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Graphical Abstract

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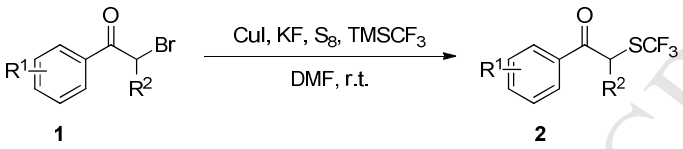

1 **2**

R^2 = H or CH_3

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Copper (I)-Mediated Trifluoromethylthiolation of α-Bromoketone with Element Sulfur and (Trifluoromethyl)trimethylsilane

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[a] *Shanghai Key Laboratory of New Drug Design, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, PR China*
[b] *Shanghai Key Laboratory of Chemical Biology, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, PR China*
[c] *Key Laboyatory of Synthetic Chemistry of Natural Substances, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road,Shanghai 200032, PR China.*

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ABSTRACT

A new method has been developed for the copper (I)-mediated trifluoromethylthiolation of α-bromoketone using commercial anhydrous potassium fluoride, elemental sulfur and (trifluoromethyl)-trimethylsilane in anhydrous *N*, *N*-dimethylformamide. This protocol provides facile access to a variety of α-trifluoromethylthiolated carbonyl compounds in moderate to excellent yields under mild and ligand free conditions.

1. Introduction

Because of the strong electron-withdrawing nature and high hydrophobic domain, the introduction of SCF_3 group into small organic molecules such as pharmaceuticals and agrochemicals could significantly alter their properties including lipophilicity, metabolic stability and bioavailability.[1] Therefore, employing new methods for introduction of trifluoromethylthio group into small organic molecules would be urgently required in synthetic chemistry.

In 1973, Haas firstly reported the synthesis of α-trifluoromethylthiolated kotones starting from ketones using trifluoromethylsulfenyl chloride as the trifluoromethylthiolation reagent.[2] Then, in 1987, Kolasa reported the α-trifluoromethylthiolation of benzoylacetic ethyl esters using trifluoromethylsulfenyl chloride as well.[3] Recently, Shen and Rueping reported the α-trifluoromethylthiolation of β-ketoesters independently to give trifluoromethylthiolated carbonyl compounds with good stero-selectivity.[4] Zard group reported a new trifluoromethylthiolation reagent, *O*-octadecyl-*S*-trifluorothiolcarbonate, which could be prepared in two steps from trifluoroacetic anhydride and sodium *O*-octadecyl-dithiocarbonate. This reagent reacts directly with α-bromoketones in the presence of potassium fluoride and pyrrolidine to give the corresponding trifluoromethyl sulfides in generally high yields.[5] In addition, Weng group reported a copper-catalyzed α-trifluoromethylthiolation of α-bromoketones using 1,10-phen as a ligand and S_8/$TMSCF_3$ as a SCF_3source.[6]

The above mentioned methods have the issues of either using toxic and unstable trifluoromethylthiolation reagents or being longer reaction time. In the current research, a method for trifluoromethylthiolation of α-bromoketones was developed under a mild and ligand free condition in a relatively short time to give the corresponding trifluoromethyl sulfides in moderate to excellent yields.

2. Results/Discussion

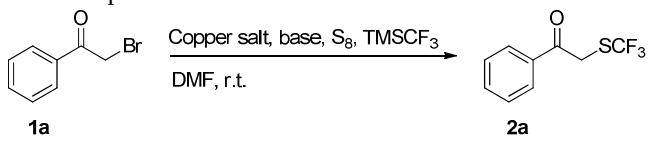
Previously, our research group reported the new trifluoromethylthiolation method of allylic halides.[7] It was found when α-bromoacetophenone was subjected to the same condition, the corresponding α-trifluoromethylthioacetophenone was obtained in 28.7 % yield. Encouraged by this result, a series of copper salts were screened in which CuI gave the best result (Table 1, Entry 3). Additional screening of bases indicated that replacement of KF with K_2CO_3, Na_2CO_3, Et_3N or DBU could not let this reaction happen and using CsF only gave the product in

∗ Corresponding author. Tel.: +0-021-642-52199; e-mail: renjm@ecust.edu.cn

∗ Corresponding author. Tel.: +0-021-642-53689; e-mail: zengbb@ ecust.edu.cn

8.0% yield. It was noteworthy that when the reaction was conducted in the absence of CuI, the yield was quite low (Table 1, Entry 9). Furthermore, no product was observed without KF which indicated that this base was essential for the reaction (Table 1, Entry 10). Following on these preliminary results, the molar equivalency of CuI and KF was investigated. The results indicated that changing the molar equivalency of CuI and KF would cause the decline of the yields.

Table 1. Optimization of reaction conditions[a]



1a **2a**

Entry	Cu salt (equiv.)	Base (equiv.)	Yield (%)[b]
1	CuSCN (0.5)	KF (4.0)	28.7
2	CuCl (0.5)	KF (4.0)	73.7
3	**CuI (0.5)**	**KF (4.0)**	**92.5**
4	CuBr (0.5)	KF (4.0)	58.9
5	$CuCl_2$(0.5)	KF (4.0)	16.1
6	$Cu(OAc)_2$ (0.5)	KF (4.0)	51.0
7	Cu (0.5)	KF (4.0)	23.9
8	CuI (0.5)	CsF (4.0)	8.0
9	-	KF (4.0)	28.4
10	CuI (0.5)	-	NR[c]
11	CuI (0.1)	KF (4.0)	38.7
12	CuI (0.2)	KF (4.0)	64.6
13	CuI (0.3)	KF (4.0)	76.3
14	CuI (1.0)	KF (4.0)	trace
15	CuI (0.5)	KF (3.0)	79.2
16	CuI (0.5)	KF (2.0)	75.2

[a] Reaction conditions: **1a** (2.0 mmol), copper salt, base, S_8 (6.0 mmol) and $TMSCF_3$ (6.0 mmol) in anhydrous DMF under N_2 at room temperature.

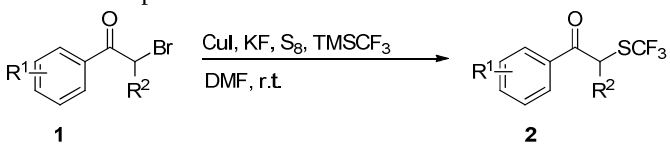
[b] Isolated yield.

[c] NR = No reaction.

Based on these, 0.5 equiv. of CuI and 4.0 equiv. of KF would be the optimal conditions.

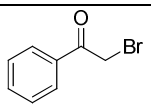
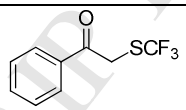
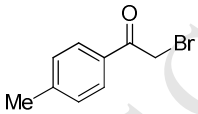
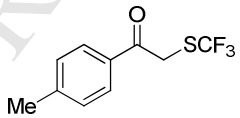
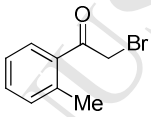
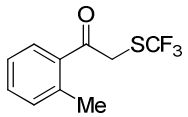
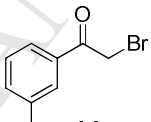
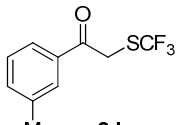
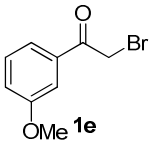
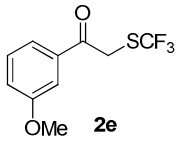
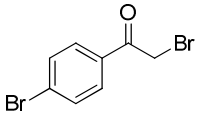
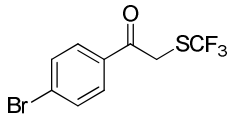
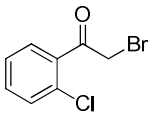
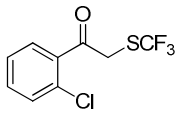
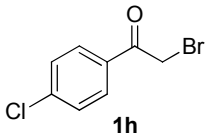
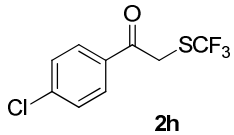
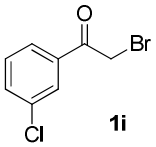
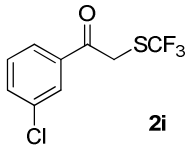
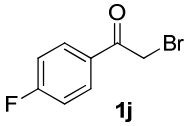
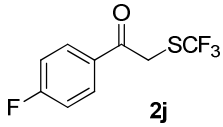
With the optimal condition in hand, the research was extent further to investigate the substrate scope of this reaction. Firstly, a series of *α*-bromoketones with different substituents at various positions of the phenyl ring were investigated. The results declared that both steric hindrance and electron density had an impact on the reaction. On the one hand, from the perspective view of steric hindrance, any *para*-substituent substrate gave the highest yield while the *ortho*-substituent substrate gave the lowest (Entries 2 and 3). On the other hand, from the perspective view of electron density, compounds bearing electron-donating group (Entries 2-4) gave higher yields than those bearing electron-withdrawing ones at the same position (Entries 7-9). Obviously, only 60.6 % of the product was obtained from substrate **1c** and even no product was detected with substrate **1g** (Table 2, Entries 3 and 7). It is noteworthy that, compounds with strong electron-withdrawing substituents gave the corresponding products in an extremely low yield or even failed to react (Entries 11 and 13). This condition equally applied to *α*-bromopropiophenones to give corresponding trifluoromethylthiolated products in moderate to good yields (Entries 14-16). *α*-Bromoacetonaphthone **1q** could also reacted smoothly under the optimized condition to give the desired product **2q** in 79.8 % yield (Entry 17). Similarly, the optimized condition could also work on the aliphatic alkane **1r** to give the corresponding product in 65.6 % yield (Entry 18).

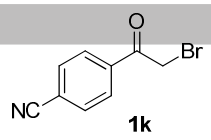
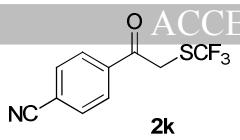
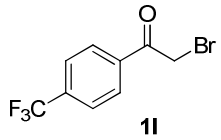
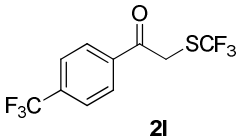
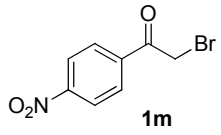
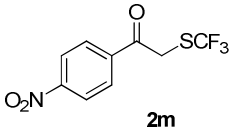
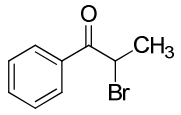
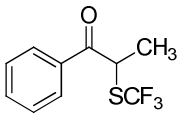
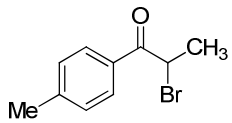
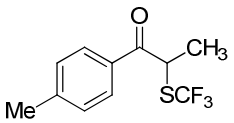
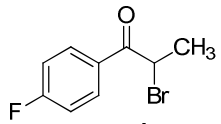
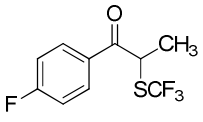
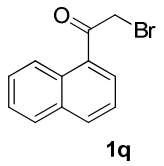
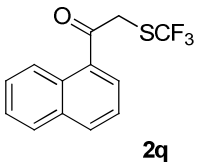
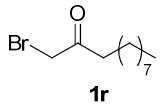
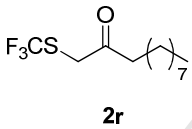
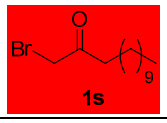
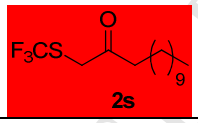
Table 2. Scope of different substrates[a]



1 **2**

R^2 = H or CH_3

Entry	Substrate	Product	Yield(%)[b]
1	 **1a**	 **2a**	92.5
2	 **1b**	 **2b**	83.2
3	 **1c**	 **2c**	60.6
4	 **1d**	 **2d**	70.2
5	 **1e**	 **2e**	78.0
6	 **1f**	 **2f**	66.2
7	 **1g**	 **2g**	ND[c]
8	 **1h**	 **2h**	67.3
9	 **1i**	 **2i**	52.9
10	 **1j**	 **2j**	72.0

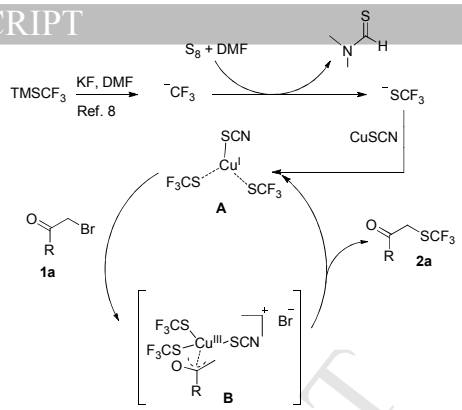
11	 **1k**	 **2k**	16.4
12	 **1l**	 **2l**	62.5
13	 **1m**	 **2m**	ND[c]
14	 **1n**	 **2n**	77.4
15	 **1o**	 **2o**	80.2
16	 **1p**	 **2p**	62.5
17	 **1q**	 **2q**	79.8
18	 **1r**	 **2r**	65.6
19	 **1s**	 **2s**	70.3

[a] Reaction conditions: 1 (2.0 mmol), CuI (1.0 mmol), KF (8.0 mmol), S_8 (6.0 mmol) and $TMSCF_3$ (6.0 mmol) in anhydrous DMF under N_2 at room temperature.

[b] Isolated yield.

[c] ND = Not detected.

Based on the previous research work,[7] a reaction mechanism was proposed as below (Scheme 1). Firstly, $TMSCF_3$ was converted to an active SCF_3 anion in the presence of KF, S_8 and DMF, which was then reacted with CuSCN to give copper (I) complex **A**. Then, substrate **1a** reacted with the resulting copper (I) complex to give a copper (III) complex **B** which then reacted to give product **2a** together with complex **A** to complete the reaction circle.



Scheme1. Proposed Mechanism

3. Conclusion

In conclusion, an efficient and convenient method for the synthesis of a series of *α*-trifluoromethylthioketones was developed. This protocol proceeds without any ligand under a mild condition and short reaction time to expressly provide the corresponding products in moderate to excellent yields. Notably, all the reagents used in the reaction are inexpensive and nontoxic.

4. Experimental section

4.1. General

Unless stated otherwise, all reagents and solvents were obtained from commercial sources without purification. Column chromatography was carried out on silica gel (200-300 μm). Melting points were determined using a digital melting-point apparatus and are uncorrected. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a spectrometer (400 MHz, 100 MHz and 376 MHz or 500 MHz, 125 MHz and 470 MHz) using TMS as internal standard. HRMS data were determined by EI ionization.

General Procedure: To an oven-dried Schlenk flask were charged with CuI (0.5 eq.), anhydrous KF (4.0 eq.) and S_8 (3.0 eq.) under N_2. Then, the solution of substrate (2.0 mmol) in DMF(12 mL) and $TMSCF_3$ (0.9 mL 3.0 eq.) were added successively via syringe. After that, the reaction mixture was stirred at room temperature for 10 min. Water was added and the mixture was filtered through celite. The resulting filtrate was extracted three times with ethyl acetate, and the combined organic layers were washed with water and dried over anhydrous sodium sulfate. The solvent was removed by rotary evaporation and the residue was purified by column chromatography on silica gel with petroleum ether and ethyl acetate.

*4.2. 1-Phenyl-2-((trifluoromethyl)thio)ethanone (**2a**)*

Colorless oil, yield 92.5 %; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 8.0, 1.4 Hz, 2H), 7.64 (tt, *J* = 8.0, 1.4 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 2H), 4.52 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.0, 134.7, 134.3, 130.7 (q, J_{C-F} = 304.4 Hz), 129.0,128.4, 38.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -41.44 (s, 3F). HRMS (EI) calcd. for $C_9H_7F_3OS$: 220.0170, found 220.0135.

*4.3. 1-(p-Tolyl)-2-((trifluoromethyl)thio)ethanone (**2b**)*

Yellow oil, yield 83.2 %; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 4.49 (s, 2H), 2.43 (s,

3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.6, 145.4, 132.2, 130.8 (q, J_{C-F} = 304.5 Hz), 129.7, 128.5, 38.4 (q, J_{C-F} = 1.8 Hz), 21.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -41.45 (s, 3F). HRMS (EI) calcd. for $C_{10}H_9F_3OS$: 234.0326, found 234.0329.

*4.4. 1-(o-Tolyl)-2-((trifluoromethyl)thio)ethanone (**2c**)*

Yellow oil, yield 60.6 %; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (dd, *J* = 6.8, 1.6 Hz, 1H), 7.45 (td, *J* = 7.6, 1.2 Hz, 1H), 7.31 (t, *J* = 6.8 Hz, 2H), 4.46 (s, 2H), 2.54 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.8, 139.8, 134.6, 132.7, 132.6, 130.7 (q, J_{C-F} = 304.4 Hz), 129.1, 126.0, 40.4, 21.6; ^{19}F NMR (470 MHz, $CDCl_3$) δ -41.36 (s, 3F); HRMS (EI) calcd. for $C_{10}H_9F_3OS$: 234.0326, found 234.0327.

*4.5. 1-(m-Tolyl)-2-((trifluoromethyl)thio)ethanone (**2d**)*

Yellow oil, yield 70.2 %; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 1H), 4.51 (s, 2H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.2, 139.0, 135.1, 134.8, 130.7 (q, J_{C-F} = 304.6 Hz), 128.9, 128.8, 125.6, 38.5, 21.3; ^{19}F NMR (470 MHz, $CDCl_3$) δ -41.41 (s, 3F); HRMS (EI) calcd. for $C_{10}H_9F_3OS$: 234.0326, found 234.0325.

*4.6. 1-(3-Methoxyphenyl)-2-((trifluoromethyl)thio)ethanone (**2e**)*

Colorless oil, yield 78.0 %; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.48 (m, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.18 (ddd, *J* = 8.0, 2.4, 1.0 Hz, 1H), 4.51 (s, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.8, 160.1, 136.0, 130.7 (q, J_{C-F} = 304.3 Hz), 130.0, 121.0, 120.7, 112.7, 55.5, 38.4 (q, J_{C-F} = 1.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -41.43 (s, 3F). HRMS (EI) calcd. for $C_{10}H_9F_3O_2S$: 250.0275, found 250.0276.

*4.7. 1-(4-Bromophenyl)-2-((trifluoromethyl)thio)ethanone (**2f**)*

Yellow oil, yield 66.2 %; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dt, *J* = 8.8, 2.0 Hz, 2H), 7.66 (dt, *J* = 8.8, 2.0 Hz, 2H), 4.46 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.1, 133.4, 132.4, 130.5 (q, J_{C-F} = 304.7 Hz), 129.9, 129.7, 38.1 (q, J_{C-F} = 1.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -41.41 (s, 3F). HRMS (EI) calcd. for $C_9H_6BrF_3OS$: 297.9275, found 297.9270.

*4.9. 1-(4-Chlorophenyl)-2-((trifluoromethyl)thio)ethanone (**2h**)*

Yellow oil, yield 67.3 %; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 4.48 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.9, 140.9, 133.0, 130.6 (q, J_{C-F} = 304.7 Hz), 129.8, 129.4, 38.2 (q, J_{C-F} = 1.9 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ -41.42 (s,3F). HRMS (EI) calcd. for $C_9H_6ClF_3OS$: 253.9780, found 253.9777.

*4.10. 1-(3-Chlorophenyl)-2-((trifluoromethyl)thio)ethanone (**2i**)*

Yellow oil, yield 52.9 %; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 4.48 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.9, 136.2, 135.4, 134.2, 130.5 (q, J_{C-F} = 304.8), 130.3, 128.4, 126.5, 38.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -41.43 (s, 3F). HRMS (EI) calcd. for $C_9H_6ClF_3OS$: 253.9780, found 253.9781.

*4.11. 1-(4-Fluorophenyl)-2-((trifluoromethyl)thio)ethanone (**2j**)*

Colorless oil, yield 72.0 %; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (m, 2H), 7.19 (m, 2H), 4.49 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.5, 167.7, 165.1, 131.3, 131.2, 130.6 (q, J_{C-F} = 304.7), 116.4, 116.1, 38.2 (q, J_{C-F} = 1.6Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -41.43 (s, 3F). HRMS (EI) calcd. for $C_9H_6F_4OS$: 238.0075, found 238.0076.

*4.12. 4-(2-((Trifluoromethyl)thio)acetyl)benzonitrile (**2k**)*

Yellow oil, yield 16.4 %; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.4 Hz, 2H), 7.83 (d, *J* = 8.4 Hz, 2H), 4.50 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ190.9, 137.5, 132.8, 130.3 (q, J_{C-F} = 305.0 Hz), 128.9, 117.6, 117.5, 38.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ -41.37 (s, 3F); HRMS (EI) calcd. for $C_{10}H_6F_3NOS$: 245.0122, found 245.0121.

*4.13. 1-(4-(Trifluoromethyl)phenyl)-2-((trifluoromethyl)thio)-ethanone (**2l**)*

Colorless oil, yield 62.5 %; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.2 Hz, 2H), 7.78 (d, *J* = 8.2 Hz, 2H), 4.52 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.3, 137.3, 135.5 (q, J_{C-F} = 32.7 Hz), 130.4 (q, J_{C-F} = 304.8 Hz), 128.8, 126.1 (q, J_{C-F} = 3.6 Hz), 123.3 (q, J_{C-F} = 271.2 Hz), 38.2 (q, J_{C-F} = 1.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -41.46 (s, 3F), -63.35 (s, 3F). HRMS (EI) calcd. for $C_{10}H_6F_6OS$: 288.0044, found 288.0046.

*4.15. 1-Phenyl-2-((trifluoromethyl)thio)propan-1-one (**2n**)*

Colorless oil, yield 77.4 %; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.6 Hz, 2H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 4.99 (q, *J* = 7.0 Hz, 1H), 1.73 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.3, 134.1, 134.0, 133.7, 130.8 (q, J_{C-F} = 305.4 Hz), 129.0, 128.7, 44.5 (q, J_{C-F} = 0.9 Hz), 41.5; ^{19}F NMR (470 MHz, $CDCl_3$) δ -39.78 (s, 3F). HRMS (EI) calcd. for $C_{10}H_9F_3OS$: 234.0326, found 234.0327.

