Supporting Information

A Redox-Economical Synthesis of Trifluoromethylated Enamides with the Langlois Reagent

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1. General Information

All reactions were carried out under argon unless otherwise stated. Oxime acetates **1** were prepared according to literature procedures using commercial reagents (Section 2).[1] All other starting materials and solvents were purchased from commercial suppliers and used as received.

^{1}H NMR and ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$ or CD_3CN on a Bruker 400 or a 500 MHz spectrometer. Chemical shifts (δ) are reported in ppm with the following abbreviations used for the observed multiplicities: s (singlet), d (doublet), t (triplet), q (quartet), br (broad), m (multiplet for unresolved lines). ^{1}H NMR chemical shifts were referenced to the residual solvent signal for $CHCl_3$ (7.26 ppm) or MeCN (1.94 ppm), and ^{13}C NMR chemical shifts were referenced to the solvent signal of $CDCl_3$ (77.0 ppm) or CD_3CN (1.32 ppm). Analytical TLC was performed on pre-coated silica gel plates. After elution, the plates were visualized by UV illumination at 254−360 nm and by staining with ethanolic $KMnO_4$ or ethanolic phosphomolybdic acid. Column chromatography was performed using Davisil 60Å silica gel (35-70 μm). HRMS data were recorded on a micrOTOF instrument using ESI techniques.

2. Experimental Procedures and Spectral Data

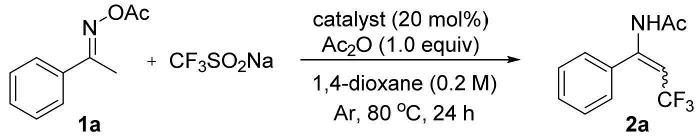
2.1. Preparation of starting materials

Oxime acetates **1** were synthesized from the corresponding ketones according to literature procedures.[1-2] All other compounds were used as received from commercial sources.

2.2. General procedure for the screening of reaction conditions

To a screw-cap vial equipped with a magnetic stirring bar were added oxime acetate **1a** (0.20 mmol), CF_3SO_2Na (0.30 mmol), $CuCl_2$ (0.04 mmol), acylating reagent (0.20 mmol), ligand or additive (0.04 mmol) and CH_3CN (1.0 mL) under argon (glove-box). The reaction mixture was stirred at 80 °C for 24 h. The mixture was then allowed to cool down to room temperature and the reaction yield was determined by ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard. The results are summarized in Table S-1, Table S-2, Table S-3 and Table S-4.

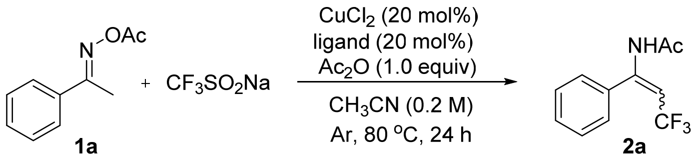
Table S-1: **Screening of catalysts**[a]



catalyst	**2a** yield (%)	E/Z
CuBr	16	1.25:1
CuI	15	1.43:1
CuTc	24	1.40:1
CuOAc	16	1.29:1
$Cu(CH_3CN)_4PF_6$	30	2.00:1
$CuCl_2$	30	1.30:1
CuF_2	**41**	**1.00:1**
$Cu(OAc)_2$	32	1.13:1
$MnCl_2{\cdot}4H_2O$	0	n.d.
$FeCl_2$	0	n.d.

[a]Yields and E/Z ratios were determined by ^{19}F NMR. n.d. = not determined.

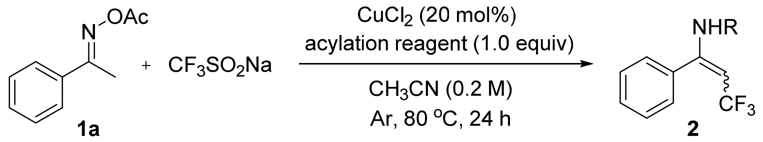
Table S-2: **Screening of ligands**[a]

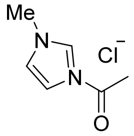
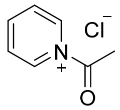


ligand	**2a** yield (%)	E/Z
none	38	1.82:1
$P(Cy)_3$	38	1.97:1
1,10-phenanthroline	3	n.d.
2,2'-biquinoline	27	2.00:1

[a]Yields and E/Z ratios were determined by ^{19}F NMR. n.d. = not determined.

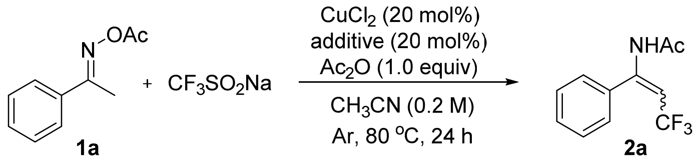
Table S-3: Screening of acylation reagents[a]



acylation reagent	**2** yield (%)	R	E/Z
CBzCl	trace	CBz	1.82:1
Boc_2O	trace	Boc	1.97:1
Piv_2O	4	Piv	n.d.
BzCl	5	Bz	n.d.
AcCl	12	Ac	5.00:1
Ac_2O	38	Ac	1.82:1
Ac_2O[b]	0	Ac	n.d.
	trace	Ac	n.d.
	13	Ac	3.25:1

[a]Yields and E/Z ratios were determined by ^{19}F NMR. n.d. = not determined.
[b]CF_3SO_2Zn (1.5 equiv) was used as CF_3 source.

Table S-4: Screening of additives[a]



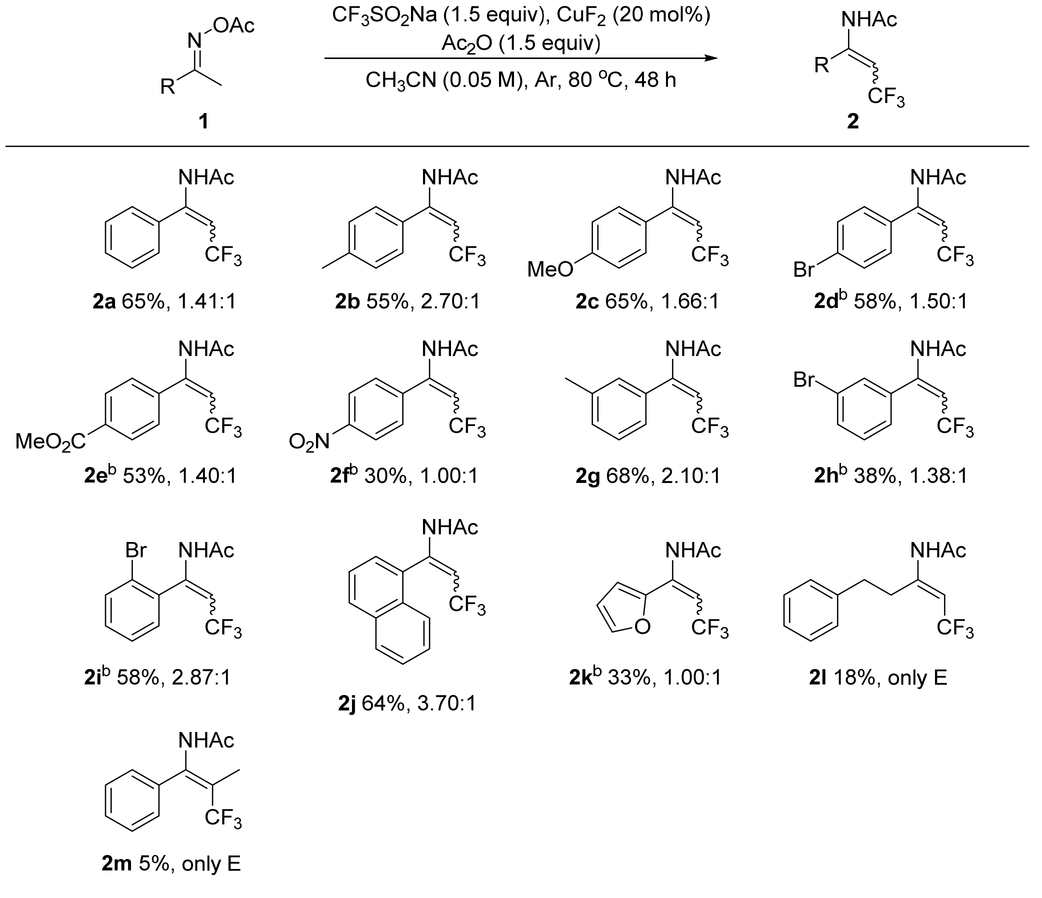
additive	**2a** yield (%)	E/Z
none	38	1.82:1
Cs_2CO_3	38	1.95:1
$NaHSO_3$	38	1.92:1
Li_2CO_3	44	1.78:1
proton sponge	22	2.17:1
LiCl (1 equiv)	44	1.92:1
Bu_4NBr	29	2.24:1
$Yb(OTf)_3.H_2O$	19	2.8:1
$Sc(OTf)_3$	40	1.86:1
$In(OTf)_3$	44	1.93:1
BEt_3	0	n.d.

[a]Yields and E/Z ratios were determined by ^{19}F NMR. n.d. = not determined.

2.3. General procedure for the copper-catalyzed trifluoromethylation of oxime acetates 1

To a screw-cap vial equipped with a magnetic stirring bar were added oxime acetates **1** (0.20 mmol), CF_3SO_2Na (0.30 mmol), CuF_2 (0.04 mmol), acetic anhydride (0.30 mmol) and CH_3CN (4.0 mL) under argon (glove-box). The reaction mixture was stirred at 80 °C for 48 h or 100 °C for 24 h. After the mixture was allowed to cool down to room temperature, the reaction yields and the *E/Z* selectivity were determined by ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard. The results are summarized in Table S-5.

Table S-5: **Substrate scope for the copper-catalyzed oxidative trifluoromethylation of oxime acetates 1 with the Langlois reagent**[a]



2a 65%, 1.41:1

2b 55%, 2.70:1

2c 65%, 1.66:1

2d[b] 58%, 1.50:1

2e[b] 53%, 1.40:1

2f[b] 30%, 1.00:1

2g 68%, 2.10:1

2h[b] 38%, 1.38:1

2i[b] 58%, 2.87:1

2j 64%, 3.70:1

2k[b] 33%, 1.00:1

2l 18%, only E

2m 5%, only E

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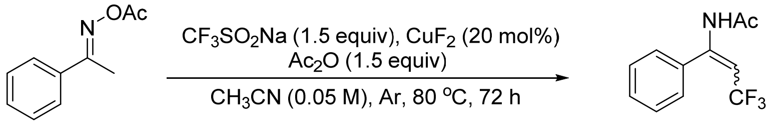
[a] Unless otherwise noted, the reactions were carried out at 80 °C using **1** (0.20 mmol), Langlois reagent (0.30 mmol), CuF_2 (0.04 mmol) and Ac_2O (0.30 mmol) in acetonitrile (4.0 mL) for 48 h. NMR yields and E/Z ratios were determined using α,α,α–trifluorotoluene as an internal standard).

[b] The reactions were carried out at 100 °C for 24 h.

2.4. General procedure for the trifluoromethylation of oxime acetates 1 and isolation of enamides 2

To a screw-cap vial equipped with a magnetic stirring bar were added oxime acetate **1** (1.0 equiv), CF_3SO_2Na (1.5 equiv), CuF_2 (0.2 equiv), acetic anhydride (1.5 equiv) and CH_3CN (20 mL/mmol) under argon (glove-box). The resulting mixture was stirred at 80 °C for 72 hours. The solvent was removed *in vacuo* and the residue was purified by column chromatography using petroleum ether:ethyl acetate 3:1 or 5:1 as the eluent system to obtain compound **2a** (Scheme S-1), **2c**, **2g** and **2j**.

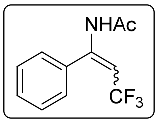
Scheme S-1 Scale-up reaction



1a (177.2 mg)

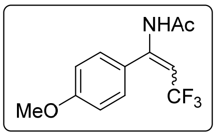
2a (130 mg), *E*:*Z* = 1.60:1, 57%

N-(3,3,3-Trifluoro-1-phenylprop-1-en-1-yl)acetamide (2a)



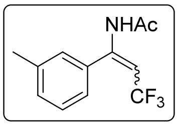
2a: (scale: 1.00 mmol, white solid, 57% yield, 130.0 mg, *E*:*Z* (isolated) = 1.60:1); ^{1}H NMR data are in accordance with literature[6] values: **^{1}H NMR** (500 MHz, $CDCl_3$): δ ppm 7.82-7.23 (m, 6H), 7.13 (br s, 1H), 7.00 (q, J = 8.4 Hz, 1H), 5.50 (q, J = 8.1 Hz, 1H), 1.96 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ ppm 169.43, 168.74 (minor isomer), 144.97 (q, J = 5.5 Hz, minor isomer), 143.93 (q, J = 6.0 Hz), 135.37 (minor isomer), 134.82, 130.08 (minor isomer), 129.61, 128.57 (minor isomer), 128.45, 128.13, 126.53 (minor isomer), 124.27 (q, J = 268.3 Hz), 122.85 (q, J = 269.7 Hz, minor isomer), 107.08 (q, J = 23.9 Hz, minor isomer), 102.75 (q, J = 34.9 Hz), 24.54, 23.23 (minor isomer); **^{19}F NMR** (376 MHz, $CDCl_3$): δ ppm -52.85 (d, J = 8.4 Hz), -57.68 (d, J = 8.1 Hz, minor isomer); **HRMS** (ESI): *m/z* calcd for $C_{11}H_{10}F_3NNaO$ $[M+Na]^+$ 252.0607, found 252.0605.

N-(3,3,3-Trifluoro-1-(4-methoxyphenyl)prop-1-en-1-yl)acetamide (2c)



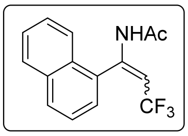
2c: (scale: 0.50 mmol, white solid, 55% yield, 71.0 mg, *E*:*Z* (isolated) = 1.62:1); ^{1}H NMR data are in accordance with literature[6] values: **^{1}H NMR** (400 MHz, $(CD_3)_2CO$): δ ppm 8.81 (brs, 1H, minor isomer), 8.69 (brs, 1H), 7.49 (d, J = 8.8 Hz, 2H, minor isomer), 7.31 (d, J = 8.7 Hz, 2H), 7.06 (q, J = 8.9 Hz, 1H), 6.97-6.93 (m, 2H (minor isomer) +2H (major isomer)), 5.80 (q, J = 8.3 Hz, 1H), 3.83 (s, 3H), 3.58 (s, 3H, minor isomer), 2.09 (s, 3H), 2.07 (s, 3H, minor isomer); **^{13}C NMR** (100 MHz, $(CD_3)_2CO$): δ ppm 170.70, 169.44 (minor isomer), 162.16 (minor isomer), 161.48, 146.78 (q, J = 6.2 Hz), 145.72 (q, J = 5.7 Hz, minor isomer), 130.73 (q, J = 1.8 Hz), 129.34, 129.11, 127.95, 126.07 (q, J = 267.0 Hz), 124.34 (q, J = 268.6 Hz, minor isomer), 114.68, 114.35, 107.17 (q, J = 33.4 Hz, minor isomer), 100.97 (q, J = 34.4 Hz), 71.14 (minor isomer), 55.66, 24.51, 23.14 (minor isomer); **^{19}F NMR** (376 MHz, $CDCl_3$): δ ppm -53.00 (d, J = 8.6 Hz), -57.48 (d, J = 8.1 Hz, minor isomer); **HRMS** (ESI): *m/z* calcd for $C_{12}H_{12}F_3NNaO_2$ $[M+Na]^+$ 282.0712, found 282.0719.

N-(3,3,3-Trifluoro-1-(*m*-tolyl)prop-1-en-1-yl)acetamide (2g)



2g: (scale: 0.50 mmol, white solid, 61% yield, 74.2 mg, *E*:*Z* (isolated) = 1.94:1); ^{1}H NMR data are in accordance with literature[6] values: **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* ppm 7.45-6.97 (m, 6H (major isomer) +5H (minor isomer)), 5.52 (q, *J* = 8.2 Hz, 1H), 2.40 (s, 3H), 2.39 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): *δ* ppm 169.25, 145.15 (q, *J* = 5.6 Hz, minor isomer), 144.01 (q, *J* = 6.1 Hz), 138.34, 135.39, 134.84, 130.95, 130.37, 128.59, 128.47, 128.38, 127.16, 125.23, 124.30 (q, *J* = 268.4 Hz), 123.74, 122.90 (q, *J* = 269.4 Hz, minor isomer), 106.87 (q, *J* = 31.9 Hz, minor isomer), 102.57 (q, *J* = 34.5 Hz), 24.64, 23.28 (minor isomer), 21.30 (minor isomer), 21.24; **^{19}F NMR** (376 MHz, $CDCl_3$): *δ* ppm -53.15 (d, *J* = 8.2 Hz), -57.72 (d, *J* = 7.8 Hz, minor isomer); **HRMS** (ESI): *m/z* calcd for $C_{12}H_{12}F_3NNaO$ [M+Na]+ 266.0763, found 266.0763.

N-(3,3,3-Trifluoro-1-(naphthalen-1-yl)prop-1-en-1-yl)acetamide (2j)

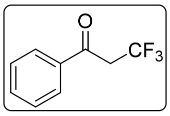


2j: (scale: 0.50 mmol, white solid, 54% yield, 75.4 mg, *E*:*Z* (isolated) = 17.5:1); **^{1}H NMR** (400 MHz, $(CD_3)_2CO$): *δ* ppm 8.92 (brs, 1H), 7.99 (t, *J* = 9.0 Hz, 2H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.65-7.48 (m, 4H), 7.44 (q, *J* = 8.9 Hz, 1H), 2.09 (s, 3H); **^{13}C NMR** (100 MHz, $(CD_3)_2CO$): *δ* ppm 170.76, 145.34 (q, *J* = 6.1 Hz), 134.37, 132.92, 131.85, 130.44, 129.13, 127.91 (q, *J* = 1.9 Hz), 127.77, 127.16, 125.94, 125.87 (q, *J* = 267.5 Hz), 125.72, 102.97 (q, *J* = 34.5 Hz), 24.47; **^{19}F NMR** (376 MHz, $CDCl_3$): *δ* ppm -54.89 (d, *J* = 8.0 Hz), -57.24 (d, *J* = 9.3 Hz, minor isomer); **HRMS** (ESI): *m/z* calcd for $C_{15}H_{12}F_3NNaO$ $[M+Na]^+$ 302.0763, found 302.0764.

2.5. General procedure for the trifluoromethylation of oxime acetates 1 and subsequent hydrolysis

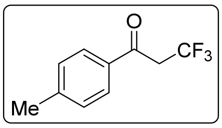
To a screw-cap vial equipped with a magnetic stirring bar were added oxime acetates **1** (0.20 mmol), CF_3SO_2Na (0.30 mmol), CuF_2 (0.04 mmol), acetic anhydride (0.30 mmol) and CH_3CN (4.0 mL) under argon (glove-box). The resulting mixture was stirred at 80 °C for 48 h or 100 °C for 24 h. The solvent was removed *in vacuo* and the residue was purified by a short column of silica gel. The resulting material was dissolved in 1,4-dioxane (1.0 mL) and treated with aqueous HCl (2 M, 1.0 mL) at 80 °C for 2 h. The mixture was then diluted with water and extracted with CH_2Cl_2. The resulting phases were separated and the organic phase was concentrated *in vacuo*. The crude products were purified by column chromatography with the indicated eluent system to obtain *α*-trifluoromethyl substituted ketones **3a-3l**.

3,3,3-Trifluoro-1-phenylpropan-1-one (3a)



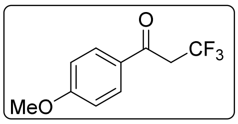
3a: (eluent: petroleum ether:ethyl acetate 30:1, white solid, 55% yield, 21.0 mg); NMR data are in accordance with literature[3] values: **^{1}H NMR** (500 MHz, $CDCl_3$): δ ppm 7.95-7.93 (m, 2H), 7.65-7.62 (m, 1H), 7.53-7.50 (m, 2H), 3.80 (q, J = 10.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ ppm 189.67 (q, J = 2.3 Hz), 135.80 (q, J = 1.7 Hz), 134.18, 128.92, 128.34, 123.98 (q, J = 276.9 Hz), 42.09 (q, J = 28.2 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$): δ ppm -62.03 (t, J = 9.9 Hz).

3,3,3-Trifluoro-1-(*p*-tolyl)propan-1-one (3b)



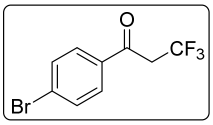
3b: (eluent: petroleum ether:ethyl acetate 30:1, white solid, 50% yield, 20.0 mg); NMR data are in accordance with literature[3] values: **^{1}H NMR** (400 MHz, $CDCl_3$): δ ppm 7.83 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 7.9 Hz, 2H), 3.79 (q, J = 10.0 Hz, 2H), 2.43 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ ppm 189.27 (q, J = 2.5 Hz), 145.28, 133.40 (q, J = 2.1 Hz), 129.59, 128.48, 124.05 (q, J = 276.9 Hz), 41.97 (q, J = 28.1 Hz), 21.69; **^{19}F NMR** (376 MHz, $CDCl_3$): δ ppm -62.03 (t, J = 9.9 Hz).

3,3,3-Trifluoro-1-(4-methoxyphenyl)propan-1-one (3c)



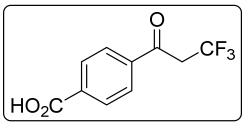
3c: (eluent: petroleum ether:ethyl acetate 30:1, white solid, 52% yield, 22.7 mg); NMR data are in accordance with literature[3] values: **^{1}H NMR** (500 MHz, $CDCl_3$): δ ppm 7.91 (d, J = 8.9 Hz, 2H), 6.97 (d, J = 8.9 Hz, 2H), 3.89 (s, 3H), 3.73 (q, J = 10.1 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ ppm 188.09 (q, J = 2.5 Hz), 164.33, 130.81, 128.94, 124.09 (q, J = 277.1 Hz), 114.08, 55.58, 41.82 (q, J = 28.1 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$): δ ppm -61.95 (t, J = 10.1 Hz).

1-(4-Bromophenyl)-3,3,3-trifluoropropan-1-one (3d)



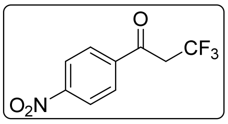
3d: (reaction conditions for the trifluoromethylation step: 24 h at 100 °C, eluent: petroleum ether:ethyl acetate 30:1, white solid, 50% yield, 26.7 mg); NMR data are in accordance with literature[4] values: **^{1}H NMR** (400 MHz, $CDCl_3$): δ ppm 7.85-7.74 (m, 2H), 7.65 (dd, J = 8.6, 1.4 Hz, 2H), 3.76 (q, J = 9.9 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ ppm 188.72 (q, J = 2.7 Hz), 134.48 (q, J = 1.8 Hz), 132.30, 129.79, 129.65, 123.78 (q, *J* = 277.0 Hz), 42.12 (q, *J* = 28.5 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$): *δ* ppm -62.00 (t, *J* = 9.9 Hz).

4-(3,3,3-Trifluoropropanoyl)benzoic acid (3e)



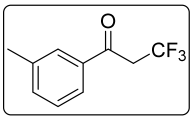
3e: (reaction conditions for the trifluoromethylation step: 24 h at 100 °C, hydrolysis was performed at 80 °C for 24 h, eluent: dichloromethane:ethanol 20:1, white solid, 52% yield, 24.0 mg); **^{1}H NMR** (400 MHz, CD_3CN): *δ* ppm 8.13 (d, *J* = 8.6 Hz, 2H), 8.03 (d, *J* = 8.5 Hz, 2H), 4.08 (q, *J* = 10.4 Hz, 3H); **^{13}C NMR** (100 MHz, CD_3CN): *δ* ppm 191.41 (q, *J* = 2.5 Hz), 166.89, 140.12 (q, *J* = 2.02 Hz), 135.69, 130.95, 129.29, 125.71 (q, *J* = 275.7 Hz), 43.06 (q, *J* = 27.6 Hz); **^{19}F NMR** (376 MHz, CD_3CN): *δ* ppm -63.18 (t, *J* = 10.2 Hz); **HRMS** (ESI): *m/z* calcd for $C_{10}H_6F_3O_3$ $[M-H]^-$ 231.0275, found 231.0273.

3,3,3-Trifluoro-1-(4-nitrophenyl)propan-1-one (3f)



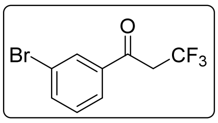
3f: (reaction conditions for the trifluoromethylation step: 24 h at 100 °C, eluent: petroleum ether:ethyl acetate 20:1, white solid, 30% yield, 14.0 mg); NMR data are in accordance with literature[3] values: **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* ppm 8.38 (d, *J* = 8.8 Hz, 2H), 8.12 (d, *J* = 8.8 Hz, 2H), 3.89 (q, *J* = 9.7 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$): *δ* ppm 188.30 (q, *J* = 2.5 Hz), 150.91, 139.91, 129.46, 124.16, 123.50 (q, *J* = 277.4 Hz), 42.70 (q, *J* = 28.8 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$): *δ* ppm -62.00 (t, *J* = 9.6 Hz).

3,3,3-Trifluoro-1-(*m*-tolyl)propan-1-one (3g)



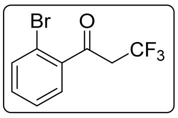
3g: (eluent: petroleum ether:ethyl acetate 30:1, white solid, 60% yield, 24 mg); NMR data are in accordance with literature[5] values: **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* ppm 7.86-7.63 (m, 2H), 7.52-7.31 (m, 2H), 3.78 (q, *J* = 10.0 Hz, 2H), 2.43 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): *δ* ppm 189.85 (q, *J* = 2.4 Hz), 138.86, 135.85, 134.95, 128.80, 128.76, 125.58, 124.02 (q, *J* = 276.9 Hz), 42.09 (q, *J* = 28.2 Hz), 21.29; **^{19}F NMR** (376 MHz, $CDCl_3$): *δ* ppm -62.06 (t, *J* = 10.1 Hz).

1-(3-Bromophenyl)-3,3,3-trifluoropropan-1-one (3h)



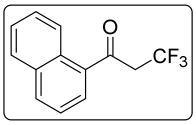
3h: (reaction conditions for the trifluoromethylation step: 24 h at 100 °C, eluent: petroleum ether:ethyl acetate 30:1, white solid, 38% yield, 20.3 mg); NMR data are in accordance with literature[3] values: **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* ppm 8.06 (t, *J* = 1.8 Hz, 1H), 7.85 (ddd, *J* = 7.9, 1.7, 1.0 Hz, 1H), 7.76 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1H), 7.41 (t, *J* = 7.9 Hz, 1H), 3.80 (q, *J* = 9.8 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* ppm 188.48 (q, *J* = 2.5 Hz), 137.08, 131.23, 130.50, 126.81, 123.68 (q, *J* = 276.9 Hz), 123.22, 42.06 (q, *J* = 28.5 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$): *δ* ppm -62.06 (t, *J* = 9.9 Hz).

1-(2-Bromophenyl)-3,3,3-trifluoropropan-1-one (3i)



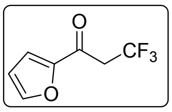
3i: (reaction conditions for the trifluoromethylation step: 24 h at 100 °C, eluent: petroleum ether:ethyl acetate 30:1, white solid, 53% yield, 28.0 mg); NMR data are in accordance with literature[5] values: **^{1}H NMR** (500 MHz, CDCl$_3$): δ ppm 7.65 (dd, J = 7.8, 1.2 Hz, 1H), 7.48-7.33 (m, 3H), 3.84 (q, J = 10.0 Hz, 2H); **^{13}C NMR** (125 MHz, CDCl$_3$): δ ppm 193.26 (q, J = 2.52 Hz), 139.98, 133.92, 132.69, 129.17, 127.77, 126.75, 123.44 (q, J = 277.6 Hz), 118.82, 45.83 (q, J = 28.4 Hz); **^{19}F NMR** (376 MHz, CDCl$_3$): δ ppm -62.13 (t, J = 10.2 Hz).

3,3,3-Trifluoro-1-(naphthalen-1-yl)propan-1-one (3j)



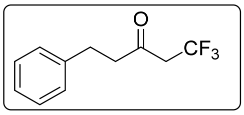
3j: (eluent: petroleum ether:ethyl acetate 30:1, white solid, 50% yield, 23.8 mg); NMR data are in accordance with literature[5] values: **^{1}H NMR** (400 MHz, CDCl$_3$): δ ppm 8.72 (d, J = 8.6 Hz, 1H), 8.06 (d, J = 8.2 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.68-7.61 (m, 1H), 7.61-7.55 (m, 1H), 7.55-7.49 (m, 1H), 3.91 (q, J = 10.0 Hz, 2H); **^{13}C NMR** (100 MHz, CDCl$_3$): δ ppm 192.81 (q, J = 2.5 Hz), 134.24, 133.99, 133.77 (q, J = 1.9 Hz), 130.15, 128.78, 128.71, 128.56, 126.89, 125.56, 124.14, 123.98 (q, J = 277.3 Hz), 44.91 (q, J = 27.9 Hz); **^{19}F NMR** (376 MHz, CDCl$_3$): δ ppm -61.93 (t, J = 10.0 Hz).

