bS*)-3*a*,6-dimethyl-3-(6-methylheptan-2-yl)tetradecahydro-6H-5*a*,9*a*-epoxyindeno[5,4-f]azulen-8-ol (SI-3): Furan **19** (120 mg, 0.27 mmol; combined material from various reactions) was dissolved in THF (7 mL) and treated with a solution of TMSOK (87 mg, 0.68 mmol) in THF (5 mL) and stirred at room temperature overnight before being concentrated and purified by flash column chromatography on silica gel to afford 28 mg (26% yield) of the title compound as a white solid suitable for X-ray crystallography (See section 5 below). **^{1}H NMR** (700 MHz, $CDCl_3$) δ 4.54 – 4.49 (m, 1H), 2.13 (dt, *J* = 13.8, 7.1 Hz, 2H), 1.95 (td, *J* = 12.5, 7.6 Hz, 1H), 1.89 – 1.79 (m, 3H), 1.77 – 1.59 (m, 5H), 1.50 (dddd, *J* = 31.3, 20.0, 13.7, 6.9 Hz, 7H), 1.39 – 1.28 (m, 4H), 1.28 – 1.19 (m, 4H), 1.17 – 1.06 (m, 3H), 1.06 – 0.96 (m, 5H), 0.91 – 0.84 (m, 8H), 0.63 (s, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 90.35, 85.84, 74.33, 56.18, 53.87, 51.44, 46.83, 46.56, 42.63, 42.18, 39.69, 36.67, 36.22, 35.82, 33.50, 32.79, 30.62, 28.18, 28.16, 24.52, 23.82, 22.96, 22.73, 21.83, 18.78, 13.38, 10.75. **IR** (cm^{-1}): 2927.99, 2867.75, 1465.26, 1435.98, 1065.41, 1042.92, 1004.09, 952.50, 930.28, 919.27, 870.46. **HRMS**: Calculated for $C_{27}H_{47}O_2^+$ $[M+H^+]^+$: 425.3390 Found:425.3365.

4. Computational Investigation of Mechanism

All quantum chemical calculations utilized density functional theory (DFT) as implemented in the Q-Chem 4.3 quantum chemistry package.[6]The unrestricted B97-D density functional[7] with singlet spin was used in combination with the 6-31G* basis set[8] to acquire gas phase geometries for the intermediates discussed. The reaction discovery tools developed by the Zimmerman group, specifically the Growing String Method (GSM)[9]were used to probe potential reaction paths and determine the exact transition state and minimum energy reaction path for each proposed elementary step. By optimizing the reaction path, GSM provides verification that the saddle point connects the reactant to product geometries through a single transition state. Frequency calculations were performed on all structures at the same level of theory to confirm that optimizations led to stable minima (intermediates) or transition states. Stable intermediates were characterized by all real frequencies, and transition states were identified by a single imaginary frequency. The ωB97X-D3[10] density functional and the triple-zeta, polarized 6-311G* basis set[8] were used to calculate energies with the SMD solvent model[11] using 1,2-dichloroethane as the implicit solvent, in the ORCA software package.[12] Thermodynamic corrections were applied to the solvated energies at a temperature of 353.15 K. For these corrections, low frequencies (<50cm^{-1}) were set to 50 cm^{-1}. Energies are either reported as solvent-phase enthalpies (H) or solvent-phase Gibbs free energies (G).

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[9] (a) Zimmerman, P.M. *J. Chem. Phys*. **2013**, *138*, 184102. (b) Zimmerman, P.M. *J. Chem. Theory Comput*. **2013**, *9*, 3043. (c) Zimmerman, P.M. *J. Comput. Chem.* **2015**, *36*, 601. (d) Jafari, M.; Zimmerman, P.M. *J. Comput. Chem.* **2017**, *38*, 645.
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[11] Marenich, A.V.; Cramer, C.J.; Truhlar, D.G. *J. Phys. Chem. B* **2009**, *113*, 6378.
[12] Neese, F. "The ORCA program system". *Wiley Interdisciplinary Reviews: Computational Molecular Science*. **2012**, *2*, 73.

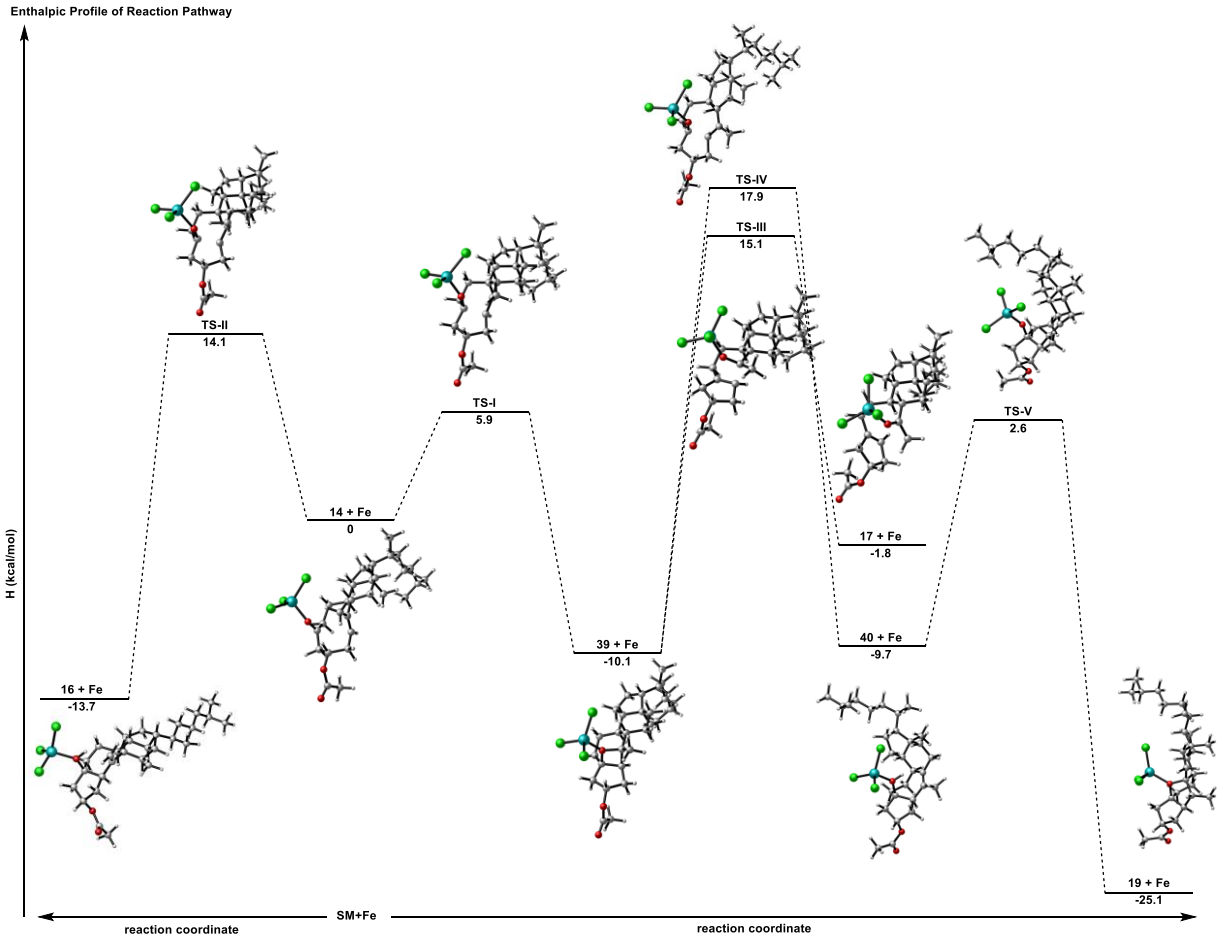

Figure A3-1: Complete reaction pathway

XYZ coordinates for all reported structures

Structure **14 + Fe**

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C	-6.29039721	0.56680898	-1.26801925
C	-6.53425772	1.35805585	0.03742002
C	-5.43994520	1.09855976	1.12060872
C	-7.87971673	0.92232853	0.65227159
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C	-5.77700044	1.75398908	2.49801778
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C	-11.68239990	3.72132403	2.59746335
C	-13.07173834	4.31355191	2.31480520
C	-13.05216043	5.75175087	1.75227350
C	-2.94729240	0.59798032	1.29377439
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O	-0.50394164	2.68899015	-1.92805381
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Cl	-5.49360701	-2.18440154	-3.42002221
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Structure **TS-I**

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Cl	-4.59318411	-2.28763788	-3.28971541
Cl	-1.50808776	-2.67422390	-1.28598993
Cl	-4.76656889	-2.59513069	0.41210644

Structure **TS-II**

C	-1.62442223	2.28562587	-1.60586270
C	-2.74134049	1.81255043	-2.55318934
C	-3.74746648	1.09949334	-1.62499955
C	-4.04048063	1.25952744	0.84093580
C	-3.71098520	2.14496636	-0.27689604
C	-5.18026538	1.03469672	-2.16739192
C	-6.23267477	0.43240297	-1.21944837
C	-6.52853656	1.24199473	0.06468807
C	-5.47453625	0.97359142	1.18494175
C	-7.89032990	0.85325870	0.66488401
C	-8.26460316	1.66121739	1.93417286
C	-7.21419956	1.39247035	3.02245228
C	-5.78901919	1.72238554	2.52543278
C	-9.16190364	0.93741259	-0.21223243
C	-10.34033623	1.01293780	0.82020403
C	-9.66352499	1.05170159	2.23043121
O	-3.22635987	-0.15172665	-1.26915283
H	-6.55228399	2.31778440	-0.18370182
H	-5.54061516	-0.10396297	1.41691392
H	-7.79251824	-0.20086457	0.98792250
C	-10.44688881	1.64516772	3.44837137
C	-11.77134732	2.37237234	3.11509574
C	-11.62557572	3.78690514	2.53365126
C	-12.98812879	4.45145744	2.28186077
C	-12.90574088	5.89626110	1.74248690
C	-3.04789259	0.37689386	1.29487097
C	-8.36587555	3.17648148	1.65657521
O	-0.59535260	3.10871332	-2.19126048
O	0.19029840	4.84141911	-3.32454207
C	-0.75832672	4.35820651	-2.74519886
C	-2.05858463	5.14050736	-2.55913486
C	-12.20503458	5.95742572	0.37133557
C	-14.31379156	6.51279327	1.65126823
H	-2.36691328	1.11841019	-3.31740658
H	-3.24412032	2.64814446	-3.06081690
H	-5.15277405	0.44504258	-3.09575841
H	-5.47582017	2.06241033	-2.44057529
H	-5.93605118	-0.58717590	-0.93332175
H	-7.16242655	0.33397994	-1.79809654
H	-7.25326418	0.32400351	3.29801583
H	-7.43065879	1.97759405	3.93238093
H	-5.67227352	2.80769942	2.37536314
H	-5.04688477	1.42121872	3.28198429
H	-9.25522976	0.07531919	-0.88728395
H	-9.13501541	1.84253571	-0.84063622
H	-11.01330750	0.14766515	0.73295721
H	-10.94895667	1.90822039	0.63631556

H	-9.45238980	-0.00403539	2.47904157
C	-10.71895126	0.52722852	4.47882404
H	-12.36831670	1.74783184	2.42789525
H	-12.36241102	2.45429380	4.04466601
H	-11.05351589	3.76050663	1.59787665
H	-11.03837192	4.40797765	3.23523113
H	-13.56683346	4.44979873	3.22335595
H	-13.56246213	3.83876781	1.56138295
H	-12.31190558	6.49217236	2.46069161
H	-1.99783082	0.68924268	1.29863215
H	-3.11511138	-0.14224568	0.09833428
H	-3.31816664	-0.37689568	2.03959914
H	-7.39668198	3.61012956	1.37135792
H	-9.07747319	3.38498542	0.84645350
H	-8.71556431	3.70299501	2.55691054
H	-2.17242051	5.80765737	-3.42316247
H	-1.95360172	5.77042606	-1.66013445
H	-2.95965928	4.52859694	-2.43951815
H	-12.73202135	5.31345990	-0.35431232
H	-11.15820278	5.61953883	0.42899708
H	-12.20731753	6.98644363	-0.02338324
H	-14.93730467	5.94155216	0.94173248
H	-14.27035003	7.55690583	1.29984932
H	-14.81703497	6.49778071	2.63201023
C	-2.32898658	2.83964178	-0.33783587
H	-1.06231053	1.38981760	-1.31256794
H	-2.47965474	3.92257371	-0.40422220
H	-1.72103488	2.65761004	0.55827274
H	-4.52051989	2.85245767	-0.48162696
H	-9.78163456	0.02889641	4.77613887
H	-11.38623223	-0.23974484	4.04880543
H	-11.20156069	0.92881571	5.38495556
H	-9.78673031	2.38144606	3.94255999
Fe	-3.56871415	-2.02663902	-1.68914772
Cl	-4.73202502	-2.25543771	-3.53211802
Cl	-1.55751915	-2.88928906	-1.82045902
Cl	-4.62314893	-2.73349855	0.14174569