*4.16. 1-(p-Tolyl)-2-((trifluoromethyl)thio)propan-1-one (**2o**)*

Colorless oil, yield 80.2 %; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.5 Hz, 2H), 7.31 (d, *J* = 8.5 Hz, 2H), 4.97 (q, *J* = 7.2 Hz, 1H), 2.44 (s, 3H), 1.71 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.9, 145.2, 131.4, 130.8 (q, J_{C-F} = 305.1), 129.7, 128.9, 44.5, 21.7, 19.9; ^{19}F NMR (470 MHz, $CDCl_3$) δ -39.81 (s, 3F); HRMS (EI) calcd. for $C_{11}H_{11}F_3OS$: 248.0483, found 248.0481.

*4.17. 1-(4-Fluorophenyl)-2-((trifluoromethyl)thio)propan-1-one (**2p**)*

Colorless oil, yield 62.5 %; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (m, 2H), 7.19 (m, 2H), 4.92 (q, J_{C-F} = 7.0 Hz, 1H), 1.72 (d, J_{C-F} = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.7, 167.3, 165.3, 131.5, 131.4, 130.7 (q, J_{C-F} = 305.3 Hz), 116.3, 116.1, 44.2, 19.6; ^{19}F NMR (470 MHz, $CDCl_3$) δ -39.81 (s, 3F); HRMS (EI) calcd. for $C_{10}H_8F_4OS$: 252.0232, found 252.0232.

*4.18. 1-(Naphthalen-1-yl)-2-((trifluoromethyl)thio)ethanone (**2q**)*

Colorless oil, yield 79.8 %;^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (d, *J* = 9.0 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.91 (t, *J* = 8.5 Hz, 2H), 7.64 (m, 1H), 7.57 (m, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 4.59 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.0, 134.4, 134.1, 132.5, 130.7 (q, J_{C-F} = 304.8), 130.3, 128.8, 128.7, 128.6, 126.9, 125.6, 124.2, 40.6; ^{19}F NMR (470 MHz, $CDCl_3$) δ -41.30 (s, 3F); HRMS (EI) calcd. for $C_{13}H_9F_3OS$: 270.0326, found 270.0325.

*4.19. 1-((Trifluoromethyl)thio)undecan-2-one (**2r**)*

Yellow oil, yield 65.6 %; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.80 (s, 2H), 2.57 (t, *J* = 7.5 Hz, 2H), 1.62 (m, 2H), 1.27 (m, 12H), 0.88 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.9, 130.5 (q, J_{C-F} = 304.8 Hz), 41.3, 40.1, 31.8, 29.4, 29.3, 29.2, 29.0, 23.7, 22.7, 14.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ -41.67 (s, 3F); HRMS (EI) calcd. for [$C_{12}H_{21}F_3OS$+H]: 271.1343, found 271.1338.

*4.20. 1-((trifluoromethyl)thio)tridecan-2-one (**2s**)*

Yellow solid, yield 70.3 %; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 (s, 2H), 2.58 (t, J = 7.5 Hz, 2H), 1.61 (m, 2H), 1.26 (m, 16H),

0.88 (t, J = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.5, 130.0 (q, JC-F = 304.6 Hz), 40.7, 39.6, 31.5, 29.1, 29.0, 28.9, 28.8, 28.6, 23.2, 22.2, 13.6; ^{19}F NMR (470 MHz, $CDCl_3$) δ -41.72 (s, 3F); HRMS (EI) calcd. for $C_{14}H_{25}F_3OS$: 298.1578, found 298.1578.

Acknowledgements

We thank the National Natural Science Foundation of China (21302053) for the generous financial support. We are also grateful for the financial support from the Fundamental Research Funds for the Central University (WY111307).

Supplementary data

^{1}H, ^{13}C and ^{19}F NMR data associated with this article.

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Copper (I)-Mediated Trifluoromethylthiolation of α-Bromoketone with Element Sulfur and (Trifluoromethyl)trimethylsilane

Jue Li [a], Fei-Fei Xie [a], Qiang-Yong Wu [a], Jiangmeng Ren [a, *], Bu-Bing Zeng [a, b, *]

[a] *Shanghai Key Laboratory of New Drug Design, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, PR China*
[b] *Key Laboyatory of Synthetic Chemistry of Natural Substances, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road,Shanghai 200032, PR China.*

Fax +86(21)64253689; E-mail: renjm@ecust.edu.cn; zengbb@ecust.edu.cn

Supporting information

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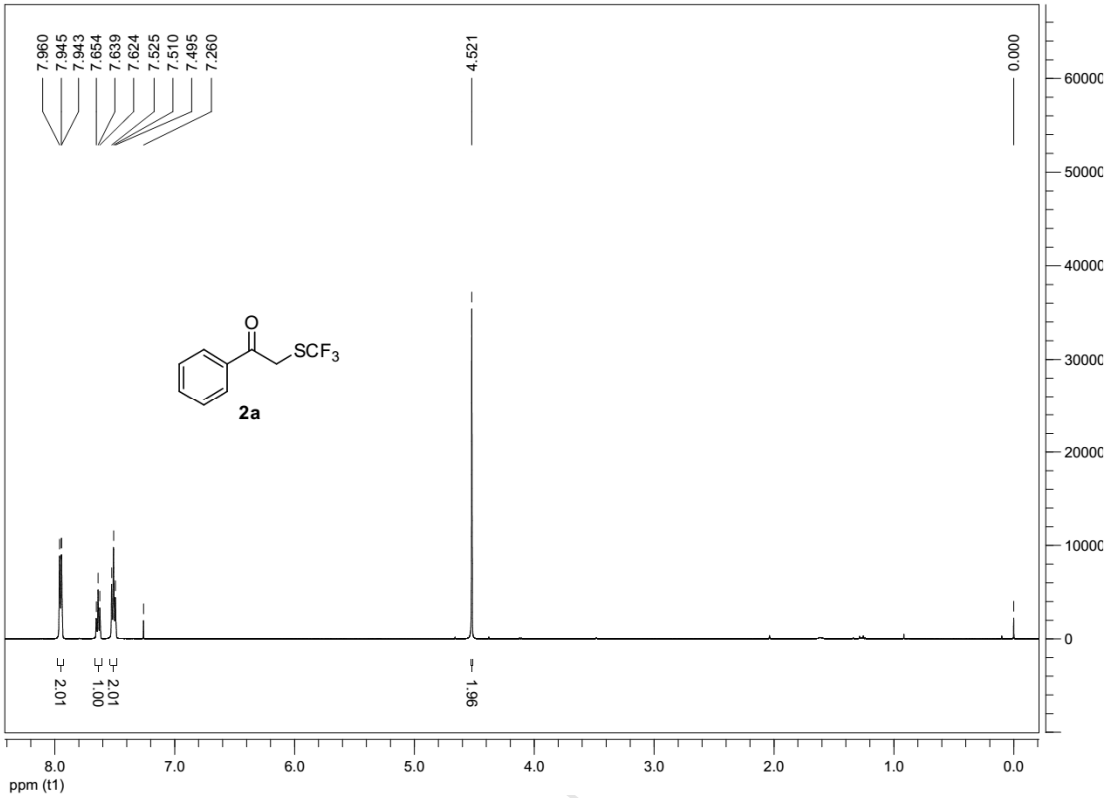
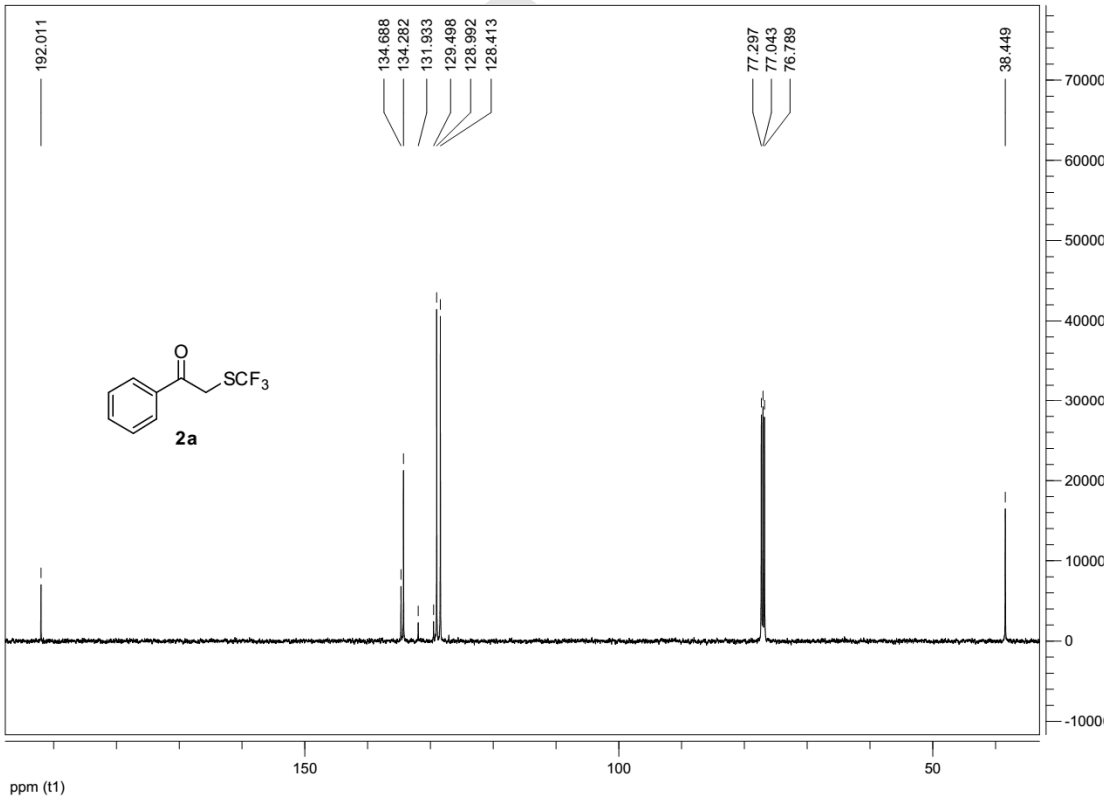
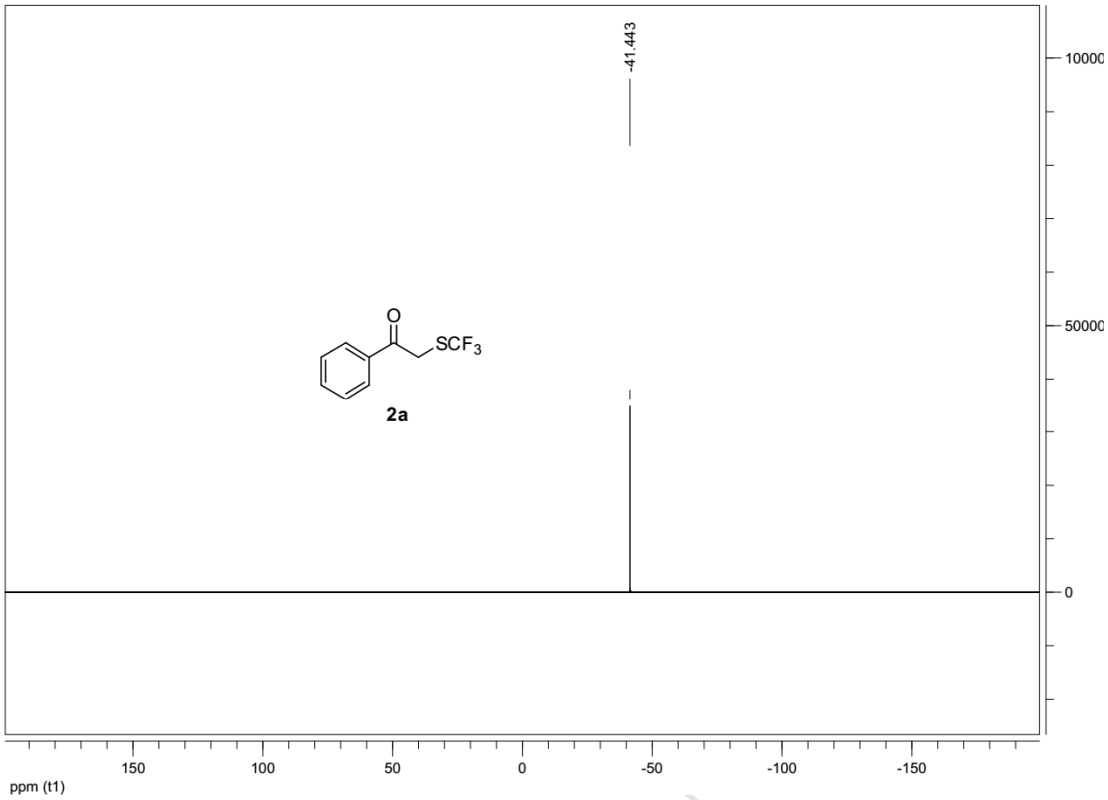
Copies of ^{1}H , ^{13}C and ^{19}F NMR Spectra.

