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SUPPORTING INFORMATION

Copper Catalysed Oxidative Sulfonylation of Branched Aldehydes Using the Acid Enhanced Reactivity of Manganese(IV) oxide.

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General Experimental Considerations

All reactions were run under an inert atmosphere (argon) with flame-dried glassware using standard techniques unless otherwise stated. Anhydrous solvents were obtained by filtration through drying columns (THF, diethyl ether, CH_2Cl_2). Acetic acid, copper(II) triflate (98% purity), manganese(IV) oxide (>99% purity) and bathophenanthroline (>99% purity) were purchased from Sigma Aldrich and used as provided. Commercial aldehydes were distilled. All other commercial reagents were used as supplied or purified by standard techniques where necessary.

All α-sulfonylation reactions were performed in microwave vials under air and sealed with Fisherbrand 20 mm aluminium, plain, centre hole, molded septa butyl, dark grey, 55° shore A, 3.0 mm caps when using polar solvents (AcOH, H_2O or Ethanol).

Flash column chromatography was performed using 230-400 mesh silica with the indicated solvent system according to standard techniques. Analytical thin-layer chromatography (TLC) was performed on precoated, glass-backed silica gel plates. Visualisation of the developed chromatogram was performed by UV absorbance (254 nm), aqueous potassium permanganate, *p*-anisaldehyde, phosphomolybdic acid or vanillin stains. Infrared spectra (ν_{max}, FTIR ATR) were recorded in reciprocal centimeters (cm^{-1}). Nuclear magnetic resonance spectra were recorded on 400 MHz spectrometers. Chemical shifts for ^1H NMR spectra are recorded in parts per million from tetramethylsilane with the solvent resonance as the internal standard (chloroform δ = 7.27 ppm, or methanol δ = 3.31 ppm). Data is reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and b = broad), coupling constant in Hz, integration, assignment]. ^{13}C NMR spectra were recorded with complete proton decoupling. Chemical shifts are reported in parts per million from tetramethylsilane with the solvent resonance as the internal standard (chloroform: δ = 77.0 ppm, methanol δ = 49.0 ppm). *J* values are reported in Hz. Assignments of $^1H/^{13}C$ spectra were made by the analysis of δ/*J* values, and COSY, HSQC, and HMBC experiments as appropriate. In cases where novel compounds are isolated as a mixture of diastereomers, both diastereomers were assigned in a single multiplet report with H_a/H_b and C_a/C_b being used to denote the proton and carbons of the two diastereomers respectively. In the case when known compounds are isolated as a mixture of diastereomers, *cis*- and *trans*-diastereomers are assigned in separate multiplet reports. ^{19}F NMR spectra were recorded with or without complete proton decoupling. Decoupling is indicated as ($^{19}F\{^1H\}$) and where relevant this is stated in each assignment and spectrum. ^{19}F spectra are indirectly referenced to $CFCl_3$, automatically via direct measurement of the absolute frequency of the deuterium lock signal by the spectrometer hardware.

Melting points are uncorrected.

The high-resolution mass spectrometry (HRMS) analyses were performed using electrospray ion source (ESI) or pneumatically assisted atmospheric pressure chemical ionization (APCI) using an atmospheric solids analysis probe (ASAP). ESI was performed using a Waters LCT Premier equipped with an ESI source operated in positive or negative ion mode. The software used was MassLynx 4.1, this software does not account for the electron and all the calibrations/references are calculated accordingly, i.e. $[M+H]^+$ is detected and the mass is calibrated to output [M+H]. APCI was performed using an Orbitrap XL or Xevo G2S using an ASAP to insert samples into the APCI source. The sample was introduced at ambient temperature and the temperature increased until the sample vaporised.

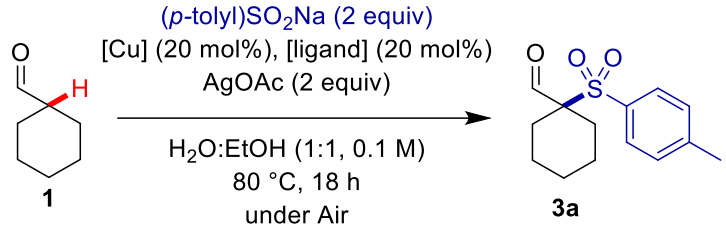
All raw and processed data for this manuscript can be found at the Imperial College London Research Data Repository:

https://doi.org/10.14469/hpc/6794

Optimisation of Reaction Conditions for Silver-Mediated Oxidative Coupling Reaction

Catalyst Screening.

Various copper salts were investigated (Table S1, Entries 1–5). Copper(II) triflate was identified as the most effective under catalytic conditions. Investigation into N,N bidentate ligand additives (entries 6–8) showed 1,10–phenanthroline as an effective ligand to promote the reaction (entry 7). Further investigation of substituted 1,10–phenanthrolines revealed bathophenanthroline as the most effective in terms of yield and mass recovery (entry 11). Conducting the reaction at higher temperature ensured full conversion to product (Entries 12,13).

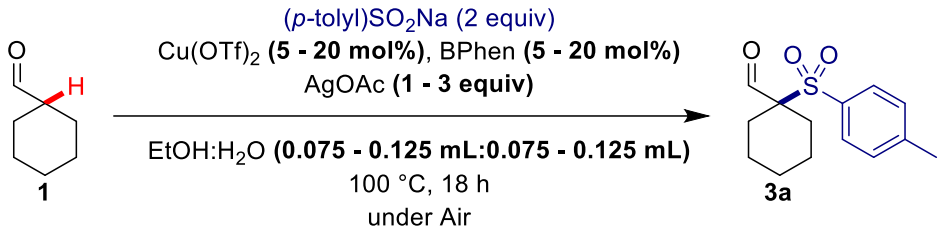


Entry	Cu (mol%)	Ligand	RSM (%)[a]	Yield 3a (%)[a]	Total (%)
1[b]	$Cu(OAc)_2$ (100)	None	14	30	44
2	$Cu(OAc)_2$ (20)	None	14	26	40
3	$CuBr_2$ (20)	None	20	26	46
4	$Cu(acac)_2$ (20)	None	15	28	43
5	$Cu(OTf)_2$ (20)	None	18	33	51
6	$Cu(OTf)_2$ (20)	2,2'-Bipyridine	17	48	65
7	$Cu(OTf)_2$ (20)	1,10-Phenanthroline	18	52	70
8	$Cu(OTf)_2$ (20)	Tetramethylethylenediamine	13	29	42
9	$Cu(OTf)_2$ (20)	4,7-Dimethoxyphenanthroline	8	38	46
10	$Cu(OTf)_2$ (20)	3,4,7,8-Tetramethylphenenanthroline	13	57	70
11	$Cu(OTf)_2$ (20)	Bathophenanthroline	19	57	76
12[c]	**$Cu(OTf)_2$ (20)**	**Bathophenanthroline**	**0**	**74**	**74**
13[d]	**$Cu(OTf)_2$ (20)**	**Bathophenanthroline**	**0**	**74**	**74**

Table S1 – Optimisation of silver mediated α–sulfonylation. Reactions performed on 0.2 mmol scale. [a] Yield determined in situ using 1,3,5-trimethoxybenzene as an internal standard. [b] 1 equiv of $Cu(OAc)_2$ used. [c] Reaction performed at 95 °C and at 1 M. [d] Reaction performed at 110 ° C and at 1 M.

DOE Optimisation of Reaction Conditions

Using JMP Pro 14 software, the following factors were investigated using a response surface design: copper loading, ligand loading, volume of EtOH, volume of H_2O and oxidant loading were investigated as these had been previously shown to have a more significant impact on the yield. Temperature was fixed to 100 °C and time at 18 h. The ranges chosen are shown below: the JMP DoE software gave 26 experiments to run (Table S2).



Entry	Cat Loading (mol%)	Ligand Loading (mol%)	Vol. EtOH (mL)	Vol. EtOH (mL)	Oxidant equiv	Yield 3a (%)[a]
1	5	20	0.125	0.125	3	24
2	20	5	0.075	0.125	1	39
3	5	20	0.075	0.075	3	36
4	12.5	12.5	0.125	0.1	2	53
5	20	20	0.125	0.075	3	34
6	20	20	0.075	0.1	1	38
7	5	5	0.075	0.125	3	42
8	5	5	0.075	0.075	1	24
9	5	20	0.125	0.075	1	24
10	12.5	5	0.1	0.1	2	54
11	5	5	0.125	0.125	1	32
12	20	5	0.125	0.125	3	46
13	12.5	20	0.075	0.125	1	50
14	20	5	0.125	0.075	1	47
15	12.5	12.5	0.075	0.075	2	56
16	5	20	0.1	0.125	2	34
17	5	5	0.125	0.075	3	55
18	20	20	0.075	0.125	3	37
19	12.5	12.5	0.1	0.1	3	48
20	5	12.5	0.075	0.1	2	26
21	5	12.5	0.1	0.1	1	35
22	20	12.5	0.1	0.125	2	53
23	12.5	5	0.1	0.1	2	54
24	20	20	0.125	0.125	1	48
25	20	20	0.1	0.075	2	58
26	20	5	0.075	0.075	3	41

Table S2 – Silver mediated α-Sulfonylation DoE data. Reactions performed on 0.2 mmol scale. [a] Yield determined in situ using 1,3,5-trimethoxybenzene as an internal standard.

The DoE software used this data to construct a model which both showed the goodness of fit of the data, comparing the predicted yield with the actual yield obtained (Figure S1)**.** The experimental data was plotted against the predicted yield given by the red line shown in Figure S1. As the points do not deviate greatly from the trendline, the model fits well to the observed data. Experimental data points in red are highlighted as potential outliers by the software. Nonetheless, the R^2 value of this data is 0.95 indicating a 95% confidence in the results obtained from the data.

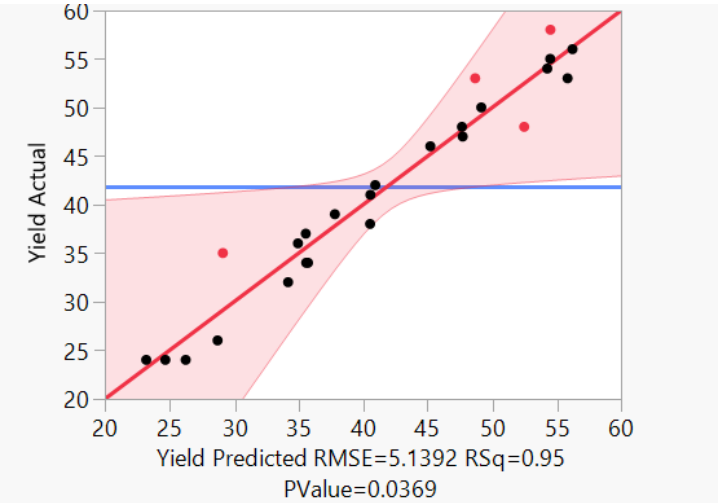


Figure S1 - Predicted vs actual yield.

The significance of each factor is shown below (Figure S2). Figure S2 denotes the log value of significance of each factor and combination of factors as calculated by JMP pro 14. A higher value for log worth signifies a higher relative significance of the factor with respect to yield of reaction. From this, it appears that the catalyst loading is most significant, with the interaction between catalyst and oxidant being next most significant.

Source	LogWorth	PValue	
Cat. Loading(5,20)	2.005	0.00989	
Cat. Loading*Cat. Loading	1.966	0.01081	
Cat. Loading*Oxidant Loading	1.580	0.02631	
Vol H2O*Vol H2O	1.495	0.03196	
Ligand Loading*Oxidant Loading	1.330	0.04679	
Vol EtOH*Vol EtOH	1.316	0.04834	
Ligand Loading(5,20)	1.277	0.05280	^
Ligand Loading*Vol EtOH	1.180	0.06603	
Cat. Loading*Ligand Loading	1.015	0.09664	
Vol EtOH(0.075,0.125)	0.604	0.24869	^
Vol H2O(0.075,0.125)	0.589	0.25762	^
Oxidant Loading*Oxidant Loading	0.501	0.31520	
Ligand Loading*Ligand Loading	0.499	0.31711	
Oxidant Loading(1,3)	0.378	0.41867	^
Vol H2O*Oxidant Loading	0.295	0.50701	
Vol EtOH*Oxidant Loading	0.223	0.59873	
Cat. Loading*Vol H2O	0.170	0.67549	
Ligand Loading*Vol H2O	0.114	0.76902	
Vol EtOH*Vol H2O	0.043	0.90540	
Cat. Loading*Vol EtOH	0.007	0.98317	

Figure S2 - Significance of each factor and interaction

The interaction plot describes the interactions of each variable (Figure S3). By focusing on this plot row by row, it is possible to understand how each of the factors interact with one another. If two factors are interacting, it would be expected that their high and low extremes (in blue and red respectively) will have different profiles to one another.

Looking at the row of catalyst loading first (row 1), box 1b shows the variation in yield at 20 mol% catalyst (in blue) and at 5 mol% (in red) as ligand loading increases from 5 to 20 mol%. Higher catalyst loading gives overall higher yield, with the increased loading of ligand having a maximum 12.5 mol%. At the lower catalyst loading, the ligand appears to have a negative interaction leading to reduced yields at high ligand loading.

This could be due to the formation of less catalytically competent copper species which is unable to effectively coordinate the substrate. For volumes of both EtOH and H_2O (rows 3a,b and 4a,b), as the line profiles at high and low catalyst loadings are very similar, this implies that no significant interaction exists between the volume of either solvent and the catalyst loading. When comparing catalyst loading and oxidant loading (box 1e) at high catalyst loading, higher oxidants loadings were not well tolerated. However, the reverse is true at low catalyst loadings where more oxidant leads to higher yields.

The lower ligand loadings gave a consistently higher yield (for any loading shown, the red line (5 mol% ligand loading) is typically higher than the blue (20 mol% ligand loading). As discussed above, the same catalyst – ligand interaction is observed (box 2a) however the decrease in yield at the extremes is more pronounced as the ligand loading is kept constant and the catalyst loading is changed. A slight interaction between the volume of EtOH and ligand loading is implied (box 2c) however no interaction is observed between volume of H_2O and ligand loading (box 2d). Finally, like catalyst loading, the oxidant loading has an interaction with the ligand loading (box 2e).

Other than the interactions discussed previously, the volumes of each respective solvent do not have any significant interactions and best yields were observed at low H_2O volume and EtOH volume.

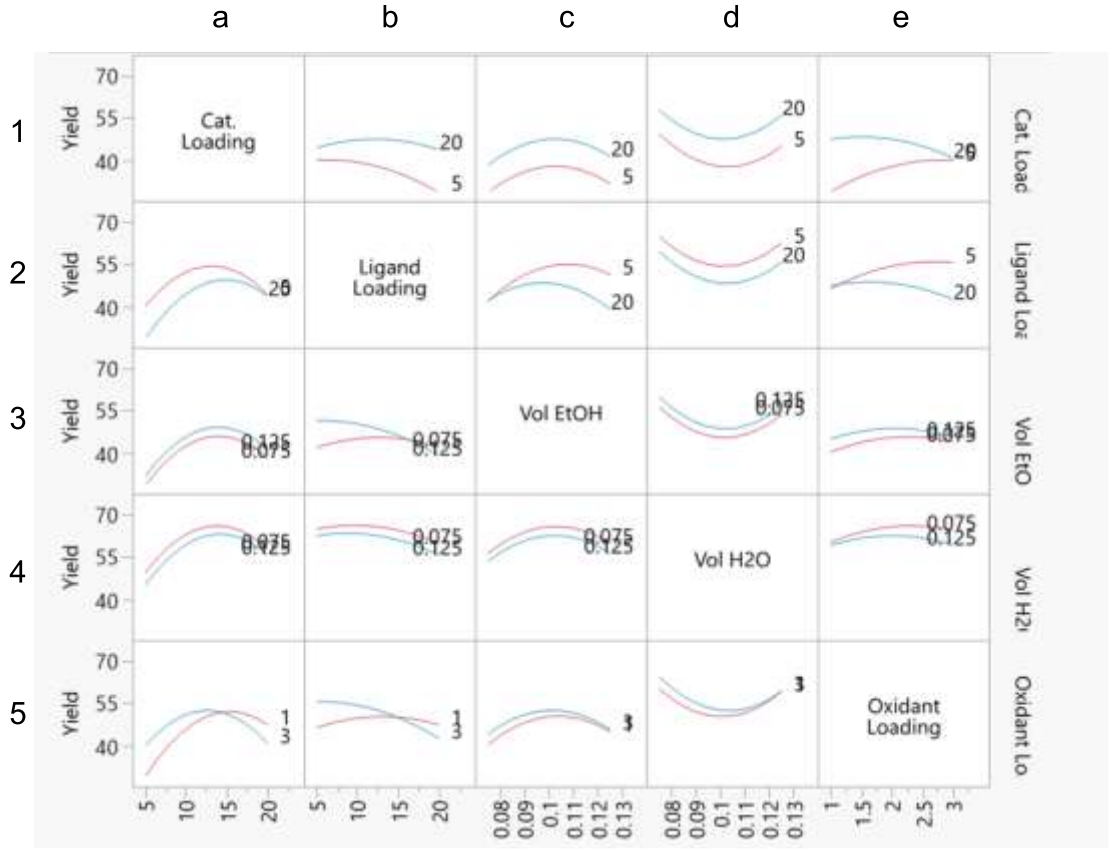


Figure S3 – DoE interaction plots

A key interaction observed from the DoE is that of oxidant and catalyst, at high catalyst loadings a low oxidant loading can be tolerated, so a model validation reaction was performed with the oxidant loading fixed at 1.5 equiv and with the loadings of other variables suggested by the model (Figure S4). Additionally, conditions which were predicted to maximise yield were also tested (Figure S5).

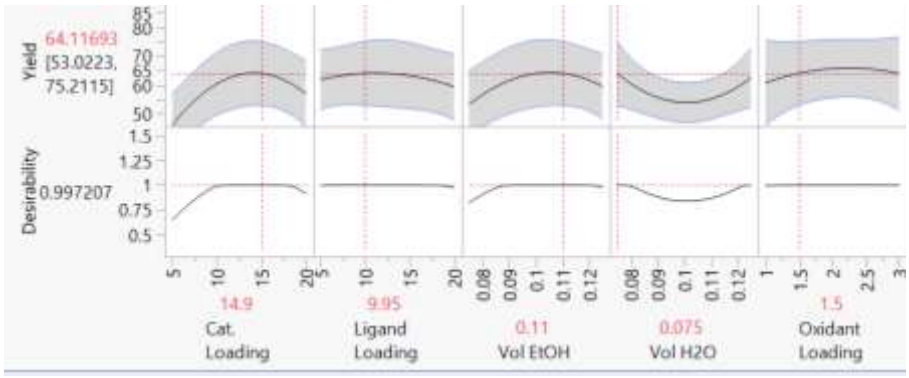


Figure S4 – Conditions predicted by model for maximum yield with 1.5 equiv of oxidant

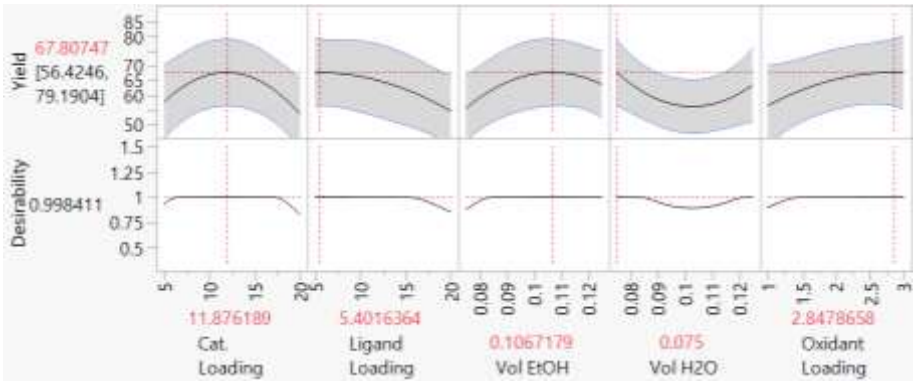
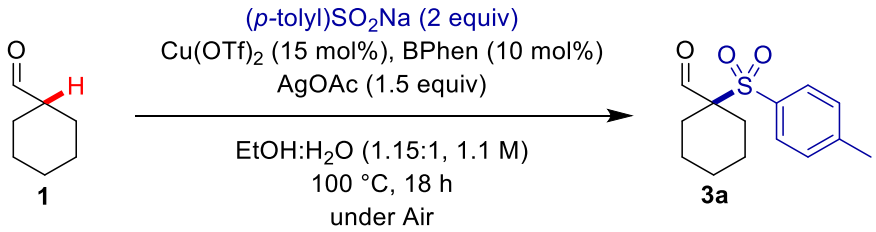


Figure S5 – Conditions predicted by model maximum yield

From the results obtained, the conditions predicted to give the highest yield with 1.5 equivalents of oxidant was in fact the highest overall yield and were chosen as the optimised conditions for this reaction (Table S3). In the absence of copper, ligand and oxidant under silver mediated conditions led to a significant reduction in yield (entries 2–4). When the reaction was performed under argon, a reduction in yield was observed implying oxygen is conducive to reactivity (entry 5). Using silver carbonate, manganese(III) acetate or MnO_2 in place of silver acetate under these conditions led to reduced yields (entries 6–8). In the presence of radical traps, the reaction does not proceed implying the silver mediated conditions proceed *via* a radical mechanism (entries 9,10).

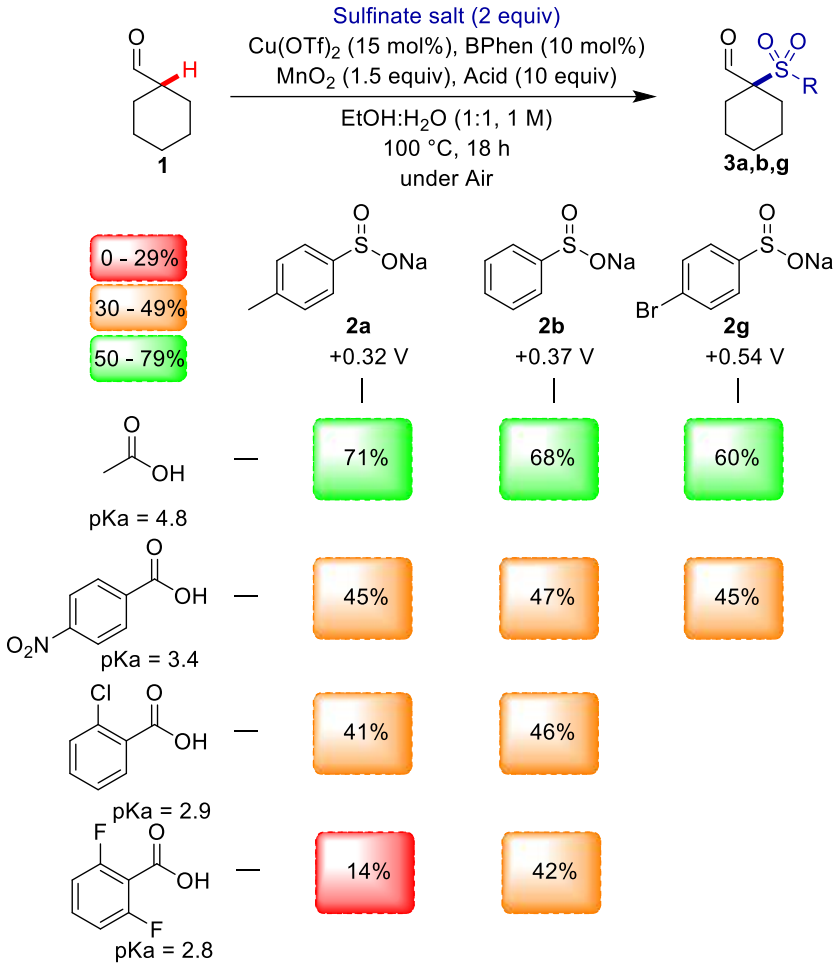


Entry	Change to conditions	Yield 3a (%)[a]
1	None	72
2	No Cu	trace
3	No Ligand	47
4	No Ag	14
5	Under argon	46
6	0.75 equiv Ag_2CO_3 instead of AgOAc	26
7	$Mn(OAc)_3$ instead of AgOAc	27
8	MnO_2 instead of AgOAc	30
9	+ 2 equiv TEMPO	0
10	+ 2 equiv dihydroanthracene	0

Table S3 – Silver mediated α-Sulfonylation control reactions. Reactions performed on 0.2 mmol scale. [a] Yield determined in situ using 1,3,5–trimethoxybenzene as an internal standard.

Investigation Into Acid Tuneable Oxidants

To overcome the limitations of the substrate scope, a stronger oxidant was needed. As MnO_2 was compatible with the reaction conditions and we understood that the electrode potential of MnO_2 could be controlled by changing the pH of the system, we hypothesised that using MnO_2 under acidic conditions could allow it to be tuned to become a stronger oxidant for the reaction (see pourbaix diagram[1]). An array of acids and sulfinates were tested to determine the most effective acid(s) to promote the reaction and identify any options for fine tuning with challenging substrates (Scheme S1b). From the results, it was clear that acetic acid was the most effective, likely due to it rendering the MnO_2 oxidising enough to promote the reaction even with the challenging salts without also enabling substrate/product degradation. Other stronger acids were less effective, and so led to MnO_2 becoming too oxidising. Therefore, acetic acid was selected for the optimised reaction conditions.



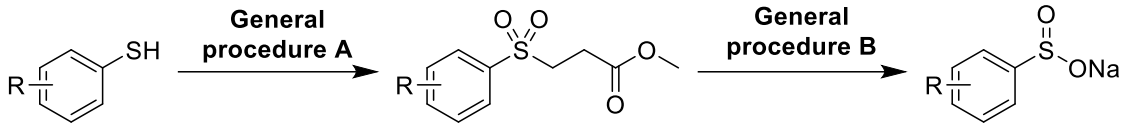
Scheme S1 – Acids and sulfinates of varying pKa and electrode potentials respectively.

The MnO_2 is mostly insoluble at the start of the reaction. As the reaction progresses, the MnO_2 reacts over the 18 h reaction time, seen visually by the disappearance of the black powder.

To investigate the potential reaction of the sulfinate salt directly with MnO_2, 2a was treated with MnO_2 in $EtOH/H_2O$ and separately in $EtOH/H_2O$/AcOH. No products of homocoupling of the sulfinates were observed, but further analysis was prevented by the polar nature of the salts, and the presence of paramagnetic manganese species.

Synthesis of Sulfinate Salts

Sulfinate salts were prepared by two methods. Either using DABSO and an ArLi reagent,[2] or by the scheme shown below (Scheme S2).



Scheme S2 – General scheme for the synthesis of sulfinate salts from thiols

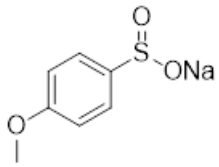
General Procedure A: Synthesis of Sulfones

Thiol (1 equiv) was added to a stirring solution of methyl acrylate (1 equiv) in THF:H_2O (1:1, 0.3 M). Sodium acetate (0.15 equiv) was added and the reaction stirred for 18 h. The reaction was concentrated *in vacuo*, then the product was extracted from the aqueous phase with ethyl acetate, dried over Na_2SO_4, filtered and concentrated *in vacuo.* The residue was dissolved in CH_2Cl_2 (0.05 M) and *m*CPBA (3 equiv) was added at rt and the reaction was stirred until completion, as determined by TLC. The reaction was quenched by the addition of 1 M NaOH then the product was extracted with CH_2Cl_2, dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford the sulfone product.

General Procedure B: Synthesis of Sulfinate Salts

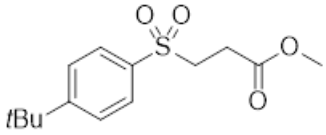
Sodium hydride as a 60% dispersion in mineral oil (1.05 equiv) was added to a stirring solution of sulfone (1 equiv) in THF (0.17 M) at rt. After 30 min, anhydrous MeOH was added dropwise, then the reaction was concentrated *in vacuo*. The precipitate was filtered off and washed with hexane to afford the sulfinic acid sodium salt.

4-Methoxybenzenesulfinic acid sodium salt (2c)



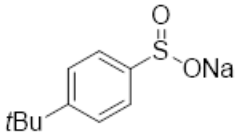
Procedure modified from Odell.[2] *n*BuLi (5.08 mL, 1.58 M in hexanes) was added dropwise to a stirring solution of 4-bromoanisole (1 mL, 8 mmol) in THF (10 mL) at –78 °C then stirred for 1 h at –78 °C. The aryl lithium solution was warmed to 0 °C and then added dropwise to another vessel containing DABSO (480 mg, 2 mmol) at –78 °C which was then stirred for 4 h at –78 °C. The reaction was quenched with the addition of aqueous Na_2CO_3 (10% w/v, 10 mL) then the aqueous phase was washed with Et_2O (3 × 10 mL). The aqueous phase was then acidified by the careful dropwise addition of H_2SO_4 (95%, 3 mL) at 0 °C followed by extraction with Et_2O (3 × 10 mL). The organic phases were basified with Na_2CO_3 (10% w/v, 10 mL) and the organic phase was extracted with a saturated aqueous solution of Na_2CO_3 (10% w/v, 3 × 30 mL) and the aqueous phase was concentrated *in vacuo*. EtOH (20 mL) was added to the crude residue and heated to reflux, then filtered. This was repeated once more with the filtrate with EtOH (20 mL) then concentrated *in vacuo* to afford sulfinic acid sodium salt **2c** as a white powder (218 mg, 28%). m.p. = >300 °C. IR (film)/cm^{-1} 2955, 2840, 1591, 1490, 1244, 1043, 974, 834, 790. ^{1}H NMR (400 MHz, CD_3OD) δ 7.58 (d, *J* = 8.7 Hz, 2 H, 2 × Ar–CH), 6.96 (d, *J* = 8.7 Hz, 2 H, 2 × Ar–CH), 3.81 (s, 3 H, CH_3). ^{13}C NMR (101 MHz, CD_3OD) δ 162.2 (Ar–C_q), 149.2 (Ar–C_q), 126.7 (2 × Ar–CH), 114.7 (2 × Ar–CH), 55.8 (CH_3). Analytical data (IR, ^{1}H NMR, ^{13}C NMR) is in agreement with the reported literature.[3]

Methyl 3-((4-(*tert*-butyl)phenyl)sulfonyl)propanoate (S1)



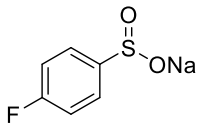
Prepared according to general procedure **A** using 4-*tert*-butylthiophenol (860 μL, 5 mmol) which afforded sulfone **S1** as a white powder (1.52 g, quant). m.p. = 85–88 °C, R_f 0.11 (20% EtOAc:hexane). IR (film)/cm^{-1} 2963, 2870, 1741 (C=O), 1595, 1319, 1252, 1156, 1111, 842, 764, 712. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* =8.6 Hz, 2 H, 2 × Ar–CH), 7.59 (d, *J* =8.6 Hz 2 H, 2 × Ar–CH), 3.65 (s, 3 H, CH_3), 3.43 (t, *J* = 7.7 Hz, 2 H, CH_2), 2.77 (t, *J* = 7.7 Hz, 2 H, CH_2), 1.36 (s, 9 H, $C(CH_3)_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5 (C=O), 158.1 (Ar–C_q), 135.4 (Ar–C_q), 128.1 (2 × Ar–CH), 126.4 (2 × Ar–CH), 52.3 (CH_3) , 51.6 (CH_2), 35.3 ($C_q(CH_3)_3$), 31.1 ($C_q(CH_3)_3$, 27.7 (CH_2). HRMS (TOF-ESI$^+$) m/z calcd. for $C_{14}H_{21}O_4S$ $[M+H]^+$: 285.1161; found: 285.1163.

4-(*tert*-Butyl)benzenesulfinic acid sodium salt (S2)



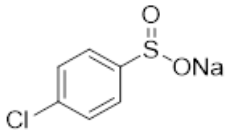
Prepared according to general procedure **B** using sulfone **S1 (**1.32 g, 5 mmol) which afforded sulfinic acid sodium salt **S2** as a white solid (1.12 g, quant). m.p. = >300 °C. IR (film)/cm^{-1} 3638, 3429, 2960, 2866, 1681, 1591, 1080, 1020, 834. ^{1}H NMR (400 MHz, CD_3OD) δ 7.59–7.56 (m, 2 H, 2 × Ar–CH), 7.49–7.46 (m, 2 H, 2 × Ar–CH), 1.33 (s, 9 H, $C(CH_3)$). ^{13}C NMR (101 MHz, CD_3OD) δ 153.9 (Ar–C_q), 153.5 (Ar–C_q), 126.0 (2 × Ar–CH), 124.7 (2 × Ar–CH), 35.3 ($C_q(CH_3)_3$), 31.5 ($C_q(CH_3)_3$). Analytical data (IR, ^{1}H NMR, ^{13}C NMR) is in agreement with the reported literature.[3]

4-Fluorobenzenesulfinic acid sodium salt (S3)



4-Fluorothiophenol (532 μL, 5 mmol), methyl acrylate (450 μL, 5 mmol), THF:H_2O (1:1, 0.3 M) and sodium acetate (61 mg, 0.75 mmol) were added sequentially to the reactionthen stirred at rt overnight. The reaction was concentrated *in vacuo*, then the product was extracted from the aqueous phase with ethyl acetate, dried over Na_2SO_4, filtered and concentrated *in vacuo.* The residue was dissolved in CH_2Cl_2 (100 mL) and *m*CPBA (2.9 g, 12.5 mmol) was added at rt and the reaction was stirred until completion, as determined by TLC. The reaction was quenched by the addition of 1 M NaOH then the product was extracted with CH_2Cl_2, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was dissolved in dry MeOH and THF (1:1, 0.5 M) under an atmosphere of argon, and sodium hydroxide (168 mg, 4.2 mmol) was added at 0 °C. The precipitate was filtered off and washed with hexane which afforded sulfinic acid sodium salt **S3** as a white powder (390 mg, 43%). m.p. = >300 °C. IR (film)/cm^{-1} 3444, 3280, 1587, 1487, 1237, 1151, 1077, 1017, 980, 827, 712. ^{1}H NMR (400 MHz, MeOD) δ 7.70–7.65 (m, 2 H, 2 × Ar–CH), 7.17–7.12 (m, 2 H, 2 × Ar–CH). ^{13}C NMR (101 MHz, MeOD) δ 164.9 (d, $^1J_{C-F}$ = 246.2 Hz, Ar–C_q), 153.5 (Ar–C_q), 127.5 (d, $^3J_{C-F}$ = 8.6 Hz, 2 × Ar–CH), 116.1 (d, $^2J_{C-F}$ = 22.1 Hz, 2 × Ar–CH). ^{19}F NMR (377 MHz, MeOD) δ -114.69. Analytical data (IR, ^{1}H NMR,^{13}C NMR and ^{19}F NMR) is in agreement with the reported literature.[3]

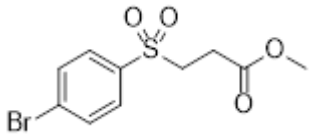
4-Chlorobenzenesulfinic acid sodium salt (S4)



4-Chlorothiophenol (720 mg, 5 mmol), methyl acrylate (450 μL, 5 mmol), THF:H_2O (1:1, 0.3 M) and sodium acetate (61 mg, 0.75 mmol) were combined sequentially then stirred at rt overnight. The reaction was concentrated *in vacuo*, then the product was extracted from the aqueous phase with ethyl acetate, dried over Na_2SO_4, filtered and concentrated *in vacuo.* The residue was dissolved in CH_2Cl_2 (100 mL) and *m*CPBA (2.9 g, 12.5 mmol) was added at rt and the reaction was stirred until completion, as determined by TLC. The reaction was quenched by the addition of 1 M NaOH then the product was extracted with CH_2Cl_2, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was dissolved in dry CH_2Cl_2 (45 mL) under an atmosphere of argon, and sodium hydroxide (5 M in MeOH, 948 μL) was added at 0 °C. The precipitate was filtered off and washed with hexane which afforded sulfinic acid sodium salt **S4** as a white powder (900 mg, 91%). m.p. = >300 °C. IR (film)/cm^{-1} 3448, 3269, 2974, 1572, 1467, 1077, 1047, 977, 828, 738, 712. ^{1}H NMR (400 MHz, MeOD) δ 7.64–7.61 (m, 2 H, 2 × Ar–CH), 7.44–7.40 (m, 2 H, 2 × Ar–CH). ^{13}C NMR (101 MHz, MeOD) δ 156.2 (Ar–C_q), 136.3

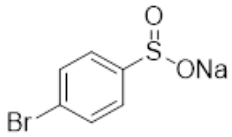
(Ar–C_q), 129.5 (2 × Ar–CH), 127.0 (2 × Ar–CH). Analytical data (IR, ^{1}H NMR and ^{13}C NMR) is in agreement with the reported literature.[3]

Methyl 3-((4-bromophenyl)sulfonyl)propanoate (S5)



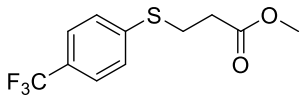
Prepared according to general procedure **A** using *p*-bromothiophenol (0.95 g, 5 mmol) which afforded sulfone **S5** as a white solid (1.52 g, 99%). m.p. = 65–69 °C. R_f 0.11 (20% EtOAc:hexane). IR (film)/cm^{-1} 2996, 3097, 2956, 1729 (C=O), 1573, 1248, 1162, 987, 798, 627. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.8 Hz, 2 H, 2 × Ar–CH), 7.74 (d, *J* = 8.8 Hz, 2 H, 2 × Ar–CH), 3.66 (s, 3 H, CH_3), 3.48–3.39 (t, *J* = 7.7 Hz, 2 H, CH_2), 2.77 (t, *J* = 7.7 Hz, 2 H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3 (C=O), 137.5 (Ar–C_q), 132.8 (2 × Ar–CH), 129.7 (2 × Ar–CH), 129.5 (Ar–C_q), 52.4 (CH_3), 51.5 (CH_2), 27.5 (CH_2). HRMS (FTMS + p APCI) m/z calcd. for $C_{10}H_{12}O_4SBr$ $[M+H]^+$: 306.9634; found: 306.9639.

4-Bromobenzenesulfinic acid sodium salt (2g)



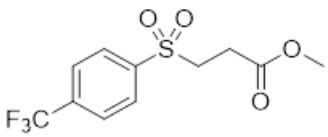
Prepared according to general procedure **B** using sulfone **S5** (1.43 g, 5 mmol) which afforded sulfinic acid sodium salt **2g** as a white powder (993 mg, 82%). m.p. = >300 °C. IR (film)/cm^{-1} 3478, 3280, 2568, 2438, 1569, 1468, 998, 927. ^{1}H NMR (400 MHz, CD_3OD) δ 7.60–7.55 (m, 4 H, 4 × Ar–CH).^{13}C NMR (101 MHz, CD_3OD) δ 156.6 (Ar–C_q), 132.5 (2 × Ar–CH), 127.3 (2 × Ar–CH), 124.5 (Ar–C_q). Analytical data (IR, ^{1}H NMR, ^{13}C NMR) is in agreement with the reported literature.[3]

Methyl 3-((4-trifluoromethylphenyl)thio)propanoate (S6)



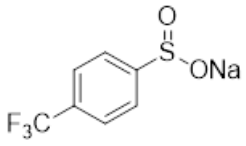
4-(Trifluoromethyl)thiophenol (1.4 mL, 10 mmol) was added to a stirring solution of methyl acrylate (0.9 mL, 10 mmol) in THF (16.7 mL) and water (16.7 mL). Sodium acetate (123 mg, 1.5 mmol) was added and the reaction stirred for 18 h. The reaction was concentrated *in vacuo*, then the product was extracted from the aqueous phase with ethyl acetate (3 × 20 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford sulfide **S6** as a white solid (2.66 g, quant.). m.p. = 74–77 °C. R_f 0.50 (40% EtOAc:hexane). IR (film)/cm^{-1} 2922, 2960, 1730 (C=O), 1603, 1438, 1323, 1252, 1163, 1096, 1062, 832, 674. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–7.53 (m, 2 H, 2 × Ar–CH), 7.40 (d, *J* = 7.9 Hz, 2 H, 2 × Ar–CH), 3.71 (s, 3 H, CH_3), 3.25 (t, *J* = 7.4 Hz, 2 H, CH_2), 2.68 (t, *J* = 7.4 Hz, 2 H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8 (C=O), 140.9 (Ar–C_q), 128.1 (4 × Ar–CH), 125.8 (q, $^2J_{C–F}$ = 3.2 Hz, Ar–C_q), 125.3 (q, $^1J_{C–F}$ = 170 Hz, CF_3), 51.9 (CH_3), 33.7 (CH_2), 27.7 (CH_2). ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.48 (CF_3). HRMS (TOF-ESI$^-$) m/z calcd. for $C_{11}H_{10}O_2SF_3$ $[M-H]^-$: 263.0354; found: 263.0347.

Methyl 3-((4-(trifluoromethyl)phenyl)sulfonyl)propanoate (S7)



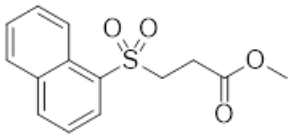
*m*CPBA (5.18 g, 30 mmol) was added to a stirring solution of sulfide **S6** (2.63 g, 10 mmol) in CH_2Cl_2 (200 mL) at rt. The reaction was quenched by the addition of 1M NaOH (100 mL) and the product was extracted with CH_2Cl_2 (3 × 100 mL), dried over Na_2SO_4, filtered then concentrated *in vacuo* which afforded sulfone **S7** as a colourless oil (2.89 g, 98%). R_f 0.11 (20% EtOAc:hexane). IR (film)/cm^{-1} 3001, 1960, 1737 (C=O), 1402, 1323, 1263, 1151, 1122, 1062, 846, 775, 734. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, $^3J_{H–H}$ = 8.1 Hz, 2 H, 2 × Ar–CH), 7.87 (d, $^3J_{H–H}$ = 8.1 Hz, 2 H, 2 × Ar–CH), 3.66 (s, 3 H, CH_3), 3.48 (t, *J* = 7.6 Hz, 2 H, CH_2), 2.80 (t, *J* = 7.6 Hz, 2 H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1 (C=O), 142.1 (Ar–C_q), 128.9 (4 × Ar–CH), 126.6 (q, $^2J_{C–F}$ = 3.8 Hz, Ar–C_q), 52.4 (CH_3), 51.5 (CH_2), 27.4 (CH_2). ^{19}F NMR (377 MHz, $CDCl_3$) δ –63.26. Analytical data (IR, ^{1}H NMR, ^{13}C NMR) is in agreement with the reported literature.[4] It was not possible to observe the quaternary *C*F_3 signal due to C–F coupling.

4-(Trifluoromethyl)benzenesulfinic acid sodium salt (2h)



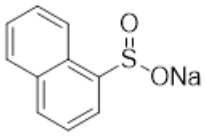
Synthesised according to general procedure **B** using sulfone **S7** (2.8 g, 9.45 mmol) which afforded sulfinic acid sodium salt **2h** as an off white solid (2.28 g, quant). m.p. = >300 °C. IR (film)/cm^{-1} 3396, 1581, 1323, 1193, 1044, 972, 741, 693. ^{1}H NMR (400 MHz, CD_3OD) δ 7.84 (d, *J* = 8.1 Hz, 2 H, 2 × Ar–CH), 7.73 (d, *J* = 8.1 Hz, 2 H, 2 × Ar–CH). ^{13}C NMR (101 MHz, CD_3OD) δ 161.4 (Ar–C_q), 132.3 (q, $^{2}J_{C-F}$ = 32.1 Hz, Ar–C_q), 126.4 (q, $^{3}J_{C-F}$ = 3.9 Hz, 2 × Ar–CH), 126.0 (2 × Ar–CH), 125.5 (q, $^{1}J_{C-F}$ = 271.4 Hz, CF_3) ^{19}F NMR (377 MHz, CD_3OD) δ -63.92. analytical data (IR, ^{1}H NMR, ^{13}C NMR) is in agreement with the reported literature.[3] Contains 8% of an inseparable impurity.

Methyl 3-(naphthalen-1-ylsulfonyl)propanoate (S8)



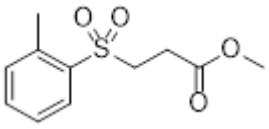
Prepared according to general procedure **A** using 1-napthalenethiol (690 μL, 5 mmol) which afforded sulfone **S8** as a colourless oil (1.43 g, quant). m.p. = 95–99 °C. R_f 0.11 (20% EtOAc:hexane). IR (film)/cm^{-1} 3064, 2983, 2937, 1733 (C=O), 1506, 1438, 1312, 1252, 1156, 1122, 1070, 9915, 772. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (dq, *J* = 8.7, 0.9 Hz, 1 H, Ar–CH), 8.31 (dd, *J* = 7.3, 1.3 Hz, 1 H, Ar–CH), 8.17 (dt, *J* = 8.4, 1.3 Hz, 1 H, Ar–CH), 8.00 (ddt, *J* = 8.1, 1.3, 0.6 Hz, 1 H, Ar–CH), 7.75 (ddd, *J* = 8.7, 6.9, 1.4 Hz, 1 H, Ar–CH), 7.68–7.61 (m, 2 H, 2 × Ar–CH), 3.66–3.62 (t, *J* = 7.6 Hz, 2 H, CH_2), 3.59 (s, 3 H, CH_3), 2.82–2.73 (t, *J* = 7.6 Hz, 2 H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4 (C=O), 135.5 (Ar–CH), 134.2 (Ar–C_q), 133.4 (Ar–C_q), 130.9 (Ar–CH), 129.3 (Ar–CH), 129.0 (Ar–CH), 128.9 (Ar–C_q), 127.2 (Ar–CH), 124.4 (Ar–CH), 124.0 (Ar–CH), 52.2 (CH_3), 51.0 (CH_2), 27.6 (CH_2). Analytical data (IR, ^{1}H NMR, ^{13}C NMR) is in agreement with the reported literature.

Naphthalene-1-sulfinic acid sodium salt (S9)



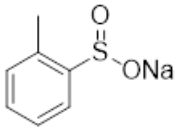
Prepared according to general procedure **B** using sulfone **S8 (**1.25 g, 4.5 mmol). The crude sulfinic acid sodium salt was dissolved in hot EtOH, then crystallised by the addition of hexane (20 ml). the precipitate was filtered off and washed with hexane to give sulfinic acid sodium salt **S9** as a white solid (408 mg, 43%). m.p. = >300 °C. IR (film)/cm^{-1} 3386, 3049, 1502, 1559, 1398, 1141, 1029, 951, 798, 772, 663. ^{1}H NMR (400 MHz, CD_3OD) δ 8.71 (ddt, *J* = 8.3, 1.5, 0.8 Hz, 1 H, Ar–CH), 8.02 (dd, *J* = 7.1, 1.3 Hz, 1 H, Ar–CH), 7.92–7.88 (m, 2 H, 2 × Ar–CH), 7.57–7.48 (m, 3 H, 3 × Ar–CH). ^{13}C NMR (101 MHz, CD_3OD) δ 152.0 (Ar–C_q), 135.4 (Ar–C_q), 131.4 (Ar–C_q), 130.9 (Ar–CH), 129.4 (Ar–CH), 127.0 (Ar–CH), 126.9 (Ar–CH), 126.3 (Ar–CH), 124.8 (Ar–CH), 121.5 (Ar–CH). Analytical data (IR, ^{1}H NMR, ^{13}C NMR) is in agreement with the reported literature.[5]

Methyl 3-(*o*-tolylsulfonyl)propanoate (S10)



Prepared according to general procedure **A** using 2-methylbenzenethiol (860 μL, 5 mmol) which afforded sulfone **S10** as a colourless oil (1.15 g, 95%). R_f 0.05 (20% EtOAc:hexane). IR (film)/cm^{-1} 3064, 2952, 1737 (C=O), 1439, 1364, 1312, 1248, 1223, 1148, 1125, 1058, 976, 730. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 7.7, 1.5 Hz, 1 H, Ar–CH), 7.54 (td, *J* = 7.7, 1.5 Hz, 1 H, Ar–CH), 7.41–7.35 (m, 2 H, 2 × Ar–CH), 3.62 (s, 3 H, OCH_3), 3.47 (t, *J* = 7.6 Hz, 2 H, CH_2), 2.77 (t, *J* = 7.6 Hz, 2 H, CH_2), 2.72 (s, 3 H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5 (C=O), 138.3 (Ar–C_q), 136.4 (Ar–C_q), 134.0 (Ar–CH), 132.9 (Ar–CH), 130.4 (Ar–CH), 126.6 (Ar–CH), 52.3 (OCH_3), 50.4 (CH_3), 27.4 (CH_2), 20.3 (CH_2). HRMS (TOF-ESI$^+$) m/z calcd. for $C_{14}H_{17}NO_4NaS$ [M+MeCN+Na]$^+$: 306.0776; found: 306.0768.

2-Methylbenzenesulfinic acid sodium salt (S11)



Prepared according to general procedure **B** using sulfone **S10 (**872 mg, 4.5 mmol). The crude sulfinic acid sodium salt was dissolved in hot EtOH, then precipitated by the addition of hexane (20 ml). The precipitate was filtered off and washed with hexane to give sulfinic acid

sodium salt **S11** as a white solid (281 mg, 35%). m.p. = >300 °C. IR (film)/cm^{-1} 3470, 3392, 3299, 1674, 999, 965, 752, 862. ^{1}H NMR (400 MHz, CD_3OD) δ 7.81 (dd, *J* = 7.1, 2.1 Hz, 1 H, Ar–CH), 7.26 (m, 2 H, 2 × Ar–CH), 7.14 (dd, *J* = 6.5, 2.1 Hz, 1 H, Ar–CH), 2.57 (s, 3 H, CH_3). ^{13}C NMR (101 MHz, CD_3OD) δ 154.0 (Ar–C_q), 136.7 (Ar–C_q), 131.5 (Ar–CH), 130.4 (Ar–CH), 127.0 (Ar–CH), 122.9 (Ar–CH), 18.4 (CH_3). Analytical data (IR, ^{1}H NMR, ^{13}C NMR) is in agreement with the reported literature.[3]

Manganese(IV) Oxide Mediated α-Sulfonylation

General Procedure C: Using MnO_2

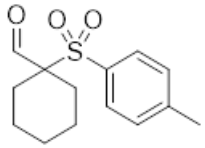
Manganese(IV) oxide (1.5 equiv), copper(II) triflate (15 mol%), bathophenanthroline (10 mol%), sulfinic acid sodium salt (2 equiv), aldehyde (1 equiv), H_2O:EtOH:AcOH (1:1:1, 0.67 M) were added sequentially to a microwave vial under air, sealed and submerged in an oil bath preheated to 100 °C for 18 h. The reaction was allowed to cool to room temperature, diluted with EtOAc, filtered through silica eluting with EtOAc then concentrated *in vacuo*. The crude product was purified by flash column chromatography.

General Procedure D: Using AgOAc

Silver acetate (1.5 equiv), copper(II) triflate (15 mol%), bathophenanthroline (10 mol%), sulfinic acid sodium salt (2 equiv), aldehyde (1 equiv), H_2O:EtOH (1.15:1, 1.1 M) were added sequentially to a microwave vial under air, sealed and submerged in an oil bath preheated to 100 °C for 18 h. The reaction was allowed to cool to room temperature, diluted with EtOAc, filtered through silica eluting with EtOAc then concentrated *in vacuo*. The crude product was purified by flash column chromatography.

Reaction Scope Varying the Sulfinate Salts

1-(4-Methylbenzene-1-sulfonyl)cyclohexane-1-carbaldehyde (3a)



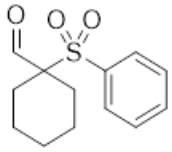
Prepared according to general procedure **C** (MnO_2) using cyclohexane carboxaldehyde **1** (48 μL, 0.4 mmol) and 4-methylbenzenesulfinic acid sodium salt **2a** (142 mg, 0.8 mmol). Purification by flash column chromatography (5–20% Et_2O:pentane) afforded *α*-sulfonyl aldehyde **3a** as a yellow solid (83.3 mg, 78%). m.p. = 77–78 °C. R_f 0.09 (20% Et_2O:pentane). IR (film)/cm^{-1} 2937, 2859, 1722 (C=O), 1595, 1454, 1316, 1144, 1088, 816. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1 H, CHO), 7.59 (d, *J* = 8.1 Hz, 2 H, 2 × Ar–CH), 7.34 (d, *J* = 8.1 Hz, 2 H, 2 × Ar–CH), 2.45 (s, 3 H, CH_3), 2.27 (d, *J* = 13.3 Hz, 2 H, 2 × C_qC*H*H), 1.91 (ddd, *J* = 13.3, 13.3, 3.3 Hz, 2 H, 2 × C_qCH*H*), 1.80–1.75 (m, 2 H, 2 × $C_q$$CH_2$C*H*H), 1.66–1.62 (m, 1 H, $C_q$$CH_2$$CH_2$C*H*H), 1.22–1.07 (m, 3 H, 2 × $C_q$$CH_2$CH*H* + $C_q$$CH_2$$CH_2$CH*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8 (CHO), 145.5 (Ar–C_q), 132.0 (Ar–C_q), 129.9 (2 × Ar–CH), 129.6 (2 × Ar–CH), 74.0 (C_q), 25.2 (2 × CH_2), 24.3 (CH_2), 21.9 (2 × CH_2), 21.7 (CH_3). HRMS (TOF-ESI$^+$) m/z calcd. For $C_{14}H_{19}O_3S$ $[M+H]^+$: 267.1055; found: 267.1060.

Prepared on 2 mmol scale with manganese conditions to afford *α*-sulfonyl aldehyde **3a** (438 mg, 82%).

For procedure on 6 mmol scale, see section on gram scale synthesis.

Also prepared using silver mediated conditions according to general procedure D which afforded α-sulfonyl aldehyde **3a** (73.1 mg, 69%).

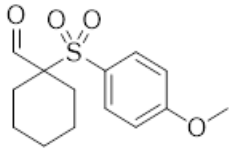
1-(Phenylsulfonyl)cyclohexane-1-carbaldehyde (3b)



Prepared according to general procedure **C** using cyclohexane carboxaldehyde **1** (48 μL, 0.4 mmol) and benzenesulfinic acid sodium salt **2b** (131 mg, 0.8 mmol). Purification by flash column chromatography (5–20% Et_2O:pentane) afforded *α*-sulfonyl aldehyde **3b** as a colourless oil (78.4 mg, 78% yield). R_f 0.21 (20% Et_2O:pentane). IR (film)/cm^{-1} 2937, 2858, 1722 (C=O), 1446, 1308, 1144, 1088, 734, 690. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (s, 1 H, CHO), 7.74–7.66 (m, 3 H, 3 × Ar–CH), 7.57–7.54 (t, *J* = 7.7 Hz, 2 H, 2 × Ar–CH), 2.27 (d, *J* = 13.0 Hz, 2 H, 2 × C_qC*H*H), 1.92 (ddd, *J* = 13.0, 13.0, 3.8 Hz, 2 H, 2 × C_qCH*H*), 1.81–1.75 (m, 2 H, 2 × $C_q$$CH_2$C*H*H), 1.66–1.63 (m, 1 H, $C_q$$CH_2$$CH_2$C*H*H), 1.19–1.11 (m, 3 H, 2 × $C_q$$CH_2$CH*H* + $C_q$$CH_2$$CH_2$CH*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6 (CHO), 135.0 (Ph–CH), 134.3 (Ph–CH), 129.9 (2 × Ph–CH), 129.0 (2 × Ph–CH), 74.0 (C_q), 25.1 (2 × CH_2), 24.3 (CH_2), 21.9 (2 × CH_2). HRMS (FTMS + p APCI) m/z calcd. For $C_{13}H_{17}O_3S$ $[M+H]^+$: 253.0893; found: 253.0890.

Also prepared using silver mediated conditions according to general procedure **D** which afforded *α*-sulfonyl aldehyde **3b** (54.2 mg, 54%).

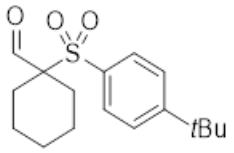
1-((4-Methoxyphenyl)sulfonyl)cyclohexane-1-carbaldehyde (3c)



Prepared according to general procedure **C** using cyclohexane carboxaldehyde **1** (48 μL, 0.4 mmol) and 4-methoxybenzenesulfinic acid sodium salt **2c** (155 mg, 0.8 mmol). Purification by flash column chromatography (20% Et_2O:hexane) afforded *α*-sulfonyl aldehyde **3c** as a colourless oil (80.5 mg, 71% yield). R_f 0.14 (20% Et_2O:hexane). IR (film)/cm^{-1} 2937, 2855, 1722 (C=O), 1595, 1498, 1315, 1263, 1140, 1088, 1021, 834, 805, 667. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (s, 1 H, CHO), 7.63 (d, *J* = 9.0 Hz, 2 H, 2 × Ar–CH), 6.99 (d, *J* = 9.0 Hz, 2 H, 2 × Ar–CH), 3.88 (s, 3 H, CH_3), 2.27 (ddd, *J* = 13.4, 2.9, 1.4 Hz, 2 H, 2 × C_qC*H*H), 1.89 (ddd, *J* = 13.4, 13.4, 3.7 Hz, 2 H, 2 × C_qCH*H*), 1.82–1.72 (m, 2 H, 2 × $C_q$$CH_2$C*H*H), 1.68–1.59 (m, 1 H, $C_q$$CH_2$$CH_2$C*H*H), 1.23–1.07 (m, 3 H, 2 × $C_q$$CH_2$CH*H* + $C_q$$CH_2$$CH_2$CH*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.0 (CHO), 164.3 (Ar–C_q), 132.1 (2 × Ar–CH), 126.3 (Ar–C_q), 114.2 (2 × Ar–CH), 74.1 (C_q), 55.7 (CH_3), 25.3 (2 × CH_2), 24.4 (CH_2), 22.0 (2 × CH_2). HRMS (FTMS + p APCI) m/z calcd. For $C_{14}H_{19}O_4S$ $[M+H]^+$: 283.0999; found: 283.0995.

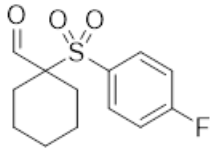
Also prepared using silver mediated conditions according to general procedure **D** which afforded *α*-sulfonyl aldehyde **3c** (48.1 mg, 43%).

1-((4-(*tert*-Butyl)phenyl)sulfonyl)cyclohexane-1-carbaldehyde (3d)



Prepared according to general procedure **C** using cyclohexane carboxaldehyde **1** (48 μL, 0.4 mmol) and 4-(*tert*-butyl)benzenesulfinic acid sodium salt **S2** (176 mg, 0.8 mmol). Purification by flash column chromatography (10% Et_2O:pentane) afforded *α*-sulfonyl aldehyde **3d** as a white solid (82.2 mg, 67%). R_f 0.52 (20% Et_2O:pent). m.p. = 98–101 °C. IR (film)/cm^{-1} 2941, 2863, 1722 (C=O), 1595, 1454, 1312, 1148, 1111, 1085, 839, 733. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1 H, CHO), 7.63 (d, *J* = 8.7 Hz, 2 H, 2 × Ar–CH), 7.54 (d, *J* = 8.7 Hz, 2 H, 2 × Ar–CH), 2.28 (d, *J* = 12.1 Hz, 2 H, 2 × C_qC*H*H), 1.92 (ddd, *J* = 12.7, 12.7, 3.8 Hz, 2 H, 2 × C_qCH*H*), 1.80–1.75 (m, 2 H, 2 × $C_q$$CH_2$C*H*H), 1.66–1.62 (m, 1 H, $C_q$$CH_2$$CH_2$C*H*H), 1.34 (s, 9 H, $C(CH_3)_3$), 1.19–1.12 (m, 3 H, 2 × $C_q$$CH_2$CH*H* + $C_q$$CH_2$$CH_2$CH*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8 (CHO), 158.3 (Ar–C_q), 132.0 (Ar–C_q), 129.7 (2 × Ar–CH), 126.0 (2 × Ar–CH), 73.9 (C_q), 35.3 (2 × $C_q$$C(CH_3)_3$), 31.0 (3 × CH_3), 25.1 (2 × CH_2), 24.3 (CH_2), 21.9 (2 × CH_2). HRMS (TOF–ESI$^+$) m/z calcd. For $C_{17}H_{25}O_3S$ $[M+H]^+$: 309.1524; found 309.1528.

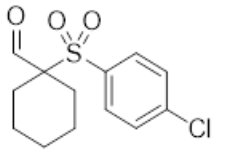
1-((4-Fluorophenyl)sulfonyl)cyclohexane-1-carbaldehyde (3e)



Prepared according to general procedure **C** using cyclohexane carboxaldehyde **1** (48 μL, 0.4 mmol) and 4-fluorobenzenesulfinic acid sodium salt **S3** (146 mg, 0.8 mmol). Purification by flash column chromatography (10–20% Et_2O:pentane) afforded *α*-sulfonyl aldehyde **3e** as a white solid (67.2 mg, 62%). R_f 0.34 (20% Et_2O:pentane).

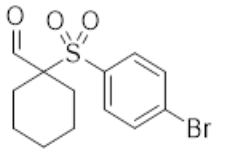
m.p. = 106–107 °C. IR (film)/cm^{-1} 2941, 2859, 1722 (C=O), 1592, 1320, 1144, 1088, 842, 663. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1 H, CHO), 7.74–7.71 (m, 2 H, 2 × Ar–CH), 7.25–7.21 (m, 2 H, 2 × Ar–CH), 2.27 (ddd, *J* = 13.5, 2.9, 1.5 Hz, 2 H, 2 × C_qC*H*H), 1.91–1.88 (m, 2 H, 2 × C_qCH_2C*H*H), 1.81–1.76 (m, 2 H, 2 × C_qCH_2C*H*H), 1.64–1.63 (m, 1 H, $C_qCH_2CH_2$C*H*H), 1.19–1.12 (m, 3 H, 2 × C_qCH_2CH*H* + $C_qCH_2CH_2$CH*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6 (CHO), 166.2 (d, $^{1}J_{C–F}$ = 257.7 Hz, F–Ar–C_q), 132.8 (d, $^{3}J_{C–F}$ = 9.7 Hz, 2 × Ar–CH), 130.9 (d, $^{4}J_{C–F}$ = 3.3 Hz, Ar–C_q), 116.4 (d, $^{2}J_{C–F}$ = 22.7 Hz, 2 × Ar–CH), 74.0 (C_q), 25.2 (2 × CH_2), 24.3 (CH_2), 21.9 (2 × CH_2). ^{19}F NMR (377 MHz, $CDCl_3$) δ -102.14. HRMS (TOF–ESI$^+$) m/z calcd. For $C_{13}H_{16}O_3SF$ $[M+H]^+$: 271.0804; found: 271.0802.

1-((4-Chlorophenyl)sulfonyl)cyclohexane-1-carbaldehyde (3f)



Prepared according to general procedure **C** using cyclohexane carboxaldehyde **1** (48 μL, 0.4 mmol) and 4-chlorobenzenesulfinic acid sodium salt **S4** (158 mg, 0.8 mmol). Purification by flash column chromatography (10–20% Et_2O:pentane) afforded α-sulfonyl aldehyde **3f** as a white solid (73 mg, 64%). R_f 0.34 (20% Et_2O:pentane). m.p. = 85–87 °C. IR (film)/cm^{-1} 2929, 2862, 1722 (C=O), 1580, 1472, 1312, 1148, 1048, 734. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1 H, CHO), 7.64 (d, *J* = 8.8 Hz, 2 H, 2 × Ar–CH), 7.53 (d, *J* = 8.8 Hz, 2 H, 2 × Ar–CH), 2.27 (d, *J* = 13.0 Hz, 2 H, 2 × C_qC*H*H), 1.91 (ddd, *J* = 13.0, 12.3, 3.8 Hz, 2 H, 2 × C_qCH_2C*H*H), 1.82–1.76 (m, 2 H, 2 × C_qCH_2CH*H*)), 1.67–1.64 (m, 1 H, $C_qCH_2CH_2$C*H*H), 1.29–1.11 (m, 3 H, 2 × C_qCH_2CH*H* + $C_qCH_2CH_2$CH*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6 (CHO), 141.4 (Ar–C_q), 133.3 (Ar–C_q), 131.4 (2 × Ar–CH), 129.3 (2 × Ar–CH), 74.1 (C_q), 25.2 (2 × CH_2), 24.3 (CH_2), 21.9 (2 × CH_2). HRMS (TOF–ESI$^-$) m/z calcd. For $C_{13}H_{14}O_3SCl$ $[M-H]^-$: 285.0352; found: 285.0347.

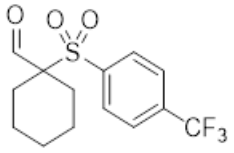
1-((4-Bromophenyl)sulfonyl)cyclohexane-1-carbaldehyde (3g)



Prepared according to general procedure **C** using cyclohexane carboxaldehyde **1** (48 μL, 0.4 mmol) and 4-bromobenzenesulfinic acid sodium salt **2g** (194 mg, 0.8 mmol). Purification by flash column chromatography (20% Et_2O:pentane) afforded α-sulfonyl aldehyde **3g** as a colourless oil (79.1 mg, 60% yield). R_f 0.38 (10% Et_2O:pentane). IR (film)/cm^{-1} 2941, 2859, 1722 (C=O), 1573, 1454, 1390, 1315, 1148, 1070, 1010, 958, 783, 746. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1 H, CHO), 7.70 (d, *J* = 8.7 Hz, 2 H, 2 × Ar–CH), 7.56 (d, *J* = 8.7 Hz, 2 H, 2 × Ar–CH), 2.27 (d, *J* = 13.0, Hz, 2 H, 2 × C_qC*H*H), 1.91 (ddd, *J* = 13.0, 13.0, 3.6 Hz, 2 H, 2 × C_qCH*H*), 1.81–1.78 (m, 2 H, 2 × C_qCH_2C*H*H), 1.78–1.64 (m, 1 H, $C_qCH_2CH_2$C*H*H), 1.20–1.12 (m, 3 H, 2 × C_qCH_2CH*H* + $C_qCH_2CH_2$CH*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.5 (CHO), 133.8 (Ar–C_q), 132.3 (2 × Ar–CH), 131.4 (2 × Ar–CH), 130.0 (Ar–C_q), 74.1 (C_q), 25.1 (2 × CH_2), 24.3 (CH_2), 21.9 (2 × CH_2). HRMS (TOF–ESI$^-$) m/z calcd. For $C_{13}H_{14}O_3SBr$ $[M-H]^-$: 328.9854; found: 328.9847.

Also prepared using silver mediated conditions according to general procedure **D** which afforded α-sulfonyl aldehyde **3g** (42 mg, 32%).

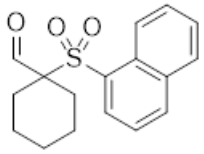
1-((4-(Trifluoromethyl)phenyl)sulfonyl)cyclohexane-1-carbaldehyde (3h)



Prepared according to general procedure **C** using cyclohexane carboxaldehyde **1** (48 μL, 0.4 mmol) and 4-(trifluoromethyl)benzenesulfinic acid sodium salt **2h** (186 mg, 0.8 mmol). Purification by flash column chromatography (10% EtOAc:pentane) afforded α-sulfonyl aldehyde **3h** as a colourless oil (79.3 mg, 62% yield). R_f 0.37 (10% EtOAc:pent). IR (film)/cm^{-1} 2945, 2863, 1722 (C=O), 1405, 1319, 1133, 1110, 1062, 1017, 846, 708. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (s, 1 H, CHO), 7.84 (d, *J* = 4.1 Hz, 4 H, 4 × Ar–CH), 2.27 (d, *J* = 13.0 Hz, 2 H, 2 × C_qC*H*H), 1.94 (ddd, *J* = 13.0, 13.0, 4.3 Hz, 2 H, 2 × C_qCH*H*), 1.83–1.79 (m, 2 H, 2 × C_qCH_2C*H*H), 1.66–1.65 (m, 1 H, $C_qCH_2CH_2$C*H*H), 1.21–1.13 (m, 3 H, 2 × C_qCH_2CH*H* + $C_qCH_2CH_2$CH*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.4 (CHO), 138.5 (Ar–C_q), 136.0 (q, $^{2}J_{C-F}$ = 33.4 Hz, Ar–C_q), 130.7 (2 × Ar–CH), 126.1 (q, $^{4}J_{C-F}$ = 3.7 Hz, 2 × Ar–CH), 125.5 (q, $^{1}J_{C-F}$ = 227 Hz, CF_3) 74.2 (C_q), 25.2 (2 × CH_2), 24.3 (CH_2), 21.9 (2 × CH_2). ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.27. HRMS (TOF–ESI$^-$) m/z calcd. For $C_{14}H_{14}O_3SF_3$ $[M-H]^-$: 319.0616; found: 319.0623.

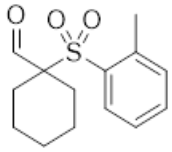
Also prepared using silver mediated conditions according to general procedure **D** which afforded α-sulfonyl aldehyde **3h** (24.3 mg, 19%).

1-(Naphthalen-1-ylsulfonyl)cyclohexane-1-carbaldehyde (3i)



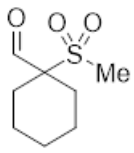
Prepared according to general procedure **C** using cyclohexane carboxaldehyde **1** (48 μL, 0.4 mmol) and napthene-1-sulfinic acid sodium salt **S9** (171 mg, 0.8 mmol). Purification by flash column chromatography (20% Et_2O:pentane) afforded α-sulfonyl aldehyde **3i** as an amorphous gum (27.5 mg, 23%). R_f 0.23 (20% Et_2O:pentane). IR (film)/cm^{-1} 2937, 2859, 1718 (C=O), 1506, 1450, 1293, 1148, 1126, 958, 768, 675. ^1H NMR (400 MHz, $CDCl_3$) δ 9.65 (d, *J* = 1.1 Hz, 1 H, CHO), 8.88 (dd, *J* = 8.7, 1.1 Hz, 1 H, Ar–CH), 8.16 (d, *J* = 8.2 Hz, 1 H, Ar–CH), 8.10 (dd, *J* = 7.5, 1.3 Hz, 1 H, Ar–CH), 7.95–7.93 (m, 1 H, Ar–CH), 7.68–7.65 (m, 1 H, Ar–CH), 7.63–7.57 (m, 2 H, 2 × Ar–CH), 2.31 (ddd, *J* = 13.0, 2.9, 1.5 Hz, 2 H, 2 × C_qCHH), 2.00 (ddd, *J* = 13.0, 13.0, 4.4 Hz, 2 H, 2 × C_qCH_2CHH), 1.81–1.71 (m, 2 H, 2 × C_qCH_2CHH), 1.67–1.59 (m, 1 H, $C_qCH_2CH_2CHH$), 1.26–1.10 (m, 3 H, 2 × C_qCH_2CHH + $C_qCH_2CH_2CHH$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.3 (CHO), 136.2 (Ar–CH), 134.2 (Ar–C_q), 133.6 (Ar–CH), 131.1 (Ar–C_q), 130.5 (Ar–C_q), 129.0 (Ar–CH), 128.7 (Ar–CH), 127.1 (Ar–CH), 125.2 (Ar–CH), 124.1 (Ar–CH), 75.8 (C_q), 25.5 (2 × CH_2), 24.4 (CH_2), 22.0 (2 × CH_2). HRMS (TOF–ESI$^+$) m/z calcd. For $C_{19}H_{21}O_3NNaS$ [M+MeCN+Na]$^+$: 366.1140; found: 366.1134.