Structure **16 + Fe**

O	2.85306450	6.62995557	20.77324482
O	5.91988746	9.85919721	20.88379529
O	3.15129961	4.75028999	22.04302187
C	5.72665182	8.83620174	17.08210869
H	4.80904634	8.22676007	17.13923405
C	6.14120561	7.68379696	14.80409107
C	2.60088296	5.33051308	21.12552588
C	6.04984720	9.02960329	15.59174410
H	7.05883042	9.48365550	15.53405809
C	5.49879783	9.50030586	13.27334262
H	6.01715546	10.31996912	12.75617569
H	4.59868626	9.27043314	12.68069165
C	7.06204638	6.65894368	16.96542992
H	7.92229532	6.12196256	17.39516628
H	6.17069094	6.03810000	17.15969334
C	5.44145248	10.15009549	17.85120256
H	6.37761682	10.56797830	18.26205173
H	5.04617103	10.90722124	17.15865564
C	6.90198477	8.01967269	17.69588223
H	7.82310660	8.59686700	17.49659176
C	5.12049053	9.90082999	14.73086831
H	5.25964565	10.97550606	14.91765349
H	4.06583060	9.66518966	14.94746052
C	6.23375698	7.28796119	12.15333777
H	5.16175058	7.02461878	12.09560992
C	7.26683097	6.84060412	15.44274557
H	7.34530108	5.85000407	14.97418107
H	8.22848892	7.35767603	15.27426721
C	6.60122000	8.03348529	10.84504658
H	7.69830817	8.17046293	10.81195374
H	6.16346169	9.04474515	10.85901830
C	6.41986725	8.23049773	13.36653126
H	7.47429106	8.56587265	13.36135954
C	6.49110815	8.14100126	8.29703520
H	7.59201853	8.20905567	8.21164882
H	6.12376589	9.17660384	8.41788912
C	5.92512804	7.56576850	6.98154608
H	4.82602486	7.50070707	7.08804610
C	6.81675111	7.81351642	19.20050381
C	6.12891709	7.33696044	9.55730509
H	5.03209968	7.20372880	9.60241651
H	6.56449607	6.32815295	9.48517374
C	4.84432298	9.12113624	20.16430773
C	4.80873291	6.89796779	14.82021535
H	4.91338084	5.97366560	14.23342265
H	3.98864220	7.48369463	14.37889022
H	4.50739824	6.61054124	15.83766525
C	4.39759288	9.96909724	18.97222268
H	4.07534863	10.94750522	19.35908900
H	3.50433350	9.47900226	18.54811217
C	5.43800059	7.70804060	19.81648217
H	4.74276460	7.27519451	19.08163518
C	3.85038133	7.33976850	21.58067164
H	3.65207874	7.13130968	22.63843262
C	6.46436439	6.15192696	6.69111790
H	6.07512383	5.77308800	5.73189243
H	6.18169179	5.43724744	7.47956772
H	7.56639546	6.17105709	6.62634228
C	7.05054856	5.98645801	12.27431204
H	7.02409863	5.41275792	11.33568884
H	6.66421584	5.33163487	13.06779876
H	8.10481523	6.21527920	12.50333922
C	5.26567014	6.93700359	21.13972913
H	5.97612890	7.29675688	21.89951598
H	5.38209910	5.85170181	21.03795583
C	1.53190011	4.74621046	20.21759202
H	1.41407050	3.67831681	20.43678055
H	1.80232682	4.89238056	19.16071816
H	0.57647857	5.26744905	20.38750311
C	3.72858520	8.83237040	21.20300465
H	3.85528873	9.45958428	22.09469270
H	2.73821213	9.05056497	20.78213411
C	6.24112425	8.51099588	5.80758405

H	7.33284189	8.59644460	5.66890287
H	5.84304818	9.52233714	5.99317186
H	5.80837987	8.13492048	4.86603433
C	7.94006940	7.80757724	19.95295675
H	7.92641617	7.61131551	21.02655923
H	8.91960420	7.95182810	19.49070348
Fe	5.86839868	11.40635620	22.16037711
Cl	7.90363995	12.13941874	21.82157703
Cl	4.25861999	12.73693890	21.51107729
Cl	5.52844351	10.54058436	24.14332065
H	6.78898984	9.63793994	20.46297822

Structure **39 + Fe**

C	-1.68994523	2.07902772	-1.50178064
C	-2.76821994	1.65669316	-2.52625784
C	-4.01515783	1.47381624	-1.67418279
C	-4.08682052	1.06582130	0.44817201
C	-3.85688710	2.35093083	-0.38729502
C	-5.36466283	1.43968283	-2.37892559
C	-6.46758313	0.74889903	-1.55005211
C	-6.64892314	1.30976789	-0.12523119
C	-5.54735232	0.86977165	0.90315111
C	-7.99325241	0.88342108	0.48946501
C	-8.30323423	1.60378479	1.82719581
C	-7.20263001	1.24829904	2.83971273
C	-5.79082744	1.54476804	2.28066115
C	-9.30031160	1.03344147	-0.32316340
C	-10.43219670	1.03922075	0.76242756
C	-9.69690200	0.99329819	2.14433714
O	-3.87054545	0.24410362	-0.81180573
H	-6.64461089	2.41062027	-0.20473309
H	-5.66410125	-0.21875311	1.04201941
H	-7.89281688	-0.19159073	0.73184726
C	-10.42332186	1.53369067	3.42123147
C	-11.75789266	2.27977132	3.17749346
C	-11.63825234	3.71284116	2.63400723
C	-13.01508204	4.35693752	2.41194394
C	-12.96962360	5.80163998	1.86810346
C	-3.04089928	0.65880242	1.47340336
C	-8.39572415	3.13553230	1.65740757
O	-0.46799564	2.60718906	-2.05506397
O	0.75720947	3.95376489	-3.31468887
C	-0.32069104	3.75715254	-2.79596868
C	-1.44874256	4.78476257	-2.88244999
C	-12.30845946	5.86896060	0.47759335
C	-14.39007666	6.39319379	1.81175827
H	-2.50445895	0.73915687	-3.07100423
H	-2.96792436	2.44327038	-3.26795873
H	-5.25825421	0.92946748	-3.34804600
H	-5.64460753	2.48867790	-2.58227137
H	-6.26559109	-0.33174617	-1.50225370
H	-7.41164899	0.86844190	-2.10198215
H	-7.26974283	0.16923719	3.06489463
H	-7.34556683	1.79184302	3.78959507
H	-5.64025840	2.63348130	2.17965747
H	-5.04829518	1.18752298	3.00847713
H	-9.42415140	0.21947897	-1.05109537
H	-9.29904671	1.97932876	-0.88897889
H	-11.10678266	0.17775913	0.65027418
H	-11.04912684	1.94010430	0.65693129
H	-9.49079950	-0.07679312	2.32796342
C	-10.66235889	0.37674596	4.41613249
H	-12.39038553	1.67995798	2.49994121
H	-12.30378658	2.33137223	4.13642124
H	-11.07617981	3.72072399	1.69225977
H	-11.05320538	4.32455112	3.34530462
H	-13.57402007	4.34423176	3.36513807
H	-13.59366618	3.73431536	1.70322693
H	-12.36689654	6.41031689	2.56788182
H	-2.05223701	0.57578371	1.00348855
H	-3.30267054	-0.31095681	1.92245895
H	-2.98724932	1.41181456	2.27323112
H	-7.42540712	3.57960682	1.39294580
H	-9.11431159	3.40730965	0.87142704
H	-8.72698117	3.60400863	2.59577548
H	-1.28507736	5.38353162	-3.78728187
H	-1.37594879	5.45573534	-2.01075769
H	-2.45935006	4.35987792	-2.89406348
H	-12.84691501	5.21552377	-0.23109045
H	-11.25523952	5.54635863	0.50423791
H	-12.33647065	6.89652252	0.08001051
H	-15.02161214	5.80688942	1.12177057
H	-14.37548444	7.43617935	1.45450871
H	-14.86741034	6.37496216	2.80530688
C	-2.43071939	2.93999111	-0.44164086
H	-1.33660273	1.16230890	-1.01358461
H	-2.49526716	3.98872213	-0.75414411
H	-1.91519548	2.91422112	0.52892797
H	-4.62527360	3.11641516	-0.22725263
H	-9.71822036	-0.13893253	4.65671953
H	-11.35309299	-0.36797654	3.98410206
H	-11.10591166	0.74837539	5.35444092
H	-9.73913186	2.24471049	3.91845915
Fe	-3.48122912	-1.64011041	-1.21367912
Cl	-4.12024062	-1.84726815	-3.30116091
Cl	-1.31029722	-1.80924803	-0.94615310
Cl	-4.65791959	-2.77796901	0.24524336

Structure **TS-III**

C	-1.63132268	2.19573336	-1.57039201
C	-2.77227206	1.63725929	-2.45980532
C	-4.03059106	1.91674912	-1.75331533
C	-3.95682655	0.93565408	0.49424587
C	-3.77799881	2.40355052	-0.40420607
C	-5.34400037	1.65375200	-2.36851885
C	-6.28687365	0.72934222	-1.53635109
C	-6.53786574	1.25869508	-0.11296884
C	-5.45415627	0.85414352	0.94436024
C	-7.89353947	0.80246108	0.45288807
C	-8.25594433	1.53555765	1.77112288
C	-7.17442787	1.22007332	2.81459561
C	-5.75531340	1.55803754	2.29271593

C	-9.17598086	0.92884215	-0.40244367
C	-10.34080399	0.92681141	0.64828602
C	-9.64787463	0.90062416	2.05111793
O	-3.61883582	-0.08157237	-0.37288215
H	-6.56782021	2.36146046	-0.18004030
H	-5.57976602	-0.22880465	1.11231383
H	-7.78059580	-0.26699143	0.70570504
C	-10.43229657	1.42678015	3.29906567
C	-11.73374488	2.21789701	3.01426834
C	-11.54575279	3.65451473	2.50255849
C	-12.87912527	4.40264752	2.34800089
C	-12.73094113	5.87570232	1.90732009
C	-2.96945782	0.94498424	1.66673365
C	-8.37283560	3.06354619	1.58595669
O	-0.61772379	2.93926772	-2.27674730
O	0.11677277	4.57887177	-3.57450039
C	-0.83314288	4.08638812	-3.00677587
C	-2.21327025	4.74855315	-3.07390513
C	-12.05769935	5.99671324	0.52660107
C	-14.10424509	6.57154814	1.89391776
H	-2.73233594	0.53036893	-2.58204088
H	-2.78434945	2.02069539	-3.49345777
H	-5.21515637	1.25597177	-3.38427269
H	-5.85373057	2.63691583	-2.42931178
H	-5.88452756	-0.28867063	-1.52339128
H	-7.23272983	0.71322425	-2.09521558
H	-7.20949939	0.14047139	3.04325506
H	-7.36179654	1.76349294	3.75656962
H	-5.63589654	2.65040849	2.18089070
H	-5.03405805	1.23882635	3.05650354
H	-9.26707412	0.10754811	-1.12744357
H	-9.17351625	1.87221970	-0.97377884
H	-11.00167513	0.05706332	0.52078627
H	-10.96443425	1.82128565	0.52172825
H	-9.42509779	-0.16369110	2.24697082
C	-10.75574677	0.24398203	4.23924893
H	-12.36116496	1.64931338	2.30584058
H	-12.30860587	2.27219088	3.95591771
H	-11.02081428	3.65095431	1.53941613
H	-10.89456020	4.20571702	3.20585293
H	-13.42640134	4.36639090	3.30750209
H	-13.50958180	3.87408323	1.60835865
H	-12.08926804	6.38726479	2.64914413
H	-1.94391750	0.83210873	1.29222246
H	-3.19672284	0.06665750	2.29194773
H	-3.04805411	1.85055873	2.28443427
H	-7.40455907	3.52714775	1.34830292
H	-9.07437531	3.31714493	0.77943840
H	-8.73775618	3.52807816	2.51318412
H	-2.37967740	5.06223767	-4.11366908
H	-2.17473848	5.66143160	-2.45884210
H	-3.06003464	4.14152909	-2.73464782
H	-12.63210906	5.43135521	-0.22832566
H	-11.02783825	5.60517146	0.53565732
H	-12.01705272	7.04957811	0.20300626
H	-14.77566734	6.07891304	1.16947995
H	-14.01092778	7.63104933	1.60352805
H	-14.58379505	6.52580164	2.88555820
C	-2.33989243	2.96739436	-0.42190686
H	-1.06610877	1.35523509	-1.15374626
H	-2.37290261	4.04297789	-0.64280721
H	-1.81276051	2.85603845	0.53171426
H	-4.53845206	3.07522079	0.01031211
H	-9.83765664	-0.29536831	4.52402930
H	-11.42601687	-0.47288018	3.73482109
H	-11.25527560	0.59214746	5.15809339
H	-9.75697065	2.10458030	3.85252563
Fe	-3.72122527	-1.88002227	-0.75673617
Cl	-3.74815120	-1.81885172	-3.01184454
Cl	-1.92324745	-2.84579511	0.08093356
Cl	-5.60182090	-2.74185544	0.06065393

