Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

Visible Light Mediated Aryl Migration by Homolytic C–N Cleavage of Aryl Amines

*Dirk Alpers, Kevin P. Cole, and Corey R. J. Stephenson**

anie_201806659_sm_miscellaneous_information.pdf

SUPPORTING INFORMATION

Table of Contents

General Information	**1**
Additional Optimization Data	**2**
Additional Mechanistic Aspects	**4**
Synthesis of Substrates	**5**
Photocatalytic Smiles Reaction	**16**
Synthesis of tetrahydrothienoazepinone 1	**23**
NMR Spectra	**24**

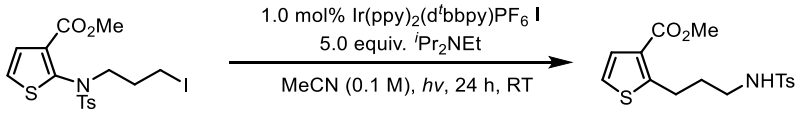
General Information

Commercially available materials were used as received without further purification. All reactions were performed using common inert atmosphere techniques, unless otherwise mentioned. Reactions were monitored by analytical thin-layer chromatography (TLC) using Merck 60 F254 precoated silica gel plates. Solvents were purified by *SciMatCo* solvent purification system. Amines were purified by *Innovative Technology* purification system. Photocatalytic reactions were irradiated with one *Kessil* H350 lamp, placed in a distance of 5 cm from the reaction vessel. HPLC analysis of reaction mixtures was performed by a *Waters ACQUITY UPLC* system with *PDA* UV-Vis detector. Nuclear magnetic resonance (NMR) spectra were recorded on a Varian MR400 400 MHz and Varian vnmrs 500 MHz spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) and referenced to chloroform (^{1}H: δ = 7.26 ppm, ^{13}C: 77.16 ppm). ^{1}H-NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), pentet (p), multiplet (m). Mass spectra were 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.

SUPPORTING INFORMATION

Additional Optimization Data

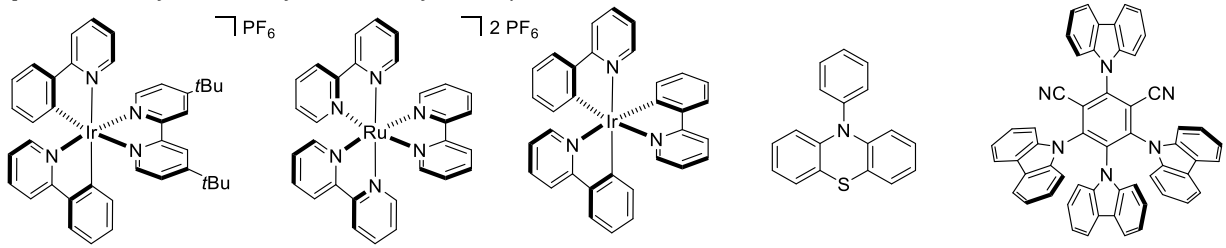
Table S1. Additional data for the optimization of Smiles reaction of **3a**.



3a **2a**

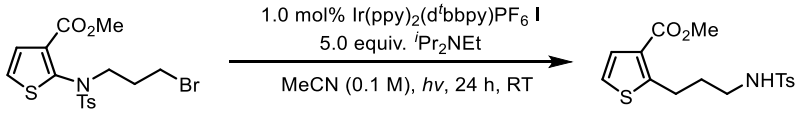
Entry	Variation of above condtions	Yield **2a** (%)[a]
1	None	>95 (87)
2	1.0 mol% $[Ru(bpy)_3](PF_6)_2$ **II**	44
3	1.0 mol% $[Ir(ppy)_3]$ **III**	81
4	10 mol% Phenylphenothiazine **IV**	29
5	5 mol% 4CzIPN **V**	>95 (83)
6	0.1 mol% IrOG	93
7	0.01 mol% IrOG	67
8	0.1 mol% $[Ir(ppy)_2d^tbbpy]PF_6$	91
9	5.0 eq. Et_3N	54
10	under air	0
11	No base	0
12	No catalyst	11
13	Exclusion of light	0
14	No catalyst, no irradiation, 60 °C	0

[a] determined by HPLC analysis; isolated yields in parentheses.



$[Ir(ppy)_2(dtbbpy)](PF_6)$ **I** $[Ru(bpy)_3](PF_6)_2$ **II** $[Ir(ppy)_3]$ **III** 10-Phenylphenothiazine **IV** 4CzIPN **V**

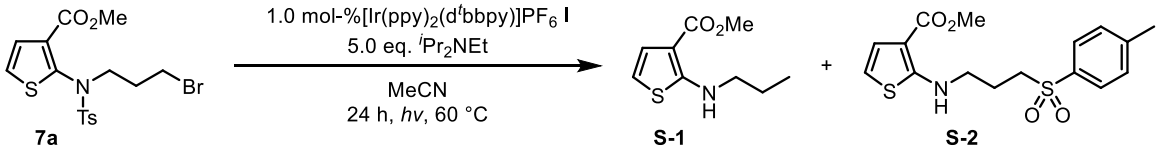
Table S2. Additional data for the optimization of Finkelstein/Smiles reaction of **5a**.



7a **2a**

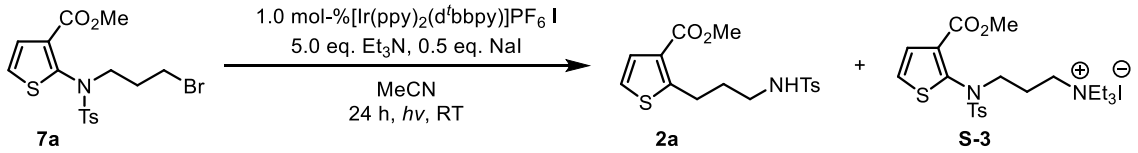
Entry	**Variation of above conditions**	Yield **2a** (%)[a]
1	none	0, see Scheme S1
2	**1.0 eq. NaI**	55
3	1.0 eq. NaI, **60 °C**	>95
4	**0.2 eq. NaI**, 60 °C	16
5	**0.5 eq. NaI**, 60 °C	>95
6	1.0 eq. NaI, **MeCN/H_2O 9:1**, 60 °C	50
7	0.5 eq. NaI, 60 °C, **DMF (0.1 M)**	74
8	0.5 eq. NaI, 60 °C, **DMSO (0.1 M)**	68
9	**1.0 eq. Bu_4NI**, 60 °C	>95
10	**0.2 eq. Bu4NI**, 60 °C	17
11	0.5 eq. NaI, **3.0 eq. $^iPr_2NEt$**, 60 °C	>95
12	0.5 eq. NaI, **3.0 eq. Et_3N**, 60 °C	26, see Scheme S2
13	0.5 eq. NaI, 3.0 eq. $^iPr_2NEt$, **40 °C**, 0.1 M	61
14	0.5 eq. NaI, 3.0 eq. $^iPr_2NEt$, 60 °C, **0.2 M**	>95
15	0.5 eq. NaI, 3.0 eq. $^iPr_2NEt$, 60 °C, **0.3 M**,	90
16	0.5 eq. NaI, 3.0 eq. $^iPr_2NEt$, 60 °C, **0.4 M**	57

[a] determined by HPLC analysis; isolated yield in parentheses.



Scheme S1. Reactivity of **7a** in absence of an iodide-source (Table S1, Entry 1).

S-1: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.01, t, J = 7.3 Hz, 3 H, CH_3), 1.72 (sextet, J = 7.3 Hz, 2 H, CH_2), 3.20 (q, J = 6.7 Hz, 2 H, CH_2), 3.79 (s, 3 H, OCH_3), 6.14 (d, J = 5.7 Hz, 1 H, Ar), 7.01 (d, J = 5.7 Hz, 1 H, Ar), 7.43 (br s, 1 H, NH) ppm.
S-2: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.97 (p, J = 7.0 Hz, 2 H, CH_2), 2.32 (s, 3 H, CH_3), 2.97 (t, J = 7.0 Hz, 2 H, CH_2), 3.36 (q, J = 6.5 Hz, 2 H, CH_2), 3.79 (s, 3 H, OCH_3), 6.16 (d, J = 5.7 Hz, 1 H, Ar), 7.01 (d, J = 5.7 Hz, 1 H, Ar), 7.10 (d, J = 8.0 Hz, 2 H, Ts), 7.27 (d, J = 8.0 Hz, 2 H, Ts), 7.42 (br s, 1 H, NH) ppm.



Scheme S2. Reaction of **7a** in presence of photocatalyst **I** and Et_3N (Table S1, Entry 11).

S-3: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.37 (t, J = 7.2 Hz, 9 H, CH_3), 2.21 (m_c, 2 H, CH_2), 2.42 (s, 3 H, CH_3), 3.50 (q, J = 7.2 Hz, 6 H, CH_2), 3.61-3.86 (m, 7 H, CH_2, OCH_3), 7.17 (d, J = 5.8 Hz, 1 H, Ar), 7.25-7.30 (m, 3 H, Ar, Ts), 7.48 (d, J = 8.2 Hz, 2 H, Ts) ppm.

Additional Mechanistic Aspects

In the course of our reaction optimization, we observed a small amount of Smiles rearrangement product **2a** being formed in absence of any photocatalyst (Table S1, Entry 12). Also, we noticed a slightly enhanced reaction rate under an aerobic atmosphere for the iridium-mediated reaction (Figure S1). These findings suggest that alternative pathways to primary alkyl radical **11** contribute to the overall reaction rate. As photolysis of the alkyl iodide does not occur in absence of an amine base, the combination of both might lead to the formation of an EDA complex, that is able to undergo charge transfer from upon irradiation.[1] The increased reaction rate under aerobic conditions suggests a pathway that is mediated by the amino radical cation of $^{i}Pr_2NEt$. It is supposedly generated by single electron oxidation by molecular oxygen and might abstract the iodine atom of **3a** to generate **11** (Scheme S3). This hypothesis is supported by the result of the electrochemical experiment depicted in Scheme S4. Herein, a potential of +1.0 V was applied to a solution of **3a** in presence of $^{i}Pr_2NEt$ and Bu_4NPF_6 as the electrolyte, and Smiles product **2a** was achieved in 20% yield.

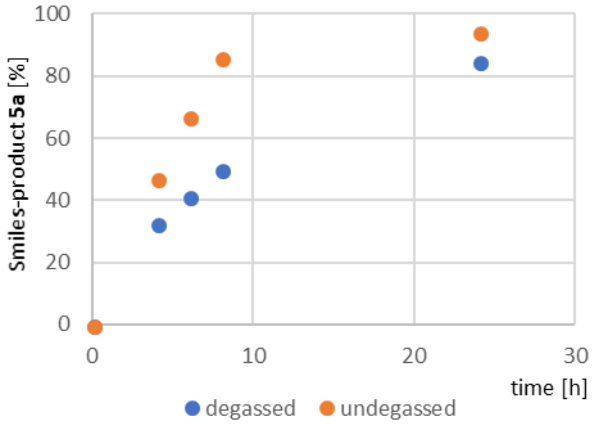
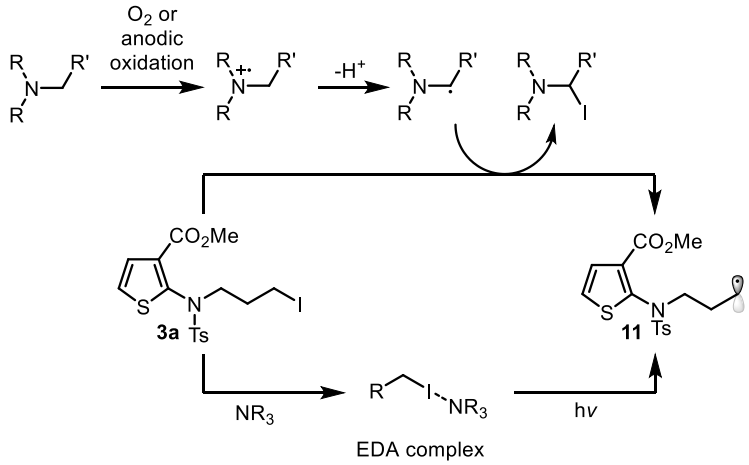
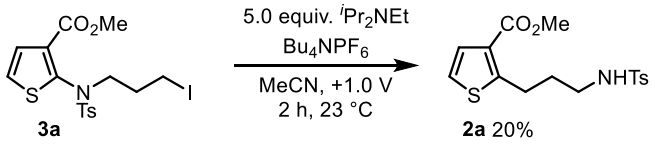


Figure S1. Time resolution of Finkelstein/Smiles reaction of **7a** under oxygen-free conditions and air atmosphere. Conditions: 1.0 mol% $[Ir(ppy)_2(d^tbbpy)]PF_6$, 3.0 equivalents $^{i}Pr_2NEt$, 0.5 equivaents NaI, MeCN (c = 0.1 M).



Scheme S3. Algternative pathways to key radical intermediate **11**.

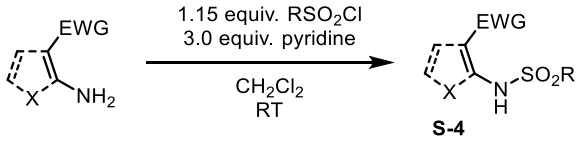


Scheme S4. Electrochemical conduction of Smiles rearrangemen

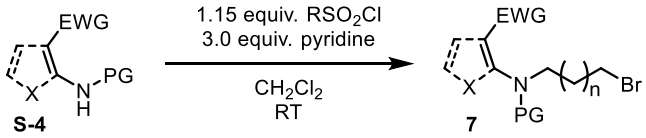
[1] a) A. Böhm, T. Bach, *Chem. Eur. J.* **2016**, *22*, 15921; b) J. F. Franz, W. B. Kraus, K. Zeitler, *Chem. Commun.* **2015**, *51*, 8280; c) D. P. Stevenson, G. M. Coppinger, *J. Am. Chem. Soc.* **1962**, *84*, 149

SUPPORTING INFORMATION

Synthesis of Substrates

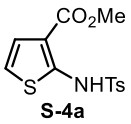


General procedure for the sulfonylation of amines (GP1): Commercially available amines (1.0 equiv.) were dissolved in CH_2Cl_2 (0.4 M) in an oven dried round bottom flask equipped with stir bar and sulfonyl chloride (1.15 equiv.) and pyridine (3.0 equiv.) were added at RT and it was stirred for the indicated time. The reaction mixture was poured into 1 N HCl/CH_2Cl_2 and extracted with CH_2Cl_2 (3x), dried over Na_2SO_4 and concentrated. Pure sulfonamides **S-4** were obtained by column chromatography using silica and hexanes/EtOAc.



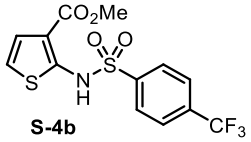
General Procedure for the bromoalkylation of protected amines S-1 with dibromoalkanes (GP2): To a solution of sulfonamides **S-4** in DMF (0.07 M) in an oven dried round bottom flask was added K_2CO_3 (5.0 equiv.) and dibromoalkane (10 equiv.) and heated to 60 °C for the indicated time. After cooling to RT, it was poured into H_2O/EtOAc and extracted with EtOAc (3x). The combined organic layers were washed with 1 N HCl (1x) and 1 M LiCl (3x), dried over Na_2SO_4 and concentrated. Pure alkylbromides **7** were obtained by column chromatography using silica and hexanes/EtOAc.

methyl 2-((4-methylphenyl)sulfonamido)thiophene-3-carboxylate S-4a



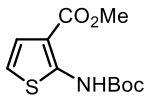
Synthesis according to GP1: 3.14 g (20.0 mmol) methyl 2-aminothiophene-3-carboxylate, 4.39 g (23.0 mmol) 4-methylbenzenesulfonyl chloride, 4.83 mL (4.75 g, 60.0 mmol) pyridine. Column chromatography hexanes/EtOAc 3:1 gave 4.94 g (15.9 mmol, 79%) of **S-4a** as a light brown solid. R_f = 0.35 (hexanes/EtOAc 2:1), ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.37 (s, 3 H, CH_3), 3.79 (s, 3 H, OCH_3), 6.64 (d, J = 5.8 Hz, 1 H, Ar), 7.06 (d, J = 5.8 Hz, 1 H, Ar), 7.25 (d, J = 8.3 Hz, 2 H, Ts), 7.79 (d, J = 8.3 Hz, 2 H, Ts), 10.12 (s, 1 H, NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.7, 51.9, 114.2, 115.7, 124.9, 127.4, 129.9, 135.9, 144.7, 150.0, 165.4 ppm.

methyl 2-((4-(trifluoromethyl)phenyl)sulfonamido)thiophene-3-carboxylate S-4b



Synthesis according to GP1: 786 mg (5.00 mmol) methyl 2-aminothiophene-3-carboxylate, 1.35 g (5.50 mmol) 4-(trifluoromethyl)benzenesulfonyl chloride, 1.21 mL (1.19 g, 15.0 mmol) pyridine. Column chromatography hexanes/EtOAc 5:1 → 3:1 gave 581 mg (1.59 mmol, 32%) of **S-4b** as a colorless solid. R_f = 0.40 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 3.81 (s, 3 H, OCH_3), 6.70 (d, J = 5.8 Hz, 1 H, Ar), 7.09 (d, J = 5.8 Hz, 1 H, Ar), 7.74 (d, J = 8.4 Hz, 1 H, Ts), 8.04 (d, J = 8.4 Hz, 1 H, Ts), 10.25 (s, 1 H, NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 52.1, 115.0, 116.3, 123.2 (q, $J_{C,F}$ = 273 Hz), 125.1, 126.5 (q, $J_{C,F}$ = 3.7 Hz), 127.9, 135.3 (q, $J_{C,F}$ = 33 Hz), 142.3, 148.9, 165.5 ppm.

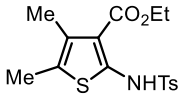
methyl 2-((tert-butoxycarbonyl)amino)thiophene-3-carboxylate S-4c



S-4c

480 mg (2.2 mmol) Boc_2O in an oven dried round bottom flask was dissolved in 50 mL of 1,4-dioxane, 3.14 mg (2.00 mmol) methyl 2-aminothiophene-3-carboxylate and 24.4 mg (0.10 mmol) DMAP were added and it was stirred at RT for 2 h. The reaction mixture was poured into water/EtOAc, extracted with EtOAc (3x) and the combined organic phases were dried over Na_2SO_4 and concentrated. Purification by column chromatography using hexanes/EtOAc 10:1 → 5:1 gave 403 mg (1.57 mmol, 78%) of **S-4c** as a colorless oil. R_f = 0.30 (hexanes/EtOAc 9:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.53 (s, 9 H, Boc), 3.86 (s, 3 H, OCH_3), 6.64 (d, J = 5.8 Hz, 1 H, Ar), 7.13 (d, J = 5.8 Hz, 1 H, Ar), 10.03 (s, NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 28.3, 51.7, 82.3, 111.1, 114.7, 124.2, 151.3, 152.2, 165.9 ppm.

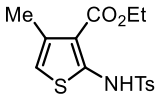
ethyl 4,5-dimethyl-2-((4-methylphenyl)sulfonamido)thiophene-3-carboxylate S-4f



S-4f

Synthesis according to GP1: 399 mg (2.00 mmol) ethyl 2-amino-4,5-dimethylthiophene-3-carboxylate, 438 mg (2.30 mmol) 4-methylbenzenesulfonyl chloride, 0.485 mL (475 mg, 6.00 mmol) pyridine. Column chromatography hexanes/EtOAc 5:1 → 3:1 gave 605 mg (1.71 mmol, 86%) of **S-4f** as a colorless solid. R_f = 0.40 (hexanes/EtOAc 3:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.32 (t, J = 7.1 Hz, 3 H, CH_3), 2.13 (s, 3 H, CH_3), 2.21 (s, 3 H, CH_3), 2.38 (s, 3 H, CH_3), 4.25 (q, J = 7.1 Hz, 2 H, OCH_2), 7.25 (d, J = 8.1 Hz, 2 H, Ts), 7.77 (d, J = 8.1 Hz, 2 H, Ts), 10.37 (s, 1 H, NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 12.7, 14.3, 14.5, 21.7, 60.8, 114.9, 123.4, 127.4, 129.8, 130.2, 136.1, 144.3, 147.1, 165.9 ppm.

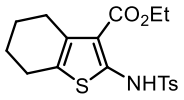
ethyl 4-methyl-2-((4-methylphenyl)sulfonamido)thiophene-3-carboxylate S-4g



S-4g

Synthesis according to GP1: 556 mg (3.00 mmol) ethyl 2-amino-4-methylthiophene-3-carboxylate, 658 mg (3.45 mmol) 4-methylbenzenesulfonyl chloride, 0.728 mL (712 mg, 9.00 mmol) pyridine. Column chromatography hexanes/EtOAc 5:1 → 3:1 gave 781 mg (2.30 mmol, 77%) of **S-4g** as a colorless solid. R_f = 0.45 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.33 (t, J = 7.1 Hz, 3 H, CH_3), 2.25 (s, 3 H, CH_3), 2.38 (s, 3 H, CH_3), 4.27 (q, J = 7.1 Hz, 2 H, OCH_2), 6.28 (s, 1 H, Ar), 7.25 (d, J = 8.3 Hz, 1 H, Ts), 7.79 (d, J = 8.3 Hz, 1 H, Ts), 10.50 (s, 1 H, NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 14.3, 18.1, 21.7, 61.0, 112.0, 114.0, 127.4, 129.8, 136.0, 144.5, 151.1, 165.9 ppm.

methyl 2-((4-methylphenyl)sulfonamido)-4,5,6,7-tetrahydrobenzothiophene-3-carboxylate S-4h

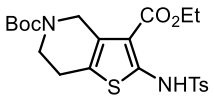


S-4h

Synthesis according to GP1: 423 mg (2.00 mmol) methyl 2-amino-4,5,6,7-tetrahydrobenzothiophene-3-carboxylate, 438 mg (2.30 mmol) 4-methylbenzenesulfonyl chloride, 0.485 mL (475 mg, 6.00 mmol) pyridine. Column chromatography hexanes/EtOAc 5:1 → 3:1 gave 446 mg (1.22 mmol, 61%) of **S-4h** as a colorless solid. R_f = 0.20 (hexanes/EtOAc 4:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.32 1.66-1.79 (m, 4 H, CH_2), 2.39 (s, 3 H, CH_3), 2.54-2.60 (m, 2 H, CH_2), 2.60-2.66 (m, 2 H, CH_2), 3.77 (s, 3 H, OCH_3), 7.26 (d, J = 8.3

Hz, 2 H, Ts), 7.80 (d, *J* = 8.3 Hz, 2 H, Ts), 10.38 (s, 1 H, NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) *δ* 21.7, 22.7, 23.0, 24.6, 26.5, 51.6, 113.2, 126.7, 127.5, 129.9, 132.1, 136.1, 144.4, 148.2, 166.4 ppm.

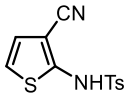
5-(*tert*-butyl) 3-ethyl 2-((4-methylphenyl)sulfonamido)-6,7-dihydrothieno[3,2-c]pyridine-3,5(4H)-dicarboxylate S-4i



S-4i

Synthesis according to GP1: 625 mg (1.91 mmol) ethyl 2-((4-methylphenyl)sulfonamido)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-3-carboxylate, 420 mg (2.20 mmol) 4-methylbenzenesulfonyl chloride, 0.464 mL (454 mg, 5.74 mmol) pyridine. Column chromatography hexanes/EtOAc 3:1 → 1:1 gave 782 mg (1.63 mmol, 85%) of **S-4i** as a colorless foam. R_f = 0.25 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) *δ* 1.31 (t, *J* = 7.1 Hz, 3 H, CH_3), 9.84 (s, 9 H, Boc), 2.39 (s, 3 H, CH_3), 2.74 (m_c, 2 H, CH_2), 3.58 (t, *J* = 5.6 Hz, 2 H, CH_2), 4.25 (q, *J* = 7.1 Hz, 2 H, OCH_2), 4.43 (s, 2 H, CH_2), 7.27 (d, *J* = 8.1 Hz, 2 H, Ts), 7.79 (d, *J* = 8.1 Hz, 2 H, Ts), 10.43 (s, 1 H, NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) *δ* 14.3, 21.7, 26.8, 28.6, 41.2, 42,7, 61.0, 80.4, 113.1, 123.4, 127.5, 129.9, 131.2, 136.3, 144.6, 149.3, 154.7, 165.5 ppm.

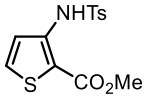
***N*-(3-cyanothiophen-2-yl)-4-methylbenzenesulfonamide S-4j**



S-4j

Synthesis according to GP1: 621 mg (5.00 mmol) 2-aminothiophene-3-carbonitrile, 1.10 g (5.75 mmol) 4-methylbenzenesulfonyl chloride, 1.21 mL (1.19 g, 15.0 mmol) pyridine. Column chromatography hexanes/EtOAc 2:1 → 3:2 gave 234 mg (0.54 mmol,11%) of **S-4j** as a colorless oil. R_f = 0.20 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) *δ* 2.42 (s, 3 H, CH_3), 6.91 (d, *J* = 5.8 Hz, 1 H, Ar), 6.96 (d, *J* = 5.8 Hz, 1 H, Ar), 7.30 (d, *J* = 8.4 Hz, 2 H, Ts), 7.65 (br s, 1 H, NH), 7.74 (d, *J* = 8.4 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) *δ* 21.8, 100.6, 113.5, 121.3, 125.8, 127.6, 130.2, 134.9, 145.4, 148.9 ppm.

