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Organocatalytic Trifluoromethylation of Imines Using Phase-Transfer Catalysis with Phenoxides. A General Platform for Catalytic Additions of Organosilanes to Imines

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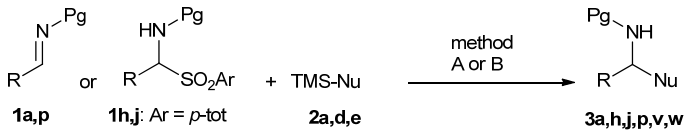
Table S1. Comparison of results obtained with control experiments with results obtained under optimised conditions.[a]



1a,p **1h,j**: Ar = *p*-tot **2a,d,e** **3a,h,j,p,v,w**

entry	**1**	R	Pg	**2**	Nu	A or B	**3**	yield (%) Optimised conditions[b]	yield (%) No TBAB[c]	yield (%) 0.10 equiv. PhONa[c]
1	**1a**	Ph	Ts	**2a**	CF_3	A	**3a**	97	31	8
2	**1j**	$Ph(CH_2)_2$	Ts	**2a**	CF_3	B	**3j**	59	15	n.p.
3	**1p**	Ph	$P(O)Ph_2$	**2a**	CF_3	A	**3p**	71	traces	6
4	**1a**	Ph	Ts	**2c**	CH_2CN	A[d]	**3v**	87	32	12
5	**1a**	Ph	Ts	**2d**	$OCH(Ph)CH_2$	A[e]	**3w**	91	traces	7

[a] Method A: **1** (0.25 mmol), **2** (0.375 mmol), TBAB (0.025 mmol), MS 5 Å, toluene (2.5 mL), then PhONa (0.275 mmol, added at 0 °C), 16-20 h RT. Method B: **1** (0.20 mmol), **2a** (2 M in THF, 0.80 mmol), TBAB (0.040 mmol), MS 5 Å, toluene (2.0 mL), then PhONa (0.44 mmol), -55 °C, 16-20 h. [b] Isolated yield after chromatography on silica gel. [c] Determined by ^{1}H NMR spectroscopy using dibenzyl as internal standard. [d] At 0 °C. [e] At -30 °C. n.p.: not performed.

As summarised in the Table, in all the examples taken into consideration the anionic amide adducts formed upon addition of the silicon nucleophiles **2** to the imines **3** were not found to be able to promote a subsequent autocatalytic cycle, as the reactions performed using 0.10 equivalents of PhONa gave roughly 10% yield in the products **3**, i.e. all reactions stopped after the initiation step.

On the other hand, the presence of the phase-transfer catalyst TBAB had a great impact on the yield obtained in all cases. If a significant acceleration was observed in the presence of TBAB in the case of **3a** and **3v** (entries 1,4)**,** in the remainders no or very little product **3j,p,w** was observed in its absence (entries 2,3,5). In all reactions where TBAB was omitted, extensive decomposition of the starting materials was observed. These data seem to indicate that under these conditions solid PhONa has some efficiency in some cases in the promotion of the reaction, despite its low solubility in toluene, but it is even more efficient in the decomposition of the imines. In the presence of TBAB catalyst, a more active (or more selective for addition) phenoxide salt is continuously formed, soluble in toluene, which selectively activates the silicon reagents **2**, anticipating imine decomposition by PhONa, and allowing production of adducts **3** in good yields.

In this respect, it is worth noting that the presence of 5 Å molecular sieves in the reaction seems to allow a prolonged "survival" of the imine into the mixture, as a reaction between **1a** and **2a** in the absence of both catalyst TBAB and molecular sieves gave a lower background yield (10%).

Taken together, these data support strongly the catalytic cycle shown in Scheme 1, wherein a soluble ammonium phenoxide is formed at each catalytic cycle by phase-transfer exchange of the anionic amide adduct with phenoxide, deriving from solid PhONa.

Experimental Details:

General Methods. ^{1}H, ^{13}C, ^{19}F NMR spectra were recorded on Varian AS 300, 400 or 600 spectrometers. Chemical shifts (δ) are reported in ppm relative to residual solvent signals for ^{1}H and ^{13}C NMR,[1] or using an external reference for ^{19}F NMR (C_6F_6, -163.0 ppm). ^{13}C NMR spectra were acquired with ^{1}H broad band decoupled mode. Mass spectra were recorded on a micromass LCT spectrometer using electrospray (ES) ionisation techniques. The optical rotation of product **3o** was measured on a Perkin-Elmer 241 polarimeter. The enantiomeric excess (ee) of product **3o** was determined by chiral stationary phase HPLC (Daicel Chiralpak AD-H).

Materials. Analytical grade solvents and commercially available reagents were used as received, unless otherwise stated. Toluene and THF were distilled from Na/benzophenone prior to use. CH_2Cl_2 was passed through a plug of basic Al_2O_3 prior to use. Chromatographic purifications were performed using 70-230 mesh silica (chromatography) or 230-400 mesh silica (flash chromatography). Imines **1a**[2] and **1g**[3] were prepared following reported procedures, and were purified by crystallisation from EtOH and toluene, respectively. Imines **1b-f,l,n,p** were prepared using modified literature procedures[4] as outlined below. 2,4,6-Trimethylbenzenesulfonamide[5] and *P*,*P*-diphenylphosphinic amide[6] used in the preparation of **1n,o** and **1p,q** were synthesised following the literature. In order to remove traces of water, crude α-amido sulfones **1h-k,m,o**[2] and **1r,s,**[7] obtained according to the literature using sodium *p*-toluensulfinate for **1h-k** and sodium benzenesulfinate for **1m**,**o,r,s** were dissolved in CH_2Cl_2, dried over $MgSO_4$, filtered and evaporated. α-Amido sulfone **1q** was obtained using *p*-toluensulfinic acid following the literature.[8]

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Preparation of imines 1b-f,l,n,p.[4]

To an oven dried round bottom flask, equipped with a magnetic stirring bar, were sequentially added under a nitrogen atmosphere the amide (5.0 mmol), CH_2Cl_2 (5 mL), THF (2.5 mL), the aldehyde (5.2 mmol), and Et_3N (15 mmol). The resulting solution was cooled to 0 °C, then $TiCl_4$ (1.0 M in CH_2Cl_2, 2.5 mL, 2.5 mmol) was added dropwise with stirring. The mixture was stirred under nitrogen at 0 °C for 1 h (4 h at RT for imine **1d**), then filtered through a short pad of Celite, and the pad washed with CH_2Cl_2. This solution was transferred in a separatory funnel, washed with sat. NH_4Cl, dried over $NaHCO_3$, filtered and evaporated. The residue was purified by crystallisation from EtOH for imines **1b-f,l,n**, or by precipitation from CH_2Cl_2 with pentane for imine **1p**.

Preparation of PhONa. PhOH (1880 mg, 20.0 mmol) was added to a flask containing an equimolar amount of NaOH (800 mg, 20.0 mmol), dissolved in H_2O (ca 3 mL). After all PhOH dissolved, indicating complete deprotonation, H_2O was removed under vacuum, the last traces stripped with toluene. The thus obtained white solid was grinded in a mortar to give a fine white powder, which was dried at 70 °C under vacuum overnight, in the presence of P_2O_5.

General procedure for the catalytic trifluoromethylation of imines: method A. To a Schlenk tube equipped with a magnetic stirring bar MS 5 Å (powder, 70 mg) were added. The molecular sieves were activated by heating with a heat gun under vacuum for a few minutes. After cooling to RT under vacuum, the Schlenk tube was filled with N_2. Imine **1a-g**,**l,n,p** (0.25 mmol) and tetra-*n*-butylammonium bromide (TBAB, 7.8 mg, 0.025 mmol, 10 mol%) were added, the Schlenk tube evacuated with vacuum then backfilled with N_2. Dry toluene (2.5 mL) was then added, and the resulting suspension was cooled to 0 °C with stirring. Trimethyl(trifluoromethyl)silane **2a** (commercial solution ca 2 M in THF, 187 µL, 0.375 mmol, 1.5 equiv.) was then added via syringe, followed by solid PhONa (31.9 mg, 0.275 mmol, 1.1 equiv.). The reaction mixture was slowly allowed to warm to RT (a few hours) and vigorously stirred overnight under a N_2 atmosphere. The initial suspension slowly turned to a slightly yellow jelly mixture. Sat. Na_2CO_3 was then added (ca 3 mL), the phases separated, and the aqueous phase extracted with EtOAc (3 x). The combined organic phases were filtered through a short pad of silica gel, the pad washed with EtOAc, then evaporated under vacuum, leaving a solid residue which was purified by (flash) chromatography on silica gel giving the trifluoromethylated adducts **3a-g,l,n,p**.

General procedure for the catalytic trifluoromethylation of imines: method B. To a Schlenk tube equipped with a magnetic stirring bar MS 5 Å (powder, 60 mg) were added. The molecular sieves were activated by heating with a heat gun under vacuum for a few minutes. After cooling to RT under vacuum, the Schlenk tube was filled with N_2. α-Amido sulfone **1h-k,m,o,q-s** (0.20 mmol) and tetra-*n*-butylammonium bromide (12.8 mg, 0.040 mmol, 20 mol%) were added, the Schlenk tube evacuated with vacuum then backfilled with N_2. Dry toluene (2.0 mL) was then added, and the resulting suspension was cooled to -55 °C with stirring. Trimethyl(trifluoromethyl)silane **2a** (commercial solution ca 2 M in THF, 400 µL, 0.80 mmol, 4.0 equiv.) was then added via syringe, followed by solid PhONa (51.0 mg, 0.44 mmol, 2.2 equiv.). The reaction mixture was vigorously stirred overnight at the same temperature. The initial suspension slowly turned to a slightly yellow jelly mixture. Sat. Na_2CO_3 was then added (ca 3 mL), the phases separated, and the aqueous phase extracted with EtOAc (3 x). The combined organic phases were filtered through a short pad of silica gel, the pad washed with EtOAc, then evaporated under vacuum, leaving a solid residue which was purified by chromatography on silica gel giving the trifluoromethylated adducts **3h-k,m,o,q-s**.

4-Methyl-*N*-(2,2,2-trifluoro-1-phenylethyl)benzenesulfonamide (3a). Following the general procedure (method A), the title compound was obtained as a white solid in 97% yield, after flash chromatography on silica gel (*n*-hexane/Et_2O 8:2-7:3). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.63-7.59 (m, 2H), 7.33-7.23 (m, 3H), 7.21-7.13 (m, 4H), 5.61 (br d, J = 6.5 Hz, 1H), 4.92 (br q, J = 6.5 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.7, 136.9, 131.8, 129.4, 129.2, 128.7, 127.7, 126.9, 123.8 (q, J = 282 Hz), 59.1 (q, J = 32 Hz), 21.4; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -74.3 (d, J = 7.6 Hz); ESI-MS 352 [M + Na^+].

The same reaction, performed using neat $TMSCF_3$ instead of the THF solution, gave **3a** in >95% yield, as determined by ^{1}H NMR spectroscopy using dibenzyl as internal standard, thus showing that the THF deriving from the $TMSCF_3$ solution has no influence on the reaction outcome.

The same reaction, performed using 0.10 equiv. of PhONa, gave **3a** in 8% yield, as determined by ^{1}H NMR spectroscopy using dibenzyl as internal standard, thus showing that the amide adduct formed upon initiation is not able to promote subsequent additions.

The same reaction, performed in the absence of TBAB catalyst, gave **3a** in 31% yield, as determined by ^{1}H NMR spectroscopy using dibenzyl as internal standard, thus showing that solid PhONa alone is not able to promote the reaction as efficiently as in the presence of TBAB. Extensive imine decomposition was also observed.

***N*-(1-(2-Bromophenyl)-2,2,2-trifluoroethyl)-4-methylbenzenesulfonamide (3b).** Following the general procedure (method A), the title compound was obtained as a white solid in 85% yield, after flash chromatography on silica gel (*n*-hexane/Et_2O 8:2-7:3). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.66-7.61 (m, 2H), 7.42 (dd, J = 8.0, 1.3 Hz, 1H), 7.31-7.26 (m, 1H), 7.19-7.14 (m, 1H), 7.15-7.08 (m, 3H), 6.62 (br s, 1H), 5.62 (br q, J = 7.1 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.1, 136.5, 133.1, 131.9, 130.7, 129.7, 129.0, 128.2, 127.2, 123.8 (q, J = 282 Hz), 57.8 (q, J = 32 Hz), 21.6; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -74.5 (d, J = 7.7 Hz); ESI-MS 430, 432 [M + Na^+].

***N*-(1-(4-Chlorophenyl)-2,2,2-trifluoroethyl)-4-methylbenzenesulfonamide (3c).** Following the general procedure (method A), the title compound was obtained as a white solid in 98% yield, after flash chromatography on silica gel (*n*-hexane/Et_2O 8:2-7:3). ^{1}H NMR (acetone-d_6, 400 MHz) δ 7.94 (d, J = 9.6 Hz, 1H), 7.59-7.54 (m, 2H), 7.45-7.41 (m, 2H), 7.32-7.27 (m, 2H), 7.22-7.18 (m, 2H), 5.24 (quint, J = 8.2 Hz, 1H), 2.33 (s, 1H); ^{13}C NMR (acetone-d_6, 100 MHz) δ 143.5, 138.4, 134.7, 131.6, 130.3, 129.5, 128.7, 127.0, 124.0 (q, J =

280 Hz), 58.5 (q, J = 32 Hz), 20.6; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -74.4 (d, J = 8.4 Hz); ESI-MS 386, 388 [M + Na^+].

4-Methyl-*N*-(2,2,2-trifluoro-1-(4-methoxyphenyl)ethyl) benzenesulfonamide (3d). Following the general procedure (method A), the title compound was obtained as a white solid in 80% yield, after flash chromatography on silica gel (*n*-hexane/Et_2O 8:2-7:3). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.66-7.58 (m, 2H), 7.18 (br d, J = 8.3 Hz, 2H), 7.14-7.06 (m, 2H), 6.81-6.74 (m, 2H), 5.58 (d, J = 8.6 Hz, 1H), 4.86 (quint, J = 8.3 Hz, 1H), 3.77 (s, 3H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 160.5, 144.0, 137.3, 129.7, 129.3, 124.3 (q, J = 282 Hz), 124.2, 114.5, 58.9 (q, J = 32 Hz), 55.7, 21.7; ^{19}F NMR ($CDCl_3$, 282 MHz) δ -74.6 (d, J = 7.3 Hz); ESI-MS 382 [M + Na^+].

4-Methyl-*N*-(2,2,2-trifluoro-1-(naphthalen-2-yl)ethyl)benzenesulfonamide (3e). Following the general procedure (method A), the title compound was obtained as a white solid in 80% yield, after flash chromatography on silica gel (*n*-hexane/Et_2O 8:2-7:3). ^{1}H NMR (acetone-d_6, 400 MHz) δ 7.99 (d, J = 10.3 Hz, 1H), 7.90-7.94 (m, 2H), 7.83-7.75 (m, 2H), 7.58-7.50 (m, 5H), 7.02-6.99 (m, 2H), 5.34 (dq, J_d = 10.1 Hz, J_q = 8.0 Hz, 1H), 2.08 (s, 3H); ^{13}C NMR (acetone-d_6, 100 MHz) δ 143.4, 138.5, 133.5, 133.0, 129.8, 129.3, 128.7, 128.6, 128.2, 127.8, 127.0, 126.7, 125.2, 125.0 (q, J = 282 Hz), 59.5 (q, J = 32 Hz), 20.4; ^{19}F NMR (acetone-d_6, 282 MHz) δ -74.5 (d, J = 8.2 Hz); ESI-MS 402 [M + Na^+].

4-Methyl-*N*-(2,2,2,-trifluoro-1-(naphtalen-1-yl)ethyl)benzenesulfonamide (3f). Following the general procedure (method A), the title compound was obtained as a white solid in 68% yield, after flash chromatography on silica gel (*n*-hexane/Et_2O 8:2-7:3). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.96 (d, J = 8.6 Hz, 1H), 7.81 (d, J = 8.2 Hz, 1H), 7.77 (d, J = 8.2 Hz, 1H), 7.56 (t, J = 7.5 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.46 (d, J = 8.6 Hz, 2H), 7.42 (d, J = 7.1 Hz, 1H), 7.32 (t, J = 7.7 Hz, 1H), 6.89 (d, J = 8.1 Hz, 2H), 5.87-5.82 (m, 2H), 2.21 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 143.8, 136.8, 133.8, 131.2, 130.1, 129.4, 128.5, 127.5, 127.1, 126.4, 125.6, 125.2, 124.4 (q, J = 280 Hz), 122.3, 54.1 (q, J = 32 Hz), 21.5; ^{19}F NMR ($CDCl_3$, 282 MHz) δ -73.5 (br s); ESI-MS 402 [M + Na^+].

4-Methyl-*N*-(2,2,2-trifluoro-1-(thiophen-2-yl)ethyl)benzenesulfonamide (3g). Following the general procedure (method A), the title compound was obtained as a white solid in 85% yield, after flash chromatography on silica gel (*n*-hexane/Et_2O 8:2-7:3). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.69-7.64 (m, 2H), 7.25 (dd, J = 5.1, 1.2 Hz, 1H), 7.24-7.20 (m, 2H), 6.97 (br d, J = 3.7 Hz, 1H), 6.90 (dd, J = 5.0, 3.2 Hz, 1H), 5.50 (d, J = 8.8 Hz, 1H), 5.23 (dq, J_d = 9.2 Hz, J_q = 7.0 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.2, 137.2, 134.0, 129.8, 128.2, 127.4, 127.3, 123.7 (q, J = 282 Hz), 55.3 (q, J = 33 Hz), 21.8; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -75.1 (d, J = 7.2 Hz); ESI-MS 358 [M + Na^+].

***N*-(1-Cyclohexyl-2,2,2-trifluoroethyl)-4-methylbenzenesulfonamide (3h).** Following the general procedure (method B), the title compound was obtained as a white solid in 91% yield, after chromatography on silica gel (*n*-hexane/EtOAc 9:1-85:15). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.76-7.61 (m, 2H), 7.31-7.26 (m, 2H), 5.11 (d, J = 10.2 Hz, 1H), 3.85-3.74 (m, 1H), 2.41 (s, 3H), 1.82-1.70 (m, 4H), 1.70-1.58 (m, 2H), 1.31-0.97 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.8, 138.2, 129.8, 127.1, 125.1 (q, J = 283 Hz), 59.8 (q, J = 29 Hz), 37.8, 30.1, 27.1, 26.2, 26.0, 25.9, 21.7; ^{19}F NMR ($CDCl_3$, 282 MHz) δ -71.7 (d, J = 8.4 Hz); ESI-MS 358 [M + Na^+].

4-Methyl-*N*-(1,1,1-trifluoro-3-methylbutan-2-yl)benzenesulfonamide (3i). Following the general procedure (method B), the title compound was obtained as a white solid in 76% yield, after chromatography on silica gel (*n*-hexane/EtOAc 85:15-8:2). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.77-7.72 (m, 2H), 7.31-7.26 (m, 2H), 5.14 (d, J = 9.9 Hz, 1H), 3.83 (ddq, J_d = 10.1, 3.8 Hz, J_q = 8.0 Hz, 1H), 2.42 (s, 3H), 2.13 (dsept, J_d = 4.1 Hz, J_{sept} = 6.9 Hz, 1H), 0.98 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.9, 138.2, 129.8, 127.1, 125.2 (q, J = 284 Hz), 59.8 (q, J = 29 Hz), 28.0, 21.8, 20.0, 16.7; ^{19}F NMR ($CDCl_3$, 282 MHz) δ -72.4 (d, J = 8.3 Hz); ESI-MS 318 [M + Na^+].

4-Methyl-*N*-(1,1,1-trifluoro-4-phenylbutan-2-yl)benzenesulfonamide (3j). Following the general procedure (method B), the title compound was obtained as a colourless thick oil in 59% yield, after chromatography on silica gel (*n*-hexane/EtOAc 9:1-8:2). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.78-7.74 (m, 2H), 7.32-7.25 (m, 4H), 7.24-7.19 (m, 1H), 7.15-7.10 (m, 2H), 5.16 (d, J = 9.9 Hz, 1H), 4.00-3.88 (m, 1H), 2.83-2.70 (m, 1H), 2.62 (ddd, J = 14.1, 9.9, 6.6 Hz, 1H), 2.42 (s, 3H), 2.13-2.03 (m, 1H), 1.85-1.73 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ

144.1, 140.1, 137.9, 129.9, 128.8, 128.6, 127.2, 126.6, 124.9 (q, J = 282 Hz), 55.2 (q, J = 31 Hz), 34.5, 31.2, 21.8; ^{19}F NMR ($CDCl_3$, 282 MHz) δ -75.8 (d, J = 7.3 Hz); ESI-MS 380 [M + Na^+].

The same reaction, performed in the absence of TBAB catalyst, gave the product **3j** in 15% yield, as determined by ^{1}H NMR spectroscopy using dibenzyl as internal standard, thus showing that solid PhONa is not able to promote efficiently the reaction, in the absence of TBAB catalyst. Extensive decomposition of the starting material was also observed.

4-Methyl-*N*-(1,1,1-trifluoropentan-2-yl)benzenesulfonamide (3k). Following the general procedure (method B), the title compound was obtained as a white solid in 78% yield, after chromatography on silica gel (*n*-hexane/EtOAc 9:1-85:15). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.76-7.72 (m, 2H), 7.31-7.26 (m, 2H), 4.97 (d, J = 9.8 Hz, 1H), 3.95-3.83 (m, 1H), 2.42 (s, 3H), 1.75-1.64 (m, 1H), 1.56-1.42 (m, 2H), 1.38-1.24 (m, 1H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.0, 138.0, 129.8, 127.1, 125.0 (q, J = 283 Hz), 55.2 (q, J = 30 Hz), 31.3, 21.8, 18.3, 13.6; ^{19}F NMR ($CDCl_3$, 282 MHz) δ -76.1 (d, J = 7.3 Hz); ESI-MS: 318 [M + Na^+].

4-Methoxy-*N*-(2,2,2-trifluoro-1-phenylethyl)benzenesulfonamide (3l). Following the general procedure (method A), the title compound was obtained as a white solid in 90% yield, after chromatography on silica gel (*n*-hexane/EtOAc 8:2-75:25). ^{1}H NMR (acetone-d_6, 400 MHz) δ 7.82 (br d, J = 9.7 Hz, 1H), 7.66-7.60 (m, 2H), 7.45-7.39 (m, 2H), 7.31-7.24 (m, 3H), 6.90-6.84 (m, 2H), 5.16 (dq, J_d = 10.1 Hz, J_q = 7.9 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (acetone-d_6, 100 MHz) δ 163.0, 130.1, 132.8, 129.1, 128.7, 128.5, 124.8 (q, J = 280 Hz), 114.1, 59.2 (q, J = 32 Hz), 55.4; ^{19}F NMR (acetone-d_6, 282 MHz) δ -74.9 (d, J = 7.7 Hz); ESI-MS 368 [M + Na^+].

***N*-(1-Cyclohexyl-2,2,2-trifluoroethyl)-4-methoxybenzenesulfonamide (3m).** Following the general procedure (method B but performing the reaction at -30 °C), the title compound was obtained as a white solid in 39% yield, after chromatography on silica gel (*n*-hexane/EtOAc 85:15-8:2). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.82-7.75 (m, 2H), 6.99-6.92 (m, 2H), 4.85 (d, J = 9.8 Hz, 1H), 3.86 (s, 3H), 3.84-3.74 (m, 1H), 1.81-1.58 (m, 6H), 1.32-0.97 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.2, 132.8, 129.3, 125.2 (q, J = 285 Hz), 114.3, 59.7 (q, J = 30 Hz), 55.8, 37.8, 30.1, 27.1, 26.2, 26.0, 25.9; ^{19}F NMR ($CDCl_3$, 282 MHz) δ -71.8 (d, J = 8.3 Hz); ESI-MS 374 [M + Na^+].

2,4,6-Trimethyl-*N*-(2,2,2-trifluoro-1-phenylethyl)benzene sulfonamide (3n). Following the general procedure (method A), the title compound was obtained as a white solid in 81% yield, after chromatography on silica gel (*n*-hexane/EtOAc 9:1-85:15). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34-7.22 (m, 3H), 7.21-7.17 (br d, J = 7.4 Hz, 2H), 6.85 (br s, 2H), 5.56 (d, J = 8.3 Hz, 1H), 4.78 (quint, J = 7.9 Hz, 1H), 2.55 (s, 6H), 2.26 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.9, 139.2, 133.9, 132.2, 132.1, 129.6, 129.0, 128.0, 124.2 (q, J = 279 Hz), 59.3 (q, J = 30 Hz), 23.0, 21.1; ^{19}F NMR ($CDCl_3$, 282 MHz) δ -74.1 (d, J = 7.5 Hz); ESI-MS 380 [M + Na^+].

***N*-(1-Cyclohexyl-2,2,2-trifluoroethyl)-2,4,6-trimethylbenzenesulfonamide (3o).** Following the general procedure (method B, but performing the reaction at -30 °C), the title compound was obtained as a white solid in 75% yield, after chromatography on silica gel (*n*-hexane/EtOAc 95:5-9:1). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.93 (s, 2H), 4.88 (d, J = 10.0 Hz, 1H), 3.76-3.64 (m, 1H), 2.61 (s, 6H), 2.29 (s, 3H), 1.83-1.58 (m, 6H), 1.35-1.02 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.4, 138.6, 135.8, 132.1, 125.3 (q, J = 284 Hz), 59.6 (q, J = 30 Hz), 37.9, 30.0, 27.2, 26.2, 26.0, 25.9, 23.1, 21.1; ^{19}F NMR ($CDCl_3$, 282 MHz) δ -72.0 (d, J = 8.0 Hz); ESI-MS 386 [M + Na^+].

***P,P*-Diphenyl-*N*-(2,2,2-trifluoro-1-phenylethyl)phosphinic amide (3p).** Following the general procedure (method A), the title compound was obtained as a white solid in 71% yield, after chromatography on silica gel (CH_2Cl_2/acetone 9:1-85:15). ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.77-7.69 (m, 2H), 7.63-7.43 (m, 8H), 7.41-7.31 (m, 5H), 6.79 (t, J = 12.0 Hz, 1H), 4.86 (dq, J_d = 11.6 Hz, J_q = 8.2 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 135.7 (d, J = 2 Hz), 134.0 (d, J = 126 Hz), 133.8 (d, J = 126 Hz), 132.4 (d, J = 2 Hz), 132.3 (d, J = 2 Hz), 132.1 (d, J = 10 Hz), 132.0 (d, J = 10 Hz), 129.2 (d, J = 13 Hz), 129.0, 128.9 (d, J = 13 Hz), 128.9, 125.9 (dq, J_q = 283 Hz, J_d = 7 Hz), 56.2 (q, J = 30 Hz); ^{19}F NMR (DMSO-d_6, 282 MHz) δ -73.2 (d, J = 8.1 Hz); ESI-MS 398 [M + Na^+].

The same reaction, performed using 0.10 equiv. of PhONa, gave **3p** in 6% yield, as determined by ^{1}H NMR spectroscopy using dibenzyl as internal standard, thus showing that the amide adduct formed upon initiation is not able to promote subsequent additions to a considerable extent.

The same reaction, performed in the absence of TBAB catalyst, gave **3p** in trace amounts, as determined by ^{1}H NMR spectroscopy, thus showing that solid PhONa alone is not able to promote the reaction. Extensive imine decomposition was also observed.

***N*-(1-Cyclohexyl-2,2,2-trifluoroethyl)-*P*,*P*-diphenylphosphinic amide (3q).** Following the general procedure (method B, but perfoming the reaction at -30 °C), the title compound was obtained as a white solid in 51% yield, after chromatography on silica gel (CH_2Cl_2/acetone 9:1-85:15). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.93-7.82 (m, 4H), 7.58-7.40 (m, 6H), 3.50-3.32 (m, 1H), 3.10 (dd, J = 12.0, 7.9 Hz, 1H), 1.95-1.46 (m, 7H), 1.35-1.06 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 132.9 (d, J = 10 Hz), 132.7 (d, J = 139 Hz), 132.5 (d, J = 3 Hz), 132.4 (d, J = 3 Hz), 132.2 (d, J = 10 Hz), 128.8 (d, J = 13 Hz), 128.6 (d, J = 13 Hz), 126.2 (dq, J_q = 283 Hz, J_d = 8 Hz), 58.0 (q, J = 28 Hz), 38.6, 30.2, 27.2, 26.5, 26.2, 26.0; ^{19}F NMR ($CDCl_3$, 282 MHz) δ -72.2 (d, J = 8.2 Hz); ESI-MS 404 [M + Na^+].

Benzyl 2,2,2-trifluoro-1-phenylethylcarbamate (3r). Following the general procedure (method B, but performing the reaction from 0 °C to RT), the title compound was obtained as a white solid in 75% yield, after chromatography on silica gel (*n*-hexane/EtOAc 9:1). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45-7.31 (m, 10H), 5.52 (br d, J = 8.6 Hz, 1H), 5.40 (br quint, J = 7.4 Hz, 1H), 5.17 (d, J = 12.6 Hz, 1H), 5.13 (d, J = 12.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 155.7, 135.9, 133.0, 129.6, 129.2, 128.9, 128.7, 128.5, 127.9, 124.8 (q, J = 285 Hz), 68.0, 56.9 (q, J = 33 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz) δ -74.1 (d, J = 7.6 Hz); ESI-MS 332 [M + Na^+].

Benzyl 1-cyclohexyl-2,2,2-trifluoroethylcarbamate (3s). Following the general procedure (method B, but performing the reaction at 0 °C), the title compound was obtained as a white solid in 53% yield, after chromatography on silica gel (*n*-hexane/EtOAc 95:5-9:1). ^{1}H NMR ($CDCl_3$, 300 MHz) δ [some signals show multiple resonances due to the presence of slowly intercorverting rotamers] 7.41-7.31 (m, 5H), 5.17 (d, J = 12.2 Hz, 1H), 5.13 (d, J = 12.2 Hz, 1H), 4.93 (d, J = 10.9 Hz, 0.85H), 4.73 (d, J = 10.4 Hz, 0.15H), 4.27-4.11 (m, 0.85H), 4.06 (br s, 0.15H), 1.87-1.57 (m, 6H), 1.39-0.91 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.3, 136.1, 128.8, 128.6, 128.4, 125.6 (q, J = 282 Hz), 67.7, 57.2 (q, J = 29 Hz), 37.5, 30.1, 29.9, 27.3, 26.2, 25.9; ^{19}F NMR ($CDCl_3$, 282 MHz) δ [the signal shows multiple resonances due to the presence of slowly intercorverting rotamers] -72.7 (d, J = 8.3 Hz, 2.55F), -72.9 (d, J = 7.5 Hz, 0.45F); ESI-MS 338 [M + Na^+].

Experimental results from the extension of the phase-transfer of phenoxides to other silicon nucleophiles.

***N*-(2,2,3,3,4,4,4-Heptafluoro-1-phenylbutyl)-4-methylbenzenesulfonamide (3t).** Following the general procedure of the trifluoromethylation reaction (method A, but with trimethylsilylheptafluoro-*n*-propyl as the nucleophile, 20 mol% TBAB catalyst and perfoming the reaction at -30 °C), the title compound was obtained as a white solid in 76% yield, after chromatography on silica gel (*n*-hexane/EtOAc 85:15). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54-7.49 (m, 2H), 7.27-7.17 (m, 3H), 7.13-7.02 (m, 4H), 5.80 (d, J = 9.9 Hz, 1H), 5.06 (dt, J_d = 15.8 Hz, J_t = 10.9 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.9, 137.1, 131.6, 129.6, 129.4, 128.9, 128.4, 127.2, 114.9 (tt, J = 258, 32 Hz), 116.5 (tq, J_q = 288 Hz, J_t = 34 Hz), 109.2 (tsext, J_t = 266 Hz, J_{sext} = 39 Hz), 58.0 (dd, J = 26, 22 Hz), 21.6; ^{19}F NMR ($CDCl_3$, 282 MHz) δ -81.1 (t, J = 11.6 Hz, 3F), -117.1 (dsext, J_d = 279 Hz, J_{sext} = 11.0 Hz, 1F), -119.6 (br d, J = 281.6 Hz, 1F), -124.8 (br t, J = 5.9 Hz, 2F); ESI-MS 452 [M + Na^+].