Structure **TS-IV**

C	-1.68858650	2.29830586	-1.36172030
C	-2.47016592	1.30026168	-2.23152023
C	-3.81372134	1.12173890	-1.49064770
C	-4.41638812	2.37536799	0.64201127
C	-4.00898965	2.63778720	-0.75095946
C	-5.04335605	0.87884126	-2.37194722
C	-6.28672868	0.56668955	-1.52215414
C	-6.65261435	1.48093313	-0.31285792
C	-5.56460466	1.55077723	0.84582491
C	-8.00359653	0.96440775	0.21255136
C	-8.39905688	1.42929488	1.62799475
C	-7.39369658	0.80019054	2.59687328
C	-5.97023581	1.33319572	2.33303757
C	-9.24893343	1.27440492	-0.65522918
C	-10.45815676	1.17063801	0.33689061
C	-9.82665891	0.82161229	1.72164128
O	-3.70122640	0.14427561	-0.50508725
H	-6.78997557	2.51935198	-0.66709497
H	-4.76238891	0.66107691	0.50942133
H	-7.91167844	-0.13373357	0.27736925
C	-10.62885704	1.10900182	3.03529763
C	-11.89166884	1.99134322	2.87768354
C	-11.62767379	3.49326632	2.69489137
C	-12.92194361	4.31676665	2.61196519
C	-12.69778361	5.84035745	2.51316903
C	-3.49308943	2.64474920	1.78988192
C	-8.41026840	2.96663997	1.74599488
O	-0.37853991	2.68567138	-1.81788155
O	1.11402342	3.51975871	-3.22274102
C	-0.06114959	3.40065194	-2.95175860
C	-1.15047131	4.07832498	-3.77987714
C	-11.93129878	6.22747477	1.23394620
C	-14.04315879	6.58588229	2.57507335
H	-1.96291398	0.33374773	-2.34265161
H	-2.67071897	1.70716752	-3.23288337
H	-4.84402444	0.02207840	-3.03453076
H	-5.20094078	1.76413327	-3.01199159
H	-6.18783885	-0.45244730	-1.12418911
H	-7.15990888	0.55225499	-2.19095149

H	-7.41632074	-0.29321842	2.46609724
H	-7.65403169	1.01814650	3.64637923
H	-5.87373111	2.30174289	2.84968608
H	-5.23823517	0.65939547	2.80332437
H	-9.33945573	0.57782924	-1.50103987
H	-9.17596946	2.29135224	-1.07596315
H	-11.18091889	0.40156259	0.02648372
H	-11.00139038	2.12472193	0.36671203
H	-9.65341374	-0.26895321	1.69851955
C	-11.01635533	-0.22706244	3.70554240
H	-12.49837210	1.61398348	2.03624275
H	-12.51288155	1.86591983	3.78253845
H	-11.02712271	3.66515522	1.79190874
H	-11.01807694	3.85802530	3.54214101
H	-13.54049101	4.10347313	3.50286929
H	-13.51175778	3.98553098	1.73652226
H	-12.09118599	6.14871657	3.38541270
H	-2.52186975	3.04153601	1.48003947
H	-3.33071551	1.72053302	2.36740345
H	-3.96860285	3.35844104	2.48582883
H	-7.40221373	3.38559679	1.60721367
H	-9.06065100	3.41498498	0.98223661
H	-8.77872682	3.27937624	2.73295931
H	-0.72736606	4.29733415	-4.76792160
H	-1.42095598	5.03366745	-3.30130506
H	-2.06623789	3.48606487	-3.89332363
H	-12.48392316	5.88516801	0.34151720
H	-10.92526282	5.77921154	1.20467285
H	-11.81671407	7.32161349	1.16205029
H	-14.67826883	6.30551556	1.71665830
H	-13.89311515	7.67746145	2.54258868
H	-14.59338607	6.33917831	3.49823044
C	-2.70944597	3.41115518	-1.05609032
H	-1.45780223	1.78086839	-0.41858407
H	-2.88520696	4.03356446	-1.94175148
H	-2.37862507	4.08197460	-0.25129268
H	-4.85942114	3.08897078	-1.27968866
H	-10.12851768	-0.86020997	3.86659720
H	-11.71831139	-0.78769613	3.06446309
H	-11.50488320	-0.05673425	4.67861596
H	-9.95145085	1.63648633	3.73350411
Fe	-3.69616745	-1.74601160	-0.34489722
Cl	-3.94041765	-2.62463171	-2.34898530
Cl	-1.77604470	-2.23965938	0.61176418
Cl	-5.41664363	-2.10620009	1.03478351

Structure **40 + Fe**

C	-0.94023988	-0.57714707	1.62475528
C	-0.84287192	-0.65395994	0.09906767
C	-0.51597839	0.79383300	-0.32624360
C	0.21249706	1.43282205	0.88612799
C	0.23333387	0.93074321	3.43442463
C	0.24812475	0.34240812	2.00888510
C	1.59459435	2.01864694	0.55292021
C	2.59359247	2.01557494	1.72258014
C	2.12095288	2.68450540	3.02558894
C	0.98925447	2.00584446	3.82028374
C	1.77395781	4.17550578	2.81962893
C	1.55042658	4.95980062	4.14135808
C	0.43612852	4.23765326	4.92182655
C	0.77080491	2.73157924	5.14535299
C	2.73004258	5.06705815	2.01129473
C	2.23867037	6.50632624	2.36936579
C	1.19999341	6.35374108	3.53520653
H	2.99370621	2.65800343	3.70355044
C	1.16295155	7.59239392	4.45559175
H	0.81229408	4.21965479	2.28360218
C	0.88556338	8.87524281	3.62848157
C	-0.42467332	8.85123997	2.82245566
C	-0.67633261	10.16350865	2.06328783
C	-1.82458423	10.07655710	1.03427388
O	-0.67396033	2.52247150	1.40140484
H	1.16409801	-0.24480205	1.84338274
O	0.27724020	-1.53653455	-0.19277610
O	1.50466437	-2.66295783	-1.66529250
C	0.48495969	-2.04087518	-1.45718300
C	-0.60516242	-1.81472205	-2.49900639
C	2.82413375	5.07395712	5.00860542
H	2.16541534	7.70985591	4.90590212
C	-3.15929311	9.67891203	1.69150484
C	-1.96441180	11.41138848	0.28031877
C	-0.75085159	0.23820379	4.36522776
H	-0.89422273	-1.57182966	2.08586686
H	-1.89897957	-0.10559515	1.88906777
H	-1.75993858	-1.03894516	-0.36645855
H	-1.45124064	1.32200166	-0.54736654
H	0.10294283	0.82807360	-1.23199924
H	1.45080525	3.03140711	0.14686961
H	2.02447315	1.40784595	-0.25657243
H	3.50019543	2.54508417	1.39244781
H	2.90121199	0.98019323	1.93739627
H	-0.50937501	4.31748762	4.35834298
H	0.26819487	4.69799078	5.90549499
H	-0.03646027	2.29152617	5.74149773
H	1.69176324	2.66096307	5.74959852
H	2.68452653	4.86177589	0.93162704
H	3.77175574	4.90928194	2.33541503
H	1.77843782	7.00595635	1.50478586
H	3.08032785	7.13784090	2.69534832
H	0.19863236	6.23965020	3.09122892
C	0.13739875	7.45199427	5.59934987
H	0.87363921	9.73821121	4.31818087
H	1.72204216	9.04467242	2.92983665
H	-1.27280585	8.64029454	3.49223280
H	-0.39544306	8.02538500	2.09183172
H	0.24974697	10.45670982	1.53503518
H	-0.89672893	10.97489538	2.78206139
H	-1.55601578	9.29014431	0.30438847
H	-0.25587004	-2.22360766	-3.45377276
H	-0.84749796	-0.74771977	-2.61506667
H	-1.53286835	-2.32985596	-2.20034745
H	3.25683724	4.09539696	5.26287463

H	3.60085225	5.66243230	4.49955316
H	2.58149676	5.58669978	5.95217112
H	-3.42345778	10.39825727	2.48716830
H	-3.10777815	8.67468294	2.14025786
H	-3.97452216	9.67768612	0.94948672
H	-2.22921446	12.22063959	0.98334694
H	-2.75327145	11.35692798	-0.48823463
H	-1.01792796	11.68853272	-0.21348808
H	-1.79566015	0.51059807	4.13617214
H	-0.56540354	0.45087225	5.42364054
H	-0.67521569	-0.85242933	4.23283688
Fe	-2.07318898	3.69156827	0.59622582
Cl	-3.84516982	2.41370032	0.35951657
Cl	-2.32365207	5.20837701	2.15583828
Cl	-1.21415223	4.41055813	-1.28168501
H	-0.48575973	2.59612483	2.37685864
H	-0.83731133	7.11168793	5.21561841
H	-0.01372260	8.42151822	6.10305894
H	0.47348845	6.73178310	6.35919327

Structure **17 + Fe**

C	-2.35763497	3.21329189	-1.49749761
C	-3.20070567	2.08156057	-2.16382360
C	-4.63281343	2.40599335	-1.78718884
C	-3.99266724	0.26092936	1.29255448
C	-4.71580533	3.56762930	-1.10476858
C	-5.76489237	1.47062585	-2.11664505
C	-5.81680496	0.28784266	-1.10874233
C	-6.24234399	0.75919655	0.30478835
C	-5.46154593	0.02278353	1.47042975
C	-7.73459134	0.52438332	0.57198071
C	-8.22063958	1.06479643	1.94041427
C	-7.46724486	0.31611503	3.05265224
C	-5.93874607	0.46178870	2.88652494
C	-8.76957131	1.07509651	-0.43520645
C	-10.11013346	1.09086227	0.37408223
C	-9.73203731	0.70462226	1.84263450
O	-3.23026538	-0.60309310	0.79908056
H	-6.02254263	1.83449347	0.39122044
H	-5.64510665	-1.05258546	1.34485904
H	-7.87491978	-0.57287408	0.60101812
C	-10.65919685	1.17619109	3.01675135
C	-11.73621262	2.22524126	2.64305854
C	-11.22419304	3.65872871	2.43503007
C	-12.33967050	4.62607056	2.01035036
C	-11.88563394	6.09495795	1.87282523
C	-3.39699329	1.59227655	1.66279940
C	-8.00364303	2.58766211	2.06891525
O	-1.34229418	3.78984472	-2.35227295
O	-0.63796937	4.72306593	-4.23584470
C	-1.59114989	4.43099651	-3.54412543
C	-3.01815681	4.82343383	-3.92406996
C	-10.76749608	6.25330506	0.82363398
C	-13.08621380	6.98976297	1.51347523
H	-2.88349396	1.08186014	-1.82592850
H	-3.06866497	2.07951276	-3.25951391
H	-5.63380908	1.06117164	-3.13184295
H	-6.72333214	2.01047075	-2.09178027
H	-4.82771388	-0.18964843	-1.10105407
H	-6.51454174	-0.48241601	-1.47058676
H	-7.73874613	-0.75307246	3.00241468
H	-7.76175883	0.68376071	4.05023378
H	-5.64753273	1.50786406	3.06300551
H	-5.41698729	-0.14977733	3.64039724
H	-8.82515828	0.45935531	-1.34410894
H	-8.50198084	2.09568846	-0.74901612
H	-10.83926580	0.37761096	-0.03777103
H	-10.57380509	2.08356253	0.31964526
H	-9.73969593	-0.39975224	1.86903925
C	-11.34228135	-0.05317209	3.65516770
H	-12.27134538	1.88730118	1.73898971
H	-12.49085832	2.25104069	3.44988040
H	-10.43097239	3.67503688	1.67609040
H	-10.75959637	4.01823053	3.37158487
H	-13.16561665	4.57326361	2.74273582
H	-12.75736105	4.29112962	1.04200237
H	-11.48767478	6.41932034	2.85255696
H	-2.39001695	1.69294368	1.24091840
H	-3.34228022	1.66959692	2.76147650
H	-4.05189974	2.39994636	1.30362697
H	-6.93733398	2.85466463	2.11639915
H	-8.43091641	3.12597599	1.21192388
H	-8.48761049	2.96654536	2.97970956
H	-3.07911604	4.84228326	-5.01974440
H	-3.19535085	5.84907149	-3.56033241
H	-3.80387068	4.18248476	-3.50815434
H	-11.09764611	5.84504095	-0.14788616
H	-9.84854384	5.72333668	1.12191236
H	-10.51407034	7.31594717	0.67679009
H	-13.49789633	6.69601356	0.53250892
H	-12.78905722	8.04957376	1.45456312
H	-13.89129319	6.89566185	2.26089400
C	-3.37655915	4.22888668	-0.87856839
H	-1.74570740	2.78206688	-0.69597896
H	-3.30347260	5.21886538	-1.35771044
H	-3.16084328	4.39568055	0.19177662
H	-5.65583119	4.00852993	-0.76236519
H	-10.59661687	-0.80237072	3.96835270
H	-12.01785131	-0.53350066	2.92688955
H	-11.93821556	0.23456938	4.53615874
H	-10.01765483	1.63215534	3.79214579
Fe	-3.33359929	-2.39990457	-0.09715134
Cl	-2.67070106	-1.88963241	-2.12158130
Cl	-1.91773007	-3.56403763	1.08099857
Cl	-5.35149538	-3.27055081	-0.05804294

Structure **TS-V**

C	-1.21360403	-0.23530620	1.48776781
C	-0.90894029	-0.48307452	0.00481428
C	-0.46450934	0.90262695	-0.49807626
C	0.22590883	1.58952537	0.72324629
C	-0.19624248	1.46820483	3.23223595