3,3,3-Trifluoro-1-(furan-2-yl)propan-1-one (3k)



3k: (reaction conditions for the trifluoromethylation step: 24 h at 100 °C, eluent: petroleum ether:ethyl acetate 30:1, colorless liquid, 28% yield, 10.1 mg); **^{1}H NMR** (400 MHz, CDCl$_3$): δ ppm 7.66 (dd, J = 1.7, 0.8 Hz, 1H), 7.32 (dd, J = 3.6, 0.8 Hz, 1H), 6.62 (dd, J = 3.6, 1.7 Hz, 1H), 3.67 (t, J = 10.2 Hz, 1H); **^{13}C NMR** (125 MHz, CDCl$_3$): δ ppm 178.19, 151.93, 147.41, 123.69 (q, J = 277.4 Hz), 118.76, 113.02, 42.19 (q, J = 28.8 Hz); **^{19}F NMR** (376 MHz, CDCl$_3$): δ ppm -61.89 (t, J = 10.2 Hz); **HRMS** (ESI): *m/z* calcd for $C_7H_5F_3NaO_2$ $[M+Na]^+$ 201.0134, found 201.0137.

1,1,1-Trifluoro-5-phenylpentan-3-one (3l)

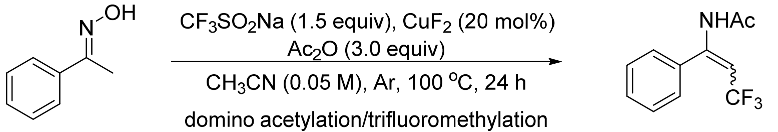


3l: (eluent: petroleum ether:ethyl acetate 30:1, white solid, 14% yield, 6.0 mg); NMR data are in accordance with literature[4] values: **^{1}H NMR** (400 MHz, CDCl$_3$): δ ppm 7.33-7.27 (m, 2H), 7.25-7.16 (m, 3H), 3.21 (q, J = 10.4 Hz, 2H), 2.96-2.90 (m, 2H), 2.89-2.83 (m, 2H); **^{13}C NMR** (100 MHz, CDCl$_3$): δ ppm 199.14 (q, J = 2.2 Hz), 140.10, 128.62, 128.28, 126.39, 123.53 (q, J = 277.1 Hz), 46.53 (q, J = 28.4 Hz), 44.96 (q, J = 2.0 Hz), 29.20; **^{19}F NMR** (376 MHz, CDCl$_3$): δ ppm -62.33 (t, J = 10.3 Hz).

2.6. Procedure for the domino acetylation/trifluoromethylation of acetophenone oxime 1a

To a screw-cap vial equipped with a magnetic stirring bar were added acetophenone oxime **4a** (0.20 mmol), CF_3SO_2Na (0.30 mmol), CuF_2 (0.04 mmol), acetic anhydride (0.60 mmol) and CH_3CN (4.0 mL) under argon (glove-box). The resulting mixture was stirred at 100 °C for 48 hours. The solvent was removed *in vacuo* and the residue purified by column chromatography using petroleum ether:ethyl acetate 5:1 as an eluent system to obtain compound **2a** (Scheme S-2).

Scheme S-2.



4a

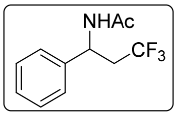
2a, *E*:*Z* = 1.73:1, 59% (61%[a])

[a]NMR yield (α,α,α−trifluorotoluene was used as an internal standard).

2.7. Procedure for the reduction of enamide 2a to compound 5a

Compound **2a** (0.10 mmol) and $NiCl_2{\cdot}6H_2O$ (0.10 mmol) were stirred in EtOH (1.0 mL) at 0 °C. $NaBH_4$ (0.50 mmol) was added and the suspension was allowed to reach room temperature and subsequently stirred for 2 hours. Another portion of $NaBH_4$ (0.50 mmol) was added and the reaction mixture was stirred for additional 2 hours. The mixture was then concentrated *in vacuo* and the residue was purified by column chromatography using petroleum ether:ethyl acetate 3:1 as eluent to obtain compound **5a**.

N-(3,3,3-Trifluoro-1-phenylpropyl)acetamide (5a)

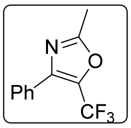


5a: (white solid, 61% yield, 14.0 mg); NMR data are in accordance with literature[4] values: **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* ppm 7.44-7.26 (m, 5H), 6.26-6.07 (m, 1H), 5.34 (td, *J* = 8.1, 5.9 Hz, 1H), 2.73 (m, 1H), 2.65-2.49 (m, 1H), 1.97 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* ppm 169.30, 139.97, 128.97, 128.14, 126.35, 125.49 (q, *J* = 277.7 Hz), 48.31 (q, *J* = 3.1 Hz), 39.45 (q, *J* = 27.4 Hz), 23.20; **^{19}F NMR** (376 MHz, $CDCl_3$): *δ* ppm -63.47 (t, *J* = 10.2 Hz).

2.8. Procedure for polysubstituted oxazole 6a

Compound **2a** (0.10 mmol) and [bis(trifluoroacetoxy)iodo]benzene (2.50 mmol) were stirred in 1,2-dichloroethane (1.0 mL) at 60 °C for 12 hours. Another portion of [bis(trifluoroacetoxy)iodo]benzene (2.50 mmol) was added and the mixture was stirred at 60 °C for an additional 12 hours. The mixture was concentrated *in vacuo* and the residue was purified by column chromatography using pentane:ethyl acetate 30:1 as eluent to obtain polysubstituted oxazole **6a**.

2-Methyl-4-phenyl-5-(trifluoromethyl)oxazole (6a)

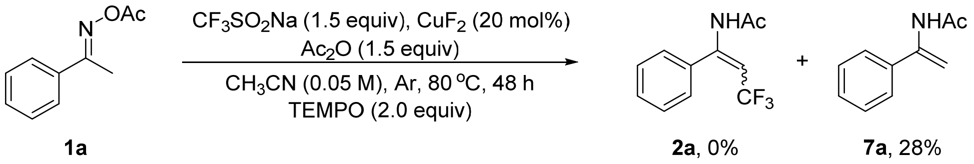


6a: (colorless oil, 53% yield, 12.0 mg); NMR data are in accordance with literature[7] values: **^{1}H NMR** (400 MHz, $CDCl_3$): δ ppm 7.67 (dd, J = 7.6, 2.0 Hz, 2H), 7.54-7.36 (m, 3H), 2.57 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ ppm 162.04, 141.33, 133.58 (q, J = 42.8 Hz), 129.42, 129.23, 128.53, 128.30, 119.67 (q, J = 267.8 Hz), 13.85; **^{19}F NMR** (376 MHz, $CDCl_3$): δ ppm -60.37.

2.9. The effect of added TEMPO to the trifluoromethylation reaction

To a screw-cap vial equipped with a magnetic stirring bar were added oxime acetate **1a** (0.10 mmol), CF_3SO_2Na (0.15 mmol), CuF_2 (0.02 mmol), acetic anhydride (0.15 mmol), TEMPO (0.20 mmol) and CH_3CN (2.0 mL) under argon (glove-box). The resulting mixture was stirred at 80 °C for 48 hours. The solvent was removed *in vacuo* and the reaction yield was determined by ^1H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard (Scheme S-3).

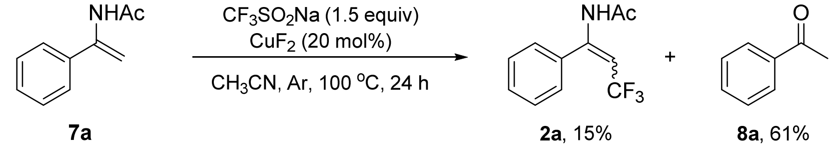
Scheme S-3.



2.10. Trifluoromethylation of enamide 7a

To a screw-cap vial equipped with a magnetic stirring bar were added enamide **7a** (0.20 mmol), CF_3SO_2Na (0.30 mmol), CuF_2 (0.04 mmol) and CH_3CN (4.0 mL) under argon (glove-box). The reaction mixture was stirred at 100 °C for 24 h. The solvent was removed *in vacuo* and the residue was purified by column chromatography using petroleum ether:ethyl acetate 30:1 to 5:1 as eluent. The low yield of **2a** explains the need of an oxidant for a catalytic turn-over. In the absence of an N-O bond as an oxidant, CuF_2 or trace amounts of O_2 may produce a CF_3 radical reacting with **7a** (Scheme S-4).

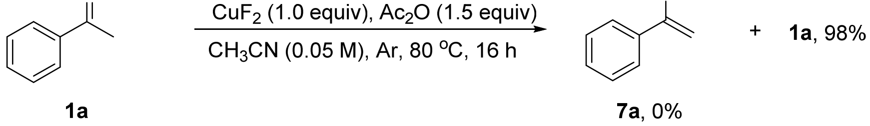
Scheme S-4.



2.11. The effect of CF_3SO_2Na for the formation of 7a

To a screw-cap vial equipped with a magnetic stirring bar were added oxime acetate **1a** (0.10 mmol), CuF_2 (0.10 mmol), acetic anhydride (0.15 mmol) and CH_3CN (2.0 mL) under argon (glove-box). The resulting mixture was stirred at 80 °C for 16 hours. The solvent was removed *in vacuo* and the reaction yield was determined by ^1H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard. Only unreacted starting material was observed (Scheme S-5).

Scheme S-5.

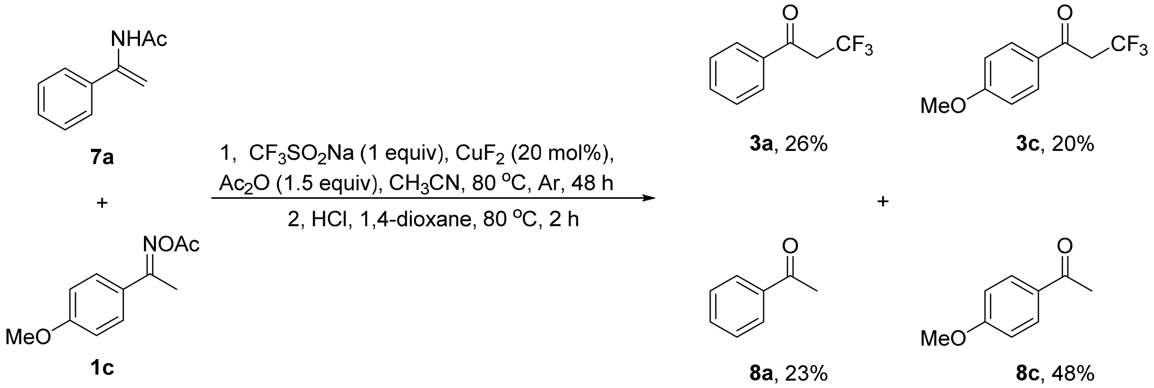


2.12. Procedure for the trifluoromethylation and subsequent hydrolysis of enamide 7a in the presence of oxime acetate 1c

To a screw-cap vial equipped with a magnetic stirring bar were added oxime acetate **1c** (0.20 mmol), enamide **7a** (0.20 mmol), CF_3SO_2Na (0.20 mmol), CuF_2 (0.04 mmol), acetic anhydride (0.30 mmol) and CH_3CN (4.0 mL) under argon (glove-box). The resulting mixture was stirred at 80 °C for 48 hours. After the solvent was removed *in vacuo*, the residue was dissolved in 1,4-dioxane (1.0 mL) and treated with aqueous HCl (2 M, 1.0 mL) at 80 °C for 2 h. The mixture was then diluted with CH_2Cl_2 and washed extracted with water. The resulting phases were separated and the organic phase was concentrated *in vacuo*. To the crude sample were added 24.5 μL of α,α,α-trifluorotoluene and a solution of 1,3,5-trimethoxybenzene in $CDCl_3$ (200 μL, 0.33 M) as internal standards. The sample was subsequently analyzed by ^1H NMR and ^{19}F NMR.

The results are summarized in Scheme S-6, Figure S-1 and Figure S-2. Compound **7a** was transformed into the trifluoromethylated product **3a** in 26% yield, and the trifluoromethylated product **3c** was obtained in 20% yield. This indicates that an enamide is a key intermediate in the trifluoromethylation reaction, and also that the N-O bond is important for the reaction to take place efficiently.

Scheme S-6 Trifluoromethylation of oxime acetate 1c and enamide 7a



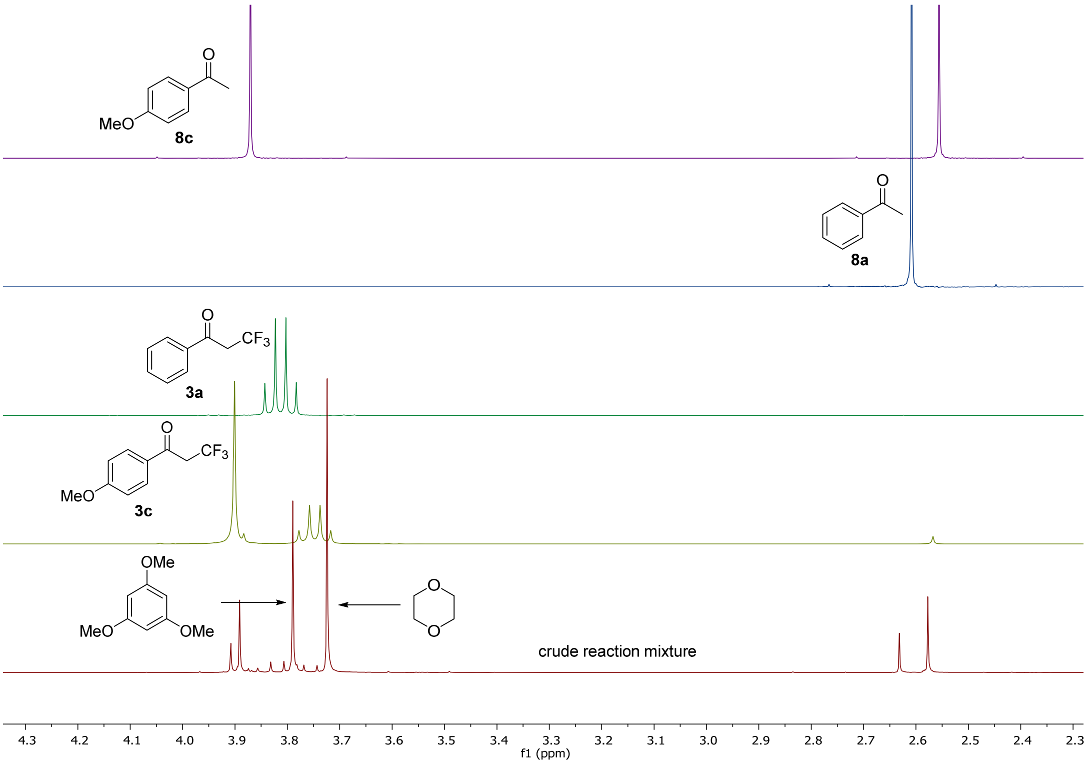


Figure S-1: ^{1}H NMR spectra of the crude reaction mixture for the trifluoromethylation and subsequent hydrolysis of oxime acetate **1c** and enamide **7a**

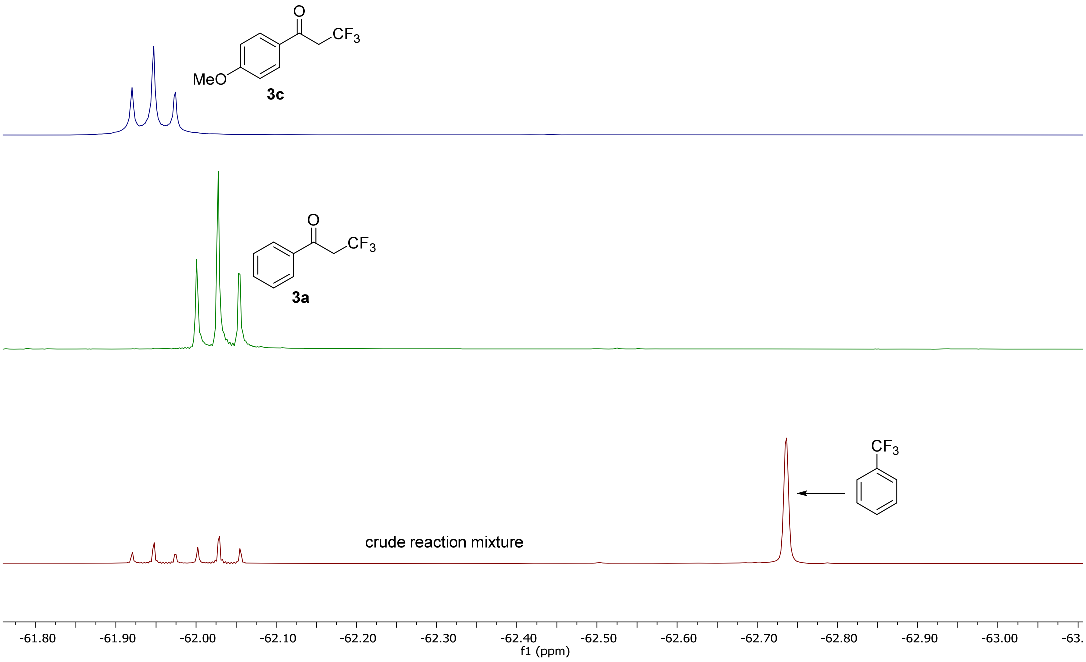


Figure S-2: ^{19}F NMR spectra of the crude reaction mixture for the trifluoromethylation and subsequent hydrolysis of oxime acetate **1c** and enamide **7a**

2.13. Monitoring the trifluoromethylation of oxime acetate 1a by ^{1}H NMR and ^{19}F NMR

To a screw-cap vial equipped with a magnetic stirring bar were added oxime acetate **1a** (0.40 mmol), CF_3SO_2Na (0.60 mmol), CuF_2 (0.08 mmol), acetic anhydride (0.60 mmol), methyl 4-chlorobenzoate (0.13 mmol, internal standard) and CH_3CN (8.0 mL) under argon (glove-box). The resulting mixture was stirred at 80 °C. At the time intervals shown below, 0.5 mL of the suspension was taken out via syringe. The samples were subsequently analyzed by ^{1}H NMR and ^{19}F NMR. The results are summarized in Figure S-3 and Figure S-4.

These data show that enamine **7a** was detectable after 2 hours. The concentration of **7a** remained in a stable concentration (approx. 0.0025 M) until completely consumed. The *E*/*Z* ratio of product **2a** decreased gradually over time, indicating a thermodynamic preference for the *Z*-isomer, possibly due to a hydrogen bond between the NH and F atom.

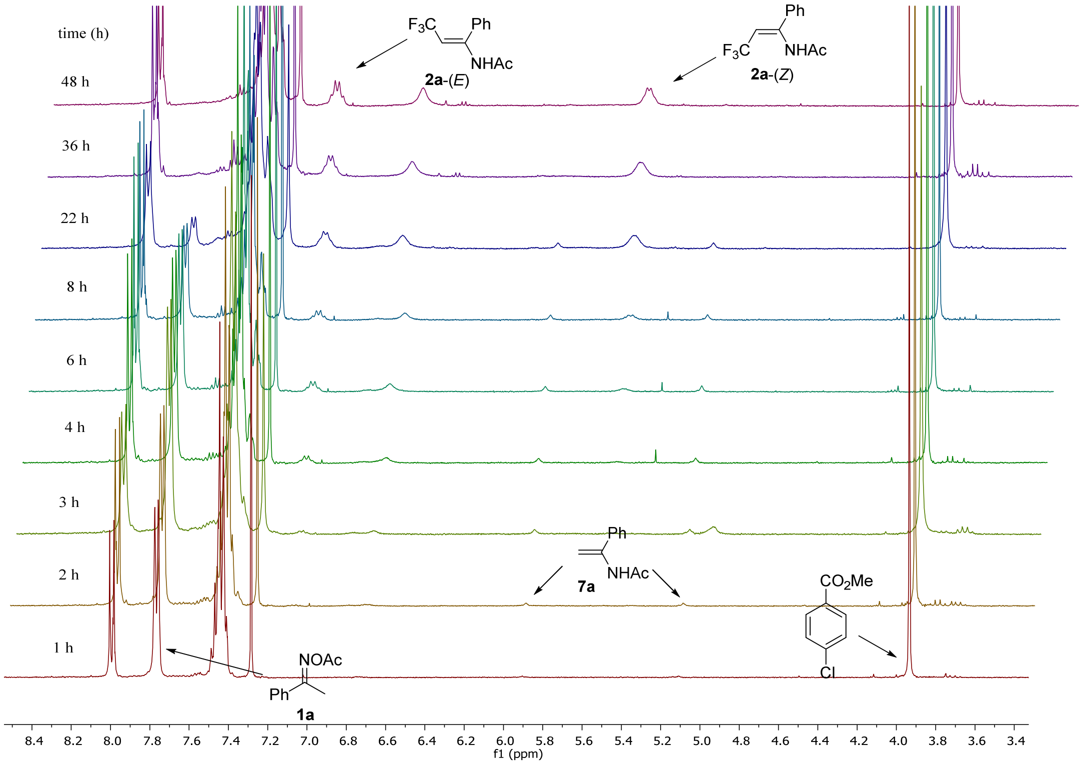


Figure S-3: ^{1}H NMR spectra of the trifluoromethylation of oxime acetate **1a** acquired at different times

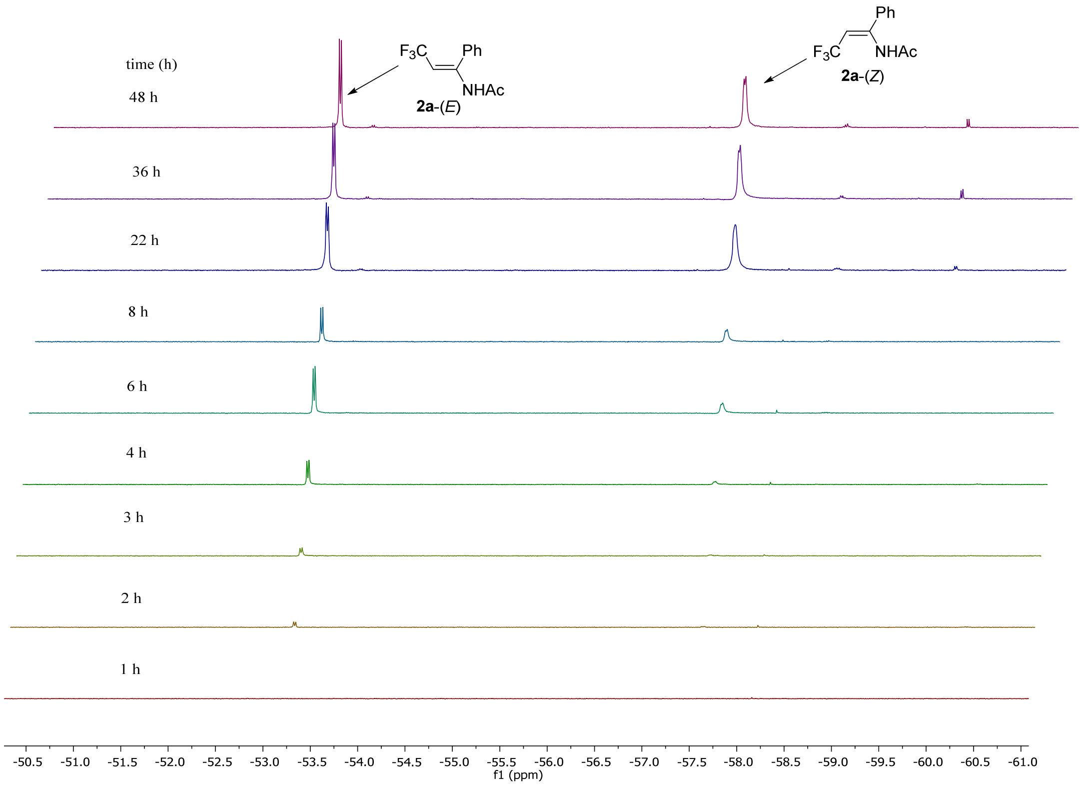
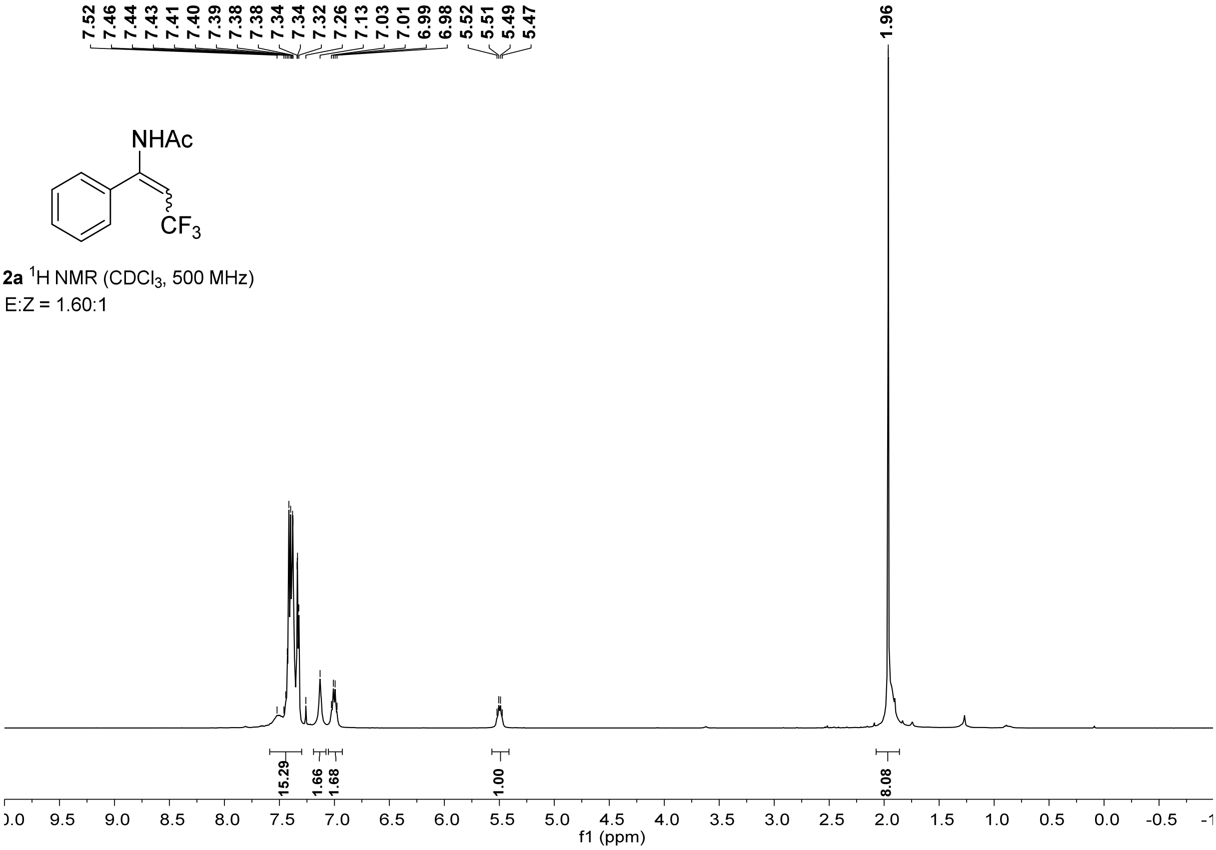
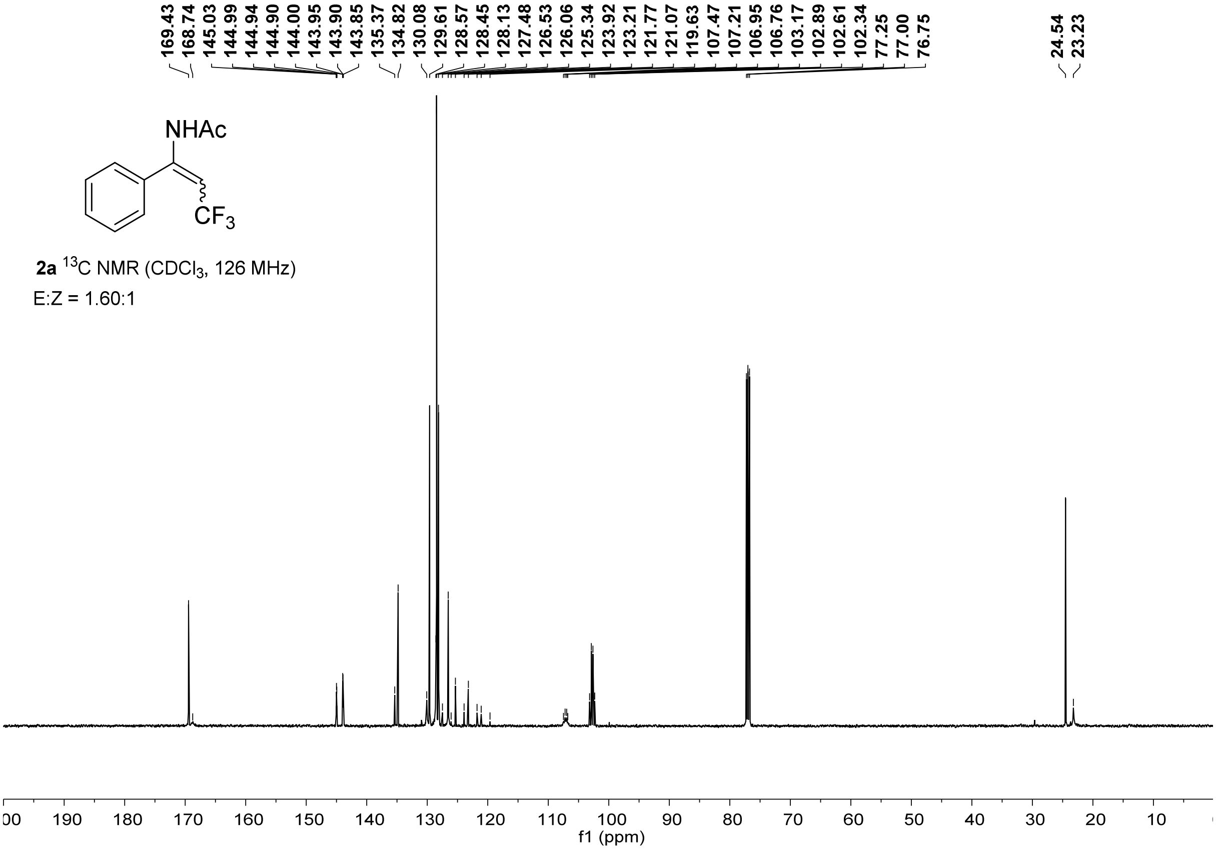


