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Supporting Information

The Formal Cross-Coupling of Amines and Carboxylic Acids to Form sp^3–sp^3 Carbon–Carbon Bonds

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Supporting Information

General Information

All reactions were conducted in oven- or flame-dried glassware under an atmosphere of nitrogen unless stated otherwise. Reactions were set up in an MBraun LABmaster Pro Glove Box (H_2O level <0.1 ppm, O_2 level <0.1 ppm), or using standard Schlenk technique with a glass vacuum manifold connected to an inlet of dry nitrogen gas. Tetrahydrofuran and dichloromethane were purified using an MBraun SPS solvent purification system by purging with nitrogen, and then passing the solvent through a column of activated alumina. 1,4-Dioxane, acetonitrile and other solvents were purchased as the anhydrous solvents and used as received. Reagents were purchased from Sigma Aldrich, Alfa Aesar, Oakwood Chemical, or TCI Chemical. All chemicals were used as received. Glass 2 dram vials (ChemGlass #CG-4912-02) were used as reaction vessels, fitted with a screw-cap with a Teflon-coated silicone septa (CG-4910-02), and magnetic stir bars (Fisher Scientific #14-513-93 or #14-513-65).

Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a Varian MR-500 MHz or Varian MR-400 MHz spectrometer and chemical shifts are reported in parts per million (ppm) using the solvent residual peak as an internal standard ($CDCl_3$ at 7.26 ppm). Data are reported using the abbreviations: app = apparent, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = complex, br = broad. Coupling constant(s) are reported in Hz. Proton-decoupled carbon nuclear magnetic resonance spectra (^{13}C NMR) spectra were recorded on a Varian MR-500 MHz or Varian MR-400 MHz spectrometer and chemical shifts are reported in ppm using the solvent as an internal standard ($CDCl_3$ at 77.16 ppm). High resolution mass spectrometry data (HRMS) were obtained on a Micromass AutoSpec Ultima Magnetic Sector instrument. Reaction analysis was typically performed by thin-layer chromatography on silica gel, or using a Waters I-class ACQUITY UPLC-MS (Waters Corporation, Milford, MA, USA) equipped with in-line photodiode array detector (PDA) and QDa mass detector (ESI positive ionization mode). 0.1 µL sample injections were taken from acetonitrile solutions of reaction mixtures or products (~1 mg/mL). A partial loop injection mode was used with the needle placement at 1.0 mm from bottom of the wells and a 0.2 µL air gap at pre-aspiration and post-aspiration. Column used: Waters Cortecs UPLC C18+ column, 2.1mm × 50 mm with (Waters #186007114) with Waters Cortecs UPLC C18+ VanGuard Pre-column 2.1mm × 5 mm (Waters #186007125), Mobile Phase A: 0.1 % formic acid in Optima LC/MS-grade water, Mobile Phase B: 0.1% formic acid in Optima LC/MS-grade MeCN. Flow rate: 1 mL/min. Column temperature: 45 °C. The PDA sampling rate was 20 points/sec. The QDa detector monitored m/z 150-750 with a scan time of 0.06 seconds and a cone voltage of 30 V. The PDA detector range was between 210 nm – 400 nm

with a resolution of 1.2 nm. 1 minute and 2 minute methods were used. The method gradients are below: 0 min: 0.8 mL/min, 95% 0.1% formic acid in water/5% 0.1% formic acid in acetonitrile; 1.5 min : 0.8 mL/min, 0.1% 0.1% formic acid in water/99.9% 0.1% formic acid in acetonitrile; 1.91 min : 0.8 mL/min, 95% 0.1% formic acid in water/5% 0.1% formic acid in acetonitrile.

Flash chromatography was performed on silica gel (230 – 400 Mesh, Grade 60) under a positive pressure of nitrogen. Thin layer chromatography was performed on 25 µm TLC Silica gel 60 F_{254} glass plates purchased from Fisher Scientific (part number: S07876). Visualization was performed using ultraviolet light (254 nm) or potassium permanganate ($KMnO_4$) stain.

Experimental

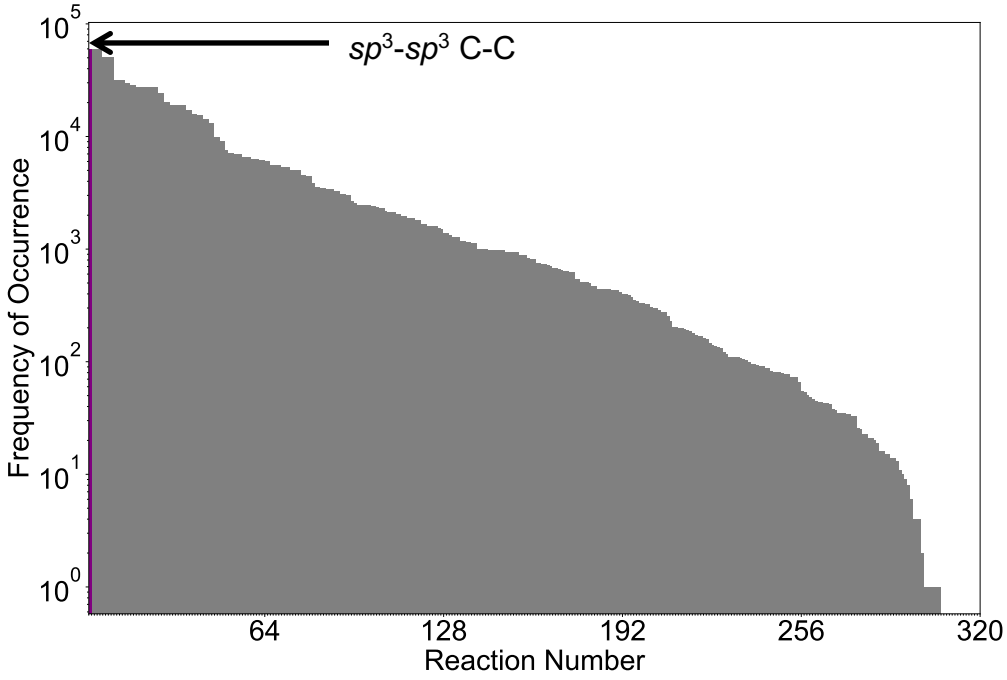


Figure S1. Plot of frequency of substructure occurrence in Drugbank versus reaction number of enumerated Acid-Amine coupling products. sp^3-sp^3 C-C coupling is the transformation with highest frequency.

General procedure for HTE screen preparation (GP-1)

Stock solutions, or suspensions, were prepared as shown in the heatmap preparation table. In an inert atmosphere glovebox, reagents were weighed and dissolved or suspended in anhydrous solvent to achieve their listed concentrations in table. Stock solutions of reagents were stirred until either a clear solution or a uniform slurry was achieved. A 24 or 96-well aluminum microvial plate (Analytical Sales & Services cat. no. 25243) was equipped with oven-dried shell vials (Analytical Sales & Services cat. no. 884001) and then moved into the glovebox. Stock solutions were dosed to the appropriate shell vials according to the plate map shown in table using single channel micropipetters. A parylene-coated stir dowel (Analytical Sales & Services cat. no. 13258) was then added to each vial. The microvial plate was sealed, removed from the glove box, and stirred on a tumble stirrer with heating to indicated temperature for planned reaction time in a heating block or under blue LED.

The reactions were quenched by opening the reaction block and adding 100 µL saturated aqueous NaCl solution and 400 µL EtOAc. Reactions were extracted by resealing the plate and shaking manually. From each reaction, a 40 µL aliquot of the quenched reaction mixture was added into a 96-well polypropylene collection plate (Analytical Sales & Services cat. no. 17P687). The solvent was evaporated by blowing nitrogen down on the analytical plate. An acetonitrile solution of caffeine as internal standard (0.05 mg/mL, 800 µL) was added, and mixed by pipetting up and down. The reactions were then analyzed by UPLC-MS. The assay yields was produced by measuring the UV absorbance (or mass signal strength) of desired product relative to the caffeine internal standard.

1,392 Machine readable reaction data points are deposited on github: https://github.com/cernaklab/Zhang-Cernak-Cross-Coupling-of-Activated-Amines-and-Acids

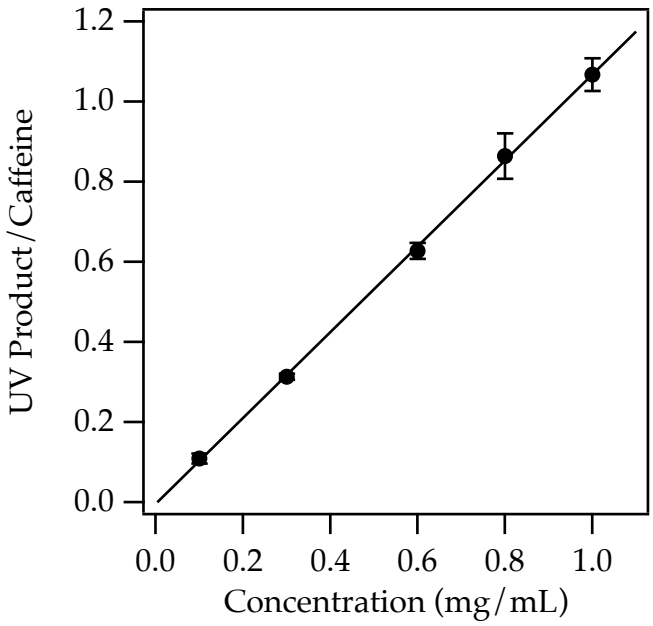


Figure S2. Calibration curve of UV integration of **4** relative to caffeine internal standard (0.050 mg/mL) versus concentration of **4**. Curve fit to $y = 1.1 * x - 0.0040$.

Reagents	C_{stock} (M)	V_{dose} (µL)	Wells
Benzyl Katritzky salt	0.60	17	All
Boc-Pro-OH	0.60	17	A1-4-H1-4 A7-10-H7-10
Boc-Pro-OH NHPI ester	0.60	17	A5,6-H5,6 A11,12-H11,12
Potassium carbonate	1.2	17	A1,7-H1,7
1,8-Diazabicyclo[5,4,0]undec-7-ene	1.2	17	A2,8-H2,8
1,4-Diazabicyclo[2,2,2]octane	1.2	17	A3,9-H3,9
2-*t*Bu-1,1,3,3-tetramethylguanidine	1.2	17	A4,10-H4,10
Zn	1.2	17	A5,11-H5,11
Tetrakis(dimethylamino)ethylene	1.2	17	A6,12-H6,12
$Ni(cod)_2$	0.12	17	A1-6-H1-6
$Ni(acac)_2$	0.12	17	A7-12-H7-12
4,4'-di-*t*Bu-2,2'-dipyridyl	0.18	17	A1-12-D1-12
4,4'-dimethoxy-2,2'-bipyridine	0.18	17	E1-12-H1-12
$(Ir[dF(CF_3)ppy]_2(dtbpy))PF_6$	0.012	17	A1-12 E1-12
$Ru(bpy)_3PF_6$	0.012	17	B1-12 F1-12
Eosin Y	0.012	17	C1-12 G1-12
2,4,6-triphenylpyrylium tetrafluoroborate	0.012	17	D1-12 H1-12

Table S1. Photoredox screen.

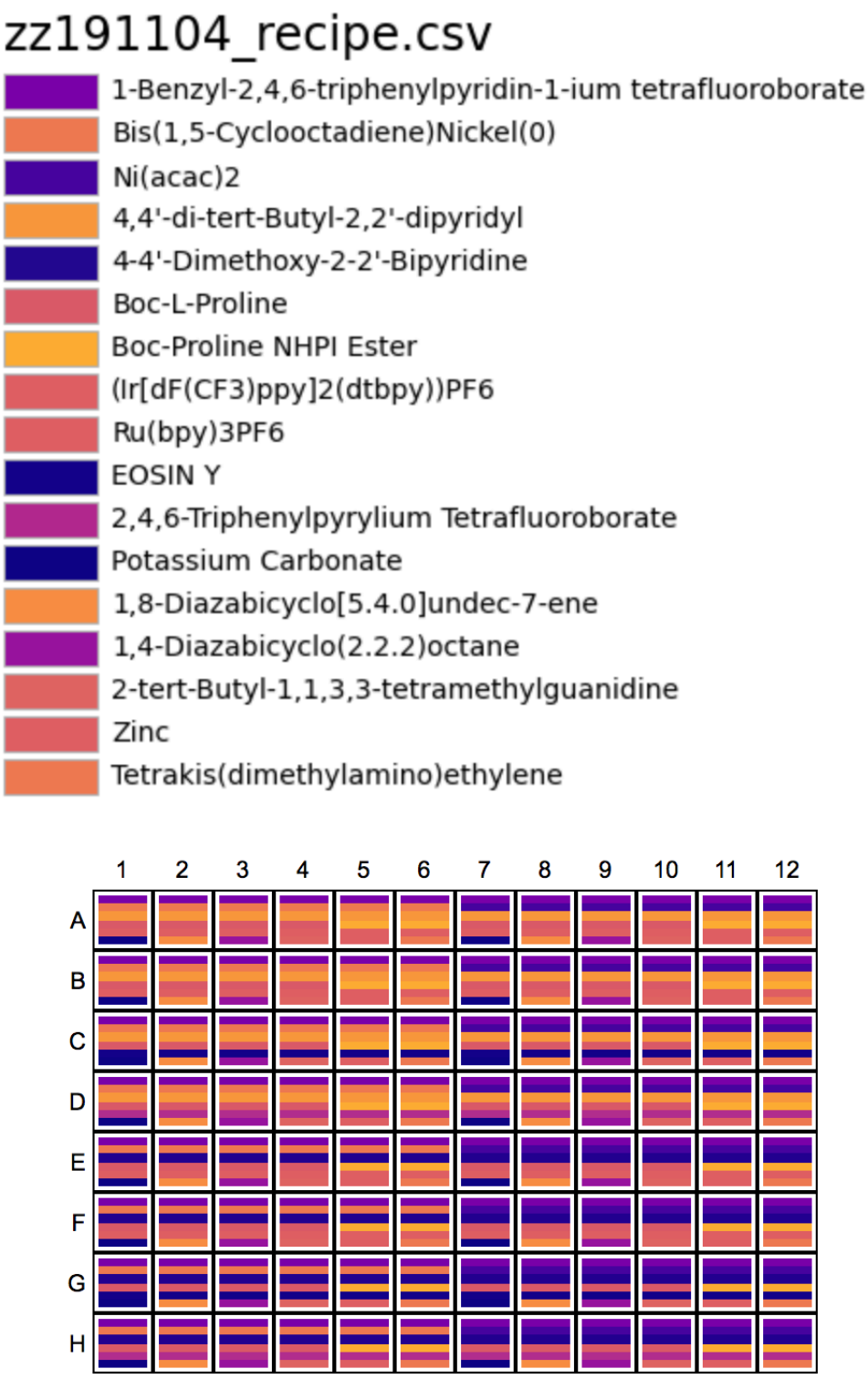
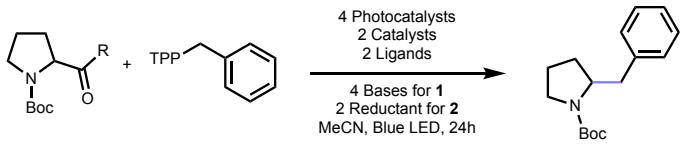


Figure S3. Recipe and grid of photoredox screen.



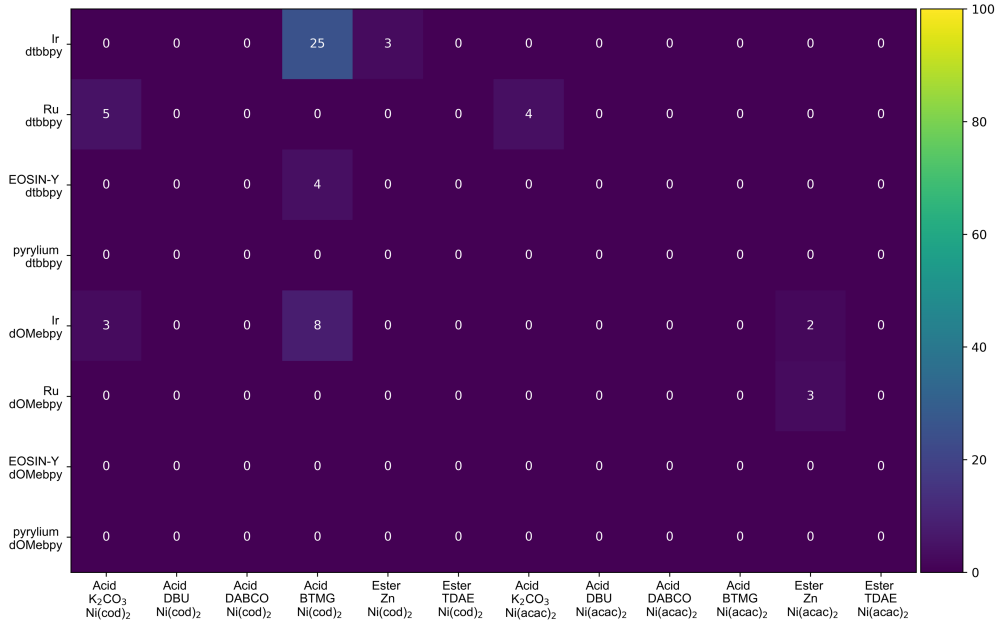


Figure S4. Heatmap of photoredox screen. Following GP-1, stock solutions were prepared and dosed according to the concentrations and well locations in **Table S1**. Screen performed at 25 ºC in MeCN under blue LED stirring at 300 rpm for 24 h.

Reagents	C_{stock} (M)	V_{dose} (µL)	Wells
Benzyl Katritzky salt	0.70	14	All
Boc-Pro-OH	0.70	14	A1-12-D1-12
Tosylpiperidine-4-carboxylic acid	0.70	14	E1-12-H1-12
K_3PO_4	0.70	14	A,C,E,G1-12
2-^{t}Bu-1,1,3,3-tetramethylguanidine	0.70	14	B,D,F,H1-12
Tricyclohexylphosphine	0.21	14	A,B,E,F1-12
1,3-Dimesitylimidazolidine	0.21	14	C,D,G,H1-12
Silver nitrate	0.70	14	A1-4-H1-4
Silver carbonate	0.70	14	A5-8-H5-8
Silver trifluoromethanesulfonate	0.70	14	A9-12-H9-12
Potassium persulfate	1.4	14	A1,5,9-H1,5,9
Ammonium persulfate	1.4	14	A2,6,10-H2,6,10
^{t}BuOO^{t}Bu	1.4	14	A3,7,11-H3,7,11
(Bis(trifluoroacetoxy)iodo)benzene	1.4	14	A4,8,12-H4,8,12
$NiBr_2$•glyme	0.14	14	All

Table S2. Minisci type decarboxylation screen.

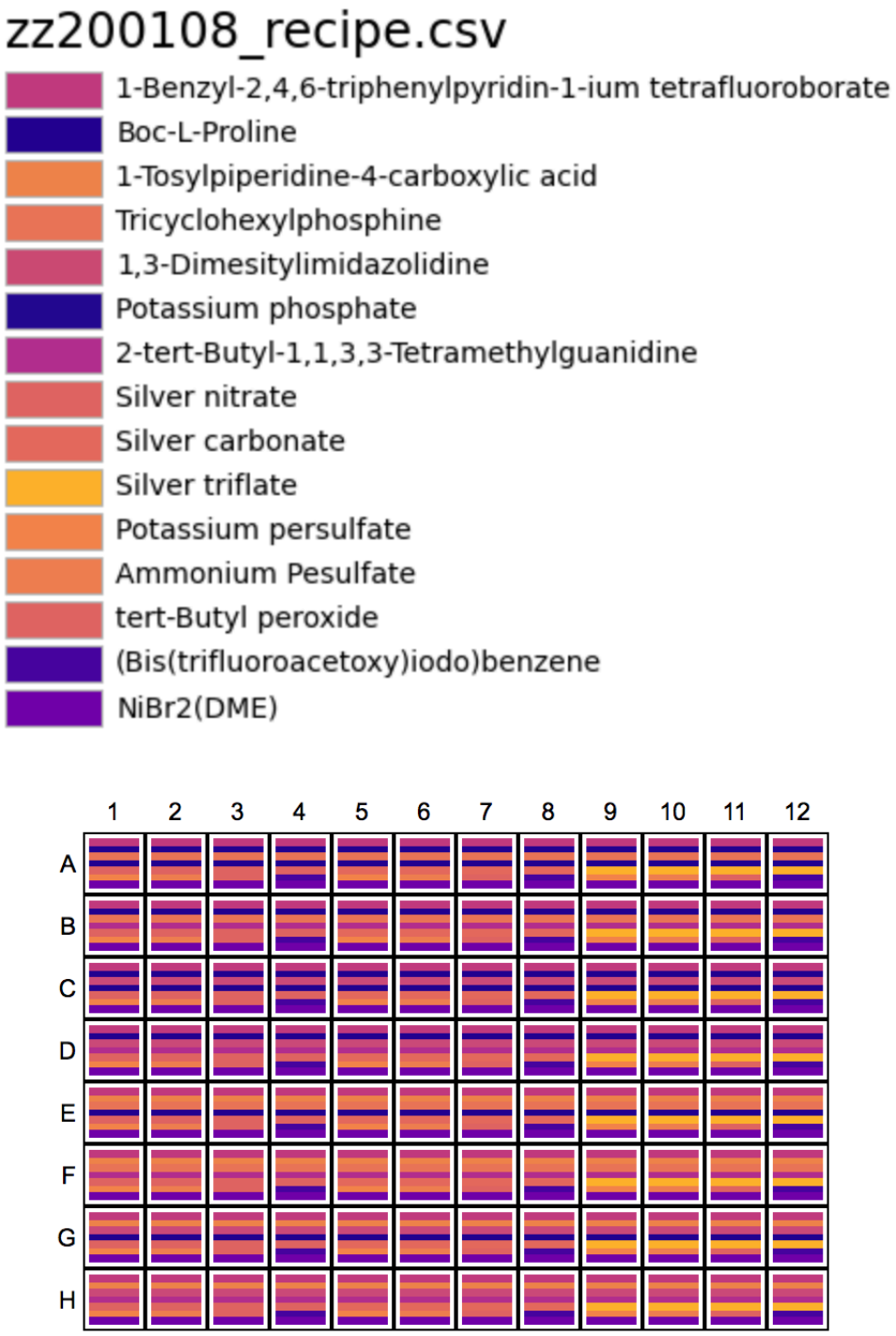
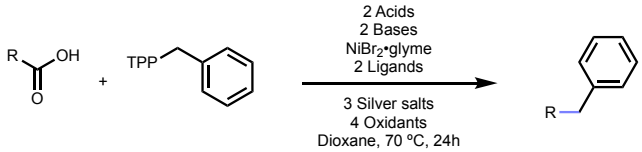


Figure S5. Recipe and grid of Minisci type decarboxylation screen.



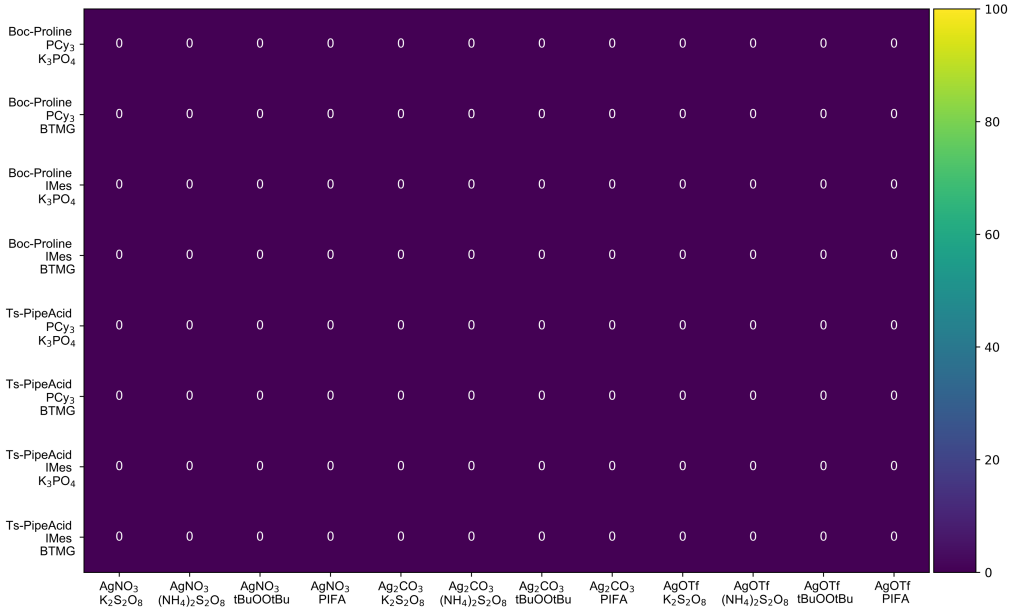


Figure S6. Heatmap of Minisci type decarboxylation screen. Following GP-1, stock solutions were prepared and dosed according to the concentrations and well locations in **Table S2**. Screen performed at 70 ºC in dioxane stirring at 300 rpm for 24 h.

Reagents	C_{stock} (M)	V_{dose} (µL)	Wells
Benzyl Katritzky salt	0.50	20	All
Boc-Pro-OH NHPI ester	0.50	20	All
Zn	1.0	20	A1-6-H1-6
Tetrakis(dimethylamino)ethylene	1.0	20	A7-12-H7-12
4,4'-di-^{t}Bu-2,2'-dipyridyl	0.15	20	A1,7-H1,7
3,4,7,8-Tetramethyl-1,10-phenanthroline	0.15	20	A2,8-H2,8
1,3-Dimesitylimidazolidine	0.15	20	A3,9-H3,9
Triphenylphosphine	0.15	20	A4,10-H4,10
1,2-Bis(dicyclohexylphosphino)ethane	0.15	20	A5,11-H5,11
2,2-Bis((4S)-(-)-4-Isopropyloxazoline)propane	0.15	20	A6,12-H6,12
$Ni(cod)_2$	0.10	20	A1-12
$NiBr_2$•glyme	0.10	20	B1-12
$Ni(acac)_2$	0.10	20	C1-12
CuBr	0.10	20	D1-12
$Cu(MeCN)_4OTf$	0.10	20	E1-12
$Cu(OAc)_2$	0.10	20	F1-12
$FeBr_2$	0.10	20	G1-12
$CoBr_2$	0.10	20	H1-12

Table S3. Hit screen.

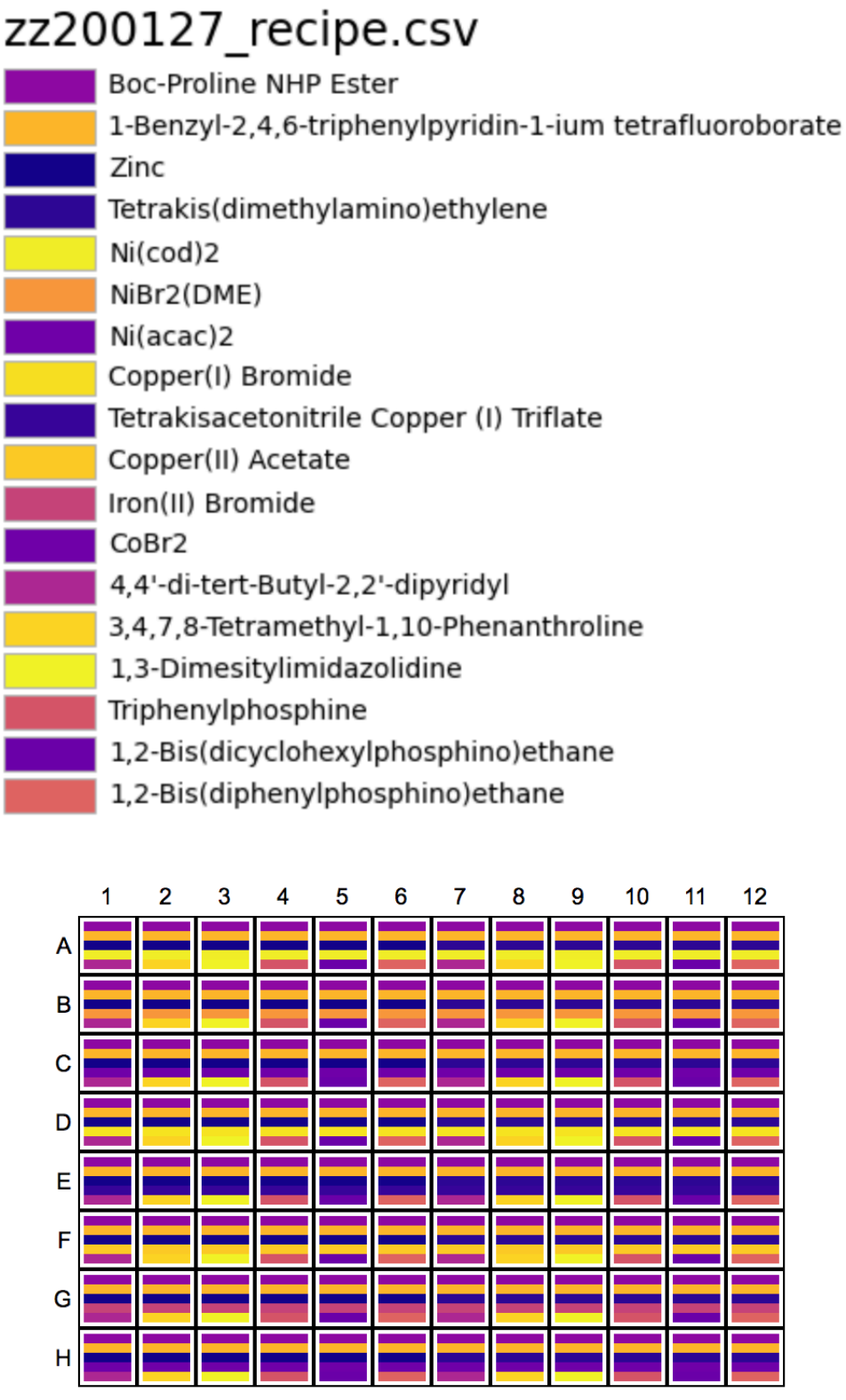
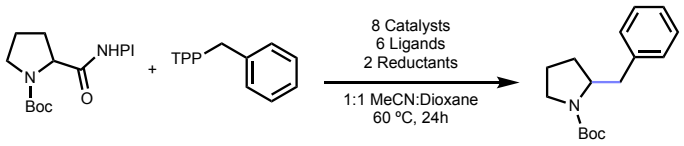


Figure S7. Recipe and grid of hit screen.



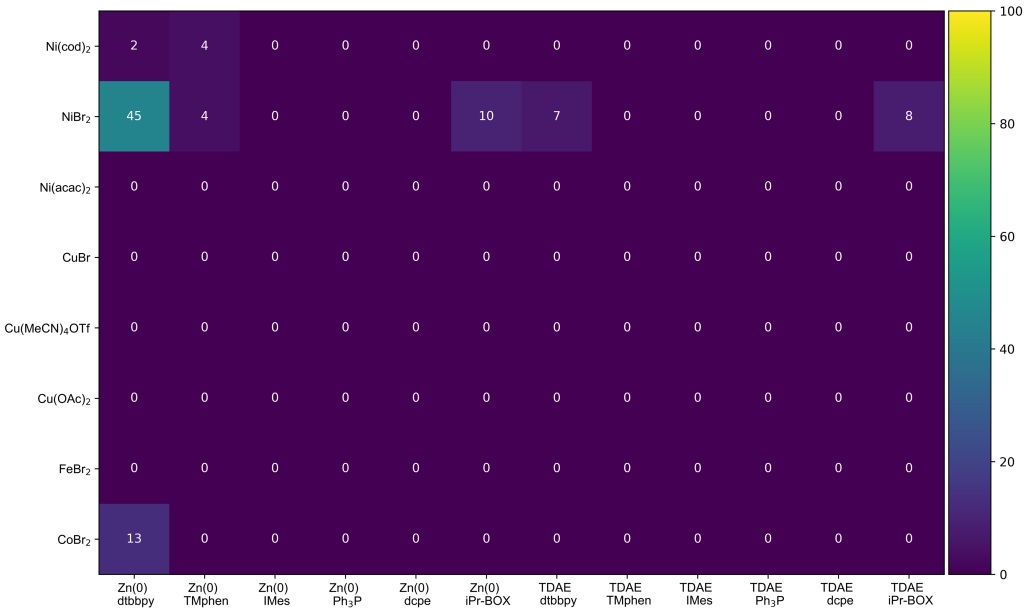


Figure S8. Heatmap of hit screen. Following GP-1, stock solutions were prepared and dosed according to the concentrations and well locations in **Table S3**. Screen performed at 60 ºC in 1:1 MeCN:dioxane stirring at 300 rpm for 24 h.

Reagents	C_{stock} (M)	V_{dose} (µL)	Wells
Benzyl Katritzky salt	0.50	20	A,C,E,G1-12
Cyclohexyl Katritzky salt	0.50	20	B,D,F,H1-12
Boc-Pro-OH NHPI ester	0.50	20	A,B,E,F1-12
Tosylpiperidine-4-carboxylic acid NHPI	0.50	20	C,D,G,H1-12
Mn	1.0	20	A1-12-D1-12
Zn	1.0	20	E1-12-H1-12
1,10-Phenanthroline	0.15	20	A1-4-H1-4
4,4'-di-^{t}Bu-2,2'-dipyridyl	0.15	20	A5-8-H5-8
4,4',4''-tri-^{t}Bu-2,2':6',2''terpyridine	0.15	20	A9-12-H9-12
NiF_2	0.10	20	A1,5,9-H1,5,9
$NiCl_2$•glyme	0.10	20	A2,6,10-H2,6,10
$NiBr_2$•glyme	0.10	20	A3,7,11-H3,7,11
NiI_2	0.10	20	A4,8,12-H4,8,12

Table S4. Substrate-reductant-catalyst-ligand screen.

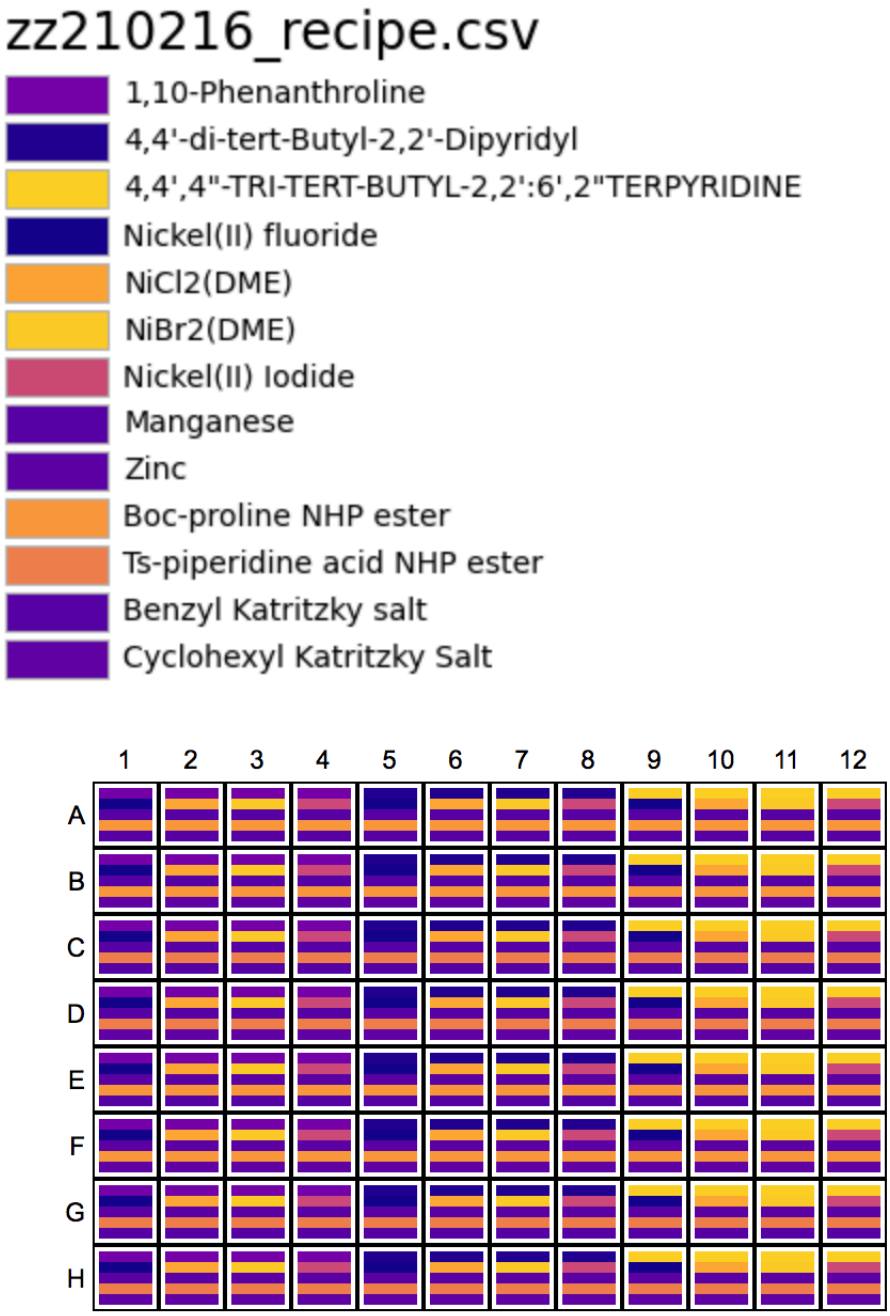
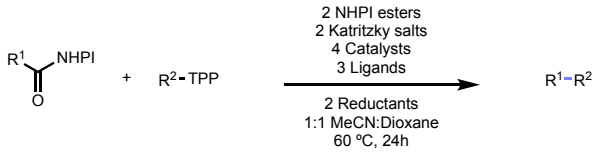


Figure S9. Recipe and grid of substrate-reductant-catalyst-ligand screen.