1-(*o*-Tolylsulfonyl)cyclohexane-1-carbaldehyde (3j)



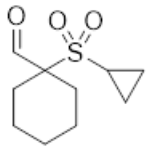
Prepared according to general procedure **C** using cyclohexane carboxaldehyde **1** (48 μL, 0.4 mmol) and 2-methylbenzenesulfinic acid sodium salt **S11** (128 mg, 0.8 mmol). Purification by flash column chromatography (10–20% Et_2O:pentane) afforded α-sulfonyl aldehyde **3j** as a colourless oil (38.9 mg, 37%). R_f 0.57 (20% Et_2O:pentane). IR (film)/cm^{-1} 2937, 2859, 1722 (C=O), 1454, 1312, 958, 805, 764, 689. ^1H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1 H, CHO), 7.73 (dd, *J* = 8.0, 1.4 Hz, 1 H, Ar–CH), 7.53 (ddd, *J* = 7.5, 1.4 Hz, 1 H, Ar–CH), 7.37–7.30 (m, 2 H, 2 × Ar–CH), 2.63 (s, 3 H, CH_3), 2.34–2.29 (m, 2 H, 2 × C_qCHH), 1.94–1.93 (m, 2 H, 2 × C_qCH_2CHH), 1.81–1.76 (m, 2 H, 2 × C_qCH_2CHH), 1.64–1.63 (m, 1 H, $C_qCH_2CH_2CHH$), 1.29–1.13 (m, 3 H, 2 × C_qCH_2CHH + $C_qCH_2CH_2CHH$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8 (CHO), 140.2 (Ar–C_q), 134.3 (Ar–CH), 133.4 (Ar–C_q), 133.3 (Ar–CH), 132.6 (Ar–CH), 126.4 (Ar–CH), 75.4 (C_q), 25.1 (2 × CH_2), 24.4 (CH_2), 22.0 (2 × CH_2) , 21.1 (CH_3). HRMS (TOF–ESI$^+$) m/z calcd. For $C_{14}H_{19}O_3S$ [M+H]$^+$: 267.1055; found: 267.1054.

1-(Methylsulfonyl)cyclohexane-1-carbaldehyde (3k)



Prepared according to general procedure **C** using cyclohexane carboxaldehyde **1** (48 μL, 0.4 mmol) and methanesulfinic acid sodium salt (81 mg, 0.8 mmol)**.** Purification by flash column chromatography (5–20% Et_2O:pentane) afforded α-sulfonyl aldehyde **3k** a colourless oil (34.6 mg, 45%). R_f 0.17 (20% Et_2O:pentane). IR (film)/cm^{-1} 2937, 3858, 1722 (C=O), 1453, 1293, 1133, 954, 752. ^1H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1 H, CHO), 2.76 (s, 3 H, CH_3), 2.49 (d, *J* = 12.3 Hz, 2 H, 2 × C_qCHH), 1.98–1.85 (m, 4 H, 2 × C_qCHH + 2 × C_qCH_2CHH), 1.74–1.70 (m, 1 H, $C_qCH_2CH_2CHH$), 1.25–1.20 (m, 3 H, 2 × C_qCH_2CHH + $C_qCH_2CH_2CHH$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.3 (CHO), 72.8 (C_q), 36.1 (CH_3), 24.6 (2 × CH_2), 24.2 (CH_2), 21.9 (2 × CH_2). HRMS (TOF-ESI$^-$) m/z calcd. For $C_8H_{13}O_3S$ [M-H]$^-$: 189.0585; found 189.0590

1-(Cyclopropylsulfonyl)cyclohexane-1-carbaldehyde (3l)



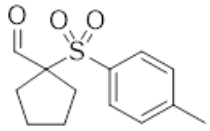
Prepared according to general procedure **C** using cyclohexane carboxaldehyde **1** (48 μL, 0.4 mmol) and cyclopropanesulfinic acid sodium salt (102 mg, 0.8 mmol)**.** Purification by flash column chromatography (30% Et_2O:hexane) afforded α-sulfonyl aldehyde **3l** as a colourless oil (47.5 mg, 55%). R_f 0.14 (30% Et_2O:hexane). IR (film)/cm^{-1} 2937, 2858, 1722, 1453, 1315, 1289, 1133, 1189, 1043, 883, 831, 693. ^1H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1 H, CHO), 2.56 (d, *J* = 12.2 Hz, 2 H, 2 × C_qCHH), 2.26 (tt, *J* = 8.0, 4.8 Hz, 1 H, SO_2CH), 1.93 (ddd, *J* = 12.2, 12.2, 4.4 Hz, 2 H, 2 × C_qCHH), 1.83 (m, 2 H, 2

× C_qCH_2CHH), 1.68 (s, 1 H, $C_qCH_2CH_2CHH$), 1.32–1.18 (m, 3 H, 2 × C_qCH_2CHH + $C_qCH_2CH_2CHH$), 1.16 (m, 2 H, $SO_2CHCHHCHH$), 1.06–0.98 (m, 2 H, $SO_2CHCHHCHH$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.5 (CHO), 73.6 (C_q), 26.2 (SO_2CH), 24.8 (2 × CH_2), 24.4 (CH_2), 21.9 (2 × CH_2), 4.8 ($SO_2CHCH_2CH_2$). HRMS (TOF–ESI$^+$) m/z calcd. For $C_{10}H_{17}O_3S$ $[M+H]^+$: 217.0898; found: 217.0894.

Reaction Scope Varying the Aldehyde

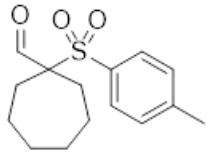
Cycloheptane carboxaldehyde **S12**, cyclooctane carboxaldehyde **S13** and 4-phenylcyclohexane carboxaldehyde **S15** were all prepared as previously reported.[6]

1-(4-Methylbenzene-1-sulfonyl)cyclopentane-1-carbaldehyde (4a)



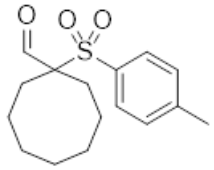
Prepared according to general procedure **C** using cyclopentanecarboxaldehyde (43 μL, 0.4 mmol) and 4-methylbenzenesulfinic acid sodium salt **2a** (142 mg, 0.8 mmol). Purification by flash column chromatography afforded α-sulfonyl aldehyde **4a** as a colourless oil (66.7 mg, 66%). R_f 0.21 (20% Et_2O:pentane). IR (film)/cm^{-1} 2960, 2874, 1722 (C=O), 1595, 1450, 1304, 1144, 1088, 1047, 816, 715, 663. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1 H, CHO), 7.66 (d, *J* = 8.2 Hz, 2 H, 2 × Ar–CH), 7.34 (d, *J* = 8.2 Hz, 1 H, 2 × Ar–CH), 2.45 (s, 3 H, CH_3), 2.30 (m, 2 H, 2 × C_qCHH), 2.19–2.07 (m, 2 H, 2 × C_qCH*H*), 1.89–1.75 (m, 2 H, 2 × C_qCH_2CHH), 1.64–1.50 (m, 2 H, 2 × C_qCH_2CH*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.7 (CHO), 145.5 (Ar–C_q), 133.9 (Ar–C_q), 129.9 (2 × Ar–CH), 129.1 (2 × Ar–CH), 81.1 (C_q), 28.8 (2 × $C_qCH_2CH_2$), 25.7 (2 × $C_qCH_2CH_2$), 21.6 (CH_3). HRMS (FTMS + p APCI) m/z calcd. For $C_{13}H_{17}O_3S$ $[M+H]^+$: 253.0893; found 253.0885.

1-(4-Methylbenzene-1-sulfonyl)cycloheptane-1-carbaldehyde (5a)



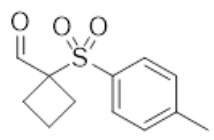
Prepared according to general procedure **C** using cycloheptanecarboxaldehyde **S12** (53 μL, 0.4 mmol) and 4-methylbenzenesulfinic acid sodium salt **2a** (142 mg, 0.8 mmol). Purification by flash column chromatography (10–20% Et_2O:pentane) afforded α-sulfonyl aldehyde **5a** as a colourless oil (82.3 mg, 73%). R_f 0.58 (20% Et_2O:pentane). IR (film)/cm^{-1} 2926, 2855, 1722 (C=O), 1595, 1461, 1290, 1141, 1085, 1040, 902, 816, 726. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (s, 1 H, CHO), 7.62 (d, *J* = 8.0 Hz, 2 H, 2 × Ar–CH), 7.34 (d, *J* = 8.0 Hz, 2 H, 2 × Ar–CH), 2.44 (s, 3 H, CH_3), 2.23–2.16 (m, 4 H, 2 × C_qCH_2), 1.82–1.71 (m, 2 H, 2 × C_qCH_2CHH), 1.60–1.45 (m, 4 H, 2 × C_qCH_2CH*H*+ 2 × $C_qCH_2CH_2CHH$), 1.41–1.30 (m, 2 H, 2 × $C_qCH_2CH_2CH$*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.5 (CHO), 145.5 (Ar–C_q), 132.7 (Ar–C_q), 129.8 (2 × Ar–CH), 129.7 (2 × Ar–CH), 77.2 (C_q), 30.1 (2 × CH_2), 27.9 (2 × CH_2), 22.9 (2 × CH_2), 21.6 (CH_3). HRMS (FTMS–p APCI) m/z calcd. For $C_{15}H_{19}O_3S$ $[M-H]^-$: 279.1049; found 279.1048.

1-(4-Methylbenzene-1-sulfonyl)cyclooctane-1-carbaldehyde (6a)



Prepared according to general procedure **C** using cyclooctanecarboxaldehyde **S13** (59 μL, 0.4 mmol) and 4-methylbenzenesulfinic acid sodium salt **2a** (142 mg, 0.8 mmol). Purification by flash column chromatography afforded α-sulfonyl aldehyde **6a** as a colourless oil (62.6 mg, 53%). R_f 0.50 (20% Et_2O:pentane). IR (film)/cm^{-1} 2922, 2855, 1722 (C=O), 1594, 1476, 1446, 1300, 1144, 1084, 816, 712. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (s, 1 H, CHO), 7.61 (d, *J* = 8.2 Hz, 2 H, 2 × Ar–CH), 7.34 (d, *J* = 8.2 Hz, 2 H, 2 × Ar–CH), 2.45 (s, 3 H, CH_3), 2.28 (ddd, *J* = 15.6, 9.0, 2.4 Hz, 2 H, 2 × C_qCHH), 2.16 (ddd, *J* = 15.6, 9.2, 2.4 Hz, 2 H, 2 × C_qCH*H*), 1.90–1.79 (m, 2 H, 2 × C_qCH_2CHH), 1.60–1.34 (m, 8 H, 2 × C_qCH_2CH*H* + 2 × $C_qCH_2CH_2CH_2$ + $C_qCH_2CH_2CH_2CH_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.5 (CHO), 145.5 (Ar–C_q), 132.8 (Ar–C_q), 129.72 (2 × Ar–CH), 129.68 (2 × Ar–CH), 77.5 (C_q), 27.8 (2 × CH_2), 24.7 (CH_2), 23.7 (2 × CH_2), 22.2 (2 × CH_2), 21.7 (CH_3). HRMS (FTMS–p APCI) m/z calcd. For $C_{16}H_{21}O_3S$ $[M-H]^-$: 293.1206; found 293.1207.

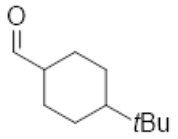
1-(4-Methylbenzene-1-sulfonyl)cyclobutane-1-carbaldehyde (7a)



Prepared according to general procedure **C** using cyclobutanecarboxaldehyde (36 μL, 0.4 mmol) and 4-methylbenzenesulfinic acid sodium salt **2a** (142 mg, 0.8 mmol). Purification by flash column chromatography afforded α-sulfonyl aldehyde **7a** as a colourless oil (9.7 mg, 10%). R_f 0.26 (20% Et_2O:pentane). IR (film)/cm^{-1} 2955, 2851, 1722 (C=O), 1595, 1315, 1252, 1316, 1156, 1118, 1080, 1039, 816, 664. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1 H, CHO), 7.66 (d, *J* = 8.4 Hz, 2 H, 2 × Ar–CH), 7.36–7.34 (m, 2 H, 2 × Ar–CH), 2.80–2.72 (m, 2 H, 2 × C_qCHH), 2.45 (s, 3 H, CH_3), 2.44–2.38 (m, 2 H, 2 × C_qCH*H*), 2.09 (dtt, *J* = 11.5, 10.0, 4.9 Hz, 1 H, C_qCH_2CHH), 1.88 (dtt, *J* = 11.5, 10.0, 8.0 Hz, 1 H, C_qCH_2CH*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5 (CHO), 145.6 (Ar–C_q), 133.1 (Ar–C_q), 130.1 (2 × Ar–CH), 128.7

(2 × Ar–CH), 72.2 (C_q), 23.5 (2 × C_qCH_2), 21.7 (CH_3), 14.5 ($C_qCH_2CH_2$). HRMS (FTMS + p APCI) m/z calcd. For $C_{12}H_{15}O_3S$ $[M+H]^+$: 239.0736; found 239.0729.

4-(*tert*-Butyl)cyclohexane-1-carbaldehyde (S14)



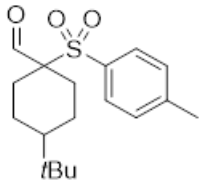
Procedure modified from Falck.[7] KO*t*Bu (359 mg, 3.20 mmol) was added to a stirred solution of (methoxymethyl)triphenylphosphonium chloride (1.09 g, 3.20 mmol) in anhydrous THF (2 mL) at rt and the reaction was stirred for 1 h. A solution of 4-(*tert*-butyl)cyclohexan-1-one (308 mg, 2.00 mmol) in anhydrous THF (2 mL) was added dropwise to the dark red solution at 0 °C and then warmed to room temperature and stirred overnight. The reaction was quenched with addition of brine (5 mL) and the product extracted with EtOAc (3 × 20 mL), the combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The intermediate enol ether was passed through a short pad of silica (10% Et_2O:pentane) and concentrated *in vacuo*. The intermediate was dissolved in THF (4 mL) and 6 M aqueous HCl (1 mL) was added and the reaction stirred at rt for 2 h. Brine (5 mL) was added to reaction, and the product was extracted with EtOAc (3 × 20 mL), the combined organic layers were dried over Na_2SO_4, filtered, then concentrated *in vacuo*. Purification by column chromatography (0–10% Et_2O:pentane) afforded aldehyde **S14** as a 1:2 mixture of *cis*- and *trans*-diasteromers as a colourless oil (203 mg, 60%). R_f 0.55 (10% Et_2O:pentane). IR (film)/cm^{-1} 2941, 2859, 2706, 1722 (C=O), 1476, 1449, 1364, 924, 697.

Cis: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1 H, CHO), 2.45–2.37 (m, 1 H, CHOC*H*), 2.30 (ddd, *J* = 13.6, 3.5, 1.8 Hz, 2 H, 2 × C*H*H), 1.72–1.64 (m, 2 H, 2 × CH*H*), 1.53 (td, *J* = 12.9, 5.2 Hz, 2 H, 2 × CHH), 1.11–0.90 (m, 3 H, 2 × CH*H* + C*H*C(CH_3)$_3$), 0.81 (s, 9 H, C(CH_3)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.1 (CHO), 47.8 (CHO*C*H), 46.5 (*C*HC(CH_3)$_3$), 27.4 (C(*C*H_3)$_3$), 25.5 (2 × CH_2), 24.1 (2 × CH_2).

Trans: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (d, *J* = 1.7 Hz, 1 H, CHO), 2.14 (ttd, *J* = 12.2, 3.7, 1.7 Hz, 1 H, CHOC*H*), 2.05–2.00 (m, 2 H, 2 × CH*H*), 1.94–1.89 (m, 2 H, 2 × C*H*H), 1.29–1.19 (m, 2 H, 2 × CH*H*), 1.09–0.96 (m, 3 H, 2 × C*H*H + C*H*C(CH_3)$_3$), 0.86 (s, 9 H, C(CH_3)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.0 (CHO), 50.5 (CHO*C*H), 47.6 (*C*HC(CH_3)$_3$), 32.5 (*C*(CH_3)$_3$), 27.5 (C(*C*H_3)$_3$), 26.5 (2 × CH_2), 26.2 (2 × CH_2).

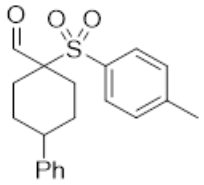
Analytical data (IR, ^{1}H NMR and ^{13}C NMR) is in agreement with the reported literature.[8]

4-(*tert*-Butyl)-1-(4-methylbenzene-1-sulfonyl)cyclohexane-1-carbaldehyde (8a)



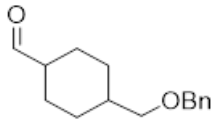
4-(*tert*-Butyl)cyclohexane-1-carboxaldehyde **S14** (70.8 mg, 0.4 mmol), manganese(IV) Oxide (52 mg, 0.6 mmol), copper(II) triflate (21.7 mg, 0.06 mmol), bathophenanthroline (13.3 mg, 0.04 mmol), 4-methylbenzenesulfinic acid sodium salt **2a** (142 mg, 0.8 mmol), water (200 μL), ethanol (200 μL) and acetic acid (200 μL, 4 mmol) were added sequentially to a microwave vial under air and the reaction was submerged in an oil bath preheated to 100 °C for 18 h. The reaction was allowed to cool to room temperature, diluted with EtOAc (2 mL) then filtered through silica eluting with EtOAc (3 × 10 mL) the concentrated *in vacuo*. Purification by flash column chromatography (20% Et_2O:pentane) afforded *α*-sulfonyl aldehyde **8a** as white amorphous gum in an inseparable 1:1 mixture of *cis*- and *trans*-diastereomers (94.7 mg, 73%). R_f 0.27 (20% Et_2O:pentane). IR (film)/cm^{-1} 2937, 2851, 1722 (C=O), 1443, 1297, 1141, 1085, 813. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (s, 1 H, CH_aO), 9.62 (s, 1 H, CH_bO), 7.64 (d, *J* = 8.4 Hz, 2 H, 2 × Ar–$CH_{a/b}$), 7.58 (d, *J* = 8.4 Hz, 2 H, 2 × Ar–$CH_{a/b}$), 7.33 (d, *J* = 7.3 Hz, 4 H, 4 × Ar–$CH_{a/b}$), 2.44 (s, 3 H, C($H_{a/b}$)$_3$), 2.43 (s, 3 H, C($H_{a/b}$)$_3$), 2.42–2.31 (m, 4 H, 2 × C($H_{a/b}$)$H_{a/b}$), 1.97–1.83 (m, 4 H, 2 × C($H_{a/b}$)$H_{a/b}$), 1.83–1.76 (m, 2 H, 2 × C(*H*$_{a/b}$)H), 1.69 (dt, *J* = 12.3, 3.7 Hz, 2 H, 2 × C(*H*$_{a/b}$)H), 1.60 (ddd, *J* = 15.0, 13.2, 4.5 Hz, 2 H, 2 × C(H)*H*$_{a/b}$), 1.04–0.92 (m, 3 H, 2 × C(H)*H*$_{a/b}$ + C($H_{a/b}$)*t*Bu), 0.88 (s, 9 H, C(C($H_{a/b}$)$_3$)$_3$), 0.85–0.80 (m, 1 H, C($H_{a/b}$)*t*Bu), 0.78 (s, 9 H, C(C($H_{a/b}$)$_3$)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.7 (CH_aO), 196.2 (CH_bO), 145.5 (2 × Ar–($C_{a/b}$)$_q$), 133.2 (Ar–($C_{a/b}$)$_q$), 132.2 (Ar–($C_{a/b}$)$_q$), 129.9 (2 × Ar–($C_{a/b}$)H), 129.8 (2 × Ar–($C_{a/b}$)H), 129.6 (2 × Ar–($C_{a/b}$)H), 129.4 (2 × Ar–($C_{a/b}$)H), 73.9 (CHO(*C*$_{a/b}$)$_q$), 72.1 (CHO(*C*$_{a/b}$)$_q$), 46.44 ((($C_{a/b}$)H*t*Bu), 46.39 ((($C_{a/b}$)H*t*Bu), 32.5 (*C*$_{a/b}$(CH_3)$_3$), 32.2 (*C*$_{a/b}$(CH_3)$_3$), 27.4 (C(*C*$_{a/b}$(H_3)$_3$), 27.3 (C(*C*$_{a/b}$(H_3)$_3$), 26.2 (4 × ($C_{a/b}$)H_2), 25.7 (2 × ($C_{a/b}$)H_2), 23.1 (2 × ($C_{a/b}$)H_2), 21.7 (2 × Ar($C_{a/b}$)H_3). HRMS (TOF–ESI$^+$) m/z calcd. For $C_{18}H_{27}O_3S$ $[M+H]^+$: 323.1681; found 323.1690.

4-Phenyl-1-(4-methylbenzene-1-sulfonyl)cyclohexane-1-carbaldehyde (9a)



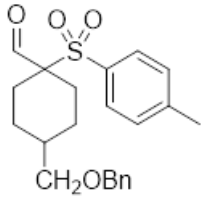
4-Phenylcyclohexane-1-carboxaldehyde **S15** (71.8 mg, 0.38 mmol), manganese(IV) oxide (52 mg, 0.6 mmol), copper(II) triflate (21.7 mg, 0.06 mmol), bathophenanthroline (13.3 mg, 0.04 mmol), 4-methylbenzenesulfinic acid sodium salt **2a** (142 mg, 0.8 mmol), water (200 μL), ethanol (200 μL) and acetic acid (200 μL, 4 mmol) were combined sequentially to a microwave vial under air and heated to 100 °C for 18 h. The reaction was allowed to cool to room temperature, diluted with EtOAc (2 mL) then filtered through silica eluting with EtOAc (3 × 10 mL) the concentrated *in vacuo*. Purification by flash column chromatography (20% Et_2O:pentane) afforded *α*-sulfonyl aldehyde **9a** as white amorphous gum in an inseparable 1:1 mixture of *cis*- and *trans*-diastereomers (51.7 mg, 40%). R_f 0.14 (20% Et_2O:pentane). IR (film)/cm^{-1} 3056, 3026, 2930, 2862, 1722 (C=O), 1595, 1490, 1446, 1301, 1237, 1140, 1088, 816, 757, 701, 664 ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1 H, CH_aO), 9.71 (s, 1 H, CH_bO), 7.69–7.64 (m, 3 H, 3 × Ar–CH_{a+b}), 7.39–7.21 (m, 13 H, 13 × Ar–$CH_{a/b}$), 7.13–7.11 (m, 2 H, 2 × Ar–$CH_{a/b}$), 2.54–2.52 (m, 3 H, 2 × $C_qC(H_{a/b})H$ + $PhCH_{a/b}$), 2.48 (s, 3 H, $C(H_{a/b})_3$), 2.47 (s, 3 H, $C(H_{a/b})_3$), 2.45–2.39 (m, 5 H, 2 × $C_qC(H_{a/b})H$ + 2 × $C_qC(H)H_{a/b}$ + $PhCH_{a+b}$), 2.15 (ddd, *J* = 13.6, 13.6, 4.1 Hz, 2 H, 2 × $C_qCH(H_{a/b})$), 1.98–1.83 (m, 6 H, 2 × $C_qCH_2C(H_{a/b})H$ + 2 × $C_qCH_2CH(H_{a+b})$), 1.41–1.37 (m, 2 H, 2 × $C_qCH_2C(H_{a/b})H$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6 ($C_{a/b}HO$), 196.4 ($C_{a/b}HO$), 145.70 (Ar–$(C_{a/b})_q$), 145.67 (Ar–$(C_{a/b})_q$), 145.2 (Ar–$(C_{a/b})_q$), 145.1 (Ar–$(C_{a/b})_q$), 132.7 (Ar–$(C_{a/b})_q$), 132.1 (Ar–$(C_{a/b})_q$), 129.9 (2 × Ar–$(C_{a/b})H$), 129.8 (2 × Ar–$(C_{a/b})H$), 129.7 (2 × Ar–$(C_{a/b})H$), 129.5 (2 × Ar–$(C_{a/b})H$), 128.5 (3 × Ar–$(C_{a/b})H$), 127.0 (2 × Ar–$(C_{a/b})H$), 126.6 (2 × Ar–$(C_{a/b})H$), 126.5 (Ar–$(C_{a/b})H$), 126.3 (2 × Ar–$(C_{a/b})H$), 73.6 ($(C_{a/b})_q$), 72.2 ($(C_{a/b})_q$), 42.5 ($(C_{a/b})HPh$), 41.0 ($(C_{a/b})HPh$), 29.5 (2 × $(C_{a/b})H_2$), 27.6 (2 × $(C_{a/b})H_2$), 25.5 (2 × $(C_{a/b})H_2$), 25.0 (2 × $(C_{a/b})H_2$), 21.71 (Ar$(C_{a/b})H_3$), 21.68 (Ar$(C_{a/b})H_3$). HRMS (TOF–ESI$^+$) m/z calcd. For $C_{22}H_{25}NO_3SNa$ [M+MeCN+Na]$^+$: 406.1453; found 406.1444.

4-((Benzyloxy)methyl)cyclohexane-1-carbaldehyde (S16)



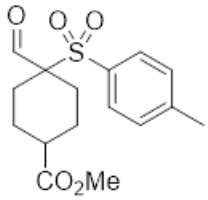
1,4-Cyclohexanedimethanol (720 mg, 5 mmol) in THF (5 mL) was added dropwise to a stirring solution of sodium hydride as a 60% dispersion in mineral oil (200 mg, 5 mmol) in THF (5 mL) and the resulting solution was stirred for 1 h at rt. Tetrabutylammonium Iodide (928 mg, 2.5 mmol), and benzyl bromide (595 mL, 5 mmol) were added and the reaction was stirred overnight at rt then at 60 °C for 30 min. The reaction was quenched by the addition of water (10 mL) and the product was extracted with Et_2O (3 × 10 mL), dried over Na_2SO_4, filtered and then concentrated *in vacuo*. Purification by flash column chromatography (20% Et_2O:pentane) afforded the mono-benzyl protected alcohol intermediate. CH_2Cl_2 (100 mL) was added to mono-benzyl protected alcohol, then the reaction was cooled to 0 °C and Dess-Martin Periodinane (3.2 g, 5 mmol) was added and the reaction stirred for 1.5 h allowing to warm to rt. The reaction was quenched by the addition of a saturated solution of $NaHCO_{3\,(aq)}$ (100 mL) and the product was extracted with CH_2Cl_2 (3 × 50 mL), dried over Na_2SO_4, filtered then concentrated *in vacuo*. Purification by flash column chromatography afforded aldehyde **S16** as a colourless oil in an inseparable 1:2 mixture of *cis*- and *trans*-diastereomers (286.4 mg, 25% over 2 steps). R_f 0.23 (10% Et_2O:pentane). IR (film)/cm^{-1} 2922, 2851, 2706, 1722 (C=O), 1450, 1360, 1092, 913, 734, 697. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (s, 1 H, CH_aO), 9.62 (d, *J* = 1.6 Hz, 1 H, CH_bO), 7.38–7.27 (m, 10 H, 10 × Ar–$CH_{a/b}$), 4.50 (s, 2 H, $OC(H_b)_2Ph$), 4.48 (s, 2 H, $OC(H_a)_2Ph$), 3.30 (d, *J* = 6.4 Hz, 2 H, $C(H_b)_2OBn$), 3.26 (d, *J* = 6.3 Hz, 2 H, $C(H_a)_2OBn$), 2.42 (pent, *J* = 4.7 Hz, 1 H, $CHOCH_a$), 2.19 (ttd, *J* = 12.3, 3.5, 1.6 Hz, 1 H, $CHOCH_b$), 2.13–2.05 (m, 2 H, 2 × $CHOCHC(H_a)H$), 2.05–1.90 (m, 4 H, 2 × $C(H_b)_2$), 1.77–1.66 (m, 3 H, CH_aCH_2OBn + 2 × $CH(H_a)CHCH_2OBn$), 1.65–1.58 (m, 3 H, 2 × $CHOCHCH(H_a)$+ CH_bCH_2OBn) 1.28 (qd, *J* = 12.9, 3.3 Hz, 2 H, 2 × $CHOCHC(H_b)H$), 1.15–0.98 (m, 4 H, 2 × $C(H_a)HCHCH_2OBn$ + 2 × $CHOCHCH(H_b)$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.5 (CH_aO), 204.6 (CH_bO), 138.5 (Ar–$(C_{a+b})_q$), 128.3 (2 × Ar–$(C_{a+b})H$), 127.5 (3 × Ar–$(C_{a+b})H$), 75.6 ($CHO(C_b)H$), 74.9 ($CHO(C_a)H$), 73.0 ($O(C_{a+b})H_2Ph$), 50.4 ($(C_b)H_2OBn$), 47.3 ($(C_a)H_2OBn$), 37.7 ($(C_b)HCH_2OBn$), 36.8 ($(C_a)HCH_2OBn$), 28.7 (2 × $(C_b)H_2$), 26.4 (2 × $(C_a)H_2$), 25.5 (2 × $(C_b)H_2$), 23.7 (2 × $(C_a)H_2$). HRMS (ESI$^+$) m/z calcd. For $C_{15}H_{21}O_2$ [M+H]$^+$: 233.1542; found 233.1540.

4-((Benzyloxy)methyl)-1-(4-methylbenzene-1-sulfonyl)cyclohexane-1-carbaldehyde (10a)



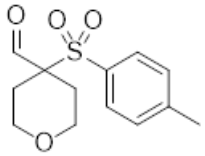
4-((Benzyloxy)methyl)cyclohexane-1-carbaldehyde **S16** (92.8 mg, 0.4 mmol), manganese(IV) oxide (52 mg, 0.6 mmol), copper(II) triflate (21.7 mg, 0.06 mmol), bathophenanthroline (13.3 mg, 0.04 mmol), 4-methylbenzenesulfinic acid sodium salt **2a** (142 mg, 0.8 mmol), water (200 μL), ethanol (200 μL) and acetic acid (200 μL) were added sequentially to a microwave vial under air and the reaction was heated to 100 °C for 18 h. The reaction was allowed to cool to room temperature, diluted with EtOAc (2 mL) then filtered through silica eluting with EtOAc (3 × 10 mL) the concentrated *in vacuo*. Purification by flash column chromatography (20% Et_2O:pentane) afforded *α*-sulfonyl aldehyde **10a** as a colourless oil in an inseparable 1:1 mixture of *cis*- and *trans*-diastereomers (112.2 mg, 73%). R_f 0.3 (30% Et_2O:pentane). IR (film)/cm^{-1} 2930, 2855, 1722 (C=O), 1453, 1300, 1144, 1085, 910, 730, 673. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (s, 1 H, $CH_{a/b}O$), 9.64 (s, 1 H, $CH_{a/b}O$), 7.61–7.58 (m, 4 H, 4 × Ar–CH_{a+b}), 7.37–7.29 (m, 14 H, 14 × Ar–CH_{a+b}), 4.53 (s, 2 H, $OC(H_{a/b})_2Ph$), 4.45 (s, 2 H, $OC(H_{a/b})_2Ph$), 3.46 (d, *J* = 7.0 Hz, 2 H, $C(H_{a/b})_2OBn$), 3.20 (d, *J* = 6.4 Hz, 2 H, $C(H_{a/b})_2OBn$), 2.45 (s, 6 H, $C(H_{a+b})_3$), 2.34 (d, *J* = 13.3 Hz, 2 H, 2 × $CHOC_qCH_{a/b}$H), 2.14 (ddd, *J* = 14.5, 10.8, 4.1 Hz, 2 H, 2 × $CHOC_qCH_{a/b}$H), 2.01–1.81 (m, 9 H, 4 × $C(H_{a/b})_2$+ $CH_{a/b}CH_2OBn$), 1.65–1.62 (m, 1 H, $CH_{a/b}CH_2OBn$), 1.53–1.45 (m, 2 H, 2 × $CHH_{a/b}$), 0.90–0.86 (m, 2 H, 2 × $CHH_{a/b}$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6 ($CH_{a/b}O$), 197.1 ($CH_{a/b}O$), 145.6 (2 × Ar–$(C_{a/b})_q$), 138.33 (Ar–$(C_{a/b})_q$), 138.29 (Ar–$(C_{a/b})_q$), 132.1 (Ar–$(C_{a/b})_q$), 132.0 (Ar–$(C_{a/b})_q$), 129.9 (2 × Ar–$(C_{a/b})$H), 129.74 (2 × Ar–$(C_{a/b})$H), 129.69 (3 × Ar–$(C_{a/b})$H), 129.66 (2 × Ar–$(C_{a/b})$H), 128.40 (2 × Ar–$(C_{a/b})$H), 128.35 (2 × Ar–$(C_{a/b})$H), 127.60 (2 × Ar–$(C_{a/b})$H), 127.56 (Ar–$(C_{a/b})$H), 127.5 (2 × Ar–$(C_{a/b})$H), 74.7 ($O(C_{a/b})H_2Ph$), 74.1 ($(C_{a/b})_q$), 73.3 ($(C_{a/b})_q$), 73.2 ($O(C_{a/b})H_2Ph$), 73.0 ($(C_{a/b})H_2OBn$), 71.4 ($(C_{a/b})H_2OBn$), 36.6 ($(C_{a/b})$H), 32.7 ($(C_{a/b})$H), 25.4 (2 × $(C_{a/b})H_2$), 24.8 (2 × $(C_{a/b})H_2$), 23.1 (2 × $(C_{a/b})H_3$), 21.7 (4 × $(C_{a/b})H_2$). HRMS (ESI^+) m/z calcd. For $C_{22}H_{26}O_4SNa$ $[M+Na]^+$: 409.1450; found 409.1443.

Methyl 4-formyl-4-(4-methylbenzene-1-sulfonyl)cyclohexane-1-carboxylate (11a)



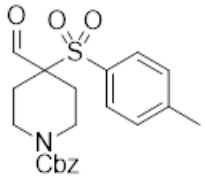
Methyl 4-formylcyclohexane-1-carboxylate (66.8 mg, 0.4 mmol), manganese(IV) oxide (52 mg, 0.6 mmol), copper(II) triflate (21.7 mg, 0.06 mmol), bathophenanthroline (13.3 mg, 0.04 mmol), 4-methylbenzenesulfinic acid sodium salt **2a** (142 mg, 0.8 mmol), water (200 μL), ethanol (200 μL) and acetic acid (200 μL, 4 mmol) were combined sequentially to a microwave vial under air and heated to 100 °C for 18 h. The reaction was allowed to cool to room temperature, diluted with EtOAc (2 mL) then filtered through silica eluting with EtOAc (3 × 10 mL) the concentrated *in vacuo*. Purification by flash column chromatography (20% Et_2O:pentane) afforded *α*-sulfonyl aldehyde **11a** a colourless oil in an inseparable 1:1 mixture of *cis*- and *trans*-diastereomers (57.2 mg, 44%). R_f 0.42 (20% Et_2O:pentane). IR (film)/cm^{-1} 2952, 2866, 1729 (C=O), 1595, 1453, 1304, 1200, 1148, 1051, 947, 820, 664. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1 H, CH_aO), 9.65 (s, 1 H, CH_bO), 7.60 (m, 4 H, 2 × Ar–CH_{a+b}), 7.35 (m, 4 H, 2 × Ar–CH_{a+b}), 3.72 (s, 3 H, $CO_2C(H_{a/b})_3$), 3.64 (s, 3 H, $CO_2C(H_{a/b})_3$), 2.57 (tt, *J* = 4.9, 3.6 Hz, 1 H, $C(H_{a/b})CO_2Me$), 2.46 (s, 3 H, $ArC(H_{a/b})_3$), 2.46 (s, 3 H, $ArC(H_{a/b})_3$), 2.41–2.34 (m, 2 H, 2 × $CH_{a/b}$H), 2.30–2.20 (m, 3 H, 2 × $CHH_{a/b}$ + $C(H_{a/b})CO_2Me$), 2.15–2.09 (m, 4 H, 2 × $CH_{a/b}$H + 2 × $CHH_{a/b}$), 2.09–1.94 (m, 4 H, 2 × $CH_{a/b}$H) + 2 × $CHH_{a/b}$) 1.47–1.44 (m, 2 H, 2 × $CH_{a/b}$H), 1.34–1.30 (m, 2 H 2 × $CHH_{a/b}$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.4 (CH_aO), 197.0 (CH_aO), 178.6 ($(C_{a/b})=O_{ester}$), 173.9 ($(C_{a/b})=O_{ester}$), 145.9 (Ar–$(C_{a/b})_q$), 145.7 (Ar–$(C_{a/b})_q$), 131.9 (2 × Ar–$(C_{a/b})_q$), 129.9 (4 × $(C_{a/b})_{Ar}$–H), 129.8 (2 × $(C_{a/b})_{Ar}$–H), 129.7 (2 × $(C_{a/b})_{Ar}$–H), 73.2 (2 × $(C_{a/b})_q$), 52.0 ($CO_2(C_{a/b})H_3$), 51.8 ($CO_2(C_{a/b})H_3$), 41.3 ($(C_{a/b})HCO_2Me$), 37.7 ($(C_{a/b})HCO_2Me$), 24.5 (2 × $(C_{a+b})H_2$), 24.4 (2 × $(C_{a+b})H_2$), 22.9 (2 × $(C_{a+b})H_2$), 22.0 (2 × $(C_{a+b})H_2$), 21.71 ($Ar(C_{a/b})H_3$), 21.69 ($Ar(C_{a/b})H_3$). HRMS (FTMS + p APCI) m/z calcd. For $C_{16}H_{21}O_5S$ $[M+H]^+$: 325.1104; found 325.1094.

4-(4-Methylbenzene-1-sulfonyl)tetrahydro-2H-pyran-4-carbaldehyde (12a)



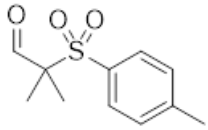
Tetrahydro-2H-pyran-4-carbaldehyde (48.7 mg, 0.4 mmol), manganese(IV) oxide (52 mg, 0.6 mmol), copper(II) triflate (21.7 mg, 0.06 mmol), bathophenanthroline (13.3 mg, 0.04 mmol), 4-methylbenzenesulfinic acid sodium salt **2a** (142 mg, 0.8 mmol), water (200 μL), ethanol (200 μL) and acetic acid (200 μL) were combined sequentially to a microwave vial under air and heated to 100 °C for 18 h. The reaction was allowed to cool to room temperature, diluted with EtOAc (2 mL) then filtered through silica eluting with EtOAc (3 × 10 mL) the concentrated *in vacuo*. Purification by flash column chromatography (40% Et_2O:pentane) afforded *α*-sulfonyl aldehyde **12a** as a colourless oil (46.4 mg, 43%). R_f 0.02 (40% Et_2O:pentane). IR (film)/cm^{-1} 2967, 2829, 2862, 1722 (C=O), 1595, 1315, 1245, 1316, 1156, 1103, 950, 816, 664. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (s, 1 H, CHO), 7.62 (d, *J* = 8.4 Hz, 2 H, 2 × Ar–CH), 7.36 (d, *J* = 8.4 Hz, 2 H, 2 × Ar–CH), 3.96 (ddd, *J* = 12.3, 4.7, 1.3 Hz, 2 H, 2 × OC*H*H), 3.24 (ddd, *J* = 12.3, 12.3, 2.4 Hz, 2 H, 2 × OCH*H*), 2.46 (s, 3 H, CH_3), 2.28 (td, *J* = 12.3, 5.4 Hz 2 H, 2 × OCH_2C*H*H), 2.12 (dd, *J* = 13.5, 2.2 Hz, 2 H, 2 × OCH_2CH*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.8 (CHO), 146.0 (Ar–C_q), 131.5 (Ar–C_q), 129.9 (4 × Ar–CH), 71.6 (C_q), 63.7 (2 × CH_2), 25.2 (2 × CH_2), 21.7 (CH_3). HRMS (EI^+) m/z calcd. For $C_{13}H_{16}O_4S$ $[M]^+$: 268.0769; found 268.0774.

Benzyl 4-formyl-4-(4-methylbenzene-1-sulfonyl)piperidine-1-carboxylate (13a)



4-Formyl-N-Cbz-piperidine (101.4 mg, 0.41 mmol), manganese(IV) oxide (52 mg, 0.6 mmol), copper(II) triflate (21.7 mg, 0.06 mmol), bathophenanthroline (13.3 mg, 0.04 mmol), 4-methylbenzenesulfinic acid sodium salt **2a** (142 mg, 0.8 mmol), water (200 μL), ethanol (200 μL) and acetic acid (200 μL) were combined sequentially to a microwave vial under air and heated to 100 °C for 18 h. The reaction was allowed to cool to room temperature, diluted with EtOAc (2 mL) then filtered through silica eluting with EtOAc (3 × 10 mL) then concentrated *in vacuo*. Purification by flash column chromatography (10% acetone:pentane) afforded *α*-sulfonyl aldehyde **13a** a colourless amorphous gum (74.2 mg, 44%). R_f 0.11 (10% acetone:pentane). IR (film)/cm^{-1} 3034, 2956, 2863, 1699 (C=O), 1595, 1431, 1319, 1282, 1237, 1148, 1088, 700, 667. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (s, 1 H, CHO), 7.60 (d, *J* = 8.4 Hz, 2 H, 2 × Ar–CH), 7.44–7.30 (m, 7 H, 7 × Ar–CH), 5.12 (s, 2 H, NCO_2CH_2), 4.21 (s, 2 H, 2 × C*H*H), 2.72 (s, 2 H, 2 × CH*H*), 2.47 (s, 3 H, CH_3), 2.27–2.05 (m, 4 H, 2 × CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.6 (CHO), 154.8 ($C{=}O_{carbamate}$), 146.2 (Ar–C_q), 136.3 (Ar–C_q), 131.5 (Ar–C_q), 129.9 (2 × Ar–CH), 129.8 (2 × Ar–CH), 128.5 (2 × Ar–CH), 128.2 (Ar–CH), 128.0 (2 × Ar–CH), 72.4 (C_q), 67.5 (OCH_2Ph), 40.0 (CH_2), 24.8 (CH_2), 21.7 (CH_3). HRMS (FTMS + p APCI) m/z calcd. For $C_{21}H_{24}NO_5S$ $[M+H_3O]^+$: 402.1370; found 402.1355.

2-Methyl-2-(4-methylbenzene-1-sulfonyl)propanal (14a)

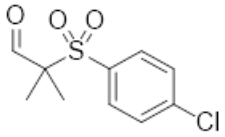


Prepared according to general procedure **C** using isobutyraldehyde (37 μL, 0.4 mmol) and 4-methylbenzenesulfinic acid sodium salt **2a** (142 mg, 0.8 mmol). Purification by flash column chromatography (30% Et_2O:pentane) afforded *α*-sulfonyl aldehyde **14a** as white crystals (34.5 mg, 38%). R_f 0.35 (30% Et_2O:pentane). m.p. = 83–84 °C. IR (film)/cm^{-1} 2986, 2937, 2848, 1729 (C=O), 1595, 1461, 1312, 1133, 1080, 916, 801, 715, 663. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1 H, CHO), 7.66 (d, *J* = 8.2 Hz, 2 H, 2 × Ar–CH), 7.36 (d, *J* = 8.2 Hz, 2 H, 2 × Ar–CH), 2.46 (s, 3 H, CH_3), 1.46 (s, 6 H, $C(CH_3)_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.3 (CHO), 145.7 (Ar–C_q), 132.2 (Ar–C_q), 129.8 (2 × Ar–CH), 129.7 (2 × Ar–CH), 70.9 (C_q), 21.7 (CH_3), 16.7 ($C(CH_3)_2$). HRMS (FTMS + p APCI) m/z calcd. For $C_{11}H_{15}O_3S$ $[M+H]^+$: 227.0736; found 227.0727.

Performed according to general procedure **C** using isobutyraldehyde (92.5 mL, 1 mmol) and 4-methylbenzenesulfinic acid sodium salt **2a** (355 mg, 2 mmol). Purification by flash column chromatography (30% Et_2O:pentane) afforded *α*-sulfonyl aldehyde **14a** as a white solid (162 mg, 71%).

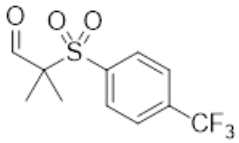
Performed according to general procedure **C** using isobutyraldehyde (546 mL, 6 mmol) and 4-methylbenzenesulfinic acid sodium salt **2a** (2.14 g mg, 12 mmol). Purification by flash column chromatography (30% Et_2O:pentane) afforded α-sulfonyl aldehyde **14a** as a white solid (886 mg, 65%).

2-Methyl-2-(4-chlorobenzene-1-sulfonyl)propanal (14f)



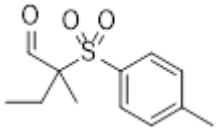
Prepared according to general procedure **C** using isobutyraldehyde (92.5 μL, 1 mmol) and 4-chlorobenzenesulfinic acid sodium salt **S4** (395 mg, 2 mmol). Purification by flash column chromatography (20% Et_2O:pentane) afforded α-sulfonyl aldehyde **14f** as a white solid (71 mg, 29%). R_f 0.14 (30% Et_2O:pentane). m.p. = 99–100 °C. IR (film)/cm^{-1} 2986, 2937, 2848, 1729 (C=O), 1595, 1461, 1312, 1133, 1080, 916, 801, 715, 663. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1 H, CHO), 7.71 (d, *J* = 8.9 Hz, 2 H, 2 × Ar–CH), 7.54 (d, *J* = 8.9 Hz, 2 H, 2 × Ar–CH), 1.47 (s, 6 H, $C(CH_3)_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.8 (CHO), 141.5 (Ar–C_q), 133.5 (Ar–C_q), 131.1 (2 × Ar–CH), 129.5 (2 × Ar–CH), 70.9 (C_q), 16.6 ($C(CH_3)_2$). HRMS (FTMS + p APCI) m/z calcd. For $C_{10}H_{12}O_3SCl$ $[M+H]^+$: 247.0190; found 247.0188.

2-Methyl-2-(4-trifluoromethylbenzene-1-sulfonyl)propanal (14h)



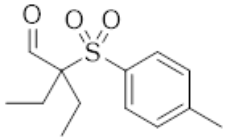
Prepared according to general procedure **C** using isobutyraldehyde (92.5 μL, 1 mmol) and 4-(trifluoromethyl)benzenesulfinic acid sodium salt **2h** (464 mg, 2 mmol). Purification by flash column chromatography (20% Et_2O:pentane) afforded α–sulfonyl aldehyde **14h** as white solid (162 mg, 58%). R_f 0.10 (20% Et_2O:pentane). m.p. = 90–91 °C. IR (film)/cm^{-1} 2982, 2945, 2847, 1743 (C=O), 1726, 1461, 1405, 1293, 1129, 838, 790, 742 ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1 H, CHO), 7.93 (d, *J* = 8.2 Hz, 1 H, 2 × Ar–CH), 7.84 (d, *J* = 8.2 Hz, 1 H, 2 × Ar–CH), 1.50 (s, 6 H, $C(CH_3)_2$).^{13}C NMR (101 MHz, $CDCl_3$) δ 195.6 (CHO), 138.7 (Ar–C_q), 136.1 (q, $^2J_{C-F}$ = 33.2 Hz, Ar–C_q), 130.4 (2 × Ar–CH), 126.3 (q, $^3J_{C-F}$ = 3.8 Hz, 2 × Ar–CH), 125.7 (q, $^1J_{C-F}$ = 270.0 Hz, CF_3), 71.0 (C_q), 16.6 ($C(CH_3)_2$). ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.32. HRMS (EI^+) m/z calcd. For $C_{11}H_{11}O_3F_3S$ $[M]^+$: 280.0376; found 280.0390.

2-Methyl-2-(4-methylbenzene-1-sulfonyl)butanal (15a)



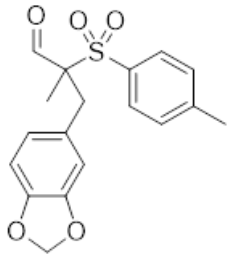
Prepared according to general procedure **C** using 2-methylbutyraldehyde (106 μL, 1 mmol) and 4-methylbenzenesulfinic acid sodium salt **2a** (355 mg, 2 mmol). Purification by flash column chromatography (5–20% Et_2O:Pentane) afforded α-sulfonyl aldehyde **15a** as a yellow solid (176.6 mg, 73%). R_f 0.31 (60% CH_2Cl_2:pentane). m.p. = 62–63 °C. IR (film)/cm^{-1} 2944, 2978, 2885, 1730 (C=O), 1300, 1148, 1080, 820, 719. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1 H, CHO), 7.64 (d, *J* = 8.3 Hz, 2 H, 2 × Ar–CH), 7.35 (d, *J* = 8.3 Hz, 2 H, 2 × Ar–CH), 2.45 (s, 3 H, $ArCH_3$), 2.33 (dq, *J* = 15.1, 7.6 Hz, 1 H, $CHHCH_3$), 1.96 (dq, *J* = 15.1, 7.6 Hz, 1 H, $CHHCH_3$), 1.35 (s, 3 H $CHOCCH_3$), 0.89 (t, *J* = 7.6 Hz, 3 H, CH_2CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.8 (CHO), 145.6 (Ar–C_q), 132.5 (Ar–C_q), 129.8 (2 × Ar–CH), 129.7 (2 × Ar–CH), 74.5 (C_q), 22.5 ($ArCH_3$), 21.7 (CH_3), 12.5 (CH_2CH_3), 7.9 (CH_2CH_3). HRMS (TOF-ESI^+) m/z calcd. for $C_{12}H_{17}O_3S$ $[M+H]^+$: 241.0898; found: 241.0903.

2-Ethyl-2-(4-methylbenzene-1-sulfonyl)butanal (16a)



Prepared according to general procedure **C** using 2-ethylbutyraldehyde (49 μL, 0.4 mmol) and 4-methylbenzenesulfinic acid sodium salt **2a** (142 mg, 0.8 mmol). Purification by flash column chromatography (20% Et_2O:pentane) afforded α-sulfonyl aldehyde **16a** as a colourless oil (49.5 mg, 49%). R_f 0.35 (20% Et_2O:pentane). IR (film)/cm^{-1} 2974, 2945, 1726 (C=O), 1595, 1434, 1315, 1148, 1126, 1080, 816, 738. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1 H, CHO), 7.61 (d, *J* = 8.0 Hz, 1 H, 2 × Ar–CH), 7.35 (d, *J* = 8.0 Hz, 2 H, 2 × Ar–CH), 2.45 (s, 3 H, CH_3), 2.03 (dq, *J* = 15.0, 7.6 Hz, 4 H, 2 × CH_2), 1.00 (t, *J* = 7.6 Hz, 6 H, 2 × CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.5 (CHO), 145.5 (Ar–C_q), 132.9 (Ar–C_q), 129.8 (2 × Ar–CH), 129.4 (2 × Ar–CH), 21.7 ($ArCH_3$), 19.0 (2 × CH_2), 7.6 (2 × CH_3).* (EI^+) m/z calcd. For $C_{13}H_{18}O_3SNa$ $[M+Na]^+$: 277.0874; found 277.0863.*quaternary carbon adjacent to aldehyde is underneath chloroform peak.

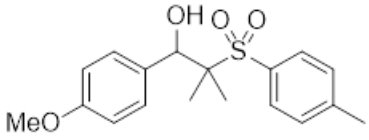
3-(Benzo[d][1,3]dioxol-5-yl)-2-methyl-2-(4-methylbenzene-1-sulfonyl)propanal (17a)



Manganese(IV) oxide (52 mg, 0.6 mmol), copper(II) triflate (21.7 mg, 0.06 mmol), bathophenanthroline (13.3 mg, 0.04 mmol), 4-methylbenzenesulfinic acid sodium salt **2a** (142 mg, 0.8 mmol), 2-Methyl-3-(3,4-methylenedioxyphenyl)propanal (66 μL, 0.4 mmol), water (200 μL), ethanol (200 μL) and acetic acid (200 μL) were combined sequentially to a microwave vial under air and heated to 100 °C for 18 h. The reaction was allowed to cool to room temperature, basified by the addition of a saturated solution of $NaHCO_{3\,(aq)}$ (1 mL) and the product extracted with CH_2Cl_2 (3 × 10 mL), dried over Na_2SO_4, filtered and then the concentrated *in vacuo*. **[NOTE:** When purifying this compound at this scale, a short plug of silica (5 cm in height in a 2.5 cm diameter column) was used and a rapid column was employed as product instability was observed.**]** Purification by flash column chromatography (30% Et_2O: pentane) afforded *α*-sulfonyl aldehyde **17a** a yellow solid (67.8 mg, 49%). R_f 0.16 (30% Et_2O:pentane) m.p. = 161–165 °C. IR (film)/cm^{-1} 3053, 2900, 2777, 1714 (C=O), 1595, 1487, 1442, 1297, 1241, 1140, 872, 813, 727. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1 H, CHO), 7.66 (d, *J* = 8.4 Hz, 2 H, 2 × Ar–CH), 7.37 (d, *J* = 7.9 Hz, 2 H, 2 × Ar–CH), 6.69 (d, *J* = 8.5 Hz, 1 H, Ar–CH), 6.58–6.48 (m, 2 H, 2 × Ar–CH), 5.93 (d, *J* = 1.5 Hz, 1 H, OC*H*HO), 5.92 (d, *J* = 1.5 Hz, 1 H, OCH*H*O), 3.71 (d, *J* = 13.8 Hz, 1 H, C*H*HAr), 3.08 (d, *J* = 13.8 Hz, 1 H, CH*H*Ar), 2.47 (s, 3 H, C_qCH_3), 1.26 (s, 3 H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.4 (CHO), 147.7 (Ar–C_q), 147.0 (Ar–C_q), 145.8 (Ar–C_q), 132.2 (Ar–C_q), 129.9 (4 × Ar–CH), 126.8 (Ar–C_q), 123.7 (Ar–CH), 110.5 (Ar–CH), 108.4 (Ar–CH), 101.1 (OCH_2O), 74.7 (C_q), 35.0 (CH_3), 21.7 (CH_2), 13.5 (C_qCH_3). HRMS (FTMS + p APCI) m/z calcd. For $C_{18}H_{18}O_5S$ $[M]^{+\bullet}$: 346.0869; found 346.0868.

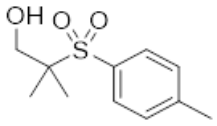
Derivatisation of Sulfonyl Aldehydes

1-(4-Methoxyphenyl)-2-methyl-2-(4-methylphenylsulfonyl)propan-1-ol (18)



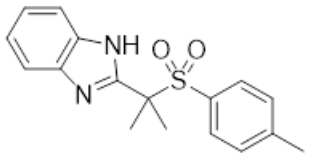
(4-Methoxyphenyl)magnesium bromide in THF (0.45 mL, 0.49 M) was added dropwise at 0 °C to a stirring solution of sulfonyl aldehyde **14a** (45 mg, 0.2 mmol) in THF (0.4 mL) and allowed to warm to rt overnight. the reaction was quenched by the addition of a saturated solution of $NH_4Cl_{(aq)}$ and the product extracted with CH_2Cl_2 (3 × 10 mL), dried over Na_2SO_4, filtered, then concentrated *in vacuo*. Purification by flash column chromatography (20% Et_2O:pentane) afforded alcohol **18** as a colourless oil (51.7 mg, 77%). R_f 0.08 (20% Et_2O:pentane). IR (film)/cm^{-1} 3448 (O–H), 2937, 1607, 1509, 1461, 1278, 1248, 1073, 1025, 865, 839, 780, 771, 686. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.3 Hz, 2 H, 2 × Ar–CH), 7.42 (d, *J* = 8.3 Hz, 2 H, 2 × Ar–CH), 7.22 (d, *J* = 8.8 Hz, 2 H, 2 × Ar–CH), 6.84 (d, *J* = 8.8 Hz, 2 H, 2 × Ar–CH), 5.13 (s, 1 H, OH), 4.28 (d, *J* = 1.1 Hz, 1 H, OHC*H*), 3.79 (s, 3 H, OCH_3), 2.49 (s, 3 H, $ArCH_3$), 1.39 (s, 3 H, $CCH_3(CH_3)$), 0.92 (s, 3 H, $CCH_3(CH_3)$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5 (Ar–C_q), 145.3 (Ar–C_q), 131.9 (Ar–C_q), 130.5 (2 × Ar–CH), 130.1 (Ar–C_q), 129.7 (2 × Ar–CH), 129.1 (2 × Ar–CH), 113.3 (2 × Ar–CH), 74.3 (OHCH), 66.6 (C_q), 55.2 (OCH_3), 21.7 ($CCH_3(CH_3)$), 21.6 ($CCH_3(CH_3)$), 13.8 ($ArCH_3$). HRMS (FTMS–pAPCI) m/z calcd. For $C_{18}H_{22}O_4SNa$ $[M+Na]^+$: 357.1137; found 357.1139.

2-Methyl-2(4-methylbenzene-1-sulfonyl)propan-1-ol (19)



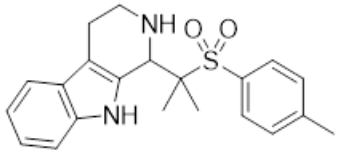
Sodium borohydride (23 mg, 0.6 mmol) was added to a stirred solution of **14a** (45 mg, 0.2 mmol) in ethanol (1 mL) at 0 °C. After 2 h, the reaction was quenched by the addition of water (10 mL), the product extracted from the aqueous phase with CH_2Cl_2 (3 × 10 mL) then dried over Na_2SO_4, filtered and concentrated in vacuo which afforded alcohol **19** as white crystals (23.7 mg, 52%). R_f 0.09 (30% Et_2O:hexane). m.p. = 89–90 °C. IR (film)/cm^{-1} 3503 (O–H), 2981, 2937, 2877, 1595, 1282, 1125, 1080, 816, 715, 682. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.2 Hz, 2 H, 2 × Ar–CH), 7.38 (d, *J* = 8.2 Hz, 2 H, 2 × Ar–CH), 3.72 (s, 2 H, CH_2), 2.48 (s, 3 H, $ArCH_3$), 1.30 (s, 6 H, $C(CH_3)_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.2 (Ar–C_q), 131.8 (Ar–C_q), 130.1 (2 × Ar–CH), 129.7 (2 × Ar–CH), 66.3 (CH_2), 62.8 (C_q), 21.6 ($ArCH_3$), 19.2 ($C(CH_3)_2$). HRMS (ESI^+) m/z calcd. For $C_{11}H_{17}O_3S$ $[M+H]^+$: 229.0989; found 229.0904.

2-(2-(4-Methylphenylsulfonyl)propan-2-yl)-1H-benzo[d]imidazole (20)



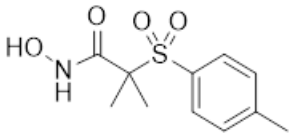
Using adapted procedure from Naali.[9] **14a** (45 mg, 0.2 mmol), *o*-phenylene diamine (22 mg, 0.2 mmol), CAN (11 mg, 0.02 mmol), MeCN (0.1 M) and H_2O_2 (30% w/w in H_2O, 0.2 mL, 0.8 mmol) were added sequentially to a microwave vial under air, sealed and heated to 50 °C for 18 h. The reaction was diluted with water then the product was extracted with CH_2Cl_2 (3 × 10 mL), the organic phase was dried over Na_2SO_4, filtered then concentrated *in vacuo.* Purification by flash column chromatography (40% Et_2O:pentane) afforded benzimidazole **20** as yellow crystals (48.5 mg, 77%). m.p. = 210–211 °C. R_f 0.08 (40% Et_2O:pentane). IR (film)/cm^{-1} 3299 (N–H), 3034, 2989, 2963, 1621, 1520, 1443, 1416, 1155, 1282, 1121, 1073, 910, 816, 742, 712. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.69 (s, 1 H, NH), 7.66 (d, *J* = 7.9 Hz, 1 H, Ar–CH), 7.52 (d, *J* = 7.9 Hz, 1 H, Ar–CH), 7.30 (d, *J* = 8.3 Hz, 2 H, 2 × Ar–CH), 7.25 (d, *J* = 8.0 Hz, 2 H, 2 × Ar–CH), 7.14 (d, *J* = 8.0 Hz, 2 H, 2 × Ar–CH), 2.35 (s, 3 H, CH_3), 1.93 (s, 6 H, $C(CH_3)_2$).^{13}C NMR (101 MHz, $CDCl_3$) δ 150.3 (NC_qNH), 145.4 (Ar–CH), 142.1 (Ar–C_q), 134.4 (Ar–C_q), 131.0 (Ar–CH), 129.5 (4 × Ar–CH), 123.8 (Ar–CH), 122.3 (Ar–CH), 119.7 (Ar–C_q), 111.3 (Ar–C_q), 63.9 (C_q), 21.6 (CH_3), 21.4 ($C(CH_3)_2$). HRMS (ESI^+) m/z calcd. For $C_{17}H_{19}N_2O_2S$ $[M+H]^+$: 315.1167; found 315.1162.

1-(2-(4-Methylbenzene-1-sulfonyl)propan-2-yl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole (21)



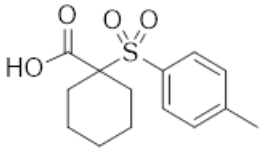
Using a method adapted from Chen.[10] Tryptamine (32 mg, 0.2 mmol), **14a** (45 mg, 0.2 mmol), CH_2Cl_2 (0.32 mL) were added sequentially to a microwave vial, followed by trifluoroacetic acid (50 μL) at rt. The reaction was monitored by TLC (≈2 h) after which the reaction was neutralised by the addition of a saturated aqueous solution of $NaHCO_3$ (1 mL) and the product was extracted with CH_2Cl_2 (3 × 5 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo.* Purification by flash column chromatography (50–100% EtOAc:Pentane) afforded sulfone **21** as a yellow oil (17.5 mg, 24%). R_f 0.5 (EtOAc). IR (film)/cm^{-1} 3373 (N–H), 3056, 2986, 2933, 2840, 1621, 1461, 1282, 1148, 1118, 1073, 816, 738. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1 H, NH), 7.89–7.79 (d,*J* = 8.0 Hz, 2 H, 2 × Ar–CH), 7.52 (dd, *J* = 7.8, 1.1 Hz, 1 H, Ar–CH), 7.48–7.36 (m, 3 H, 3 × Ar–CH), 7.20 (ddd, *J* = 8.0, 7.0, 1.2 Hz, 1 H, Ar–CH), 7.15–7.07 (m, 1 H, Ar–CH), 4.79 (s, 1 H, C*H*NH), 3.23–3.13 (ddd, *J* = 12.3, 12.3, 5.3 Hz, 1 H, CH_2CHHNH), 3.07 (ddd, *J* = 12.3, 6.7, 5.2 Hz, 1 H, CH_2CHHNH), 2.77 (m, 2 H, C$H_2$$CH_2$NH), 2.48 (s, 3 H, CH_3), 1.46 (s, 3 H, CH_3), 1.25 (s, 3 H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.2 (Ar–C_q), 135.4 (Ar–C_q), 132.0 (Ar–C_q), 131.2 (Ar–C_q), 130.7 (2 × Ar–CH), 129.7 (2 × Ar–CH), 126.8 (Ar–C_q), 121.8 (Ar–CH), 118.9 (Ar–CH), 117.9 (Ar–CH), 111.29 (Ar–CH), 111.25 (Ar–C_q) 68.5 (C_q), 53.3 (CHNH), 42.9 (CH_2*C*H_2NH), 22.5 (*C*$H_2$$CH_2$NH), 22.2 ($CH_3$), 21.7 ($CH_3$), 19.1 ($CH_3$). HRMS (ESI$^+$)m/z calcd. For $C_{21}H_{25}O_2S$ $[M+H]^+$: 369.1637; found 369.1635.

N-Hydroxy-2-methyl-2-(4-methylphenylsulfonyl)propanamide (22)



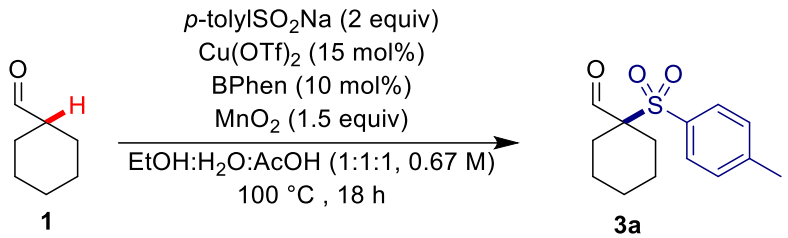
Using a method adapted from De Luca.[11] Sulfonyl aldehyde **14a** (45 mg, 0.2 mmol) was added to a stirring solution of *N*-hydroxysuccinimide (24 mg, 0.21 mmol) and diacetoxyiodobenzene (70.8 mg, 0.21 mmol) in MeCN (0.28 mL) at 0 °C and stirred for 2 h. Hydroxyamine hydrochloride (50% w/w in H_2O, 0.4 mmol) was added and the reaction stirred overnight at rt. The reaction was concentrated *in vacuo*. Purification by flash column chromatography (20% Et_2O:pentane) afforded hydroxamic acid **22** as a white powder (15.9 mg, 31%). m.p. = 145–150 °C. R_f 0.20 (20% Et_2O:pentane). IR (film)/cm^{-1} 3396 (O–H), 3045, 2989, 2937, 1595, 1409, 1274, 1151, 1125, 1080, 968, 842, 812, 715. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 2 H, 2 × Ar–CH), 7.55 (s, 1 H, OH), 7.35 (m, 3 H, NH + 2 × Ar–CH), 2.46 (s, 3 H, CH_3), 1.50 (s, 6 H, C(CH_3)$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.1 (C=O), 145.1 (Ar–C_q), 131.9 (Ar–C_q), 130.3 (2 × Ar–CH), 129.4 (2 × Ar–CH), 63.8 (C_q), 21.7 (CH_3), 19.4 (C(*C*H_3)$_2$). HRMS (FTMS-pAPCI) m/z calcd. For $C_{11}H_{16}NO_4S$ $[M+H]^+$: 258.0795; found 258.0805.

1-(4-Methylphenylsulfonyl)cyclohexane-1-carboxylic acid (23)

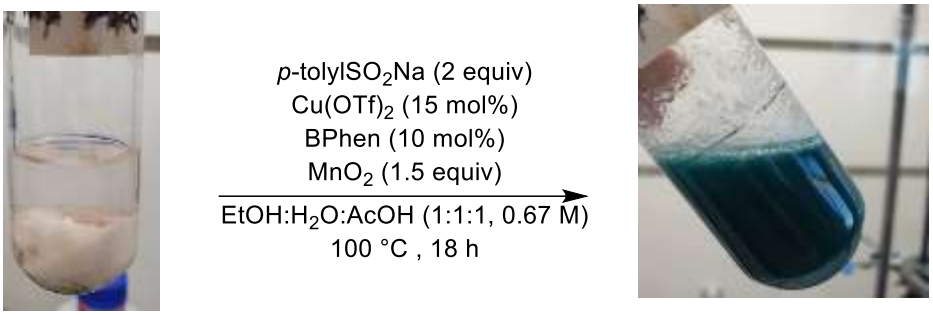


Using method adapted from Montanari.[12] Hydrogen peroxide (30% w/w in H_2O, 102 μL, 1 mmol) and NaH_2PO_4 (261.8 mg, 2.2 mmol) in H_2O (1 mL) were added to a stirring solution of sulfonyl aldehyde **14a** (133 mg, 0.5 mmol) in MeCN (4 mL). $NaClO_2$ (180 mg, 2 mmol) in H_2O (1.6 mL) was added to the stirring solution at 0 °C. The reaction was stirred for 1.5 h, allowing the solution to slowly warm to rt. $Na_2S_2O_3$ was added to quench any unreacted $NaClO_2$ and H_2O_2, then the reaction was acidified by the addition of aqueous 1 M HCl and the product extracted with EtOAc (3 × 10 mL) and concentrated *in vacuo* to afford sulfonyl acid **23** as a white solid (124.4 mg, 88%). m.p. = 175–179 °C. IR (film)/cm^{-1} 3045, 2937, 2858, 2546 (O–H, br), 1692 (C=O), 1595, 1312, 1264, 1148, 973, 820, 715. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.3 Hz, 2 H, 2 × Ar–CH), 7.35 (d, *J* = 8.3 Hz, 2 H, 2 × Ar–CH), 2.46 (s, 3 H, CH_3), 2.36 (d, *J* = 13.0 Hz, 2 H, 2 × C_qC*H*H), 1.93–1.80 (m, 4 H, 2 × C_qCH*H* + 2 × $C_q$$CH_2$C*H*H), 1.69 (d, *J* = 11.6 Hz, 1 H, $C_q$$CH_2$$CH_2$C*H*H), 1.39–1.15 (m, 3 H, 2 × $C_q$$CH_2$CH*H* + $C_q$$CH_2$$CH_2$CH*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3 (C=O), 145.5 (Ar–C_q), 131.9 (Ar–C_q), 130.4 (2 × Ar–CH), 129.5 (2 × Ar–CH), 74.0 (C_q), 28.1 (2 × CH_2) , 24.5 (CH_2), 23.0 (2 × CH_2), 21.7 (CH_3). HRMS (FTMS–pAPCI) m/z calcd. For $C_{14}H_{17}O_4S$ $[M-H]^-$: 281.0842; found 281.0851.