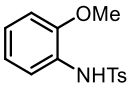
***N*-(3-cyanothiophen-2-yl)-4-methylbenzenesulfonamide S-4k**



S-4k

Synthesis according to GP1: 393 mg (2.50 mmol) methyl 3-aminothiophene-2-carboxylate 548 mg (2.87 mmol) 4-methylbenzenesulfonyl chloride, 1.01 mL (989 mg, 12.5 mmol) pyridine. Column chromatography hexanes/EtOAc 6:1 gave 185 mg (0.59 mmol,24%) of **S-4k** as a colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) *δ* 2.25 (s, 3 H, CH_3), 3.70 (s, 3 H, CH_3), 7.12 (d, *J* = 8.3 Hz, 2 H, Ts), 7.61 (d, *J* = 8.3 Hz, 2 H, Ts), 9.46 (s, 1 H, NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) *δ* 21.5, 52.0, 110.5, 120.5, 127.0, 129.8, 131.9, 136.4, 143.6, 144.1, 164.2 ppm.

methyl 2-((4-methylphenyl)sulfonamido)benzoate S-4l

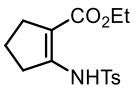


S-4l

Synthesis according to GP1: 572 mg (4.64 mmol) methoxyaniline, 974 mg (5.11 mmol) 4-methylbenzenesulfonyl chloride, 1.13 mL (1.10 g, 13.9 mmol) pyridine. Column chromatography hexanes/EtOAc 5:1 → 4:1 gave 1.24 g (0.59 mmol, 96%) of **S-4l** as a colorless oil. R_f = 0.15 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) *δ* 2.35 (s, 3 H, CH_3) 3.64 (s, 3 H, OCH_3), 6.73 (d, J = 7.9 Hz, 1 H, Ar),

6.89 (t, *J* = 7.4 Hz, 1 H, Ar), 6.95-7.11 (m, 2 H, NH, Ar), 7.18 (d, *J* = 7.6 Hz, 2 H, Ts), 7.51 (s, *J* = 7.6 Hz, 1 H, Ar), 7.64 (d, *J* = 7.6 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.6, 55.7, 110.7, 121.1, 121.2, 125.3, 126.2, 127.4, 129.5, 136.4, 143.7, 149.6 ppm.

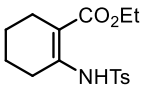
ethyl 2-((4-methylphenyl)sulfonamido)cyclopent-1-ene-1-carboxylate S-4m



S-4m

Synthesis according to GP1: 310 mg (2.00 mmol) ethyl 2-aminocyclopentene-1-carboxylate, 438 mg (2.30 mmol) 4-methylbenzenesulfonyl chloride, 0.485 mL (475 mg, 6.00 mmol) pyridine. Column chromatography hexanes/EtOAc 4:1 → 1:1 gave 188 mg (0.608 mmol, 30%) of **S-4m** as a colorless solid. R_f = 0.45 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.27 (t, J = 7.1 Hz, 3 H, CH_3), 1.78, (p, J = 7.6 Hz, 2 H, CH_2), 2.41-2.48 (m, 5 H, CH_2, CH_3), 2.72 (t, J = 7.7 Hz, 2 H, CH_2), 4.18 (q, J = 7.1 Hz, 2 H, OCH_2), 7.31 (d, J = 8.3 Hz, 2 H, Ts), 7.77 (d, J = 8.3 Hz, 2 H, Ts), 10.09 (s, 1 H, NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 14.5, 20.7, 21.7, 28.8, 32.6, 60.2, 107.6, 127.2, 130.0, 137.8, 144.2, 152.7, 167.6 ppm.

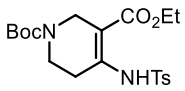
ethyl 2-((4-methylphenyl)sulfonamido)cyclohex-1-ene-1-carboxylate S-4n



S-4n

Synthesis according to GP1: 422 mg (2.49 mmol) ethyl 2-aminocyclopentene-1-carboxylate, 547 mg (2.87 mmol) 4-methylbenzenesulfonyl chloride, 0.603 mL (592 mg, 7.48 mmol) pyridine. Column chromatography hexanes/EtOAc 9:1 gave 577 mg (1.78 mmol, 72%) of **S-4n** as a colorless solid. R_f = 0.25 (hexanes/EtOAc 9:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.27 (t, J = 7.1 Hz, 3 H, CH_3), 1.50 (m_c, 4 H, CH_2), 2.19-2.25 (m, 2 H, CH_2), 2.40-2.46 (m, 5 H, CH_2, CH_3), 4.18 (q, J = 7.1 Hz, 2 H, OCH_2), 7.29 (d, J = 8.2 Hz, 2 H, Ts), 7.75 (d, J = 8.2 Hz, 2 H, Ts), 11.60 (s, 1 H, NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 14.3, 21.6, 21.7, 21.7, 24.1, 26.6, 60.6, 105.2, 127.2, 129.9, 138.1, 143.9, 149.6, 170.0 ppm.

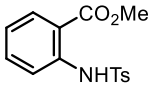
1-(*tert*-butyl) 3-ethyl 4-((4-methylphenyl)sulfonamido)-5,6-dihydropyridine-1,3(2*H*)-dicarboxylate S-4o



S-4o

synthesis according to GP1: 541 mg (2.00 mmol) ethyl 2-aminocyclopentene-1-carboxylate, 438 mg (2.30 mmol) 4-methylbenzenesulfonyl chloride, 0.485 mL (475 mg, 6.00 mmol) pyridine. Column chromatography hexanes/EtOAc 6:1 → 3:1 gave 313 mg (0.74 mmol, 37%) of **S-4o** as a pale yellow foam along with 129 mg (0.477 mmol, 24%) of starting material. R_f = 0.25 (hexanes/EtOAc 4:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.27 (t, J = 7.1 Hz, 3 H, CH_3), 1.42 (s, 9 H, Boc), 2.42 (s, 3 H, CH_3), 2.54 (m_c, 2 H, CH_2), 3.38 (t, J = 5.8 Hz, 2 H, CH_2), 4.03 (br s, 2 H, CH_2), 4.19 (q, J = 7.1 Hz, 2 H, OCH_2) 7.30 (d, J = 8.2 Hz, 2 H, Ts), 7.74 (d, J = 8.2 Hz, 2 H, Ts), 11.45 (s, 1 H, NH) ppm.^{13}C-NMR ($CDCl_3$, 100 MHz) δ 14.2, 21.7, 26.3, 28.4, 39.0, 41.4, 61.0, 80.3, 127.1, 130.1, 137.6, 144.3, 154.3, 167.9 ppm.

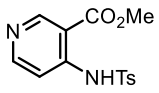
methyl 2-((4-methylphenyl)sulfonamido)benzoate S-4p



S-4p

synthesis according to GP1: 302 mg (2.00 mmol) methyl 2-aminobenzoate, 438 mg (2.30 mmol) 4-methylbenzenesulfonyl chloride, 0.485 mL (475 mg, 6.00 mmol) pyridine. Column chromatography hexanes/EtOAc 3:1 → 2:1 gave 491 mg (1.61 mmol, 80%) of **S-4p** as a colorless solid. R_f = 0.35 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.35 (s, 3 H, CH_3), 3.87 (s, 3 H, OCH_3), 7.02 (t, J = 7.6 Hz, 1 H, Ar), 7.21 (d, J = 8.1 Hz, 2 H, Ts), 7.44 (t, J = 7.8 Hz, 1 H, Ar), 7.68 (d, J = 8.4 Hz, 1 H, Ar), 7.73 (d, J = 8.1 Hz, 1 H, Ts), 7.91 (d, J = 7.9 Hz, 1 H, Ar), 10.61 (s, 1 H, NH) ppm.

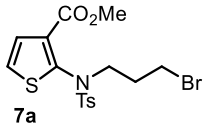
methyl 4-((4-methylphenyl)sulfonamido)nicotinate S-4q



S-4q

synthesis according to GP1: 304 mg (2.00 mmol) methyl 4-aminonicotinate, 438 mg (2.30 mmol) 4-methylbenzenesulfonyl chloride, 0.485 mL (475 mg, 6.00 mmol) pyridine. Column chromatography hexanes/EtOAc 1:1 → 1:2 gave 124 mg (0.405 mmol, 20%) of **S-4q** as a colorless solid. R_f = 0.15 (hexanes/EtOAc 1:2). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.40 (s, 3 H, CH_3), 3.96 (s, 3 H, OCH_3), 7.30 (d, J = 8.2 Hz, 2 H, Ts), 7.53 (d, J = 5.9 Hz, 1 H, Ar), 7.84 (d, J = 8.2 Hz, 2 H, Ts), 8.47 (d, J = 5.9 Hz, 1 H, Ar), 9.04 (s, 1 H, Ar), 10.92 (br s, 1 H, NH) ppm.^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.8, 52.9, 110.7, 111.0, 127.5, 130.2, 136.1, 145.0, 147.5, 152.7, 154.0, 167.8 ppm.

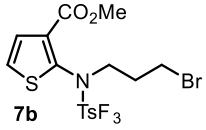
methyl 2-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)thiophene-3-carboxylate 7a



7a

Synthesis according to GP2: 1.72 g (5.52 mmol) methyl 2-((4-methylphenyl)sulfonamido)thiophene-3-carboxylate **S-4a**, 3.82 g (27.6 mmol) K_2CO_3, 5.60 mL (11.2 g, 55.2 mmol) 1,3-dibromopropane. Column chromatography hexanes/EtOAc 3:1 → 2:1 gave 1.64 g (3.79 mmol, 67%) of **7a** as a colorless solid. R_f = 0.30 (hexanes/EtOAc 3:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.14 (m_c, 2 H, CH_2), 2.42 (s, 3 H, CH_3), 3.50 (t, J = 6.6 Hz, 2 H, CH_2), 3.64 (s, 3 H, OCH_3), 3.79 (t, J = 6.6 Hz, 2 H, CH_2), 7.16 (d, J = 5.9 Hz, 1 H, Ar), 7.27 (d, J = 8.2 Hz, 2 H, Ts), 7.32 (d, J = 5.9 Hz, 1 H, Ar), 7.58 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.7, 30.2, 32.1, 51.8, 51.9, 124.0, 128.0, 128.2, 129.6, 130.2, 135.2, 144.1, 146.0, 162.1 ppm. ESI-HRMS for $C_{16}H_{18}BrNO_4S_2$, $[M+H]^+$ calc. 431.9933, found 431.9934. IR: $\tilde{\nu}$ = 2950 (-C-H), 1715 (C=O), 1435, 1350, 1265, 1160, 1090 cm^{-1}.

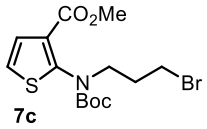
methyl 2-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)thiophene-3-carboxylate 7b



7b

Synthesis according to GP2: 550 mg (1.51 mmol) methyl 2-((4-(trifluoromethyl)phenyl)sulfonamido)thiophene-3-carboxylate **S-4b**, 1.04 g (7.53 mmol) K_2CO_3, 1.53 mL (3.04 g, 15.1 mmol) 1,3-dibromopropane. Column chromatography hexanes/EtOAc 3:1 → 2:1 gave 1.64 g (3.79 mmol, 67%) of **7b** as a colorless solid. R_f = 0.45 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.17 (p, J = 6.6 Hz, 2 H, CH_2), 3.49 (t, J = 6.5 Hz, 2 H, CH_2), 3.57 (s, 3 H, OCH_3), 3.87 (t, J = 6.7 Hz, 2 H, CH_2), 7.22 (d, J = 5.9 Hz, 1 H, Ar), 7.32 (d, J = 5.9 Hz, 1 H, Ar), 7.74 (d, J = 8.4 Hz, 2 H, Ts), 7.83 (d, J = 8.4 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 29.9, 32.1, 51.8, 52.1, 123.4 ($J_{C,F}$ = 273 Hz), 124.6, 126.1 ($J_{C,F}$ = 3.7 Hz), 128.3, 128.5, 129.7, 134.8 ($J_{C,F}$ = 32.7 Hz), 141.8, 145.4, 161.7 ppm. ESI-HRMS for $C_{16}H_{15}BrF_3NO_4S_2$, $[M+H]^+$ calc. 485.9651, found 485.9644. IR: $\tilde{\nu}$ = 2955 (-C-H), 1720 (C=O), 1360, 1320, 1270, 1170, 1135, 1060 cm^{-1}.

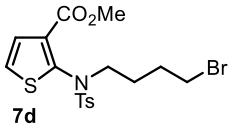
methyl 2-((3-bromopropyl)(*tert*-butoxycarbonyl)amino)thiophene-3-carboxylate 7c



7c

Synthesis according to GP2: 400 mg (1.55 mmol) methyl 2-((tert-butoxycarbonyl)amino)thiophene-3-carboxylate **S-4c**, 1.07 g (7.77 mmol) K_2CO_3, 1.58 mL (3.14 g, 15.5 mmol) 1,3-dibromopropane. Column chromatography hexanes/EtOAc 10:1 → 4:1 gave 440 mg (1.16 mmol, 75%) of **7c** as a colorless oil. R_f = 0.40 (hexanes/EtOAc 4:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.20-1.60 (m, 9 H, Boc), 2.16 (p, J = 6.8 Hz, 2 H, CH_2), 3.44 (t, J = 6.7 Hz, 2 H, CH_2), 3.76 (t, J = 6.8 Hz, 2 H, CH_2), 3.81 (s, 3 H, OCH_3), 7.05 (d, J = 5.8 Hz, 1 H, Ar), 7.30 (d, J = 5.8 Hz, 1 H, Ar) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 28.2, 30.7, 31.6, 50.5, 51.9, 81.2, 121.5, 127.5, 127.7, 151.2, 154.0, 162.5 ppm. ESI-HRMS for $C_{14}H_{20}BrNO_4S_2$, $[M+Na]^+$ calc. 400.0189, found 400.0183. IR: $\tilde{\nu}$ = 2975 (-C-H), 1705 (C=O), 1365, 1260, 1145 cm^{-1}.

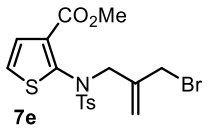
methyl 2-((*N*-(3-bromobutyl)-4-methylphenyl)sulfonamido)thiophene-3-carboxylate 7d



7d

Synthesis according to GP2: 623 mg (2.00 mmol) methyl 2-((4-methylphenyl)sulfonamido)thiophene-3-carboxylate **S-4a**, 1.38 g (10.0 mmol) K_2CO_3, 2.36 mL (4.32 g, 20.0 mmol) 1,3-dibromobutane. Column chromatography hexanes/EtOAc 8:1 → 3:1 gave 511 mg (1.14 mmol, 57%) of **7d** as a colorless oil. R_f = 0.35 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.72 (p, J = 7.2 Hz, 2 H, CH_2), 1.97(p, J = 7.1 Hz, 2 H, CH_2), 2.42 (s, 3 H, CH_3), 3.40 (t, J = 6.6 Hz, 2 H, CH_2), 3.63 (s, 3 H, OCH_3), 3.71 (t, J = 6.9 Hz, 2 H, CH_2), 7.15 (d, J = 5.9 Hz, 1 H, Ar), 7.25 (d, J = 8.1 Hz, 2 H, Ts), 7.32 (d, J = 5.9 Hz, 1 H, Ar), 7.58 (d, J = 8.1 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.5, 27.2, 29.6, 33.0, 51.6, 52.1, 123.8, 127.9, 128.1, 129.5, 130.1, 135.6, 143.8, 146.0, 162.0 ppm. ESI-HRMS for $C_{17}H_{20}BrNO_4S_2$, $[M+H]^+$ calc. 446.0090, found 446.0088. IR: $\tilde{\nu}$ = 2950 (-C-H), 1715 (C=O), 1435, 1350, 1285, 1155, 1090 cm^{-1}.

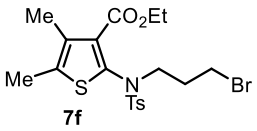
methyl 2-((*N*-(2-(bromomethyl)allyl)-4-methylphenyl)sulfonamido)thiophene-3-carboxylate 7e



7e

Synthesis according to GP2: 167 mg (0.536 mmol) methyl 2-((4-methylphenyl)sulfonamido)thiophene-3-carboxylate **S-4a**, 371 mg (2.68 mmol) K_2CO_3, 5.74 mg (2.68 mmol) 3-bromo-2-(bromomethyl)prop-1-ene. Column chromatography hexanes/EtOAc 8:1 → 1:1 gave 58.9 mg (0.144 mmol, 27%) of **7e** as a colorless oil. R_f = 0.25 (hexanes/EtOAc2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.40 (s, 3 H, CH_3), 3.62 (s, 3 H, OCH_3), 4.05 (s, 2 H, CH_2), 4.37 (s, 2 H, CH_2), 5.07 (s, 1 H, =CH_2), 5.25 (s, 1 H, =CH_2), 7.11 (d, J = 5.9 Hz, 1 H, Ar), 7.22 – 7.29 (m, 3 H, Ar, Ts), 7.58 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.7, 33.3, 51.8, 55.3, 120.3, 123.8, 128.0, 128.1, 129.6, 129.9, 135.0, 140.3, 144.2, 145.8, 162.1 ppm.

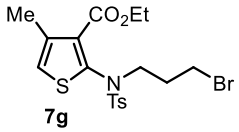
ethyl 2-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)-4,5-dimethylthiophene-3-carboxylate 7f



7f

Synthesis according to GP2: 527 mg (1.49 mmol) ethyl 4,5-dimethyl-2-((4-methylphenyl)sulfonamido)thiophene-3-carboxylate **S-4f**, 1.03 g (7.45 mmol) K_2CO_3, 1.51 mL (3.01 g, 14.9 mmol) 1,3-dibromopropane. Column chromatography hexanes/EtOAc 5:1 → 3:1 gave 505 mg (1.06 mmol, 71%) of **7f** as a colorless oil. R_f = 0.35 (hexanes/EtOAc 3:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.34 (t, J = 7.1 Hz, 3 H, CH_3), 2.16 (p, J = 6.6 Hz, 2 H, CH_2), 2.20 (s, 3 H, CH_3), 2.28 (s, 3 H, CH_3), 2.42 (s, 3 H, CH_3), 3.50 (t, J = 6.6 Hz, 2 H, CH_2), 3.67 (m_c, 2 H, CH_2), 4.19 (q, J = 7.1 Hz, 2 H, OCH_2), 7.27 (d, J = 8.1 Hz, 2 H, Ts), 7.59 (d, J = 8.1 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 13.5, 14.3, 21.7, 30.4, 31.8, 51.8, 61.0, 128.1, 129.6, 132.2, 132.7, 132.8, 135.1, 139.6, 143.9, 163.6 ppm. ESI-HRMS for $C_{19}H_{24}BrNO_4S_2$, $[M+H]^+$ calc. 474.0403, found 474.0401. IR: $\tilde{\nu}$ = 2925 (-C-H), 1710 (C=O), 1350, 1260, 1165, 1090 cm^{-1}.

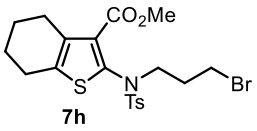
ethyl 2-((N-(3-bromopropyl)-4-methylphenyl)sulfonamido)-4-methylthiophene-3-carboxylate 7g



7g

Synthesis according to GP2: 750 mg (2.21 mmol) ethyl 4-methyl-2-((4-methylphenyl)sulfonamido)thiophene-3-carboxylate **S-4g**, 1.53 g (11.0 mmol) K_2CO_3, 2.24 mL (4.46 g, 22.1 mmol) 1,3-dibromopropane. Column chromatography hexanes/EtOAc 10:1 → 4:1 gave 846 mg (1.84 mmol, 83%) of **7g** as a colorless oil. R_f = 0.20 (hexanes/EtOAc 5:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.35 (t, J = 7.1 Hz, 3 H, CH_3), 2.16 (p, J = 6.6 Hz, 2 H, CH_2), 2.34 (s, 3 H, CH_3), 2.42 (s, 3 H, CH_3), 3.51 (t, J = 6.6 Hz, 2 H, CH_2), 3.71 (t, J = 6.2 Hz, 2 H, CH_2), 4.22 (q, J = 7.1 Hz, 2 H, OCH_2), 6.78 (s, 1 H, Ar), 7.26 (d, J = 8.3 Hz, 1 H, Ts), 7.57 (d, J = 8.3 Hz, 1 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 14.3, 17.2, 21.7, 30.3, 31.9, 51.8, 61.1, 119.9, 128.1, 129.7, 131.8, 134.8, 137.8, 144.1, 144.7, 163.2 ppm. ESI-HRMS for $C_{18}H_{22}BrNO_4S_2$, $[M+H]^+$ calc. 460.0246, found 460.0244. IR: $\tilde{\nu}$ = 2980, 2925 (-C-H), 1715 (C=O), 1355, 1260, 1160, 1090 cm^{-1}

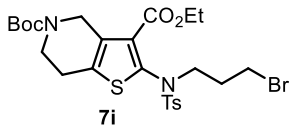
ethyl 2-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)-4-methylthiophene-3-carboxylate 7h



7h

Synthesis according to GP2: 431 mg (1.18 mmol) methyl 2-((4-methylphenyl)sulfonamido)-4,5,6,7-tetrahydrobenzothiophene-3carboxylate **S-4h**, 815 mg (5.90 mmol) K_2CO_3, 1.20 mL (2.38 g, 11.8 mmol) 1,3-dibromopropane. Column chromatography hexanes/EtOAc 7:1 → 3:1 gave 366 mg (0.752 mmol, 64%) of **7h** as a colorless solid. R_f = 0.35 (hexanes/EtOAc 3:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.61-1.76 (m, 4 H, CH_2), 2.04 (p, J = 6.5 Hz, 2 H, CH_2), 2.31 (s, 3 H, CH_3), 2.51-2.57 (m, 2 H, CH_2), 2.57-2.65 (m, 2 H, CH_2), 3.38 (t, J = 6.6 Hz, 2 H, CH_2) 3.52-3.61 (m, 5 H, CH_2, OCH_3), 7.16 (d, J = 8.0 Hz, 2 H, Ts), 7.50 (d, J = 8.0 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.7, 22.5, 22.9, 25.3, 25.8, 30.4, 31.9, 51.6, 51.8, 128.1, 129.7, 130.7, 134.8, 135.4, 135.4, 141.4, 143.9, 163.4 ppm. ESI-HRMS for $C_{20}H_{24}BrNO_4S_2$, $[M+H]^+$ calc. 486.0403, found 486.0399. IR: $\tilde{\nu}$ = 2935, (-C-H), 1715 (C=O), 1350, 1265, 1245, 1165, 1090 cm^{-1}.

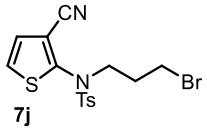
5-(*tert*-butyl) 3-ethyl 2-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)-6,7-dihydrothieno[3,2-c]pyridine-3,5(4*H*)-dicarboxylate 7i



7i

Synthesis according to GP2: 718 mg (1.49 mmol) 5-(*tert*-butyl) 3-ethyl 2-((4-methylphenyl)sulfonamido)-6,7-dihydrothieno[3,2-c]pyridine-3,5(4*H*)-dicarboxylate **S-4i**, 1.03 g (7.47 mmol) K_2CO_3, 1.52 mL (3.02 g, 14.9 mmol) 1,3-dibromopropane. Column chromatography hexanes/EtOAc 3:1 → 2:1 gave 590 mg (0.981 mmol, 66%) of **7i** as a pale yellow foam. R_f = 0.35 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.30 (t, J = 7.0 Hz, 3 H, CH_3), 1.46 (s, 9 H, Boc), 2.14 (m_c, 2 H, CH_2), 2.40 (s, 3 H, CH_3), 2.82 (m_c, 2 H, CH_2), 3.44 (t, J = 6.6 Hz, 2 H, CH_2), 3.63 (m_c, 2 H, CH_2), 3.68 (m_c, 2 H, CH_2), 4.09-4.22 (m, 2 H, CH_2), 4.48 (s, 2 H, CH_2), 7.25 (d, J = 8.0 Hz, 2 H, Ts), 7.58 (d, J = 8.0 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 14.2, 21.6, 26.2, 28.5, 30.0, 31.9, 41.2, 43.0, 52.0, 60.9, 80.4, 128.1, 129.7, 130.6, 131.7, 133.7, 135.4, 143.1, 144.0, 154.6, 162.3 ppm. ESI-HRMS for $C_{25}H_{33}BrN_2O_6S_2$, $[M+H]^+$ calc. 601,1036, found 601.1022. IR: $\tilde{\nu}$ = 2975 (-C-H), 1695 (C=O), 1420, 1365, 1240, 1165 cm^{-1}.

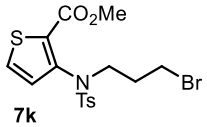
***N*-(3-bromopropyl)-*N*-(3-cyanothiophen-2-yl)-4-methylbenzenesulfonamide 7j**



7j

Synthesis according to GP2: 207 mg (0.744 mmol) *N*-(3-cyanothiophen-2-yl)-4-methylbenzenesulfonamide **S-4j**, 514 mg (3.72 mmol) K_2CO_3, 0.754 mL (1.50 g, 7.44 mmol) 1,3-dibromopropane. Column chromatography hexanes/EtOAc 3:1 → 2:1 gave 226 mg (0.566 mmol, 76%) of **7j** as a colorless solid. R_f = 0.15 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.11 (p, J = 6.5 Hz, 2 H, CH_2), 2.45 (s, 3 H, CH_3), 3.46 (t, J = 6.4 Hz, 2 H, CH_2), 3.81 (t, J = 6.7 Hz, 2 H, CH_2), 7.08 (d, J = 5.8 Hz, 1 H, Ar), 7.29 (d, J = 5.8 Hz, 1 H, Ar), 7.33 (d, J = 8.2 Hz, 2 H, Ts), 7.65 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.8, 29.5, 31.7, 51.6, 110.7, 113.1, 126.3, 127.3, 128.2, 130.2, 133.6, 145.2, 150.7 ppm. ESI-HRMS for $C_{16}H_{18}BrNO_4S_2$, $[M+NH_4]^+$ calc. 416.0097, found 416.0092. IR: $\tilde{\nu}$ = 3110 (=C-H), 2925 (-C-H), 2235 (C≡N), 1355, 1240, 1165, 1090 cm^{-1}.