C	-0.00542853	0.60899436	1.94141257
C	1.72114627	1.89261097	0.48973971
C	2.61587471	1.85732739	1.74638995
C	2.15004196	2.58770476	3.02470629
C	0.96182528	2.10099209	3.80571425
C	1.78101580	4.11236157	2.81730340
C	1.68623757	4.91083279	4.14417201
C	0.62711799	4.24290662	5.03806047
C	0.91113597	2.69145400	5.17638466
C	2.67594126	4.96091930	1.89860458
C	2.25808200	6.41478168	2.29572114
C	1.29590441	6.29158335	3.52161090
H	3.01164471	2.58436044	3.71138511
C	1.29222680	7.55181426	4.40883795
H	0.78167466	4.13201553	2.36510258
C	0.90260002	8.79105665	3.55633168
C	-0.44943293	8.67634794	2.82823605
C	-0.83109025	9.96933523	2.08866887
C	-2.01288367	9.79519169	1.10999372
O	-0.45688180	2.78869473	1.06235371
H	0.85214645	-0.06619765	2.04711325
O	0.20167767	-1.42655182	-0.03126761
O	1.60904718	-2.69443727	-1.19343005
C	0.58341805	-2.04613358	-1.19796092
C	-0.33332910	-1.91262803	-2.40877549
C	3.02879852	5.02086220	4.89625461
H	2.32052129	7.72099738	4.77703534
C	-3.28711202	9.30784286	1.82341835
C	-2.28144913	11.10950527	0.35535442
C	-1.34713725	1.08088778	4.17733269
H	-1.34798306	-1.16488814	2.05785381
H	-2.14288457	0.35297976	1.53177842
H	-1.76909057	-0.89231519	-0.54264140
H	-1.35141301	1.48547795	-0.78134980
H	0.19880368	0.83893193	-1.37164497
H	1.78536154	2.86901436	-0.01303949
H	2.12815654	1.14166728	-0.20558691
H	3.58802165	2.30131996	1.48164002
H	2.82630227	0.80969026	2.01372700
H	-0.37439313	4.37782930	4.60780460
H	0.62193682	4.65391695	6.05609372
H	0.15312626	2.22885828	5.81638426
H	1.89502679	2.57293844	5.65545507
H	2.48481010	4.75471764	0.83794975
H	3.74249668	4.77427899	2.10012487
H	1.75433298	6.92386825	1.46510649
H	3.14186647	7.01186764	2.57150459
H	0.27227316	6.16260078	3.13872393
C	0.35962456	7.41530869	5.62885785
H	0.88947134	9.67495383	4.21877208
H	1.68960344	8.97426033	2.80582312
H	-1.24122999	8.40799675	3.54583253
H	-0.40922764	7.86008095	2.08912982
H	0.04543265	10.32813008	1.51722057
H	-1.07488327	10.76392529	2.81906247
H	-1.71964704	9.02318550	0.37554873
H	0.14647437	-2.41267049	-3.25797049
H	-0.53378634	-0.86011075	-2.65866382
H	-1.30619943	-2.39084372	-2.20737464
H	3.42998669	4.04019931	5.19834208
H	3.79080250	5.51750921	4.27973323
H	2.89517777	5.61943240	5.81001581
H	-3.57601401	10.01381697	2.62302250
H	-3.14223264	8.31547234	2.27626075
H	-4.12683841	9.23656833	1.11285757
H	-2.57660158	11.90617741	1.06097643
H	-3.09593536	10.98558321	-0.37710661
H	-1.38037258	11.44971804	-0.18210248
H	-2.22103599	0.76400627	3.59845021
H	-1.66438878	1.94001486	4.78159676
H	-1.05786914	0.25431868	4.84673699
Fe	-1.66162168	4.14506786	0.72544363
Cl	-3.29368466	3.41858564	-0.58166927
Cl	-2.42020943	4.61294138	2.78931628
Cl	-0.54560826	5.85445132	-0.15458653
H	-0.53466541	2.45405767	2.64763479
H	-0.62688288	7.02840600	5.33033374
H	0.20943590	8.39567200	6.11009693
H	0.77823914	6.73683129	6.38804073

Structure **19 + Fe**

C	-0.52370568	-1.26470976	1.81228391
C	-0.76559758	-1.17318962	0.30129762
C	-0.88601432	0.34322290	0.05739996
C	0.12594482	0.97974292	1.03521928
C	0.42648201	0.55898229	3.45133493
C	0.48426250	-0.12778825	2.07284979
C	1.35411775	1.63834256	0.41112473
C	2.34628815	2.06320648	1.51564893
C	1.67745846	2.74977373	2.73745092
C	0.33465130	2.07782412	3.14052841
C	1.42543974	4.25275597	2.56325697
C	0.95311762	4.94997323	3.87648337
C	-0.41464233	4.34620853	4.25286175
C	-0.39138802	2.80438732	4.27823160
C	2.59210953	5.12109824	2.05835533
C	2.21419061	6.56214394	2.51587267
C	0.92699139	6.43409529	3.39233041
H	2.35738191	2.62055210	3.59249473
C	0.82098159	7.55855836	4.44300856
H	0.59663891	4.37730350	1.84034226
C	0.83647426	8.95102369	3.76038214
C	-0.30470803	9.18510153	2.75509032
C	-0.33898654	10.62697938	2.22602239
C	-1.37051761	10.86091524	1.10135872
O	-0.51766475	2.04976257	1.89023969
H	1.49579444	-0.49560894	1.85842666
O	0.43743255	-1.69113303	-0.33380855
O	1.56112923	-2.20834555	-2.18068682
C	0.48362761	-1.95618477	-1.68467665
C	-0.83190060	-1.95925763	-2.45388681
C	1.95993252	4.78384905	5.03437395

H	1.72170557	7.50549828	5.08197333
C	-2.80870244	10.57073786	1.56997132
C	-1.25964035	12.29896159	0.56335062
C	1.57346588	0.17247971	4.39546757
H	-0.15840744	-2.25425639	2.12053191
H	-1.47569747	-1.05781166	2.32854853
H	-1.64703449	-1.73539979	-0.03731794
H	-1.91176647	0.65145127	0.30208314
H	-0.68829988	0.63137659	-0.98099261
H	1.02787273	2.49613653	-0.19482615
H	1.82793776	0.91204869	-0.26757090
H	3.10727752	2.73786392	1.09951585
H	2.88203467	1.16778613	1.86445196
H	-1.16287950	4.69192654	3.53187530
H	-0.75836654	4.68622615	5.24057069
H	-1.41639754	2.40487169	4.34196040
H	0.12641417	2.47474576	5.19406185
H	2.72098863	5.04287415	0.96880991
H	3.53607166	4.79230288	2.52347737
H	2.03987945	7.23320673	1.66240809
H	3.02906011	7.00586766	3.11055896
H	0.05331073	6.51512829	2.72930542
C	-0.41599841	7.42462723	5.35508554
H	0.77989248	9.71872798	4.55367667
H	1.80182885	9.10027393	3.24832777
H	-1.26825552	8.94127501	3.22876143
H	-0.19700056	8.49555647	1.90011740
H	0.66533179	10.89638243	1.84971809
H	-0.55677328	11.32000918	3.06055532
H	-1.13095777	10.16368371	0.27673613
H	-0.61178223	-2.17254144	-3.50611236
H	-1.35617051	-0.99480142	-2.37364310
H	-1.50748314	-2.73451280	-2.05669653
H	2.07632736	3.73499093	5.34728202
H	2.95216947	5.17046604	4.75659731
H	1.61264437	5.35261747	5.90971364
H	-3.06312813	11.20614227	2.43705886
H	-2.93683412	9.51832427	1.86616125
H	-3.53248466	10.78642192	0.76696738
H	-1.48602107	13.02669447	1.36215188
H	-1.97068106	12.46999907	-0.26161244
H	-0.24198564	12.50726841	0.19311808
H	1.52567130	-0.90403293	4.62102033
H	1.51210265	0.72103808	5.34829486
H	2.55324806	0.38129350	3.93994043
Fe	-1.87177945	3.33472035	1.04987313
Cl	-3.70524828	2.28929581	1.70120717
Cl	-2.14429611	5.49118143	1.39870771
Cl	-1.53839508	3.28057633	-1.13150745
H	-0.52879804	0.28644460	3.92877916
H	-1.33368492	7.28176572	4.76375676
H	-0.54171813	8.33538628	5.96433947
H	-0.32014344	6.57345170	6.04376027

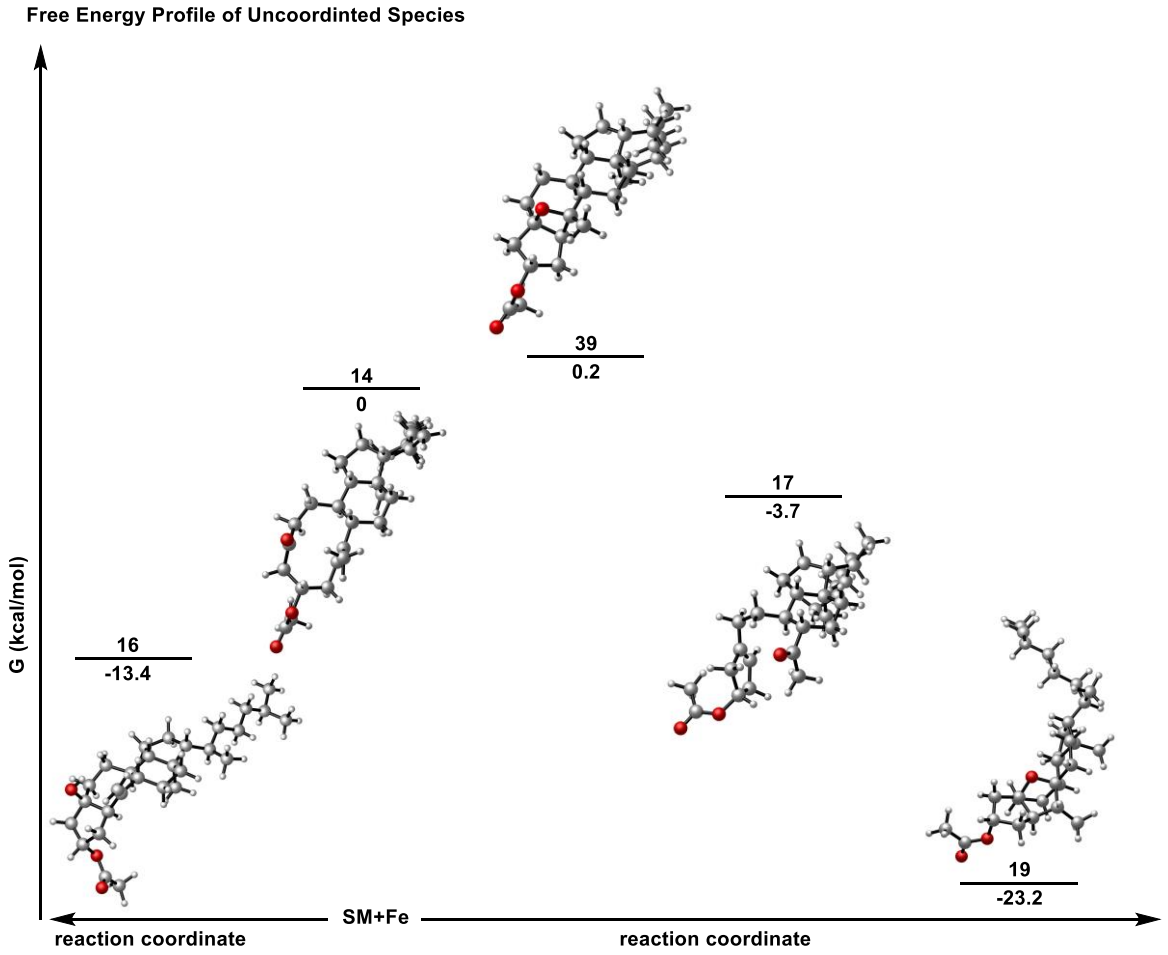


Figure A3-2: Relative energies of species uncoordinated from $FeCl_3$

XYZ coordinates for structures uncoordinated to $FeCl_3$

Structure **14**

C	-1.81147049	2.19611853	-1.44318721
C	-2.78237303	1.90840493	-2.61575721
C	-3.85231203	0.88372479	-2.17868169
C	-4.02191812	1.55349370	0.76451196
C	-3.74582340	2.69736801	0.10255946
C	-5.31550597	1.31886435	-2.28217788
C	-6.28757559	0.64488962	-1.28875445
C	-6.54084790	1.40246632	0.04124007
C	-5.44324198	1.14661435	1.12311312
C	-7.88312443	0.95869030	0.65791045
C	-8.25672524	1.70936807	1.96185756
C	-7.18544416	1.41322067	3.02213652
C	-5.78450658	1.79023591	2.50316851
C	-9.17849315	1.03449945	-0.18861303
C	-10.34049448	1.04448765	0.86349178
C	-9.64097728	1.07015872	2.26316361
O	-3.52506921	-0.25001415	-1.84733693
H	-6.60042165	2.48156987	-0.18310172
H	-5.44258544	0.05008572	1.27375774
H	-7.74967238	-0.10308121	0.94512570
C	-10.41096214	1.63372694	3.50489403
C	-11.78364508	2.28452389	3.20660484
C	-11.72535436	3.70587193	2.62403212
C	-13.12434136	4.26909703	2.32988272
C	-13.12916072	5.70609084	1.76433591
C	-2.95508573	0.60353232	1.25088677
C	-8.38713494	3.23162350	1.73393961
O	-0.46767776	2.56104729	-1.88011403
O	1.06247597	3.79186693	-2.90121182
C	-0.09789650	3.69422136	-2.55572829
C	-1.10304537	4.81611571	-2.81053455
C	-12.40784775	5.78831740	0.40494449
C	-14.57498248	6.21960444	1.63284733
H	-2.19191887	1.44723749	-3.42214090
H	-3.26334974	2.81963402	-2.99911351
H	-5.61270213	1.05295470	-3.31624290
H	-5.38464863	2.41564751	-2.22146916
H	-5.92580545	-0.37470673	-1.07628410
H	-7.25408261	0.53815305	-1.80191184
H	-7.20862978	0.33183474	3.24872847
H	-7.40124565	1.95159589	3.96145146