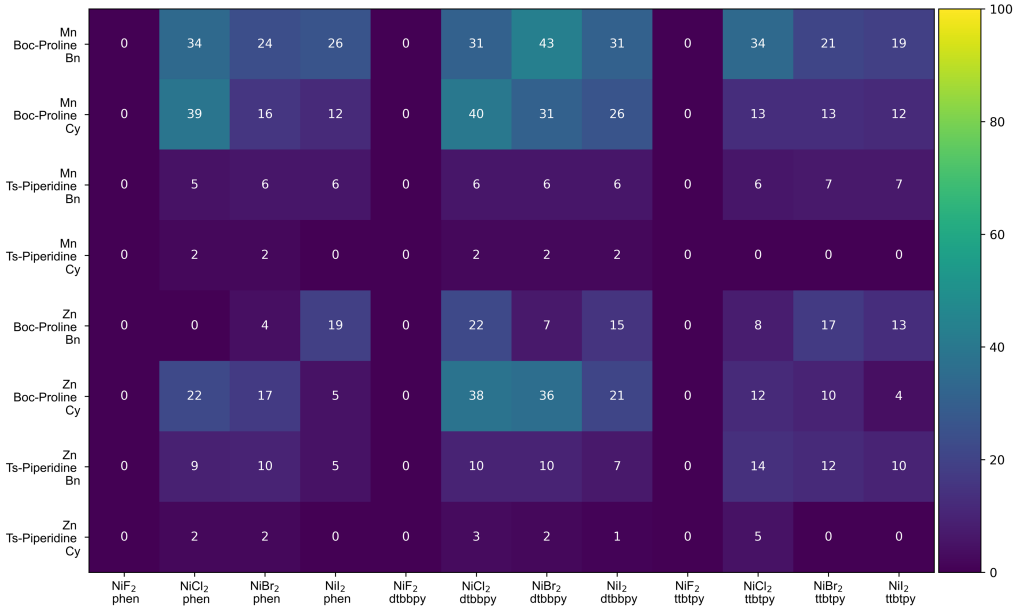


Figure S10. Heatmap of substrate-reductant-catalyst-ligand screen. Following GP-1, stock solutions were prepared and dosed according to the concentrations and well locations in **Table S4**. Screen performed at 60 ºC in 1:1 MeCN:dioxane stirring at 300 rpm for 24 h.

Reagents	C_{stock} (M)	V_{dose} (µL)	Wells
Benzyl Katritzky salt	0.50	20	All
Boc-Pro-OH NHPI ester	0.50	20	All
Mn	1.0	20	All
$NiBr_2$•glyme	0.10	20	A1,2-H1,2
$NiCl_2$•glyme	0.10	20	A3,4-H3,4
NiI_2	0.10	20	A5,6-H5,6
$Ni(cod)_2$	0.10	20	A7,8-H7,8
$Ni(acac)_2$	0.10	20	A9,10-H9,10
$Ni(OAc)_2$	0.10	20	A11,12-H11,12
4,4'-di-^{t}Bu-2,2'-dipyridyl	0.15	20	A1,3,5,7,9,11
2,2'-Bipyridyl	0.15	20	A2,4,6,8,10,12
4,4'-Dimethoxy-2,2'-bipyridine	0.15	20	B1,3,5,7,9,11
4,4'-Bis(trifluoromethyl)-2,2'-bipyridine	0.15	20	B2,4,6,8,10,12
2,2':6',2''-Terpyridine	0.15	20	C1,3,5,7,9,11
4,4',4''-Tri-^{t}Bu-2,2':6',2''-terpyridine	0.15	20	C2,4,6,8,10,12
(2Z,6Z)-N′2,N′6-Dicyanopyridine-2,6-bis(carboximidamide)	0.15	20	D1,3,5,7,9,11
Pyridine-2,6-bis(carboximidamide) dihydrochloride	0.15	20	D2,4,6,8,10,12
2,2-Bis((4S)-(-)-4-Isopropyloxazoline)propane	0.15	20	E1,3,5,7,9,11
2,6-Bis[(4R)-(+)-Isopropyl-2-oxazolin-2-yl]pyridine	0.15	20	E2,4,6,8,10,12
1,10-Phenanthroline	0.15	20	F1,3,5,7,9,11
3,4,7,8-Tetramethyl-1,10-phenanthroline	0.15	20	F2,4,6,8,10,12
4,7-Dichlro-1,10-phenanthroline	0.15	20	G1,3,5,7,9,11
4,7-Dimethoxy-1,10-phenanthroline	0.15	20	G2,4,6,8,10,12
Neocuproine	0.15	20	H1,3,5,7,9,11
Blank	0.15	20	H2,4,6,8,10,12

Table S5. Catalyst-ligand screen.

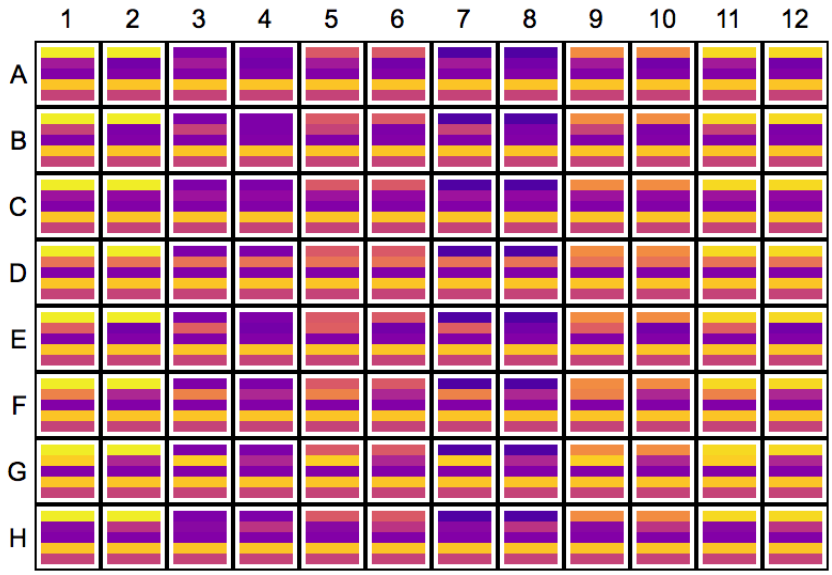
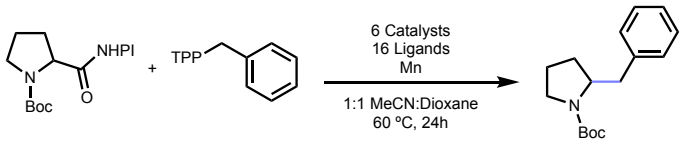


Figure S11. Recipe and grid of catalyst-ligand screen.



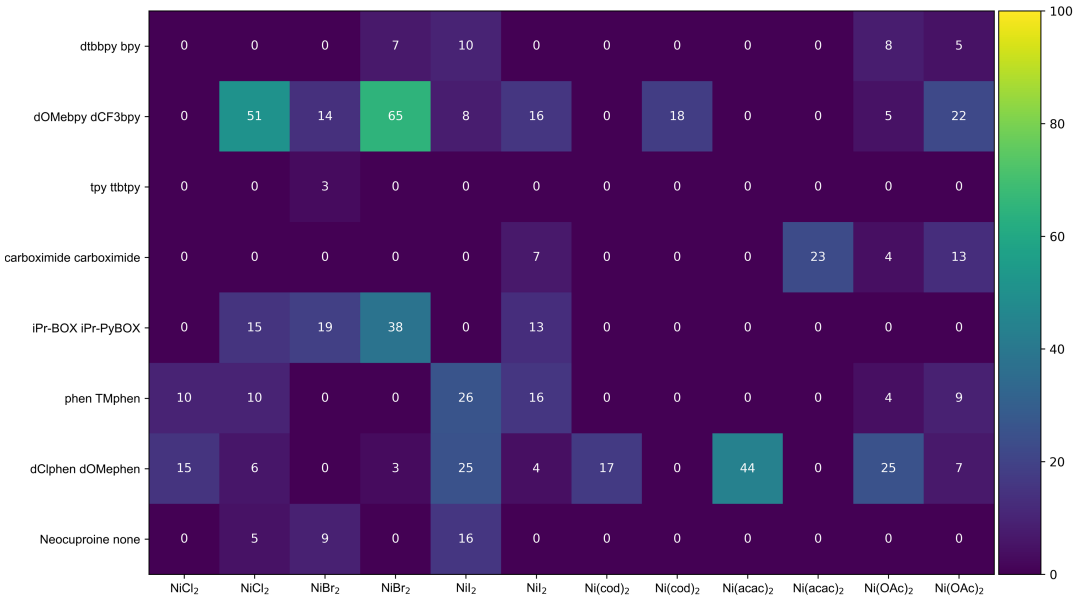
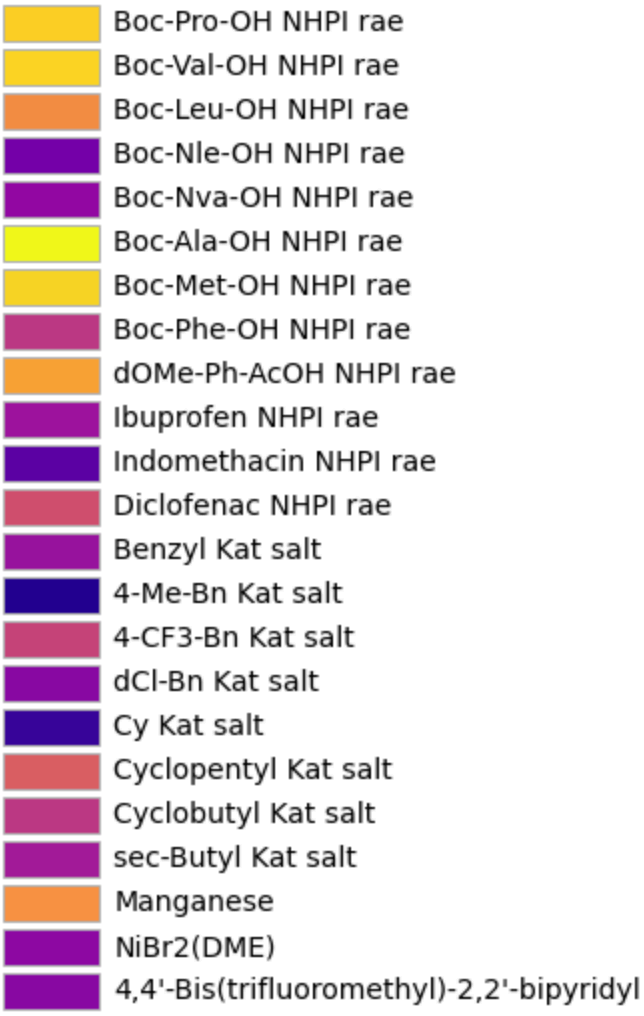


Figure S12. Heatmap of catalyst-ligand screen. Following GP-1, stock solutions were prepared and dosed according to the concentrations and well locations in **Table S5**. Screen performed at 60 ºC in 1:1 MeCN:dioxane stirring at 300 rpm for 24 h.

Reagents	C_{stock} (M)	V_{dose} (µL)	Wells
$NiBr_2$•glyme	0.10	20	All
4,4'-Bis(trifluoromethyl)-2,2'-bipyridine	0.10	20	All
Mn	1.0	20	All
Benzyl Katritzky salt	0.50	20	A1-12
4-Methylbenzyl Katritzky salt	0.50	20	B1-12
4-Trifluoromethylbenzyl Katritzky salt	0.50	20	C1-12
2,4-Dichlorobenzyl Katritzky salt	0.50	20	D1-12
Cyclohexyl Katritzky salt	0.50	20	E1-12
Cyclopentyl Katritzky salt	0.50	20	F1-12
Cyclobutyl Katritzky salt	0.50	20	G1-12
sec-Butyl Katritzky salt	0.50	20	H1-12
Boc-Pro-OH NHPI ester	0.50	20	A1-H1
Boc-Val-OH NHPI ester	0.50	20	A2-H2
Boc-Leu-OH NHPI ester	0.50	20	A3-H3
Boc-Nle-OH NHPI ester	0.50	20	A4-H4
Boc-Nva-OH NHPI ester	0.50	20	A5-H5
Boc-Ala-OH NHPI ester	0.50	20	A6-H6
Boc-Met-OH NHPI ester	0.50	20	A7-H7
Boc-Phe-OH NHPI ester	0.50	20	A8-H8
3,4-Dimethoxyphenylacetic acid NHPI ester	0.50	20	A9-H9
Indomethacin NHPI ester	0.50	20	A10-H10
Ibuprofen NHPI ester	0.50	20	A11-H11
Naproxen NHPI ester	0.50	20	A12-H12

Table S6. Substrate screen.

zz210406_recipe.csv



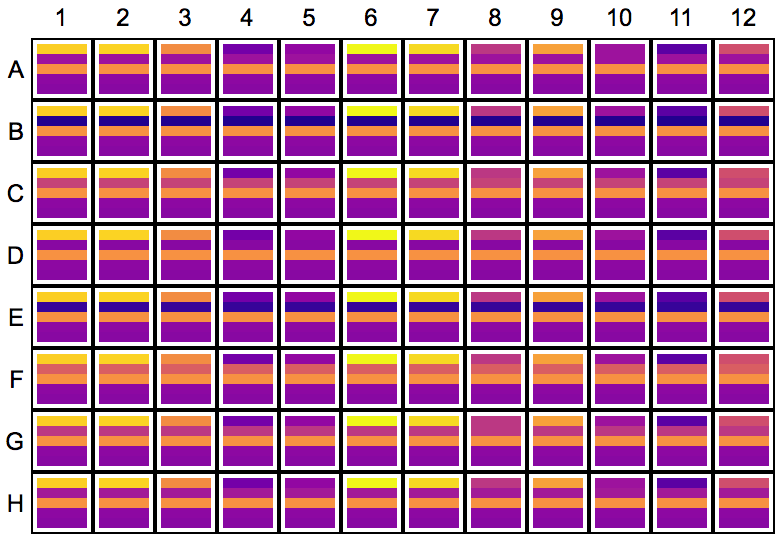
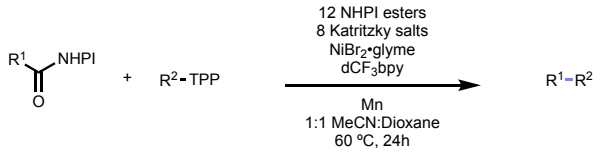


Figure S13. Recipe and grid of substrate screen.



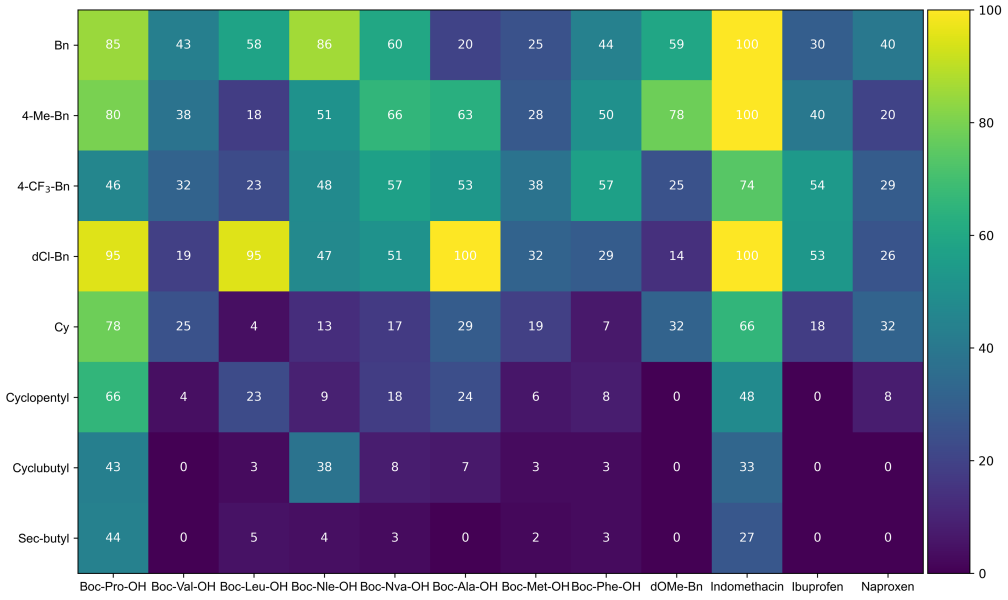


Figure S14. Heatmap of substrate screen. Following GP-1, stock solutions were prepared and dosed according to the concentrations and well locations in **Table S6**. Screen performed at 60 ºC in 1:1 MeCN:dioxane stirring at 300 rpm for 24 h.

Reagents	C_{stock} (M)	V_{dose} (µL)	Wells
Boc-Pro-OH	0.60	17	All
Benzyl Katritzky salt	0.60	17	All
2-^{t}Bu-1,1,3,3-tetramethylguanidine	1.2	17	All
4,4'-di-^{t}Bu-2,2'-dipyridyl	0.12	17	A1-4-H1-4
4,7-Dichlro-1,10-phenanthroline	0.12	17	A5-8-H5-8
BINAP	0.12	17	A9-12-H9-12
$Ni(cod)_2$	0.12	17	A1,5,9-H1,5,9
$NiCl_2$	0.12	17	A2,6,10-H2,6,10
$Cu(OAc)_2$	0.12	17	A3,7,11-H3,7,11
CuOTf	0.12	17	A4,8,12-H4,8,12
$(Ir[dF(Me)ppy]_2(dtbpy))PF_6$	0.012	17	A1-12
$[Ir(ppy)_2](dtbpy))PF_6$	0.012	17	B1-12
$Ir(ppy)_3PF_6$	0.012	17	C1-12
$(Ir[dF(CF_3)ppy]_2(dtbpy))PF_6$	0.012	17	D1-12
$Ru(bpy)_3PF_6$	0.030	17	E1-12
Perylene	0.060	17	F1-12
Benzophenone	0.060	17	G1-12
TiO_2	0.30	17	H1-12

Table S7. Photoredox screen of photocatalyst, catalyst, and ligand.

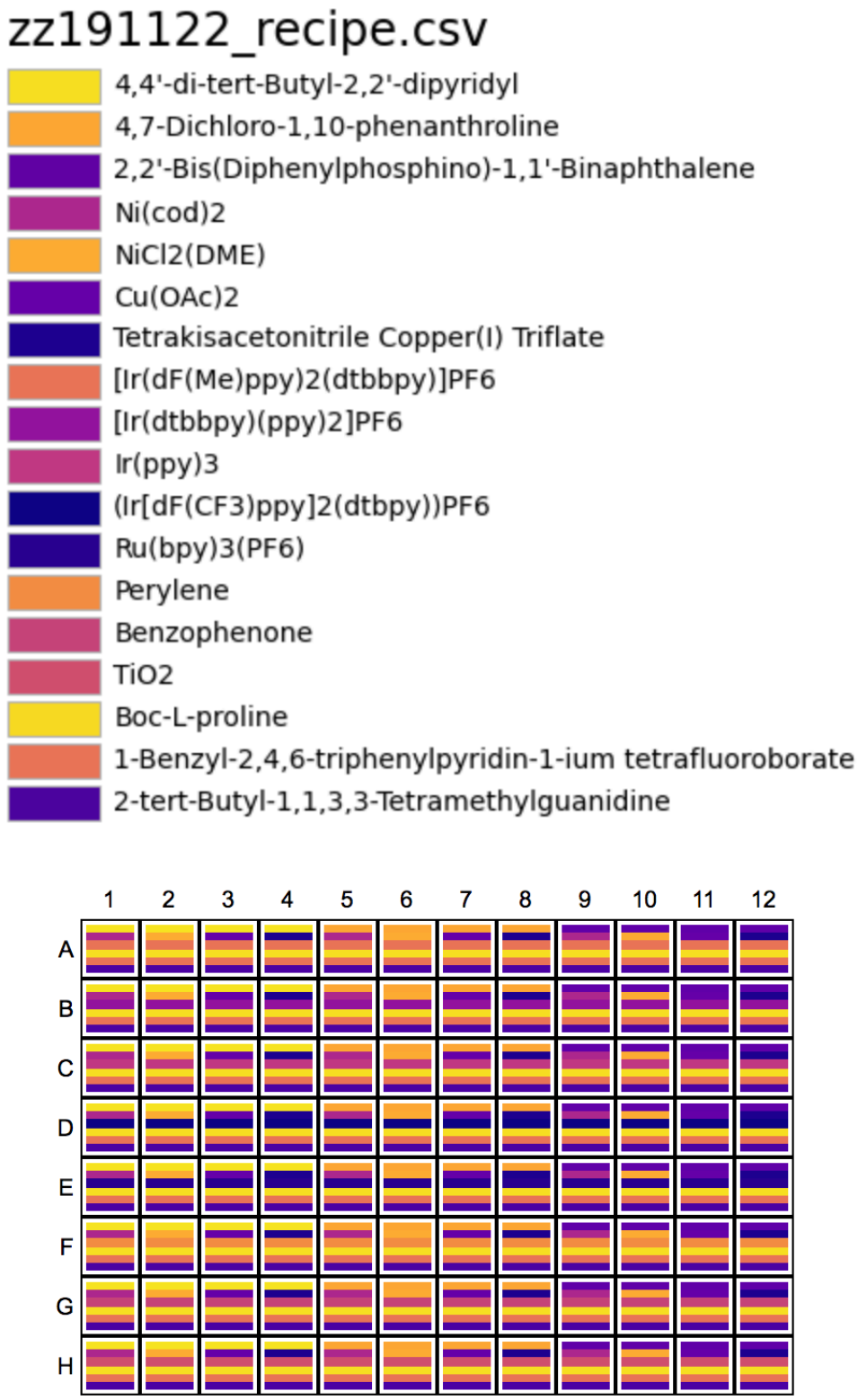
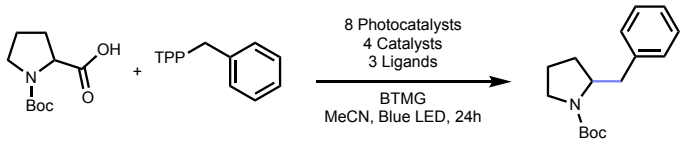


Figure S15. Recipe and grid of photocatalyst-catalyst-ligand screen.



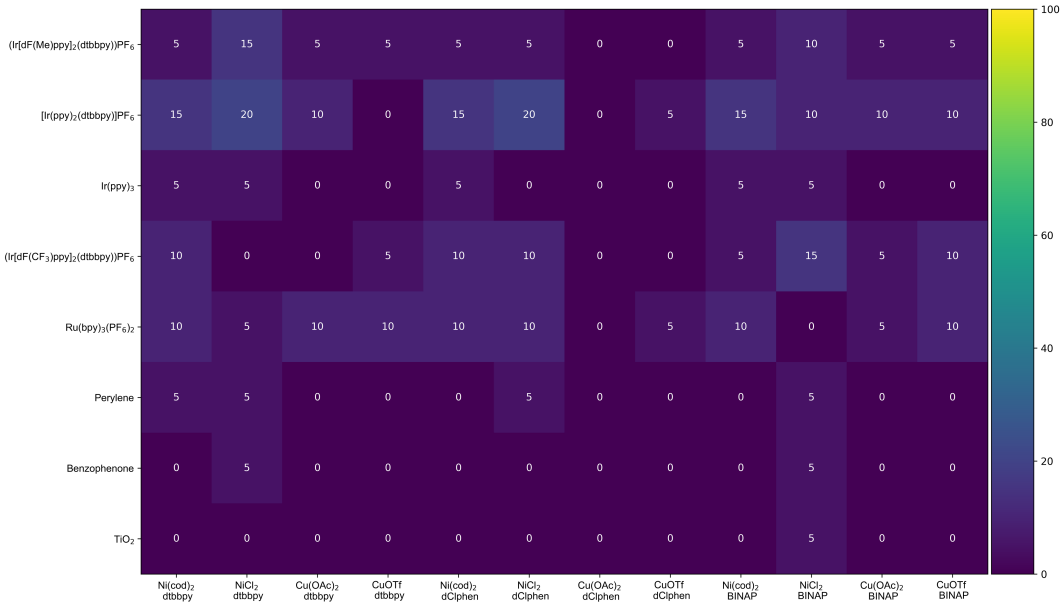


Figure S16. Heatmap of photocatalyst-catalyst-ligand screen. Following GP-1, stock solutions were prepared and dosed according to the concentrations and well locations in **Table S7**. Screen performed at 25 ºC in MeCN under blue LED stirring at 300 rpm for 24 h.

Reagents	C_{stock} (M)	V_{dose} (µL)	Wells
Benzyltrimethylammonium triflate	0.60	17	A3-6-H3-6 A9,10-H9,10 A12-H12
Benzyl Katritzky salt	0.60	17	A1,2-H1,2 A7,8-H7,8 A11-H11
Tos-Pro-OH	0.60	17	A1-4-H1-4
Boc-Pro-OH	0.60	17	A5,6-H5,6
1-Tosylpiperidine-4-carboxylic acid	0.60	17	A7-10-H7-10
Potassium (*tert*-butoxycarbonyl)prolinate	0.60	17	A11,12-H11,12
2-^{t}Bu-1,1,3,3-tetramethylguanidine	0.60	17	A1,3,5,7,9- H1,3,5,7,9
K_2CO_3	1.2	17	A2,4,6,8,10- H2,4,6,8,10
Blank	-	17	A11,12-H11,12
$Ni(cod)_2$	0.12	17	A,B,E,F1-12
$NiBr_2$•glyme	0.12	17	C,D,G,H1-12
4,4'-di-^{t}Bu-2,2'-dipyridyl	0.18	17	A,C,E,G1-12
Triphenylphosphine	0.18	17	B,D,F,H1-12
$(Ir[dF(CF_3)ppy]_2(dtbpy))PF_6$	0.012	17	A-D1-12
$[Ir(ppy)_2](dtbpy))PF_6$	0.012	17	E-H1-12

Table S8. Photoredox screen including benzyltrimethylammonium triflate.

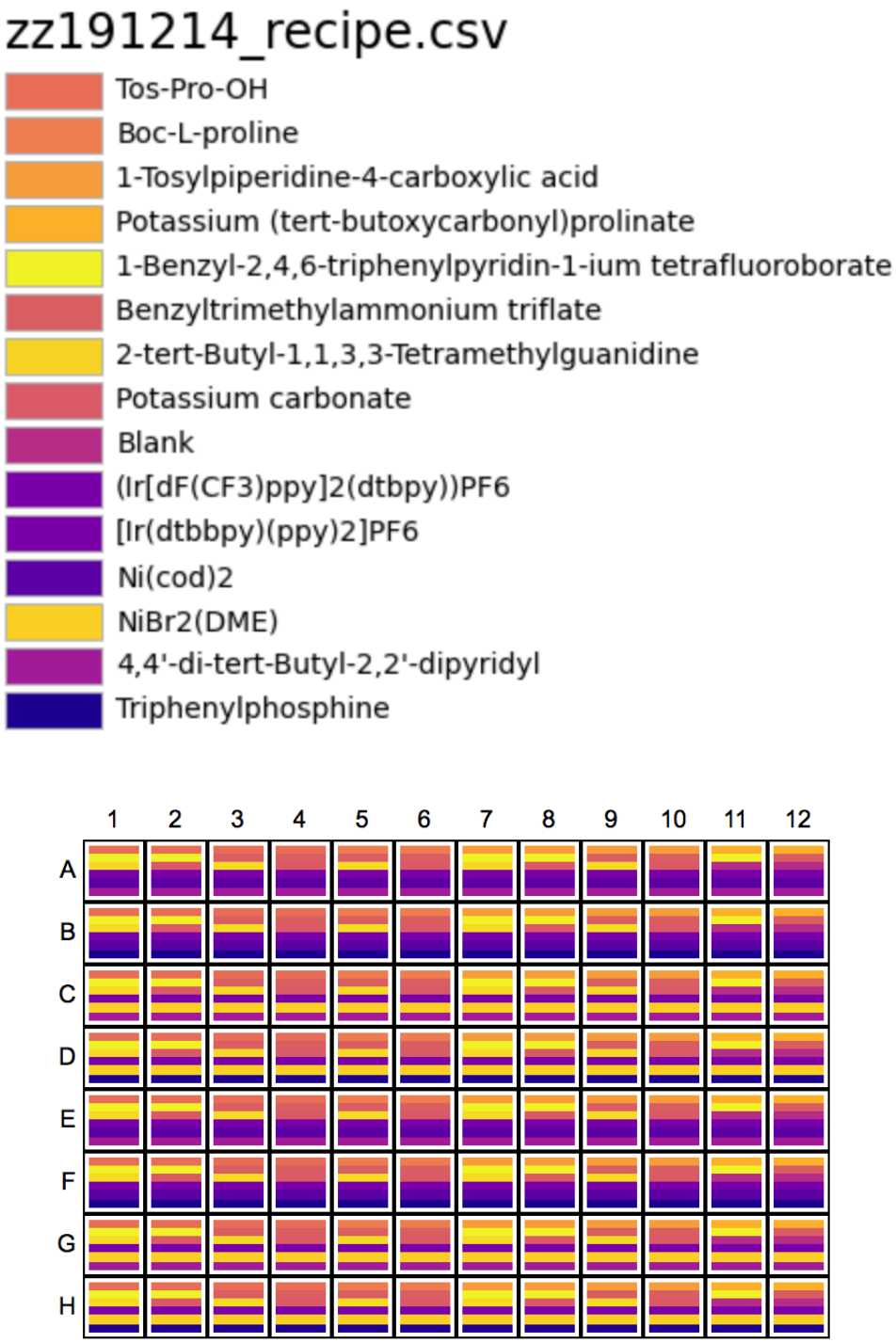


Figure S17. Recipe and grid of photoredox screen including benzyltrimethylammonium triflate.

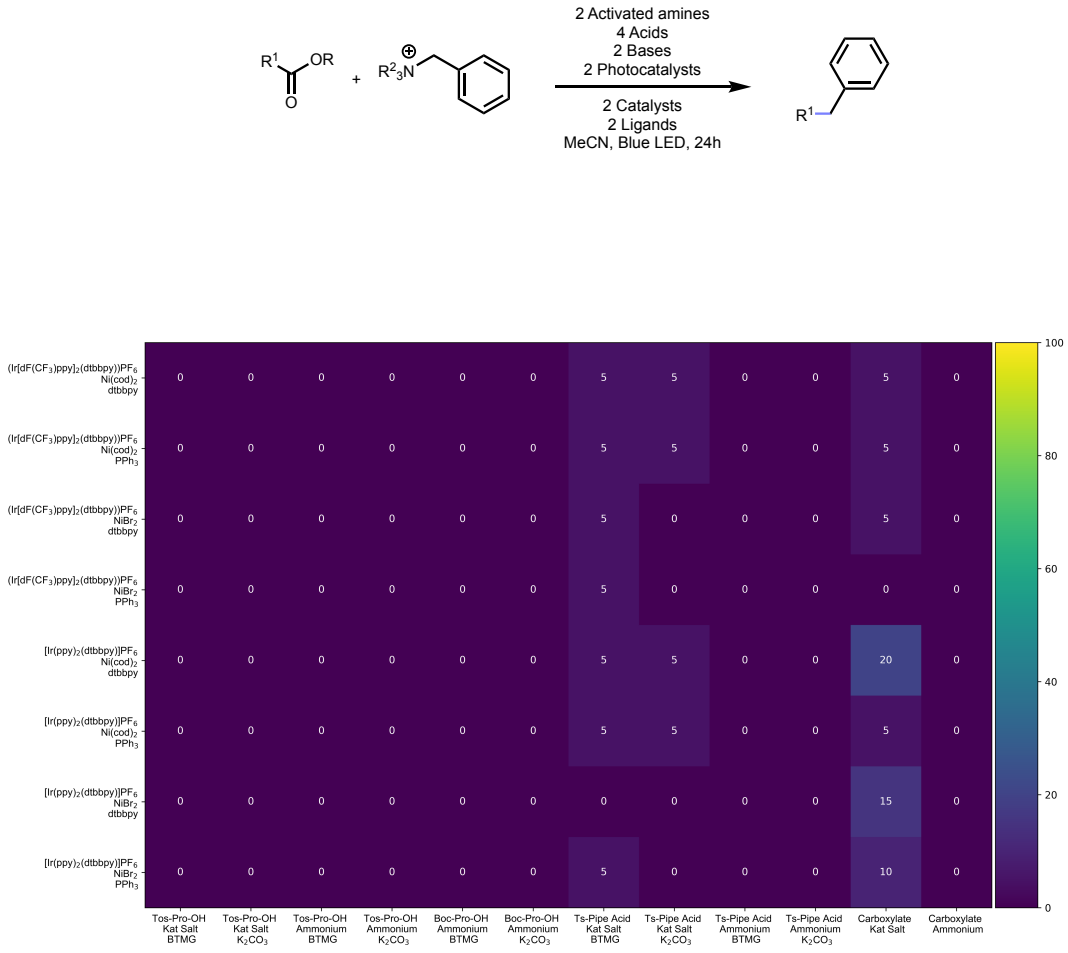


Figure S18. Heatmap of photoredox screen including benzyltrimethylammonium triflate. Following GP-1, stock solutions were prepared and dosed according to the concentrations and well locations in **Table S8**. Screen performed at 25 ºC in MeCN under blue LED stirring at 300 rpm for 24 h.

Reagents	C_{stock} (M)	V_{dose} (µL)	Wells
Potassium persulfate	0.80	13	All
Silver nitrate	0.160	13	All
Potassium phosphate	0.80	13	All
Boc-Pro-OH	0.80	13	A,B1-6
1-Tosylpiperidine-4-carboxylic acid	0.80	13	C,D1-6
Benzyl Katritzky salt	0.80	13	A,C1-6
Benzyltrimethylammonium Triflate	0.80	13	B,D1-6
$Ni(cod)_2$	0.16	13	A1,3,5-D1,3,5
$NiBr_2$•glyme	0.16	13	A2,3,6-D2,4,6
4,7-Diphenyl-1,10-phenanthroline	0.24	13	A1,2-D1,2
Tricyclohexylphosphine	0.24	13	A3,4-D3,4
1,3-Bis(2,4,6-trimethylphenyl)imidazolinium chloride	0.24	13	A5,6-D5,6

Table S9. Minisci type decarboxylation 24-well screen.

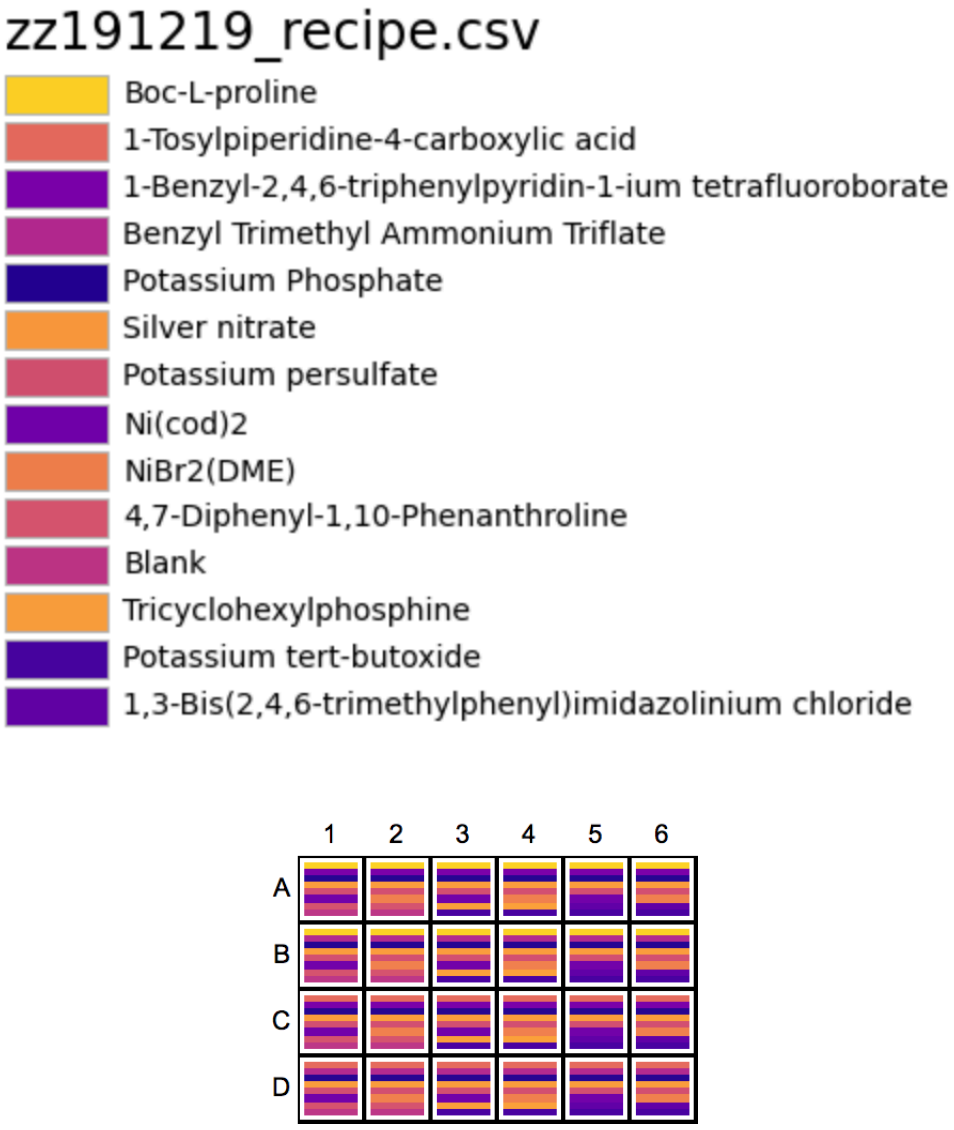
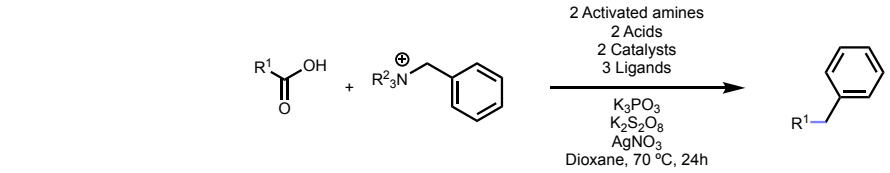


Figure S19. Recipe and grid of Minisci type decarboxylation 24-well screen.