Compound **2a**



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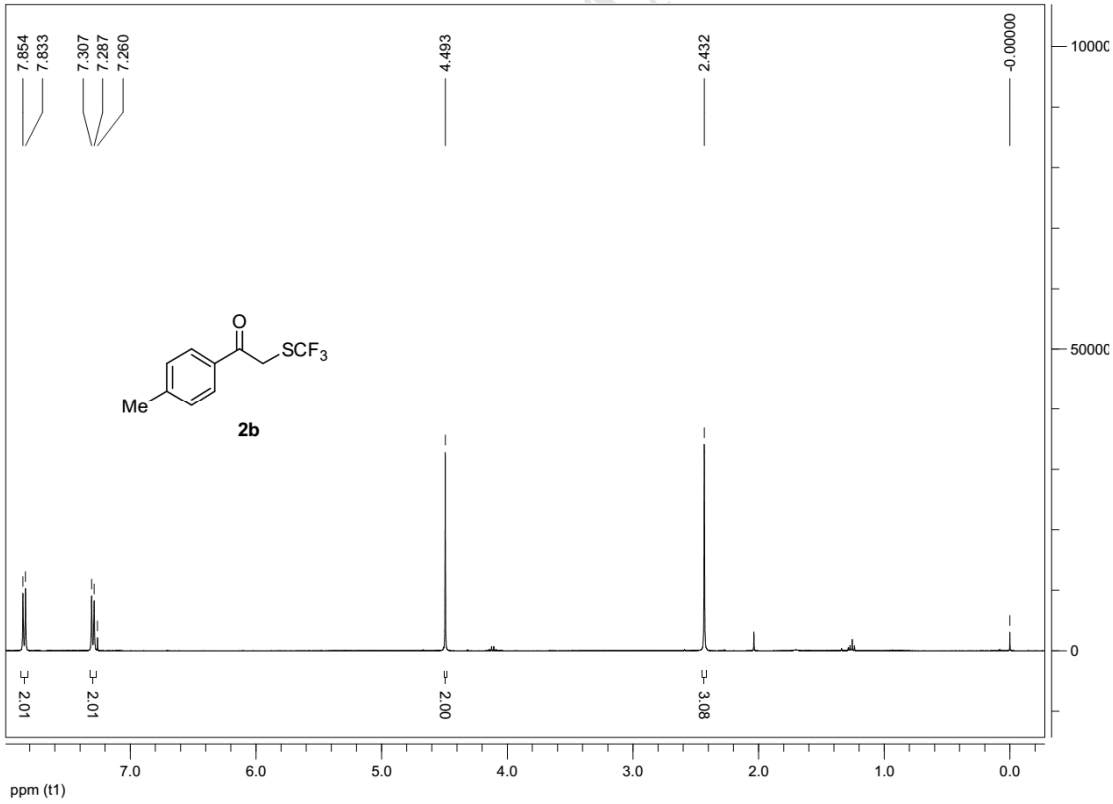
Compound **2b**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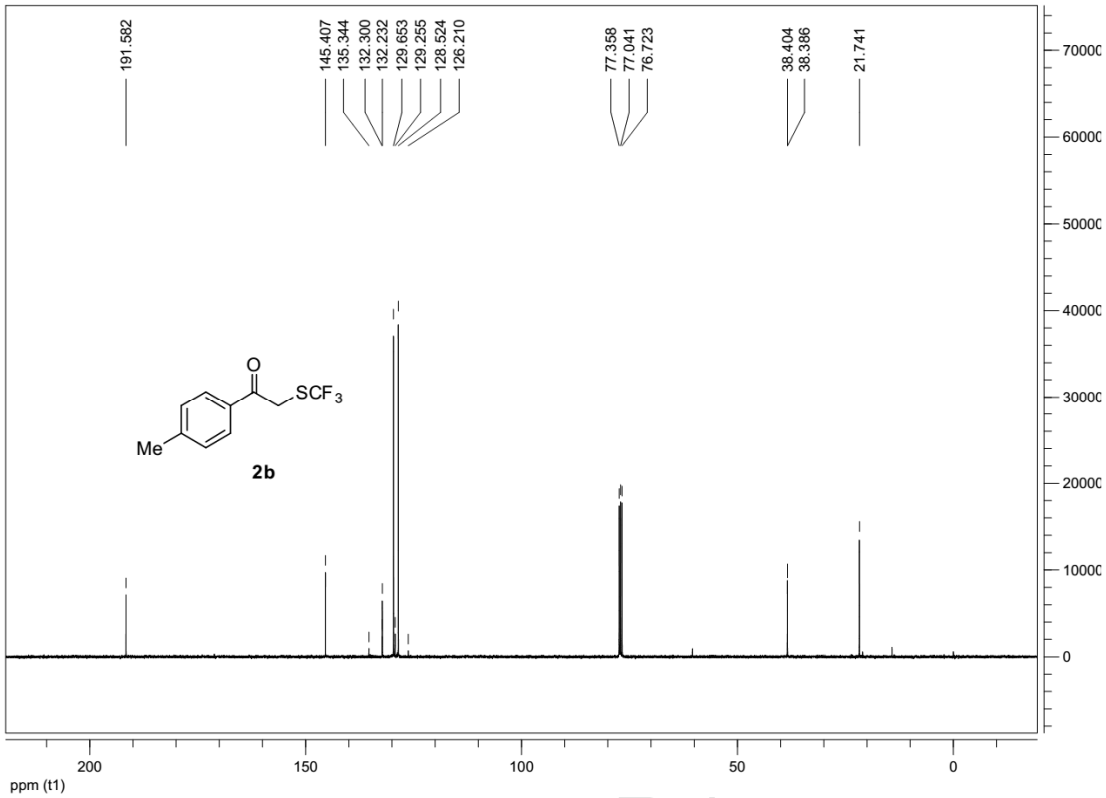
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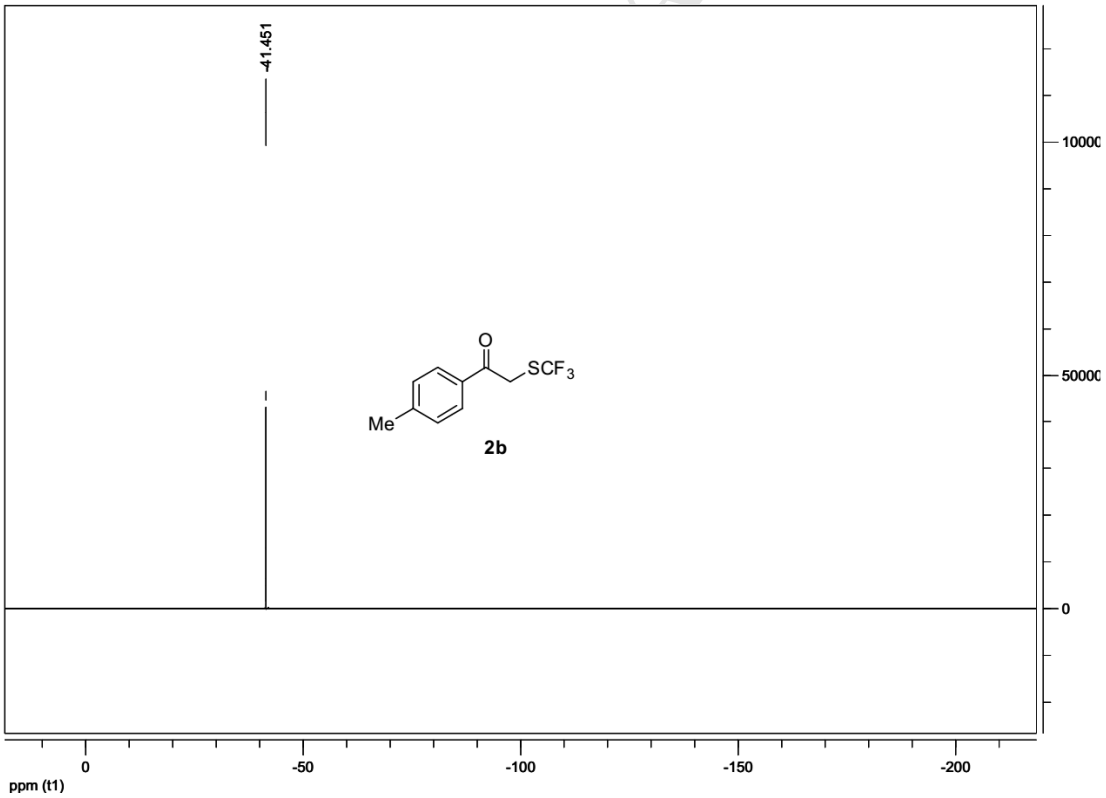
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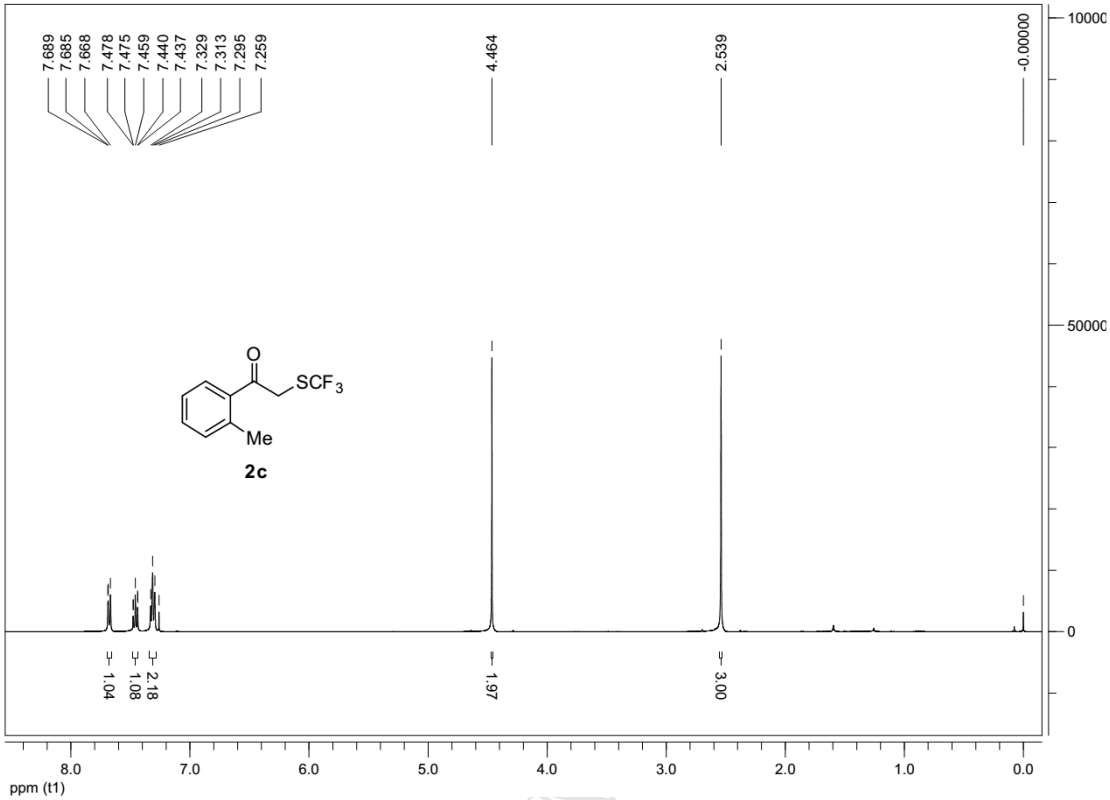
Compound **2c**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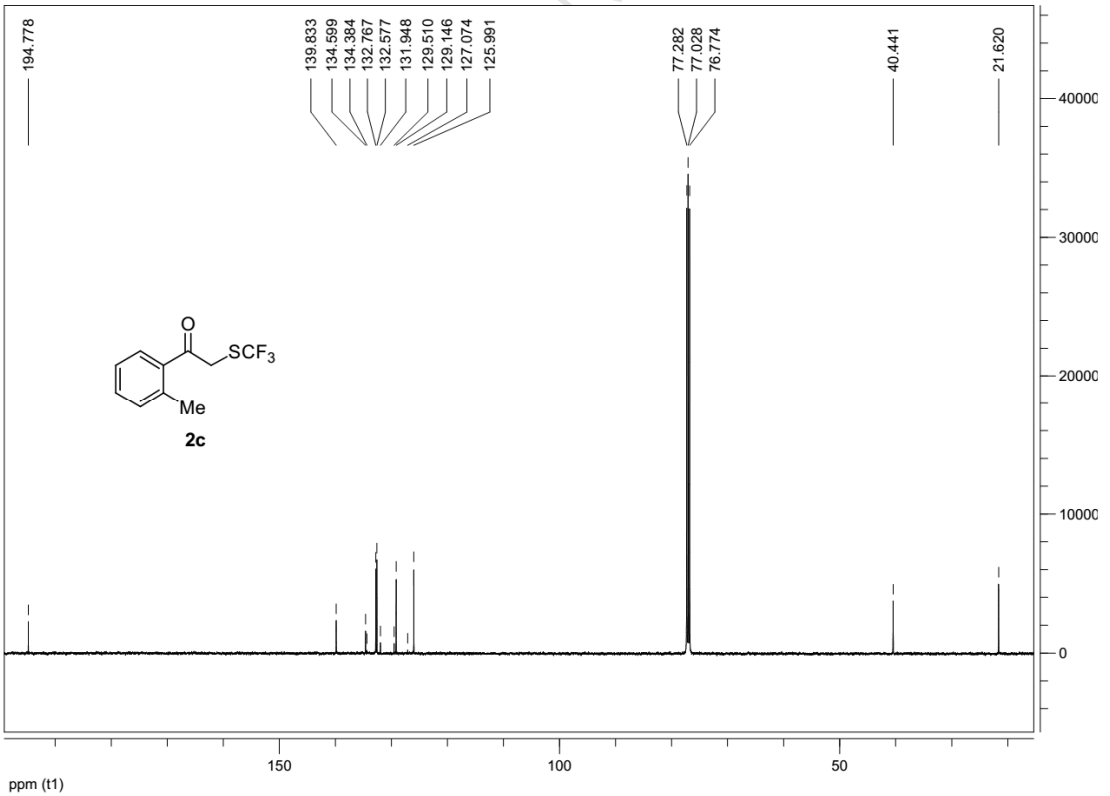
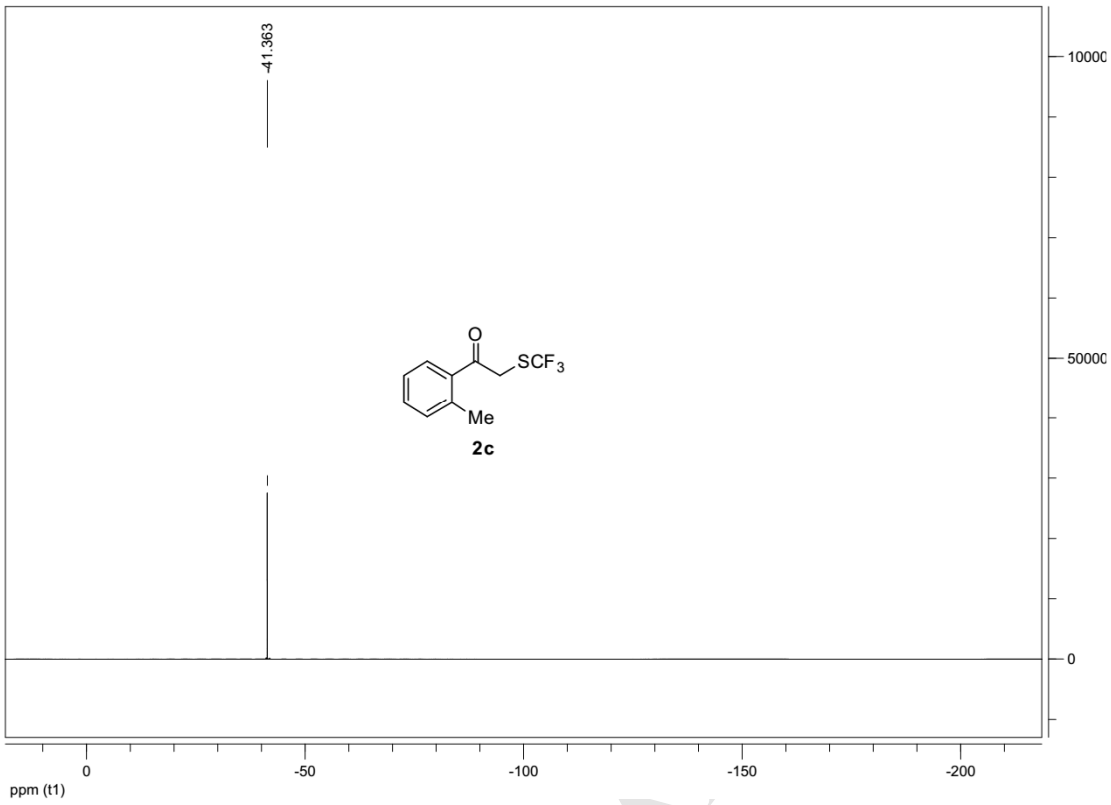
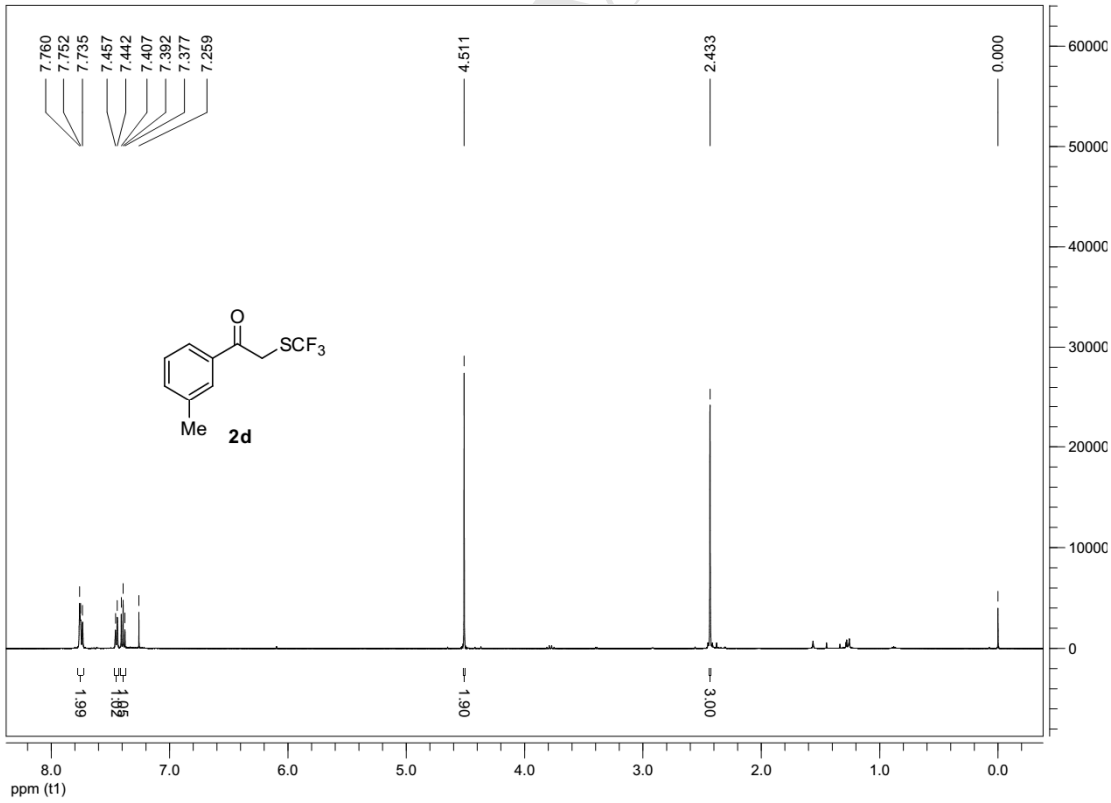
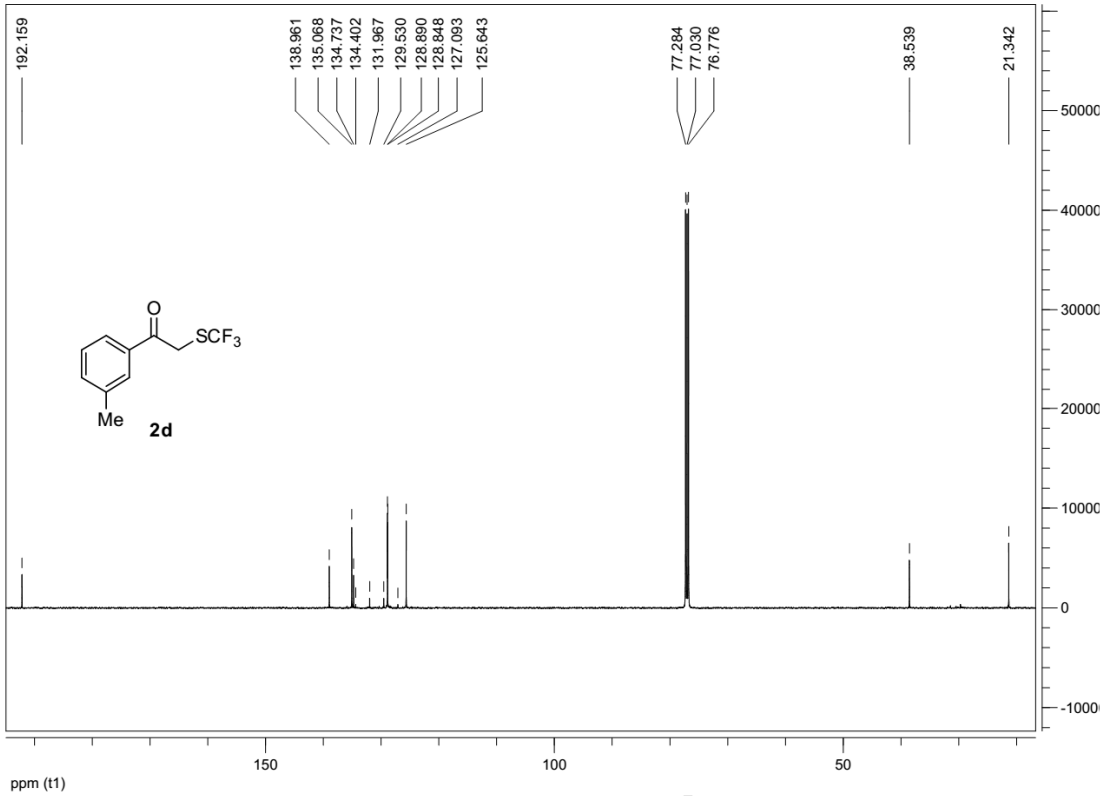
2c
ppm (t1)

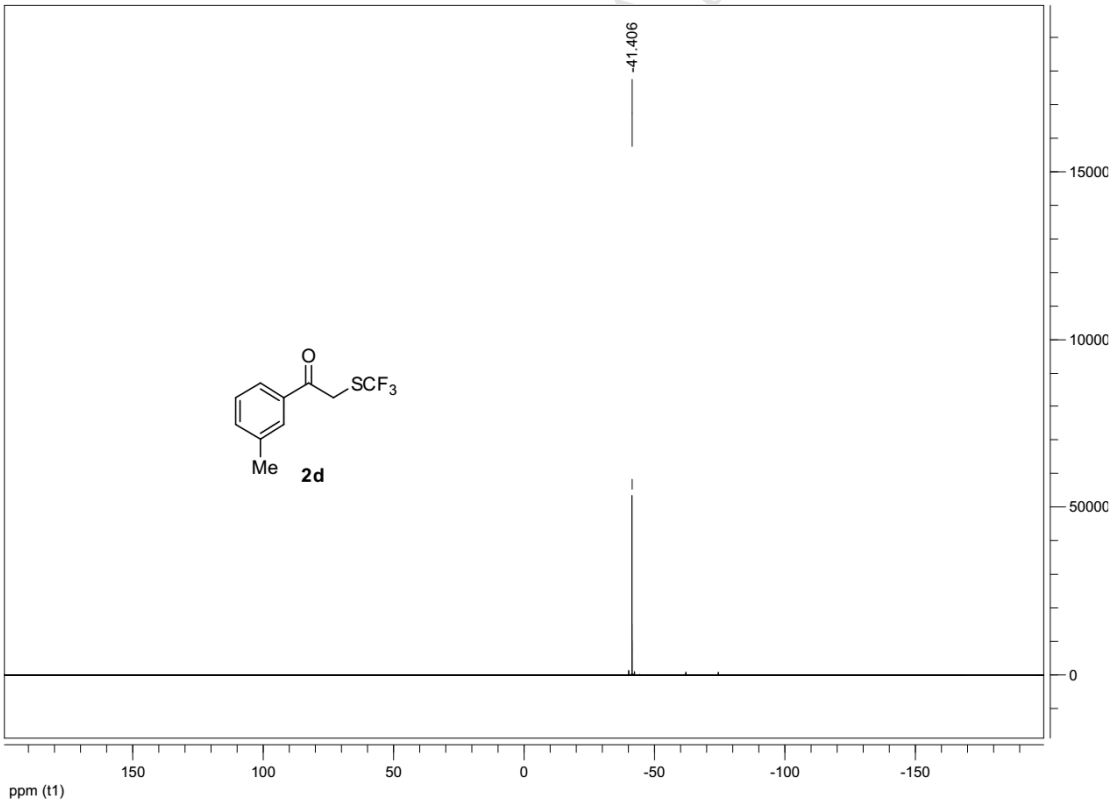

194.778
139.833
134.599
134.384
132.767
132.577
131.948
129.510
129.146
127.074
125.991
77.282
77.028
76.774
40.441
21.620
O
SCF3
Me
2c
ppm (t1)


-41.363
O
SCF3
Me
2c
10000
50000
0
0
-50
-100
-150
-200
ppm (t1)

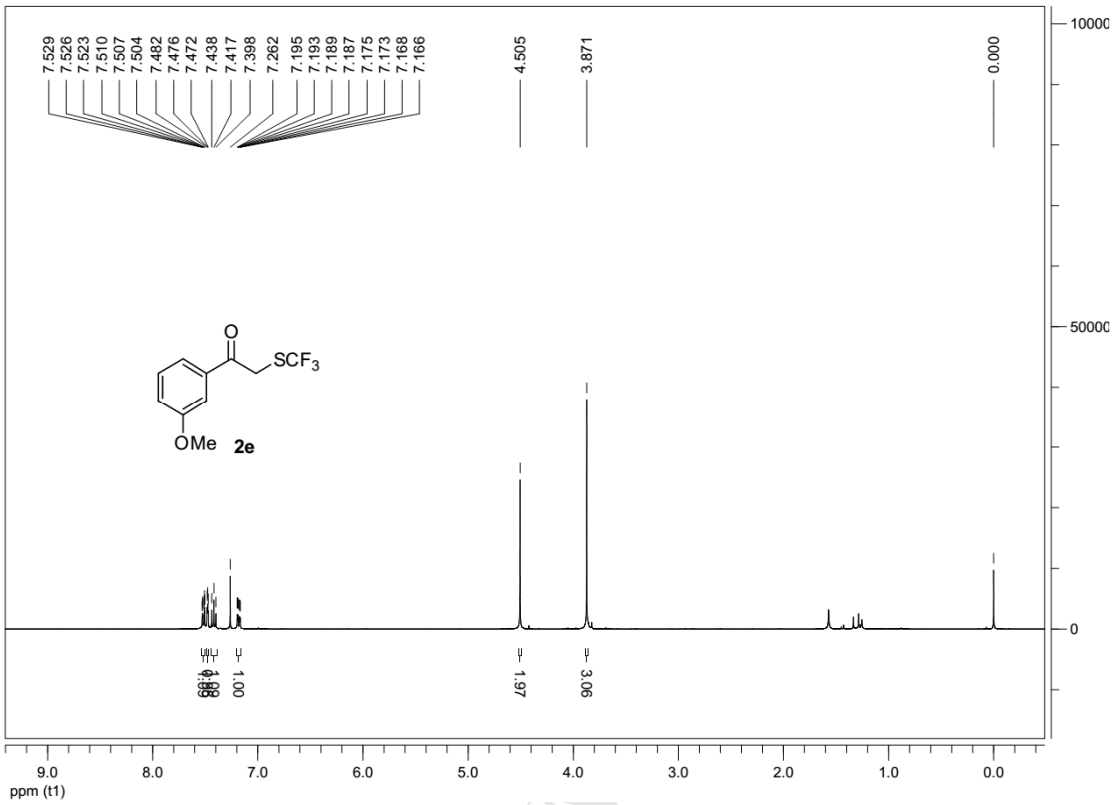
Compound **2d**

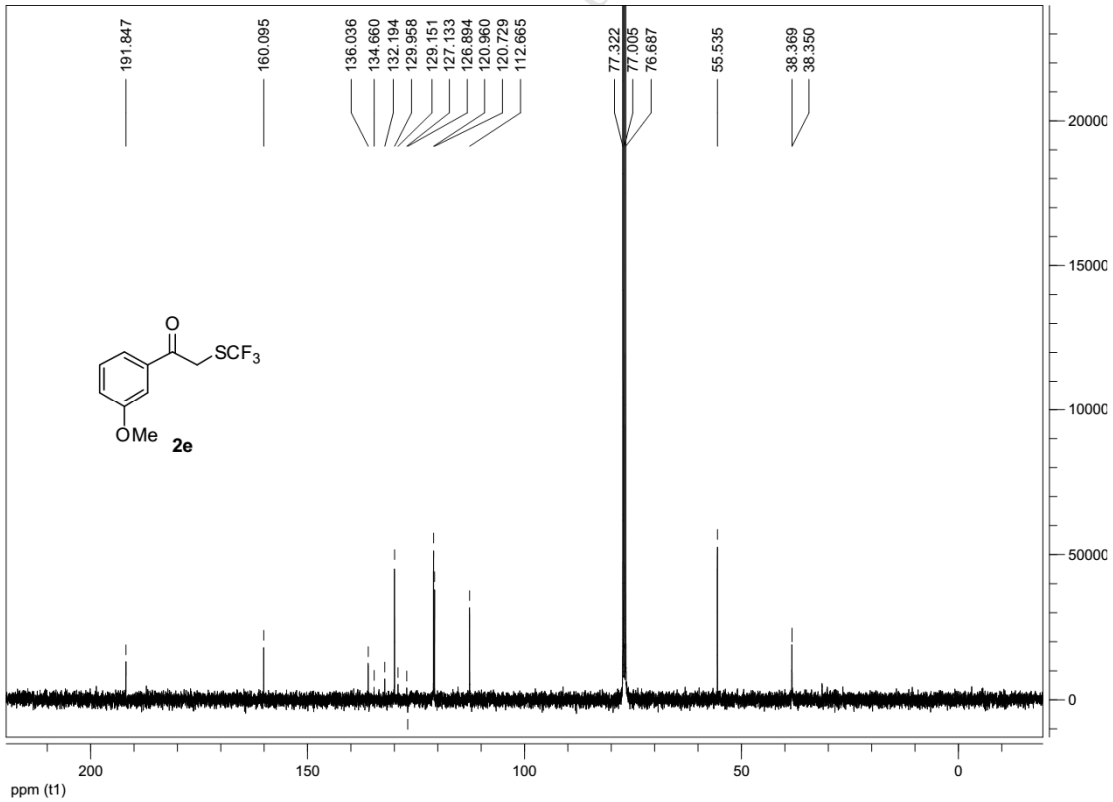

7.760
7.752
7.735
7.457
7.442
7.407
7.392
7.377
7.259
4.511
2.433
0.000
O
SCF3
Me
2d
1.99
1.95
1.90
3.00
60000
50000
40000
30000
20000
10000
0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