H	-5.69504956	2.88353371	2.40342362
H	-5.01752154	1.48414967	3.23426661
H	-9.26458961	0.19354646	-0.89164111
H	-9.18957489	1.95992824	-0.78753465
H	-10.98653831	0.15916058	0.76625896
H	-10.98275428	1.92078645	0.70793796
H	-9.41045580	0.01291545	2.48893371
C	-10.58758991	0.52015539	4.56003715
H	-12.35729082	1.63016863	2.52734834
H	-12.36083400	2.33007182	4.14734044
H	-11.12501754	3.71688484	1.70610229
H	-11.20423921	4.36999030	3.33782618
H	-13.72309968	4.24170614	3.25820652
H	-13.63814122	3.60598849	1.60795030
H	-12.59267305	6.35558135	2.48104433
H	-1.95307782	1.05661478	1.26489727
H	-2.92476568	-0.28206828	0.59268534
H	-3.19404385	0.24990460	2.26811251
H	-7.43162857	3.68496058	1.43575068
H	-9.12245338	3.45000297	0.94716496
H	-8.71764042	3.73060978	2.65739051
H	-0.78263167	5.35237704	-3.71289126
H	-1.06244070	5.52017716	-1.96368516
H	-2.13894321	4.47962716	-2.92115099
H	-12.88369939	5.10260990	-0.31793037
H	-11.34417019	5.51407105	0.48512022
H	-12.46335843	6.80891401	-0.00755440
H	-15.14032379	5.58923546	0.92444496
H	-14.60144507	7.25694508	1.25993702
H	-15.09660320	6.18821193	2.60368701
C	-2.37027285	3.14140451	-0.35077522
H	-1.61573444	1.22145223	-0.98028837
H	-2.43039024	4.16957844	-0.73032039
H	-1.64450897	3.14022362	0.47967321
H	-4.58312712	3.32336590	-0.21725098
H	-9.61706089	0.06803227	4.82197839
H	-11.24007939	-0.28094496	4.17099787
H	-11.04766886	0.91600900	5.48051877
H	-9.77666409	2.41114399	3.96753706

Structure **16**

O	2.90271702	6.80028416	20.81940883
O	6.28030758	9.67963305	20.97086292
H	7.10319186	9.50133297	20.47330314
O	3.00756175	4.90290554	22.09462600
C	5.96735711	8.74447586	17.08406814
H	4.97907019	8.25915204	17.14910410
C	6.19585636	7.60606500	14.76976597
C	2.52130581	5.54080451	21.17704703
C	6.28449736	8.93278770	15.59129788
H	7.34095380	9.26047523	15.52108896
C	5.74219544	9.52205159	13.29410455
H	6.33918944	10.28530269	12.77459707
H	4.80535216	9.41060660	12.72481642
C	7.02806900	6.42581315	16.88558065
H	7.82745845	5.78186807	17.28502808
H	6.07539805	5.90475465	17.08255890
C	5.87197679	10.06648001	17.88866145
H	6.86245341	10.33747934	18.29676712
H	5.57918507	10.88788560	17.21710359
C	7.03838855	7.77171092	17.65735085
H	8.01993171	8.24124210	17.45854827
C	5.45394825	9.93285625	14.76956205
H	5.73212885	10.97693010	14.97401337
H	4.38335848	9.82741235	15.00976830
C	6.18257677	7.26387833	12.11089137
H	5.08513593	7.13313387	12.07441181
C	7.22489446	6.61961380	15.36398621
H	7.17958765	5.63855239	14.87008629
H	8.23710070	7.02553510	15.18509981
C	6.60777478	7.98859262	10.80854615
H	7.71272329	8.01917302	10.76494872
H	6.27031784	9.03723897	10.84382037
C	6.50690780	8.15102931	13.33776830
H	7.59383857	8.35748131	13.31401467
C	6.48297474	8.14572722	8.26224454
H	7.58594276	8.12851404	8.17685967
H	6.19763491	9.20582729	8.39145604
C	5.87561159	7.62687861	6.94140636
H	4.77450359	7.65331103	7.04340996
C	6.94848993	7.53043219	19.15919750
C	6.05974146	7.36071045	9.51533319
H	4.95582796	7.32650912	9.57021509
H	6.40103202	6.31811184	9.42207803
C	5.20864035	9.09104495	20.21482816
C	4.77848633	6.98821364	14.80124141
H	4.75071810	6.07803172	14.18396770
H	4.02617984	7.68583835	14.40419329
H	4.47308257	6.70776251	15.81854451
C	4.83225719	9.99540176	19.02649990
H	4.65071693	11.00425231	19.43233803
H	3.87838523	9.63560657	18.60109898
C	5.58444026	7.61026625	19.80103414
H	4.82284738	7.28303223	19.07508838
C	4.00043340	7.40074085	21.59507502
H	3.80523510	7.20469060	22.65658999
C	6.29593567	6.17461854	6.64371154
H	5.89097558	5.83995037	5.67454875
H	5.94071015	5.47892704	7.41958410
H	7.39647376	6.09955540	6.59634168
C	6.83648397	5.87056860	12.18867168
H	6.71091111	5.31945541	11.24457445
H	6.39520011	5.25622751	12.98543236
H	7.91739279	5.96280294	12.38739278
C	5.34680490	6.84141394	21.11354051
H	6.11019891	7.12116432	21.85446422
H	5.34008540	5.74968424	21.00541924
C	1.40892827	5.05671981	20.25893305
H	1.79512170	4.94978973	19.23259578
H	0.59012847	5.79146702	20.22678354
H	1.03725496	4.08878688	20.61635017
C	4.03316150	8.89905812	21.21956621

H	4.21350588	9.52134218	22.10708348
H	3.07148501	9.20116969	20.78076019
C	6.27469972	8.54825897	5.77377706
H	7.37012182	8.53987229	5.63776577
H	5.96479430	9.58916478	5.96431558
H	5.81369347	8.21596461	4.82907757
C	8.07424602	7.32010865	19.87222239
H	8.05797617	7.10331958	20.94114534
H	9.05246843	7.32541774	19.38301531

Structure **39**

C	-1.72907568	2.14439021	-1.48791391
C	-2.78793345	1.68085044	-2.51004586
C	-4.01832151	1.44035537	-1.63498345
C	-4.07915821	1.08159658	0.42998057
C	-3.90136924	2.38631895	-0.39084125
C	-5.36080533	1.36220473	-2.36675921
C	-6.44802209	0.65521581	-1.53205485
C	-6.65300353	1.25426596	-0.12526680
C	-5.53998708	0.85757743	0.90986676
C	-7.99691115	0.83028707	0.49050111
C	-8.31774975	1.56516769	1.81770669
C	-7.22171098	1.22504913	2.83905081
C	-5.81021933	1.52699552	2.28336459
C	-9.30330998	0.96613878	-0.32877796
C	-10.44165605	0.99240917	0.75033270
C	-9.71225142	0.95689597	2.13441796
O	-3.82471629	0.26396049	-0.77372098
H	-6.66647663	2.35263715	-0.23521100
H	-5.62755634	-0.23726393	1.04550060
H	-7.89382973	-0.24155026	0.74914581
C	-10.44572964	1.50440019	3.40386307
C	-11.76629773	2.27256267	3.15145754
C	-11.61734710	3.70422802	2.61241918
C	-12.97854619	4.38805540	2.41370816
C	-12.89754361	5.83883976	1.89007078
C	-3.03835139	0.74732159	1.49672201
C	-8.41126999	3.09472376	1.63014282
O	-0.49241121	2.66539407	-2.03440433
O	0.74511942	3.98343336	-3.31191327
C	-0.33827560	3.79473347	-2.79627492
C	-1.46830629	4.81646414	-2.91404933
C	-12.24493722	5.90850923	0.49577680
C	-14.30058372	6.47195149	1.85396877
H	-2.48163243	0.76914503	-3.04299901
H	-3.01520781	2.45862338	-3.25484430
H	-5.22820269	0.82301826	-3.32106850
H	-5.67826154	2.39041666	-2.61764755
H	-6.18626526	-0.40963509	-1.43590327
H	-7.39559909	0.71590304	-2.08963709
H	-7.28549430	0.14646222	3.07115319
H	-7.37731861	1.77303632	3.78516999
H	-5.66646313	2.61687820	2.18421938
H	-5.06949081	1.18023847	3.01854964
H	-9.42632706	0.14051965	-1.04399617
H	-9.29866611	1.90187503	-0.91122502
H	-11.12471209	0.13629530	0.64424334
H	-11.05046262	1.89834166	0.63493772
H	-9.50567329	-0.11183438	2.32696129
C	-10.71335757	0.34747341	4.39165124
H	-12.40489912	1.68509551	2.46869512
H	-12.31695247	2.33253721	4.10750789
H	-11.06964659	3.70122578	1.66238477
H	-11.00480863	4.29566262	3.31771796
H	-13.52870115	4.37819619	3.37229561
H	-13.58109552	3.79180774	1.70233157
H	-12.27233539	6.41956910	2.59388904
H	-2.03702291	0.71090211	1.04567867
H	-3.25385479	-0.23722025	1.94170760
H	-3.02951587	1.49912841	2.30054353
H	-7.43997709	3.53434844	1.36438237
H	-9.12611132	3.35659539	0.83731426
H	-8.74735717	3.57285395	2.56211662
H	-1.28564821	5.41492842	-3.81561524
H	-1.42547207	5.48779224	-2.04088204
H	-2.47298967	4.37983230	-2.95022590
H	-12.80515373	5.27917116	-0.21790495
H	-11.20041748	5.55857062	0.51047897
H	-12.24949208	6.94211992	0.11296920
H	-14.95461279	5.91459079	1.16095573
H	-14.25756704	7.51890492	1.51078035
H	-14.77045211	6.45391480	2.85114336
C	-2.49263181	3.01706584	-0.45593923
H	-1.38099952	1.24357089	-0.96922835
H	-2.58395883	4.05482735	-0.79885887
H	-1.97870414	3.02977086	0.51651476
H	-4.68669940	3.13921754	-0.24266272
H	-9.77844754	-0.17955630	4.64363328
H	-11.40616469	-0.38761410	3.94632827
H	-11.16633485	0.72015432	5.32532724
H	-9.75536502	2.20285126	3.91011341

Structure **17**

C	-2.55841385	3.44327830	-1.33719032
C	-3.24974636	2.16161562	-1.89782273
C	-4.73360828	2.46385691	-1.80739750
C	-3.93942419	0.32908672	1.29066570
C	-4.95785641	3.71325206	-1.35171075
C	-5.77411500	1.43150713	-2.14756429
C	-5.79154315	0.27626843	-1.10955184
C	-6.22851237	0.75403783	0.30028274
C	-5.43404966	0.02034128	1.44288686
C	-7.72619450	0.52566489	0.54226385
C	-8.22055276	1.01576016	1.92584808
C	-7.48733903	0.20816211	3.01035306
C	-5.95538041	0.35265756	2.86916234
C	-8.75060196	1.12231945	-0.44960371
C	-10.09945811	1.11991437	0.34548516
C	-9.73654622	0.68119639	1.80269257
O	-3.16342158	-0.48514397	0.80120549
H	-6.01617662	1.83260068	0.37844880

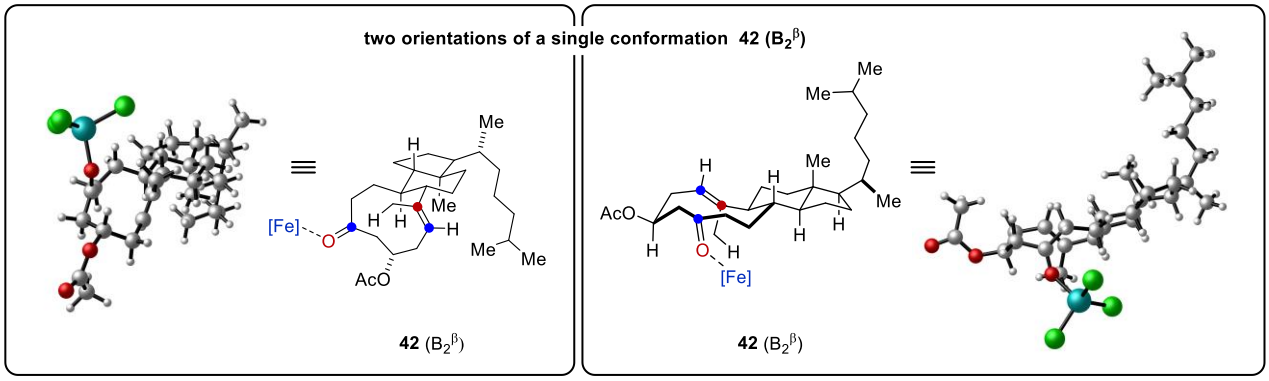
H	-5.54542566	-1.06232965	1.26680004
H	-7.87732453	-0.57186644	0.53510313
C	-10.66611779	1.12762160	2.98470408
C	-11.72055882	2.20966095	2.64363847
C	-11.17824279	3.63746937	2.47664733
C	-12.26694112	4.63636912	2.05531457
C	-11.78159315	6.09830128	1.95364730
C	-3.46110844	1.72316440	1.69809712
C	-7.97997274	2.52897635	2.11366340
O	-1.44195464	3.92525818	-2.12660205
O	-0.49083330	4.62523780	-4.00140760
C	-1.52592195	4.34612309	-3.43036756
C	-2.88362294	4.51126937	-4.11374373
C	-10.65006628	6.25619777	0.91910324
C	-12.95954188	7.02588844	1.60176627
H	-2.96766830	1.27057281	-1.31489967
H	-2.93840294	1.96324378	-2.93812607
H	-5.56404405	1.00546923	-3.14479373
H	-6.76656500	1.90518830	-2.19054469
H	-4.79006196	-0.17671813	-1.07365993
H	-6.47728729	-0.51376337	-1.45924528
H	-7.76990337	-0.85478375	2.89969621
H	-7.79876280	0.52569499	4.02092297
H	-5.67008811	1.38126574	3.13714010
H	-5.44824521	-0.30806395	3.59166412
H	-8.80408551	0.54780195	-1.38601404
H	-8.46895063	2.15267534	-0.71876203
H	-10.83078947	0.42706390	-0.09735374
H	-10.55741535	2.11667445	0.32347164
H	-9.75978384	-0.42339842	1.79450538
C	-11.37856038	-0.10947496	3.57410765
H	-12.26271351	1.91048958	1.72981343
H	-12.47519566	2.22754082	3.45097273
H	-10.37182679	3.65288737	1.73251190
H	-10.72260046	3.96682887	3.42843885
H	-13.10560435	4.58678117	2.77348483
H	-12.67630553	4.33023384	1.07379085
H	-11.38749813	6.39453324	2.94373728
H	-2.40719936	1.84007332	1.41564794
H	-3.56398591	1.86936151	2.78582369
H	-4.07355921	2.49475852	1.20428271
H	-6.91044218	2.76862979	2.19296495
H	-8.37609846	3.10330297	1.26487781
H	-8.47755103	2.88704105	3.02541439
H	-2.77402211	4.17784700	-5.15478267
H	-3.11544836	5.58866621	-4.13792580
H	-3.72259685	3.99257028	-3.63801731
H	-10.98366224	5.88843015	-0.06739648
H	-9.74993857	5.69013024	1.20724279
H	-10.36402193	7.31498589	0.80815087
H	-13.37253444	6.75716655	0.61414260
H	-12.63764394	8.07942239	1.56065747
H	-13.77080938	6.93930779	2.34359440
C	-3.69196684	4.48821452	-1.07148287
H	-2.06488784	3.20002979	-0.39033703
H	-3.58591543	5.37074807	-1.72474258
H	-3.64514438	4.86552878	-0.03520826
H	-5.95360295	4.14276755	-1.21518740
H	-10.64986245	-0.88345295	3.86607205
H	-12.05834094	-0.55077761	2.82483410
H	-11.97636574	0.15828483	4.46050125
H	-10.02155755	1.54180945	3.78153810