Gram Scale Synthesis

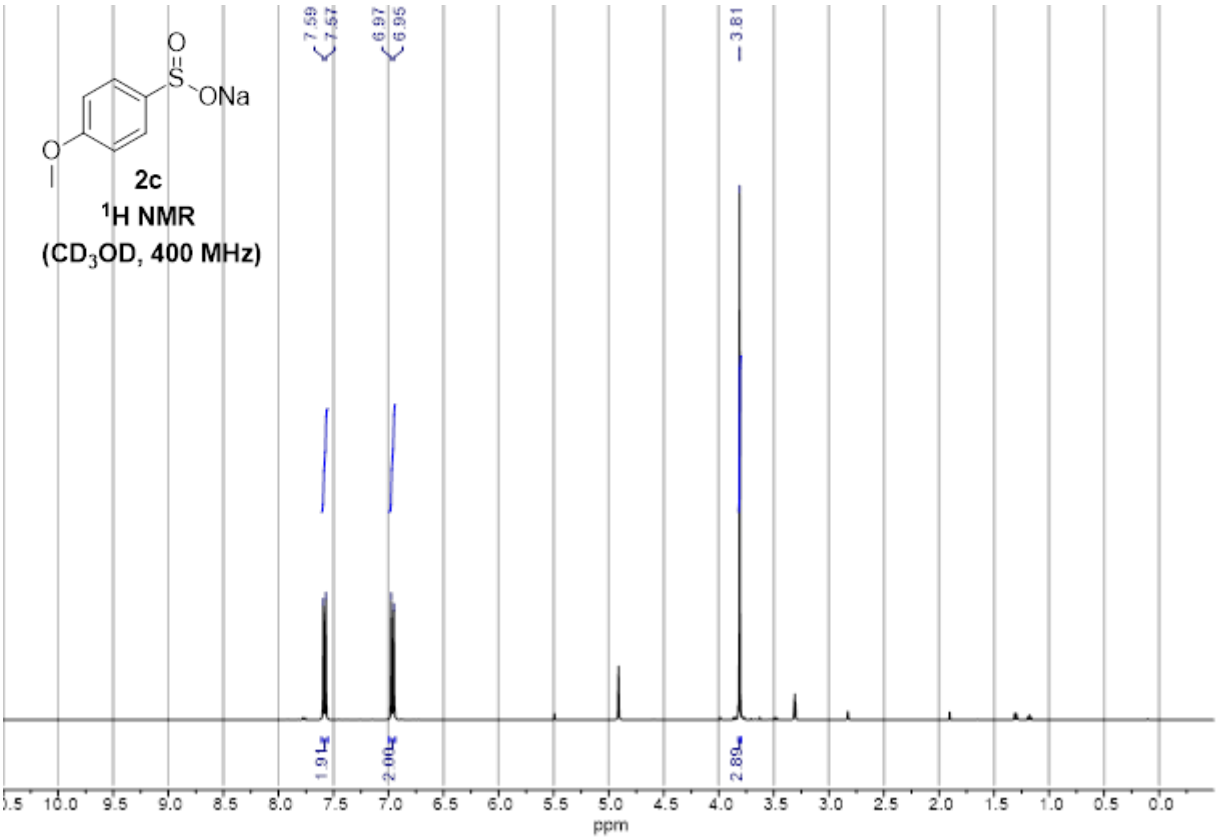


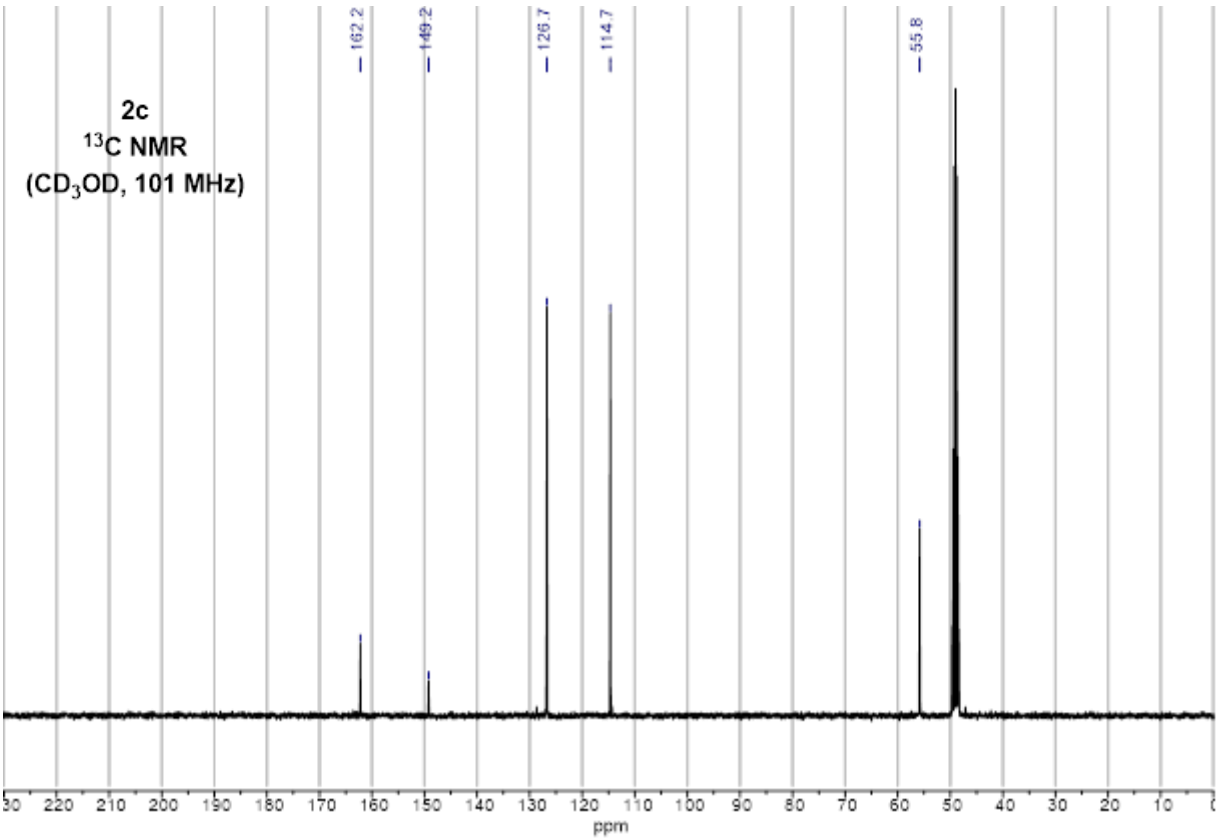
Manganese(IV) oxide (786.2 mg, 9 mmol), copper(II) triflate (324.7 mg, 0.9 mmol), Bathophenanthroline (199.2 mg, 0.6 mmol), 4-methylbenzenesulfinic acid sodium salt **2a** (2.14 g, 12 mmol), cyclohexane carboxaldehyde (726 μL, 6 mmol), H_2O (3 mL), EtOH (3 mL) and AcOH (3 mL) were added sequentially to a 25 mL microwave vial under air, sealed and submerged in an oil bath preheated to 100 °C for 18 h so that the level of the oil was the same as the level of the solvent in the reaction. [**NOTE:** in the course of the reaction, a white precipitate forms early in the reaction (≈1 h) which can interfere with stirring, an increased stirring rate (1000 rpm) was employed to ensure constant stirring. In the majority of cases, the precipitate re-dissolves over the course of the reaction.]. The reaction was allowed to cool to room temperature, diluted with EtOAc (10 mL), filtered through silica eluting with EtOAc (3 × 10 mL) then concentrated *in vacuo*. Purification by flash column chromatography (5–20% Et_2O:pentane) afforded *α*-sulfonyl aldehyde **3a** as a yellow solid (1.36 g, 85%).

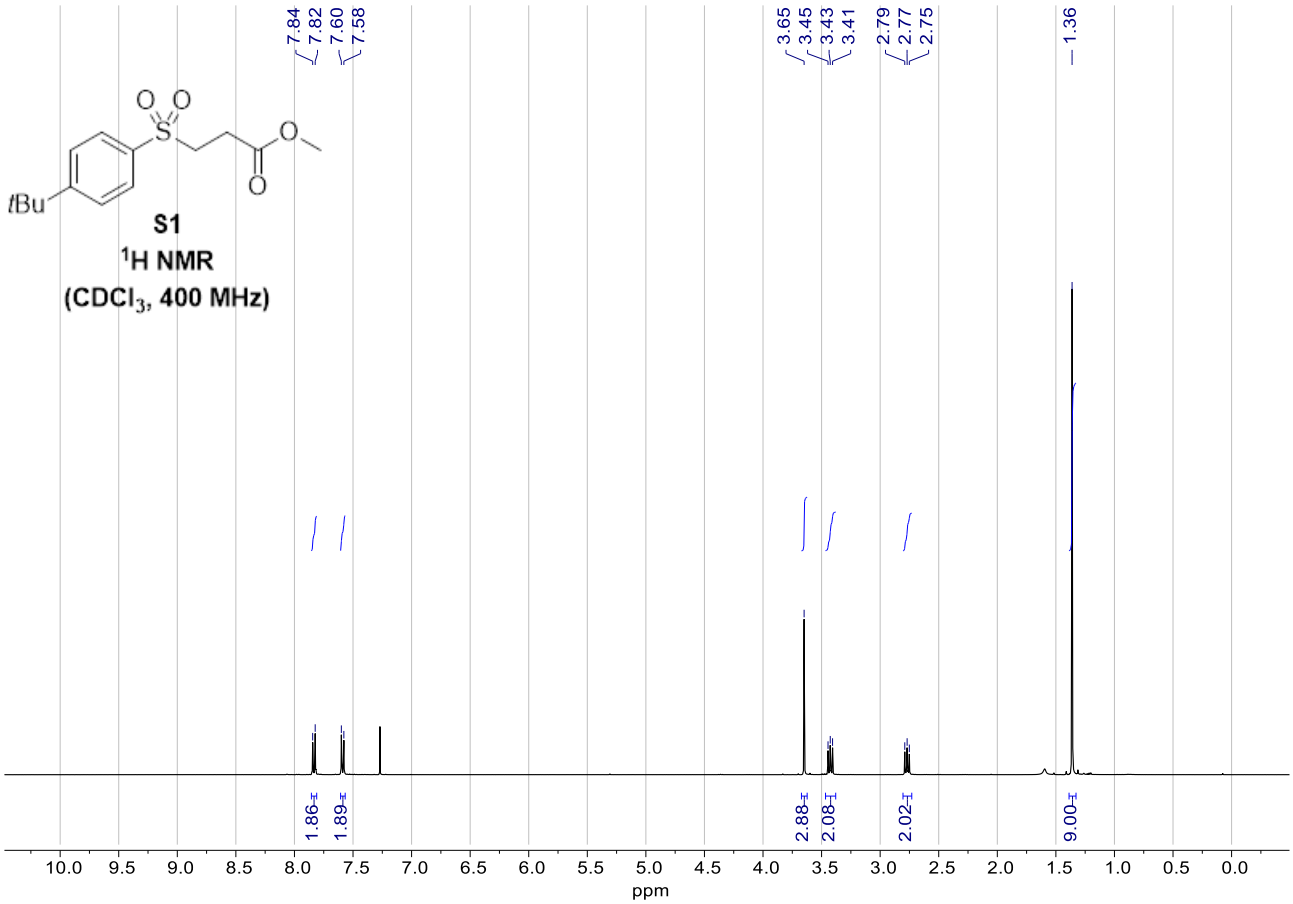


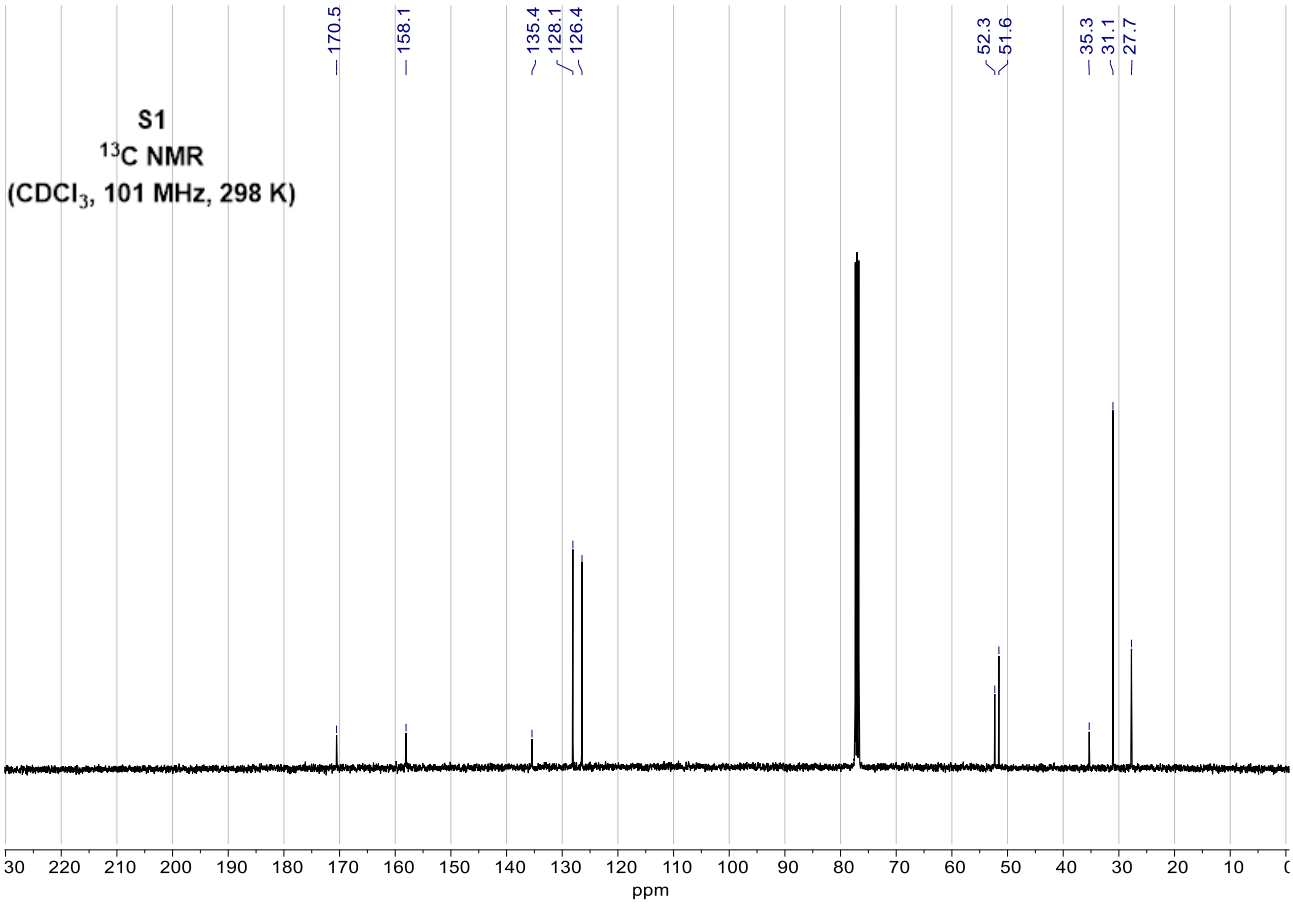
From left to right: Reaction mixture after addition of aldehyde and solvents. Reaction mixture after heating to 100 °C for 18 h.

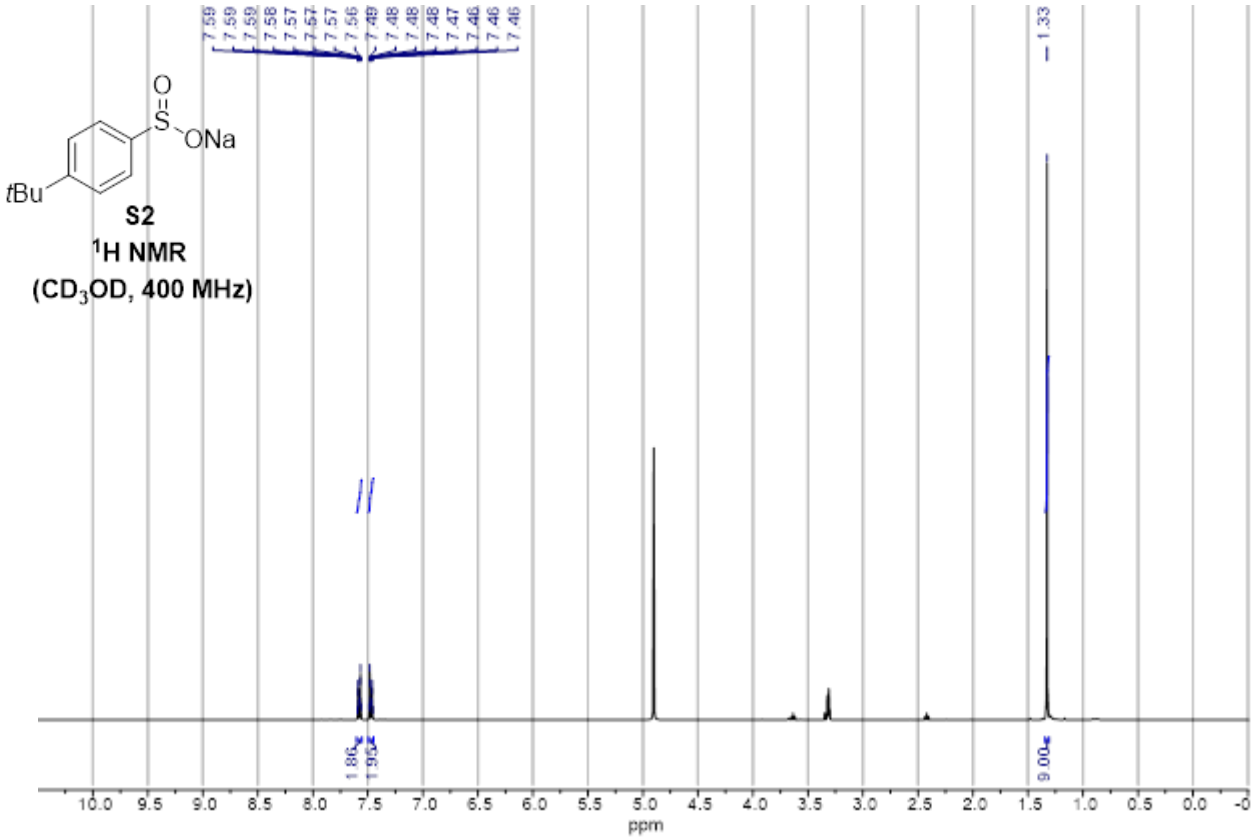
^{1}H and ^{13}C Spectra of Selected Compounds

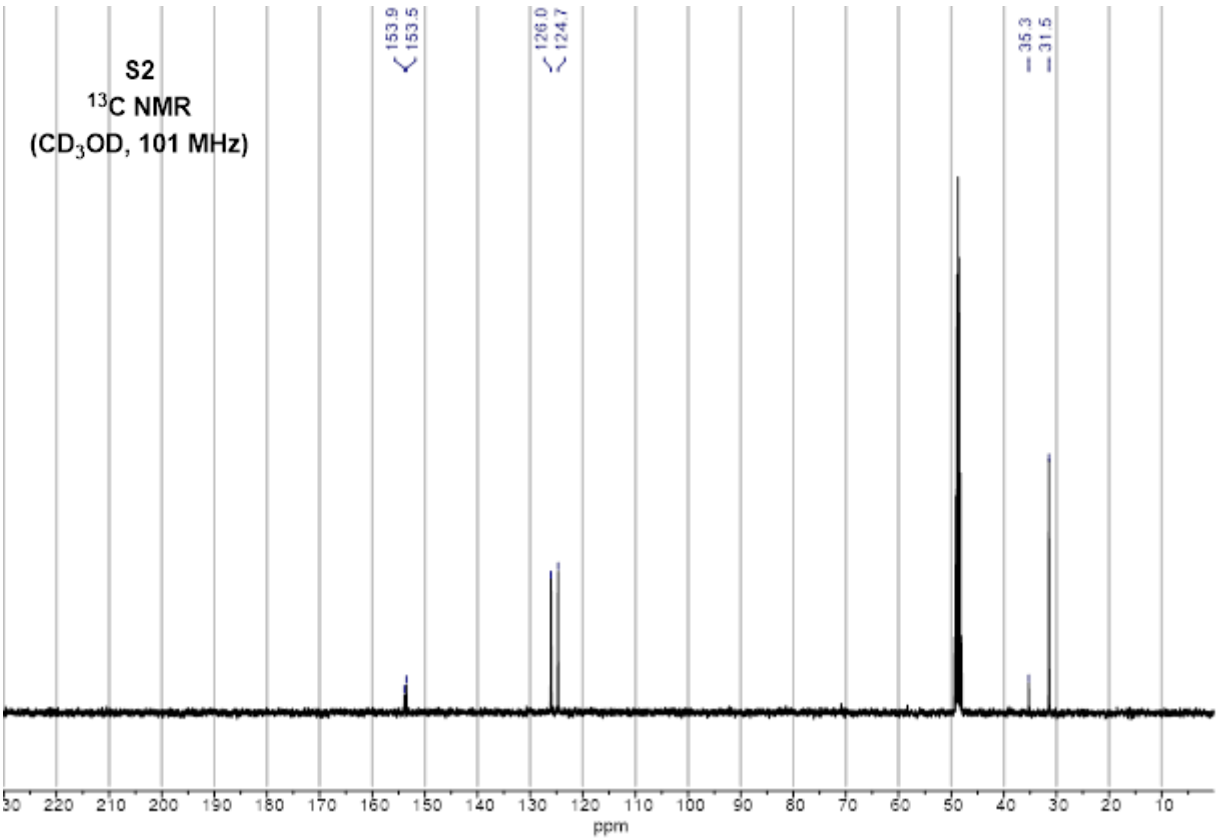

2c
^{1}H NMR
(CD$_3$OD, 400 MHz)
7.59
7.57
6.97
6.95
3.81
1.91
2.00
2.89
ppm

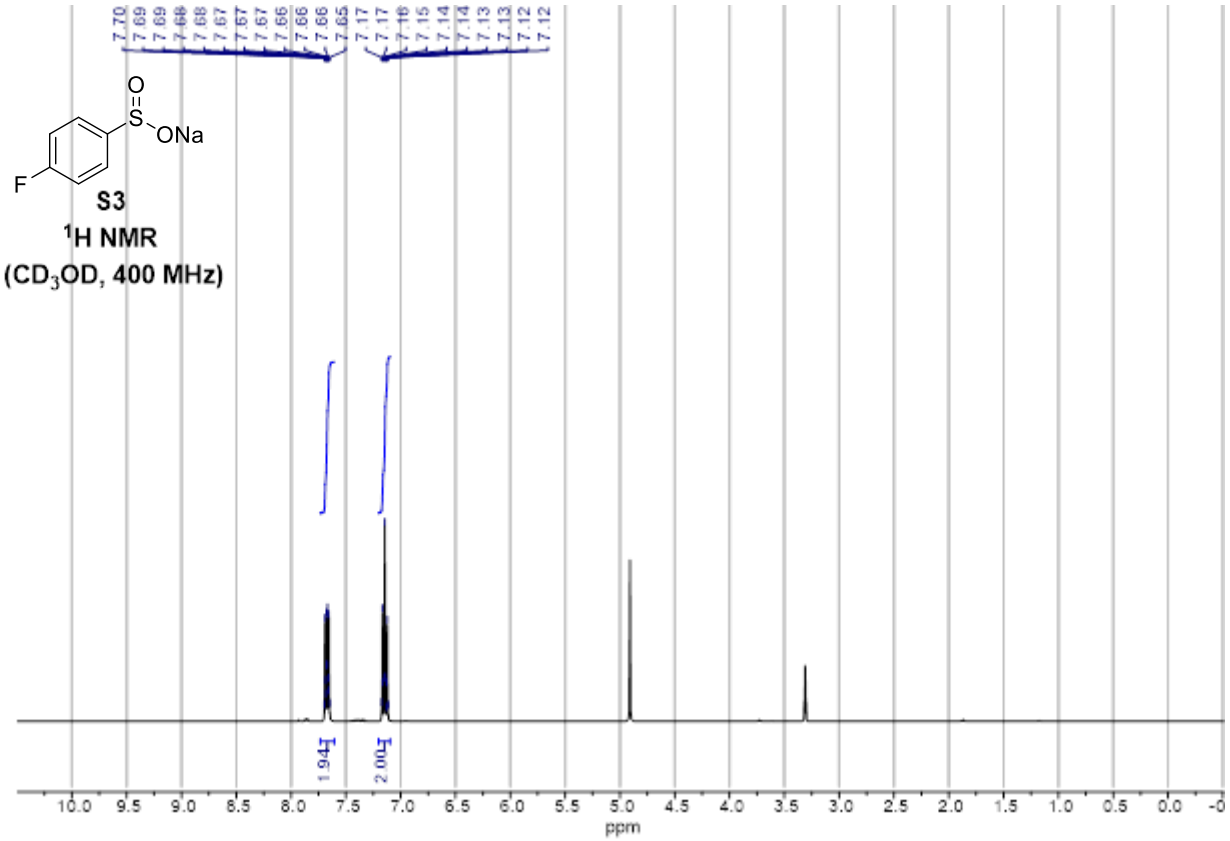

2c
^{13}C NMR
(CD$_3$OD, 101 MHz)
162.2
149.2
126.7
114.7
55.8
ppm

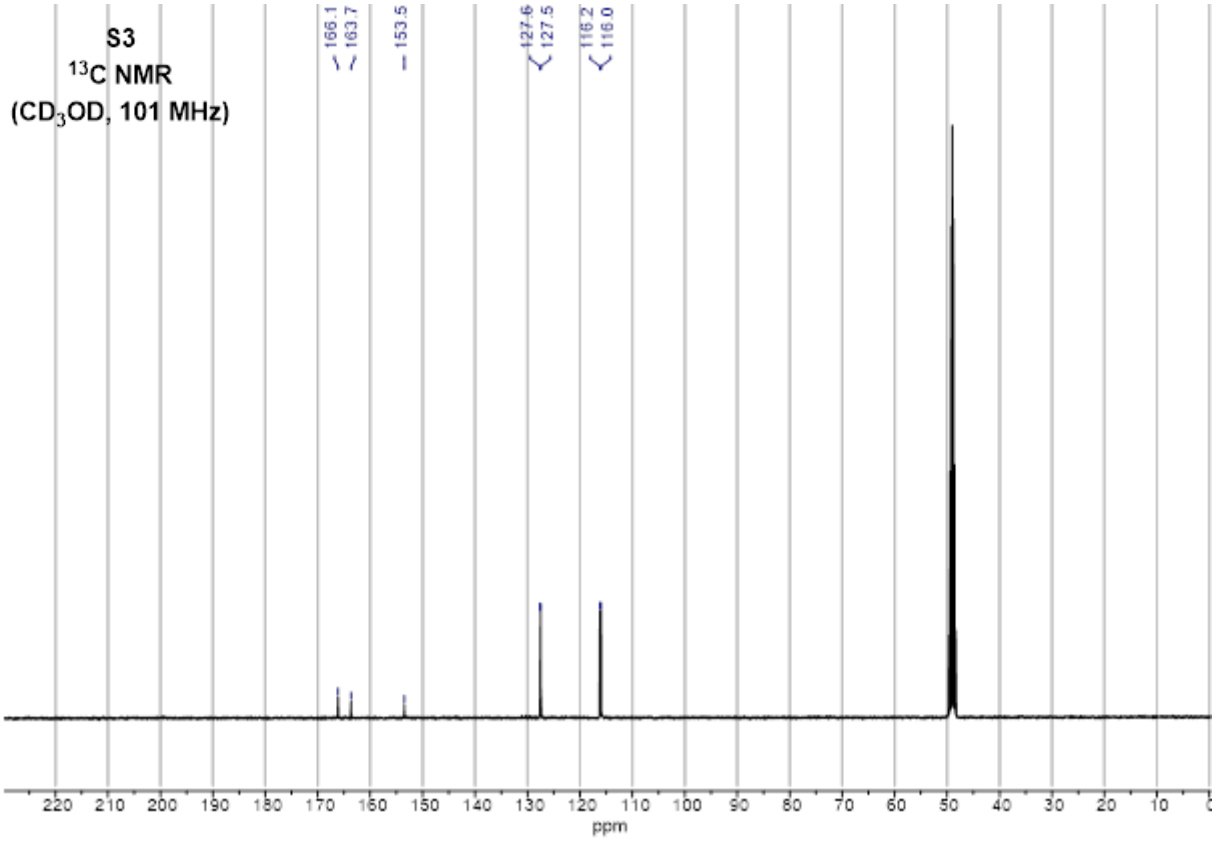

7.84
7.82
7.60
7.58
3.65
3.45
3.43
3.41
2.79
2.77
2.75
1.36
tBu
S1
1H NMR
(CDCl3, 400 MHz)
1.86
1.89
2.88
2.08
2.02
9.00
ppm

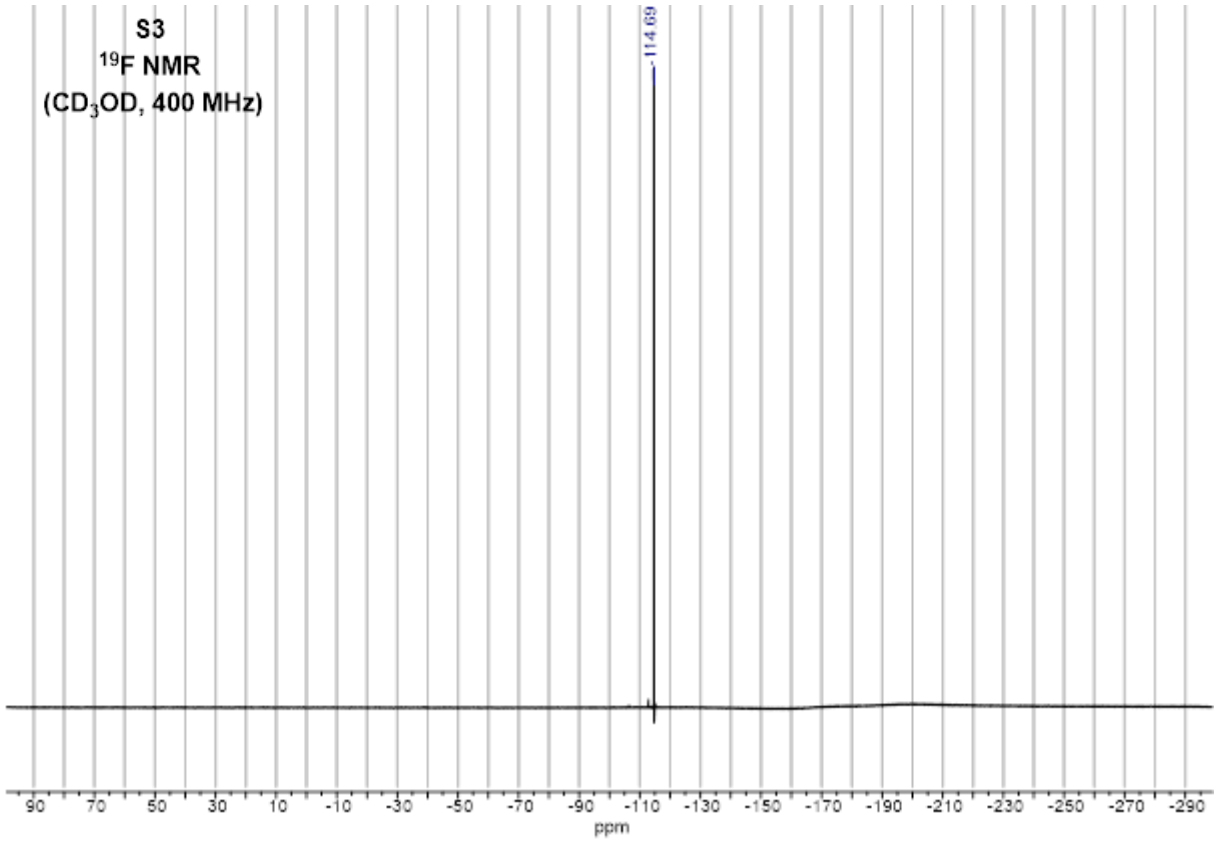

170.5
158.1
135.4
128.1
126.4
52.3
51.6
35.3
31.1
27.7
S1
13C NMR
(CDCl3, 101 MHz, 298 K)
ppm

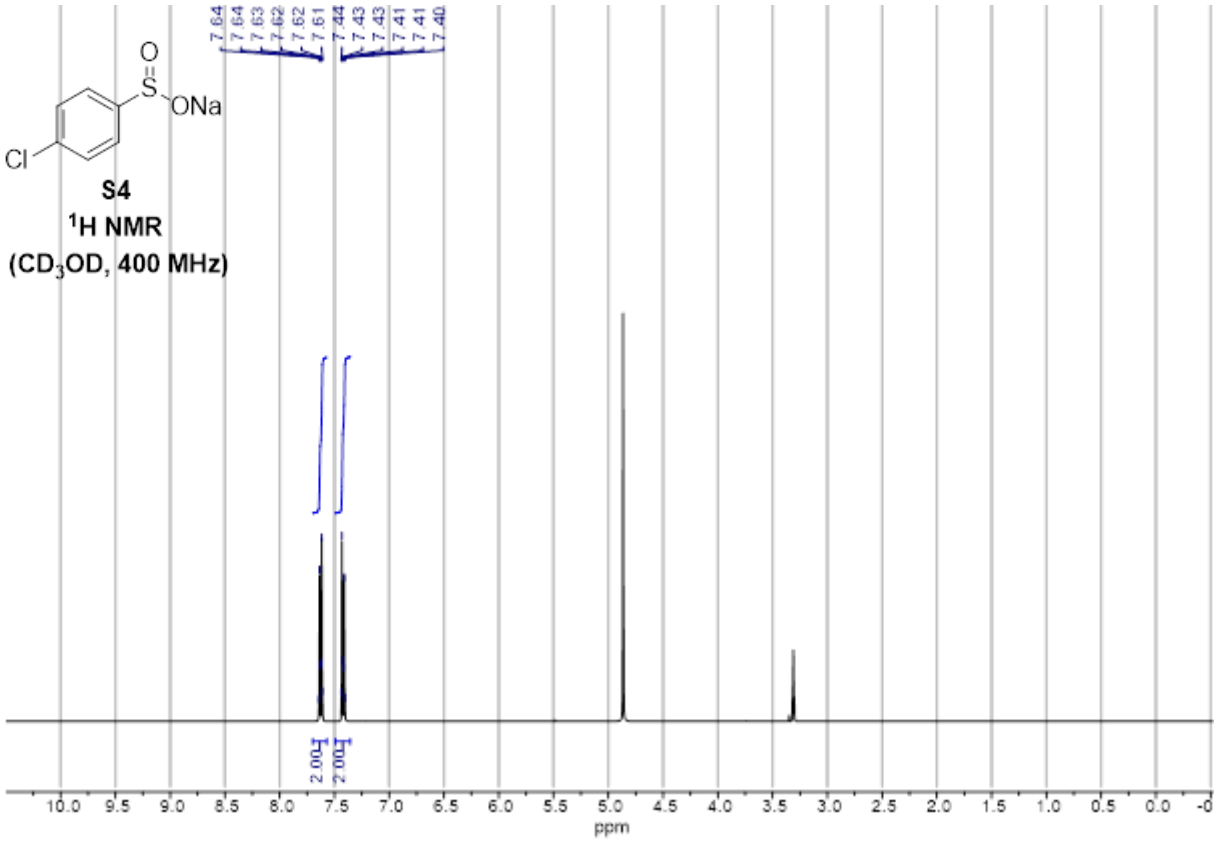

tBu
S
O
ONa
S2
1H NMR
(CD3OD, 400 MHz)
7.59
7.59
7.59
7.58
7.57
7.57
7.57
7.56
7.49
7.48
7.48
7.48
7.47
7.46
7.46
7.46
1.33
1.86
1.95
9.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

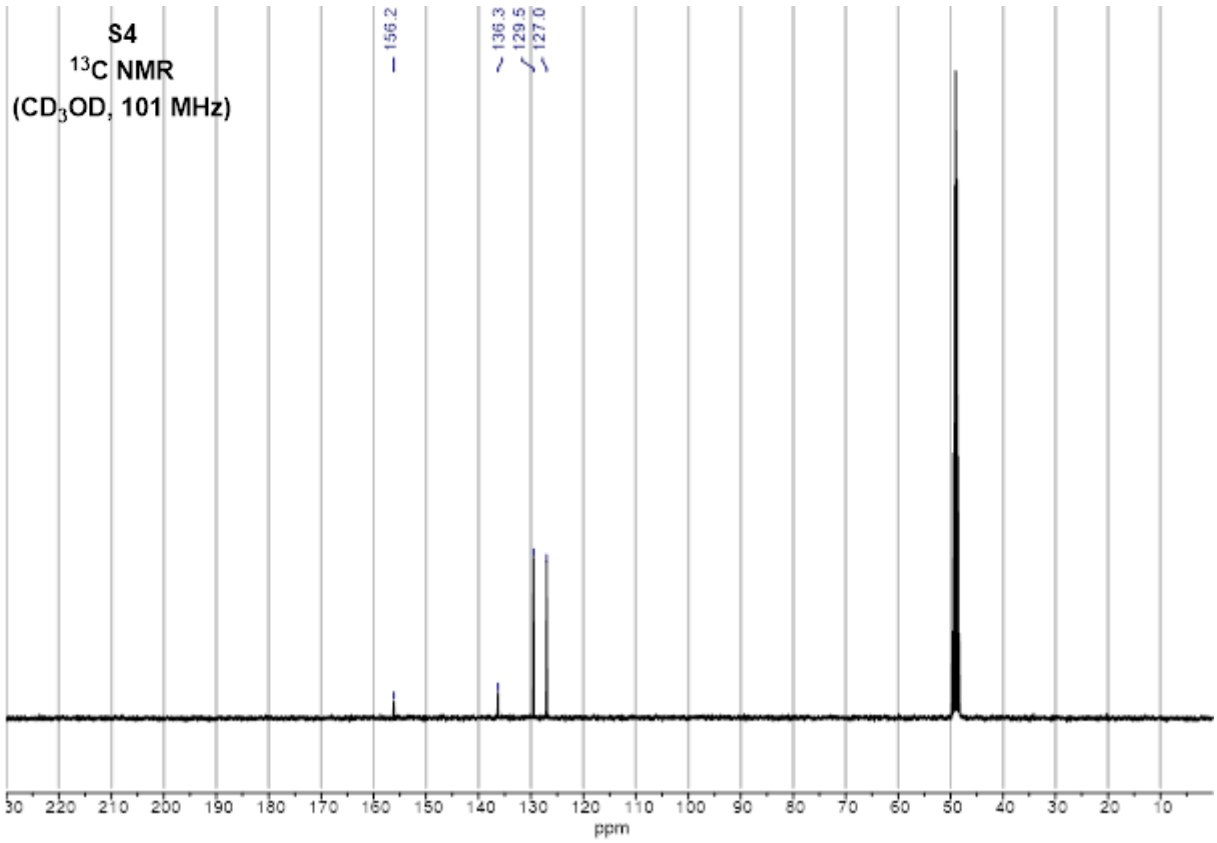

S2
13C NMR
(CD3OD, 101 MHz)
153.9
153.5
126.0
124.7
35.3
31.5
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

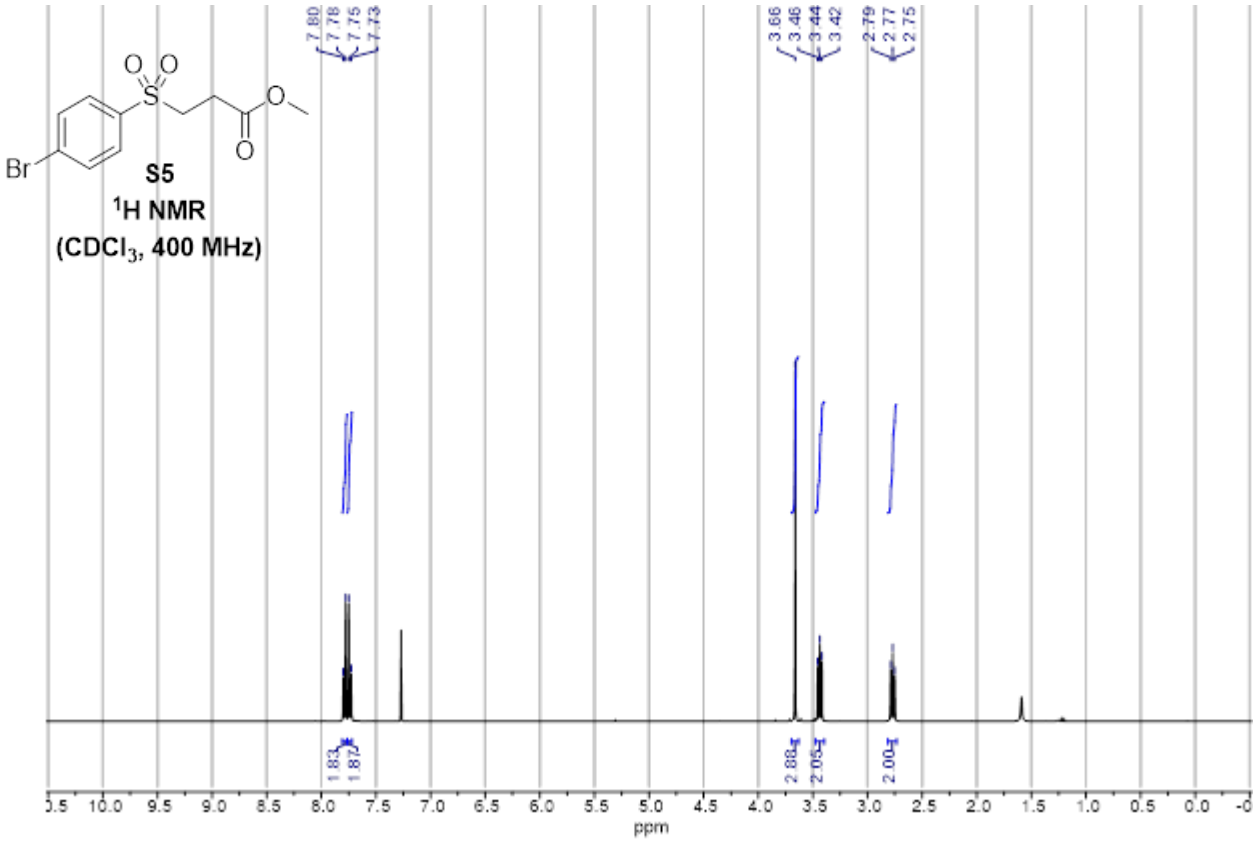

S3
^{1}H NMR
(CD$_3$OD, 400 MHz)
ppm

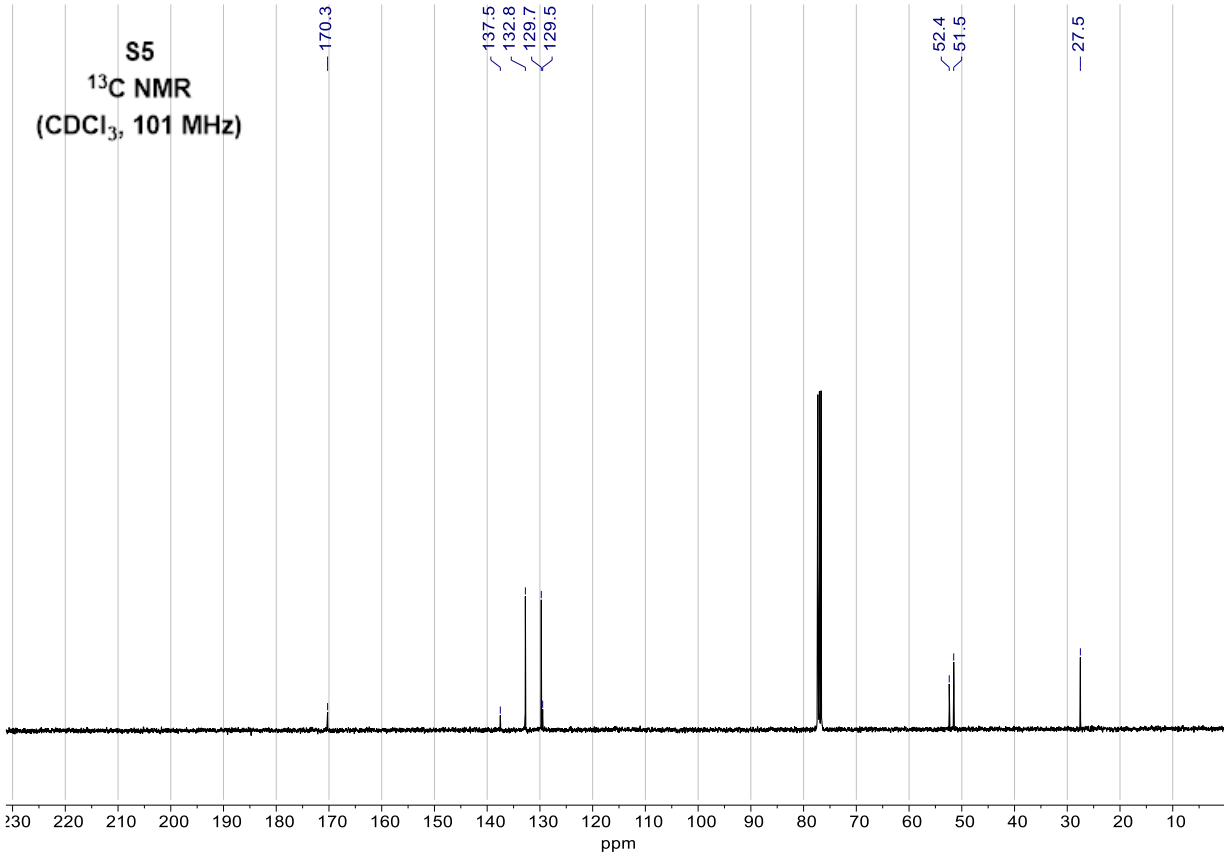

S3
^{13}C NMR
(CD$_3$OD, 101 MHz)
ppm

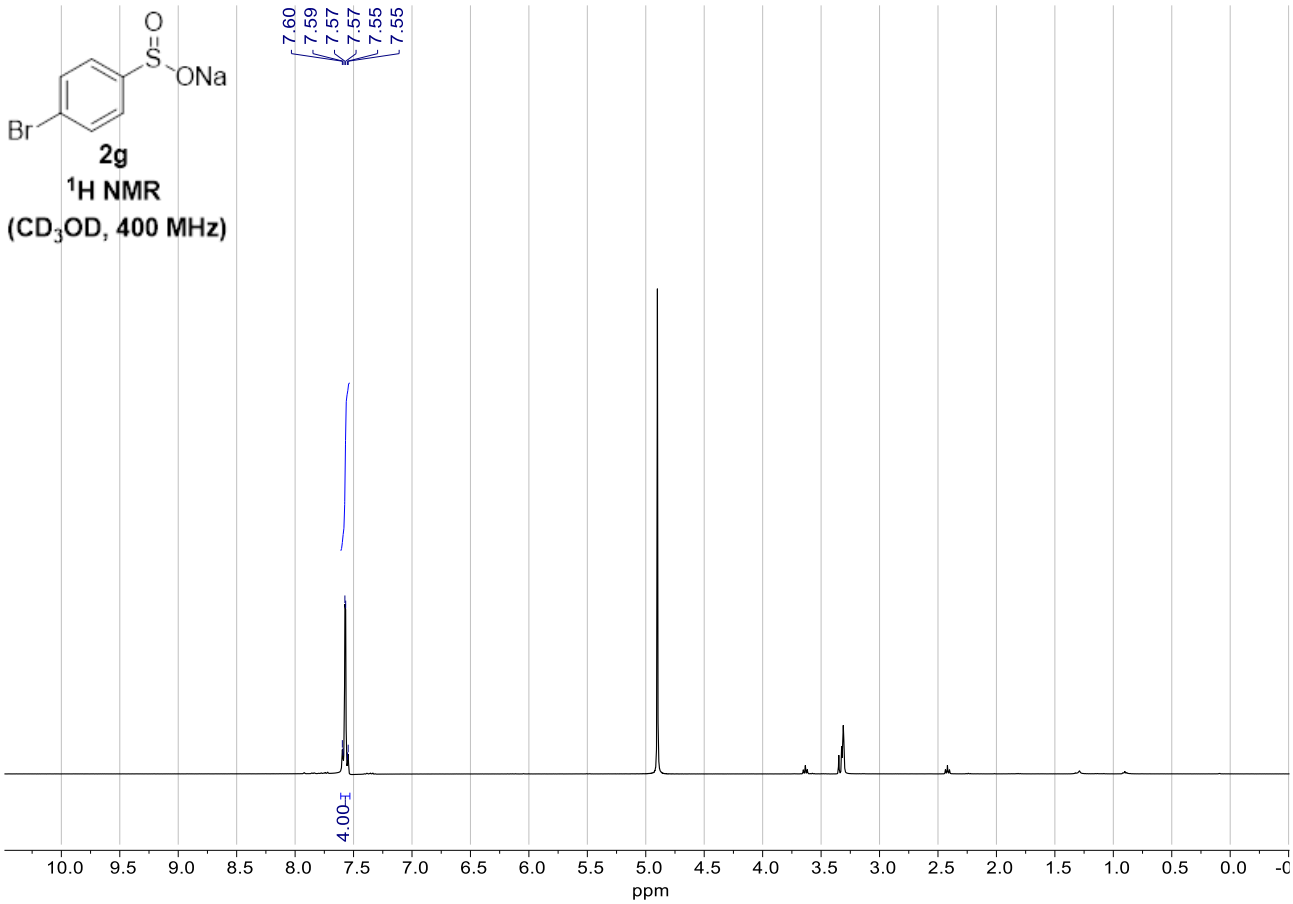

S3
19F NMR
(CD3OD, 400 MHz)
-114.69
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
-230
-250
-270
-290
ppm

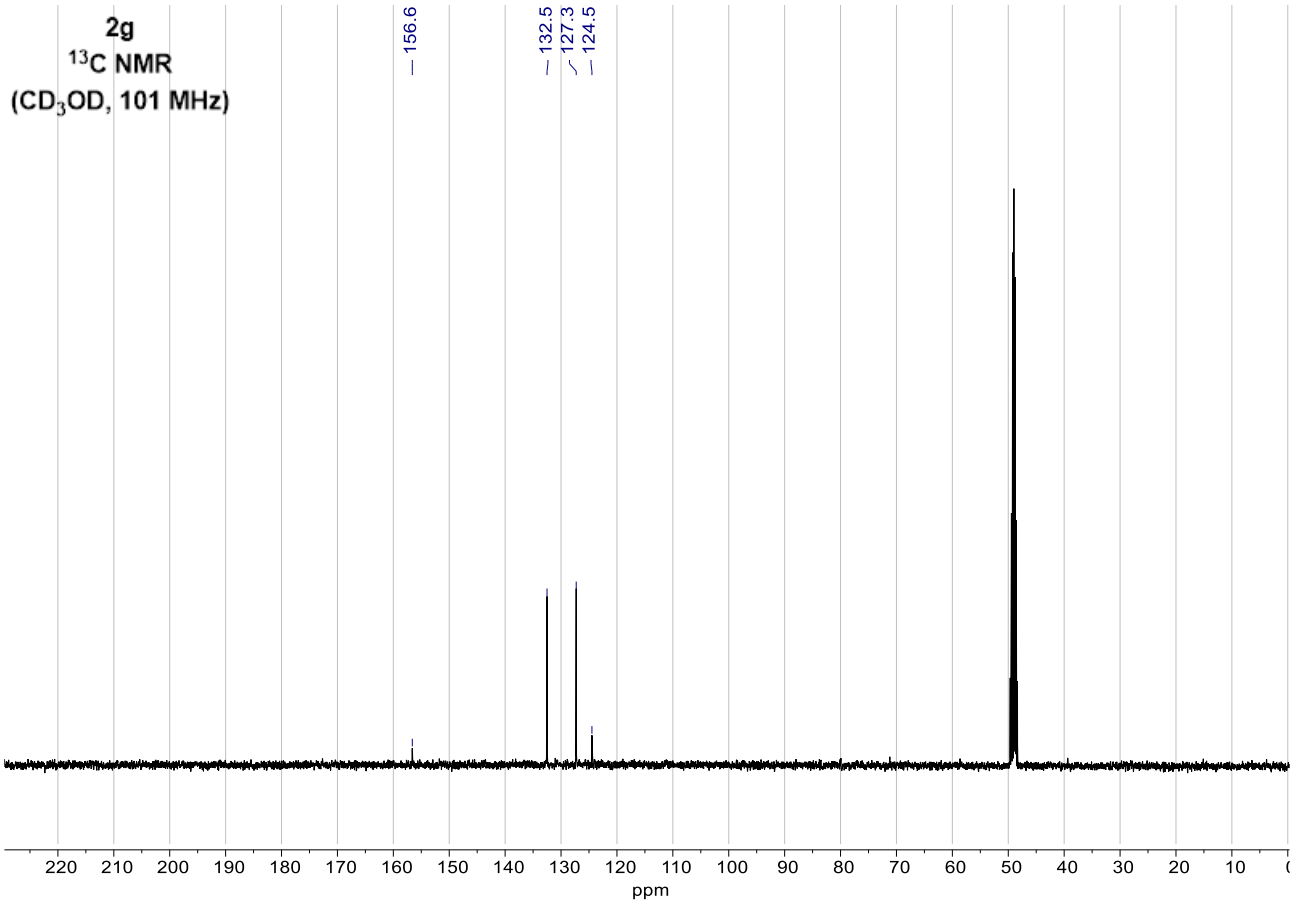

S4
^{1}H NMR
(CD_3OD, 400 MHz)
7.64
7.64
7.63
7.62
7.62
7.61
7.44
7.43
7.43
7.41
7.41
7.40
2.00
2.00
ppm

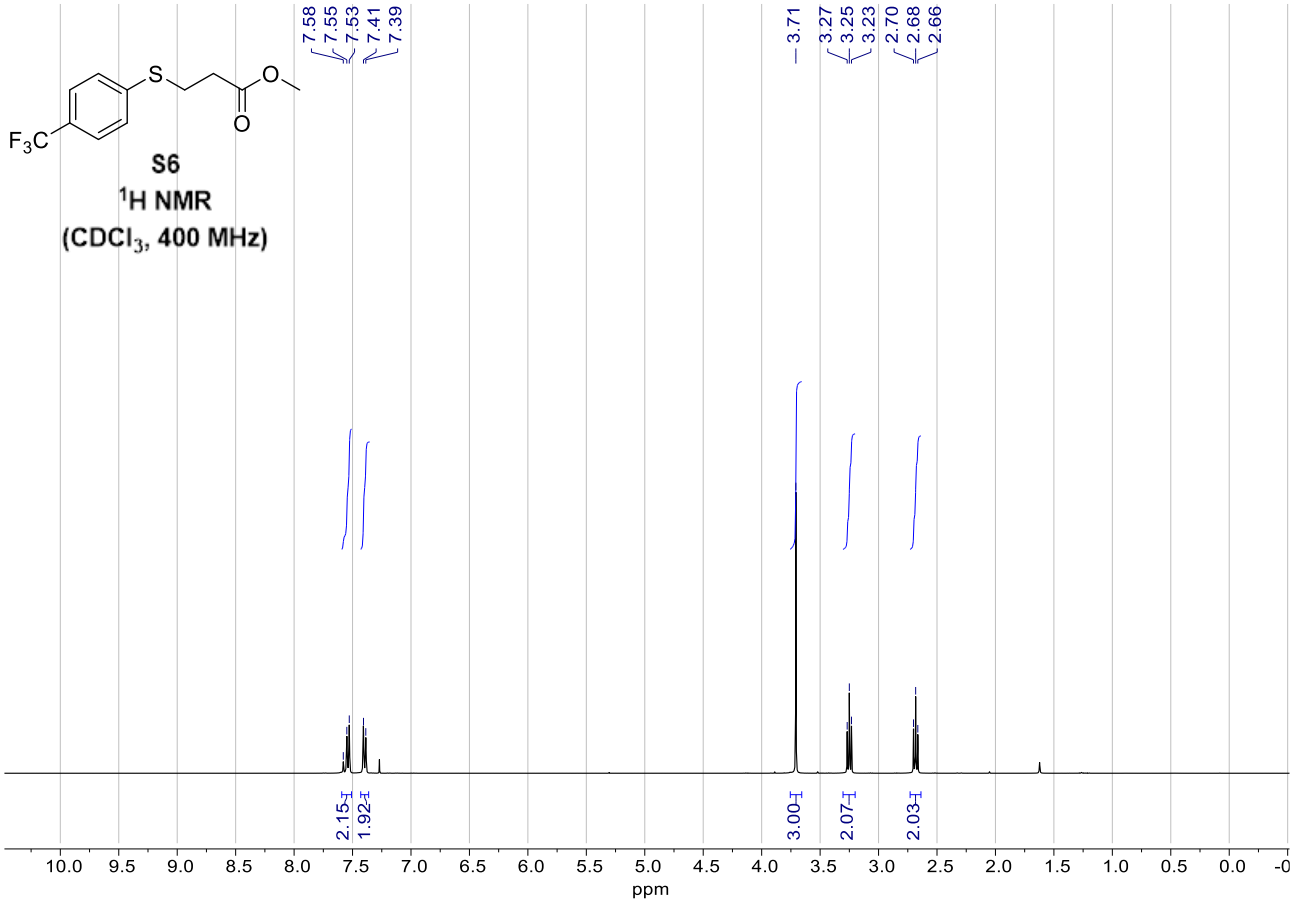

S4
^{13}C NMR
(CD_3OD, 101 MHz)
156.2
136.3
129.5
127.0
ppm

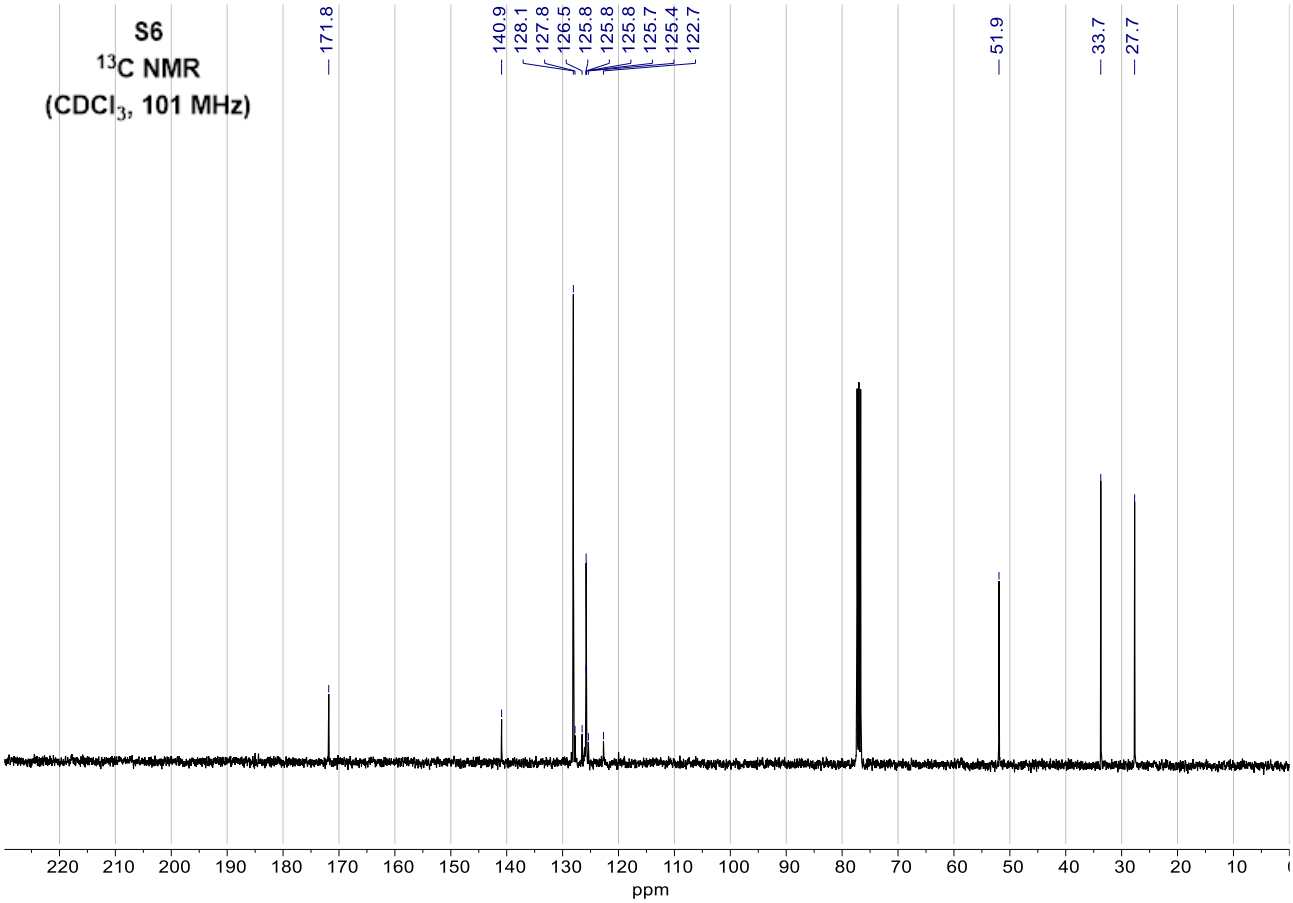

S5
^{1}H NMR
(CDCl$_3$, 400 MHz)
Br
O
O
S
O
O
7.80
7.78
7.75
7.73
3.66
3.46
3.44
3.42
2.79
2.77
2.75
1.83
1.87
2.88
2.05
2.00
ppm

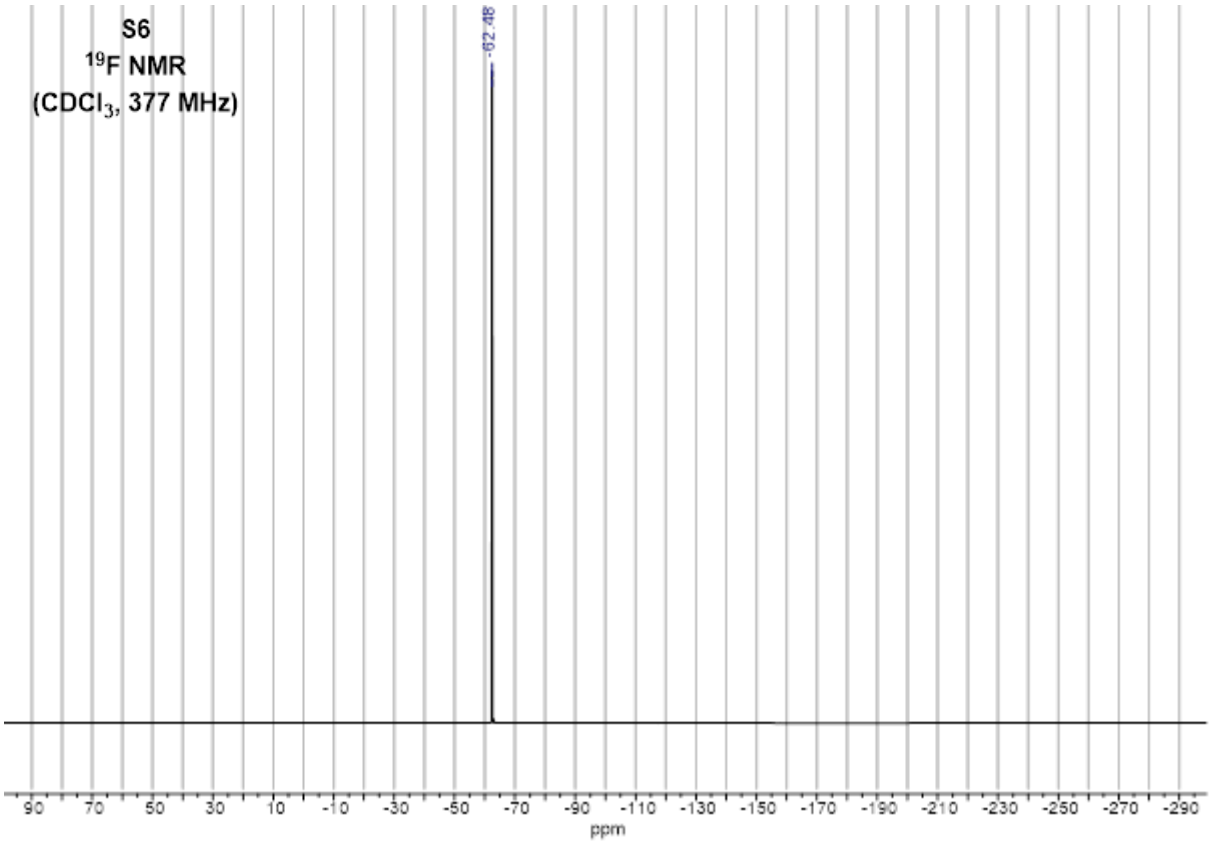

S5
^{13}C NMR
(CDCl$_3$, 101 MHz)
170.3
137.5
132.8
129.7
129.5
52.4
51.5
27.5
ppm

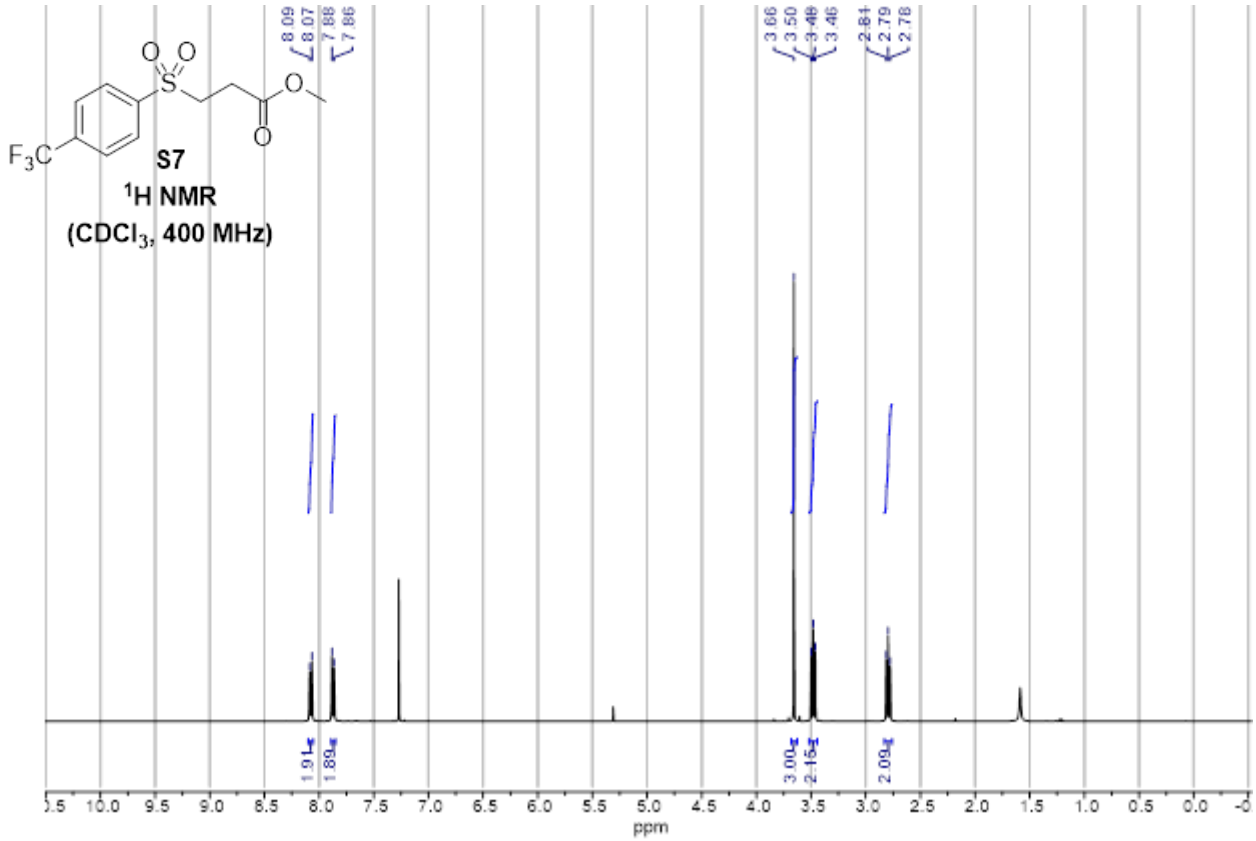

O
S
ONa
Br
2g
^{1}H NMR
(CD$_3$OD, 400 MHz)
7.60
7.59
7.57
7.57
7.55
7.55
4.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

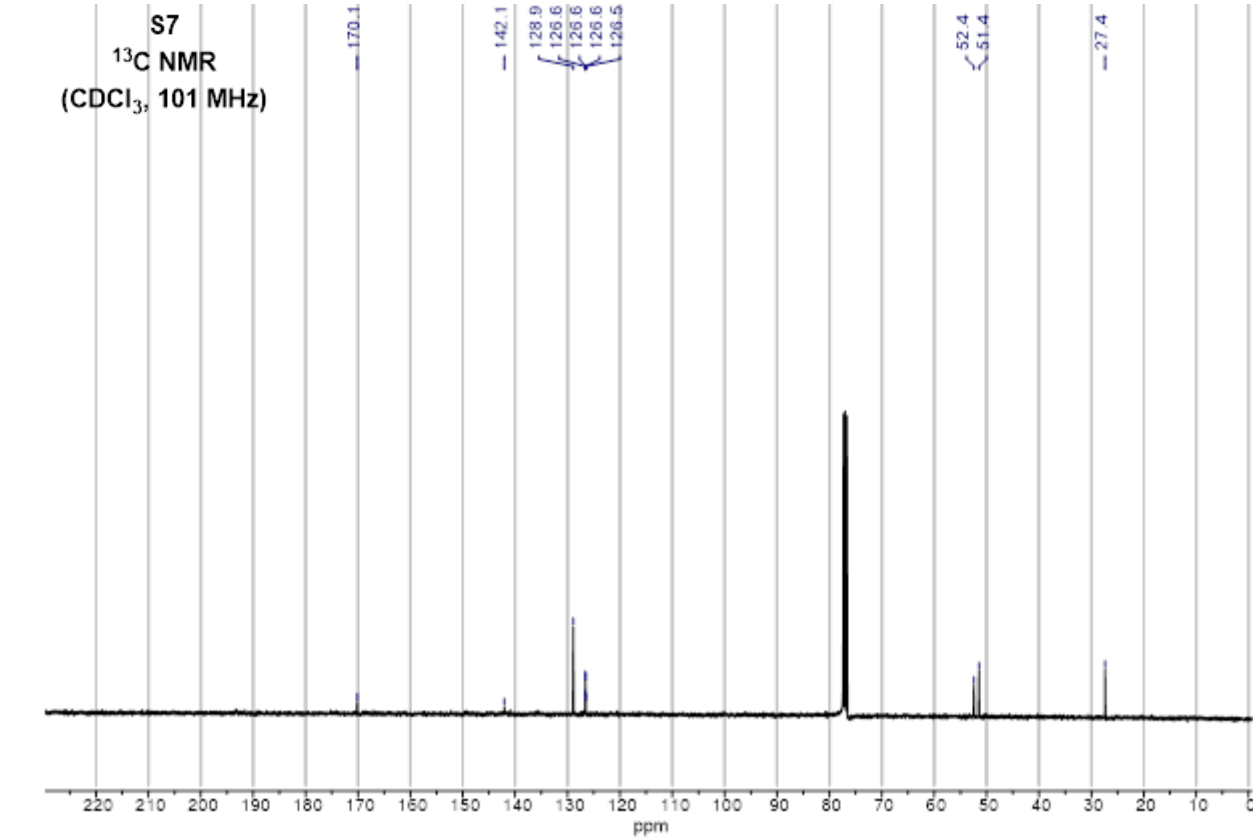

2g
^{13}C NMR
(CD$_3$OD, 101 MHz)
156.6
132.5
127.3
124.5
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

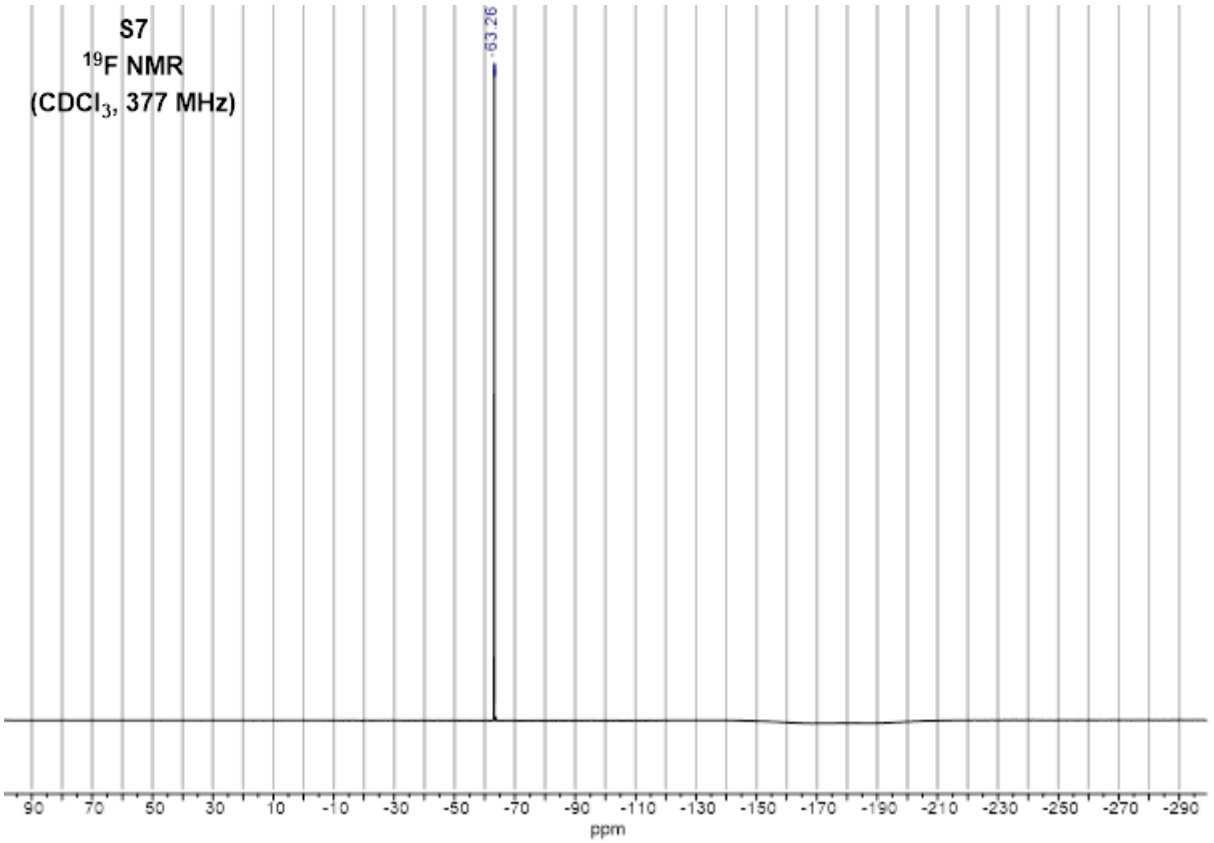

S6
^{1}H NMR
(CDCl$_3$, 400 MHz)
F$_3$C
S
O
O
7.58
7.55
7.53
7.41
7.39
3.71
3.27
3.25
3.23
2.70
2.68
2.66
2.15
1.92
3.00
2.07
2.03
ppm