Figure S-4: ^{19}F NMR spectra of the trifluoromethylation of oxime acetate **1a** acquired at different times

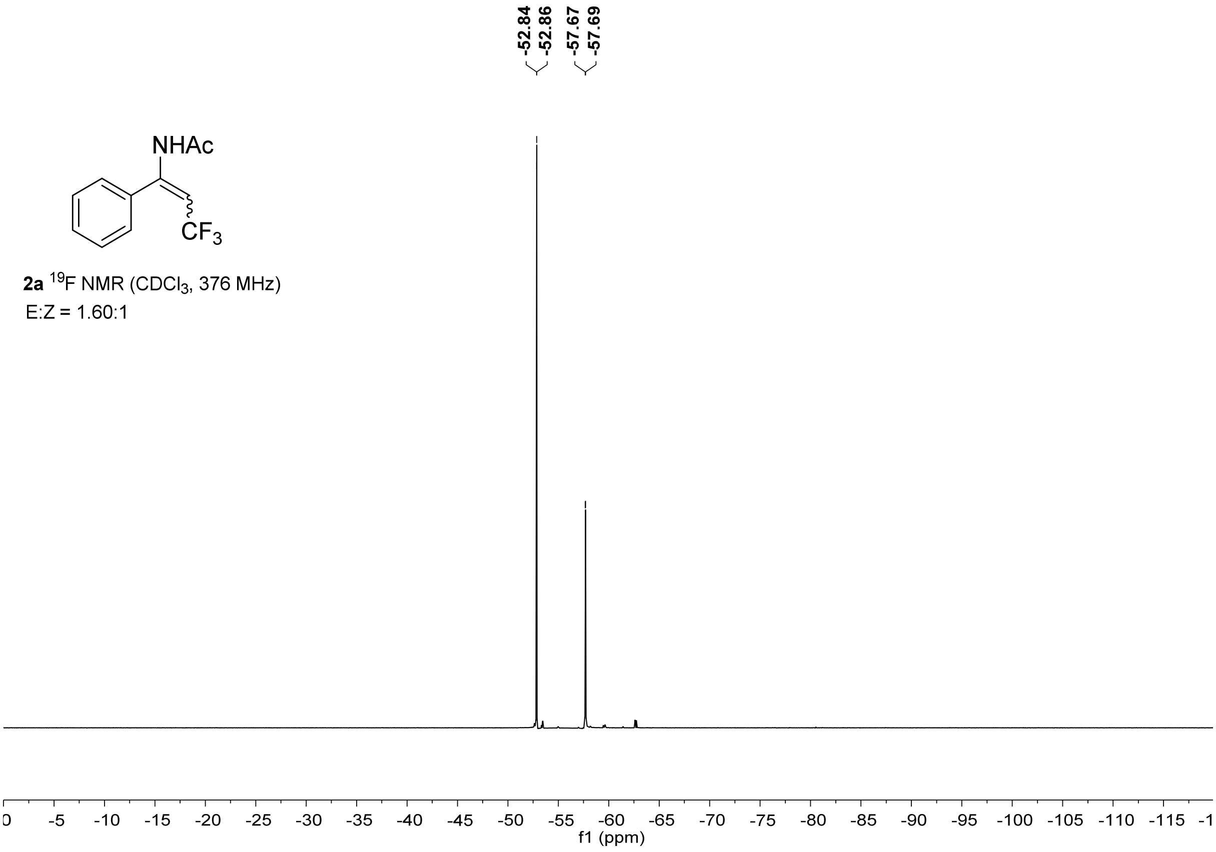
3. ^{1}H, ^{13}C and ^{19}F NMR Spectra



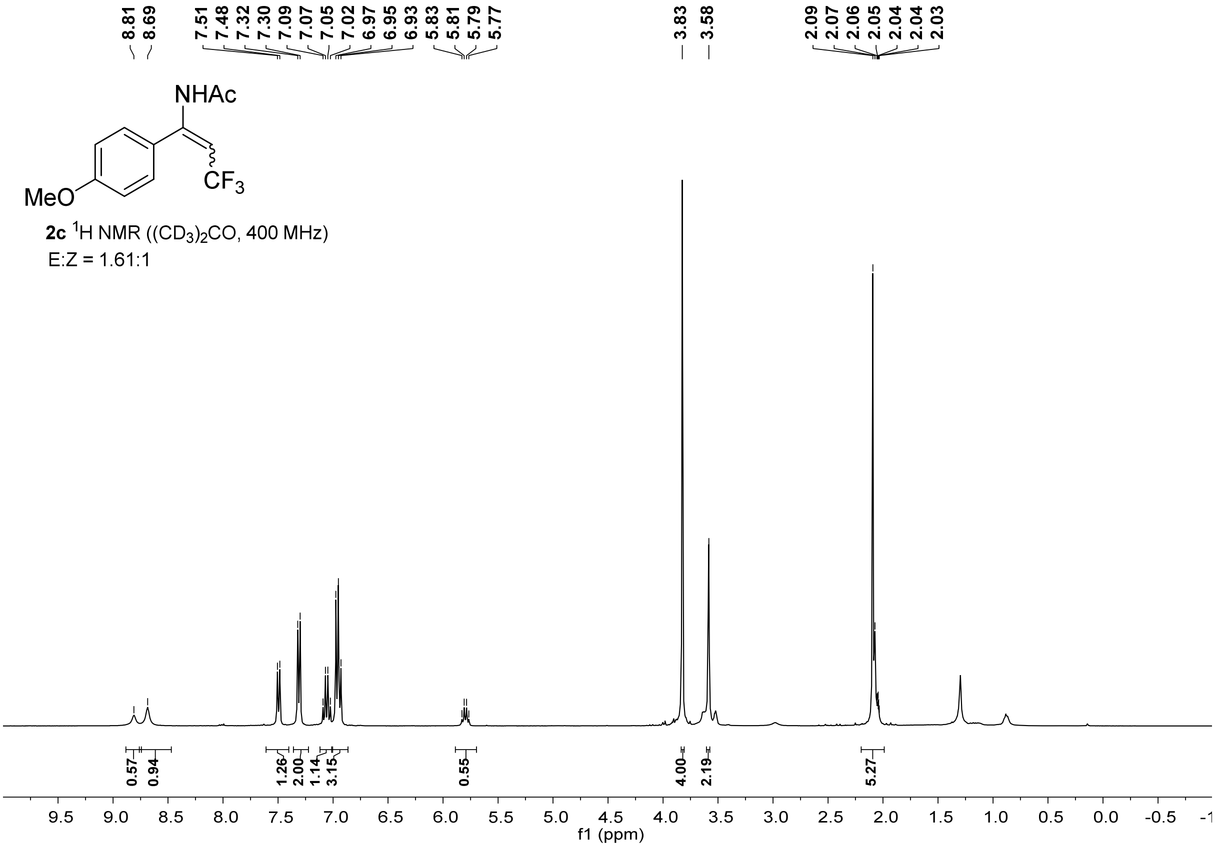
2a ^{1}H NMR ($CDCl_3$, 500 MHz)
E:Z = 1.60:1

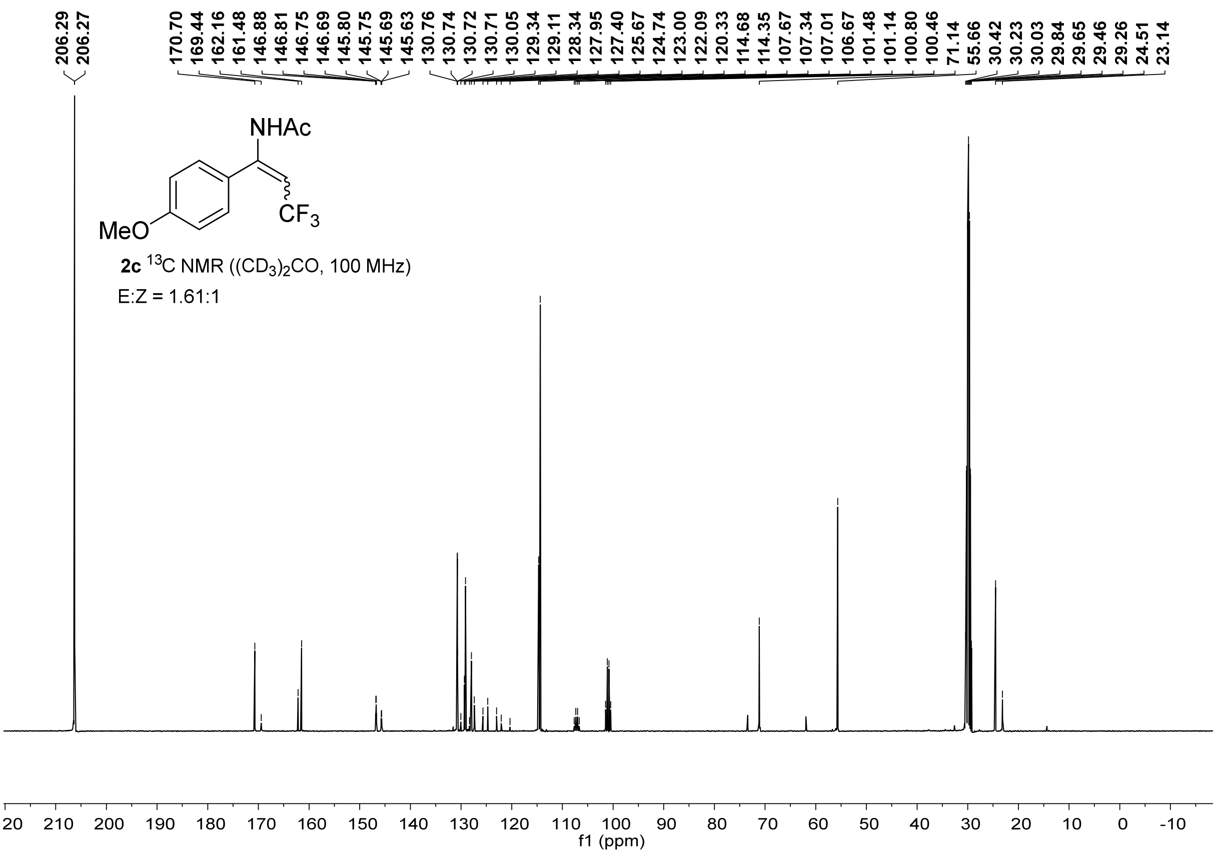


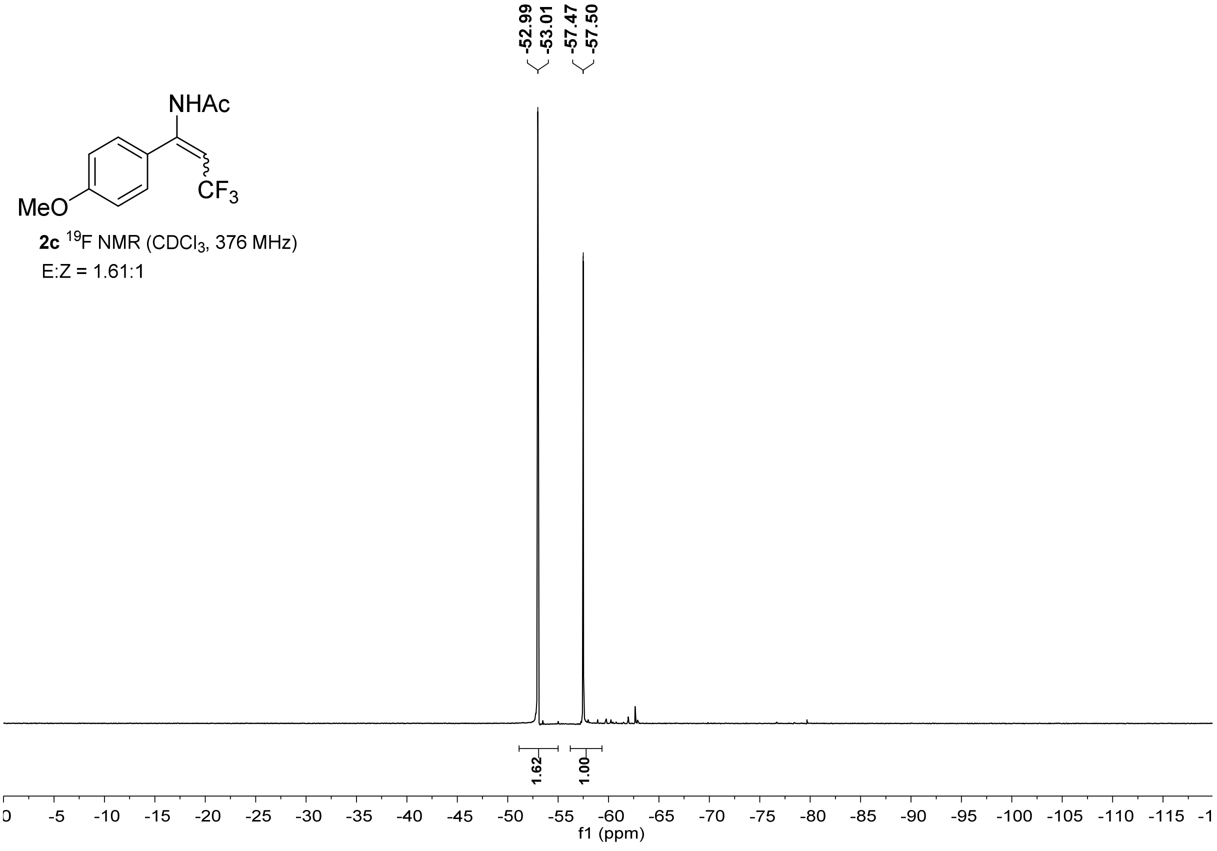
2a ^{13}C NMR ($CDCl_3$, 126 MHz)
E:Z = 1.60:1



2a ^{19}F NMR ($CDCl_3$, 376 MHz)
E:Z = 1.60:1

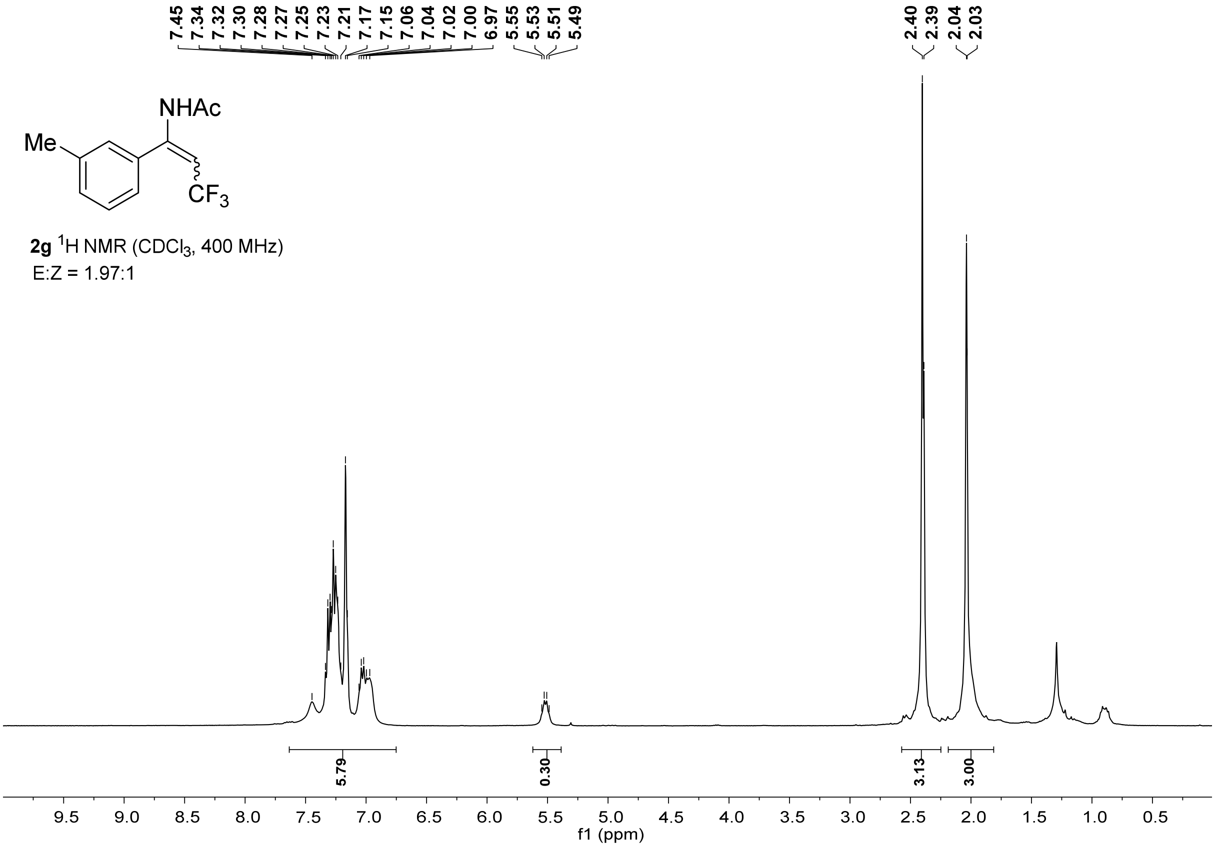

8.81
8.69
7.51
7.48
7.32
7.30
7.09
7.07
7.05
7.02
6.97
6.95
6.93
5.83
5.81
5.79
5.77
3.83
3.58
2.09
2.07
2.06
2.05
2.04
2.04
2.03
NHAc
CF3
MeO
2c 1H NMR ((CD3)2CO, 400 MHz)
E:Z = 1.61:1
0.57
0.94
1.26
2.00
1.14
3.15
0.55
4.00
2.19
5.27
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

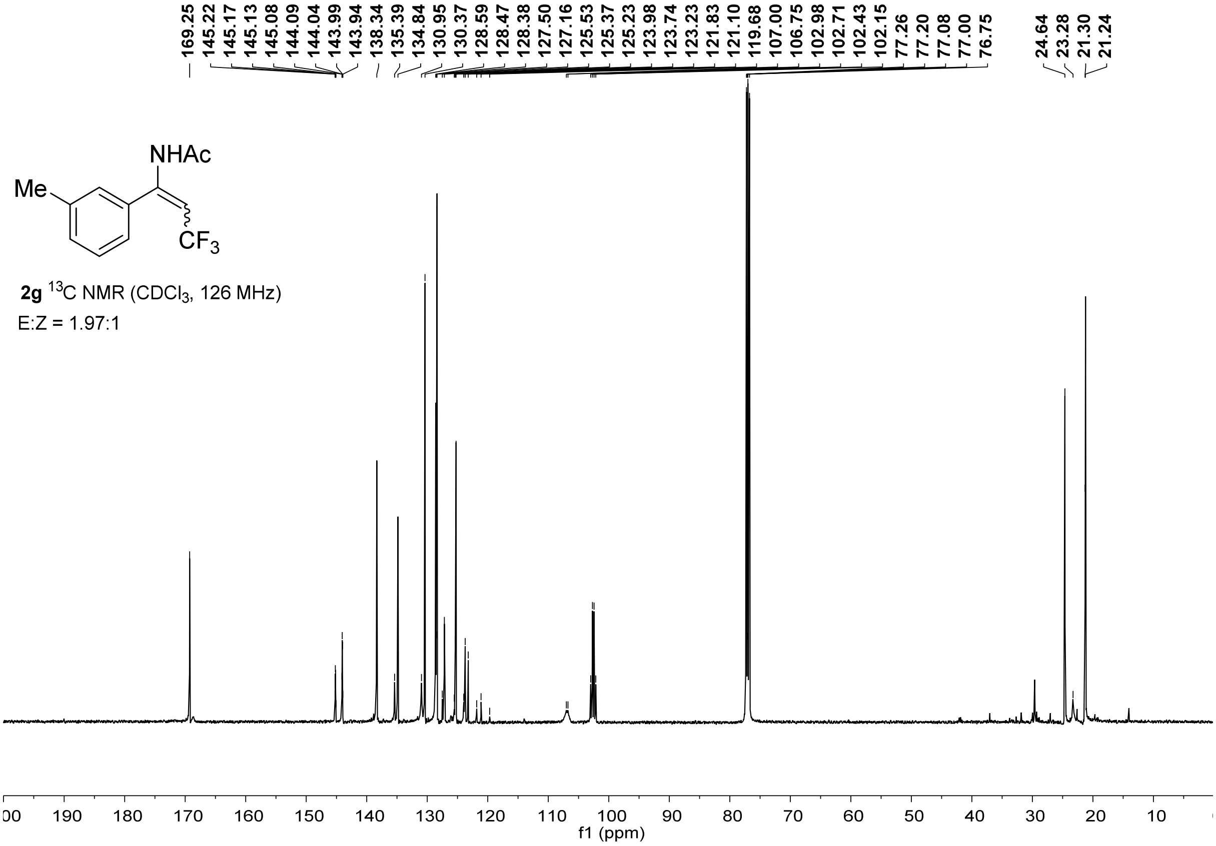

206.29
206.27
170.70
169.44
162.16
161.48
146.88
146.81
146.75
146.69
145.80
145.75
145.69
145.63
130.76
130.74
130.72
130.71
130.05
129.34
129.11
128.34
127.95
127.40
125.67
124.74
123.00
122.09
120.33
114.68
114.35
107.67
107.34
107.01
106.67
101.48
101.14
100.80
100.46
71.14
55.66
30.42
30.23
30.03
29.84
29.65
29.46
29.26
24.51
23.14
NHAc
CF3
MeO
2c 13C NMR ((CD3)2CO, 100 MHz)
E:Z = 1.61:1
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



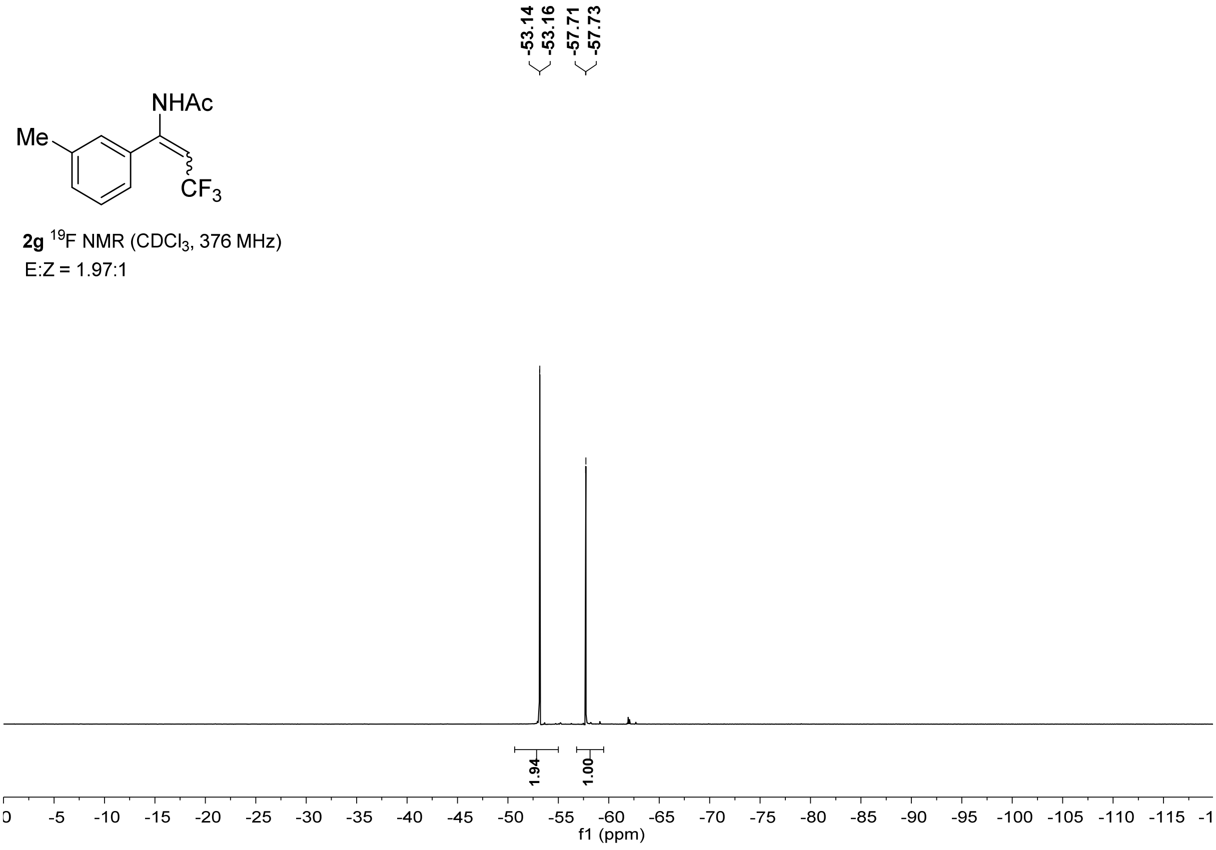
2c ^{19}F NMR ($CDCl_3$, 376 MHz)

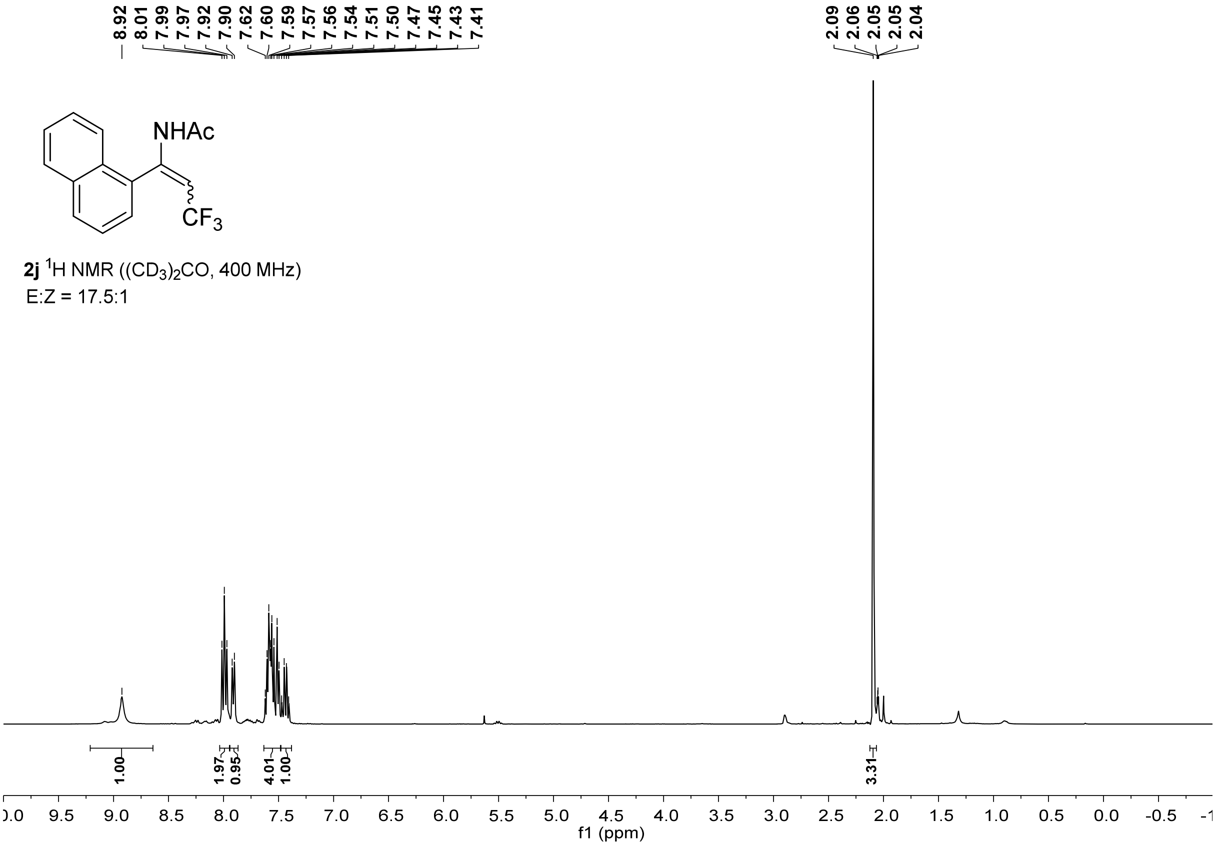
E:Z = 1.61:1


7.45
7.34
7.32
7.30
7.28
7.27
7.25
7.23
7.21
7.17
7.15
7.06
7.04
7.02
7.00
6.97
5.55
5.53
5.51
5.49
2.40
2.39
2.04
2.03
NHAc
Me
CF3
2g 1H NMR (CDCl3, 400 MHz)
E:Z = 1.97:1
5.79
0.30
3.13
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