Structure **19**

C	-0.53139295	-1.17993665	1.78254982
C	-0.85913651	-0.93697683	0.30279740
C	-0.83595288	0.60119762	0.17061222
C	0.23542035	1.07380715	1.18042015
C	0.63187752	0.43405157	3.51908164
C	0.58590675	-0.15998183	2.08618269
C	1.48167603	1.71214712	0.55186096
C	2.51507987	2.01862722	1.65786085
C	1.86356371	2.67284418	2.90225498
C	0.50932682	1.97384982	3.26935763
C	1.57990112	4.16652549	2.68539242
C	0.98342182	4.88322232	3.92800106
C	-0.36917263	4.20994116	4.23846087
C	-0.21471864	2.68325044	4.41924404
C	2.74116101	5.07501841	2.23684574
C	2.25371740	6.51164453	2.60284101
C	0.91034196	6.34699407	3.38713635
H	2.55332834	2.55856906	3.75396432
C	0.67133627	7.49479782	4.39061854
H	0.79937292	4.22400380	1.90657099
C	0.69971358	8.87625531	3.68906181
C	-0.40502007	9.09921979	2.64218993
C	-0.39361736	10.53039357	2.08221410
C	-1.41290544	10.78493331	0.95119047
O	-0.35542820	2.02261156	2.10203238
H	1.55443686	-0.58853079	1.79396805
O	0.24413882	-1.52306085	-0.45412020
O	1.16441032	-2.07543217	-2.40157125
C	0.16827898	-1.71228165	-1.80985329
C	-1.18276578	-1.49414499	-2.48702129
C	1.91712798	4.82164818	5.15598934
H	1.51709660	7.49106418	5.10251881
C	-2.86316363	10.57464472	1.42537266
C	-1.23813290	12.20544726	0.38364012
C	1.82226615	-0.00856747	4.37942816
H	-0.25030312	-2.22515265	1.97694663
H	-1.43033248	-0.93978116	2.37441910
H	-1.80794936	-1.39606060	-0.01174971
H	-1.81372269	1.01008687	0.46830760
H	-0.62281964	0.92841471	-0.85756082
H	1.17019066	2.63456183	0.03434445
H	1.90973168	1.02643886	-0.19724135
H	3.31443837	2.67083858	1.27469999
H	2.99751320	1.07498358	1.95311254
H	-1.05744150	4.39866227	3.39775720
H	-0.83341229	4.62609422	5.14428065
H	-1.20818156	2.21741388	4.52565602
H	0.34118643	2.46490258	5.34626607

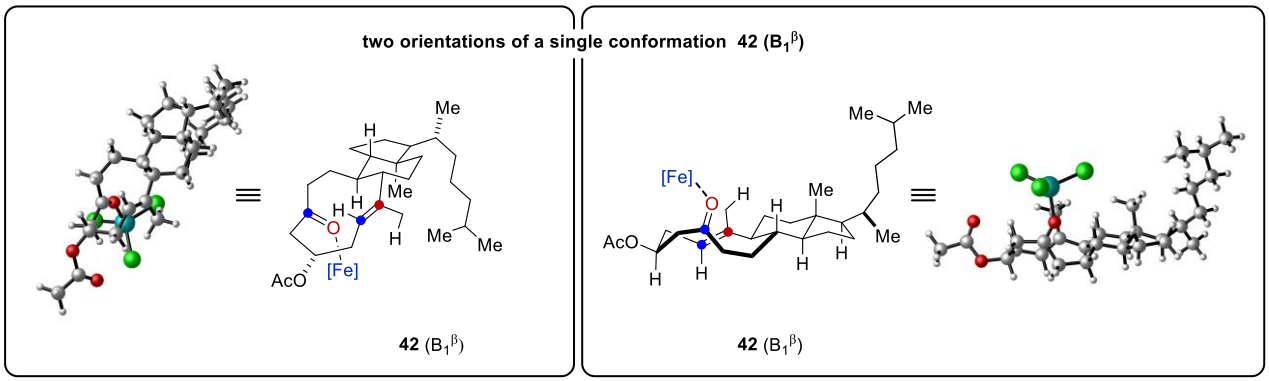
H	2.96080206	4.96741251	1.16429795
H	3.66367726	4.82069248	2.78475413
H	2.11618574	7.13970639	1.70968735
H	2.99343358	7.02592567	3.23769964
H	0.08111673	6.35601081	2.65678076
C	-0.62736066	7.33424420	5.20773200
H	0.60838915	9.65351037	4.46987500
H	1.68204701	9.02609262	3.21089597
H	-1.38643810	8.88596503	3.09451345
H	-0.28202988	8.38611187	1.80775793
H	0.62028535	10.75878039	1.70543763
H	-0.58946437	11.24458481	2.90414560
H	-1.20587673	10.06059711	0.14103429
H	-1.04876242	-1.62260340	-3.56727287
H	-1.58657885	-0.49359955	-2.27424423
H	-1.91833023	-2.22933031	-2.12038298
H	2.12163268	3.78791905	5.46973578
H	2.88145540	5.30694688	4.94234610
H	1.45628094	5.34797961	6.00649315
H	-3.09199468	11.25615036	2.26377947
H	-3.03620825	9.54271064	1.76822033
H	-3.57654329	10.78688225	0.61197692
H	-1.43742441	12.95688202	1.16735405
H	-1.93707252	12.39132777	-0.44863343
H	-0.21065098	12.36286683	0.01604438
H	1.79004956	-1.09592464	4.55482812
H	1.80530208	0.49237800	5.36186283
H	2.78170032	0.22729444	3.89475886
H	-0.29440598	0.13859199	4.04130579
H	-1.48394271	7.10094606	4.55532710
H	-0.85673351	8.26716237	5.74998199
H	-0.53946824	6.52714602	5.94885648

Possible Reactive conformations:



The above computational results suggest that conformation **14** (B_2^{β}) is the one leading to product formation (**14**, **16** and **19**) under our optimized reaction conditions for $FeCl_3$-catalyzed transannular carbonyl-olefin metathesis.

In comparison, conformation **14** (B_1^{β}) was found to lead to the preferential formation of diastereomeric product *epi*-**16** that is not observed experimentally under our optimal reaction conditions, suggesting it is not a reactive conformation for the transannular reactions discussed in this report.



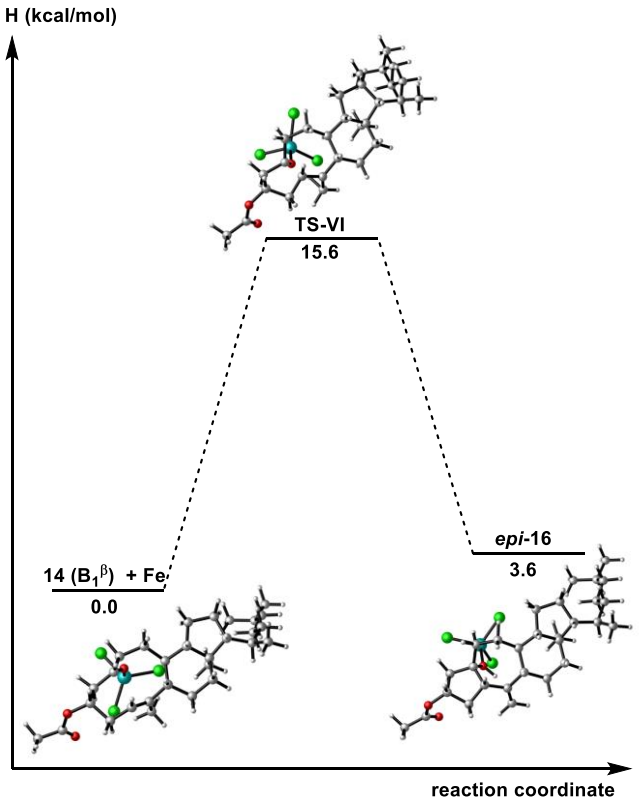


Figure A3-3: Computed Reaction pathway of 14 (B1β) + Fe

Structure **14 (B_1^{β}) + Fe**

C	-1.96198776	2.12734063	-1.82223758
C	-3.10356447	2.88960728	-2.53785776
C	-4.51656819	2.53965206	-2.12985490
C	-4.21513008	2.51826727	0.73498957
C	-3.08340397	1.87463404	0.36044720
C	-4.97513714	1.11314283	-1.96349945
C	-6.28612418	0.91379280	-1.15584829
C	-6.57293353	1.73306012	0.13399798
C	-5.42404741	1.71510030	1.20503180
C	-7.84529954	1.13697947	0.76314614
C	-8.30462990	1.84850991	2.05798554
C	-7.20822203	1.64738175	3.11604797
C	-5.86444701	2.21718488	2.61730513
C	-9.12815523	1.06582125	-0.09841060
C	-10.29460398	0.95645843	0.94012714
C	-9.61969777	1.06919141	2.34690623
O	-5.39672533	3.43368976	-2.10624383
H	-6.78253381	2.77114374	-0.15853982
H	-5.12309361	0.65616278	1.31054123
H	-7.59002069	0.09955783	1.05985340
C	-10.46800184	1.55653562	3.57054284
C	-11.89145288	2.06514350	3.23802353
C	-11.95246228	3.47887200	2.63719193
C	-13.37887374	3.88459887	2.23740876
C	-13.49978592	5.30940850	1.65571865
C	-4.34989182	4.02468914	0.73455659
C	-8.57662068	3.34982079	1.81798111
O	-0.70377155	2.31010836	-2.53317225
O	-0.58408898	4.55798102	-2.06679870
C	-0.12031907	3.55429307	-2.57217994
C	1.18501014	3.47420549	-3.34355125
C	-12.68609015	5.47316324	0.35699406
C	-14.97945110	5.65625219	1.40667595
H	-3.04387235	2.64040842	-3.61426175
H	-2.96028215	3.97283124	-2.44123502
H	-4.15246256	0.50953514	-1.56710273
H	-5.15103784	0.74685702	-2.99533934
H	-6.33058188	-0.15944562	-0.90280743
H	-7.12794716	1.10823831	-1.83479826
H	-7.10993605	0.56470151	3.31454623
H	-7.47903696	2.13223620	4.06962022
H	-5.94179600	3.31269304	2.60325608
H	-5.05631007	1.97287971	3.32645471
H	-9.10899833	0.21775646	-0.79849344
H	-9.22654230	1.98413398	-0.69965369
H	-10.83872588	0.00486254	0.84479650
H	-11.02605270	1.75564391	0.76953279
H	-9.28182378	0.04471968	2.58899340
C	-10.54928331	0.43150486	4.62526809
H	-12.38669081	1.35065822	2.55732097
H	-12.48953665	2.06541812	4.16690363
H	-11.29605791	3.54763441	1.76058929
H	-11.55343987	4.20189155	3.37202552
H	-14.03991831	3.79849618	3.11928958
H	-13.76199271	3.16420050	1.48966336
H	-13.09885709	6.01655879	2.40579353
H	-4.22316988	4.41557476	1.75769109
H	-5.35230932	4.33428904	0.40282281
H	-3.61254194	4.52452509	0.09694413
H	-7.66749528	3.89448053	1.53241120
H	-9.30038900	3.49955058	1.00573199
H	-8.98220656	3.82044373	2.72552158
H	1.63804490	4.47145942	-3.38818418
H	0.99978885	3.09639801	-4.36079356
H	1.87125749	2.76819637	-2.85062418
H	-13.02321487	4.74128119	-0.39815560
H	-11.60845836	5.32054380	0.52226460
H	-12.82212277	6.48206849	-0.06520380
H	-15.41152953	4.96914140	0.65832820
H	-15.08921561	6.68477419	1.02551161
H	-15.57043818	5.56373536	2.33309560
C	-1.87080876	2.45902244	-0.31076515
H	-2.12361212	1.04610553	-1.93550403
H	-1.78458974	3.54158104	-0.17654799
H	-0.94854014	1.99207414	0.07279560
H	-3.08507603	0.78016998	0.43079228
H	-9.54166004	0.08412361	4.90708844
H	-11.10490974	-0.43349430	4.22324533
H	-11.06629929	0.77643404	5.53578213
H	-9.92964508	2.39821340	4.04265853