4-Methyl-*N*-((perfluorophenyl)(phenyl)methyl)benzenesulfonamide (3u). Following the general procedure of the trifluoromethylation reaction (method A, but with trimethylsilylpentafluorobenzene as the nucleophile, and using 20 mol% TBAB catalyst), the title compound was obtained as a white solid in 82% yield, after chromatography on silica gel (*n*-hexane/EtOAc 85:15). ^{1}H NMR (acetone-d_6, 400 MHz) δ 7.71-7.73 (m, 3H), 7.37-7.26 (m, 7H), 6.07 (d, J = 9.4 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (acetone-d_6, 100 MHz) δ 143.6, 144.3 (br d, J = 248 Hz), 141.0 (br d, J = 248 Hz), 138.8, 137.7 (br dt, J_d = 251 Hz, J_t = 15 Hz), 137.6, 129.5, 129.0, 128.4, 127.0, 126.6, 114.9 (t, J = 17 Hz), 51.6, 20.6; ^{19}F NMR (acetone-d_6, 282 MHz) δ -143.2- -143.5 (m, 2F), -157.8 (t, J = 20.8 Hz, 1F), -164.5 (dd, J = 21.9, 8.2 Hz, 1F), -164.6 (dd, J = 21.9, 7.7 Hz, 1F); ESI-MS 427 [M + Na^+].

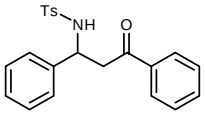
***N*-(2-Cyano-1-phenylethyl)-4-methylbenzenesulfonamide (3v).** Following the general procedure of the trifluoromethylation reaction (method A, but using trimethylsilylacetonitrile as the nucleophile and performing the reaction at 0 °C), the title compound was obtained as a white solid in 87% yield, after chromatography on silica gel (*n*-hexane/EtOAc 7:3-6:4). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.68-7.62 (m, 2H), 7.28-7.19 (m, 5H), 7.14-7.09 (m, 2H), 5.66 (d, J = 7.3 Hz, 1H), 4.57 (br q, J = 7.3 Hz, 1H), 2.92 (dd, J = 16.6, 5.7 Hz, 1H), 2.87 (dd, J =

17.0, 7.4 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.2, 137.4, 136.8, 130.0, 129.3, 129.1, 127.3, 126.5, 116.8, 54.5, 26.6, 21.7; ESI-MS 323 [M + Na^+].

The same reaction, performed using 0.10 equiv. of PhONa, gave **3v** in 12% yield, as determined by ^{1}H NMR spectroscopy using dibenzyl as internal standard, thus showing that the amide adduct formed upon initiation is not able to promote subsequent additions to a considerable extent.

The same reaction, performed in the absence of TBAB catalyst, gave **3v** in 32% yield, as determined by ^{1}H NMR spectroscopy using dibenzyl as internal standard, thus showing that solid PhONa alone is not able to promote the reaction as efficiently as in the presence of TBAB catalyst. Extensive imine decomposition was also observed.

4-Methyl-*N*-(3-oxo-1,3-diphenylpropyl)benzenesulfonamide (3w). Following the general procedure of the trifluoromethylation reaction (method A, but using 1-phenyl-1-trimethylsiloxyethylene as the nucleophile, 140 mg MS 5 Å and performing the reaction at -30 °C), the title compound was obtained as a white solid in 91% yield, after chromatography on silica gel (*n*-hexane/EtOAc 8:2-7:3). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.81-7.77 (m, 2H), 7.64-7.59 (m, 2H), 7.53 (dt, J_d = 7.4 Hz, J_t = 1.3 Hz, 1H), 7.42-7.37 (m, 2H), 7.19-7.11 (m, 7H), 5.91 (d, J = 7.0 Hz, 1H), 4.88 (q, J = 6.2 Hz, 1H), 3.56 (dd, J = 17.2, 5.7 Hz, 1H), 3.44 (dd, J = 17.2, 6.4 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 197.9, 143.4, 140.2, 137.5, 136.5, 133.8, 129.7, 128.9, 128.7, 128.3, 127.8, 127.4, 127.0, 54.6, 45.1, 21.7; ESI-MS 402 [M + Na^+].

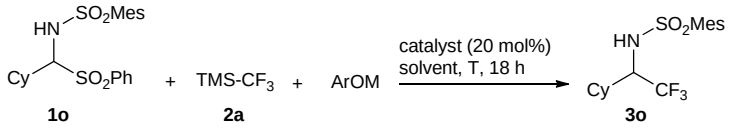


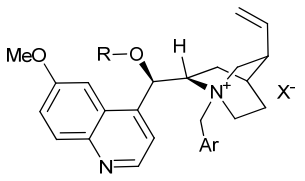
The same reaction, performed using 0.10 equiv. of PhONa, gave **3w** in 7% yield, as determined by ^{1}H NMR spectroscopy using dibenzyl as internal standard, thus showing that the amide adduct formed upon initiation is not able to promote subsequent additions to a considerable extent.

The same reaction, performed in the absence of TBAB catalyst, gave **3w** in trace amounts, as determined by ^{1}H NMR spectroscopy, thus showing that solid PhONa alone is not able to promote the reaction, if the anion is not transferred in the toluene phase by the catalyst.

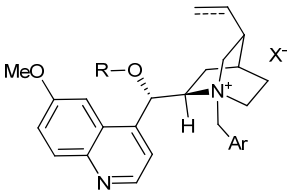
Selected experimental results from the extension of the phase-transfer of phenoxides to the use of chiral, enantiopure catalysts.

Table S2. Representative results from the screening of different chiral catalysts and reaction conditions in the trifluoromethylation reaction of **1o**.[a]

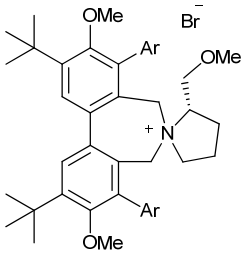




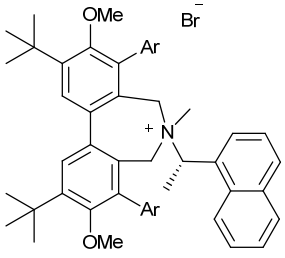
QN-1: Ar = 2-$NO_2C_6H_4$, R = CO*t*-Bu
QN-2: Ar = 9-anthracenyl, R = CO*t*-Bu



QD-1: Ar = 2-$NO_2C_6H_4$, R = CO*t*-Bu
QD-2: Ar = Ph, R = CO*t*-Bu
QD-3: Ar = 2-$NO_2C_6H_4$, R = Allyl
QD-4: Ar = 2-$NO_2C_6H_4$, R = H
QD-5: Ar = 3,5-$(CF_3)_2C_6H_3$, R = CO*t*-Bu
QD-6: Ar = 2,3,4-$F_3C_6H_2$, R = CO*t*-Bu
QD-7: Ar = 2,6-$F_2C_6H_3$, R = CO*t*-Bu
QD-8: Ar = 2-$NO_2C_6H_4$, R = COPh
QD-9: Ar = 2-$NO_2C_6H_4$, R = 1-adamantoyl
QD-10: Ar = 2-NCC_6H_4, R = CO*t*-Bu
QD-11: Ar = 2-FC_6H_4, R = CO*t*-Bu
QD-12: Ar = 2-$MeOC_6H_4$, R = CO*t*-Bu
QD-13: Ar = 2-pyridyl-N-oxide, R = CO*t*-Bu
QD-14: Ar = 2-$CF_3C_6H_4$, R = CO*t*-Bu
QD-15: Ar = 2-NO_2-4,5-$(MeO)_2C_6H_2$, R = CO*t*-Bu
DHQD-16 (4): Ar = 2-NO_2-4,5-$(MeO)_2C_6H_2$, R = CO*t*-Bu



LY-1: Ar = 3,5-$(CF_3)_2C_6H_3$
LY-2: Ar = 1-naphthyl



LY-3: Ar = 3,5-$(CF_3)_2C_6H_3$
LY-4: Ar = 1-naphthyl

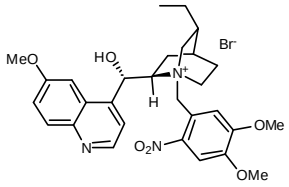
cat.	solvent (M)	T (°C)	ArOM	ee[b] (%)
QD-1	Toluene (0.05)	-20, 30 min then 0	PhONa	30
QD-1	Toluene (0.05)	-20, 30 min then 0	2-naphtholateNa	26
QD-1	Toluene (0.05)	-20, 30 min then 0	2,4,6-$Me_3C_6H_2ONa$	24
QD-1	Toluene (0.05)	-20, 30 min then 0	4-$MeOC_6H_4ONa$	30
QD-1	Toluene (0.05)	-20, 30 min then 0	4-MeC_6H_4ONa	30
QD-1	Toluene (0.05)	-20, 30 min then 0	3,5-$Me_2C_6H_3ONa$	29
QD-1	Toluene (0.05)	-20, 30 min then 0	2,5-$Me_2C_6H_3ONa$	31
QD-1	Toluene (0.05)	-20, 30 min then 0	2,4-$Me_2C_6H_3ONa$	32
QD-1	Toluene (0.05)	-20, 30 min then 0	4-PhC_6H_4ONa	29
QD-1	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	34
QD-1	Toluene/DCM 1:1 (0.05)	-20, 30 min then 0	PhONa	27
QD-1	DCM (0.05)	-20, 30 min then 0	PhONa	20
QD-1	Toluene/DCM/TBME 1:1:1 (0.05)	-20, 30 min then 0	PhONa	30
LY-1	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	3
LY-2	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	0

cat.	solvent (M)	T (°C)	ArOM	ee[b] (%)
LY-3	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	2
LY-4	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	0
QD-1	Toluene/DCM 5:1 (0.05)	-78, 30 min then 0	PhONa	35
QD-2	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	23
QN-1	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	-25
QD-3	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	20
QD-4	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	10
QD-5	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	11
QD-6	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	30
QD-7	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	5
QN-2	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	0
QD-8	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	30
QD-9	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	30
QD-10	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	33
QD-11	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	27
QD-12	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	29
QD-13	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	15
QD-14	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	20
QD-15	Toluene/DCM 5:1 (0.05)	-20, 30 min then 0	PhONa	46
QD-15	Toluene/DCM 5:1 (0.05)	-20	PhONa	48
QD-15	Toluene (0.05)	-20	PhONa	48
QD-15	Toluene/DCM 5:1 (0.10)	-20	PhONa	40
QD-15	Toluene/DCM 5:1 (0.025)	-20	PhONa	50
QD-15	Toluene/DCM 5:1 (0.025)	-35	PhONa	56
QD-15	Toluene/DCM 5:1 (0.025)	-45	PhONa	58
DHQD-16[c]	Toluene/DCM 5:1 (0.025)	-45	PhONa	61

[a] Conditions: **1o** (0.05 mmol), **2a** (ca 2 M in THF, 0.20 mmol, 4 equiv.), catalyst (0.01 mmol, 20 mol%), solvent, ArONa (0.11 mmol, 2.2 equiv.), MS 5 Å. [b] Determined by chiral stationary phase HPLC. [c] 0.125 mmol of **2a** (2.5 equiv.) were used.

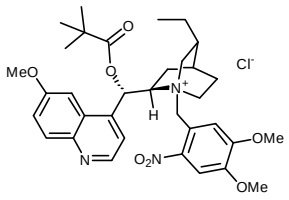
Preparation and characterisation of catalyst 4.[9]

N-4,5-dimethoxy-2-nitrobenzyl hydroquinidinium bromide.



To a stirred suspension of hydroquinidine (163 mg, 0.50 mmol) in toluene/THF 1:1 (2.0 mL), 4,5-dimethoxy-2-nitro-benzyl bromide (166 mg, 0.60 mmol) was added. The resulting mixture was then heated up to 70°C and stirred for 20 h at the same temperature. After cooling to r.t., the precipitate was collected by Bückner filtration and washed with tol/THF 1:1 (ca 10 ml) and several times with Et_2O, affording the title compound as a yellow solid in 75% yield. ^{1}H NMR (CD_3OD, 400 MHz) δ 8.80 (d, J = 5.0 Hz, 1H), 8.03 (d, J = 9.9 Hz, 1H), 7.96 (d, J = 5.1 Hz, 1H), 7.87 (s, 1H), 7.54 (dd, J = 9.4, 2.5 Hz, 1H), 7.49-7.46 (m, 2H), 6.63 (br s, 1H), 5.60 (d, J = 13.9 Hz, 1H), 5.48 (d, J = 12.1 Hz, 1H), 4.27-4.19 (m, 1H), 4.15 (s, 3H), 4.07 (s, 3H), 4.06-3.95 (m, 1H), 3.99 (s, 3H), 3.94-3.81 (m, 2H), 3.54 (br t, J = 9.7 Hz, 1H), 3.13 (br q, J = 9.7 Hz, 1H), 2.48 (br t, J = 10.4 Hz, 1H), 1.98-1.74 (m, 3H), 1.71-1.53 (m, 2H), 1.16-1.05 (m, 1H), 0.93 (t, J = 7.6 Hz, 3H); ^{13}C NMR (CD_3OD, 100 MHz) δ 159.2, 153.5, 151.1, 146.6, 145.3, 144.2, 143.0, 130.1, 126.4, 122.7, 120.5, 117.9, 115.6, 109.5, 101.2, 68.7, 67.8, 65.9, 59.1, 57.9, 56.5, 56.4, 55.9, 35.8, 25.3, 24.6, 24.3, 21.0, 10.4; $[\alpha]_D^{25}$ +225 (0.36 in CH_3OH); ESI-MS 522 [Q^+].

N-4,5-Dimethoxy-*O*-pivaloyl-2-nitrobenzyl hydroquinidinium chloride (4).



To a stirred suspension of *N*-4,5-dimethoxy-2-nitrobenzyl hydroquinidinium bromide (0.15 mmol) in CH_2Cl_2 (2.0 mL), were sequentially added pivaloyl chloride (0.75 mmol) and a 30% w/w NaOH solution (0.21 mL). After 30 min of vigorous stirring, H_2O and CH_2Cl_2 were added. The two layers were separated and the aqueous layer extracted with CH_2Cl_2, the combined extracted phases were dried over $MgSO_4$, filtered off and evaporated under reduced pressure. The crude product was dissolved in CH_2Cl_2 (ca 2 mL), poured onto Et_2O (20 mL) with stirring. The resulting precipitate was collected and washed several times with Et_2O, giving **4** as a yellow solid in 61% yield. ^{1}H NMR (CD_3OD, 400 MHz) δ 8.76 (d, J = 5.4 Hz, 1H), 8.04 (d, J = 9.4 Hz, 1H), 7.89 (s, 1H), 7.73 (d, J = 3.9 Hz, 1H), 7.56 (dd, J = 9.2, 2.7 Hz, 1H), 7.51-7.47 (m, 3H), 5.72 (d, J = 13.6 Hz, 1H), 5.00 (d, J = 13.1 Hz, 1H), 4.16 (br t, J = 10.1 Hz, 2H), 4.12 (s, 3H), 4.06 (s, 3H), 3.99 (s, 3H), 3.69-3.60 (m, 1H), 3.48-3.33 (m, 2H), 2.70 (br t, J = 12.6 Hz, 1H), 2.08-2.00 (m, 1H), 2.00-1.81 (m, 3H), 1.72-1.49 (m, 3H), 1.44 (s, 9H), 0.92 (t, J = 7.6 Hz, 3H); ^{13}C NMR (CD_3OD, 100 MHz) δ 176.6, 159.4, 153.7, 151.3, 146.7, 143.9, 143.7, 140.4, 130.8, 126.1, 122.2,

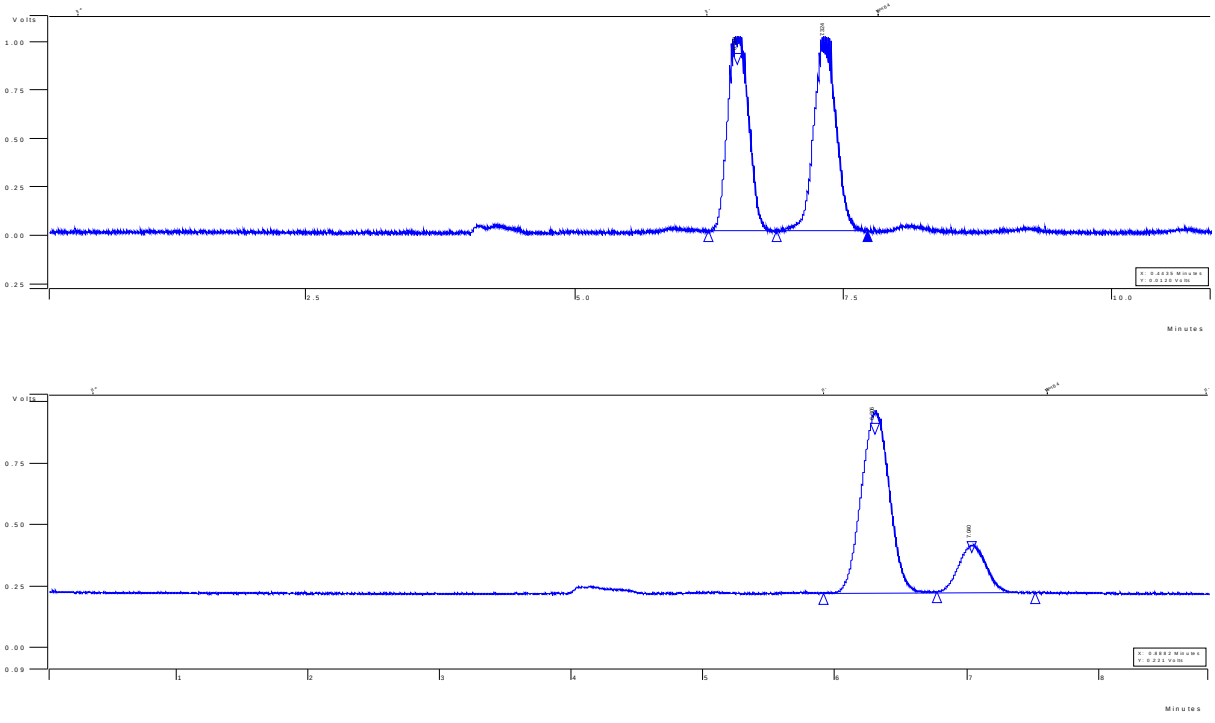
[9] Procedure adapted from: C. Gioia, F. Fini, A. Mazzanti, L. Bernardi and A. Ricci, *J. Am. Chem. Soc.*, 2009, **131**, 9614.

119.6, 117.8, 115.1, 109.6, 101.7, 67.6, 67.1, 59.4, 58.0, 57.2, 56.5, 55.9, 55.6, 39.1, 35.9, 26.4, 24.8, 24.3, 23.9, 22.3, 10.4; $[\alpha]_D^{25}$ +264 (0.26 in CH_3OH); ESI-MS 606 [Q^+].

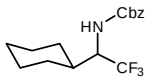
Catalytic enantioselective trifluoromethylation.

(+)-*N*-(1-Cyclohexyl-2,2,2-trifluoroethyl)-2,4,6-trimethylbenzenesulfonamide ((+)-3o). To a Schlenk tube equipped with a magnetic stirring bar MS 5 Å (powder, 60 mg) were added. The molecular sieves were activated by heating with a heat gun under vacuum for a few minutes. After cooling to RT under vacuum, the Schlenk tube was filled with N_2. α-Amido sulfone **1o** (0.10 mmol) and catalyst **4** (20 mol%) were added, the Schlenk tube evacuated with vacuum then backfilled with N_2. A toluene/CH_2Cl_2 mixture (5:1, 4.8 mL) was then added, and the resulting suspension was cooled to -45 °C with stirring. Trimethyl(trifluoromethyl)silane **2a** (commercial solution ca 2 M in THF, 125 µL, 0.25 mmol, 2.5 equiv.) was then added via syringe, followed by solid PhONa (26.0 mg, 0.22 mmol, 2.2 equiv.). The reaction mixture was vigorously stirred at the same temperature for 22 h. Sat. Na_2CO_3 was then added (ca 3 mL), the phases separated, and the aqueous phase extracted with EtOAc (3 x). The combined organic phases were filtered through a short pad of silica gel, the pad washed with EtOAc, then evaporated under vacuum, leaving a solid residue which was purified by chromatography on silica gel (*n*-hexane/EtOAc 95:5-9:1) giving the trifluoromethylated adduct (+)-**3o** in 59% yield. The enantiomeric excess of the product was determined by chiral stationary phase HPLC (Chiralpak AD-H column, *n*-hexane/*i*-PrOH 95:5, 0.75 mL/min, λ 215 nm, t_{maj} 5.8 min, t_{min} 6.7 min, 61% ee). $[\alpha]_D^{25}$ +17 (1.0 in CH_2Cl_2). Spectral data were identical to compound **3o**.

HPLC traces for racemic **3o** and **(+)-3o**:

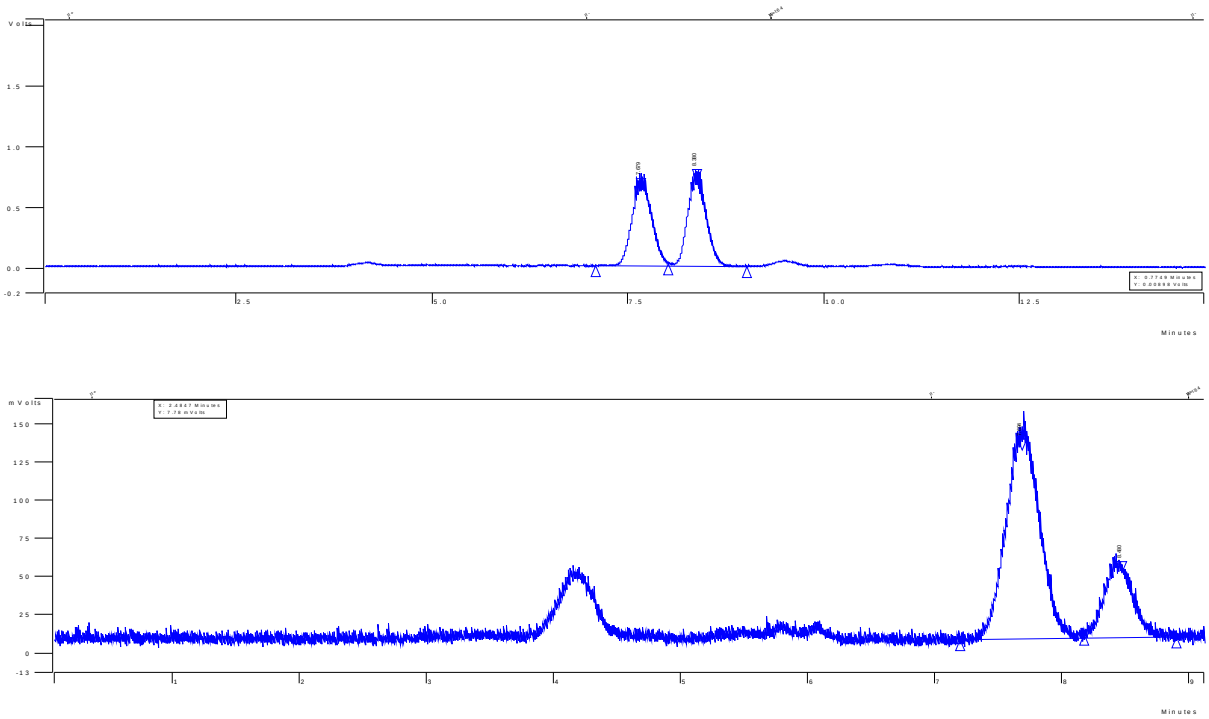


Deprotection of the mesitylenesulfonyl group in (+)-3o.[10]

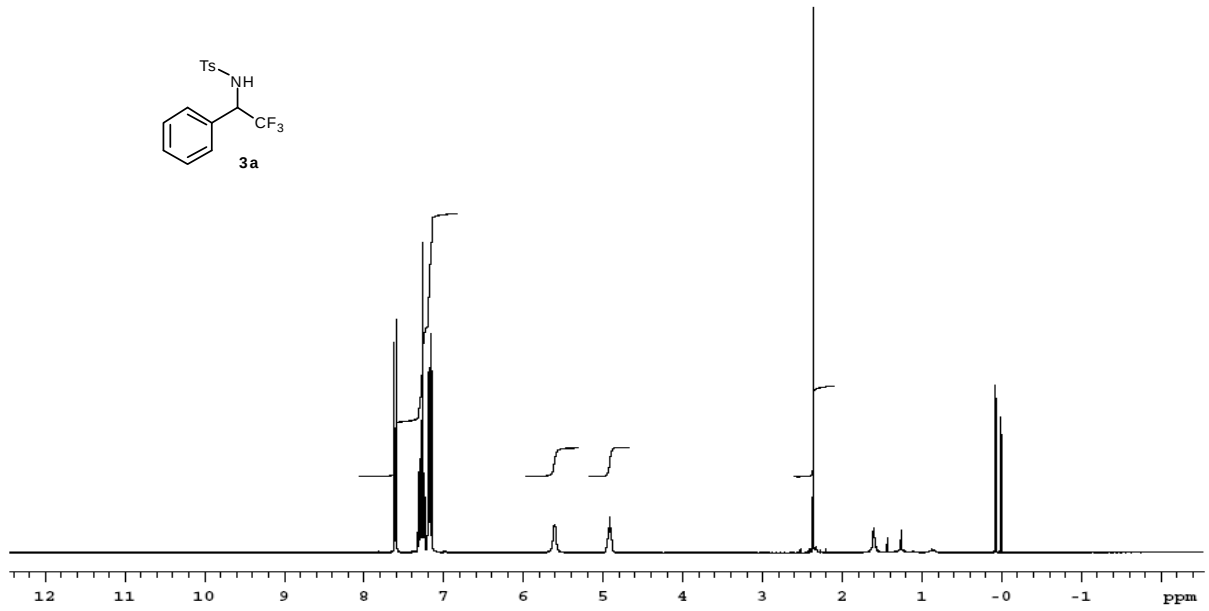


(-)-Benzyl 1-cyclohexyl-2,2,2-trifluoroethylcarbamate ((-)-3s). In a vial equipped with a magnetic stirring bar, a sample of compound **(+)-3o** (0.035 mmol) of 61% ee was dissolved in 87 μL of thioanisole (0.70 mmol), and 0.70 mL of trifluoroacetic acid. The resulting solution was cooled to 0 °C, then a 48% w/w aqueous HBr solution (79 μL, 0.70 mmol) was added. The brown solution was allowed to warm to room temperature, then stirred for 2 h. The volatiles were then removed under reduced pressure, leaving a residue which was dissolved in dioxane (1.0 mL). 50% w/w aqueous K_2CO_3 (200 μL), and CbzCl (9 μL, 0.05 mmol) were sequentially added, and the resulting biphasic mixture was stirred for 2 h at RT. The mixture was then poured onto water, and extracted with CH_2Cl_2 (3 x). The combined organic extracts were dried over $MgSO_4$, filtered and evaporated, leaving a residue which was purified by chromatography on silica gel (*n*-hexane/EtOAc 95:5-9:1), affording **(-)-3s** as a white solid in 72% yield. The enantiomeric excess of the product was determined by chiral stationary phase HPLC (Chiralpak AD-H column, *n*-hexane/*i*-PrOH 90:10, 0.75 mL/min, λ 215 nm, t_{maj} 7.7 min, t_{min} 8.4 min, 60% ee). $[\alpha]_D^{25}$ -18 (0.080 in CH_2Cl_2). Spectral data were identical to compound **3s**.