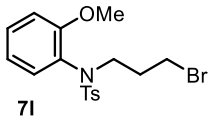
methyl 3-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)thiophene-2-carboxylate 7k



7k

Synthesis according to GP2: 100 mg (0.321 mmol) *N*-(3-cyanothiophen-2-yl)-4-methylbenzenesulfonamide **S-4k**, 222 mg (1.61 mmol) K_2CO_3, 0.327 mL (648 mg, 3.21 mmol) 1,3-dibromopropane. Column chromatography hexanes/EtOAc 3:1 gave 117 mg (0.271 mmol, 84%) of **7k** as a colorless oil. R_f = 0.25 (hexanes/EtOAc 3:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.08 (p, J = 6.6 Hz, 2 H, CH_2), 2.41 (s, 3 H, CH_3), 3.48 (t, J = 6.6 Hz, 2 H, CH_2), 3.65 (s, 3 H, OCH_3), 3.74 (t, J = 6.6 Hz, 2 H, CH_2), 6.94 (d, J = 5.3 Hz, 1 H, Ar), 7.24 (d, J = 8.3 Hz, 2 H, Ts), 7.46 (d, J = 5.3 Hz, 1 H, Ar), 7.54 (d, J = 8.3 Hz, 2 H Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.7, 30.4, 32.6, 50.3, 52.1, 127.7, 128.9, 129.5, 129.6, 130.0, 136.0, 140.9, 143.7, 160.7 ppm. ESI-HRMS for $C_{16}H_{18}BrNO_4S_2$, $[M+H]^+$ calc. 431.9933, found 431.9933. IR: $\tilde{\nu}$ = 2950 (-C-H), 1720 (C=O), 1435, 1350, 1260, 1230, 1160, 1090 cm^{-1}.

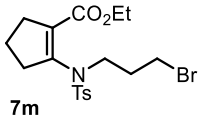
_N_-(3-bromopropyl)-_N_-(2-methoxyphenyl)-4-methylbenzenesulfonamide 7l



7l

Synthesis according to GP2: 1.19 g (4.29 mmol) methyl 2-((4-methylphenyl)sulfonamido)benzoate **S-4l**, 2.97 g (21.5 mmol) K_2CO_3, 4.35 mL (8.66 g, 42.9 mmol) 1,3-dibromopropane. Column chromatography hexanes/EtOAc 9:1 → 3:1 gave 117 mg (0.271 mmol, 84%) of **7l** as a colorless solid. R_f = 0.30 (hexanes/EtOAc 3:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.99 (p, J = 6.7 Hz, 2 H, CH_2), 2.39 (s, 3 H, CH_3), 3.41 (s, 3 H, OCH_3), 3.45 (t, J = 6.7 Hz, 2 H, CH_2), 3.68 (m_c, 2 H, CH_2), 6.79 (d, J = 8.3 Hz, 1 H, Ar), 6.91 (t, J = 7.5 Hz, 1 H, Ar), 7.19 (d, J = 7.6 Hz, 1 H, Ar), 7.22 (d, J = 8.2 Hz, 2 H, Ts), 7.28 (t, J = 7.7 Hz, 1 H, Ar), 7.54 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.6, 30.6, 32.4, 48.9, 55.1, 111.9, 120.9, 126.9, 127.8, 129.2, 130.1, 132.8, 137.2, 143.0, 156.8 ppm. ESI-HRMS for $C_{17}H_{20}BrNO_3S$, $[M+H]^+$ calc. 398.0420, found 398.0419. IR: $\tilde{\nu}$ = 2940 (-C-H), 1495, 1340, 1255, 1155, 1090, 1025 cm^{-1}.

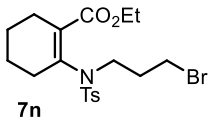
ethyl 2-((_N_-(3-bromopropyl)-4-methylphenyl)sulfonamido)cyclopent-1-ene-1-carboxylate 7m



7m

Synthesis according to GP2: 127 mg (0.410 mmol) ethyl 2-((4-methylphenyl)sulfonamido)cyclopent-1-ene-1-carboxylate **S-4m**, 284 mg (2.05 mmol) K_2CO_3, 0.416 mL (829 mg, 4.10 mmol) 1,3-dibromopropane. Column chromatography hexanes/EtOAc 5:1 → 2:1 gave 117 mg (0.271 mmol, 84%) of **7m** as a colorless solid. R_f = 0.45 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.25 (t, J = 7.1 Hz, 3 H, CH_3), 1.86, (p, J = 7.6 Hz, 2 H, CH_2), 2.10 (p, J = 6.4 Hz, 2 H, CH_2), 2.36-2.47 (m, 5 H, CH_2, CH_3), 2.68 (m_c, 2 H, CH_2), 3.49 (t, J = 6.4Hz, 2 H, CH_3), 3.56 (t, J = 6.5 Hz, 2 H, CH_2), 4.09 (q, J = 7.1 Hz, 2 H, OCH_2), 7.28 (d, J = 8.3 Hz, 2 H, Ts), 7.68 (d, J = 8.3Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 14.2, 20.6, 21.7, 30.7, 32.3, 32.6, 34.7, 47.7, 60.5, 127.5, 129.7, 131.6, 136.8, 143.7, 146.1, 164.5 ppm. ESI-HRMS for $C_{18}H_{24}BrNO_4S$, $[M+H]^+$ calc. 430.0682, found 430.0682. IR: $\tilde{\nu}$ = 2960 (-C-H), 1710 (C=O), 1350, 1235, 1160, 1090 cm^{-1}.

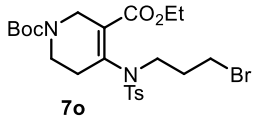
ethyl 2-((_N_-(3-bromopropyl)-4-methylphenyl)sulfonamido)cyclohex-1-ene-1-carboxylate 7n



7n

Synthesis according to GP2: 323 mg (1.00 mmol) ethyl 2-((4-methylphenyl)sulfonamido)cyclohex-1-ene-1-carboxylate **S-4n**, 691 mg (5.00 mmol) K_2CO_3, 1.01 mL (2.02 g, 10.0 mmol) 1,3-dibromopropane. Column chromatography hexanes/EtOAc 8:1 → 3:1 gave 393 mg (0.884 mmol, 88%) of 7**n** as a colorless solid. R_f = 0.20 (hexanes/EtOAc 4:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.28 (t, J = 7.1 Hz, 3 H, CH_3), 1.48-2.73 (m, 13 H), 3.09-3.76 (m, 4 H), 4.12 (q, J = 7.1 Hz, 2 H, OCH_2), 7.26, (d, J = 8.2 Hz, 2 H, Ts), 7.66 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 14.2, 21.6, 22.5, 27.6, 27.7, 31.2, 32.1, 46.4, 60.8, 127.4, 129.7, 133.5, 137.3, 138.0, 143.5, 167.9 ppm. ESI-HRMS for $C_{19}H_{26}BrNO_4S$, $[M+H]^+$ calc. 444.0893, found 444.0839. IR: $\tilde{\nu}$ = 2935 (-C-H), 1710 (C=O), 1350, 1230, 1155, 1090, 1050 cm^{-1}.

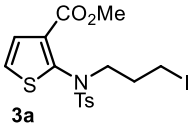
1-(*tert*-butyl) 3-ethyl 4-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)-5,6-dihydropyridine-1,3(2*H*)-dicarboxylate 7o



7o

Synthesis according to GP2: 250 mg (0.589 mmol) 1-(*tert*-butyl) 3-ethyl 4-((4-methylphenyl)sulfonamido)-5,6-dihydropyridine-1,3(2*H*)-dicarboxylate **S-4o**, 407 mg (2.94 mmol) K_2CO_3, 0.597 mL (1.19 g, 5.89 mmol) 1,3-dibromopropane. Column chromatography hexanes/EtOAc 5:1 → 2:1 gave 198 mg (0.363 mmol, 62%) of **7o** as a colorless oil. R_f = 0.15 (hexanes/EtOAc 3:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.29 (m_c, 3 H, CH_3), 1.48 (s, 9 H, Boc), 2.08 (m, 2 H, CH_2), 2.16 (p, J = 6.6 Hz, 2 H, CH_2), 2.42 (s, 3 H, CH_3), 3.39-3.56 (m, 6 H), 4.13 (m_c, 2 H, CH_2), 4.23 (br s, 2 H, CH_2), 7.28 (d, J = 8.2 Hz, 2 H, Ts), 7.67 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 14.2, 21.6, 28.6, 29.8, 30.7, 32.4, 40.4, 44.6, 47.1, 61.2, 80.6, 127.6, 129.9, 130.2 137.4, 138.8, 143.9 154.6, 165.1 ppm. ESI-HRMS for $C_{16}H_{18}BrNO_4S_2$, $[M+NH_4]^+$ calc. 562.1581, found 562.1571. IR: $\tilde{\nu}$ = 2980 (-C-H), 1700 (C=O), 1355, 1240, 1160 cm^{-1}.

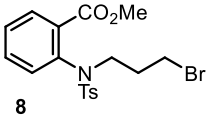
methyl 2-((*N*-(3-iodopropyl)-4-methylphenyl)sulfonamido)thiophene-3-carboxylate 3a



3a

To a solution of 432 mg (1.00 mmol) alkylbromide **7a** in 10.0 mL MeCN in an oven dried round bottom flask were added 749 mg (5.00 mmol) of NaI and the reaction mixture was heated to 60 °C for 18 h. After cooling to RT, the mixture was poured into brine/EtOAc and extracted with EtOAc (3x). The combined organic layers were washed with water (1x), dried over Na_2SO_4, and concentrated *in vacuo*. Column chromatography hexanes/EtOAc 4:1 → 3:1 gave 454 mg (0.947 mmol, 95%) of **3a** as a colorless solid. R_f = 0.30 (hexanes/EtOAc 3:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.11 (p, J = 6.8 Hz, 2 H, CH_2), 2.42 (s, 3 H, CH_3), 3.25 (t, J = 6.8 Hz, 2 H, CH_2), 3.63 (s, 3 H, CH_3), 3.73 (t, J = 6.8 Hz, 2 H, CH_2), 7.16 (d, J = 5.9 Hz, 1 H, Ar), 7.27 (d, J = 8.2 Hz, 2 H, Ts), 7.31 (d, J = 5.9 Hz, 1 H, Ar), 7.58 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 2.2, 21.7, 32.9, 51.8, 53.8, 124.0, 128.0, 128.2, 129.6, 130.2, 135.2, 144.1, 146.0, 162.1 ppm. IR: $\tilde{\nu}$ = 2950 (-C-H), 1715 (C=O), 1435, 1350, 1275, 1155, 1090 cm^{-1}

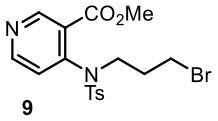
methyl 2-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)benzoate 8



8

Synthesis according to GP2: 464 mg (1.52 mmol) methyl 2-((4-methylphenyl)sulfonamido)benzoate **S-4p**, 1.05 g (7.60 mmol) K_2CO_3, 1.54 mL (3.07 g, 15.2 mmol) 1,3-dibromopropane. Column chromatography hexanes/EtOAc 5:1 → 2:1 gave 402 mg (0.943 mmol, 62%) of **8** as colorless solid. R_f = 0.35 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.17 (m_c, 2 H, CH_2), 2.42 (s, 3 H, CH_3), 3.50 (t, J = 6.6 Hz, 2 H, CH_2), 3.78 (br s, 2 H, CH_2), 3.83 (s, 3 H, OCH_3), 6.92 (d, J = 7.4 Hz, 1 H, Ar), 7.24 (d, J = 7.9 Hz, 2 H, Ts), 7.40 (p, J = 7.3 Hz, 2 H, Ar), (d, J = 7.9 Hz, 2 H, Ts), 7.86 (d, J = 7.2 Hz, 1 H, Ar) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.6, 30.7, 32.2, 50.5, 52.3, 127.9, 128.3, 129.6, 131.5, 132.2, 133.2, 136.2, 138.5, 143.5, 166.6 ppm

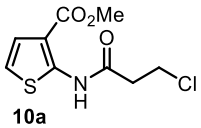
methyl 4-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)nicotinate 9



9

Synthesis according to GP2: 124 mg (0.405 mmol) methyl 4-((4-methylphenyl)sulfonamido)nicotinate **S-4q**, 280 mg (2.02 mmol) K_2CO_3, 0.411 mL (0.817 g, 4.05 mmol) 1,3-dibromopropane. Column chromatography using pure EtOAc gave 116 mg (0.271 mmol, 67%) of **9** as colorless oil. R_f = 0.10 (EtOAc). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.32 (p, J = 6.4 Hz, 2 H, CH_2), 2.39 (s, 3 H, CH_3), 3.34 (t, J = 5.9 Hz, 2 H, CH_2), 3.84 (s, 3 H, OCH_3), 4.16 (t, J = 6.8 Hz, 2 H, CH_2), 7.25 (d, J = 8.0 Hz, 2 H, Ts), 7.50 (d, J = 7.4 Hz, 1 H, Ar), 7.59 (d, J = 7.4 Hz, 1 H, Ar), 7.91 (d, J = 8.0 Hz, 2 H, Ts), 8.09 (s, 1 H, Ar) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.6, 28.6, 32.8, 52.6, 55.8, 116.5, 119.2, 165.2, 129.2, 139.4, 141.1, 142.0, 143.7, 159.1, 164.4 ppm

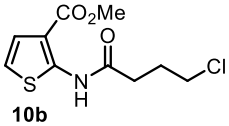
methyl 2-(3-chloropropanamido)thiophene-3-carboxylate 10a



10a

In an oven dried round bottom flask was added 0.101 mL (134 mg, 1.00 mmol) of 3-chloropropanoyl chloride dropwise to a solution of 157 mg (1.00 mmol) methyl 2-aminothiophene-3-carboxylate and 0.0807 mL (79.1mg, 1.00 mmol) pyridine in 4.0 mL of CH_2Cl_2. It was stirred at RT for 2 h and quenched by addition of of 1 N HCl. It was extracted with CH_2Cl_2 (3x), dried over Na_2SO_4, and concentrated *in vacuo*. Purification by column chromatography using hexanes/EtOAc 2:1 → 1:1 gave 233 mg (0.941 mmol, 94%) of **10a** as a colorless solid. R_f = 0.30 (hexanes/EtOAc 1:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.95 (t, J = 6.5 Hz, 2 H, CH_2), 3.80-3.93 (m, 5 H, CH_2, OCH_3), 6.73 (d, J = 5.7 Hz, 1 H, Ar), 7.17 (d, J = 5.7 Hz, 1 H, Ar), 11.06 (s, 1 H, NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 39.2, 39.7, 51.9, 113.0, 116.5, 123.8, 148.4, 166.1, 166.7 ppm.

methyl 2-(3-chlorobutanamido)thiophene-3-carboxylate 10b

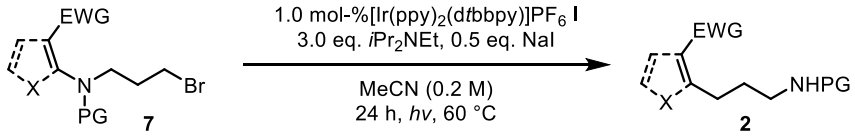


10b

In an oven dried round bottom flask was added 0.112 mL (142 mg, 1.00 mmol) of 4-chlorobutanoyl chloride dropwise to a solution of 157 mg (1.00 mmol) methyl 2-aminothiophene-3-carboxylate and 0.0807 mL (79.1mg, 1.00 mmol) pyridine in 4.0 mL of CH_2Cl_2. It was stirred at RT for 2 h and quenched by addition of of 1 N HCl. It was extracted with CH_2Cl_2 (3x), dried over Na_2SO_4, and concentrated *in vacuo*. Purification by column chromatography using hexanes/EtOAc 3:1 → 1:1 gave 243 mg (0.928 mmol, 93%) of **10b** as a colorless oil. R_f = 0.30 (hexanes/EtOAc 1:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.23 (p, J = 6.6 Hz, 2 H, CH_2), 2.70 (t, J = 7.1 Hz, 2 H, CH_2), 3.65 (t, J = 6.2 Hz, 2 H, CH_2), 3.88 (s, 3 H, OCH_3), 6.73 (d, J = 5.7 Hz, 1 H, Ar), 7.18 (d, J = 5.7 Hz, 1 H, Ar), 11.01 (s, 1 H, NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 27.7, 33.4, 44.2, 51.9, 112.6, 116.2, 123.8, 148.7, 166.1, 169.0 ppm.

SUPPORTING INFORMATION

Photocatalytic Smiles Reactions



General procedure for the one-pot Finkelstein/photocatalytic Smiles reaction (GP3): To 0.10 mmol of alkylbromides **7** in a 2-dram-vial equipped with a stir bar was added 0.300 mL of a freshly prepared solution of NaI in MeCN (0.167 M, 0.0500 mmol), 0.149 mL of $[Ir(ppy)_2(dtbbpy)]PF_6$ **I** in MeCN (6.71 mM, 1.00 µmol) and 51.0 µL iPr_2NEt (38.8 mg, 0.300 mmol). To reactions run at 0.05 M was added 1.5 mL of MeCN. The reaction vessel was sealed, heated to 60 °C using an oil bath and irradiated by one Kessil H350 lamp for 24 h. The solvent was removed under reduced pressure and the Smiles products **2** was purified by column chromatography using silica and hexanes/EtOAc.

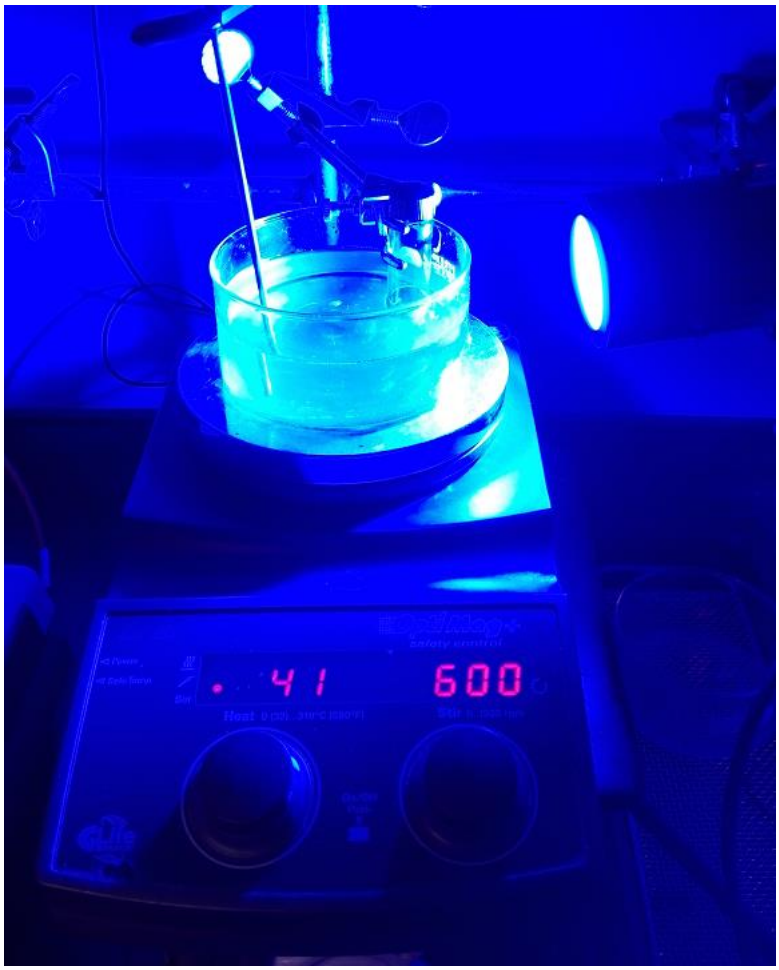
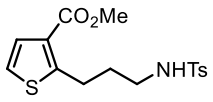


Figure S2. Experimental setup of Finkelstein/Smiles reaction.

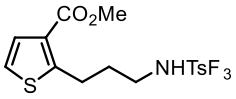
methyl 2-(3-((4-methylphenyl)sulfonamido)propyl)thiophene-3-carboxylate 2a



2a

Synthesis according to GP3: 43.2 mg (0.100 mmol) methyl 2-((4-methylphenyl)sulfonamido)thiophene-3-carboxylate **7a**, column chromatography hexanes/EtOAc 3:1 → 2:1 gave 33.6 mg (0.0951 mmol, 95%) of **2a** as a colorless oil. R_f = 0.25 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.84 (p, J = 6.9 Hz, 2 H, CH_2), 2.40 (s, 3 H, Me), 2.95 (q, J = 6.4 Hz, 2 H, CH_2), 3.17 (t, J = 7.3 Hz, 2 H, CH_2), 3.83 (s, 3 H, OMe), 5.24 (t, J = 6.2 Hz, 1 H, NH), 7.02 (d, J = 5.4 Hz, 1 H, Ar), 7.27 (d, J = 8.2 Hz, 2 H, Ts), 7.32 (d, J = 5.4 Hz, 1 H, Ar), 7.73 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.6, 25.8, 31.6, 42.0, 51.8, 122.1, 127.2, 128.1, 129.1, 129.7, 137.3, 143.3, 153.6, 164.2 ppm. ESI-HRMS for $C_{16}H_{19}NO_4S_2$, $[M+H]^+$ calc. 354.0828, found 354.0836. IR: $\tilde{\nu}$ = 3275 (N-H), 2945 (-C-H), 1705 (C=O), 1435, 1325, 1260, 1155, 1095 cm^{-1}.

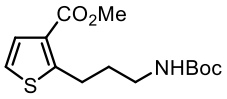
methyl 2-(3-((4-(trifluoromethyl)phenyl)sulfonamido)propyl)thiophene-3-carboxylate 2b



2b

Synthesis according to GP3: 48.6 mg (0.100 mmol) methyl 2-((*N*-(3-bromopropyl)-4-(trifluoromethyl)phenyl)sulfonamido)thiophene-3-carboxylate **7b**, concentration of reaction mixture 0.05 M, column chromatography hexanes/EtOAc 10:1 → 2:1 gave 20.5 mg (0.0503 mmol, 50%) of **2b** as a colorless oil. R_f = 0.30 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.87 (p, J = 6.7 Hz, 2 H, CH_2), 3.00 (q, J = 6.2 Hz, 2 H, CH_2), 3.20 (t, J = 7.1 Hz, 2 H, CH_2), 3.85 (s, 3 H, OCH_3), 5.56 (m_c, 1 H, NH), 7.05 (d, J = 5.4 Hz, 1 H, Ar), 7.32 (d, J = 5.4Hz, 1 H, Ar), 7.76 (d, J = 8.2 Hz, 2 H, Ar), 7.99 (d, J = 8.2 Hz, 2 H, Ar) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 25.4, 31.7, 41.8, 52.0, 122.4, 123.4 ($J_{C,F}$ = 273 Hz), 126.3, 127.6, 128.2, 129.1, 134.3 ($J_{C,F}$ = 32.7 Hz), 144.2, 153.4, 164.5 ppm. ESI-HRMS for $C_{16}H_{16}F_3NO_4S_2$, $[M+H]^+$ calc. 408.0546, found 408.0542. IR: $\tilde{\nu}$ = 3280 (N-H), 2925 (-C-H), 1710 (C=O), 1320, 1255, 1160, 1130, 1060 cm^{-1}.

methyl 2-(3-((*tert*-butoxycarbonyl)amino)propyl)thiophene-3-carboxylate 2c



2c

Synthesis according to GP3: 43.2 mg (0.100 mmol) methyl 2-((3-bromopropyl)(*tert*-butoxycarbonyl)amino)thiophene-3-carboxylate **7c**, concentration of reaction mixture 0.05 M. After 24 h of reaction time the crude reaction mixture showed signals, that likely belong to spiro compound S-5 the solvent was removed, and the residue was dissolved in 2 mL of EtOAc and 2 mL of 1 N aqueous HCl was added. The biphasic mixture was stirred vigorously for 3 h, and then poured into sat. $NaHCO_3$/EtOAc. It was extracted with EtOAc (3x), dried over Na_2SO_4 and concentrated. Column chromatography hexanes/EtOAc 5:1 → 3:1 gave 20.1 mg (0.0671 mmol, 67%) of **2c** as a colorless oil. R_f = 0.25 (hexanes/EtOAc) ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.45 (s, 9 H, Boc), 1.88 (p, J = 7.1 Hz, 2 H, CH_2), 3.17 (m_c, 2 H, CH_2), 3.23 (t, J = 7.5 Hz, 2 H, CH_2), 3.84 (s, 3 H, OCH_3), 4.83, (br s, 1 H, NH), 7.04, (d, J = 5.2 Hz, 1 H, Ar), 7.37 (d, J = 5.2 Hz, 1 H, Ar) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 26.6, 28.6, 32.0, 40.0, 51.6, 79.3, 121.8, 128.0, 129.4, 154.3, 156.1, 164.1 ppm. ESI-HRMS for $C_{14}H_{21}NO_4S$, $[M+H]^+$ calc. 300.1264, found 300.1262. IR: $\tilde{\nu}$ = 35370 (N-H), 2975 (-C-H), 1695 (C=O), 1530, 1260, 1165 cm^{-1}.