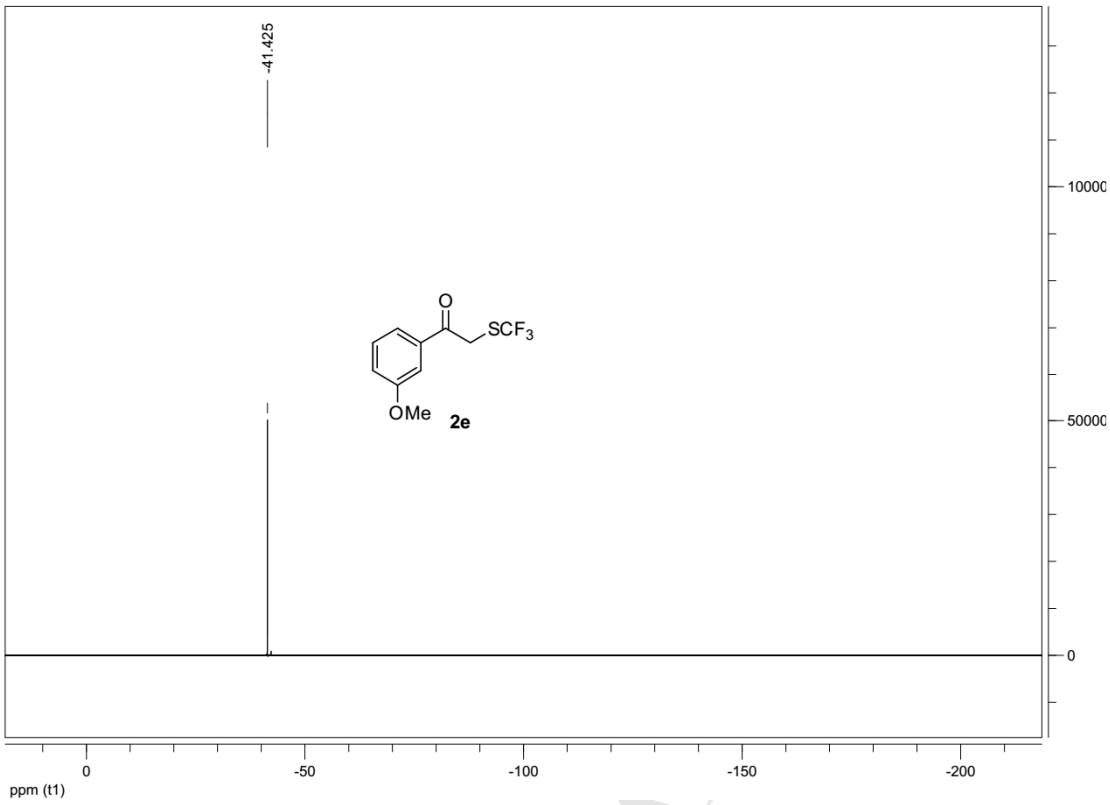

192.159
138.961
135.068
134.737
134.402
131.967
129.530
128.890
128.848
127.093
125.643
77.284
77.030
76.776
38.539
21.342
O
SCF3
Me
2d
50000
40000
30000
20000
10000
0
-1000
150
100
50
ppm (t1)


-41.406
O
SCF3
Me
2d
15000
10000
50000
0
150
100
50
0
-50
-100
-150
ppm (t1)

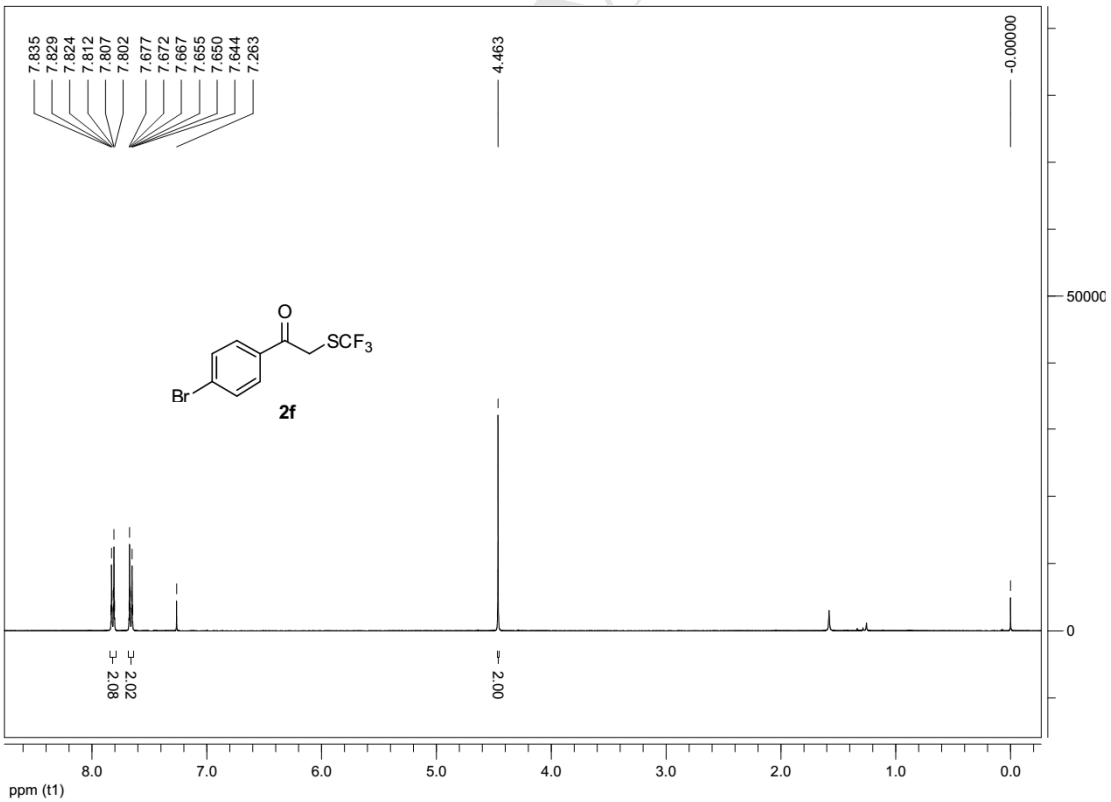
Compound **2e**

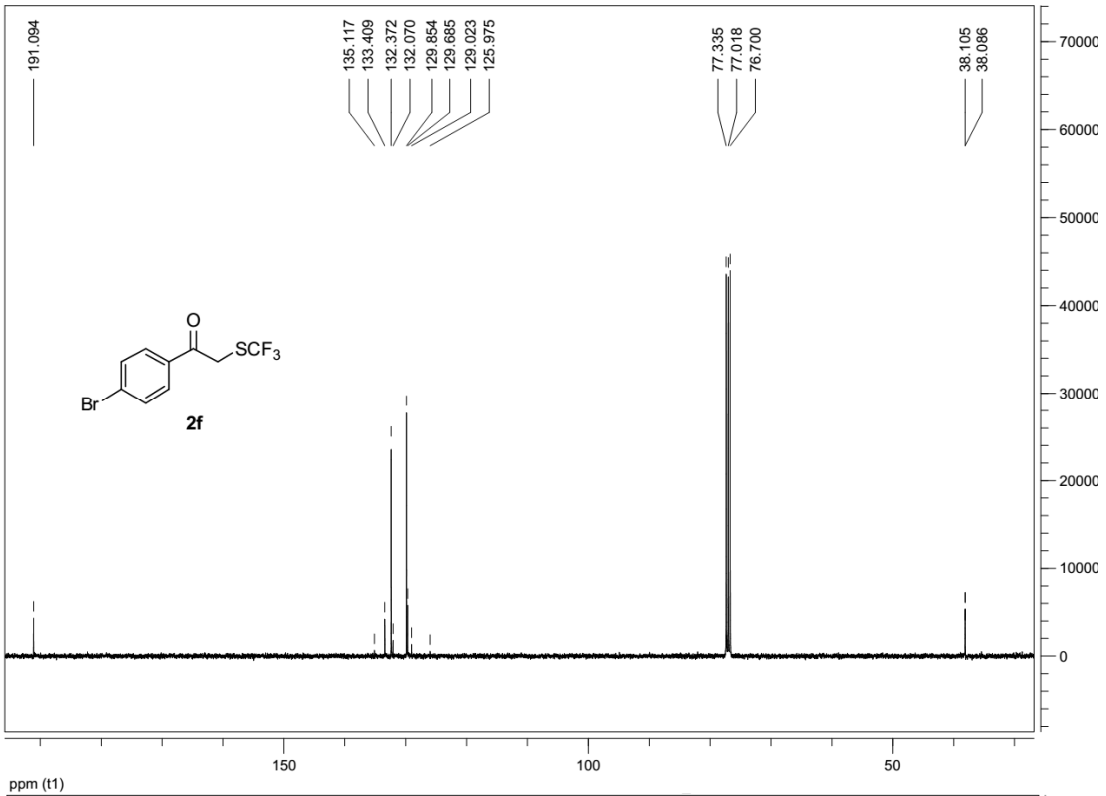

7.529
7.526
7.523
7.510
7.507
7.504
7.482
7.476
7.472
7.438
7.417
7.398
7.262
7.195
7.193
7.189
7.187
7.175
7.173
7.168
7.166
4.505
3.871
0.000
O
SCF3
OMe
2e
1.00
1.97
3.06
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

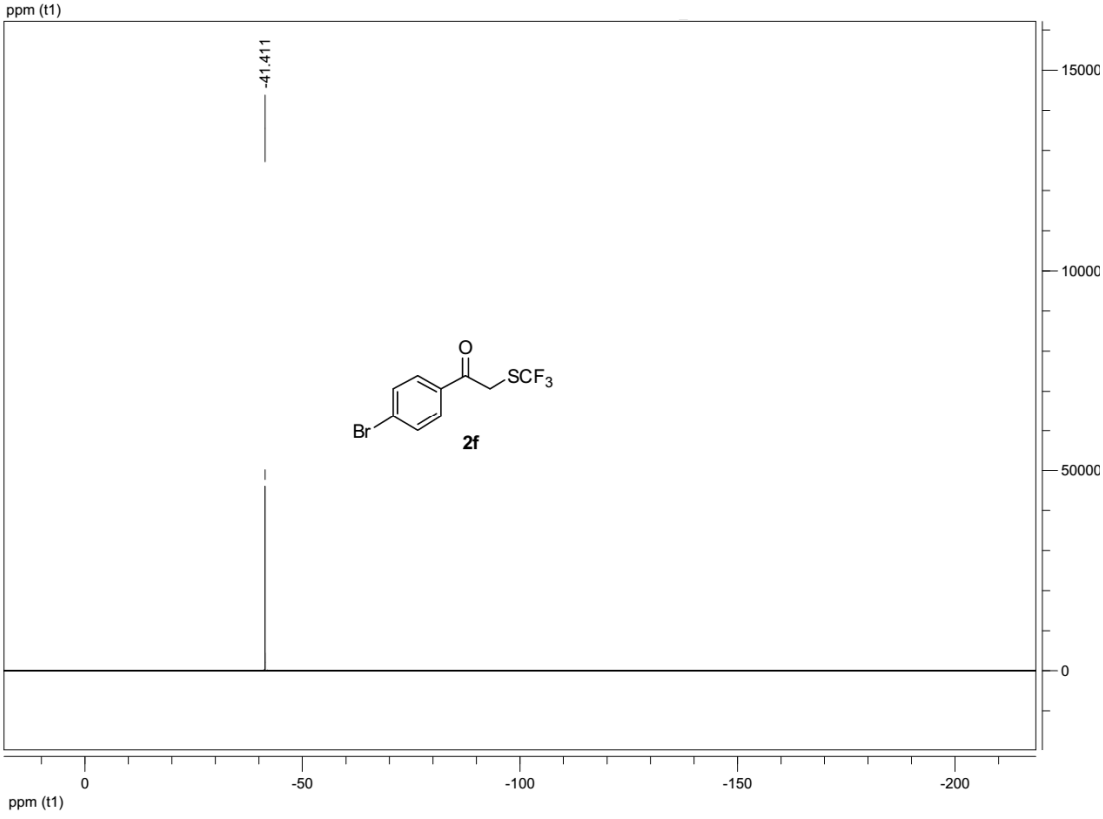

191.847
160.095
136.036
134.660
132.194
129.958
129.151
127.133
126.894
120.960
120.729
112.665
77.322
77.005
76.687
55.535
38.369
38.350
O
SCF3
OMe
2e
200
150
100
50
0
ppm (t1)


-41.425
O
SCF3
OMe
2e
10000
50000
0
0
-50
-100
-150
-200
ppm (t1)

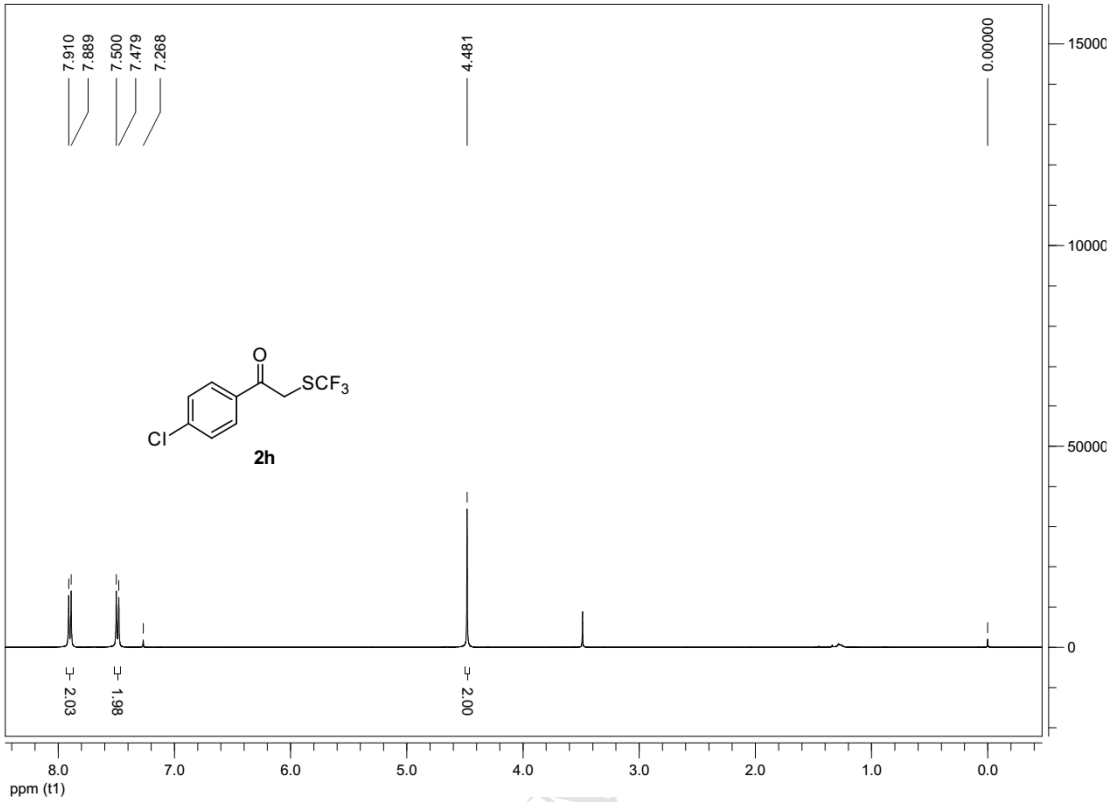
Compound **2f**

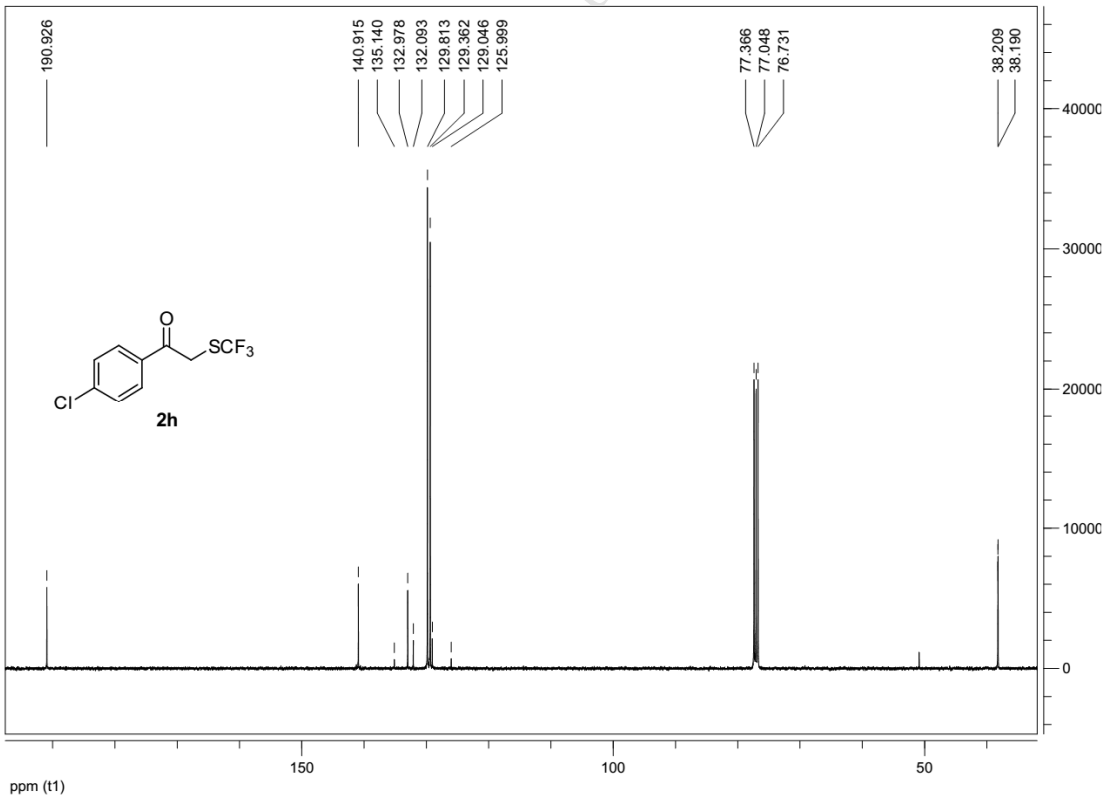

7.835
7.829
7.824
7.812
7.807
7.802
7.677
7.672
7.667
7.655
7.650
7.644
7.263
4.463
-0.00000
O
SCF3
Br
2f
50000
0
2.08
2.02
2.00
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

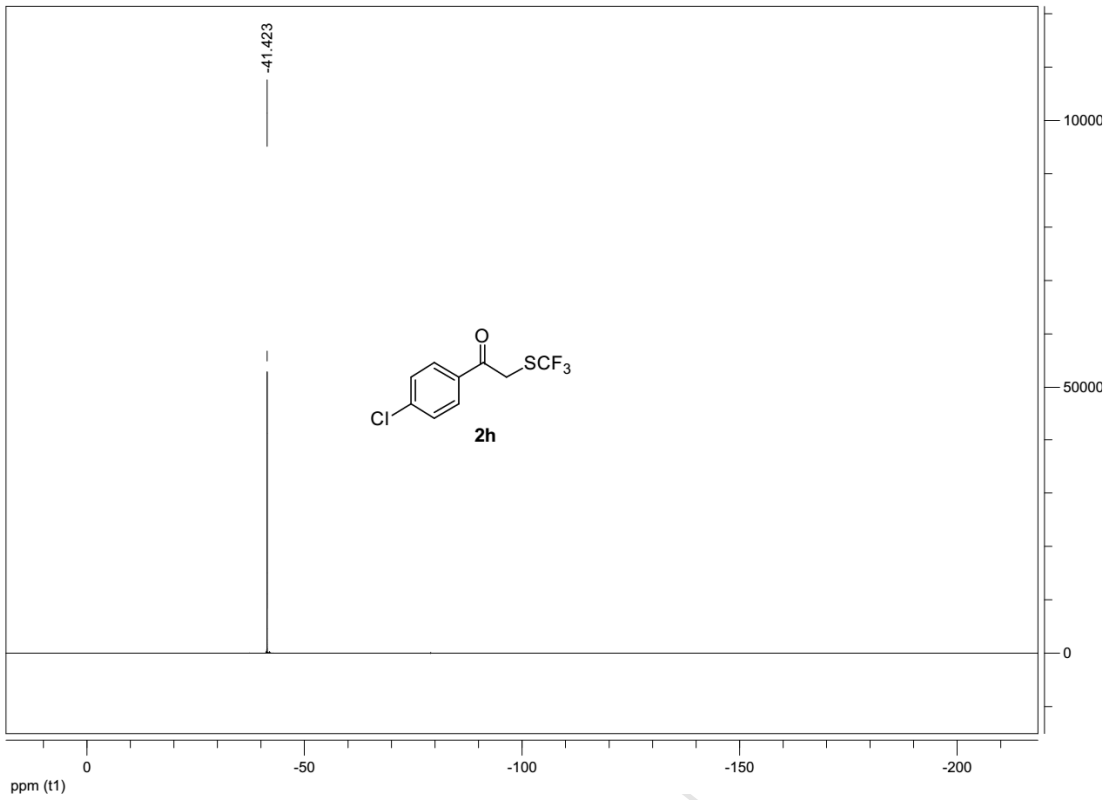

191.094
135.117
133.409
132.372
132.070
129.854
129.685
129.023
125.975
77.335
77.018
76.700
38.105
38.086
O
SCF3
Br
2f
150
100
50
ppm (t1)


-41.411
O
SCF3
Br
2f
0
-50
-100
-150
-200
ppm (t1)