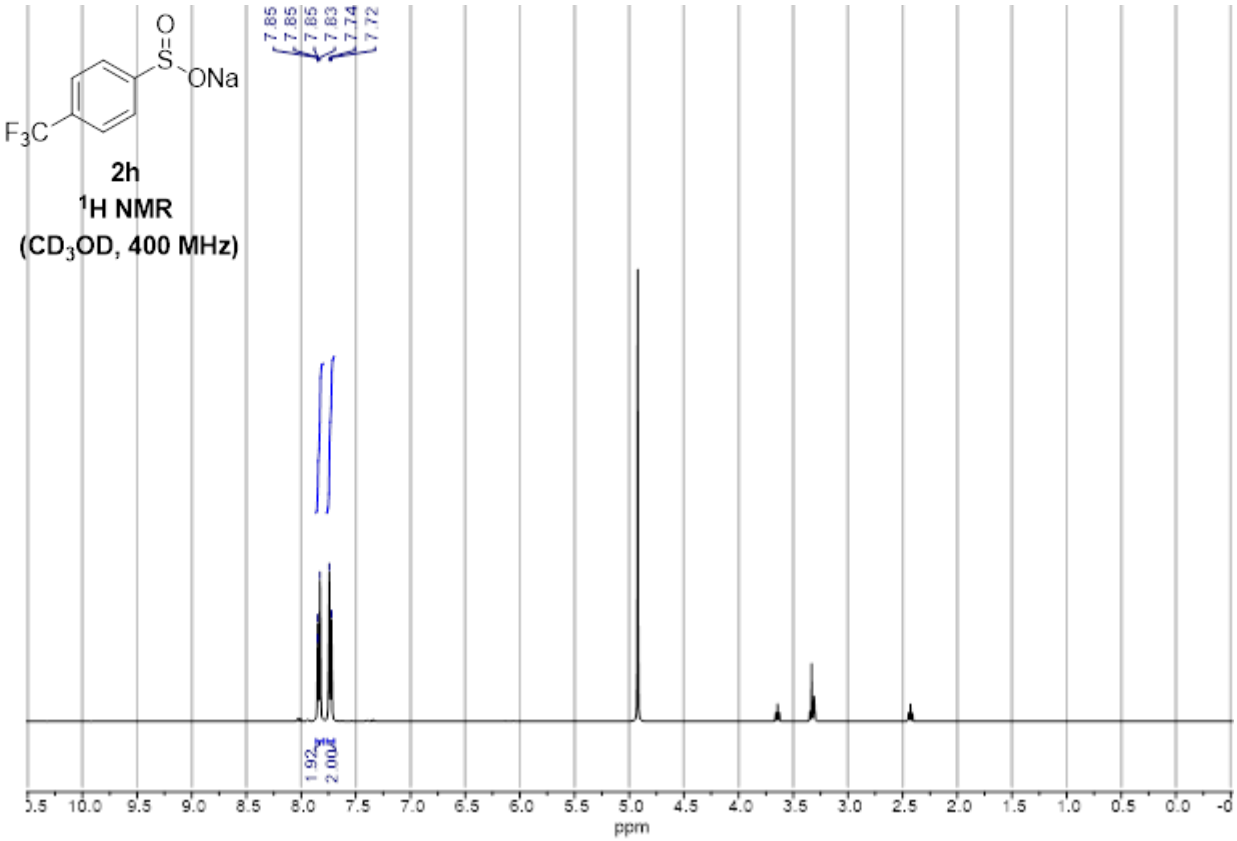

S6
^{13}C NMR
(CDCl$_3$, 101 MHz)
171.8
140.9
128.1
127.8
126.5
125.8
125.8
125.8
125.7
125.4
122.7
51.9
33.7
27.7
ppm

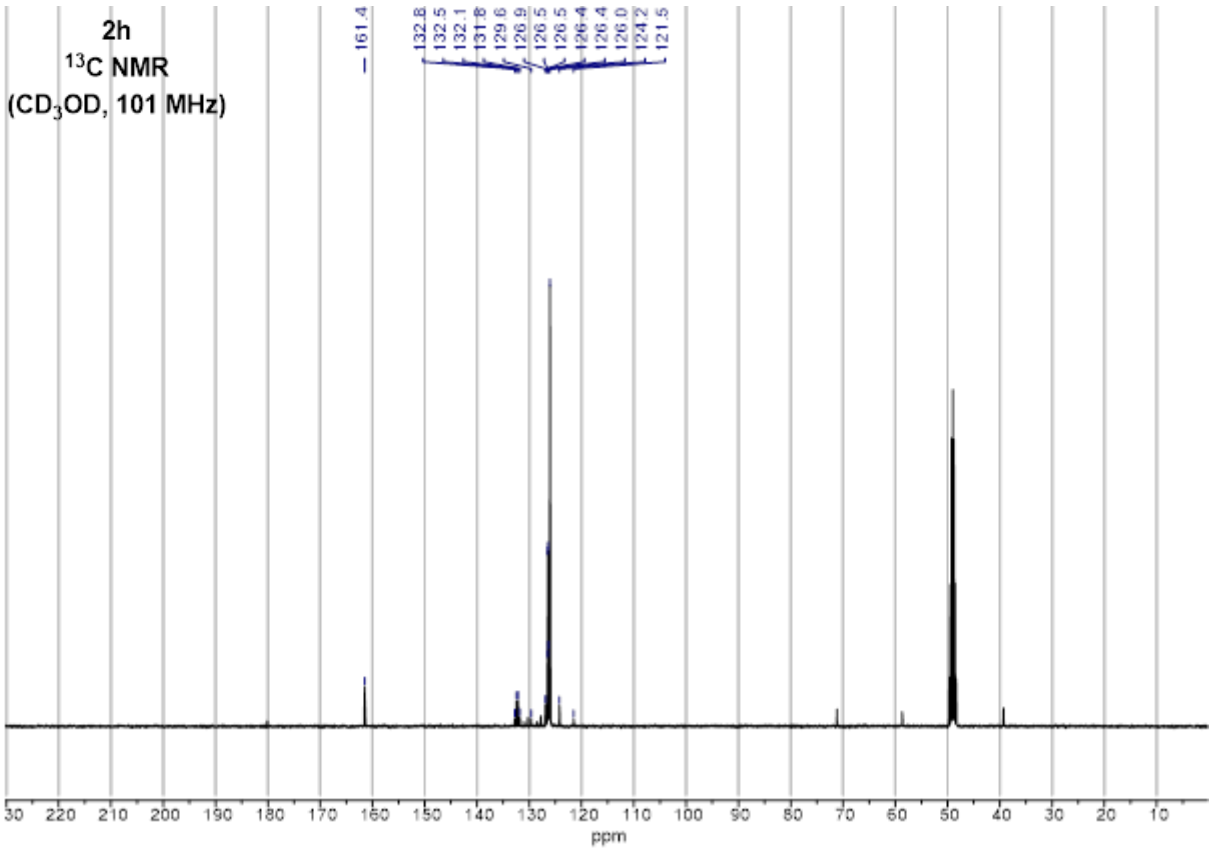

S6
^{19}F NMR
($CDCl_3$, 377 MHz)
-62.48
90 70 50 30 10 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190 -210 -230 -250 -270 -290
ppm

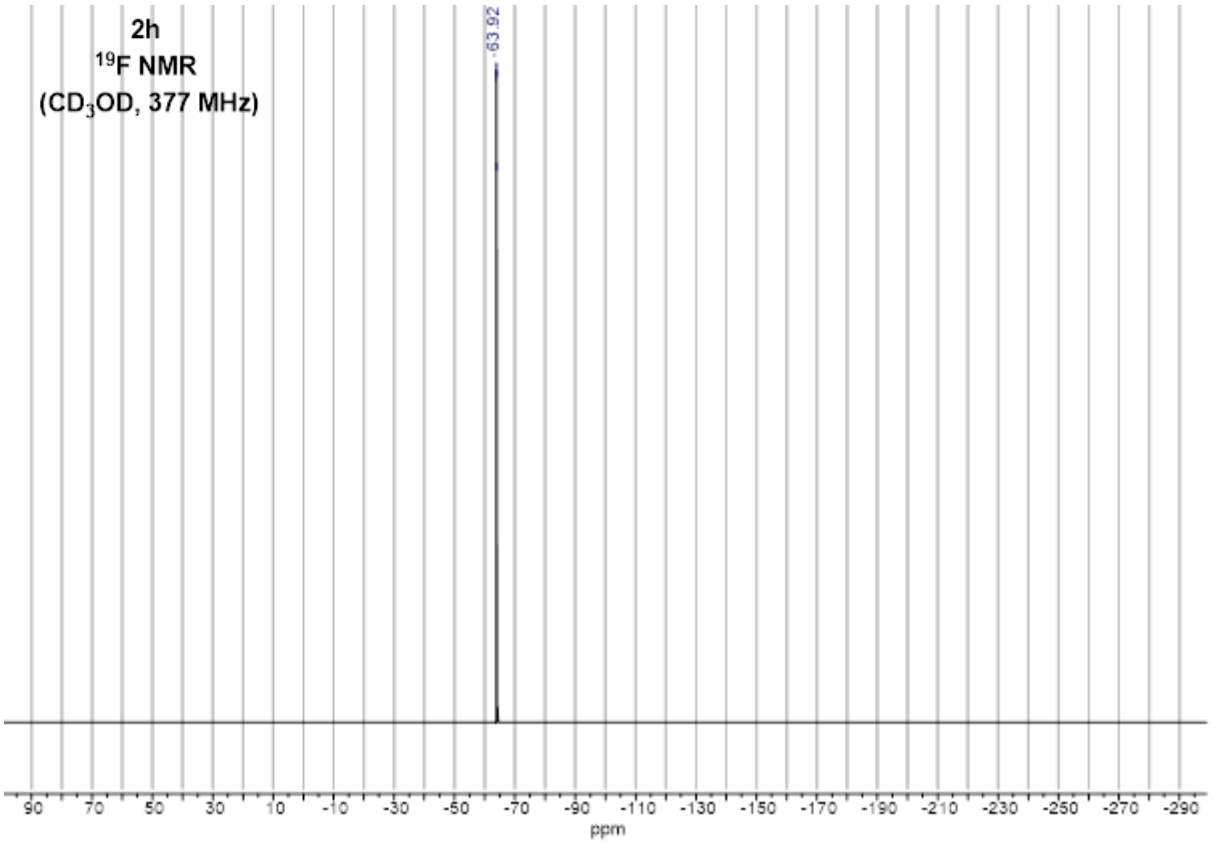

S7
^{1}H NMR
(CDCl$_3$, 400 MHz)
8.09
8.07
7.88
7.86
3.66
3.50
3.48
3.46
2.84
2.79
2.78
1.91
1.89
3.00
2.16
2.09
ppm

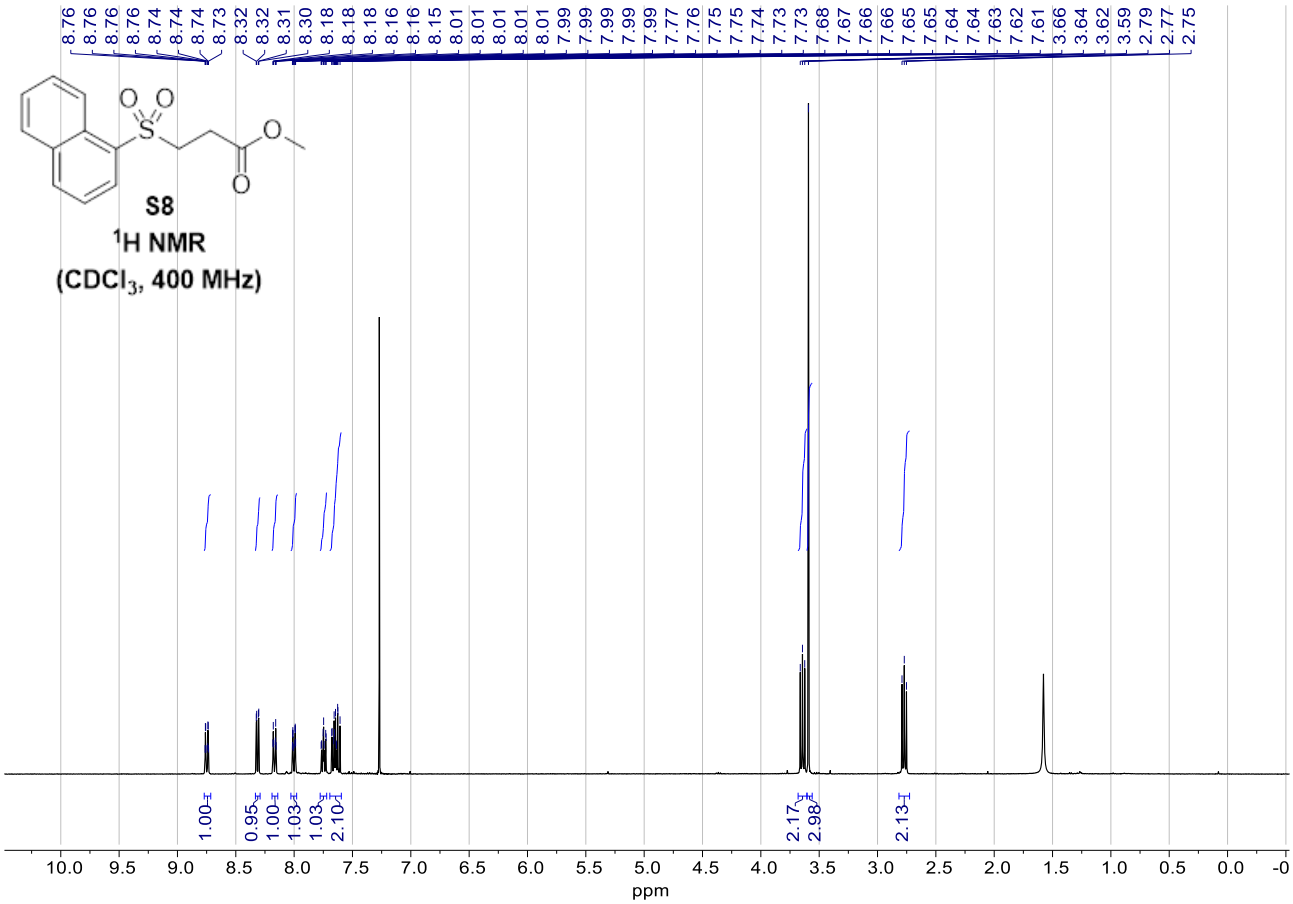

S7
^{13}C NMR
(CDCl$_3$, 101 MHz)
170.1
142.1
128.9
126.6
126.6
126.6
126.5
52.4
51.4
27.4
ppm

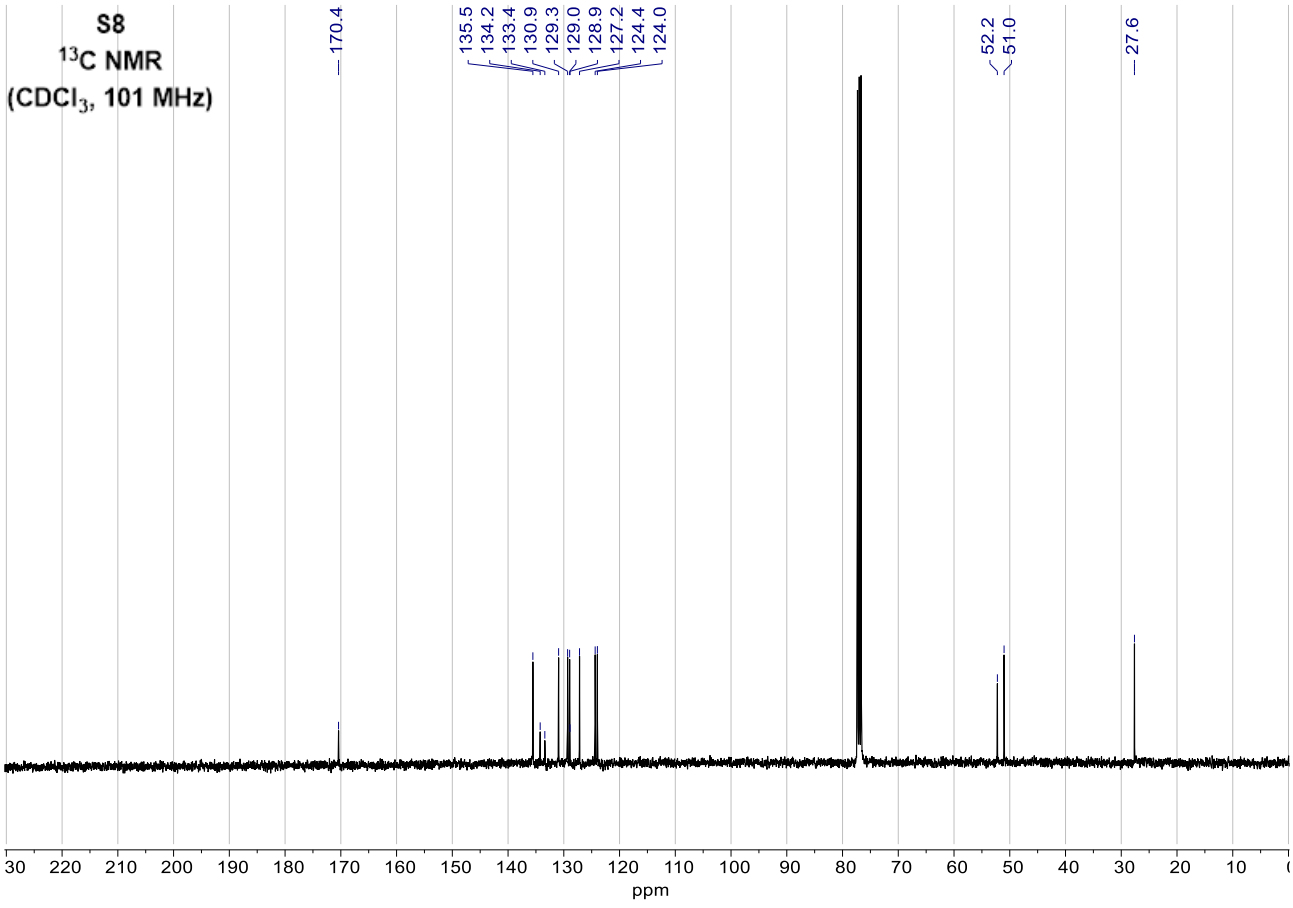

S7
^{19}F NMR
($CDCl_3$, 377 MHz)
-63.26
90 70 50 30 10 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190 -210 -230 -250 -270 -290
ppm

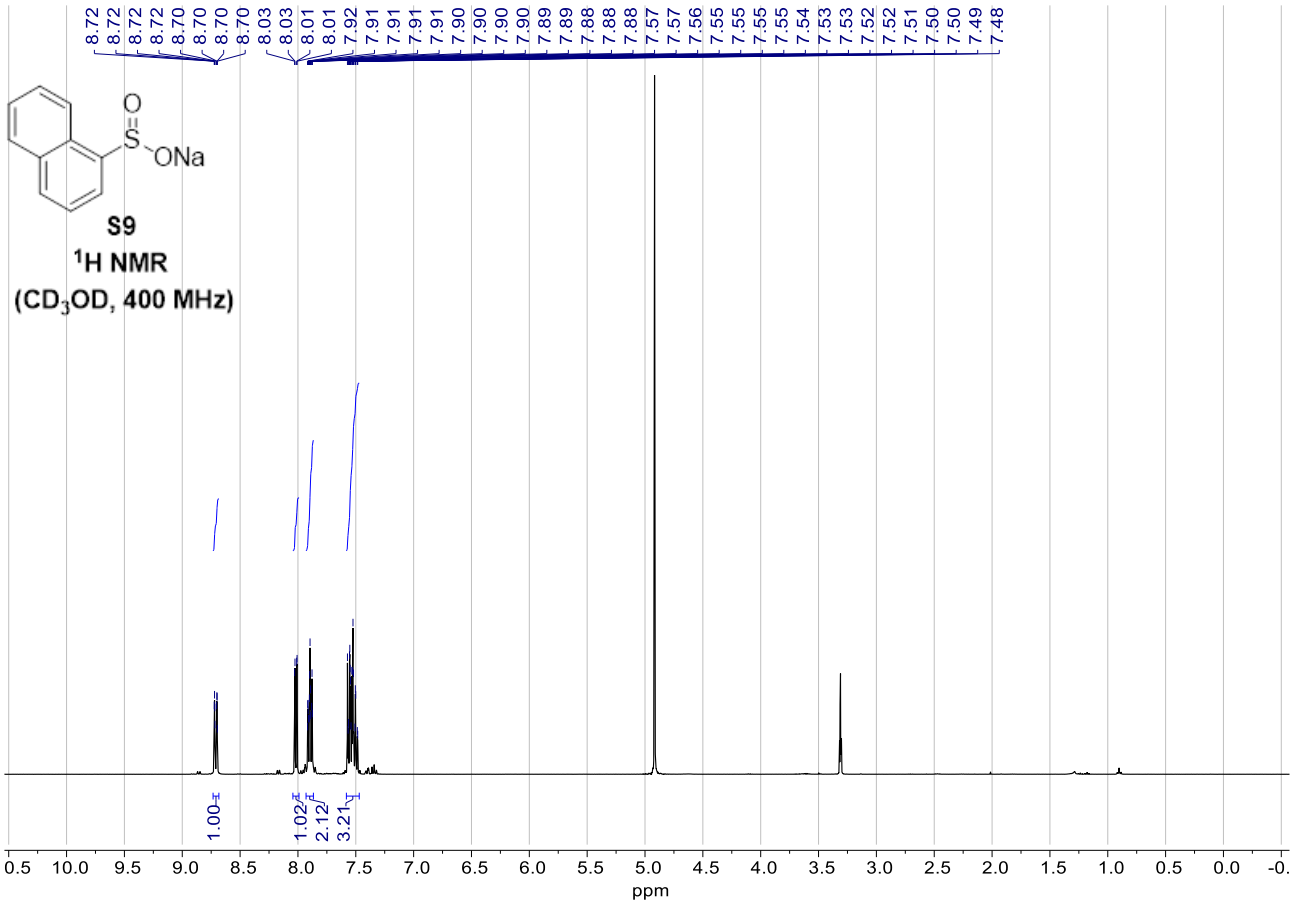

O
S
ONa
F3C
2h
1H NMR
(CD3OD, 400 MHz)
7.85
7.85
7.85
7.83
7.74
7.72
1.92
2.00
ppm

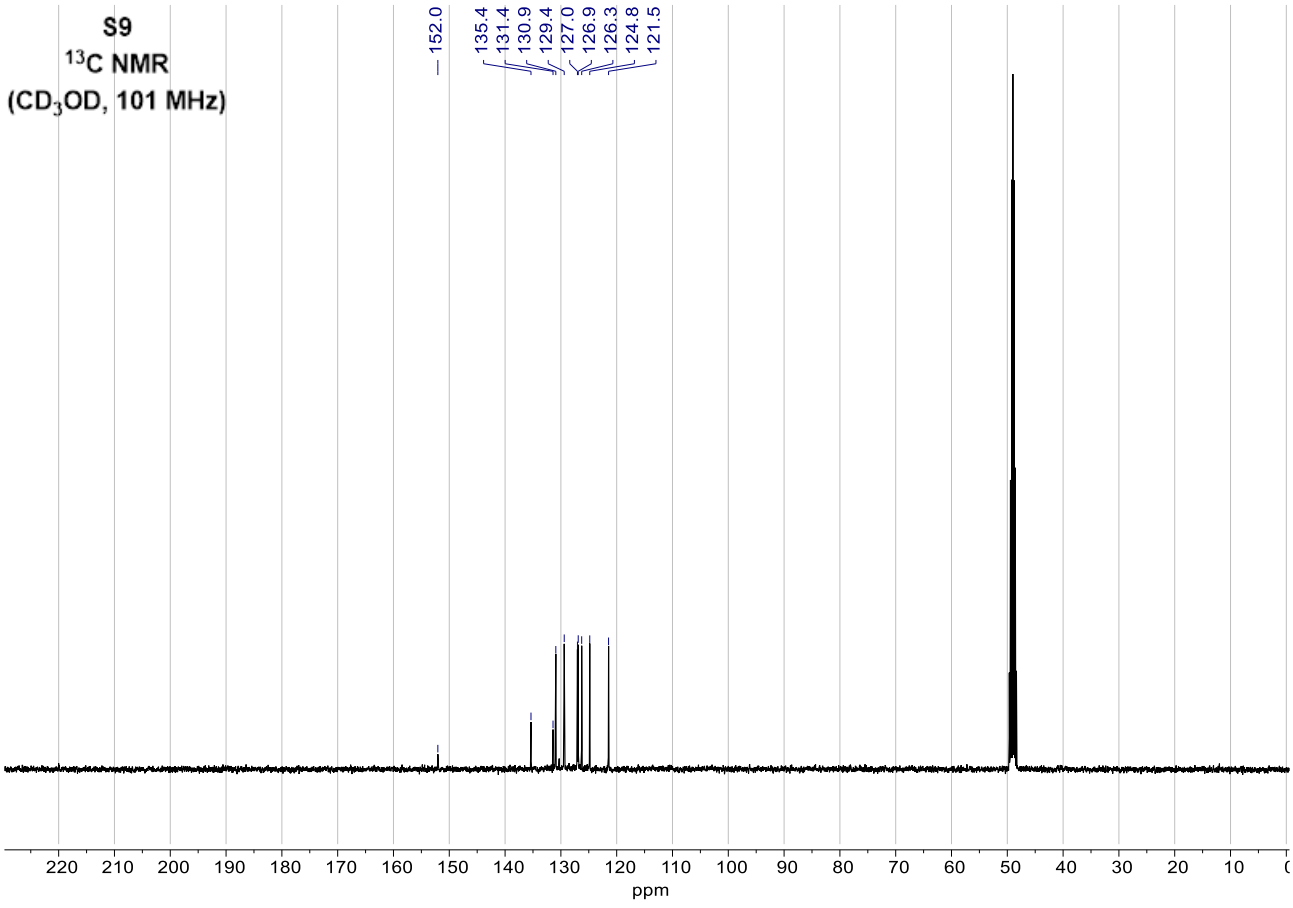

2h
13C NMR
(CD3OD, 101 MHz)
161.4
132.8
132.5
132.1
131.8
129.6
126.9
126.5
126.5
126.4
126.4
126.0
124.2
121.5
ppm

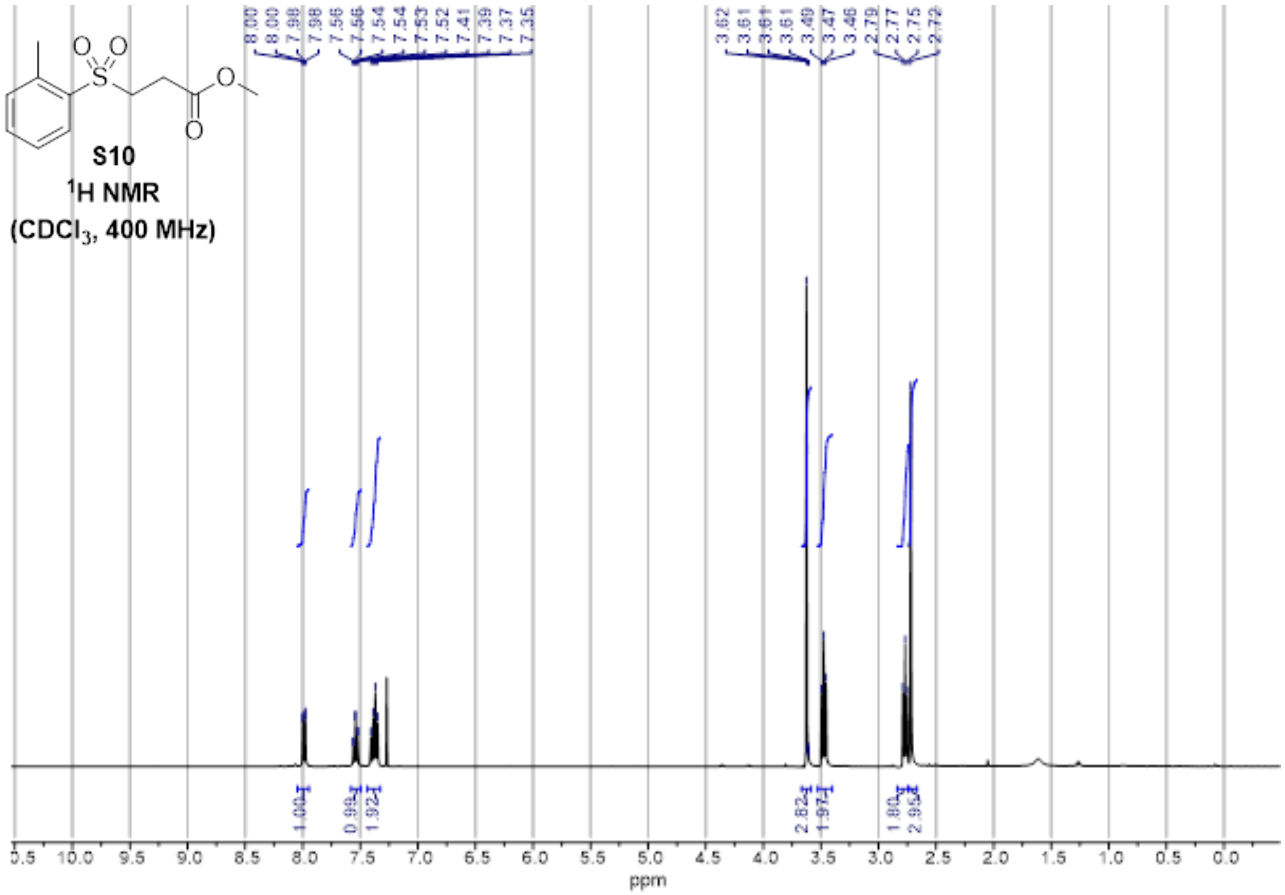

2h
19F NMR
(CD3OD, 377 MHz)
-63.92
90 70 50 30 10 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190 -210 -230 -250 -270 -290
ppm

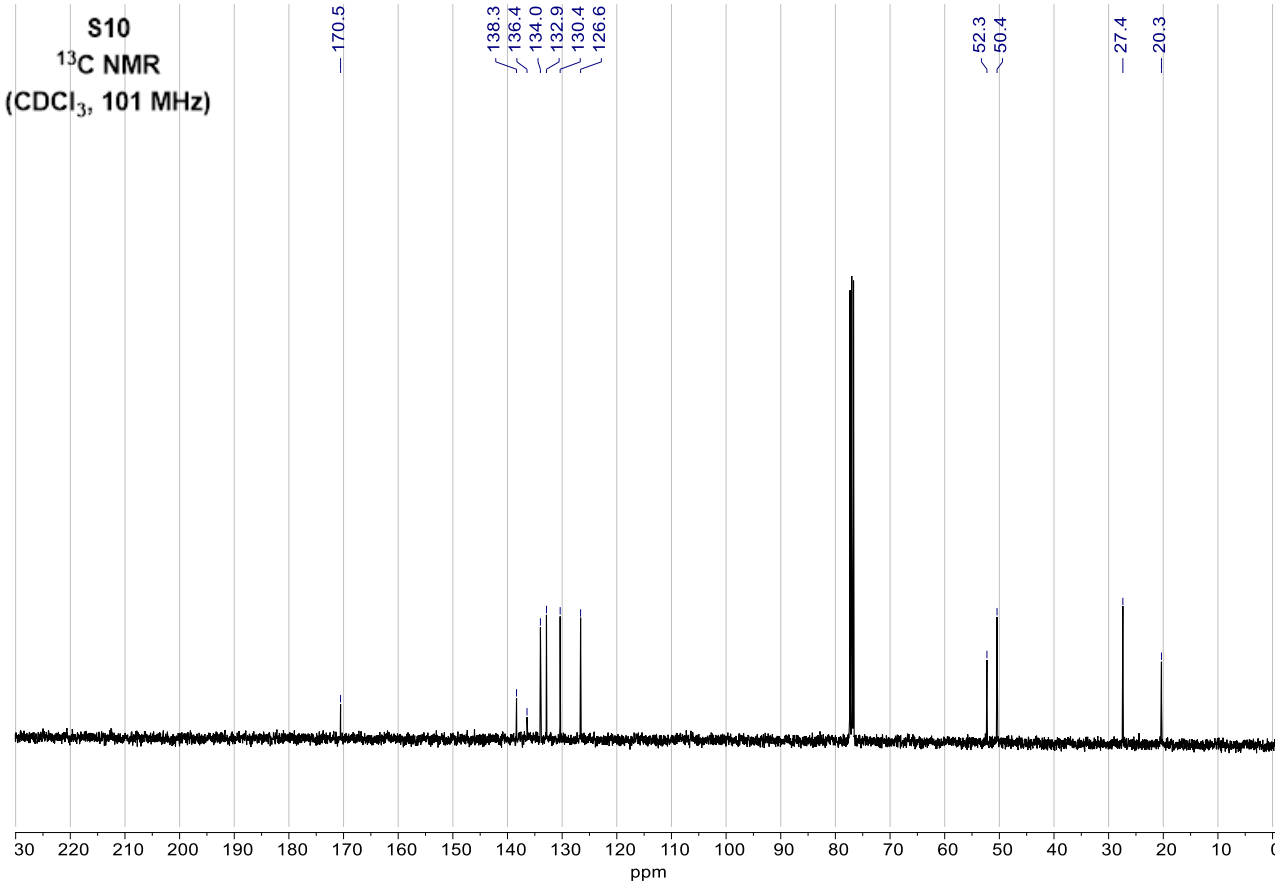

S8
^{1}H NMR
(CDCl$_3$, 400 MHz)
ppm

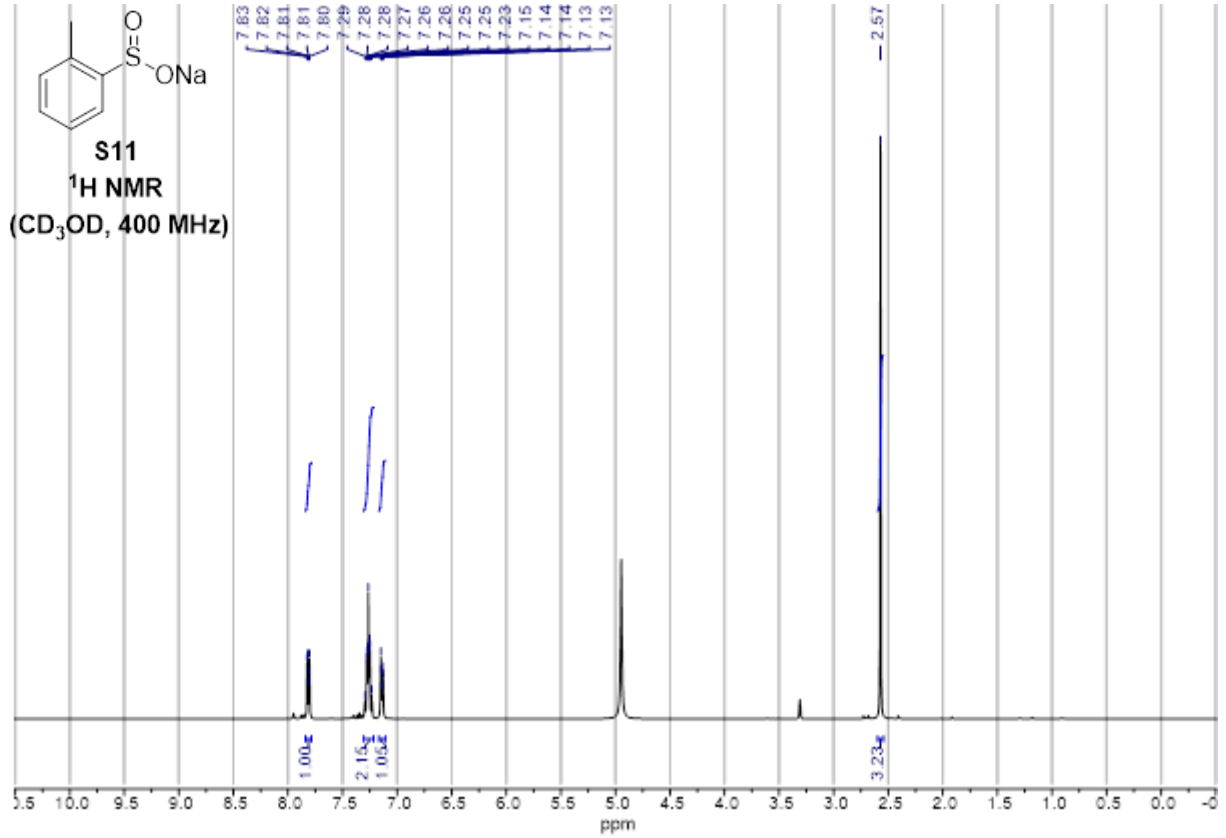

S8
^{13}C NMR
(CDCl$_3$, 101 MHz)
ppm

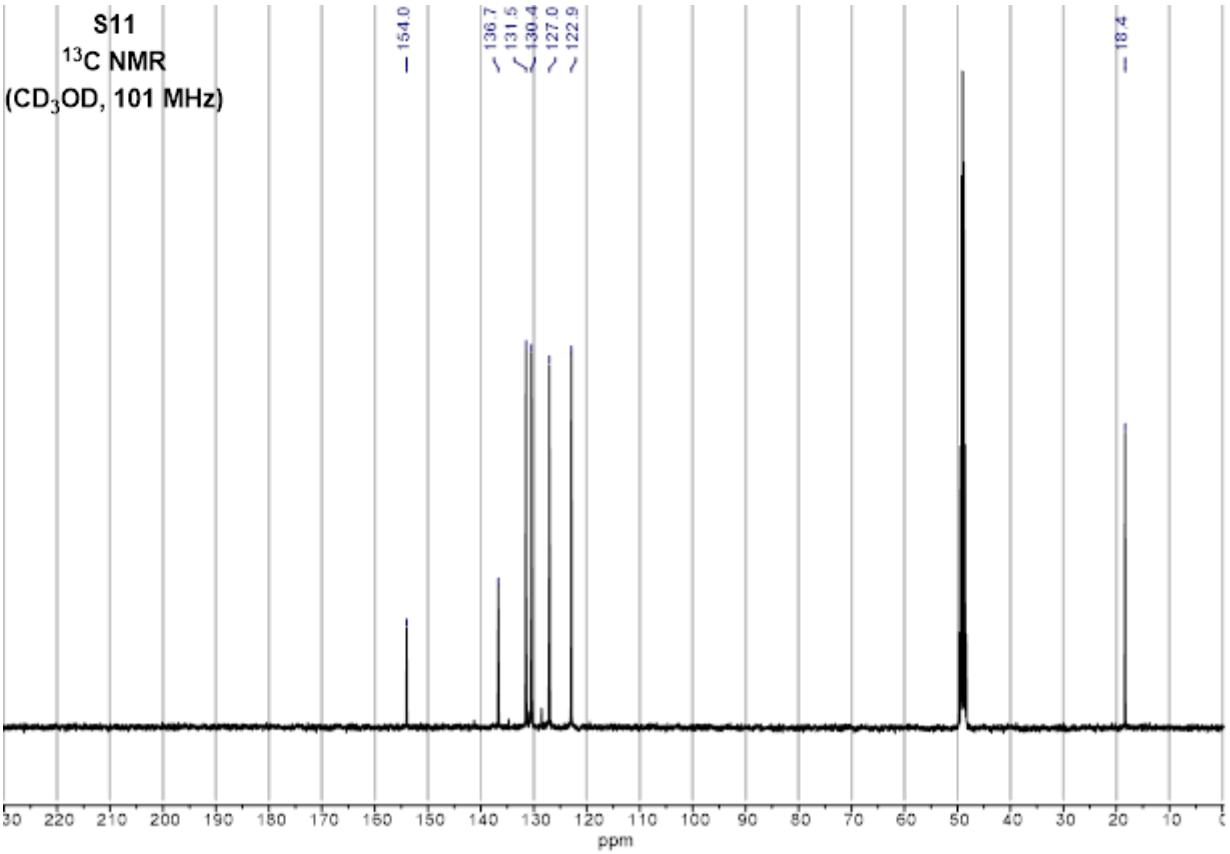

8.72 8.72 8.72 8.72 8.70 8.70 8.70 8.03 8.03 8.01 8.01 7.92 7.91 7.91 7.91 7.90 7.90 7.90 7.90 7.89 7.89 7.88 7.88 7.88 7.57 7.57 7.56 7.55 7.55 7.55 7.55 7.54 7.53 7.53 7.52 7.52 7.51 7.50 7.50 7.49 7.48
O
S
ONa
S9
1H NMR
(CD3OD, 400 MHz)
1.00
1.02
2.12
3.21
0.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

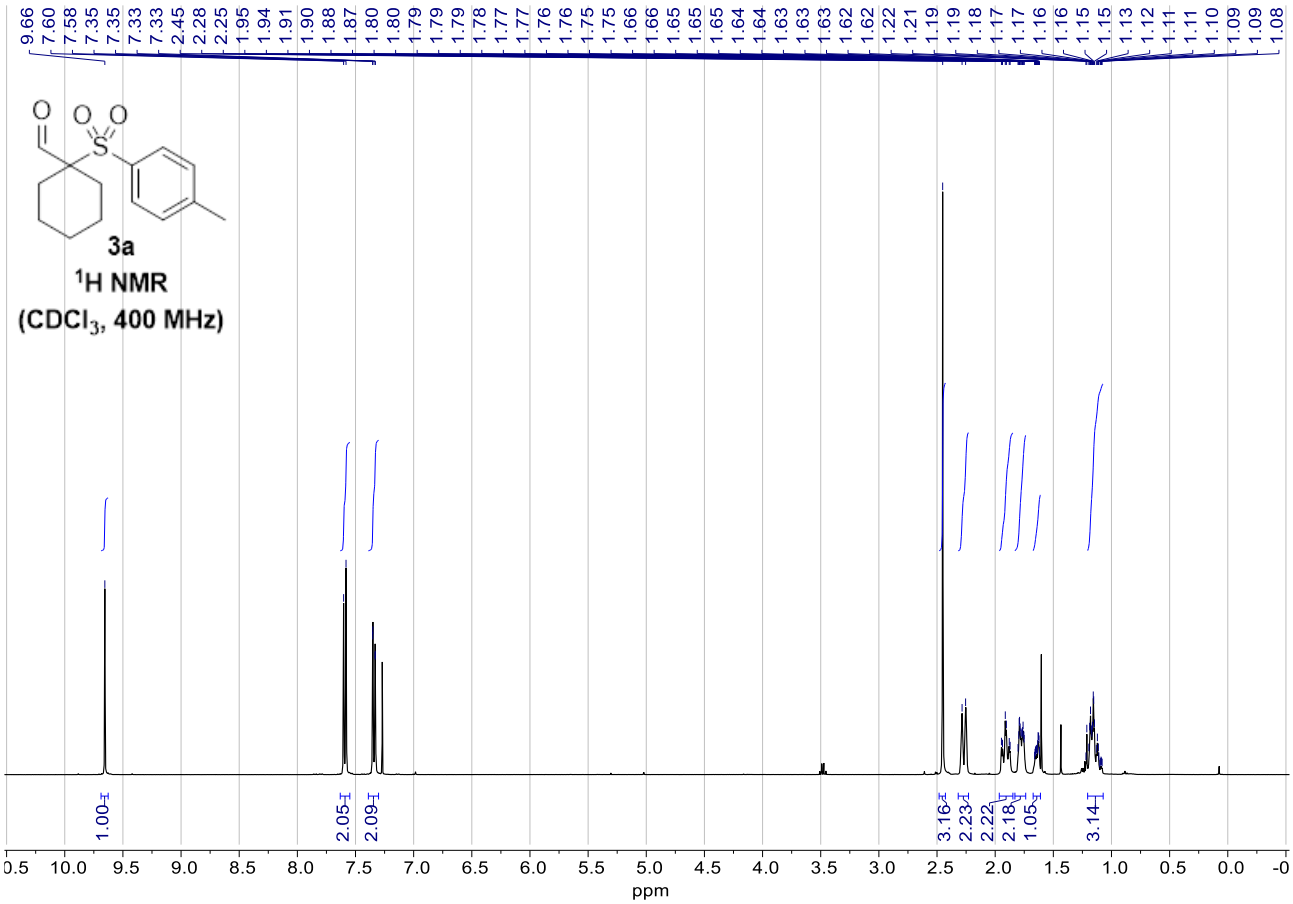

S9
13C NMR
(CD3OD, 101 MHz)
152.0
135.4
131.4
130.9
129.4
127.0
126.9
126.3
124.8
121.5
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

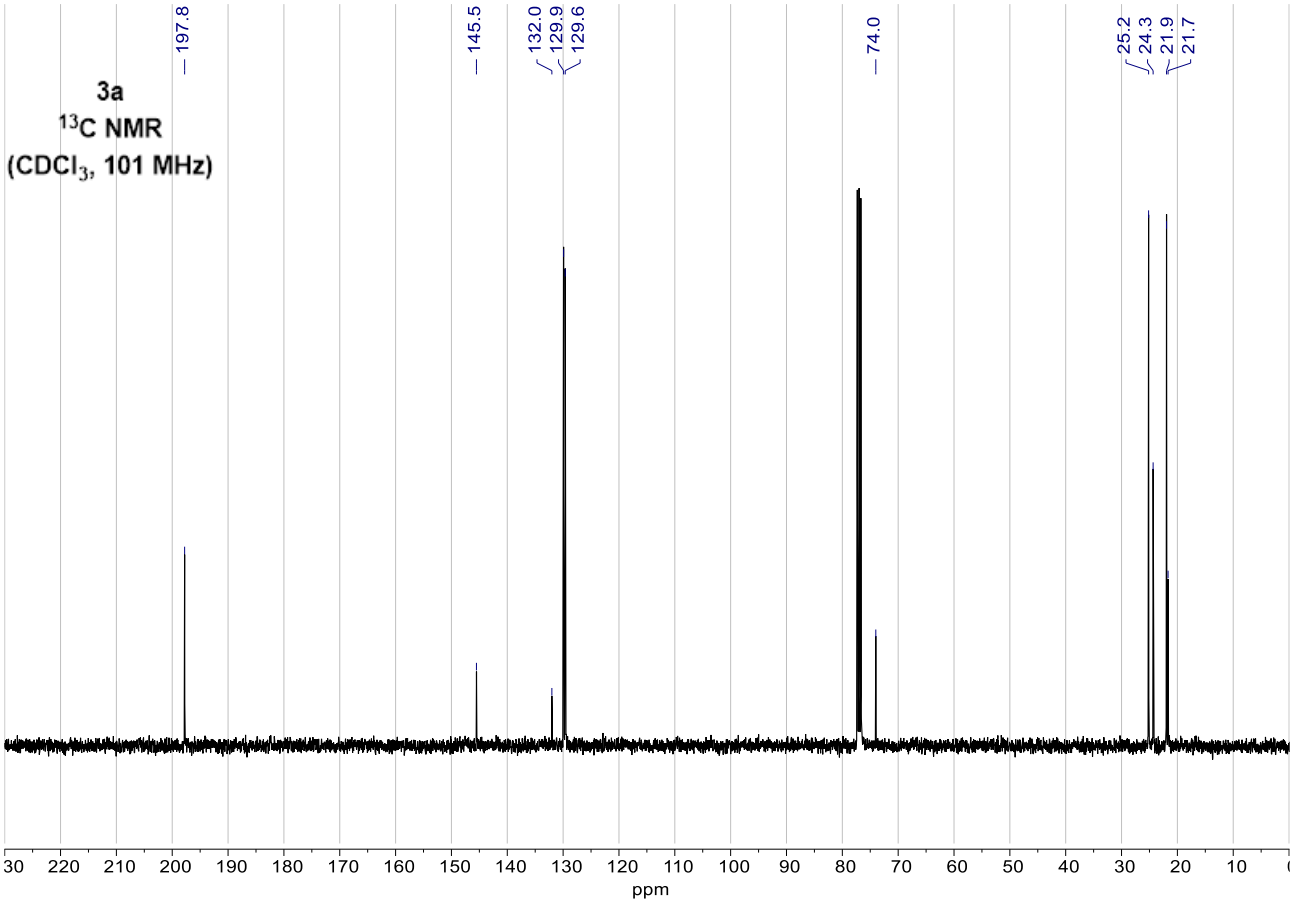

S10
^{1}H NMR
(CDCl$_3$, 400 MHz)
ppm

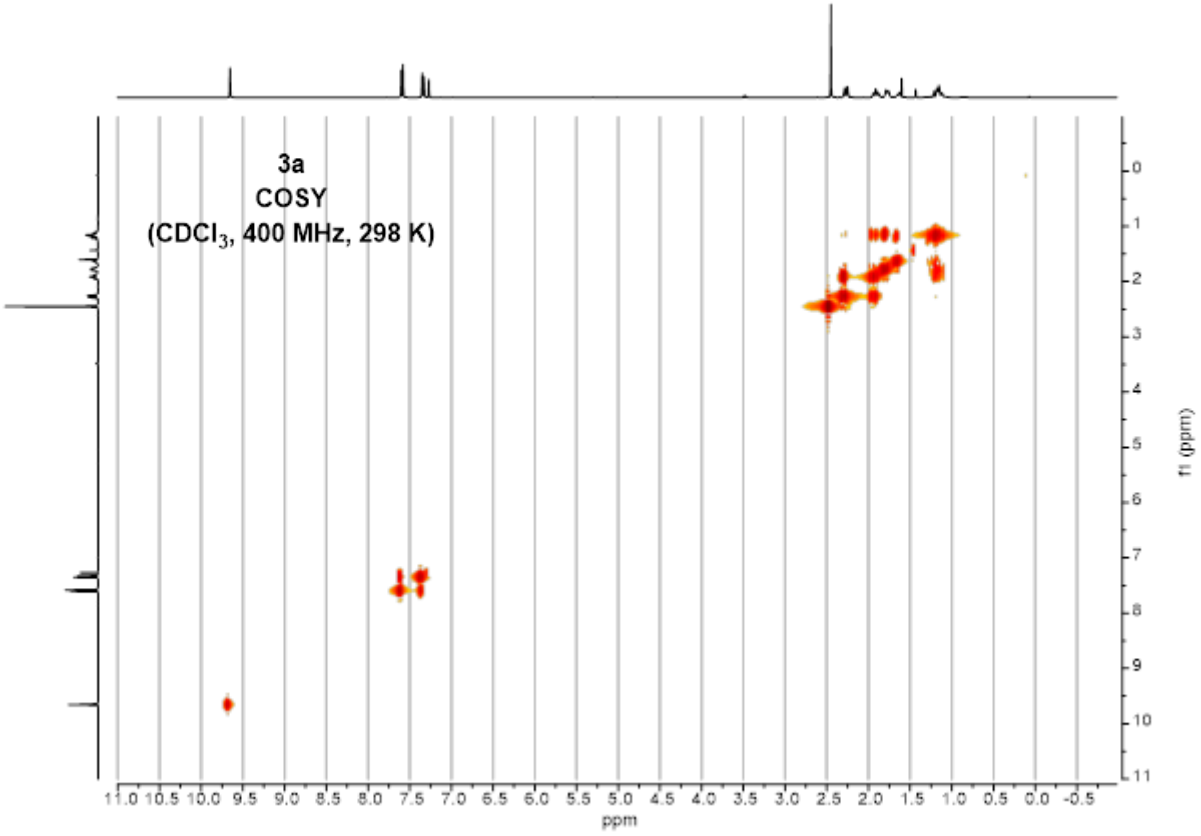

S10
^{13}C NMR
(CDCl$_3$, 101 MHz)
170.5
138.3
136.4
134.0
132.9
130.4
126.6
52.3
50.4
27.4
20.3
ppm

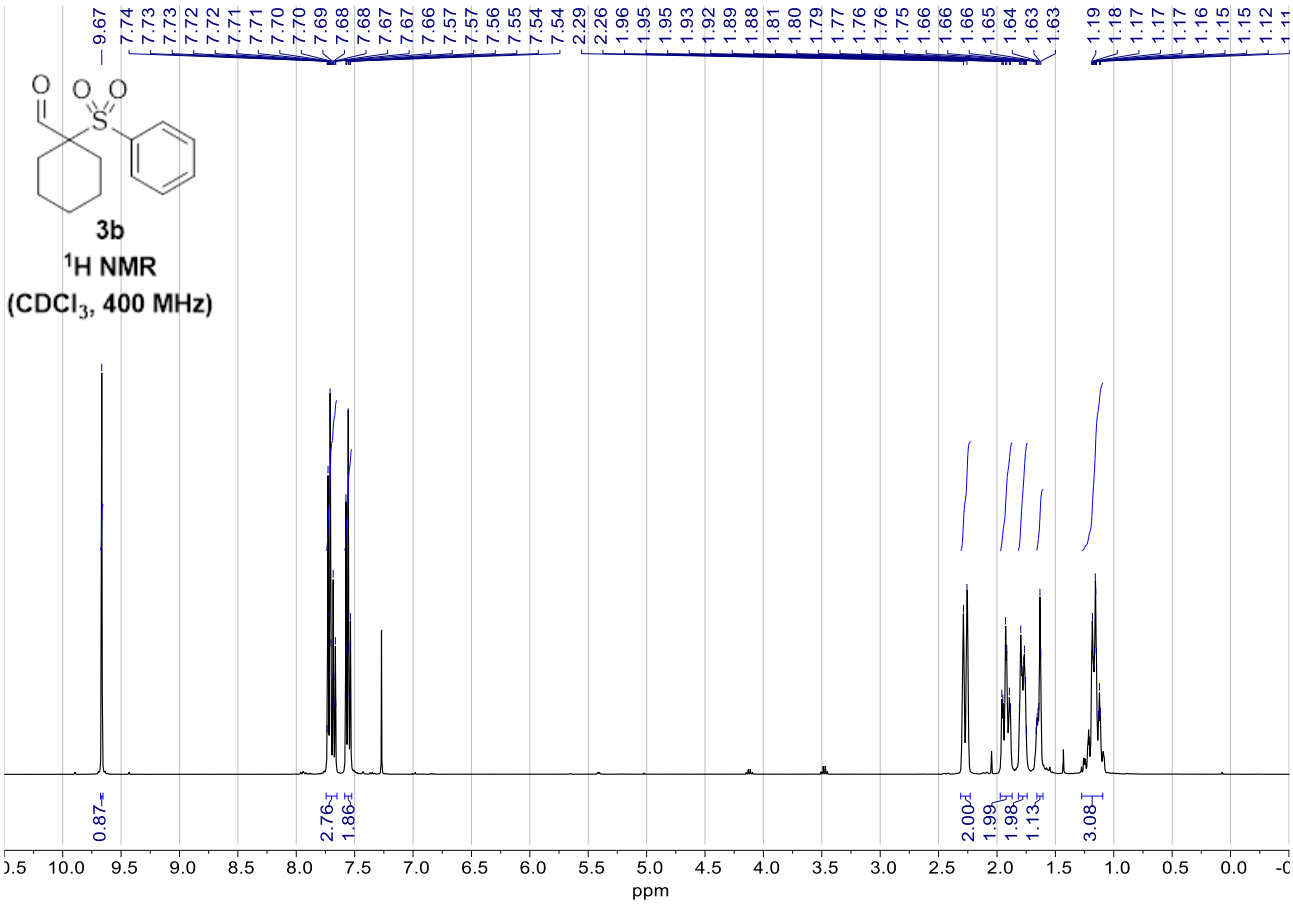

S11
^{1}H NMR
(CD_3OD, 400 MHz)
ONa
7.83
7.82
7.81
7.81
7.80
7.29
7.28
7.28
7.27
7.26
7.26
7.25
7.25
7.23
7.15
7.14
7.14
7.13
7.13
2.57
1.00
2.15
1.05
3.23
ppm

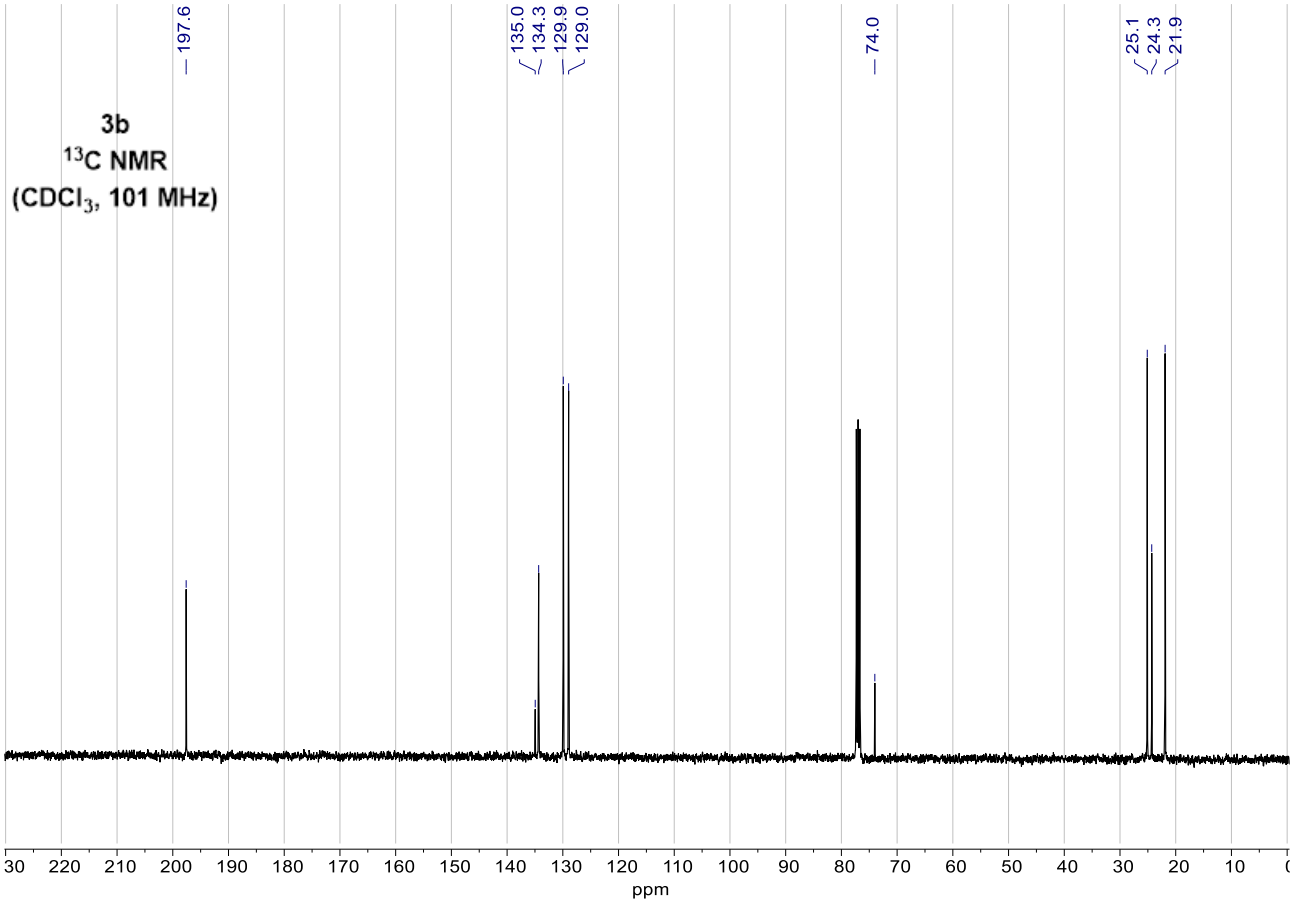

S11
^{13}C NMR
(CD_3OD, 101 MHz)
154.0
136.7
131.5
130.4
127.0
122.9
18.4
ppm

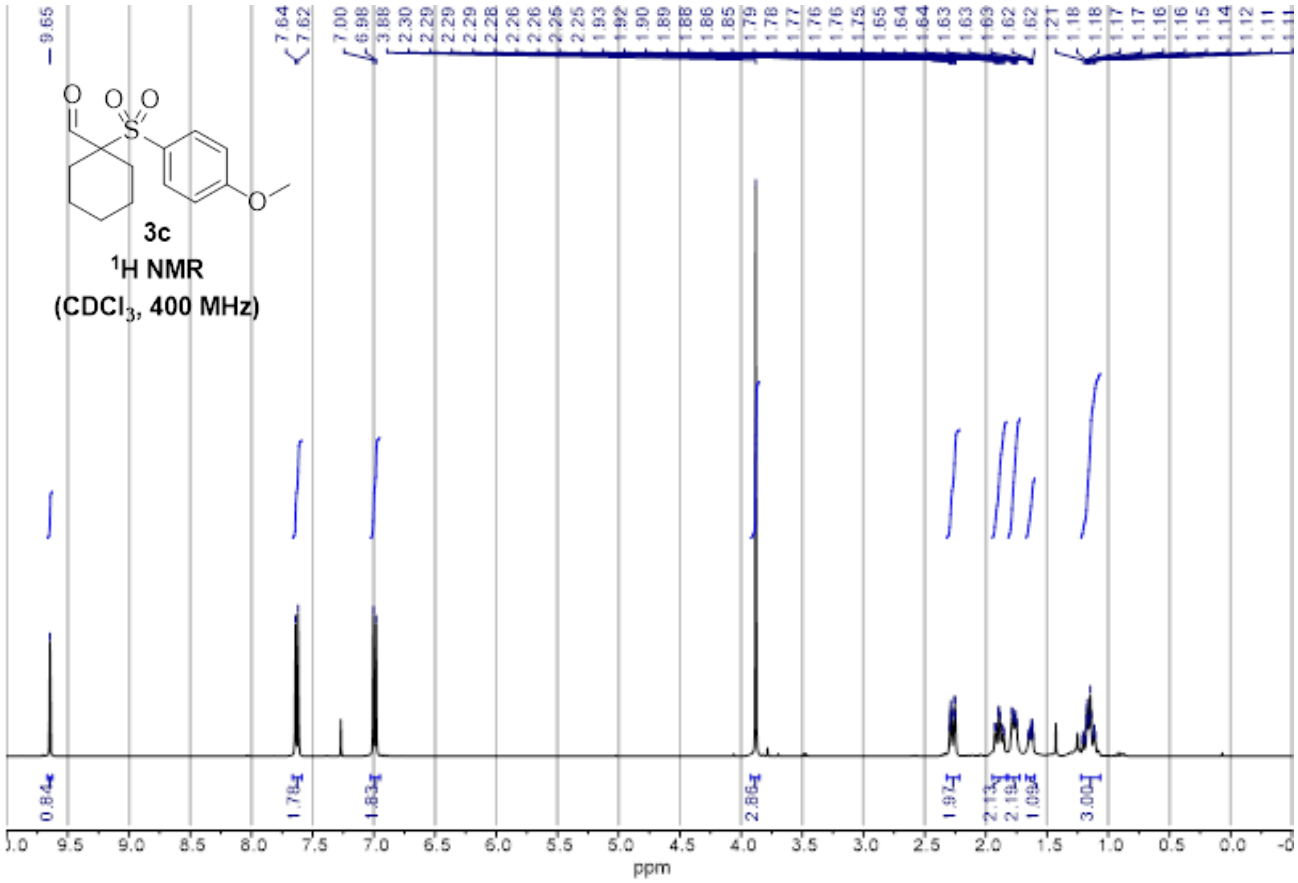

9.66 7.60 7.58 7.35 7.35 7.33 7.33 2.45 2.28 2.25 1.95 1.94 1.91 1.90 1.88 1.87 1.80 1.80 1.79 1.79 1.79 1.78 1.77 1.77 1.76 1.76 1.75 1.75 1.66 1.66 1.65 1.65 1.65 1.64 1.64 1.63 1.63 1.63 1.62 1.62 1.22 1.21 1.19 1.19 1.18 1.17 1.17 1.16 1.16 1.15 1.15 1.13 1.12 1.11 1.11 1.10 1.09 1.09 1.08
3a
^{1}H NMR
($CDCl_3$, 400 MHz)
1.00 2.05 2.09 3.16 2.23 2.22 2.18 1.05 3.14
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

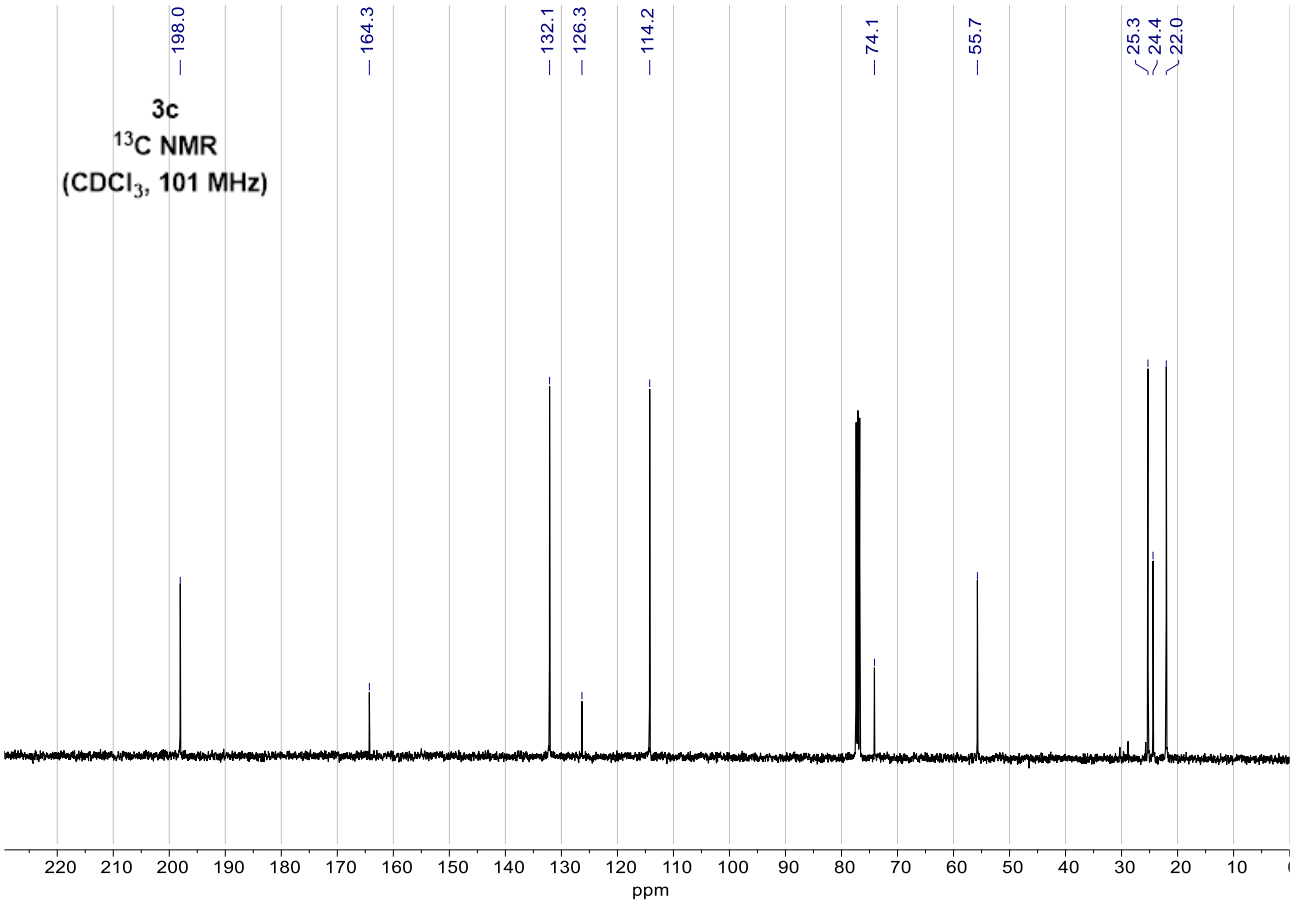

3a
^{13}C NMR
($CDCl_3$, 101 MHz)
197.8 145.5 132.0 129.9 129.6 74.0 25.2 24.3 21.9 21.7
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