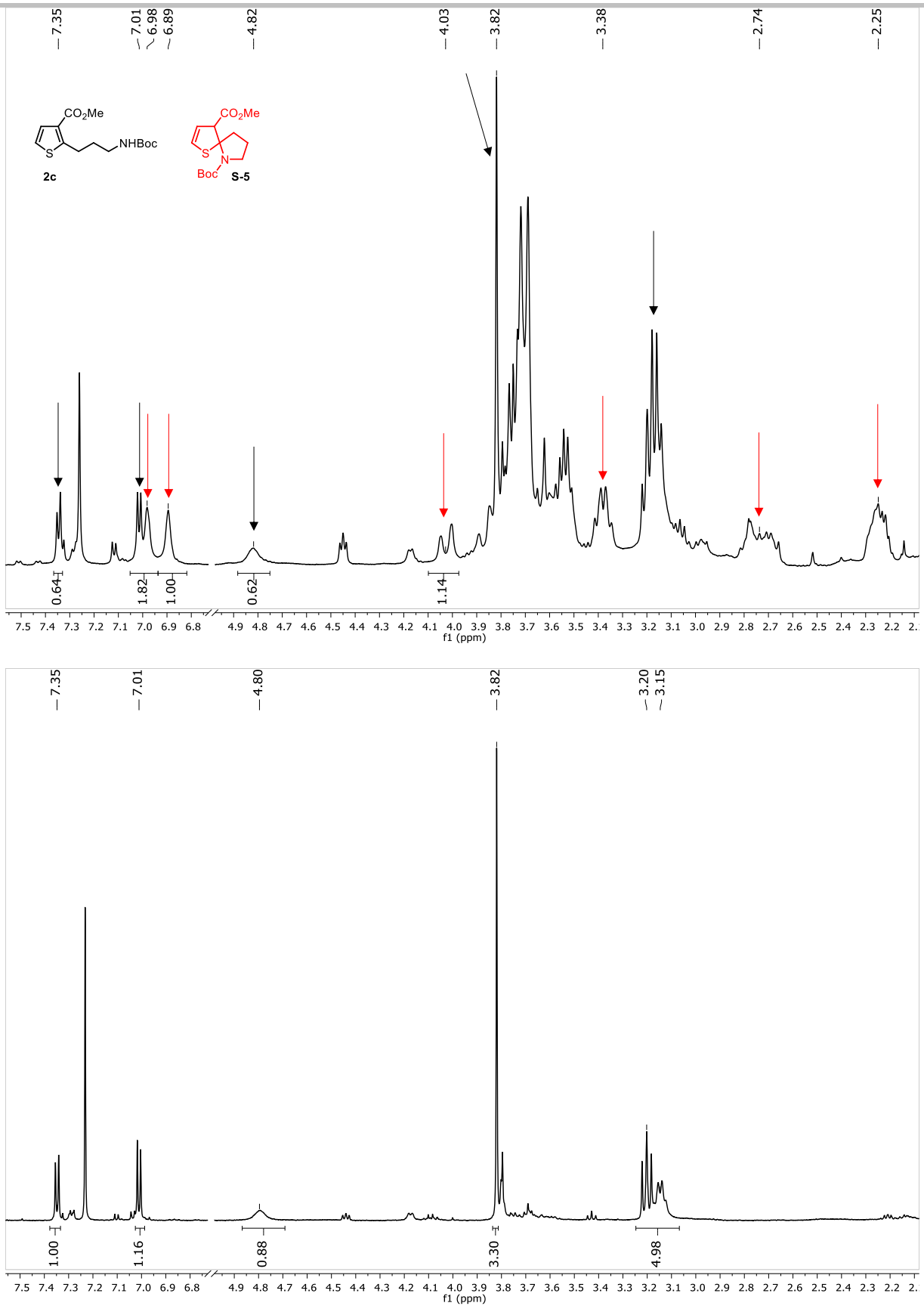
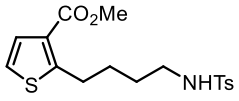


Figure S3. Top: ^{1}H-NMR of crude reaction mixture of Finkelstein/Smiles reaction of **7c** prior to acidic treatment, showing signals of proposed side product **S-5**; bottom: after acidic treatment.

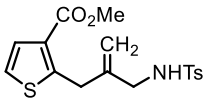
methyl 2-(4-((4-methylphenyl)sulfonamido)butyl)thiophene-3-carboxylate 2d



2d

Synthesis according to GP3: 44.6 mg (0.100 mmol) methyl 2-((*N*-(3-bromobutyl)-4-methylphenyl)sulfonamido)thiophene-3-carboxylate **7d**, concentration of reaction mixture 0.05 M, column chromatography hexanes/EtOAc 4:1 → 3:1 gave 31.4 mg (0.0854 mmol, 85%) of **2d** as a colorless oil. R_f = 0.25 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.51-1.61 (m, 2 H, CH_2), 1.63-1.72 (m, 2 H CH_2), 2.42 (s, 3 H, CH_3), 3.00 (q, J = 6.6 Hz, 2 H, CH_2), 3.10 (m_c, 2 H, CH_2), 4.71-4.80 (m, 1 H, NH), 7.01 (d, J = 5.4Hz, 1 H, Ar), 7.29 (d, J = 8.2 Hz, 2 H, Ts), 7.36 (d, J = 5.4 Hz, 1 H, Ar), 7.75 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.7, 28.4, 28.5, 29.0, 42.6, 51.7, 121.6, 127.2, 127.5, 129.3, 129.8, 137.2, 143.4, 154.7, 164.1 ppm. ESI-HRMS for $C_{17}H_{21}NO_4S_2$, $[M+H]^+$ calc. 368.0985, found 368.0985. IR: $\tilde{\nu}$ = 3275 (N-H), 2945 (-C-H), 1705 (C=O), 1435, 1325, 1260, 1155, 1095 cm^{-1}.

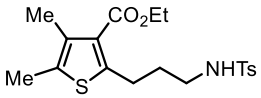
methyl 2-(2-(((4-methylphenyl)sulfonamido)methyl)allyl)thiophene-3-carboxylate 2e



2e

Synthesis according to GP3: 38.0 mg (0.0855 mmol) methyl 2-((*N*-(2-(bromomethyl)allyl)-4-methylphenyl)sulfonamido)thiophene-3-carboxylate **7e**, column chromatography hexanes/EtOAc 2:1 → 1:1 gave 18.4 mg (0.0503 mmol, 59%) of **2e** as a colorless oil. R_f = 0.20 (hexnes/EtOAc 1:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.40 (s, 3 H, CH_3), 2.53 (t, J = 6.3 Hz, 1 H, NH), 3.61 (s, 3 H, OCH_3), 4.23 (d, J = 5.7 Hz, 2 H, CH_2), 4.27 (s, 2 H, CH_2), 4.86 (s, 1 H, =CH_2), 5.06 (s, 1 H, =CH_2), 7.11 (d, J = 5.8 Hz, 1 H, Ar), 7.21-7.29 (m, 3 H, Ar, Ts), 7.56 (d, J = 8.1 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.7, 51.9, 55.4, 63.7, 116.4, 123.8, 128.0, 128.2, 129.7, 129.8, 134.9, 143.3, 144.3, 145.8, 162.4 ppm. IR: $\tilde{\nu}$ = 3525 (N-H), 2950 (-C-H), 1715 (C=O), 1440, 1350, 1275, 1160 cm^{-1}.

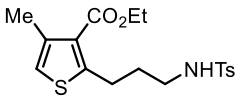
ethyl 4,5-dimethyl-2-(3-((4-methylphenyl)sulfonamido)propyl)thiophene-3-carboxylate 2f



2f

Synthesis according to GP3: 47.4 mg (0.100 mmol) ethyl 2-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)-4,5-dimethylthiophene-3-carboxylate **7f**, column chromatography hexanes/EtOAc 3:1 → 2:1 gave 32.5 mg (0.0822 mmol, 82%) of **2f** as a colorless oil. R_f = 0.30 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.35 (t, J = 7.1 Hz, 3 H, CH_3), 1.79 (p, J = 6.8 Hz, 2 H, CH_2), 2.17 (s, 3 H, CH_3), 2.25 (s, 3 H, CH_3), 2.41 (s, 3 H, CH_3), 2.91-3.03 (m, 4 H, CH_2), 4.31 (q, J = 7.1 Hz, 2 H, CH_2), 5.26 (t, J = 6.2 Hz, 1 H, NH), 7.27 (d, J = 8.2 Hz, 2 H, Ts), 7.73 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.7, 51.9, 55.4, 63.7, 116.4, 123.8, 128.0, 128.2, 129.7, 129.8, 134.9, 143.3, 144.3, 145.8, 162.4 ppm. ESI-HRMS for $C_{19}H_{25}NO_4S_2$, $[M+H]^+$ calc. 396.1298, found 396.1299. IR: $\tilde{\nu}$ = 3275 (N-H), 2925 (-C-H), 1700 (C=O), 1325, 1260, 1155 1090 cm^{-1}.

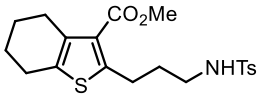
ethyl 4-methyl-2-(3-((4-methylphenyl)sulfonamido)propyl)thiophene-3-carboxylate 2g



2g

Synthesis according to GP3: 46.0 mg (0.100 mmol) ethyl 2-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)-4-methylthiophene-3-carboxylate **7g**, column chromatography hexanes/EtOAc 3:1 → 2:1 gave 34.3 mg (0.0899 mmol, 90%) of **2g** as a colorless oil. R_f = 0.30 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.35 (t, J = 7.1 Hz, 3 H, CH_3), 1.83 (p, J = 6.9 Hz, 2 H, CH_2), 2.32 (s, 3 H, CH_3) 2.41 (s, 3 H, CH_3), 2.95 (q, J = 9.6 Hz, 2 H, CH_2), 3.07 (t, J = 7.3 Hz, 2 H, CH_2), 4.31 (q, J = 7.1 Hz, 2 H, CH_2) 5.18-5.29 (m, 1 H, NH), 6.67 (s, 1 H, Ar), 7.27 (d, J = 8.2 Hz, 1 H, Ts), 7.73 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 14.4, 17.6, 21.6 (CH_3), 26.7, 31.6, 42.0, 60.7, 51.8, 119.0, 127.2, 128.5, 129.7, 137.4, 139.1, 143.3, 153.1, 164.7 ppm. ESI-HRMS for $C_{18}H_{23}NO_4S_2$, $[M+H]^+$ calc. 382.1141, found 382.1141. IR: $\tilde{\nu}$ = 3270 (N-H), 2925 (-C-H), 1700 (C=O), 1325, 1255, 1155, 1090 cm^{-1}.

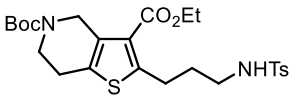
methyl 2-(3-((4-methylphenyl)sulfonamido)propyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate 2h



2h

Synthesis according to GP3: 48.6 mg (0.100 mmol) methyl 2-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate **7h**, column chromatography hexanes/EtOAc 3:1 → 2:1 gave 34.3 mg (0.0899 mmol, 90%) of **2h** as a colorless oil. R_f = 0.35 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.58-1.80 (m, 6 H, CH_2), 2.32 (s, 3 H, CH_3), 2.55 (t, J = 5.6 Hz, 2 H, CH_2), 2.61 (t, J = 5.8 Hz, 2 H, CH_2), 2.87 (q, J = 6.4 Hz, 2 H, CH_2), 2.94 (t, J = 7.2 Hz, 2 H, CH_2), 3.73 (s, 3 H, OCH_3), 5.17 (t, J = 6.2 Hz, 1 H, NH), 7.19 (d, J = 8.2 Hz, 2 H, Ts), 7.65 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.8, 22.8, 23.1, 25.1, 26.2, 26.6, 31.6, 41.9, 51.5, 127.2, 127.6, 129.7, 133.6, 135.7, 137.4, 143.2, 149.7, 165.1 ppm. ESI-HRMS for $C_{20}H_{25}F_3NO_4S_2$, $[M+H]^+$ calc. 408.1298, found 408.1296. IR: $\tilde{\nu}$ = 3275 (N-H), 2930 (-C-H), 1705 (C=O), 1325, 1155, 1095 cm^{-1}.

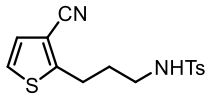
5-(*tert*-butyl) 3-ethyl 2-(3-((4-methylphenyl)sulfonamido)propyl)-6,7-dihydrothieno[3,2-c]pyridine-3,5(4*H*)-dicarboxylate 2i



2i

Synthesis according to GP3: 58.8 mg (0.0977 mmol) 5-(*tert*-butyl) 3-ethyl 2-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)-6,7-dihydrothieno[3,2-c]pyridine-3,5(4*H*)-dicarboxylate **7i**, column chromatography hexanes/EtOAc 3:1 → 2:1 gave 34.4 mg (0.0658 mmol, 67%) of **2i** as a colorless oil. R_f = 0.25 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.34 (t, J = 7.1 Hz, 3 H, CH_3), 1.47 (s, 9H, Boc), 1.81 (p, J = 6.8 Hz, 2 H, CH_2), 2.41 (s, 3 H, OCH_3), 2.82 (m_c, 2 H, CH_2), 2.96 (q, J = 6.4 Hz, 2 H, CH_2), 3.08 (t, J = 7.2 Hz, 2 H, CH_2), 3.61 (t, J = 5.5 Hz, 2 H, CH_2), 4.29 (q, J = 7.1 Hz, 2 H, OCH_2), 4.49 (s, 2 H, CH_2), 5.21 (m_c, 1 H, NH), 7.27 (d, J = 8.2 Hz, 2 H, Ts), 7.73 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 14.4, 21.6, 26.4, 27.1, 28.6, 31.7, 41.3, 42.1, 43.2, 60.7, 80.3, 127.3, 127.5, 129.7, 130.1, 134.9, 137.8, 143.3, 151.0, 154.7, 164.1 ppm. ESI-HRMS for $C_{25}H_{34}N_2O_6S_2$, $[M+NH_4]^+$ calc. 540.2197, found 540.2188. IR: $\tilde{\nu}$ = 3265 (N-H), 2980 (-C-H), 1690 (C=O), 1415, 1325, 1235, 1155, 1095, 1020 cm^{-1}.

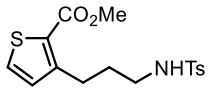
_N_-(3-(3-cyanothiophen-2-yl)propyl)-4-methylbenzenesulfonamide 2j



2j

Synthesis according to GP3: 39.9 mg (0.100 mmol) *N*-(3-bromopropyl)-*N*-(3-cyanothiophen-2-yl)-4-methylbenzenesulfonamide **7j**, column chromatography hexanes/EtOAc 3:1 → 1:1 gave 25.8 mg (0.0805 mmol, 81%) of **2j** as a colorless oil. R_f = 0.25 (hexanes/EtOAc 3:2). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.90 (p, J = 7.2 Hz, 2 H, CH_2), 2.42 (s, 3 H, CH_3), 2.93-3.09 (m, 4 H, CH_2), 4.84_4.94 (m, 1 H, NH), 7.09 (d, J = 5.3 Hz, 1 H, Ar), 7.17 (d, J = 5.3 Hz, 1 H, Ar), 7.31 (d, J = 8.0 Hz, 2 H, Ts), 7.74 (d, J = 8.0 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.7, 26.4, 31.3, 42.3, 108.7, 115.0, 124.7, 127.2, 128.4, 129.9, 136.8, 143.7, 155.5 ppm. ESI-HRMS for $C_{15}H_{16}N_2O_2S_2$, $[M+H]^+$ calc. 321.0726, found 321.0726. IR: $\tilde{\nu}$ = 3270 (N-H), 2925 (-C-H), 2225 (C≡N), 1325, 1155, 1090 cm^{-1}.

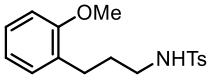
methyl 3-(3-((4-methylphenyl)sulfonamido)propyl)thiophene-2-carboxylate 2k



2k

Synthesis according to GP3: 43.2 mg (0.100 mmol) methyl 3-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)thiophene-2-carboxylate **7k**, column chromatography hexanes/EtOAc 3:1 → 3:2 gave 27.0 mg (0.0764 mmol, 76%) of **2k** as a colorless oil. R_f = 0.20 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.78 (p, J = 6.8 Hz, 2 H, CH_2), 2.41 (s, 3 H, CH_3), 2.91 (q, J = 6.4 Hz, 2 H, CH_2), 2.99 (t, J = 7.2 Hz, 2 H, CH_2), 3.84 (s, 3 H, OCH_3), 5.11-5.24 (m, 1 H, NH), 6.87 (d, J = 5.0 Hz, 1 H, Ar), 7.27 (d, J = 8.2 Hz, 2 H, Ts), 7.39 (d, J = 5.0 Hz, 1 H, Ar), 7.73 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.6, 26.0, 30.2, 42.1, 52.1, 126.7, 127.2, 129.7, 130.7, 131.0, 137.4, 143.3, 149.8, 163.4 ppm. ESI-HRMS for $C_{16}H_{19}NO_4S_2$, $[M+H]^+$ calc. 354.0828, found 354.0828. IR: $\tilde{\nu}$ = 3280 (N-H), 2950 (-C-H), 1705 (C=O), 1435, 1325, 1260, 1160, 1080 cm^{-1}.

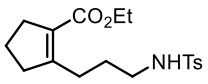
_N_-(3-(2-methoxyphenyl)propyl)-4-methylbenzenesulfonamide 2l



2l

Synthesis according to GP3: 39.8 mg (0.100 mmol) *N*-(3-bromopropyl)-*N*-(2-methoxyphenyl)-4-methylbenzenesulfonamide **7l**, concentration 0.05 M of starting material, column chromatography hexanes/EtOAc 5:1 → 1:1 gave 14.2 mg (0.0445 mmol, 45%) of **2l** as a colorless oil. R_f = 0.55 (hexanes/EtOAc 1:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.73 (p, J = 7.0 Hz, 2 H, CH_2), 2.42 (s, 3 H, CH_3), 2.60 (t, J = 7.3 Hz, 2 H, CH_2), 2.93 (q, J = 6.6 Hz, 2 H, CH_2), 3.79 (s, 3 H, OCH_3), 4.58 (t, J = 5.9 Hz, 1 H, NH), 6.82 (d, J = 8.2 Hz, 1 H, Ar), 6.85 (t, J = 7.4 Hz, 1 H, Ar), 7.01 (d, J = 7.4 Hz, 1 H, Ar), 7.17 (t, J = 7.8 Hz, 1 H, Ar), 7.29 (d, J = 8.0 Hz, 2 H, Ts), 7.72 (d, J = 8.0 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.7, 26.9, 29.9, 42.6, 55.4, 110.5, 120.8, 127.2, 127.6, 129.2, 129.8, 130.2, 137.3, 143.4, 157.4 ppm. ESI-HRMS for $C_{17}H_{21}NO_3S$, $[M+H]^+$ calc. 320.1315, found 320.1314. IR: $\tilde{\nu}$ = 3280 (N-H), 2922 (-C-H), 1495, 1325, 1245, 1155, 1095 cm^{-1}.

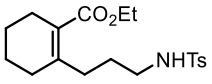
ethyl 2-(3-((4-methylphenyl)sulfonamido)propyl)cyclopent-1-ene-1-carboxylate 2m



2m

Synthesis according to GP3: 43.0 mg (0.100 mmol) ethyl 2-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)cyclopent-1-ene-1-carboxylate **7m**, column chromatography hexanes/EtOAc 3:1 → 1:1 gave 32.7 mg (0.0930 mmol, 93%) of **2m** as a colorless oil. R_f = 0.15 (hexanes/EtOAc 3:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.28 (t, J = 7.1 Hz, 3 H, CH_3), 1.65 (p, J = 6.6 Hz, 2 H, CH_2), 1.73 (p, J = 7.5 Hz, 2 H, CH_2), 2.35 (t, J = 7.5 Hz, 2 H, CH_2), 2.41 (s, 3 H, CH_3), 2.49-2.59 (m, 4 H, CH_2), 2.87 (q, J = 6.3 Hz, 2 H, CH_2), 4.19 (q, J = 7.1 Hz, 2 H, OCH_2), 5.60-5.69 (m, 1 H, NH), 7.27 (d, J = 8.2 Hz, 2 H, Ts), 7.72 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 14.4, 21.5, 21.6, 26.1, 27.0, 33.6, 37.8, 41.9, 60.3, 127.1, 129.1, 129.6, 137.6, 143.1, 158.1, 166.8 ppm. ESI-HRMS for $C_{18}H_{25}NO_4S$, $[M+H]^+$ calc. 352.1577, found 352.1576. IR: $\tilde{\nu}$ = 3275 (N-H), 2925 (-C-H), 1685 (C=O), 1325, 1260, 1155, 1090 cm^{-1}.

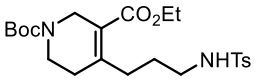
ethyl 2-(3-((4-methylphenyl)sulfonamido)propyl)cyclohex-1-ene-1-carboxylate 2n



2n

Synthesis according to GP3: 44.4 mg (0.100 mmol) ethyl 2-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)cyclohex-1-ene-1-carboxylate **7n**, column chromatography hexanes/EtOAc 4:1 → 2:1 gave 29.9 mg (0.0818 mmol, 82%) of **2n** as a colorless oil. R_f = 0.15 (hexanes/EtOAc 3:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) 1.28 (t, J = 7.1 Hz, 3 H, CH_3), 1.53 (m_c, 4 H, CH_2), 1.65 (p, J = 6.2 Hz, 2 H, CH_2), 1.99 (m, 2 H, CH_2), 2.19 (m, 2 H, CH_2), 2.33 (t, J = 7.2 Hz, 2 H, CH_2), 2.41 (s, 3 H, CH_3), 2.89 (q, J = 6.2 Hz, 2 H, CH_2), 4.18 (q, J = 7.1 Hz, 2 H, OCH_2), 5.65 (t, J = 6.2 Hz, 1 H, NH), 7.27 (d, J = 8.2 Hz, 2 H, Ts), 7.73 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 14.4, 21.6, 22.1, 22.3, 26.6, 27.3, 30.8, 31.5, 42.1, 60.5, 126.1, 127.2, 129.6, 137.5, 143.1, 147.6, 169.5 ppm. ESI-HRMS for $C_{19}H_{27}NO_4S$, $[M+H]^+$ calc. 366.1734, found 366.1727. IR: $\tilde{\nu}$ = 3275 (N-H), 2930 (-C-H), 1705 (C=O), 1325, 1230, 1155, 1090 cm^{-1}.

1-(*tert*-butyl) 3-ethyl 4-(3-((4-methylphenyl)sulfonamido)propyl)-5,6-dihydropyridine-1,3(2*H*)-dicarboxylate 2o

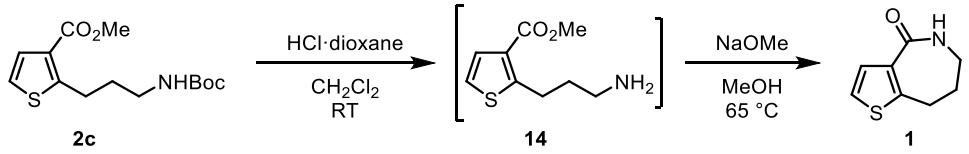


2o

Synthesis according to GP3: 54.5 mg (0.100 mmol) ethyl 2-((*N*-(3-bromopropyl)-4-methylphenyl)sulfonamido)cyclohex-1-ene-1-carboxylate **7o**, column chromatography hexanes/EtOAc 4:1 → 1:1 gave 32.0 mg (0.0686 mmol, 69%) of **2o** as a colorless oil. R_f = 0.15 (hexanes/EtOAc 2:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.28 (t, J = 7.2 Hz, 3 H, CH_3), 1.46 (s, 9 H, Boc), 1.66 (m, 2 H, CH_2), 2.14 (m_c, 2 H, CH_2), 2.41 (s, 3 H, CH_3), 2.47 (t, J = 7.2 Hz, 2 H, CH_2), 2.91 (q, J = 6.2 Hz, 2 H, CH_2), 3.39 (t, J = 5.7 Hz, 2 H, CH_2), 4.04 (br s, 2 H, CH_2), 4.19 (m_c, 2 H, OCH_2), 5.42 (br s, 1 H, NH), 7.28 (d, J = 8.2 Hz, 2 H, Ts), 7.73 (d, J = 8.2 Hz, 2 H, Ts) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 14.3, 21.6, 27.8, 28.6, 31.0, 31.4, 39.7, 42.4, 43.6, 60.7, 80.1, 123.6, 127.2, 129.7, 137.8, 143.2, 149.1, 154.7, 166.5 ppm. ESI-HRMS for $C_{23}H_{34}N_2O_6S$, $[M+H]^+$ calc. 467.2210, found 467.2206. IR: $\tilde{\nu}$ = 3275 (N-H), 2980 (-C-H), 1690 (C=O), 1240, 1155, 1095 cm^{-1}.