HPLC traces for racemic **3s** and **(-)-3s**:



[10] Deprotection procedure adapted from: (*a*) T. Ooi, Y. Uematsu and K. Maruoka, *J. Am. Chem. Soc.* 2006, **128**, 2548; (*b*) T. Akindele, K.-i. Yamada, T. Sejima, M. Maekawa, Y. Yamamoto, M. Nakano and K. Tomioka, *Chem. Pharm. Bull.* 2010, **58**, 265. Cbz-derivatisation adapted from: (*c*) S. Fustero, A. Navarro, B. Pina, J. García Soler, A. Bartolomé, A. Asensio, A. Simón, P. Bravo, G. Fronza, A. Volonterio and M. Zanda, *Org. Lett.* 2001, **3**, 2621.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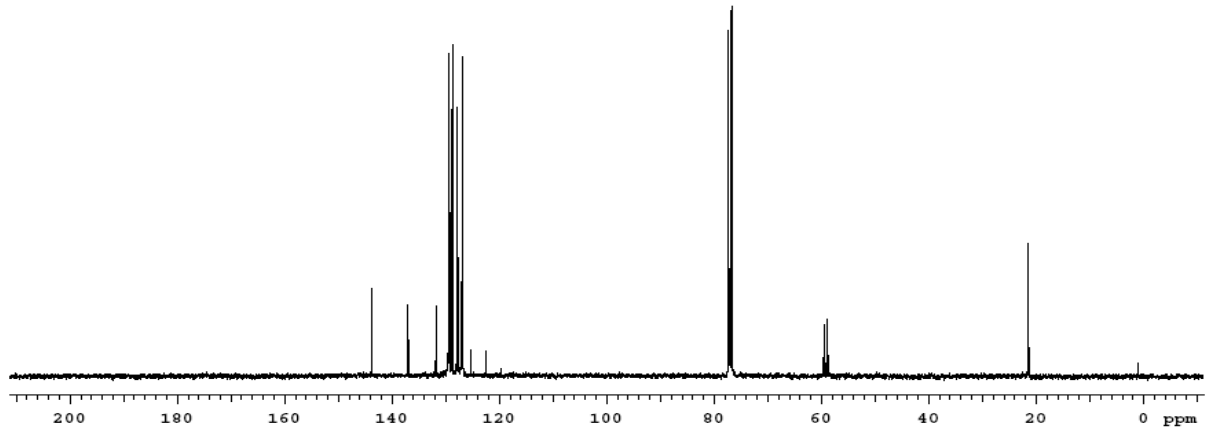
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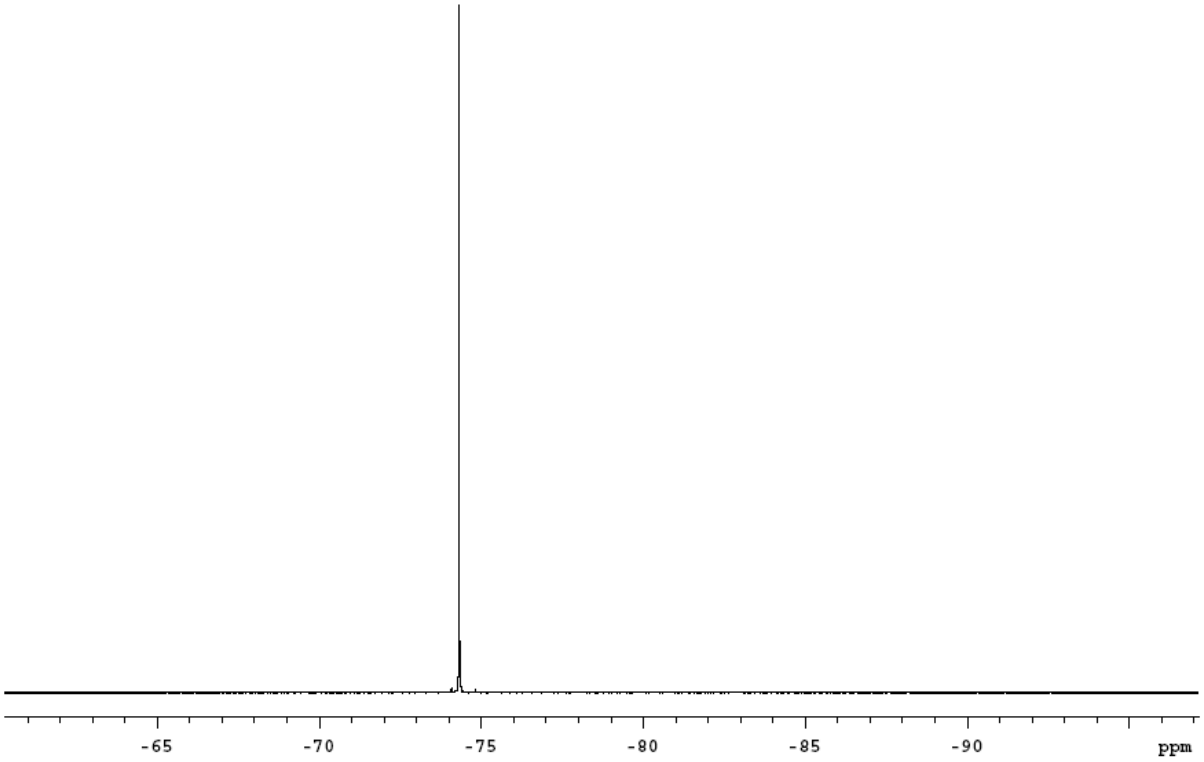
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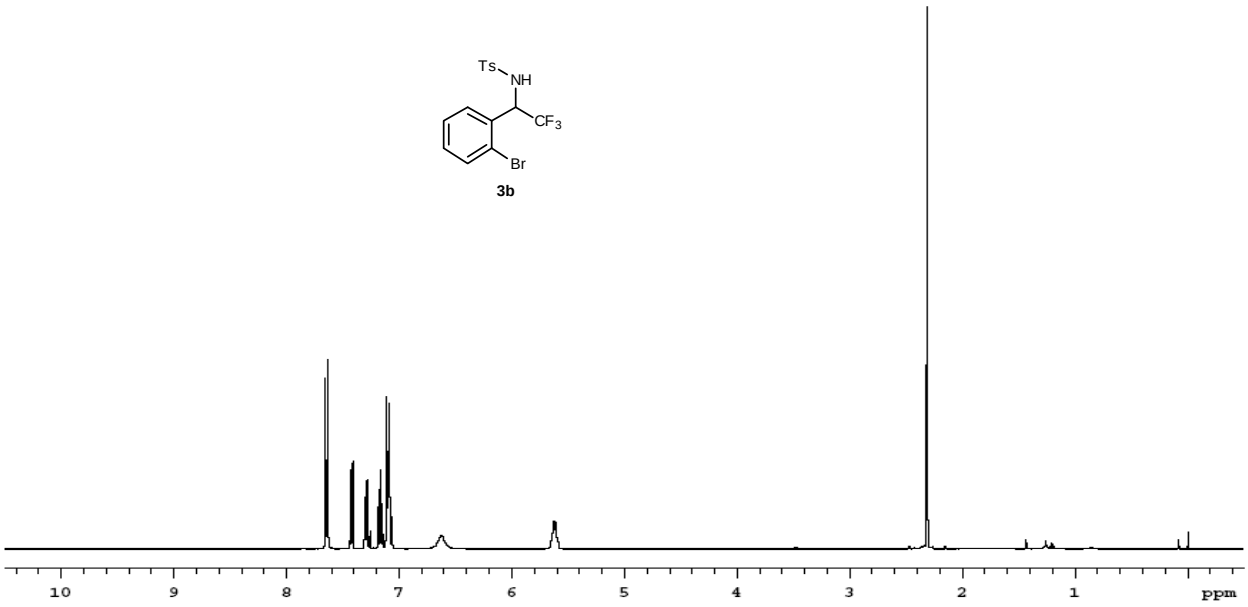
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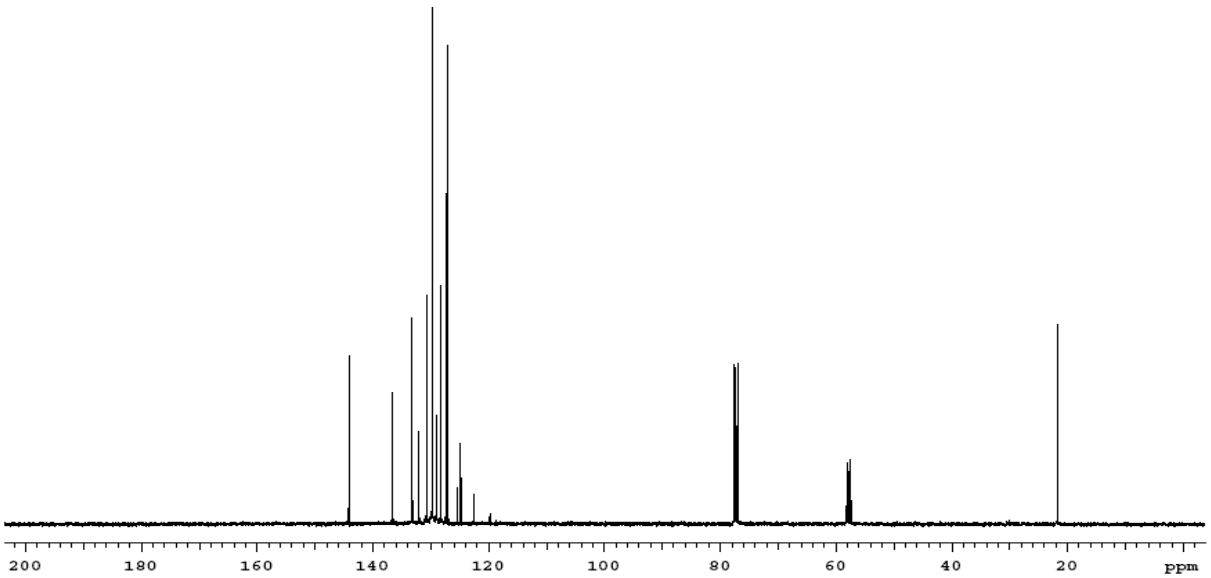
ppm