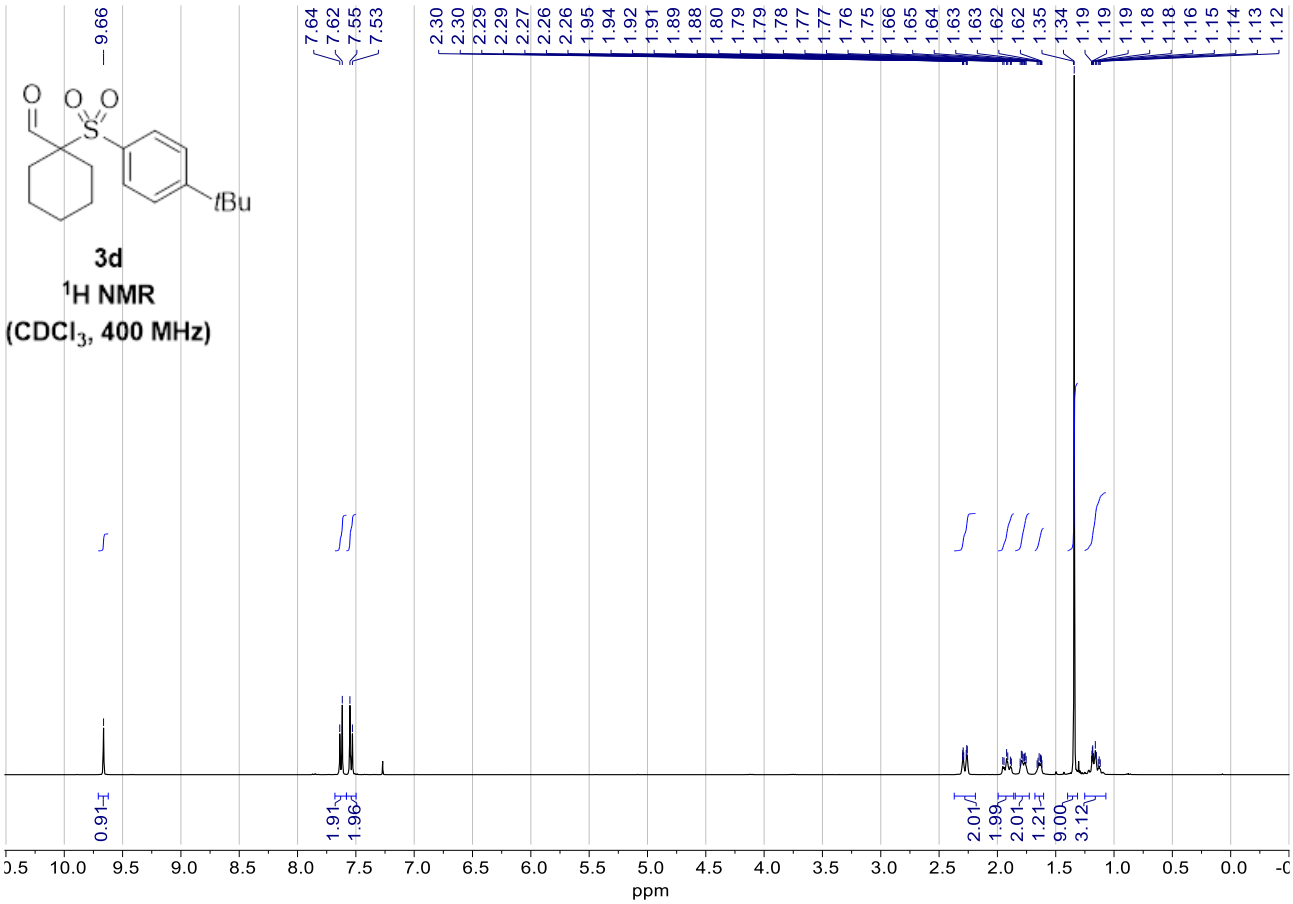

3a
COSY
(CDCl3, 400 MHz, 298 K)
f1 (ppm)
ppm

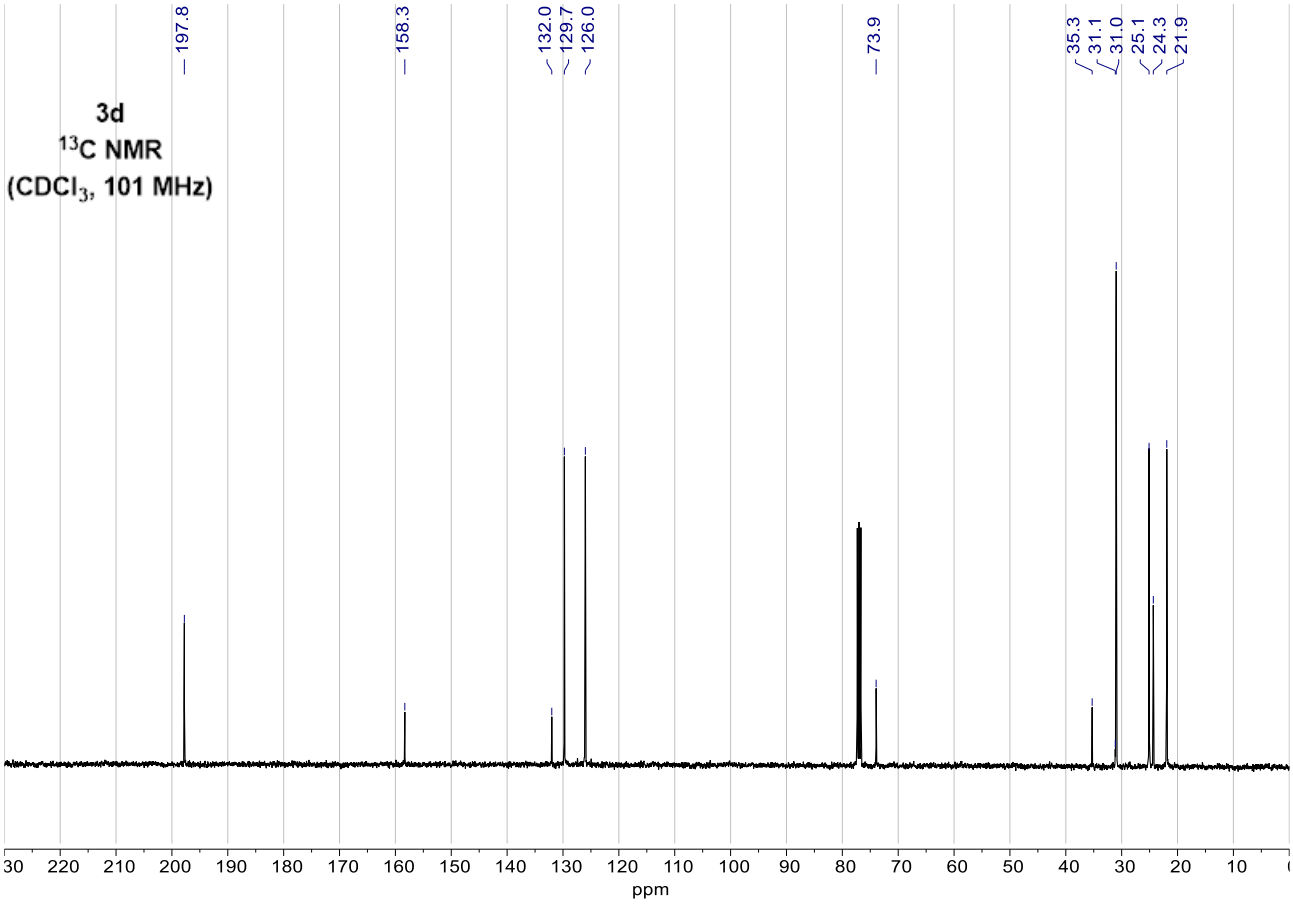

3b
^{1}H NMR
(CDCl$_3$, 400 MHz)
ppm

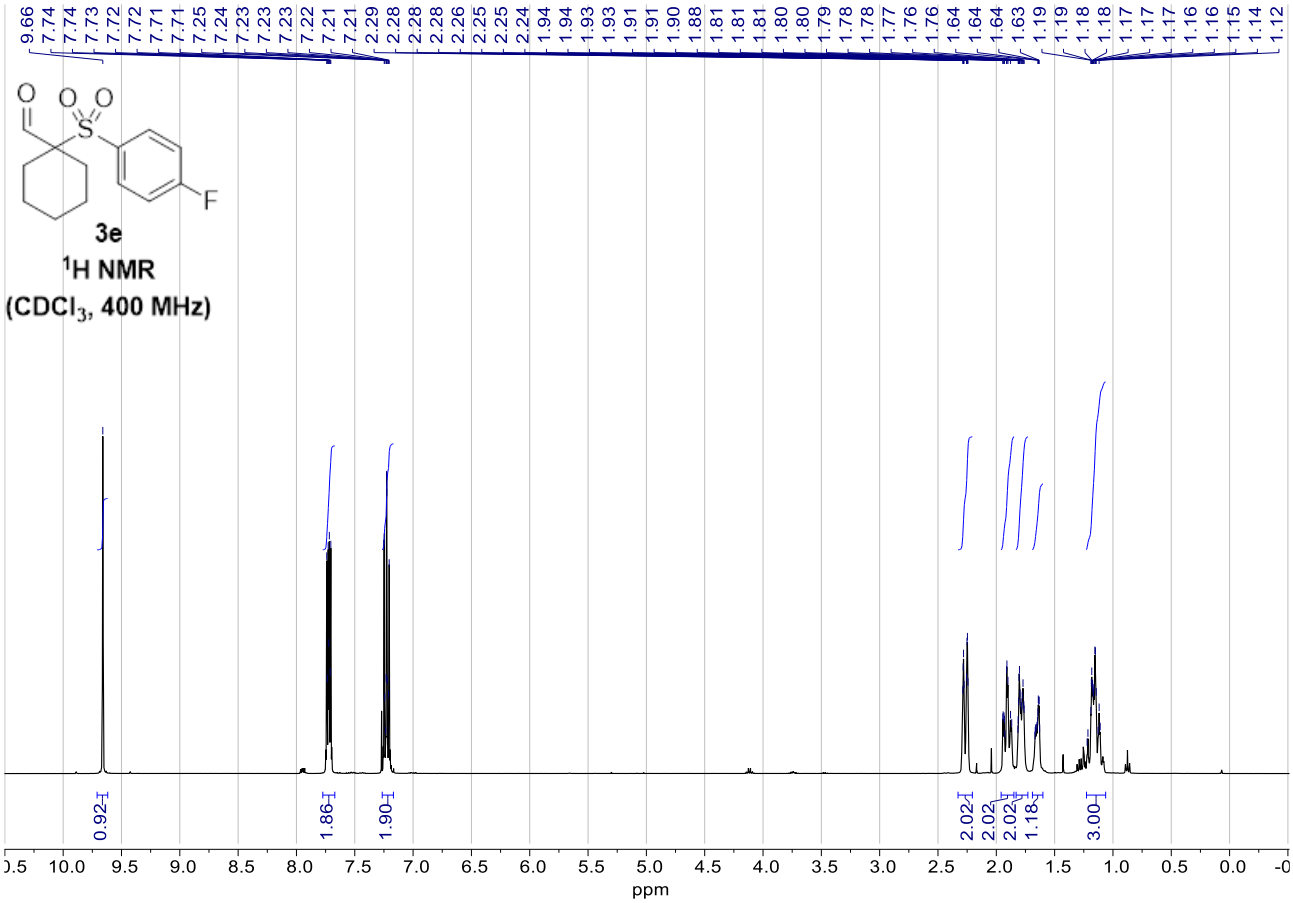

3b
^{13}C NMR
(CDCl$_3$, 101 MHz)
ppm

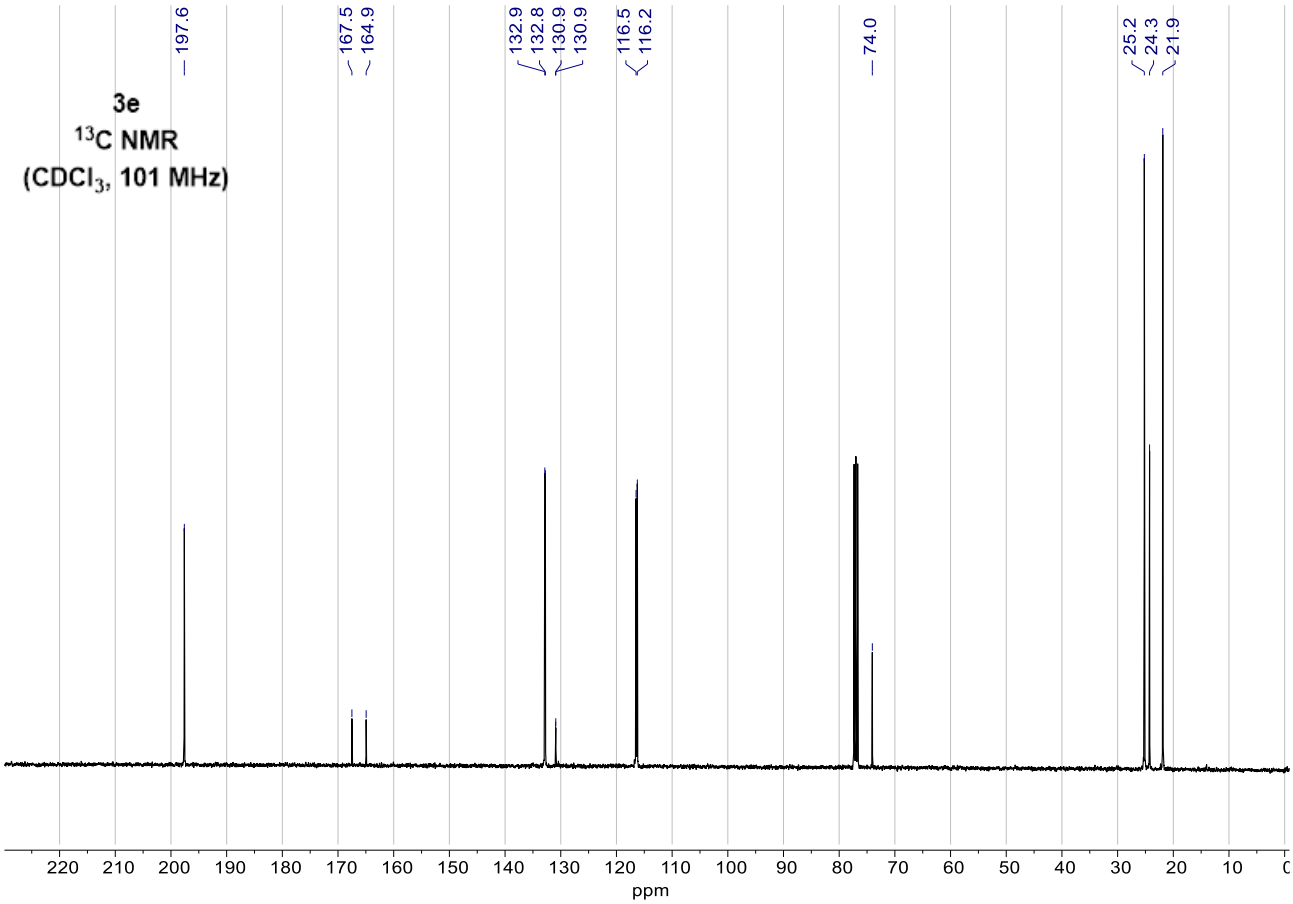

3c
^{1}H NMR
(CDCl$_3$, 400 MHz)
ppm

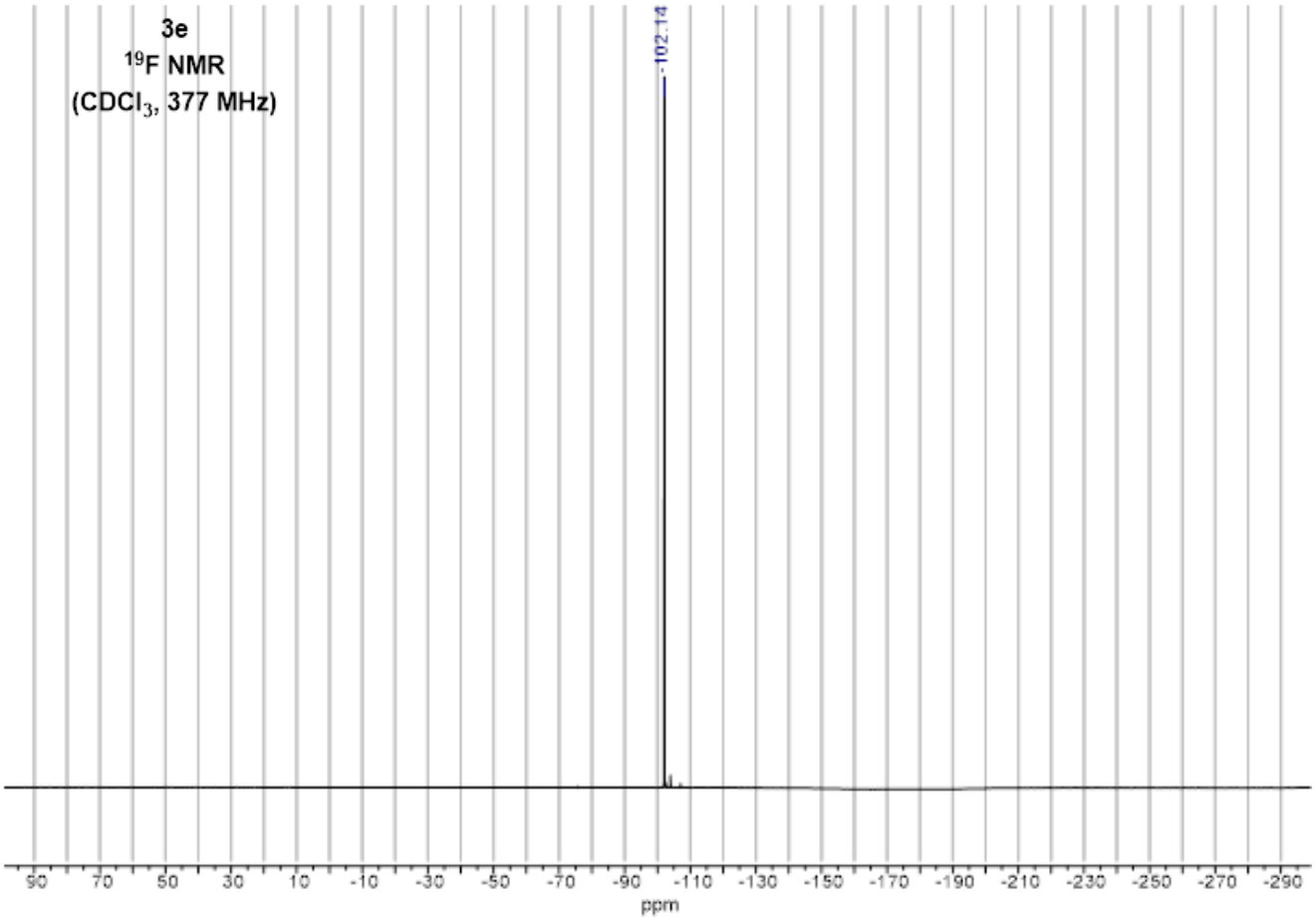

3c
^{13}C NMR
(CDCl$_3$, 101 MHz)
198.0
164.3
132.1
126.3
114.2
74.1
55.7
25.3
24.4
22.0
ppm

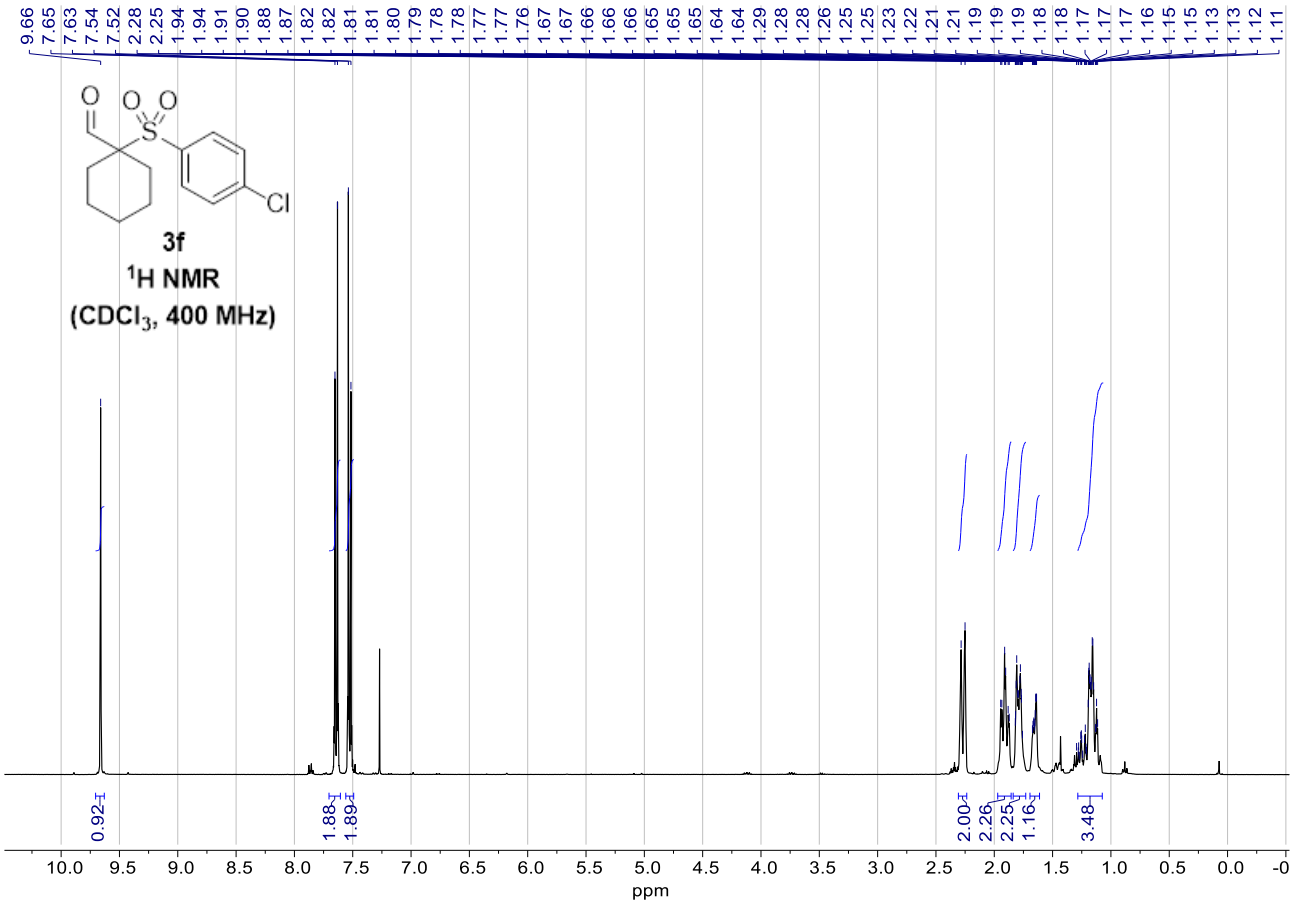

9.66
7.64
7.62
7.55
7.53
2.30
2.30
2.29
2.29
2.27
2.26
2.26
1.95
1.94
1.92
1.91
1.89
1.88
1.80
1.79
1.79
1.78
1.77
1.77
1.76
1.75
1.66
1.65
1.64
1.63
1.63
1.62
1.62
1.35
1.34
1.19
1.19
1.19
1.18
1.18
1.16
1.15
1.14
1.13
1.12
tBu
3d
^{1}H NMR
($CDCl_3$, 400 MHz)
0.91
1.91
1.96
2.01
1.99
2.01
1.21
9.00
3.12
ppm

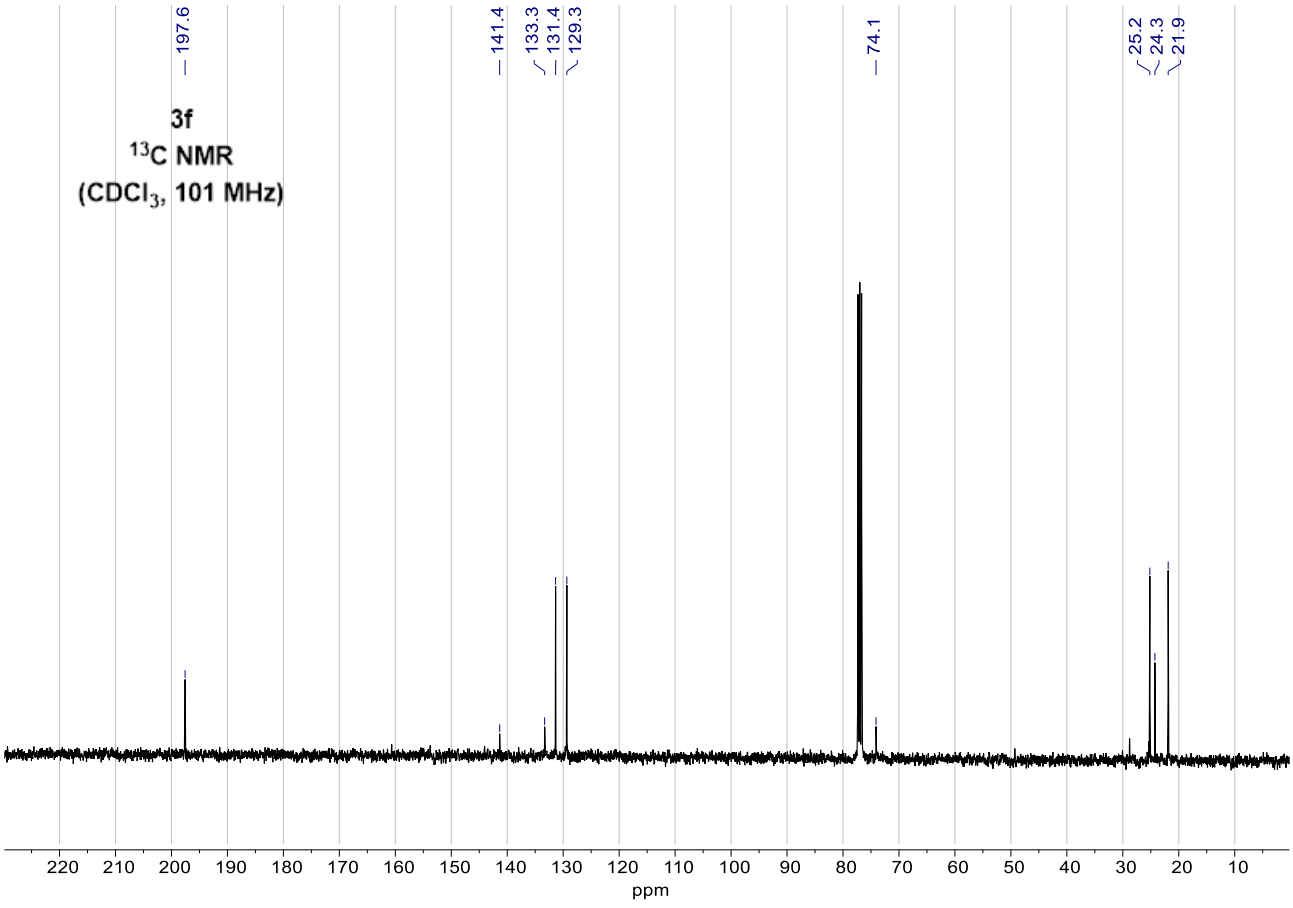

197.8
158.3
132.0
129.7
126.0
73.9
35.3
31.1
31.0
25.1
24.3
21.9
3d
^{13}C NMR
($CDCl_3$, 101 MHz)
ppm

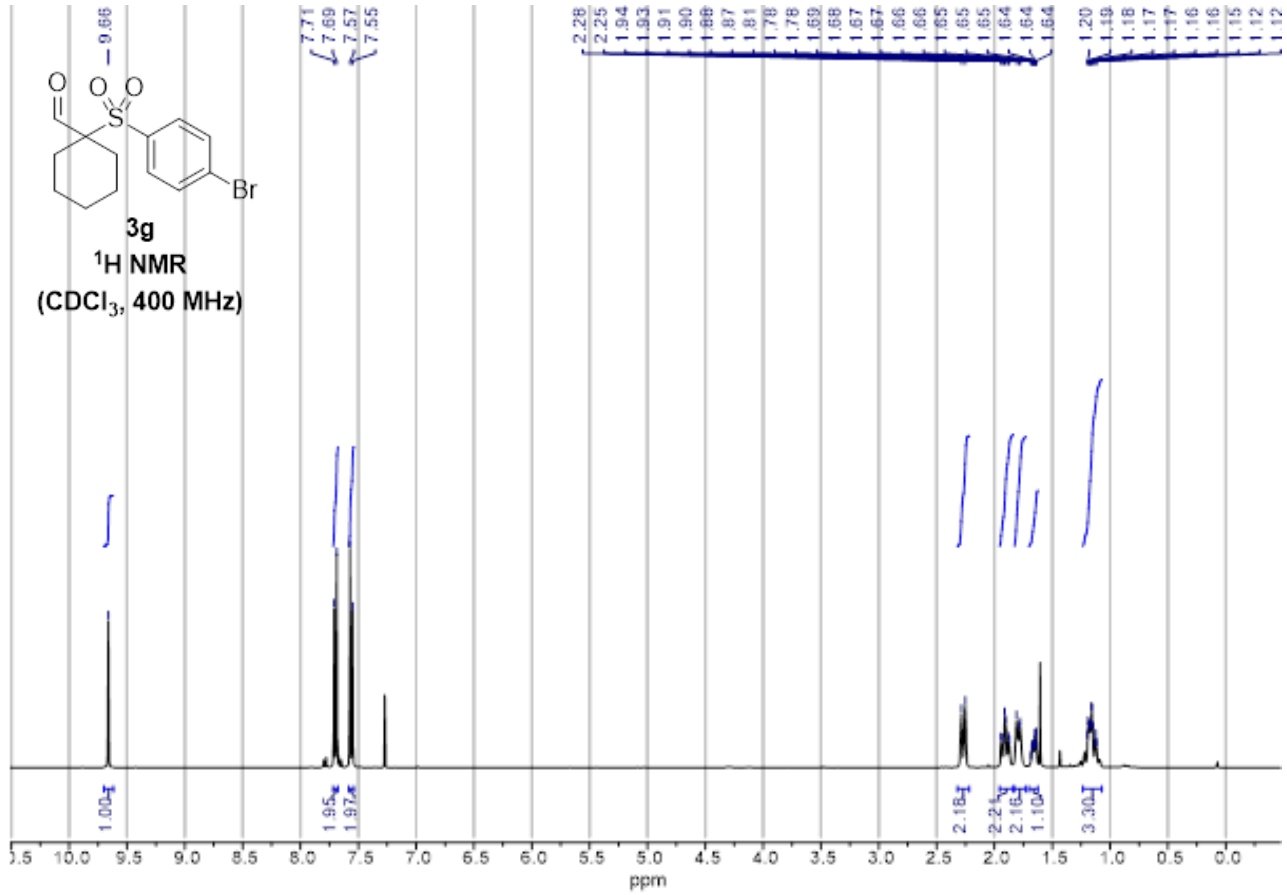

3e
^{1}H NMR
(CDCl$_3$, 400 MHz)
ppm

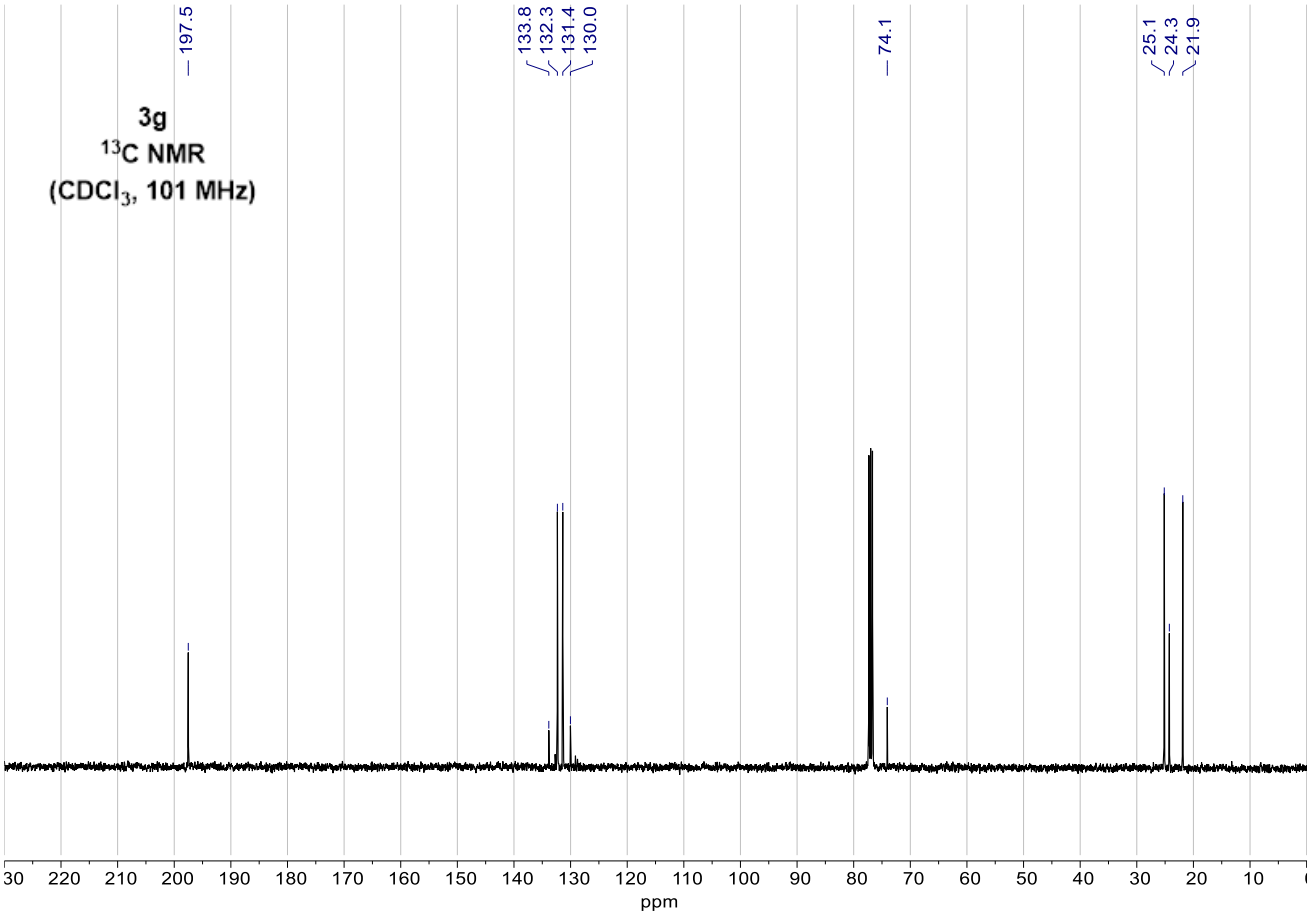

3e
^{13}C NMR
(CDCl$_3$, 101 MHz)
ppm

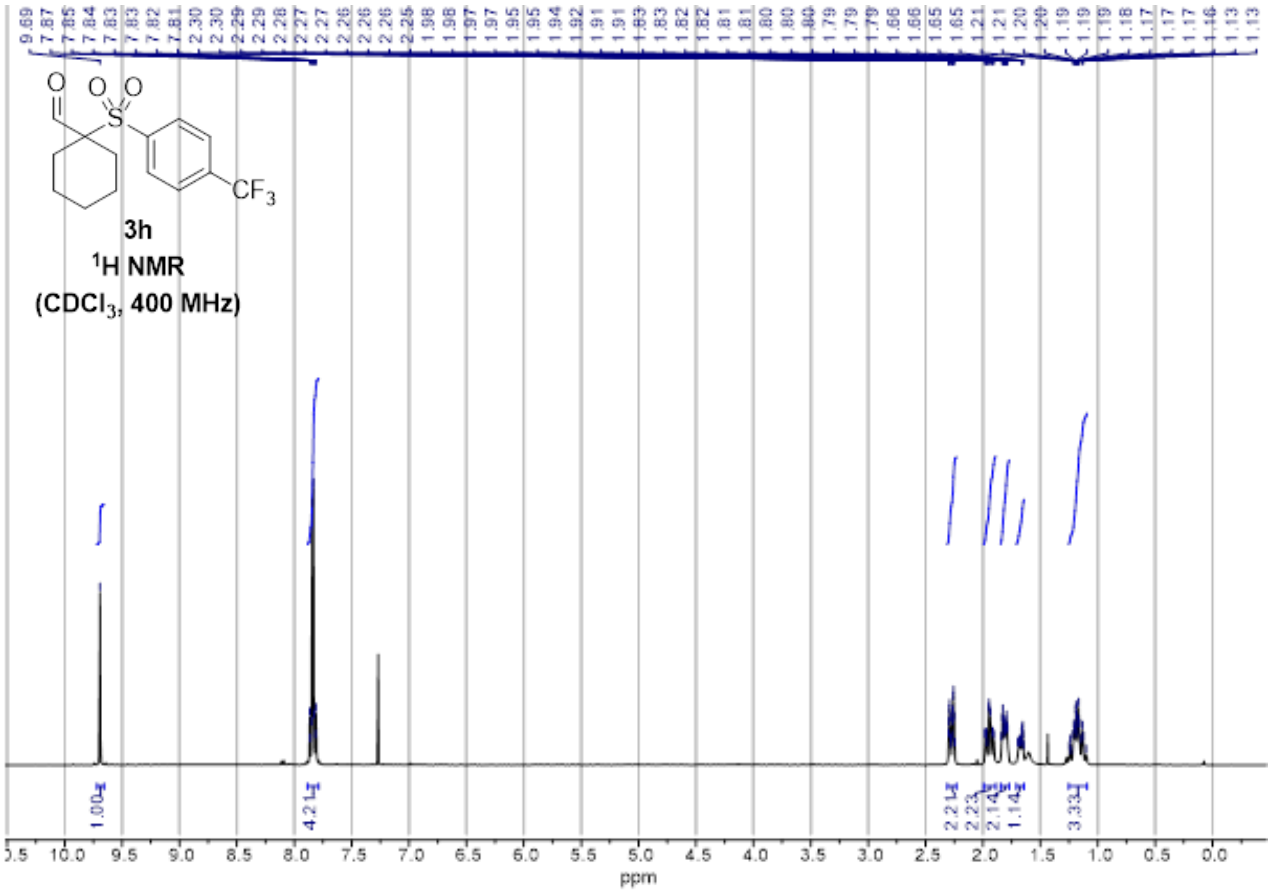

3e
^{19}F NMR
($CDCl_3$, 377 MHz)
-102.14
90 70 50 30 10 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190 -210 -230 -250 -270 -290
ppm

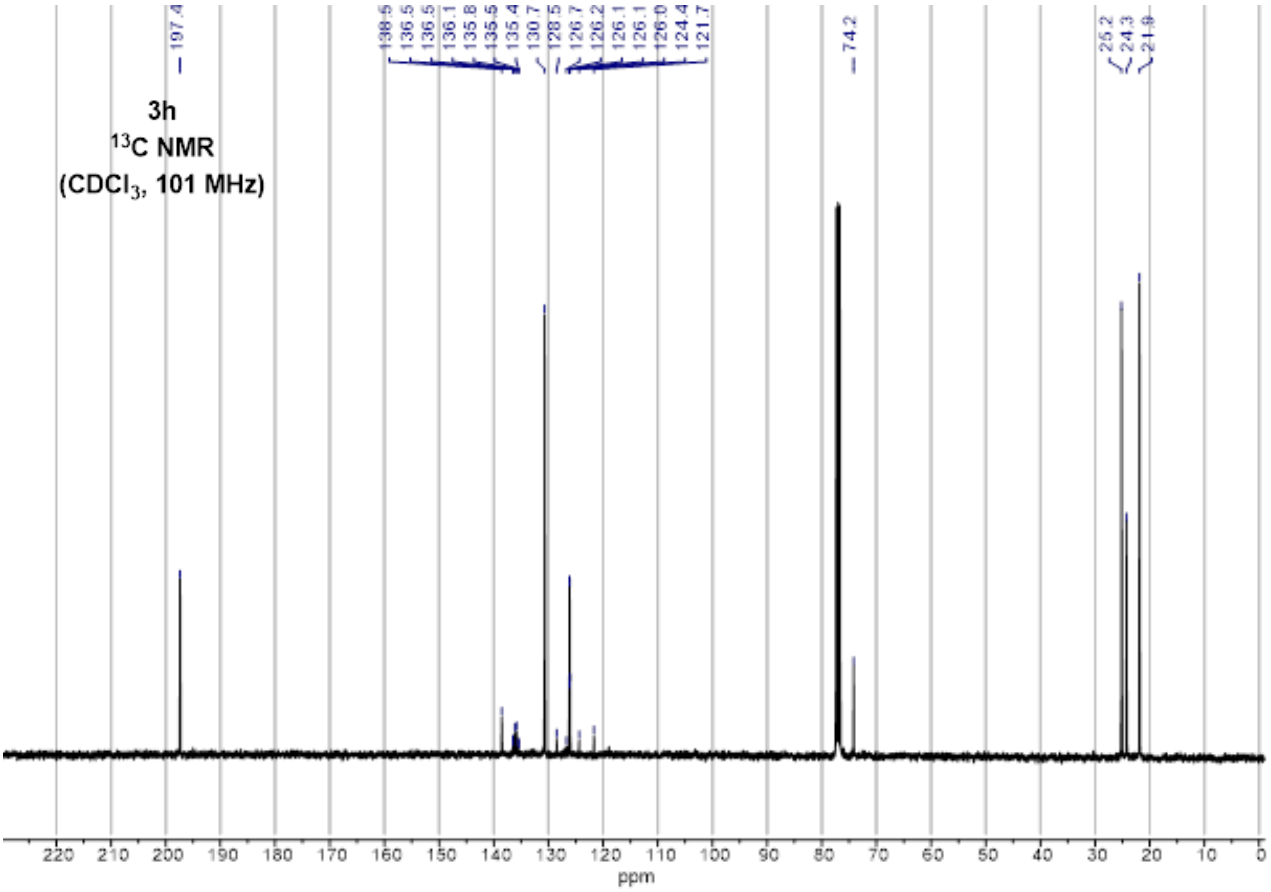

9.66 7.65 7.63 7.54 7.52 2.28 2.25 1.94 1.94 1.91 1.90 1.88 1.87 1.82 1.82 1.81 1.81 1.80 1.79 1.78 1.78 1.77 1.77 1.76 1.67 1.67 1.66 1.66 1.66 1.65 1.65 1.65 1.64 1.64 1.29 1.28 1.28 1.26 1.25 1.25 1.23 1.22 1.21 1.21 1.19 1.19 1.19 1.18 1.18 1.17 1.17 1.17 1.16 1.15 1.15 1.13 1.13 1.12 1.11
O
O
O
S
Cl
3f
^{1}H NMR
($CDCl_3$, 400 MHz)
0.92
1.88
1.89
2.00
2.26
2.25
1.16
3.48
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
ppm

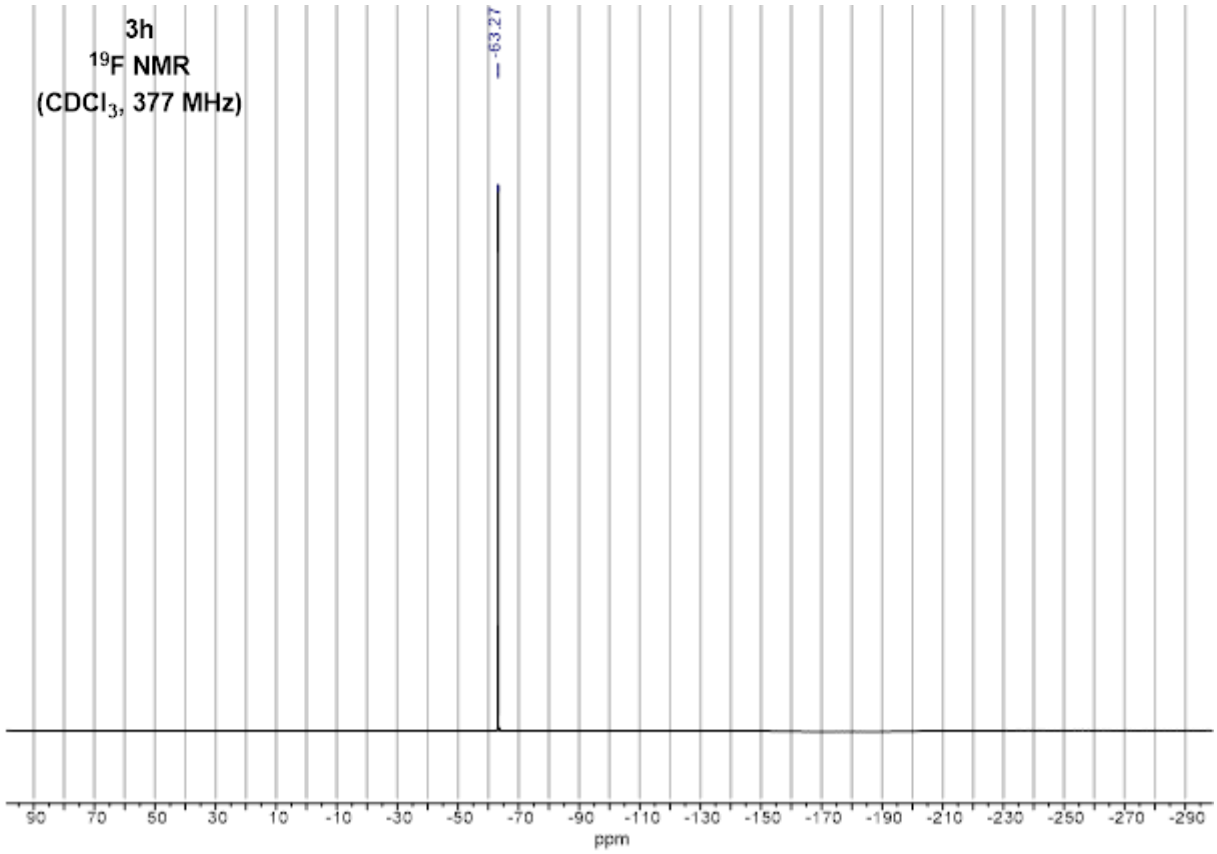

197.6
141.4
133.3
131.4
129.3
74.1
25.2
24.3
21.9
3f
^{13}C NMR
($CDCl_3$, 101 MHz)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

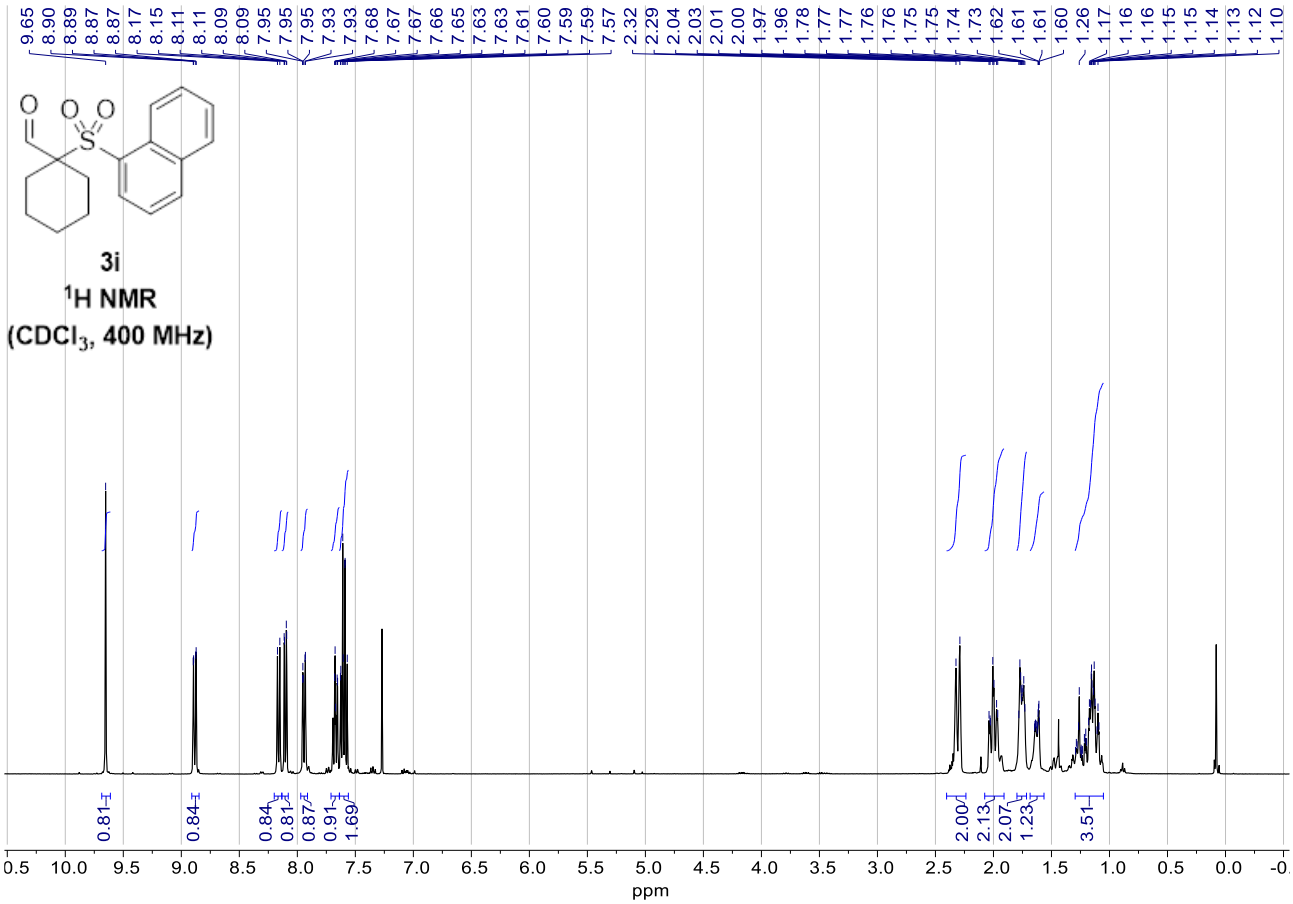

3g
^{1}H NMR
(CDCl$_3$, 400 MHz)
ppm

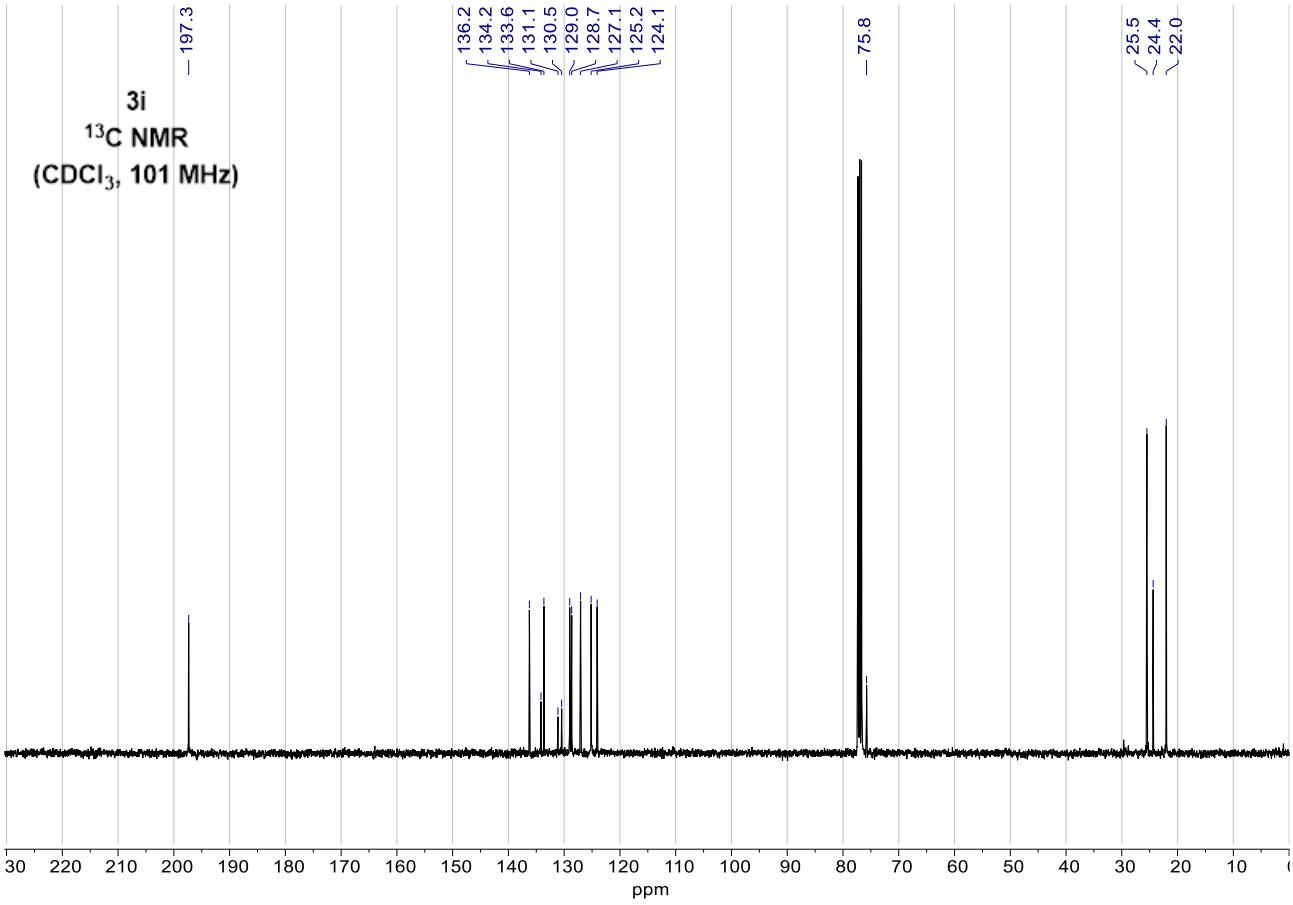

3g
^{13}C NMR
(CDCl$_3$, 101 MHz)
ppm

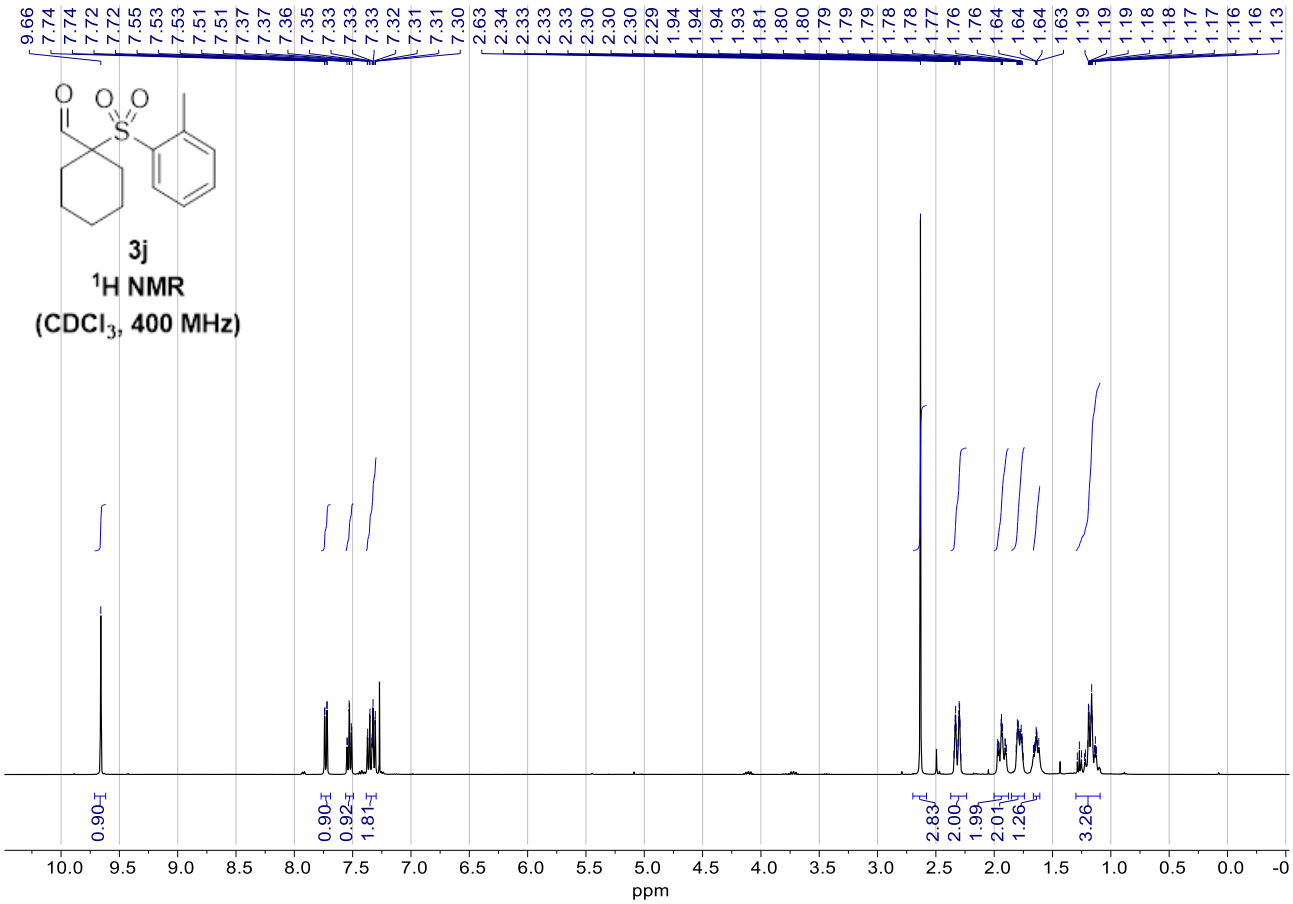

3h
^{1}H NMR
($CDCl_3$, 400 MHz)
ppm

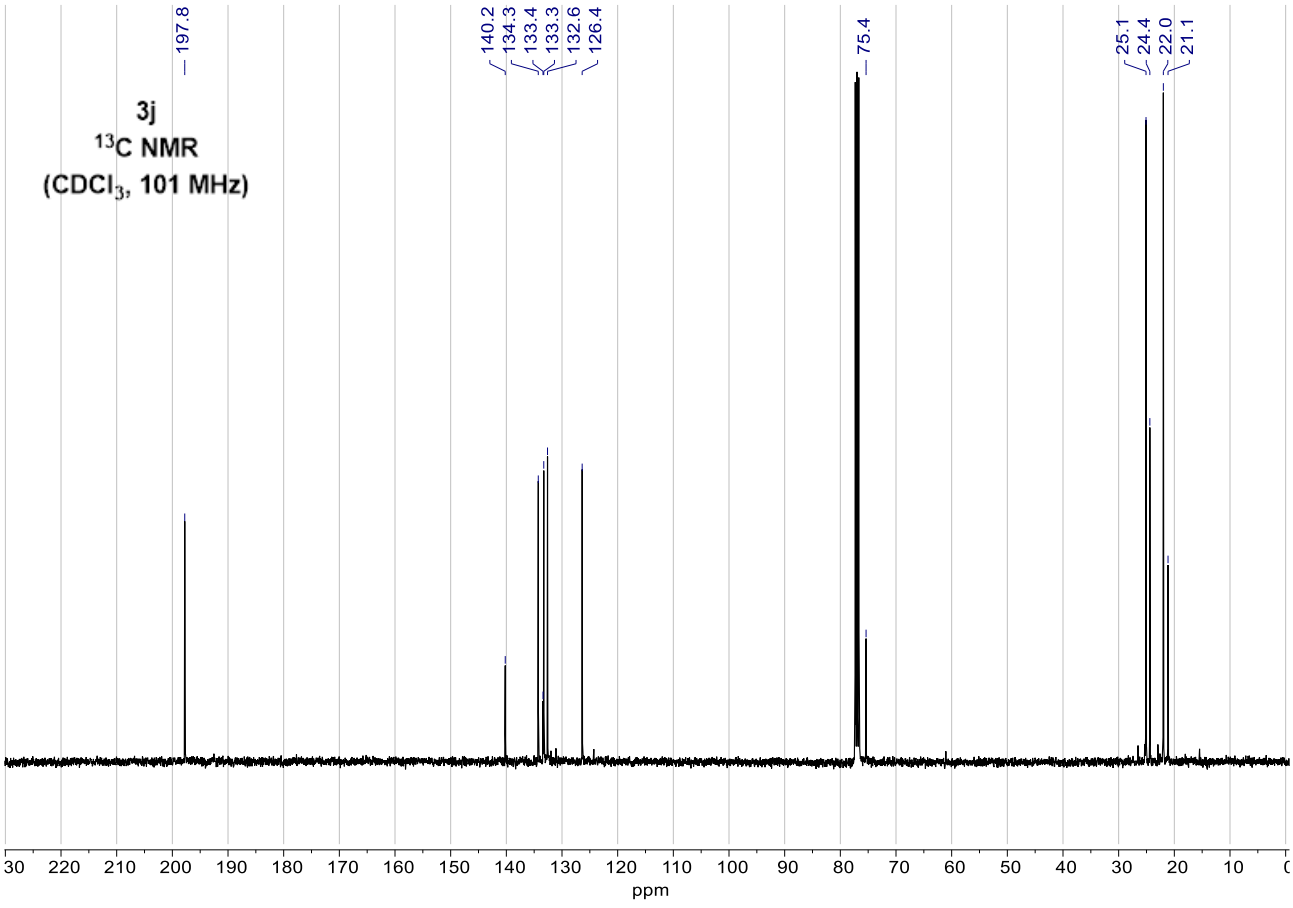

3h
^{13}C NMR
($CDCl_3$, 101 MHz)
ppm

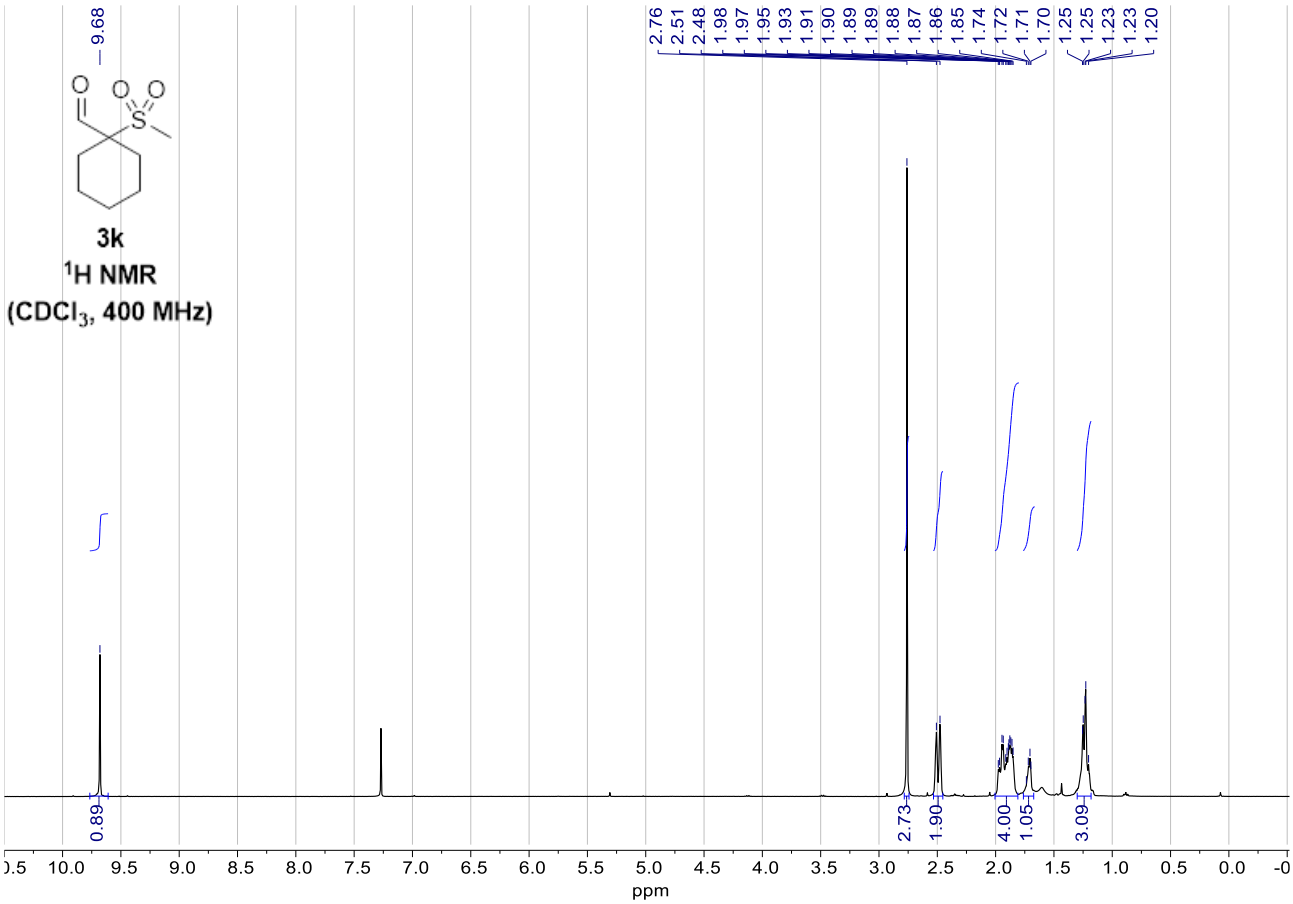

3h
^{19}F NMR
($CDCl_3$, 377 MHz)
-63.27
90 70 50 30 10 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190 -210 -230 -250 -270 -290
ppm