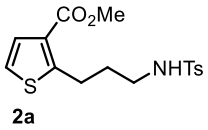
SUPPORTING INFORMATION

Synthesis of tetrahydrothienoazepinone 1

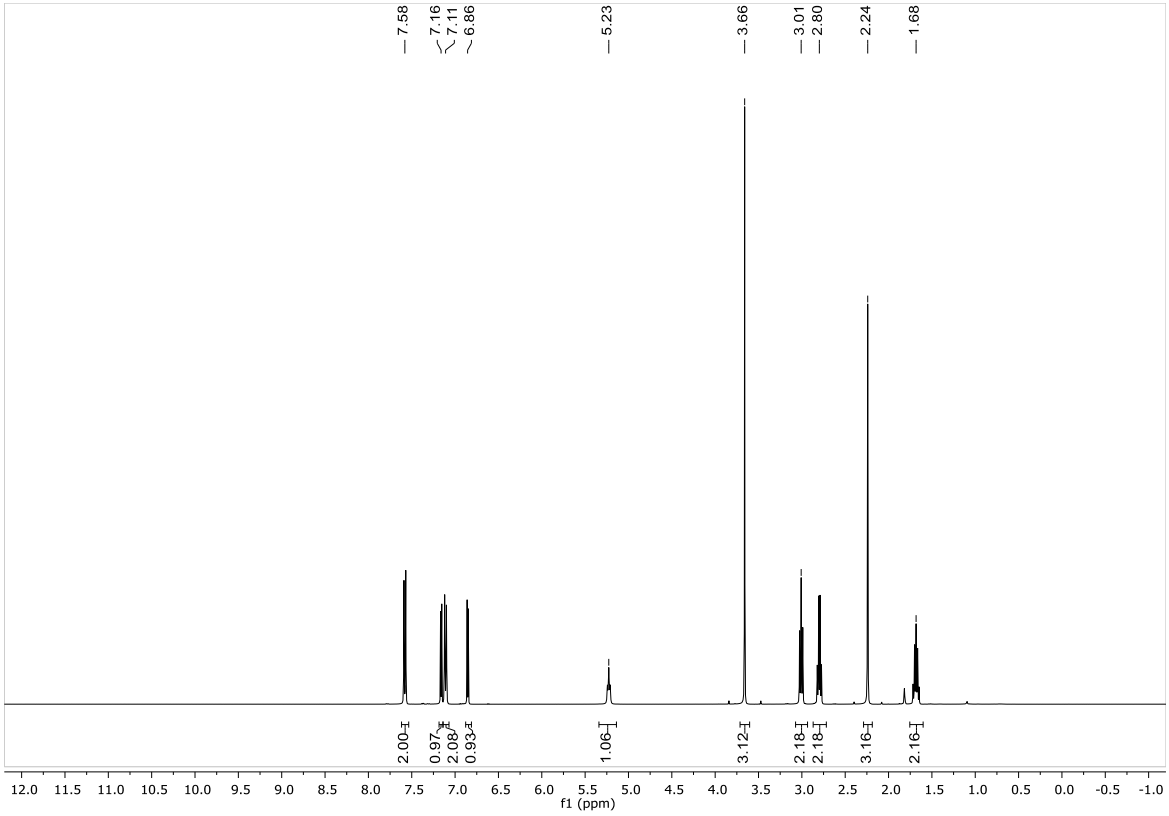


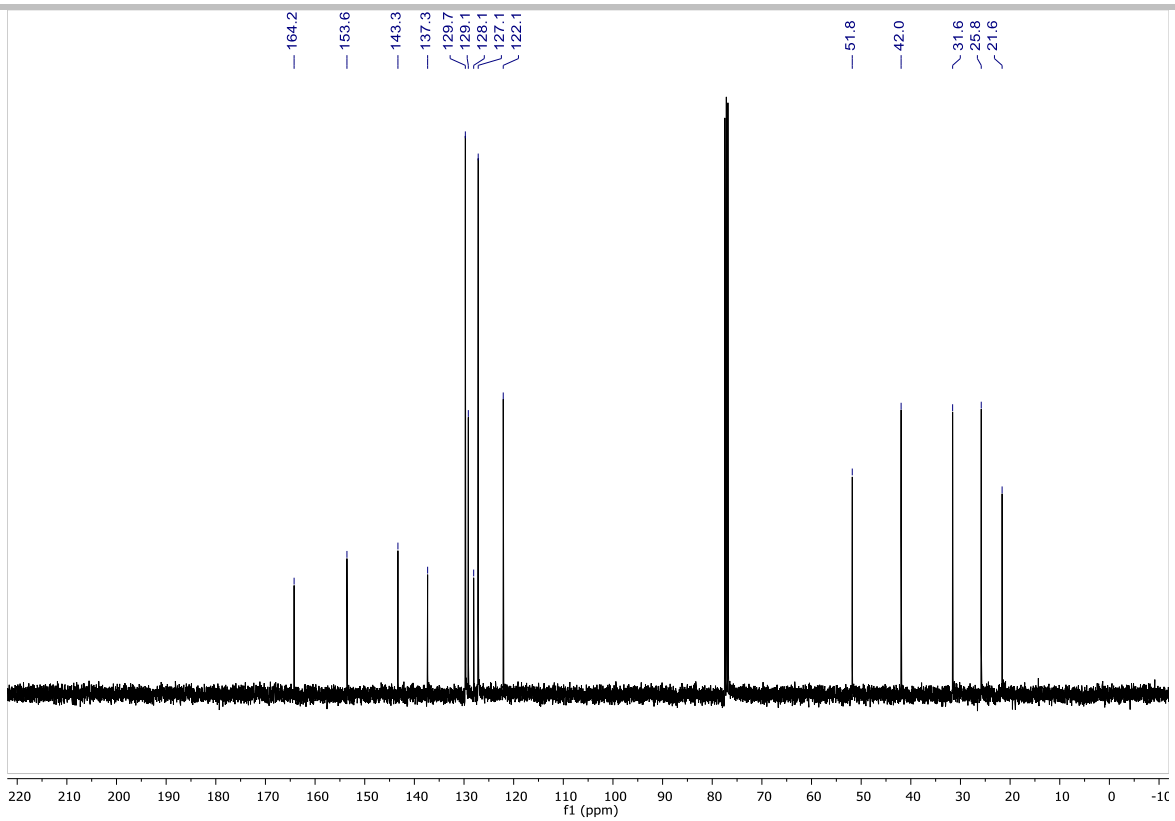
In a round bottom flask open to air 181 mg (0.605 mmol) of methyl 2-(3-((*tert*-butoxycarbonyl)amino)propyl)thiophene-3-carboxylate **2c** were dissolved in 4.5 mL of CH_2Cl_2 and 0.756 mL of a 4.0 M solution of HCl (3.02 mmol) in 1,4-dioxane were added and it was stirred for 6 h at RT. The reaction mixture was added to sat. $NaHCO_3$/EtOAc and extracted with EtOAc (3x), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was redissolved in 6.0 mL of MeOH, 49.1 mg (0.909 mmol) of NaOMe were added and it was heated to 60 °C for 24 h. The reaction mixture was poured into water, extracted with EtOAc (3x), dried over Na_2SO_4 and concentrated in vacuo. Column chromatography (CH_2Cl2/MeOH 19:1) gave 58.4 mg (0.349 mmol, 58%) of 5,6,7,8-tetrahydro-4*H*-thieno[3,2-c]azepin-4-one **1** as a colorless solid. R_f = 0.15 (CH_2Cl_2/MeOH 19:1). ^{1}H-NMR ($CDCl_3$, 400 MHz) 2.10 (p, J = 6.4 Hz, 2 H, CH_2), 3.09 (t, J = 7.1 Hz, 2 H, CH_2), 3.30 (m, 2 H, CH_2), 7.04 (d, J = 5.3 Hz, 1 H, Ar), 7.28-7.42 (m, 2 H, Ar, NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 26.9, 29.4, 41.2, 122.4, 129.8, 133.6, 145.8, 169.3 ppm. ESI-HRMS for $C_8H_{10}NOS$, $[M+H]^+$ calc. 168.0478, found 168.0479.

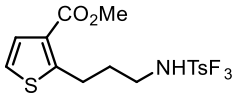
NMR Spectra



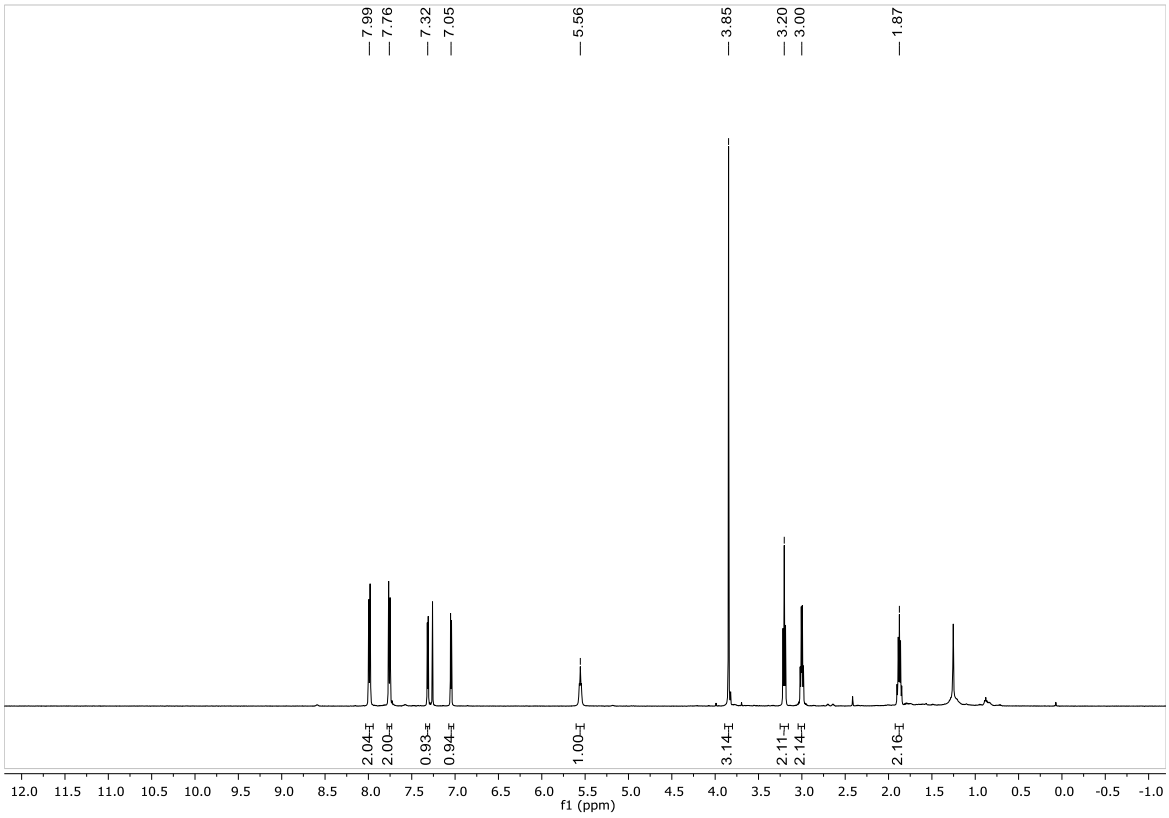
2a

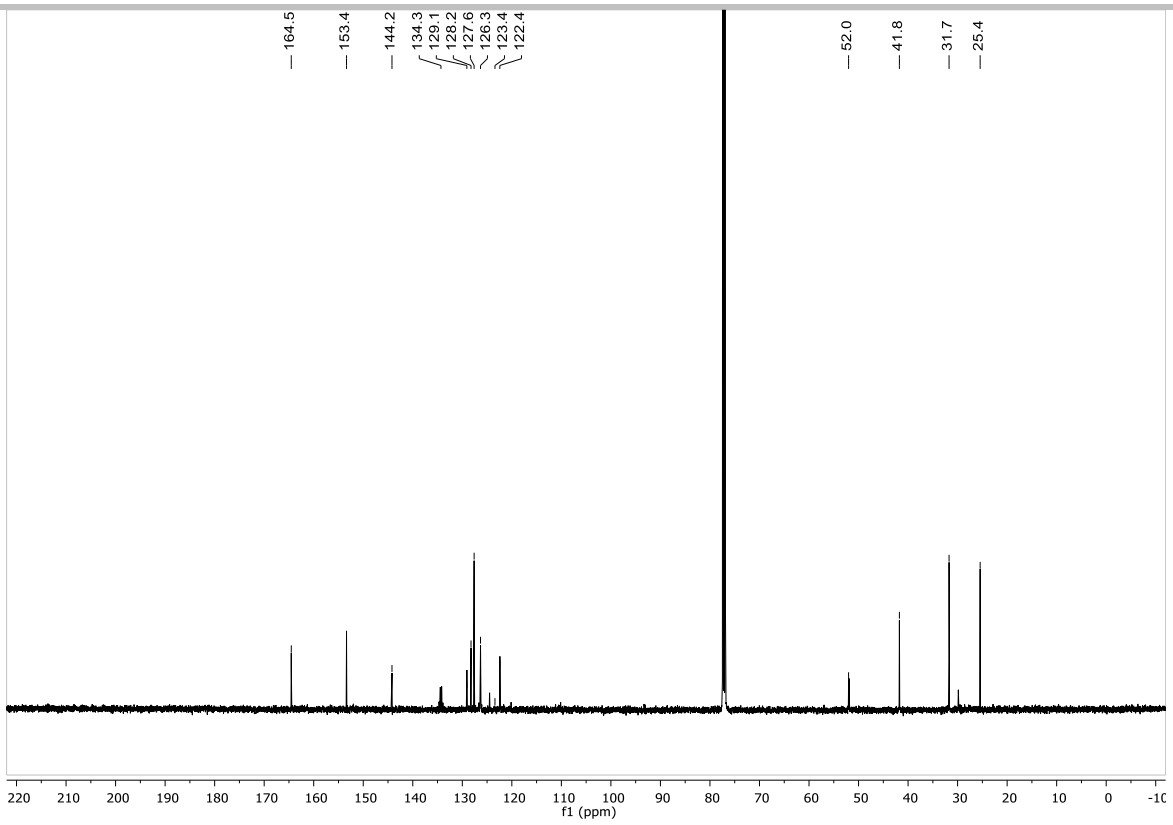


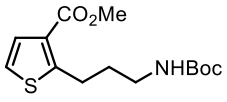

164.2
153.6
143.3
137.3
129.7
129.1
128.1
127.1
122.1
51.8
42.0
31.6
25.8
21.6
f1 (ppm)


CO2Me
NHTsF3
S

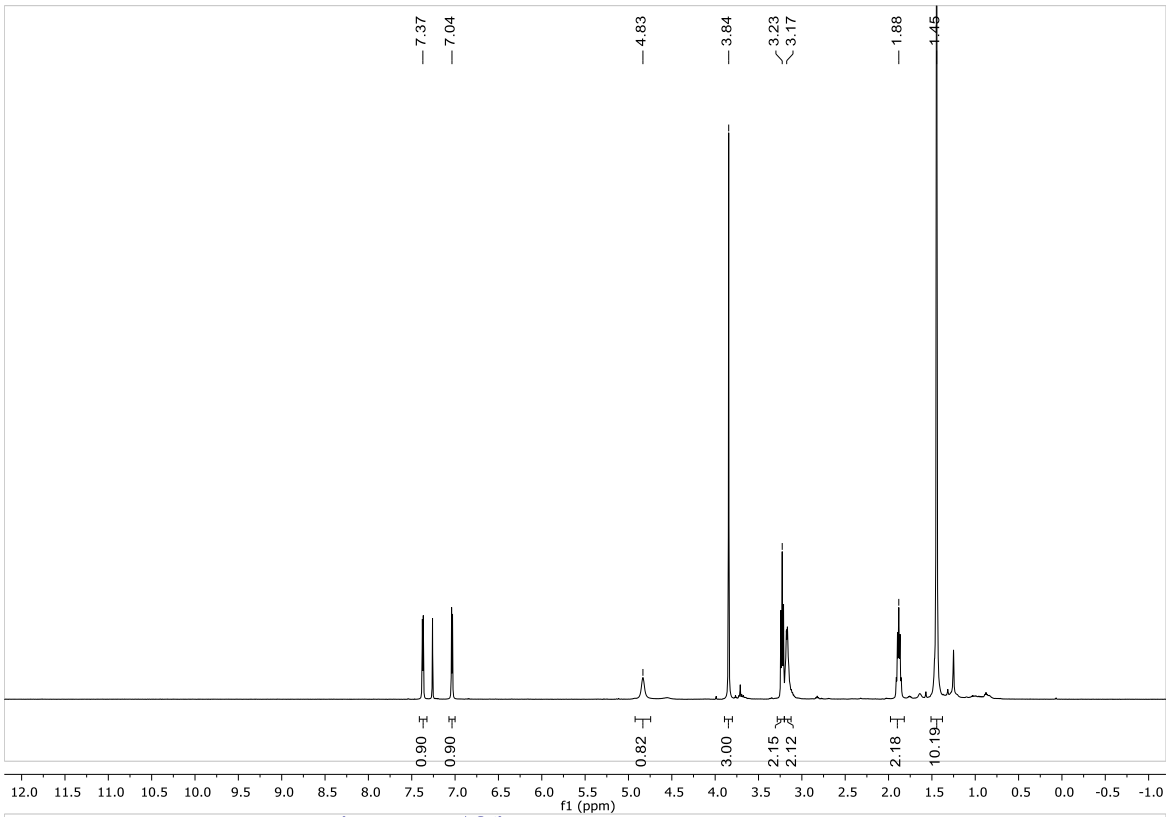
2b

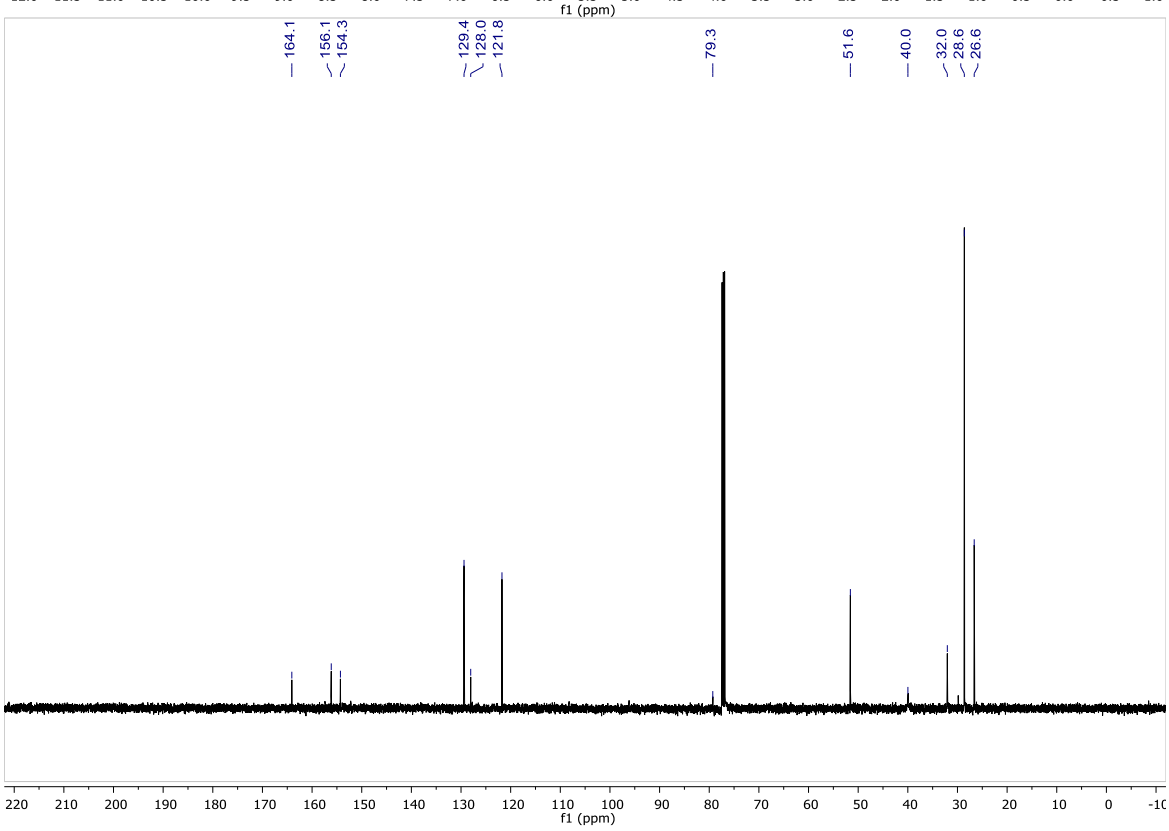

7.99
7.76
7.32
7.05
5.56
3.85
3.20
3.00
1.87
2.04
2.00
0.93
0.94
1.00
3.14
2.11
2.14
2.16
f1 (ppm)

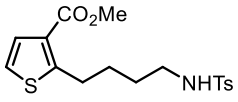

164.5
153.4
144.2
134.3
129.1
128.2
127.6
126.3
123.4
122.4
52.0
41.8
31.7
25.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


CO2Me
NHBoc
S

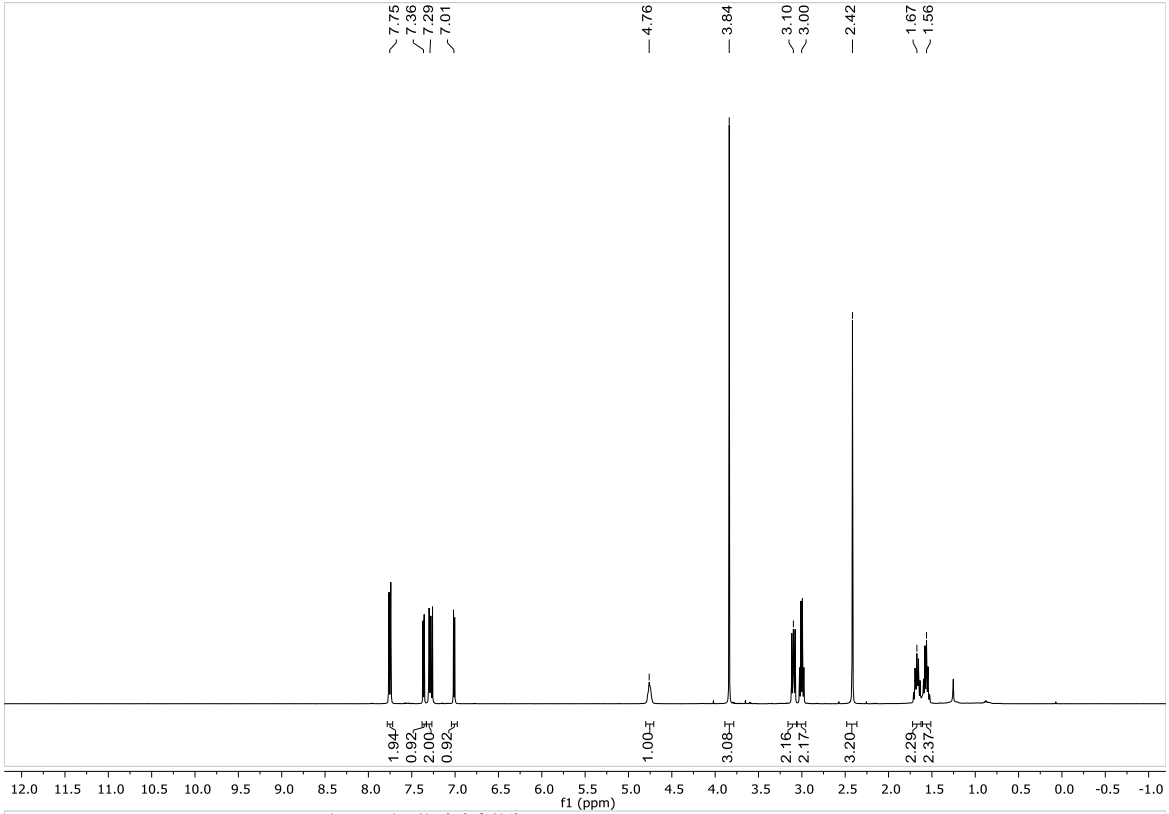
2c

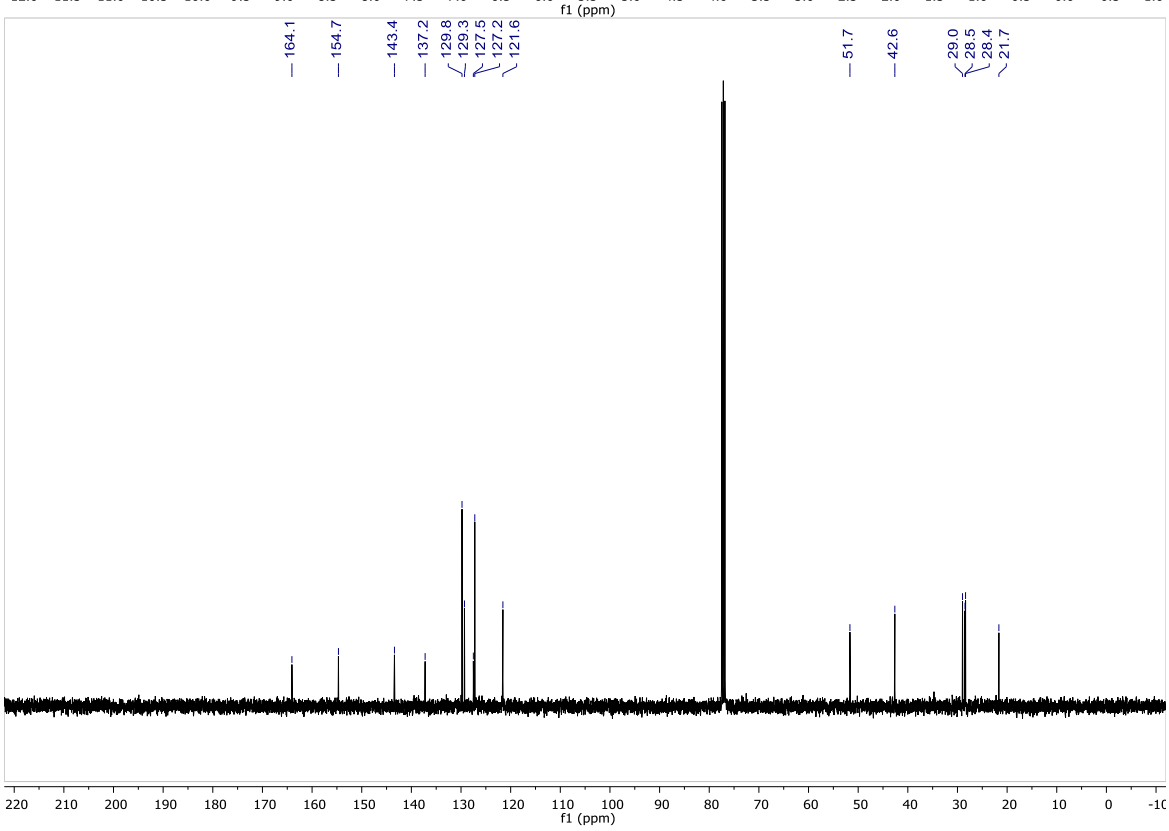

7.37
7.04
4.83
3.84
3.23
3.17
1.88
1.45
0.90
0.90
0.82
3.00
2.15
2.12
2.18
10.19
f1 (ppm)

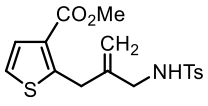

164.1
156.1
154.3
129.4
128.0
121.8
79.3
51.6
40.0
32.0
28.6
26.6
f1 (ppm)