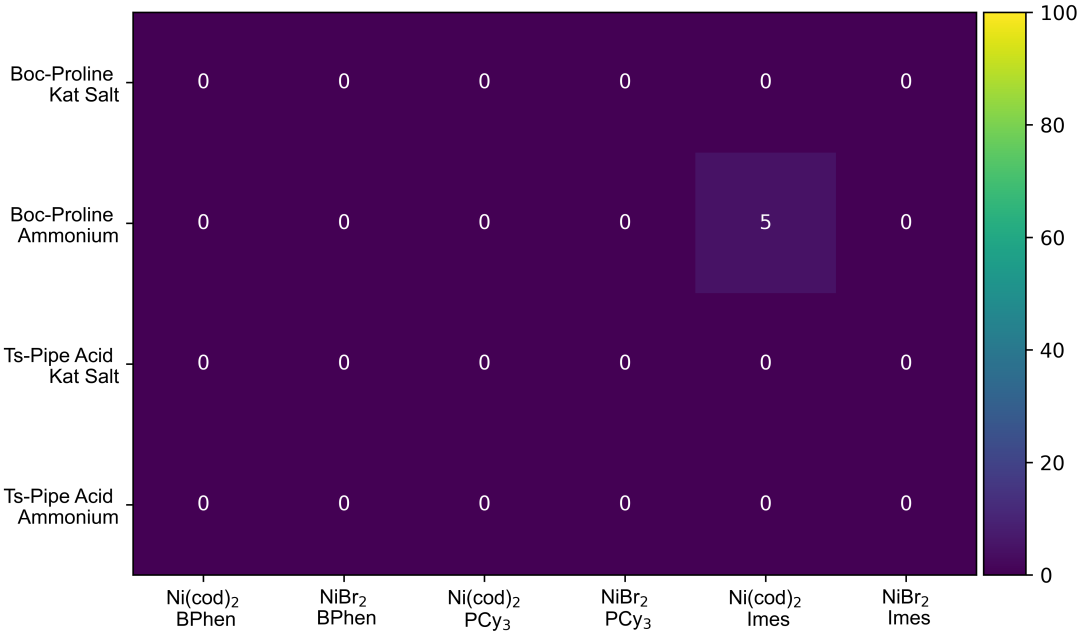


Figure S20. Heatmap of Minisci type decarboxylation 24-well screen. Following GP-1, stock solutions were prepared and dosed according to the concentrations and well locations in **Table S9**. Screen performed at 70 ºC in dioxane stirring at 300 rpm for 24 h.

Reagents	C_{stock} (M)	V_{dose} (µL)	Wells
Benzyl Katritzky salt	0.50	20	All
Boc-Pro-OH NHPI ester	0.50	20	All
Mn	1.0	20	All
NiF_2	0.10	20	A1-6
$NiBr_2$•glyme	0.10	20	B1-6
$NiCl_2$•glyme	0.10	20	C1-6
NiI_2	0.10	20	D1-6
4,4'-di-^{t}Bu-2,2'-dipyridyl	0.10	20	A1-D1
4,4'-Bis(trifluoromethyl)-2,2'-bipyridine	0.10	20	A2-D2
5,5'-Bis(trifluoromethyl)-2,2'-bipyridine	0.15	20	A3-D3
Dimethyl 2,2′-bipyridine-4,4′-dicarboxylate	0.15	20	A4-D4
4,4'-Dibromo-2,2'-bipyridine	0.15	20	A5-D5
2,2′-Bipyridine-5,5′-dicarboxylic Acid	0.15	20	A6-D6

Table S10. Catalyst-ligand 24-well screen.

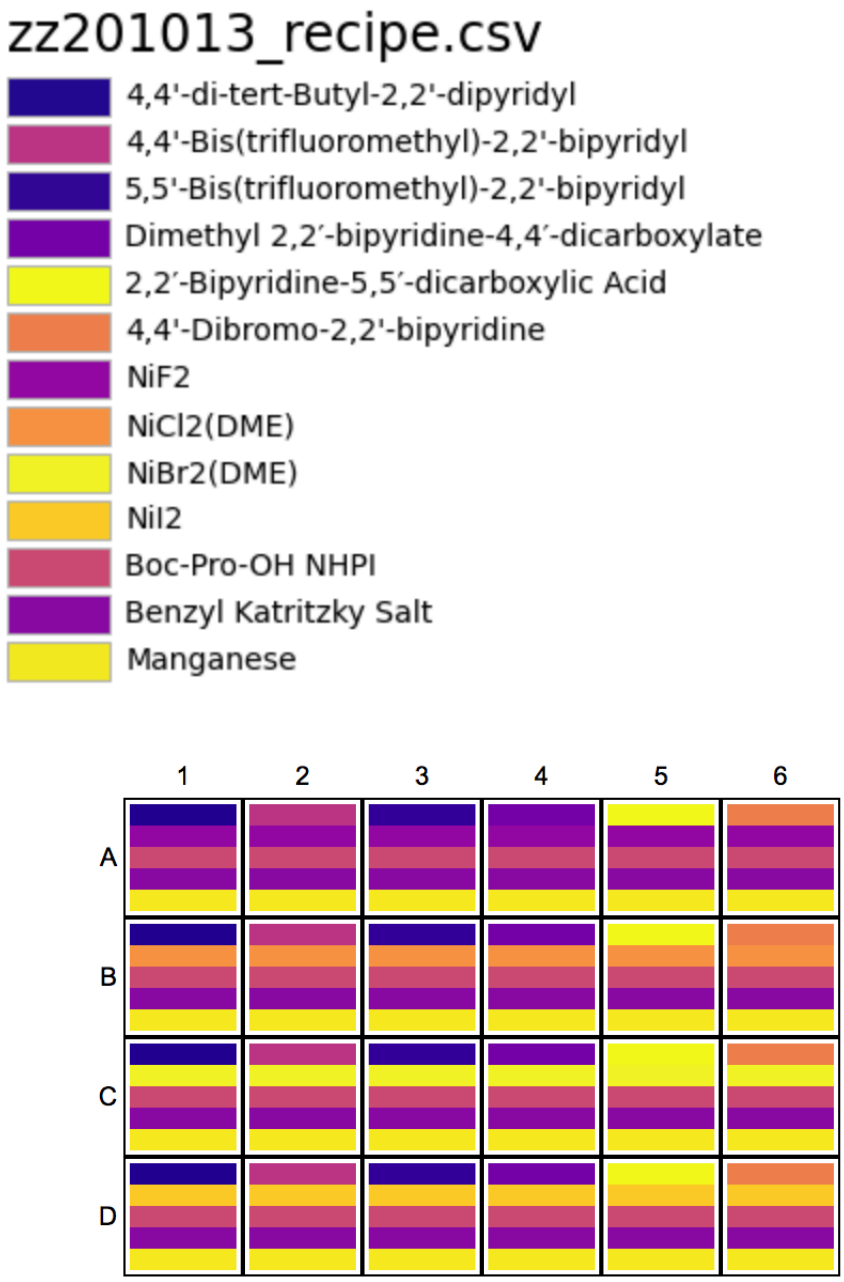
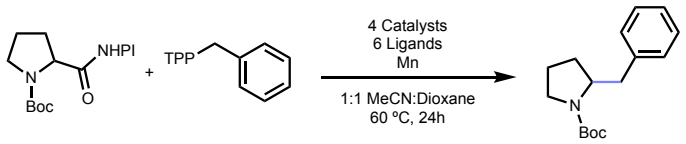


Figure S21. Recipe and grid of catalyst-ligand 24-well screen



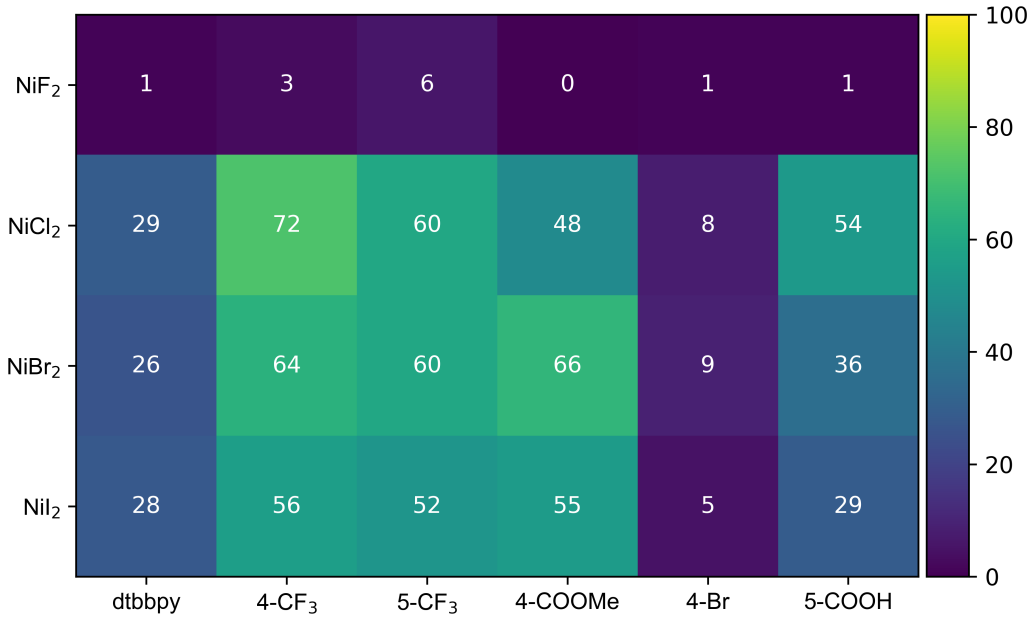
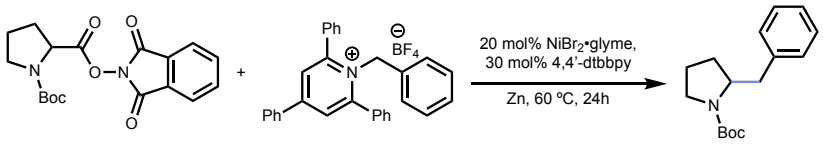
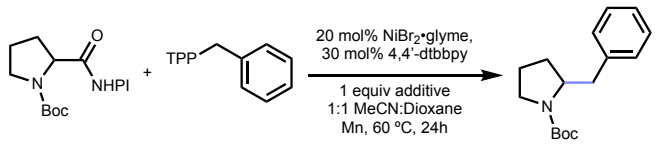


Figure S22. Heatmap of catalyst-ligand 24-well screen. Following GP-1, stock solutions were prepared and dosed according to the concentrations and well locations in **Table S10**. Screen performed at 60 ºC in 1:1 MeCN:dioxane stirring at 300 rpm for 24 h.



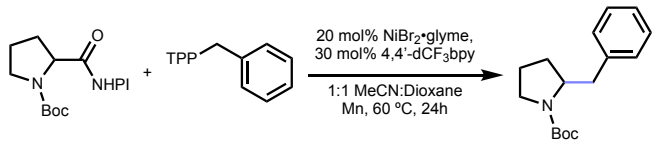
Solvents	(LC Yield) Isolated Yield
Dioxane	(36%)
MeCN	(25%)
DMF/Toluene/^{t}BuOH/H_2O	0%
DCE	(15%)
MeCN:Dioxane 3:7	(56%)
MeCN:Dioxane 1:1	(70%) 41%
MeCN:Dioxane 7:3	(61%)
THF	(30%)
MeCN:THF 1:1	(46%)
Diglyme	(10%)
MeCN:Diglyme 1:1	(60%)
DMF:Dioxane 1:1	11%
DMA: Dioxane 1:1	27%
NMP:Dioxane 1:1	32%
MeCN:Dioxane:^{i}PrOH 2:2:1	37%

Table S11. Solvent study. Reaction run with Boc-proline NHPI ester (**2**, 0.10 M, 0.050 mmol), benzyl Katritzky salt (**3**, 0.10 M), $NiBr_2$•glyme (0.020 M), dtbbpy (0.030 M), and Mn (0.20 M) in various solvents at 60 ºC for 24 hours. Reagents were first weighed into the reaction vessel, followed by addition of the solvent, and lastly placed on the heating plate.



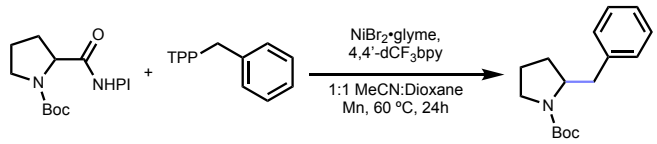
Additives	(LC Yield) Isolated Yield
None	(51%) 48%
CsF	0
AgF	(29%)
LiCl	(32%)
TMSCl	(36%)
KBr	(45%) 38%
Diethyl bromomalonate	(41%) 40%
NaI	(24%)
Bu_4NI	(20%)
CH_3COOH	0
DBU	0
^{i}PrOH	(42%) 33%

Table S12. Additive study. Reaction run with Boc-proline NHPI ester (**2**, 0.10 M, 0.050 mmol), benzyl Katritzky salt (**3**, 0.10 M), $NiBr_2$•glyme (0.020 M), dtbbpy (0.030 M), Mn (0.20 M) and indicated additive (0.10 M) in 1:1 MeCN:dioxane at 60 ºC for 24 hours. Reagents were first weighed into the reaction vessel, followed by addition of the solvent, and lastly placed on the heating plate.



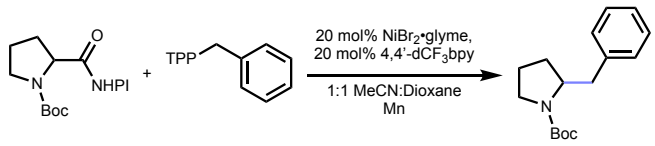
Premixed	First	Second	Last	(LC Yield) Isolated Yield
2, **3**, $NiBr_2$, **L1**, Mn	MeCN	Dioxane	–	(47%)
2, **3**, $NiBr_2$, **L1**, Mn	Dioxane	MeCN	–	(28%)
2, **3**, $NiBr_2$, **L1**	MeCN	Dioxane	Mn	(39%)
2, **3**, $NiBr_2$, **L1**	Dioxane	MeCN	Mn	(64%) 68%
2, **3**, $NiBr_2$, Mn	MeCN	Dioxane	**L1**	(32%)
2, **3**, $NiBr_2$, Mn	Dioxane	MeCN	**L1**	(24%)
$NiBr_2$, **L1**	MeCN	Dioxane	Mn, **2**, **3**	(51%)
$NiBr_2$, **L1**	Dioxane	MeCN	Mn, **2**, **3**	(61%) 61%

Table S13. Order of addition study. Reaction run with Boc-proline NHPI ester (**2**, 0.10 M, 0.050 mmol), benzyl Katritzky salt (**3**, 0.10 M), $NiBr_2$•glyme (0.020 M), dCF_3bpy (**L1**, 0.030 M), and Mn (0.20 M) in 1:1 MeCN:dioxane at 60 ºC for 24 hours. Premixed reagents were first weighed into the reaction vessel, followed by sequential addition of the two solvents with stirring for 10 minutes in between, and lastly the final reagent, as in the order shown above.



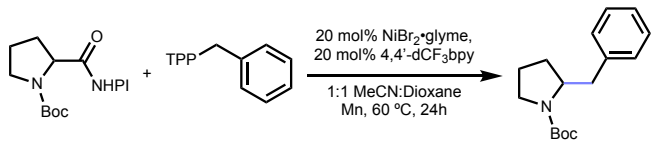
2 (eq.)	**3** (eq.)	Mn (eq.)	$NiBr_2$•glyme (mol%)	**L1** (mol%)	(LC Yield) Isolated Yield
1.0	1.0	2.0	20%	30%	68%
2.0	1.0	2.0	20%	30%	74%
1.0	2.0	2.0	20%	30%	48%
1.0	1.0	1.0	20%	30%	58%
1.0	1.0	4.0	20%	30%	61%
1.0	2.0	2.0	10%	30%	(48%)
1.0	2.0	2.0	20%	20%	66%

Table S14. Stoichiometry study. Reaction run with Boc-proline NHPI ester (**2**), benzyl Katritzky salt (**3**), $NiBr_2$•glyme, dCF_3bpy, and Mn at the indicated stoichiometry (0.10 M, 0.050 mmol limiting reagent) in 1:1 MeCN:dioxane at 60 ºC for 24 hours. Order of addition follows entry 4 of **Table S13**.



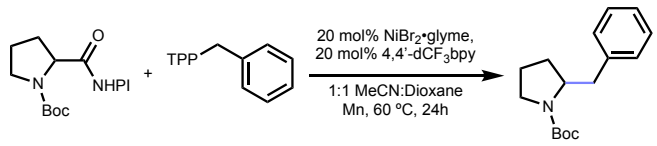
Temperature	Time	Yield
70 ºC	12h	55%
60 ºC	24h	68%
50 ºC	36h	65%
50 ºC	72h	70%

Table S15. Temperature study. Reaction run with Boc-proline NHPI ester (**2**, 0.10 M, 0.050 mmol), benzyl Katritzky salt (**3**, 0.10 M), $NiBr_2$•glyme (0.020 M), dCF_3bpy (0.020 M), and Mn (0.20 M) in 1:1 MeCN:dioxane at the temperature and time shown above. Order of addition follows entry 4 of **Table S13**.



Concentration	Yield
0.25 M	53%
0.10 M	68%
0.050 M	75%
0.025 M	81%

Table S16. Concentration study. Reaction run with Boc-proline NHPI ester (**2**, 1.0 eq., 0.050 mmol), benzyl Katritzky salt (**3**, 1.0 eq.), $NiBr_2$•glyme (20 mol%), dCF_3bpy (20 mol%), and Mn (2.0 eq.) in 1:1 MeCN:dioxane at the indicated concentration at 60 ºC for 24 hours. Order of addition follows entry 4 of **Table S13**.



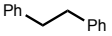
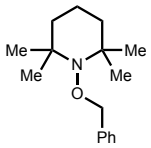
Variation	Result
No variation	81%
No NHPI ester	
No Katritzky salt	Side products
No Mn	No reaction
No $NiBr_2$•glyme	No reaction
No ligand	Trace product
Complete dark	77%
With TEMPO	No reaction 
With 1,5-hexadiene	82% (81% at 10 mol% Ni loading)
$NiCl_2$, ttbtpy in NMP (Watson-Weix)	No C-C or ketone product observed
BnBr instead of Katritzky salt	No product observed

Table S17. Control experiments. Reaction run with Boc-proline NHPI ester (**2**, 0.050 M, 0.050 mmol), benzyl Katritzky salt (**3**, 0.050 M), $NiBr_2$•glyme (0.010 M), dCF_3bpy (0.010 M), and Mn (0.10 M) in 1:1 MeCN:dioxane at 60 ºC for 24 hours with the shown variation. Order of addition follows entry 4 of **Table S13**.

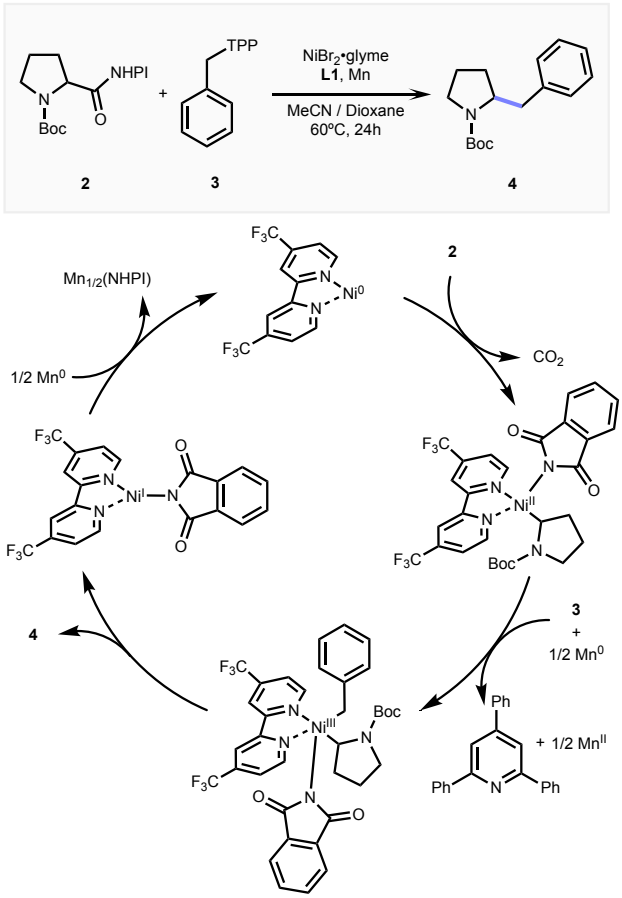
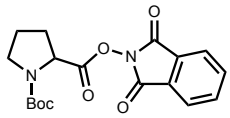


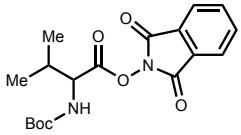
Figure S23. Proposed mechanism of the deaminative decarboxylative coupling.

General procedure for NHPI ester synthesis (GP-2)

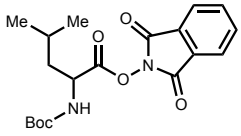
A 20 mL scintillation vial equipped with a magnetic stir bar was charged with carboxylic acid (5.0 mmol, 1.0 eq.), *N*-Hydroxyphthalimide (5.0 mmol, 815.7 mg, 1.0 eq.), and 4-Dimethylaminopyridine (0.50 mmol, 61.1 mg, 10 mol%). Dichloromethane (10 mL, 0.5 M) was added and the mixture was stirred for 5 minutes, after which *N*,*N*′-Diisopropylcarbodiimide (5.25 mmol, 822 µL, 1.05 eq.) was added dropwise. The vial was capped and the reaction stirred at 25 ºC for 12 h. The crude mixture was loaded on silica column and purified with 20-40% EtOAc/Hexanes to give the isolated product.



1-(*tert*-Butyl) 2-(1,3-dioxoisoindolin-2-yl) pyrrolidine-1,2-dicarboxylate (**2**)
Following GP-2, using Boc-Pro-OH (1.1 g) affords 1.4 g (80%) **2**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (dt, *J* = 7.4, 3.8 Hz, 2H), 7.80 (dq, *J* = 7.2, 4.3 Hz, 2H), 4.61 (dd, *J* = 8.8, 3.7 Hz, 1H), 3.63 (ddd, *J* = 10.4, 7.9, 4.5 Hz, 1H), 3.49 (dt, *J* = 10.4, 7.5 Hz, 1H), 2.44 (dtd, *J* = 13.2, 9.2, 7.2 Hz, 1H), 2.36 (ddt, *J* = 13.3, 10.8, 4.0 Hz, 1H), 2.18 – 2.03 (m, 1H), 1.98 (dddd, *J* = 11.9, 8.8, 7.1, 4.5 Hz, 1H), 1.52 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.80, 161.86, 153.65, 134.95, 129.06, 124.12, 81.28, 57.34, 46.42, 31.58, 28.25, 23.71. [Ref1] HRMS (ESI): calculated $C_{18}H_{20}N_2O_6$ [M-$C_5H_8O_2$+H]$^+$: 261.0875, found: 261.0870.

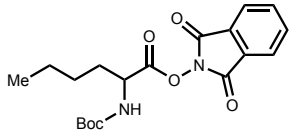


1,3-Dioxoisoindolin-2-yl (*tert*-butoxycarbonyl)valinate (**12**)
Following GP-2, using Boc-Val-OH (1.1 g) affords 0.95 g (52%) **12**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (dt, *J* = 7.6, 3.9 Hz, 2H), 7.79 (dd, *J* = 5.5, 3.1 Hz, 2H), 5.05 (d, *J* = 9.4 Hz, 1H), 4.66 (dd, *J* = 9.4, 4.9 Hz, 1H), 2.36 (dd, *J* = 12.6, 6.3 Hz, 1H), 1.50 (s, 9H), 1.11 (d, *J* = 8.0 Hz, 3H), 1.08 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.09, 161.69, 155.30, 134.97, 129.00, 124.16, 80.58, 57.23, 31.97, 28.43, 18.88, 17.52. [Ref2] HRMS (ESI): calculated $C_{18}H_{22}N_2O_6$ [M-$C_5H_8O_2$+H]$^+$: 263.1032, found: 263.1025.

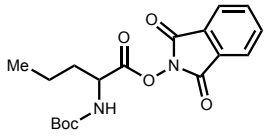


1,3-Dioxoisoindolin-2-yl (*tert*-butoxycarbonyl)leucinate (**13**)

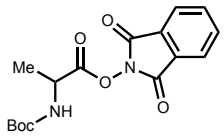
Following GP-2, using Boc-Leu-OH (1.2 g) affords 1.5 g (80%) **13**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.79 (dd, *J* = 5.5, 3.1 Hz, 2H), 4.91 (d, *J* = 8.9 Hz, 1H), 4.74 (dt, *J* = 12.9, 6.3 Hz, 1H), 1.98 – 1.80 (m, 2H), 1.71 (qd, *J* = 9.1, 8.7, 4.1 Hz, 1H), 1.50 (s, 9H), 1.10 – 0.98 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.11, 161.70, 155.04, 134.95, 129.03, 124.16, 80.66, 50.75, 42.03, 28.43, 24.89, 22.91, 22.01. [Ref3] HRMS (ESI): calculated $C_{19}H_{24}N_2O_6$ [M-$C_5H_8O_2$+H]$^+$: 277.1188, found: 277.1183.



1,3-Dioxoisoindolin-2-yl 2-((*tert*-butoxycarbonyl)amino)hexanoate (**14**)
Following GP-2, using Boc-Nle-OH (1.2 g) affords 1.1 g (60%) **14**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (dt, *J* = 7.6, 3.8 Hz, 2H), 7.79 (dd, *J* = 5.5, 3.1 Hz, 2H), 5.01 (d, *J* = 8.8 Hz, 1H), 4.73 (d, *J* = 7.1 Hz, 1H), 2.02 (dq, *J* = 14.3, 7.3, 6.9 Hz, 1H), 1.86 (dq, *J* = 14.5, 7.4 Hz, 1H), 1.65 – 1.35 (m, 13H), 0.95 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.72, 161.67, 155.03, 134.96, 129.01, 124.16, 80.62, 52.10, 32.81, 28.43, 27.18, 22.37, 13.97. HRMS (ESI): calculated $C_{19}H_{24}N_2O_6$ [M-$C_5H_8O_2$+H]$^+$: 277.1188, found: 277.1184.

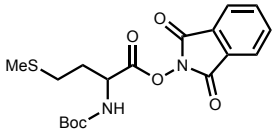


1,3-Dioxoisoindolin-2-yl 2-((*tert*-butoxycarbonyl)amino)pentanoate (**15**)
Following GP-2, using Boc-Nva-OH (1.1 g) affords 1.5 g (83%) **15**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.80 (dd, *J* = 5.4, 3.1 Hz, 2H), 5.00 (d, *J* = 8.8 Hz, 1H), 4.74 (q, *J* = 7.4 Hz, 1H), 1.99 (q, *J* = 9.9, 6.2 Hz, 1H), 1.84 (dq, *J* = 14.2, 7.4 Hz, 1H), 1.69 – 1.55 (m, 2H), 1.55 (s, 9H), 1.02 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.74, 161.69, 155.01, 134.97, 129.02, 124.17, 80.63, 51.94, 35.19, 28.44, 18.54, 13.78. HRMS (ESI): calculated $C_{18}H_{22}N_2O_6$ [M-$C_5H_8O_2$+H]$^+$: 263.1032, found: 263.1026.

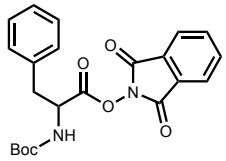


1,3-Dioxoisoindolin-2-yl (*tert*-butoxycarbonyl)alaninate (**16**)
Following GP-2, using Boc-Ala-OH (0.95 g) affords 1.3 g (75%) **16**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.80 (dd, *J* = 5.5, 3.1 Hz, 2H), 5.03 (d, *J* = 7.7 Hz, 1H), 4.84 – 4.72 (m, 1H), 1.63 (d, *J* = 7.2 Hz, 3H),

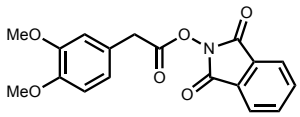
1.47 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.15, 161.64, 154.79, 134.98, 129.02, 124.19, 80.69, 47.87, 28.43, 19.09. [Ref4] HRMS (ESI): calculated $C_{16}H_{18}N_2O_6$ [M-$C_5H_8O_2$+H]$^+$: 235.0719, found: 235.0717.



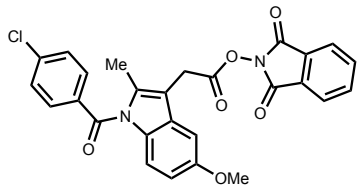
1,3-Dioxoisoindolin-2-yl (*tert*-butoxycarbonyl)methioninate (**17**)
Following GP-2, using Boc-Met-OH (1.3 g) affords 1.8 g (91%) **17**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.80 (dd, *J* = 5.5, 3.1 Hz, 2H), 5.19 (d, *J* = 8.5 Hz, 1H), 4.91 (s, 1H), 2.69 (td, *J* = 14.0, 13.5, 7.3 Hz, 2H), 2.39 – 2.26 (m, 1H), 2.20 (s, 1H), 2.17 (s, 3H), 1.50 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.23, 161.61, 154.95, 135.04, 128.97, 124.23, 80.87, 51.48, 32.56, 29.70, 28.42, 15.61. [Ref2] HRMS (ESI): calculated $C_{18}H_{22}N_2O_6S$ [M-$C_5H_8O_2$+H]$^+$: 295.0753, found: 295.0747.



1,3-Dioxoisoindolin-2-yl (*tert*-butoxycarbonyl)phenylalaninate (**18**)
Following GP-2, using Boc-Phe-OH (1.3 g) affords 1.9 g (90%) **18**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 – 7.85 (m, 2H), 7.80 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.46 – 7.27 (m, 5H), 5.07 – 4.99 (m, 1H), 4.93 (d, *J* = 8.8 Hz, 1H), 3.36 (dd, *J* = 14.2, 6.0 Hz, 1H), 3.26 (dd, *J* = 14.2, 6.0 Hz, 1H), 1.44 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.77, 161.59, 154.77, 134.99, 134.84, 129.88, 128.97, 128.84, 127.51, 124.20, 80.66, 52.82, 38.38, 28.37. [Ref2] HRMS (ESI): calculated $C_{22}H_{22}N_2O_6$ [M-$C_5H_8O_2$+H]$^+$: 311.1032, found: 311.1028.



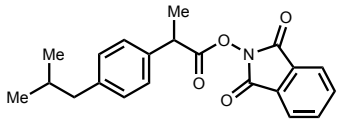
1,3-Dioxoisoindolin-2-yl 2-(3,4-dimethoxyphenyl)acetate (**19**)
Following GP-2, using 2-(3,4-dimethoxyphenyl)acetic acid (0.98 g) affords 1.2 g (72%) **19**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.82 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.00 – 6.92 (m, 2H), 6.89 (d, *J* = 8.1 Hz, 1H), 3.97 (s, 2H), 3.95 (s, 3H), 3.91 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.00, 162.00, 149.32, 148.76, 134.95, 129.04, 124.15, 124.04, 121.68, 112.26, 111.41, 56.09, 56.04, 37.50. [Ref5] HRMS (ESI): calculated $C_{18}H_{15}NO_6$ [M+Na]$^+$: 364.0797, found: 364.0790.



1,3-Dioxoisoindolin-2-yl 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)acetate (**20**)

Following GP-2, using Indomethacin (1.8 g) affords 0.91 g (36%) **20**.

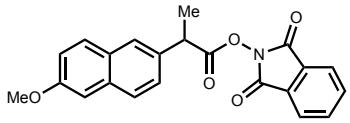
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.79 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.71 – 7.66 (m, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 2.5 Hz, 1H), 6.93 (d, *J* = 9.0 Hz, 1H), 6.71 (dd, *J* = 9.0, 2.5 Hz, 1H), 4.04 (s, 2H), 3.89 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.46, 167.17, 161.94, 156.38, 139.58, 136.61, 134.98, 133.83, 131.46, 130.90, 130.10, 129.33, 129.03, 124.18, 115.19, 112.62, 110.33, 100.78, 55.90, 27.29, 13.61. [Ref5] HRMS (ESI): calculated $C_{27}H_{19}ClN_2O_6$ $[M+H]^+$: 503.1010, found: 503.1016.



1,3-Dioxoisoindolin-2-yl 2-(4-isobutylphenyl)propanoate (**21**)

Following GP-2, using Ibuprofen (1.0 g) affords 1.3 g (71%) **21**.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.77 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.34 – 7.28 (m, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 4.10 (q, *J* = 7.2 Hz, 1H), 2.47 (d, *J* = 7.2 Hz, 2H), 1.87 (dp, *J* = 13.6, 6.8 Hz, 1H), 1.66 (d, *J* = 7.2 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.11, 162.03, 141.42, 135.70, 134.85, 129.76, 129.10, 127.40, 124.06, 45.21, 42.73, 30.30, 22.55, 19.17. [Ref6] HRMS (ESI): calculated $C_{21}H_{21}NO_4$ $[M+Na]^+$: 374.1368, found: 374.1356.

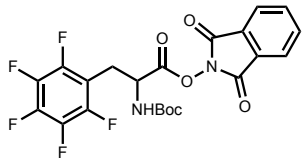


1,3-Dioxoisoindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate (**22**)

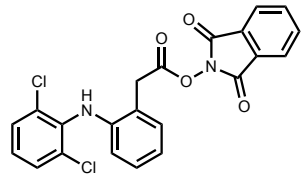
Following GP-2, using Naproxen (1.2 g) affords 1.4 g (72%) **22**.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 – 7.82 (m, 2H), 7.82 – 7.72 (m, 5H), 7.49 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.17 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.14 (d, *J* = 2.5 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 1H), 3.92 (s, 3H), 1.75 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.05, 161.98, 158.00, 134.83, 134.11, 133.56, 129.56, 129.06,

129.03, 127.67, 126.49, 126.02, 124.02, 119.32, 105.76, 55.44, 43.05, 19.14. [Ref11] HRMS (ESI): calculated $C_{22}H_{17}NO_5$ $[M+H]^+$: 376.1185, found: 376.1182.



1,3-Dioxoisoindolin-2-yl 2-((*tert*-butoxycarbonyl)amino)-3-(perfluorophenyl)propanoate (**S1**)
Following GP-2, using Boc-F_5Phe-OH (1.8 g) affords 1.8 g (72%) **S1**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.82 (dd, *J* = 5.5, 3.1 Hz, 2H), 5.14 (d, *J* = 9.2 Hz, 1H), 5.08 – 4.96 (m, 1H), 3.55 – 3.39 (m, 1H), 3.24 (dd, *J* = 14.2, 9.8 Hz, 1H), 1.39 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.95, 161.39, 154.67, 154.19, 146.75, 144.78, 141.81, 139.79, 138.65, 136.62, 135.12, 128.84, 124.30, 109.40, 81.16, 51.17, 28.12, 26.63. HRMS (ESI): calculated $C_{22}H_{17}N_2O_6F_5$ $[M-C_5H_8O_2+H]^+$: 401.0561, found: 401.0552.

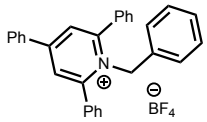


1,3-Dioxoisoindolin-2-yl 2-(2-((2,6-dichlorophenyl)amino)phenyl)acetate (**S2**)
Following GP-2, using Diclofenac (1.5 g) affords 1.9 g (88%) **S2**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.79 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.37 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.19 (td, *J* = 7.7, 1.6 Hz, 1H), 7.09 – 7.04 (m, 1H), 6.98 (t, *J* = 8.0 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 6.29 (s, 1H), 4.20 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.43, 161.79, 142.96, 138.26, 134.95, 131.21, 129.39, 129.04, 128.98, 128.92, 124.21, 123.52, 123.24, 119.97, 35.12. HRMS (ESI): calculated $C_{22}H_{14}Cl_2N_2O_4$ $[M+H]^+$: 441.0409, found: 441.0401.

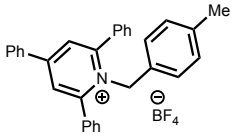
General procedure for Katritzky salt synthesis (GP-3)

A round-bottom flask equipped with a magnetic stir bar was charged with triphenylpyrylium (1.98 g, 5.0 mmol, 1.0 eq.). Ethanol (5 mL, 1.0 M) was added and amine (6.0 mmol, 1.2 eq.) was added while the mixture was stirred. Reaction was heated to reflux for 5 hours with stirring. After reaction was allowed to cool to room temperature, Et_2O (25 mL) was added and the mixture was stirred rigorously overnight for precipitation. The desired product was collected by

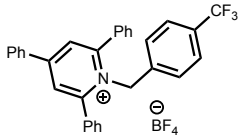
filtration and washed with Et_2O (25 mL). If no solid formed with Et_2O addition, the mixture was concentrated in vacuo and the residue was purified by chromatography with 1-20% Acetone/DCM to give isolated product.



1-Benzyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (**3**)
Following GP-3, using benzylamine (0.66 mL) affords 1.9 g (80%) **3**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 1.8 Hz, 2H), 7.86 – 7.81 (m, 2H), 7.65 (d, *J* = 7.3 Hz, 4H), 7.62 – 7.53 (m, 3H), 7.53 – 7.44 (m, 6H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.10 (dd, *J* = 8.3, 6.7 Hz, 2H), 6.47 (d, *J* = 7.6 Hz, 2H), 5.78 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.78, 156.46, 134.42, 134.00, 132.88, 132.52, 131.11, 129.95, 129.31, 129.20, 128.94, 128.36, 128.30, 126.74, 126.36, 58.36. [Ref7] HRMS (ESI): calculated $C_{30}H_{24}N$ $[M]^+$: 398.1909, found: 398.1929.

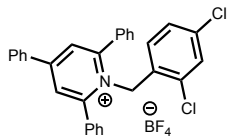


1-(4-Methylbenzyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (**5**)
Following GP-3, using 4-methylbenzylamine (0.76 mL) affords 2.3 g (90%) **5**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (s, 2H), 7.83 (dt, *J* = 6.9, 1.5 Hz, 2H), 7.65 (d, *J* = 7.3 Hz, 4H), 7.57 (ddd, *J* = 14.5, 7.9, 6.2 Hz, 3H), 7.53 – 7.43 (m, 6H), 6.90 (d, *J* = 7.9 Hz, 2H), 6.34 (d, *J* = 7.9 Hz, 2H), 5.73 (s, 2H), 2.24 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.74, 156.34, 138.33, 134.03, 132.93, 132.47, 131.38, 131.08, 129.94, 129.55, 129.28, 129.22, 128.29, 126.74, 126.27, 58.20, 21.19. [Ref8] HRMS (ESI): calculated $C_{31}H_{26}N$ $[M]^+$: 412.2065, found: 412.2048.