3b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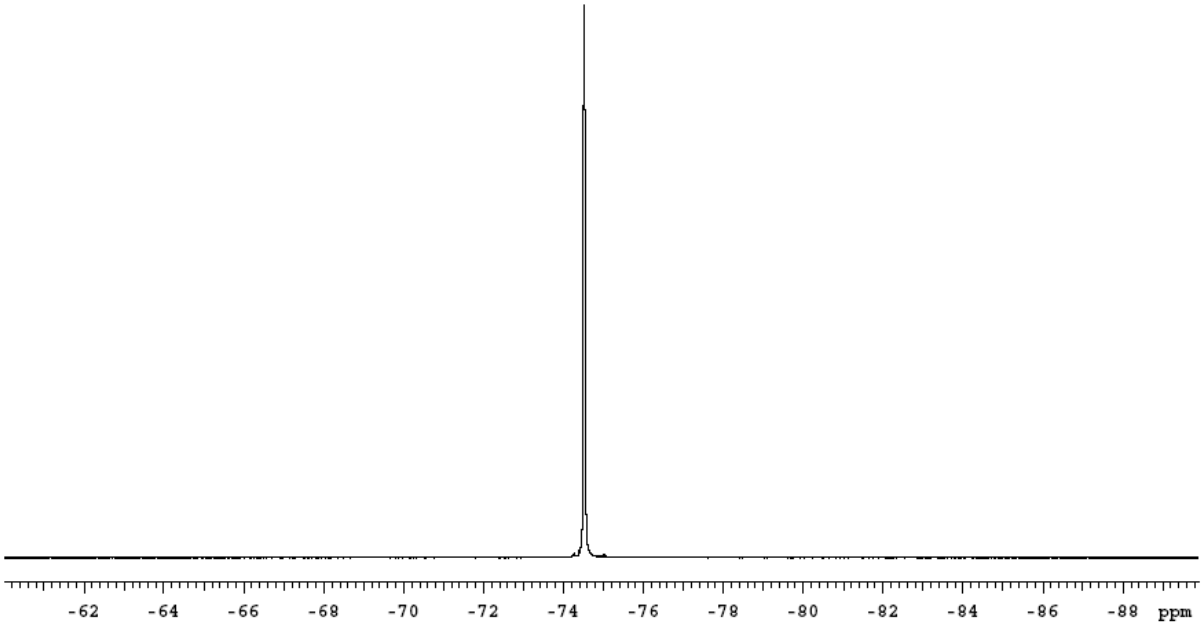
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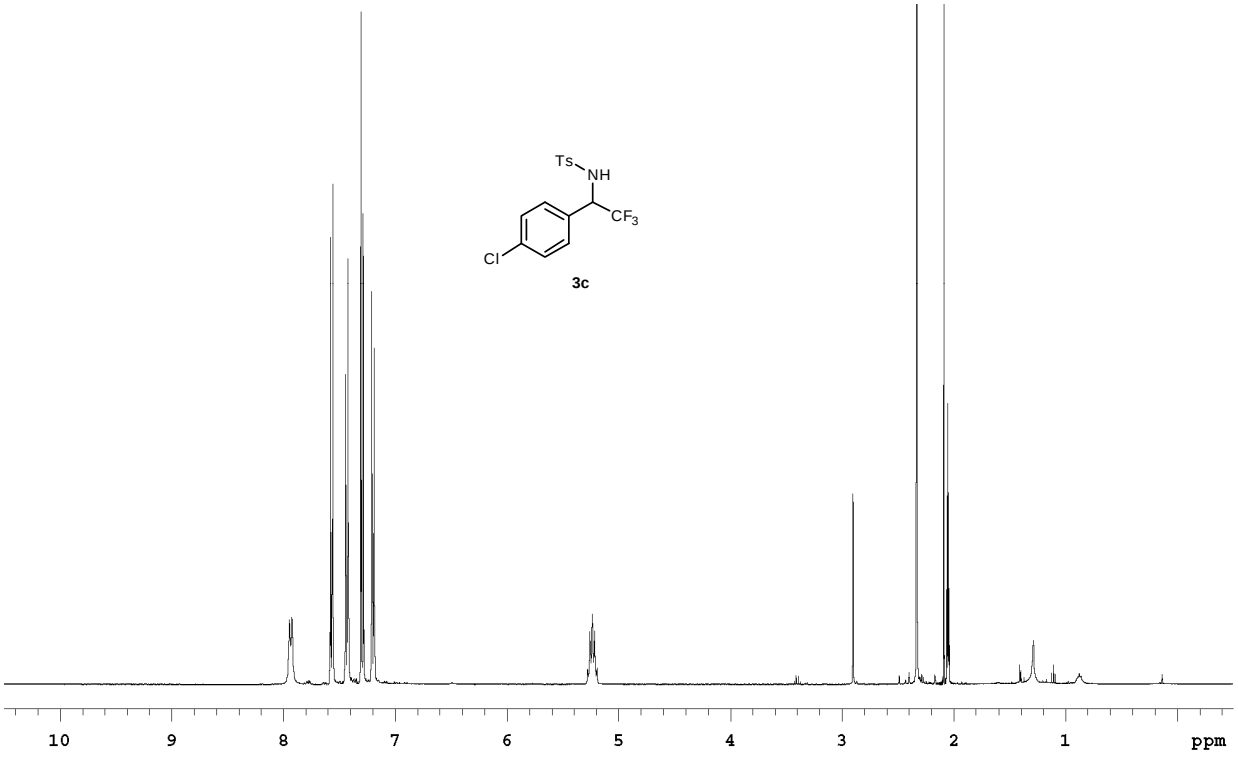
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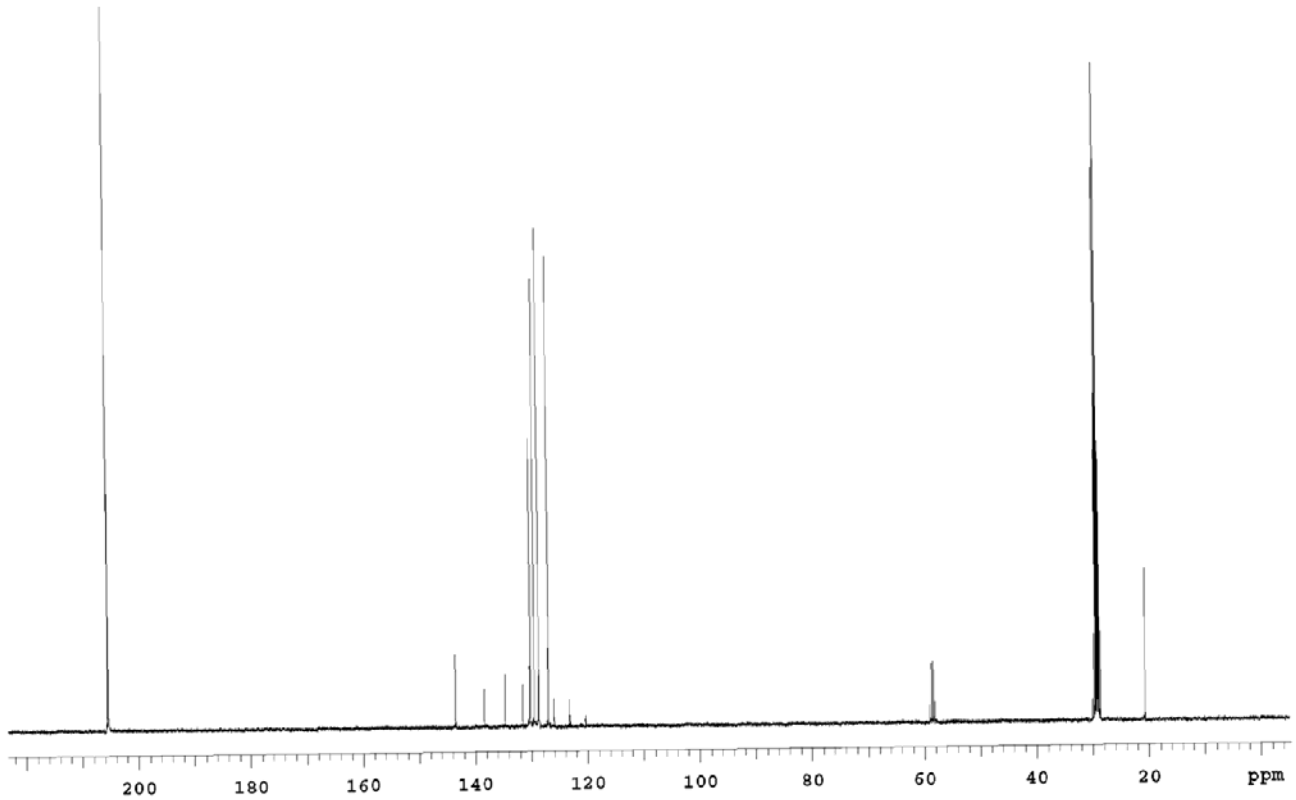
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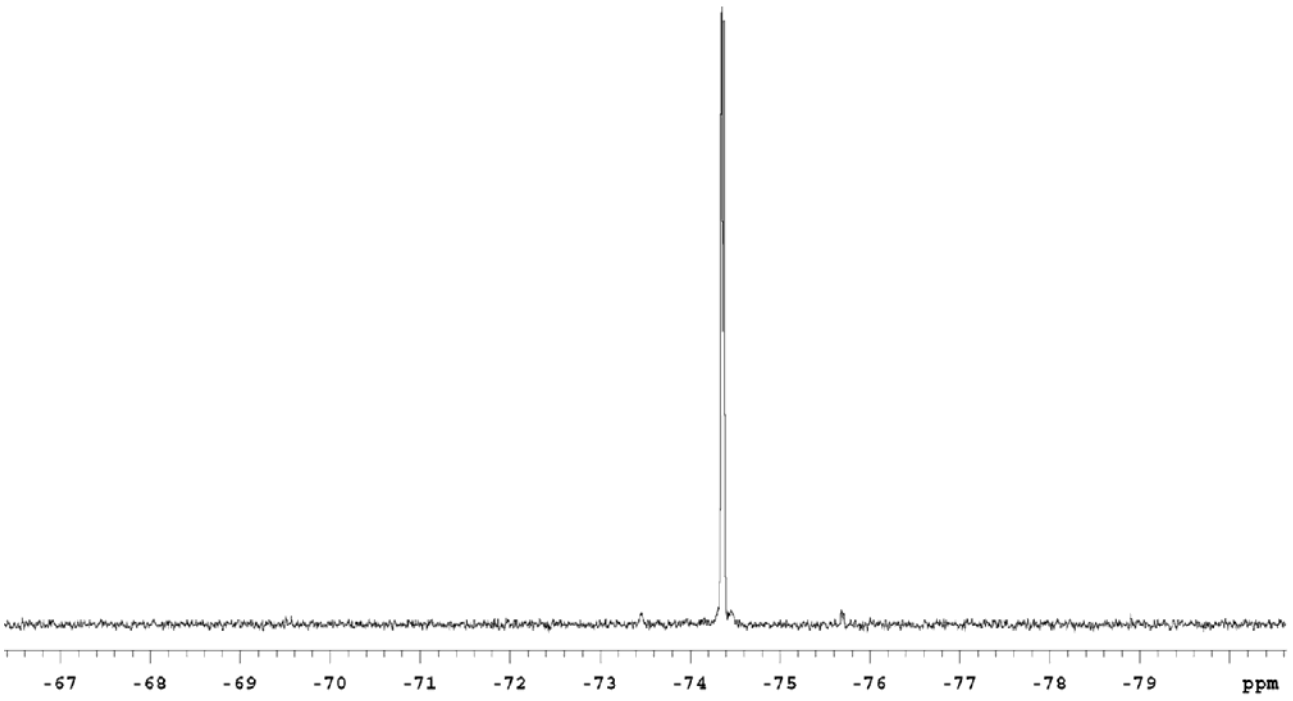
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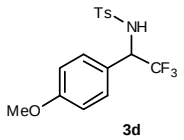
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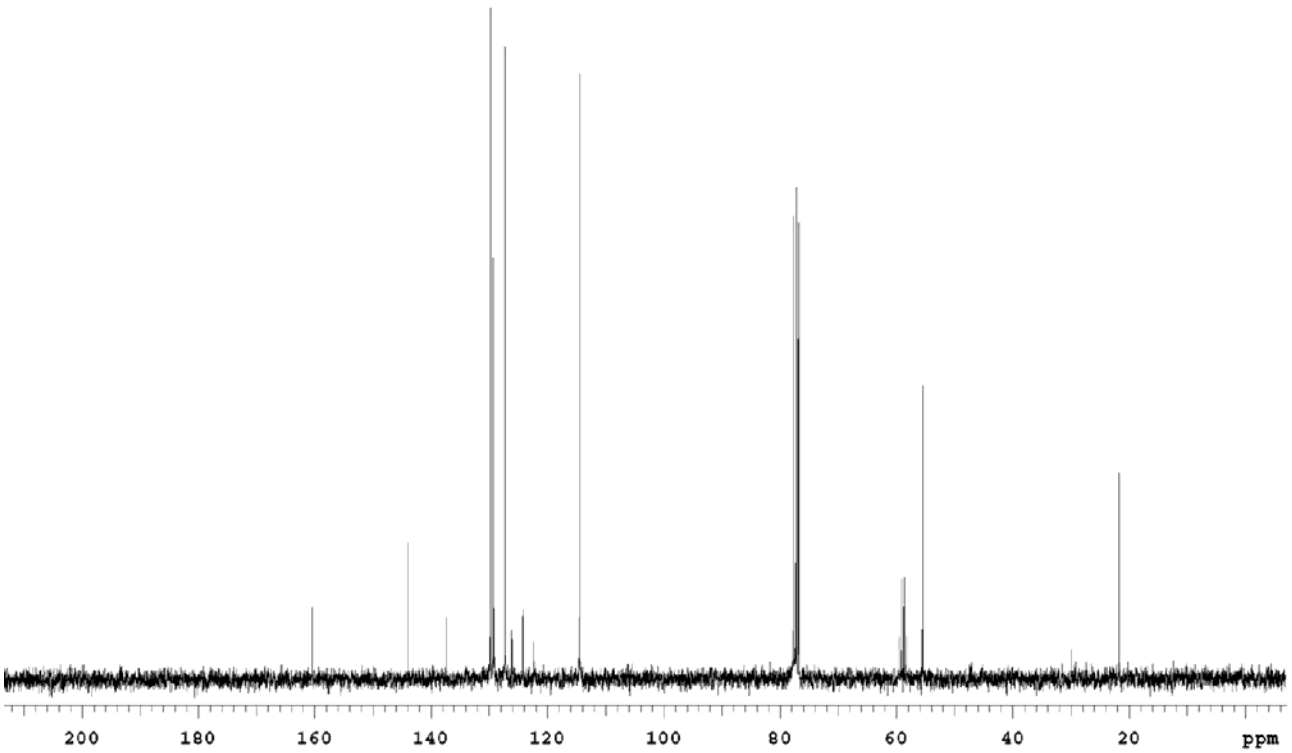
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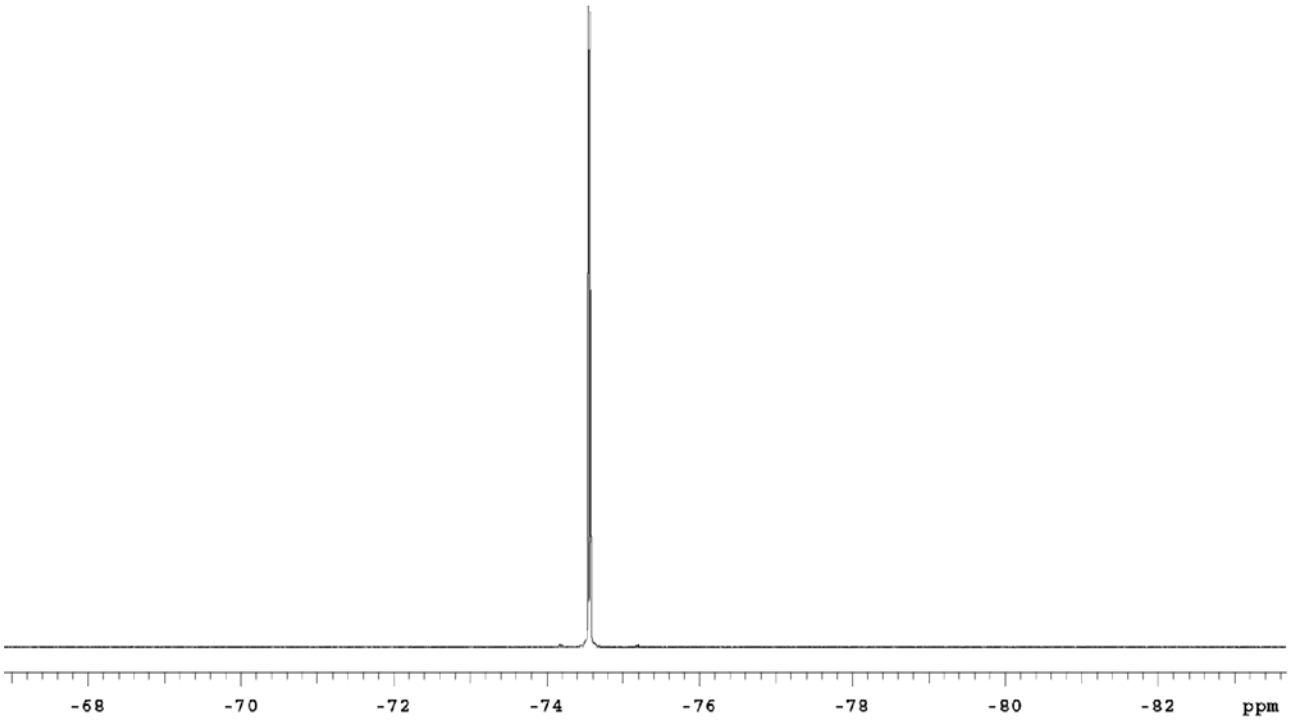
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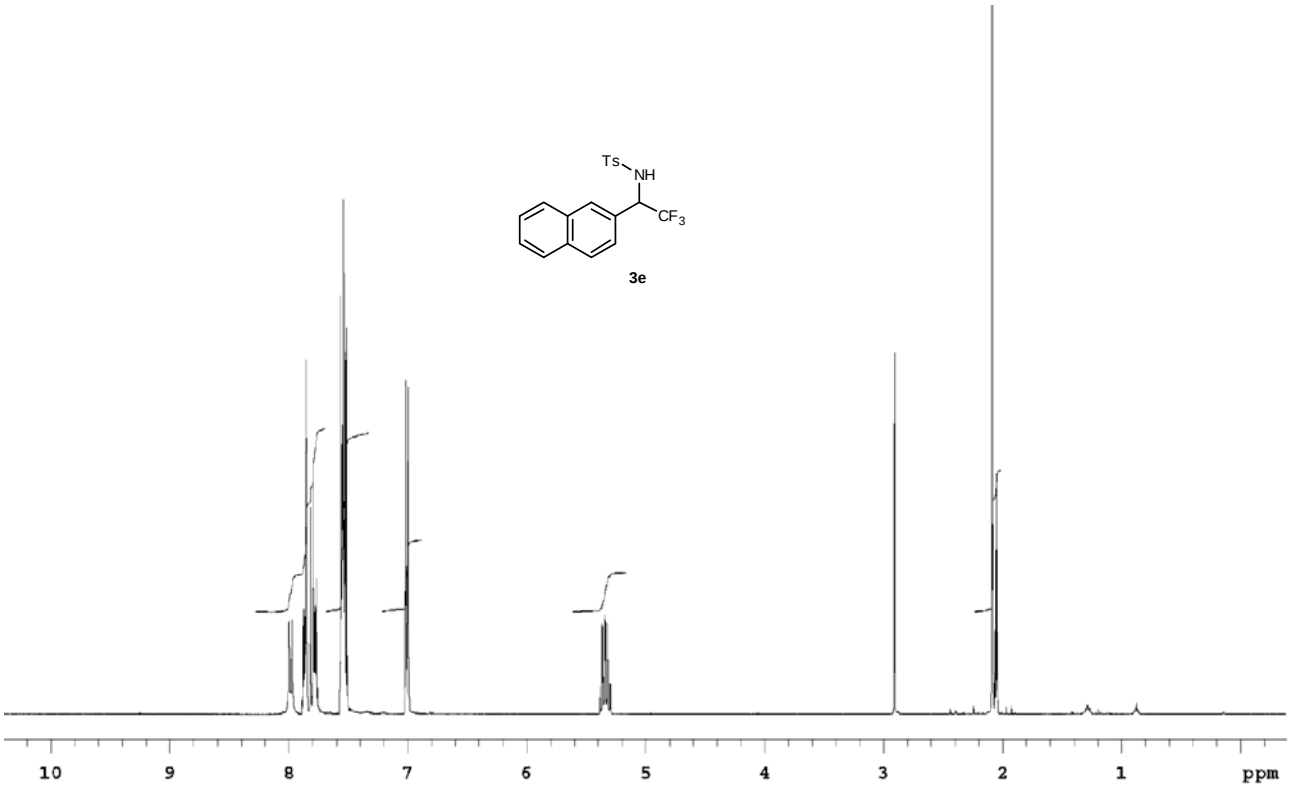
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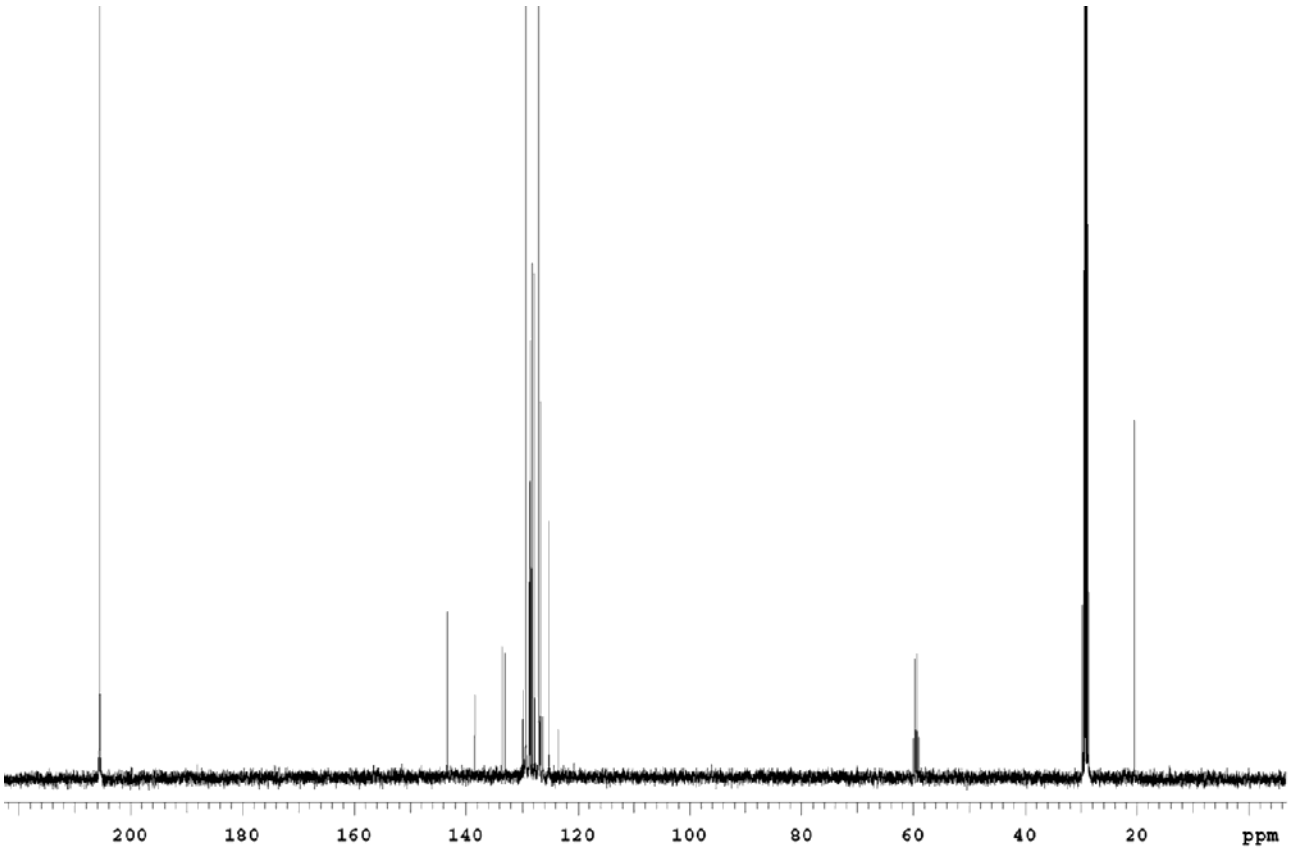
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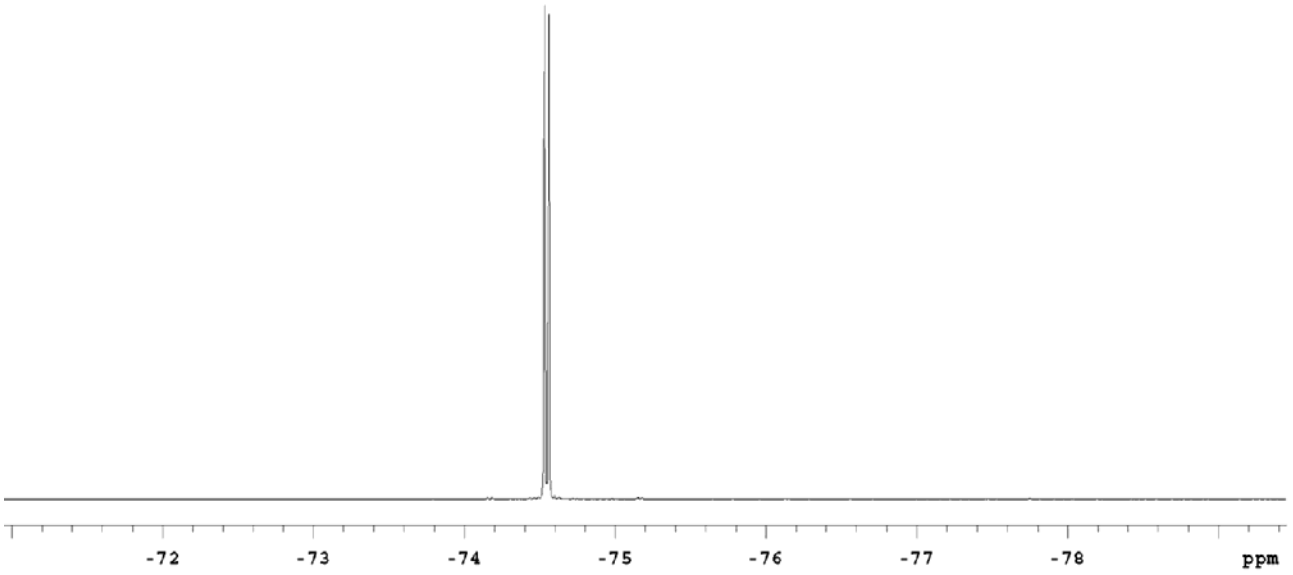
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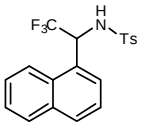
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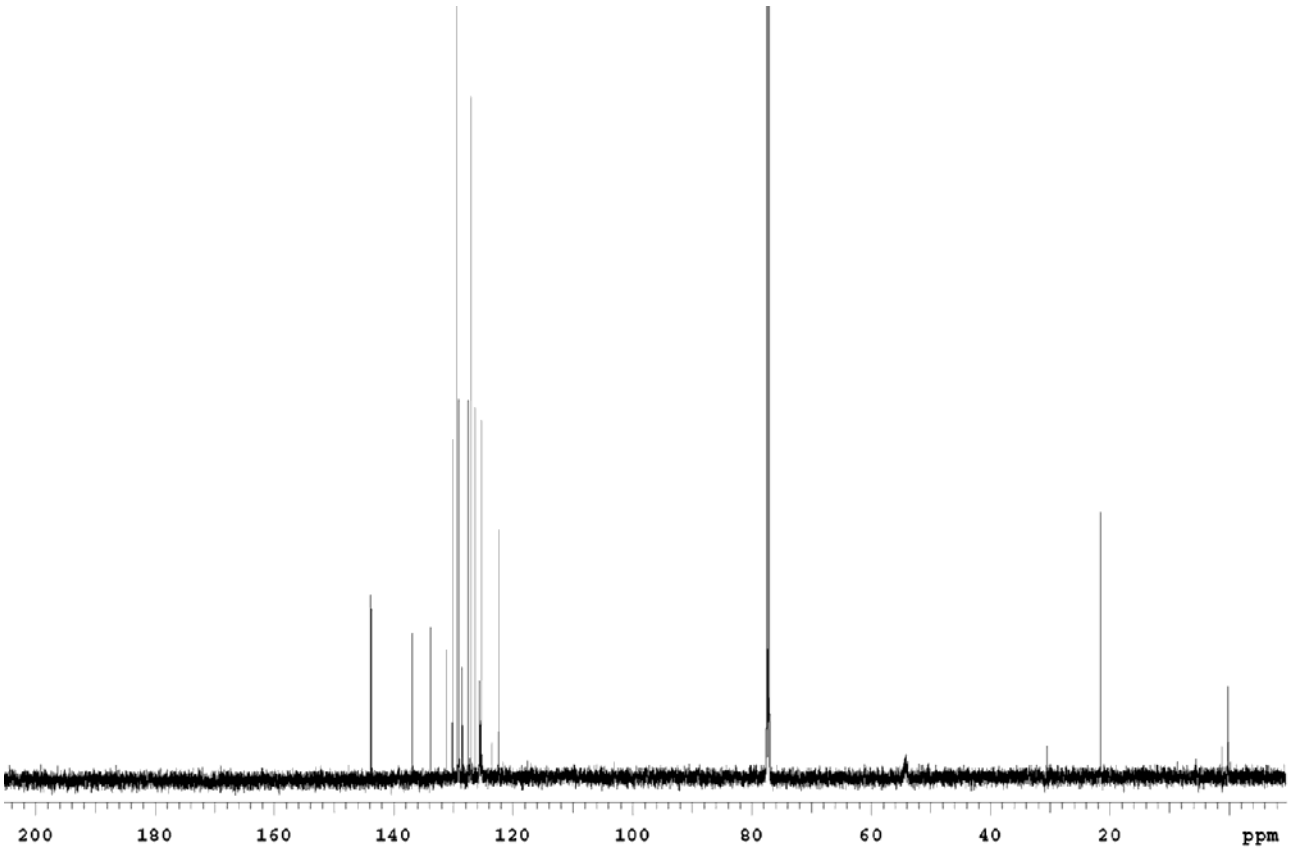
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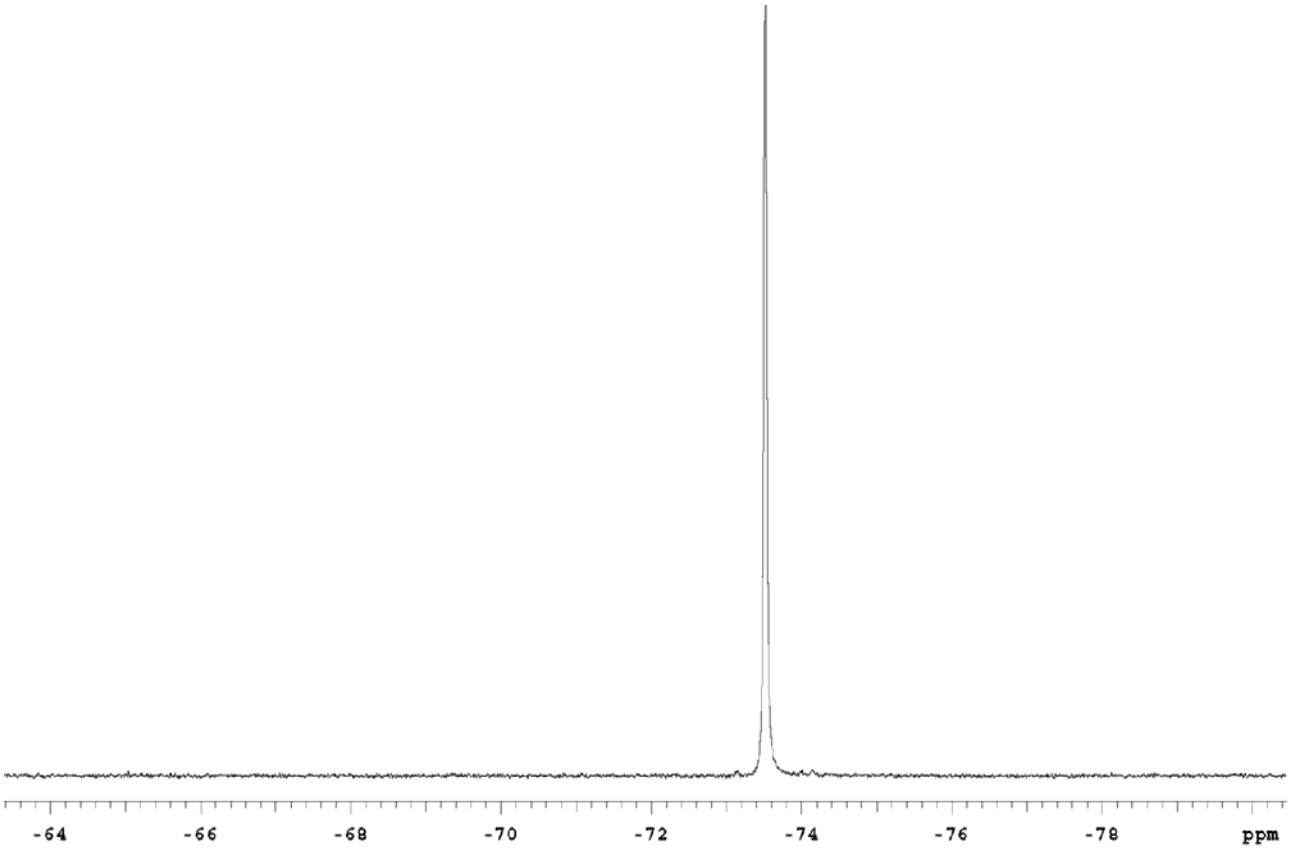
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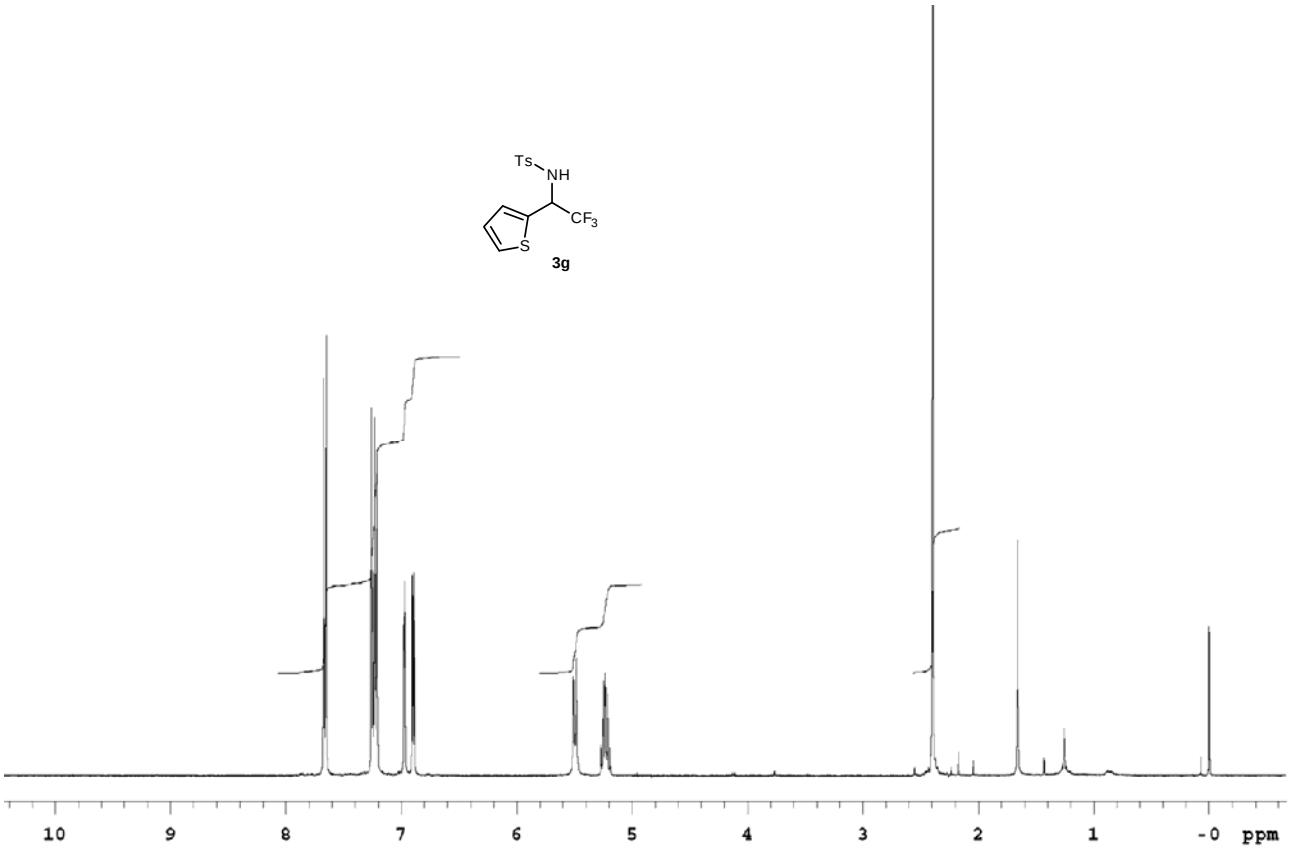
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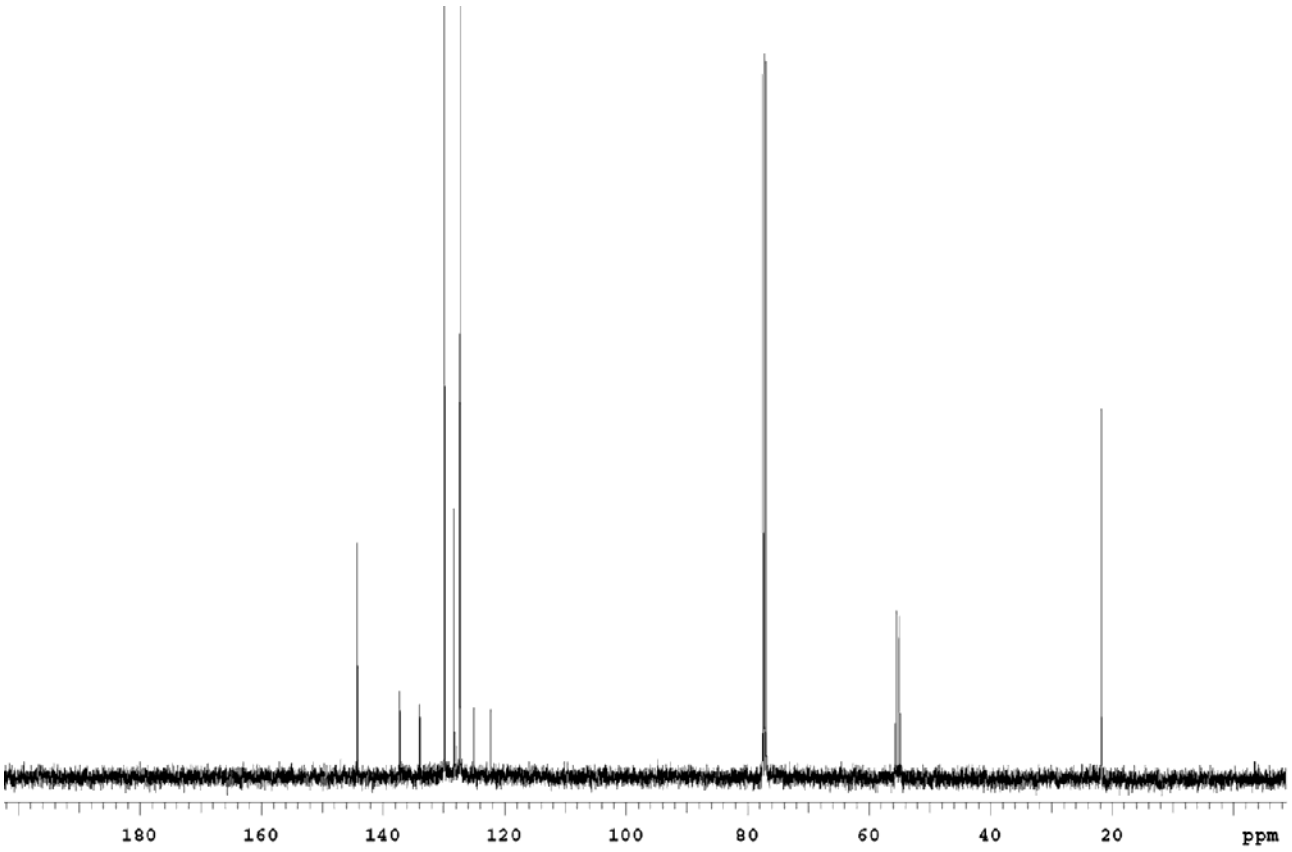
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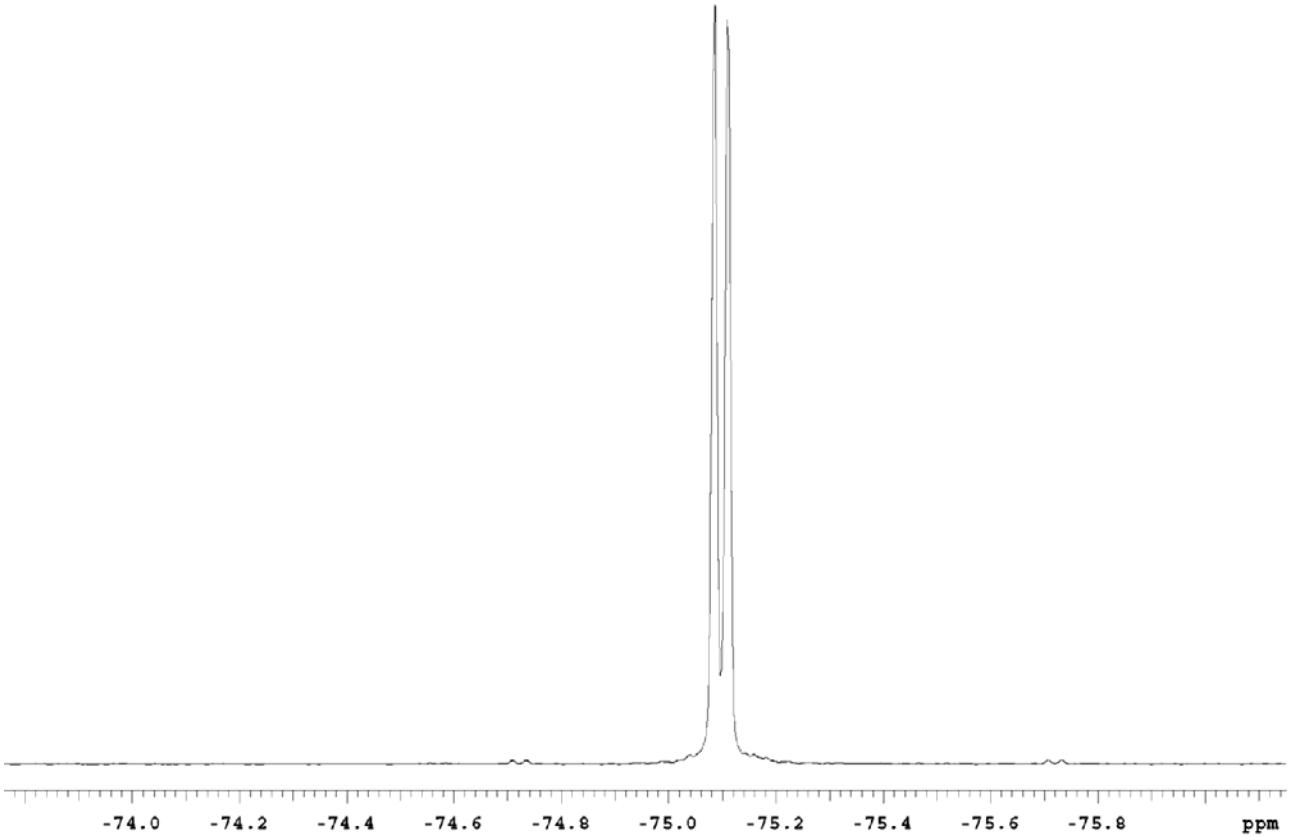
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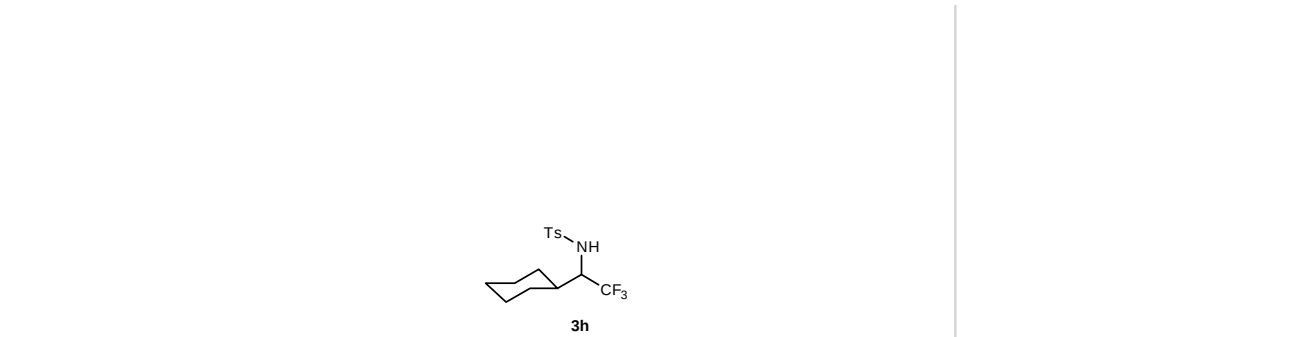
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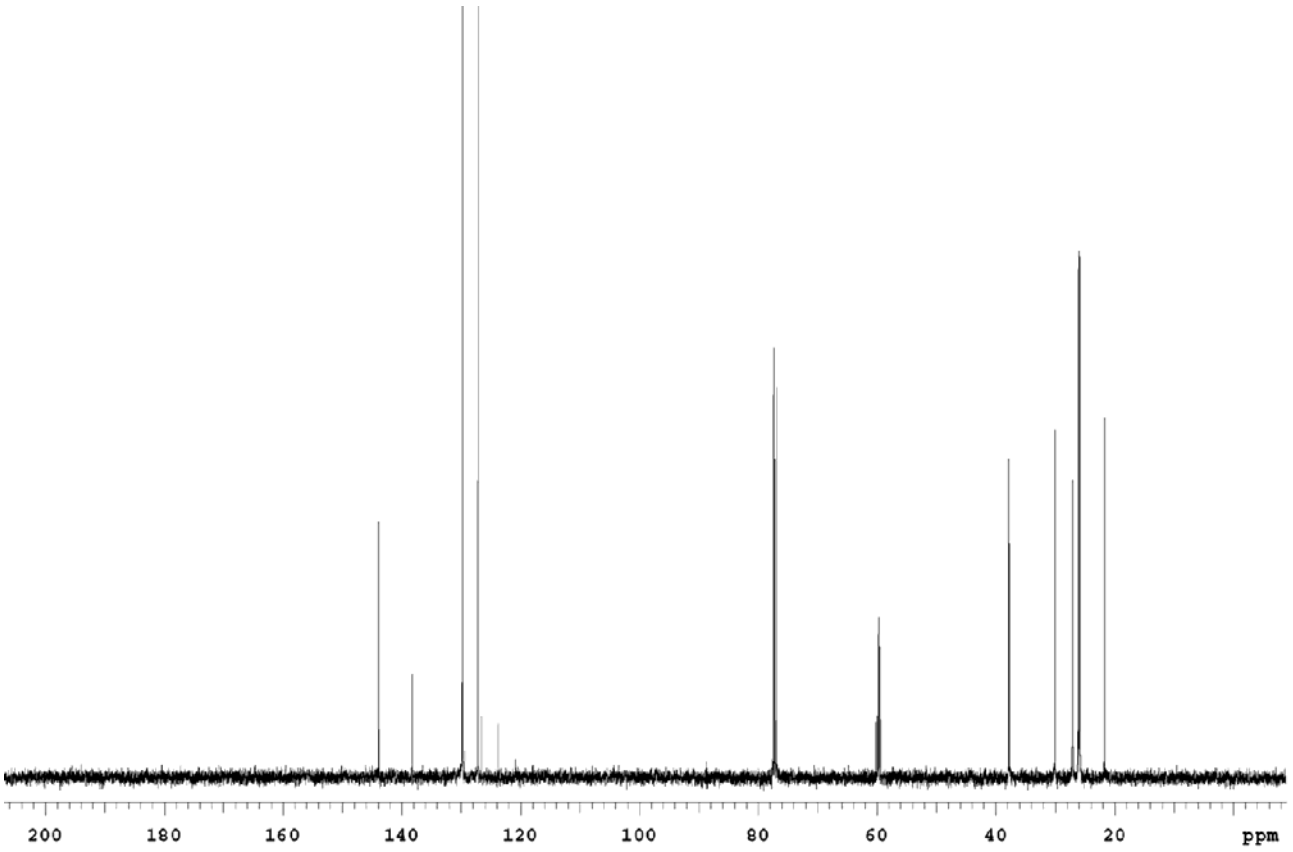
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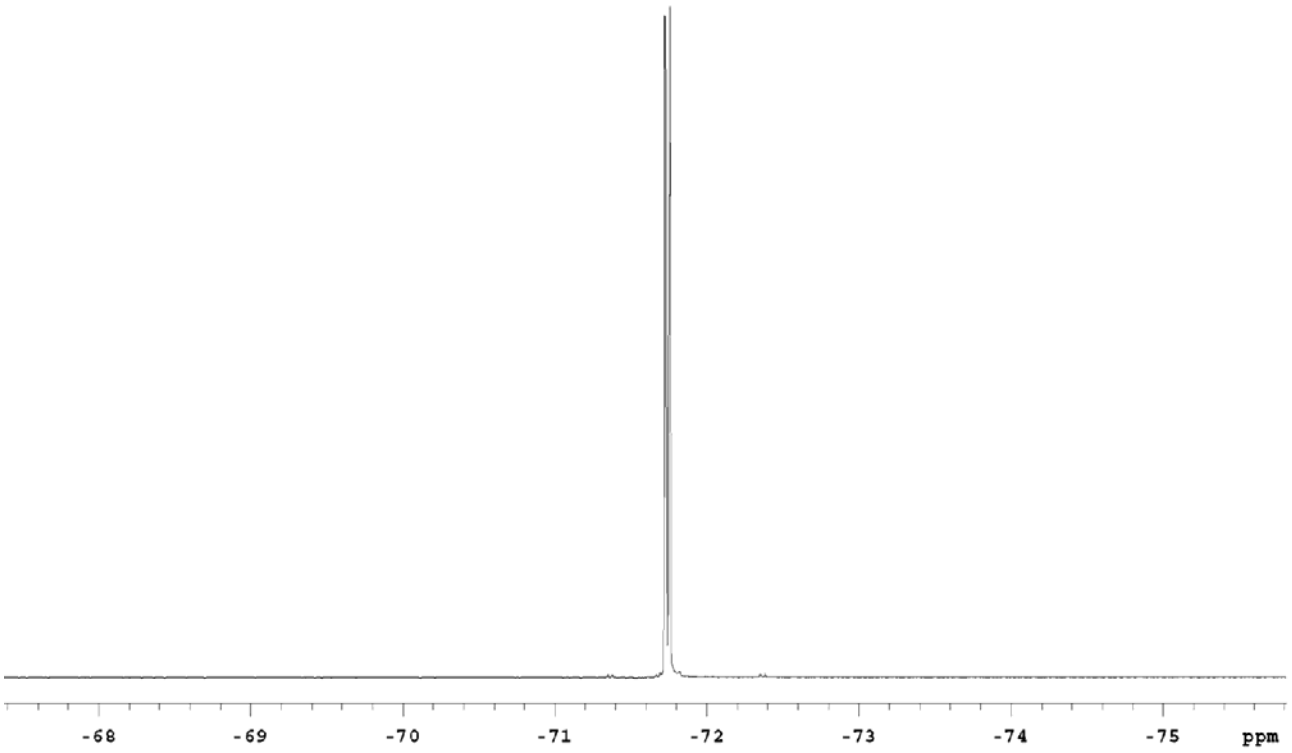