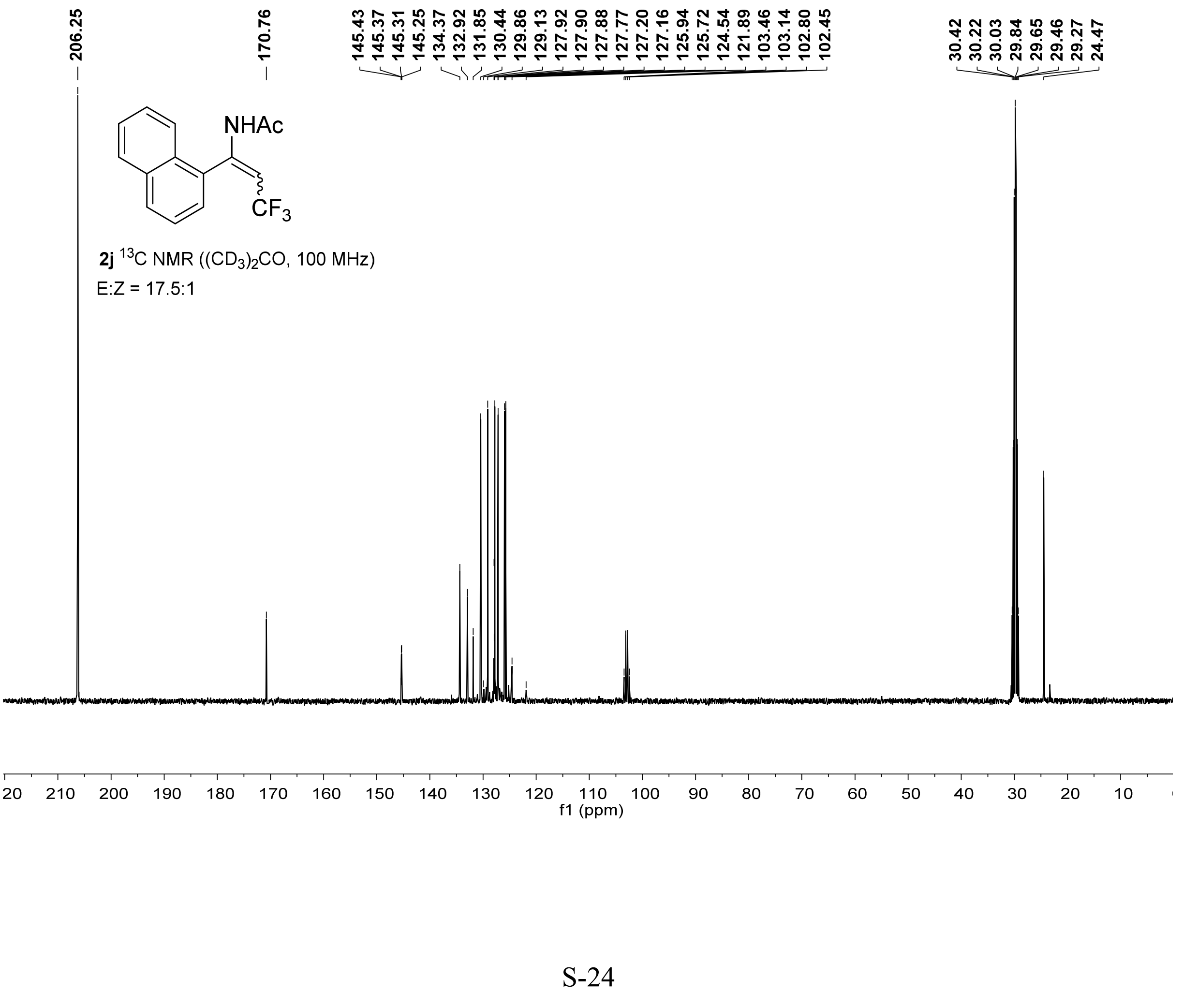

169.25
145.22
145.17
145.13
145.08
144.09
144.04
143.99
143.94
138.34
135.39
134.84
130.95
130.37
128.59
128.47
128.38
127.50
127.16
125.53
125.37
125.23
123.98
123.74
123.23
121.83
121.10
119.68
107.00
106.75
102.98
102.71
102.43
102.15
77.26
77.20
77.08
77.00
76.75
24.64
23.28
21.30
21.24
NHAc
Me
CF3
2g 13C NMR (CDCl3, 126 MHz)
E:Z = 1.97:1
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

2g ^{19}F NMR (CDCl$_3$, 376 MHz)
E:Z = 1.97:1

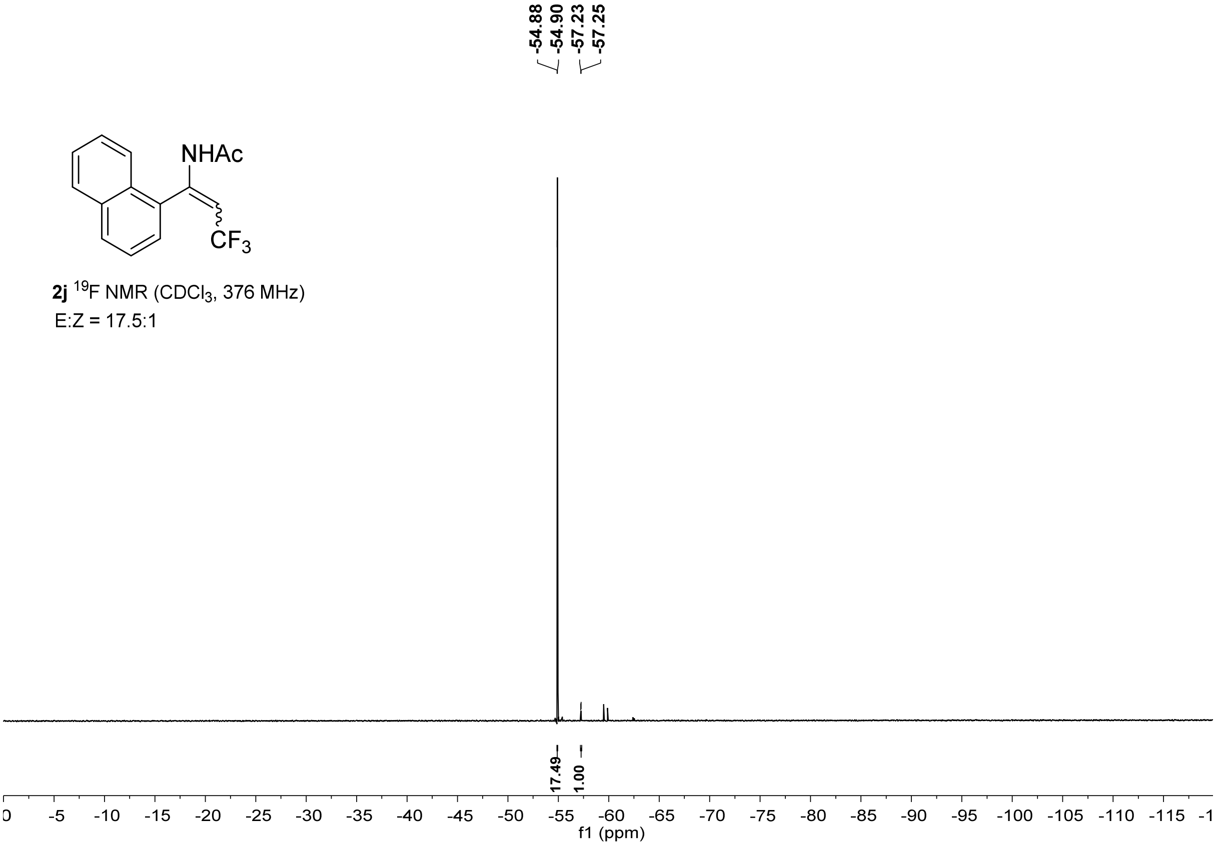




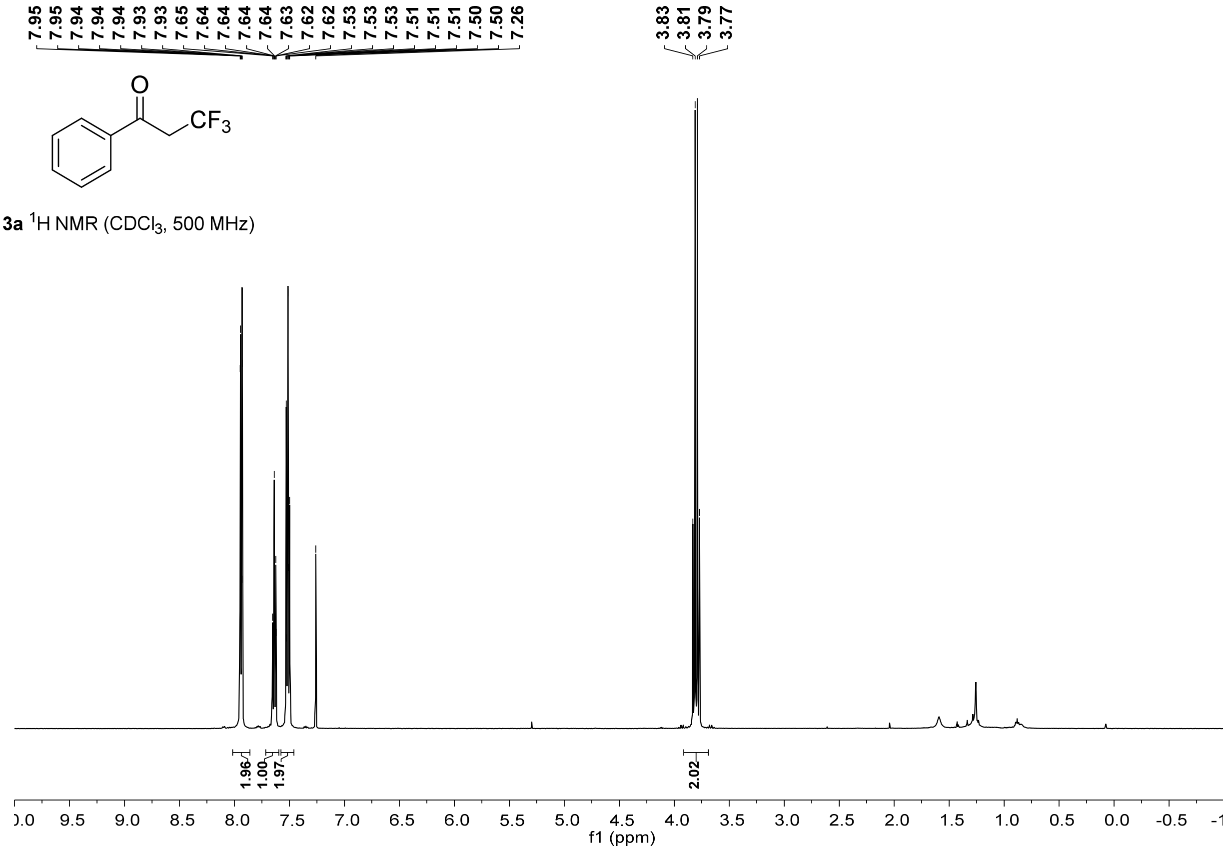
2j ^{1}H NMR ((CD$_3$)$_2$CO, 400 MHz)
E:Z = 17.5:1

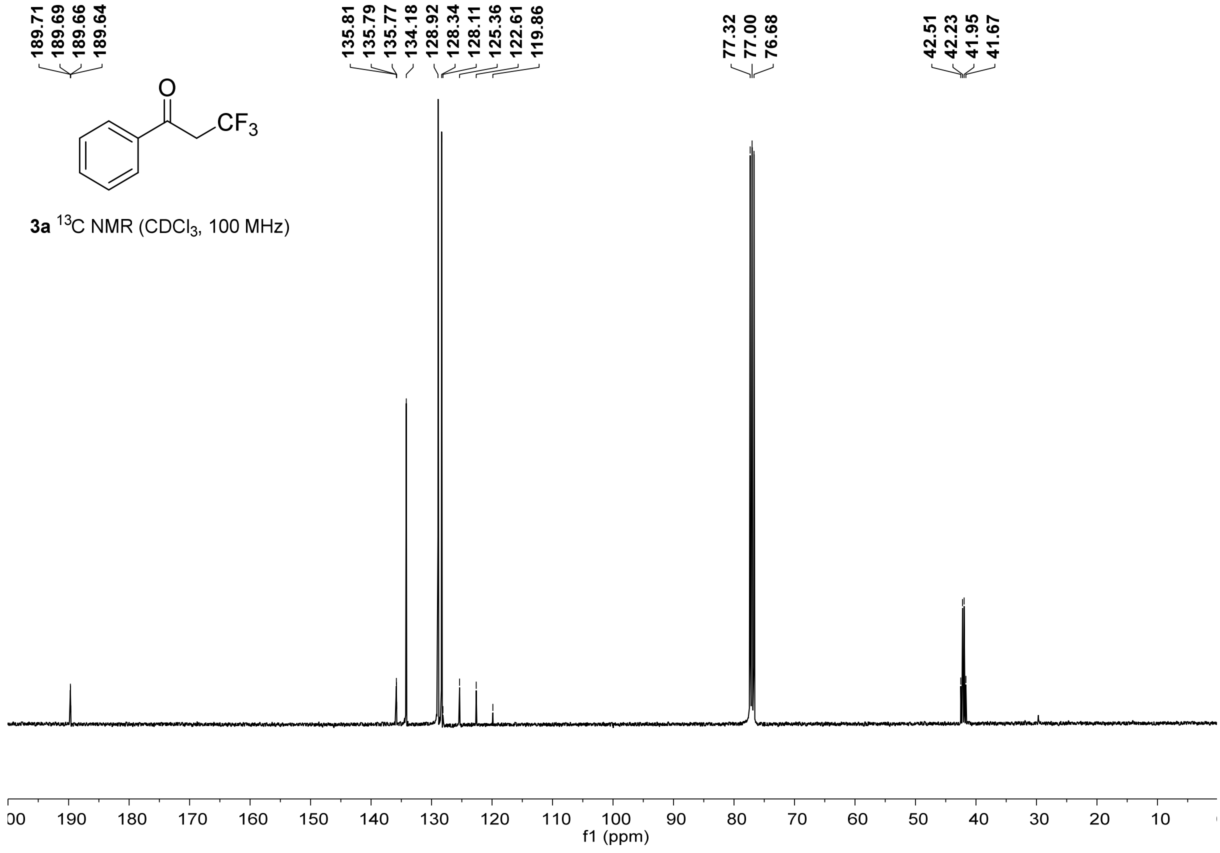


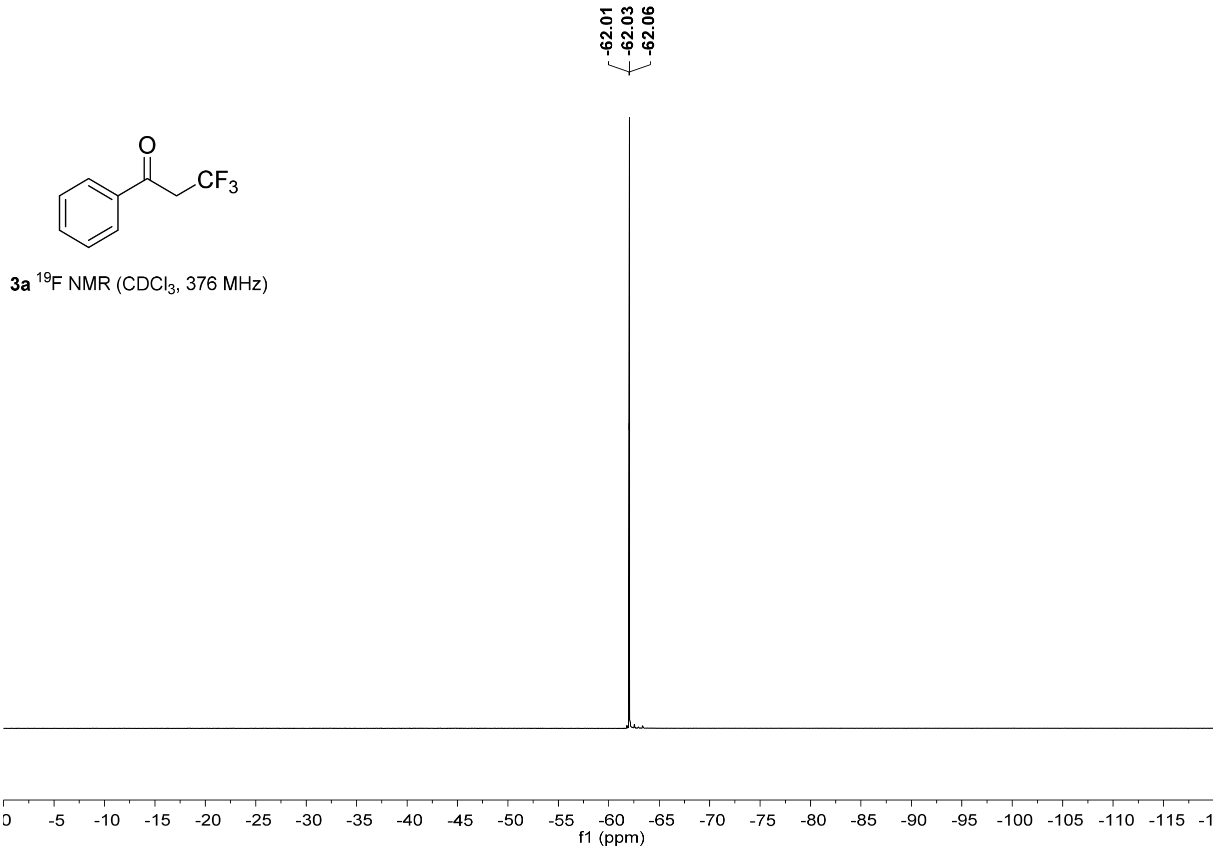
2j ^{13}C NMR ((CD$_3$)$_2$CO, 100 MHz)
E:Z = 17.5:1



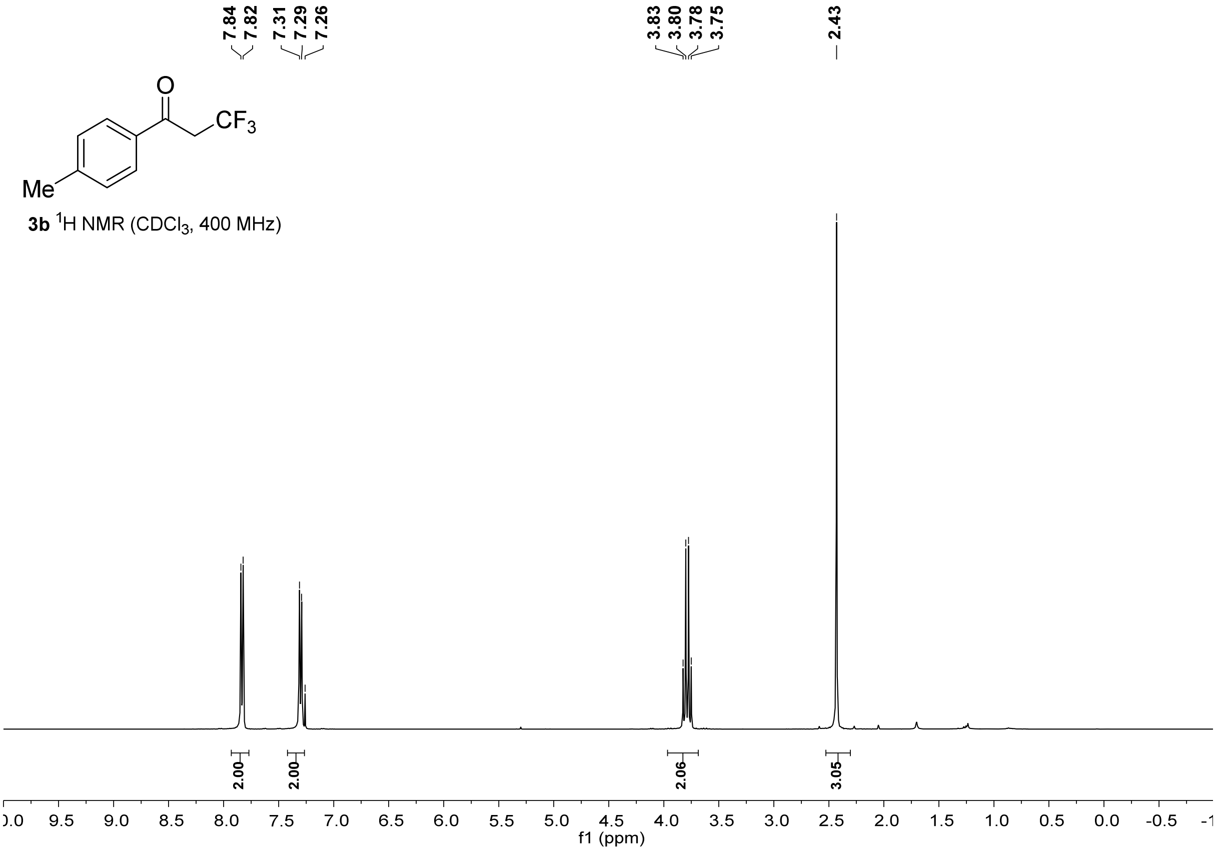
2j ^{19}F NMR ($CDCl_3$, 376 MHz)
E:Z = 17.5:1


7.95
7.95
7.94
7.94
7.94
7.93
7.93
7.65
7.64
7.64
7.64
7.63
7.62
7.62
7.53
7.53
7.53
7.51
7.51
7.51
7.50
7.50
7.26
3.83
3.81
3.79
3.77
O
CF3
3a ¹H NMR (CDCl3, 500 MHz)
1.96
1.00
1.97
2.02
).0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

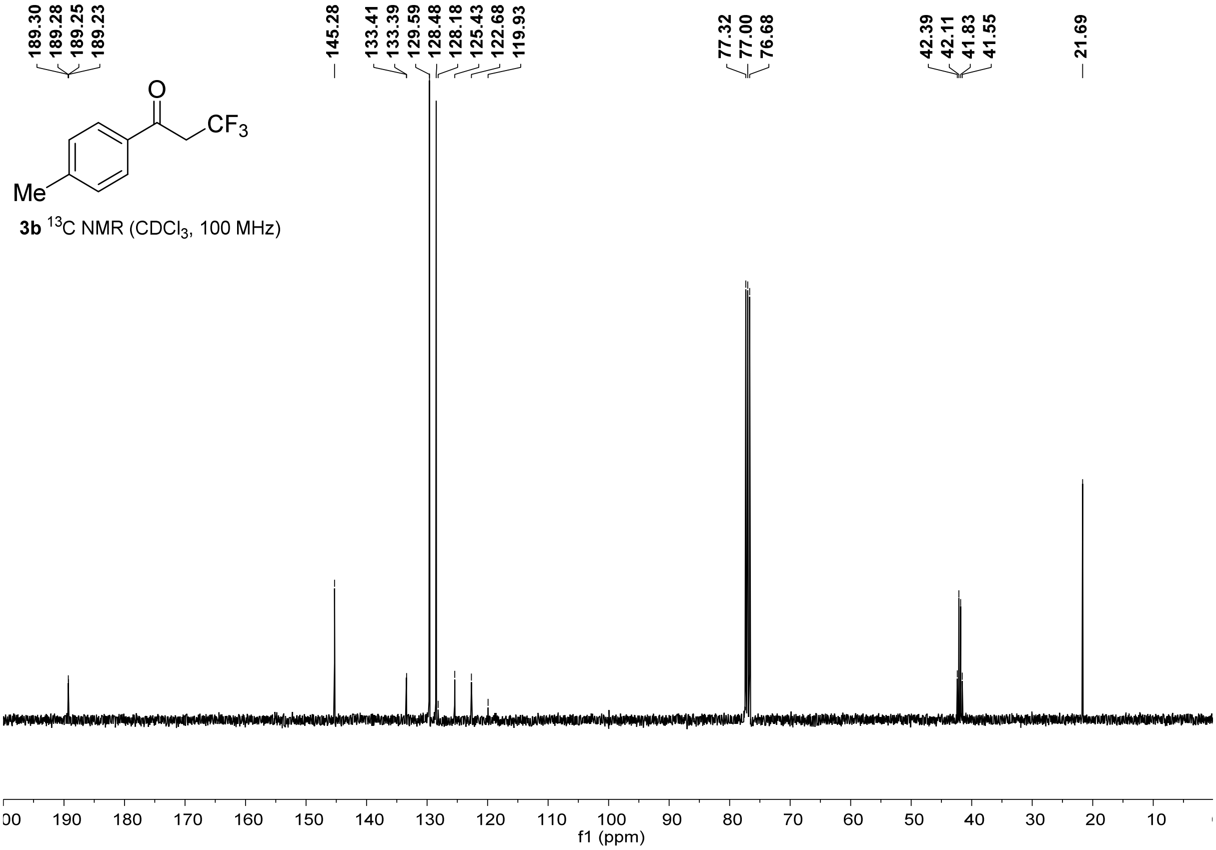

189.71
189.69
189.66
189.64
135.81
135.79
135.77
134.18
128.92
128.34
128.11
125.36
122.61
119.86
77.32
77.00
76.68
42.51
42.23
41.95
41.67
O
CF3
3a ¹³C NMR (CDCl3, 100 MHz)
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



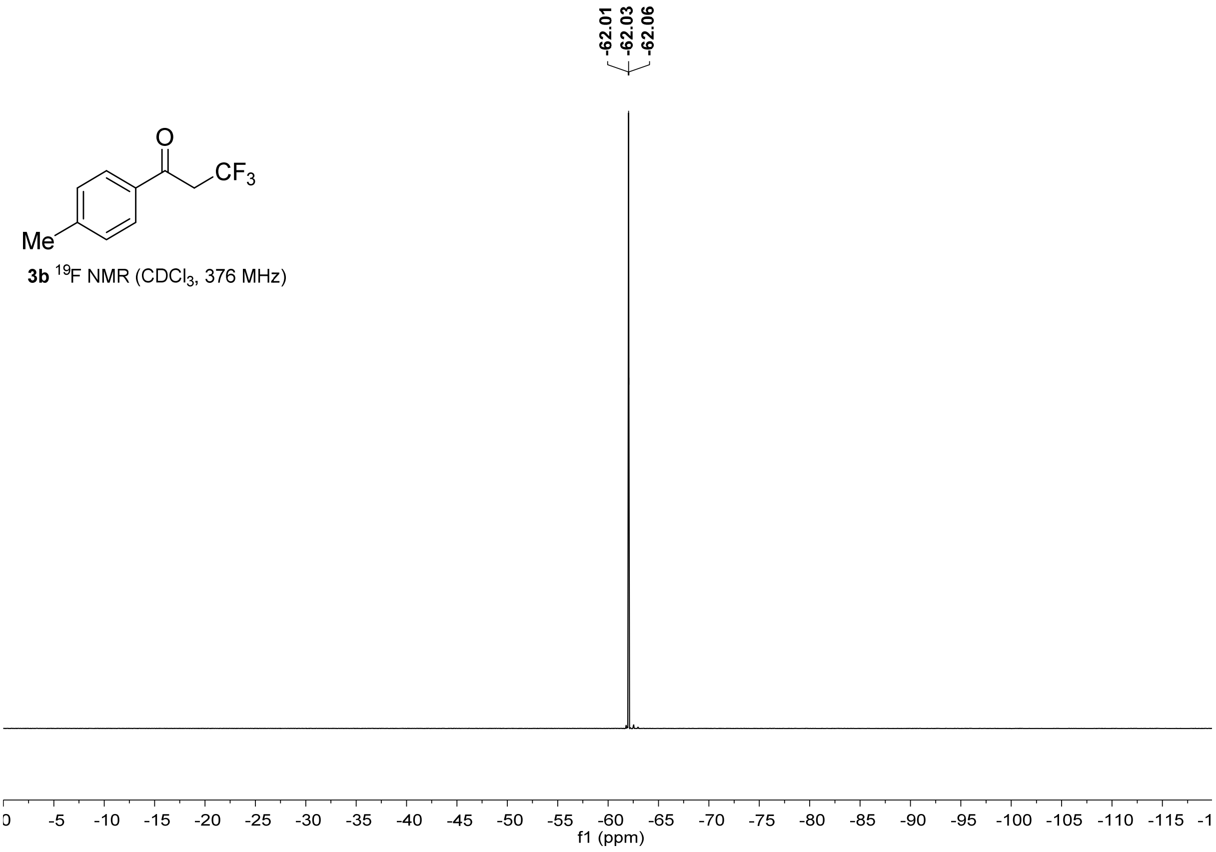
3a ^{19}F NMR ($CDCl_3$, 376 MHz)