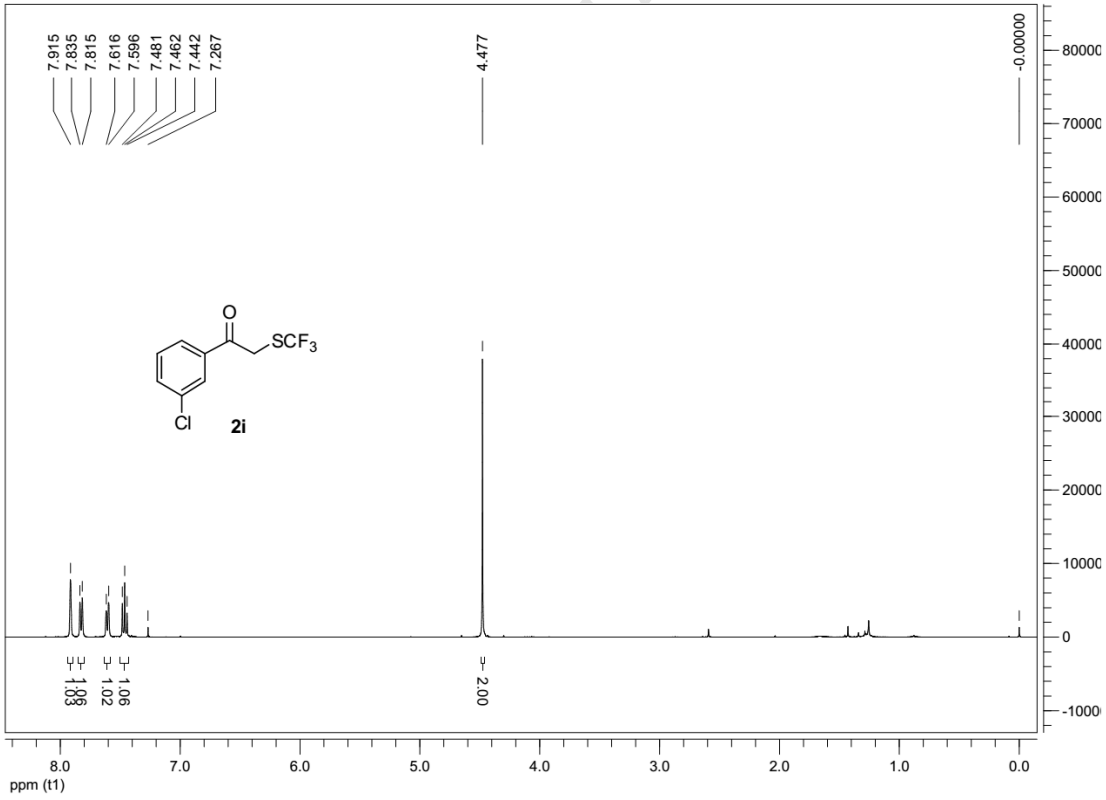
Compound **2h**

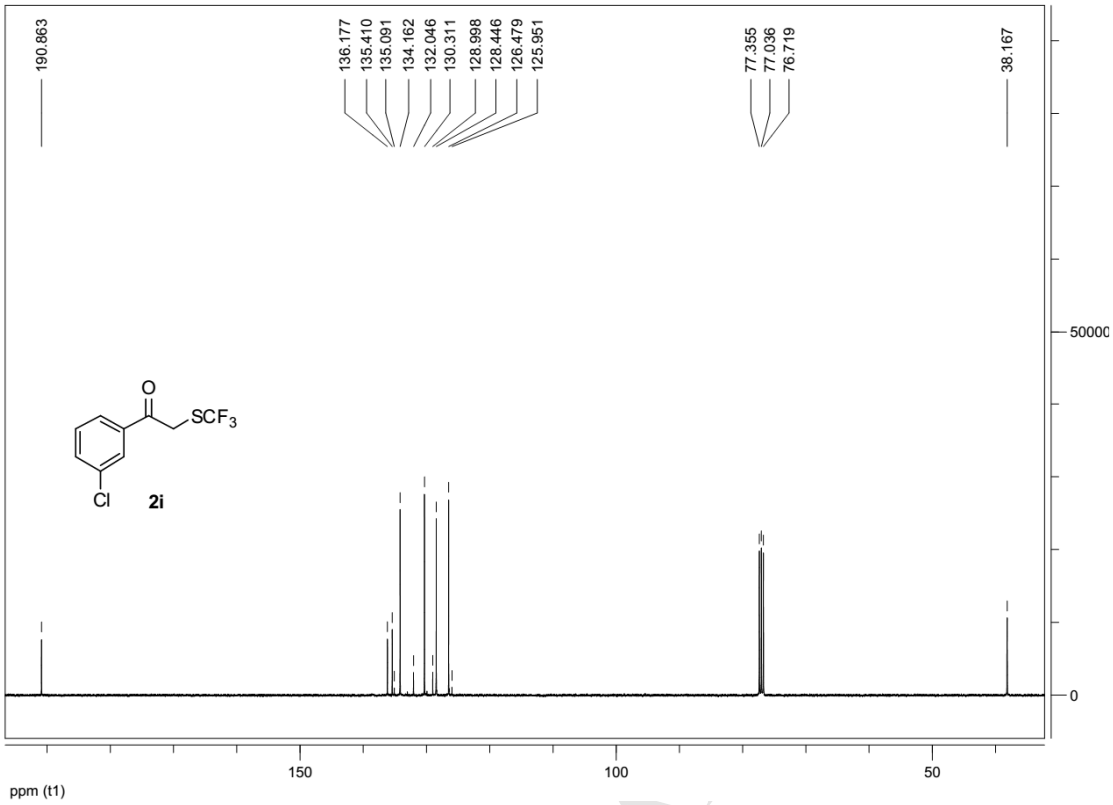

7.910
7.889
7.500
7.479
7.268
4.481
0.00000
15000
10000
50000
0
O
SCF3
Cl
2h
2.03
1.98
2.00
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

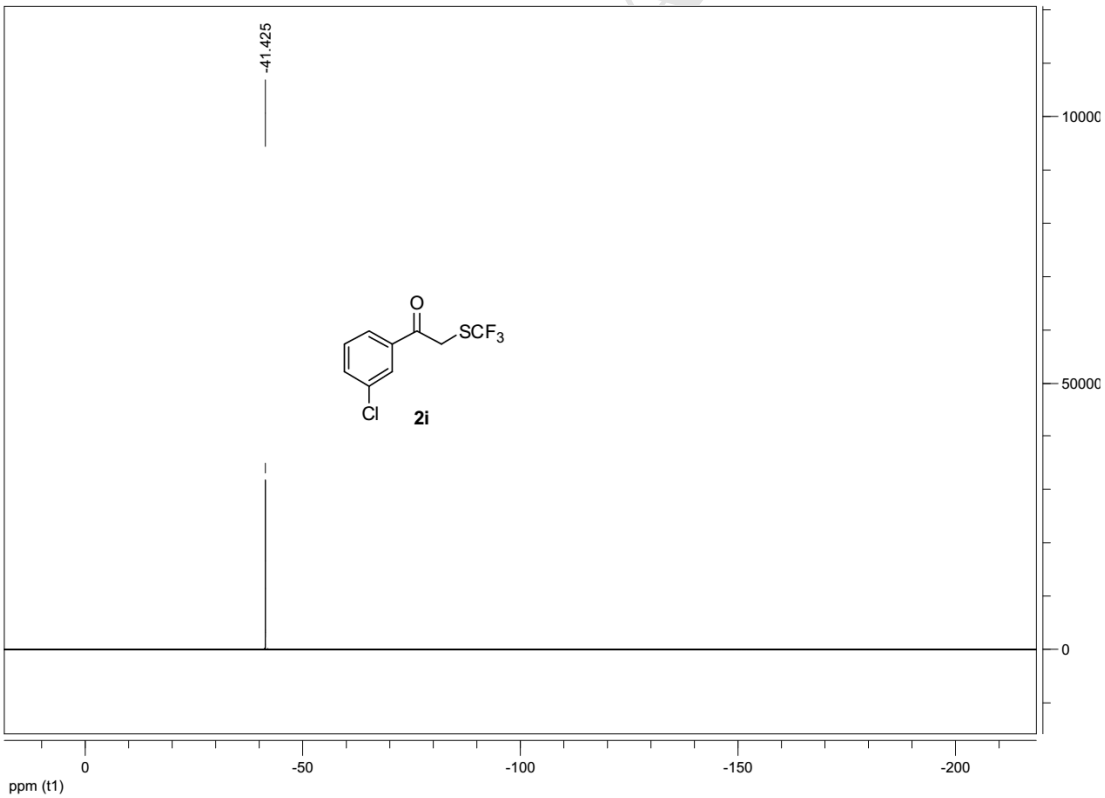

190.926
140.915
135.140
132.978
132.093
129.813
129.362
129.046
125.999
77.366
77.048
76.731
38.209
38.190
40000
30000
20000
10000
0
O
SCF3
Cl
2h
150
100
50
ppm (t1)


-41.423
O
SCF3
Cl
2h
10000
50000
0
0
-50
-100
-150
-200
ppm (t1)

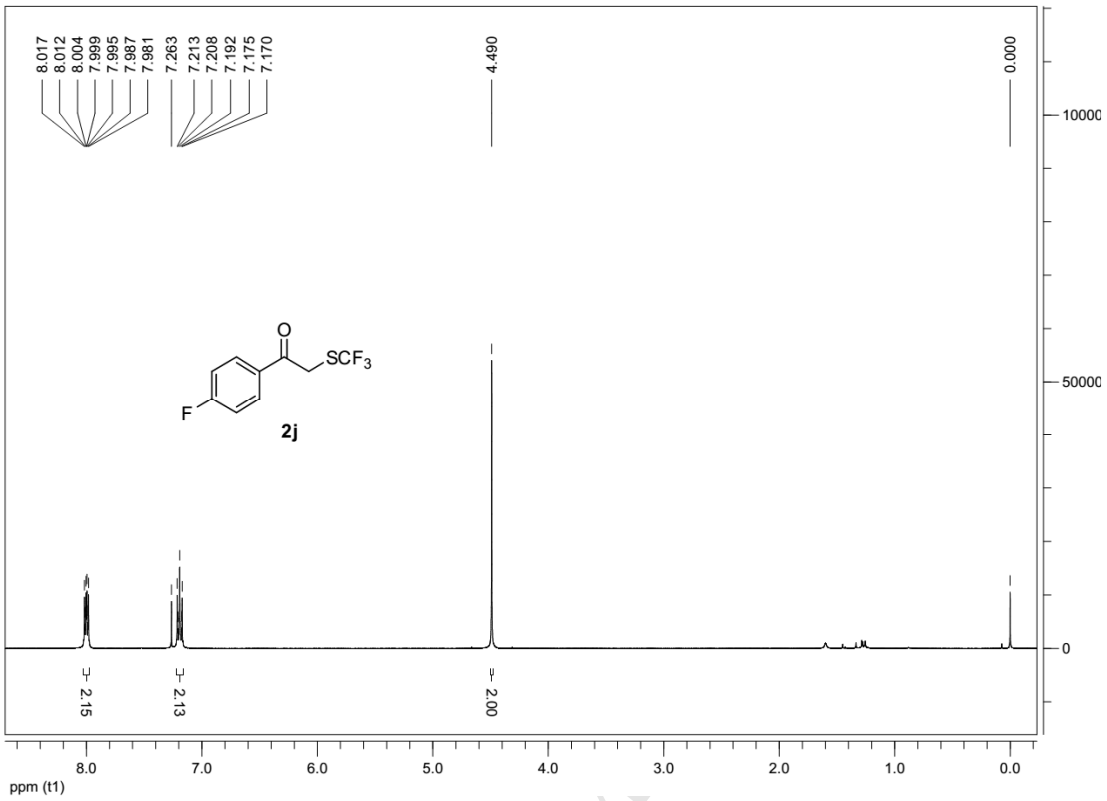
Compound **2i**

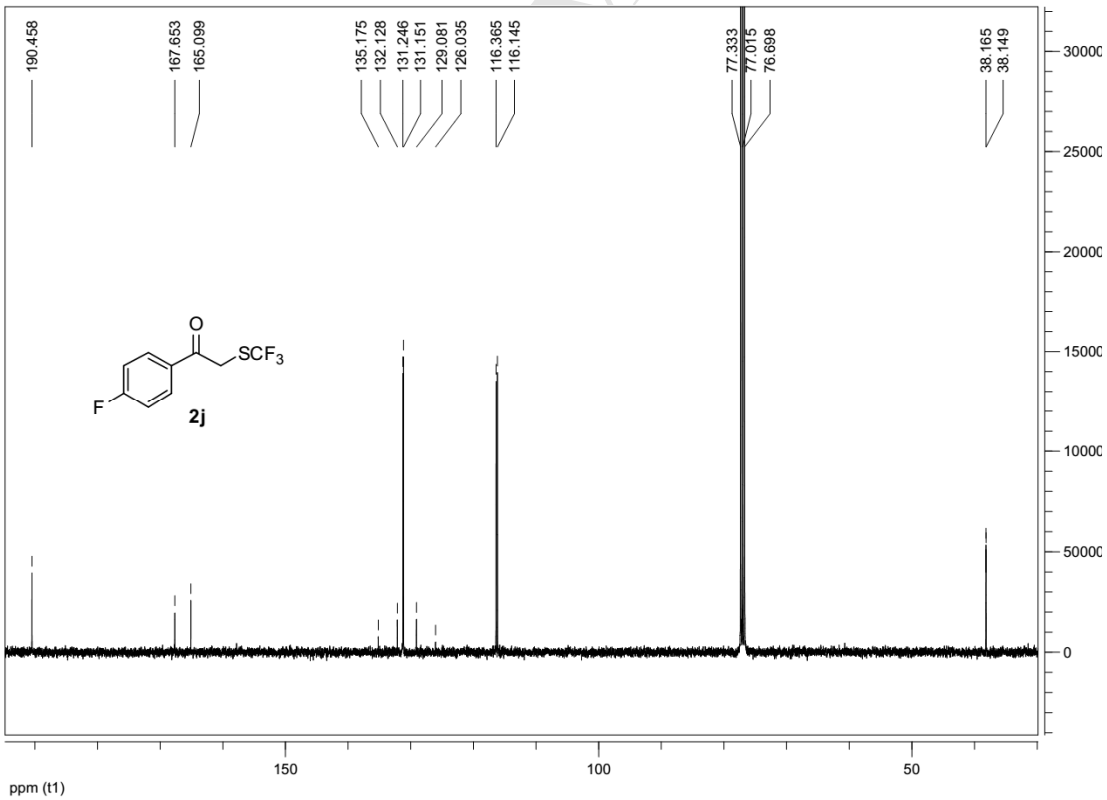

7.915
7.835
7.815
7.616
7.596
7.481
7.462
7.442
7.267
4.477
-0.00000
O
SCF3
Cl
2i
1.03
1.08
1.02
1.06
2.00
80000
70000
60000
50000
40000
30000
20000
10000
0
-1000
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

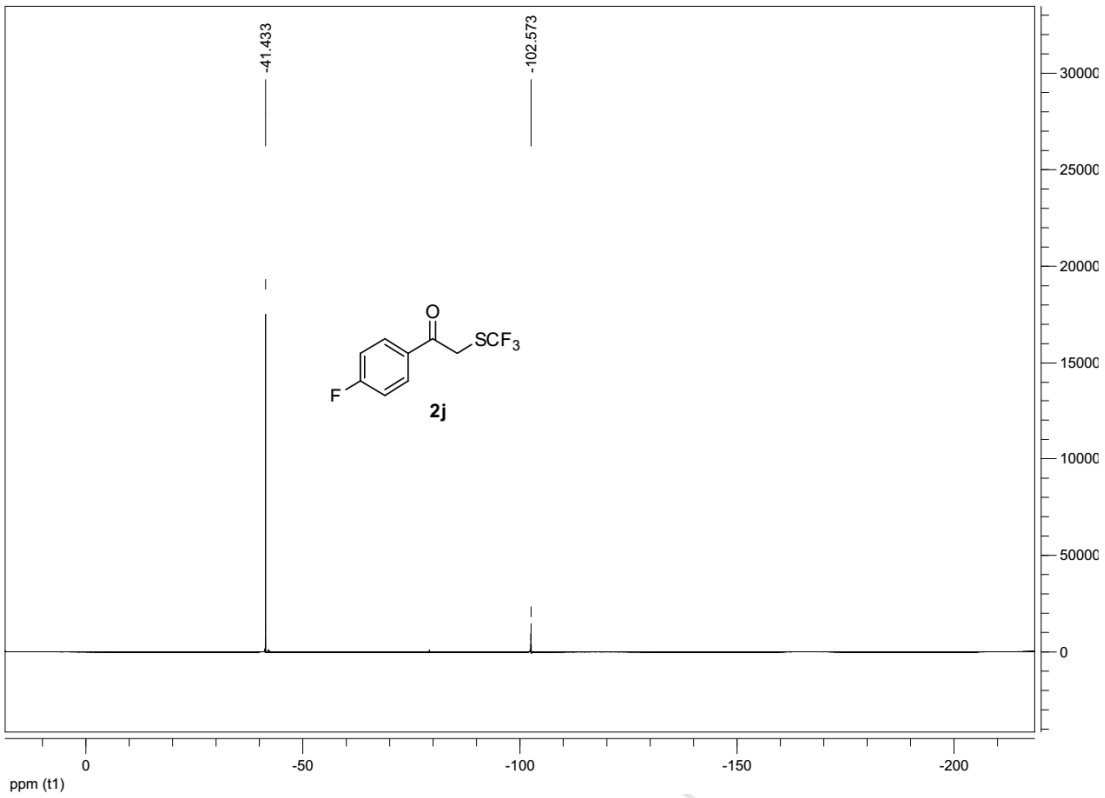

190.863
136.177
135.410
135.091
134.162
132.046
130.311
128.998
128.446
126.479
125.951
77.355
77.036
76.719
38.167
50000
0
150
100
50
ppm (t1)
O
SCF3
Cl
2i


-41.425
10000
50000
0
0
-50
-100
-150
-200
ppm (t1)
O
SCF3
Cl
2i

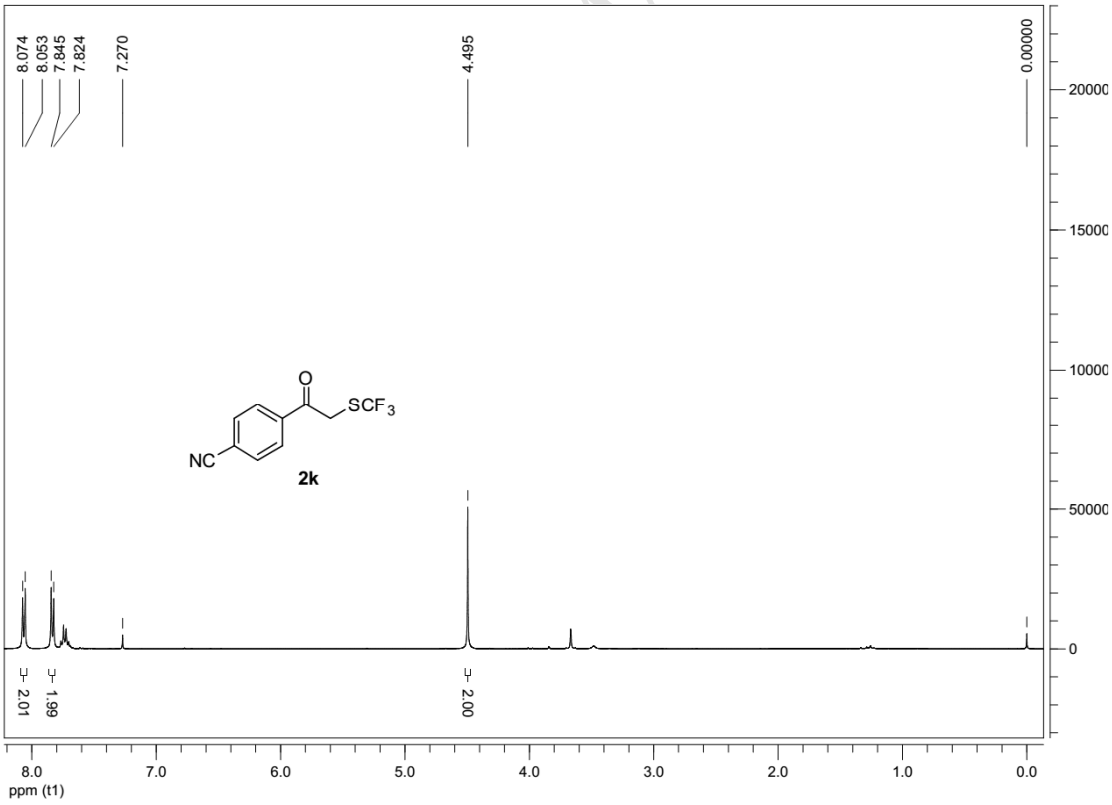
Compound **2j**

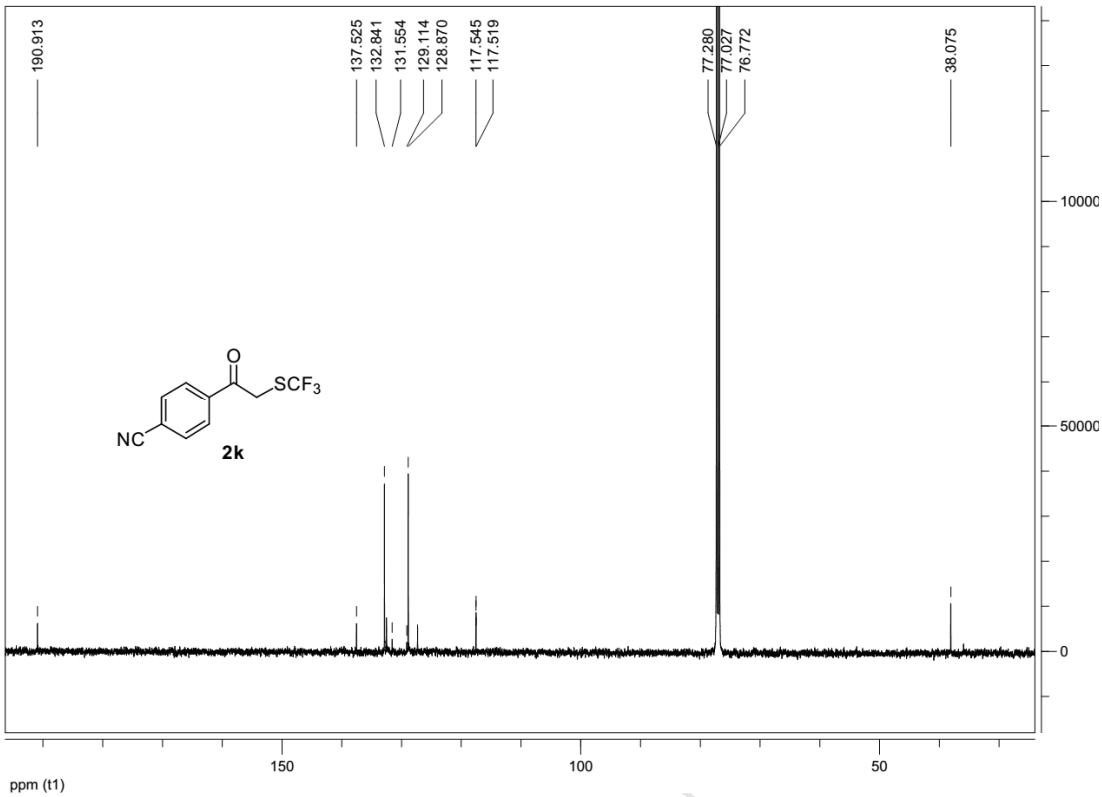

8.017
8.012
8.004
7.999
7.995
7.987
7.981
7.263
7.213
7.208
7.192
7.175
7.170
4.490
0.000
O
SCF3
F
2j
2.15
2.13
2.00
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