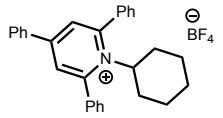


2,4,6-Triphenyl-1-(4-(trifluoromethyl)benzyl)pyridin-1-ium tetrafluoroborate (**6**)
Following GP-3, using 4-(trifluoromethyl)benzylamine (0.71 mL) affords 1.5 g (54%) **6**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (s, 2H), 7.87 – 7.81 (m, 2H), 7.65 (d, *J* = 7.4 Hz, 4H), 7.63 – 7.46 (m, 9H), 7.37 (d, *J* = 8.1 Hz, 2H), 6.64 (d, *J* = 8.0 Hz, 2H), 5.86 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.54, 156.87, 137.99, 133.80, 132.66, 132.59, 131.26, 129.90, 129.38, 129.17, 128.34, 126.88, 126.83, 125.90,

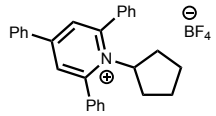
125.87, 125.84, 125.81, 124.75, 122.59, 57.81. [Ref8] HRMS (ESI): calculated $C_{31}H_{23}NF_3$ $[M]^+$: 466.1783, found: 466.1789.



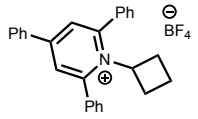
1-(2,4-Dichlorobenzyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (**7**)
Following GP-3, using 2,4-dichlorobenzylamine (0.67 mL) affords 2.6 g (95%) **7**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 1.9 Hz, 2H), 7.84 (dd, *J* = 7.2, 2.0 Hz, 2H), 7.72 – 7.64 (m, 4H), 7.64 – 7.56 (m, 3H), 7.56 – 7.48 (m, 6H), 7.12 (d, *J* = 2.1 Hz, 1H), 7.02 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.55 (d, *J* = 8.4 Hz, 1H), 5.82 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.06, 156.98, 135.18, 133.90, 132.99, 132.77, 132.69, 131.49, 130.56, 130.38, 130.01, 129.57, 129.09, 128.37, 127.69, 126.83, 57.09. HRMS (ESI): calculated $C_{30}H_{22}NCl_2$ $[M]^+$: 466.1129, found: 466.1126.



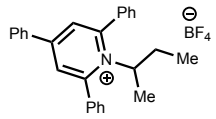
1-Cyclohexyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (**8**)
Following GP-3, using cyclohexylamine (0.68 mL) affords 1.8 g (75%) **8**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (s, 2H), 7.76 (m, 6H), 7.64 – 7.56 (m, 6H), 7.51 (ddt, *J* = 10.6, 8.5, 4.6 Hz, 3H), 4.63 (tt, *J* = 12.3, 2.9 Hz, 1H), 2.14 (d, *J* = 12.1 Hz, 2H), 1.59 (d, *J* = 14.0 Hz, 2H), 1.49 (qd, *J* = 12.3, 3.2 Hz, 2H), 1.35 (d, *J* = 13.3 Hz, 1H), 0.82 – 0.70 (m, 2H), 0.62 (dddd, *J* = 16.8, 13.1, 8.4, 3.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.20, 155.28, 134.26, 134.19, 132.00, 130.96, 129.72, 129.52, 129.03, 128.95, 128.44, 72.03, 33.73, 26.65, 24.80. [Ref9] HRMS (ESI): calculated $C_{29}H_{28}N$ $[M]^+$: 390.2222, found: 390.2205.



1-Cyclopentyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (**9**)
Following GP-3, using cyclopentylamine (0.59 mL) affords 1.8 g (80%) **9**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (s, 2H), 7.78 (ddt, *J* = 8.4, 6.0, 2.8 Hz, 6H), 7.59 (dd, *J* = 5.1, 1.9 Hz, 6H), 7.51 (ddd, *J* = 14.4, 7.9, 6.1 Hz, 3H), 5.06 (p, *J* = 9.0 Hz, 1H), 2.23 (dt, *J* = 15.1, 7.3 Hz, 2H), 2.03 (td, *J* = 13.5, 5.7 Hz, 2H), 1.31 – 1.10 (m, 2H), 1.05 – 0.86 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.84, 155.15, 134.27, 134.18, 132.06, 130.89, 129.75, 129.73, 129.11, 128.46, 128.39, 70.75, 33.91, 24.73. [Ref8] HRMS (ESI): calculated $C_{28}H_{26}N$ $[M]^+$: 376.2065, found: 376.2050.



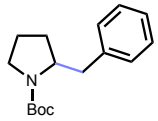
1-Cyclobutyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (**10**)
Following GP-3, using cyclobutylamine (0.51 mL) affords 1.4 g (64%) **10**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 – 7.85 (m, 4H), 7.85 – 7.76 (m, 4H), 7.62 – 7.47 (m, 9H), 5.64 – 5.51 (m, 1H), 1.81 (dt, *J* = 12.3, 6.1 Hz, 2H), 1.28 (d, *J* = 9.3 Hz, 1H), 1.23 – 1.11 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.43, 155.58, 134.19, 132.19, 131.59, 129.86, 129.67, 129.43, 128.19, 126.20, 126.17, 64.36, 33.19, 14.26. [Ref9] HRMS (ESI): calculated $C_{27}H_{24}N$ $[M]^+$: 362.1909, found: 362.1897.



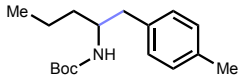
1-(*sec*-Butyl)-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (**11**)
Following GP-3, using *sec*-butylamine (0.61 mL) affords 1.1 g (49%) **11**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 – 7.74 (m, 2H), 7.74 – 7.62 (m, 6H), 7.56 (d, *J* = 8.8 Hz, 6H), 7.50 (d, *J* = 6.4 Hz, 1H), 7.44 (t, *J* = 7.9 Hz, 2H), 4.79 (p, *J* = 6.8 Hz, 1H), 1.86 (dp, *J* = 14.4, 7.3 Hz, 1H), 1.45 (dt, *J* = 14.9, 7.6 Hz, 1H), 1.38 (t, *J* = 5.5 Hz, 3H), 0.60 (q, *J* = 7.1, 6.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.32, 155.23, 134.05, 134.03, 133.98, 132.04, 130.99, 129.68, 129.37, 128.94, 128.38, 68.67, 30.17, 21.33, 11.29. [Ref10] HRMS (ESI): calculated $C_{27}H_{26}N$ $[M]^+$: 364.2065, found: 364.2048.

General procedure for decarboxylative deaminative coupling (GP4)

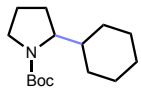
To a flame-dried 2-dram vial equipped with a magnetic stir bar in glovebox, NHPI ester (0.20 mmol, 1.3 eq.), Katritzky salt (0.15 mmol, 1.0 eq.), $NiBr_2$•glyme (9.3 mg, 0.030 mmol, 20mol%), and **L1** (8.8 mg, 0.030 mmol, 20mol%) were weighed. Dioxane (1.5 mL) was added and mixture was stirred for 10 minutes in glovebox before sequential addition of MeCN (1.5 mL) and Mn (16.5 mg, 0.30 mmol, 2 eq.). The vial was brought out of glovebox, sealed with parafilm and electrical tape, and heated at 60 ºC for 24h with stirring at 300 rpm. The reaction was quenched by saturated NaCl (1 mL), extracted with EtOAc (3 × 1 mL), dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by column chromatography (0-10% EtOAc/Hexanes) to give isolated product.



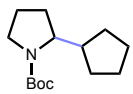
tert-Butyl 2-benzylpyrrolidine-1-carboxylate (**4,** 81%)
Following GP-4, using **2** (72 mg) and **3** (73 mg) affords 32 mg (81%) **4**. At 10 mol% Ni loading, 29 mg (74%) **4** is isolated.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (m, 2H), 7.24 – 7.14 (m, 3H), 4.09 – 3.92 (m, 1H), 3.43 – 3.22 (m, 2H), 3.21 – 2.98 (m, 1H), 2.62 – 2.46 (m, 1H), 1.81 – 1.66 (m, 4H), 1.51 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.56, 139.24, 129.40, 128.42, 126.22, 79.27, 58.89, 46.32, 40.61, 29.66, 28.63, 22.66. HRMS (ESI): calculated $C_{16}H_{23}NO_2$ [M- C_4H_8+H]$^+$: 206.1181, found: 206.1171.



tert-Butyl (1-(*p*-tolyl)pentan-2-yl)carbamate (**23,** 66%)
Following GP-4, using **15** (72 mg) and **5** (75 mg) affords 28 mg (66%) **23**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (d, *J* = 7.8 Hz, 2H), 7.06 (d, *J* = 7.9 Hz, 2H), 4.37 – 4.23 (m, 1H), 3.79 (s, 1H), 2.72 (qd, *J* = 13.6, 13.0, 6.1 Hz, 2H), 2.32 (s, 3H), 1.50 – 1.18 (m, 13H), 0.88 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.63, 135.78, 135.29, 129.56, 129.08, 79.03, 51.47, 41.00, 36.41, 28.54, 21.14, 19.36, 14.06. HRMS (ESI): calculated $C_{17}H_{27}NO_2$ [M- C_4H_8+H]$^+$: 222.1494, found: 222.1495

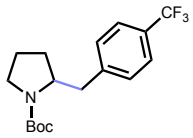


tert-Butyl 2-cyclohexylpyrrolidine-1-carboxylate (**24,** 47%)
Following GP-4, using **2** (72 mg) and **8** (72 mg) affords 18 mg (47%) **24**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.66 (q, *J* = 5.2 Hz, 1H), 3.52 – 3.38 (m, 1H), 3.19 (dt, *J* = 11.5, 5.8 Hz, 1H), 1.76 (tdd, *J* = 14.5, 10.4, 4.5 Hz, 6H), 1.70 – 1.54 (m, 4H), 1.45 (s, 9H), 1.27 – 1.05 (m, 3H), 0.96 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.24, 78.95, 61.98, 46.82, 41.32, 30.29, 28.70, 28.12, 27.21, 26.80, 26.71, 26.49, 24.11. HRMS (ESI): calculated $C_{15}H_{27}NO_2$ [M- C_4H_8+H]$^+$: 198.1494, found: 198.1489.

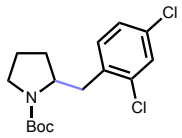


tert-Butyl 2-cyclopentylpyrrolidine-1-carboxylate (**25,** 51%)
Following GP-4, using **2** (72 mg) and **9** (69 mg) affords 18 mg (51%) **25**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87 – 3.77 (m, 1H), 3.45 (dt, *J* = 13.3, 7.1 Hz, 1H), 3.25 (td, *J* = 9.3, 7.5, 3.9 Hz, 1H), 2.05 (h, *J* = 8.1 Hz, 1H), 1.82 (m, 3H), 1.73 –

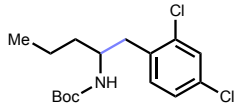
1.57 (m, 5H), 1.57 – 1.48 (m, 2H), 1.46 (s, 9H), 1.42 – 1.32 (m, 1H), 1.17 (dq, *J* = 12.2, 8.4, 7.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.35, 79.00, 60.86, 46.43, 44.50, 30.14, 29.02, 28.96, 28.71, 25.48, 25.23, 23.56. HRMS (ESI): calculated $C_{14}H_{25}NO_2$ [M- C_4H_8+H]$^+$: 184.1338, found: 184.1338.



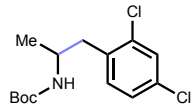
tert-Butyl 2-(4-(trifluoromethyl)benzyl)pyrrolidine-1-carboxylate (**26,** 60%)
Following GP-4, using **2** (72 mg) and **6** (83 mg) affords 30 mg (60%) **26**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (t, *J* = 7.3 Hz, 2H), 7.29 (m, 2H), 4.00 (m, 1H), 3.52 – 3.24 (m, 2H), 3.14 (m, 1H), 2.63 (p, *J* = 11.1 Hz, 1H), 1.97 – 1.59 (m, 4H), 1.49 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.57, 143.48, 129.79, 128.89, 125.45, 123.35, 79.60, 58.70, 46.42, 40.66, 29.96, 28.69, 22.80. HRMS (ESI): calculated $C_{17}H_{22}F_3NO_2$ [M- C_4H_8+H]$^+$: 274.1055, found: 274.1037.



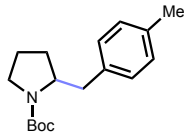
tert-Butyl 2-(2,4-dichlorobenzyl)pyrrolidine-1-carboxylate (**27,** 53%)
Following GP-4, using **2** (72 mg) and **7** (83 mg) affords 26 mg (53%) **27**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (s, 1H), 7.25 – 7.06 (m, 2H), 4.10 (m, 1H), 3.41 (p, *J* = 8.1, 6.3 Hz, 1H), 3.31 (dd, *J* = 17.6, 8.2 Hz, 1H), 3.08 (m, 1H), 2.93 – 2.69 (m, 1H), 1.94 – 1.71 (m, 3H), 1.67 (ddt, *J* = 12.3, 6.0, 2.7 Hz, 1H), 1.57 – 1.42 (m, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.64, 135.75, 135.17, 132.80, 132.52, 129.36, 127.17, 79.55, 57.26, 46.20, 37.18, 29.96, 28.64, 22.82. HRMS (ESI): calculated $C_{16}H_{21}Cl_2NO_2$ [M- C_4H_8+H]$^+$: 274.0402, found: 274.0392.



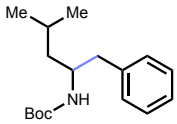
tert-Butyl (1-(2,4-dichlorophenyl)pentan-2-yl)carbamate (**28,** 61%)
Following GP-4, using **15** (72 mg) and **7** (83 mg) affords 31 mg (61%) **28**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (s, 1H), 7.21 – 7.09 (m, 2H), 4.33 (d, *J* = 9.3 Hz, 1H), 3.86 (d, *J* = 8.1 Hz, 1H), 2.91 (dd, *J* = 13.8, 5.5 Hz, 1H), 2.76 (dd, *J* = 13.9, 8.3 Hz, 1H), 1.55 – 1.16 (m, 13H), 0.90 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.45, 135.33, 135.20, 132.70, 132.26, 129.26, 127.01, 79.16, 50.91, 38.66, 37.29, 28.44, 19.39, 14.04. HRMS (ESI): calculated $C_{16}H_{23}NO_2Cl_2$ [M- C_4H_8+H]$^+$: 276.0558, found: 276.0547



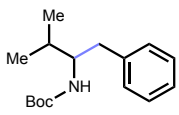
tert-Butyl (1-(2,4-dichlorophenyl)propan-2-yl)carbamate (**29,** 58%)
Following GP-4, using **16** (67 mg) and **7** (83 mg) affords 26 mg (58%) **29**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (s, 1H), 7.16 (s, 2H), 4.42 (s, 1H), 3.97 (p, *J* = 7.2 Hz, 1H), 2.85 (d, *J* = 6.6 Hz, 2H), 1.37 (s, 9H), 1.15 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.18, 135.21, 135.17, 132.84, 132.30, 129.33, 127.07, 79.32, 47.00, 39.90, 28.46, 20.76. HRMS (ESI): calculated $C_{14}H_{19}NO_2Cl_2$ [M- C_4H_8+H]$^+$: 248.0245, found: 248.0231



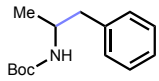
tert-Butyl 2-(4-methylbenzyl)pyrrolidine-1-carboxylate (**30,** 80%)
Following GP-4, using **2** (72 mg) and **5** (75 mg) affords 33 mg (80%) **30**. At 10 mol% Ni loading, 32 mg (77%) **30** is isolated.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (s, 4H), 4.01 – 3.91 (m, 1H), 3.32 (d, *J* = 6.4 Hz, 2H), 3.06 (dd, *J* = 13.0, 3.5 Hz, 1H), 2.50 (dd, *J* = 13.0, 9.5 Hz, 1H), 2.32 (s, 3H), 1.82 – 1.65 (m, 4H), 1.55 – 1.46 (m, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.56, 136.13, 135.63, 129.35, 129.06, 79.12, 58.90, 46.53, 39.72, 29.29, 28.64, 22.97, 21.06. HRMS (ESI): calculated $C_{17}H_{25}NO_2$ [M- $C_5H_8O_2$+H]$^+$: 176.1439.1338, found: 176.1433.



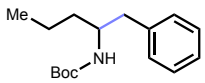
tert-Butyl (4-methyl-1-phenylpentan-2-yl)carbamate (**31,** 72%)
Following GP-4, using **13** (75 mg) and **3** (73 mg) affords 30 mg (72%) **31**. At 10 mol% Ni loading, 27 mg (64%) **31** is isolated.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (t, *J* = 7.5 Hz, 2H), 7.24 – 7.20 (m, 1H), 7.17 (d, *J* = 7.5 Hz, 2H), 4.25 (d, *J* = 9.0 Hz, 1H), 3.91 (h, *J* = 7.2 Hz, 1H), 2.76 (d, *J* = 6.2 Hz, 2H), 1.68 (qd, *J* = 13.4, 6.7 Hz, 1H), 1.40 (s, 9H), 1.24 (t, *J* = 7.1 Hz, 2H), 0.88 (dd, *J* = 9.1, 6.6 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.50, 138.40, 129.74, 128.35, 126.30, 79.04, 49.68, 43.62, 41.92, 28.54, 24.95, 23.36, 22.10. HRMS (ESI): calculated $C_{17}H_{27}NO_2$ [M- C_4H_8+H]$^+$: 222.1494 found: 222.1487.



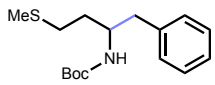
tert-Butyl (3-methyl-1-phenylbutan-2-yl)carbamate (**32,** 44%)
Following GP-4, using **12** (72 mg) and **3** (73 mg) affords 17 mg (44%) **32**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.25 (m, 2H), 7.19 (dt, *J* = 7.4, 3.3 Hz, 3H), 4.33 (d, *J* = 9.7 Hz, 1H), 3.75 (m, 1H), 2.79 (dd, *J* = 13.9, 6.3 Hz, 1H), 2.67 (dd, *J* = 14.0, 8.0 Hz, 1H), 1.72 (ddd, *J* = 13.8, 9.5, 6.2 Hz, 1H), 1.36 (s, 9H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.83, 138.89, 129.37, 128.44, 126.27, 79.02, 56.67, 38.82, 30.79, 28.50, 19.83, 17.37. HRMS (ESI): calculated $C_{16}H_{25}NO_2$ [M- C_4H_8+H]$^+$: 208.1338, found: 208.1324.



tert-Butyl (1-phenylpropan-2-yl)carbamate (**33,** 65%)
Following GP-4, using **16** (67 mg) and **3** (73 mg) affords 23 mg (65%) **33**.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 2H), 7.24 – 7.20 (m, 1H), 7.20 – 7.14 (m, 2H), 4.38 (s, 1H), 3.91 (s, 1H), 2.84 (dd, *J* = 13.4, 5.5 Hz, 1H), 2.65 (dd, *J* = 13.4, 7.4 Hz, 1H), 1.43 (s, 9H), 1.08 (d, *J* = 6.7, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.31, 138.38, 129.63, 128.43, 126.41, 79.23, 47.55, 43.14, 28.54, 20.29. HRMS (ESI): calculated $C_{14}H_{21}NO_2$ [M- C_4H_8+H]$^+$: 180.1025 found: 180.1033.

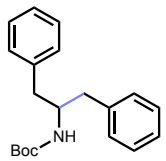


tert-Butyl (1-phenylpentan-2-yl)carbamate (**34,** 75%)
Following GP-4, using **15** (72 mg) and **3** (73 mg) affords 30 mg (75%) **34**. At 10 mol% Ni loading, 27 mg (68%) **34** is isolated.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (t, *J* = 7.5 Hz, 2H), 7.23 – 7.20 (m, 1H), 7.18 (d, *J* = 7.5 Hz, 2H), 4.29 (d, *J* = 8.9 Hz, 1H), 3.83 (s, 1H), 2.75 (m, 2H), 1.49 – 1.22 (m, 13H), 0.88 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.60, 138.47, 129.68, 128.40, 126.33, 79.09, 51.45, 41.53, 36.51, 28.54, 19.37, 14.06. HRMS (ESI): calculated $C_{16}H_{25}NO_2$ [M- C_4H_8+H]$^+$: 208.1338 found: 208.1319.

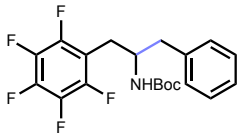


tert-Butyl (4-(methylthio)-1-phenylbutan-2-yl)carbamate (**35,** 42%)
Following GP-4, using **17** (79 mg) and **3** (73 mg) affords 18 mg (42%) **35**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (m, 2H), 7.24 – 7.20 (m, 1H), 7.19 – 7.14 (m, 2H), 4.37 (d, *J* = 8.9 Hz, 1H), 3.92 (s, 1H), 2.82 (t, *J* = 9.8 Hz, 1H), 2.76 (dd, *J* = 13.4, 6.9 Hz, 1H), 2.56 (ddd, *J* = 12.9, 9.5, 5.2 Hz, 1H), 2.49 (ddd, *J* = 13.0, 9.3, 6.6 Hz, 1H), 2.05 (s, 3H), 1.85 – 1.75 (m, 1H), 1.59 (dhept, *J* = 9.3, 5.2 Hz, 1H), 1.40 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.57, 137.99, 129.60, 128.55,

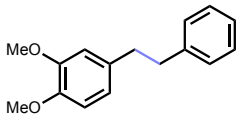
126.57, 79.37, 51.24, 41.50, 34.01, 30.98, 28.51, 15.72. HRMS (ESI): calculated $C_{16}H_{25}NO_2S$ [M- $C_5H_8O_2$+H]$^+$: 196.1160 found: 196.1150.



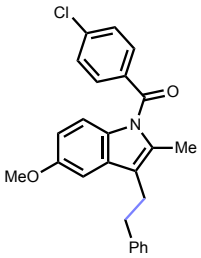
tert-Butyl (1,3-diphenylpropan-2-yl)carbamate (**36,** 64%)
Following GP-4, using **18** (82 mg) and **3** (73 mg) affords 30 mg (64%) **36**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (t, *J* = 7.4 Hz, 4H), 7.23 (d, *J* = 7.2 Hz, 2H), 7.20 (d, *J* = 7.7 Hz, 4H), 4.47 – 4.29 (m, 1H), 4.22 – 4.07 (m, 1H), 2.82 (dd, *J* = 13.8, 6.2 Hz, 2H), 2.79 – 2.67 (m, 2H), 1.36 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.40, 138.31, 129.54, 128.52, 126.49, 79.22, 52.66, 40.36, 28.45. HRMS (ESI): calculated $C_{20}H_{25}NO_2$ [M- C_4H_8+H]$^+$: 256.1338 found: 256.1329.



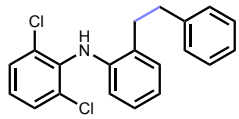
tert-Butyl (1-(perfluorophenyl)-3-phenylpropan-2-yl)carbamate (**37,** 51%)
Following GP-4, using **S1** (100 mg) and **3** (73 mg) affords 31 mg (51%) **37**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.5 Hz, 2H), 7.27 – 7.24 (m, 1H), 7.22 (t, *J* = 7.9 Hz, 2H), 4.40 (d, *J* = 9.3 Hz, 1H), 4.13 (s, 1H), 2.99 – 2.79 (m, 3H), 2.73 (dd, *J* = 13.9, 9.9 Hz, 1H), 1.31 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.27, 137.31, 129.31, 128.77, 126.93, 79.67, 51.45, 41.49, 28.24, 28.12. HRMS (ESI): calculated $C_{20}H_{20}F_5NO_2$ [M- C_4H_8+H]$^+$: 302.0968, found: 302.1410.



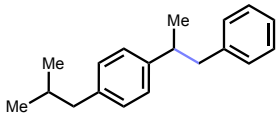
1,2-Dimethoxy-4-phenethylbenzene (**38,** 48%)
Following GP-4, using **19** (68 mg) and **3** (73 mg) affords 17 mg (48%) **38**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.23 – 7.15 (m, 3H), 6.80 (d, *J* = 8.1 Hz, 1H), 6.73 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.64 (d, *J* = 2.0 Hz, 1H), 3.87 (s, 3H), 3.83 (s, 3H), 2.95 – 2.83 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.78, 147.32, 141.88, 134.51, 128.67, 128.44, 126.02, 120.35, 111.97, 111.25, 56.03, 55.88, 38.29, 37.65. HRMS (ESI): calculated $C_{16}H_{18}O_2$ [M+H]$^+$: 243.1385, found: 243.1381.



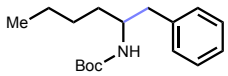
(4-Chlorophenyl)(5-methoxy-3-phenethyl-1*H*-indol-1-yl)methanone (**39,** 51%)
Following GP-4, using **17** (100 mg) and **3** (73 mg) affords 30 mg (51%) **39**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 – 7.55 (m, 2H), 7.47 – 7.43 (m, 2H), 7.30 – 7.25 (m, 2H), 7.24 – 7.19 (m, 1H), 7.16 – 7.11 (m, 2H), 7.04 (d, *J* = 9.0 Hz, 1H), 6.91 (d, *J* = 2.5 Hz, 1H), 6.70 (dd, *J* = 9.0, 2.6 Hz, 1H), 3.85 (s, 3H), 2.99 – 2.88 (m, 4H), 1.98 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.42, 156.07, 141.74, 139.05, 134.39, 131.26, 131.22, 131.12, 129.13, 128.83, 128.47, 126.17, 118.91, 115.18, 111.15, 101.50, 55.89, 35.91, 26.45, 13.25. HRMS (ESI): calculated $C_{24}H_{20}ClNO_2$ $[M+H]^+$: 404.1417, found: 404.1409.



2,6-Dichloro-*N*-(2-phenethylphenyl)aniline (**40,** 41%)
Following GP-4, using **S2** (88 mg) and **3** (73 mg) affords 21 mg (41%) **40**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.1 Hz, 2H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.24 (m, 3H), 7.18 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.07 (td, *J* = 7.7, 1.6 Hz, 1H), 7.02 (t, *J* = 8.1 Hz, 1H), 6.94 (t, *J* = 7.4 Hz, 1H), 6.48 (d, *J* = 8.0 Hz, 1H), 5.69 – 5.40 (m, 1H), 3.06 (q, *J* = 3.1 Hz, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.91, 141.34, 137.70, 130.31, 130.26, 129.81, 129.00, 128.66, 128.61, 126.74, 126.22, 124.61, 121.88, 116.85, 35.75, 33.76. HRMS (ESI): calculated $C_{20}H_{17}Cl_2N$ $[M+H]^+$: 343.0816, found: 343.0830.

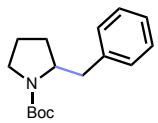


1-Isobutyl-4-(1-phenylpropan-2-yl)benzene (**41,** 46%)
Following GP-4, using **21** (70 mg) and **3** (73 mg) affords 17 mg (46%) **41**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (dd, *J* = 8.1, 6.6 Hz, 2H), 7.19 – 7.14 (m, 1H), 7.11 – 7.03 (m, 6H), 2.95 (ddd, *J* = 17.0, 13.3, 6.5 Hz, 2H), 2.78 – 2.67 (m, 1H), 2.44 (d, *J* = 7.2 Hz, 2H), 1.85 (dh, *J* = 13.5, 6.8 Hz, 1H), 1.22 (d, *J* = 6.7 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.38, 141.14, 139.42, 129.33, 129.14, 128.18, 126.83, 125.90, 45.33, 45.19, 41.59, 30.39, 22.55, 21.18. HRMS (ESI): calculated $C_{19}H_{24}$ $[M]^-$: 252.1878, found: 252.1869.



tert-Butyl (1-phenylhexan-2-yl)carbamate (**S3,** 72%)
Following GP-4, using **14** (75 mg) and **3** (73 mg) affords 30 mg (72%) **S3**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (t, *J* = 7.5 Hz, 2H), 7.23 – 7.13 (m, 3H), 4.29 (s, 1H), 3.81 (s, 1H), 2.76 (d, *J* = 6.6 Hz, 2H), 1.53 – 1.44 (m, 1H), 1.41 (s, 9H), 1.38 – 1.19 (m, 5H), 0.87 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.62, 138.50, 129.66, 128.39, 126.33, 79.09, 51.66, 41.50, 34.02, 28.53, 28.29, 22.66, 14.15. HRMS (ESI): calculated $C_{17}H_{27}NO_2$ [M- C_4H_8+H]$^+$: 222.1494 found: 222.1486.

Spectra



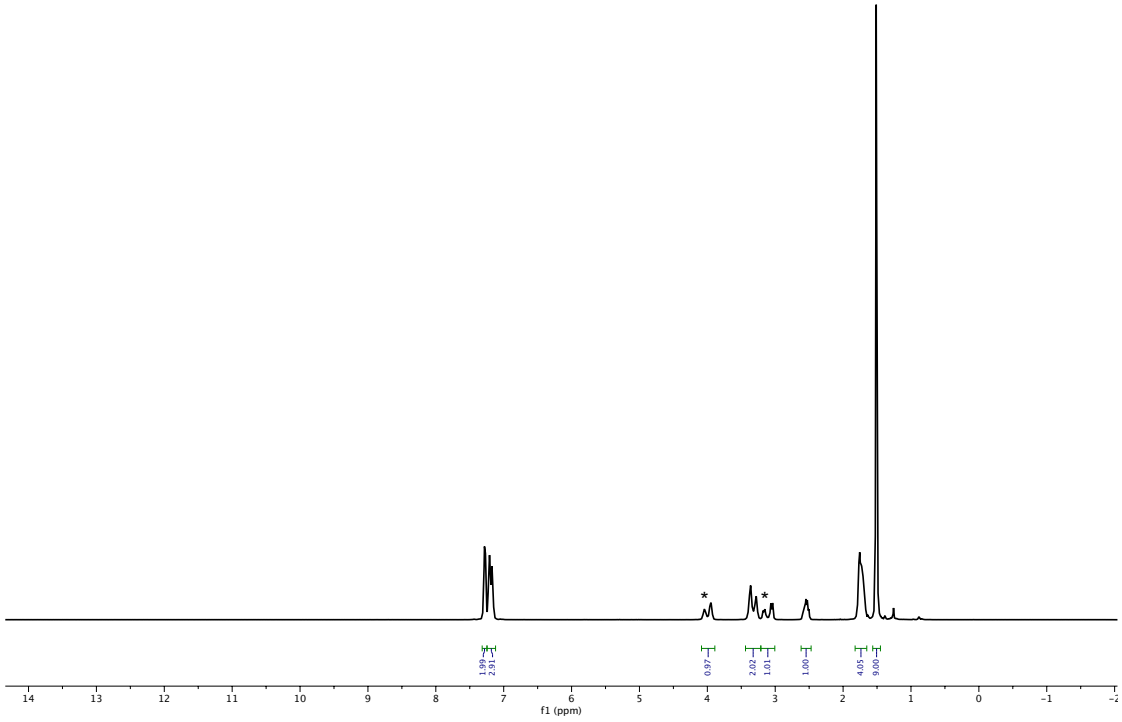


Figure S23. ^{1}H NMR of **4** in $CDCl_3$ at 25 ºC
*: Rotamer

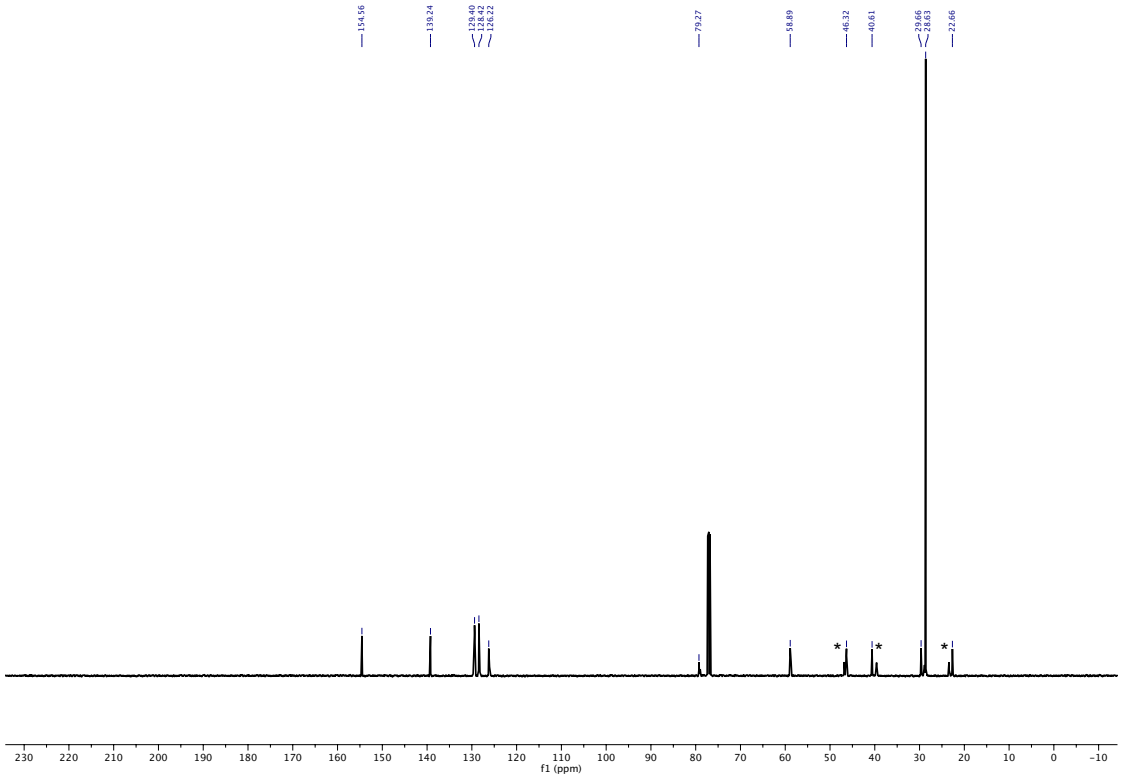
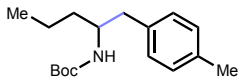


Figure S24. ^{13}C NMR of **4** in $CDCl_3$ at 25 ºC
*: Rotamer



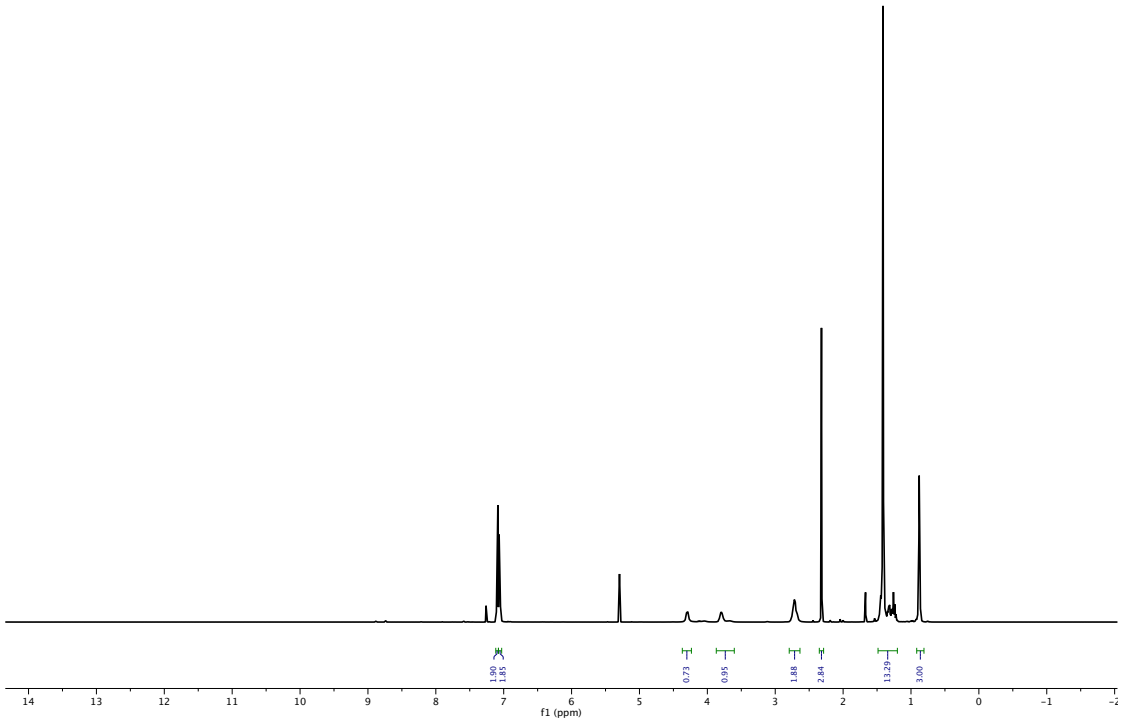


Figure S25. ^{1}H NMR of **23** in $CDCl_3$ at 25 ºC

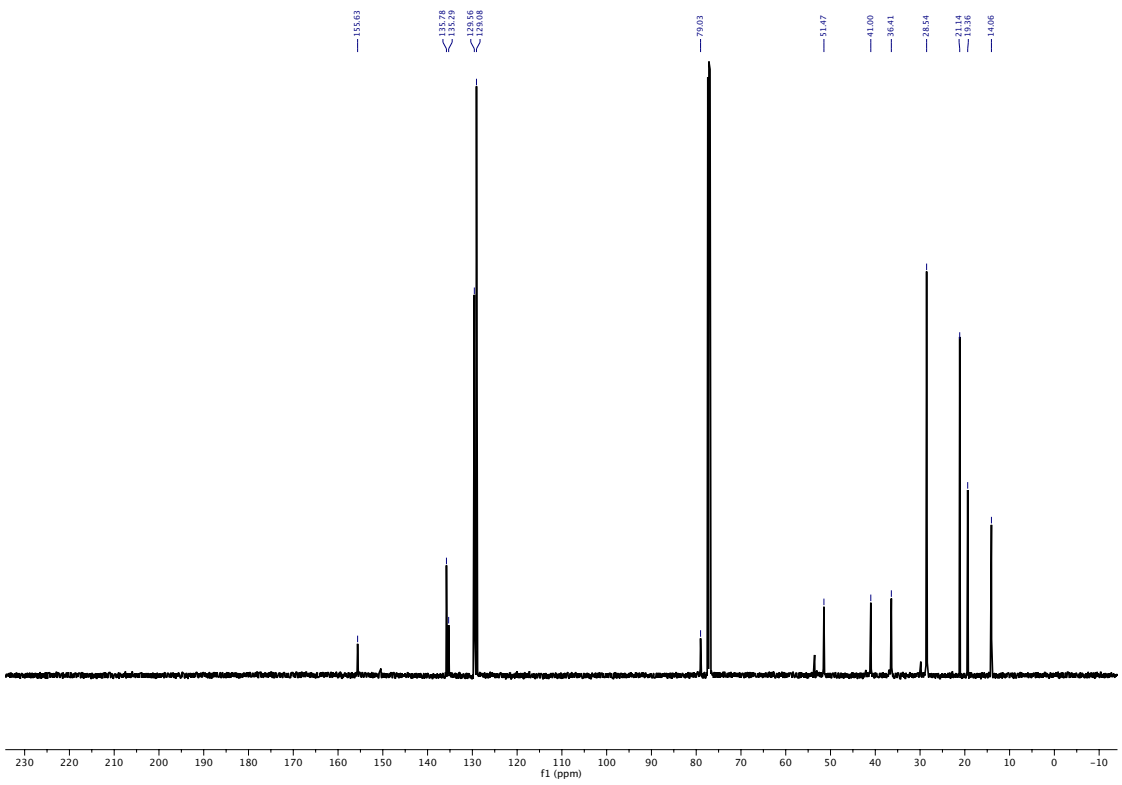


Figure S26. ^{13}C NMR of **23** in $CDCl_3$ at 25 ºC

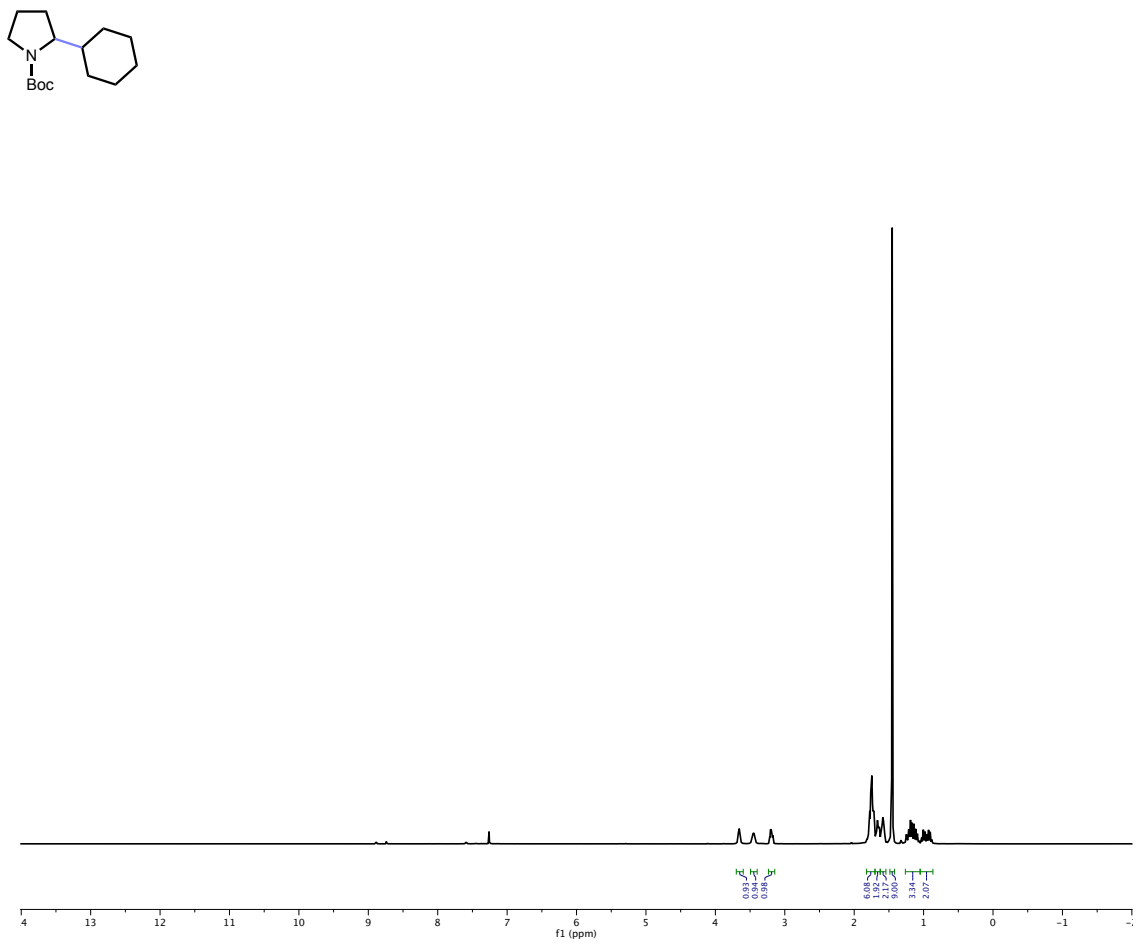


Figure S27. ^{1}H NMR of **24** in $CDCl_3$ at 25 ºC.