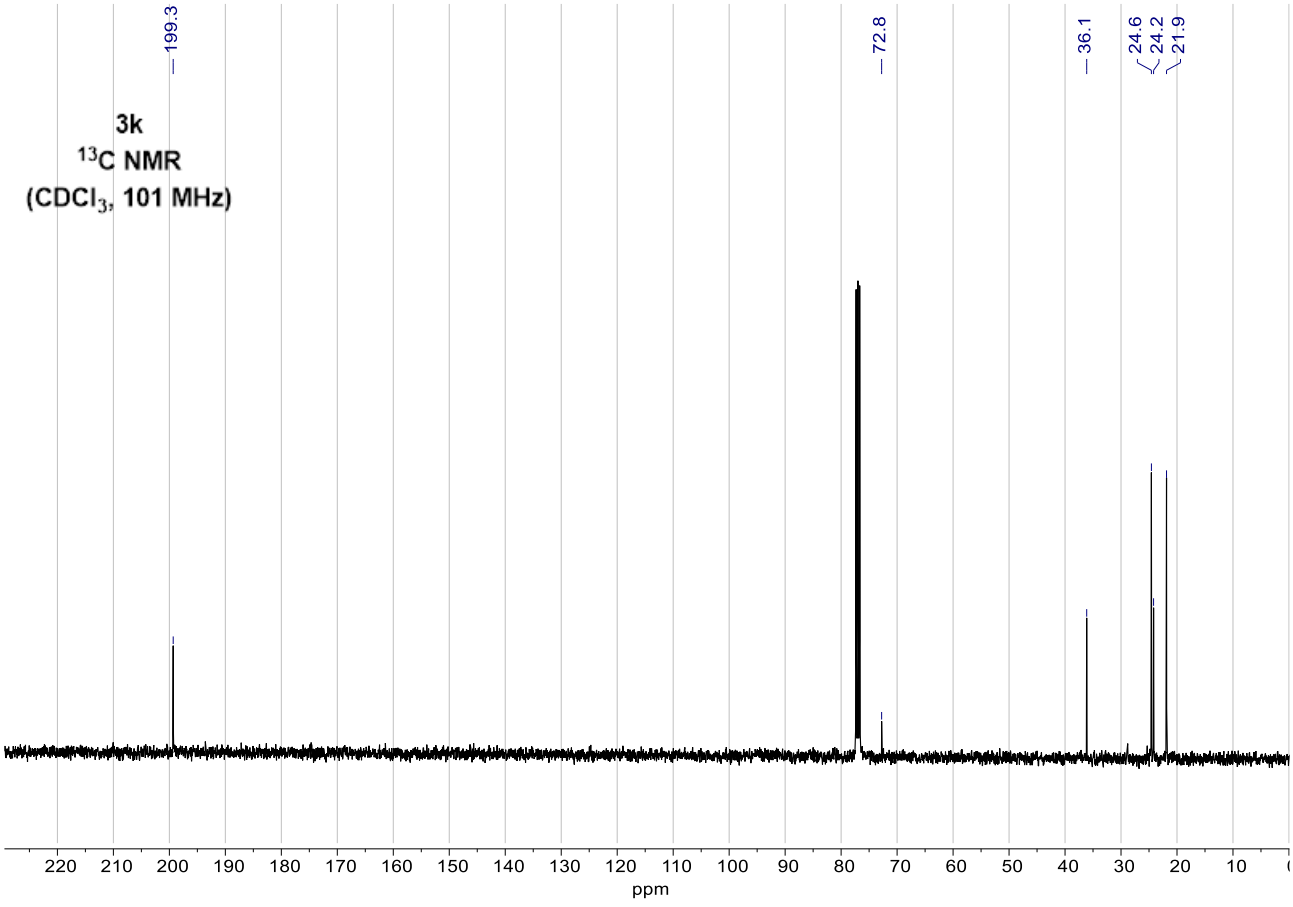

3i
^{1}H NMR
(CDCl$_3$, 400 MHz)
ppm

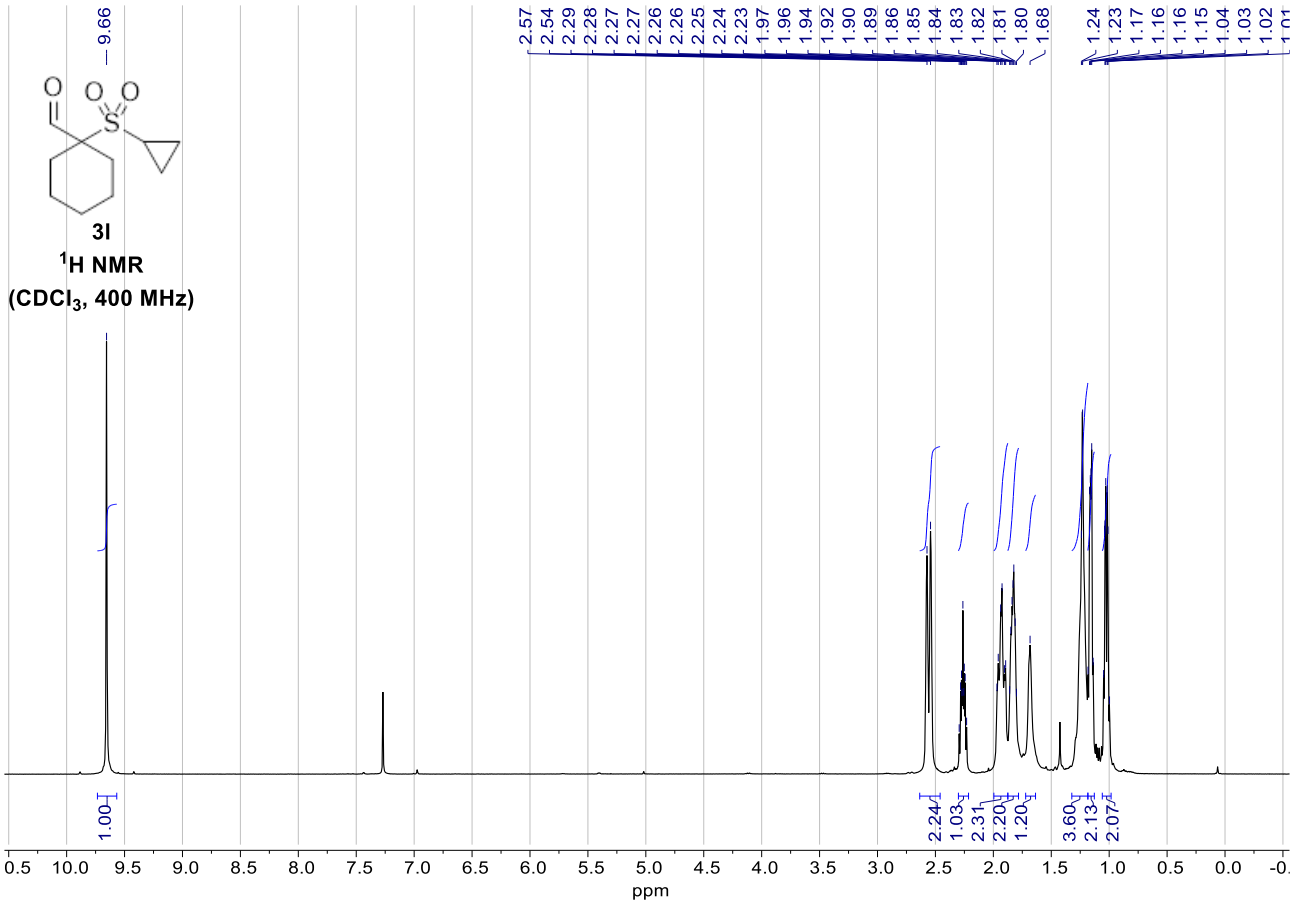

3i
^{13}C NMR
(CDCl$_3$, 101 MHz)
ppm

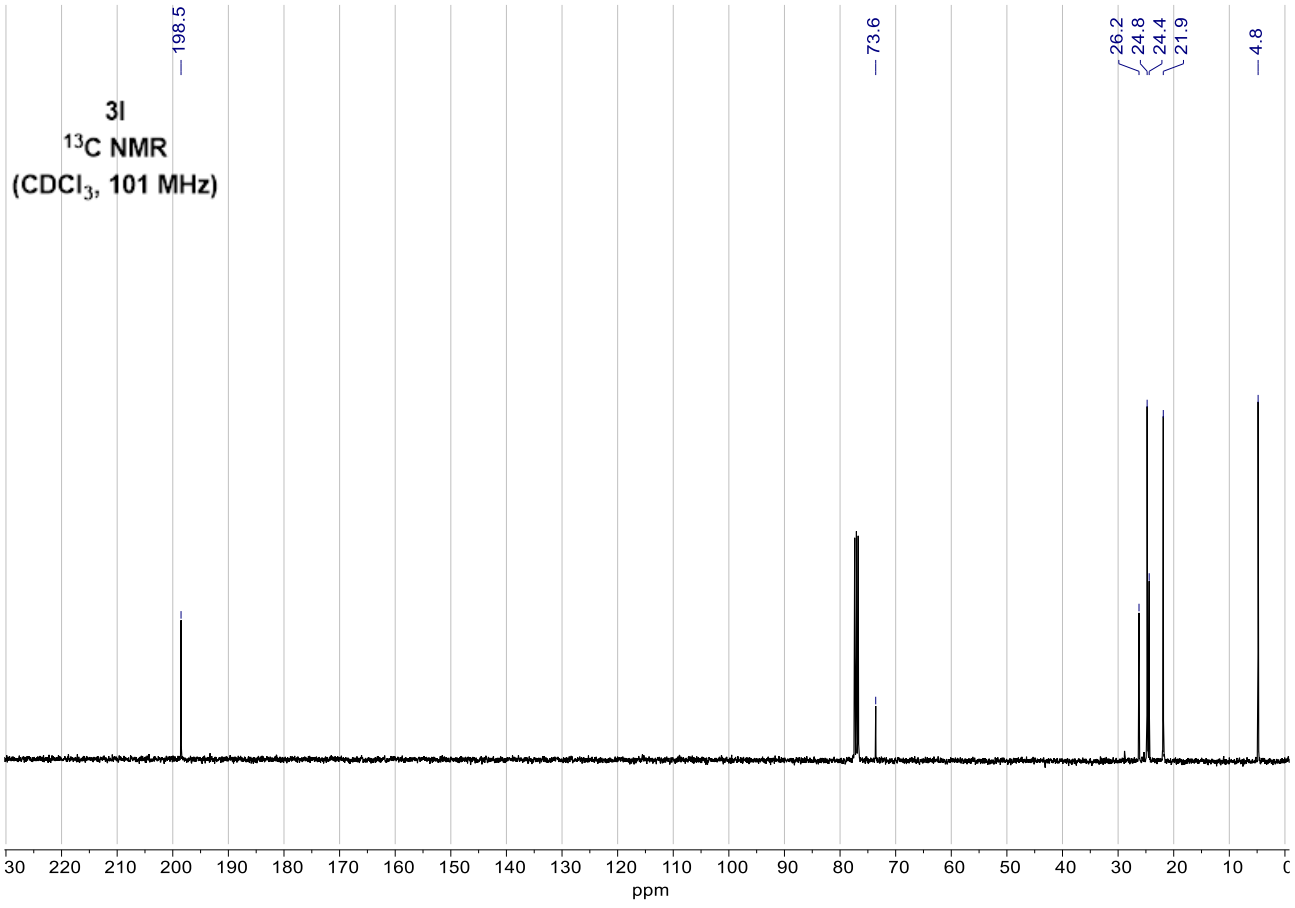

3j
^{1}H NMR
(CDCl$_3$, 400 MHz)
ppm

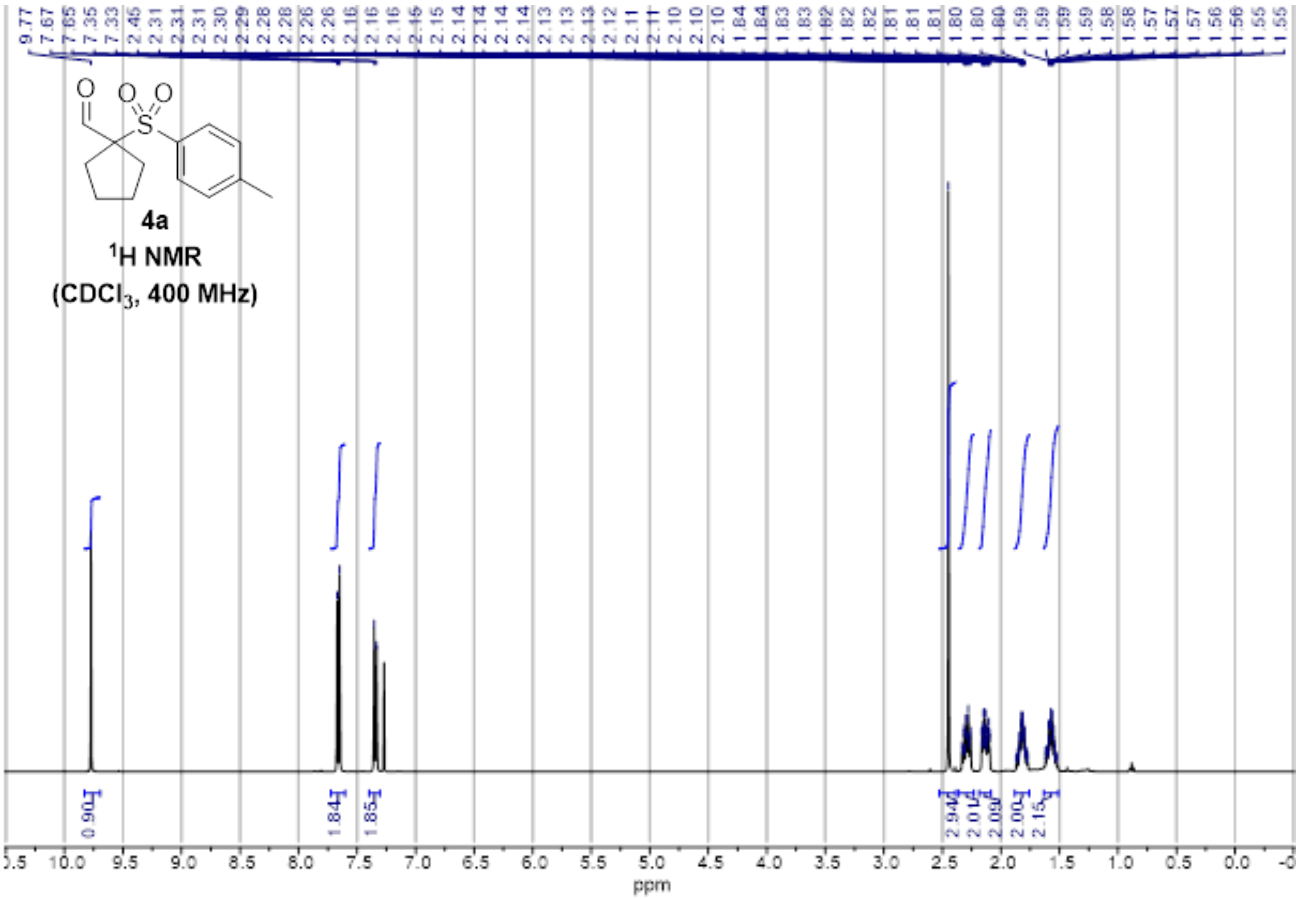

3j
^{13}C NMR
(CDCl$_3$, 101 MHz)
ppm

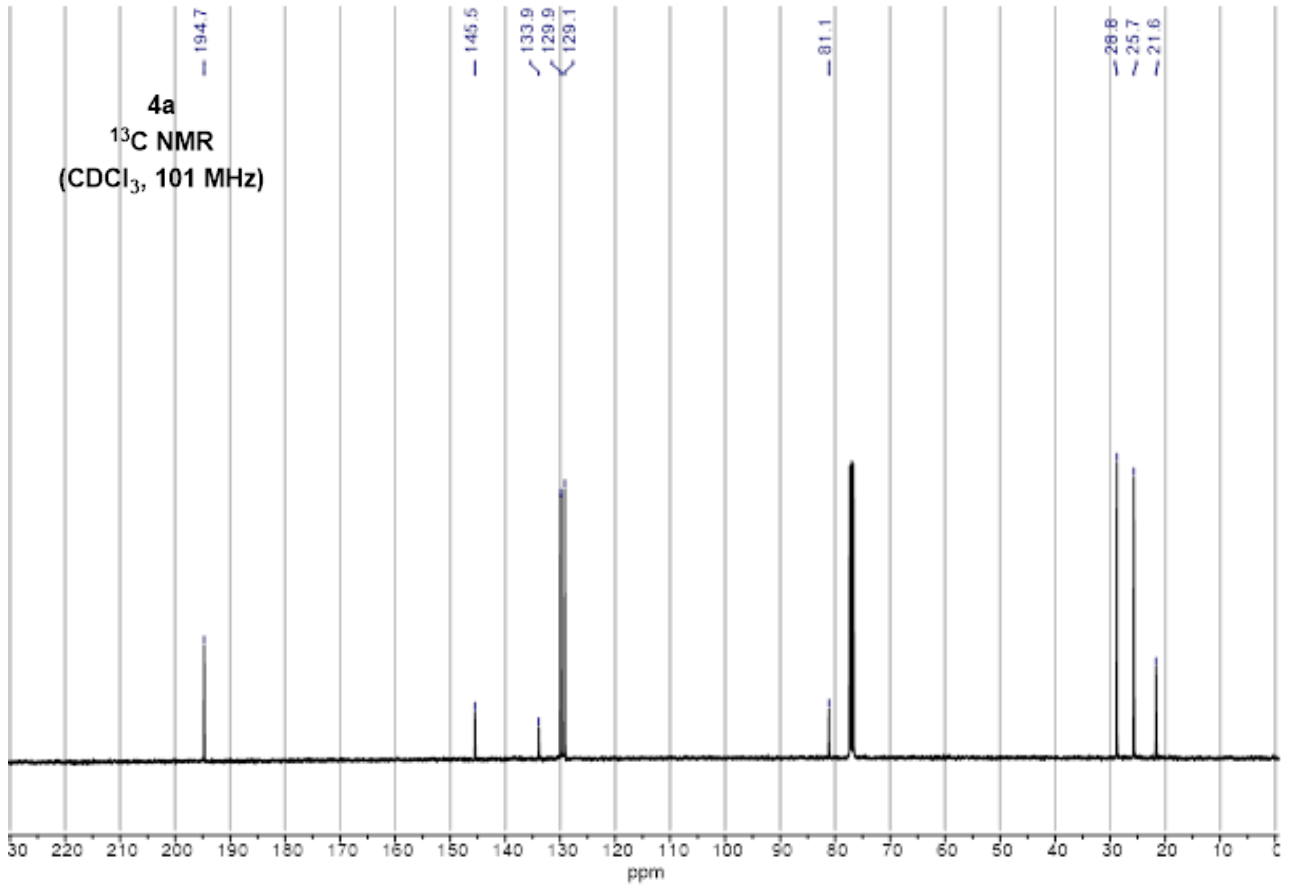

9.68
2.76
2.51
2.48
1.98
1.97
1.95
1.93
1.91
1.90
1.89
1.89
1.88
1.87
1.86
1.85
1.74
1.72
1.71
1.70
1.25
1.25
1.23
1.23
1.20
3k
^{1}H NMR
(CDCl$_3$, 400 MHz)
0.89
2.73
1.90
4.00
1.05
3.09
ppm

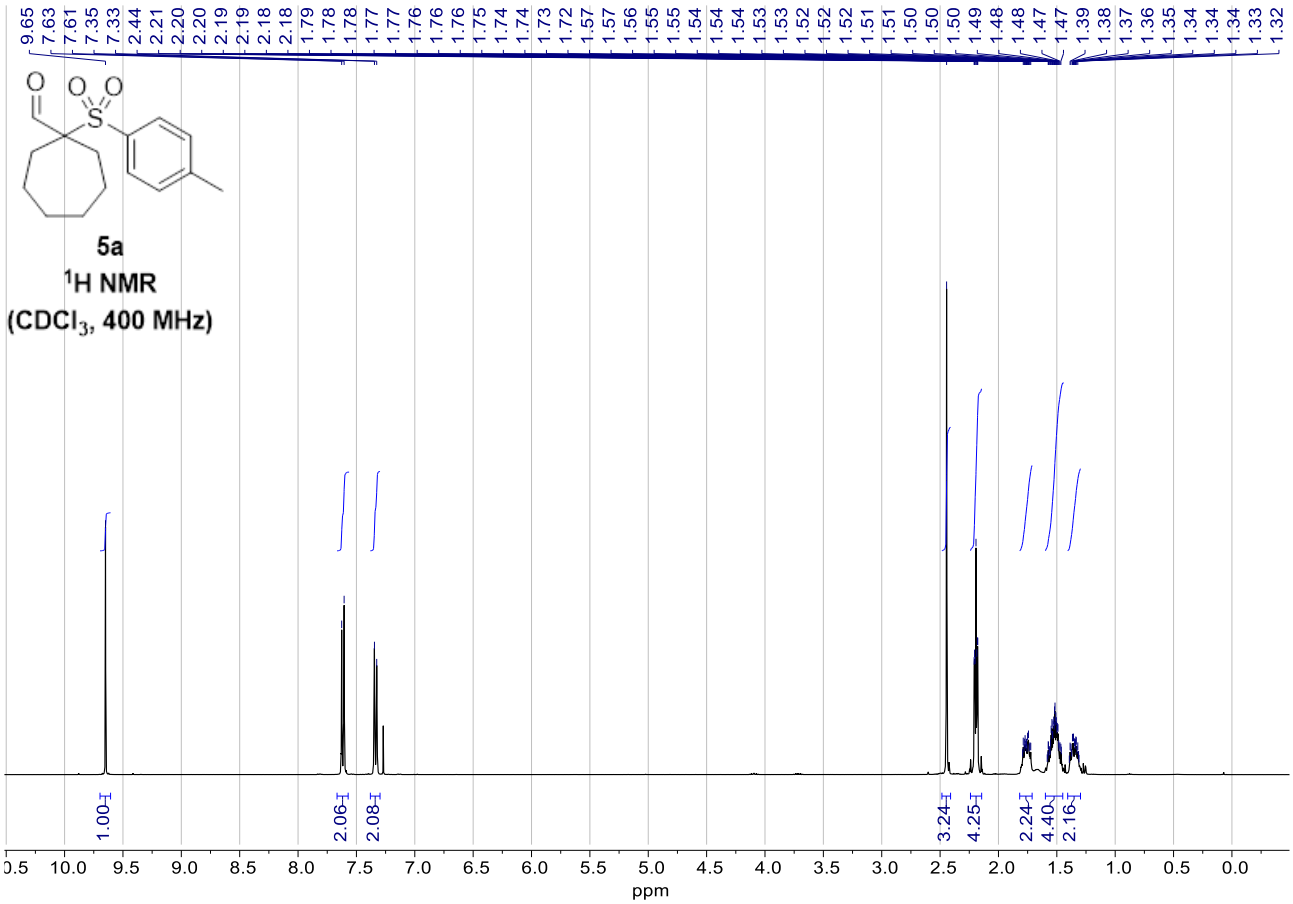

199.3
72.8
36.1
24.6
24.2
21.9
3k
^{13}C NMR
(CDCl$_3$, 101 MHz)
ppm

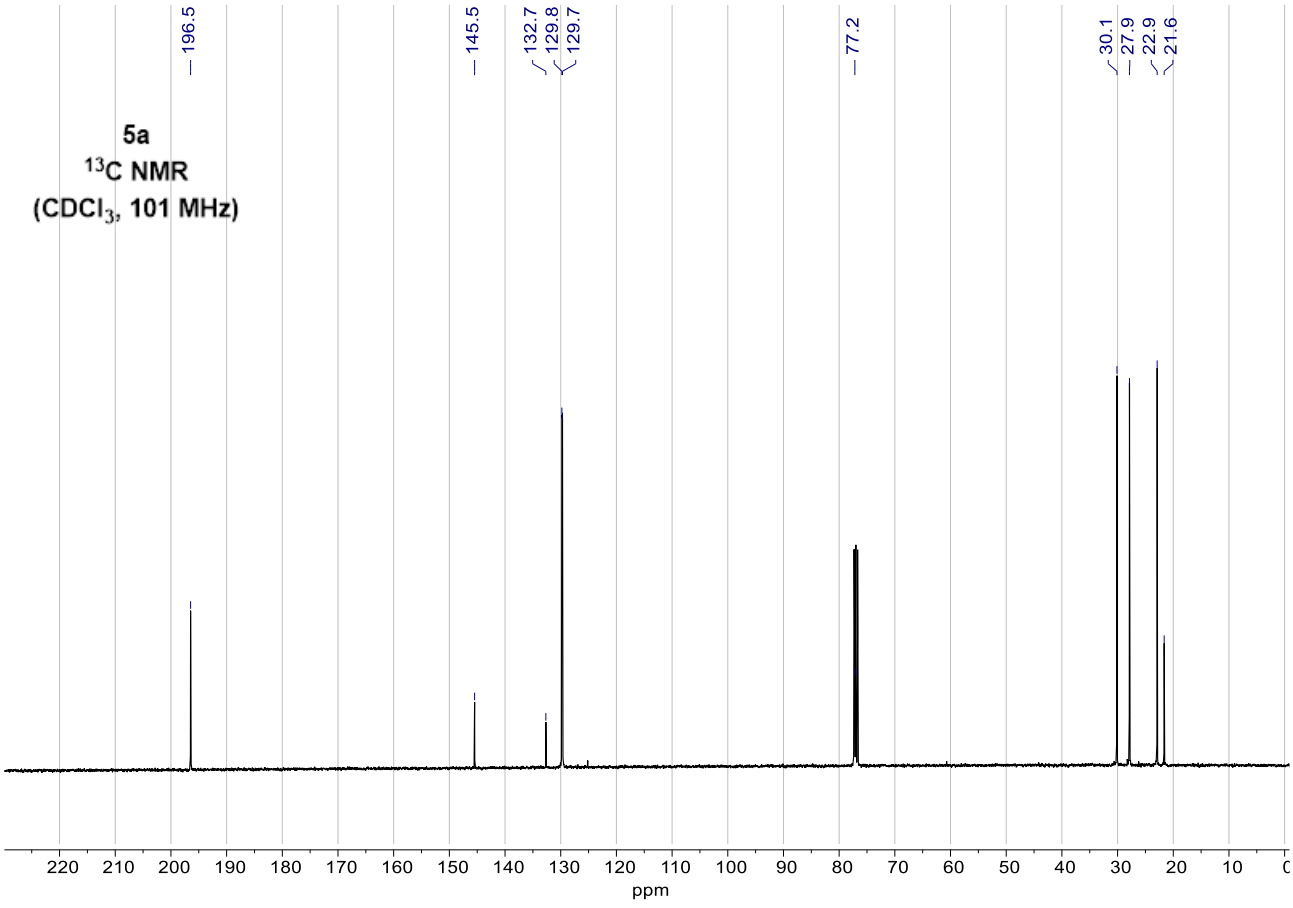

9.66
2.57
2.54
2.29
2.28
2.27
2.27
2.26
2.26
2.25
2.24
2.23
1.97
1.96
1.94
1.92
1.90
1.89
1.86
1.85
1.84
1.83
1.82
1.81
1.80
1.68
1.24
1.23
1.17
1.16
1.16
1.15
1.04
1.03
1.02
3l
^{1}H NMR
($CDCl_3$, 400 MHz)
1.00
2.24
1.03
2.31
2.20
1.20
3.60
2.13
2.07
ppm

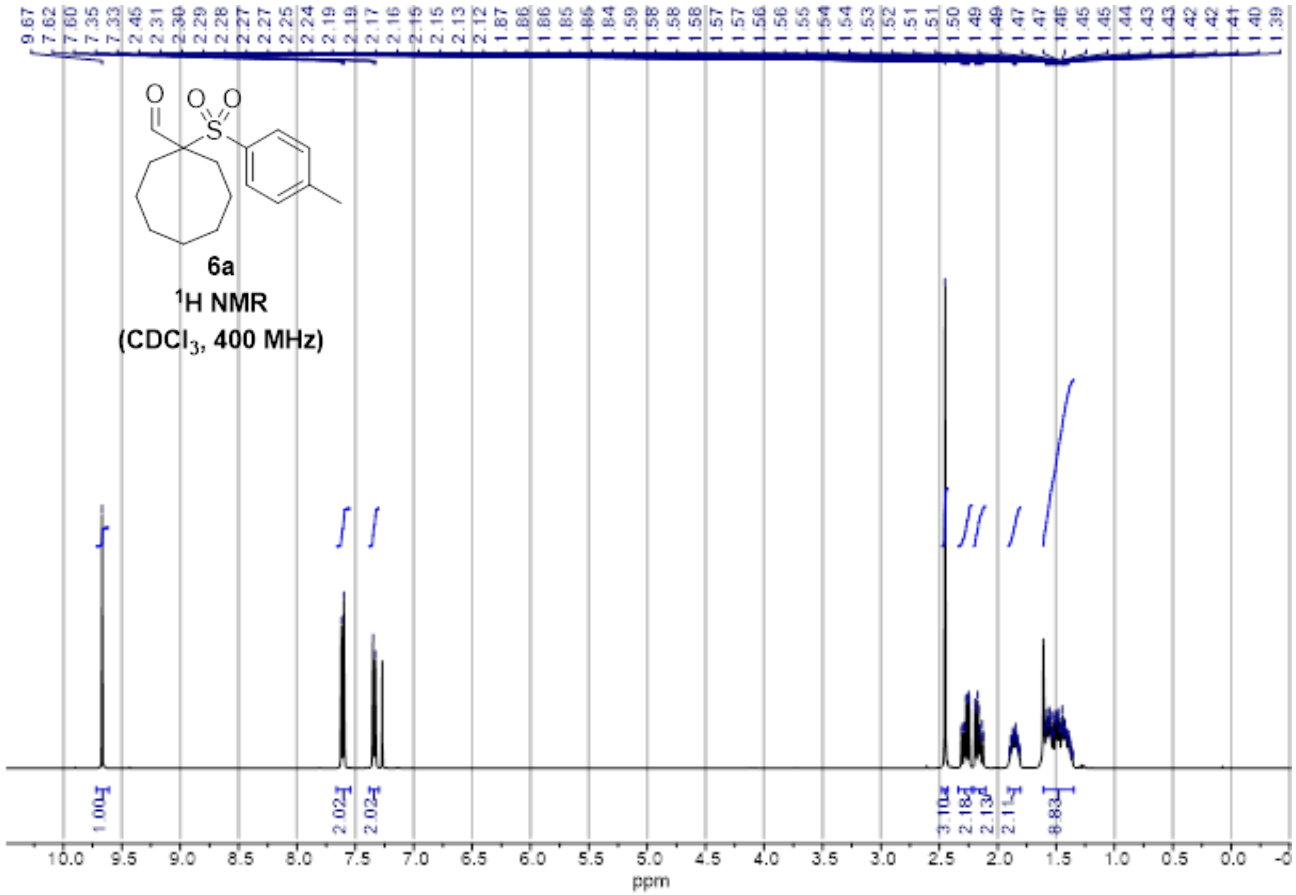

198.5
73.6
26.2
24.8
24.4
21.9
4.8
3l
^{13}C NMR
($CDCl_3$, 101 MHz)
ppm

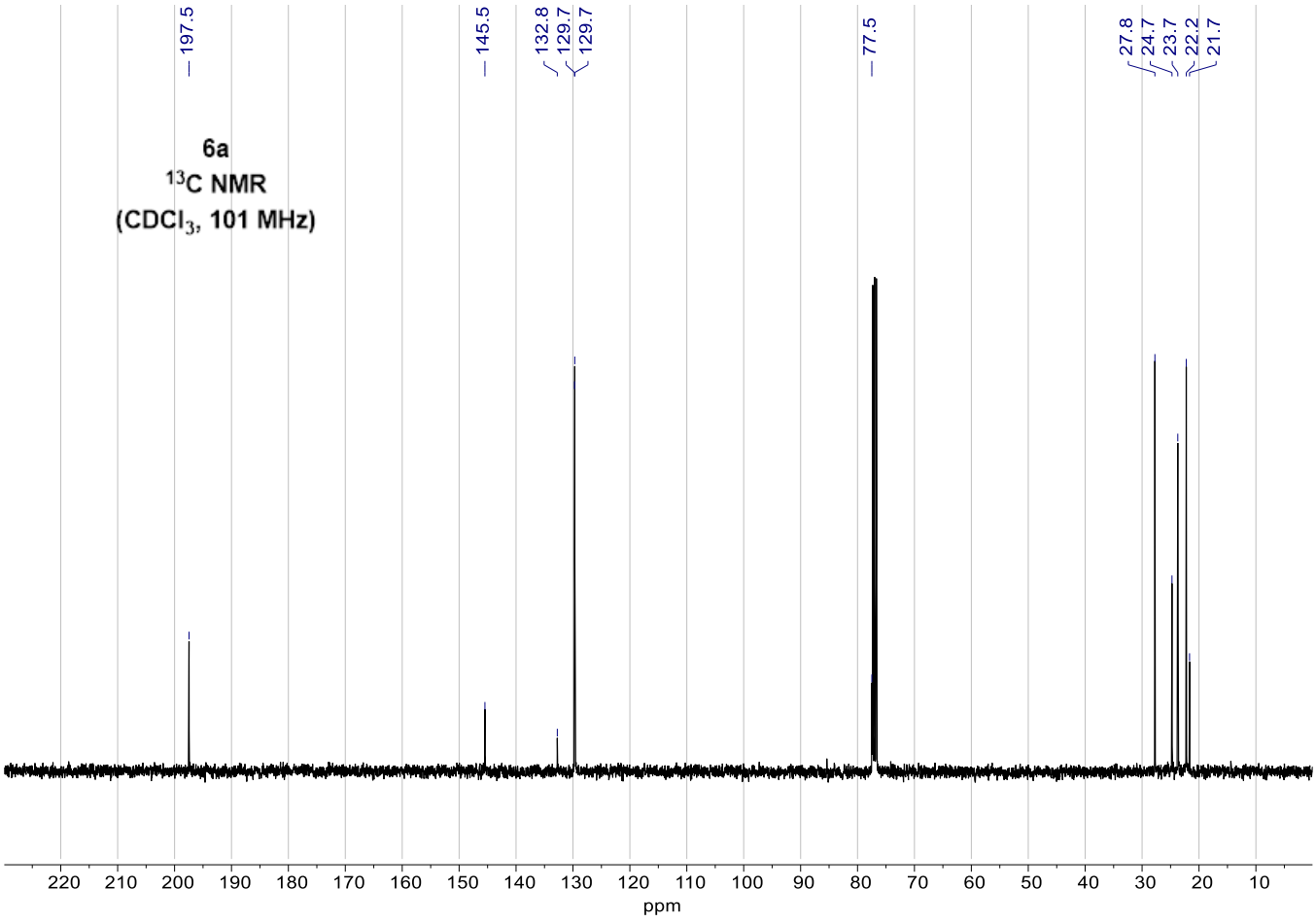

4a
^{1}H NMR
($CDCl_3$, 400 MHz)
ppm

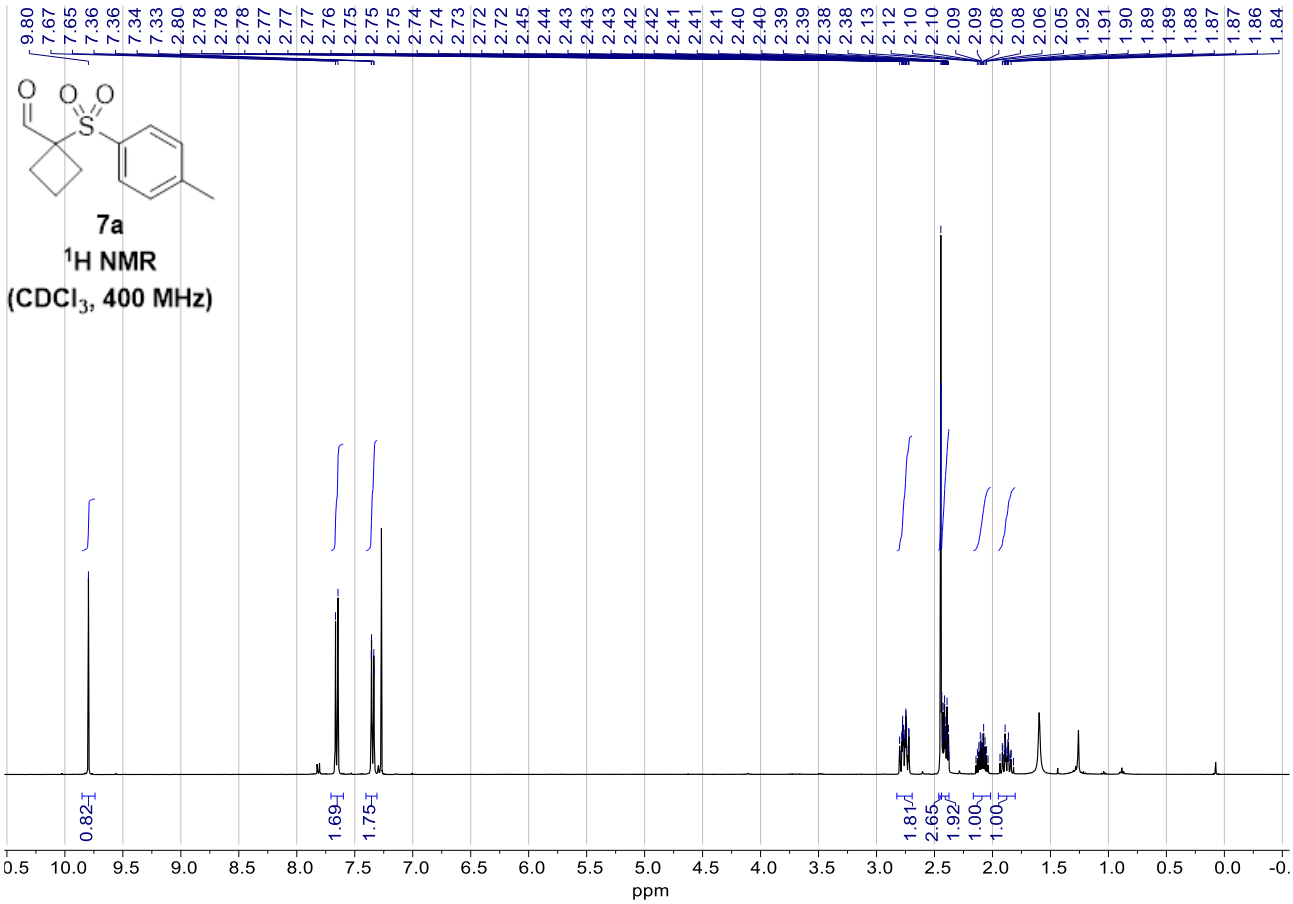

4a
^{13}C NMR
($CDCl_3$, 101 MHz)
194.7
145.5
133.9
129.9
129.1
81.1
28.8
25.7
21.6
ppm

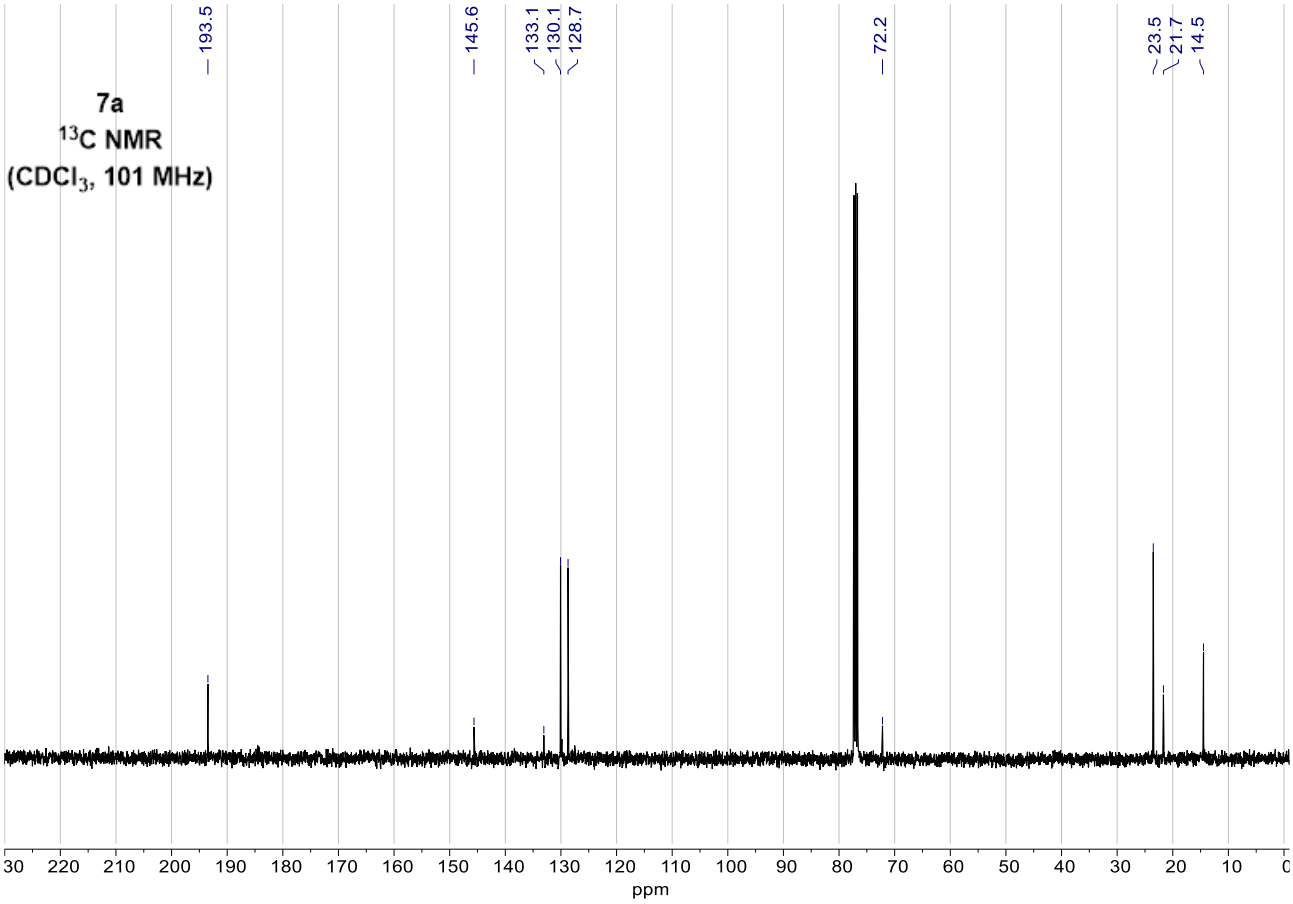

9.65 7.63 7.61 7.35 7.33 2.44 2.21 2.20 2.20 2.19 2.19 2.18 2.18 1.79 1.78 1.78 1.77 1.77 1.76 1.76 1.76 1.75 1.74 1.74 1.73 1.72 1.57 1.56 1.55 1.55 1.54 1.54 1.54 1.53 1.53 1.52 1.52 1.52 1.51 1.51 1.50 1.50 1.50 1.49 1.48 1.48 1.47 1.47 1.39 1.38 1.37 1.36 1.35 1.34 1.34 1.34 1.33 1.32
O O O S
5a
^{1}H NMR
($CDCl_3$, 400 MHz)
1.00 2.06 2.08 3.24 4.25 2.24 4.40 2.16
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

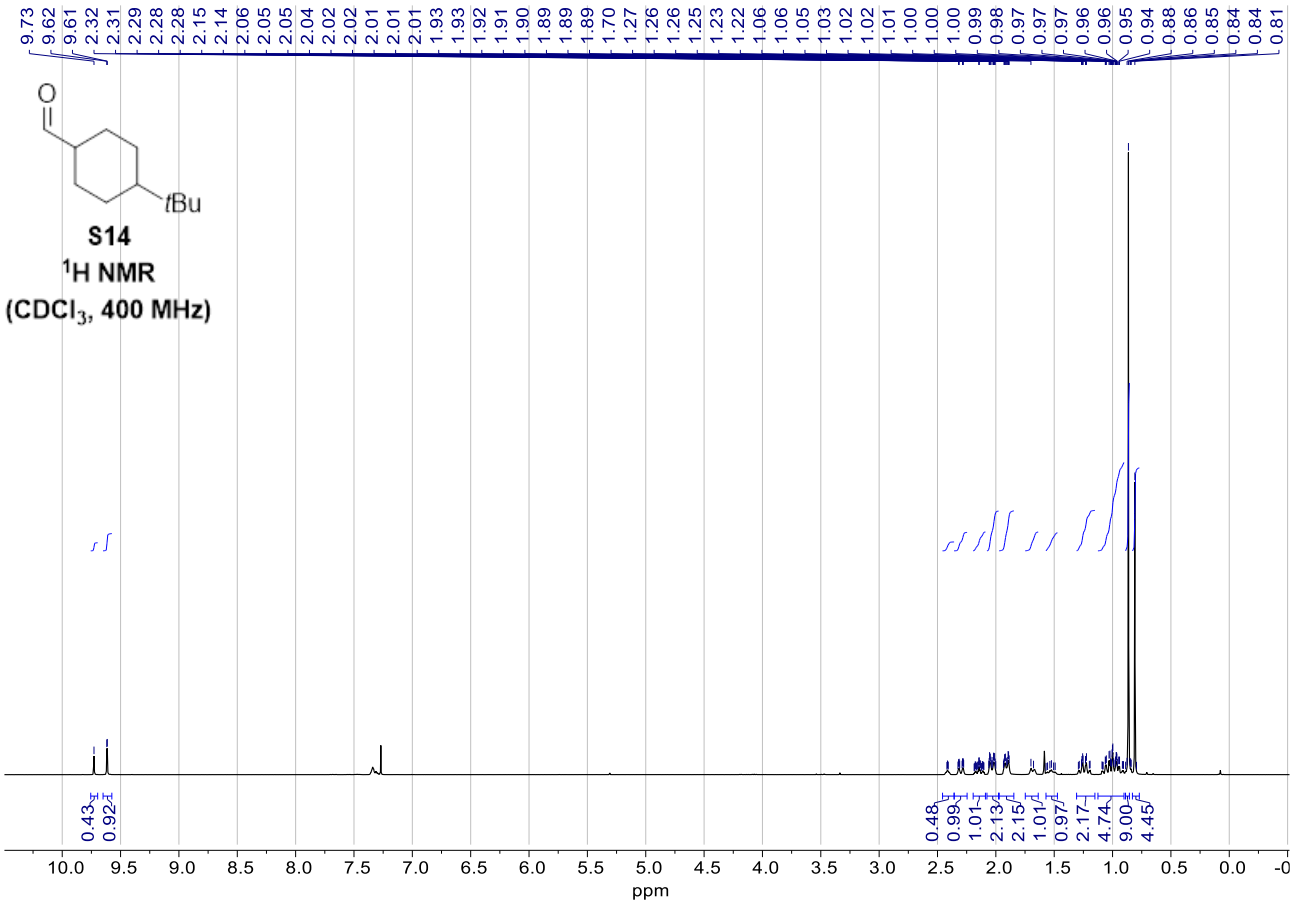

196.5
145.5
132.7
129.8
129.7
77.2
30.1
27.9
22.9
21.6
5a
^{13}C NMR
($CDCl_3$, 101 MHz)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

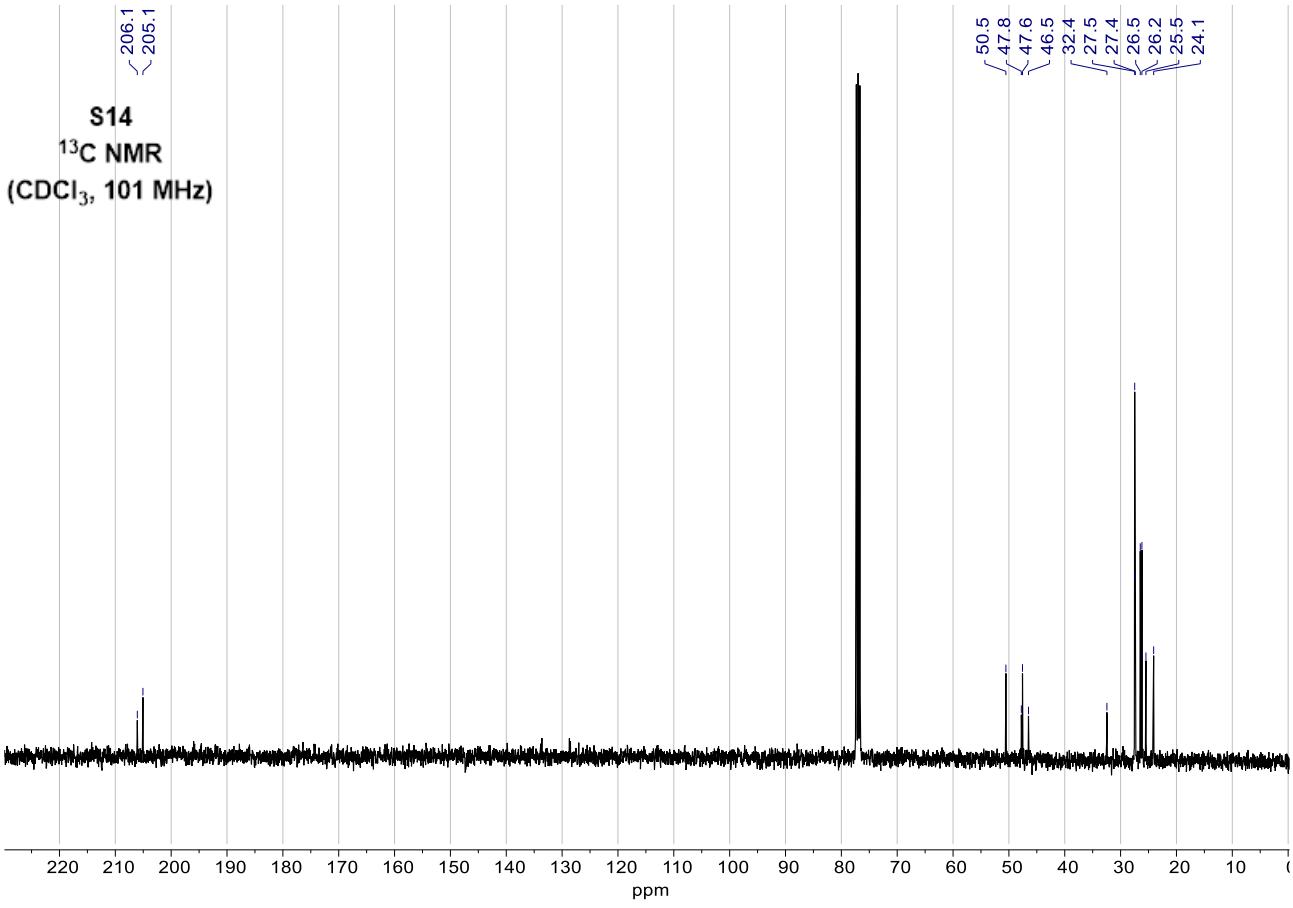

6a
^{1}H NMR
(CDCl$_3$, 400 MHz)
ppm

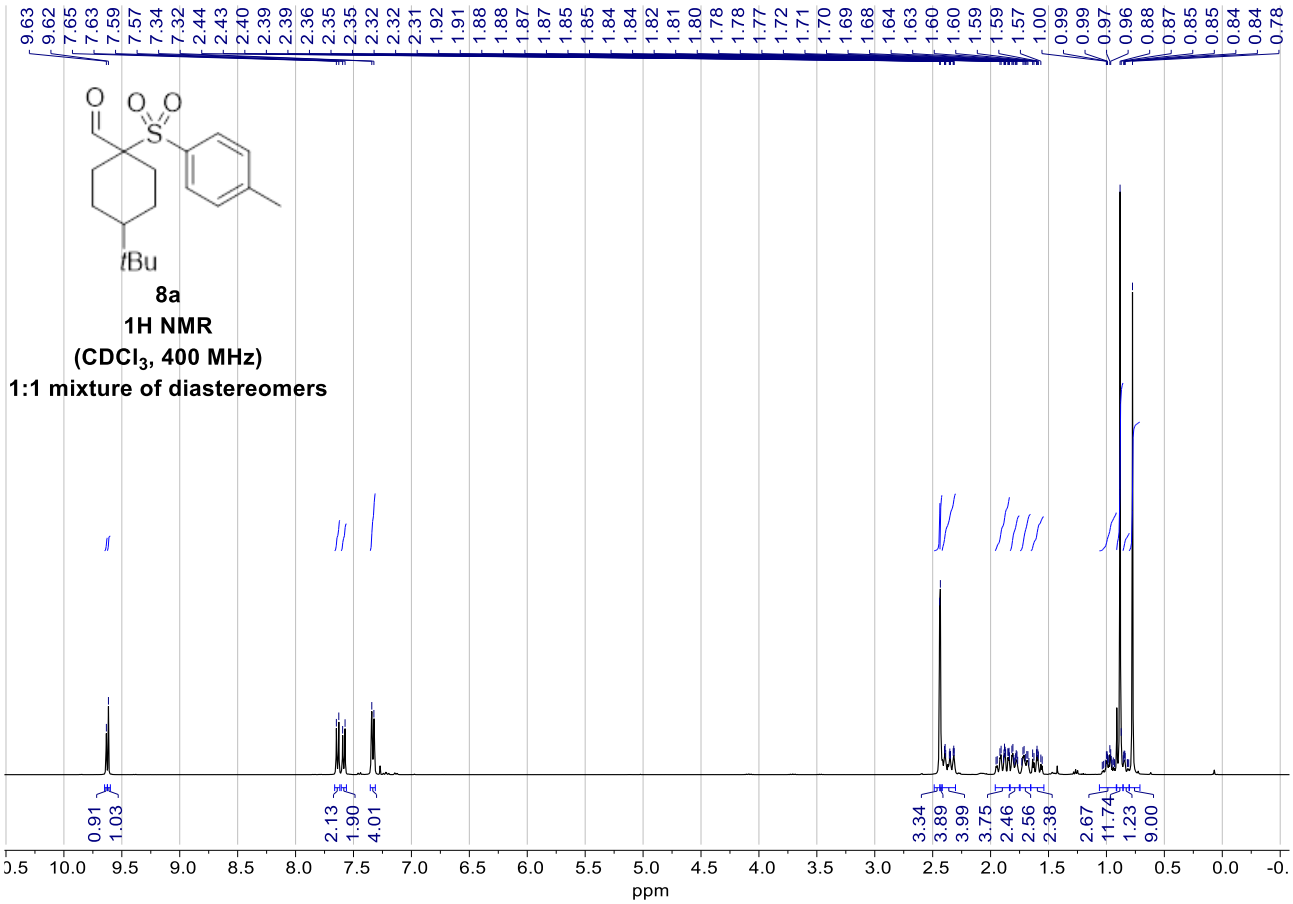

6a
^{13}C NMR
(CDCl$_3$, 101 MHz)
197.5
145.5
132.8
129.7
129.7
77.5
27.8
24.7
23.7
22.2
21.7
ppm

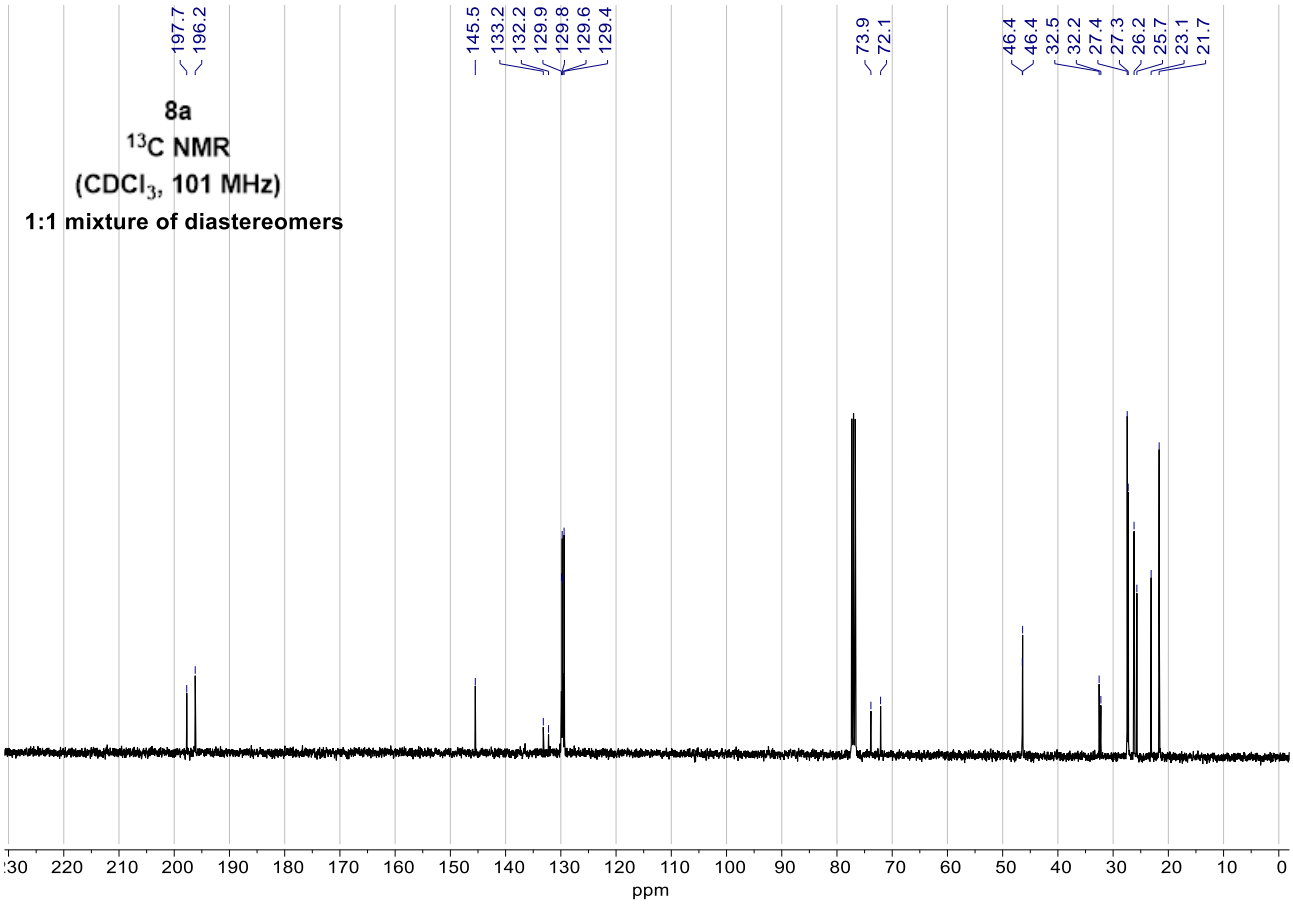

9.80 7.67 7.65 7.36 7.36 7.34 7.33 2.80 2.78 2.78 2.77 2.77 2.76 2.75 2.75 2.75 2.74 2.74 2.73 2.72 2.72 2.45 2.44 2.43 2.43 2.42 2.42 2.41 2.41 2.41 2.40 2.40 2.39 2.39 2.38 2.38 2.13 2.12 2.10 2.10 2.09 2.09 2.08 2.08 2.06 2.05 1.92 1.91 1.90 1.89 1.89 1.88 1.87 1.87 1.86 1.84
O O O S
7a
^{1}H NMR
($CDCl_3$, 400 MHz)
0.82 1.69 1.75 1.81 2.65 1.92 1.00 1.00
0.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
ppm

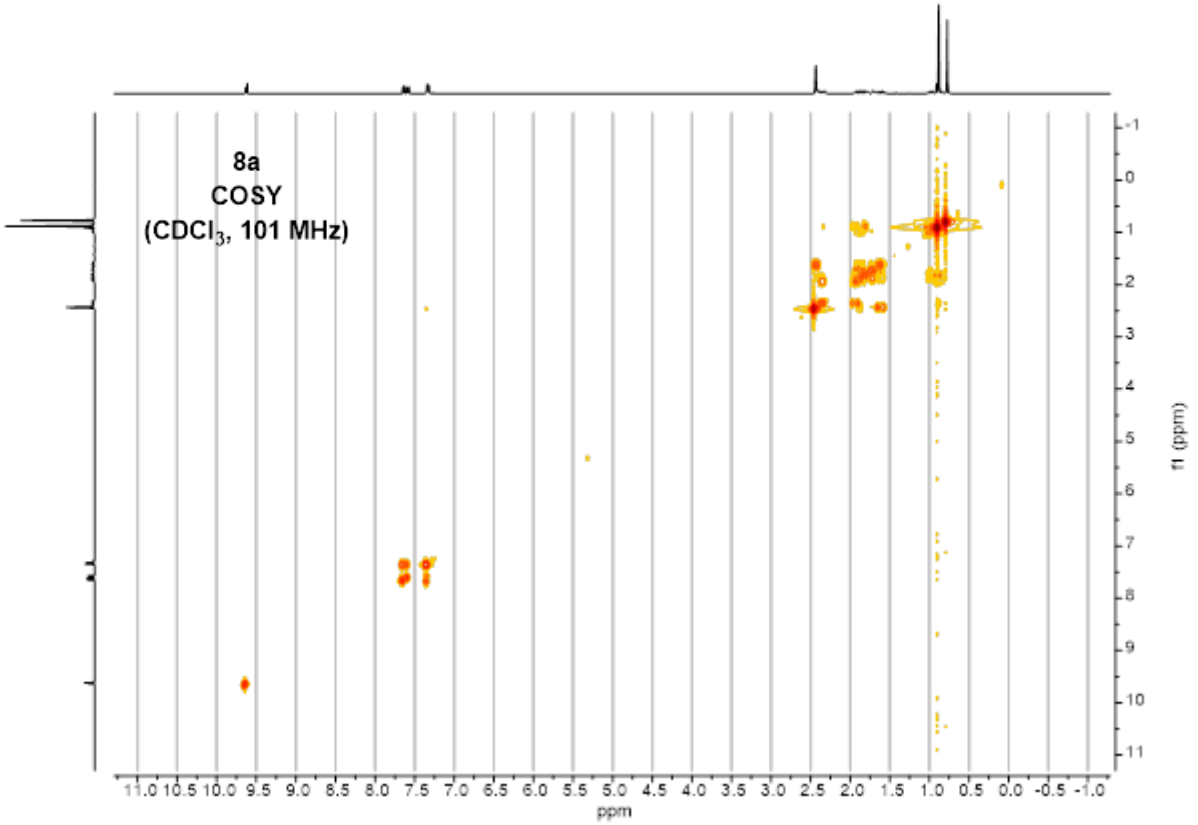

193.5 145.6 133.1 130.1 128.7 72.2 23.5 21.7 14.5
7a
^{13}C NMR
($CDCl_3$, 101 MHz)
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

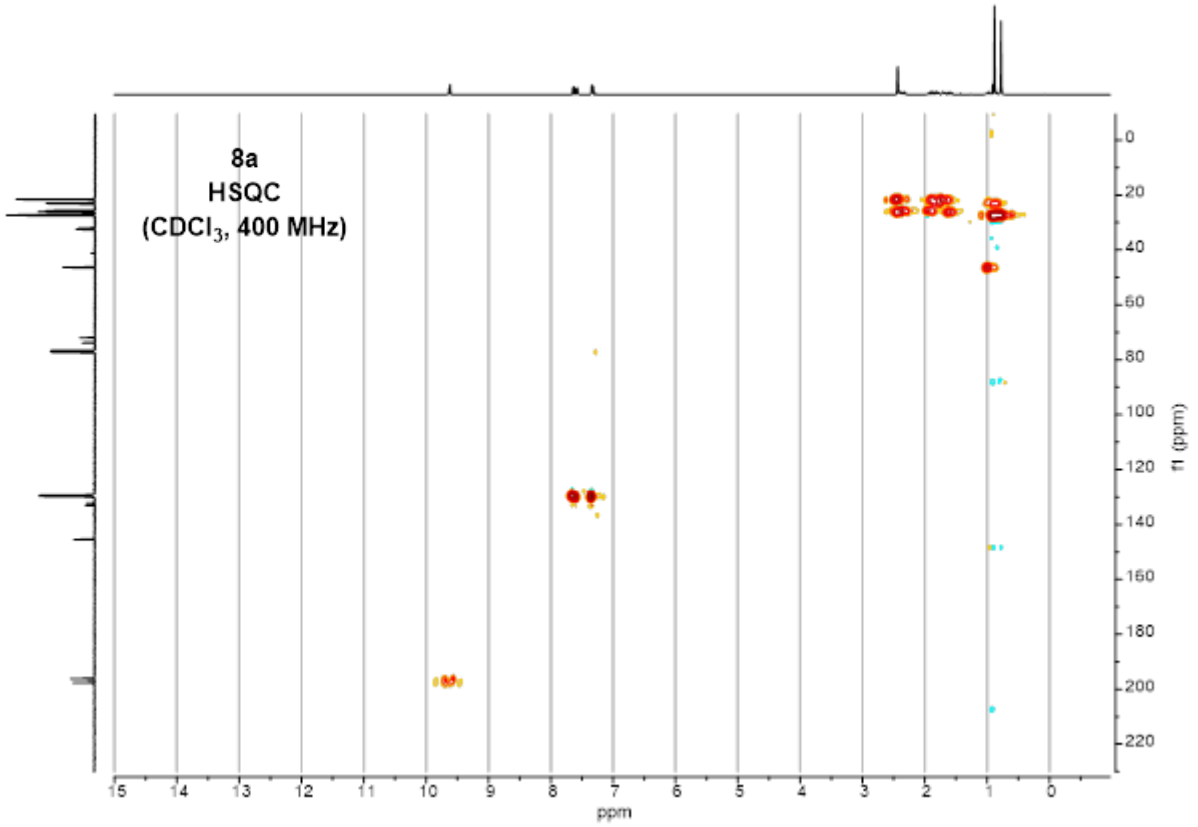

9.73 9.62 9.61 2.32 2.31 2.29 2.28 2.28 2.15 2.14 2.06 2.05 2.05 2.04 2.02 2.02 2.01 2.01 2.01 1.93 1.93 1.92 1.91 1.90 1.89 1.89 1.89 1.70 1.27 1.26 1.26 1.25 1.23 1.22 1.06 1.06 1.05 1.03 1.02 1.02 1.01 1.00 1.00 1.00 0.99 0.98 0.97 0.97 0.97 0.96 0.96 0.95 0.94 0.88 0.86 0.85 0.84 0.84 0.81
O
tBu
S14
1H NMR
(CDCl3, 400 MHz)
0.43 0.92 0.48 0.99 1.01 2.13 2.15 1.01 0.97 2.17 4.74 9.00 4.45
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
ppm

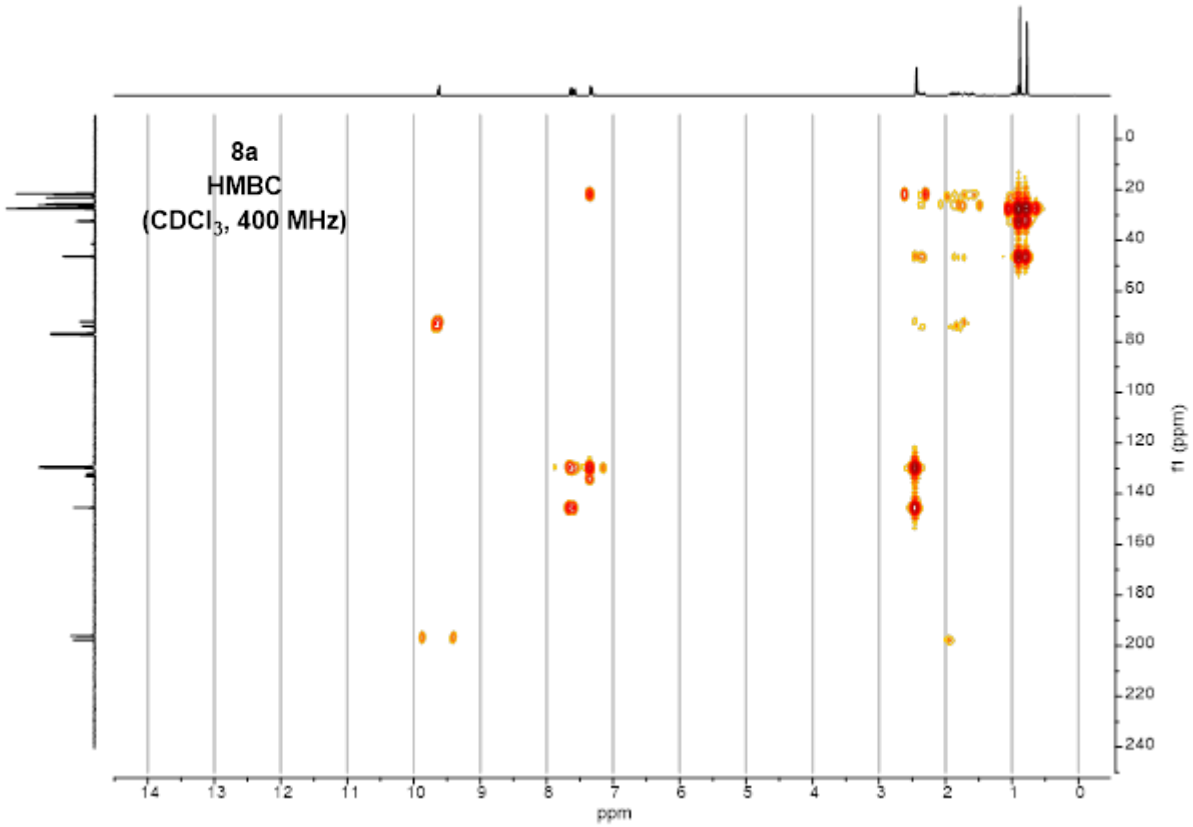

206.1 205.1
50.5 47.8 47.6 46.5 32.4 27.5 27.4 26.5 26.2 25.5 24.1
S14
13C NMR
(CDCl3, 101 MHz)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

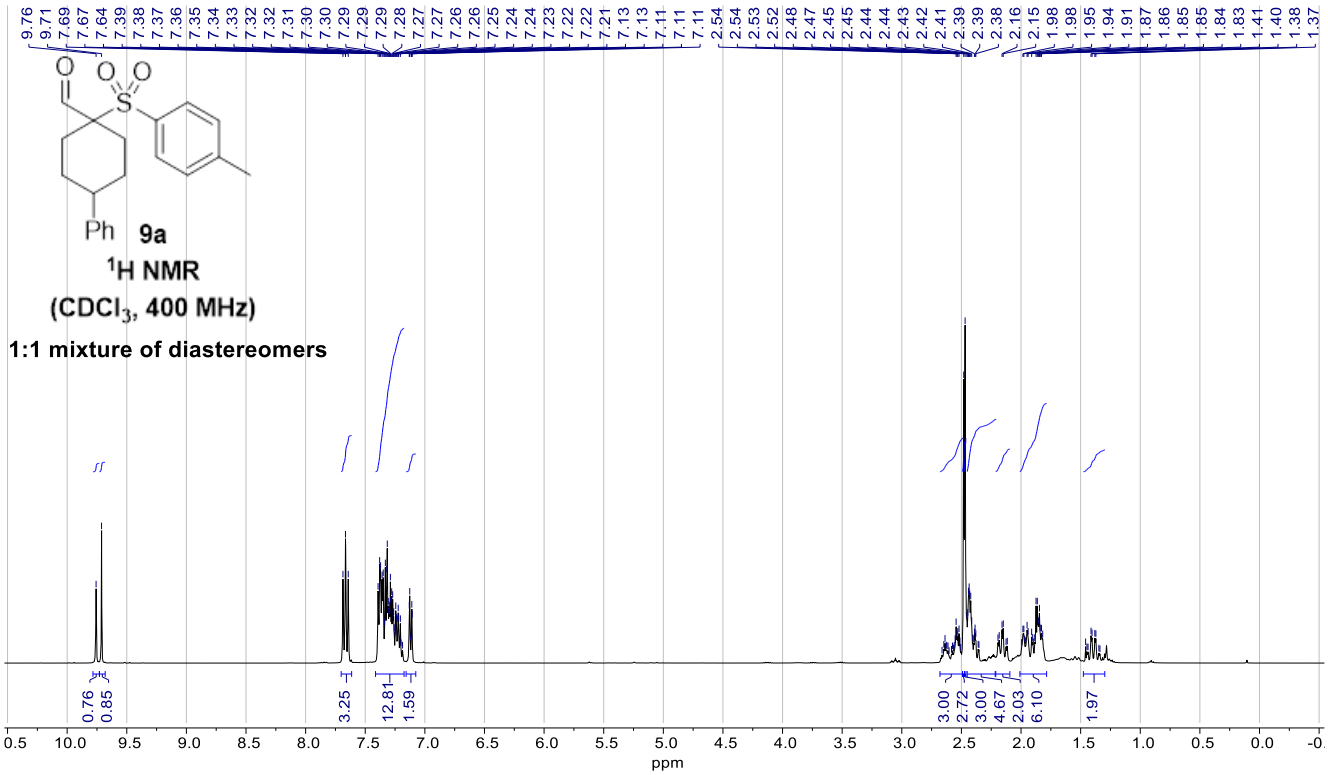

9.63 9.62 7.65 7.63 7.59 7.57 7.34 7.32 2.44 2.43 2.40 2.39 2.39 2.36 2.35 2.35 2.32 2.32 2.31 1.92 1.91 1.88 1.88 1.87 1.87 1.85 1.85 1.84 1.84 1.82 1.81 1.80 1.78 1.78 1.77 1.72 1.71 1.70 1.69 1.68 1.64 1.63 1.60 1.60 1.59 1.59 1.57 1.00 0.99 0.99 0.97 0.96 0.88 0.87 0.85 0.85 0.84 0.84 0.78
O O O S tBu
8a
1H NMR
(CDCl3, 400 MHz)
1:1 mixture of diastereomers
0.91 1.03 2.13 1.90 4.01 3.34 3.89 3.99 3.75 2.46 2.56 2.38 2.67 11.74 1.23 9.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

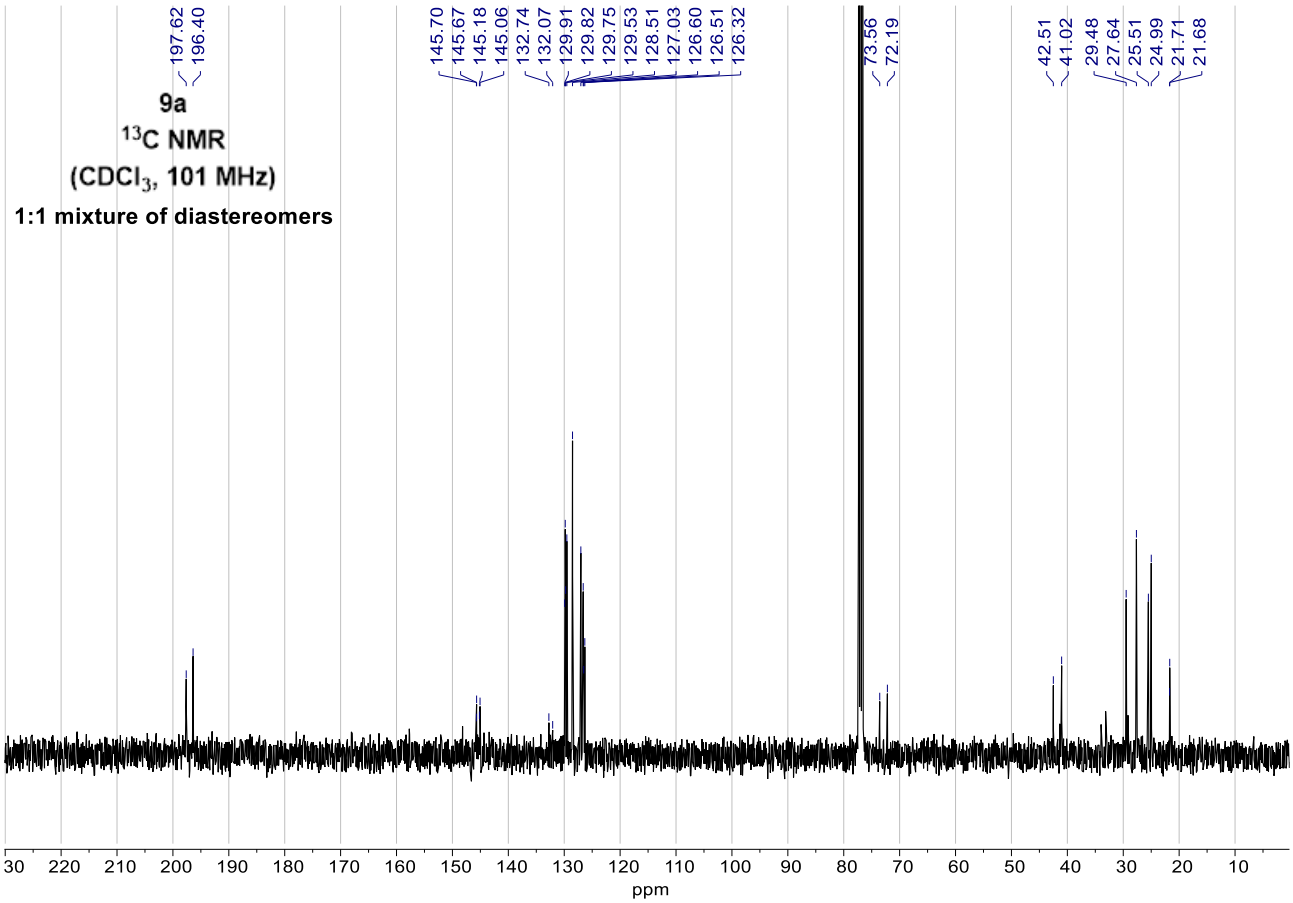

197.7 196.2 145.5 133.2 132.2 129.9 129.8 129.6 129.4 73.9 72.1 46.4 46.4 32.5 32.2 27.4 27.3 26.2 25.7 23.1 21.7
8a
13C NMR
(CDCl3, 101 MHz)
1:1 mixture of diastereomers
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

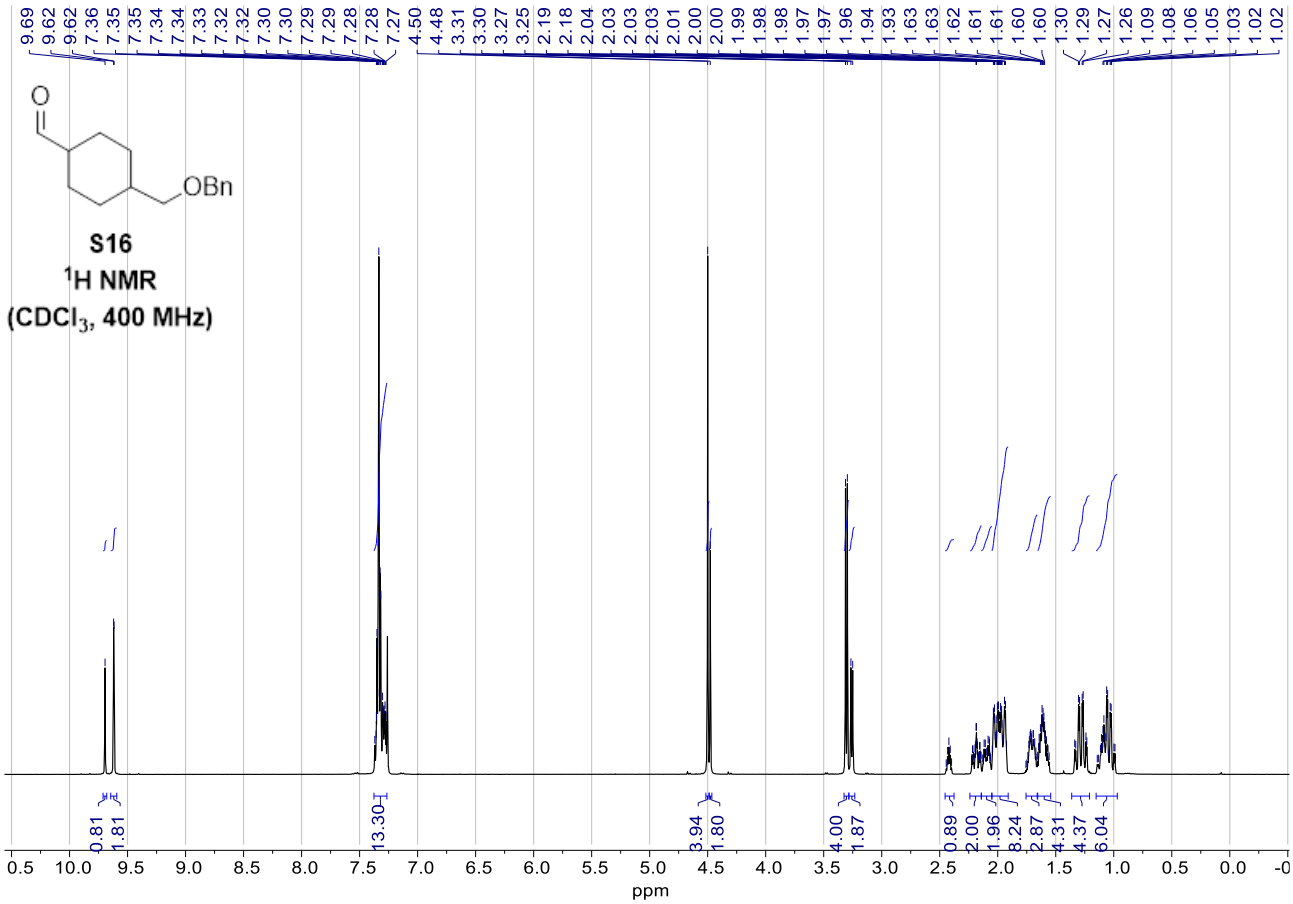

8a
COSY
(CDCl3, 101 MHz)
ppm
f1 (ppm)