Fe	-5.70672007	5.36718901	-2.42423813
Cl	-3.93313875	6.54432811	-1.91385093
Cl	-6.13919090	5.38368104	-4.57241319
Cl	-7.43941912	5.76212949	-1.13156900

Structure **TS-VI**

C	-1.80091994	1.96574531	-2.03856917
C	-2.90457670	2.86608297	-2.61762826
C	-4.13113492	2.70731031	-1.67581063
C	-4.13800929	2.54847314	0.83758699
C	-3.43687989	1.95453548	-0.30271494
C	-5.21427565	1.75177672	-2.18598916
C	-6.14603668	1.11120251	-1.12299960
C	-6.53564193	1.91300038	0.14794572
C	-5.41867830	1.89107263	1.29217076
C	-7.79323073	1.26272750	0.76304907
C	-8.31895194	1.95524881	2.04462774
C	-7.24108388	1.82105845	3.13093154
C	-5.91773204	2.44826577	2.65281491
C	-9.05603929	1.12269688	-0.12534607
C	-10.23622317	0.96790892	0.89123152
C	-9.59442091	1.10637338	2.30908941
O	-4.65677433	3.95931784	-1.35711781
H	-6.74707402	2.95536103	-0.12106354
H	-5.18822008	0.81590371	1.41840382
H	-7.49060571	0.24037368	1.06726773
C	-10.48842332	1.54480750	3.51902870
C	-11.92804185	1.98775593	3.16114978
C	-12.04287644	3.40205081	2.56989707
C	-13.48064184	3.75575599	2.16152394
C	-13.64732252	5.18043777	1.59038799
C	-3.84327490	3.89574575	1.13488960
C	-8.67288560	3.43694814	1.78755971
O	-0.47961923	2.17590625	-2.59821269
O	-0.28292686	4.32945664	-1.81135293
C	0.15177237	3.38286694	-2.44279719
C	1.47631546	3.35731912	-3.18492224
C	-12.82936023	5.38384472	0.29991425
C	-15.13621379	5.47770429	1.33281256
H	-3.16597936	2.60463629	-3.65307324
H	-2.57690156	3.91080008	-2.58306260
H	-4.71139701	0.93817942	-2.73507963
H	-5.81652317	2.30751981	-2.91862526
H	-5.72322067	0.14726574	-0.78782761
H	-7.07278088	0.86239325	-1.65516943
H	-7.09314977	0.74808321	3.35057102
H	-7.55472442	2.30842770	4.06913603
H	-6.07164667	3.53200021	2.57040687
H	-5.12378898	2.29658746	3.40261496
H	-8.98578561	0.26075536	-0.80426580
H	-9.18174909	2.02095405	-0.74725256
H	-10.74109753	-0.00388528	0.78537668
H	-10.99402009	1.73895850	0.70645775
H	-9.20821596	0.09948242	2.55374547
C	-10.53715246	0.40891768	4.56397875
H	-12.37511461	1.25615294	2.46543560
H	-12.54309848	1.95199919	4.07810215
H	-11.38327935	3.50381057	1.69928327
H	-11.67913899	4.13494000	3.31329768
H	-14.14520588	3.63830303	3.03706438
H	-13.83048409	3.02813363	1.40459015
H	-13.27736719	5.89434850	2.35000699
H	-4.36823773	4.40618181	1.94116325
H	-4.37696317	4.18724607	0.01740769
H	-2.82791739	4.26106077	0.95240098
H	-7.79614124	4.04529449	1.53115493
H	-9.37804316	3.53440274	0.95176326
H	-9.14001598	3.87880164	2.67958002
H	2.00540962	4.30143875	-3.01008706
H	1.29622641	3.22351153	-4.26304667
H	2.08841736	2.50764963	-2.84591212
H	-13.13439393	4.64800631	-0.46476643
H	-11.74831002	5.26719268	0.47219757
H	-12.99693217	6.39134216	-0.11400368
H	-15.53830366	4.78345324	0.57445295
H	-15.27894949	6.50553572	0.96085802
H	-15.73082393	5.35578767	2.25353094
C	-1.92789503	2.14059132	-0.51311710
H	-2.00016400	0.91445936	-2.29638040
H	-1.59135836	3.14598494	-0.24321026
H	-1.34249645	1.39712610	0.04749091
H	-3.69074992	0.89305559	-0.40630966
H	-9.52037294	0.10572158	4.86379985
H	-11.04411984	-0.47744407	4.14467266
H	-11.08735946	0.72159424	5.46653612
H	-10.00057093	2.40858058	4.00606797
Fe	-6.07661920	5.12167016	-1.92562288
Cl	-5.28866660	6.29401688	-3.60779770
Cl	-7.92183313	4.04790026	-2.50913456
Cl	-6.38749368	6.25860887	-0.04797680

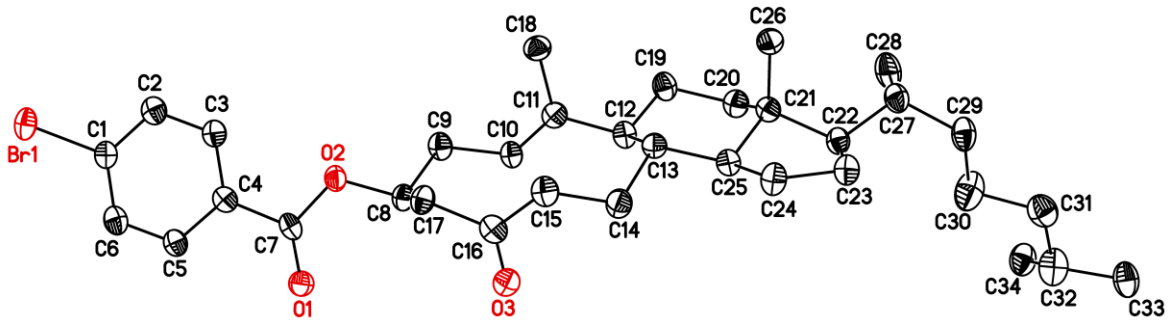
Structure ***epi*-16**

C	-1.82224847	1.95031416	-2.04819790
C	-2.99981645	2.73049616	-2.67084491
C	-4.14528502	2.56526235	-1.64078038
C	-4.13130194	2.55008505	0.92187282
C	-3.46411650	1.99657284	-0.32862477
C	-5.30237791	1.68491658	-2.11726380
C	-6.14975388	1.01215334	-1.01590848
C	-6.55230645	1.84767356	0.22879648
C	-5.43506004	1.87344860	1.35183285
C	-7.81847574	1.21666028	0.84342827
C	-8.34767859	1.94207024	2.10436678
C	-7.27359487	1.82798193	3.19491546
C	-5.94337836	2.43419750	2.70807165
C	-9.07734621	1.05995969	-0.04768721
C	-10.26900228	0.95386126	0.96279573
C	-9.63287538	1.11266172	2.38055111
O	-4.68969117	3.91906592	-1.34476528
H	-6.78015619	2.87717148	-0.08426340
H	-5.18393734	0.80521508	1.51148303
H	-7.52468225	0.20073910	1.17648588

C	-10.52857146	1.58323104	3.57643924
C	-11.95808301	2.04674938	3.20410836
C	-12.04820788	3.45574368	2.59663013
C	-13.48445915	3.84104934	2.21164394
C	-13.62971329	5.27097845	1.64791098
C	-3.61490817	3.64176968	1.53353013
C	-8.68809371	3.42008446	1.81155532
O	-0.52854730	2.21589145	-2.64818972
O	-0.48835316	4.43547788	-2.04468149
C	0.01194480	3.47298668	-2.59914637
C	1.32985495	3.48501994	-3.35432039
C	-12.82395993	5.46339249	0.34823414
C	-15.11522778	5.60019611	1.41070406
H	-3.27771927	2.36966880	-3.66941456
H	-2.72941818	3.78915025	-2.74404726
H	-4.87063616	0.89221713	-2.75098393
H	-5.94687660	2.28530066	-2.77768765
H	-5.63812925	0.10065921	-0.65916661
H	-7.06371275	0.66341328	-1.51501916
H	-7.13261956	0.75899907	3.43714834
H	-7.58788043	2.33574470	4.12260481
H	-6.07385209	3.52338134	2.62025375
H	-5.15606104	2.27647684	3.46284654
H	-9.01544744	0.17494211	-0.69748311
H	-9.18921114	1.93807384	-0.70167937
H	-10.79586575	-0.00808617	0.87536965
H	-11.00826034	1.73786399	0.75646572
H	-9.25721749	0.10731405	2.64671858
C	-10.60599330	0.46242177	4.63611238
H	-12.41480667	1.31464387	2.51536746
H	-12.57800389	2.03320471	4.11852854
H	-11.40322755	3.53047056	1.71214534
H	-11.65272291	4.18808950	3.32437811
H	-14.13696400	3.73586184	3.09773004
H	-13.86236424	3.12319566	1.45901138
H	-13.23551662	5.97378626	2.40576845
H	-4.07731663	4.09651900	2.40764896
H	-4.57328575	4.11769380	-0.37896609
H	-2.68149825	4.09598689	1.19999724
H	-7.79865618	4.00302304	1.53777593
H	-9.39436404	3.50558001	0.97544624
H	-9.14332789	3.89194545	2.69447228
H	1.80817741	4.46337969	-3.22797647
H	1.14491243	3.29732545	-4.42379476
H	1.99052347	2.68430717	-2.98888443
H	-13.15565885	4.73935283	-0.41657686
H	-11.74393890	5.31968410	0.50649112
H	-12.97337748	6.47705087	-0.05774292
H	-15.54132318	4.91819603	0.65437534
H	-15.24163355	6.63264596	1.04557746
H	-15.70027345	5.48598532	2.33844093
C	-1.95385574	2.22341671	-0.53886493
H	-1.94717493	0.87280940	-2.23356759
H	-1.65974710	3.26071448	-0.34750429
H	-1.34032886	1.55286576	0.07891456
H	-3.64084717	0.90997713	-0.35579220
H	-9.59701823	0.14575010	4.94771090
H	-11.12502300	-0.42035444	4.22400852
H	-11.15781612	0.79657678	5.52993707
H	-10.02826353	2.44446866	4.05591284
Fe	-5.91063303	5.07650014	-2.43284598
Cl	-5.58136975	6.97226068	-1.39337100
Cl	-5.14993209	4.90292650	-4.47488266
Cl	-7.97111781	4.34510876	-2.22894888

5. X-Ray Crystallographic Data

Structure Determination of (3*R*,3*aR*,5*aS*,9*S*,13*aR*,13*bS*,*E*)-3a,6-dimethyl-3-(6-methylheptan-2-yl)-11-oxo-2,3,3*a*,4,5,5*a*,8,9,10,11,12,13,13*a*,13*b*-tetradecahydro-1H-cyclodeca[e]inden-9-yl 4-bromobenzoate (SI-2)



(CCDC 1861046)

Colorless needles of **SI-2** were grown from a diethyl ether solution of the compound at 23 deg. C. A crystal of dimensions 0.19 x 0.08 x 0.07 mm was mounted on a Rigaku AFC10K Saturn 944+ CCD-based X-ray diffractometer equipped with a low temperature device and Micromax-007HF Cu-target micro-focus rotating anode (l = 1.54187 A) operated at 1.2 kW power (40 kV, 30 mA). The X-ray intensities were measured at 85(1) K with the detector placed at a distance 42.00 mm from the crystal. A total of 2028 images were collected with an oscillation width of 1.0° in w. The exposure times were 1 sec. for the low angle images, 3 sec. for high angle. Rigaku d*trek images were exported to CrysAlisPro for processing and corrected for absorption. The crystal was determined to be a two component non-merohedral twin. The twin domains are related by a 180 deg. rotation about the direct (1 0 0) axis. Reflections from both domains as well as overlaps were used as the basis for a HKLF5 reflection file for refinement. The integration of the data yielded a total of 38308 reflections to a maximum 2q value of 138.56° of which 10306 were independent and 10028 were greater than 2s(I). The final cell constants (Table 1) were based on the xyz centroids 14185 reflections above 10s(I). Analysis of the data showed negligible decay during data collection. The structure was solved and refined with the Bruker SHELXTL (version 2016/6) software package, using the space group P2(1) with Z = 2 for the formula $C_{34}H_{49}O_3Br$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. The twin fraction refined to a BASF = 0.419(2). Full matrix least-squares refinement based on F^2 converged at R1 = 0.0595 and wR2 = 0.1696 [based on I > 2sigma(I)], R1 = 0.0601 and wR2 = 0.1706 for all data. Additional details are presented in Table 1 and are given as Supporting Information in a CIF file. Acknowledgement is made for funding from NSF grant CHE-0840456 for X-ray instrumentation.

G.M. Sheldrick (2015) "Crystal structure refinement with SHELXL", Acta Cryst., C71, 3-8 (Open Access).