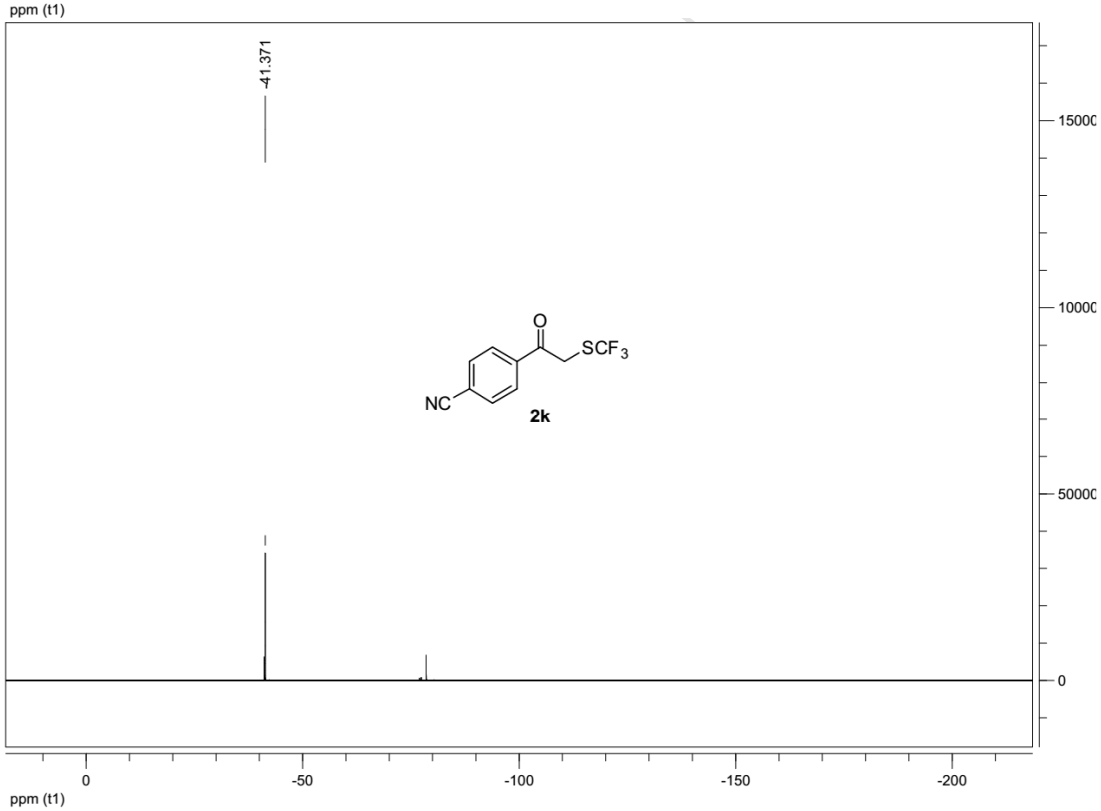

190.458
167.653
165.099
135.175
132.128
131.246
131.151
129.081
126.035
116.365
116.145
77.333
77.015
76.698
38.165
38.149
O
SCF3
F
2j
150
100
50
ppm (t1)


-41.433
-102.573
O
SCF3
F
2j
30000
25000
20000
15000
10000
50000
0
0
-50
-100
-150
-200
ppm (t1)

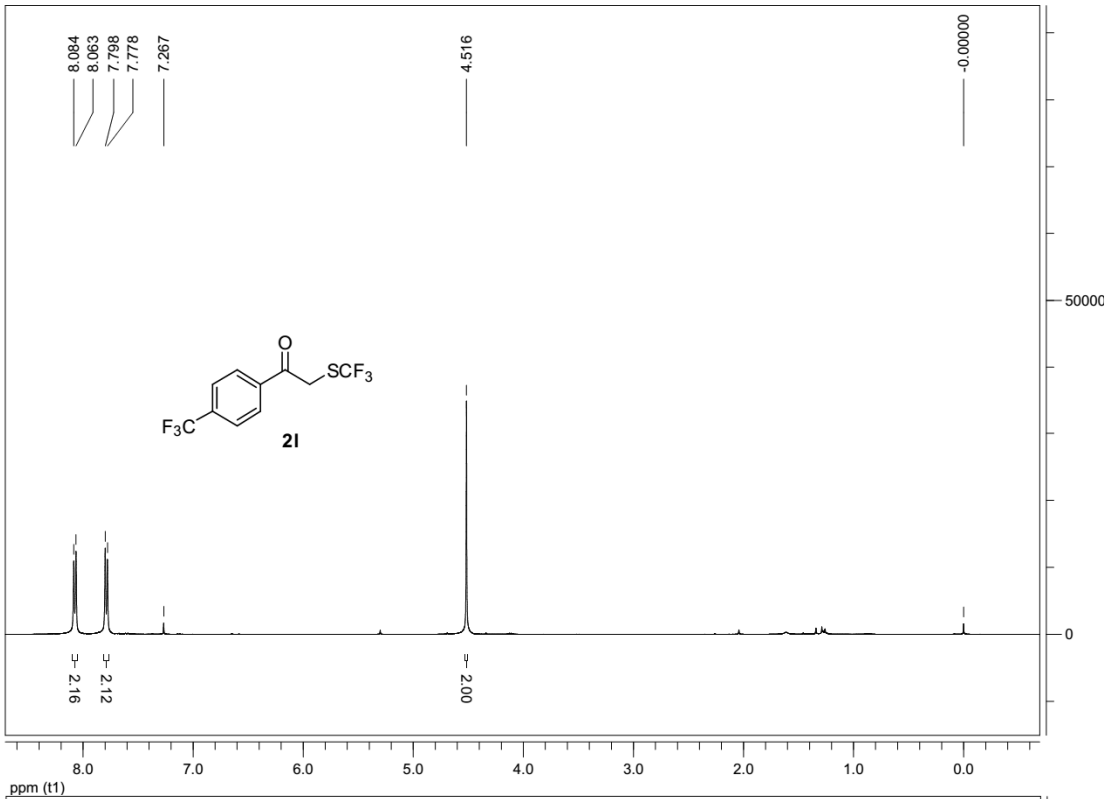
Compound **2k**

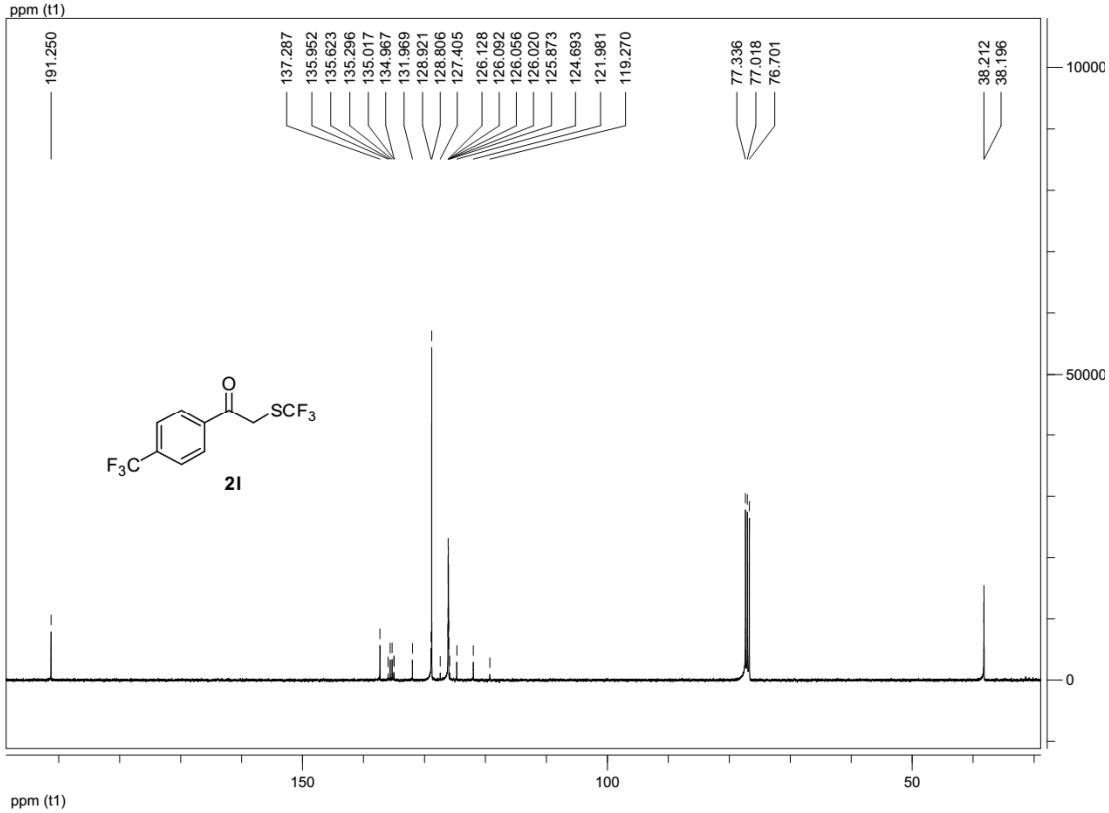

8.074
8.053
7.845
7.824
7.270
4.495
0.00000
O
SCF3
NC
2k
2.01
1.99
2.00
20000
15000
10000
50000
0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

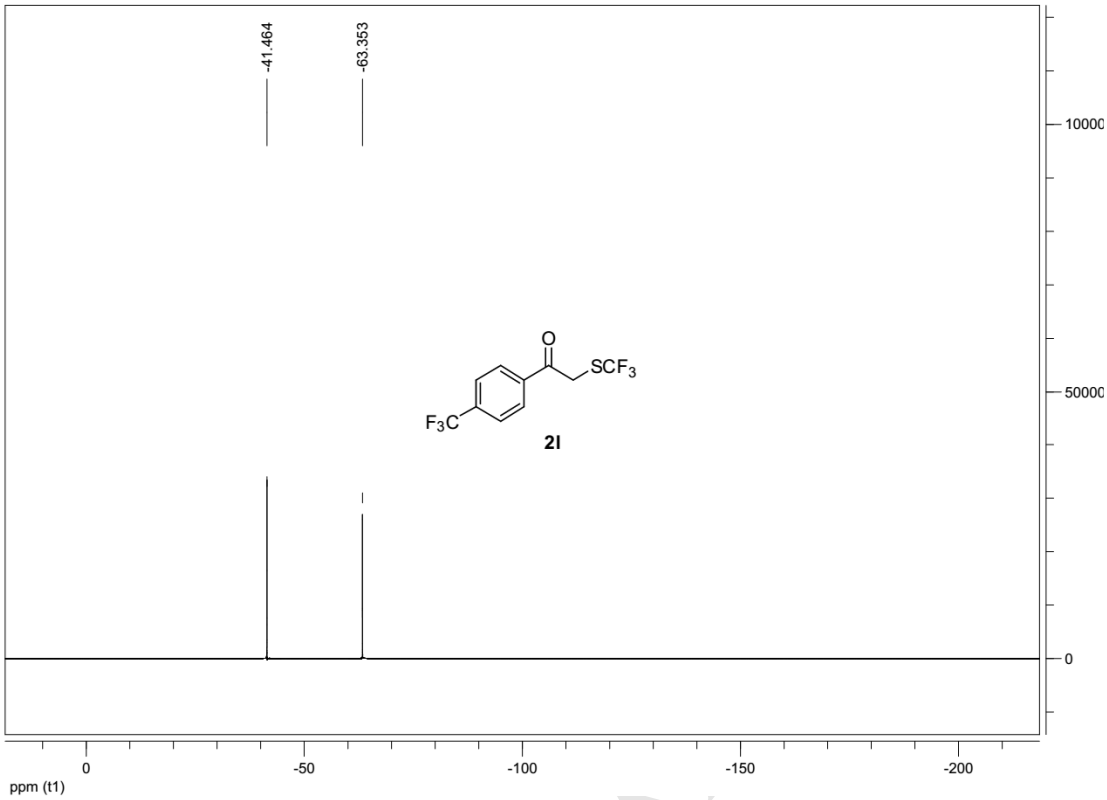

190.913
137.525
132.841
131.554
129.114
128.870
117.545
117.519
77.280
77.027
76.772
38.075
10000
50000
0
O
SCF3
NC
2k
150
100
50
ppm (t1)


-41.371
15000
10000
50000
0
O
SCF3
NC
2k
0
-50
-100
-150
-200
ppm (t1)

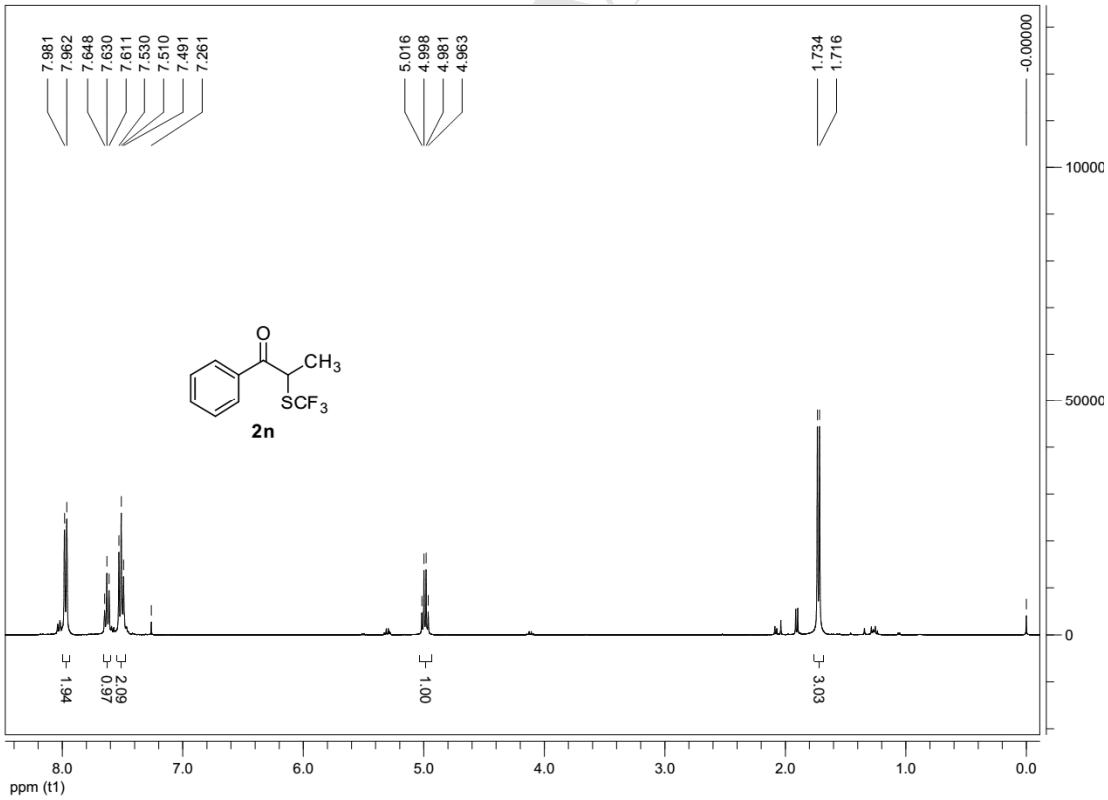
Compound **2l**

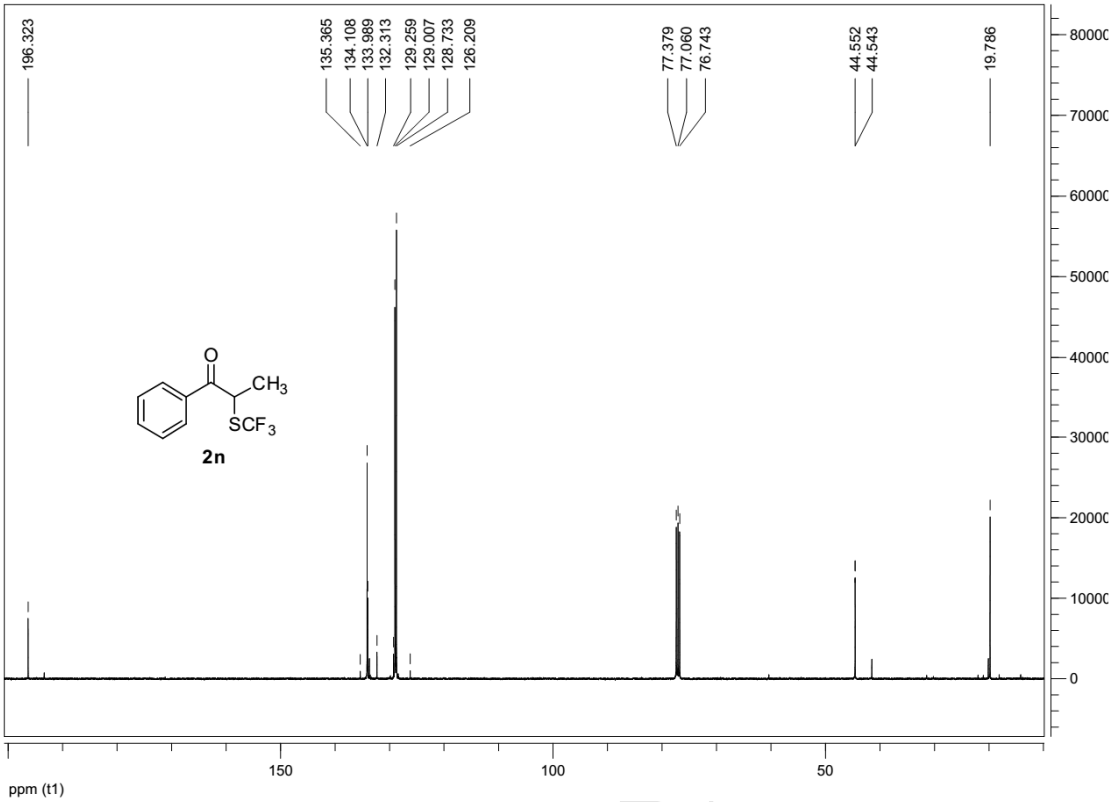

8.084
8.063
7.798
7.778
7.267
4.516
-0.00000
50000
0
2.16
2.12
2.00
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)
O
SCF3
F3C
2l

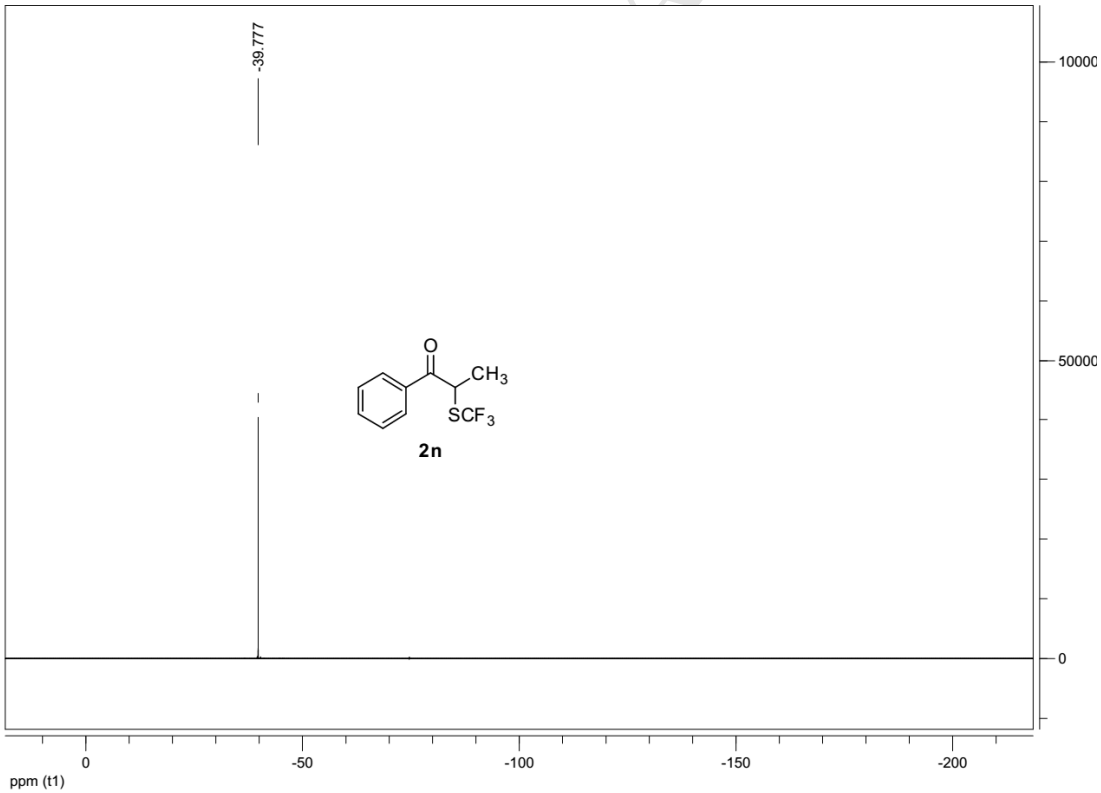

191.250
137.287
135.952
135.623
135.296
135.017
134.967
131.969
128.921
128.806
127.405
126.128
126.092
126.056
126.020
125.873
124.693
121.981
119.270
77.336
77.018
76.701
38.212
38.196
10000
50000
0
150
100
50
ppm (t1)
O
SCF3
F3C
2l