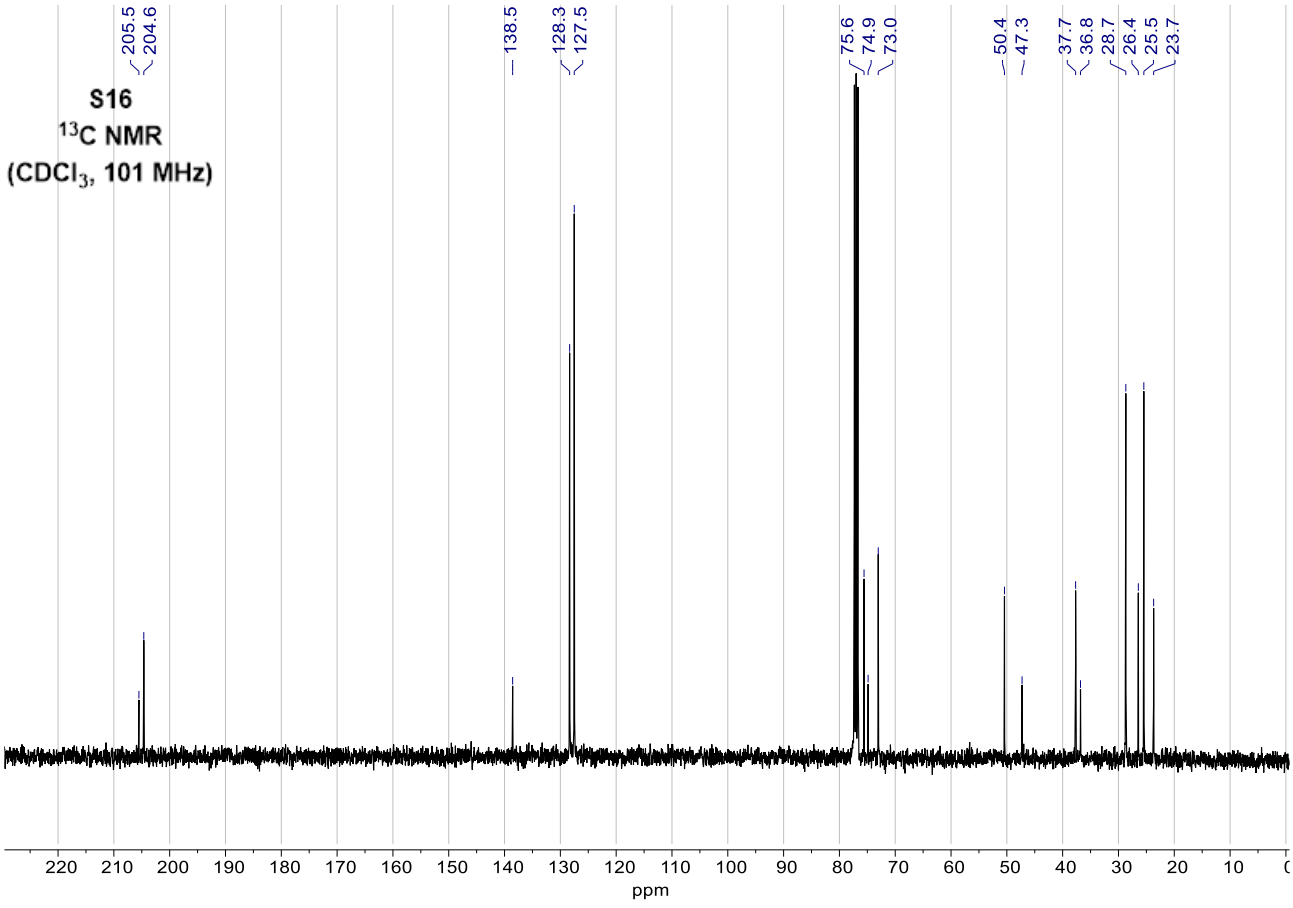

8a
HSQC
(CDCl3, 400 MHz)
ppm
f1 (ppm)

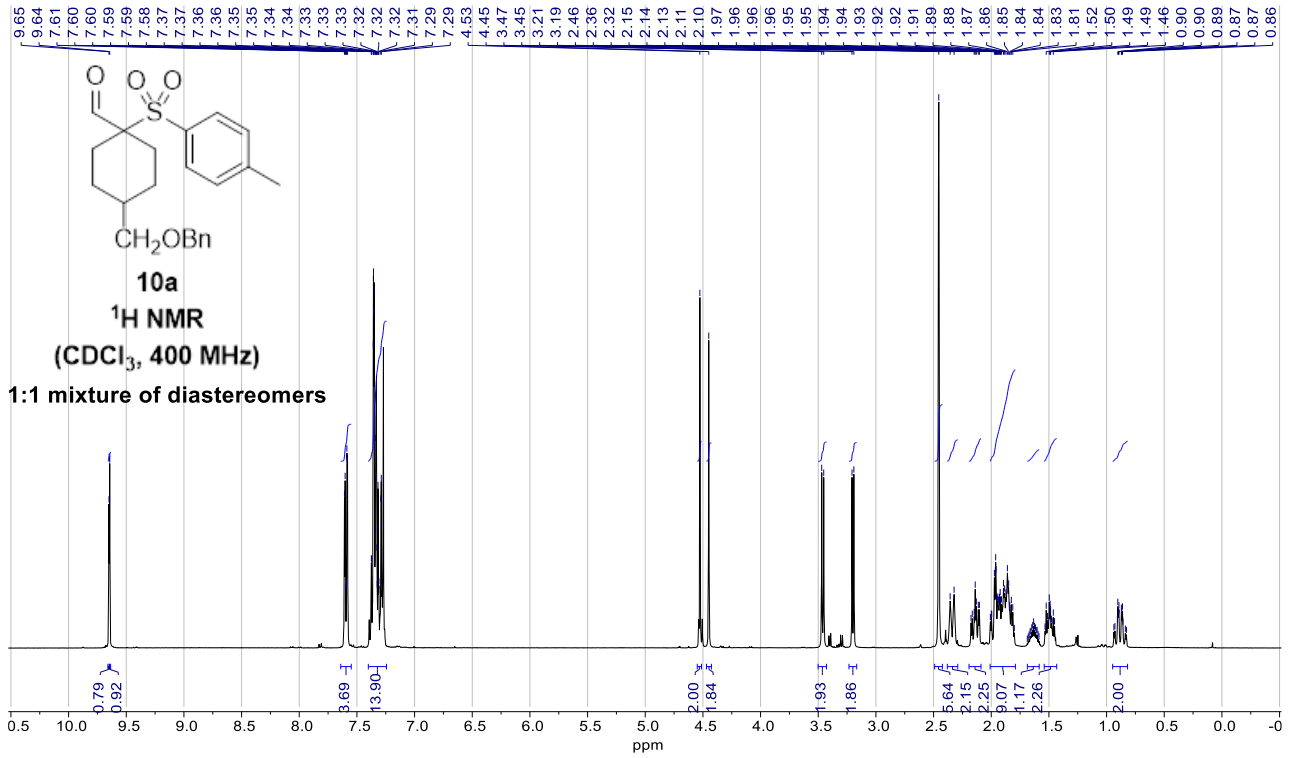

8a
HMBC
(CDCl3, 400 MHz)
ppm
f1 (ppm)

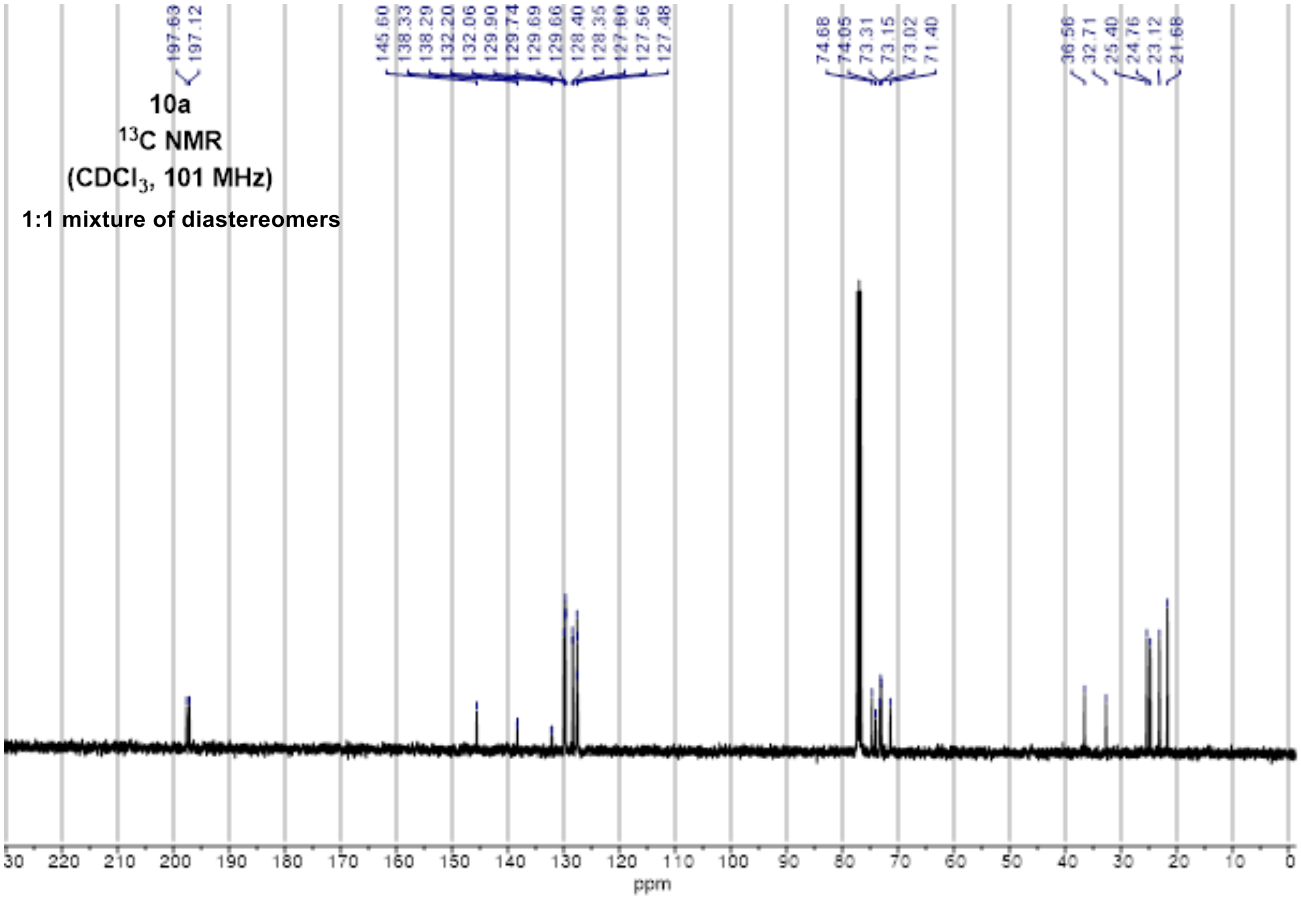

9a
^{1}H NMR
($CDCl_3$, 400 MHz)
1:1 mixture of diastereomers
ppm

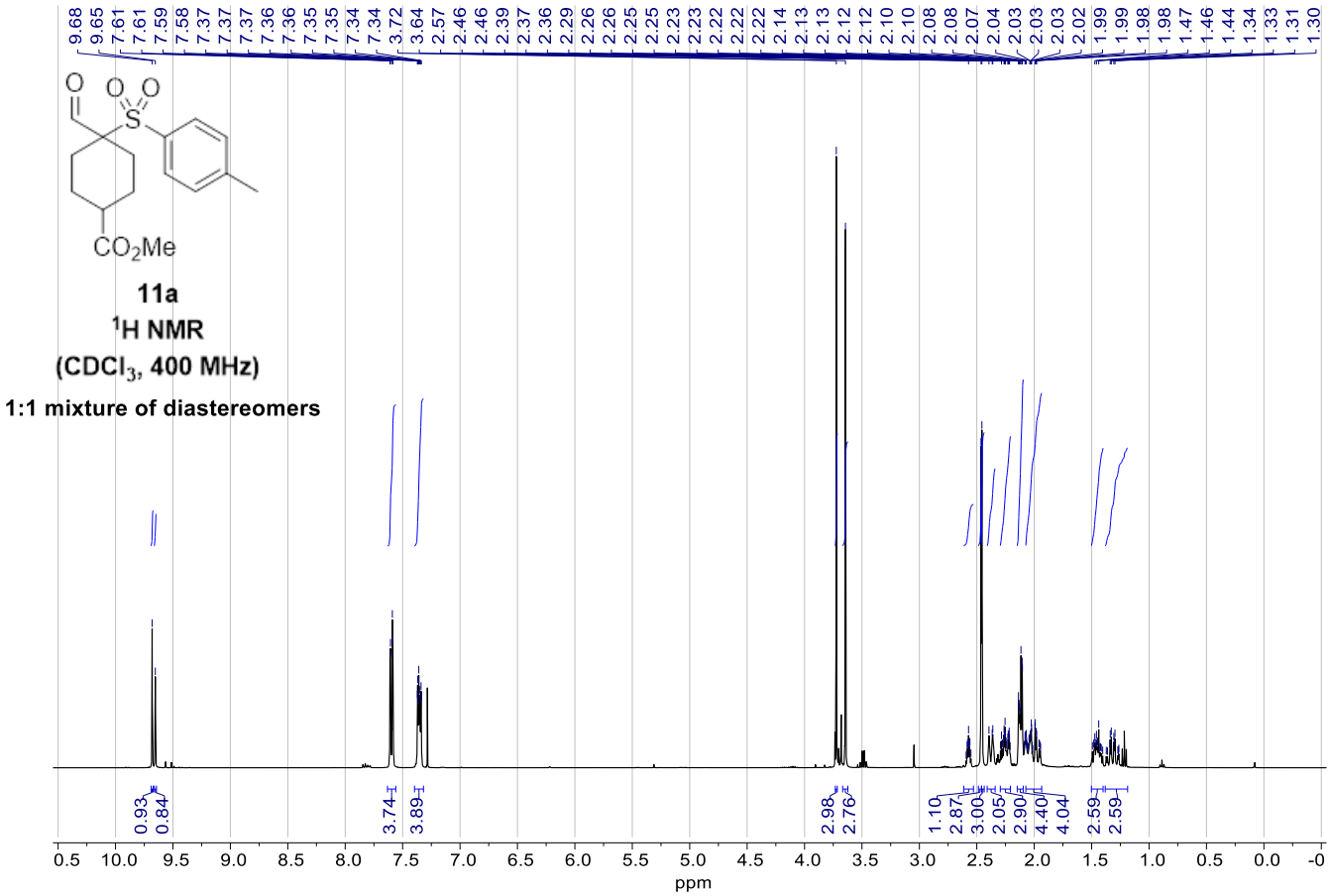

9a
^{13}C NMR
($CDCl_3$, 101 MHz)
1:1 mixture of diastereomers
ppm

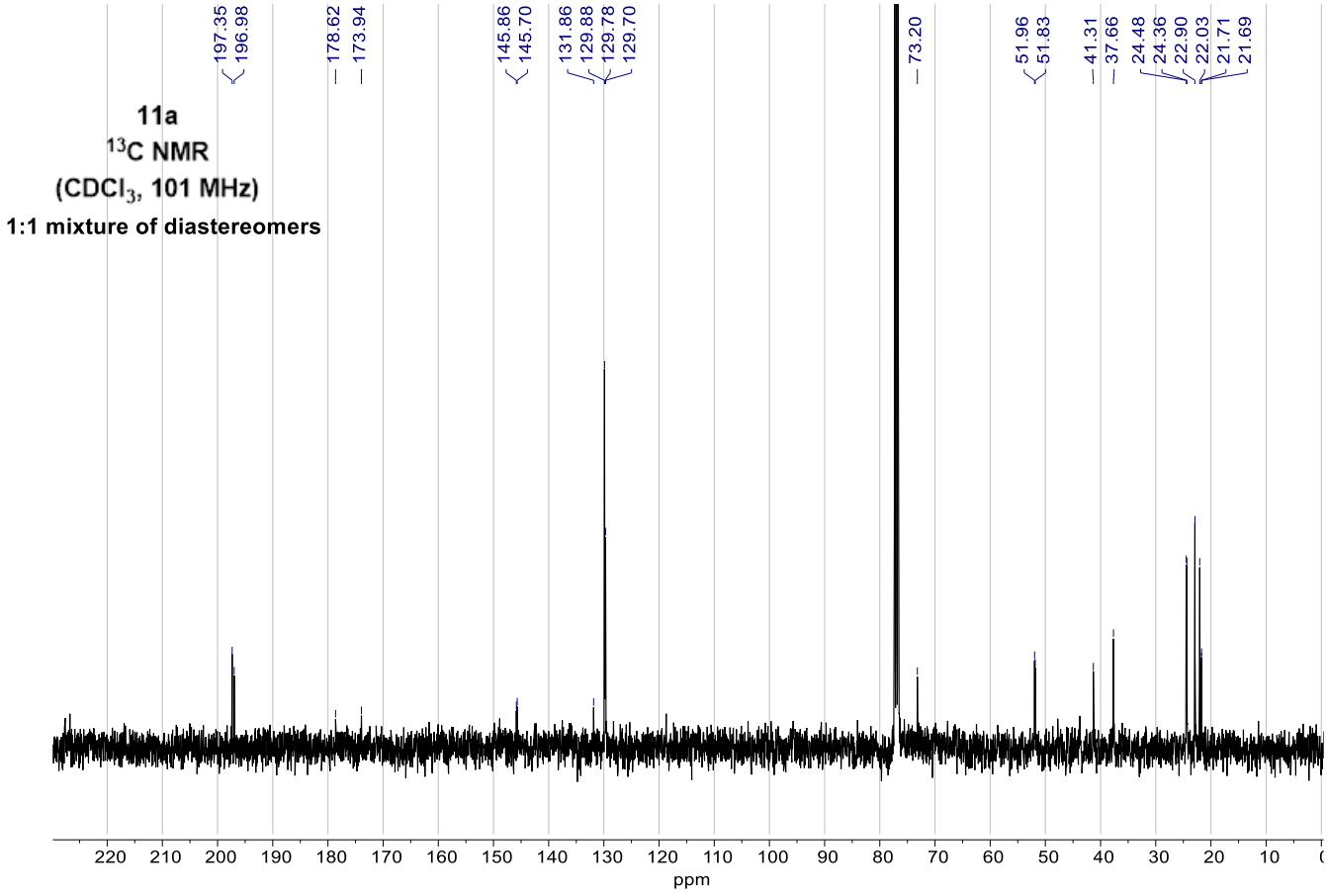

OBn
S16
^{1}H NMR
(CDCl$_3$, 400 MHz)
ppm

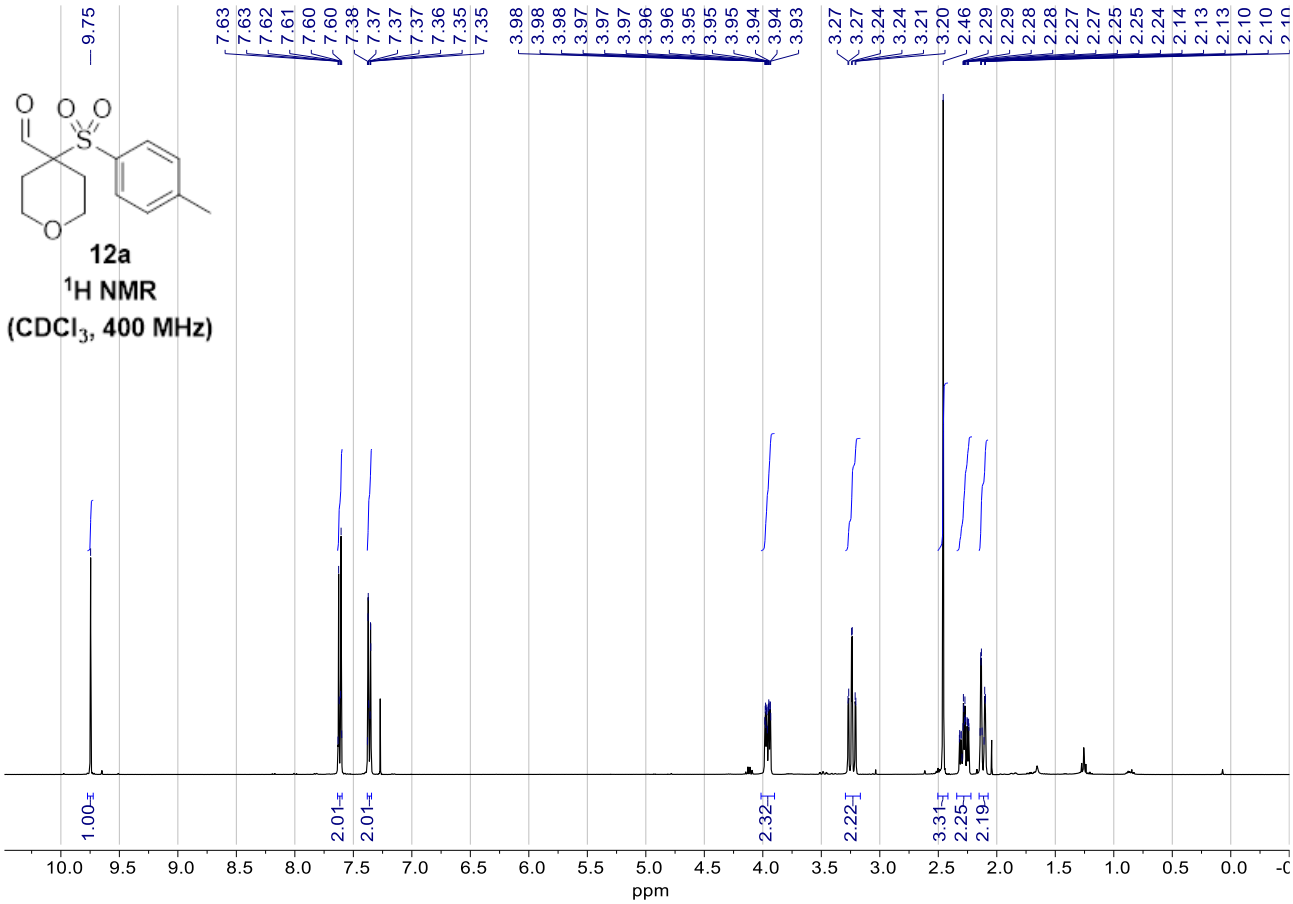

S16
^{13}C NMR
(CDCl$_3$, 101 MHz)
ppm

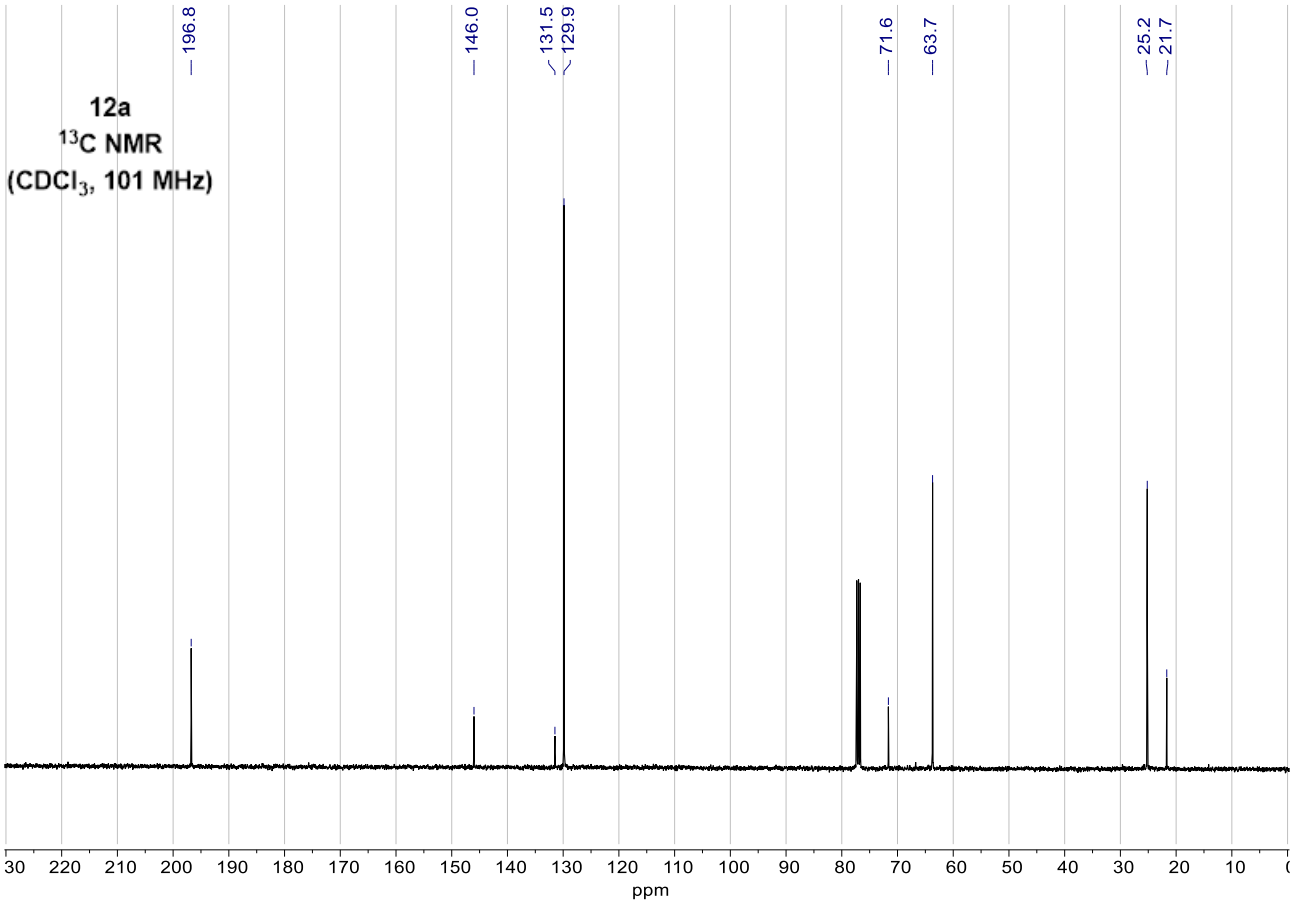

10a
^{1}H NMR
(CDCl$_3$, 400 MHz)
1:1 mixture of diastereomers
CH$_2$OBn
ppm

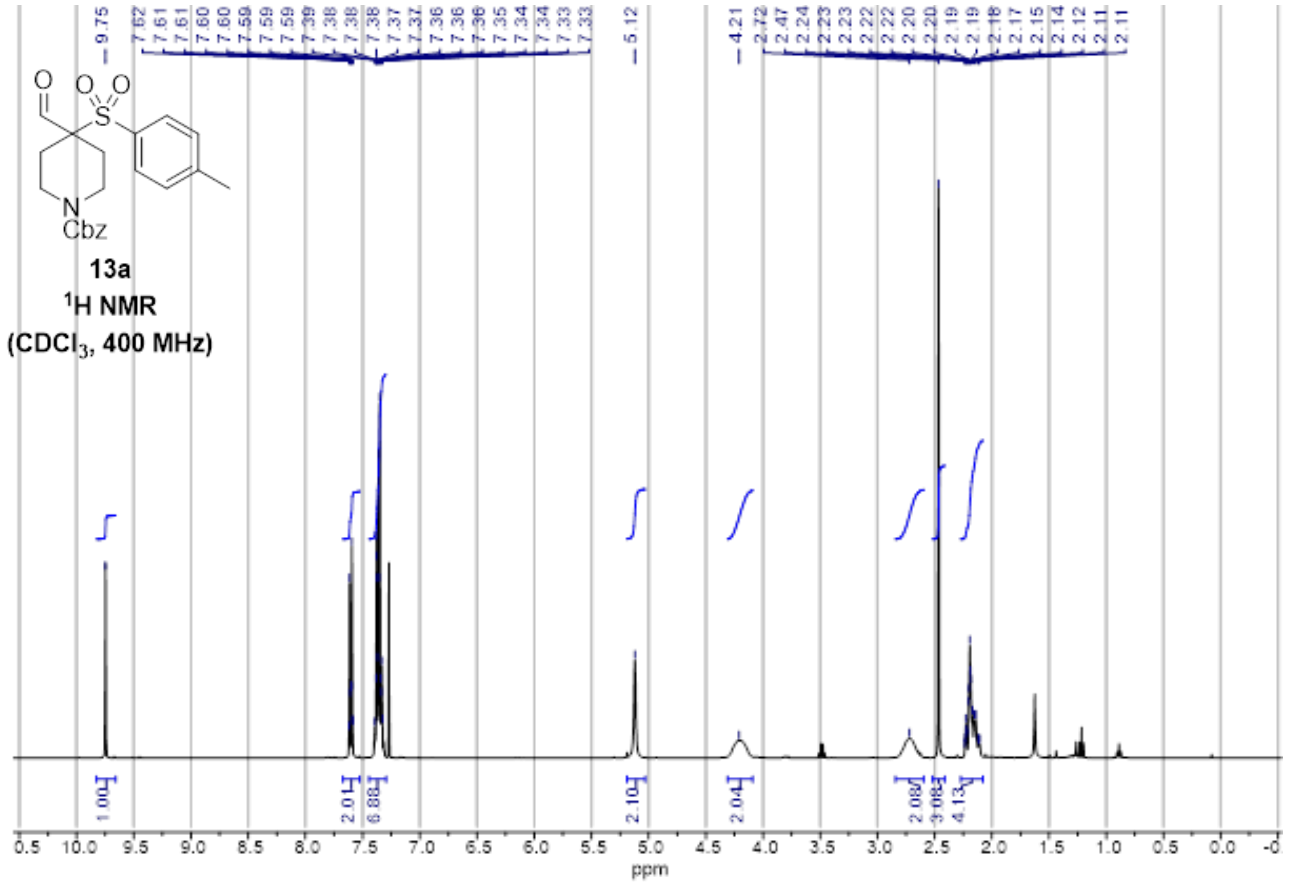

10a
^{13}C NMR
(CDCl$_3$, 101 MHz)
1:1 mixture of diastereomers
ppm

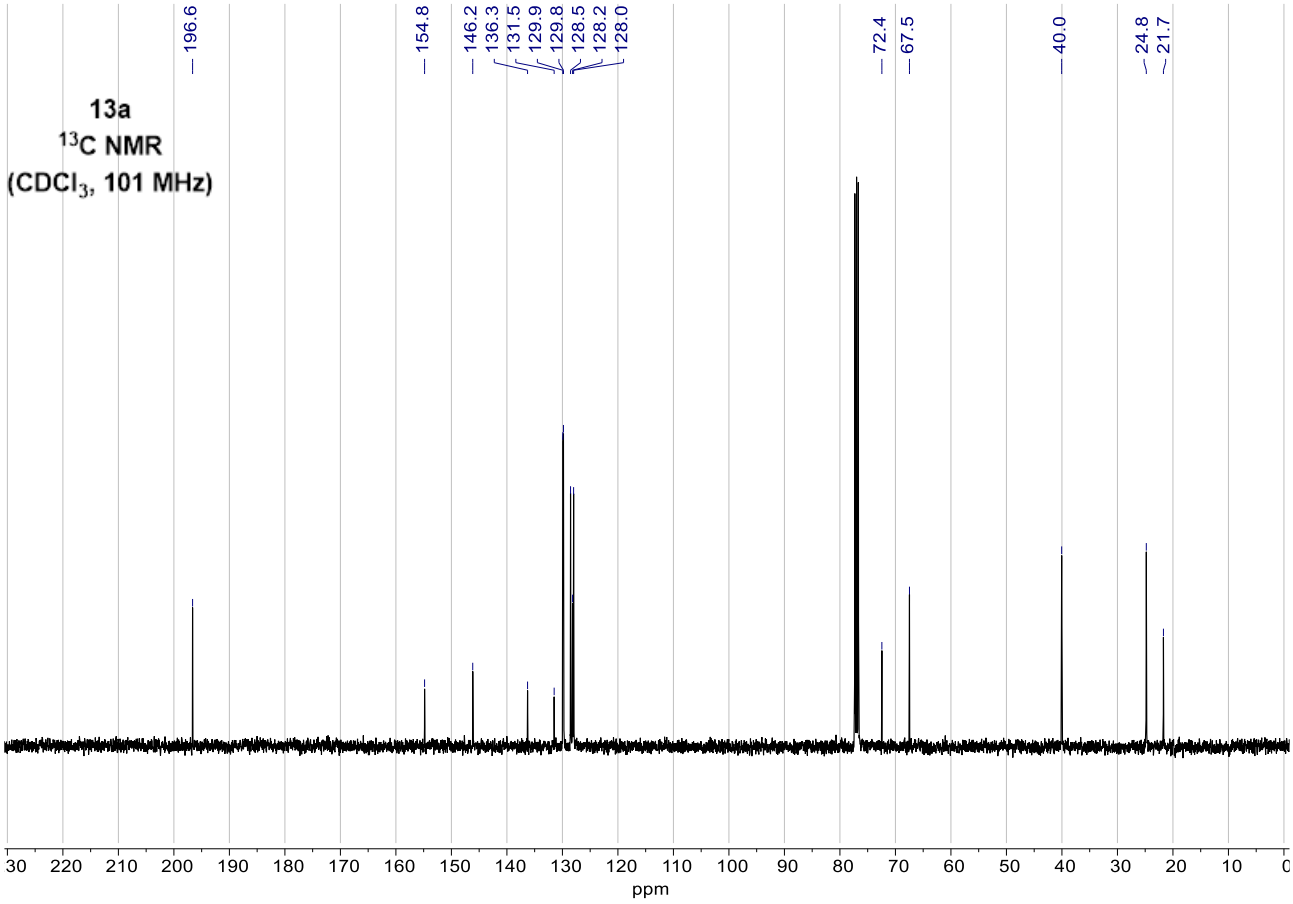

11a
^{1}H NMR
(CDCl$_3$, 400 MHz)
1:1 mixture of diastereomers
CO$_2$Me
ppm

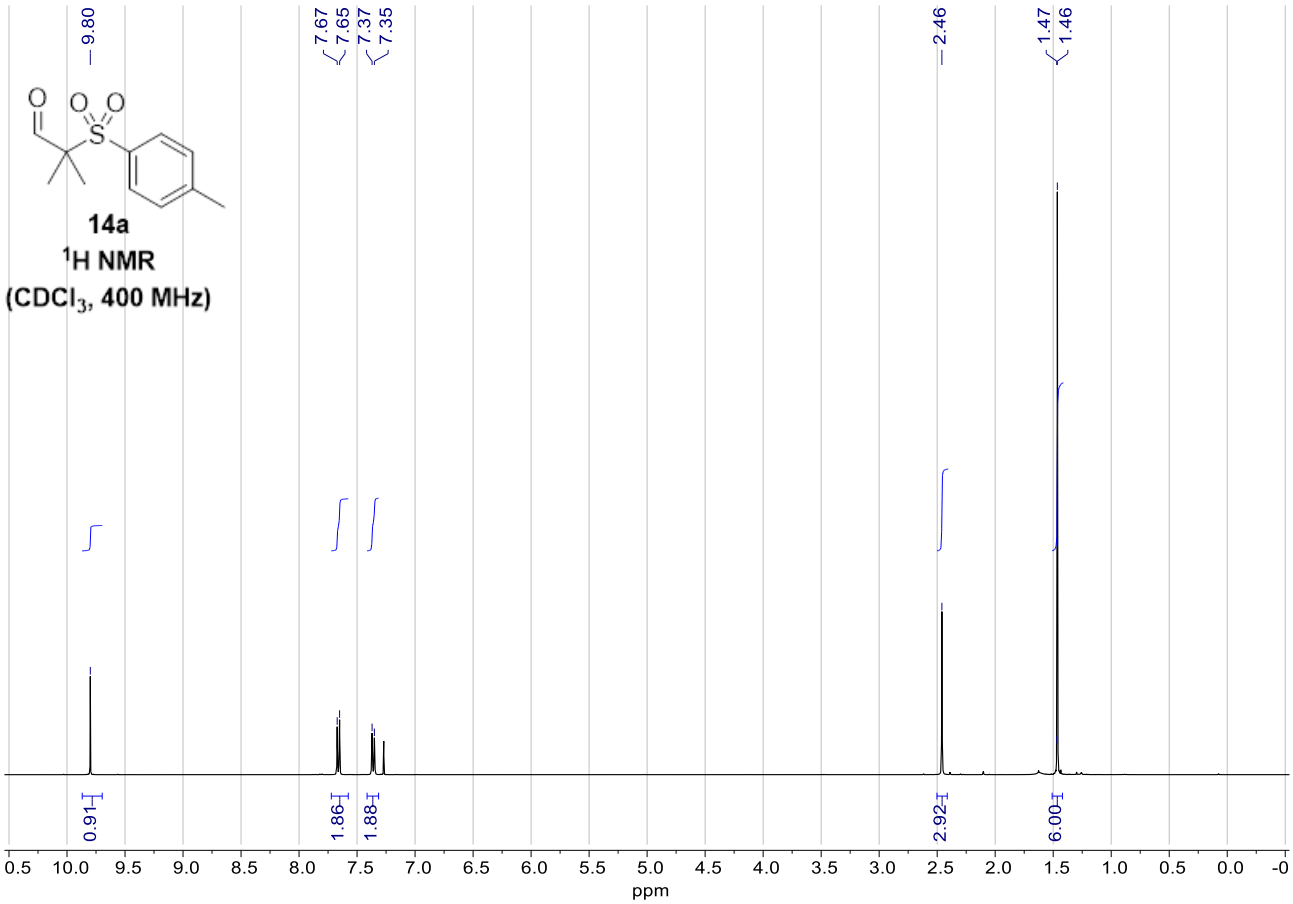

11a
^{13}C NMR
(CDCl$_3$, 101 MHz)
1:1 mixture of diastereomers
ppm

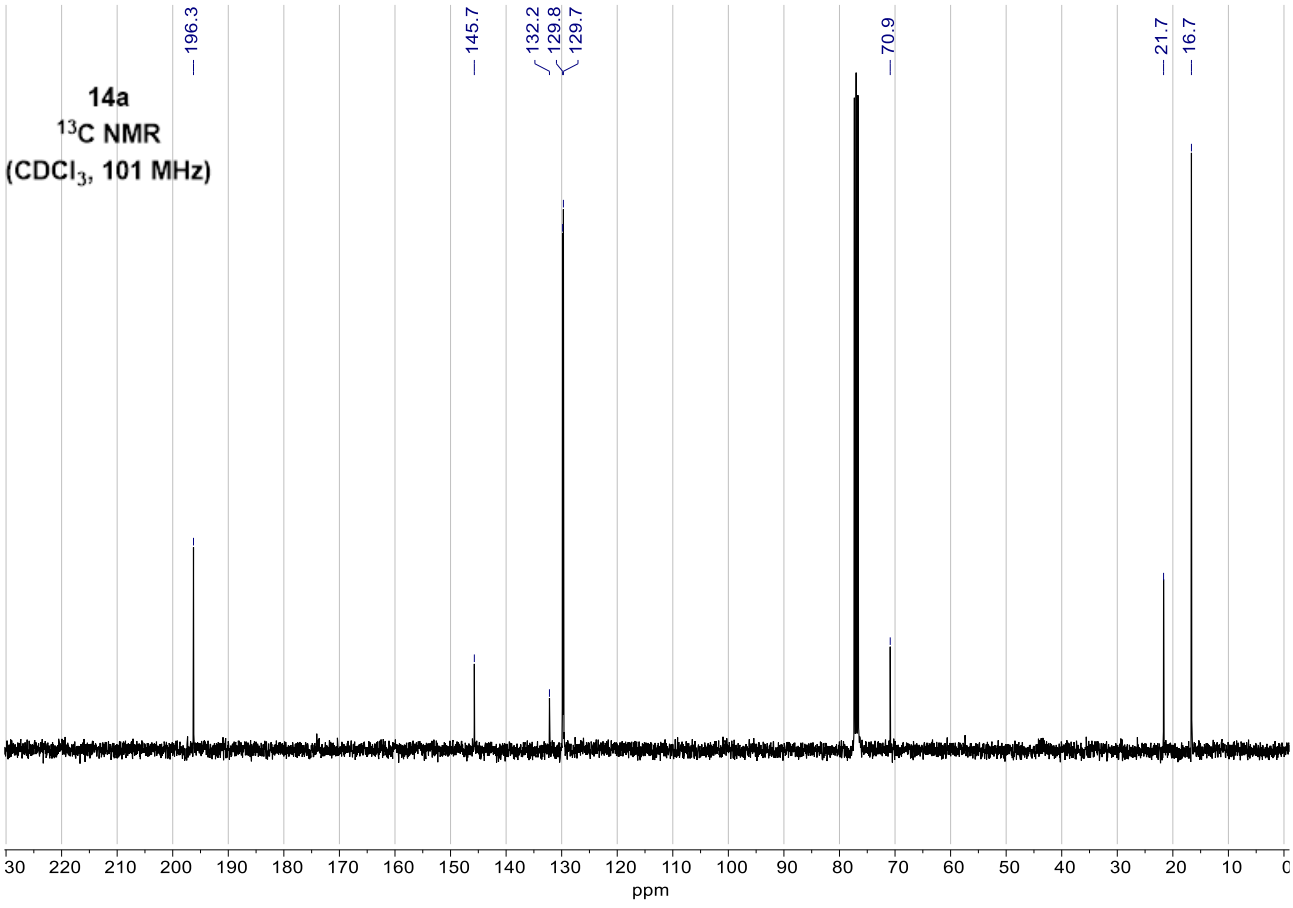

12a
^{1}H NMR
(CDCl$_3$, 400 MHz)
ppm

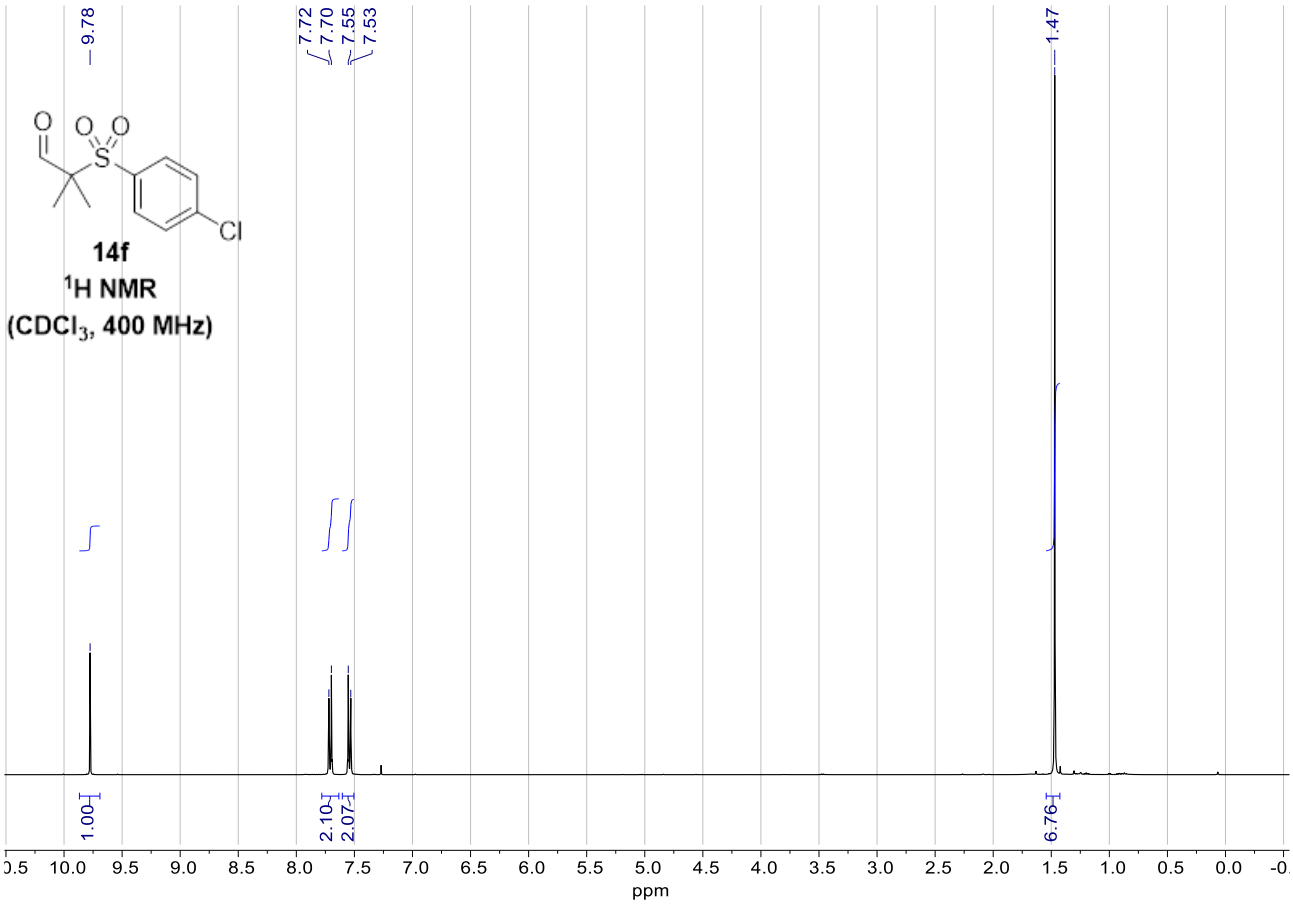

12a
^{13}C NMR
(CDCl$_3$, 101 MHz)
ppm

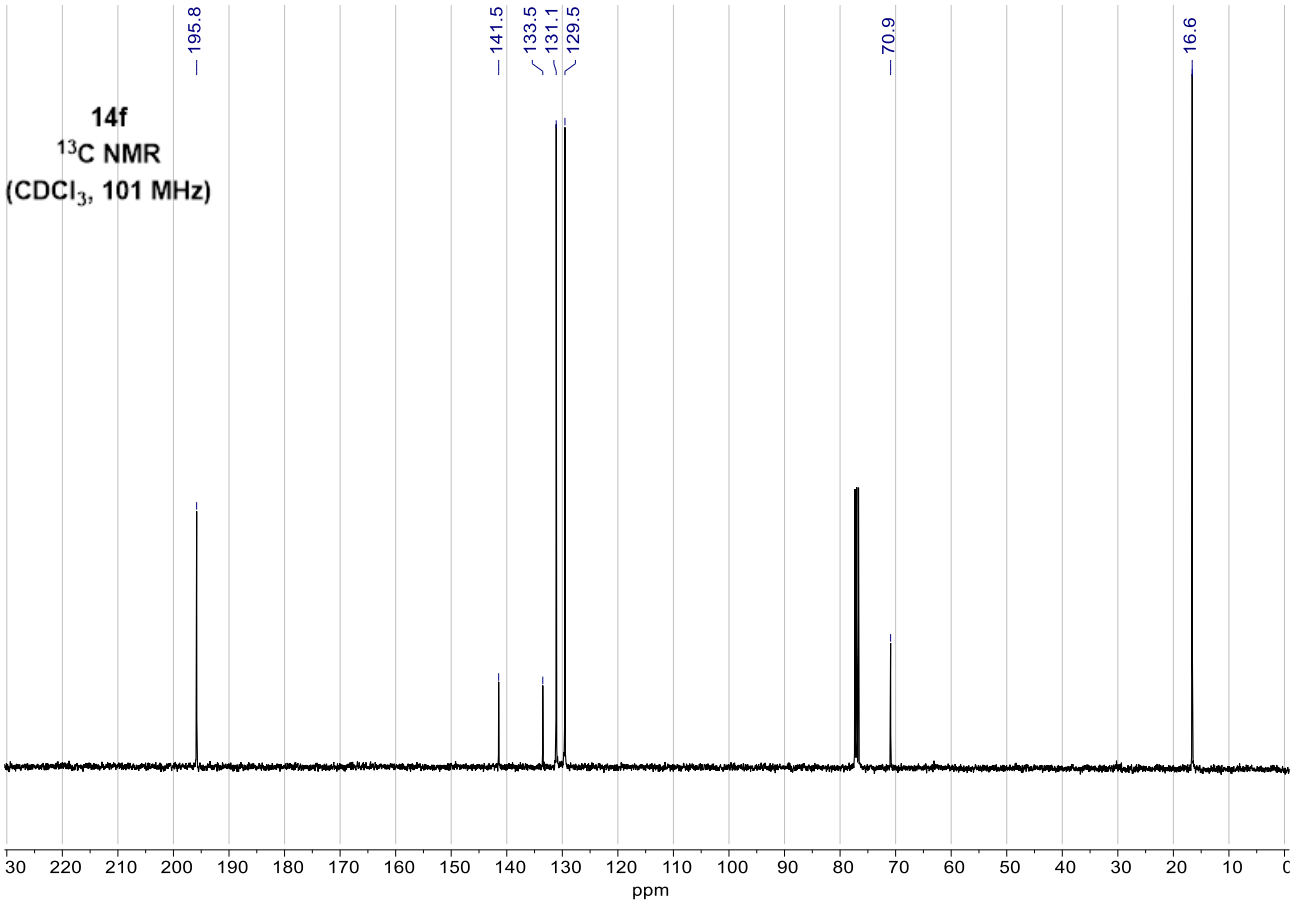

13a
^{1}H NMR
(CDCl$_3$, 400 MHz)
Cbz
ppm

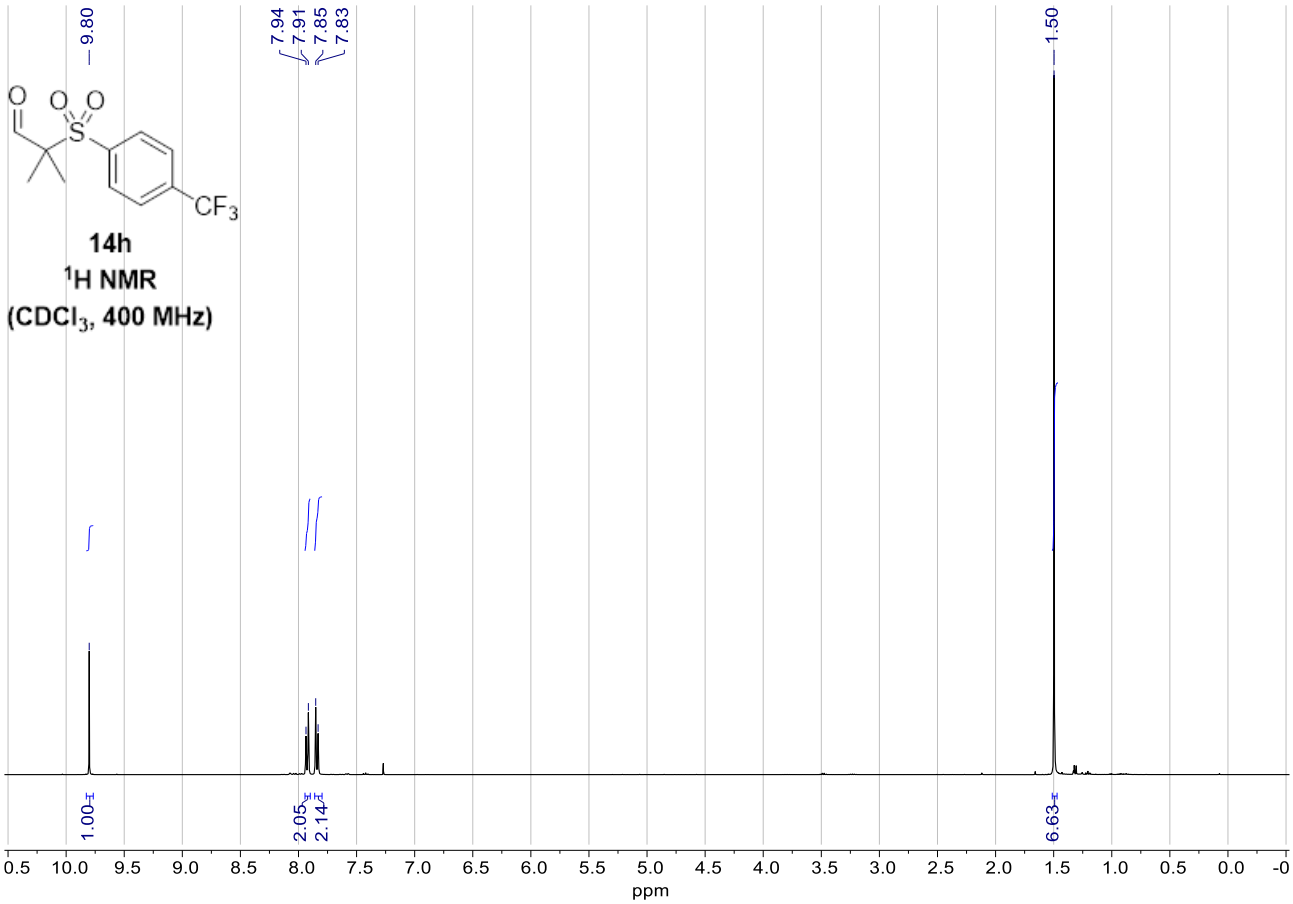

13a
^{13}C NMR
(CDCl$_3$, 101 MHz)
196.6
154.8
146.2
136.3
131.5
129.9
129.8
128.5
128.2
128.0
72.4
67.5
40.0
24.8
21.7
ppm

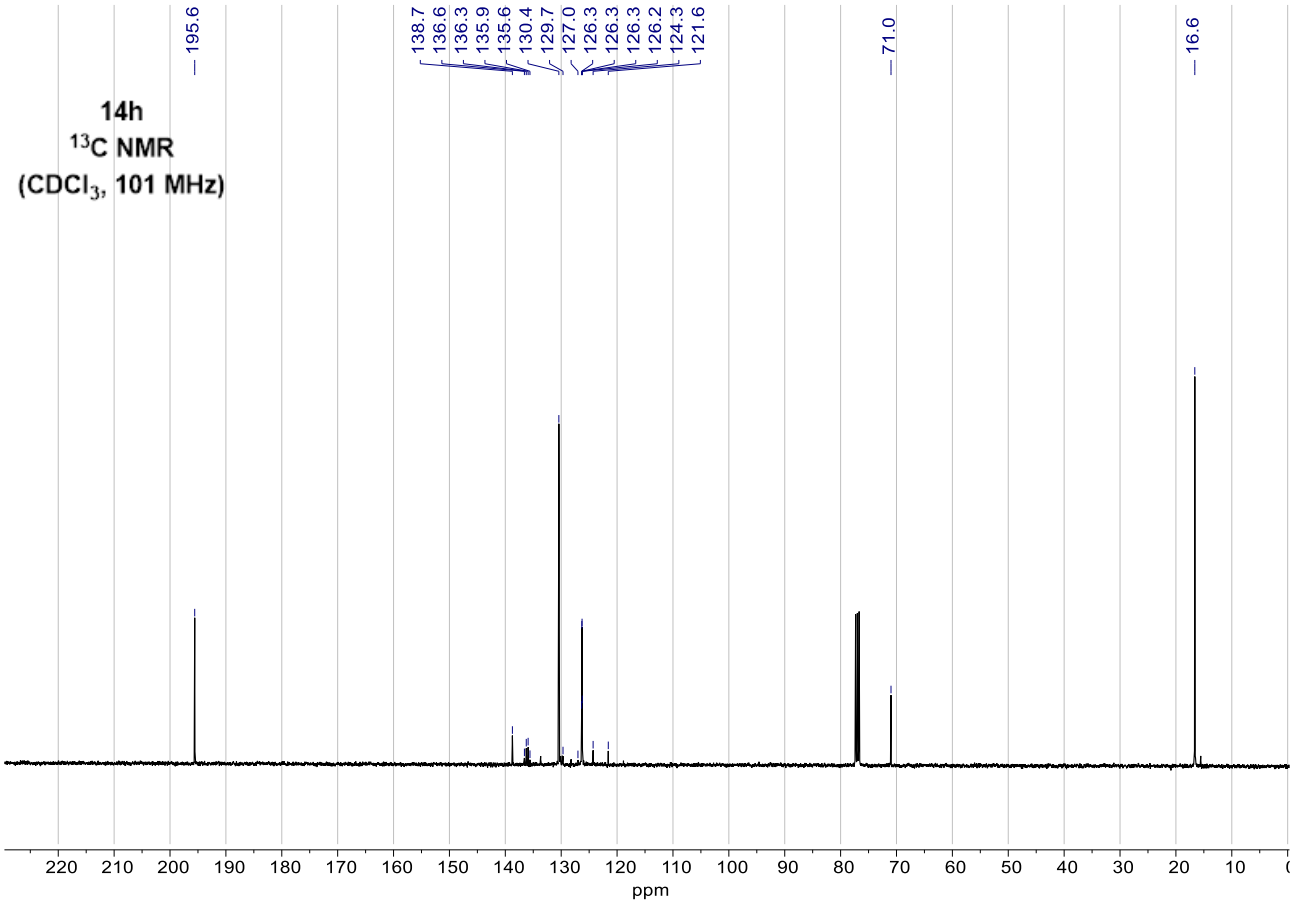

9.80
7.67
7.65
7.37
7.35
2.46
1.47
1.46
14a
^{1}H NMR
($CDCl_3$, 400 MHz)
0.91
1.86
1.88
2.92
6.00
ppm

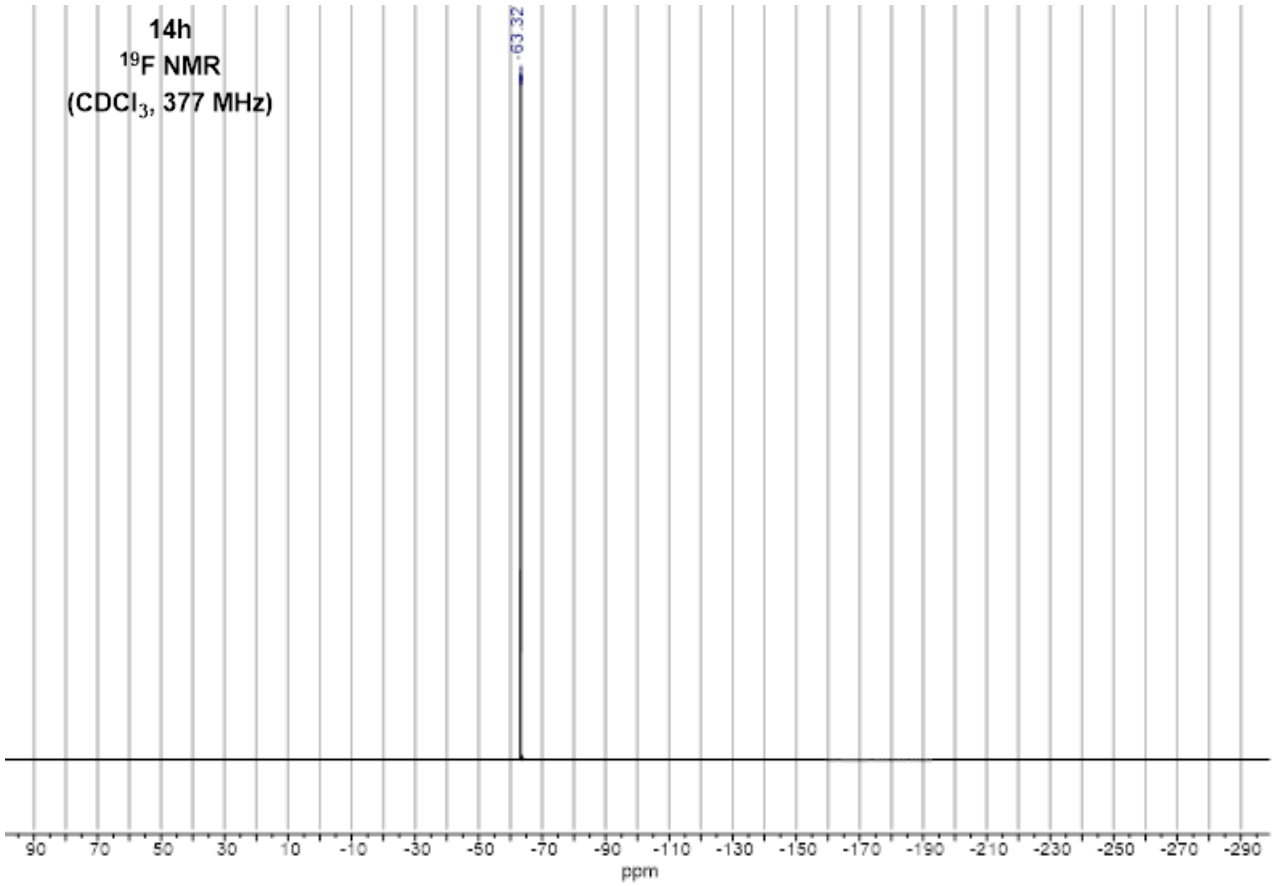

196.3
145.7
132.2
129.8
129.7
70.9
21.7
16.7
14a
^{13}C NMR
($CDCl_3$, 101 MHz)
ppm

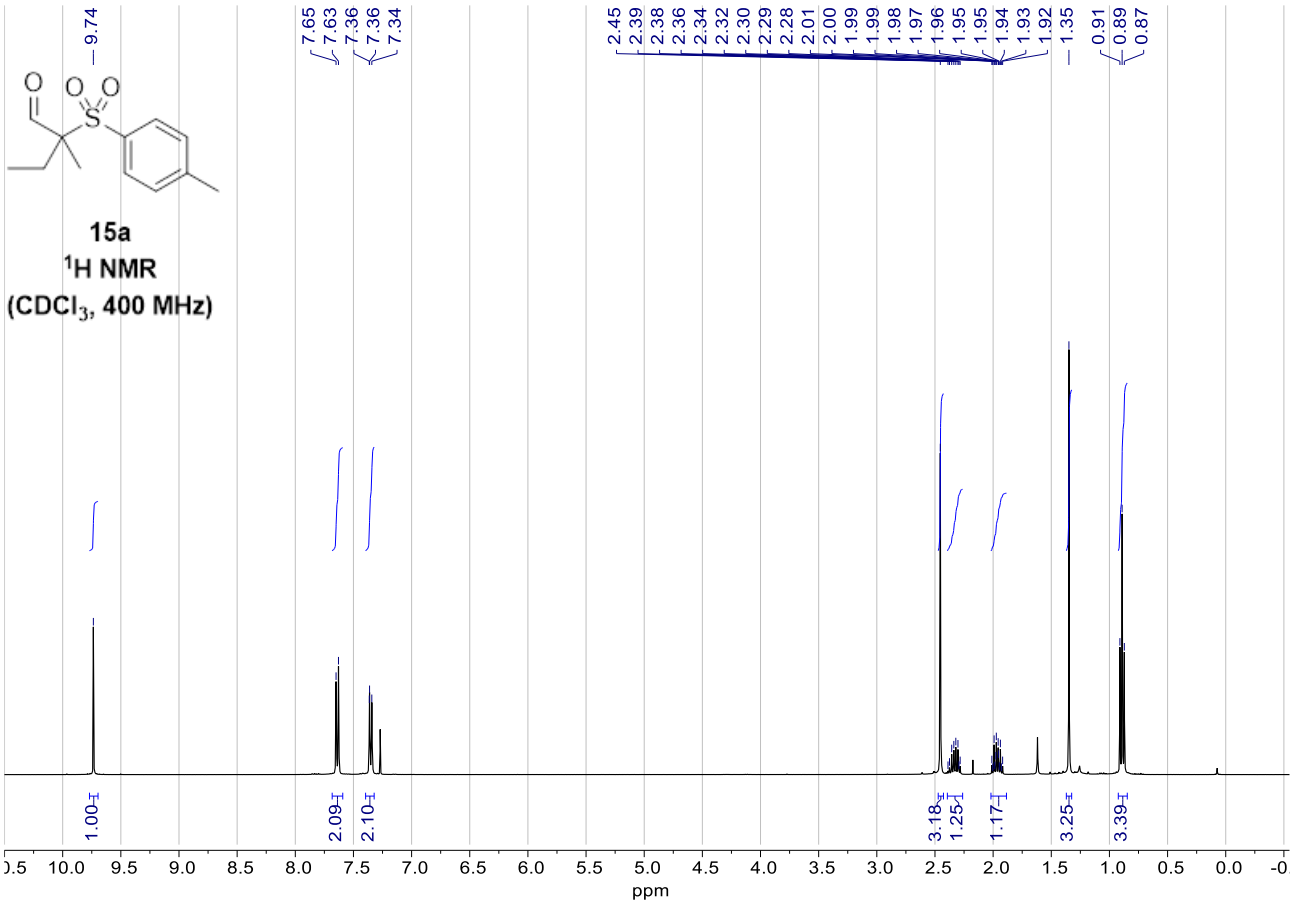

9.78
7.72
7.70
7.55
7.53
1.47
14f
^{1}H NMR
($CDCl_3$, 400 MHz)
1.00
2.10
2.07
6.76
ppm

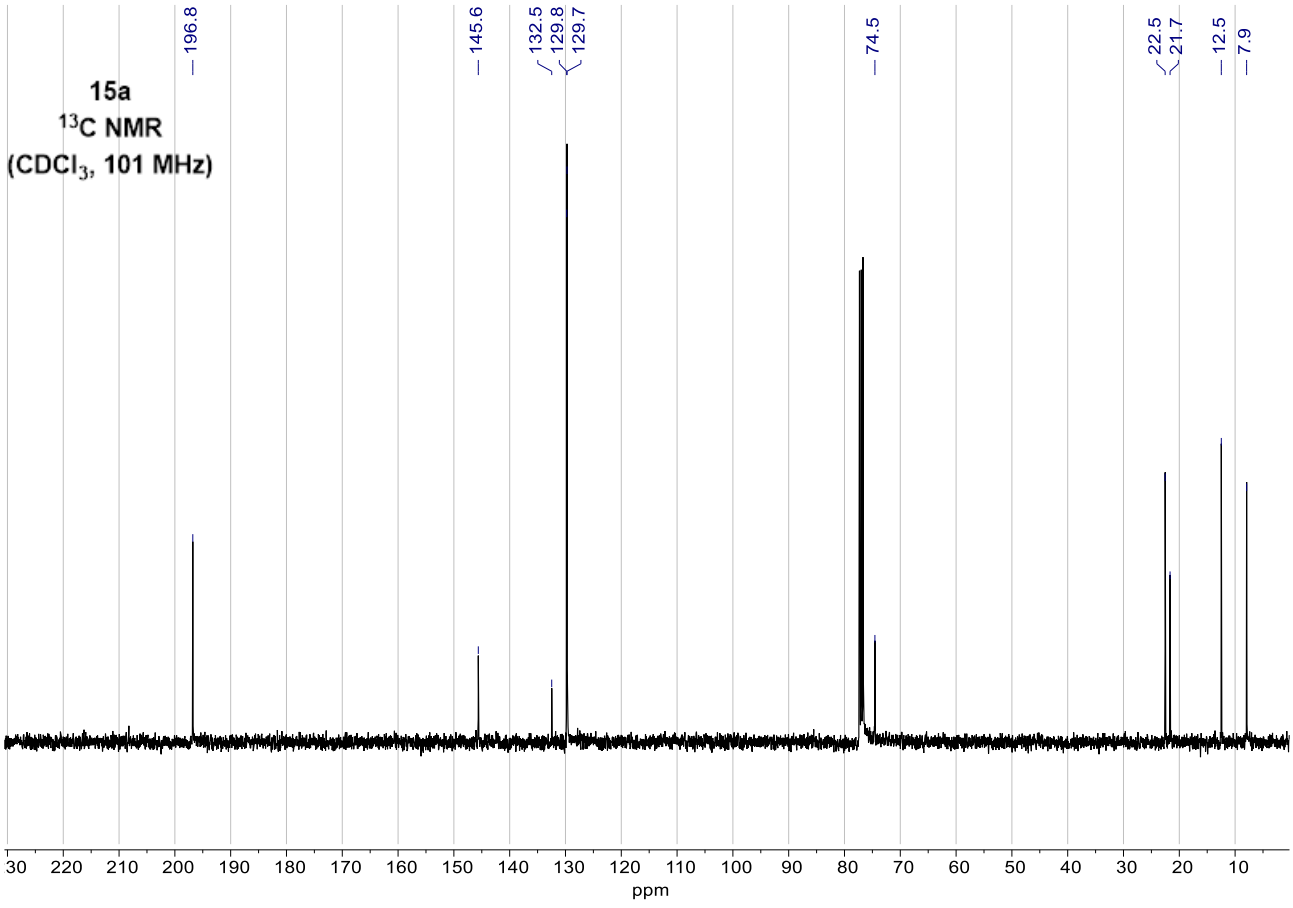

195.8
141.5
133.5
131.1
129.5
70.9
16.6
14f
^{13}C NMR
($CDCl_3$, 101 MHz)
ppm

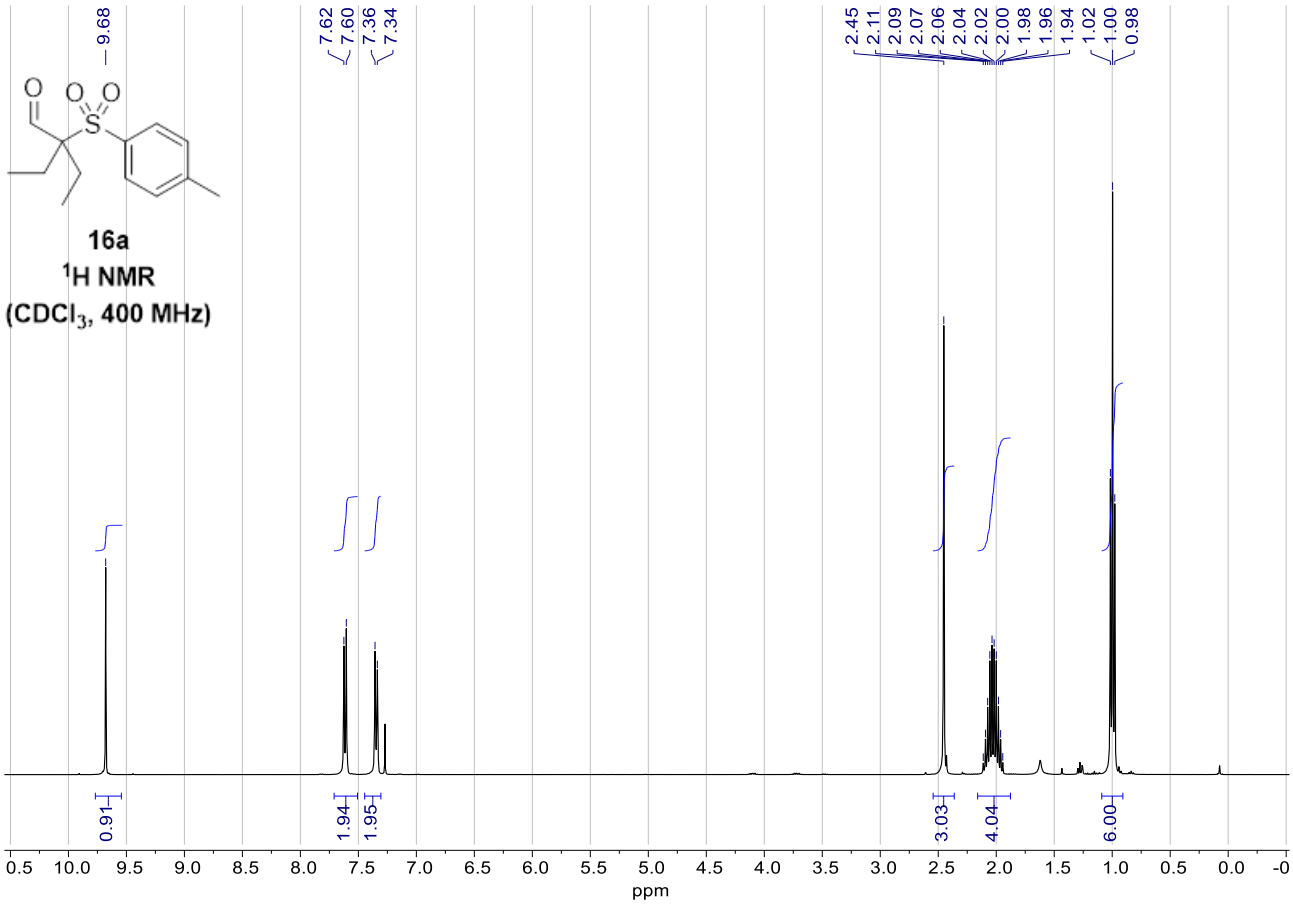

9.80
7.94
7.91
7.85
7.83
1.50
14h
^{1}H NMR
($CDCl_3$, 400 MHz)
1.00
2.05
2.14
6.63
ppm