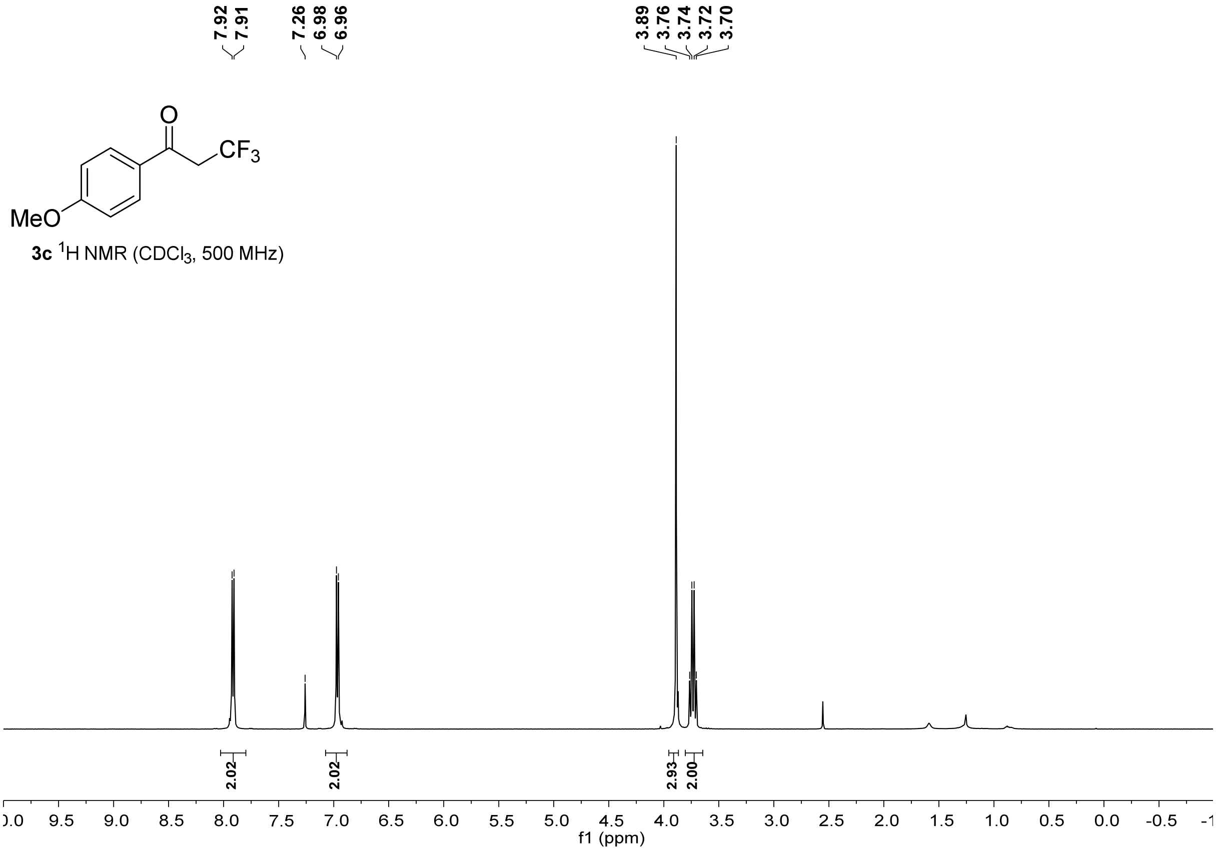


3b ^{1}H NMR ($CDCl_3$, 400 MHz)

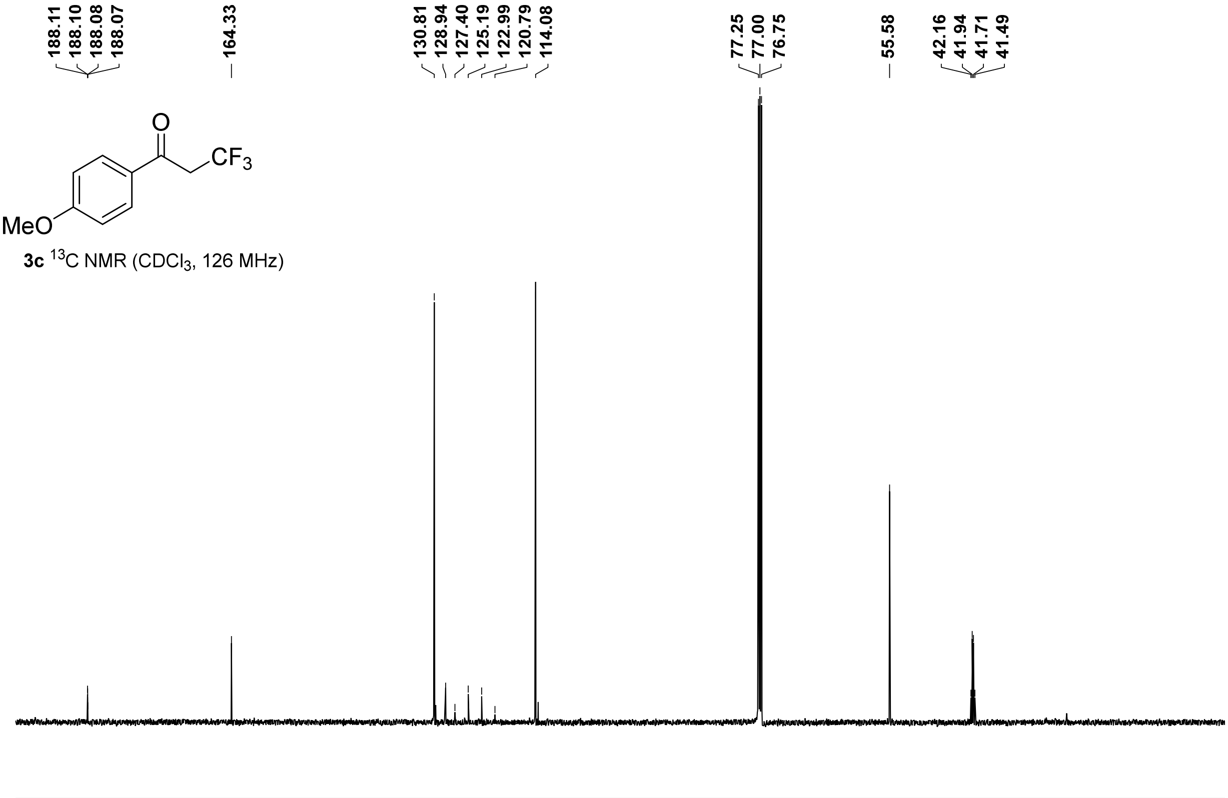


3b ^{13}C NMR ($CDCl_3$, 100 MHz)

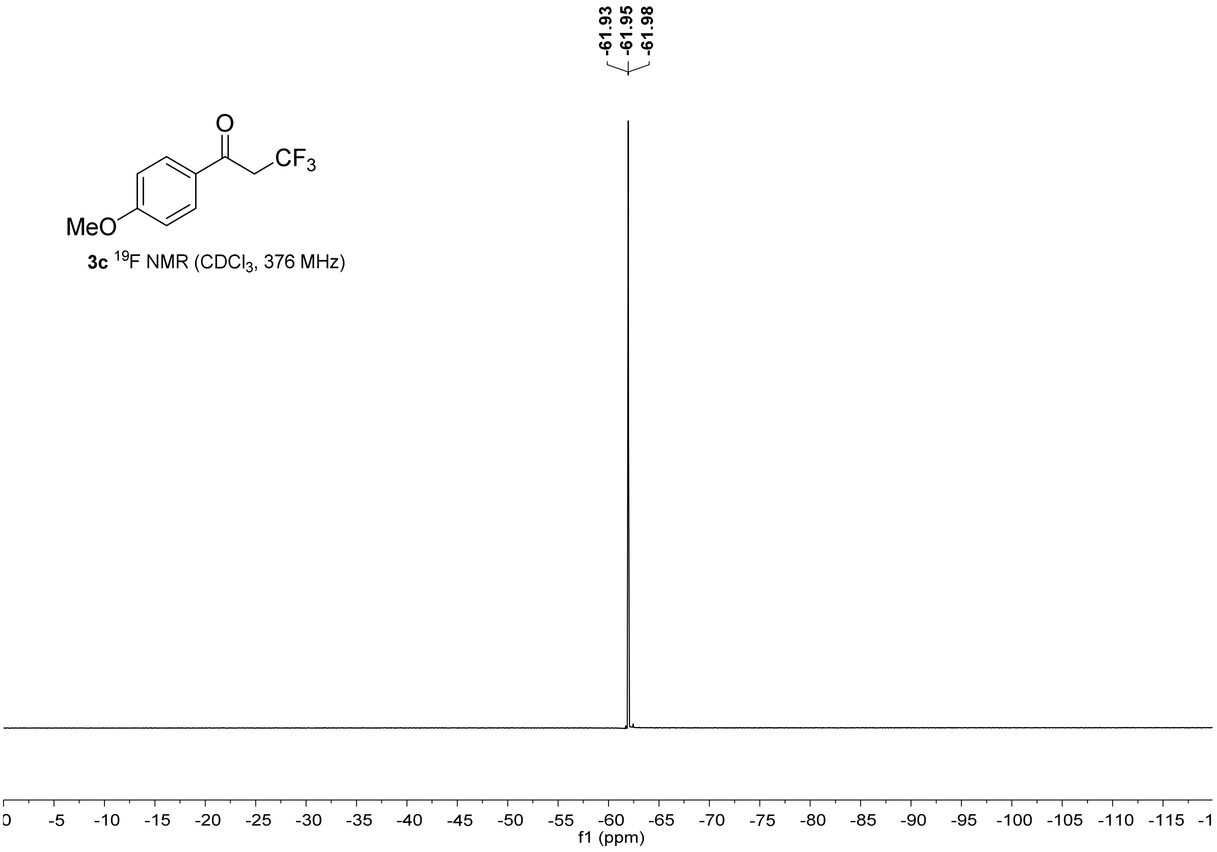

3b ^{19}F NMR (CDCl$_3$, 376 MHz)



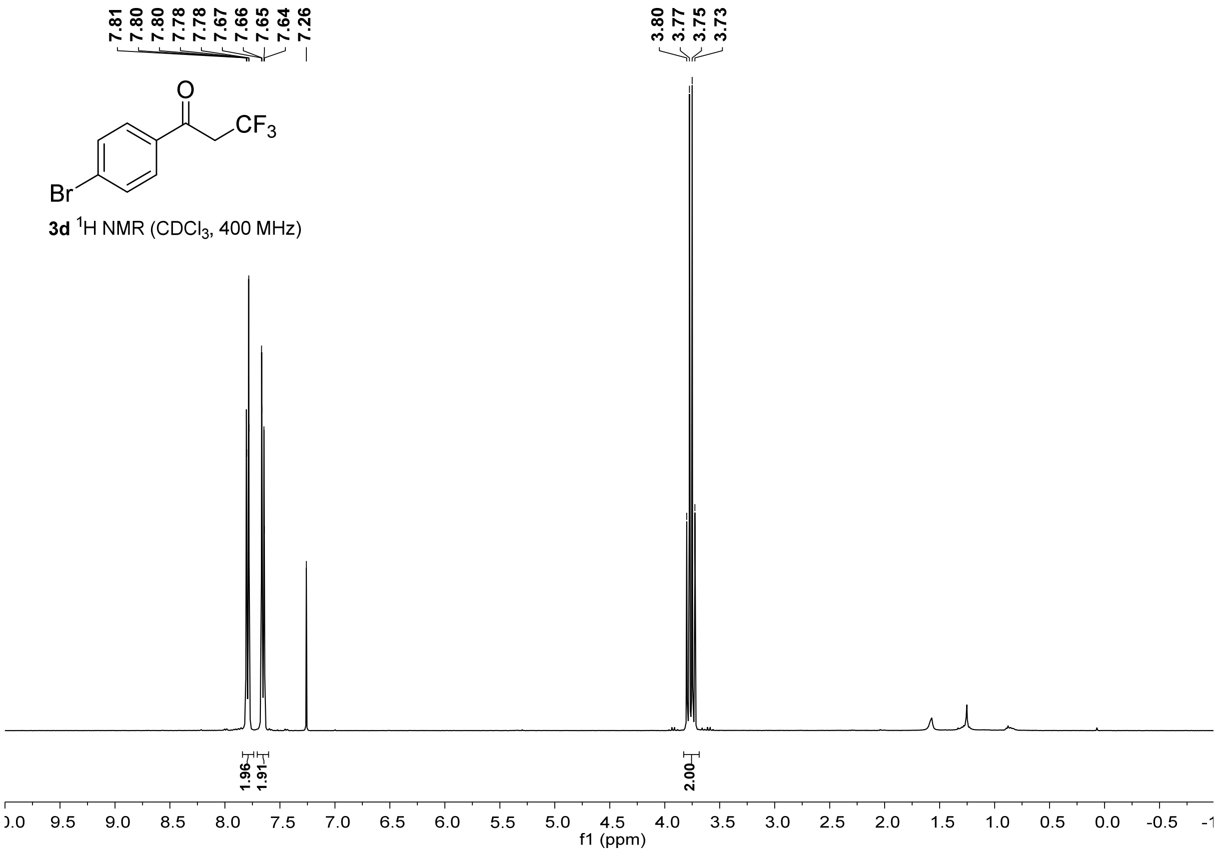
3c ^{1}H NMR ($CDCl_3$, 500 MHz)



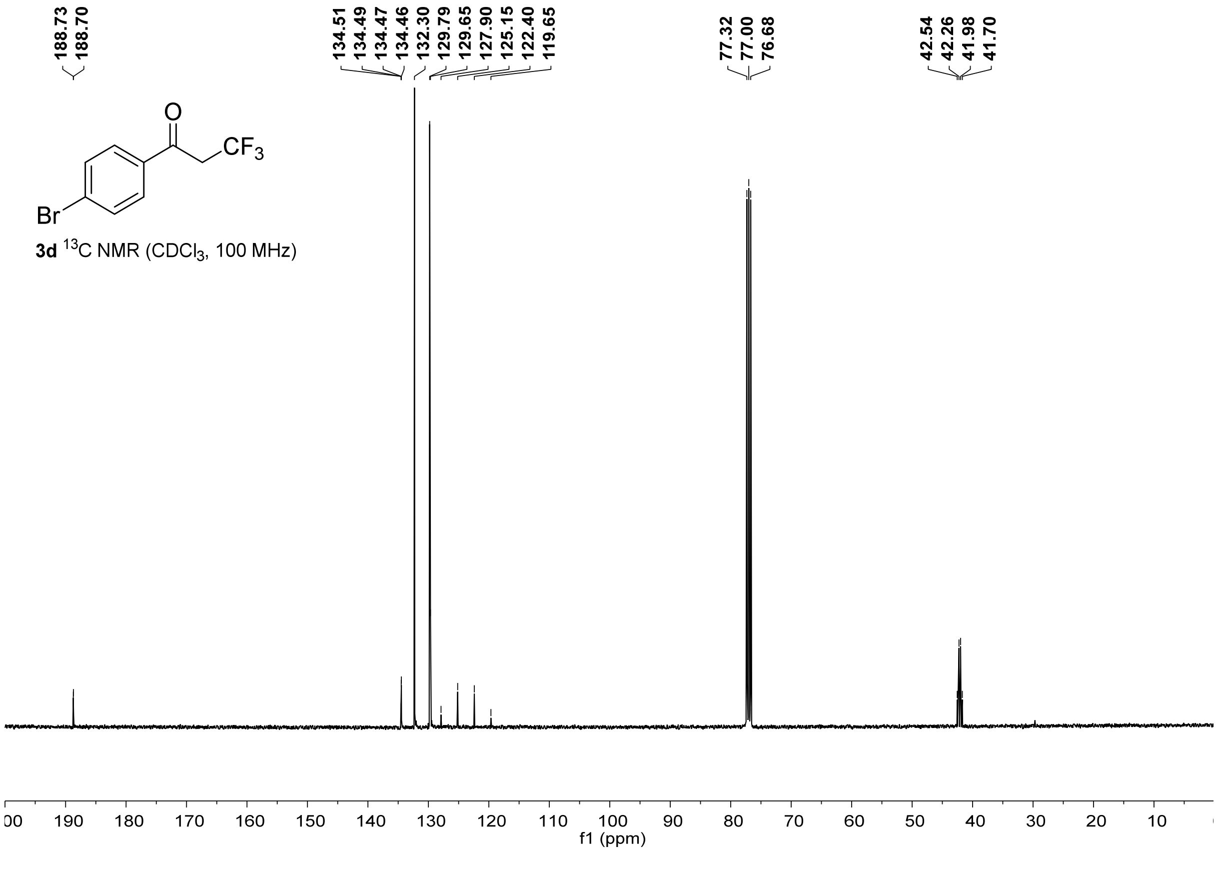
3c ^{13}C NMR ($CDCl_3$, 126 MHz)



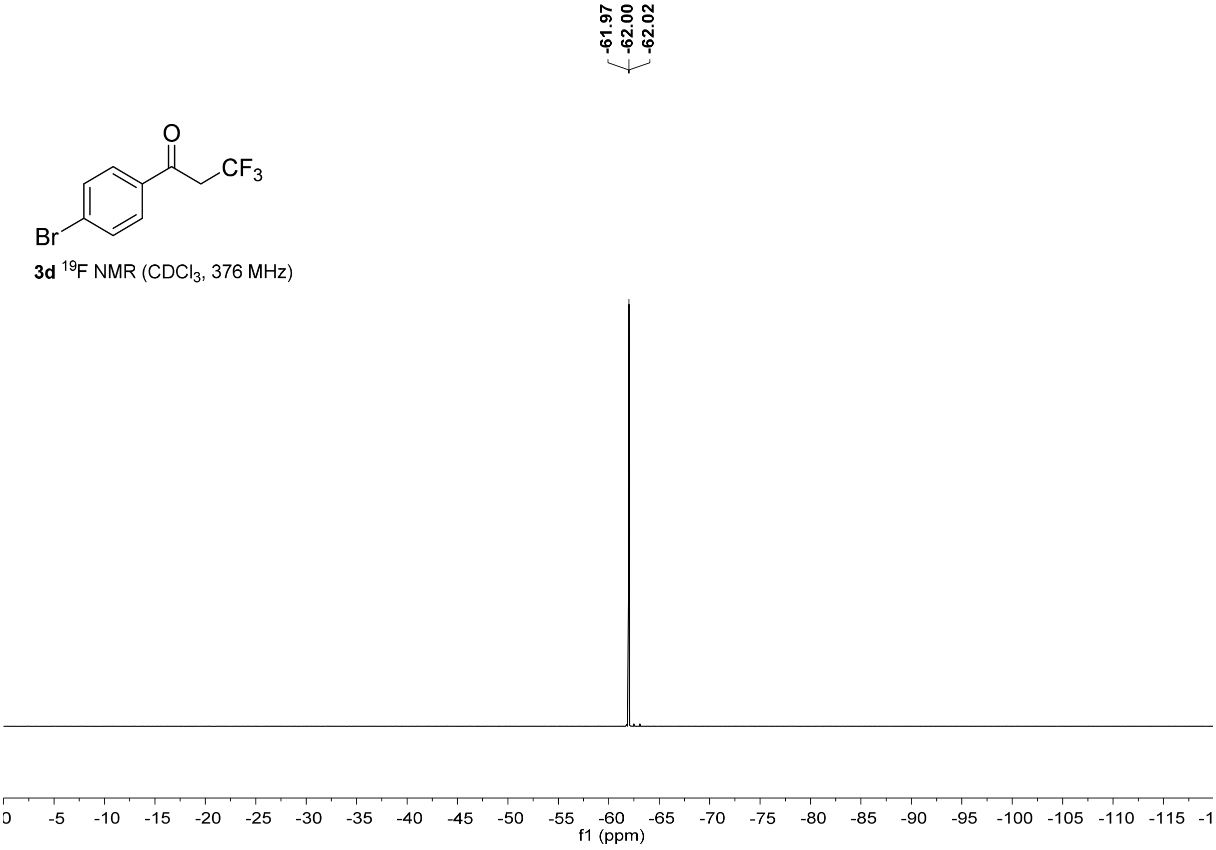
3c ^{19}F NMR ($CDCl_3$, 376 MHz)



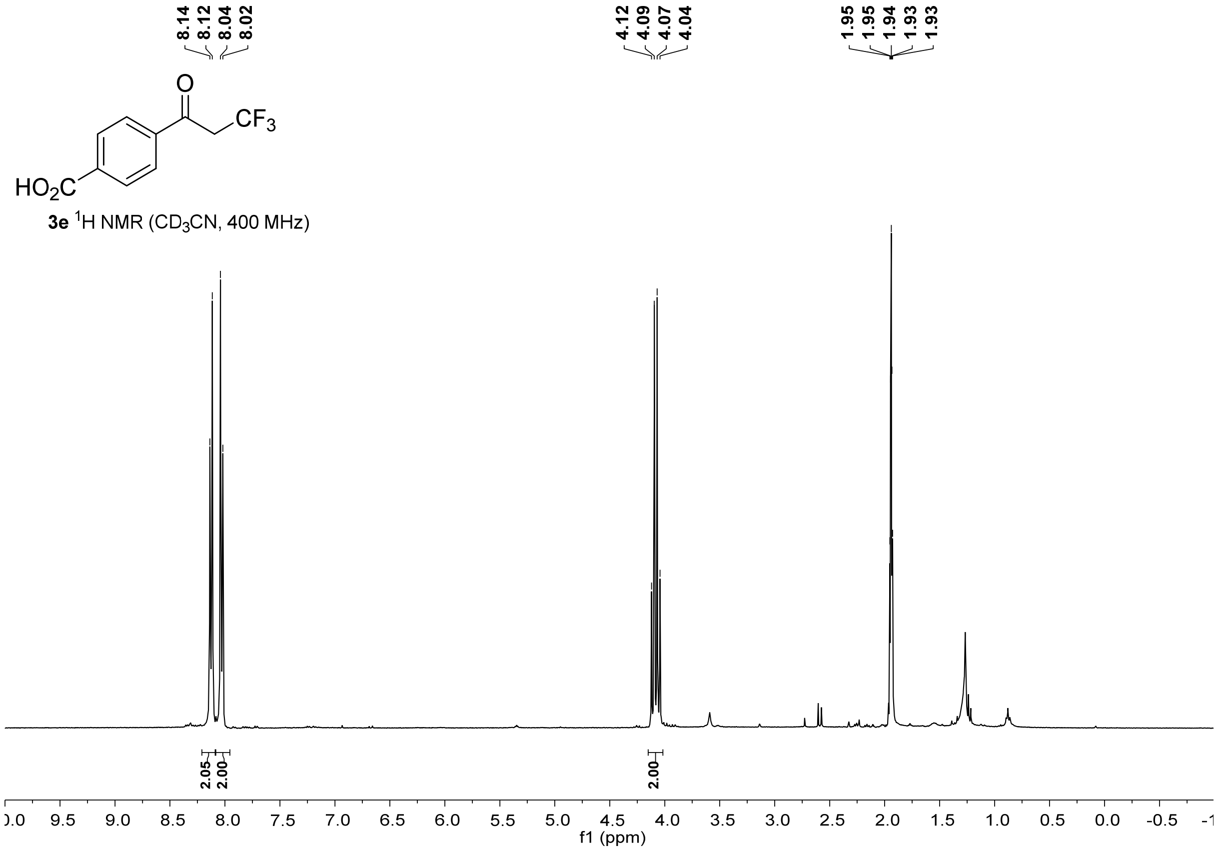
3d ^{1}H NMR ($CDCl_3$, 400 MHz)



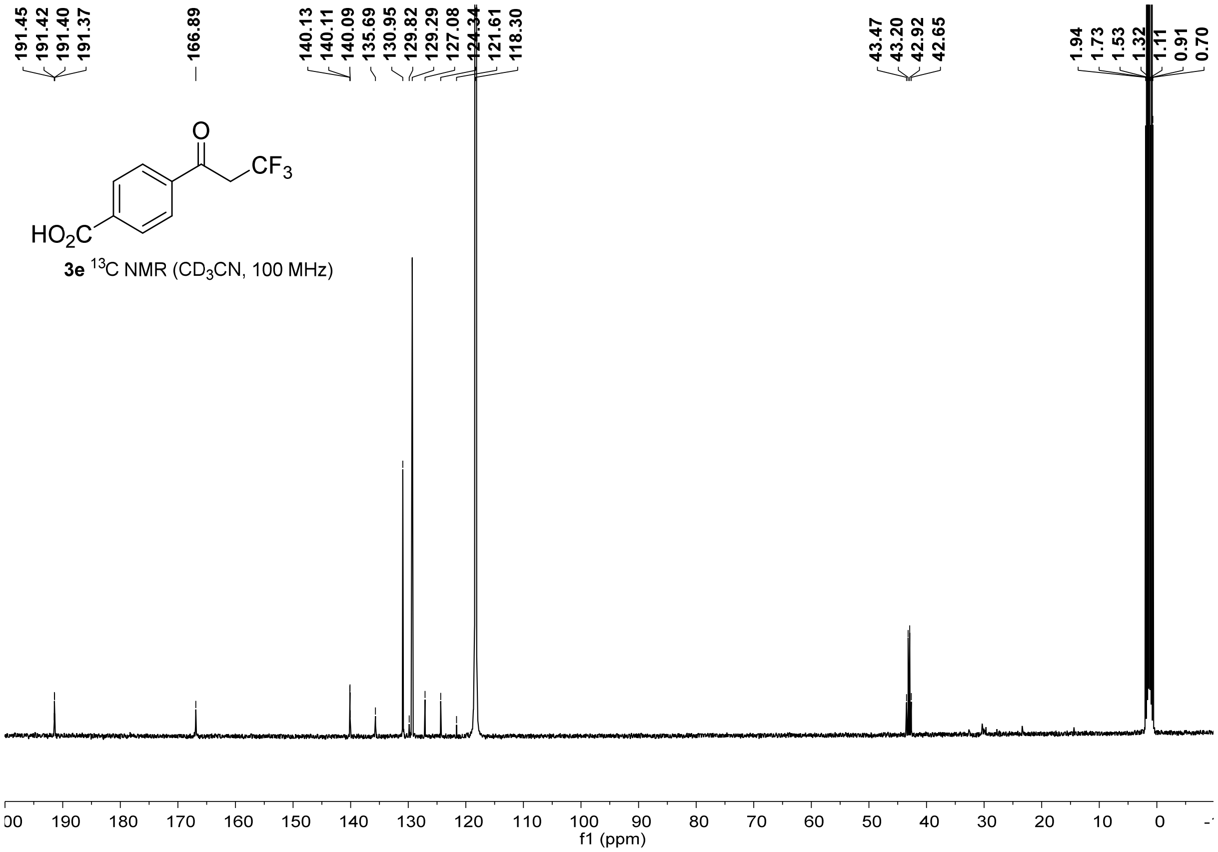
3d ^{13}C NMR ($CDCl_3$, 100 MHz)