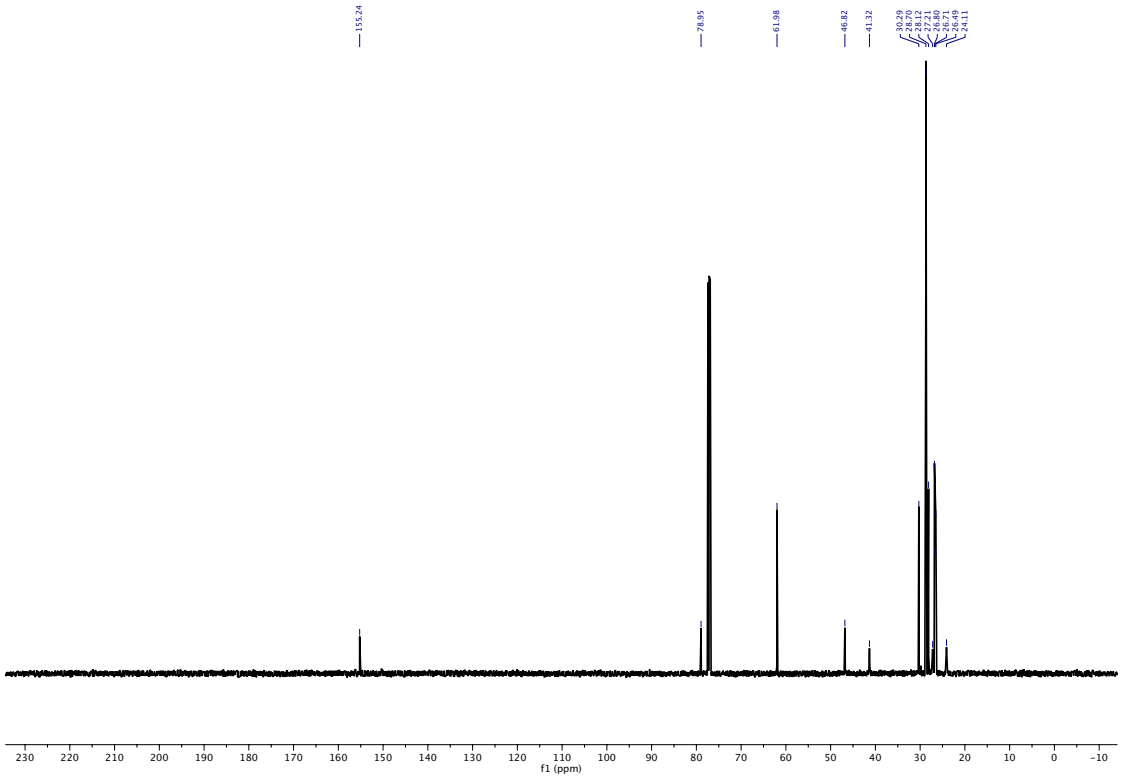
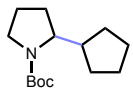


Figure S28. ^{13}C NMR of **24** in $CDCl_3$ at 25 ºC



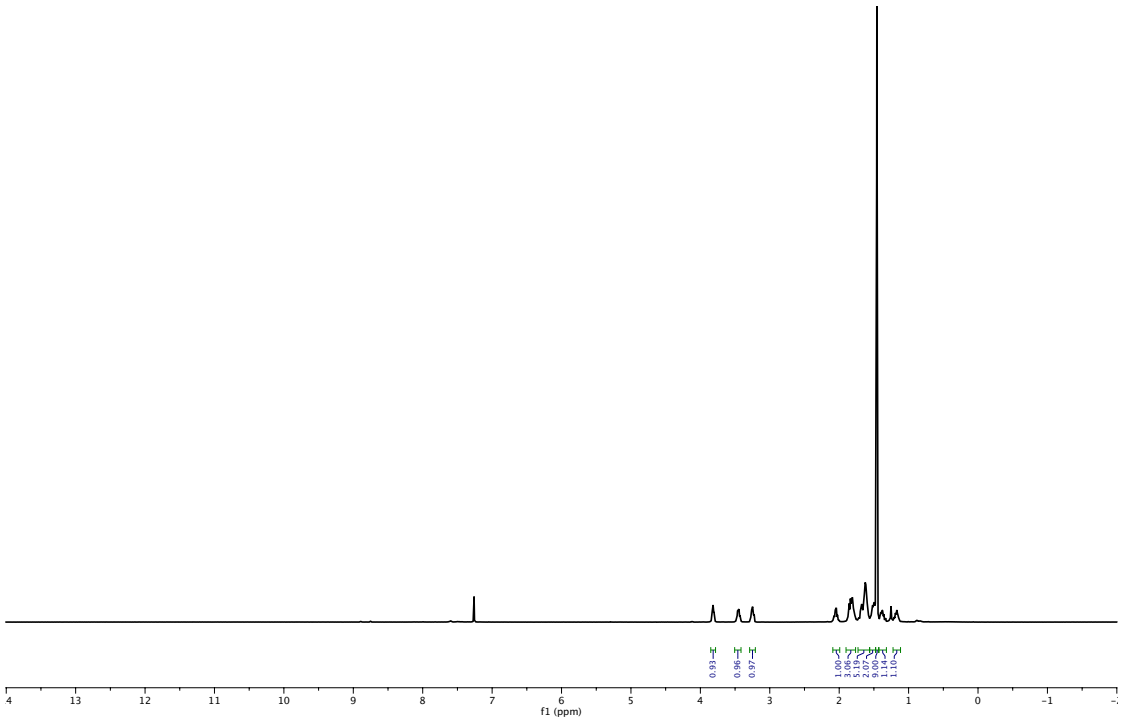


Figure S29. ^{1}H NMR of **25** in $CDCl_3$ at 25 ºC

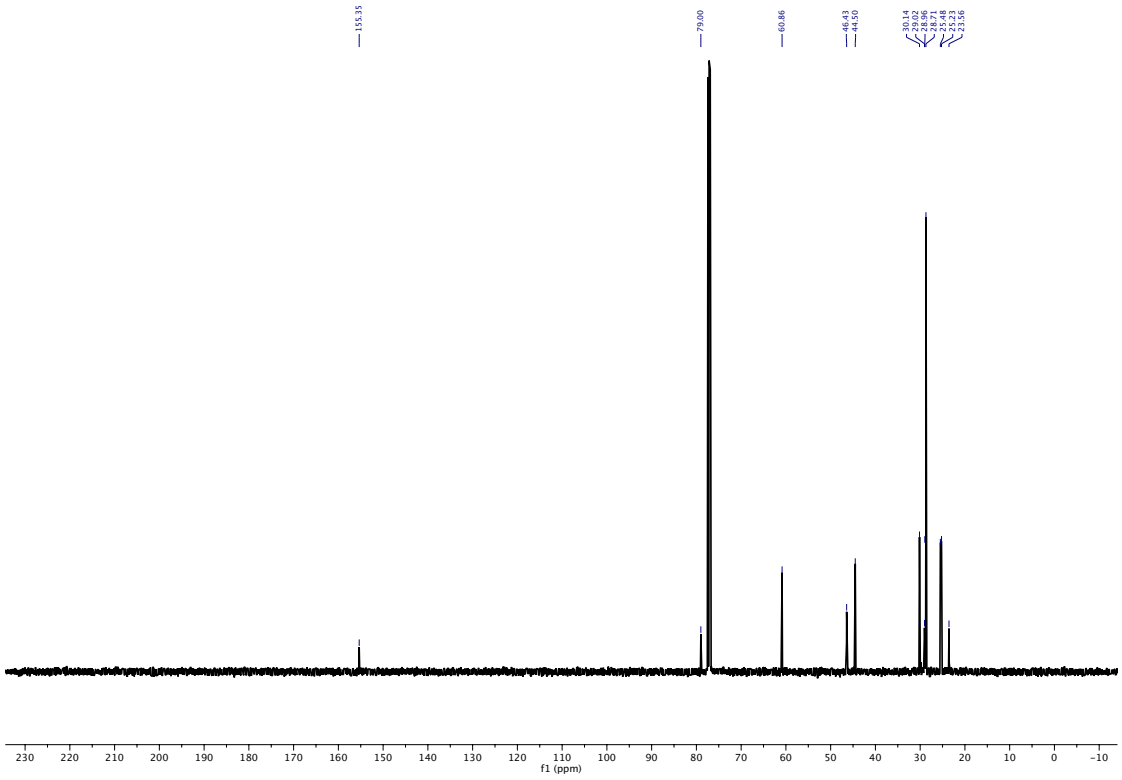


Figure S30. ^{13}C NMR of **25** in $CDCl_3$ at 25 ºC

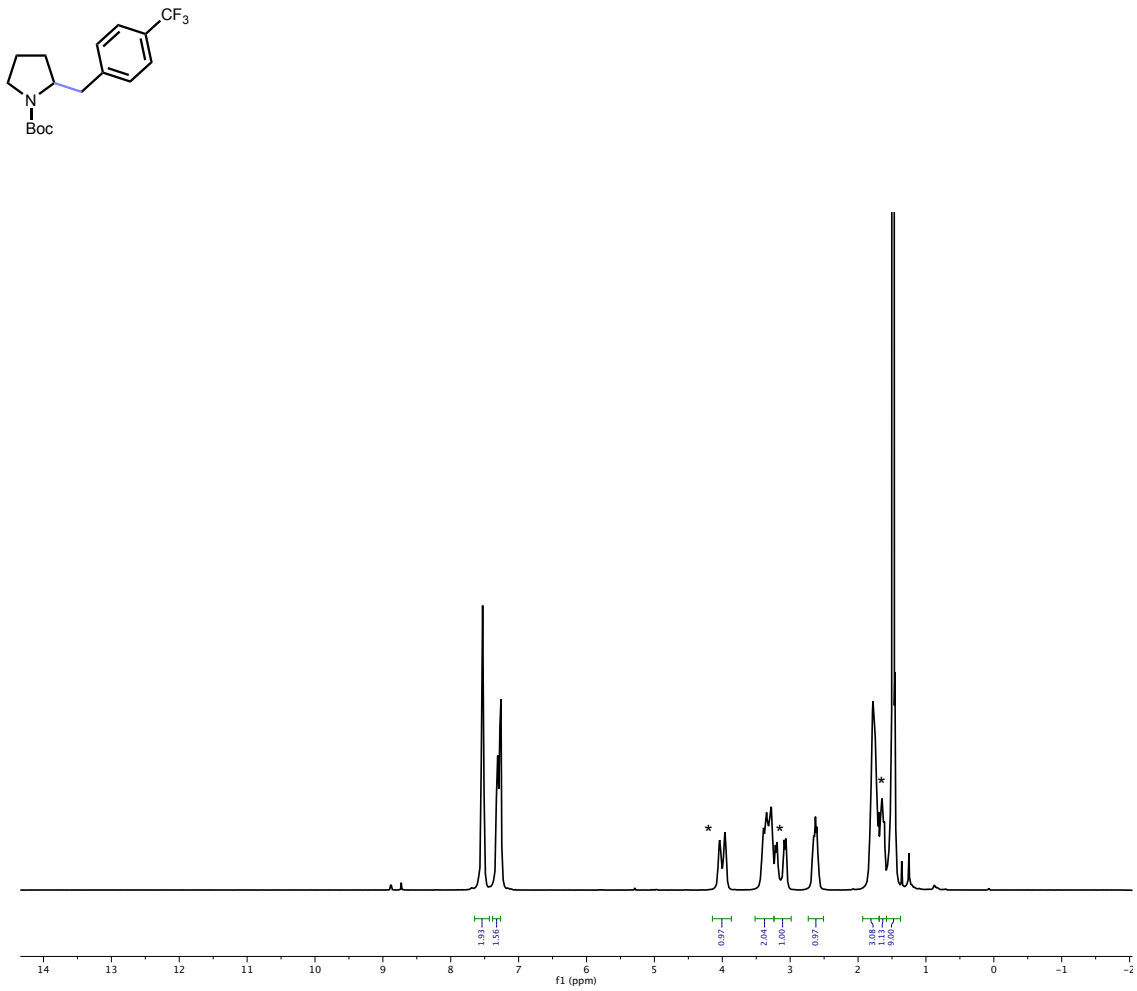


Figure S31. ^{1}H NMR of **26** in $CDCl_3$ at 25 ºC
*: Rotamer

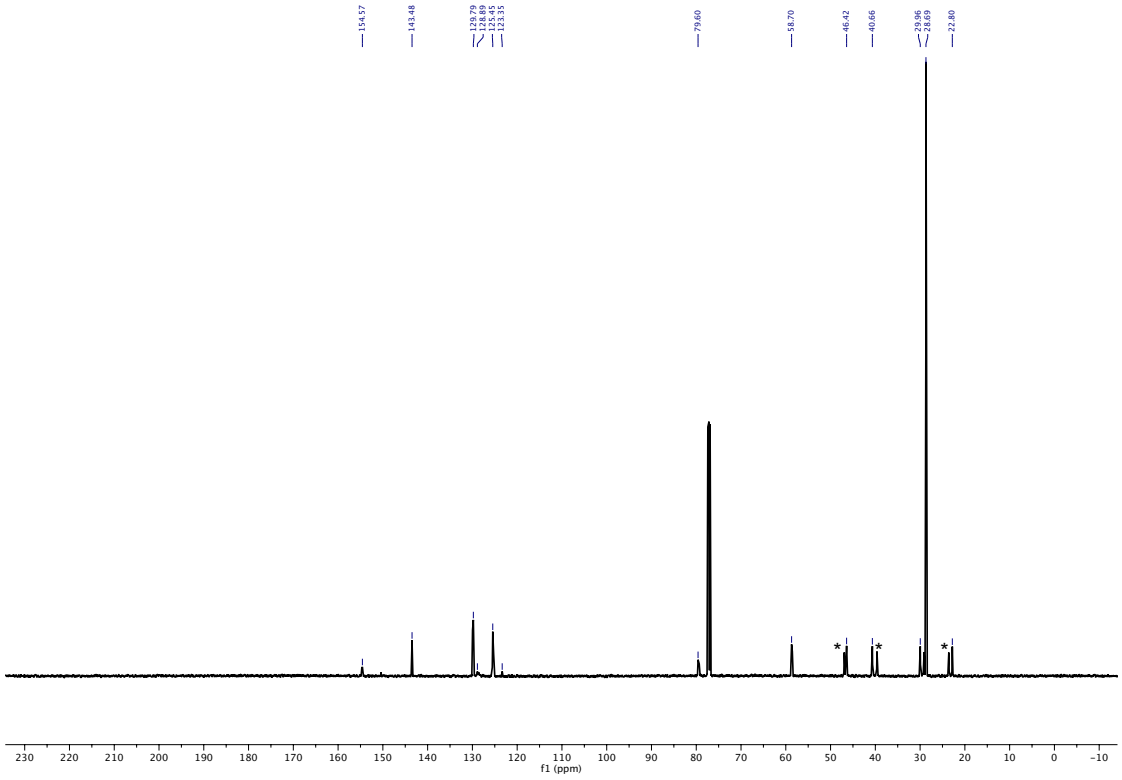


Figure S32. ^{13}C NMR of **26** in $CDCl_3$ at 25 ºC
*: Rotamer

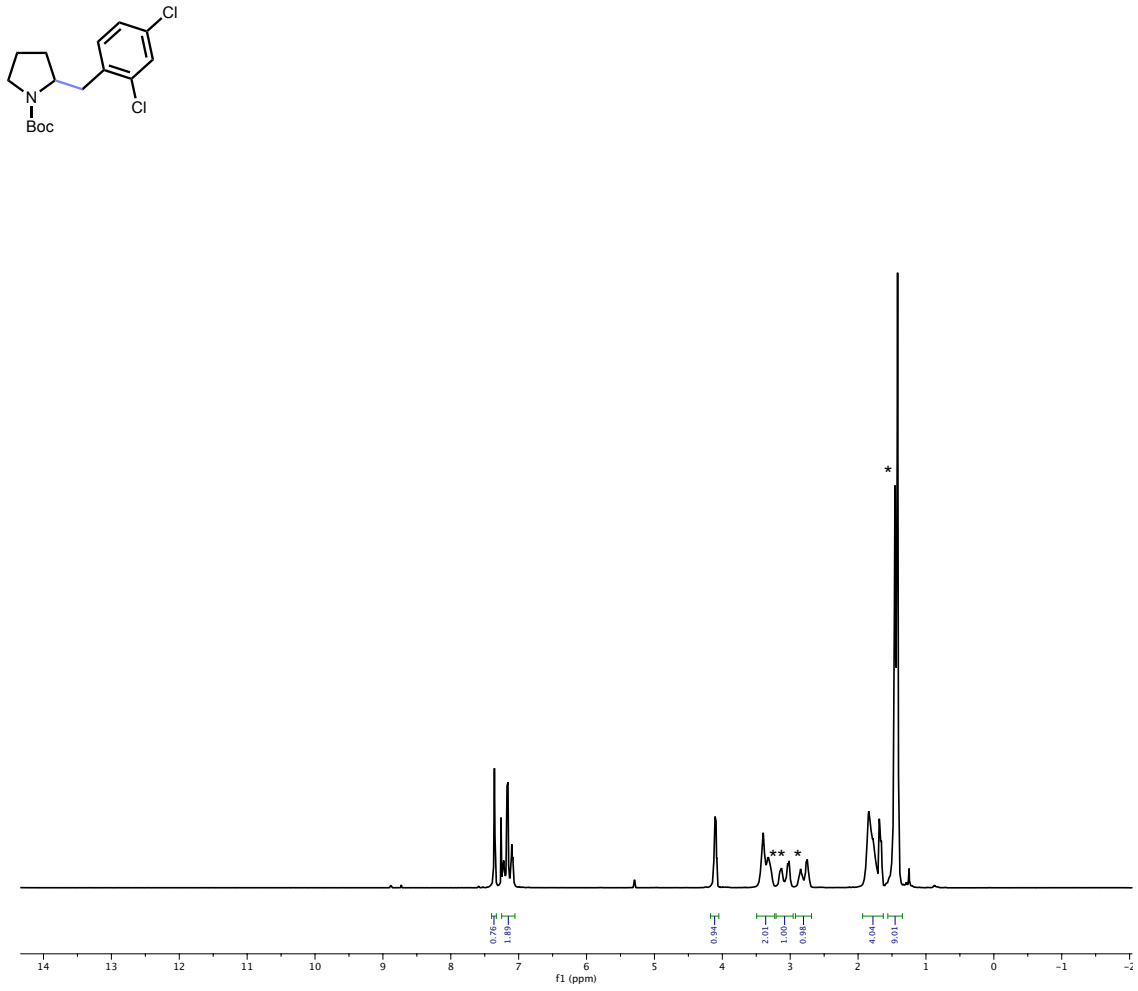


Figure S33. ^{1}H NMR of **27** in $CDCl_3$ at 25 ºC
*: Rotamer

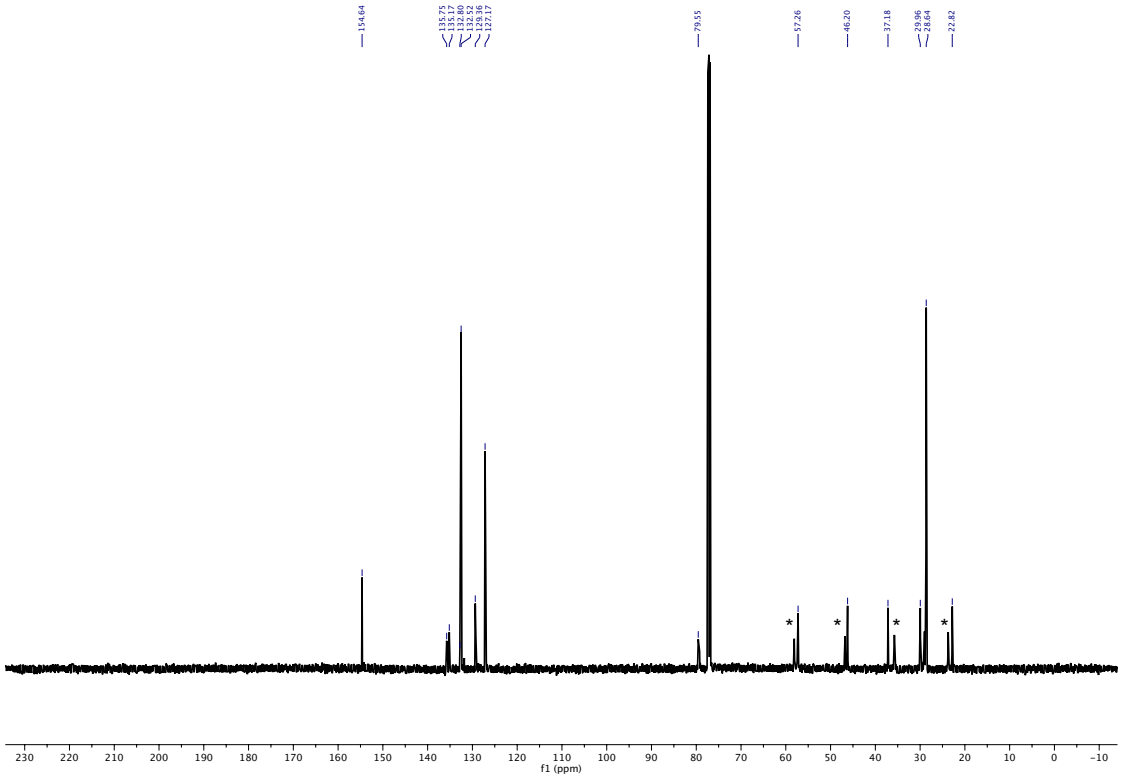


Figure S34. ^{13}C NMR of **27** in $CDCl_3$ at 25 ºC
*: Rotamer

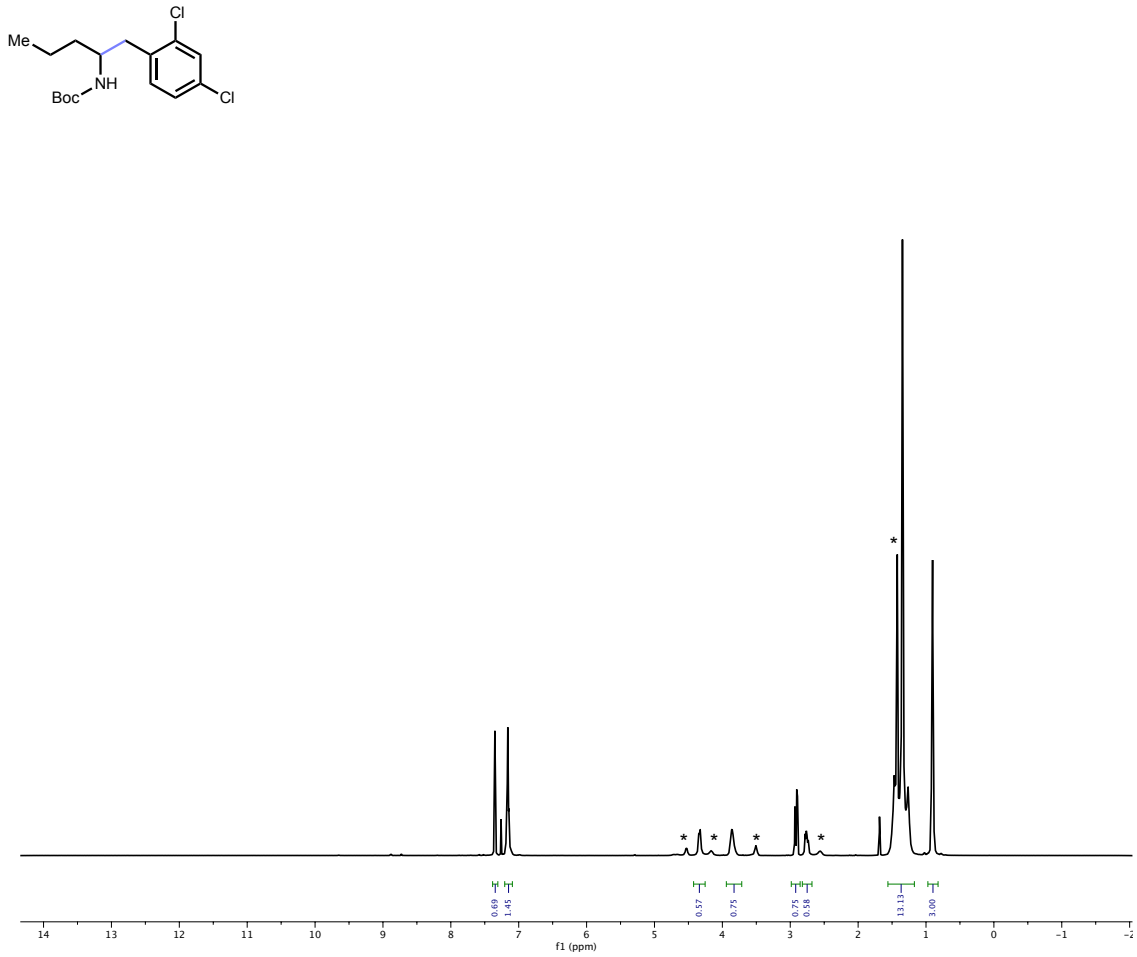


Figure S35. ^{1}H NMR of **28** in $CDCl_3$ at 25 ºC
*: Rotamer

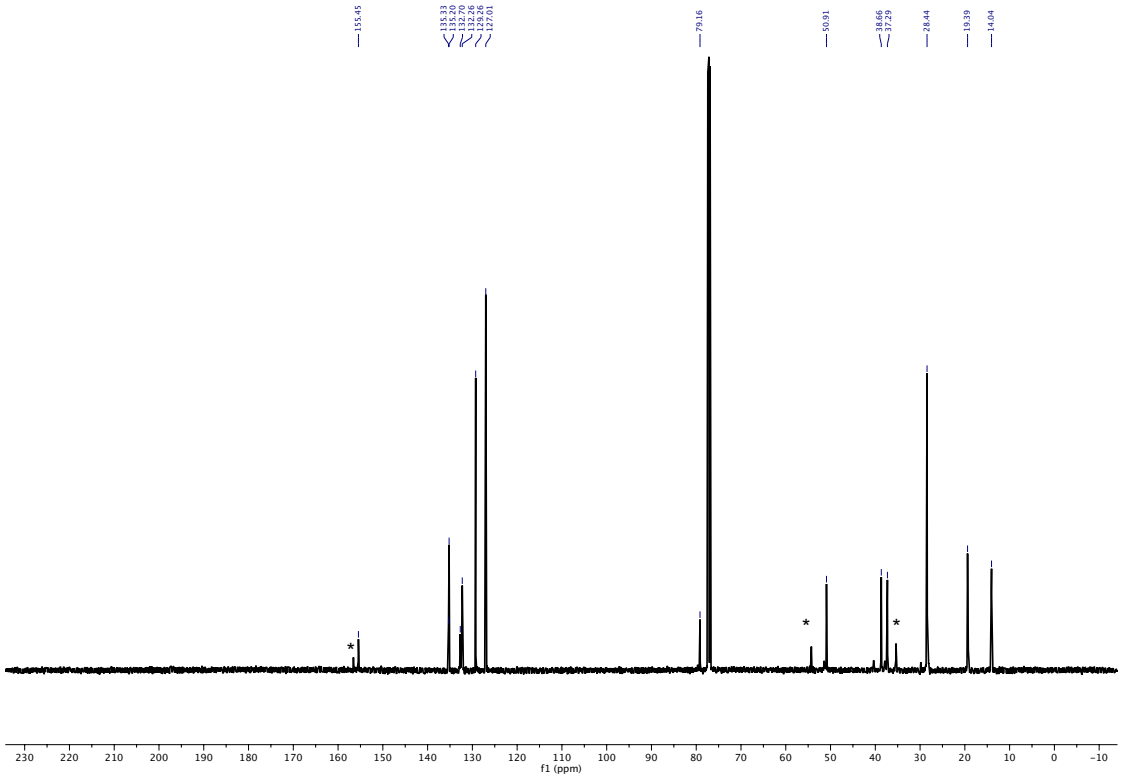


Figure S36. ^{13}C NMR of **28** in $CDCl_3$ at 25 ºC
*: Rotamer

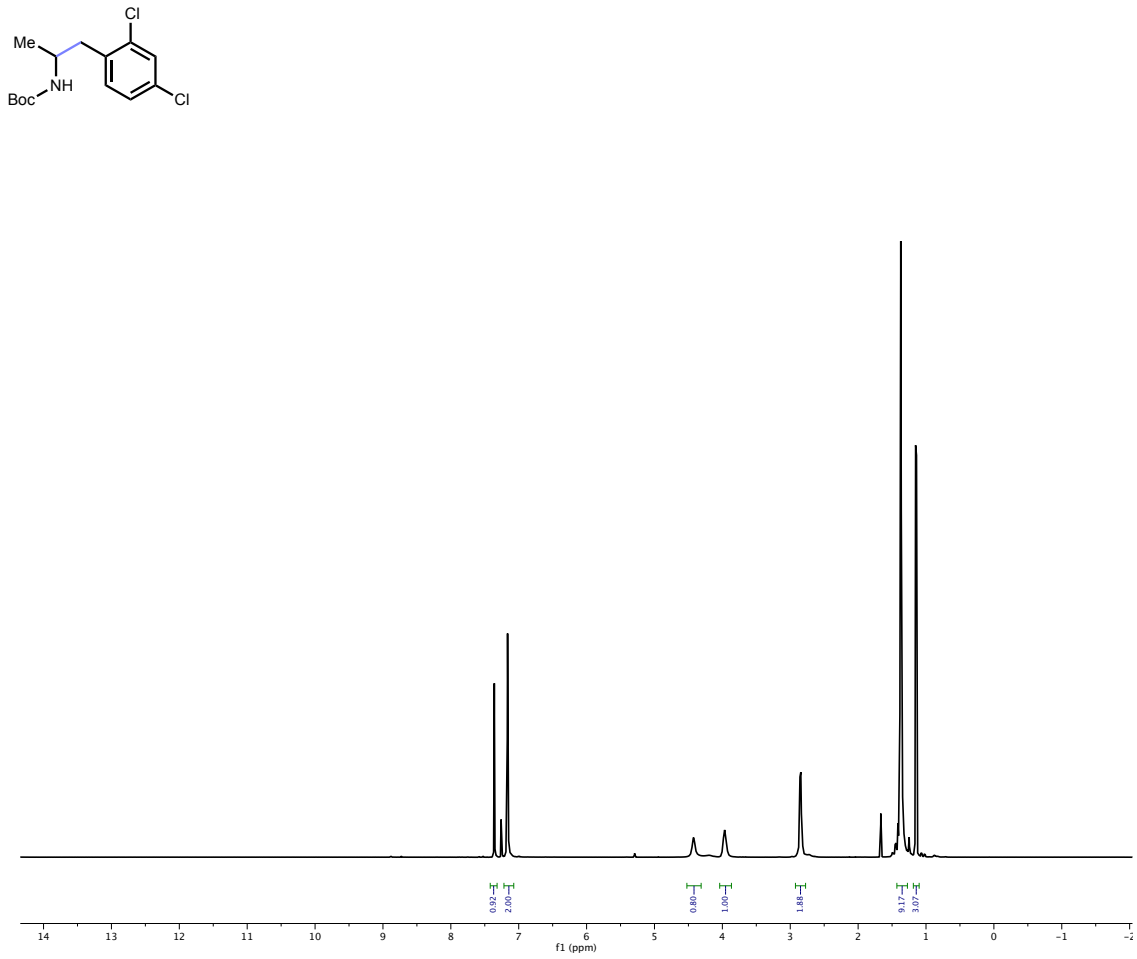


Figure S37. ^{1}H NMR of **29** in $CDCl_3$ at 25 ºC

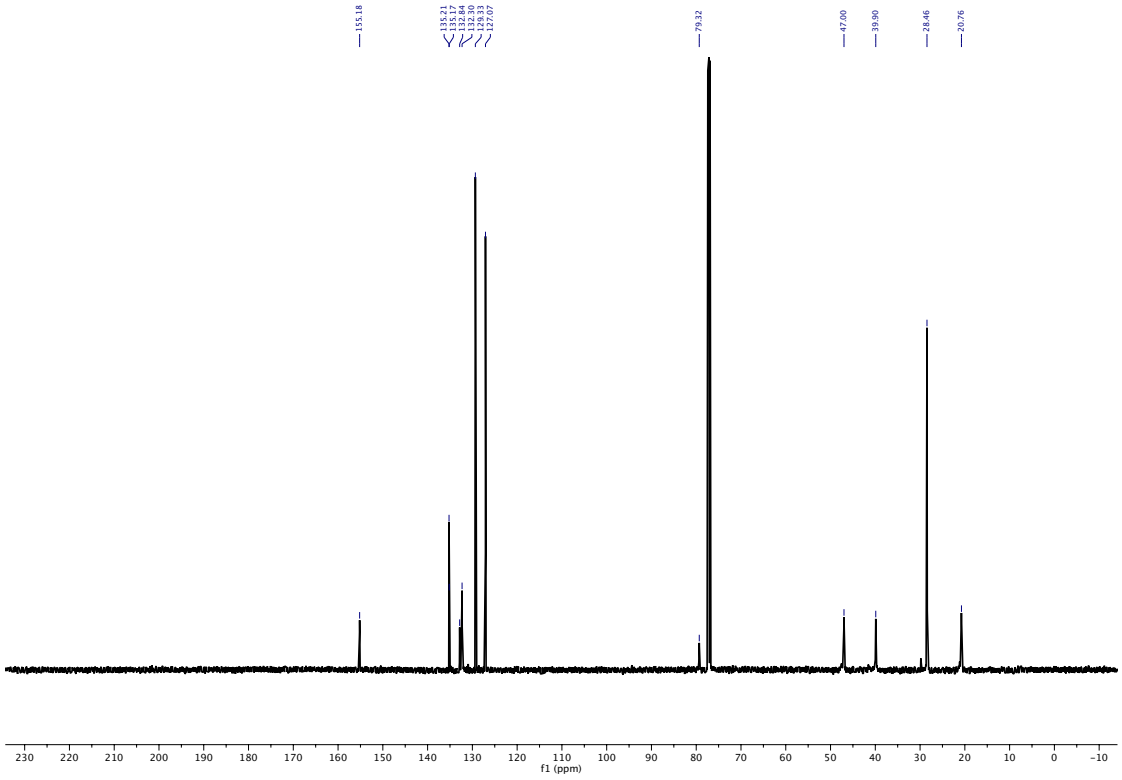


Figure S38. ^{13}C NMR of **29** in $CDCl_3$ at 25 ºC

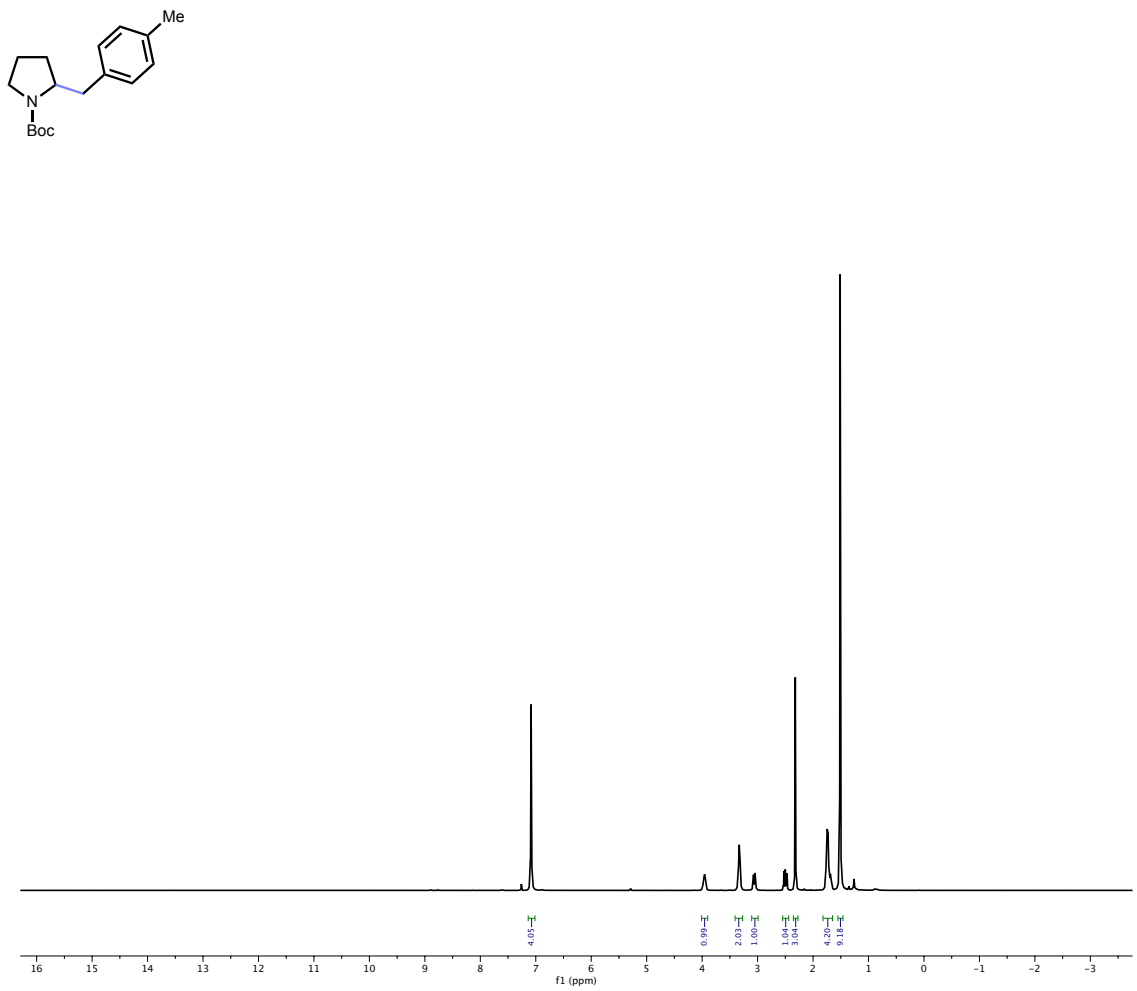


Figure S39. ^{1}H NMR of **30** in $CDCl_3$ at 25 ºC.