-41.464
-63.353
O
SCF3
F3C
2l
10000
50000
0
0
-50
-100
-150
-200
ppm (t1)

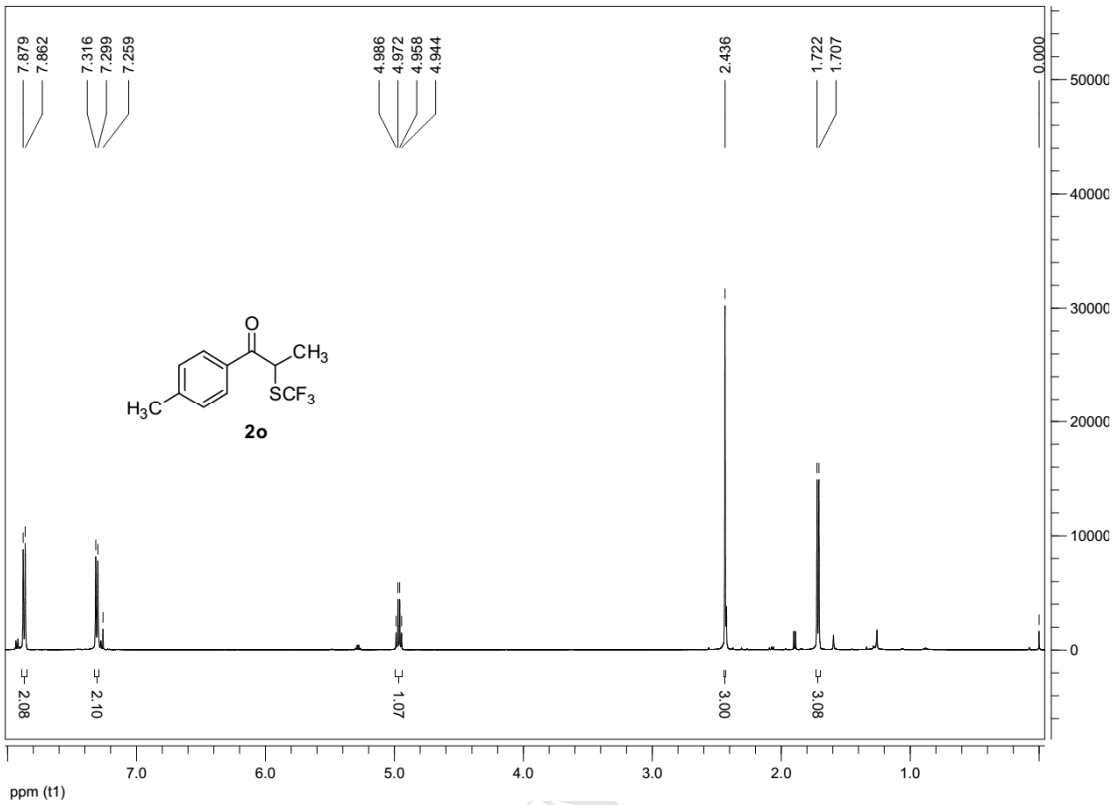
Compound **2n**

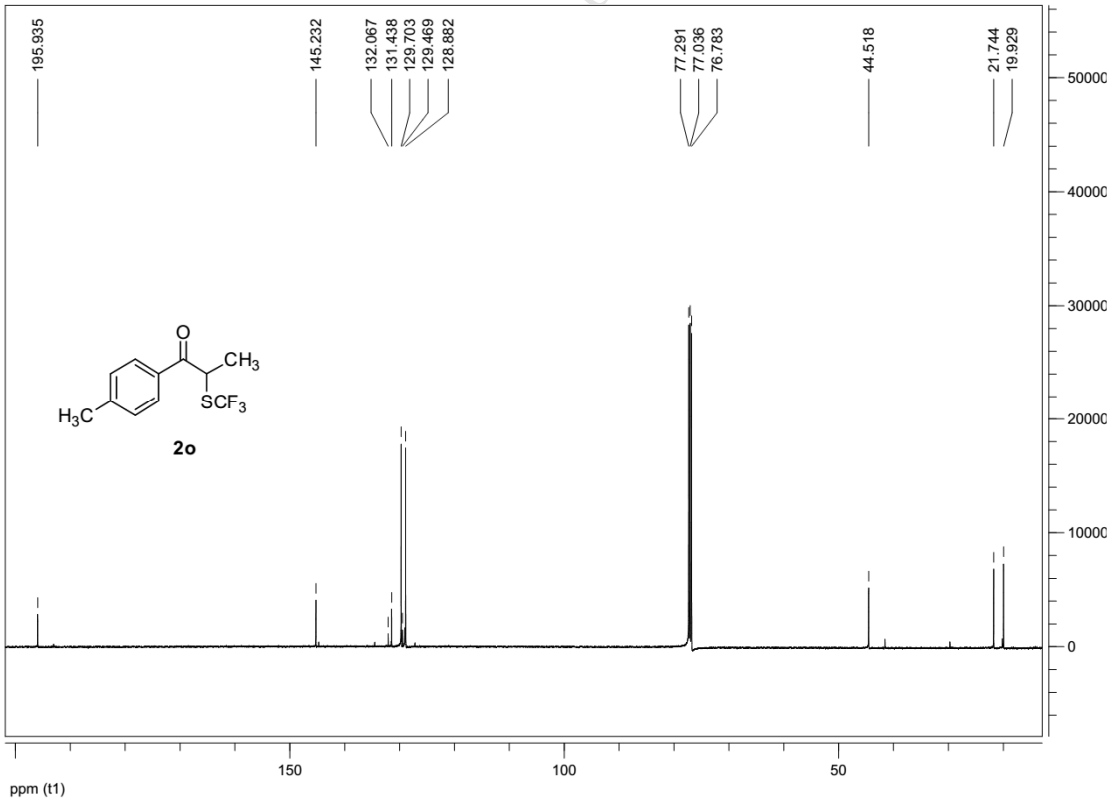

7.981
7.962
7.648
7.630
7.611
7.530
7.510
7.491
7.261
5.016
4.998
4.981
4.963
1.734
1.716
-0.00000
O
CH3
SCF3
2n
1.94
0.97
2.69
1.00
3.03
10000
50000
0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

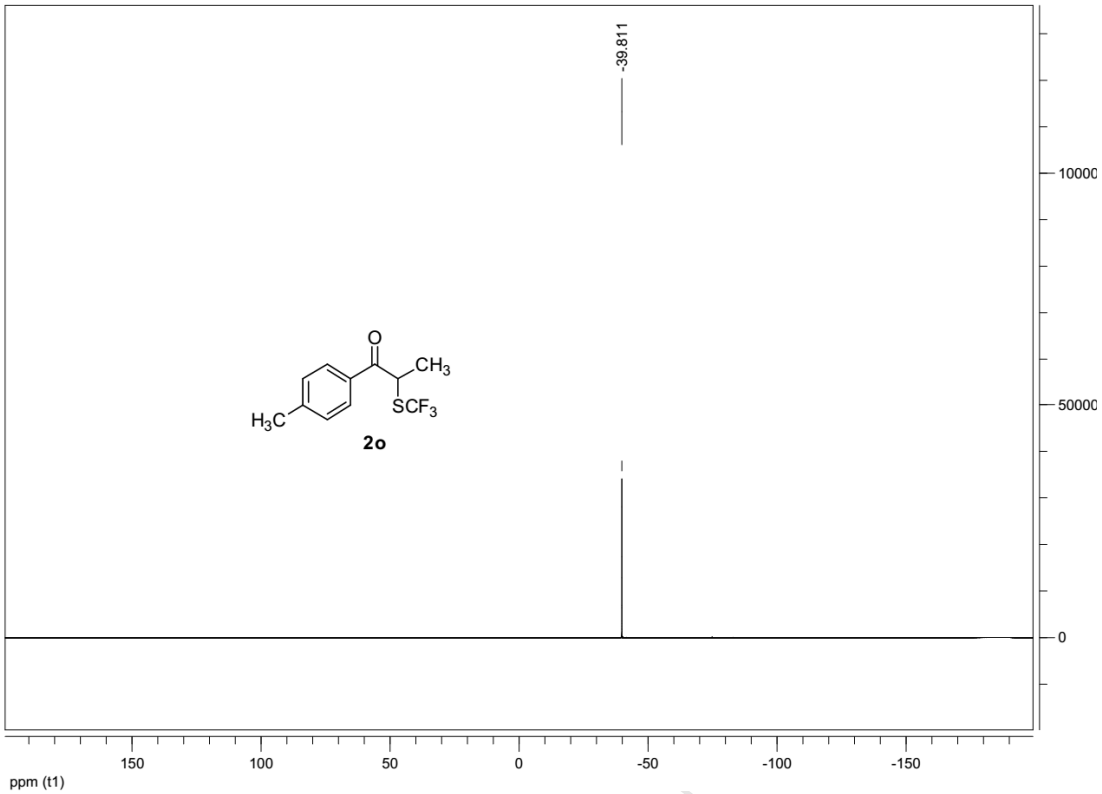

196.323
135.365
134.108
133.989
132.313
129.259
129.007
128.733
126.209
77.379
77.060
76.743
44.552
44.543
19.786
O
CH3
SCF3
2n
ppm (t1)


-39.777
O
CH3
SCF3
2n
ppm (t1)

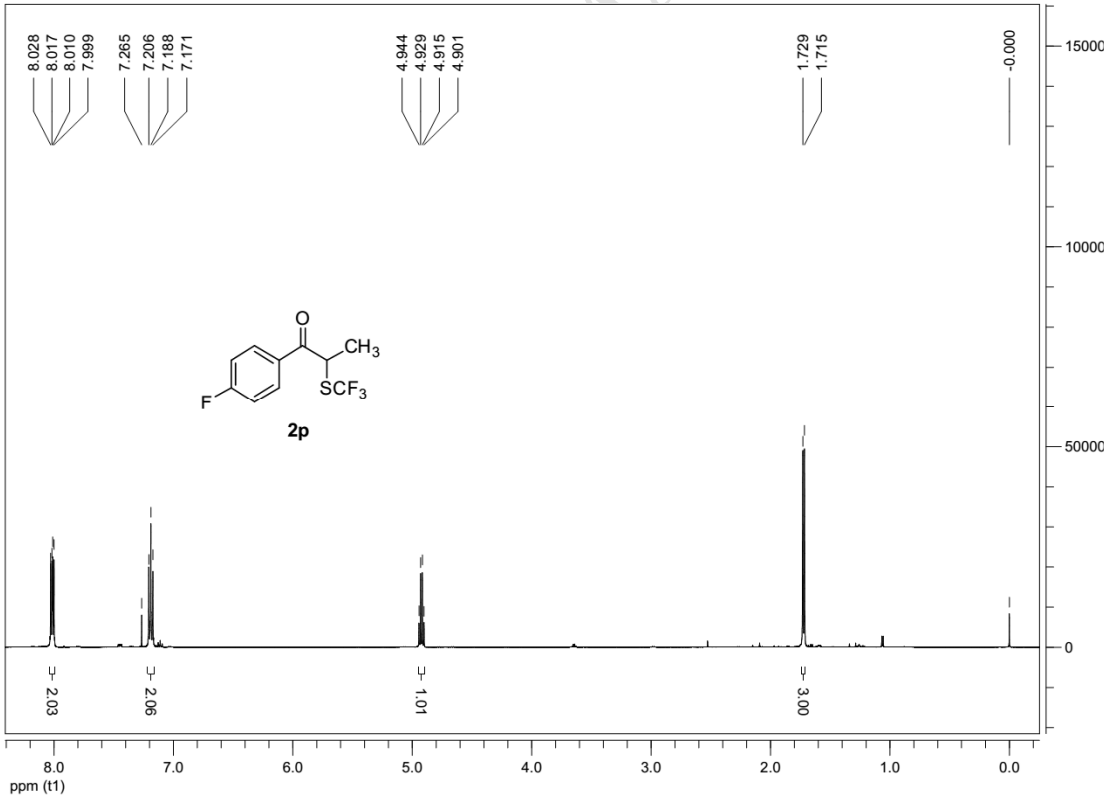
Compound **2o**

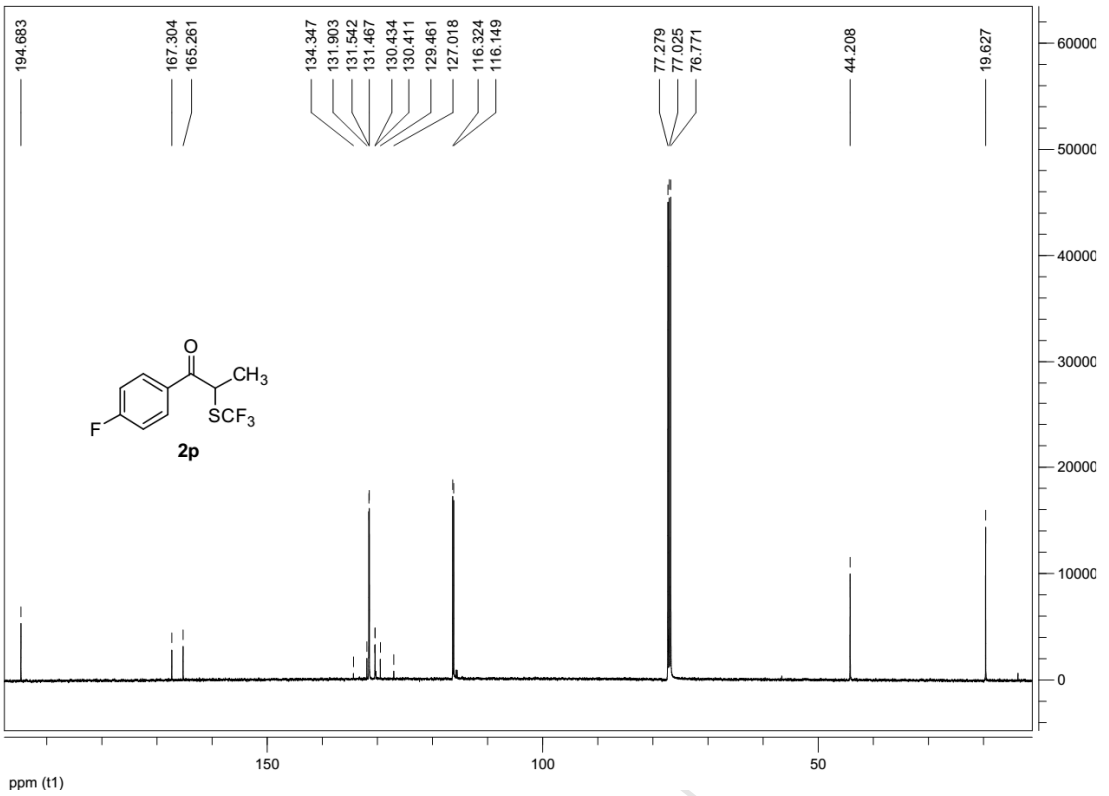

7.879
7.862
7.316
7.299
7.259
4.986
4.972
4.958
4.944
2.436
1.722
1.707
0.000
2.08
2.10
1.07
3.00
3.08
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)
O
CH3
SCF3
H3C
2o

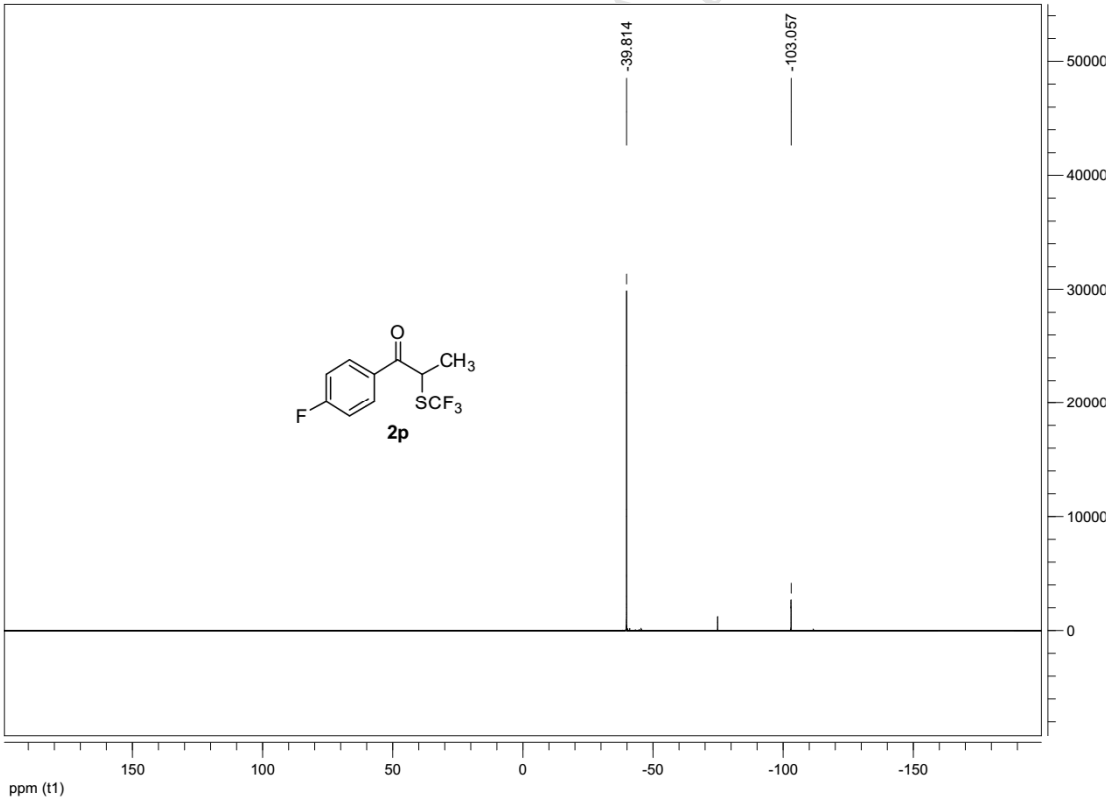

195.935
145.232
132.067
131.438
129.703
129.469
128.882
77.291
77.036
76.783
44.518
21.744
19.929
150
100
50
ppm (t1)
O
CH3
SCF3
H3C
2o


-39.811
10000
50000
0
O
CH3
SCF3
H3C
2o
150
100
50
0
-50
-100
-150
ppm (t1)

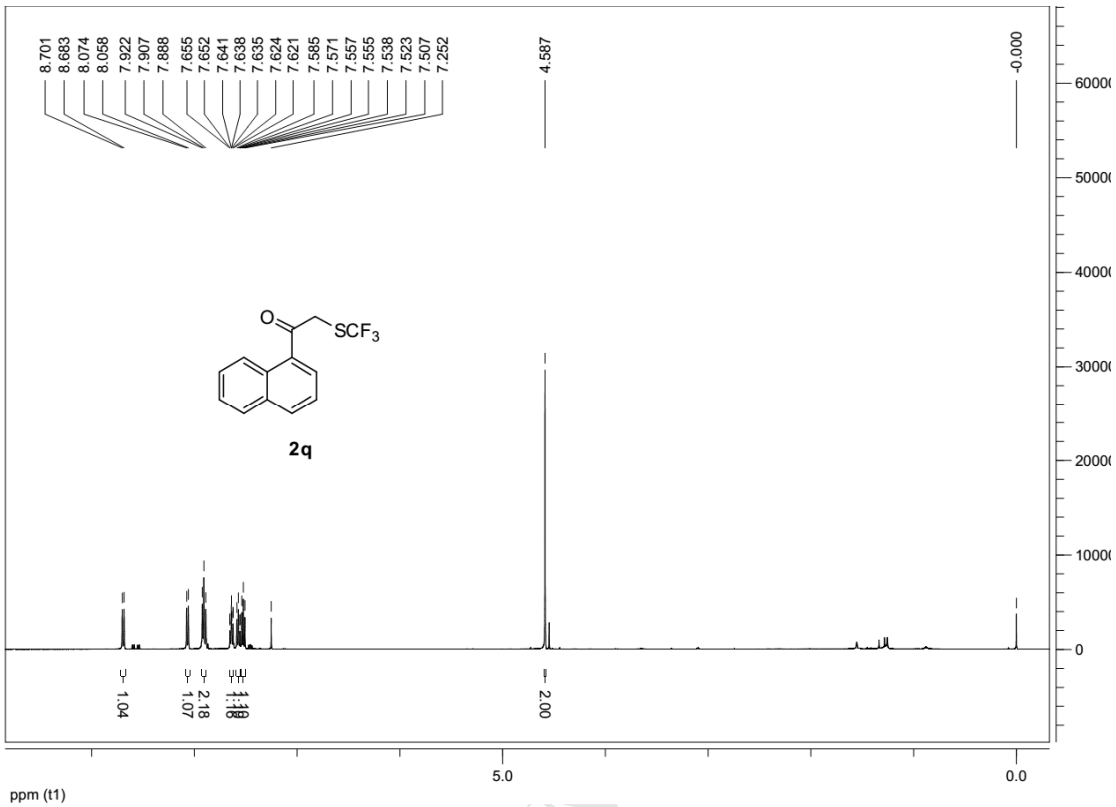
Compound **2p**

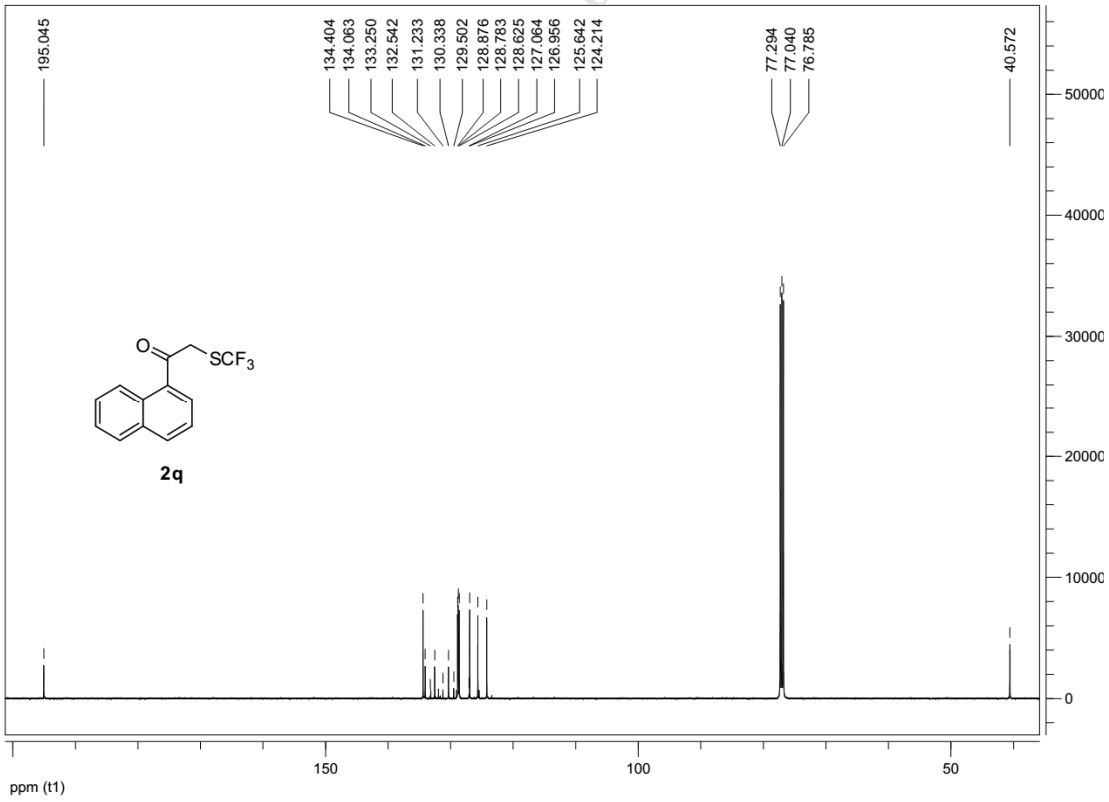

8.028
8.017
8.010
7.999
7.265
7.206
7.188
7.171
4.944
4.929
4.915
4.901
1.729
1.715
-0.000
15000
10000
50000
0
O
CH3
SCF3
F
2p
2.03
2.06
1.01
3.00
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