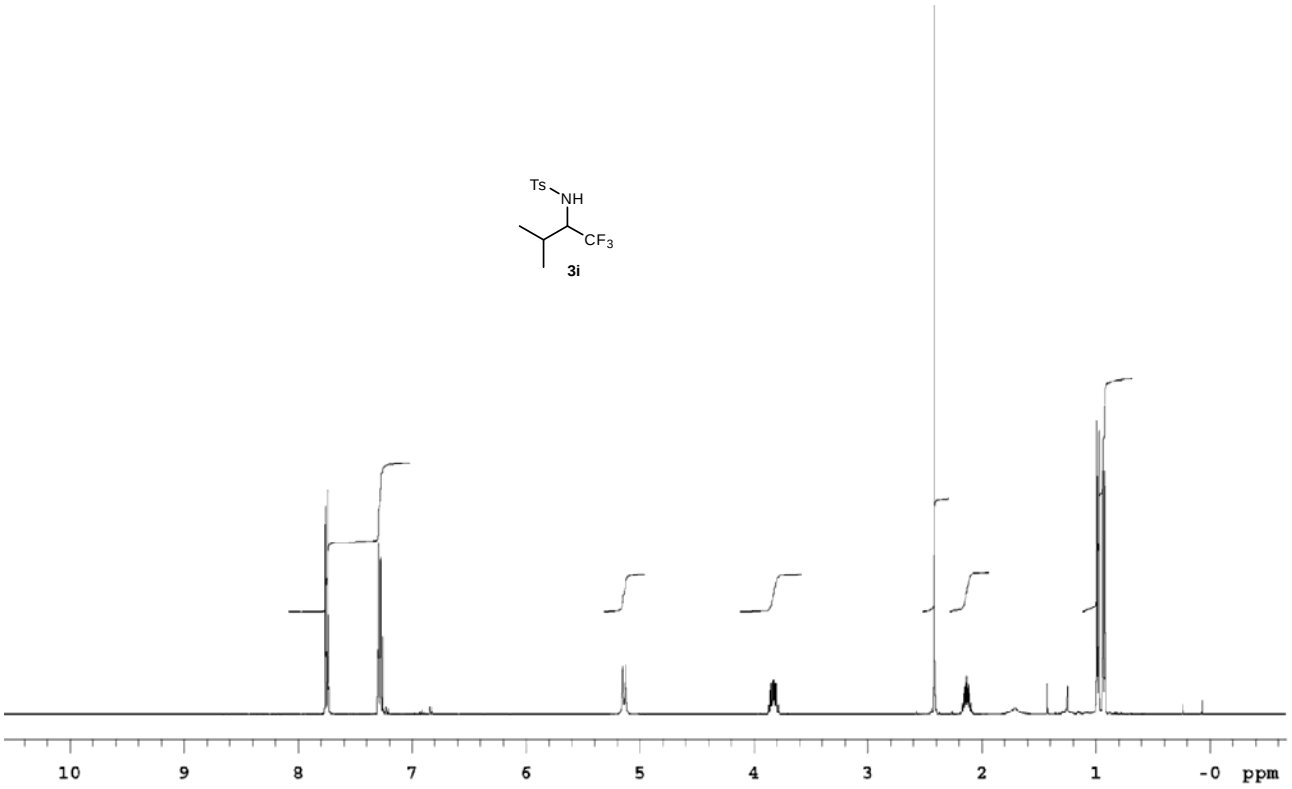
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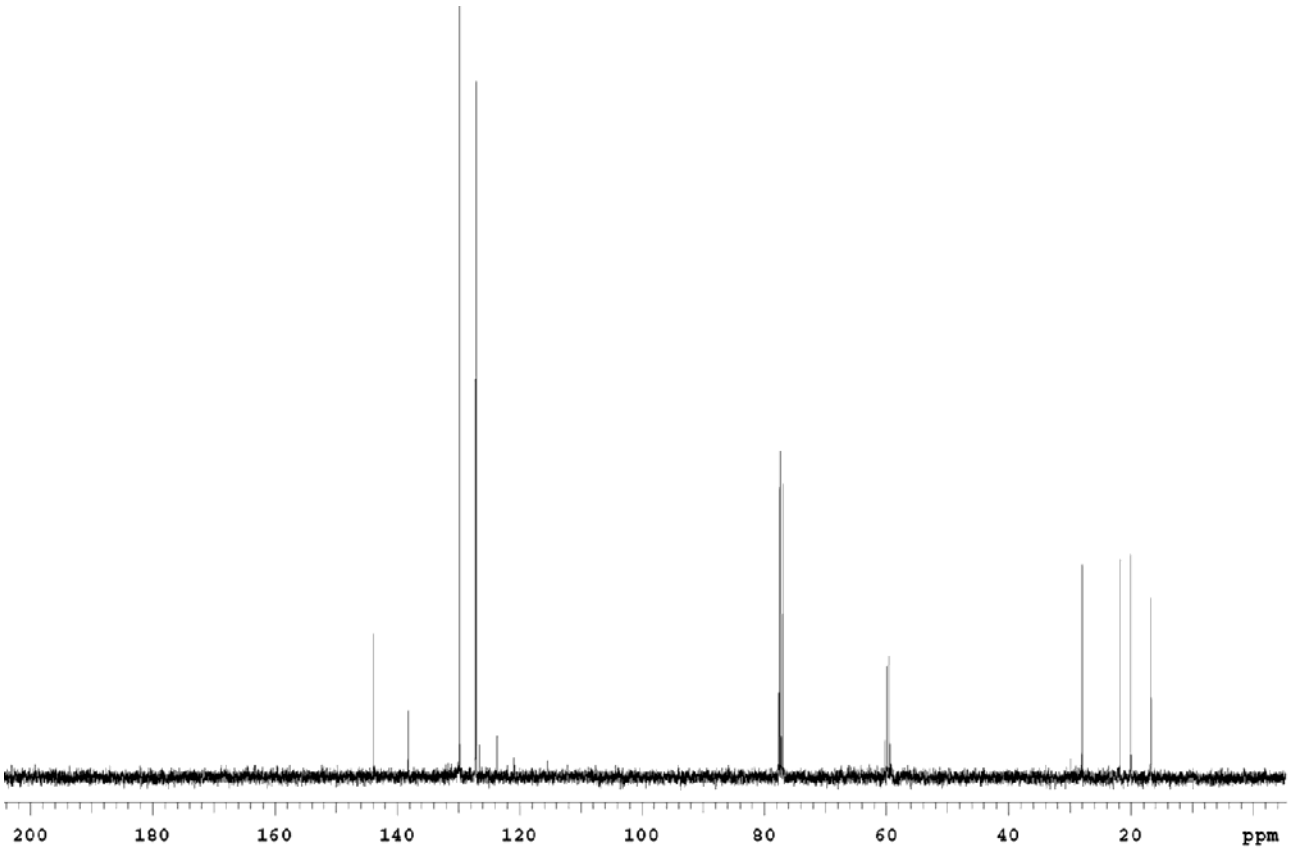
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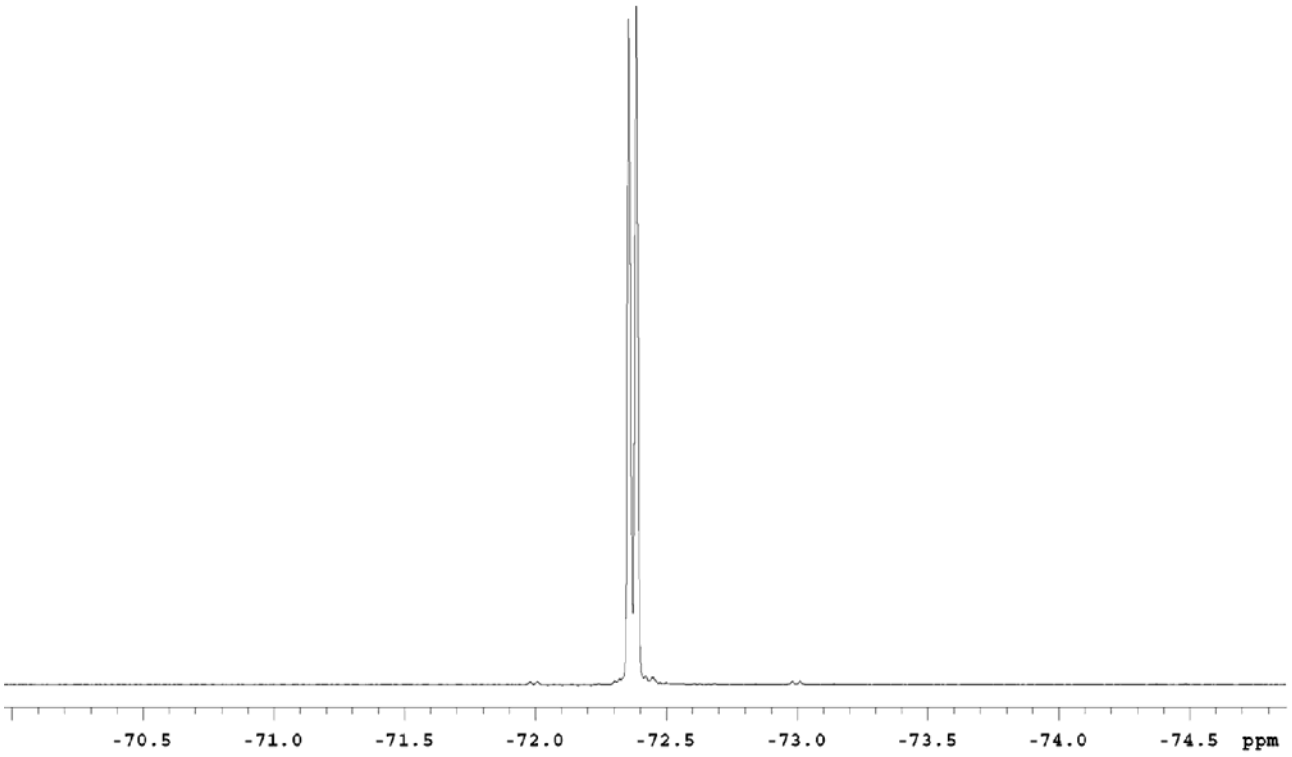

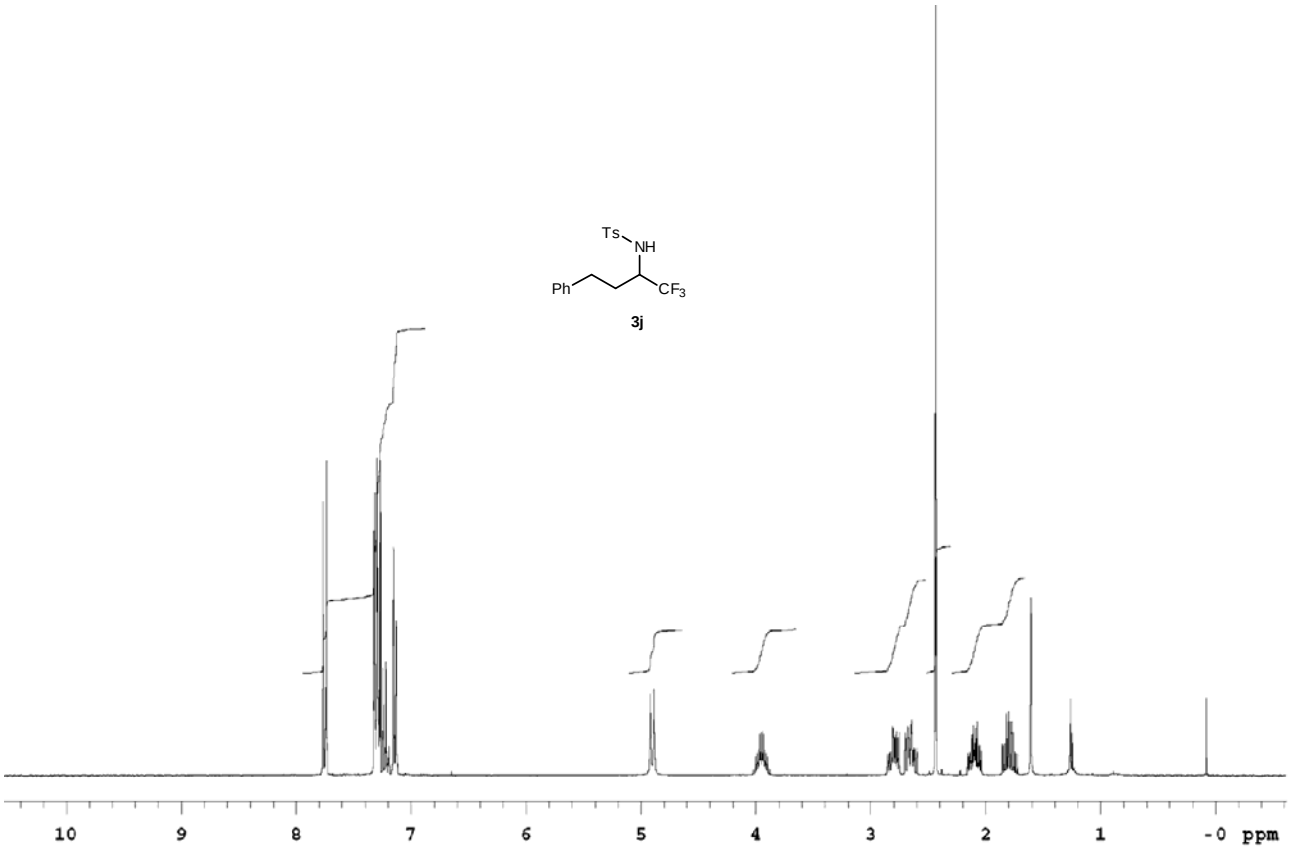
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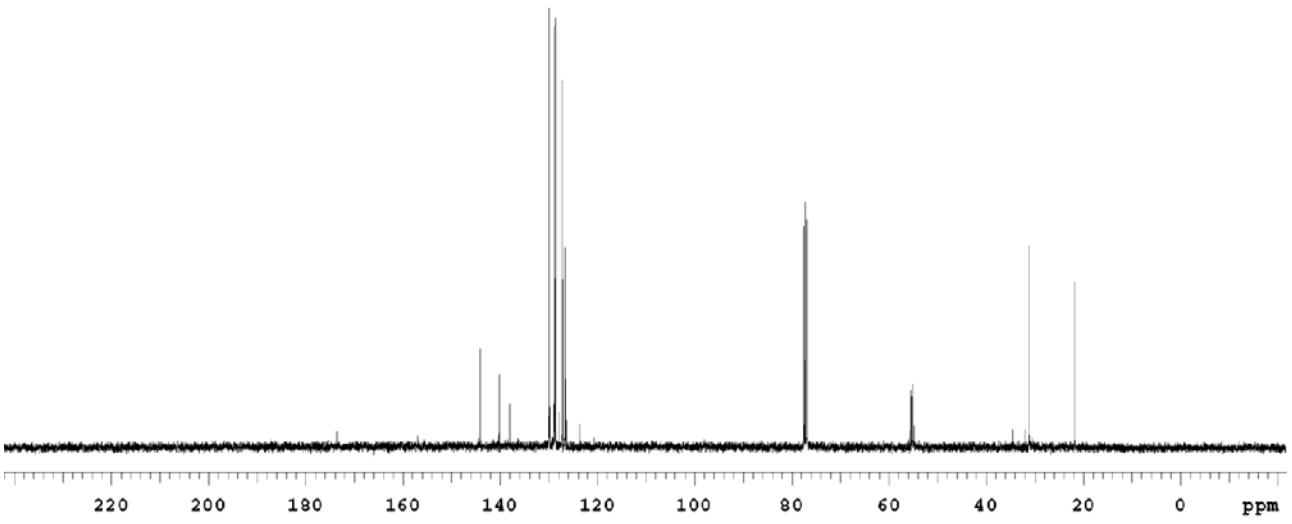
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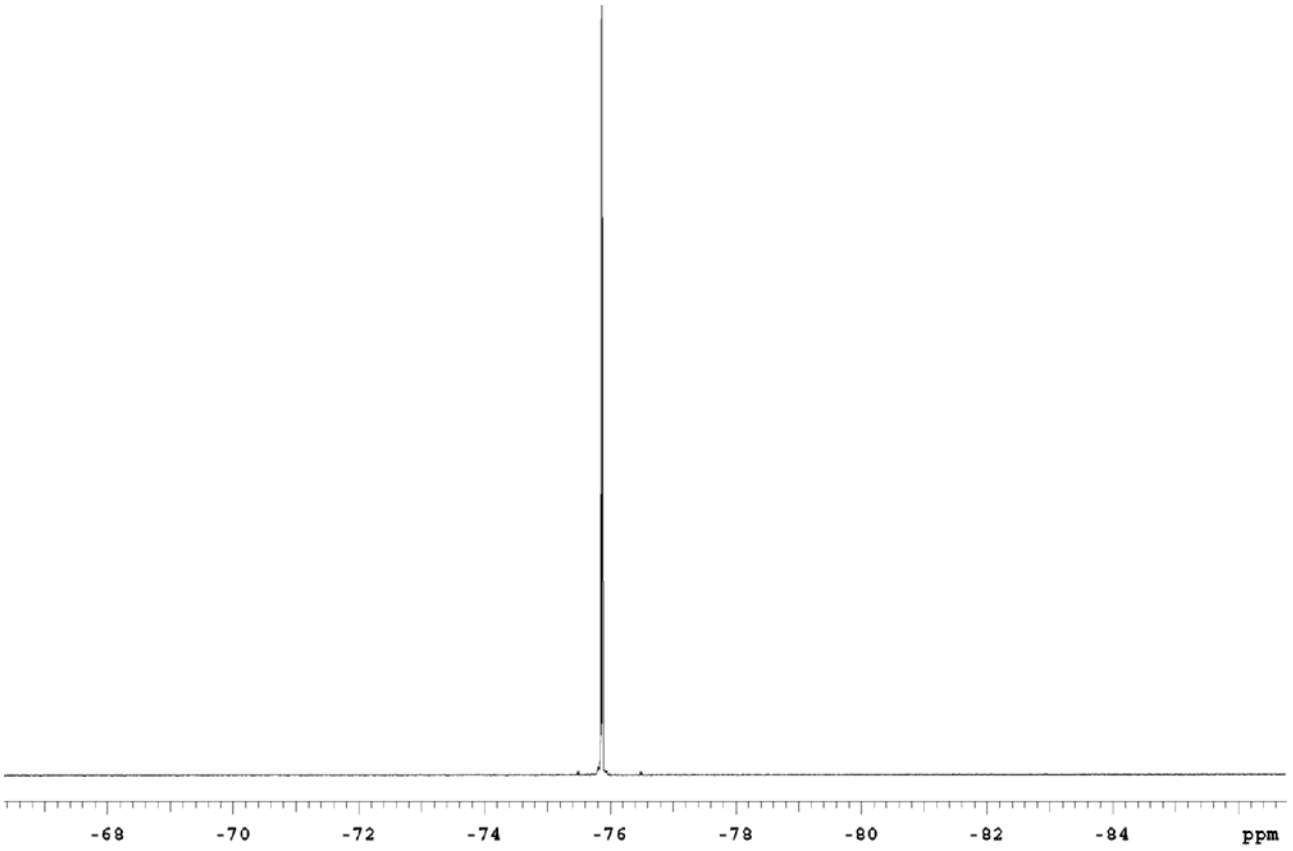
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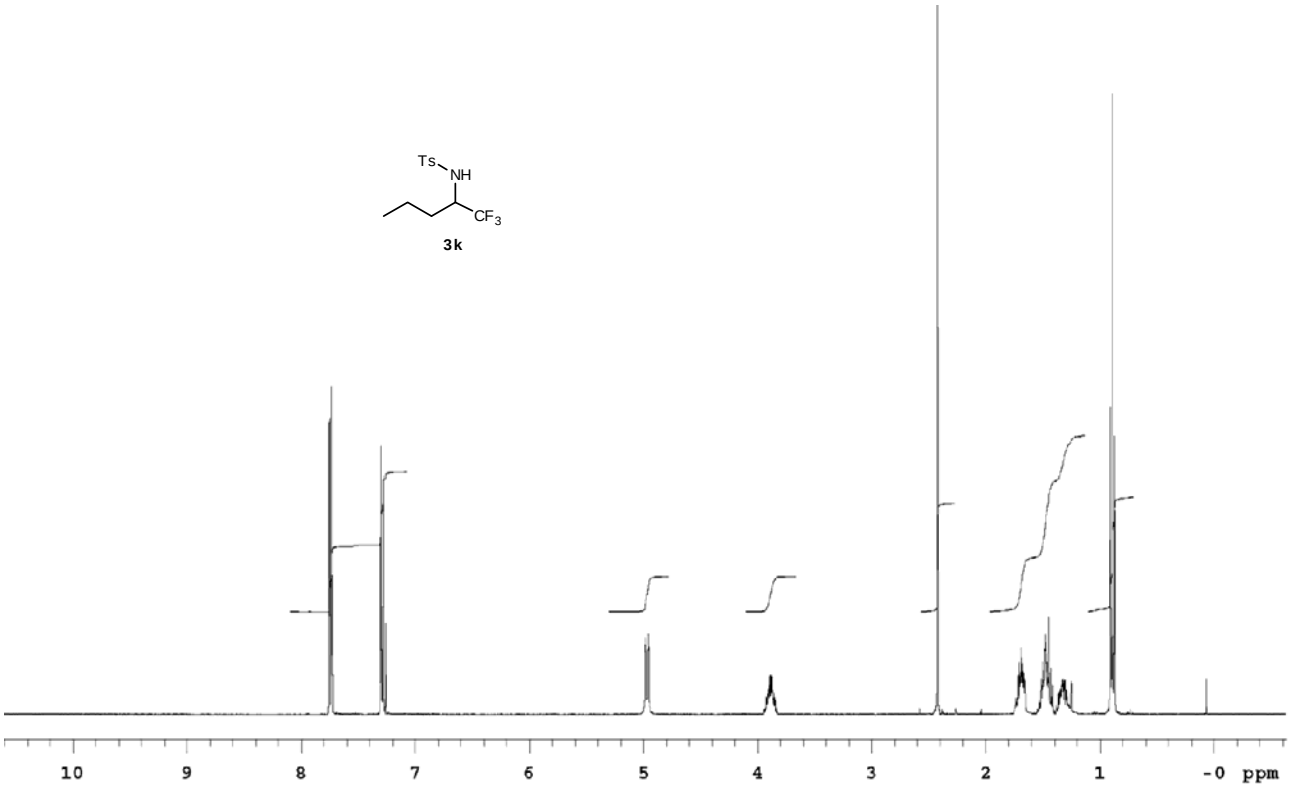
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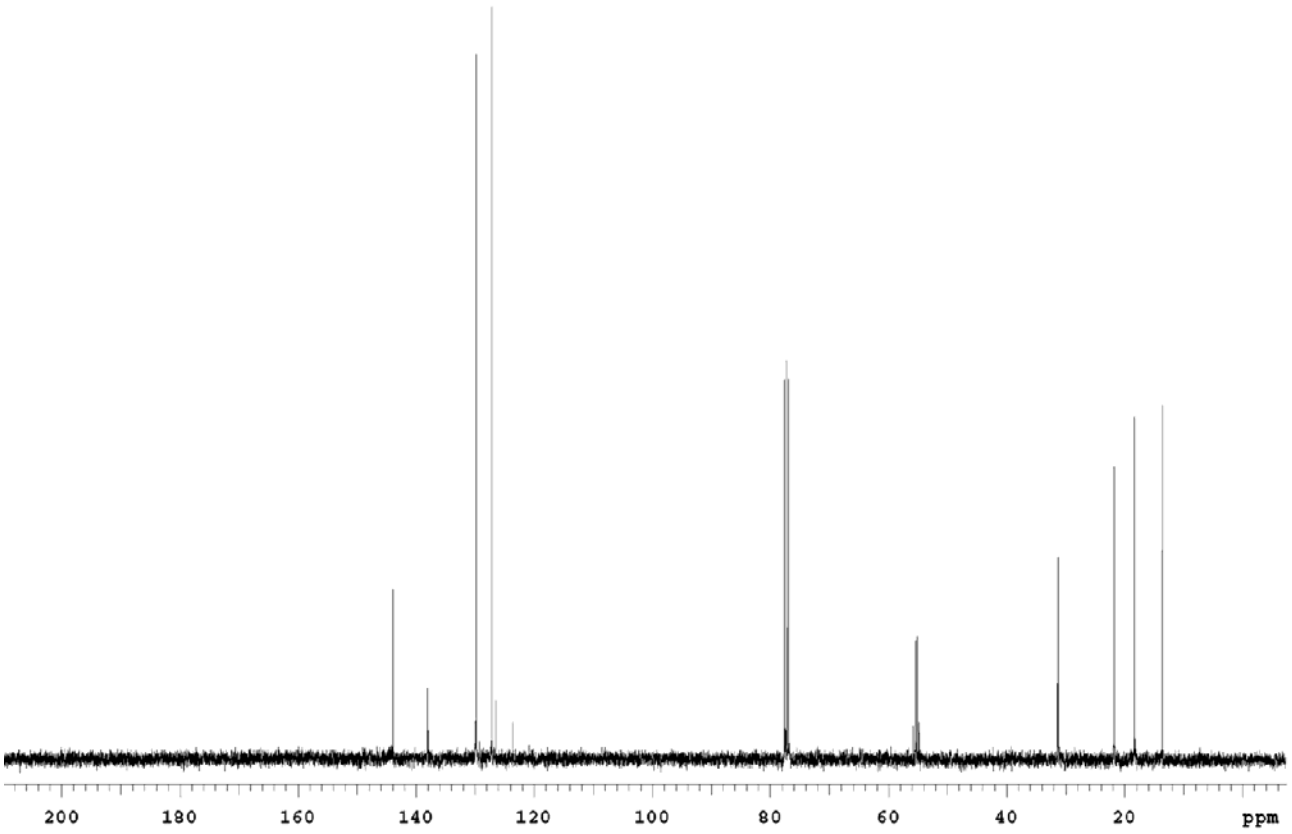
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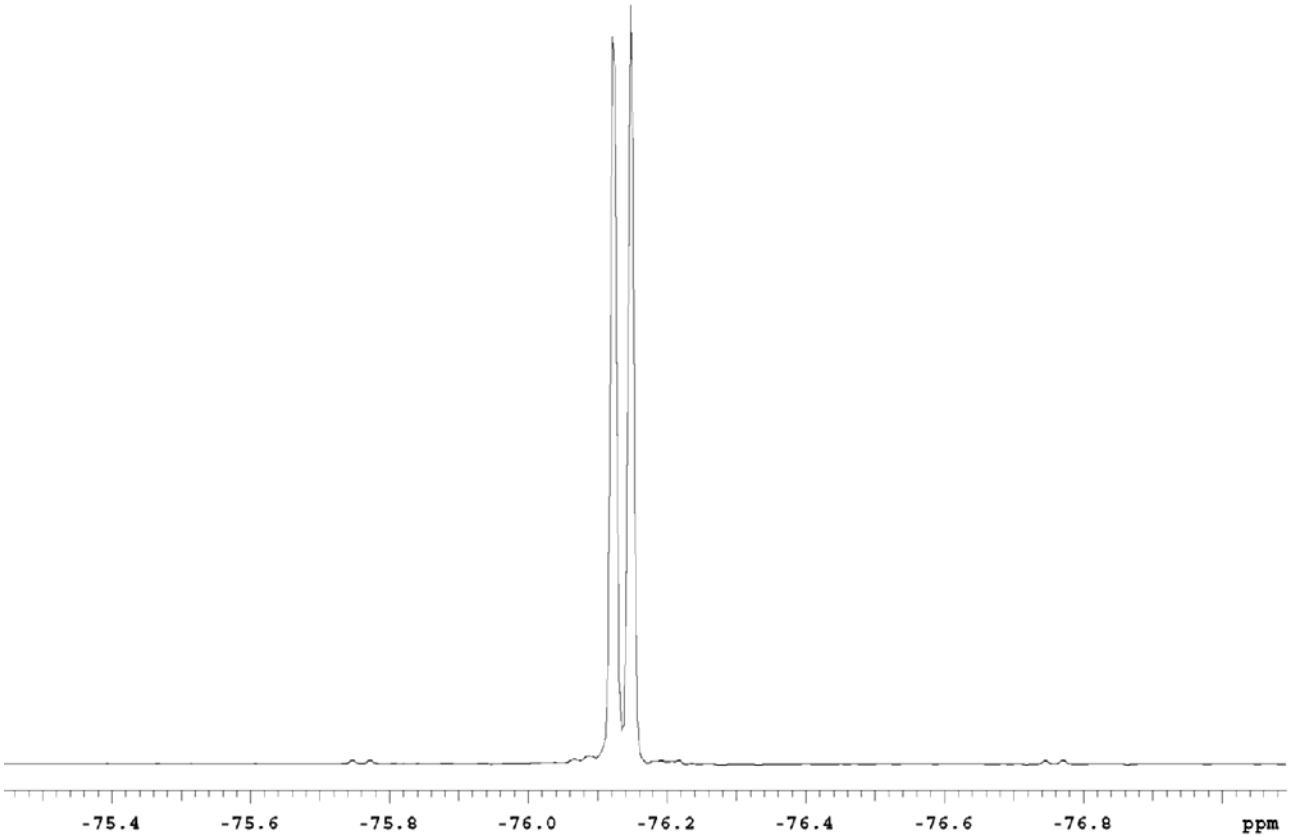
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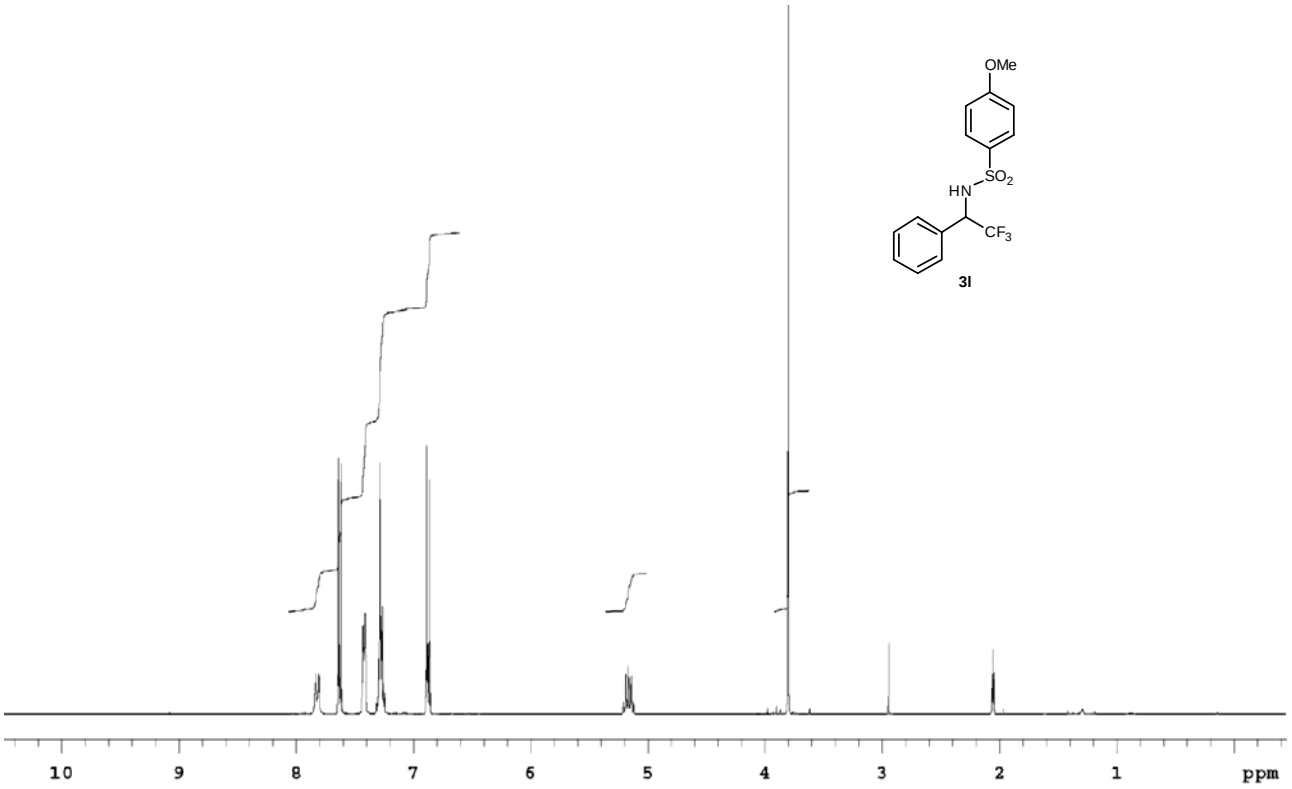
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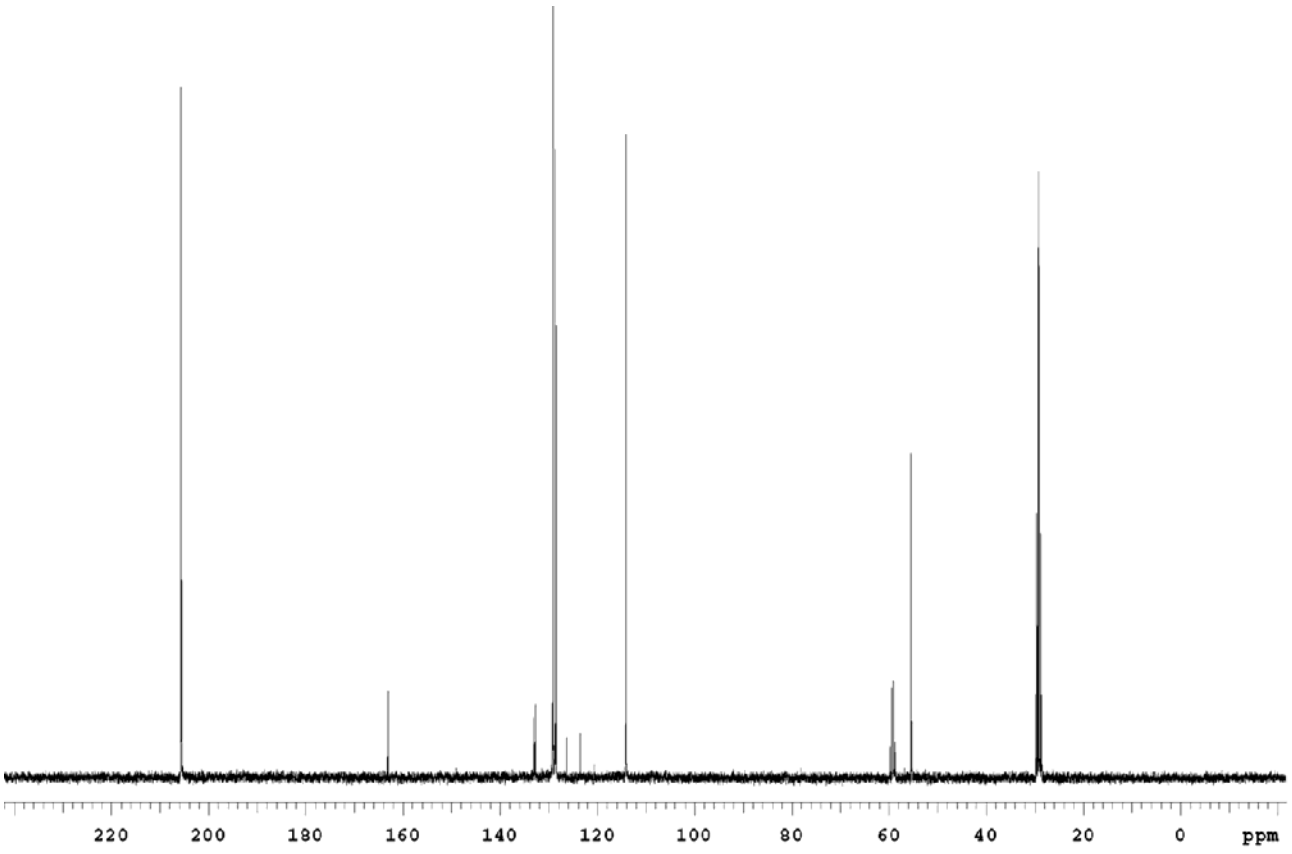
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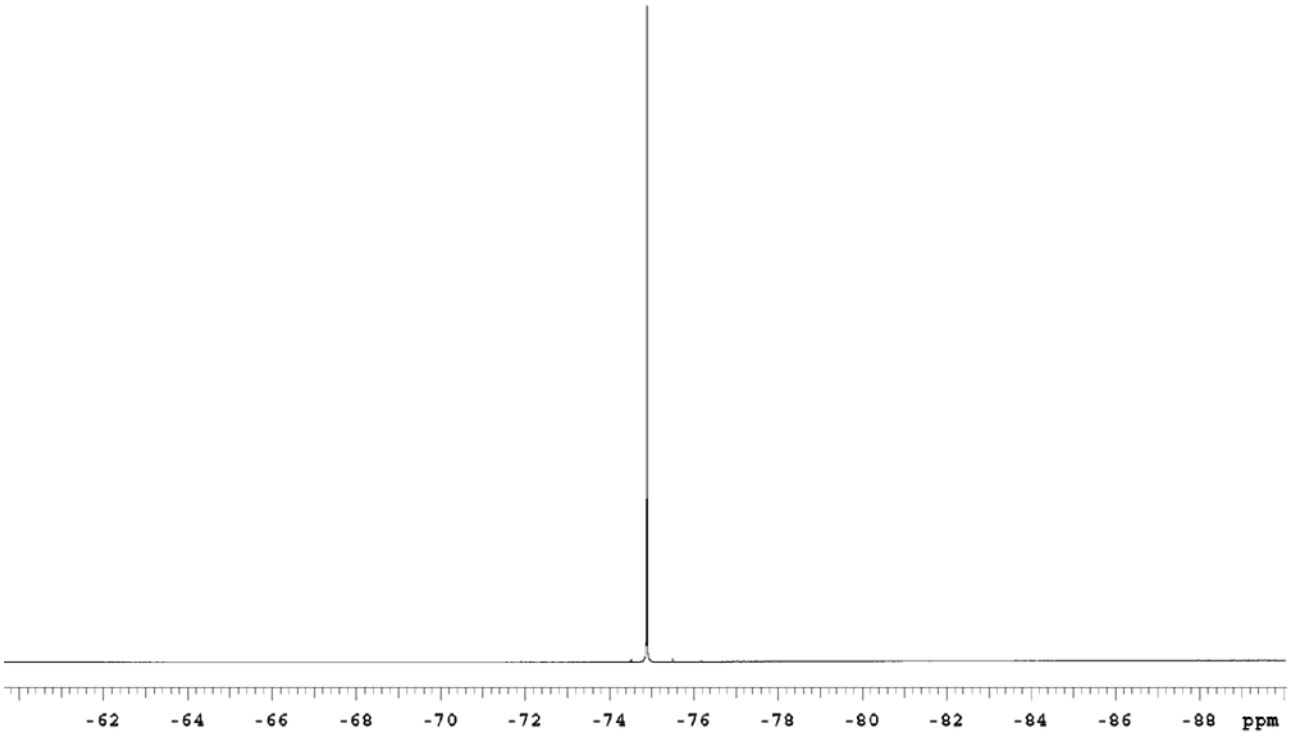
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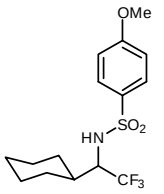
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HN
SO2
CF3