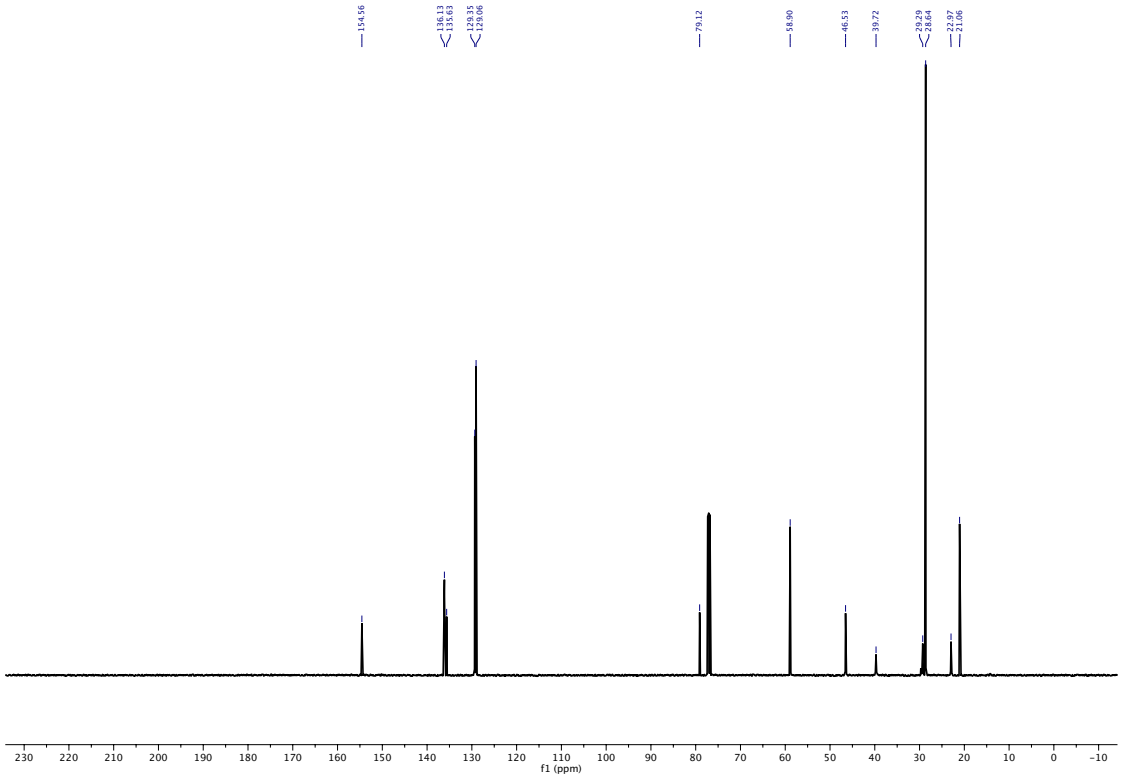
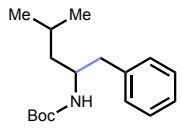


Figure S40. ^{13}C NMR of **30** in $CDCl_3$ at 25 ºC



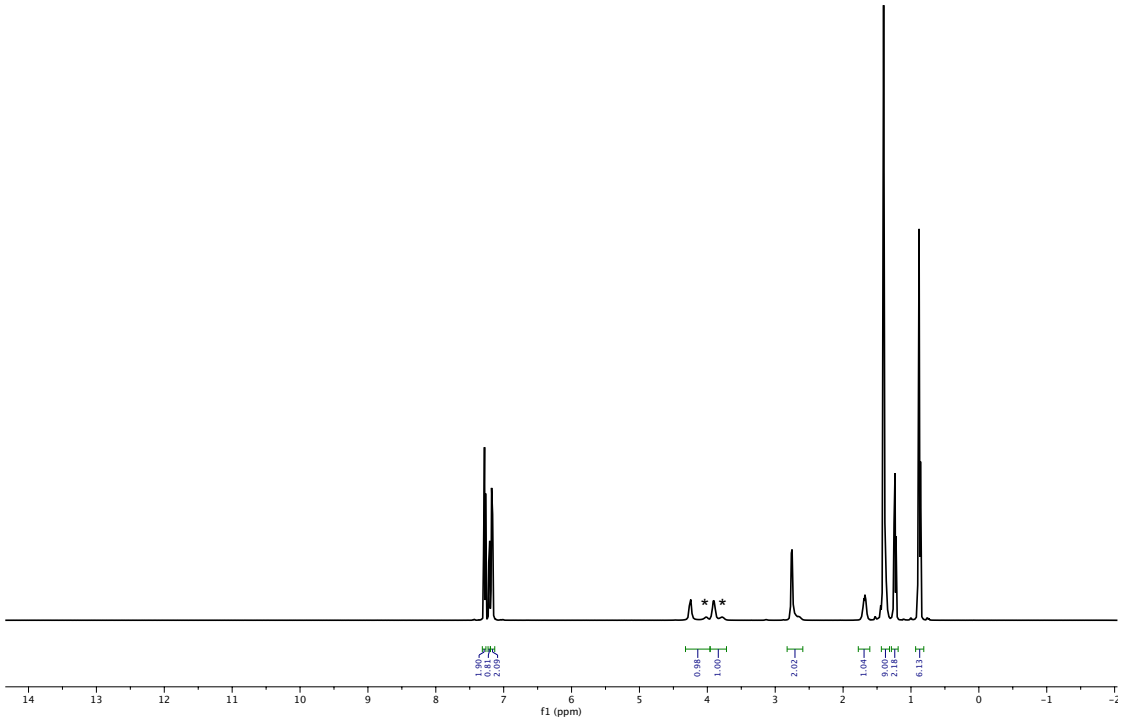


Figure S41. ^{1}H NMR of **31** in $CDCl_3$ at 25 ºC
*: Rotamer

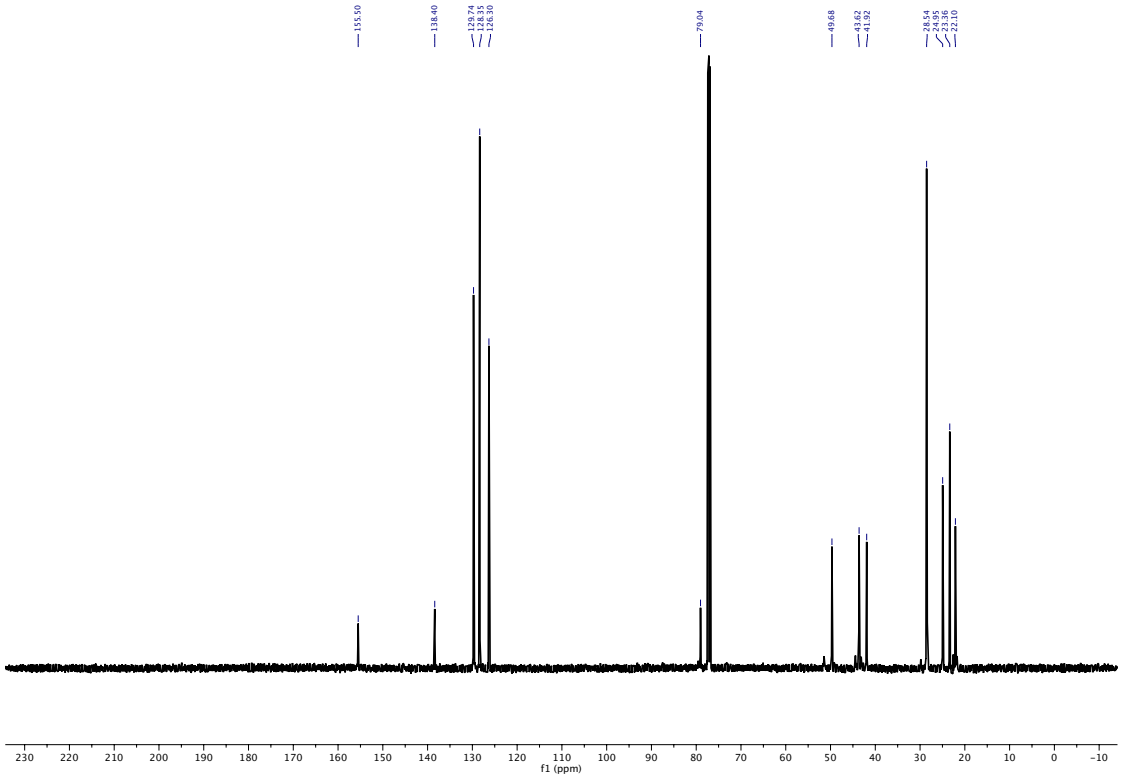
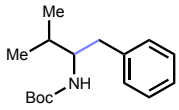