CO2Me
S
NHTs

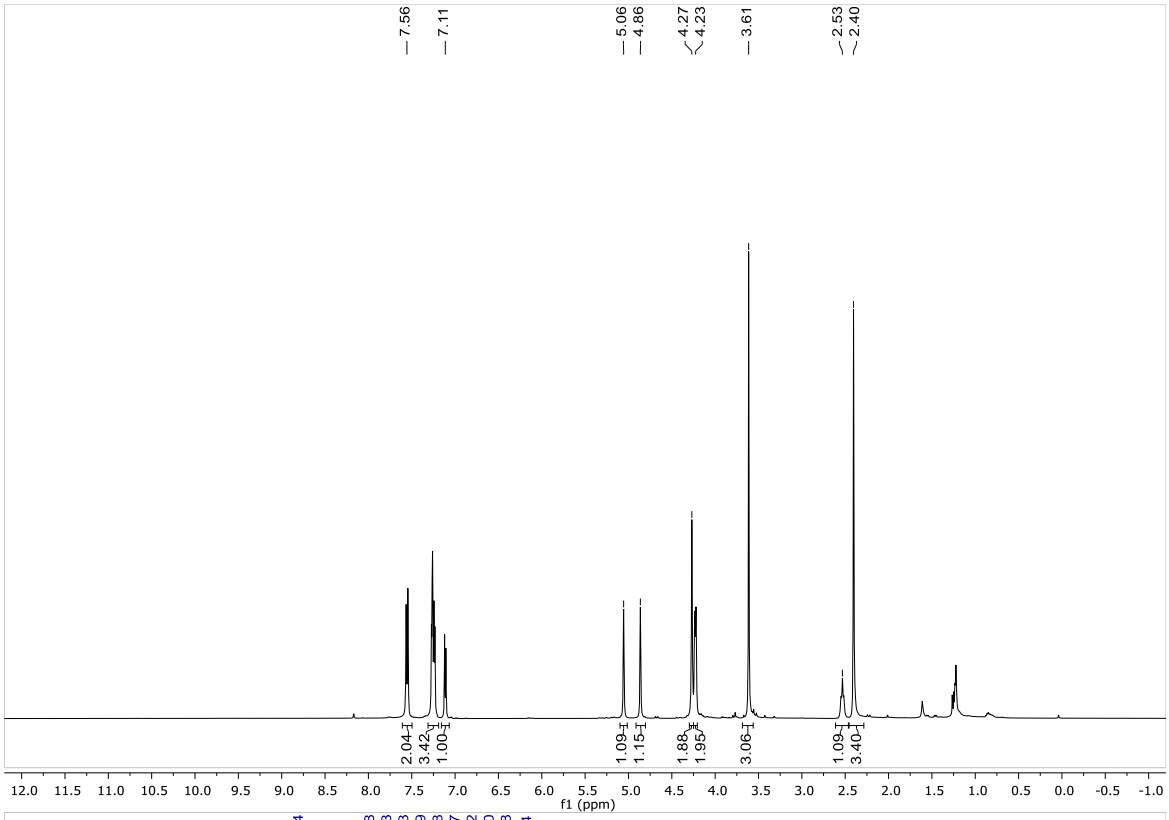
2d

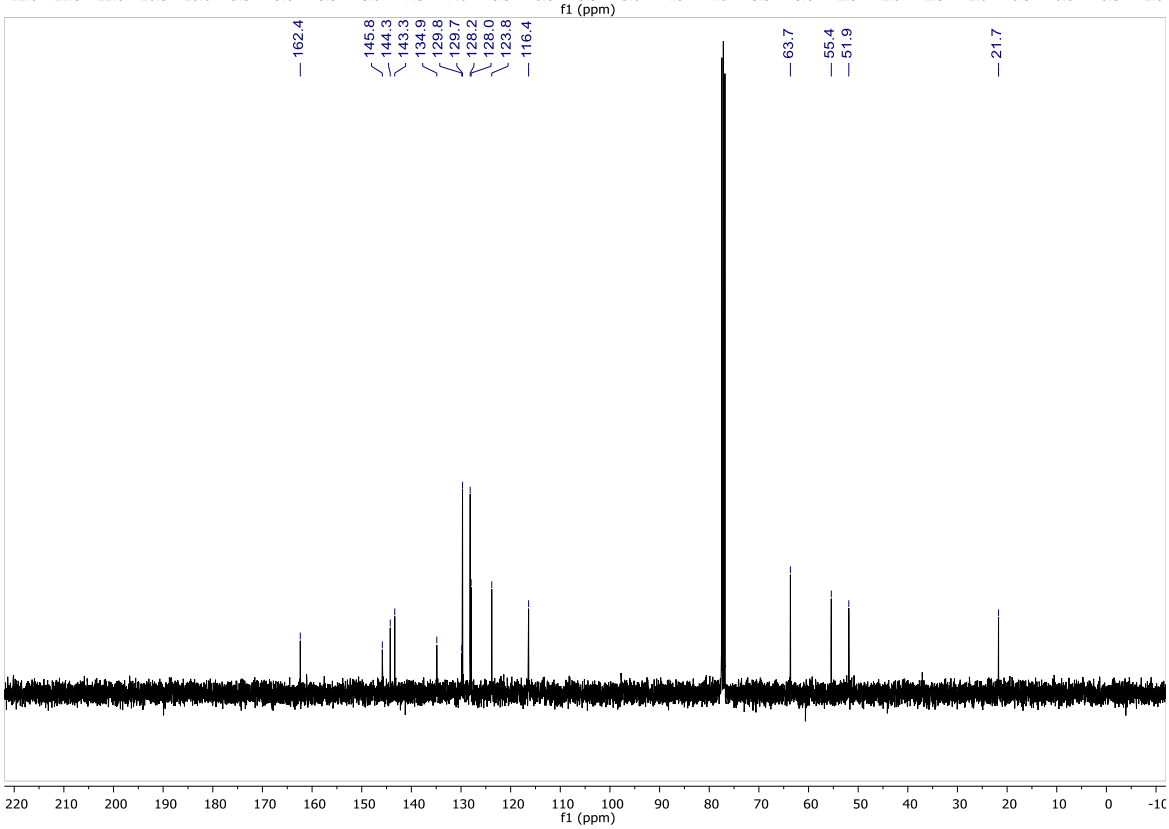

7.75
7.36
7.29
7.01
4.76
3.84
3.10
3.00
2.42
1.67
1.56
1.94
0.92
2.00
0.92
1.00
3.08
2.16
2.17
3.20
2.29
2.37
f1 (ppm)

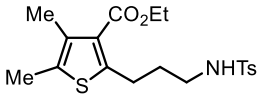

164.1
154.7
143.4
137.2
129.8
129.3
127.5
127.2
121.6
51.7
42.6
29.0
28.5
28.4
21.7
f1 (ppm)


CO2Me
CH2
NHTs
S

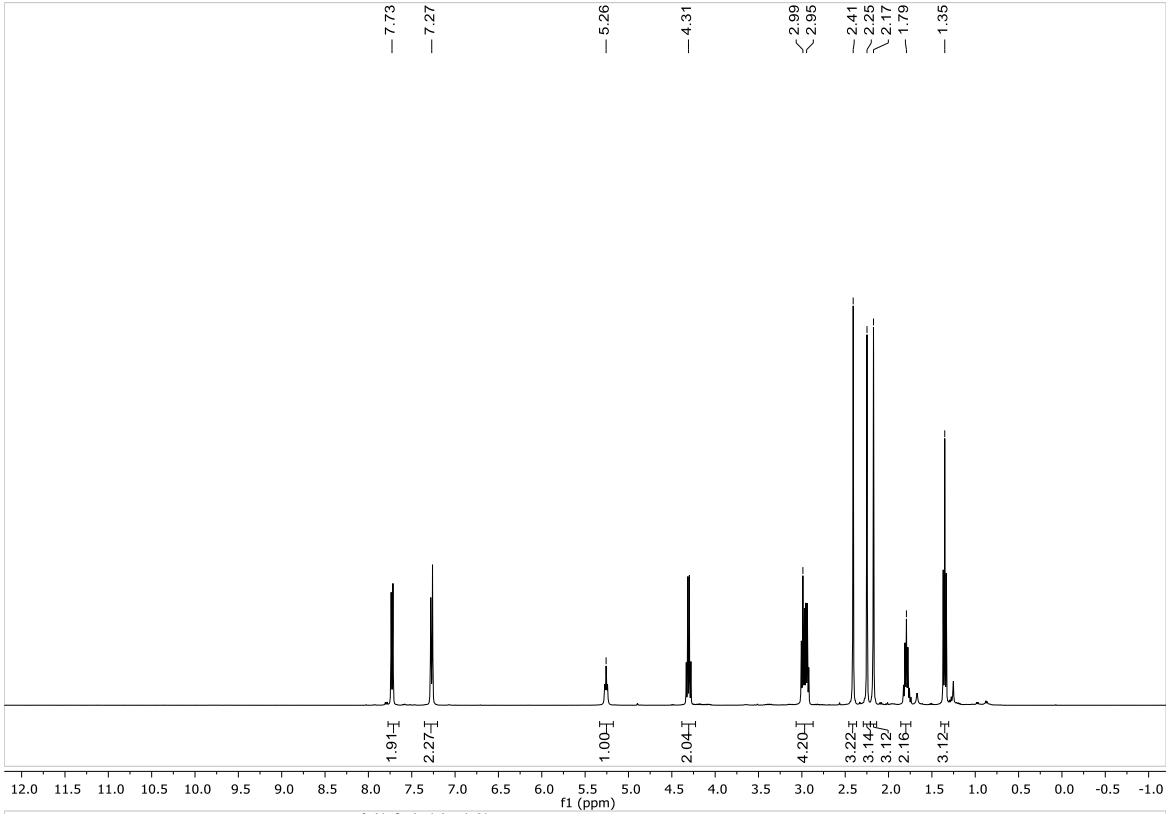
2e

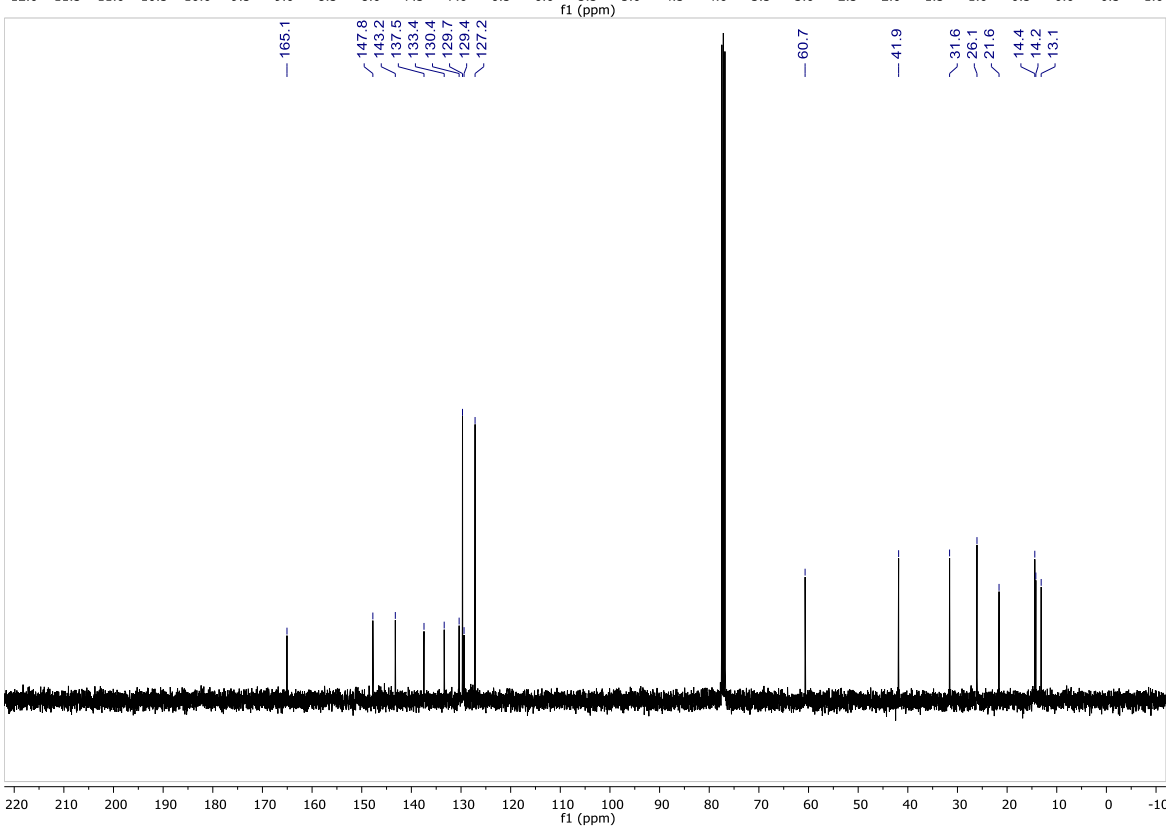

7.56
7.11
5.06
4.86
4.27
4.23
3.61
2.53
2.40
2.04
3.42
1.00
1.09
1.15
1.88
1.95
3.06
1.09
3.40
f1 (ppm)

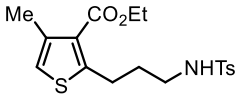

162.4
145.8
144.3
143.3
134.9
129.8
129.7
128.2
128.0
123.8
116.4
63.7
55.4
51.9
21.7
f1 (ppm)


Me
CO2Et
Me
S
NHTs

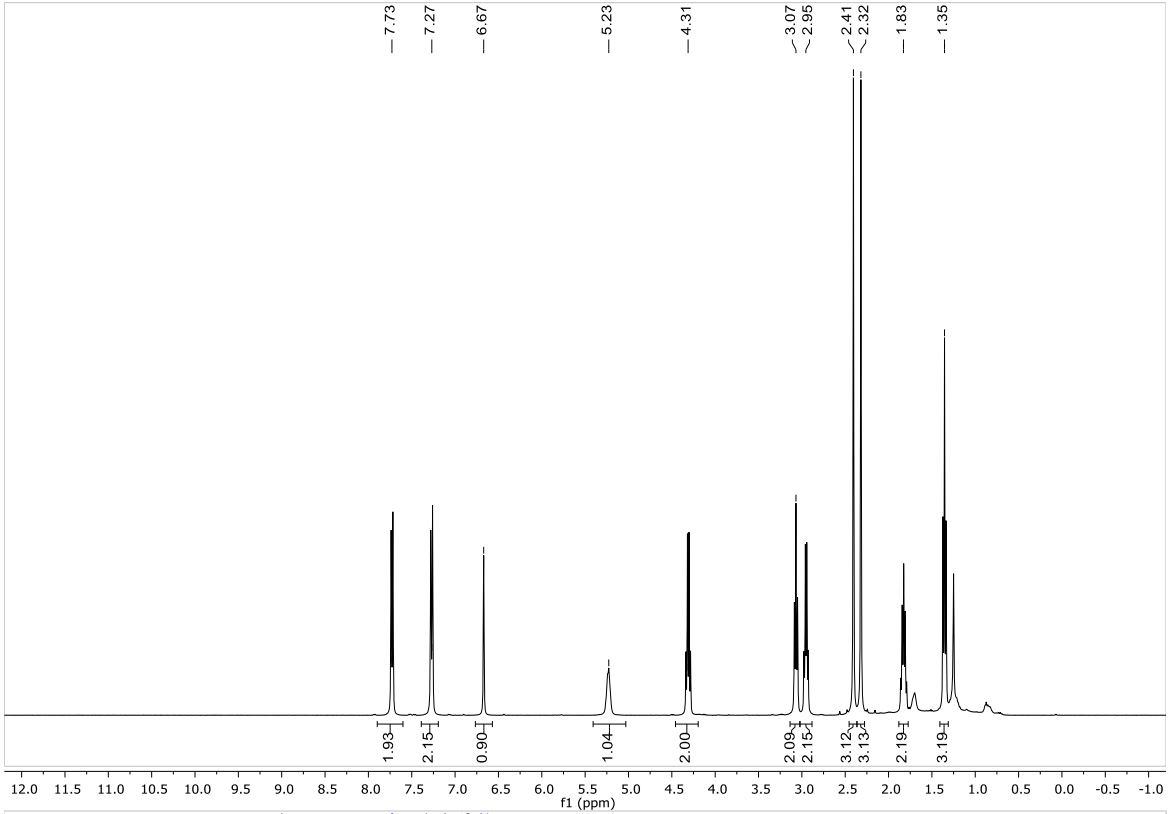
2f

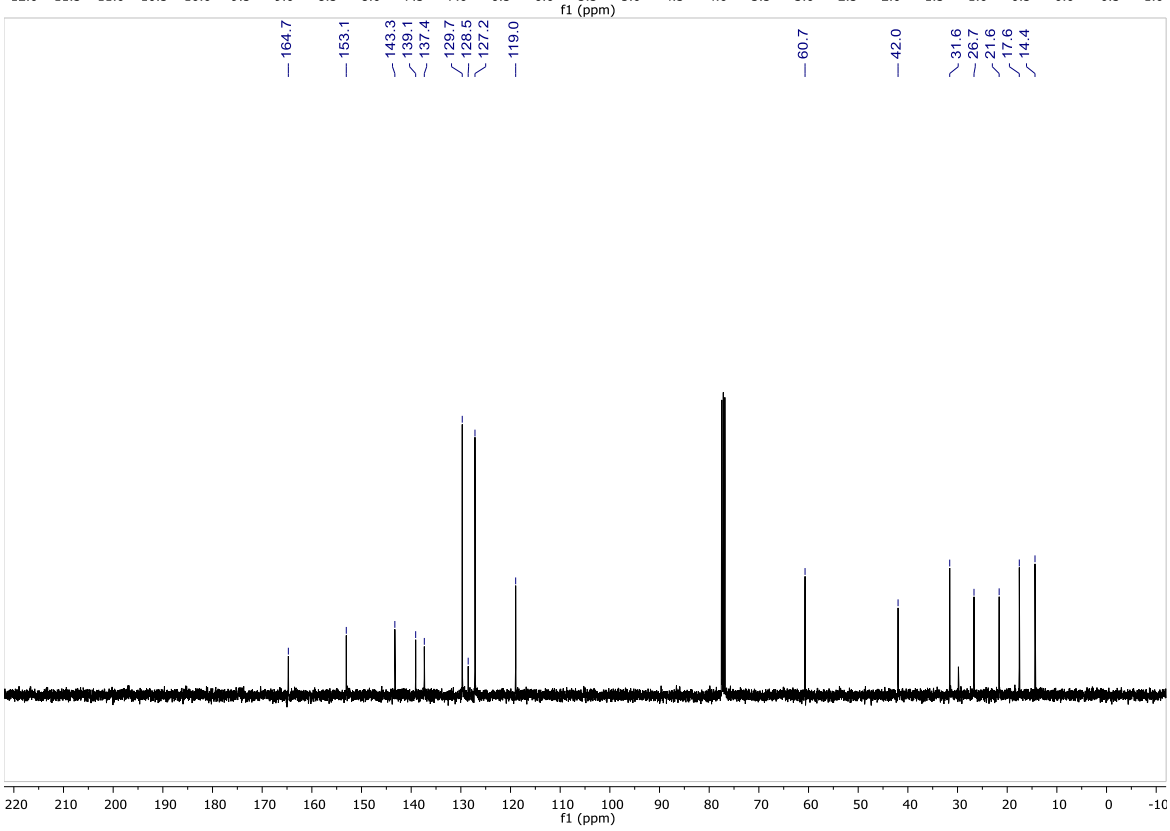

7.73
7.27
5.26
4.31
2.99
2.95
2.41
2.25
2.17
1.79
1.35
1.91
2.27
1.00
2.04
4.20
3.22
3.14
3.12
2.16
3.12
f1 (ppm)

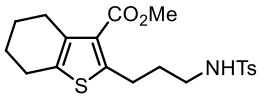

165.1
147.8
143.2
137.5
133.4
130.4
129.7
129.4
127.2
60.7
41.9
31.6
26.1
21.6
14.4
14.2
13.1
f1 (ppm)


Me
CO2Et
NHTs
S

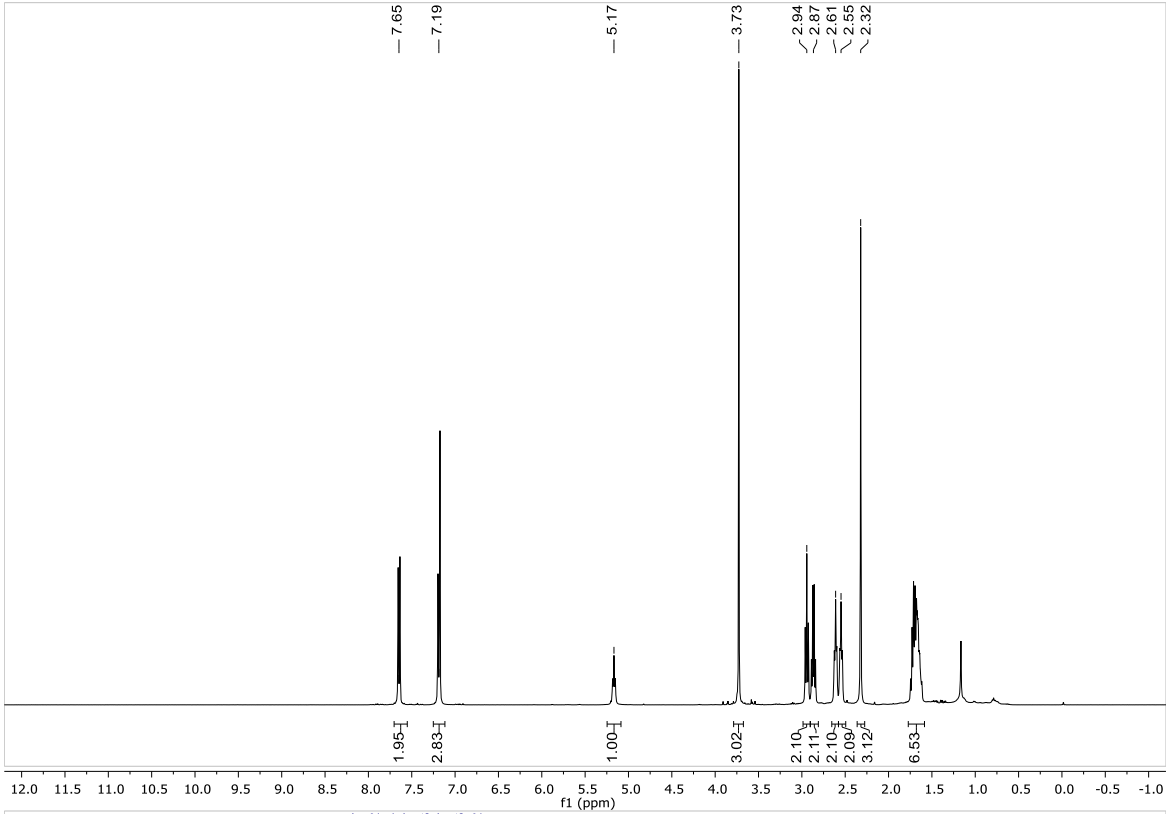
2g

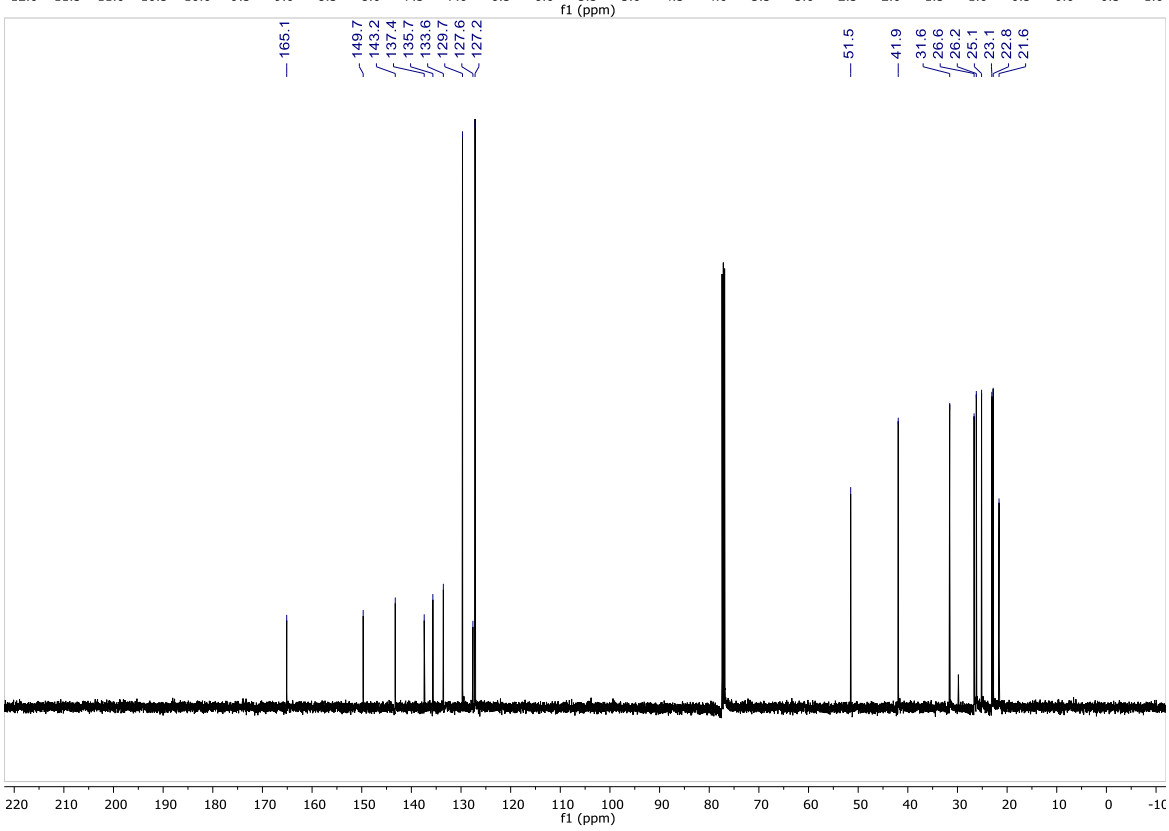

7.73
7.27
6.67
5.23
4.31
3.07
2.95
2.41
2.32
1.83
1.35
1.93
2.15
0.90
1.04
2.00
2.09
2.15
3.12
3.13
2.19
3.19
f1 (ppm)

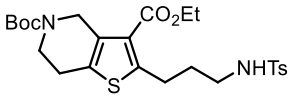

164.7
153.1
143.3
139.1
137.4
129.7
128.5
127.2
119.0
60.7
42.0
31.6
26.7
21.6
17.6
14.4
f1 (ppm)