3m

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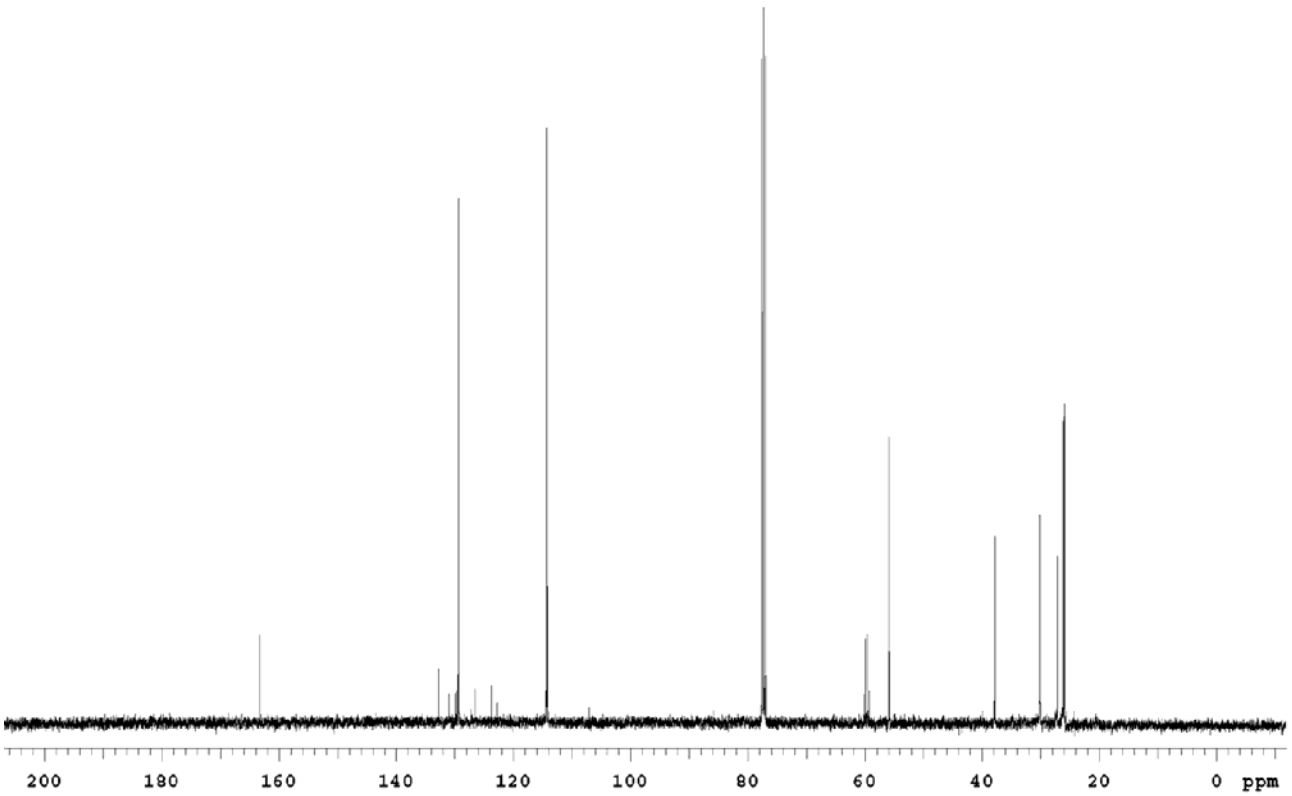
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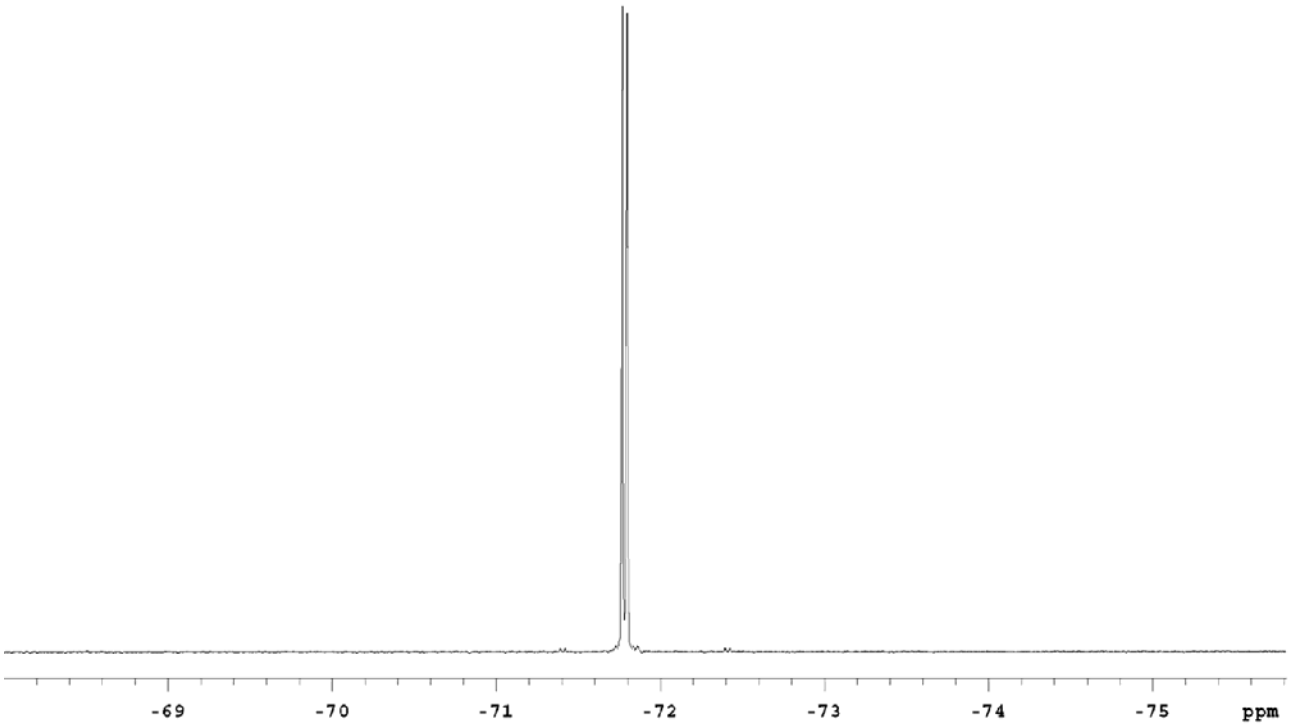

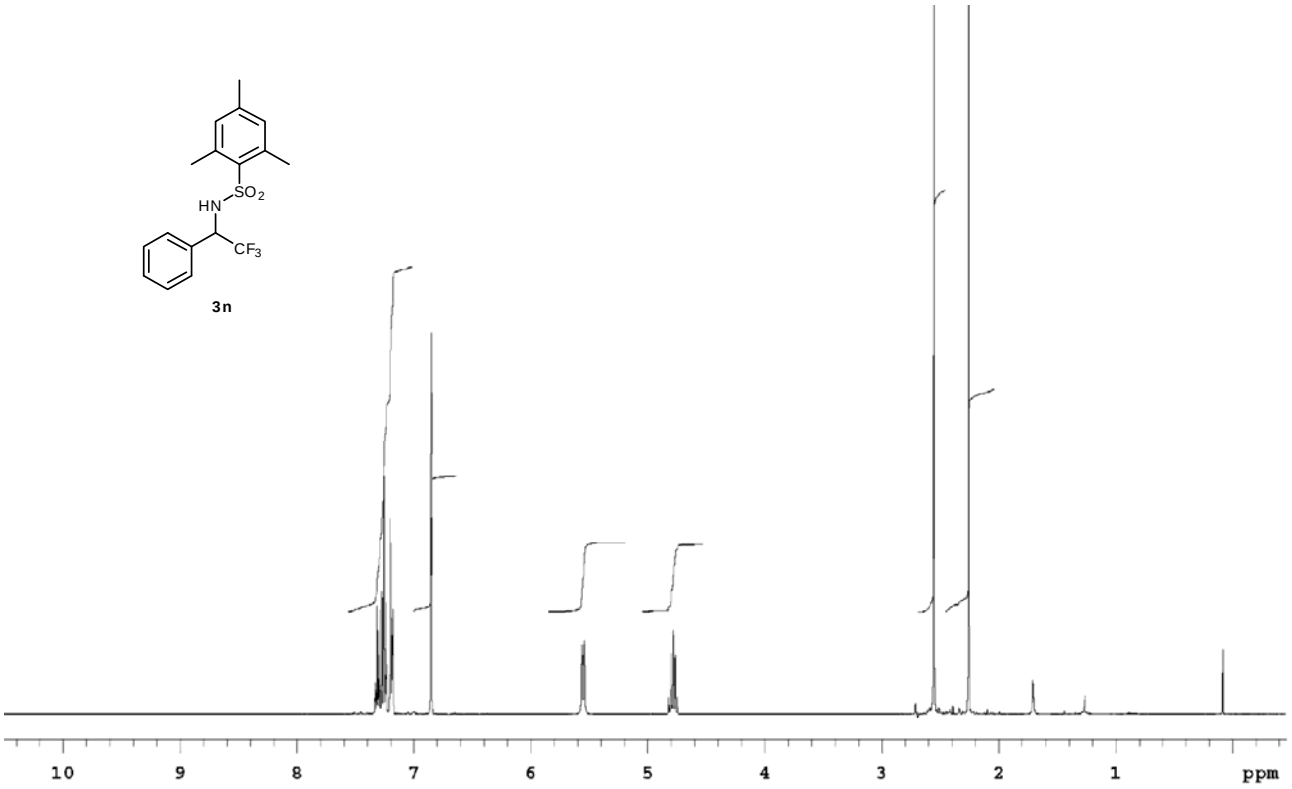
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SO2
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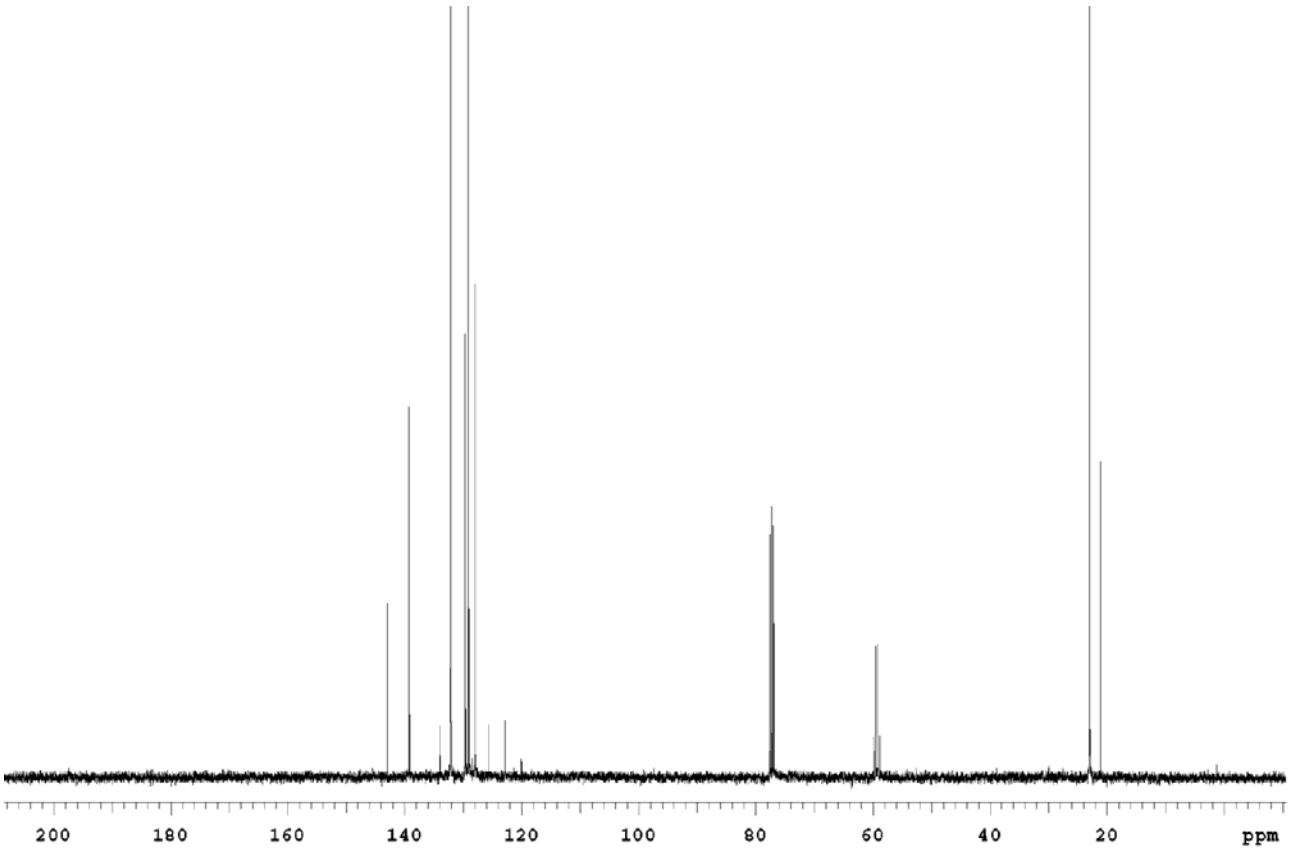
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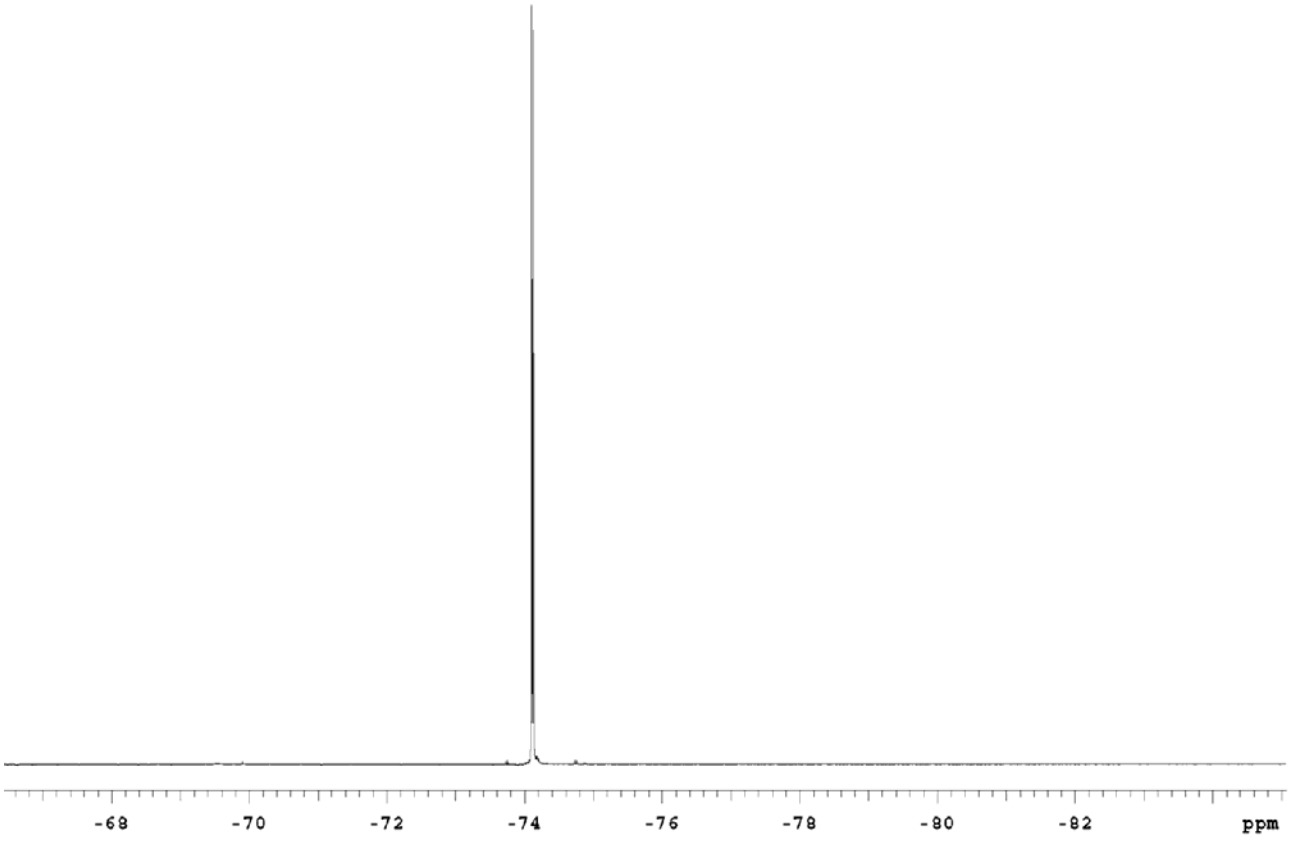
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-82
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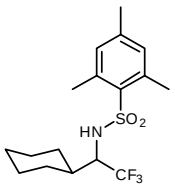

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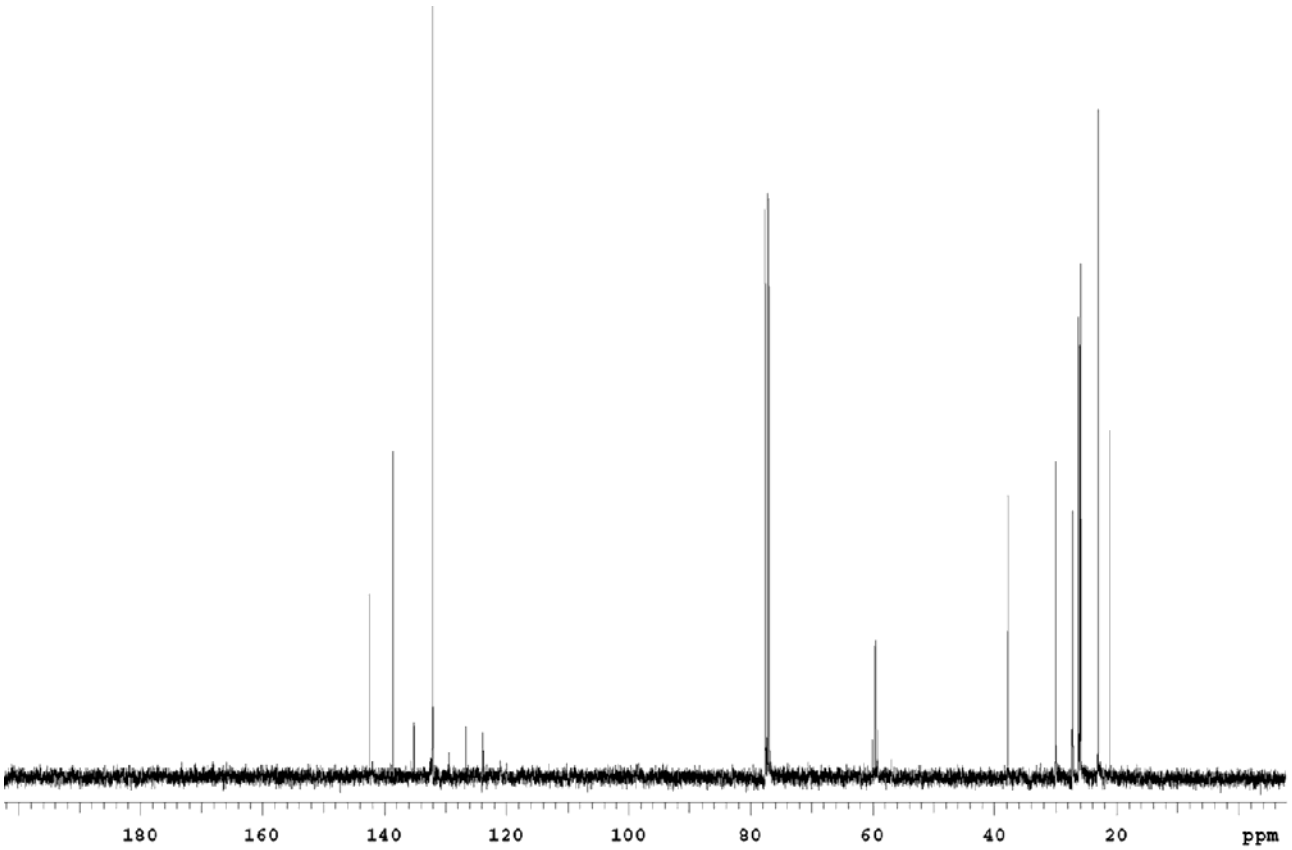

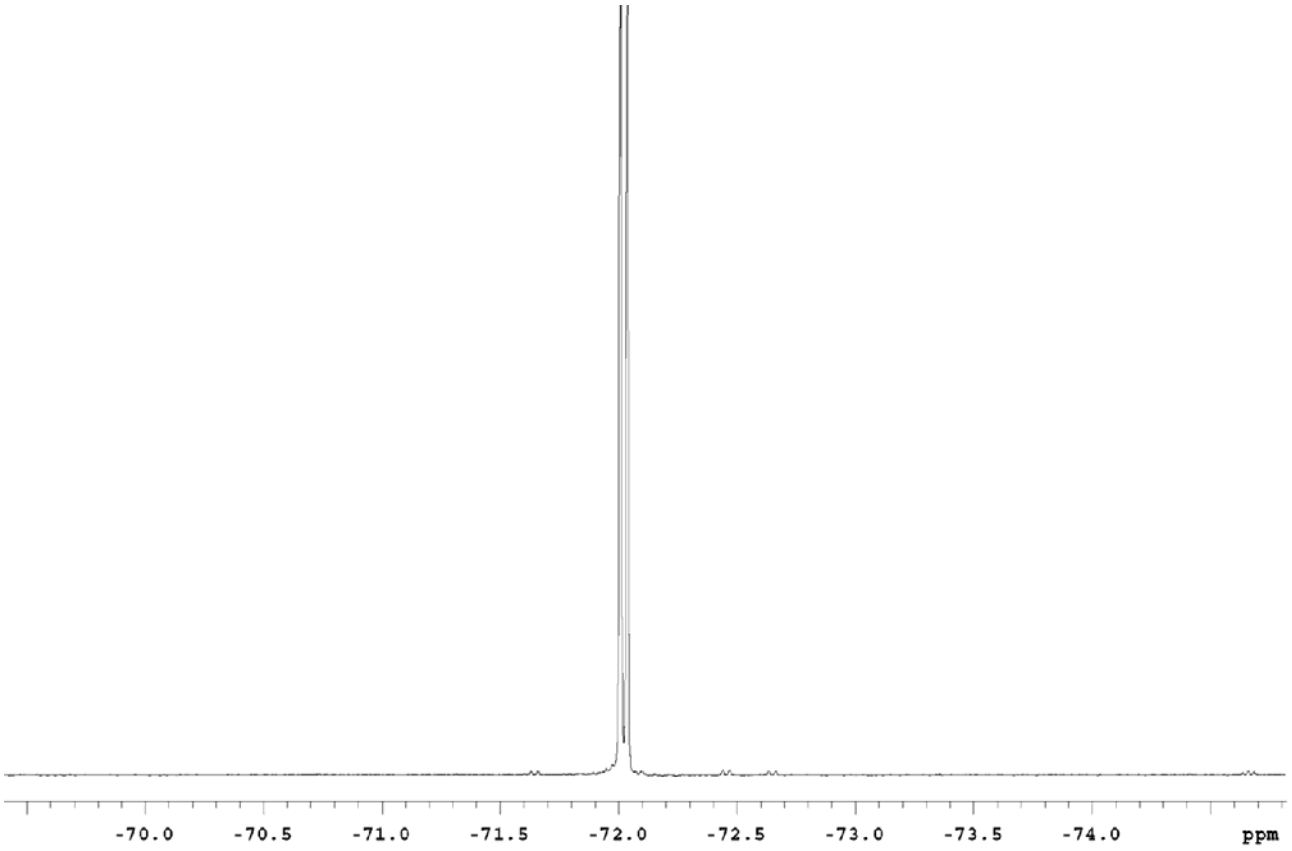
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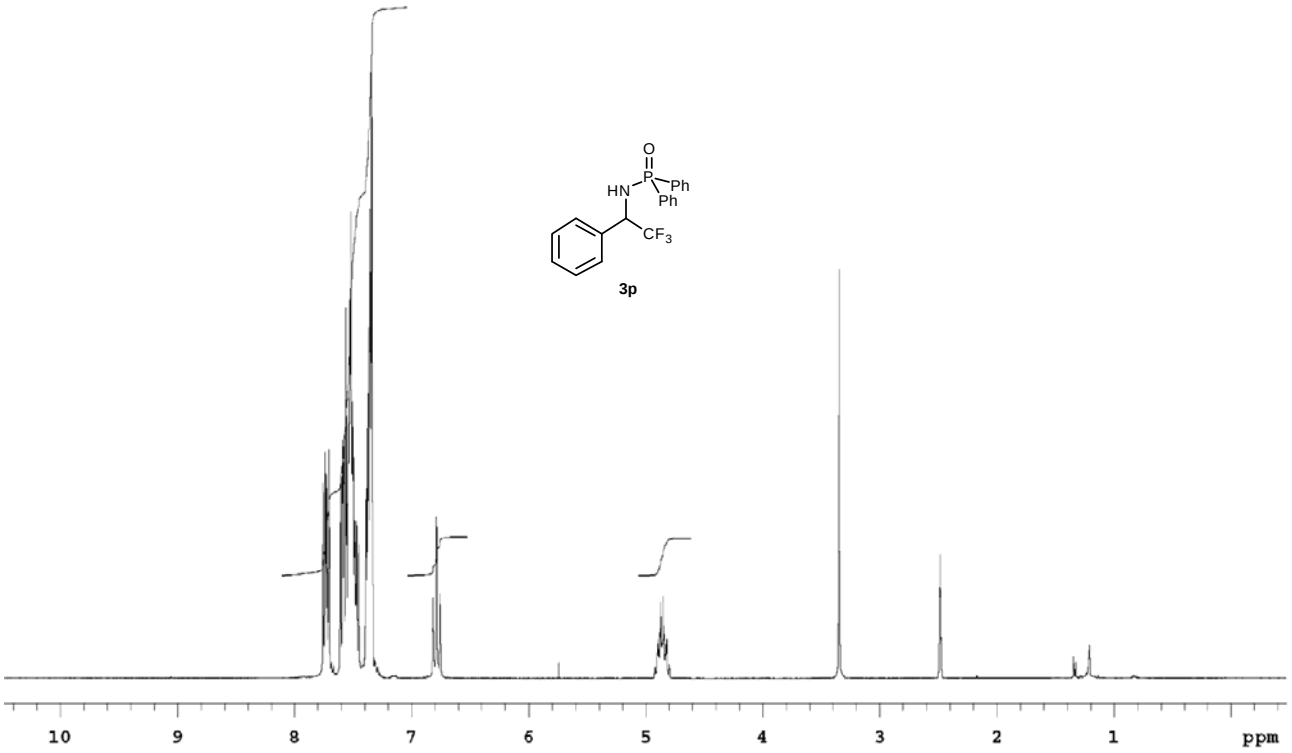
ppm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P
Ph
Ph
CF3
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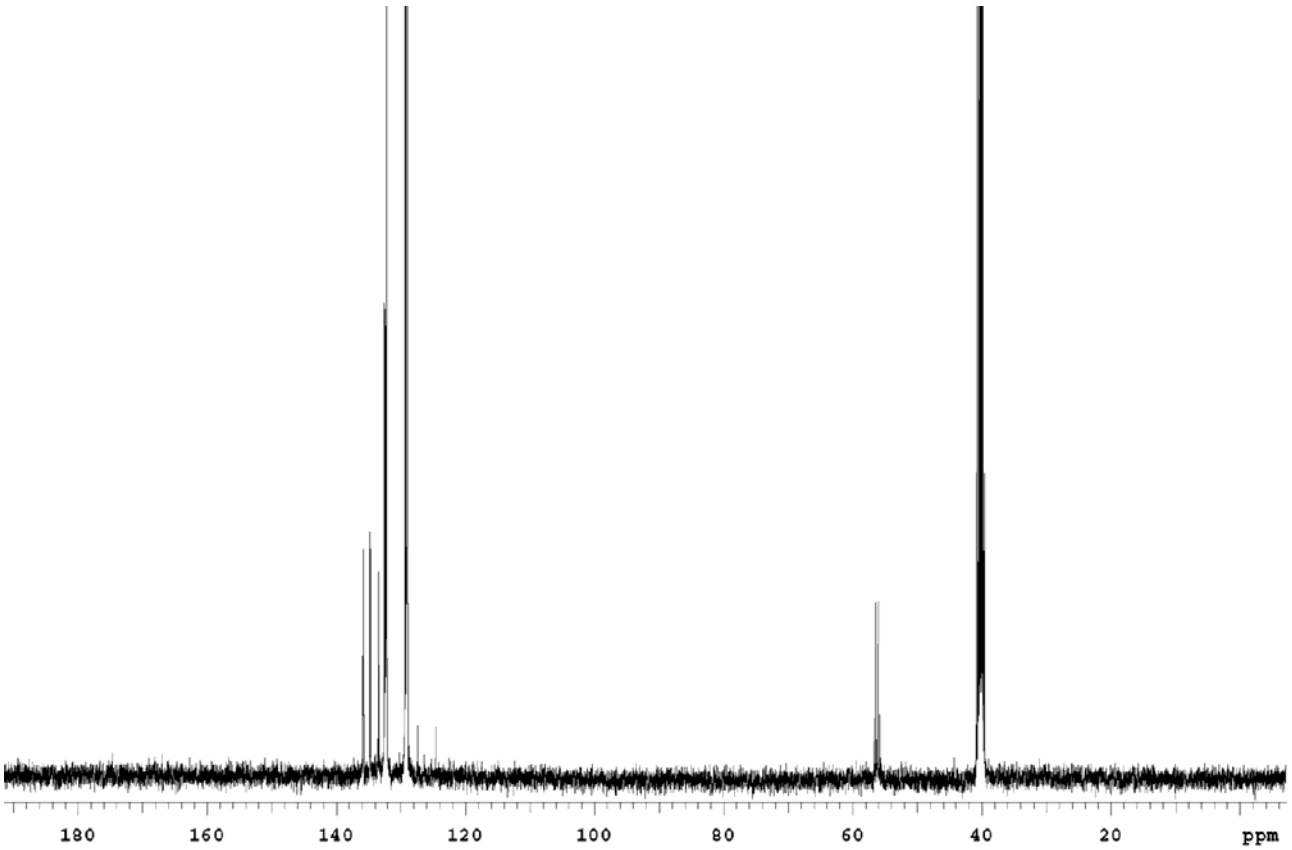
8
7
6
5
4
3
2
1
ppm