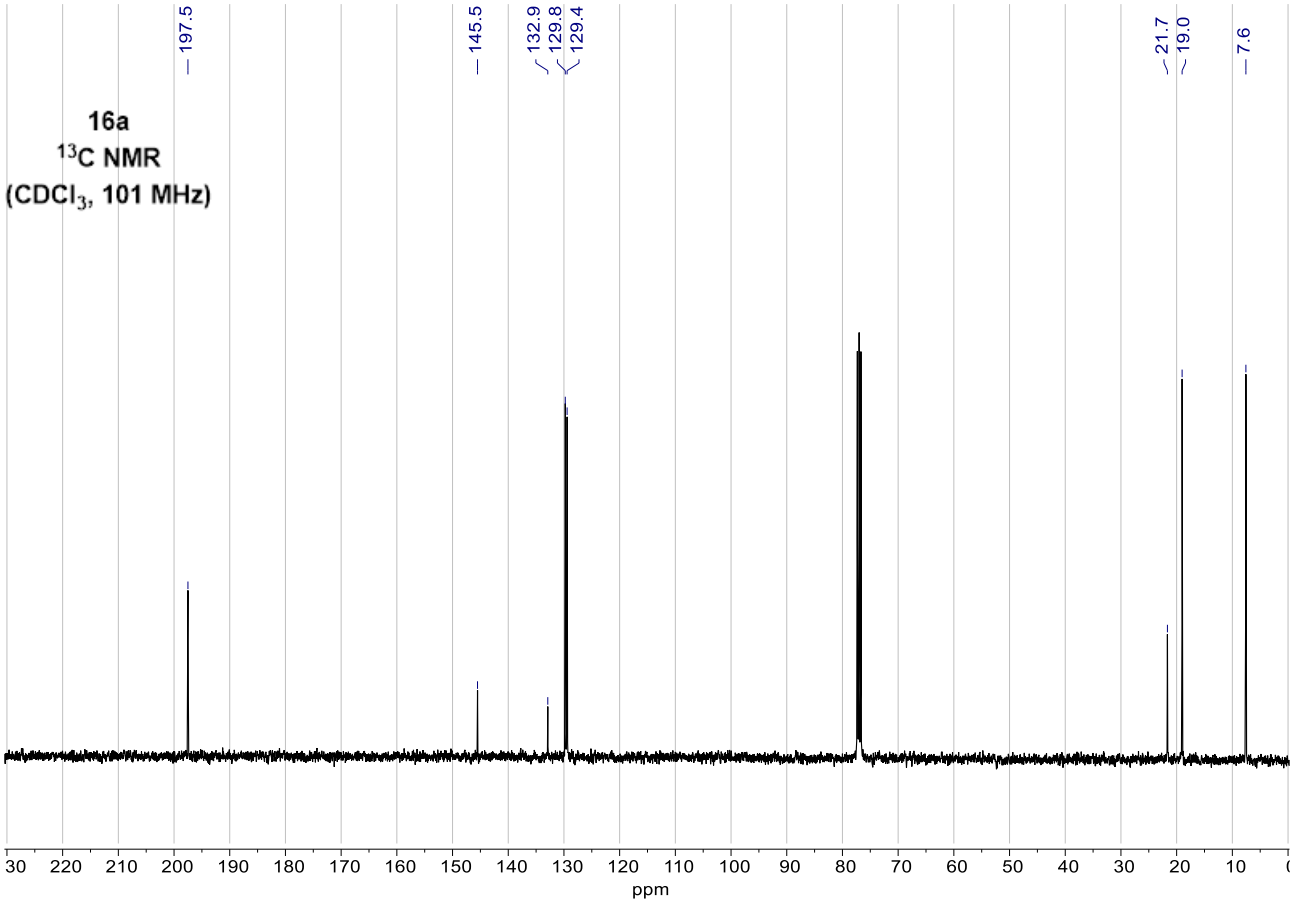

195.6
138.7
136.6
136.3
135.9
135.6
130.4
129.7
127.0
126.3
126.3
126.3
126.2
124.3
121.6
71.0
16.6
14h
^{13}C NMR
($CDCl_3$, 101 MHz)
ppm

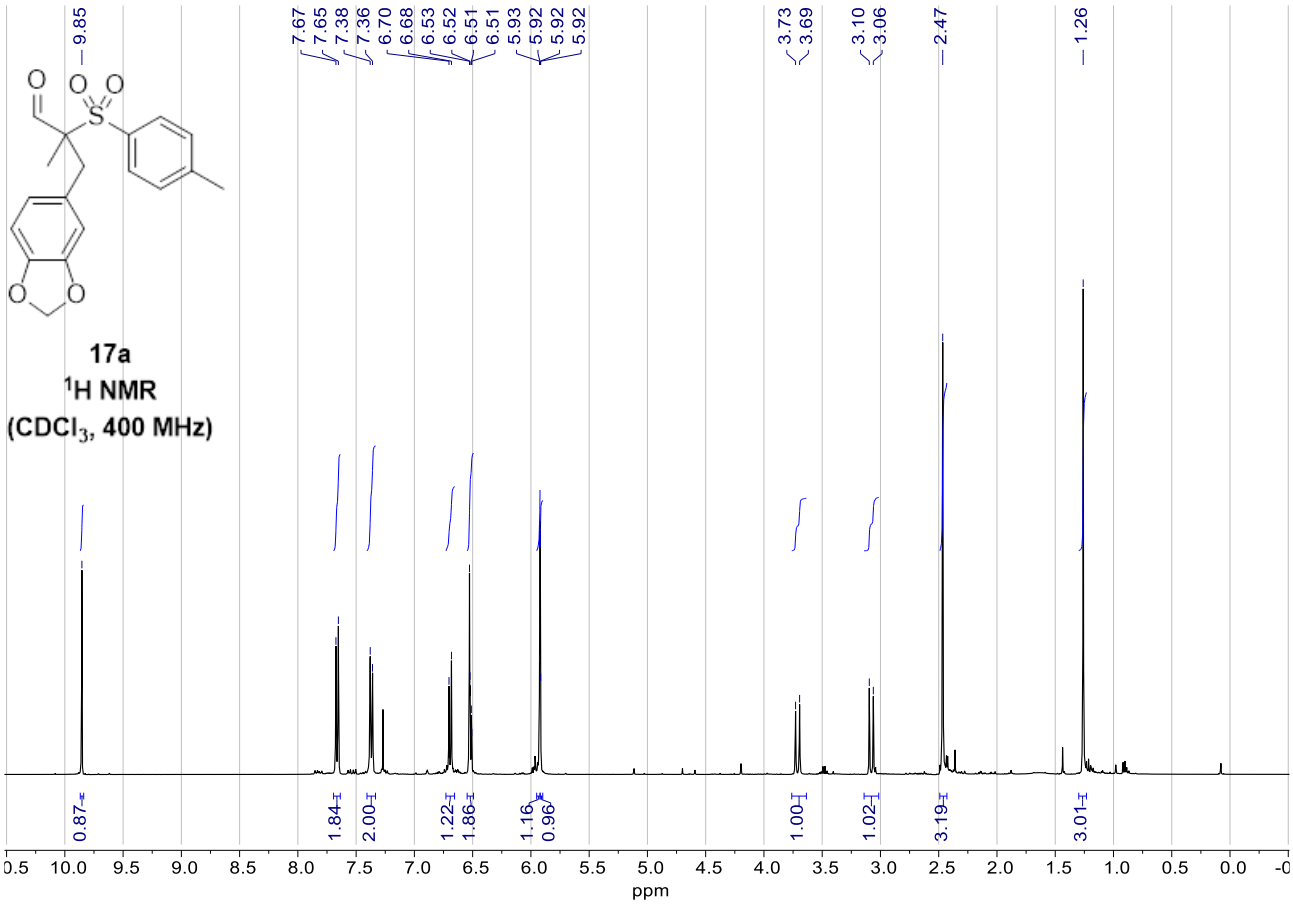

14h
^{19}F NMR
($CDCl_3$, 377 MHz)
-63.32
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
-230
-250
-270
-290
ppm

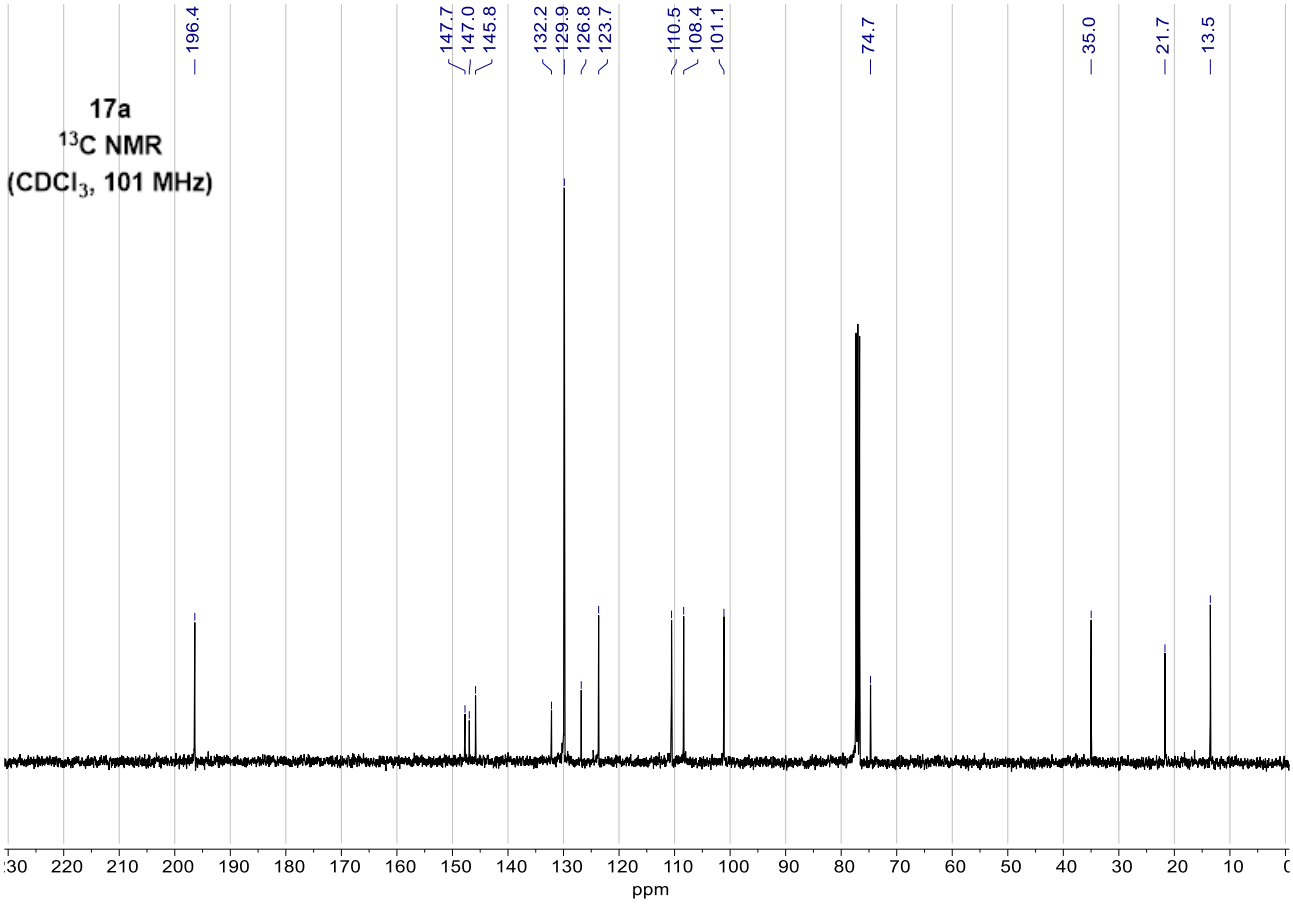

9.74
7.65
7.63
7.36
7.36
7.34
2.45
2.39
2.38
2.36
2.34
2.32
2.30
2.29
2.28
2.01
2.00
1.99
1.99
1.98
1.97
1.96
1.95
1.95
1.94
1.93
1.92
1.35
0.91
0.89
0.87
15a
^{1}H NMR
($CDCl_3$, 400 MHz)
1.00
2.09
2.10
3.18
1.25
1.17
3.25
3.39
ppm

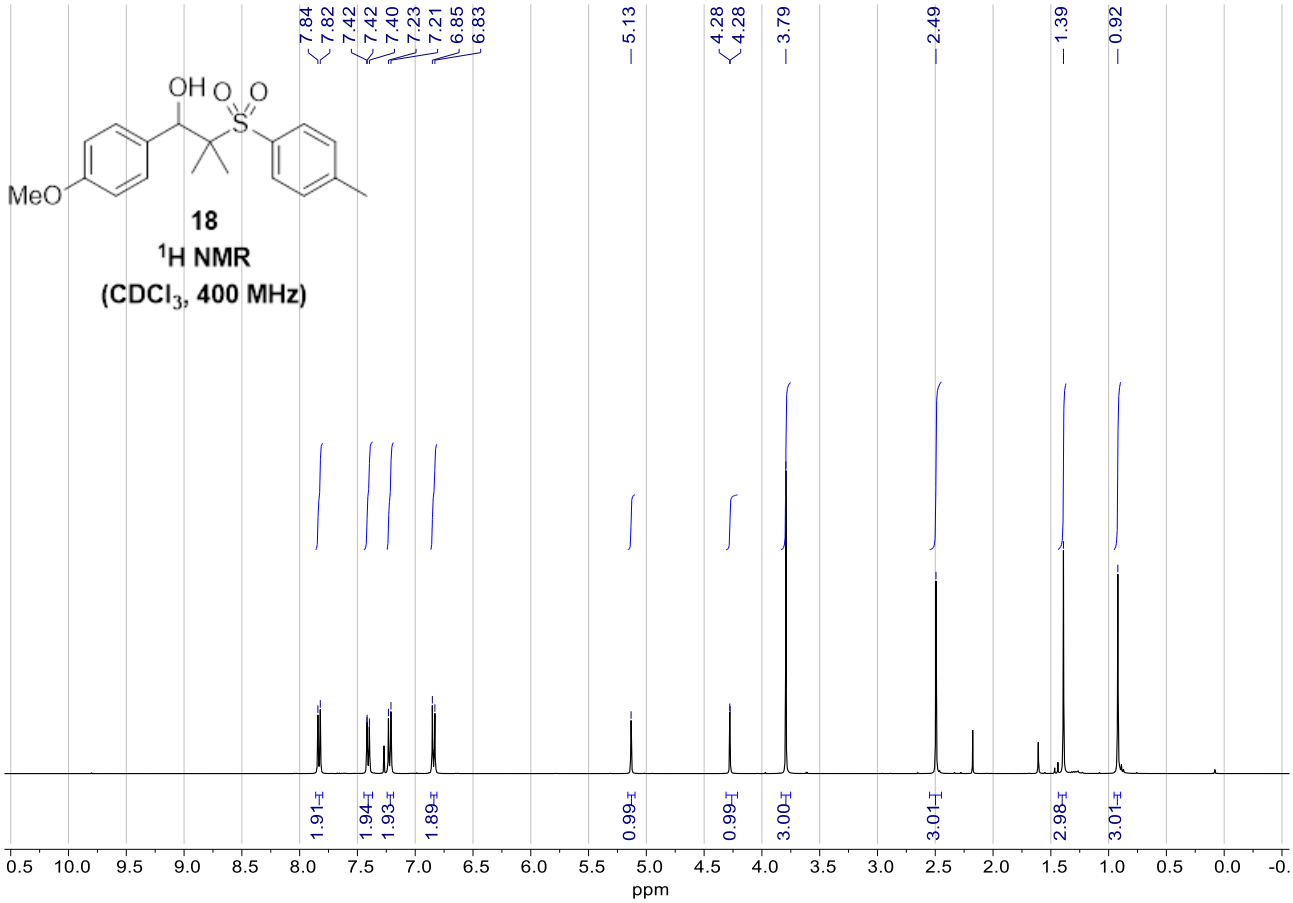

196.8
145.6
132.5
129.8
129.7
74.5
22.5
21.7
12.5
7.9
15a
^{13}C NMR
($CDCl_3$, 101 MHz)
ppm

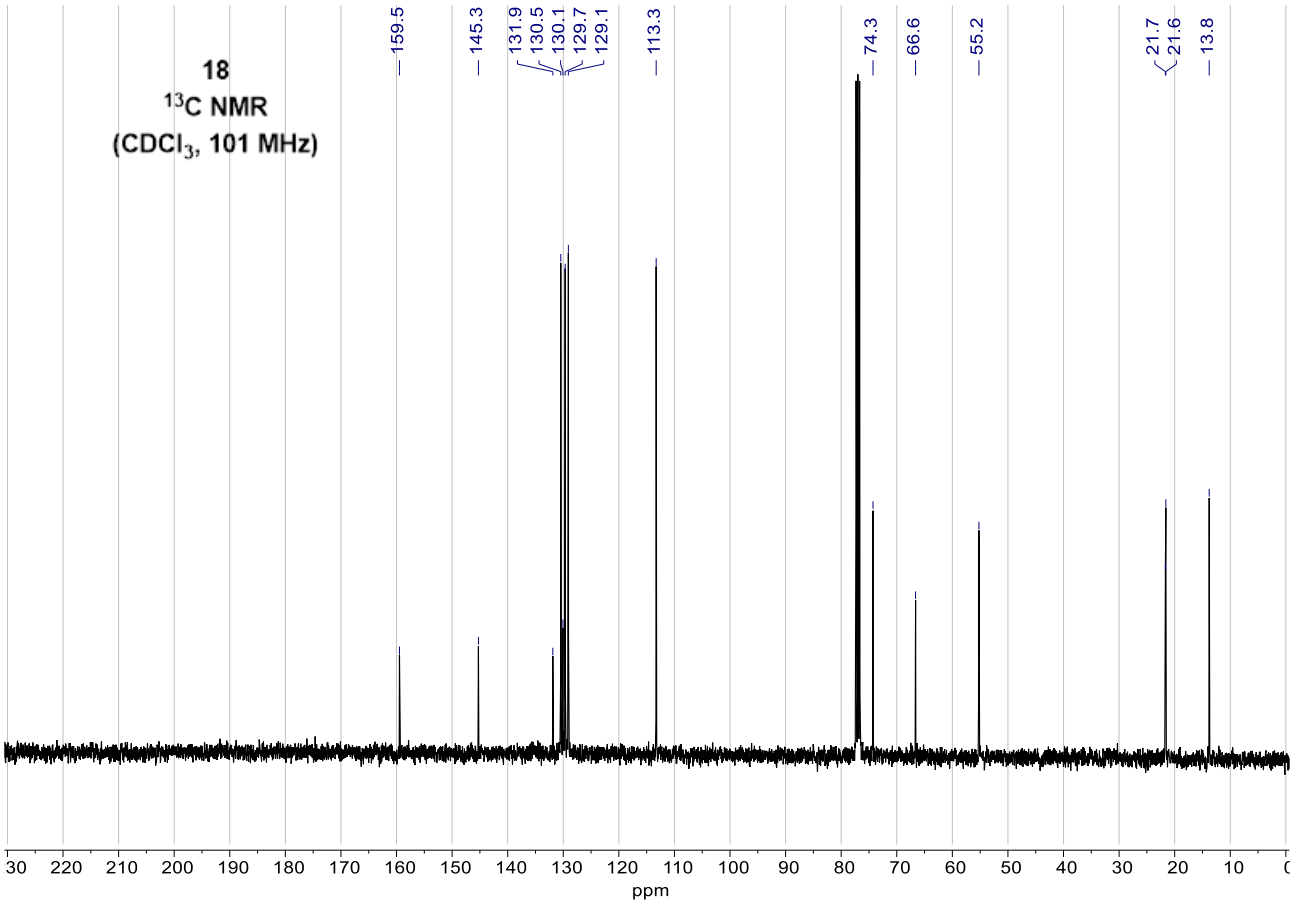

9.68
7.62
7.60
7.36
7.34
2.45
2.11
2.09
2.07
2.06
2.04
2.02
2.00
1.98
1.96
1.94
1.02
1.00
0.98
16a
1H NMR
(CDCl3, 400 MHz)
0.91
1.94
1.95
3.03
4.04
6.00
ppm

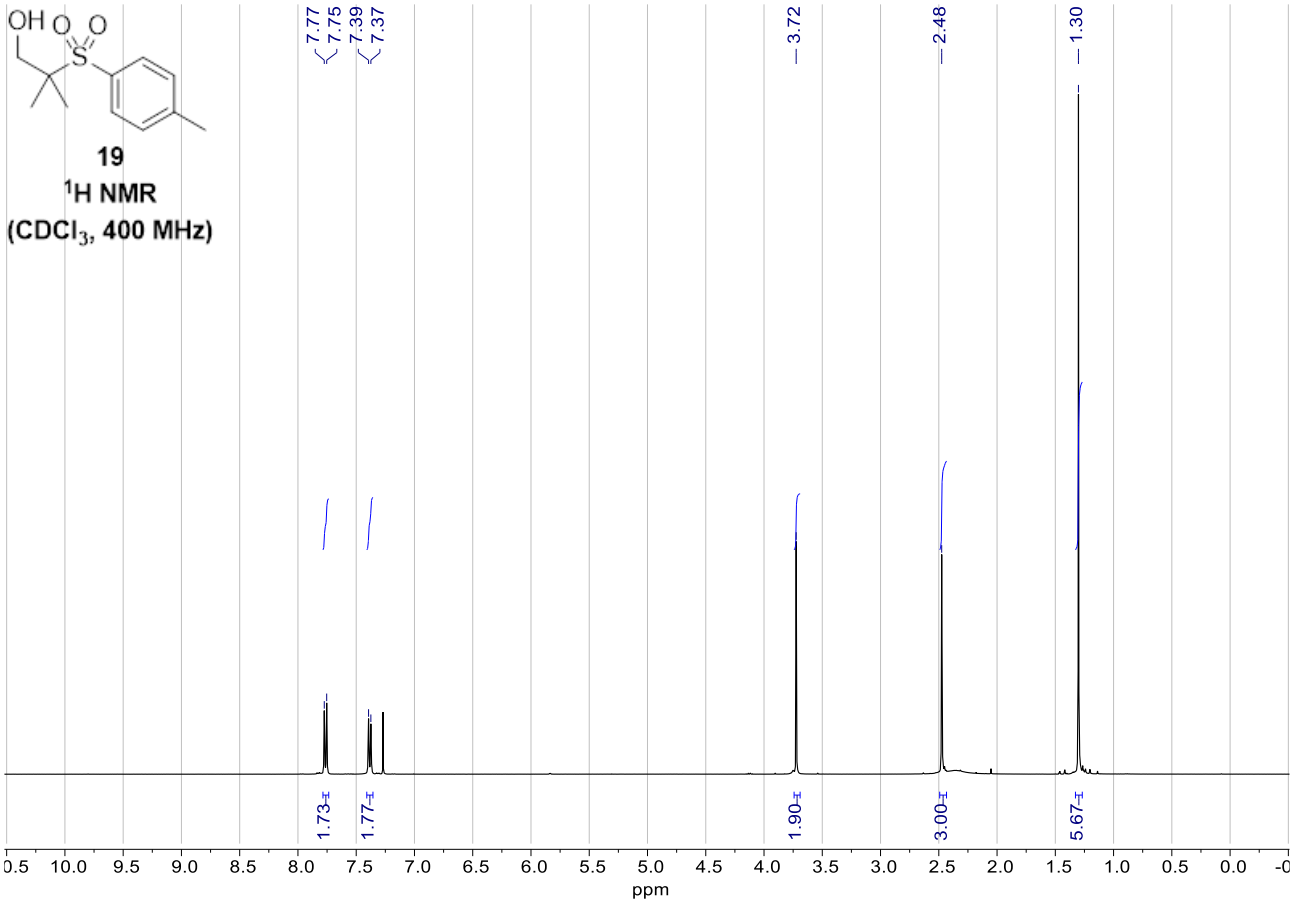

197.5
145.5
132.9
129.8
129.4
21.7
19.0
7.6
16a
13C NMR
(CDCl3, 101 MHz)
ppm

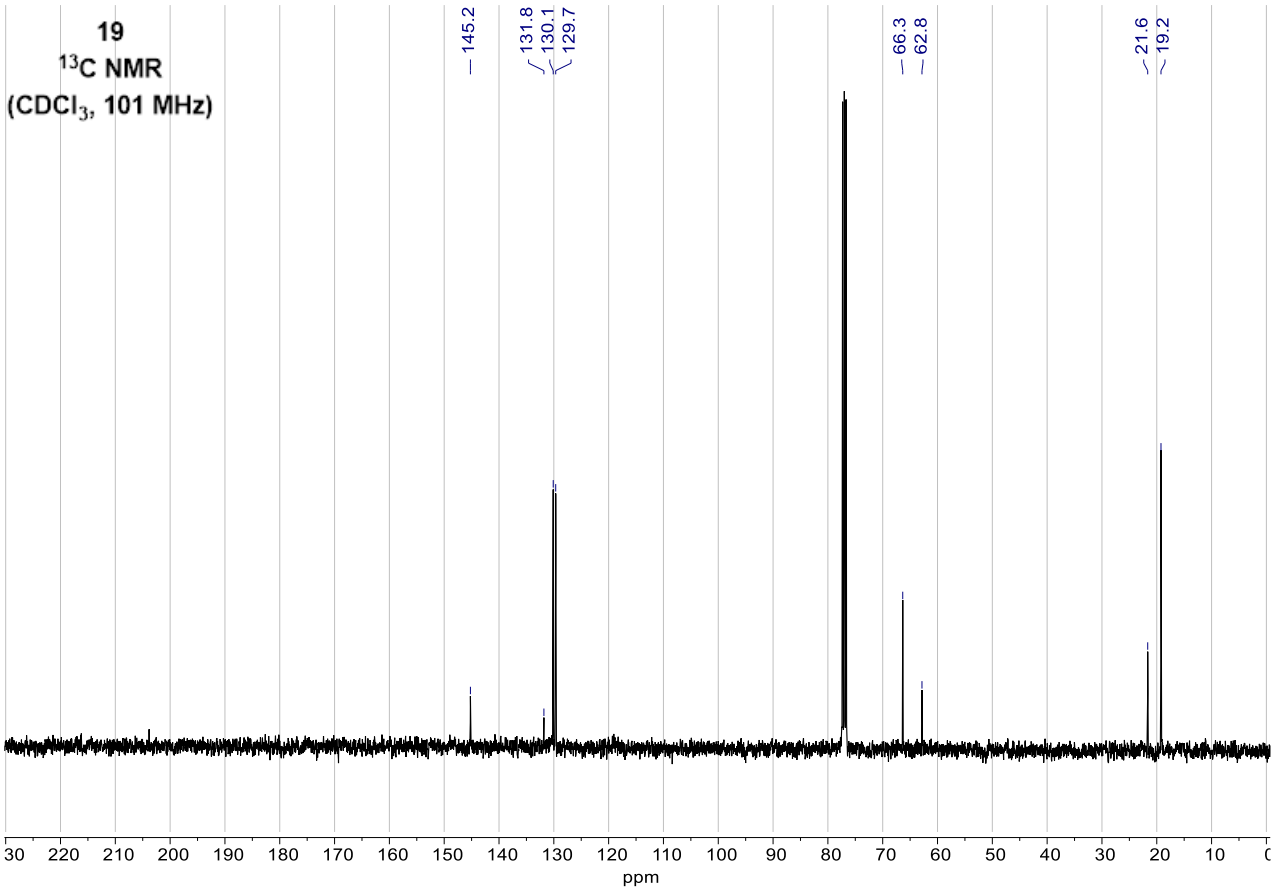

17a
^{1}H NMR
(CDCl$_3$, 400 MHz)
9.85
7.67
7.65
7.38
7.36
6.70
6.68
6.53
6.52
6.51
6.51
5.93
5.92
5.92
5.92
3.73
3.69
3.10
3.06
2.47
1.26
0.87
1.84
2.00
1.22
1.86
1.16
0.96
1.00
1.02
3.19
3.01
ppm

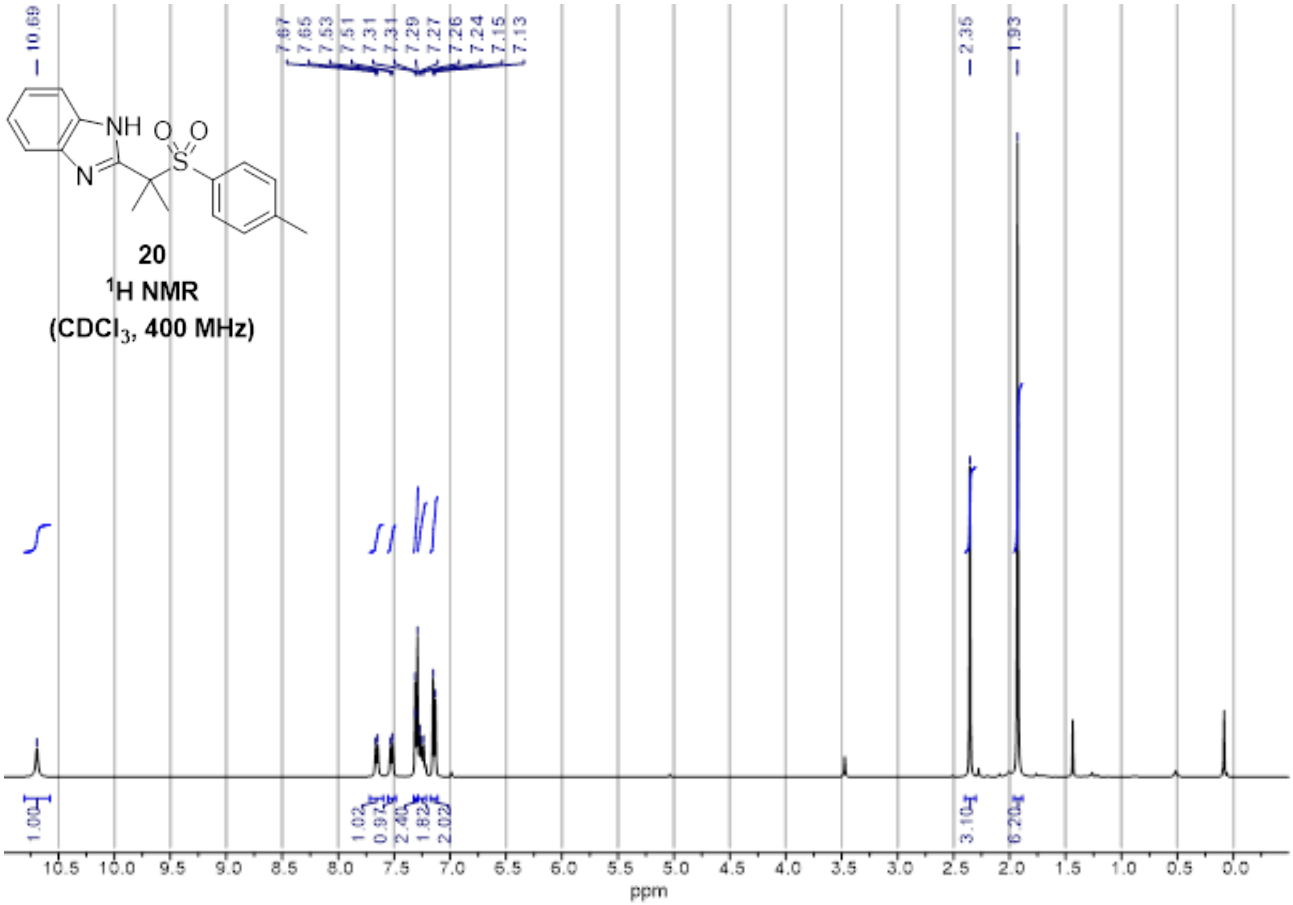

17a
^{13}C NMR
(CDCl$_3$, 101 MHz)
196.4
147.7
147.0
145.8
132.2
129.9
126.8
123.7
110.5
108.4
101.1
74.7
35.0
21.7
13.5
ppm

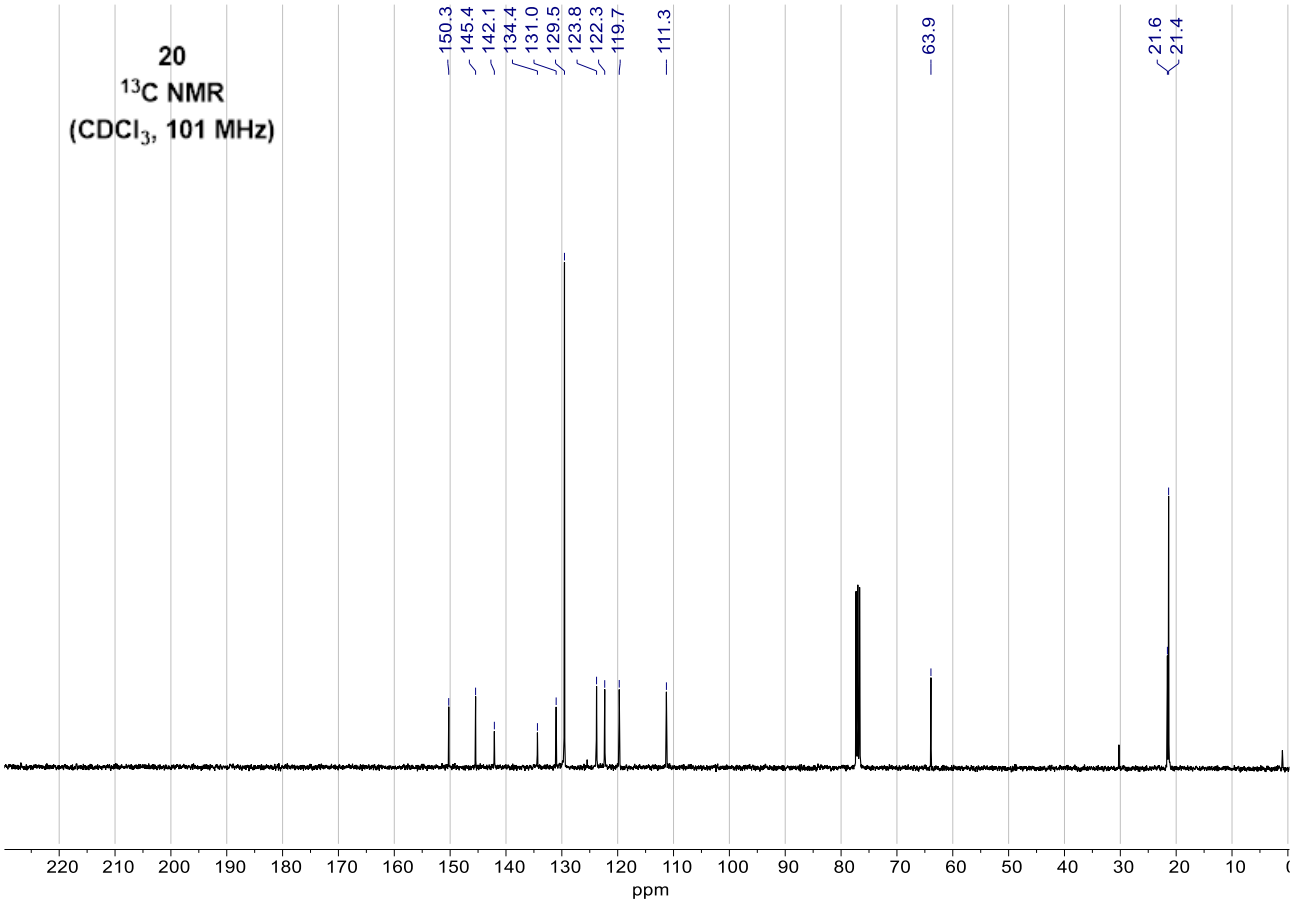

7.84
7.82
7.42
7.42
7.40
7.23
7.21
6.85
6.83
5.13
4.28
4.28
3.79
2.49
1.39
0.92
OH
O
O
S
MeO
18
^{1}H NMR
(CDCl$_3$, 400 MHz)
1.91
1.94
1.93
1.89
0.99
0.99
3.00
3.01
2.98
3.01
ppm

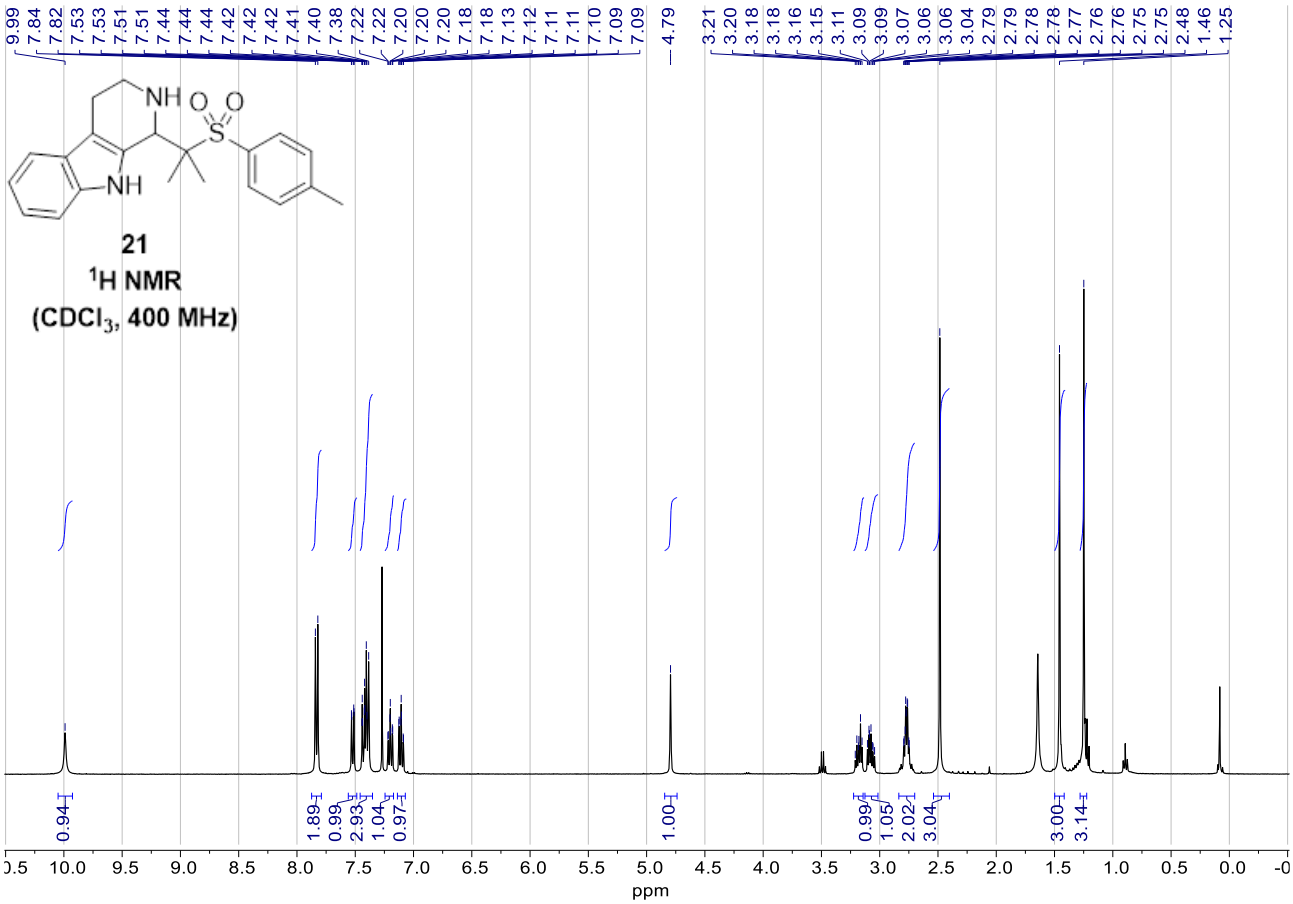

18
^{13}C NMR
(CDCl$_3$, 101 MHz)
159.5
145.3
131.9
130.5
130.1
129.7
129.1
113.3
74.3
66.6
55.2
21.7
21.6
13.8
ppm

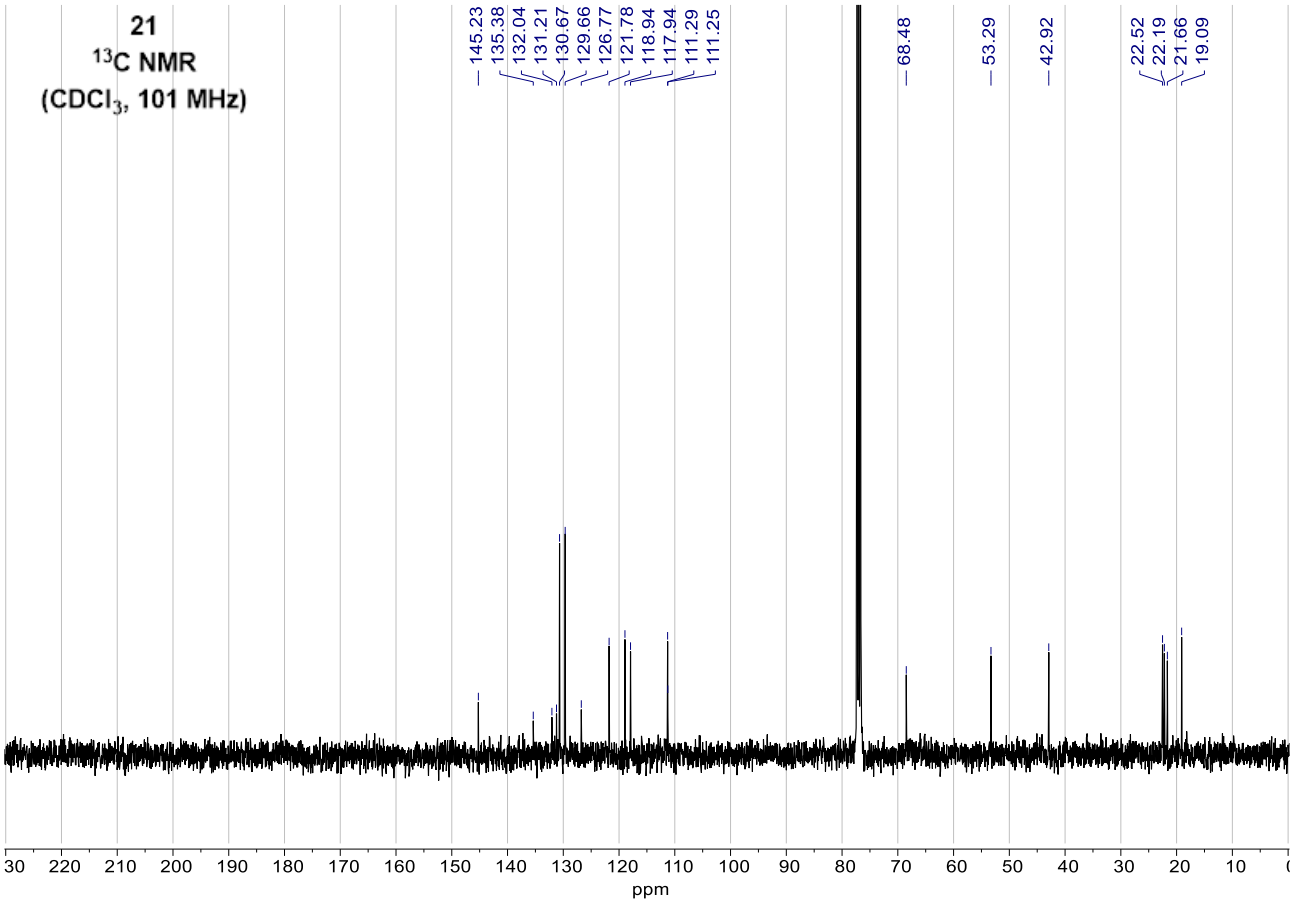

OH
O
O
S
19
^{1}H NMR
(CDCl$_3$, 400 MHz)
7.77
7.75
7.39
7.37
3.72
2.48
1.30
1.73
1.77
1.90
3.00
5.67
ppm

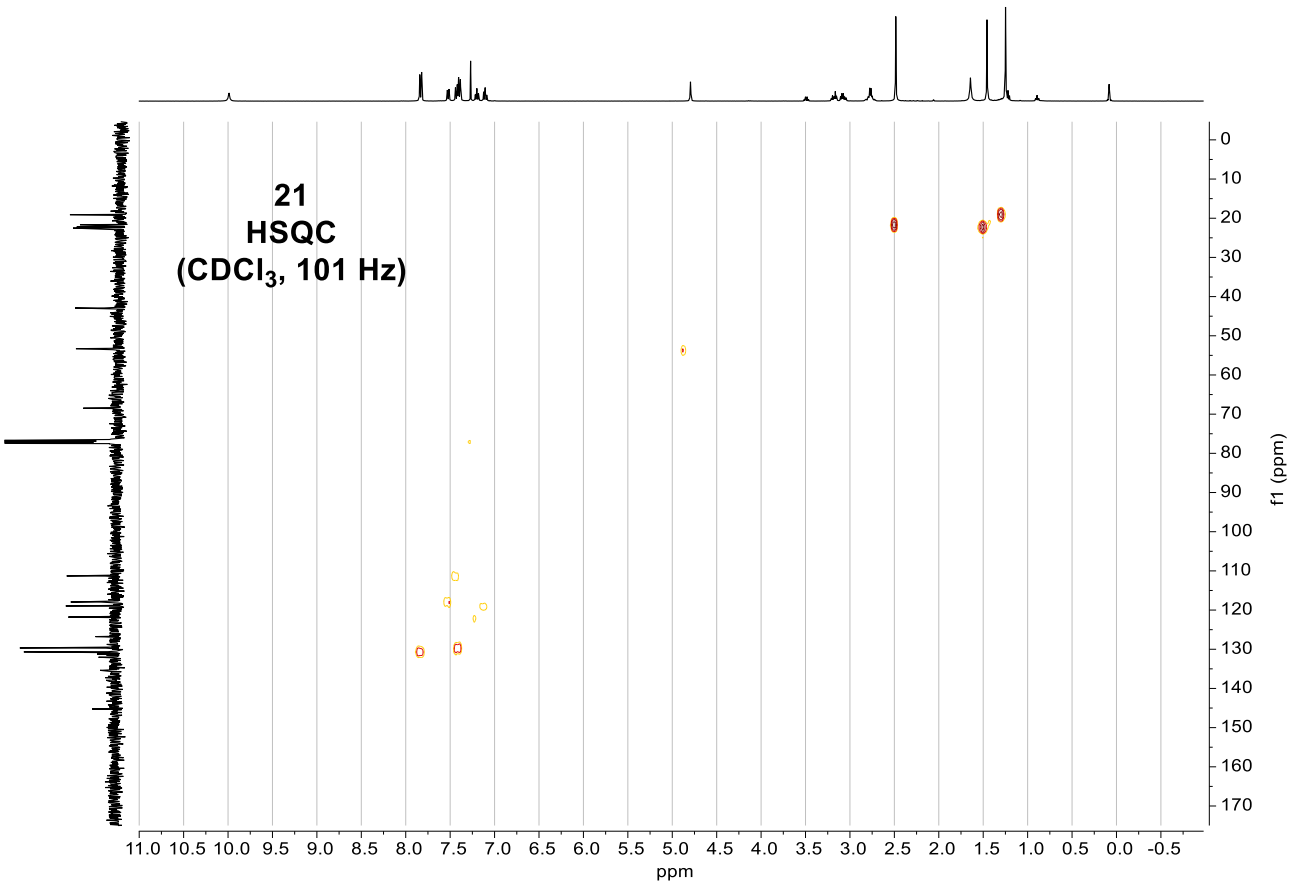

19
^{13}C NMR
(CDCl$_3$, 101 MHz)
145.2
131.8
130.1
129.7
66.3
62.8
21.6
19.2
ppm

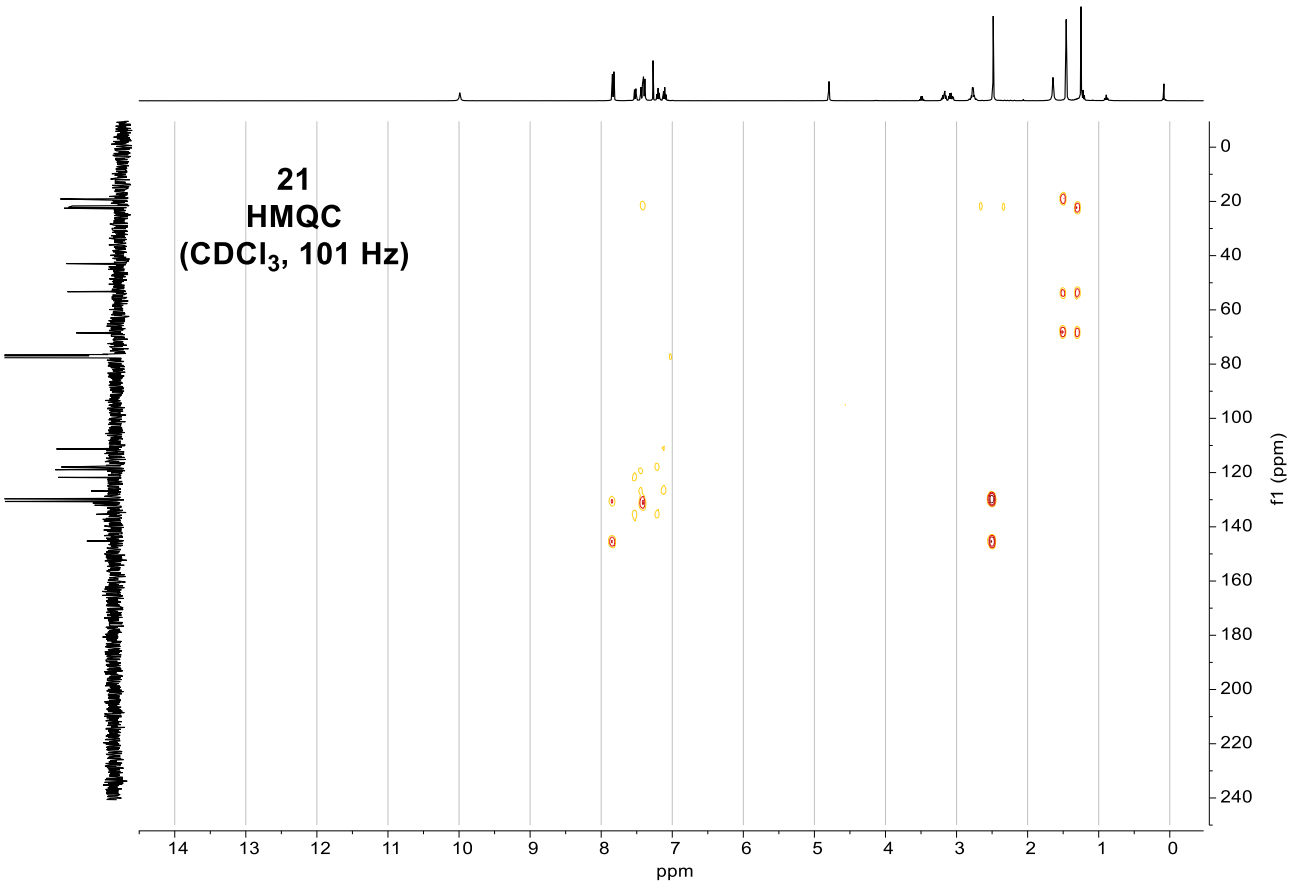

10.69
7.67
7.65
7.53
7.51
7.31
7.31
7.29
7.27
7.26
7.24
7.15
7.13
2.35
1.93
NH
O
O
S
N
20
^{1}H NMR
(CDCl$_3$, 400 MHz)
1.00
1.02
0.97
2.48
1.82
2.02
3.10
6.20
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

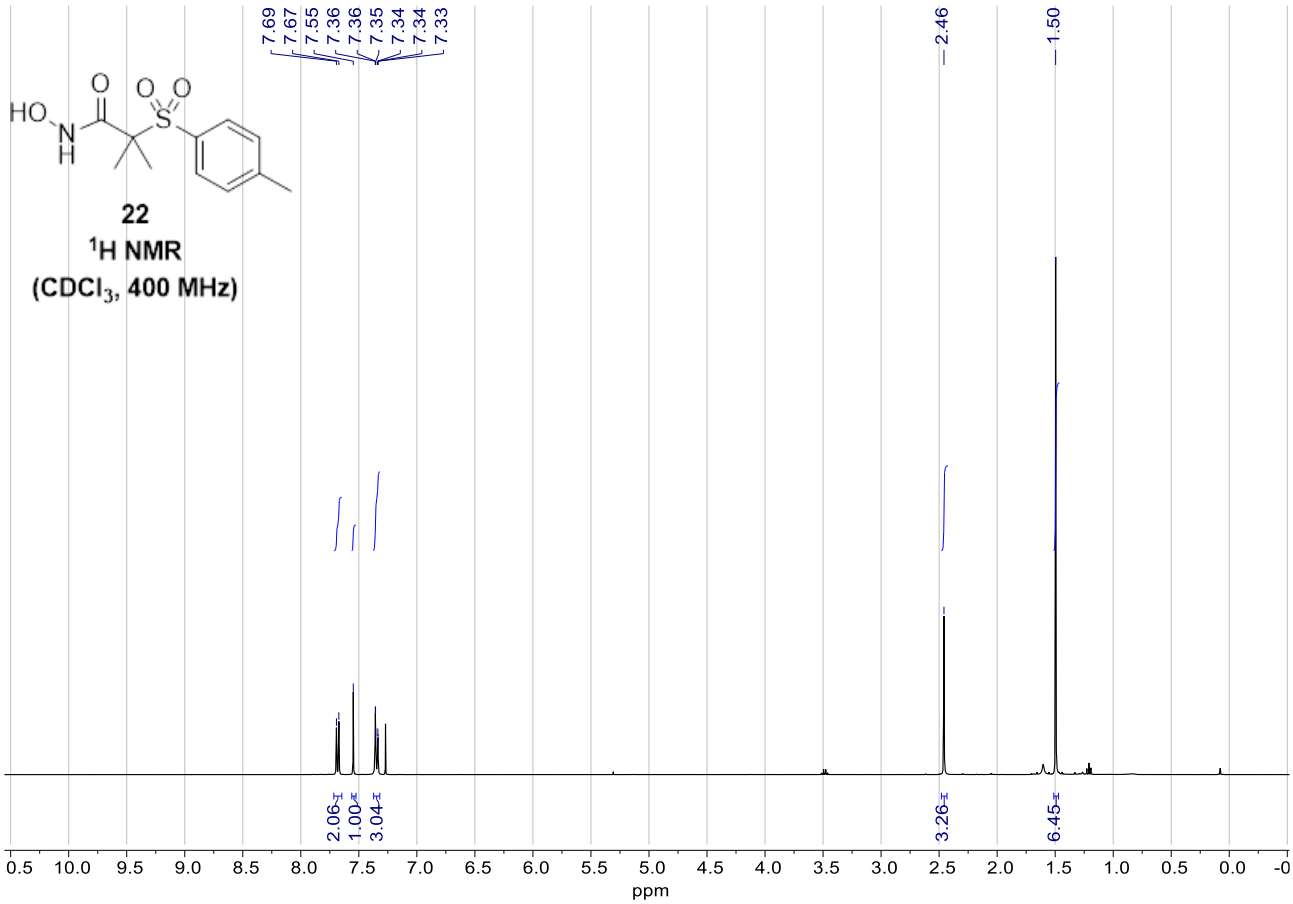

20
^{13}C NMR
(CDCl$_3$, 101 MHz)
150.3
145.4
142.1
134.4
131.0
129.5
123.8
122.3
119.7
111.3
63.9
21.6
21.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

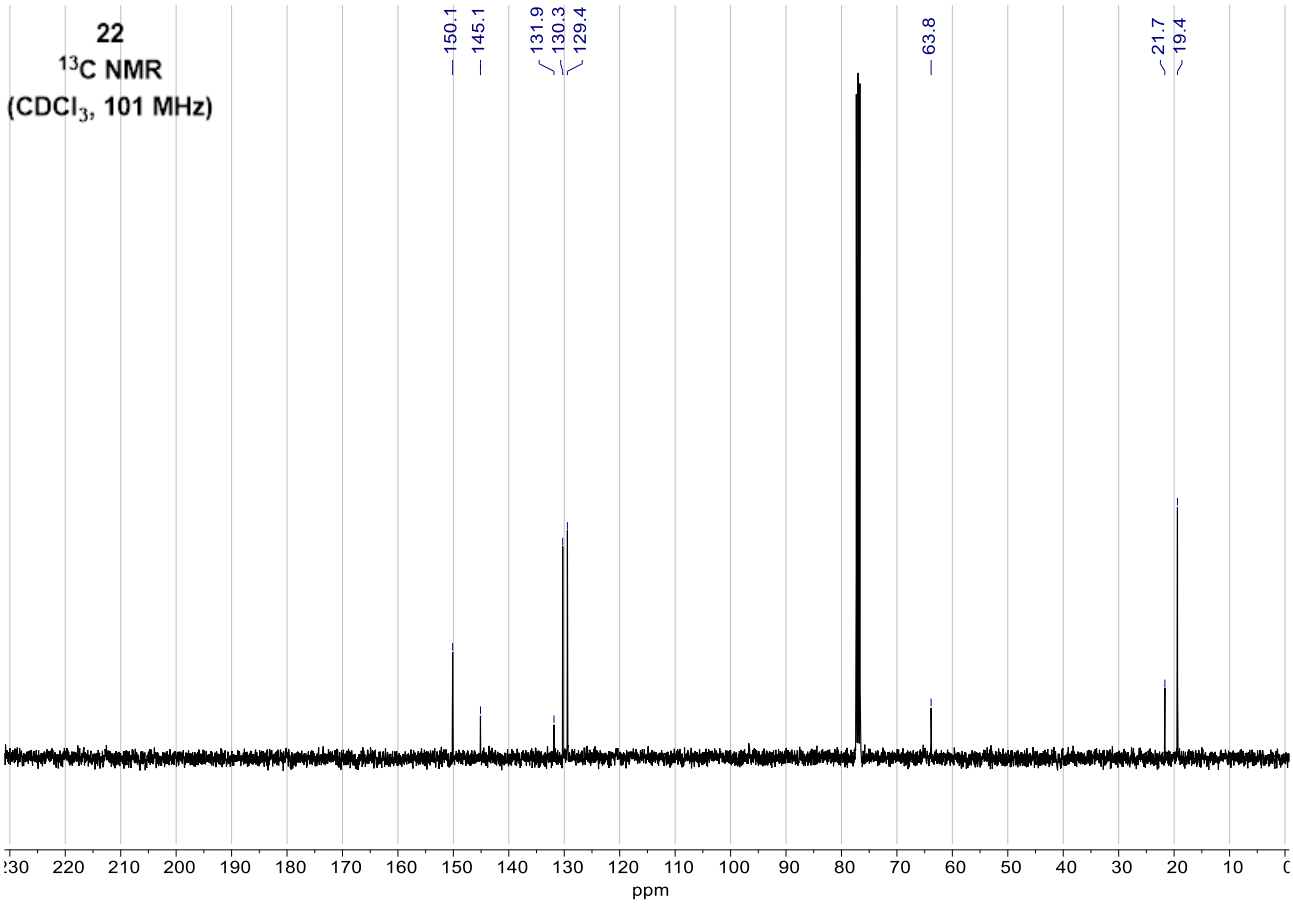

9.99 7.84 7.82 7.53 7.53 7.51 7.51 7.44 7.44 7.44 7.42 7.42 7.42 7.41 7.40 7.38 7.22 7.22 7.20 7.20 7.20 7.18 7.18 7.13 7.12 7.11 7.11 7.10 7.09 7.09 4.79
3.21 3.20 3.18 3.18 3.16 3.15 3.11 3.09 3.09 3.07 3.06 3.06 3.04 2.79 2.79 2.78 2.78 2.77 2.76 2.76 2.75 2.75 2.48 1.46 1.25
NH
O O
S
NH
21
^{1}H NMR
($CDCl_3$, 400 MHz)
0.94 1.89 0.99 2.93 1.04 0.97 1.00 0.99 1.05 2.02 3.04 3.00 3.14
ppm

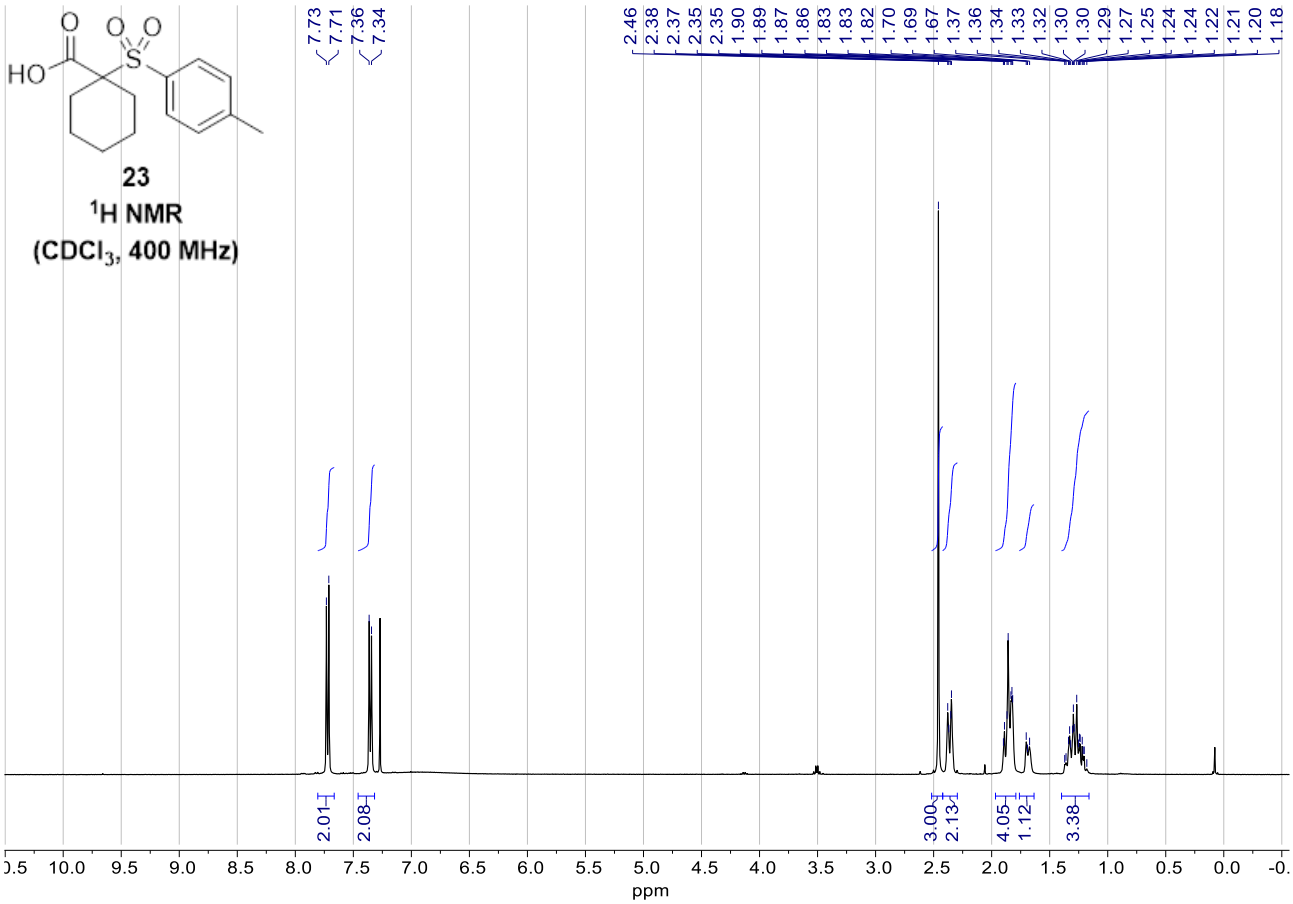

21
^{13}C NMR
($CDCl_3$, 101 MHz)
145.23 135.38 132.04 131.21 130.67 129.66 126.77 121.78 118.94 117.94 111.29 111.25
68.48
53.29
42.92
22.52 22.19 21.66 19.09
ppm

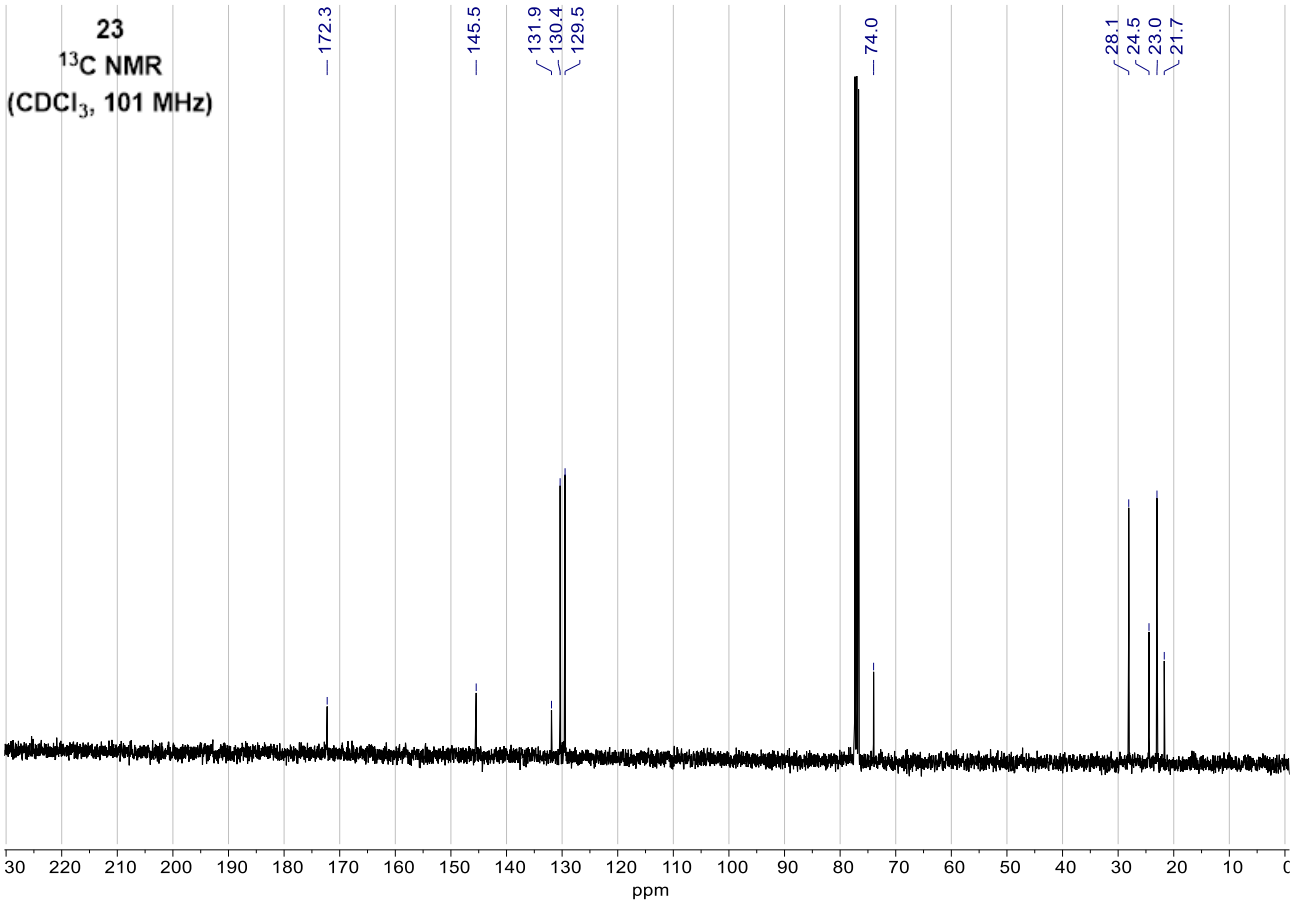

21
HSQC
(CDCl3, 101 Hz)
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170
f1 (ppm)


21
HMQC
(CDCl3, 101 Hz)
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
ppm
0 20 40 60 80 100 120 140 160 180 200 220 240
f1 (ppm)


22
^{1}H NMR
($CDCl_3$, 400 MHz)
7.69
7.67
7.55
7.36
7.36
7.35
7.34
7.34
7.33
2.46
1.50
2.06
1.00
3.04
3.26
6.45
ppm


22
^{13}C NMR
($CDCl_3$, 101 MHz)
150.1
145.1
131.9
130.3
129.4
63.8
21.7
19.4
ppm


23
^{1}H NMR
(CDCl$_3$, 400 MHz)
7.73
7.71
7.36
7.34
2.46
2.38
2.37
2.35
2.35
1.90
1.89
1.87
1.86
1.83
1.83
1.82
1.70
1.69
1.67
1.37
1.36
1.34
1.33
1.32
1.30
1.30
1.29
1.27
1.25
1.24
1.24
1.22
1.21
1.20
1.18
2.01
2.08
3.00
2.13
4.05
1.12
3.38
ppm


23
^{13}C NMR
(CDCl$_3$, 101 MHz)
172.3
145.5
131.9
130.4
129.5
74.0
28.1
24.5
23.0
21.7
ppm

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