Figure S42. ^{13}C NMR of **31** in $CDCl_3$ at 25 ºC



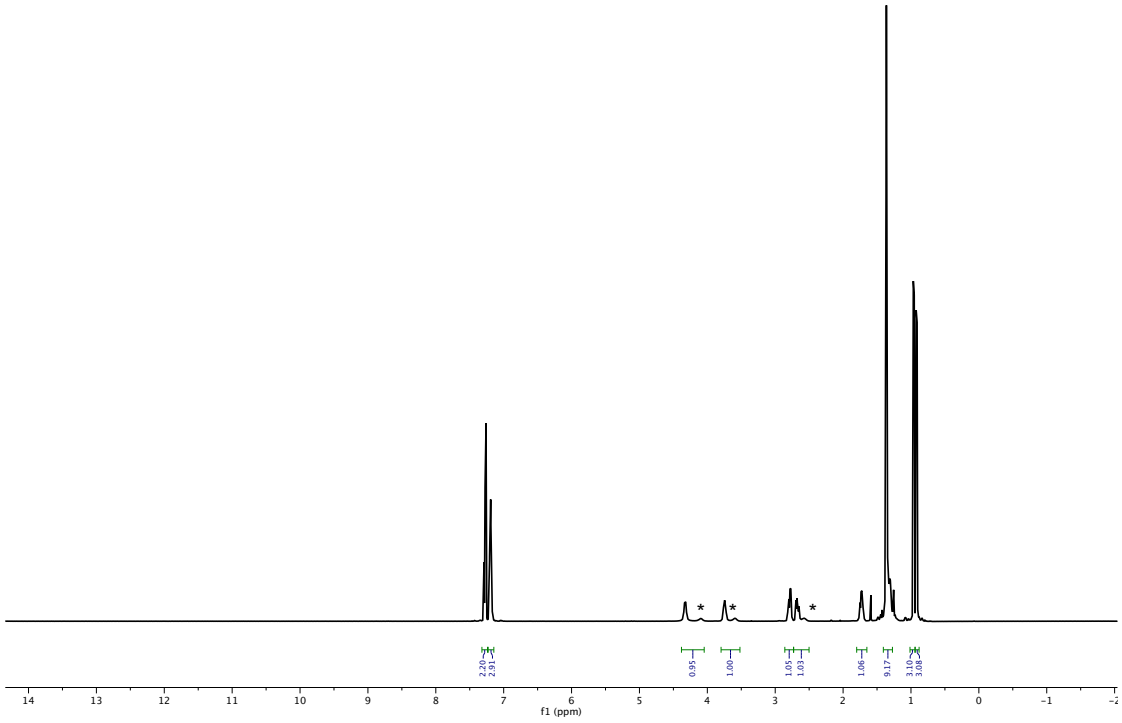


Figure S43. ^{1}H NMR of **32** in $CDCl_3$ at 25 ºC
*: Rotamer

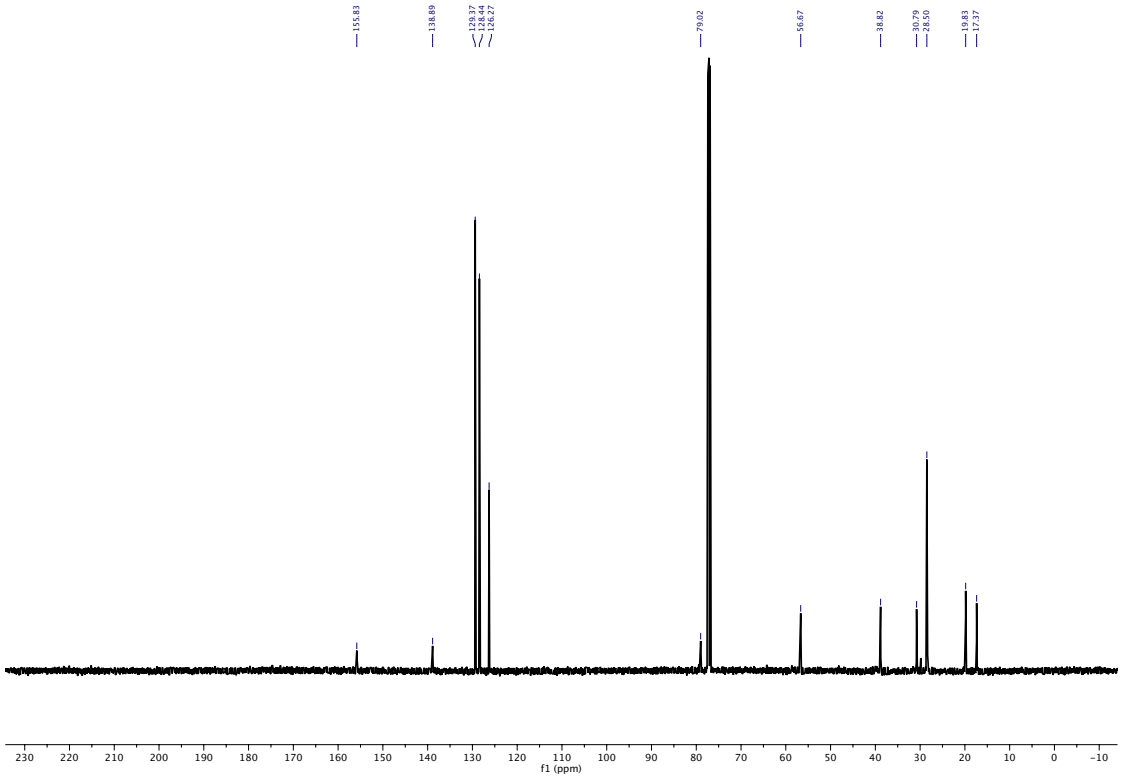


Figure S44. ^{13}C NMR of **32** in $CDCl_3$ at 25 ºC

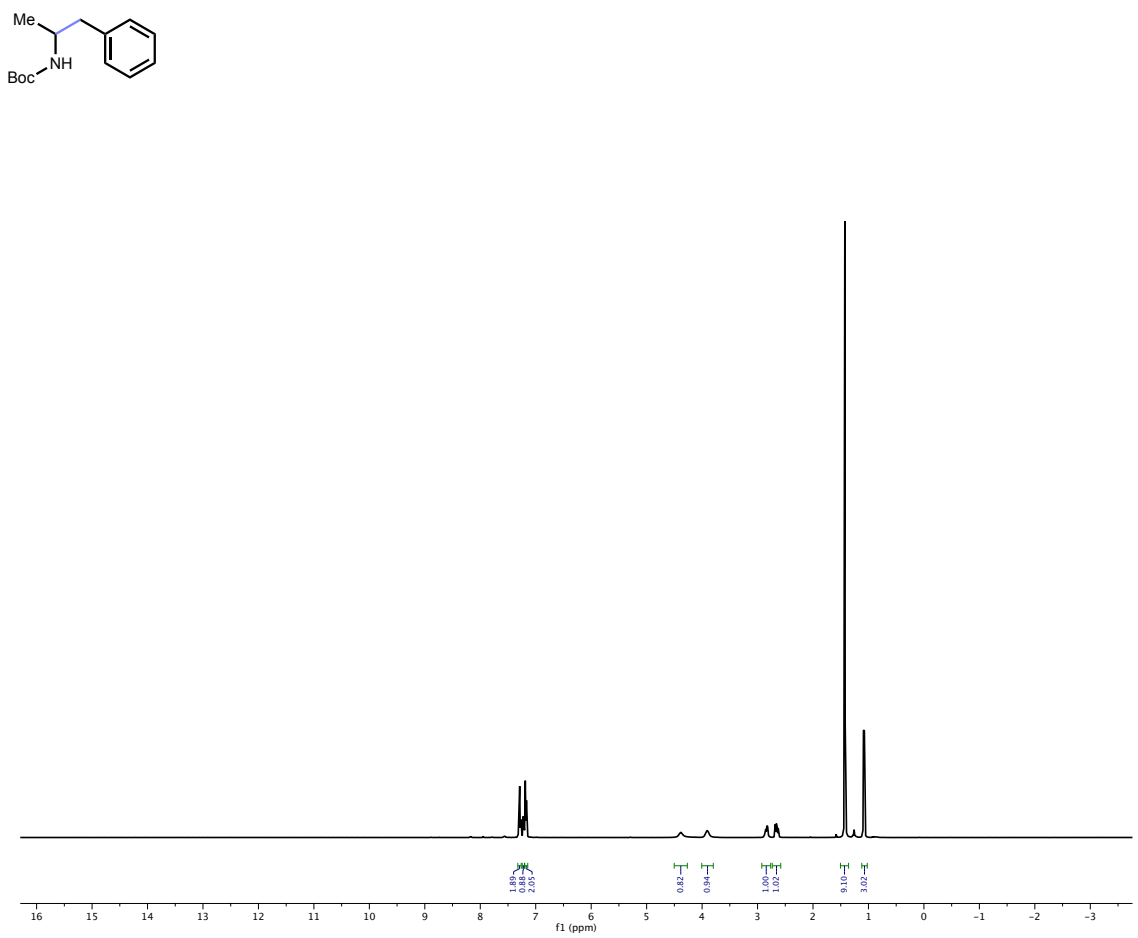


Figure S45. ^{1}H NMR of **33** in $CDCl_3$ at 25 ºC

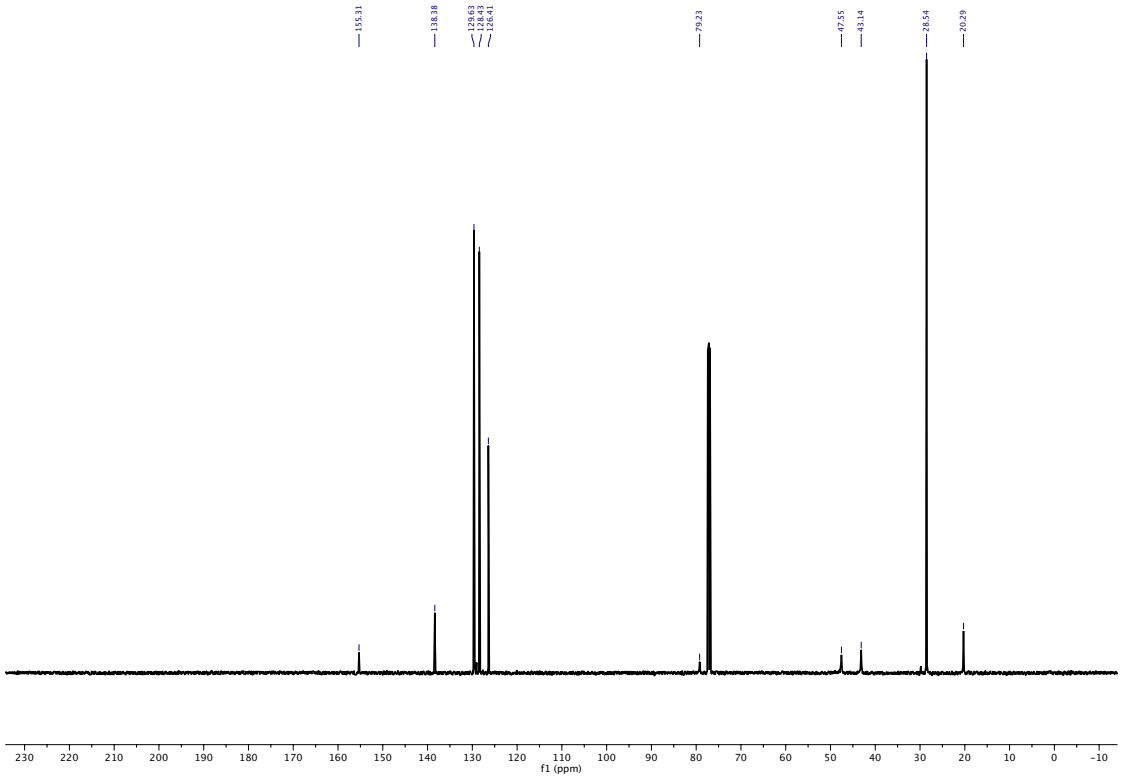


Figure S46. ^{13}C NMR of **33** in $CDCl_3$ at 25 ºC

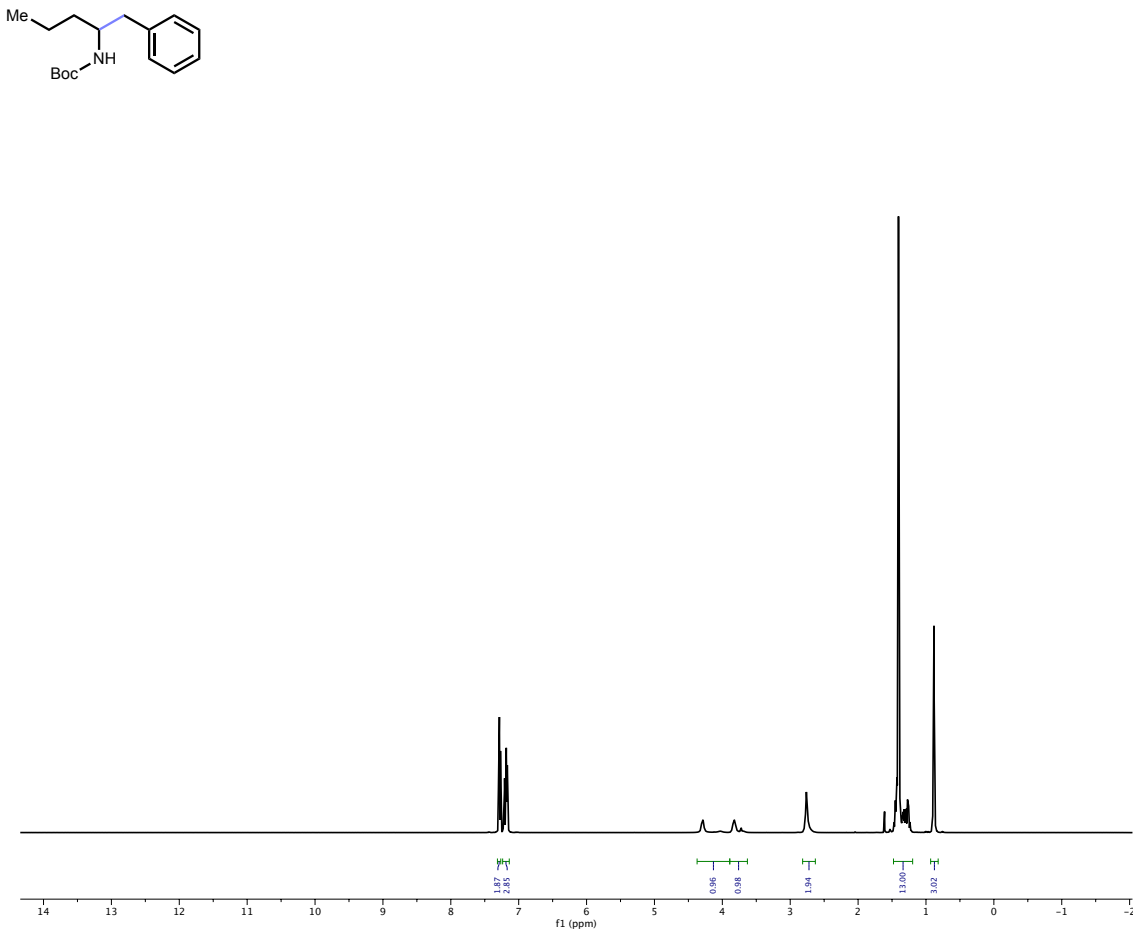


Figure S47. ^{1}H NMR of **34** in $CDCl_3$ at 25 ºC

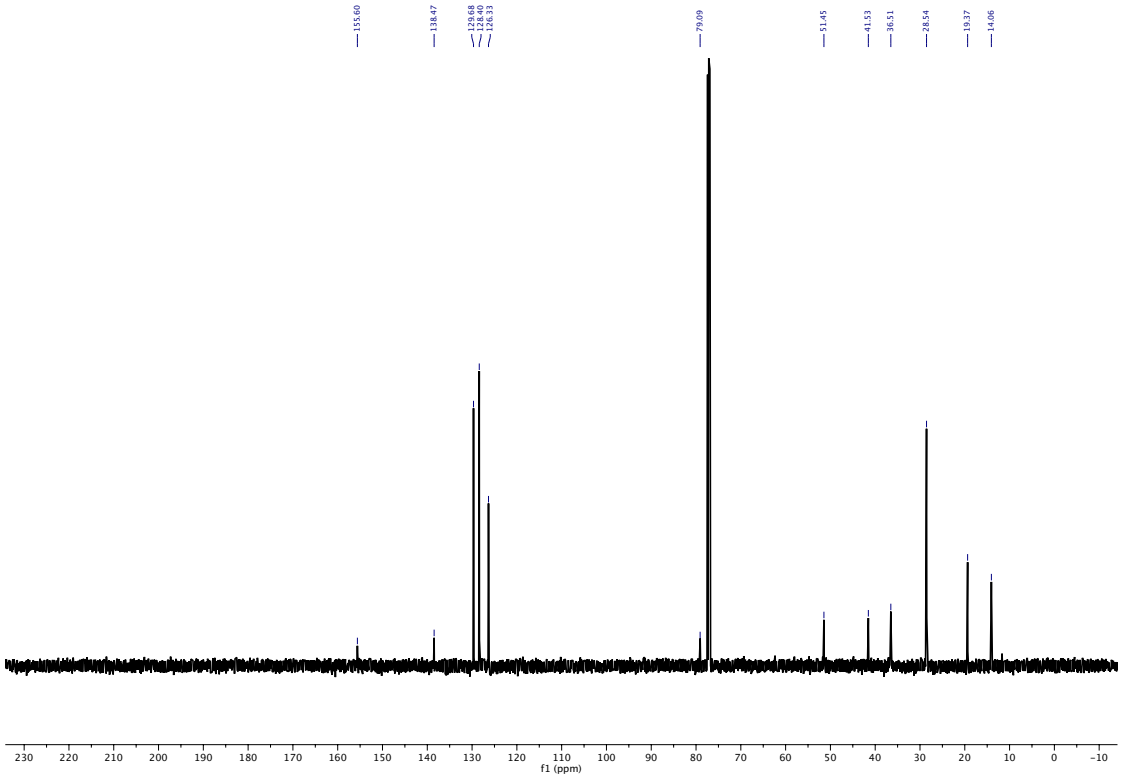


Figure S48. ^{13}C NMR of **34** in $CDCl_3$ at 25 ºC

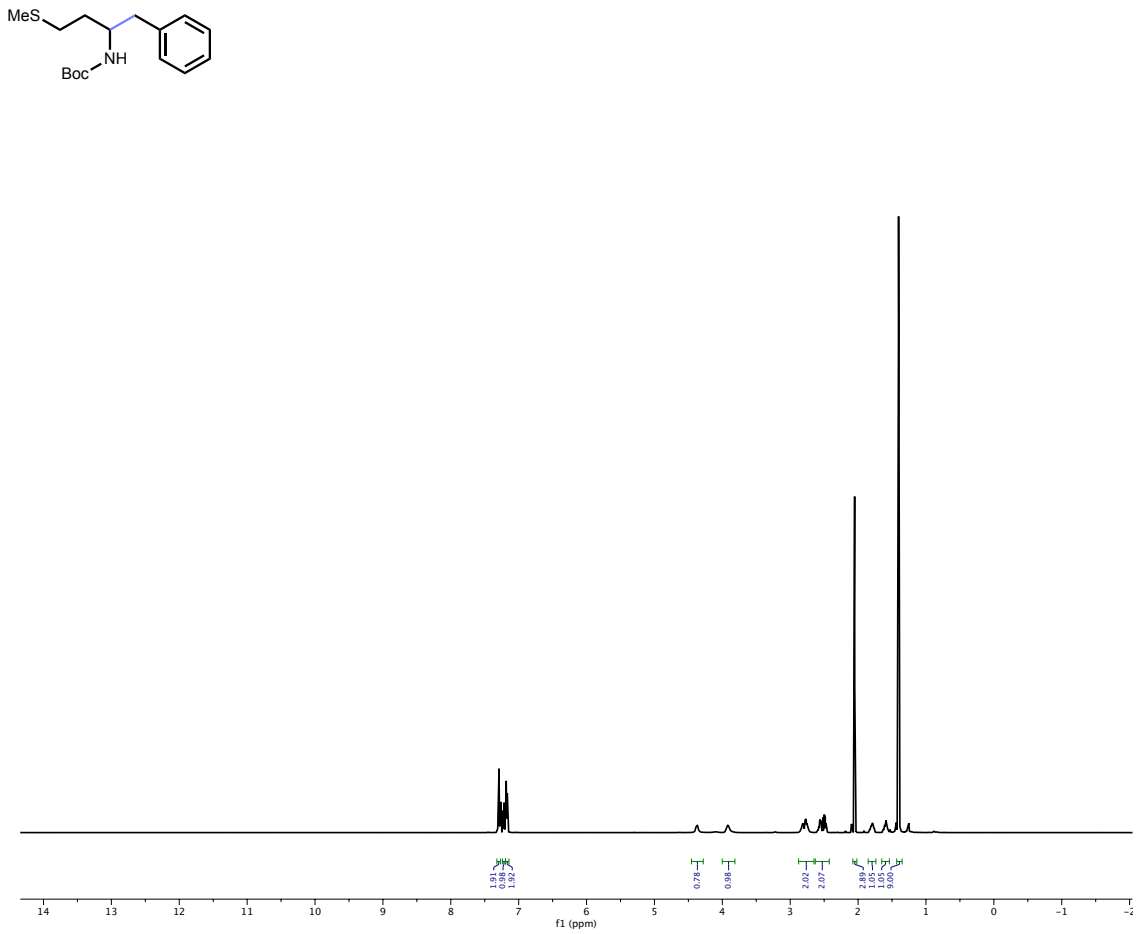


Figure S49. ^{1}H NMR of **35** in $CDCl_3$ at 25 ºC

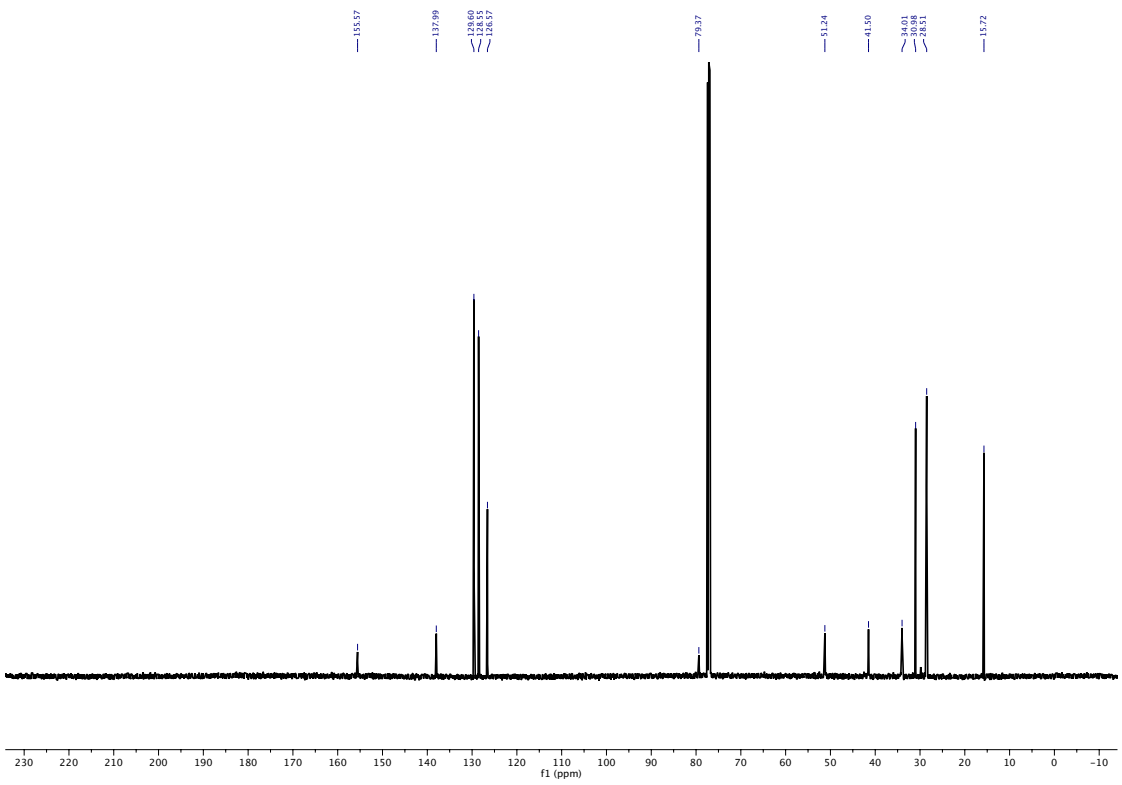


Figure S50. ^{13}C NMR of **35** in $CDCl_3$ at 25 ºC

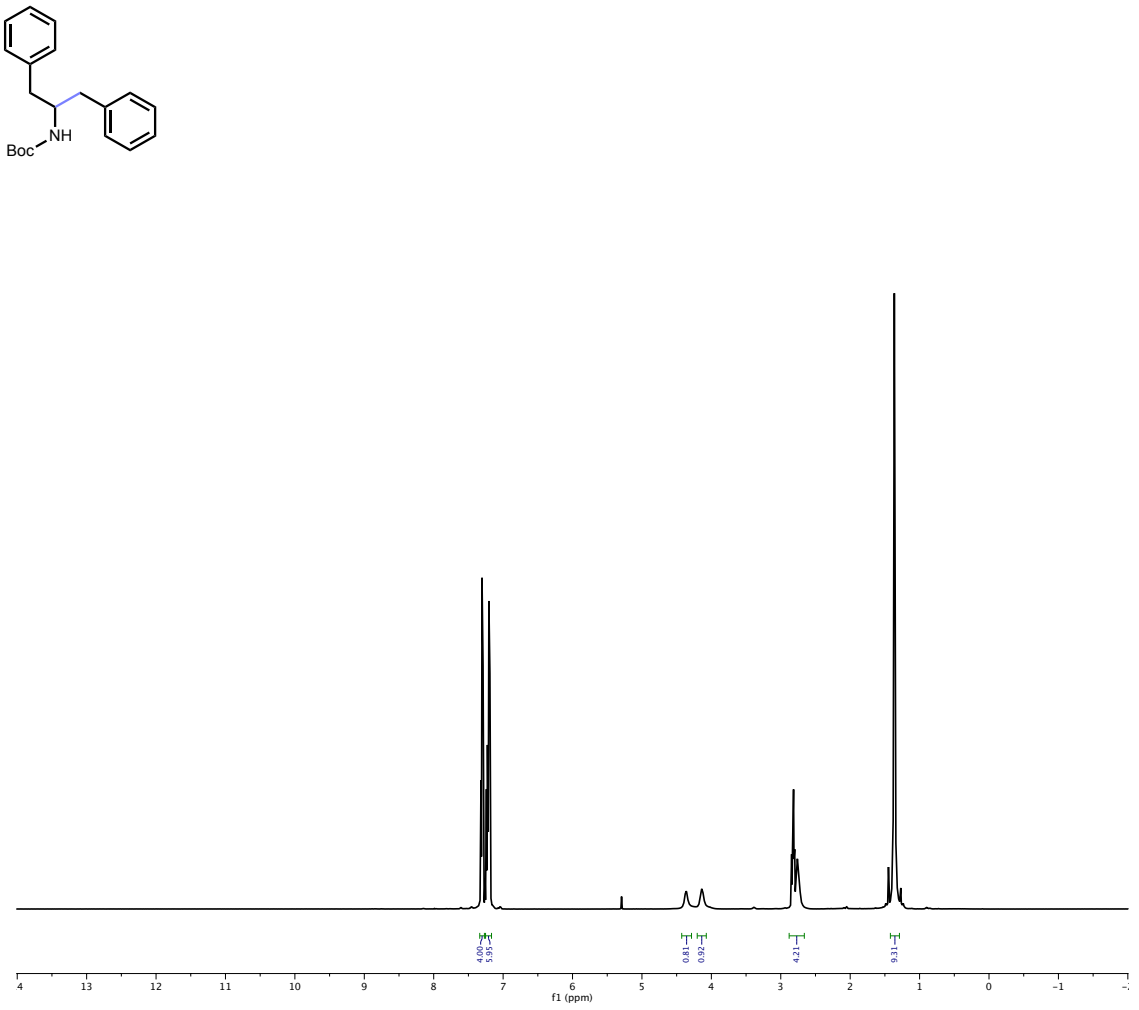


Figure S51. ^{1}H NMR of **36** in $CDCl_3$ at 25 ºC

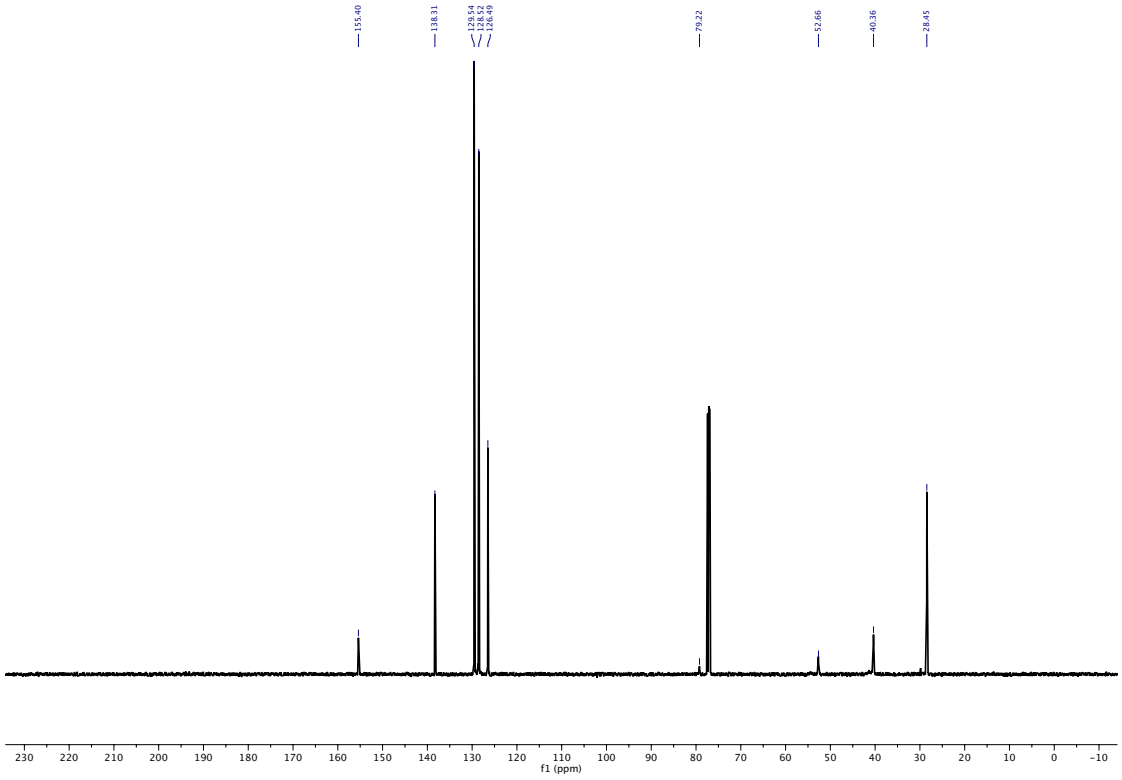
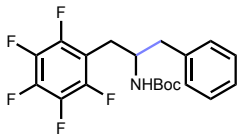


Figure S52. ^{13}C NMR of **36** in $CDCl_3$ at 25 ºC



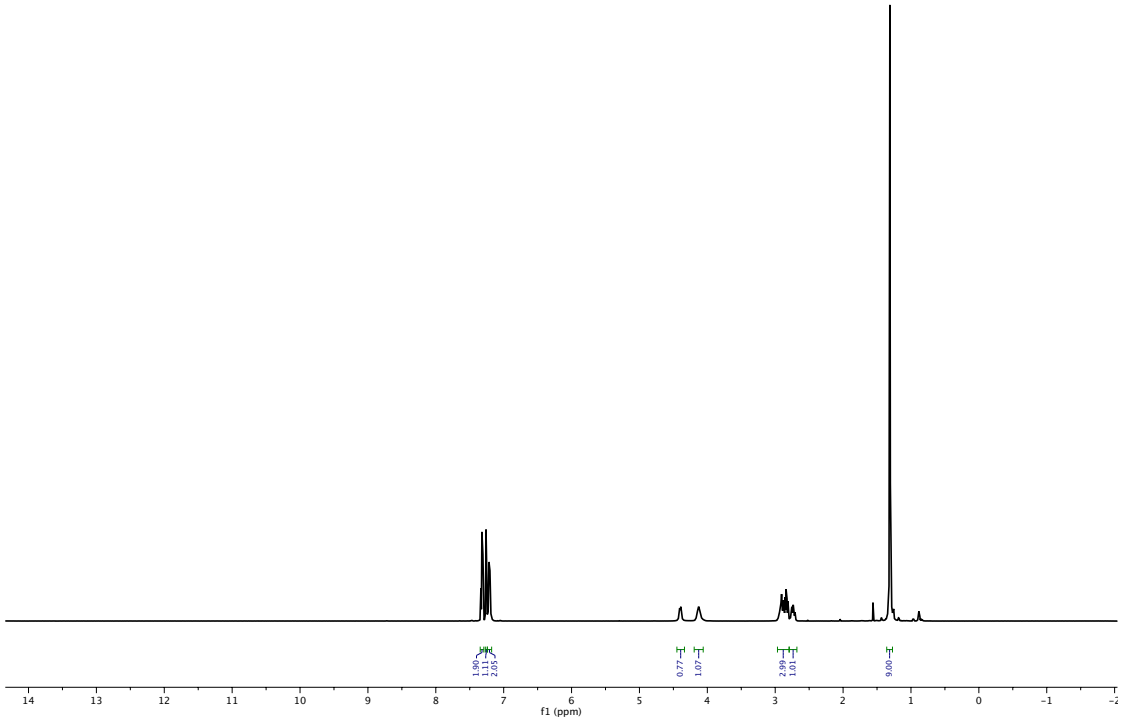


Figure S53. ^{1}H NMR of **37** in $CDCl_3$ at 25 ºC

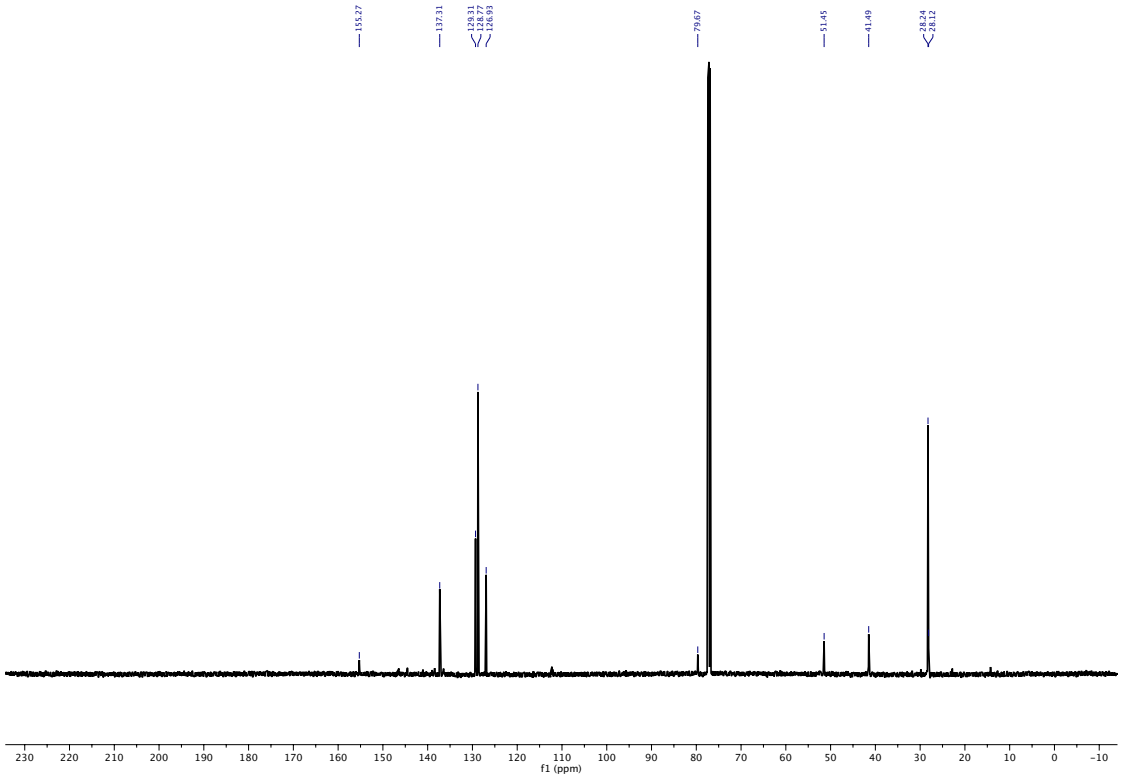


Figure S54. ^{13}C NMR of **37** in $CDCl_3$ at 25 ºC

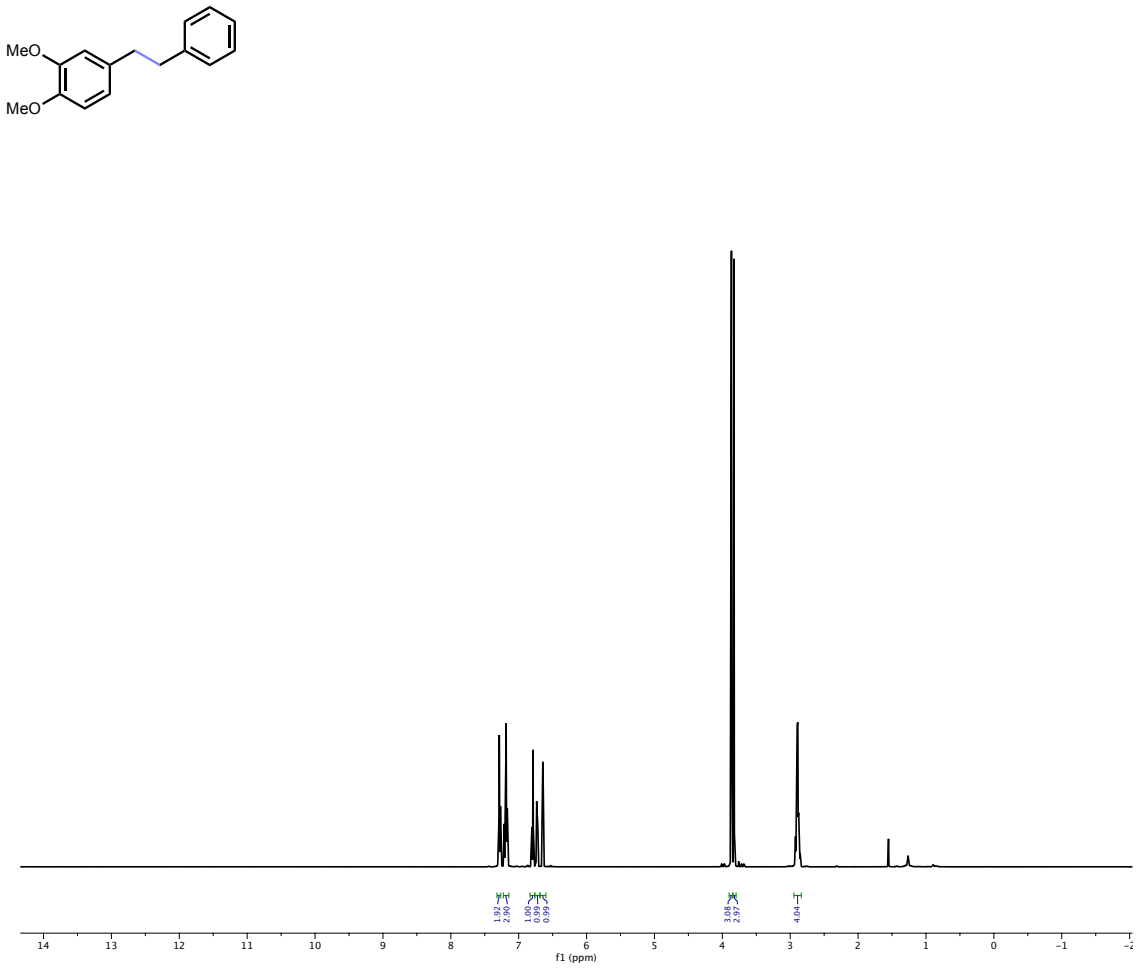


Figure S55. ^{1}H NMR of **38** in $CDCl_3$ at 25 ºC

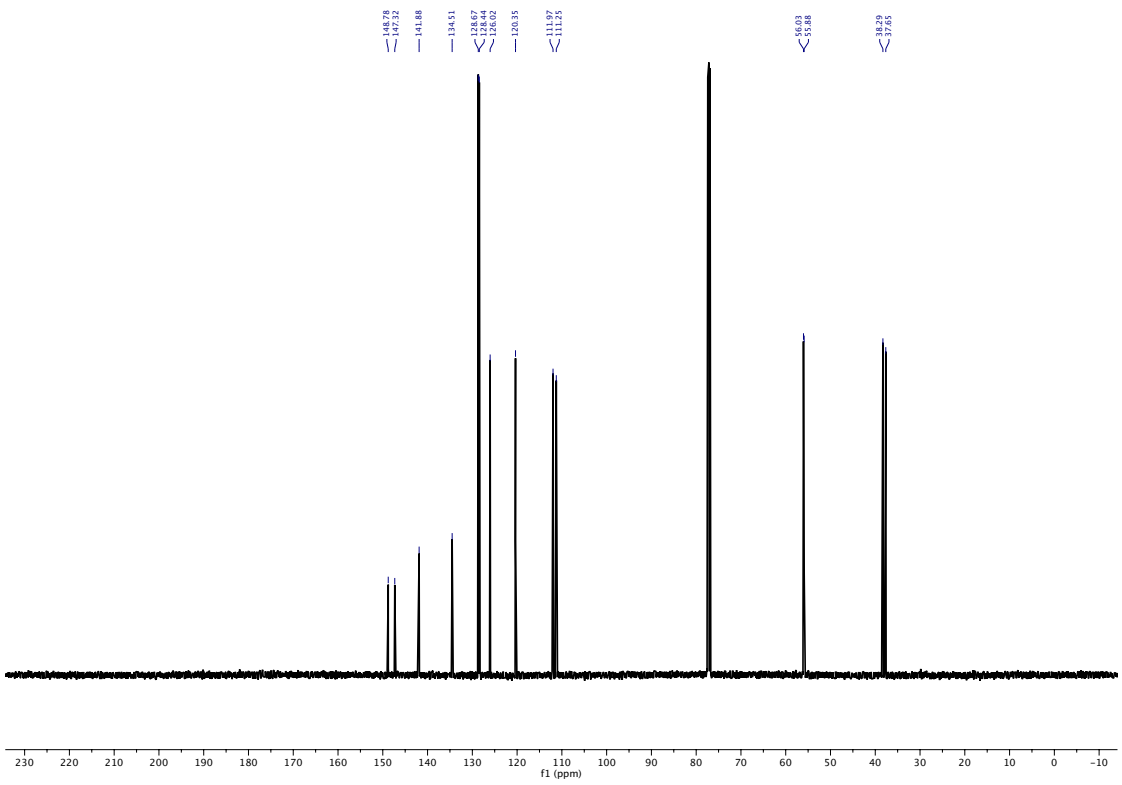


Figure S56. ^{13}C NMR of **38** in $CDCl_3$ at 25 ºC

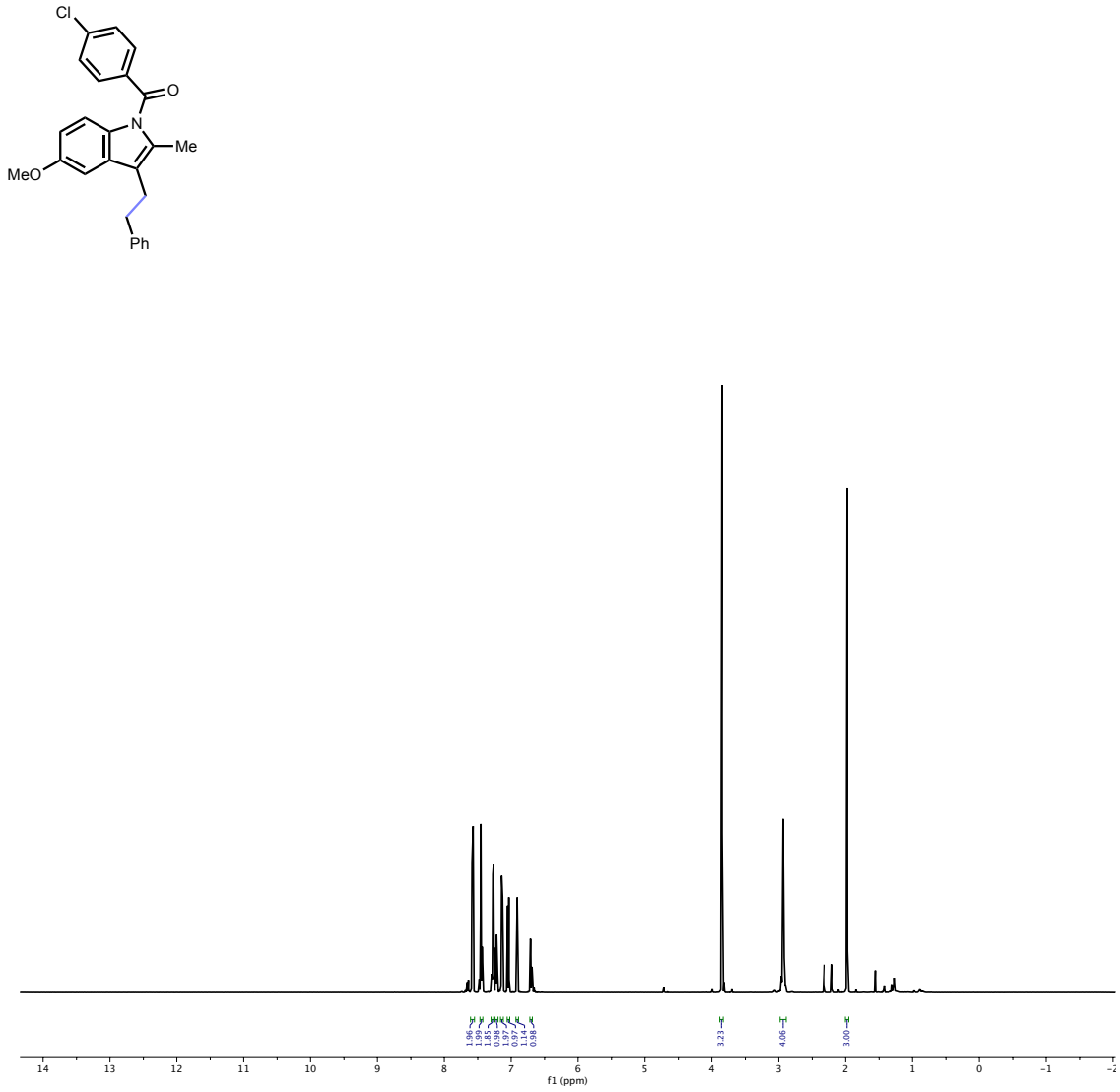


Figure S57. ^{1}H NMR of **39** in $CDCl_3$ at 25 ºC

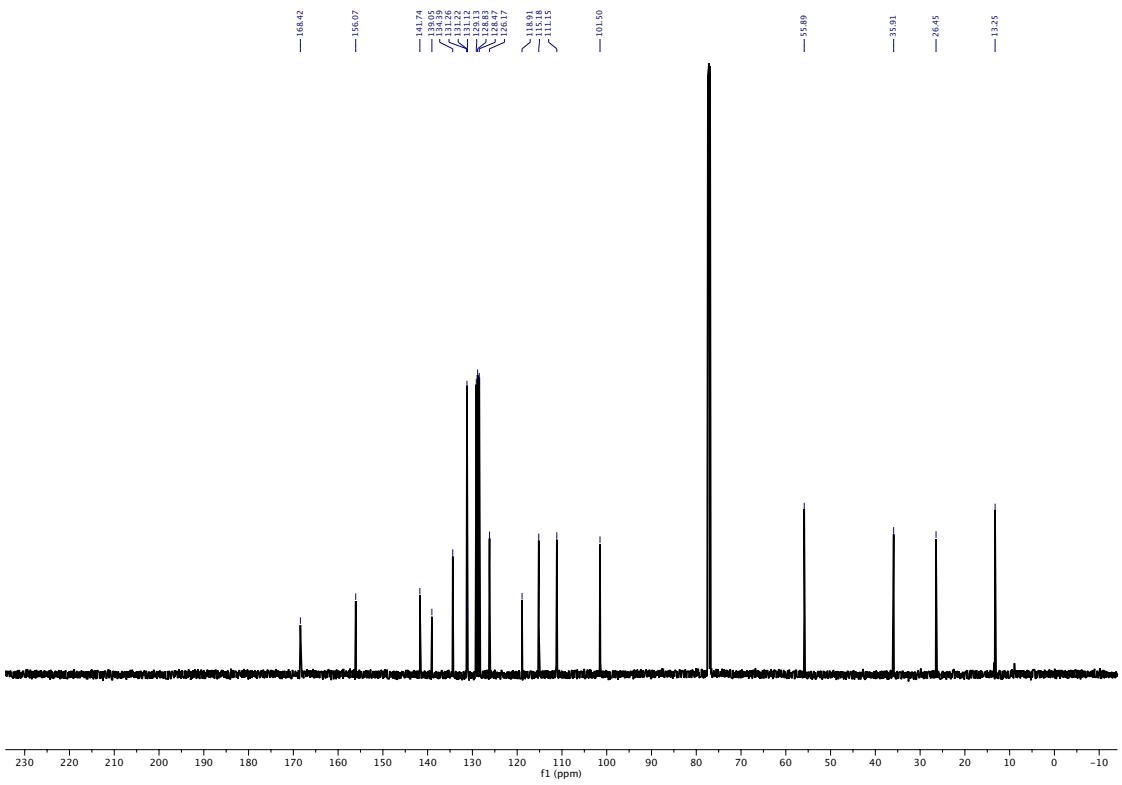


Figure S58. ^{13}C NMR of **39** in $CDCl_3$ at 25 ºC

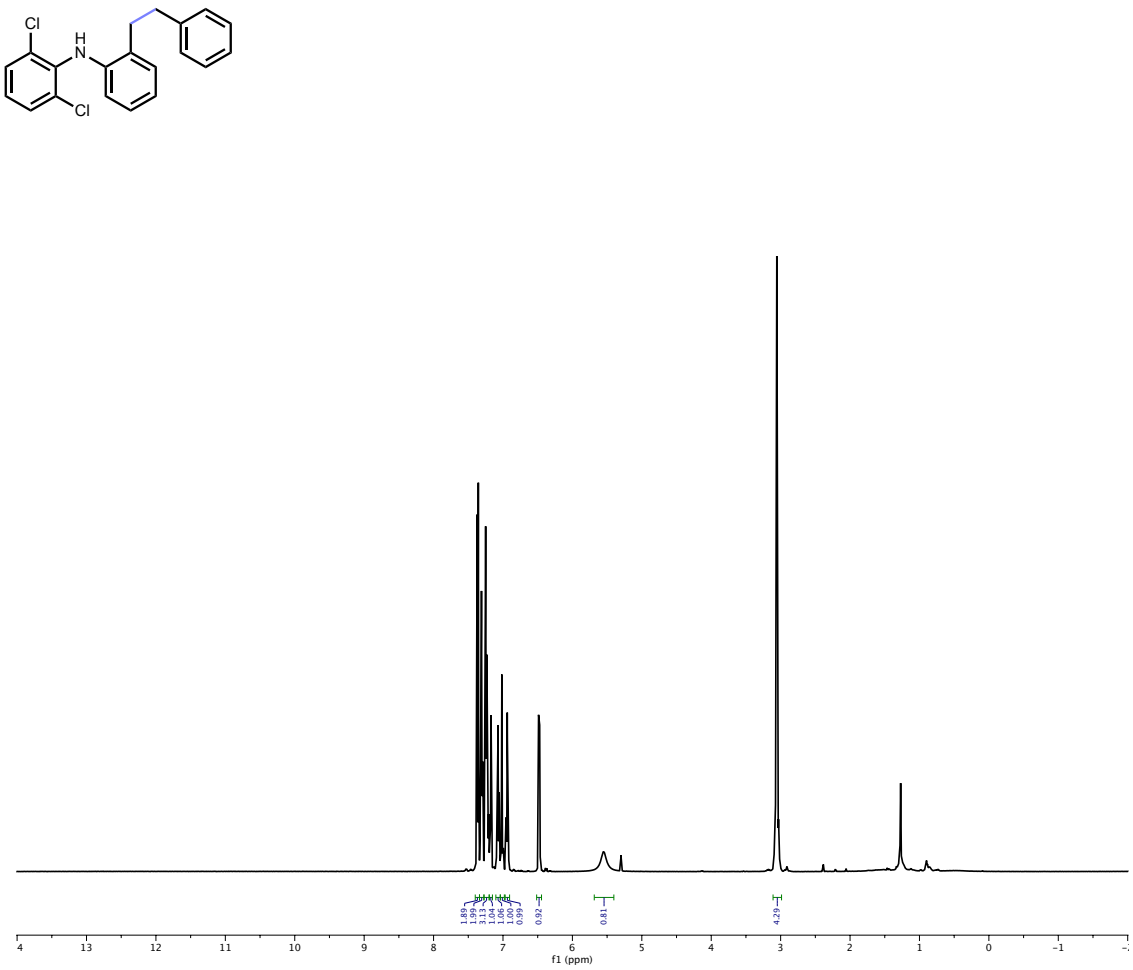


Figure S59. ^{1}H NMR of **40** in $CDCl_3$ at 25 ºC

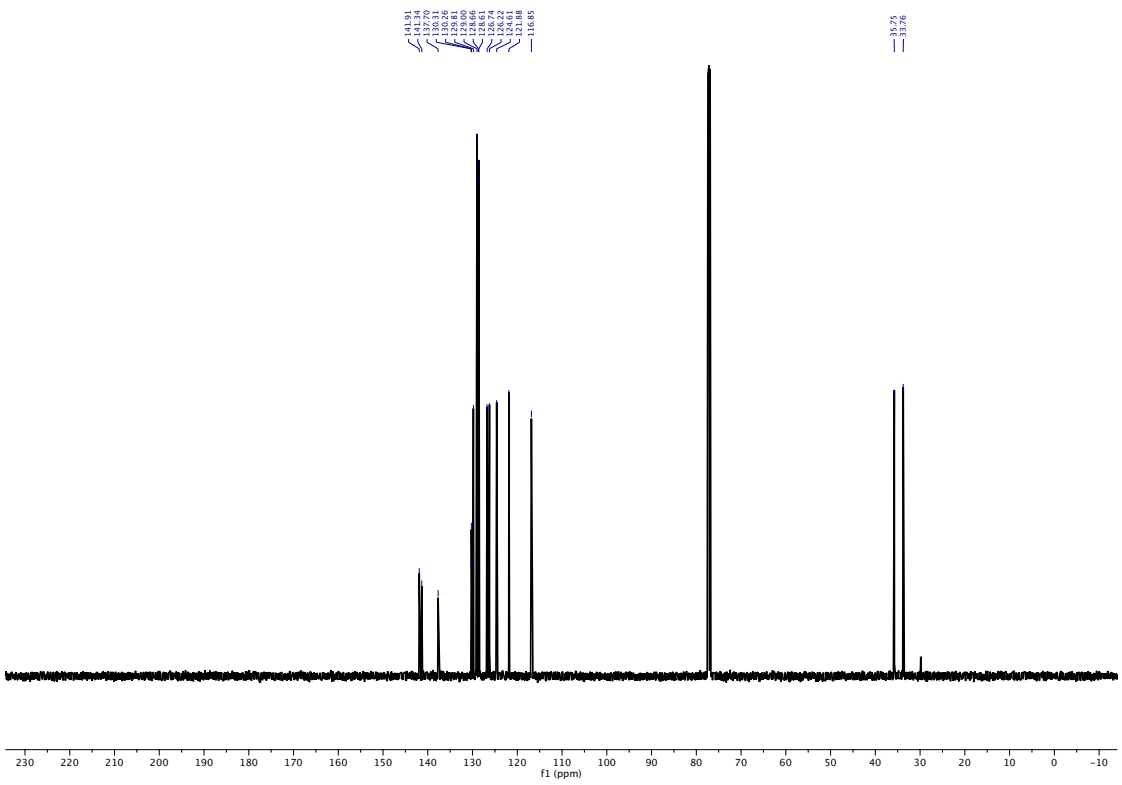


Figure S60. ^{13}C NMR of **40** in $CDCl_3$ at 25 ºC

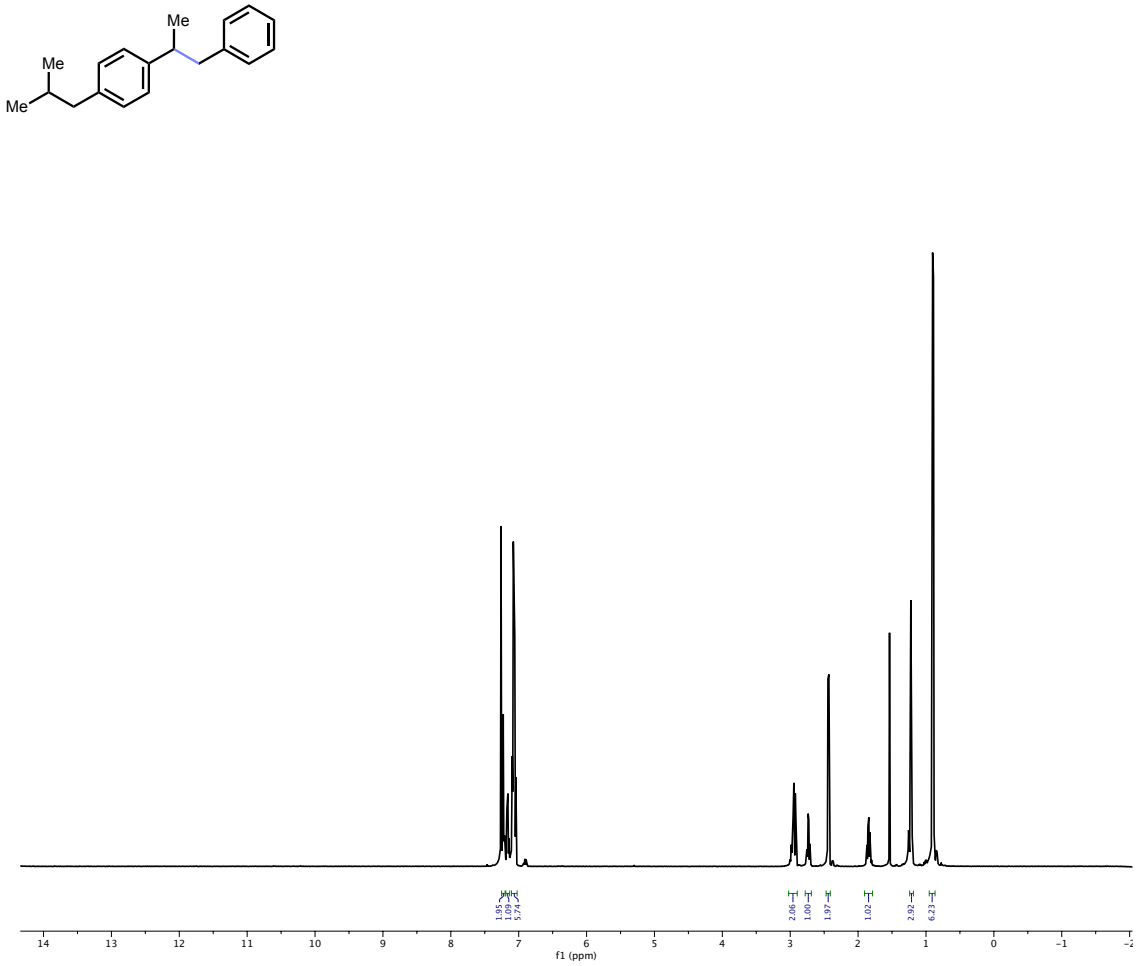


Figure S61. ^{1}H NMR of **41** in $CDCl_3$ at 25 ºC

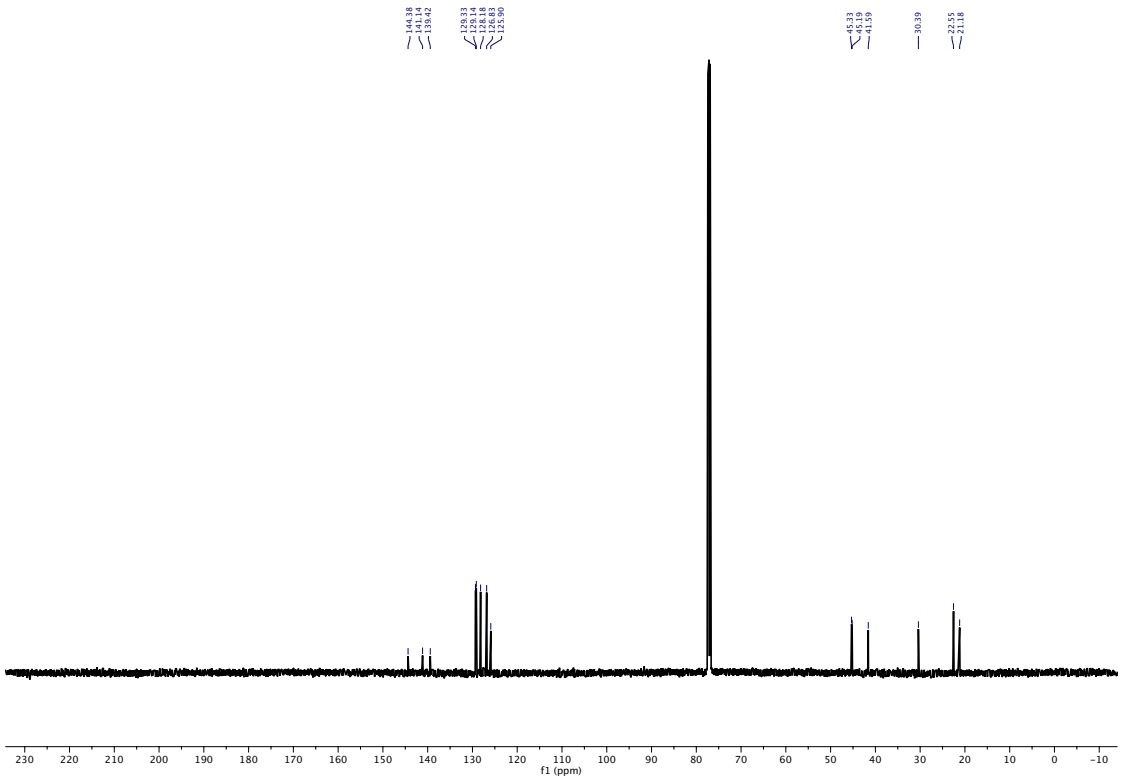
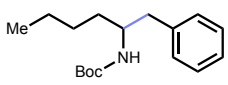