CO2Me
NHTs
S

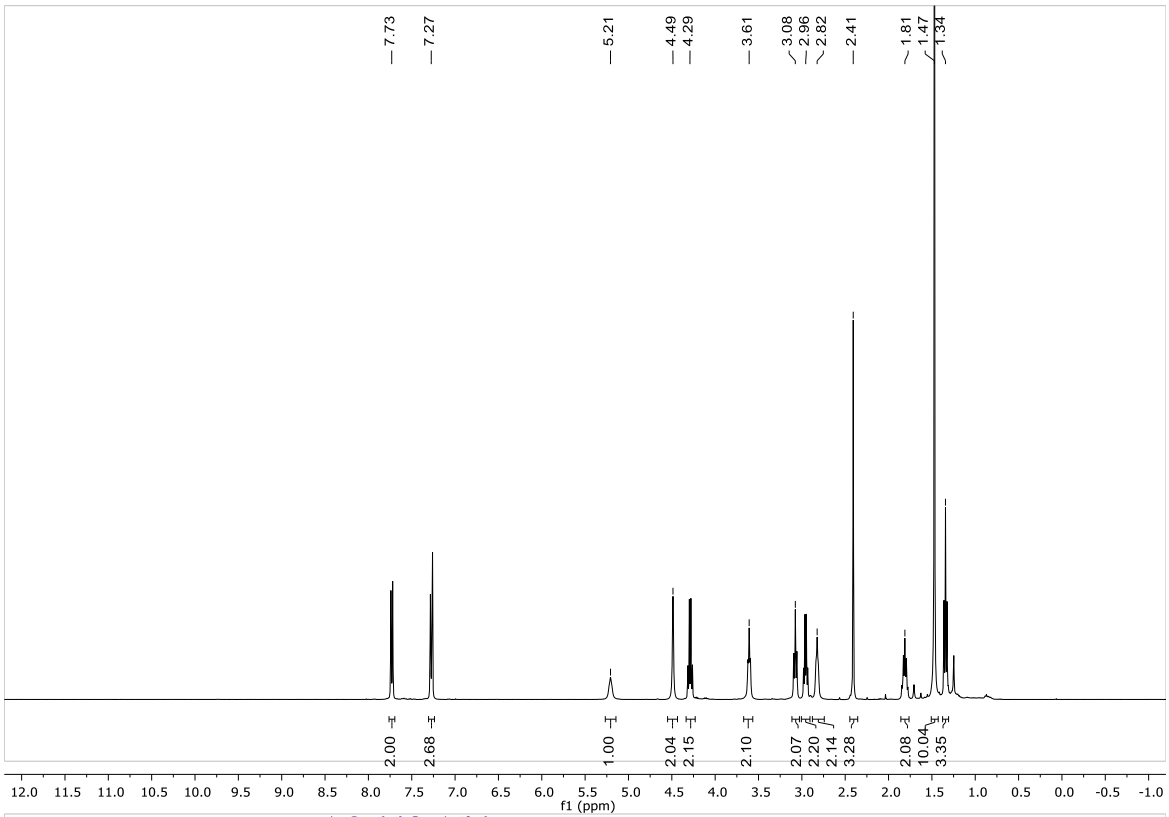
2h

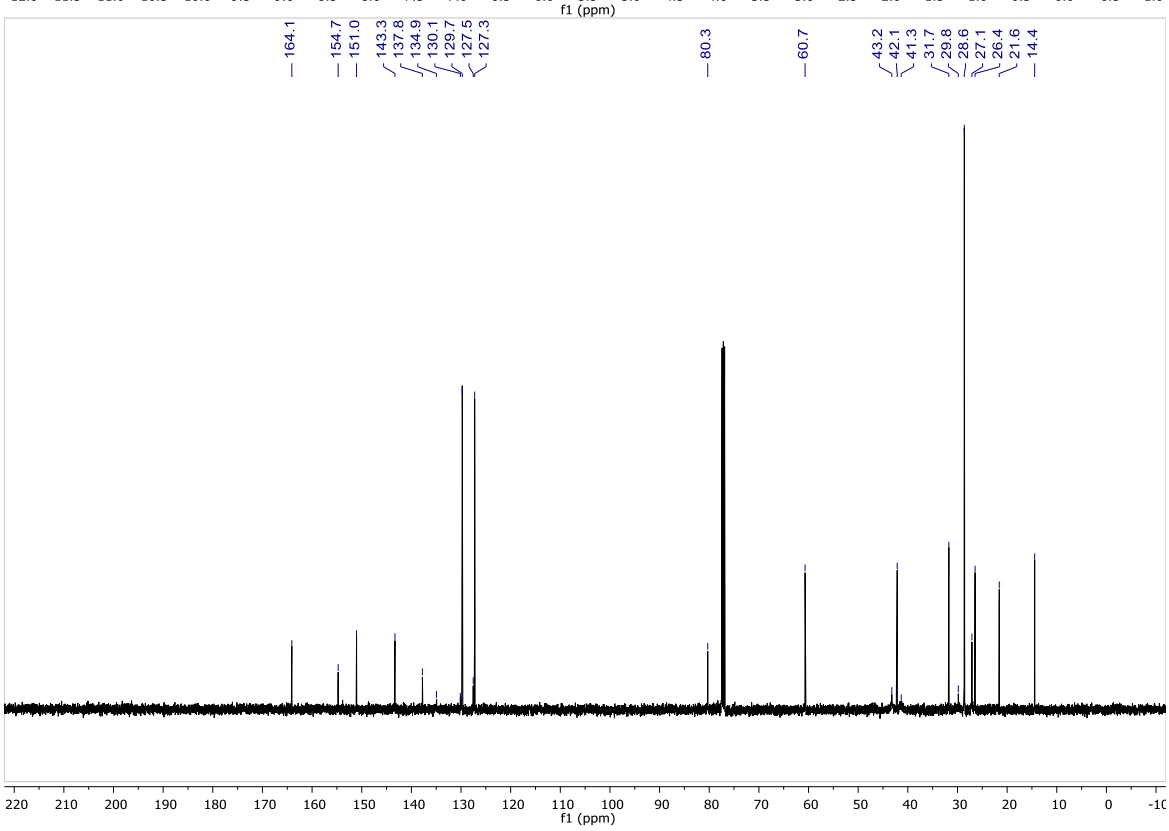

7.65
7.19
5.17
3.73
2.94
2.87
2.61
2.55
2.32
1.95
2.83
1.00
3.02
2.10
2.11
2.10
2.09
3.12
6.53
f1 (ppm)

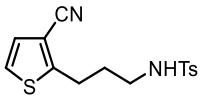

165.1
149.7
143.2
137.4
135.7
133.6
129.7
127.6
127.2
51.5
41.9
31.6
26.6
26.2
25.1
23.1
22.8
21.6
f1 (ppm)


BocN
CO2Et
NHTs
S

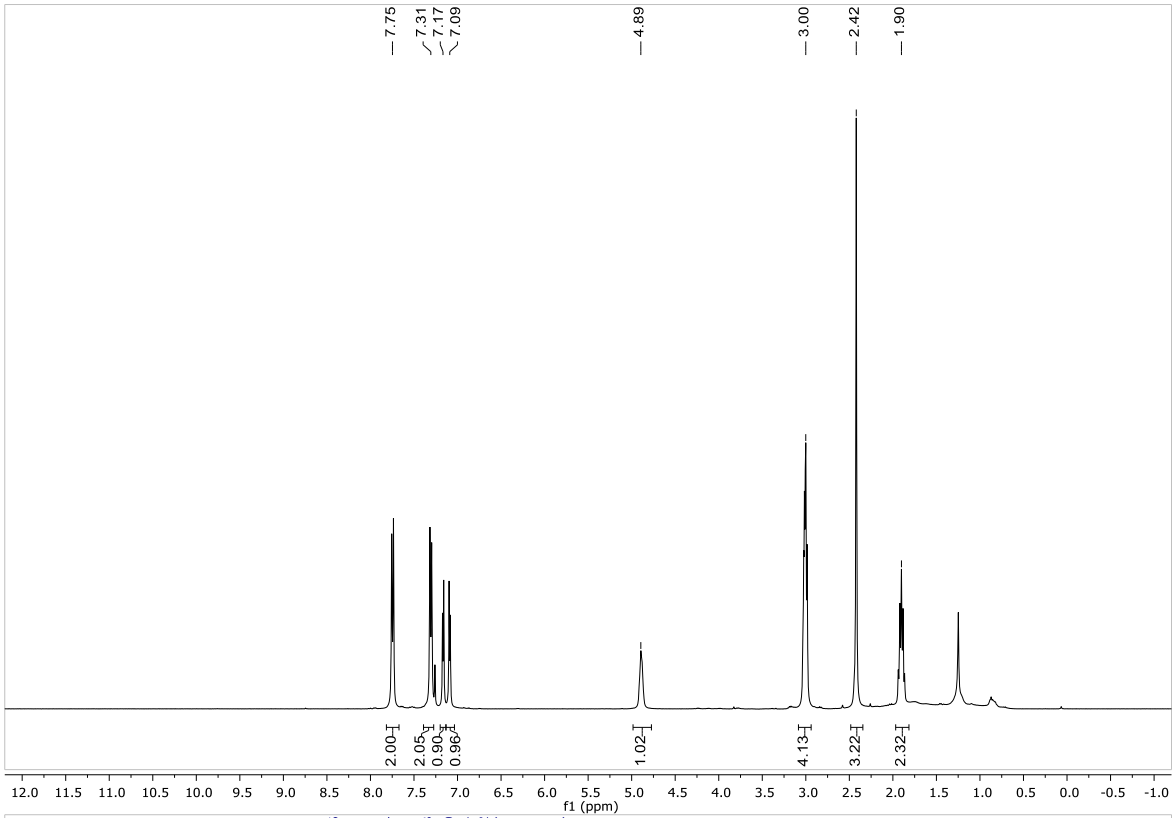
2i

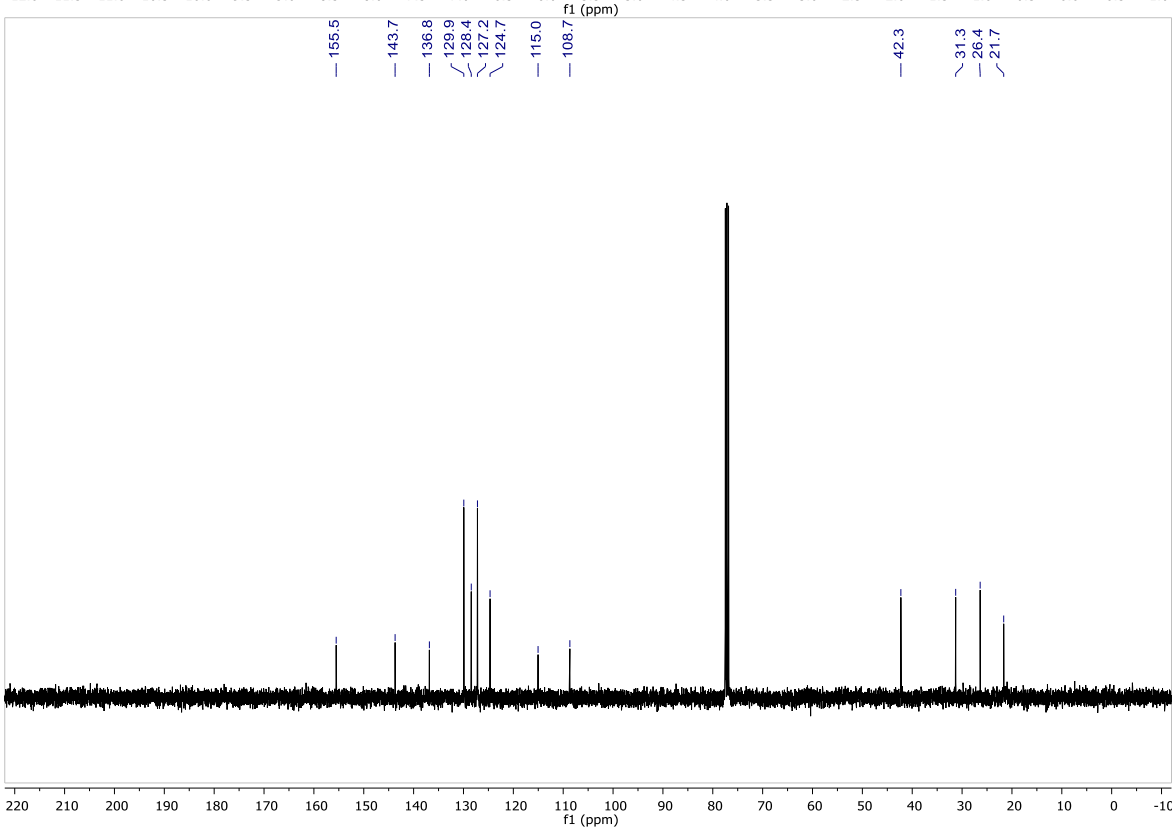

7.73
7.27
5.21
4.49
4.29
3.61
3.08
2.96
2.82
2.41
1.81
1.47
1.34
2.00
2.68
1.00
2.04
2.15
2.10
2.07
2.20
2.14
3.28
2.08
10.04
3.35
f1 (ppm)

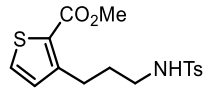

164.1
154.7
151.0
143.3
137.8
134.9
130.1
129.7
127.5
127.3
80.3
60.7
43.2
42.1
41.3
31.7
29.8
28.6
27.1
26.4
21.6
14.4
f1 (ppm)


CN
NHTs
S

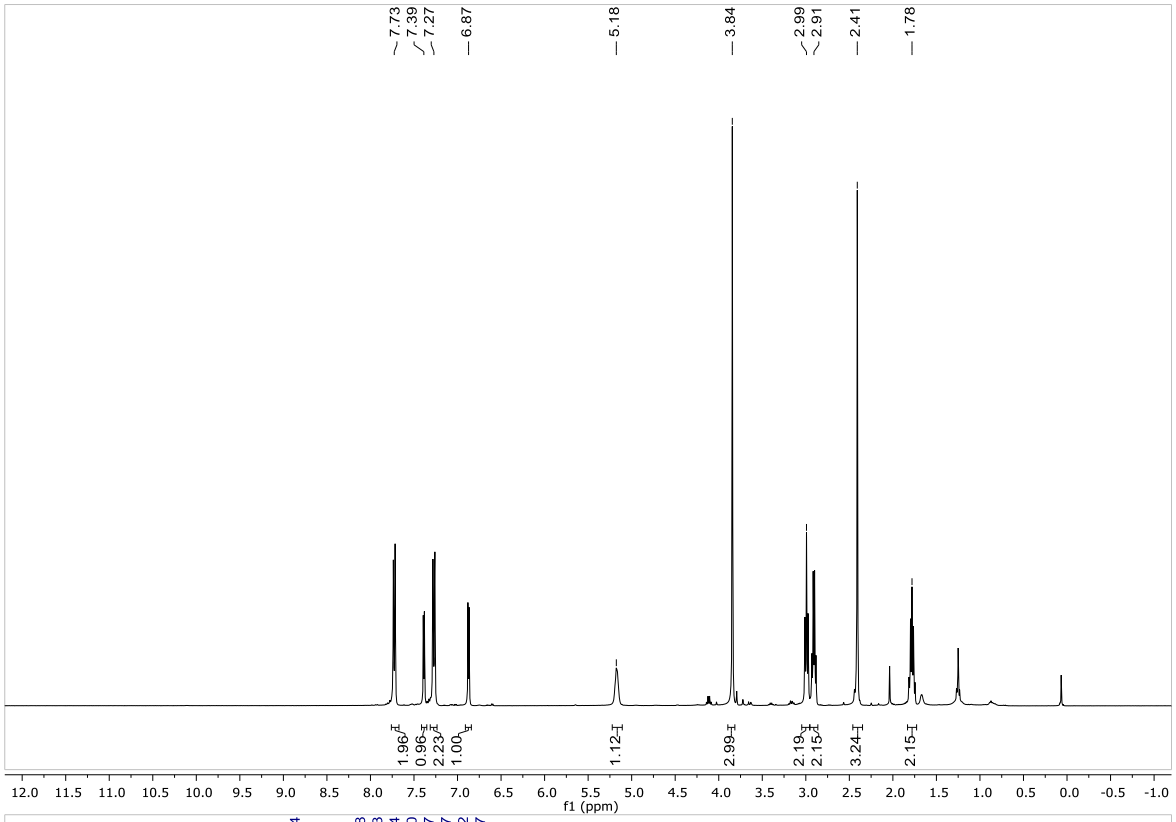
2j

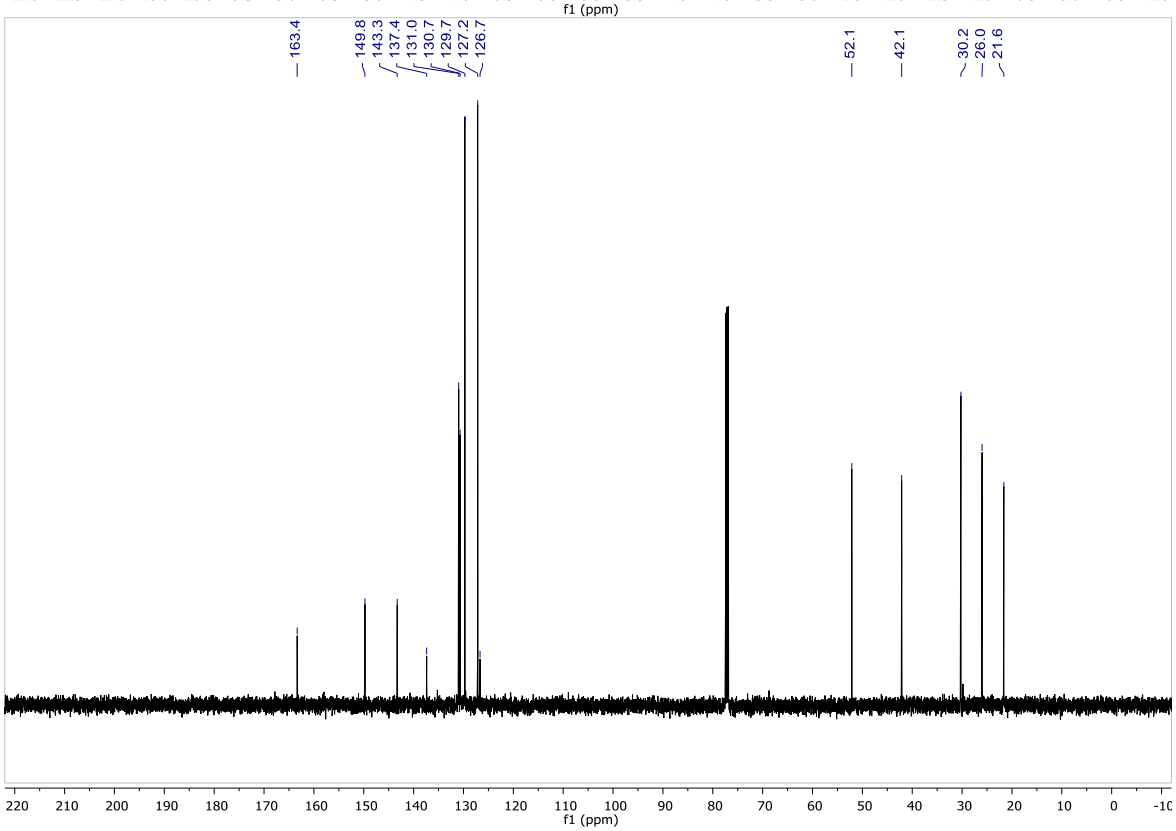

7.75
7.31
7.17
7.09
4.89
3.00
2.42
1.90
2.00
2.05
0.90
0.96
1.02
4.13
3.22
2.32
f1 (ppm)

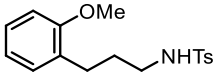

155.5
143.7
136.8
129.9
128.4
127.2
124.7
115.0
108.7
42.3
31.3
26.4
21.7
f1 (ppm)


CO2Me
S
NHTs

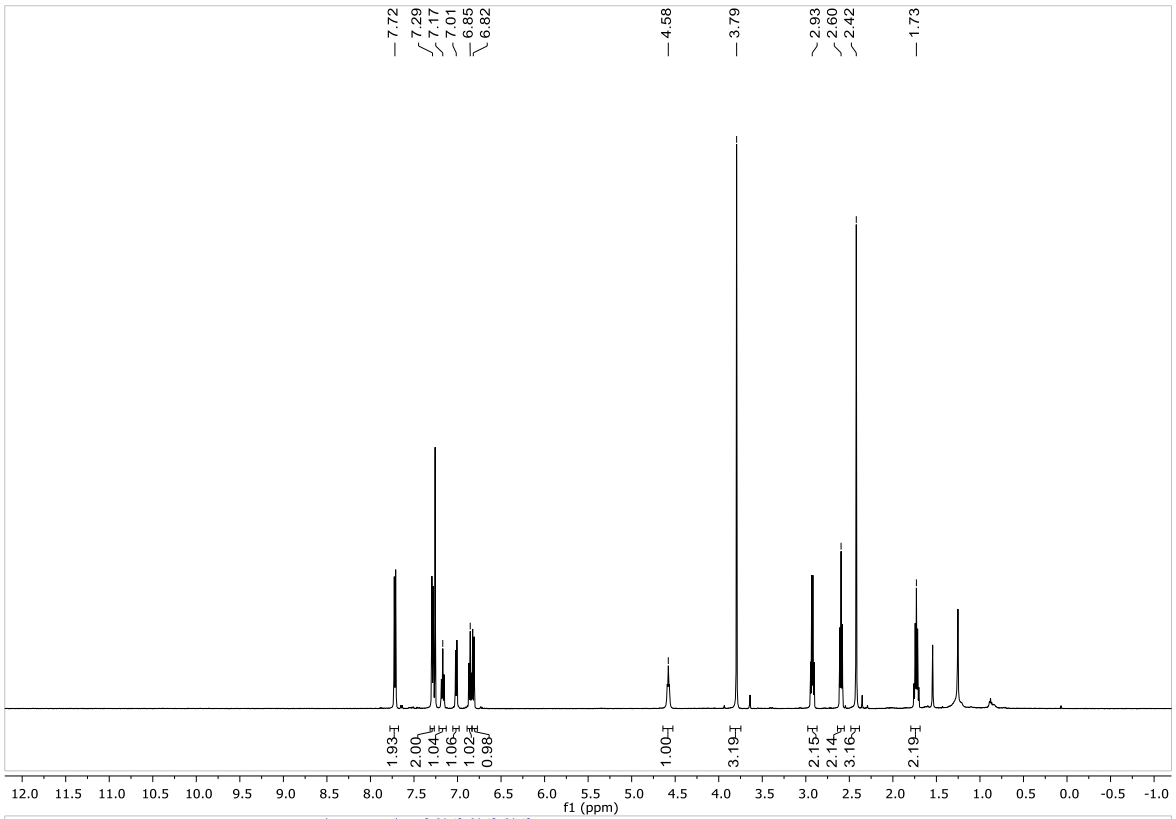
2k

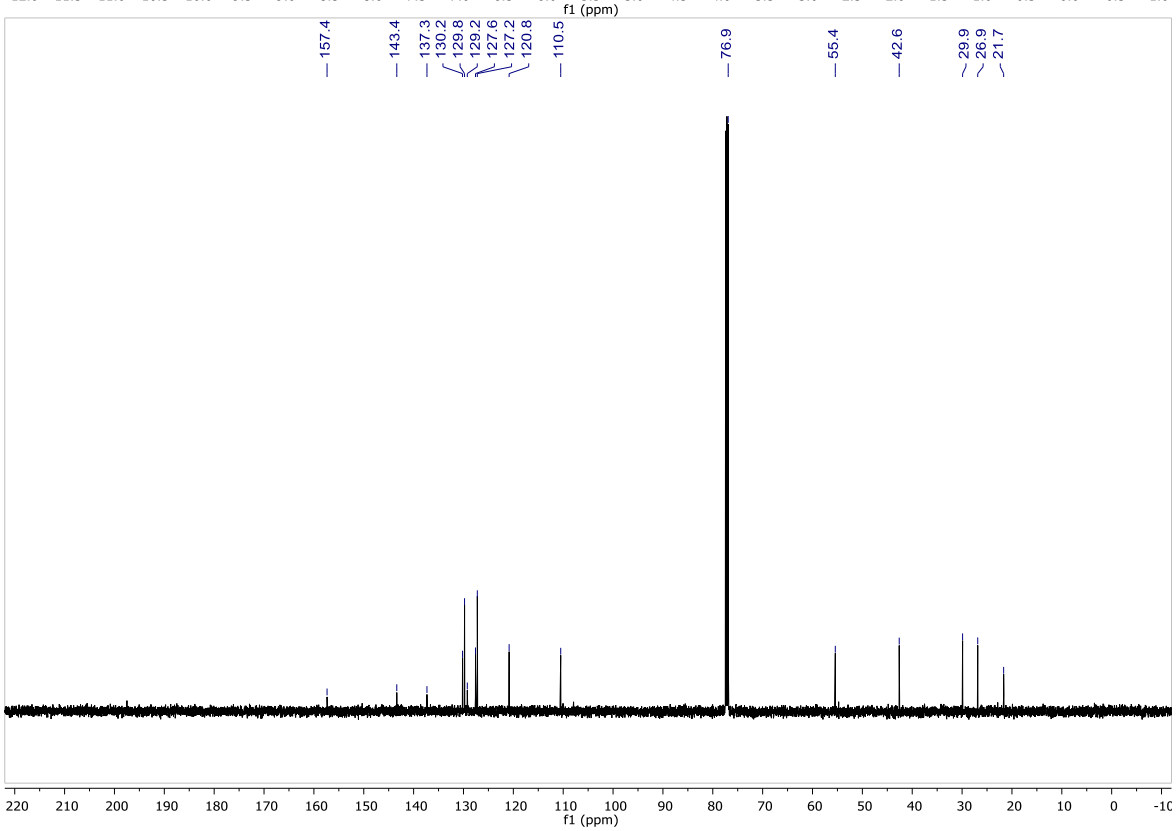

7.73
7.39
7.27
6.87
5.18
3.84
2.99
2.91
2.41
1.78
1.96
0.96
2.23
1.00
1.12
2.99
2.19
2.15
3.24
2.15
f1 (ppm)

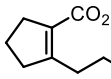

163.4
149.8
143.3
137.4
131.0
130.7
129.7
127.2
126.7
52.1
42.1
30.2
26.0
21.6
f1 (ppm)