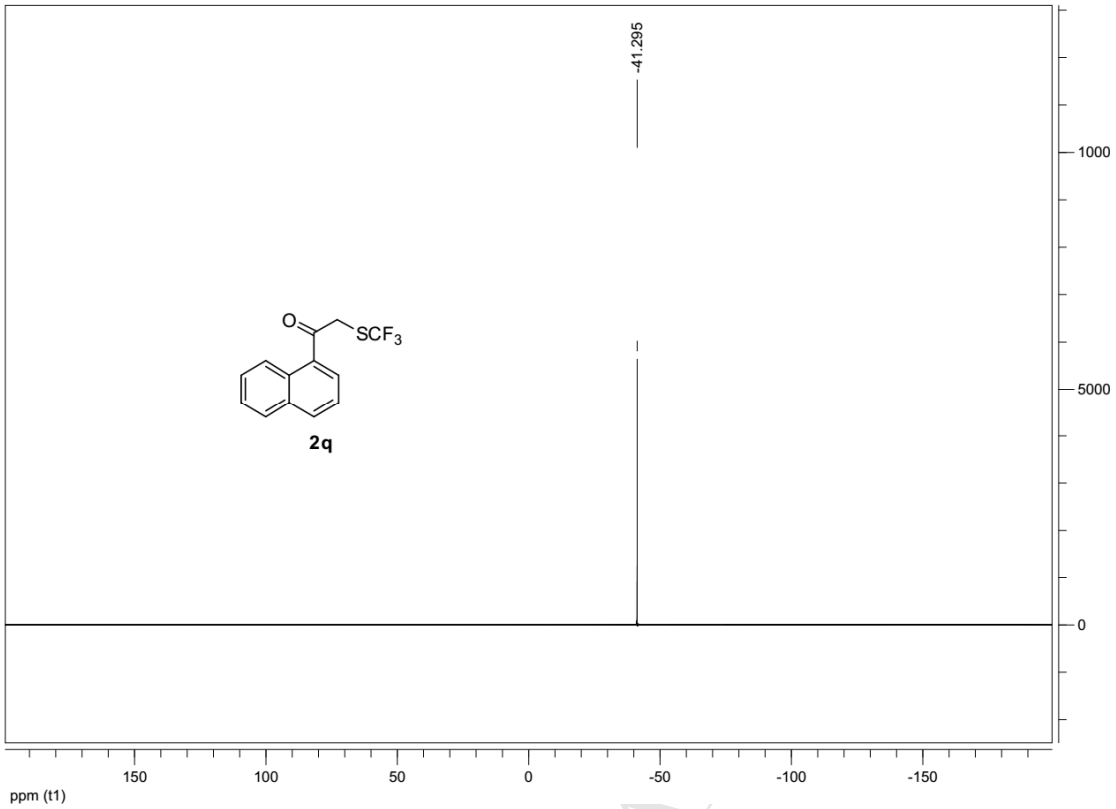

194.683
167.304
165.261
134.347
131.903
131.542
131.467
130.434
130.411
129.461
127.018
116.324
116.149
77.279
77.025
76.771
44.208
19.627
60000
50000
40000
30000
20000
10000
0
150
100
50
ppm (t1)
O
CH3
SCF3
F
2p


-39.814
-103.057
50000
40000
30000
20000
10000
0
150
100
50
0
-50
-100
-150
ppm (t1)
O
CH3
SCF3
F
2p

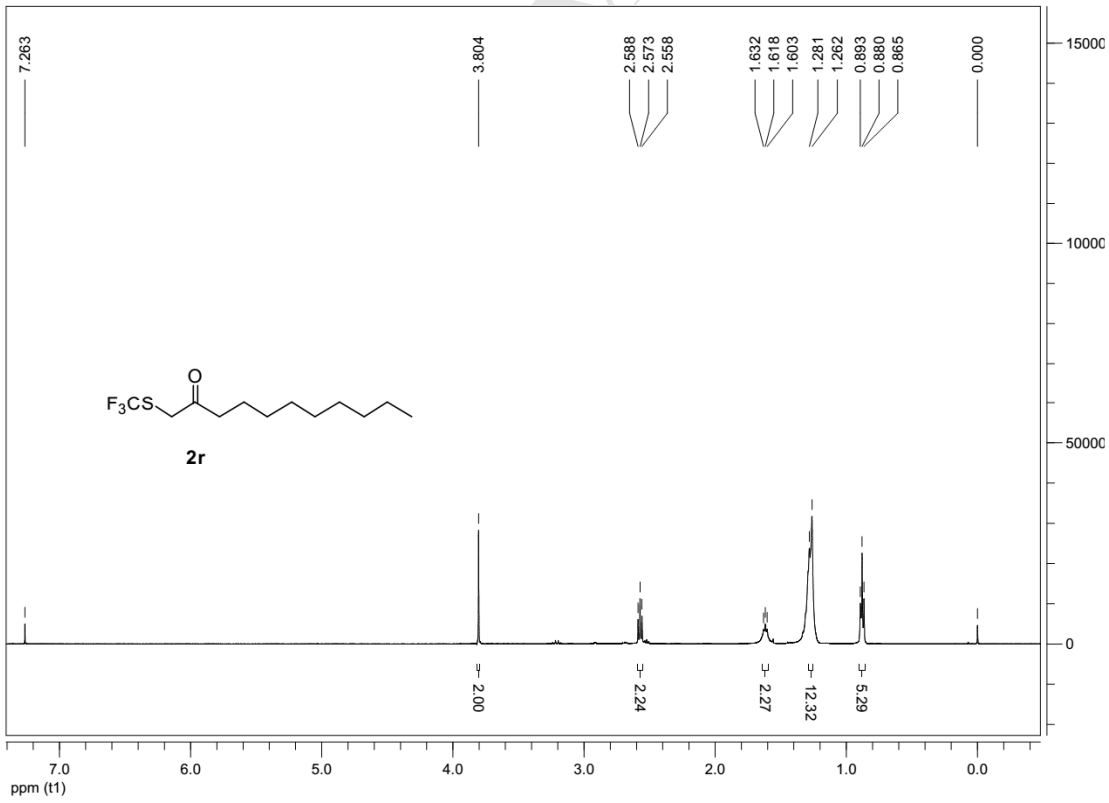
Compound **2q**

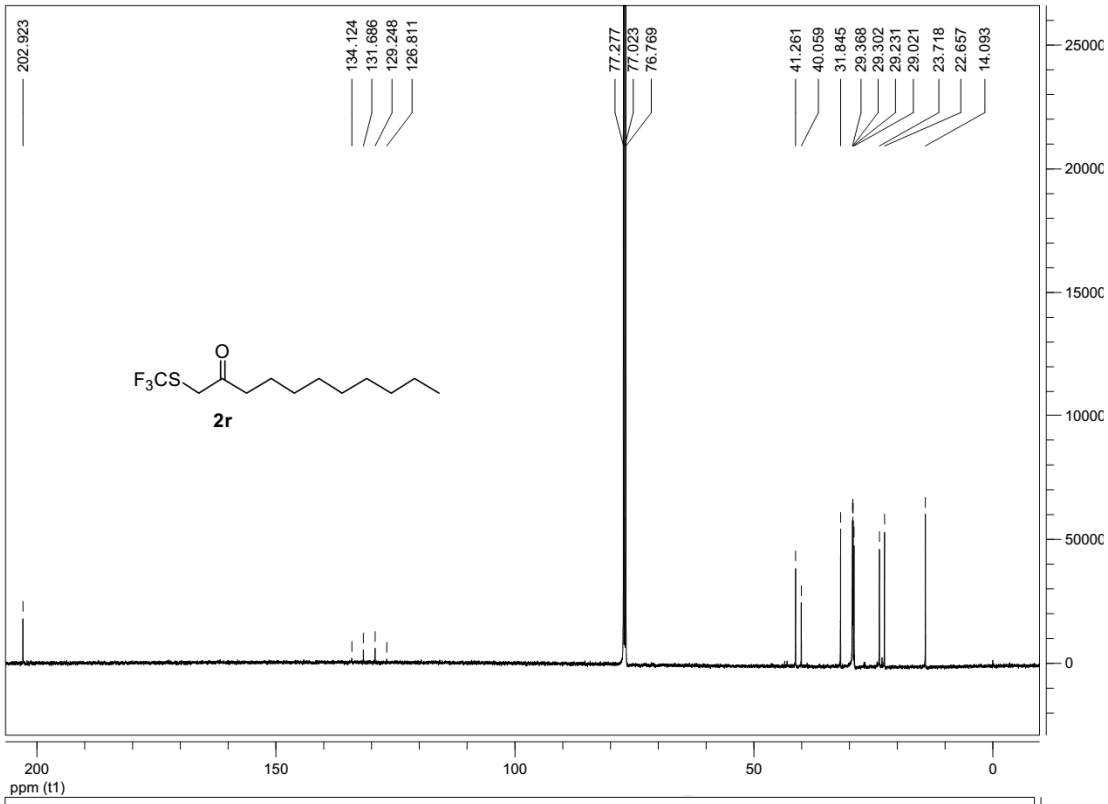

8.701
8.683
8.074
8.058
7.922
7.907
7.888
7.655
7.652
7.641
7.638
7.635
7.624
7.621
7.585
7.571
7.557
7.555
7.538
7.523
7.507
7.252
4.587
-0.000
O
SCF3
2q
1.04
1.07
2.18
2.00
5.0
0.0
ppm (t1)

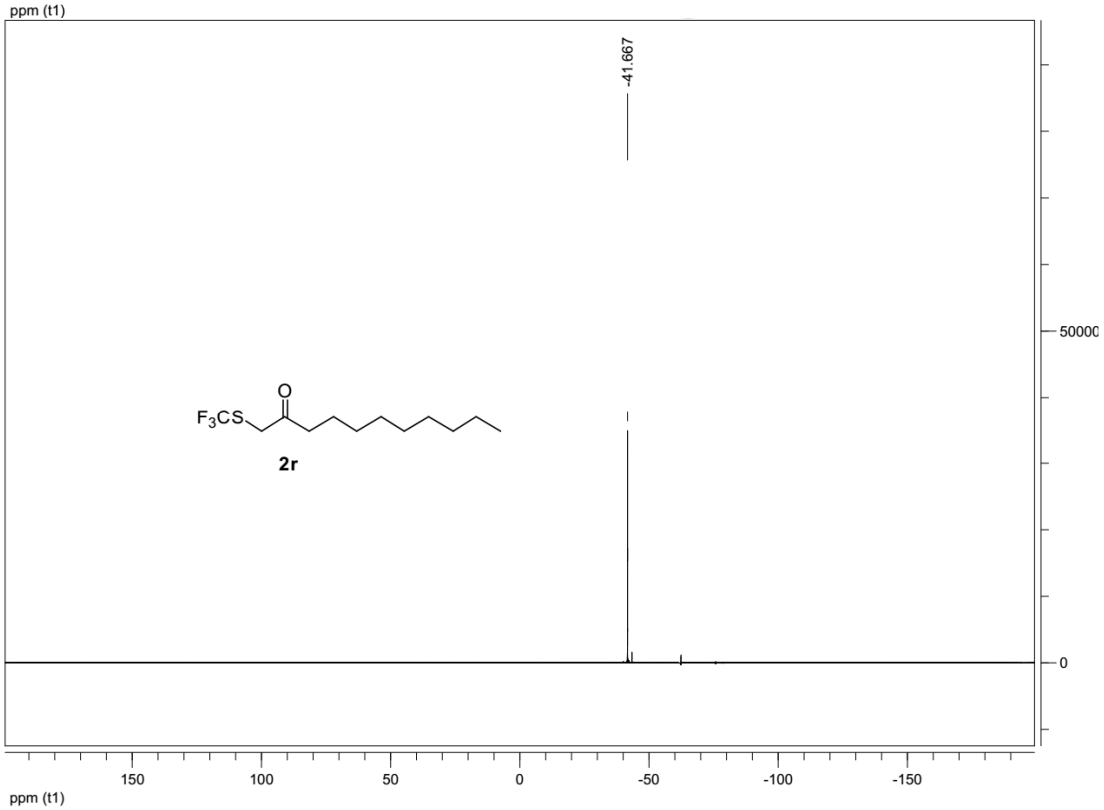

195.045
134.404
134.063
133.250
132.542
131.233
130.338
129.502
128.876
128.783
128.625
127.064
126.956
125.642
124.214
77.294
77.040
76.785
40.572
O
SCF3
2q
150
100
50
ppm (t1)


-41.295
1000
5000
0
O
SCF3
2q
150
100
50
0
-50
-100
-150
ppm (t1)

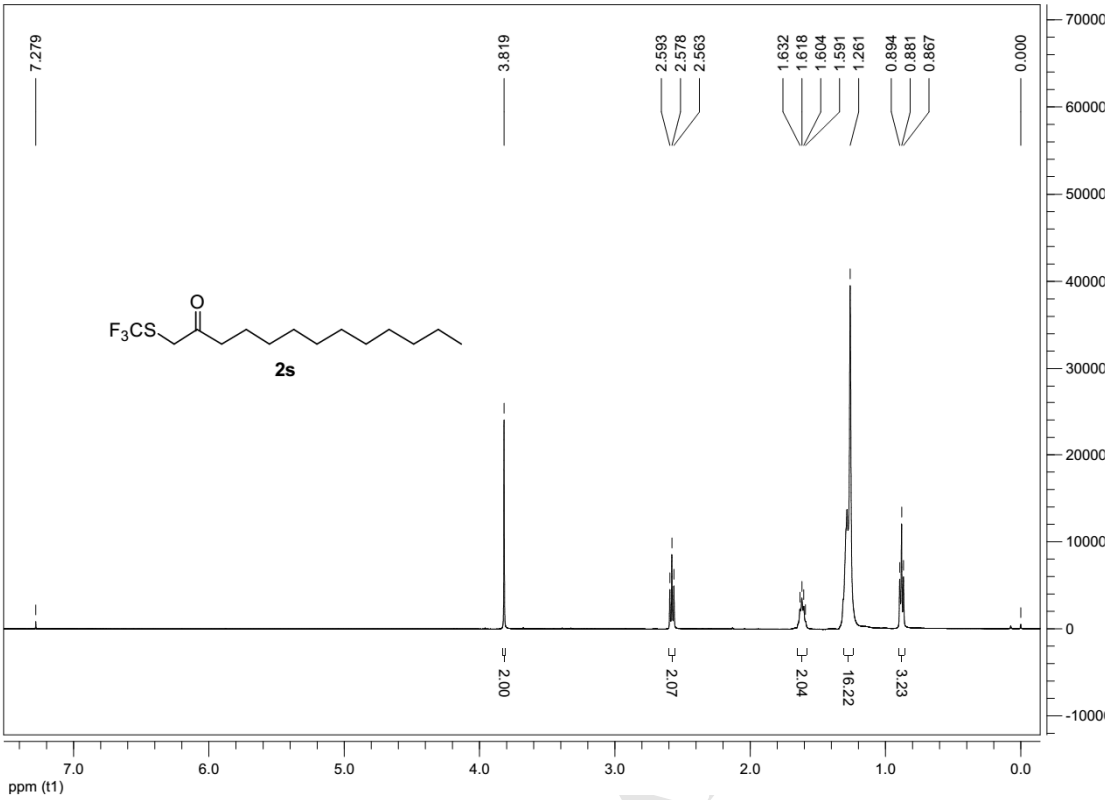
Compound **2r**

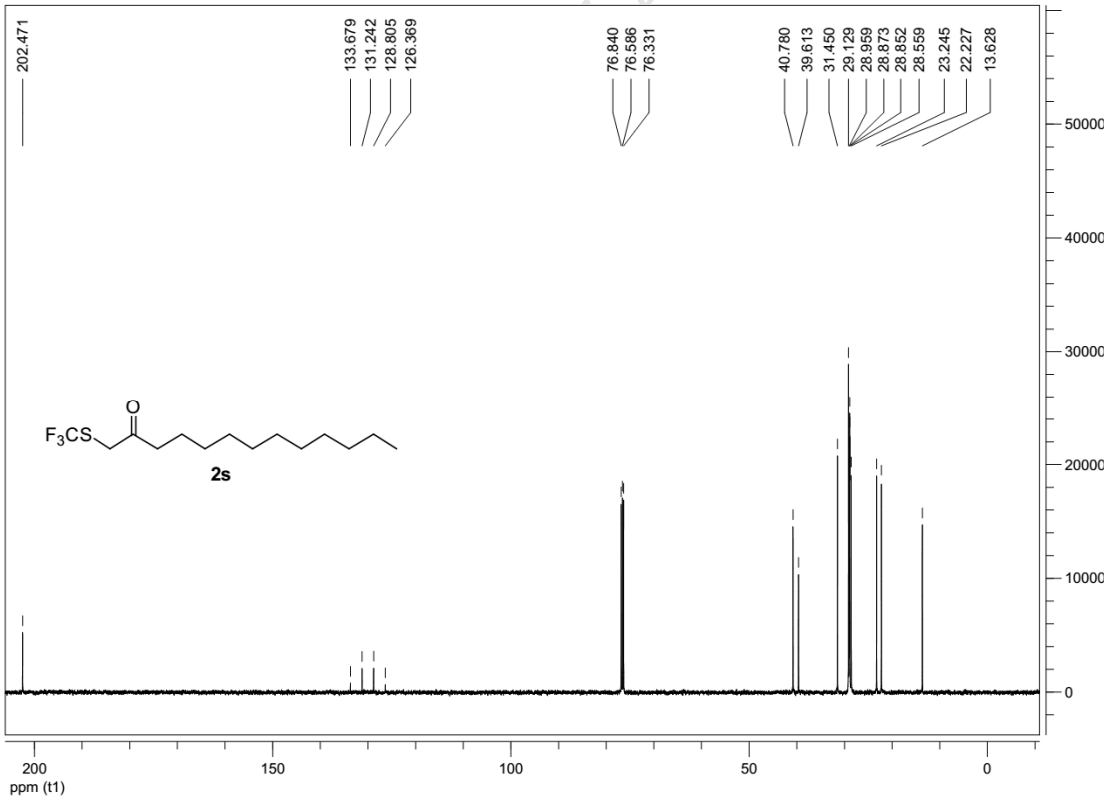

7.263
3.804
2.588
2.573
2.558
1.632
1.618
1.603
1.281
1.262
0.893
0.880
0.865
0.000
15000
10000
50000
0
O
F3CS
2r
2.00
2.24
2.27
12.32
5.29
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


202.923
134.124
131.686
129.248
126.811
77.277
77.023
76.769
41.261
40.059
31.845
29.368
29.302
29.231
29.021
23.718
22.657
14.093
25000
20000
15000
10000
50000
0
O
F3CS
2r
200
150
100
50
0
ppm (t1)


-41.667
50000
0
O
F3CS
2r
150
100
50
0
-50
-100
-150
ppm (t1)

Compound **2s**


7.279
3.819
2.593
2.578
2.563
1.632
1.618
1.604
1.591
1.261
0.894
0.881
0.867
0.000
O
F3CS
2s
2.00
2.07
2.04
16.22
3.23
ppm (t1)


202.471
133.679
131.242
128.805
126.369
76.840
76.586
76.331
40.780
39.613
31.450
29.129
28.959
28.873
28.852
28.559
23.245
22.227
13.628
O
F3CS
2s
ppm (t1)