Figure S62. ^{13}C NMR of **41** in $CDCl_3$ at 25 ºC



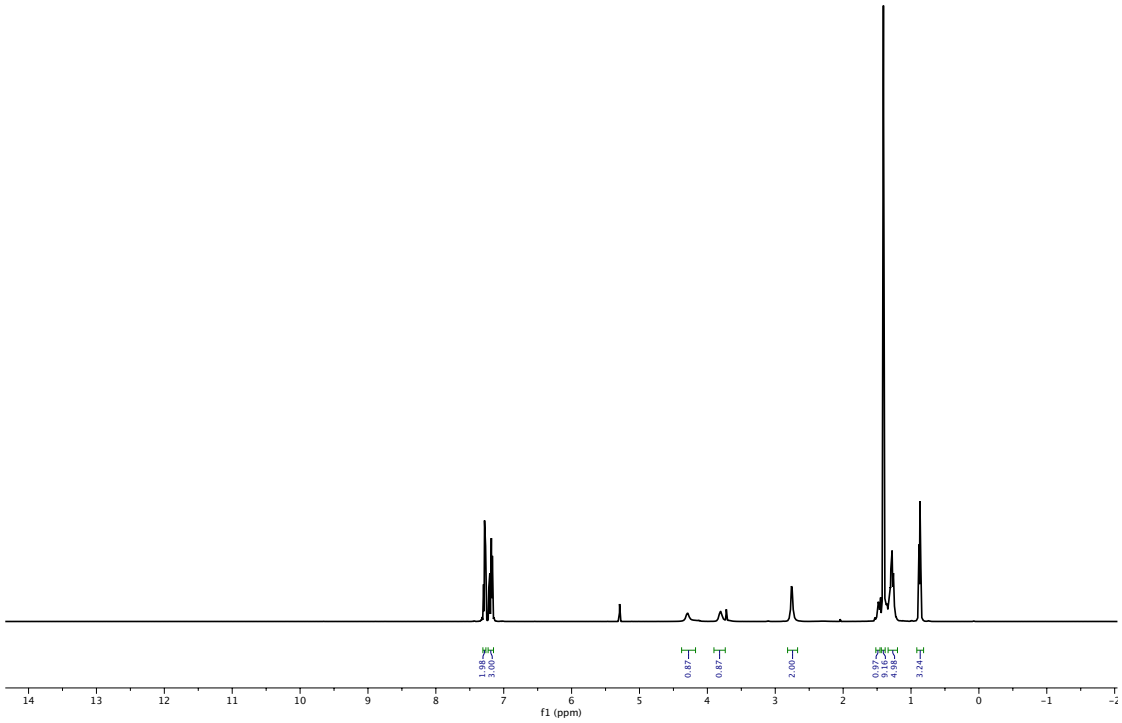


Figure S63. ^{1}H NMR of **S3** in $CDCl_3$ at 25 ºC

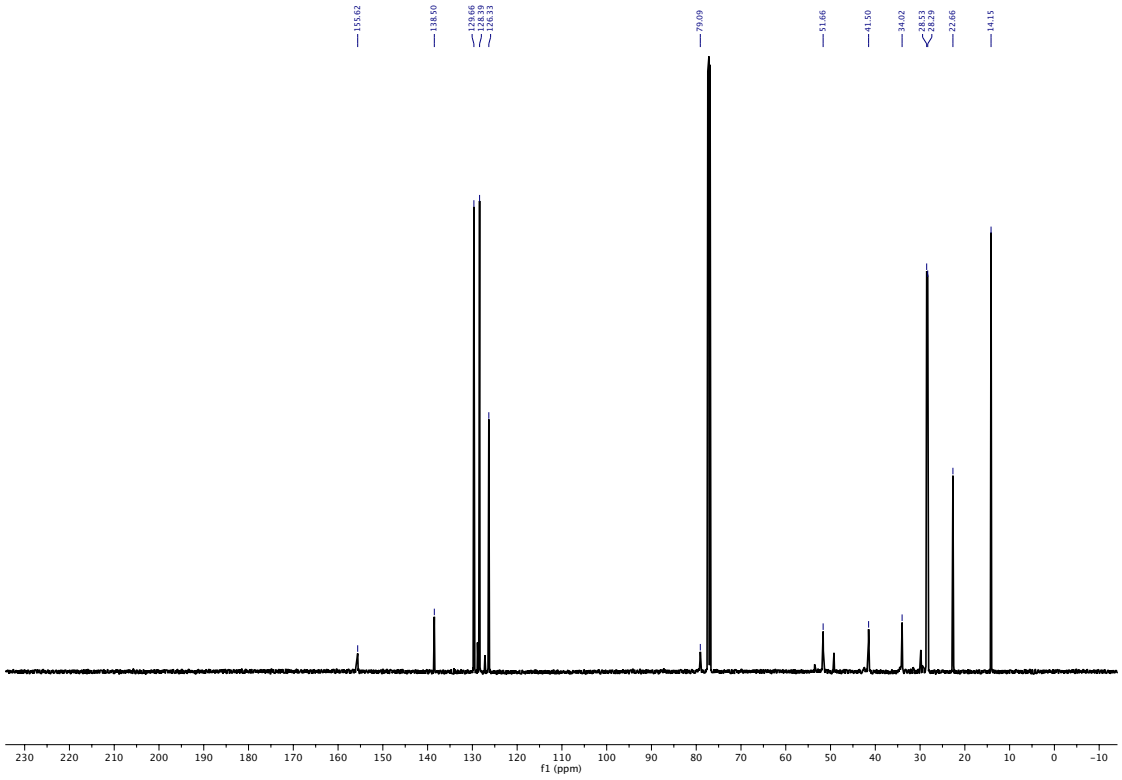


Figure S64. ^{13}C NMR of **S3** in $CDCl_3$ at 25 ºC

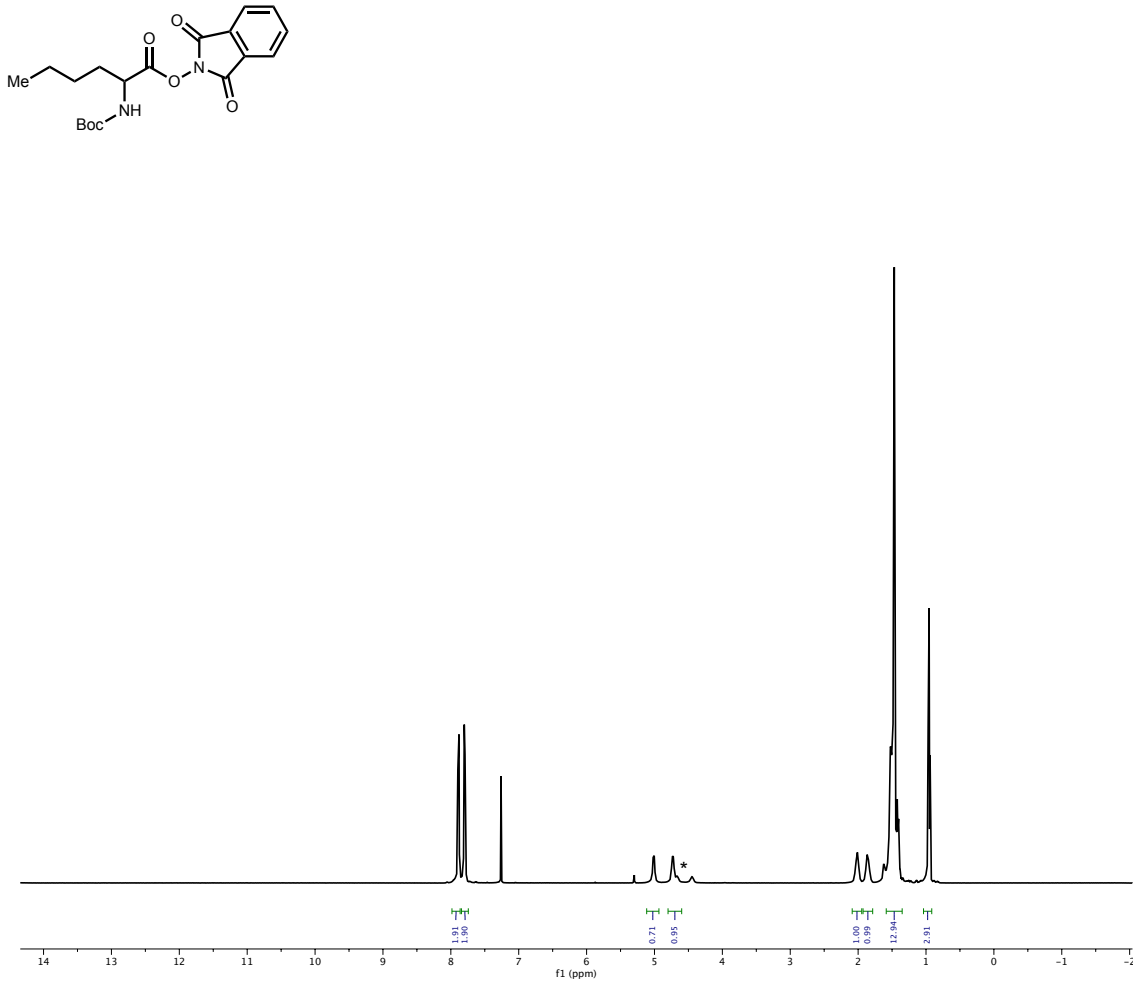


Figure S65. ^{1}H NMR of **14** in $CDCl_3$ at 25 ºC
*: Rotamer

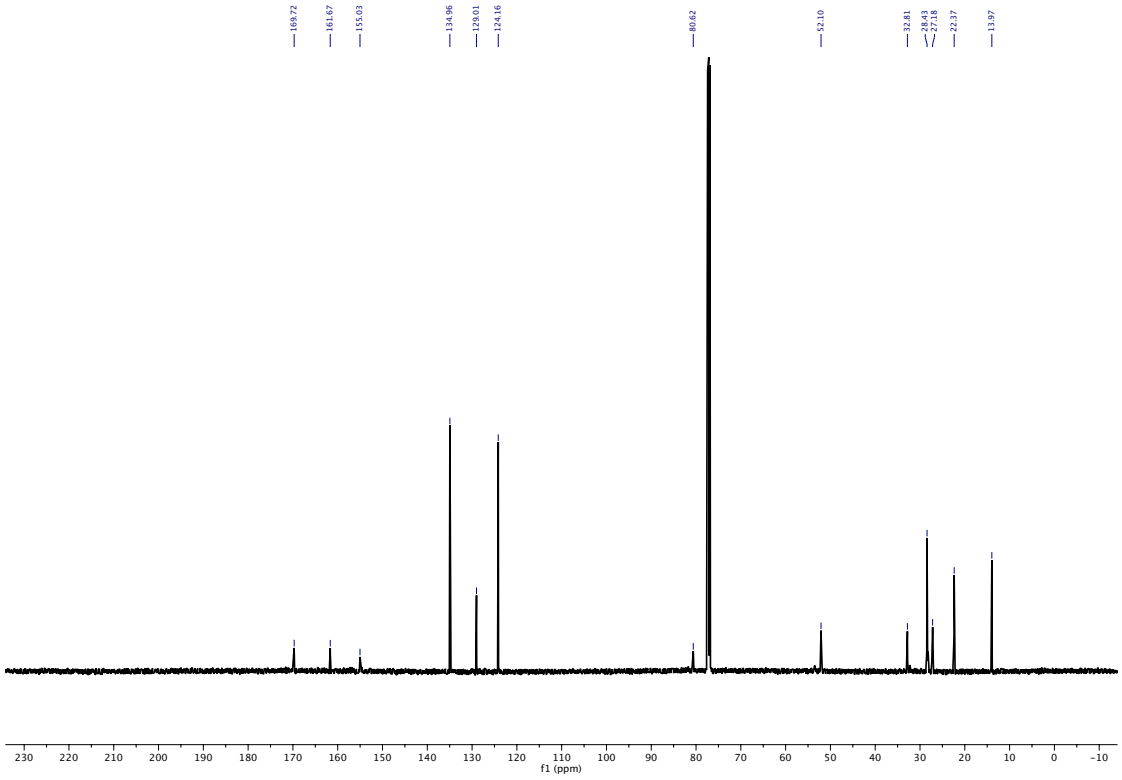


Figure S66. ^{13}C NMR of **14** in $CDCl_3$ at 25 ºC

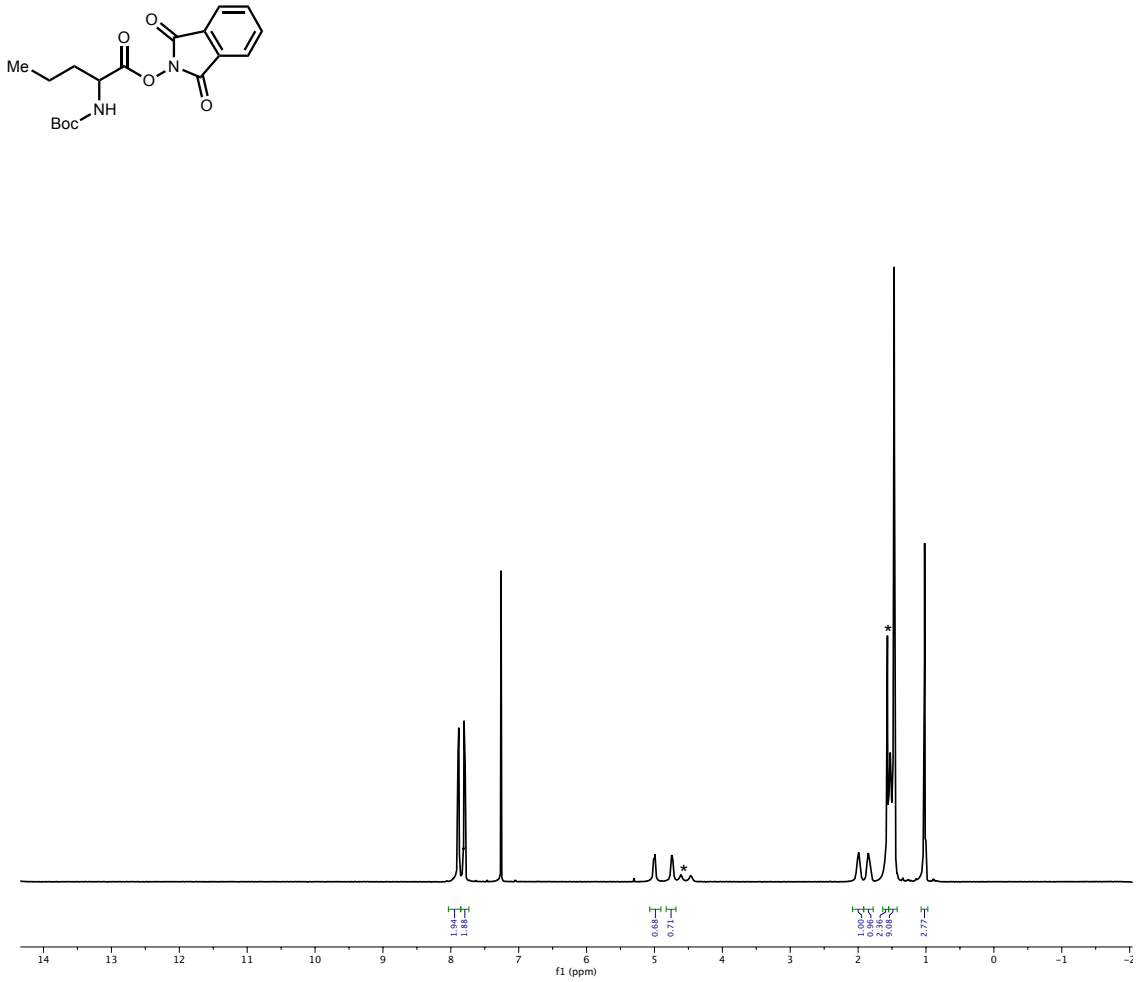


Figure S67. ^{1}H NMR of **15** in $CDCl_3$ at 25 ºC
*: Rotamer

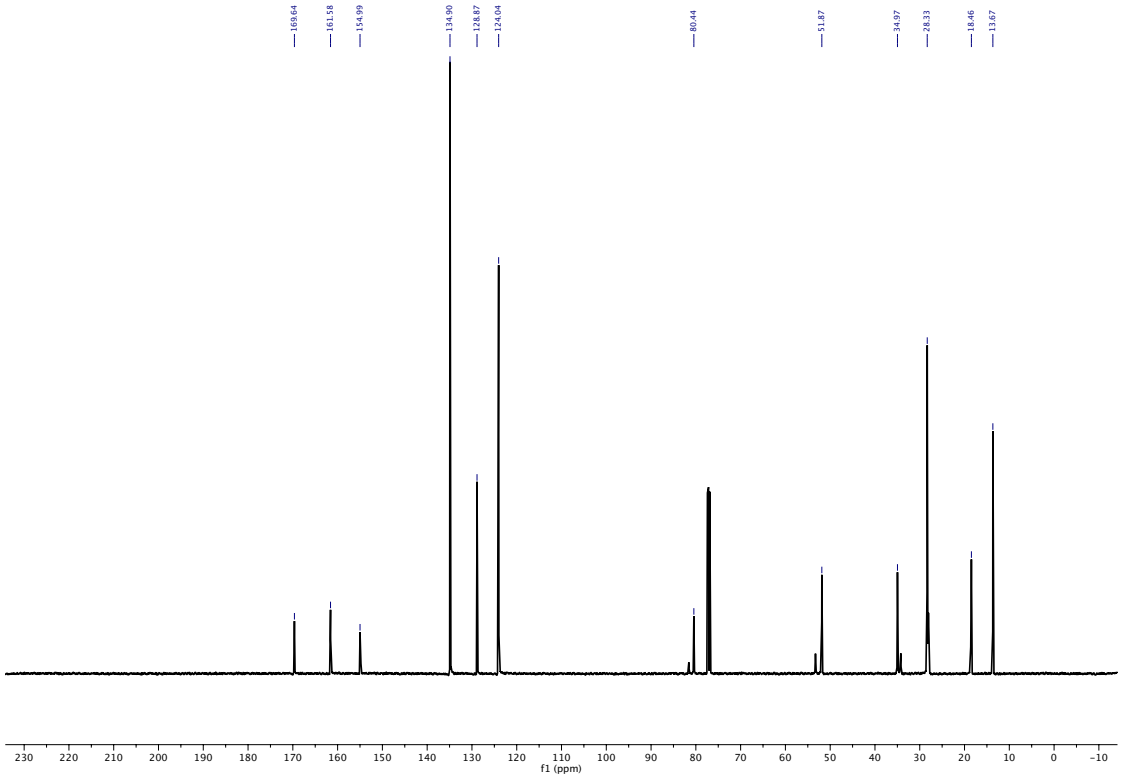


Figure S68. ^{13}C NMR of **15** in $CDCl_3$ at 25 ºC

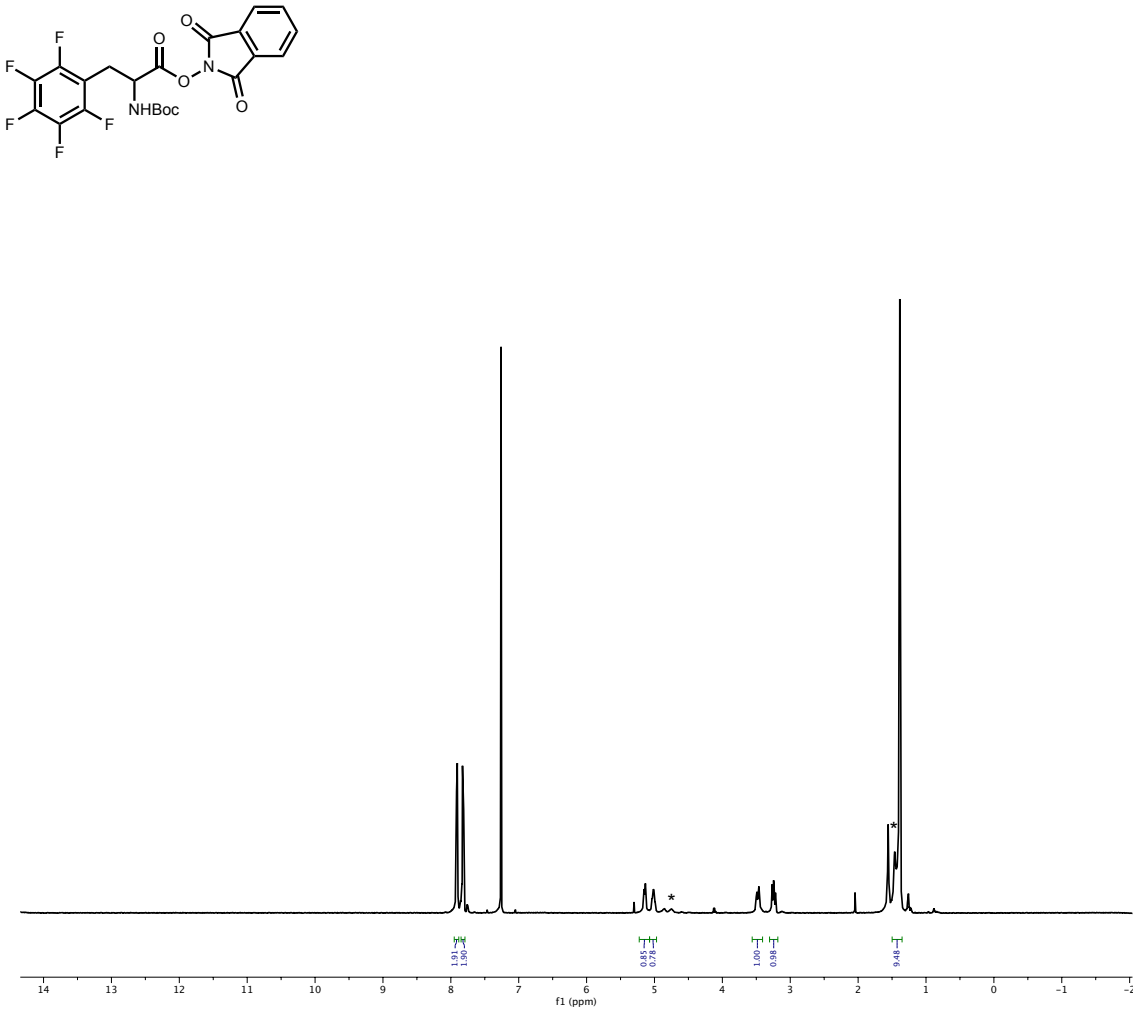


Figure S69. ^{1}H NMR of **S1** in $CDCl_3$ at 25 ºC
*: Rotamer

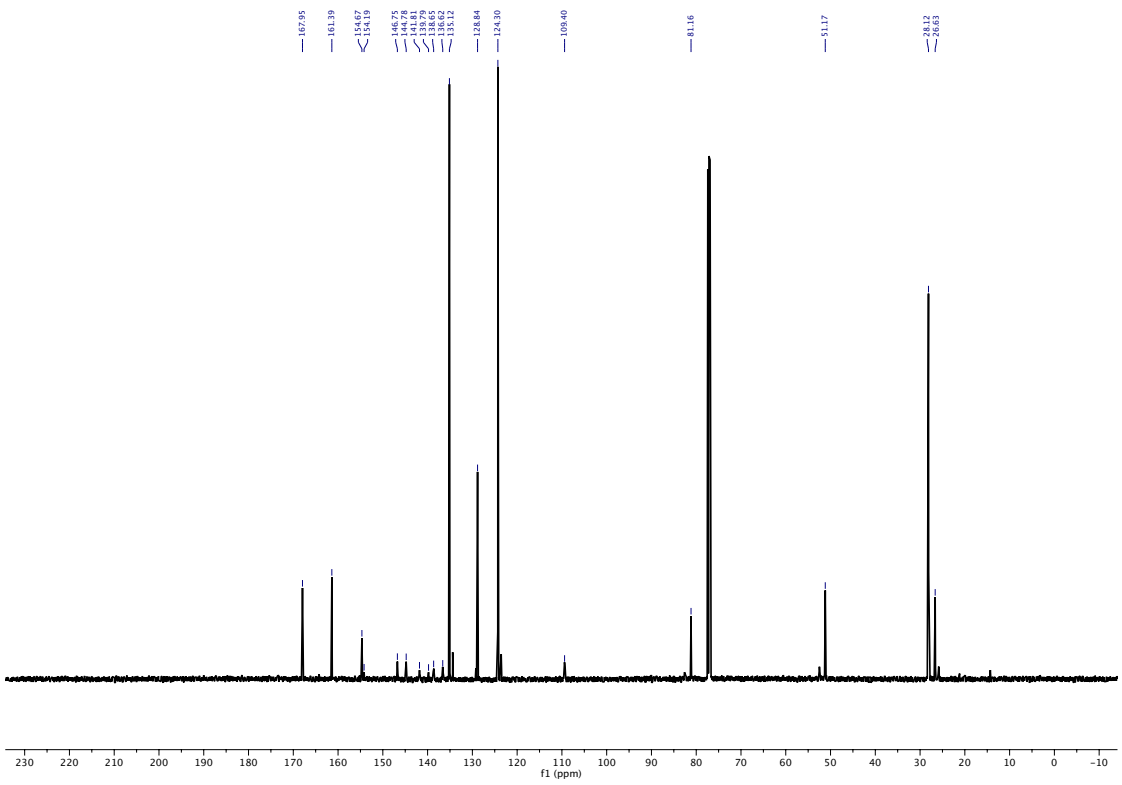


Figure S70. ^{13}C NMR of **S1** in $CDCl_3$ at 25 ºC

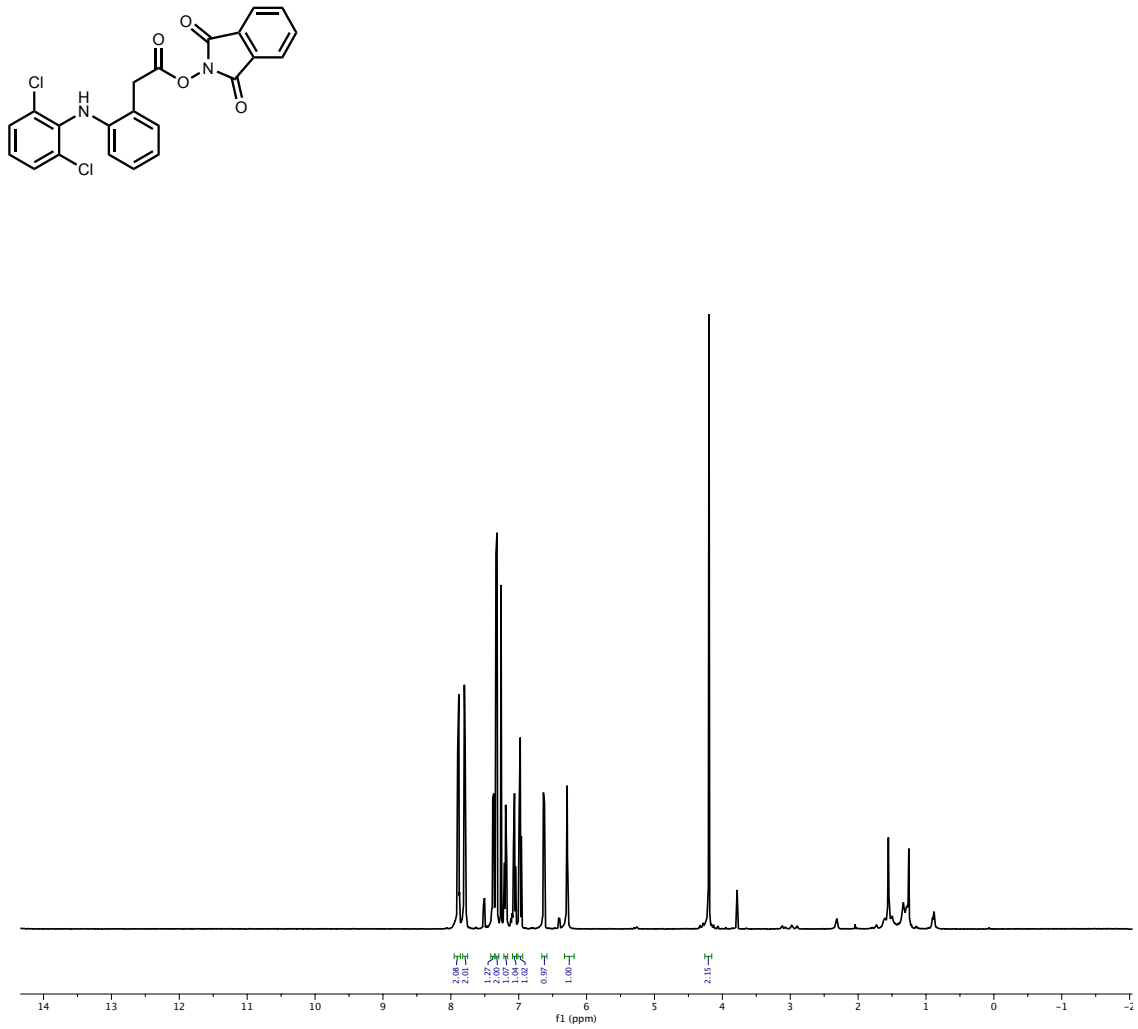


Figure S71. ^{1}H NMR of **S2** in $CDCl_3$ at 25 ºC

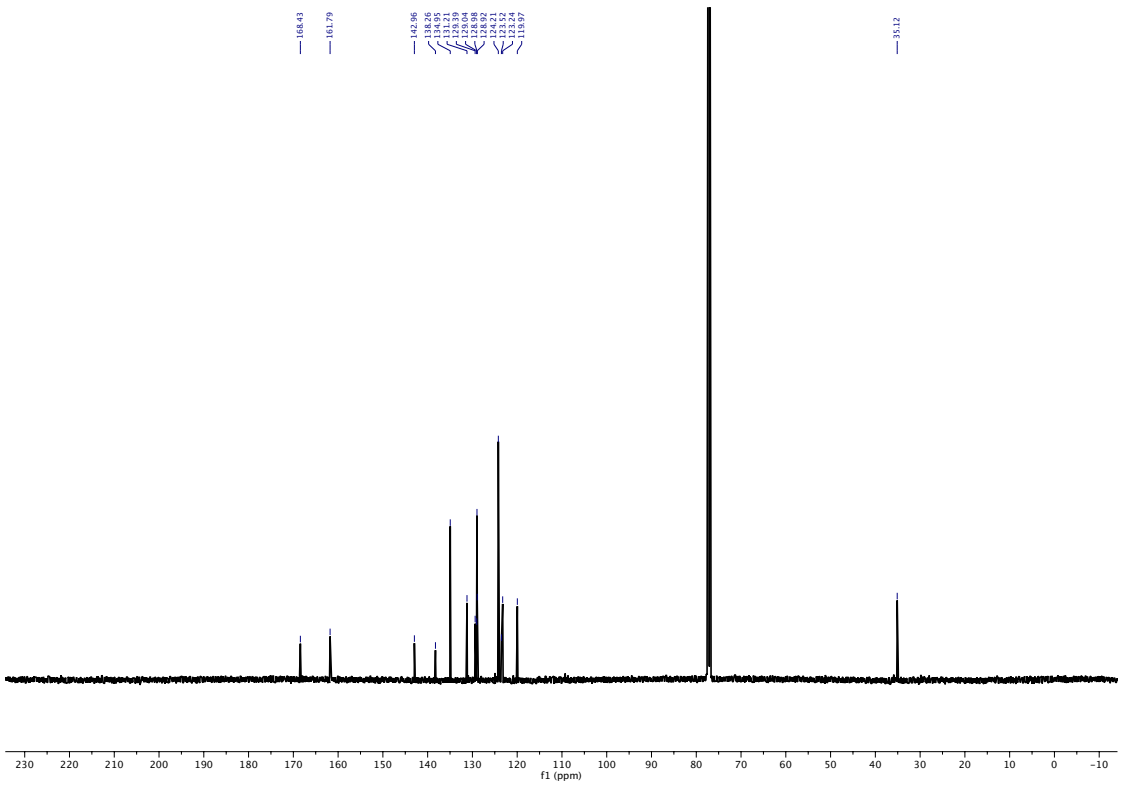
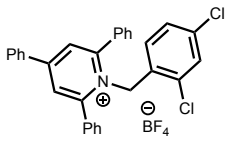


Figure S72. ^{13}C NMR of **S2** in $CDCl_3$ at 25 ºC



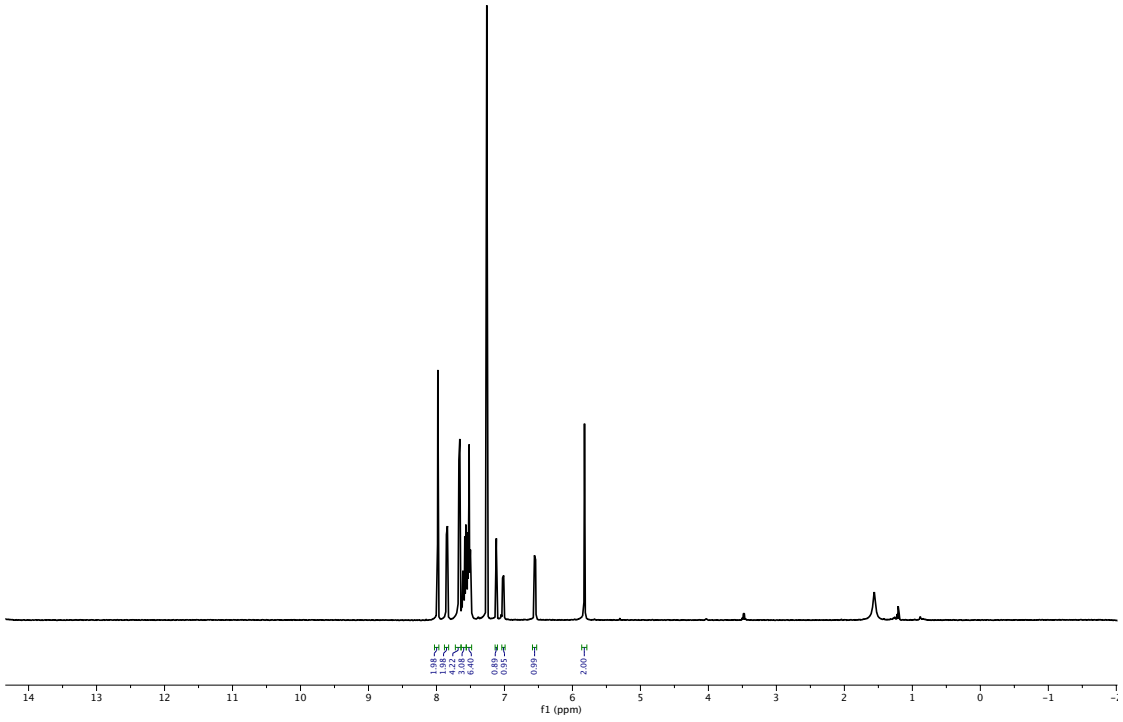


Figure S73. ^{1}H NMR of **7** in $CDCl_3$ at 25 ºC

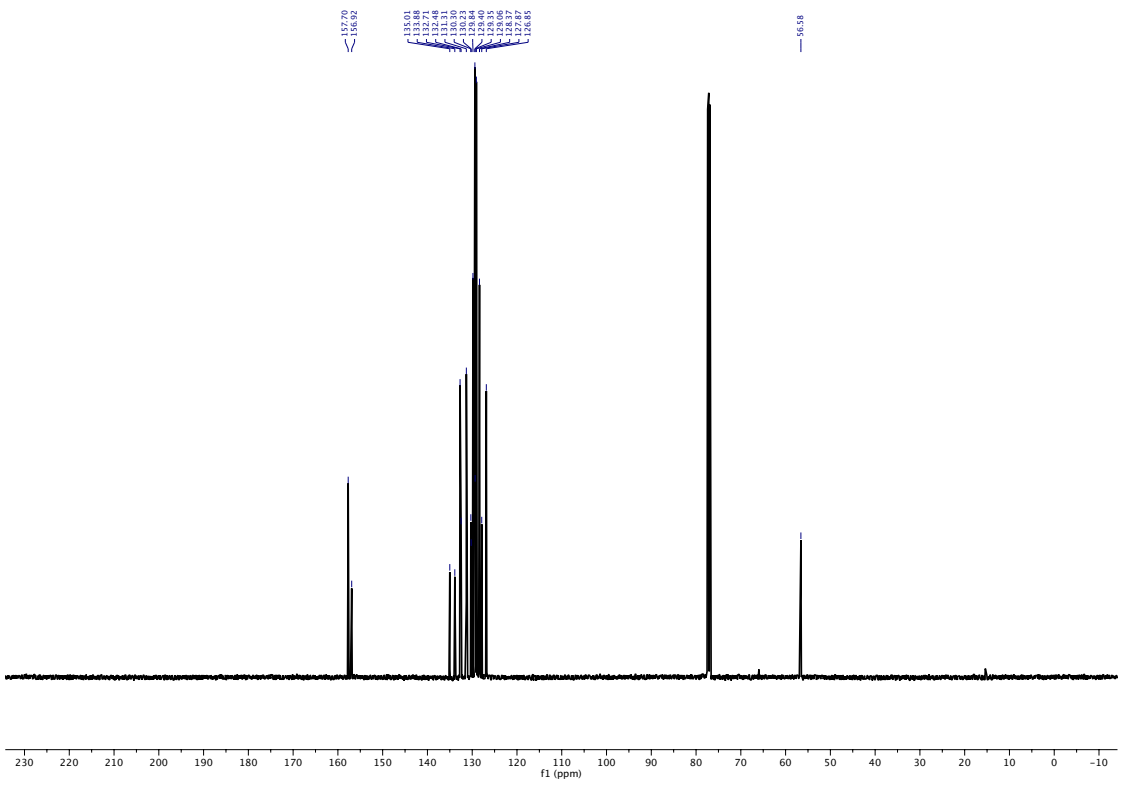


Figure S74. ^{13}C NMR of **7** in $CDCl_3$ at 25 ºC

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