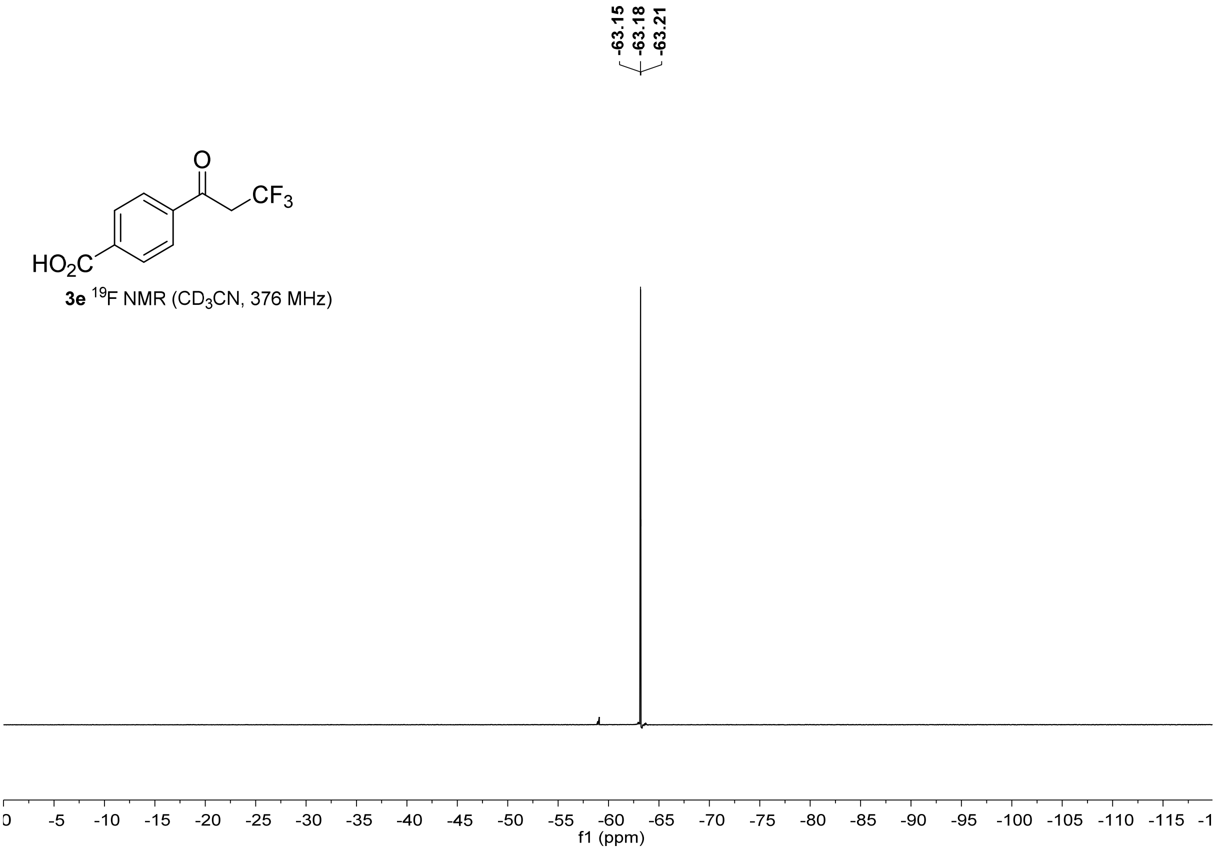
3d ^{19}F NMR ($CDCl_3$, 376 MHz)



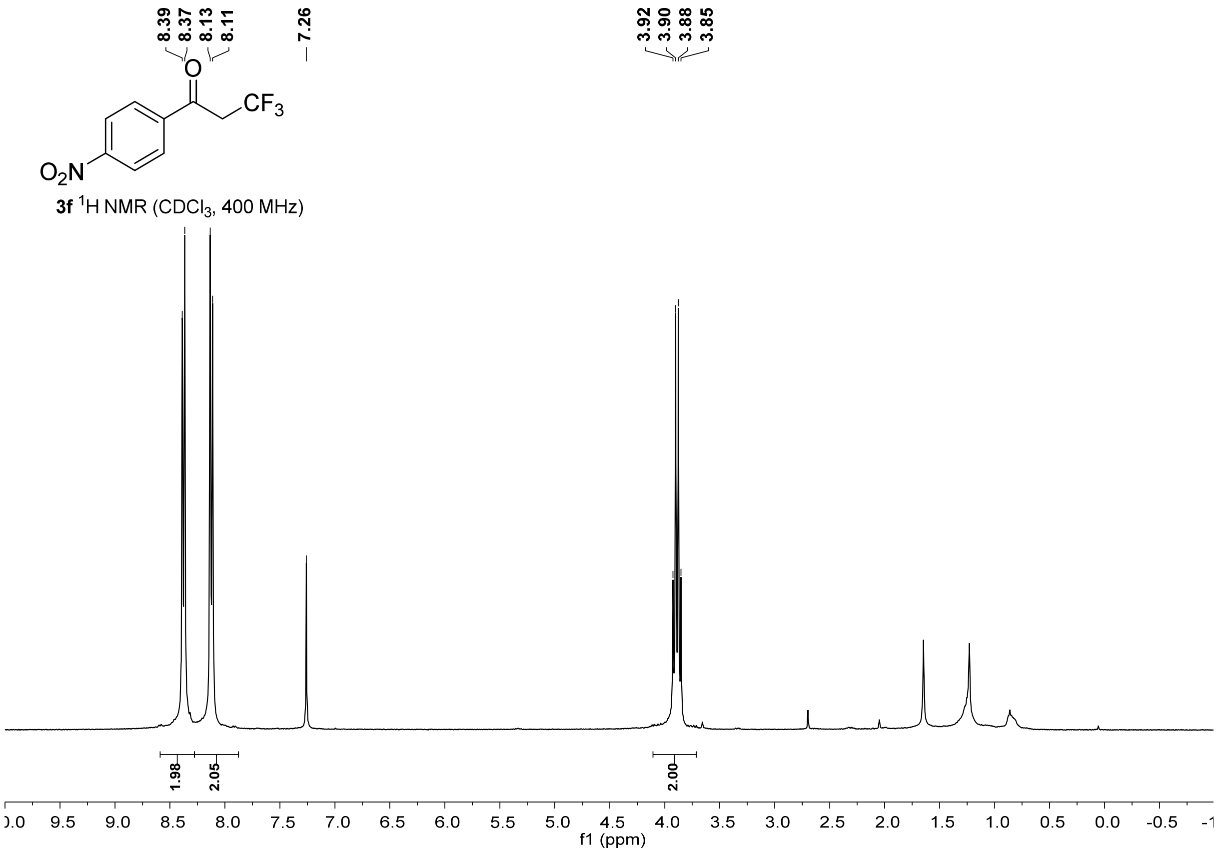
3e ^{1}H NMR (CD_3CN, 400 MHz)



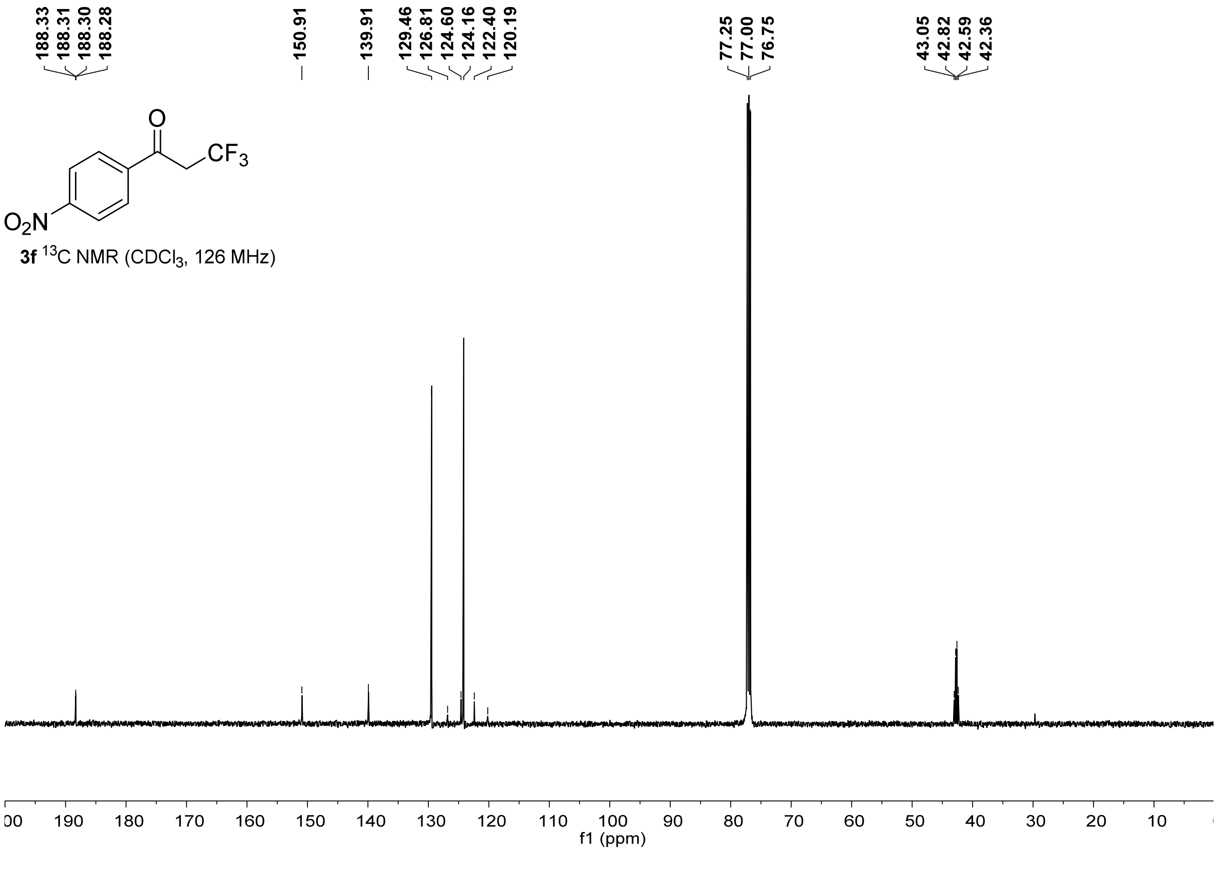
3e ^{13}C NMR (CD_3CN, 100 MHz)



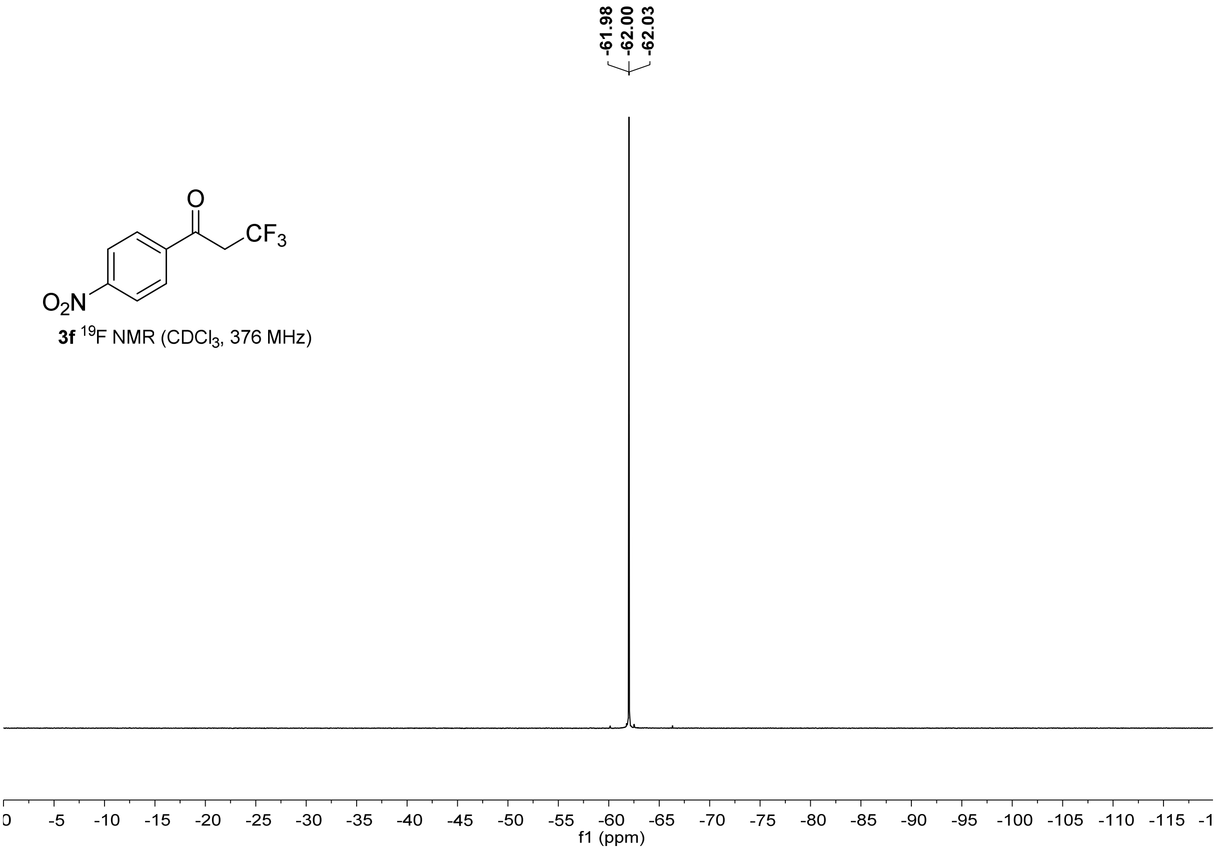
3e ^{19}F NMR (CD_3CN, 376 MHz)



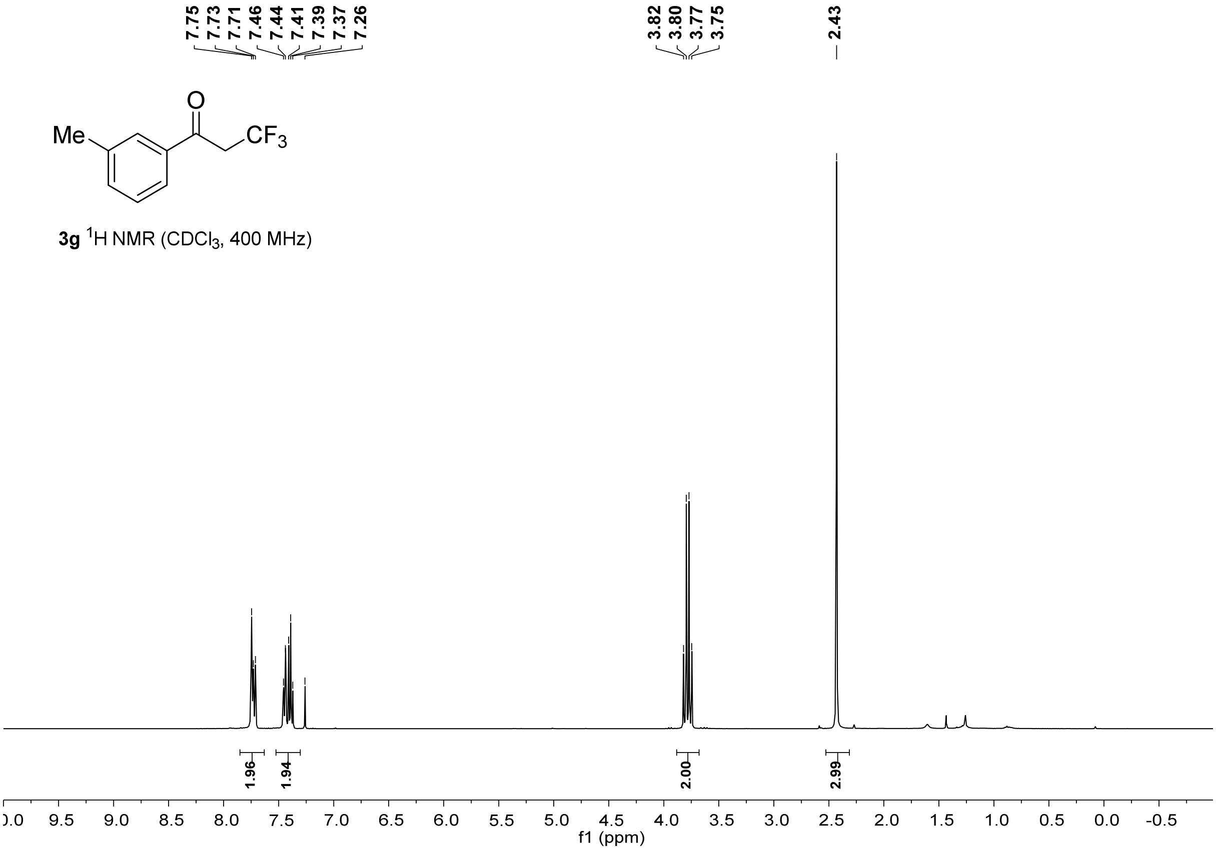
3f ^{1}H NMR (CDCl$_3$, 400 MHz)



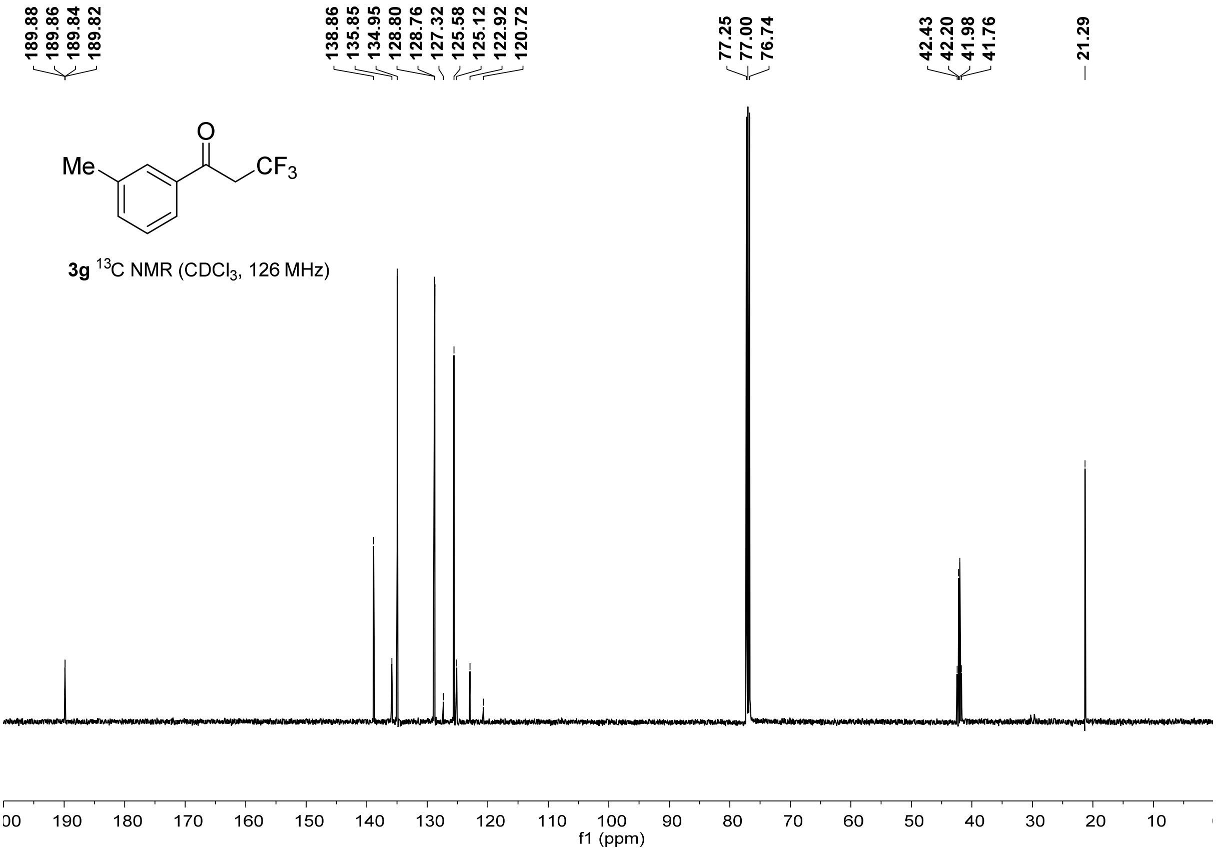
3f ^{13}C NMR (CDCl$_3$, 126 MHz)



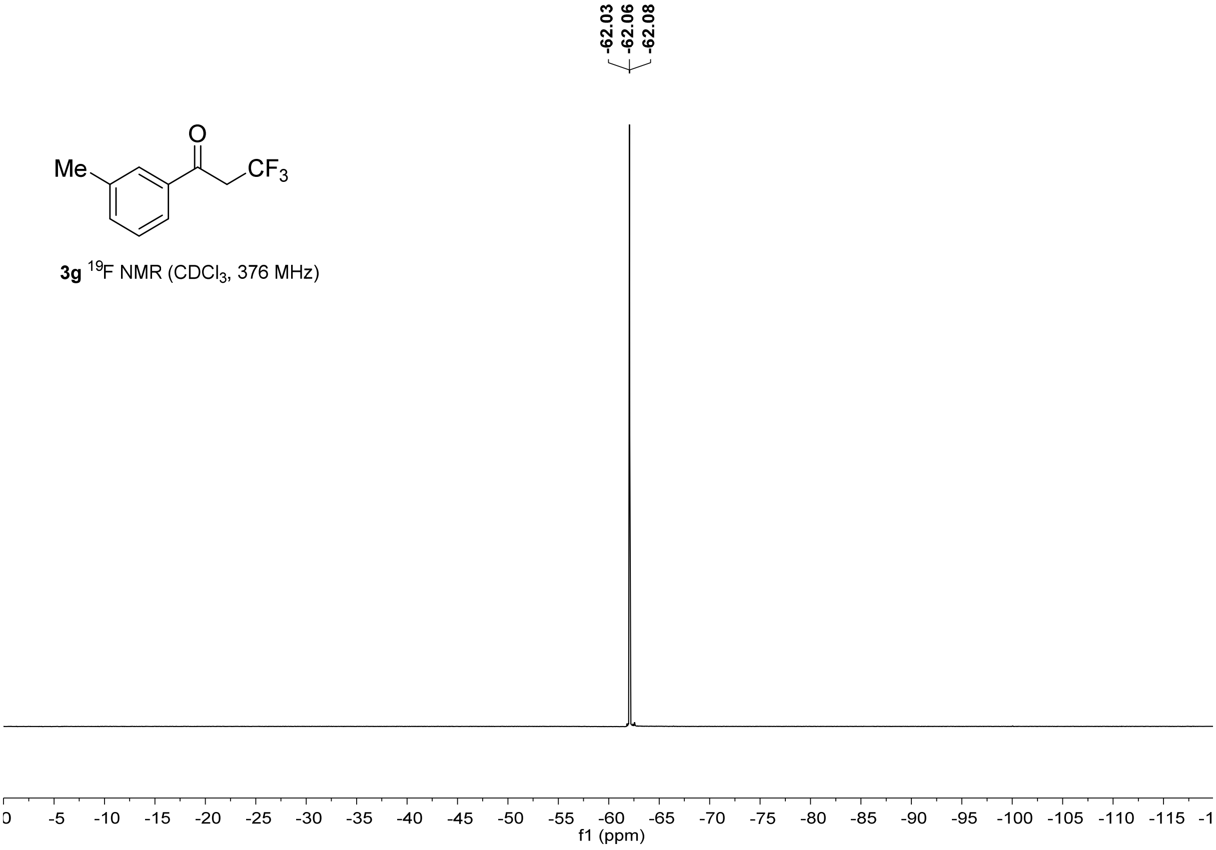
3f ^{19}F NMR ($CDCl_3$, 376 MHz)

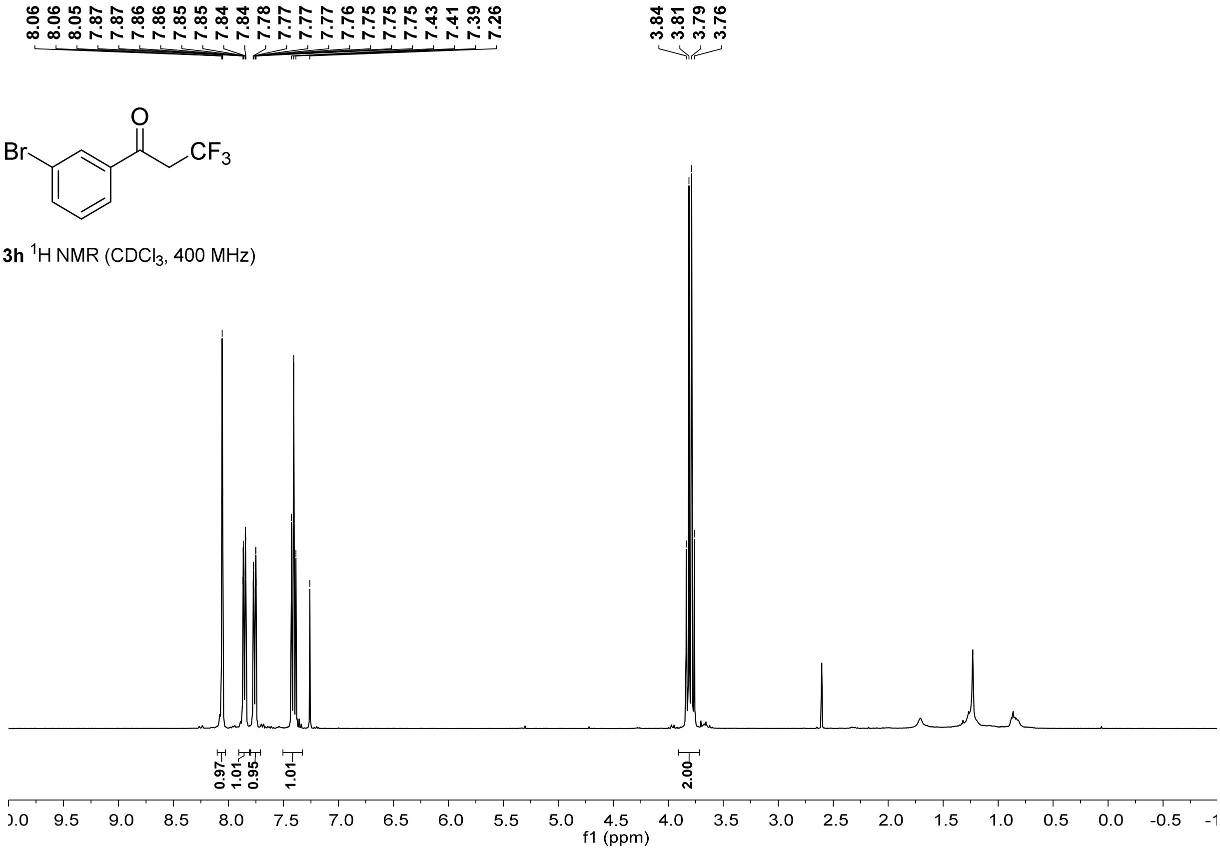


3g ^{1}H NMR ($CDCl_3$, 400 MHz)

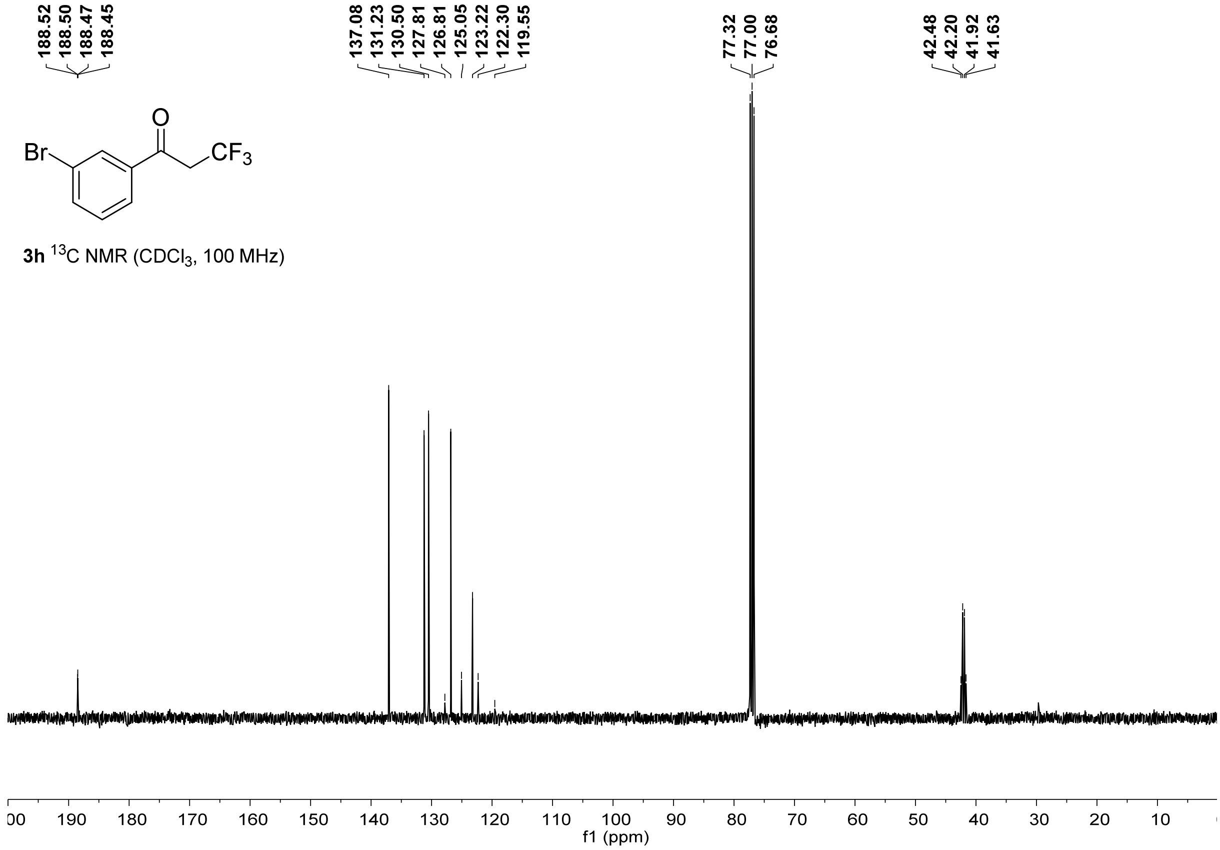


3g ^{13}C NMR ($CDCl_3$, 126 MHz)