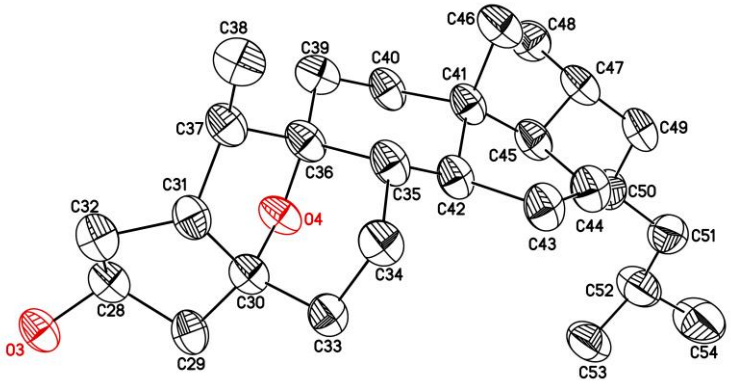
CrystalClear Expert 2.0 r16, Rigaku Americas and Rigaku Corporation (2014), Rigaku Americas, 9009, TX, USA 77381-5209, Rigaku Tokyo, 196-8666, Japan.

CrysAlisPro 1.171.38.41 (Rigaku Oxford Diffraction, 2015).

Crystal data and structure refinement for **(3*R*,3*aR*,5*aS*,9*S*,13*aR*,13*bS*,*E*)-3a,6-dimethyl-3-(6-methylheptan-2-yl)-11-oxo-2,3,3*a*,4,5,5*a*,8,9,10,11,12,13,13*a*,13*b*-tetradecahydro-1H-cyclodeca[e]inden-9-yl 4-bromobenzoate (SI-2)**

Identification code	**(3*R*,3*aR*,5*aS*,9*S*,13*aR*,13*bS*,*E*)-3a,6-dimethyl-3-(6-methylheptan-2-yl)-11-oxo-2,3,3*a*,4,5,5*a*,8,9,10,11,12,13,13*a*,13*b*-tetradecahydro-1H-cyclodeca[e]inden-9-yl 4-bromobenzoate (SI-2)**
Empirical formula	C34 H49 Br O3
Formula weight	585.64
Temperature	85(2) K
Wavelength	1.54184 A
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 14.8070(5) A alpha = 90 deg. b = 6.83670(10) A beta = 102.062(3) deg. c = 15.3104(4) A gamma = 90 deg.
Volume	1515.67(7) A^3
Z, Calculated density	2, 1.283 Mg/m^3
Absorption coefficient	2.085 mm^-1
F(000)	624
Crystal size	0.190 x 0.080 x 0.070 mm
Theta range for data collection	2.951 to 69.260 deg.
Limiting indices	-17<=h<=17, -8<=k<=8, -18<=l<=18
Reflections collected / unique	38308 / 10296 [R(int) = 0.0766]
Completeness to theta = 67.684	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.62051
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	10296 / 1 / 350
Goodness-of-fit on F^2	1.071
Final R indices [I>2sigma(I)]	R1 = 0.0595, wR2 = 0.1696
R indices (all data)	R1 = 0.0601, wR2 = 0.1706
Absolute structure parameter	-0.026(17)
Extinction coefficient	0.0060(14)
Largest diff. peak and hole	0.975 and -0.588 e.A^-3

Structure Determination of (3*R*,3*aR*,5*aS*,6*R*,6*aR*,8*S*,9*aR*,11*aS*,11*bS*)-3*a*,6-dimethyl-3-(6-methylheptan-2-yl)tetradecahydro-6H-5*a*,9*a*-epoxyindeno[5,4-f]azulen-8-ol (SI-3)



(CCDC 1861045)

Colorless needles of **SI-3** were grown from an ethyl acetate solution of the compound at 20 deg. C. A crystal of dimensions 0.06 x 0.01 x 0.01 mm was mounted on a Rigaku AFC10K Saturn 944+ CCD-based X-ray diffractometer equipped with a low temperature device and Micromax-007HF Cu-target micro-focus rotating anode (l = 1.54187 A) operated at 1.2 kW power (40 kV, 30 mA). The X-ray intensities were measured at 85(1) K with the detector placed at a distance 42.00 mm from the crystal. A total of 2028 images were collected with an oscillation width of 1.0° in w. The exposure times were 10 sec. for the low angle images, 60 sec. for high angle. Rigaku d*trek images were exported to CrysAlisPro for processing and corrected for absorption. The integration of the data yielded a total of 40651 reflections to a maximum 2q value of 139.36° of which 9030 were independent and 5521 were greater than 2s(I). The final cell constants (Table 1) were based on the xyz centroids of 3749 reflections above 10s(I). Analysis of the data showed negligible decay during data collection. The structure was solved and refined with the Bruker SHELXTL (version 2016/6) software package, using the space group P2(1)2(1)2(1) with Z = 8 for the formula $C_{27}H_{46}O_2$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0934 and wR2 = 0.2218 [based on I > 2sigma(I)], R1 = 0.1451 and wR2 = 0.2753 for all data. Additional details are presented in Table 1 and are given as Supporting Information in a CIF file. Acknowledgement is made for funding from NSF grant CHE-0840456 for X-ray instrumentation.

G.M. Sheldrick (2015) "Crystal structure refinement with SHELXL", Acta Cryst., C71, 3-8 (Open Access).
CrystalClear Expert 2.0 r16, Rigaku Americas and Rigaku Corporation (2014), Rigaku Americas, 9009, TX, USA 77381-5209, Rigaku Tokyo, 196-8666, Japan.

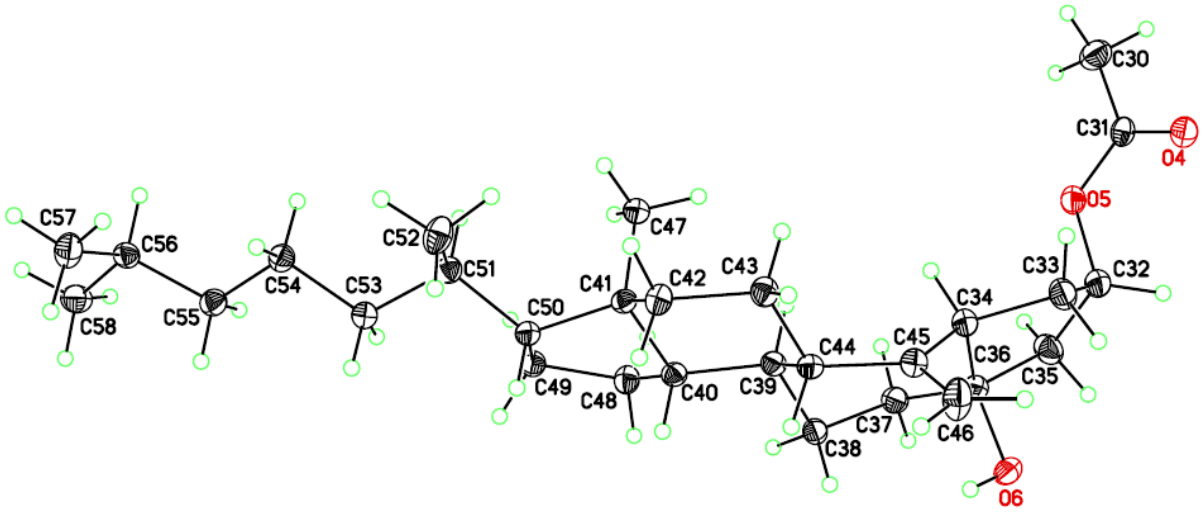
CrysAlisPro 1.171.38.41 (Rigaku Oxford Diffraction, 2015).

Crystal data and structure refinement for **(3*R*,3*aR*,5*aS*,6*R*,6*aR*,8*S*,9*aR*,11*aS*,11*bS*)-3*a*,6-dimethyl-3-(6-methylheptan-2-yl)tetradecahydro-6H-5*a*,9*a*-epoxyindeno[5,4-f]azulen-8-ol (SI-3)**

Identification code	**(3*R*,3*aR*,5*aS*,6*R*,6*aR*,8*S*,9*aR*,11*aS*,11*bS*)-3*a*,6-dimethyl-3-(6-methylheptan-2-yl)tetradecahydro-6H-5*a*,9*a*-epoxyindeno[5,4-f]azulen-8-ol (SI-3)**
Empirical formula	C27 H46 O2
Formula weight	402.64
Temperature	85(2) K

Wavelength	1.54184 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 6.1663(4) A alpha = 90 deg.
	b = 17.4271(17) A beta = 90 deg.
	c = 45.499(4) A gamma = 90 deg.
Volume	4889.3(7) A^3
Z, Calculated density	8, 1.094 Mg/m^3
Absorption coefficient	0.502 mm^-1
F(000)	1792
Crystal size	0.060 x 0.010 x 0.010 mm
Theta range for data collection	2.715 to 69.680 deg.
Limiting indices	-7<=h<=7, -20<=k<=20, -55<=l<=54
Reflections collected / unique	40651 / 9030 [R(int) = 0.1360]
Completeness to theta = 67.684	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.44226
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9030 / 0 / 536
Goodness-of-fit on F^2	1.063
Final R indices [I>2sigma(I)]	R1 = 0.0935, wR2 = 0.2218
R indices (all data)	R1 = 0.1451, wR2 = 0.2753
Absolute structure parameter	0.3(3)
Extinction coefficient	0.0041(5)
Largest diff. peak and hole	0.421 and -0.357 e.A^-3

Structure determination of (3*R*,3*aR*,5*aS*,6*aR*,8*S*,9*aR*,11*aR*,11*bS*)-9a-hydroxy-3a-methyl-6-methylene-3-(6-methylheptan-2-yl)hexadecahydro-1H-indeno[5,4-f]azulen-8-yl acetate (16)



(CCDC 1914933)

Colorless plates of **16** were grown from an ethyl acetate solution of the compound at 23 deg. C. A crystal of dimensions 0.24 x 0.03 x 0.03 mm was mounted on a Rigaku AFC10K Saturn 944+ CCD-based X-ray diffractometer equipped with a low temperature device and Micromax-007HF Cu-target micro-focus rotating anode (λ = 1.54187 A) operated at 1.2 kW power (40 kV, 30 mA). The X-ray intensities were measured at 85(1) K with the detector placed at a distance 42.00 mm from the crystal. A total of 2028 images were collected with an oscillation width of 1.0° in ω. The exposure times were 1 sec. for the low angle images, 5 sec. for high angle. Rigaku d*trek images were exported to CrysAlisPro for processing and corrected for absorption. The integration of the data yielded a total of 80727 reflections to a maximum 2□ value of 138.62□ of which 9793 were independent and 9616 were greater than 2□(I). The final cell constants (Table 1) were based on the xyz centroids of 45003 reflections above 10□(I). Analysis of the data showed negligible decay during data collection. The structure was solved and refined with the Bruker SHELXTL (version 2018/3) software package, using the space group P2(1)2(1)2(1) with Z = 8 for the formula $C_{29}H_{48}O_3$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in a combination of idealized and refined positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0305 and wR2 = 0.0767 [based on I > 2sigma(I)], R1 = 0.0312 and wR2 = 0.0773 for all data. Additional details are presented in Table 1 and are given as Supporting Information in a CIF file. Acknowledgement is made for funding from NSF grant CHE-0840456 for X-ray instrumentation.

G.M. Sheldrick (2015) "Crystal structure refinement with SHELXL", Acta Cryst., C71, 3-8 (Open Access).
CrystalClear Expert 2.0 r16, Rigaku Americas and Rigaku Corporation (2014), Rigaku Americas, 9009, TX, USA 77381-5209, Rigaku Tokyo, 196-8666, Japan.

CrysAlisPro 1.171.38.41 (Rigaku Oxford Diffraction, 2015).

Crystal data and structure refinement for **(3*R*,3*aR*,5*aS*,6*aR*,8*S*,9*aR*,11*aR*,11*bS*)-9a-hydroxy-3a-methyl-6-methylene-3-(6-methylheptan-2-yl)hexadecahydro-1H-indeno[5,4-f]azulen-8-yl acetate (16)**

Identification code	**(3*R*,3*aR*,5*aS*,6*aR*,8*S*,9*aR*,11*aR*,11*bS*)-9a-hydroxy-3a-methyl-6-methylene-3-(6-methylheptan-2-yl)hexadecahydro-1H-indeno[5,4-f]azulen-8-yl acetate (16)**
Empirical formula	C29 H48 O3
Formula weight	444.67
Temperature	85(2) K
Wavelength	1.54184 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 10.32230(10) A alpha = 90 deg. b = 11.39260(10) A beta = 90 deg. c = 44.7577(6) A gamma = 90 deg.
Volume	5263.41(10) A^3
Z, Calculated density	8, 1.122 Mg/m^3
Absorption coefficient	0.540 mm^-1
F(000)	1968
Crystal size	0.240 x 0.030 x 0.030 mm
Theta range for data collection	3.951 to 69.307 deg.
Limiting indices	-12<=h<=12, -13<=k<=13, -51<=l<=54
Reflections collected / unique	80727 / 9793 [R(int) = 0.0502]
Completeness to theta = 67.684	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.84450
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9793 / 0 / 595
Goodness-of-fit on F^2	1.011
Final R indices [I>2sigma(I)]	R1 = 0.0305, wR2 = 0.0767
R indices (all data)	R1 = 0.0312, wR2 = 0.0773
Absolute structure parameter	-0.04(5)
Extinction coefficient	n/a
Largest diff. peak and hole	0.197 and -0.170 e.A^-3