3p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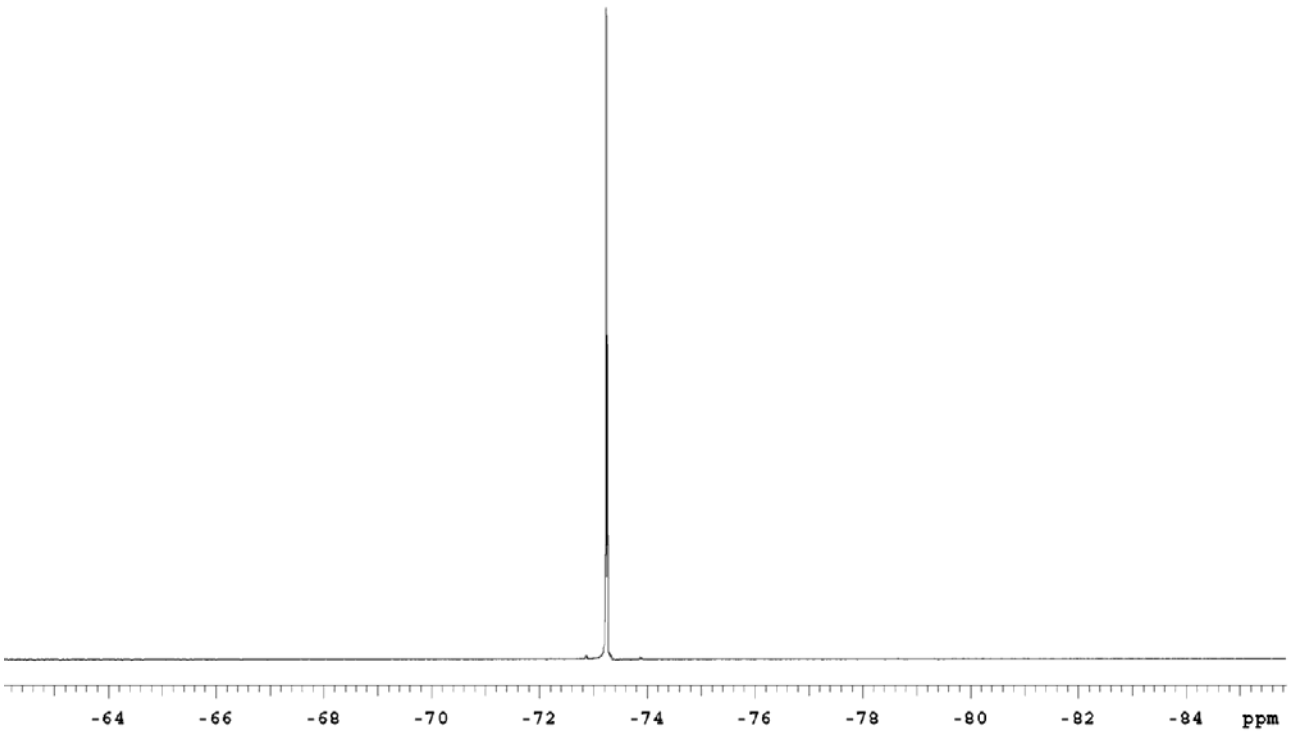
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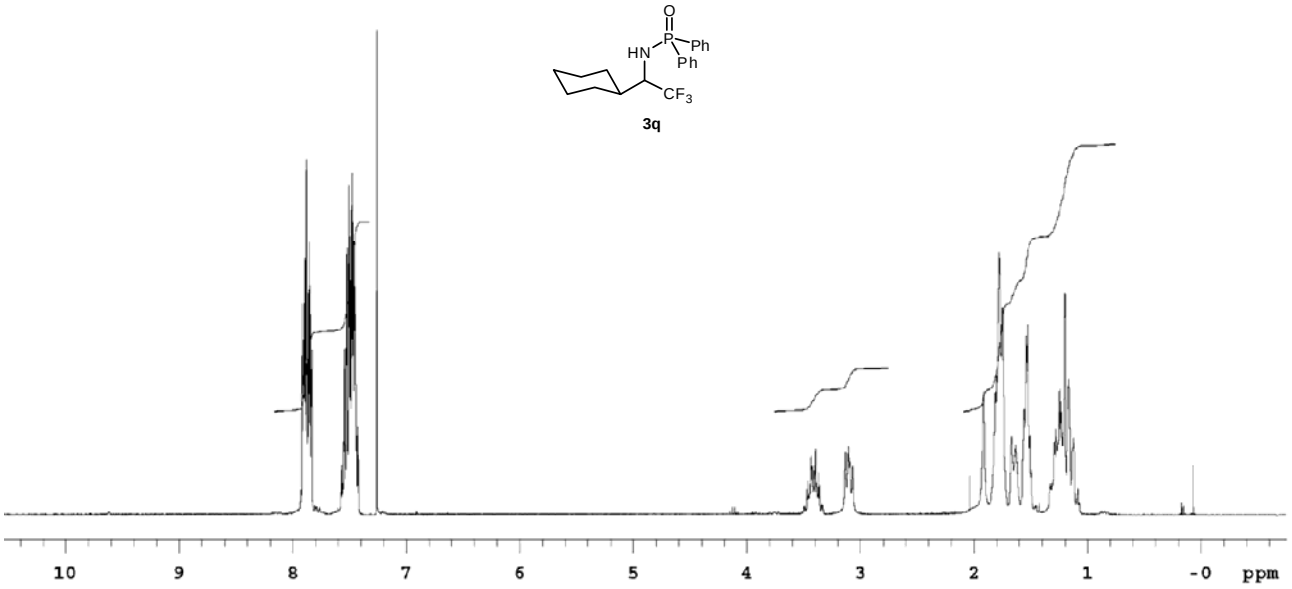
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P
Ph
Ph
CF3
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6
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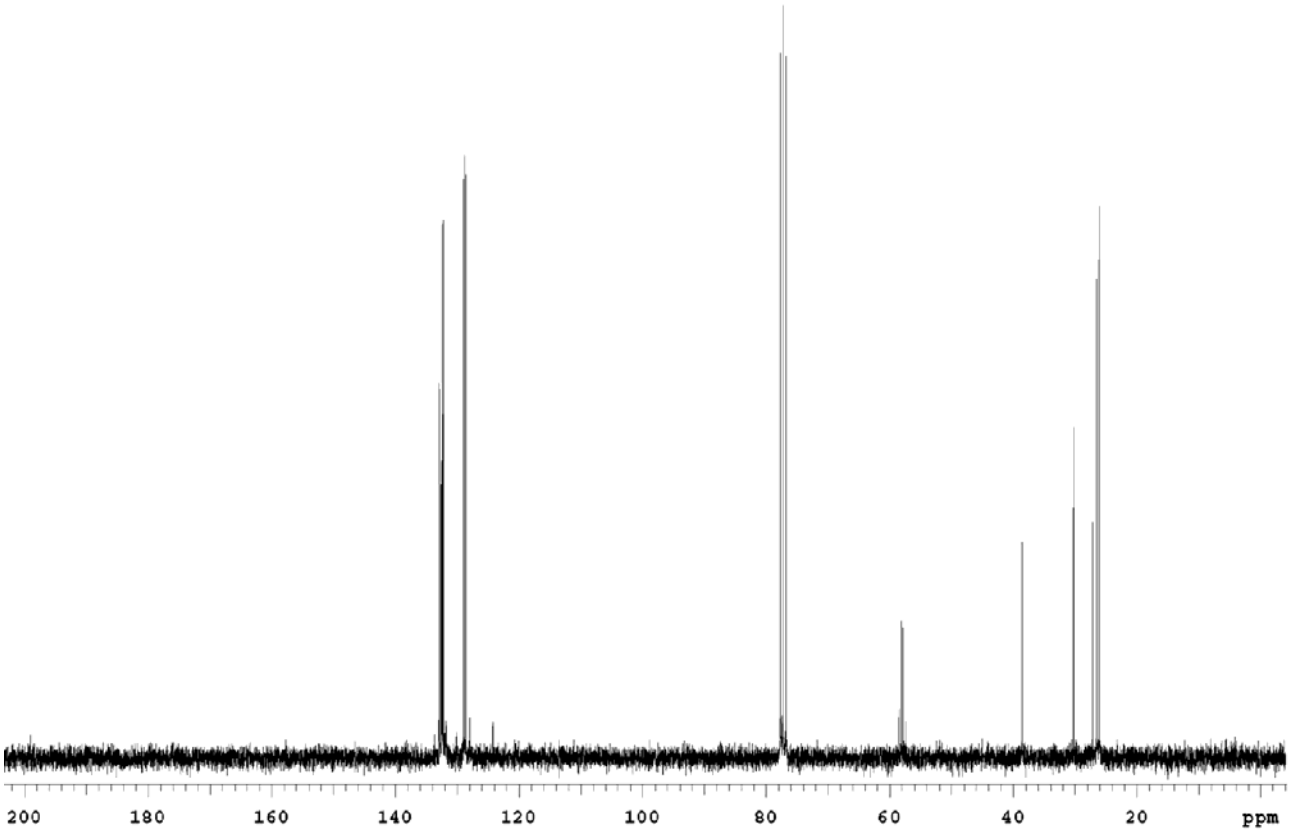
3
2
1
-0
ppm

3q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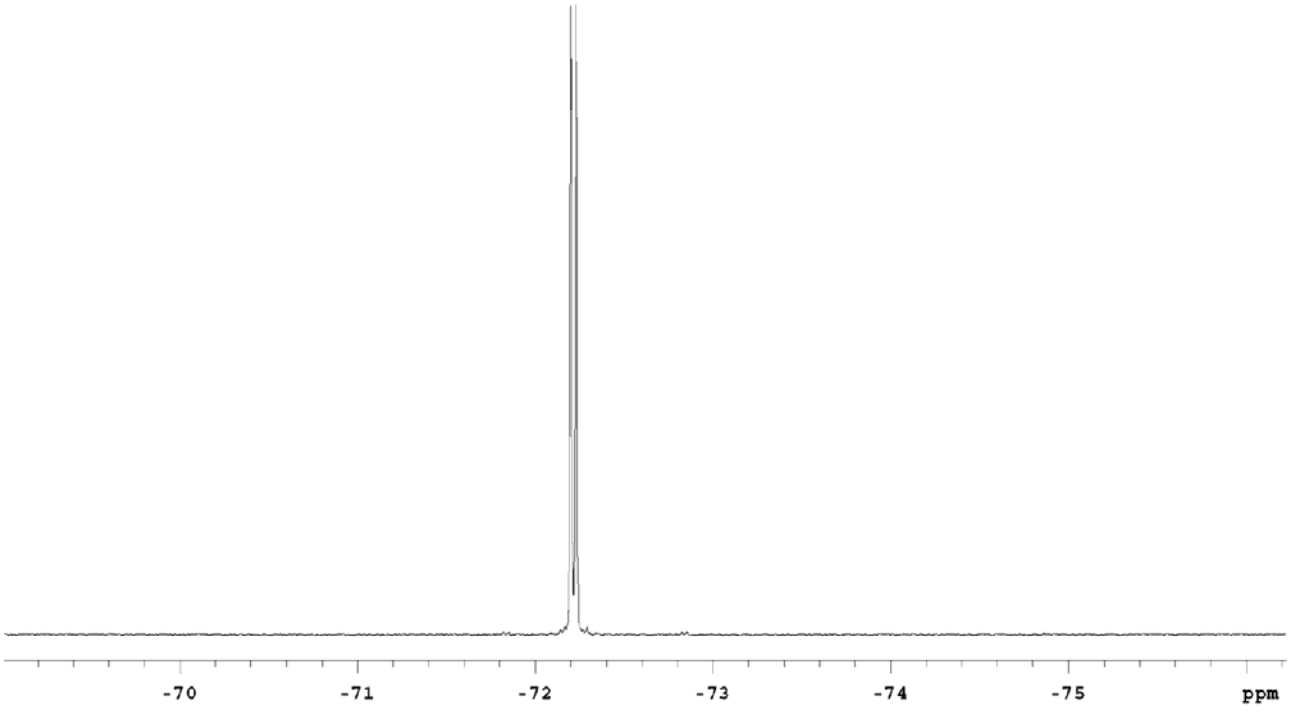
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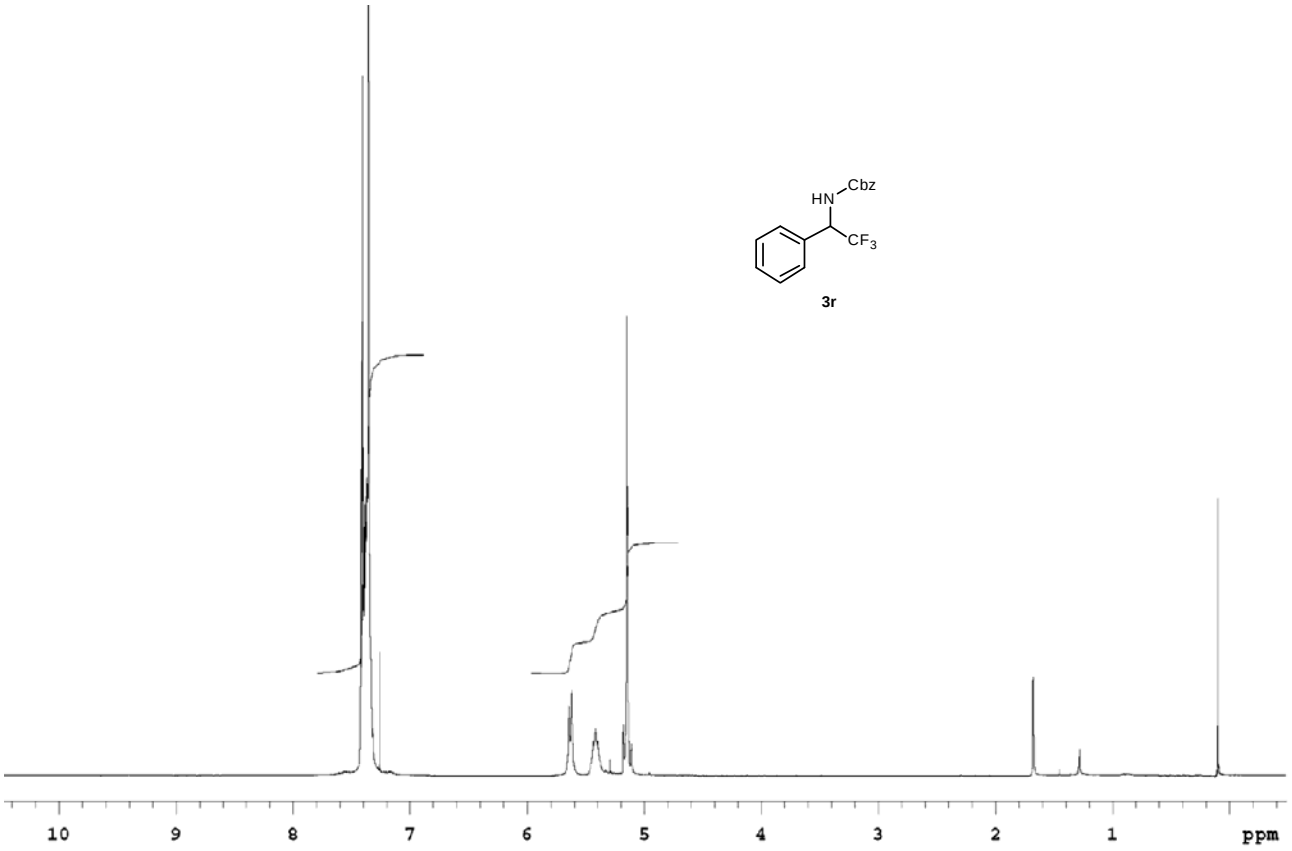

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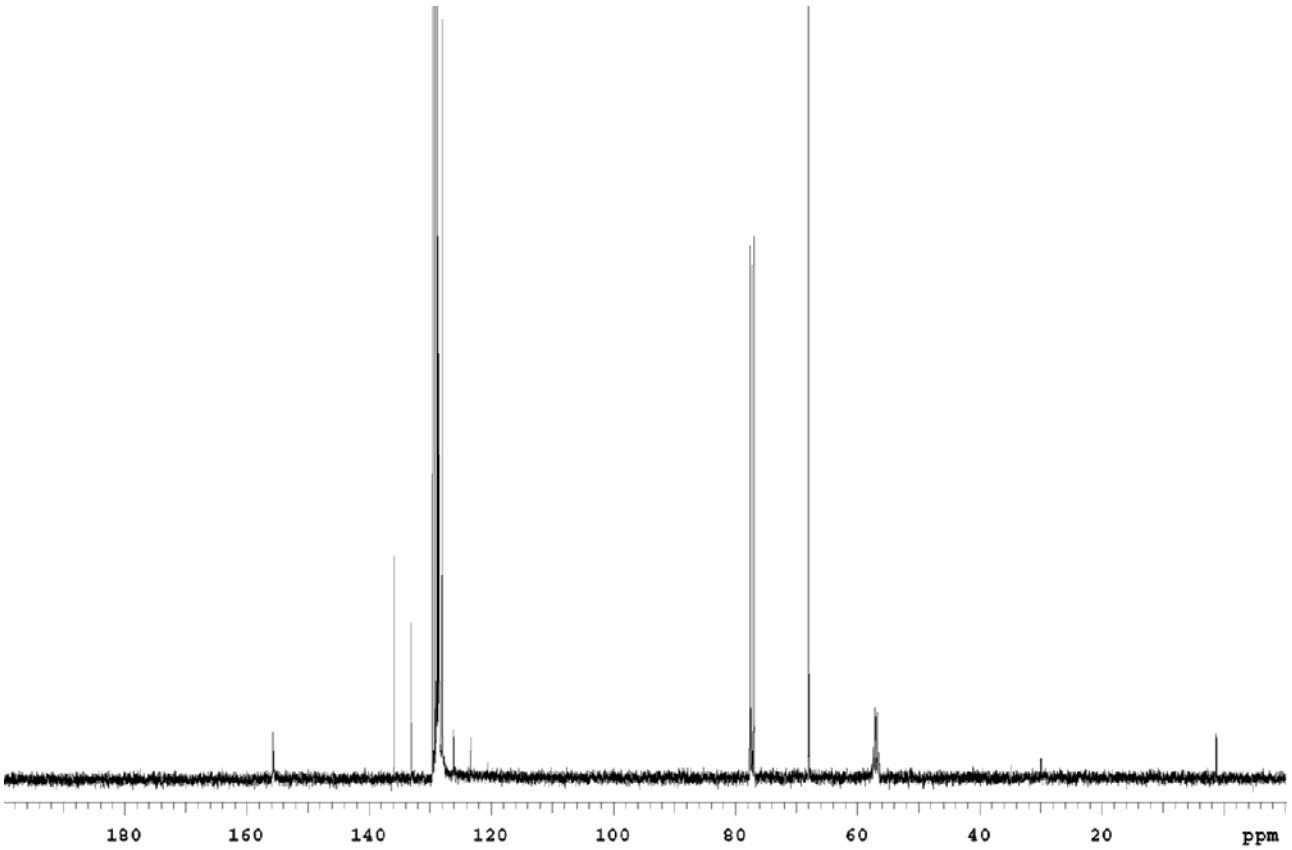