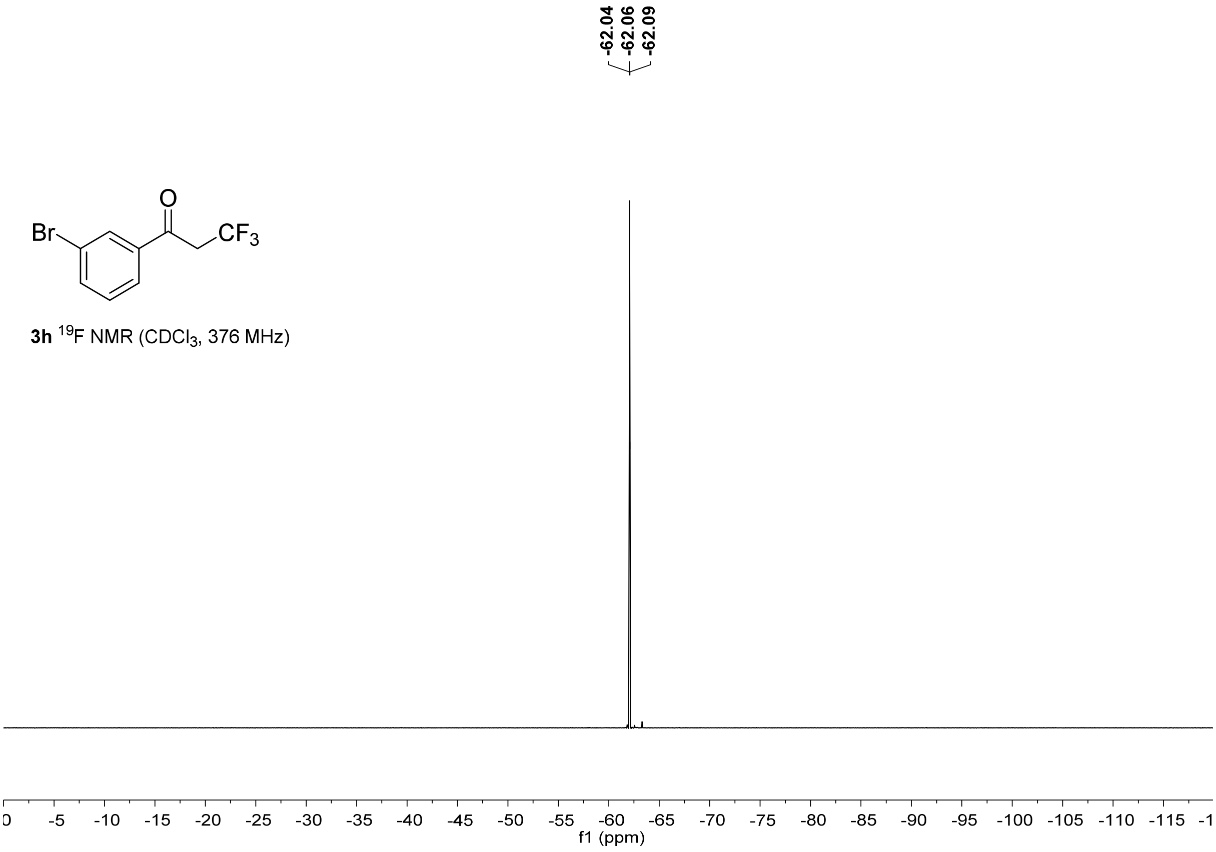

-62.03
-62.06
-62.08
Me
O
CF3
3g 19F NMR (CDCl3, 376 MHz)
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-1
f1 (ppm)

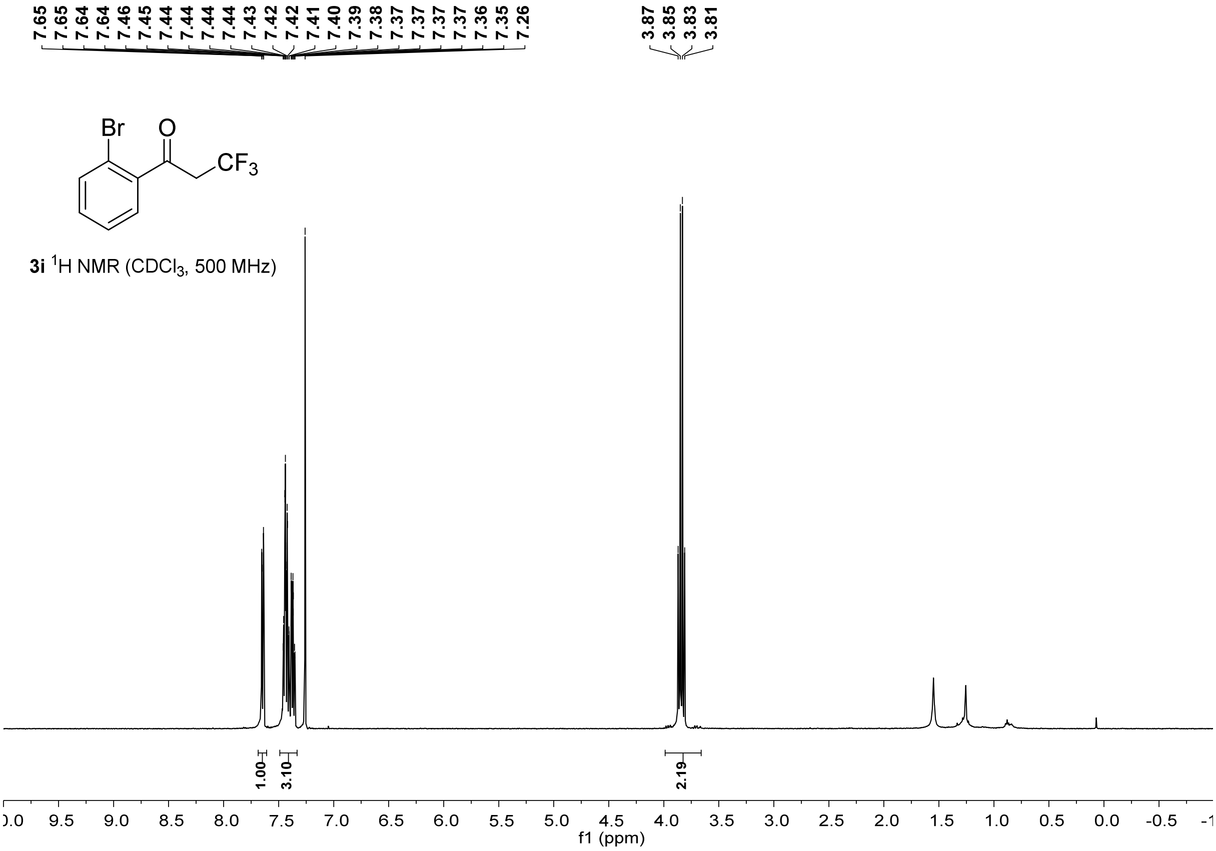


3h ^{1}H NMR (CDCl$_3$, 400 MHz)

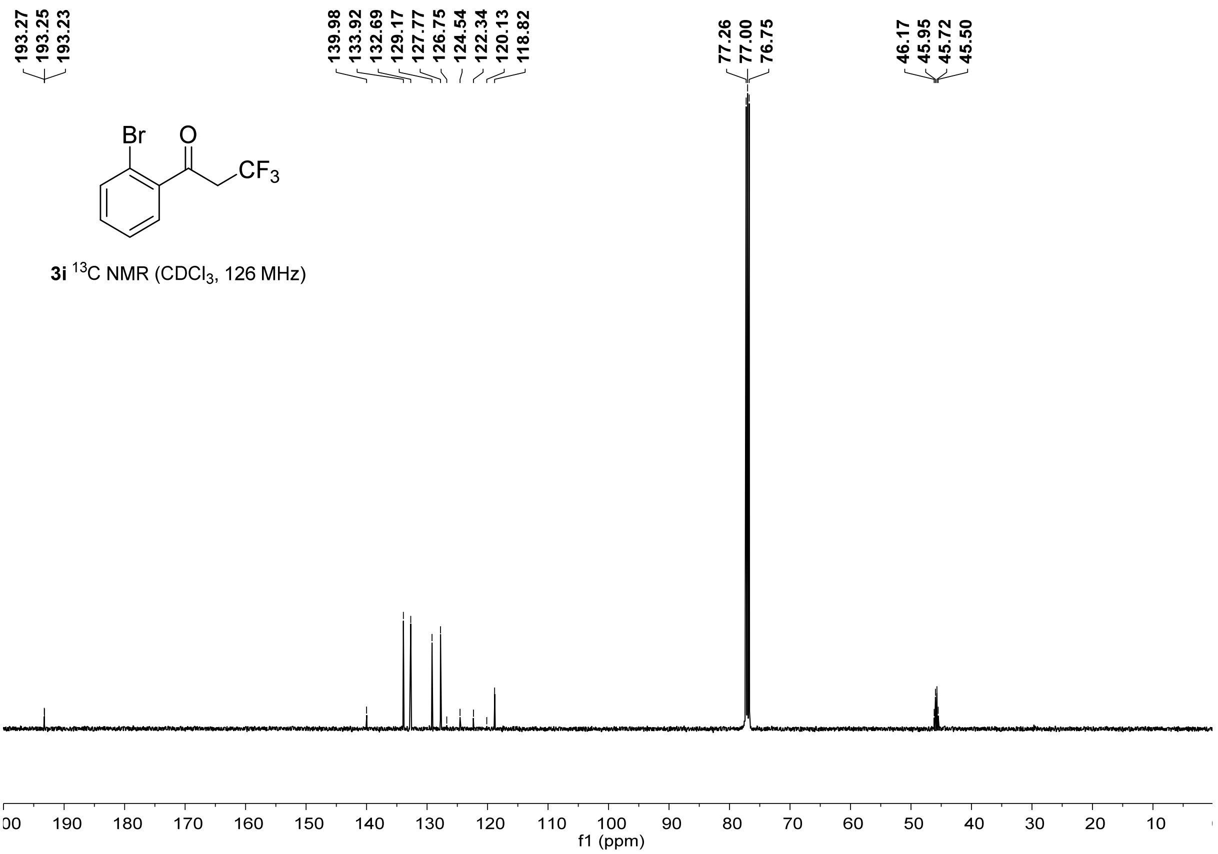


3h ^{13}C NMR (CDCl$_3$, 100 MHz)

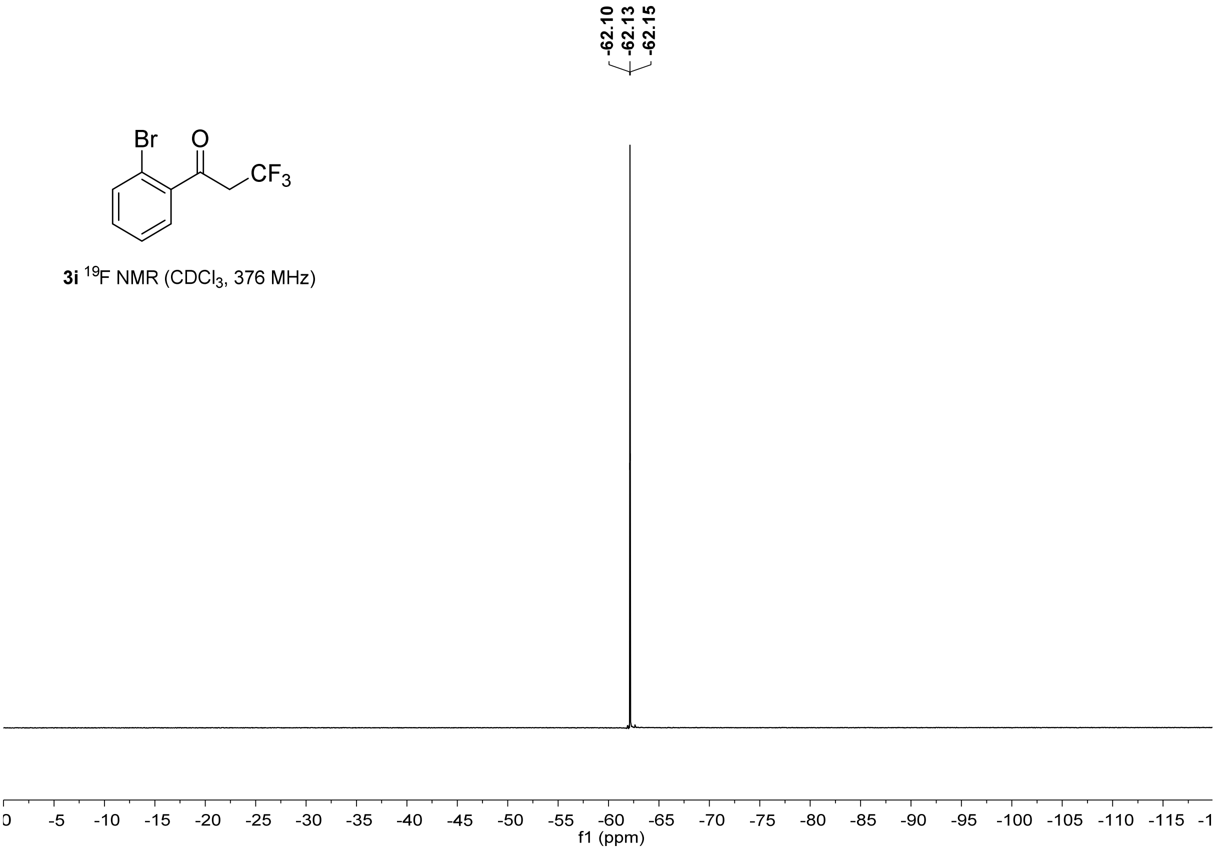

-62.04
-62.06
-62.09
O
Br
CF3
3h ¹⁹F NMR (CDCl3, 376 MHz)
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-1
f1 (ppm)



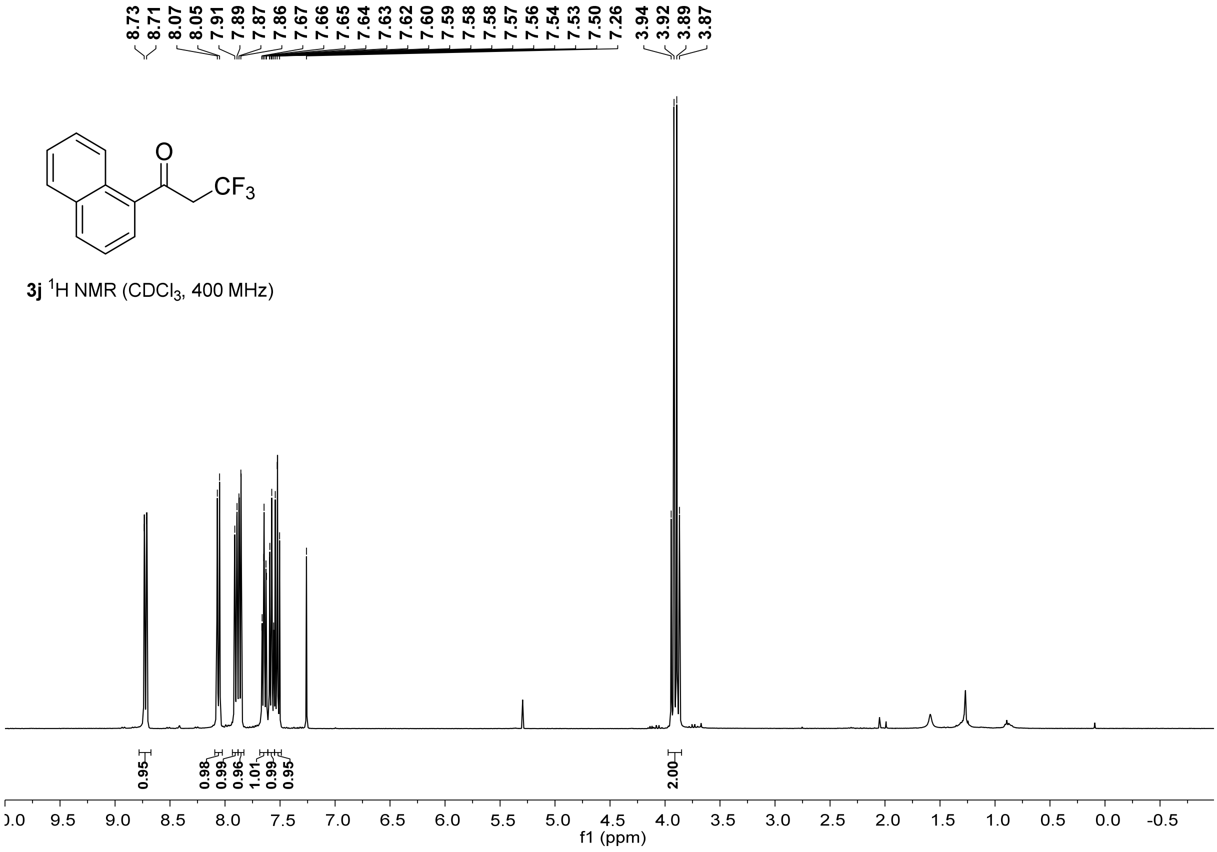
3i ^{1}H NMR ($CDCl_3$, 500 MHz)



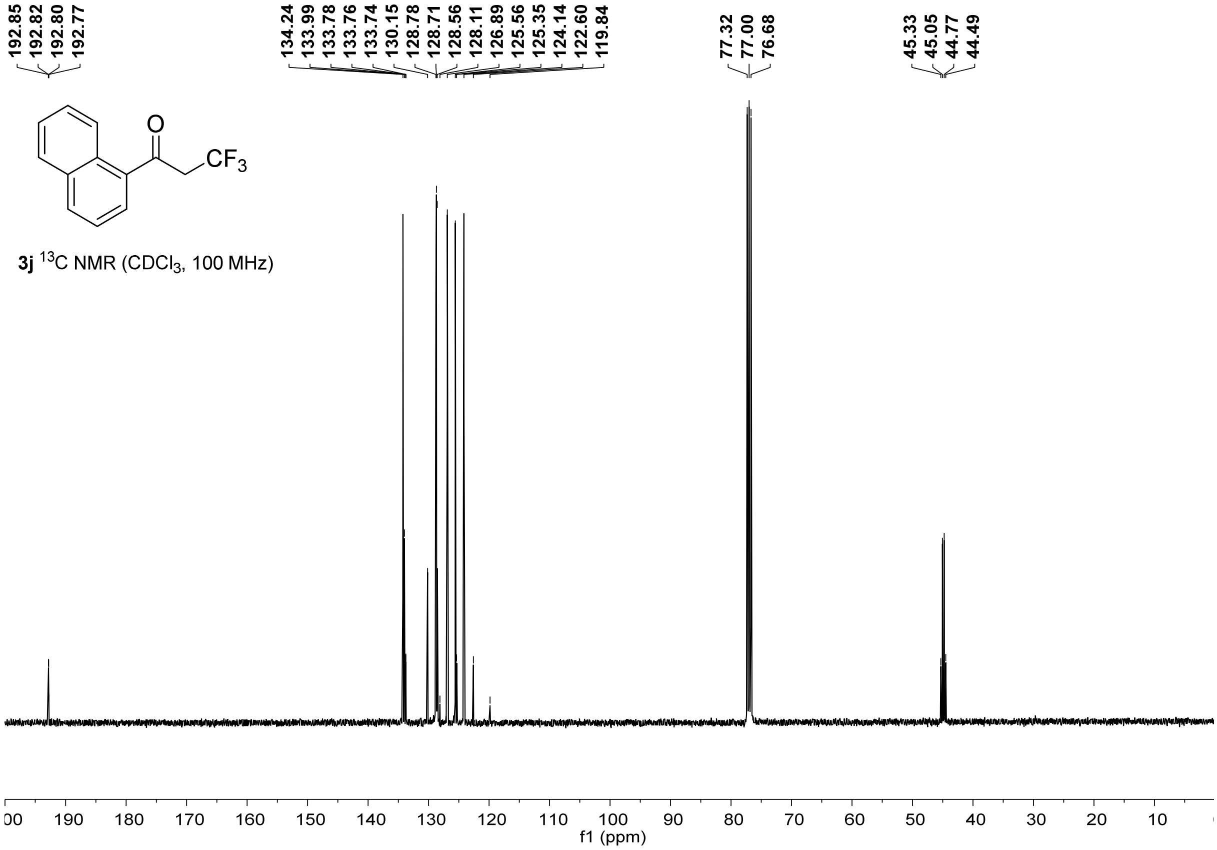
3i ^{13}C NMR ($CDCl_3$, 126 MHz)



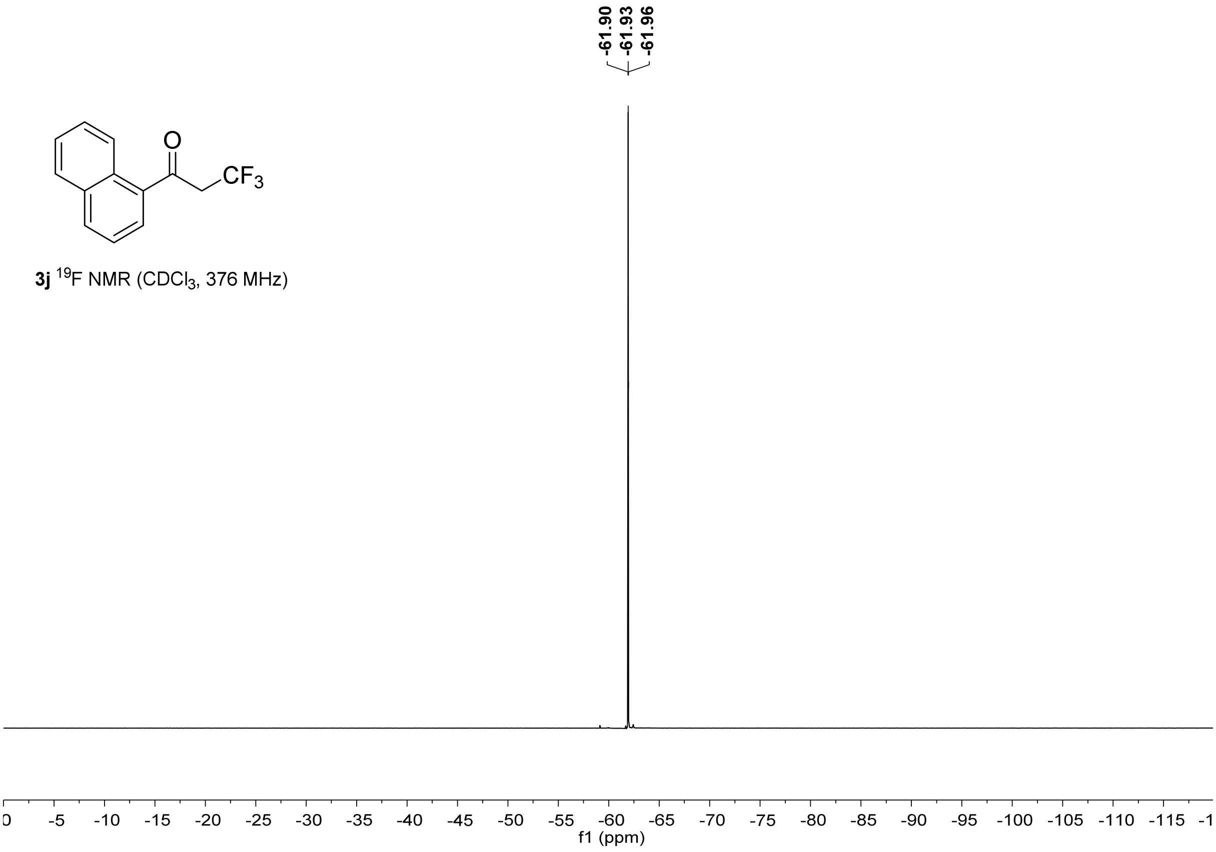
3i ^{19}F NMR ($CDCl_3$, 376 MHz)

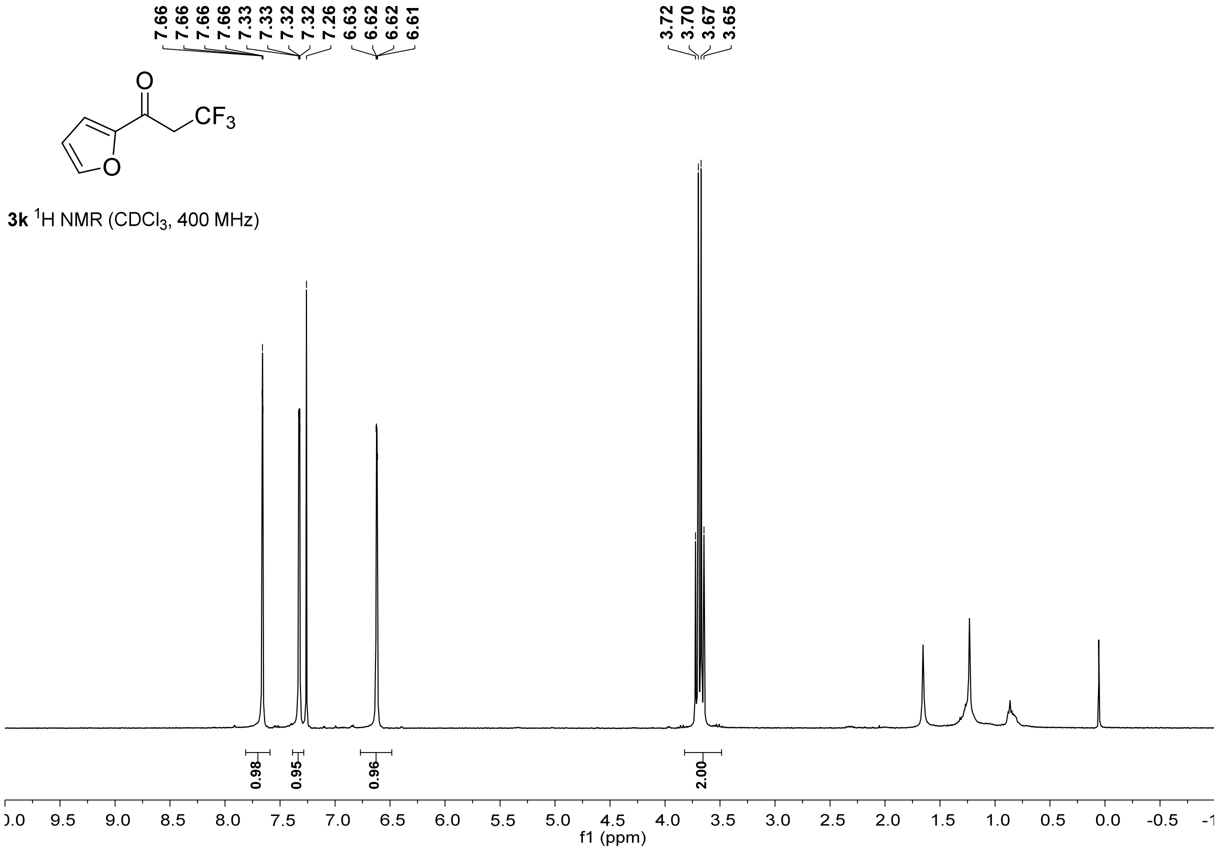


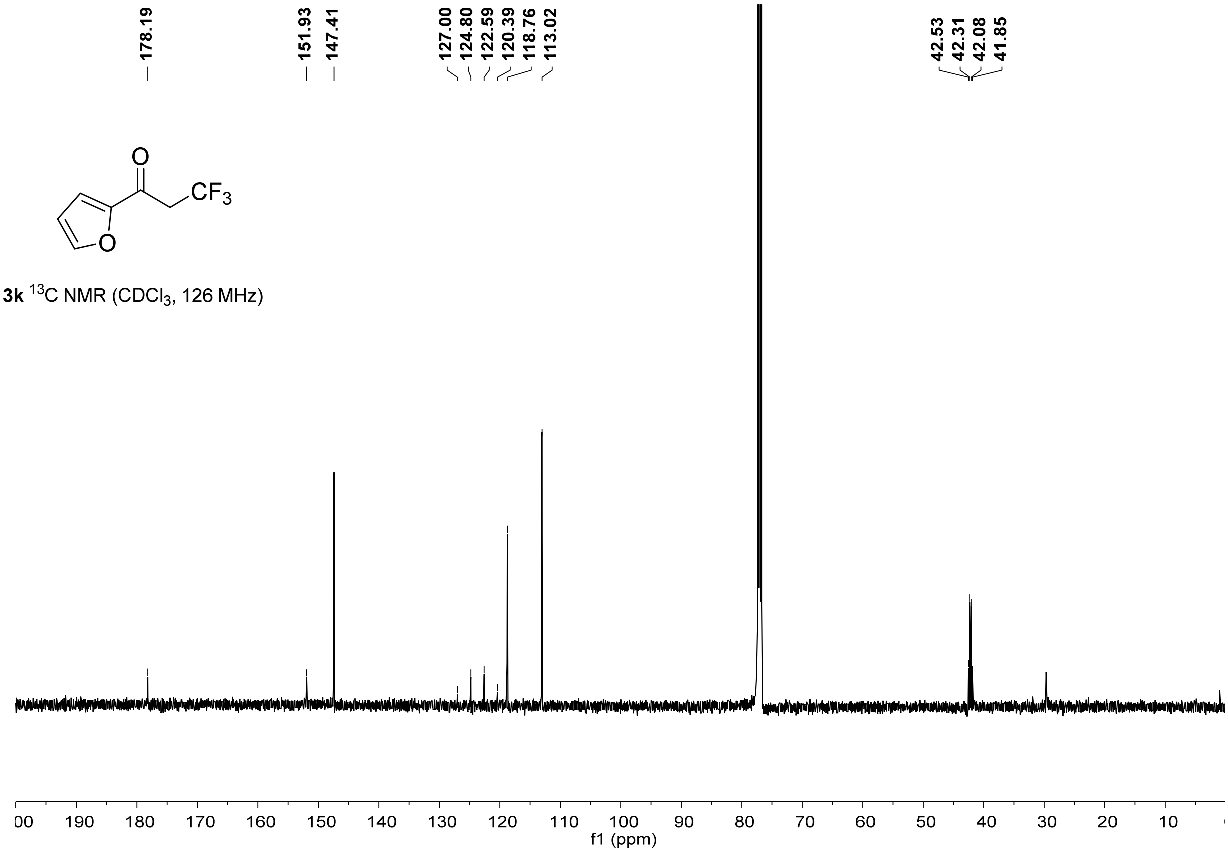
3j ^{1}H NMR ($CDCl_3$, 400 MHz)