OMe
NHTs

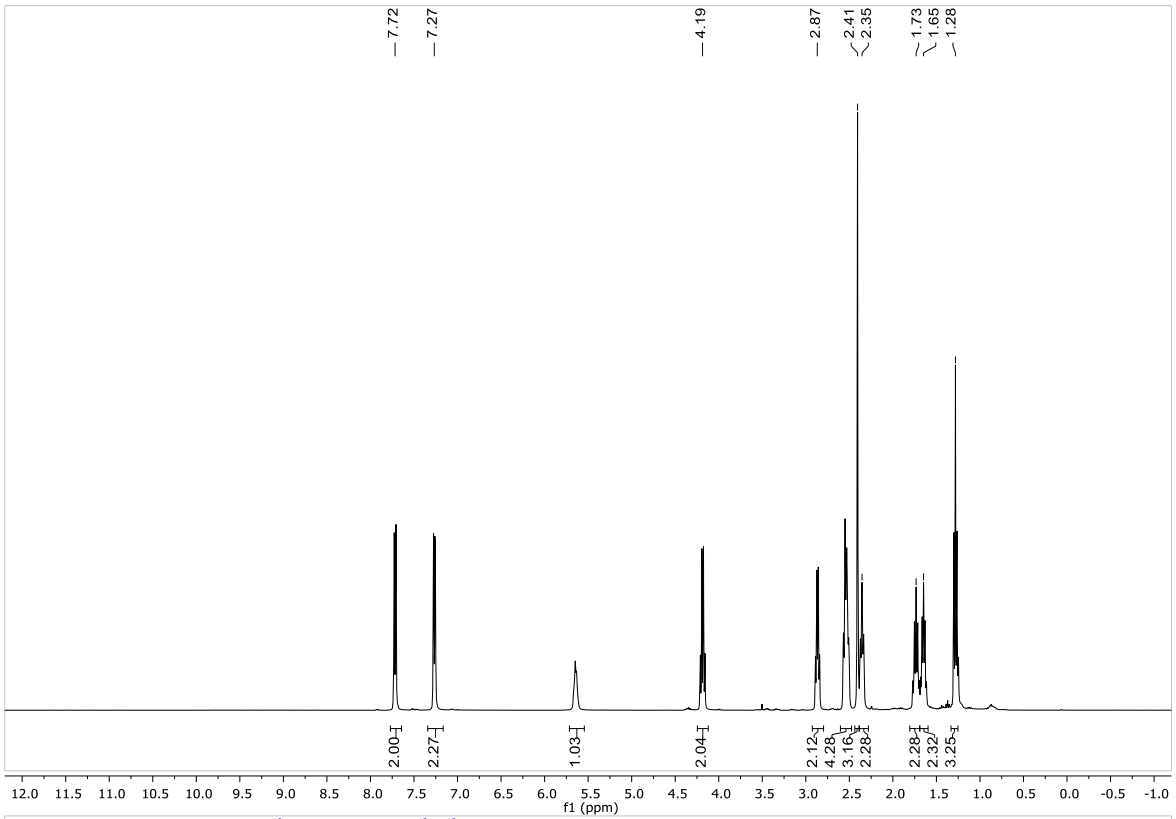
2l

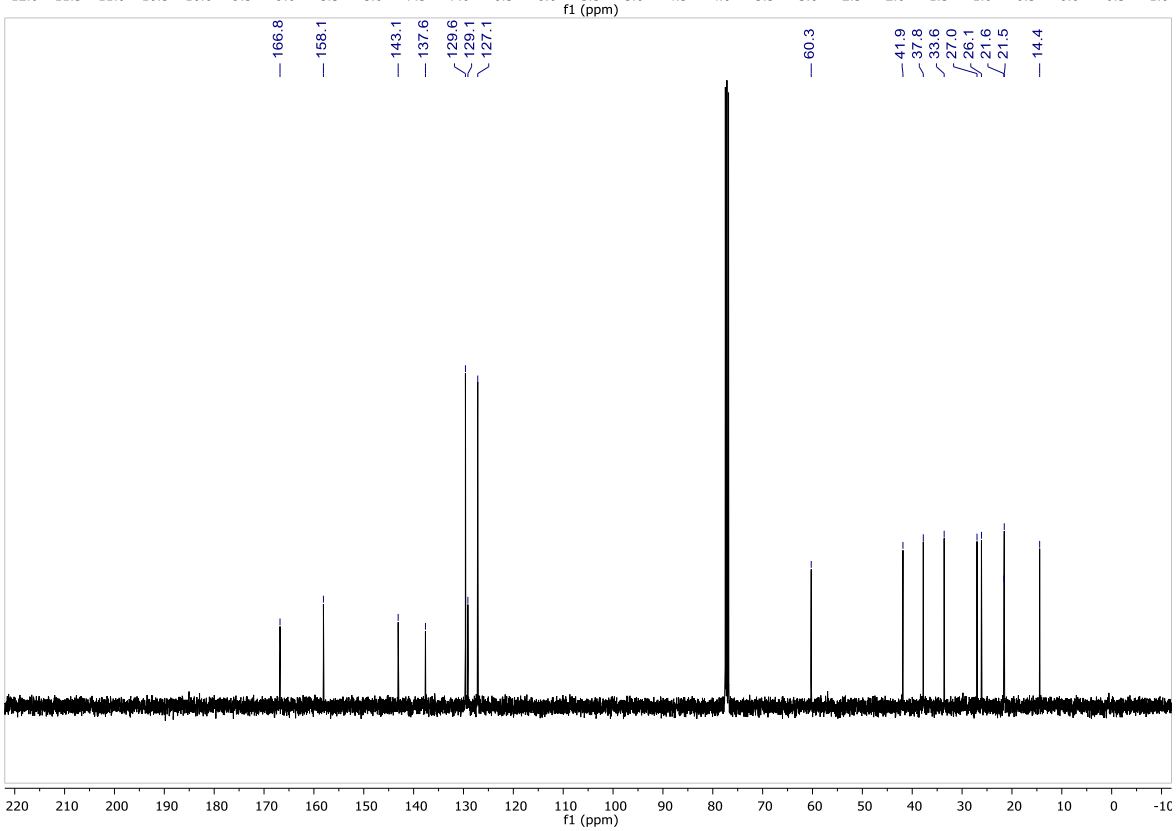

7.72
7.29
7.17
7.01
6.85
6.82
4.58
3.79
2.93
2.60
2.42
1.73
1.93
2.00
1.04
1.06
1.02
0.98
1.00
3.19
2.15
2.14
3.16
2.19
f1 (ppm)

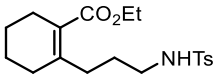

157.4
143.4
137.3
130.2
129.8
129.2
127.6
127.2
120.8
110.5
76.9
55.4
42.6
29.9
26.9
21.7
f1 (ppm)


CO2Et
NHTs

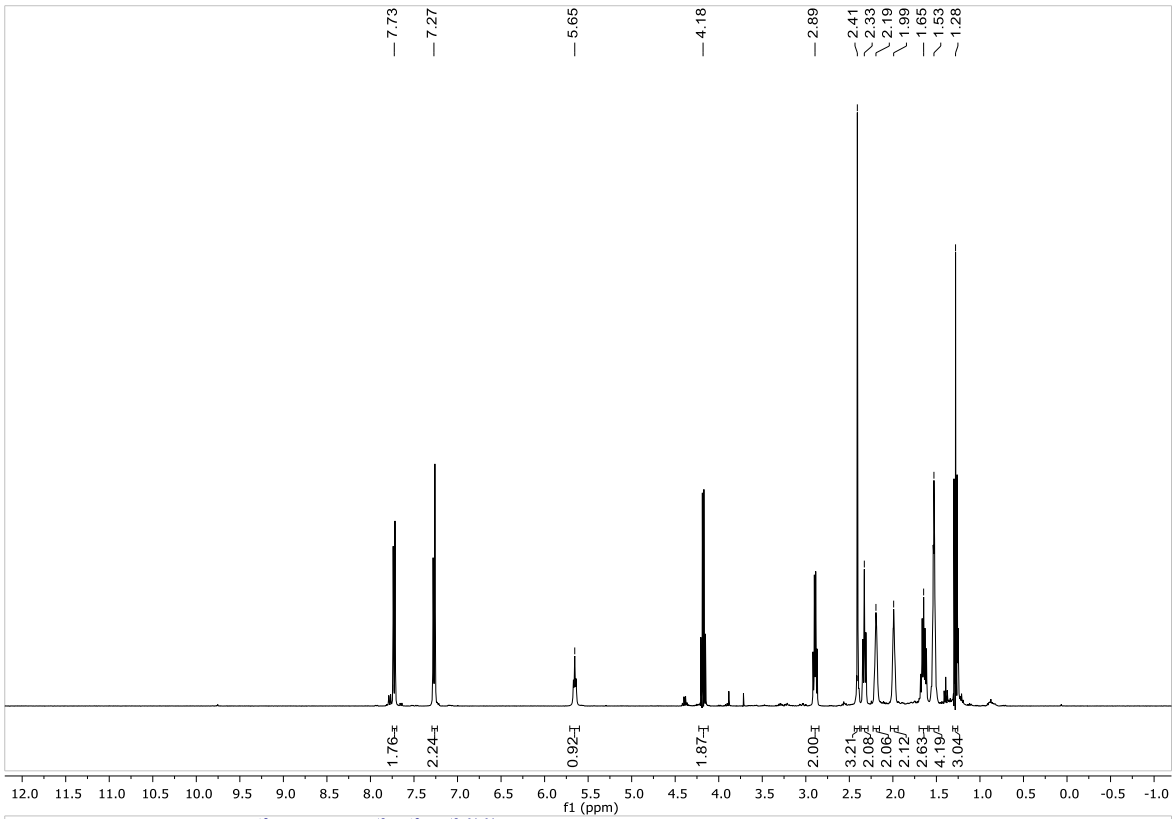
2m

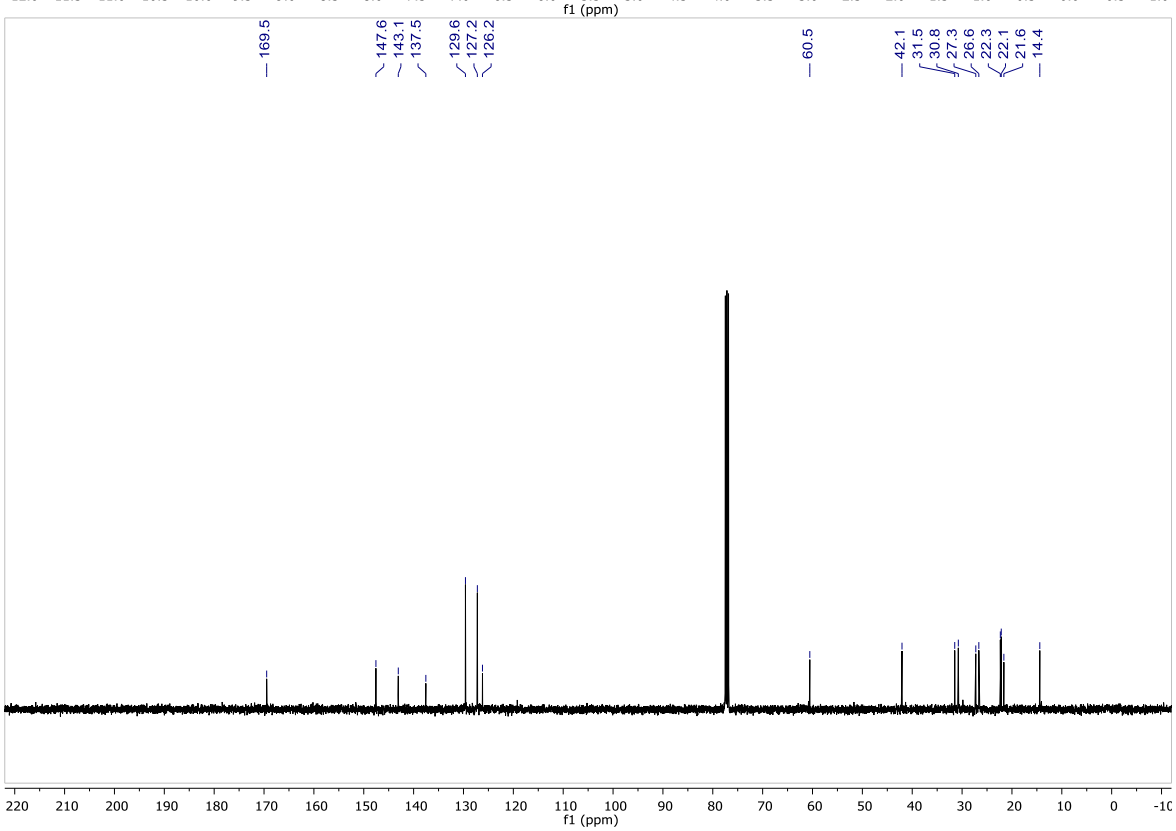

7.72
7.27
4.19
2.87
2.41
2.35
1.73
1.65
1.28
2.00
2.27
1.03
2.04
2.12
4.28
3.16
2.28
2.28
2.32
3.25
f1 (ppm)

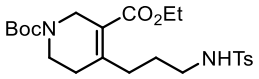

166.8
158.1
143.1
137.6
129.6
129.1
127.1
60.3
41.9
37.8
33.6
27.0
26.1
21.6
21.5
14.4
f1 (ppm)


CO2Et
NHTs

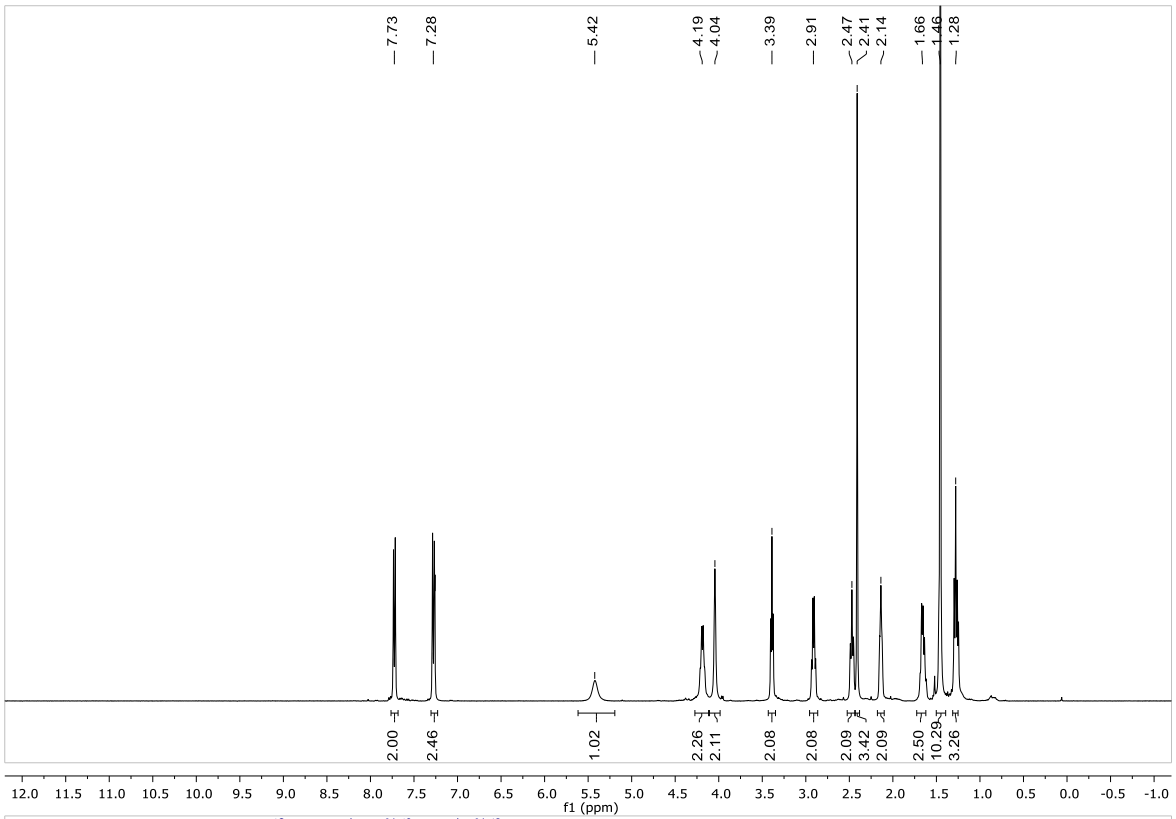
2n

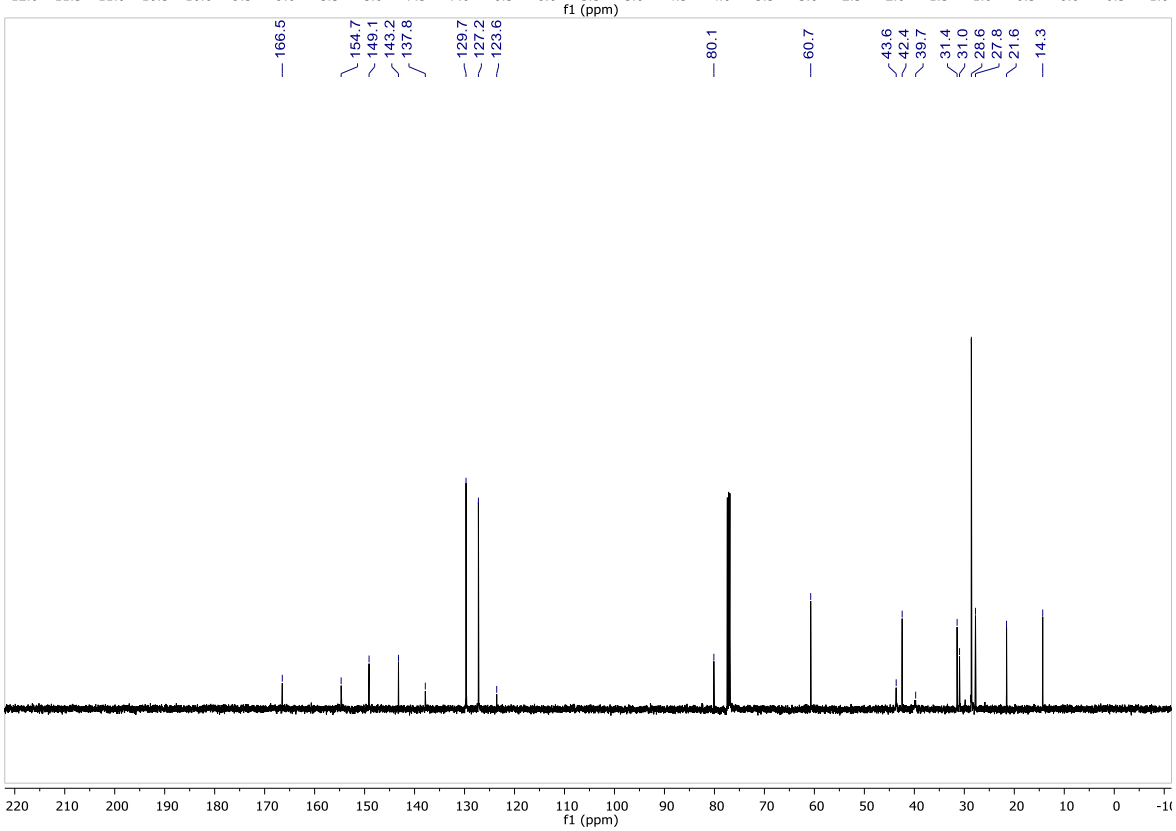

7.73
7.27
5.65
4.18
2.89
2.41
2.33
2.19
1.99
1.65
1.53
1.28
1.76
2.24
0.92
1.87
2.00
3.21
2.08
2.06
2.12
2.63
4.19
3.04
f1 (ppm)

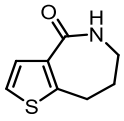

169.5
147.6
143.1
137.5
129.6
127.2
126.2
60.5
42.1
31.5
30.8
27.3
26.6
22.3
22.1
21.6
14.4
f1 (ppm)


BocN
CO2Et
NHTs

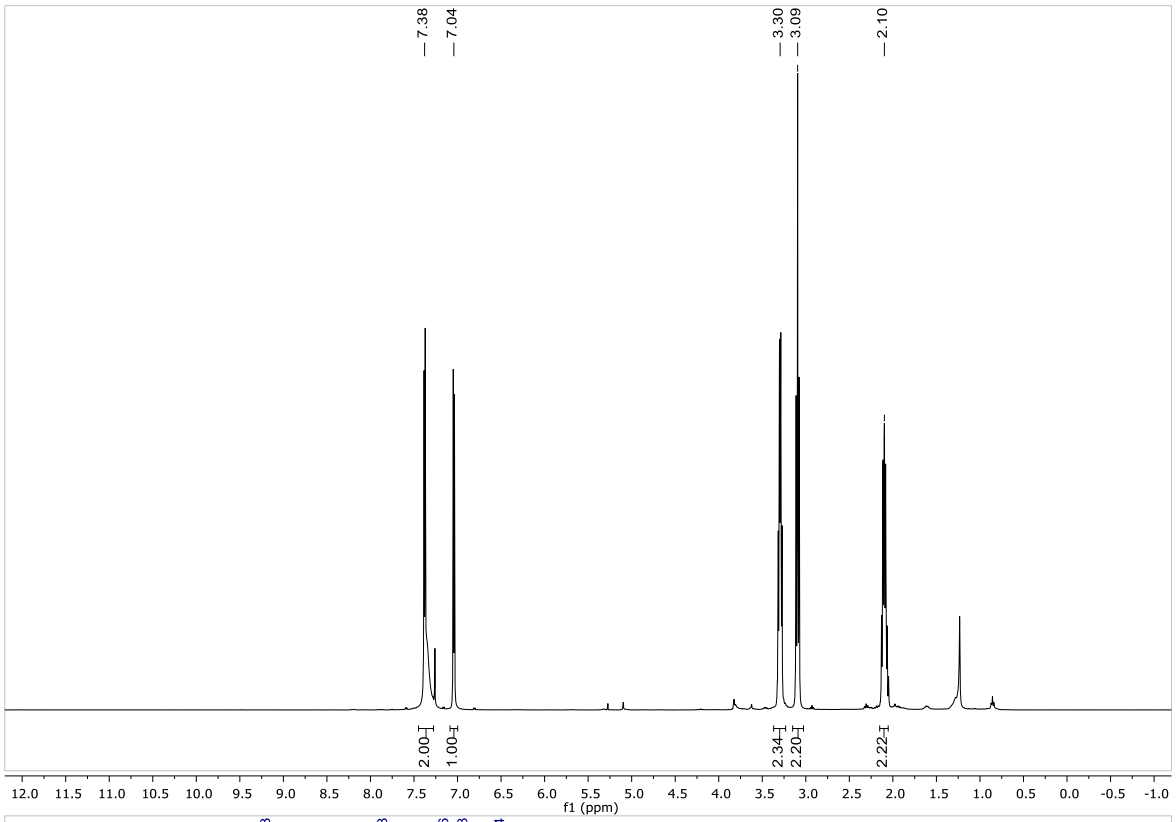
2o

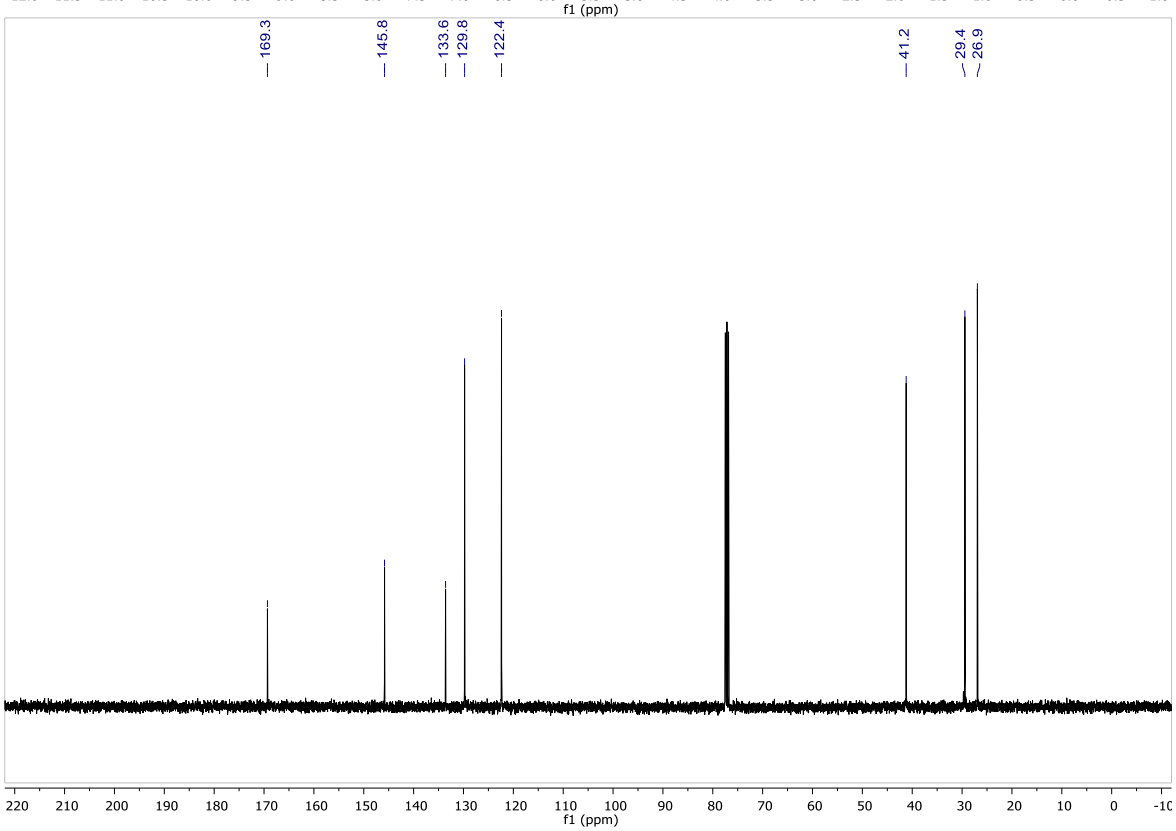

7.73
7.28
5.42
4.19
4.04
3.39
2.91
2.47
2.41
2.14
1.66
1.46
1.28
2.00
2.46
1.02
2.26
2.11
2.08
2.08
2.09
3.42
2.09
2.50
10.29
3.26
f1 (ppm)


166.5
154.7
149.1
143.2
137.8
129.7
127.2
123.6
80.1
60.7
43.6
42.4
39.7
31.4
31.0
28.6
27.8
21.6
14.3
f1 (ppm)


O
H
N
S

1


7.38
7.04
3.30
3.09
2.10
2.00
1.00
2.34
2.20
2.22
f1 (ppm)


169.3
145.8
133.6
129.8
122.4
41.2
29.4
26.9
f1 (ppm)