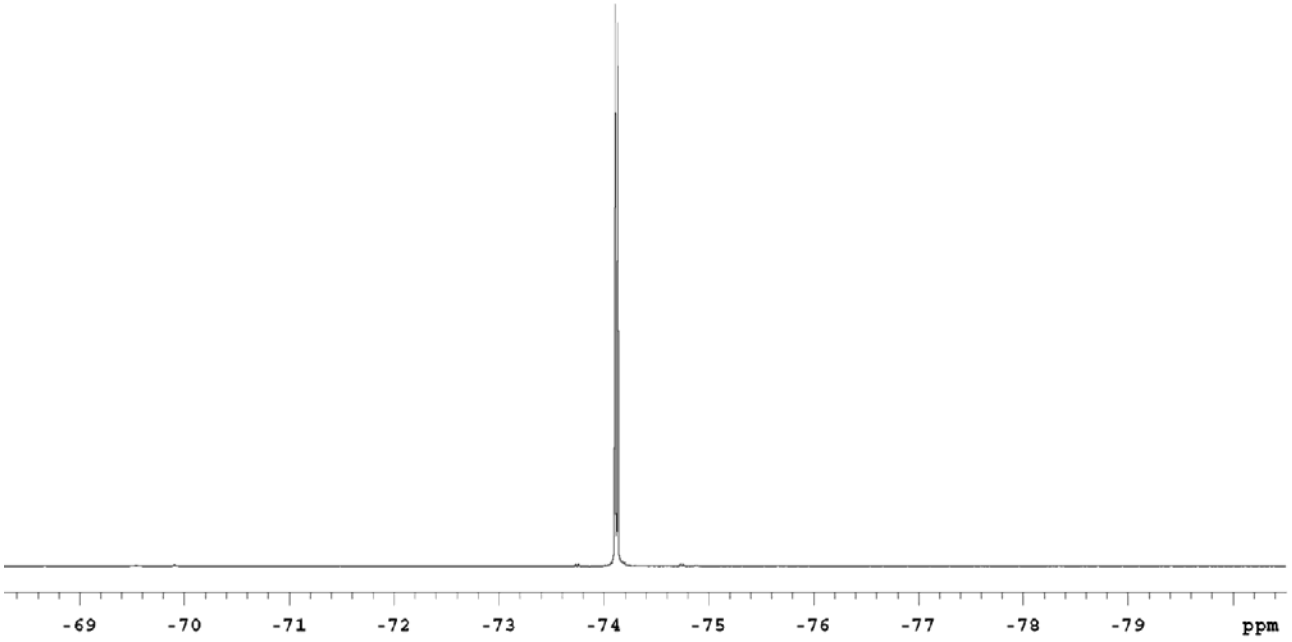
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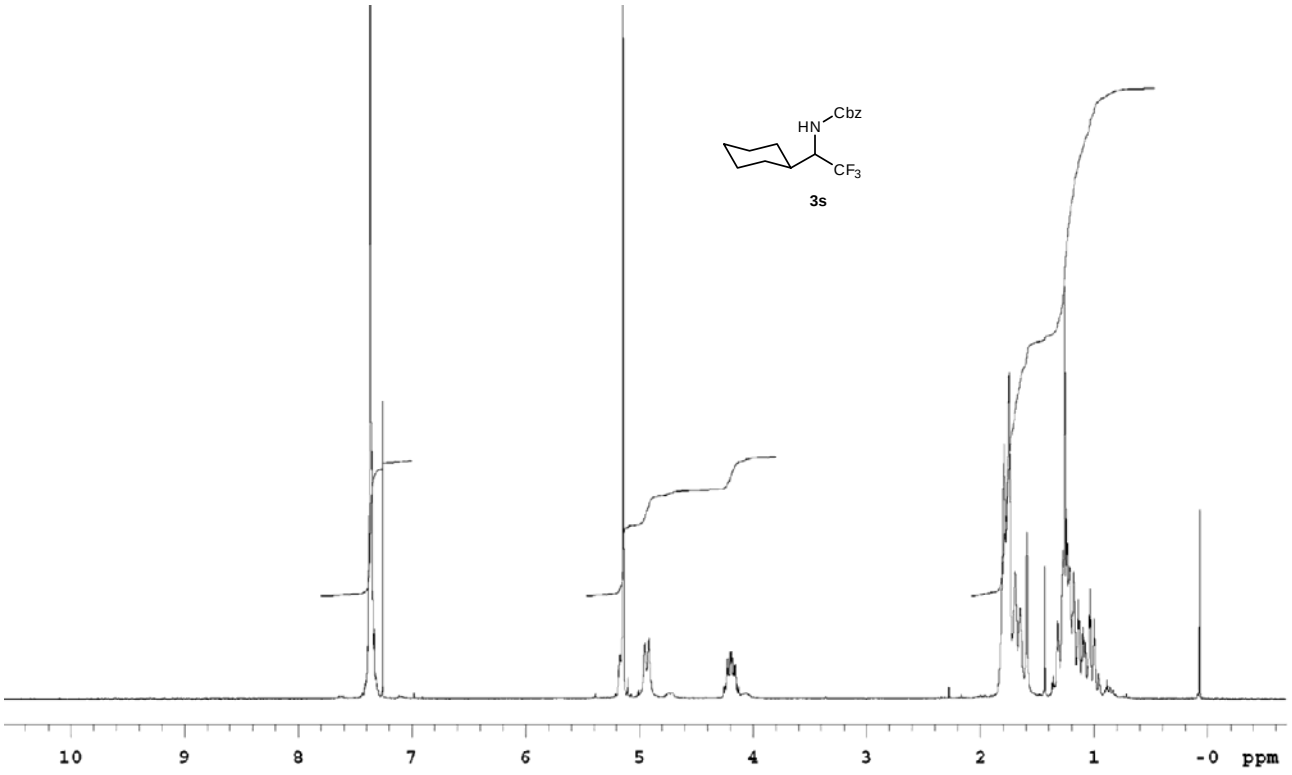
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2
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-0
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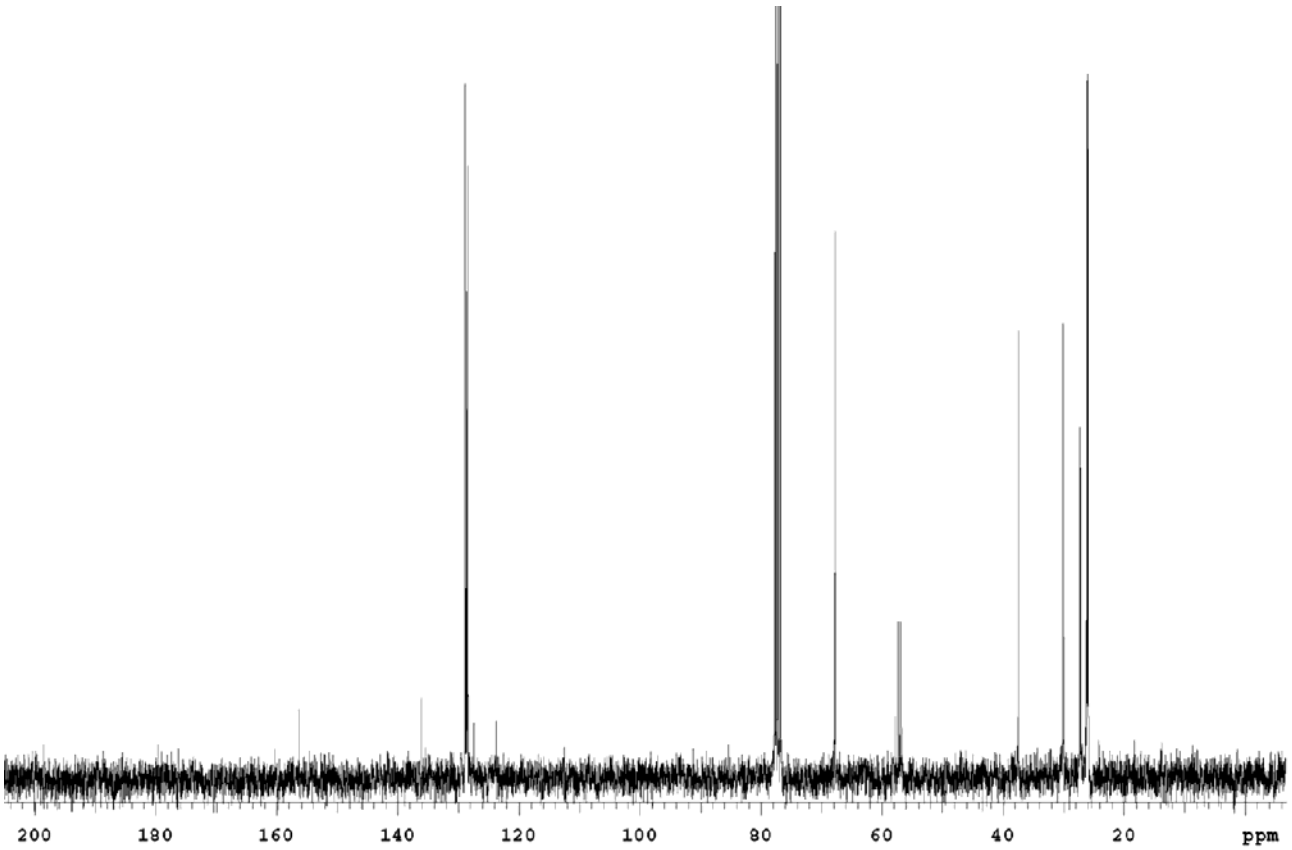
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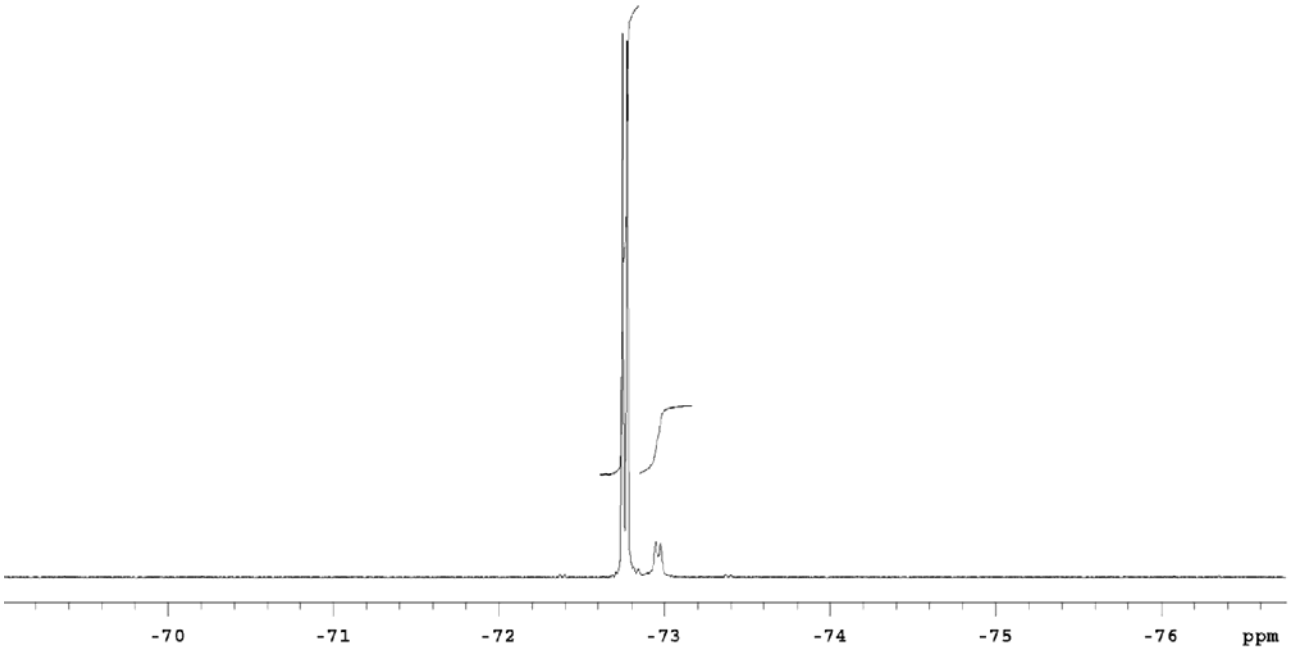
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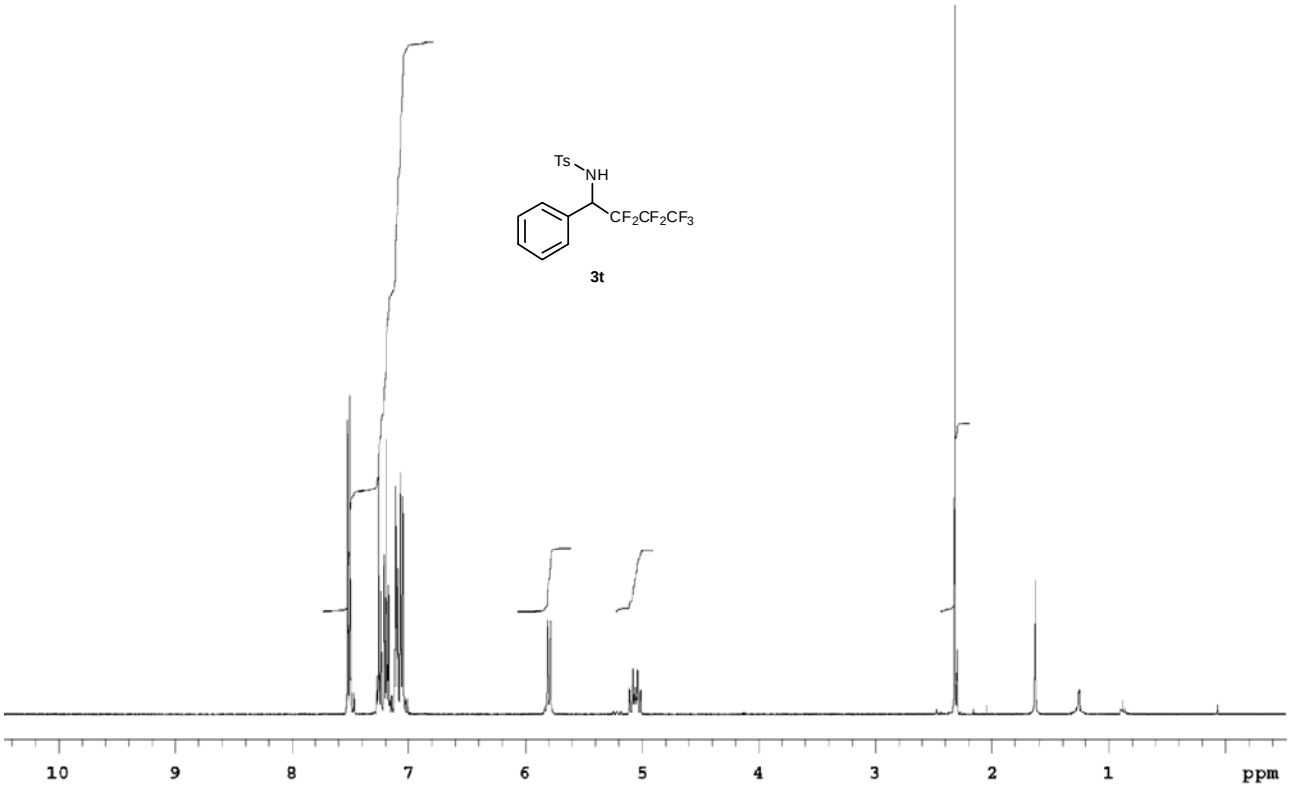
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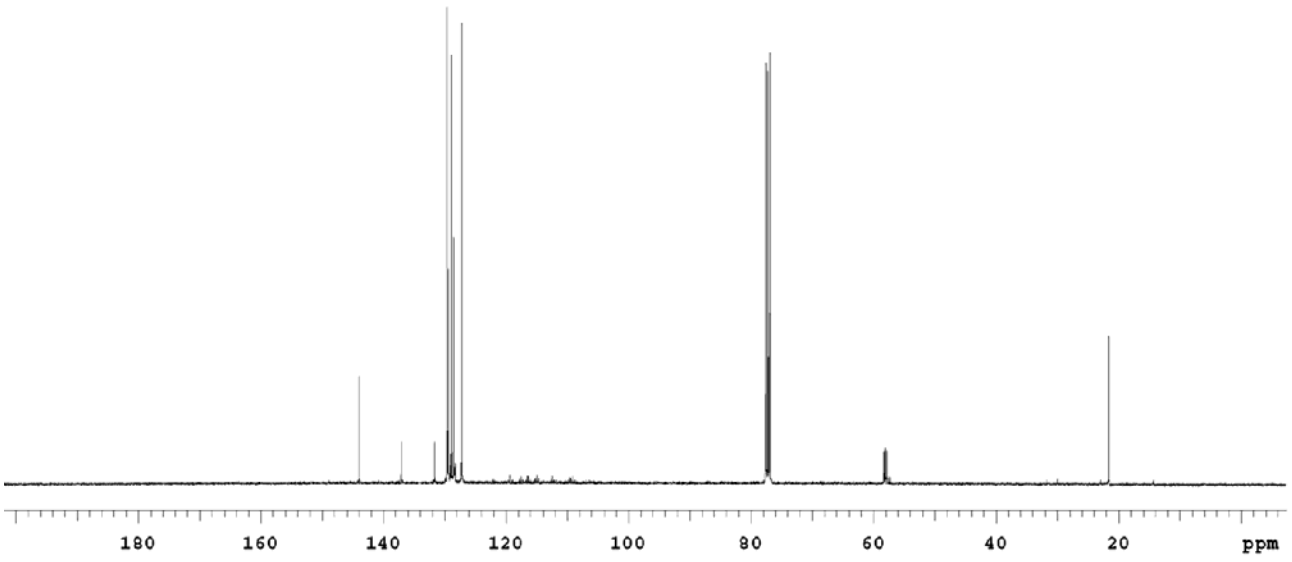
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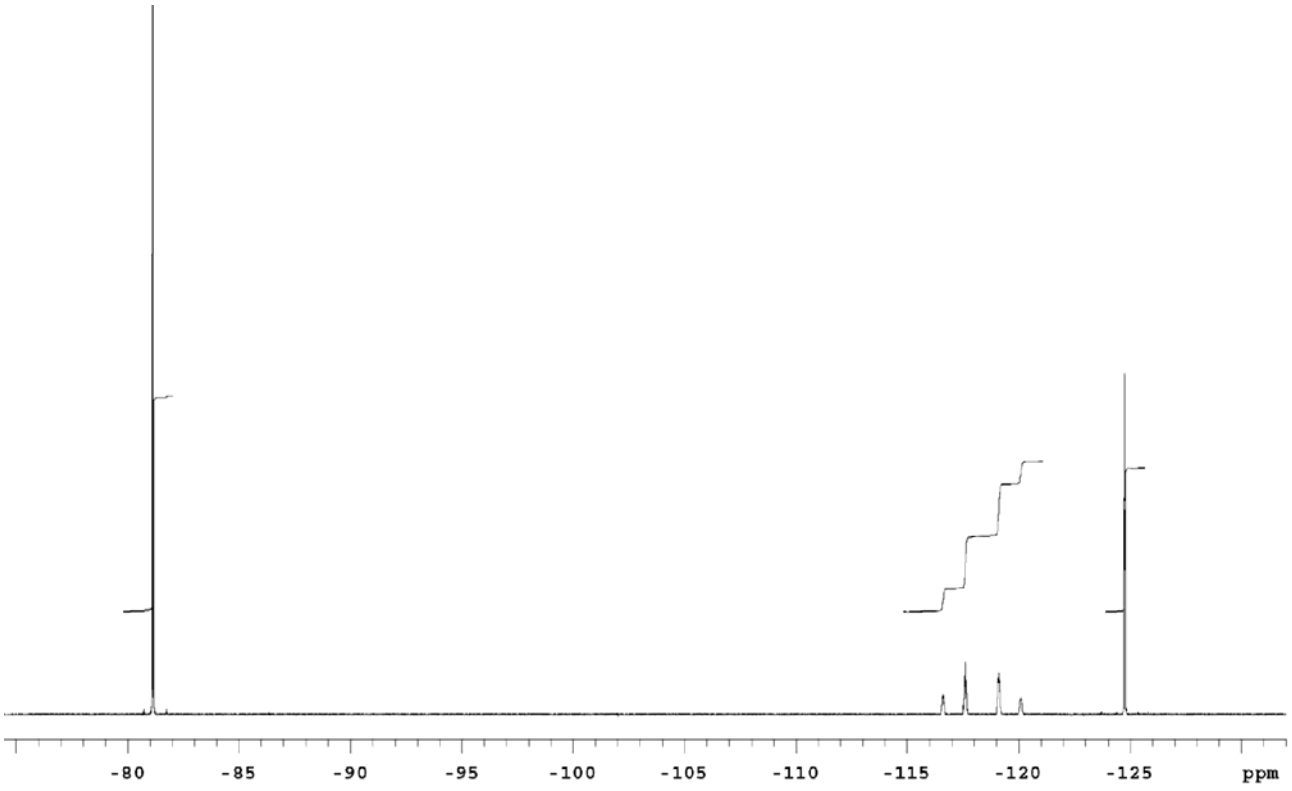
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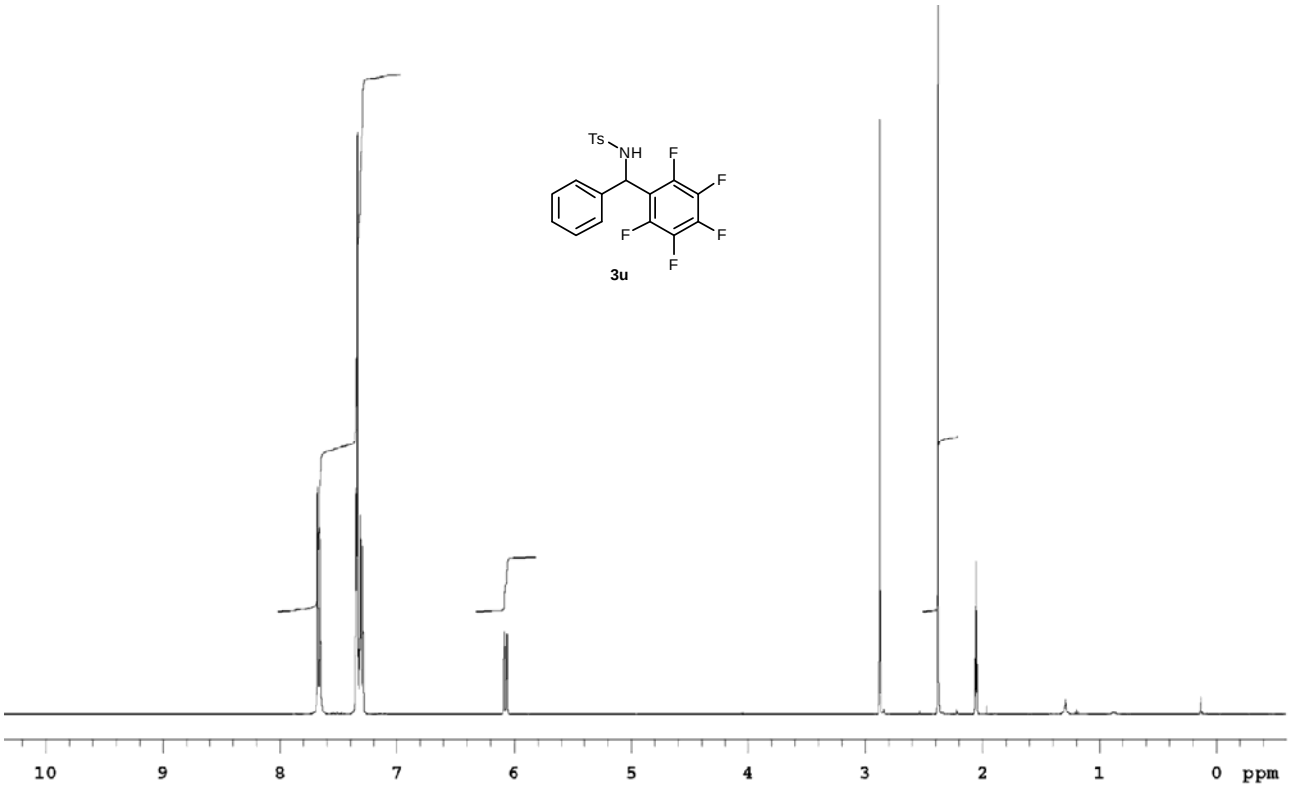
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F
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F
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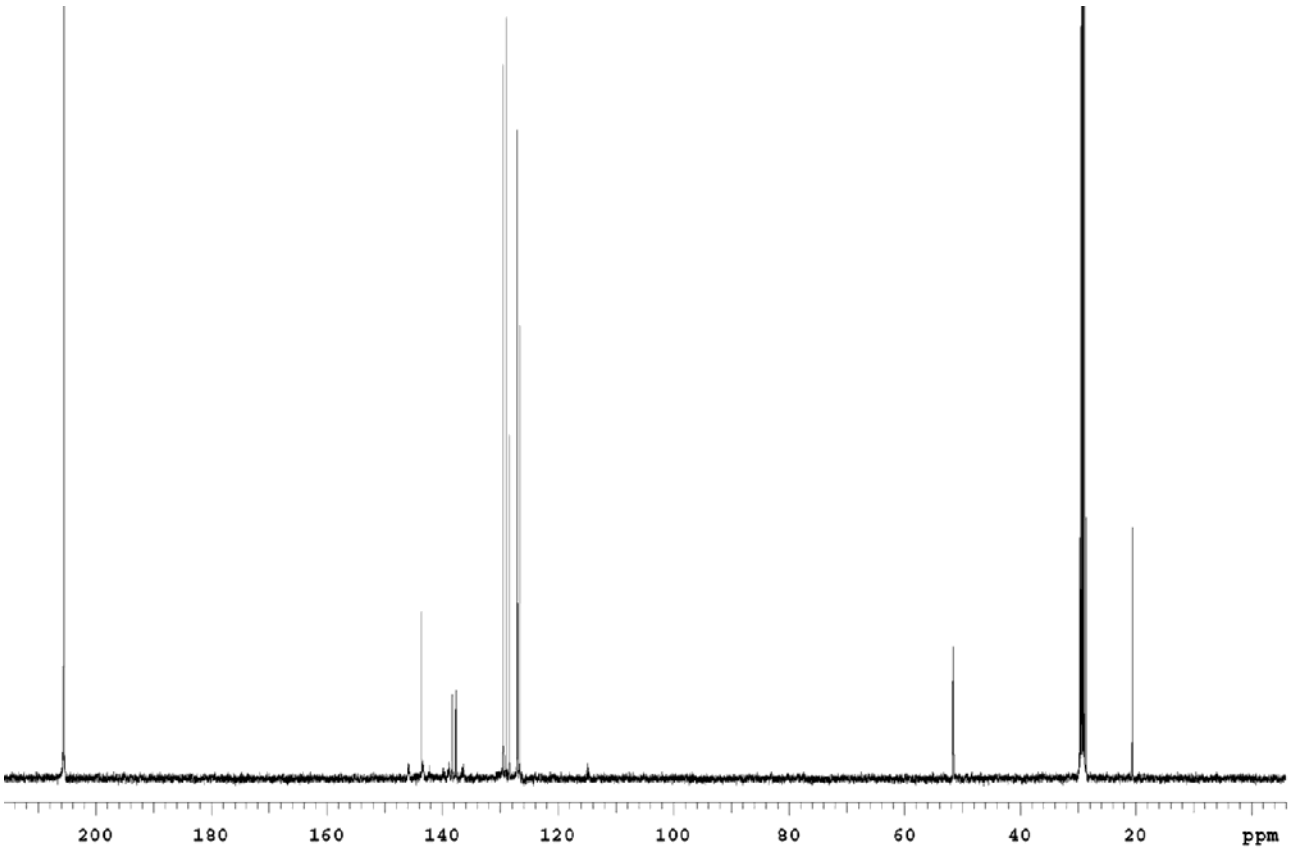
ppm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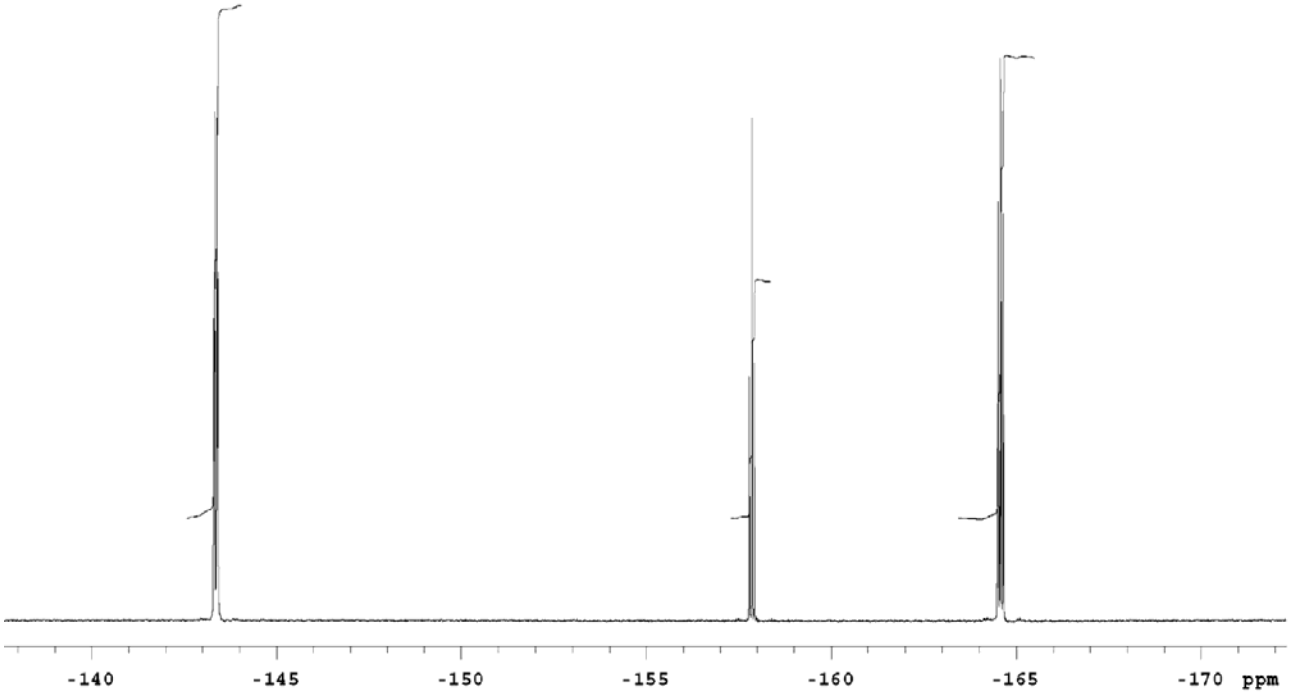

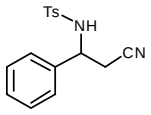

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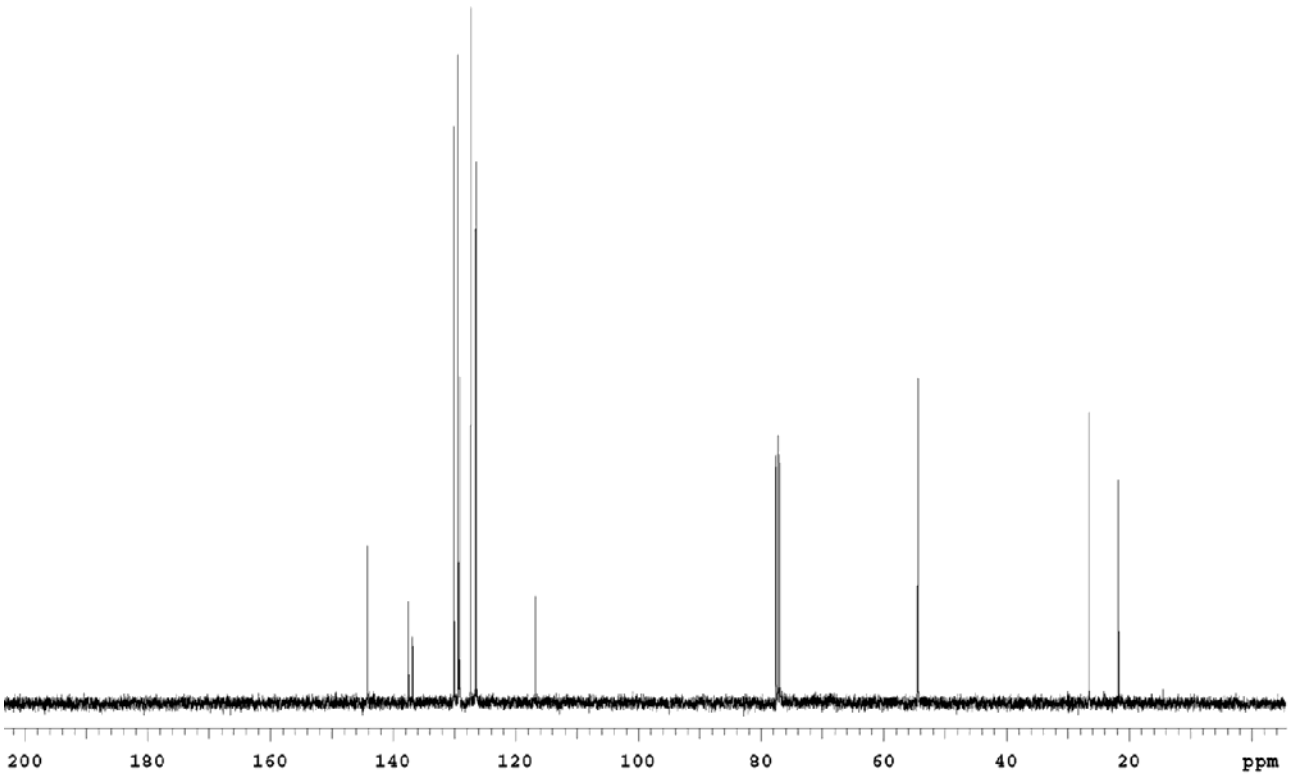

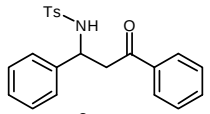
Ts
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O

3w

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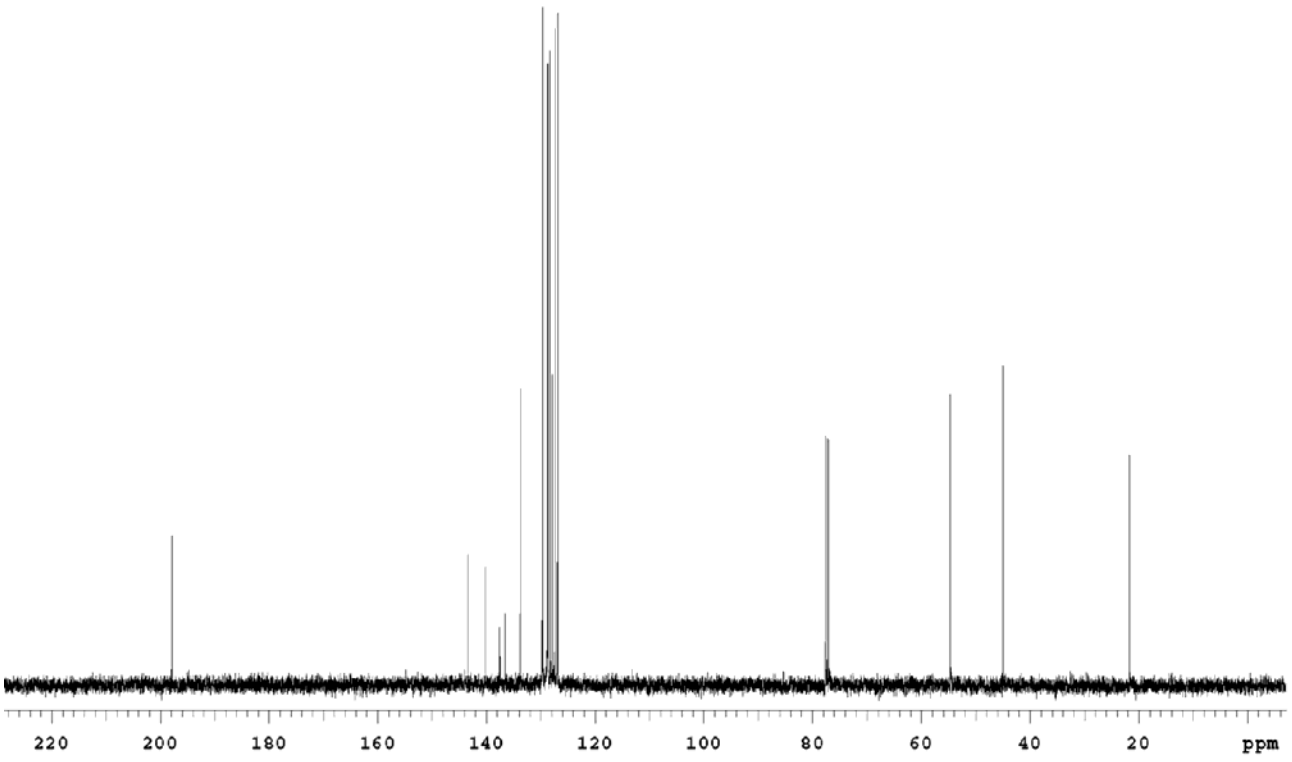
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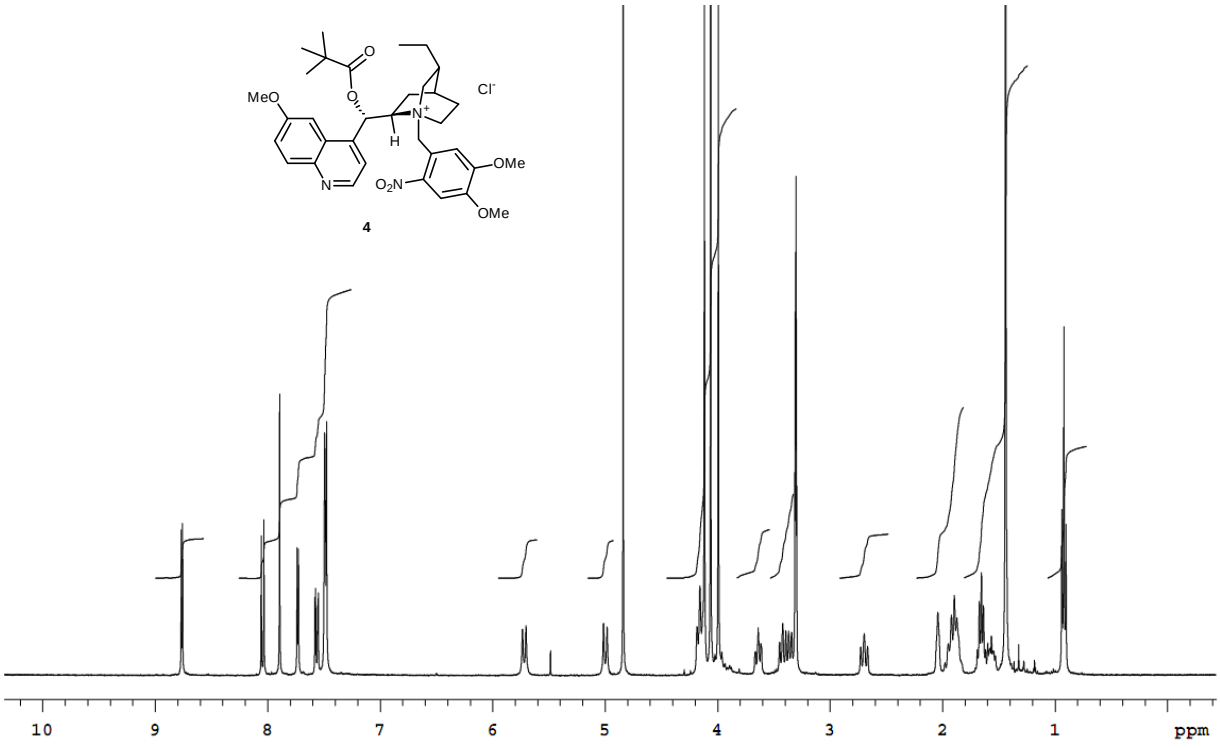
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3
2
1
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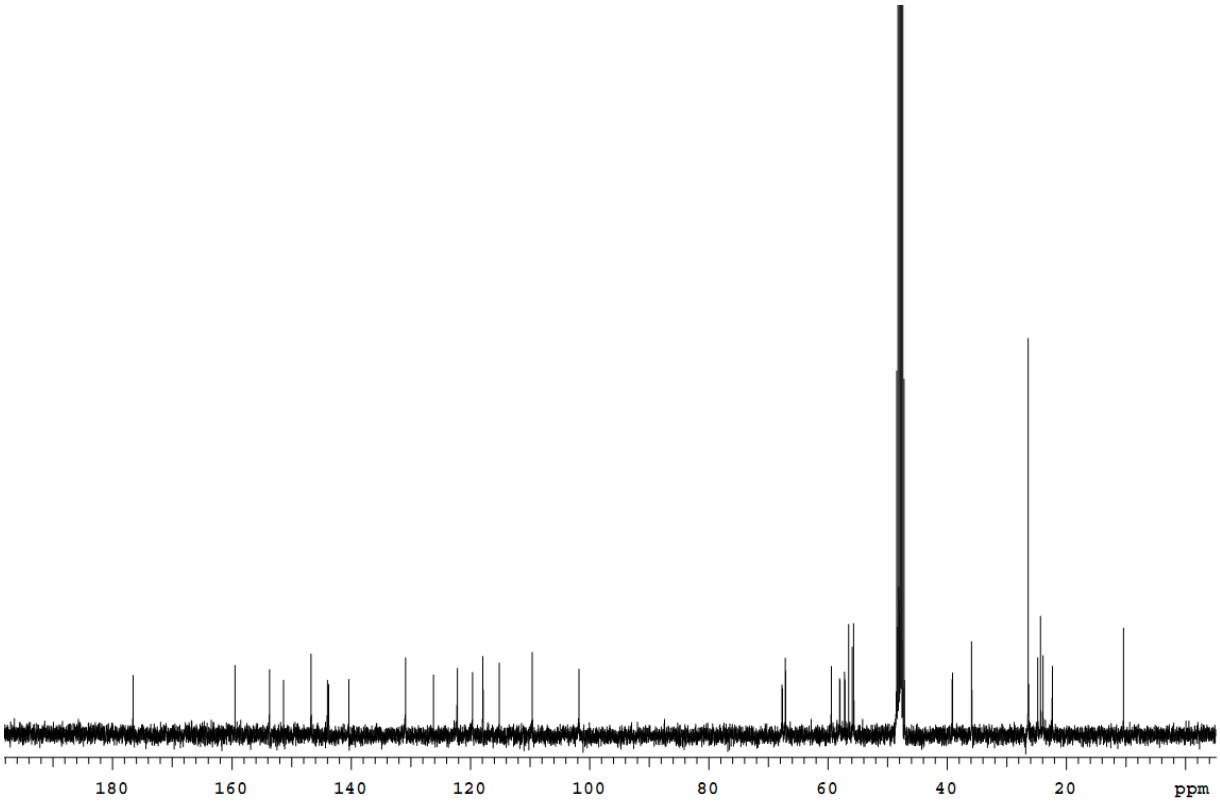
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20
ppm