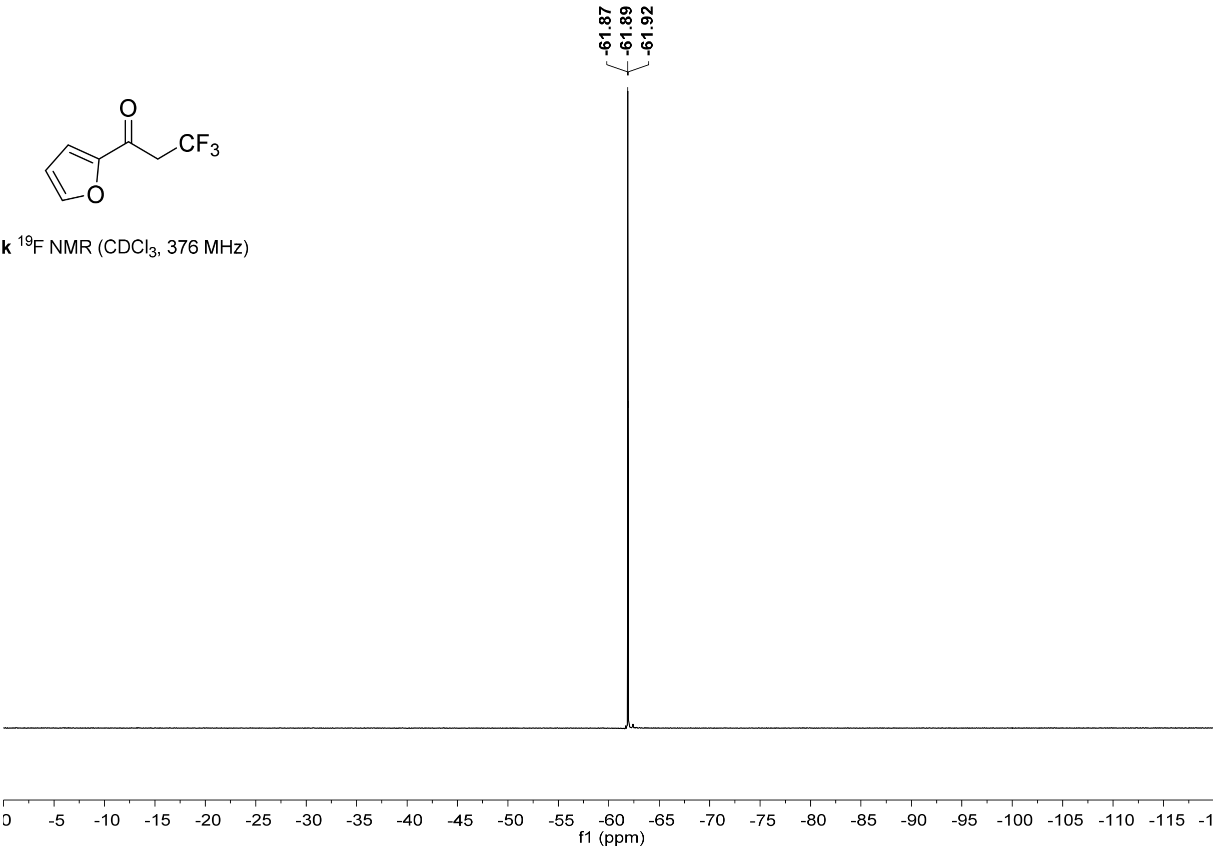


3j ^{13}C NMR ($CDCl_3$, 100 MHz)

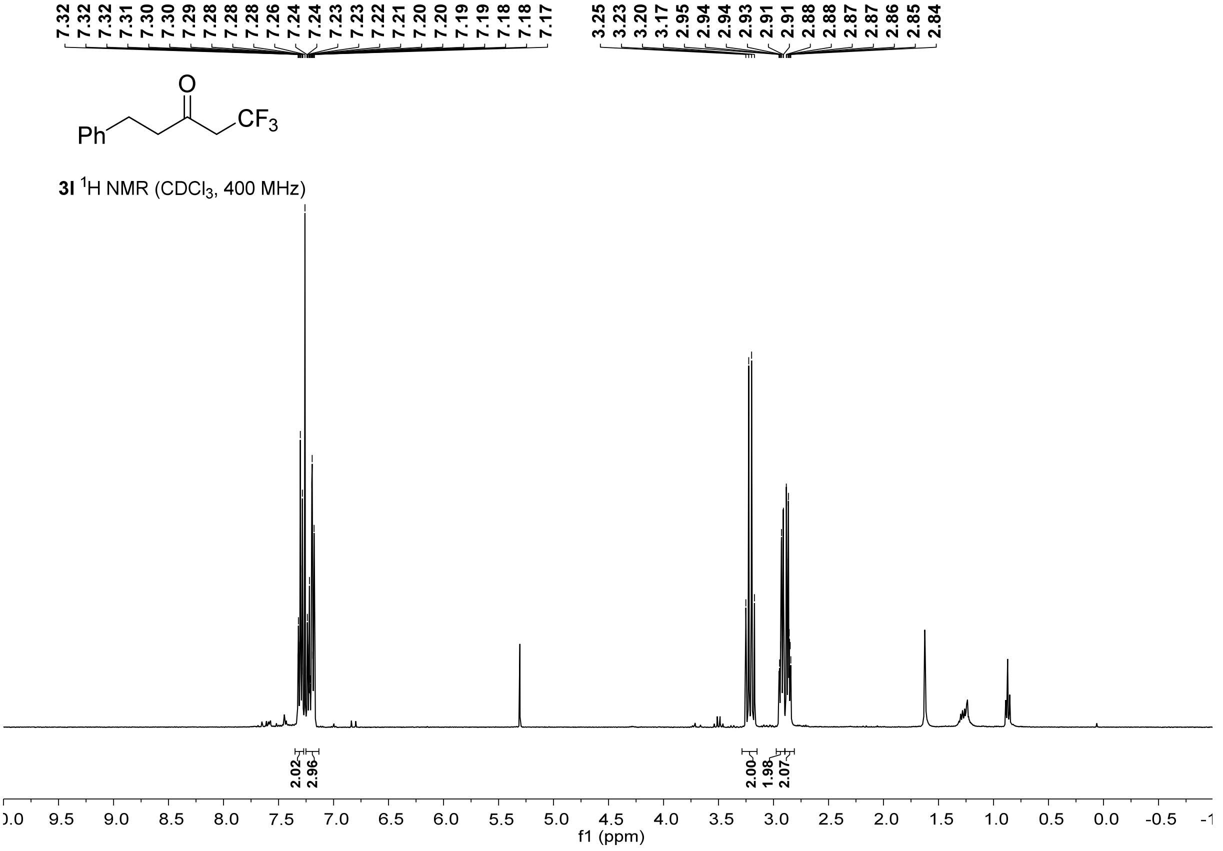

3j ^{19}F NMR ($CDCl_3$, 376 MHz)


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

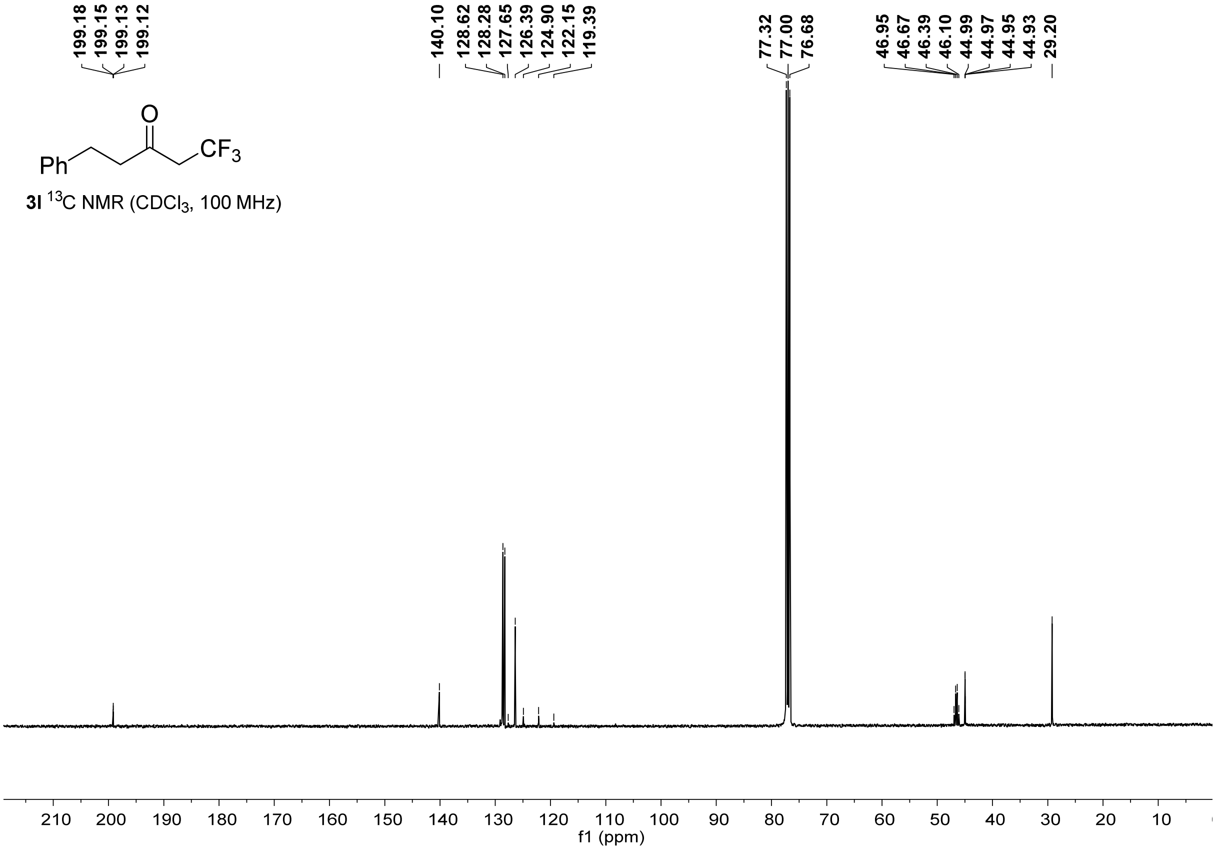

3k ^{13}C NMR (CDCl$_3$, 126 MHz)



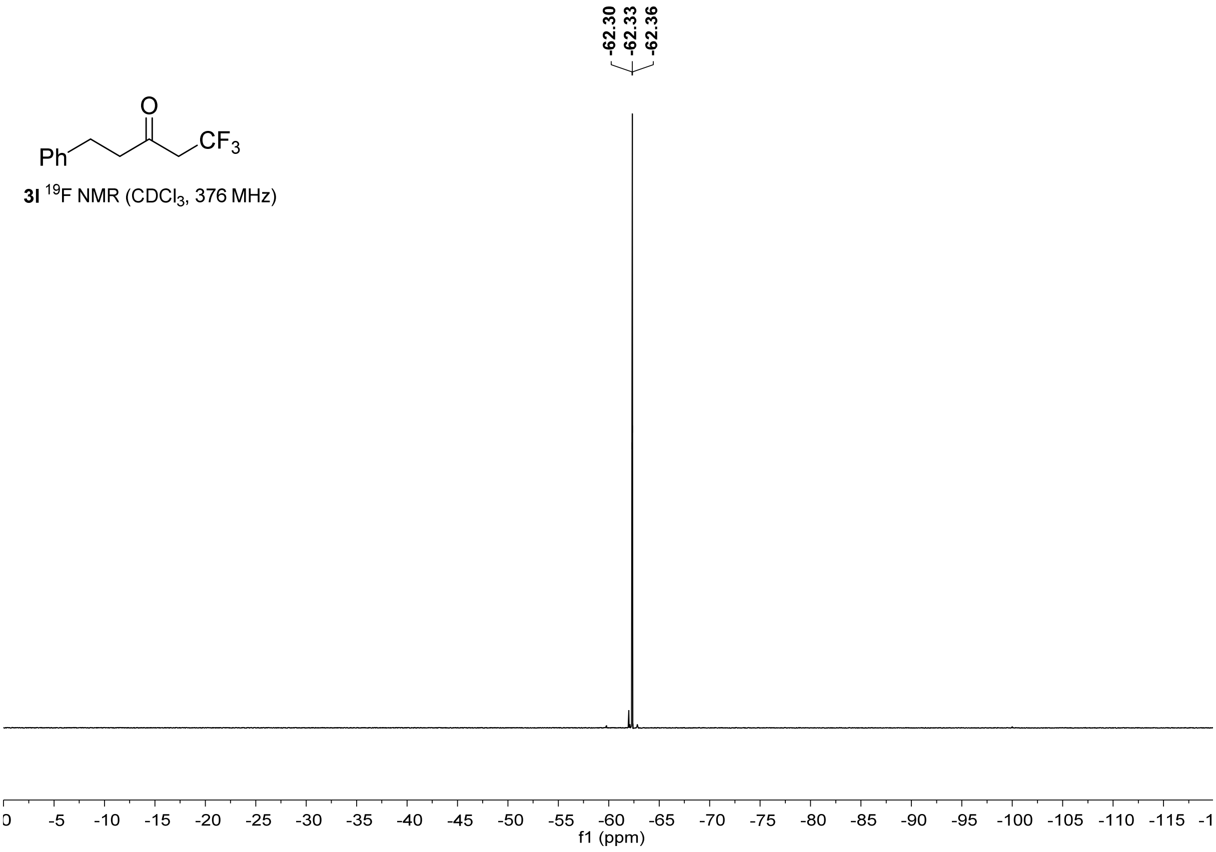
3k ^{19}F NMR ($CDCl_3$, 376 MHz)



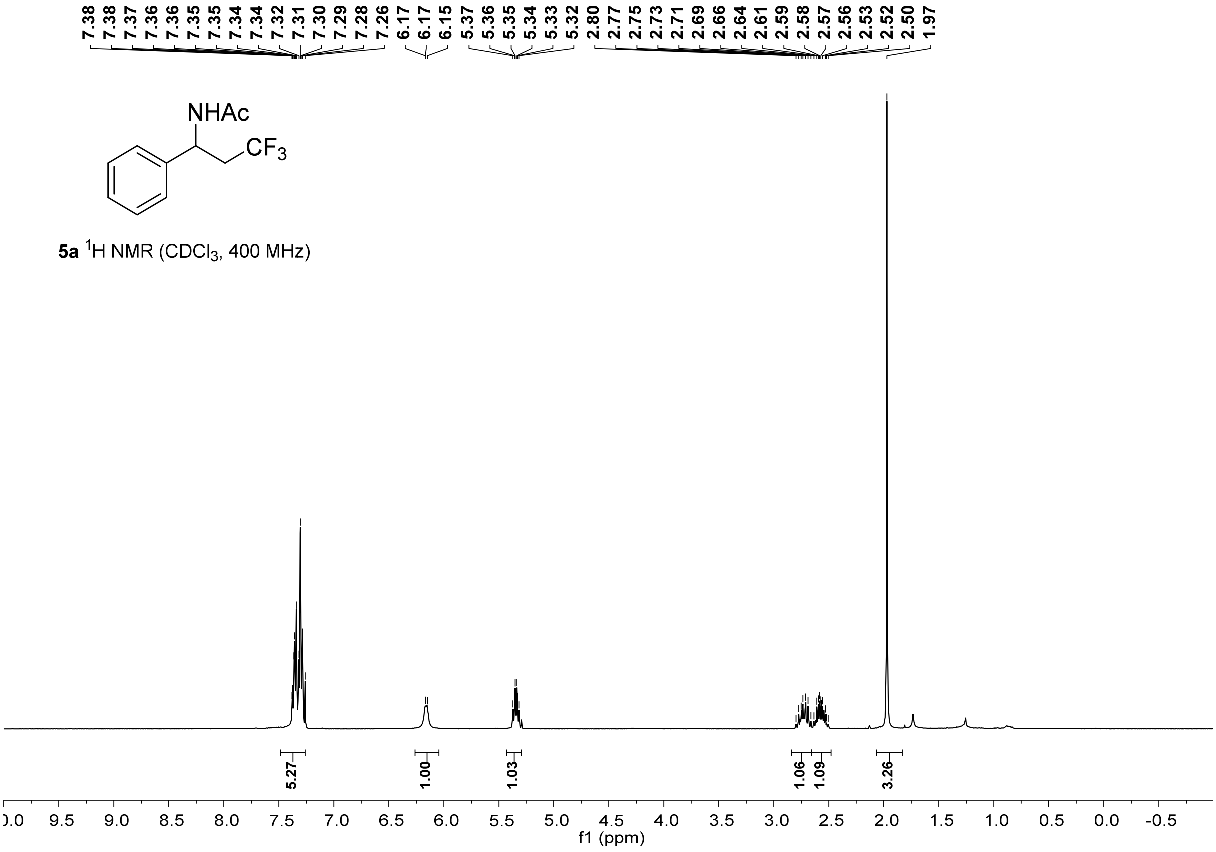
3l ^{1}H NMR (CDCl$_3$, 400 MHz)



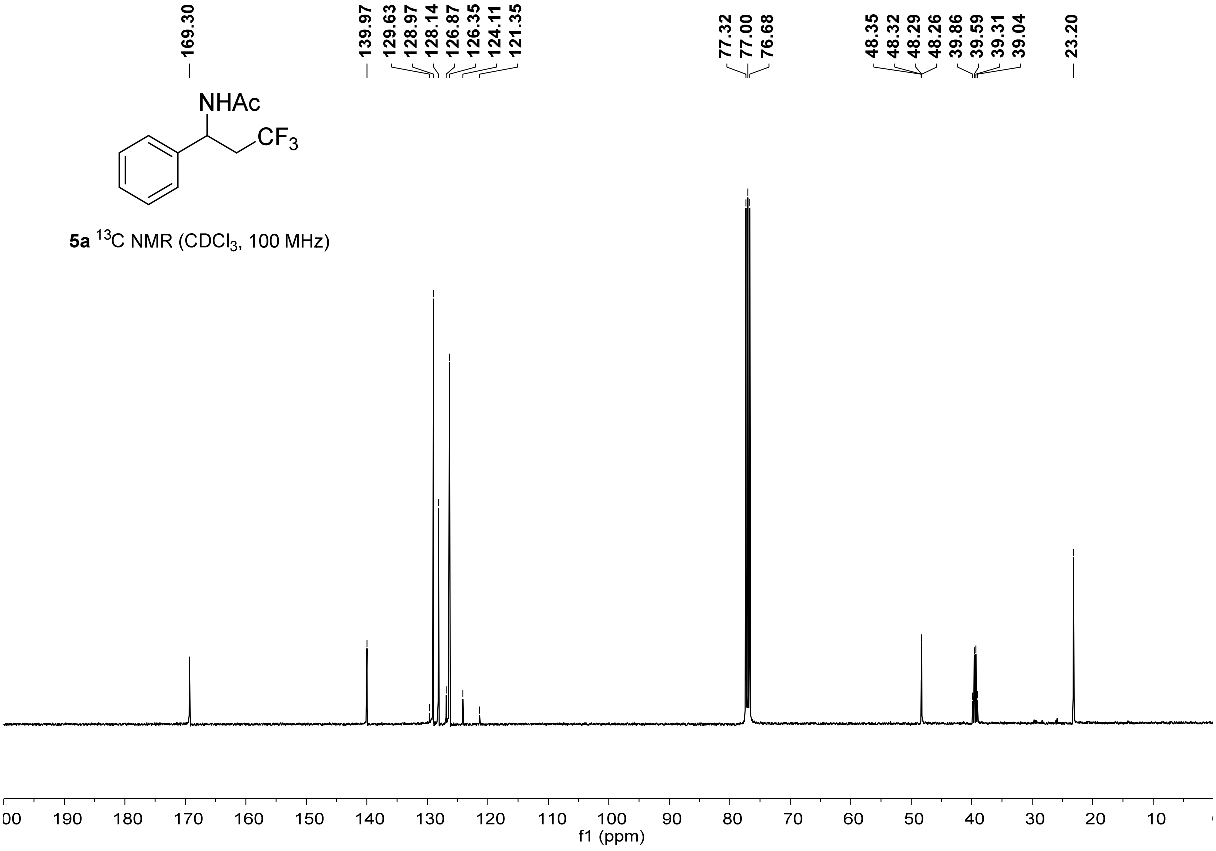
3l ^{13}C NMR (CDCl$_3$, 100 MHz)



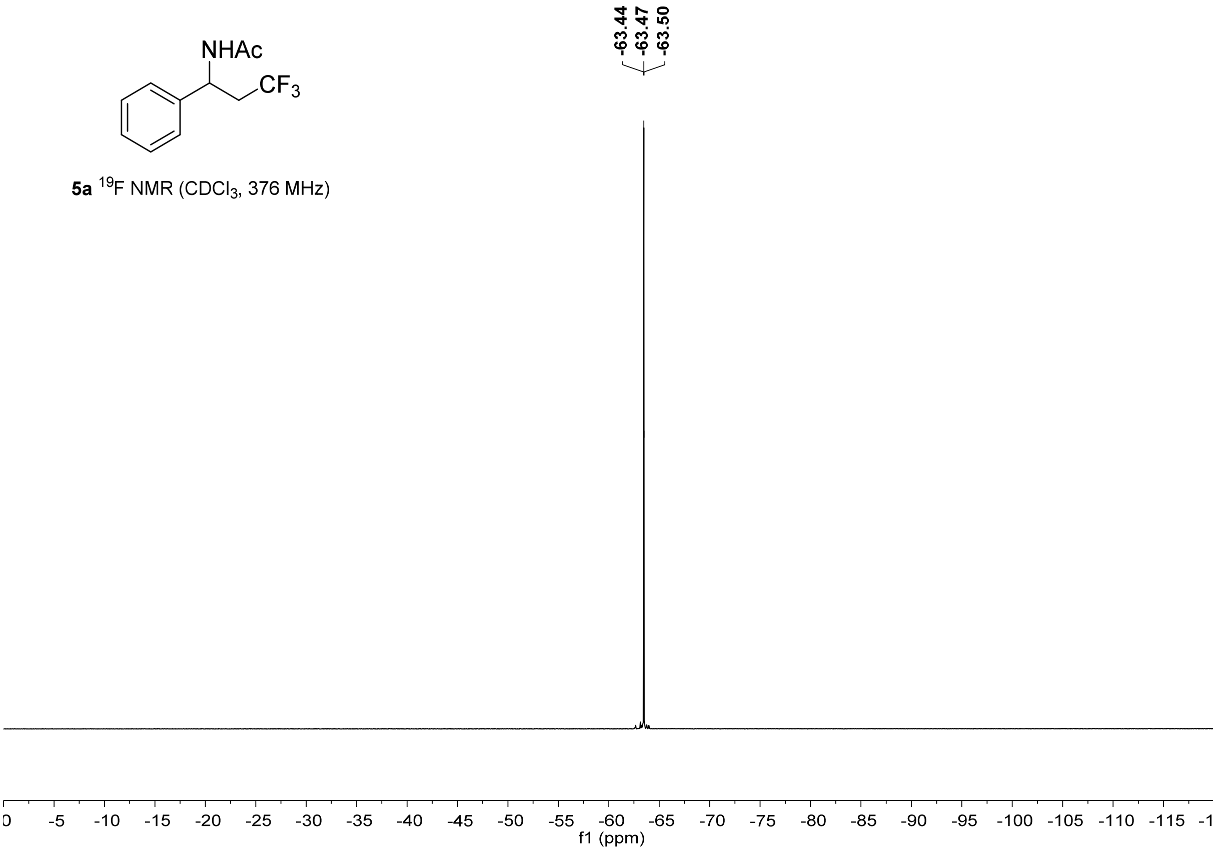
3l ^{19}F NMR (CDCl$_3$, 376 MHz)



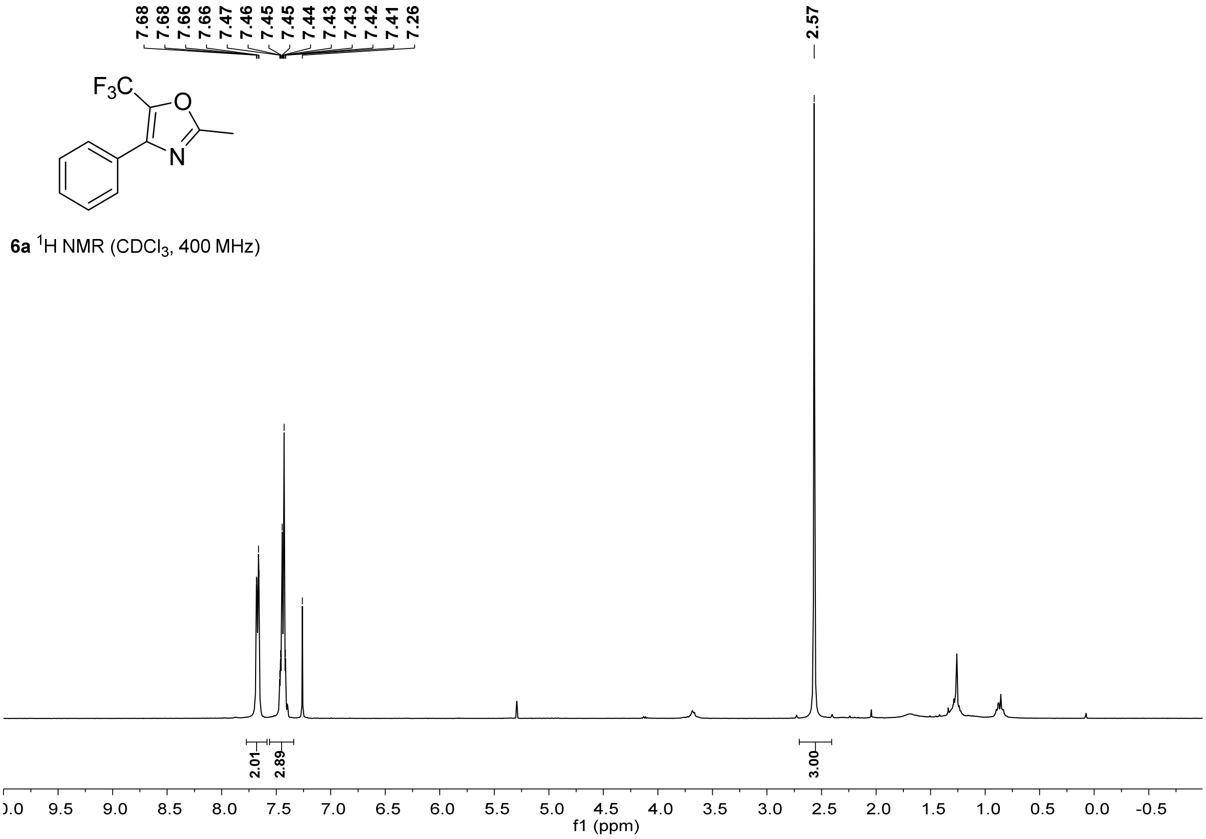
5a ^{1}H NMR ($CDCl_3$, 400 MHz)



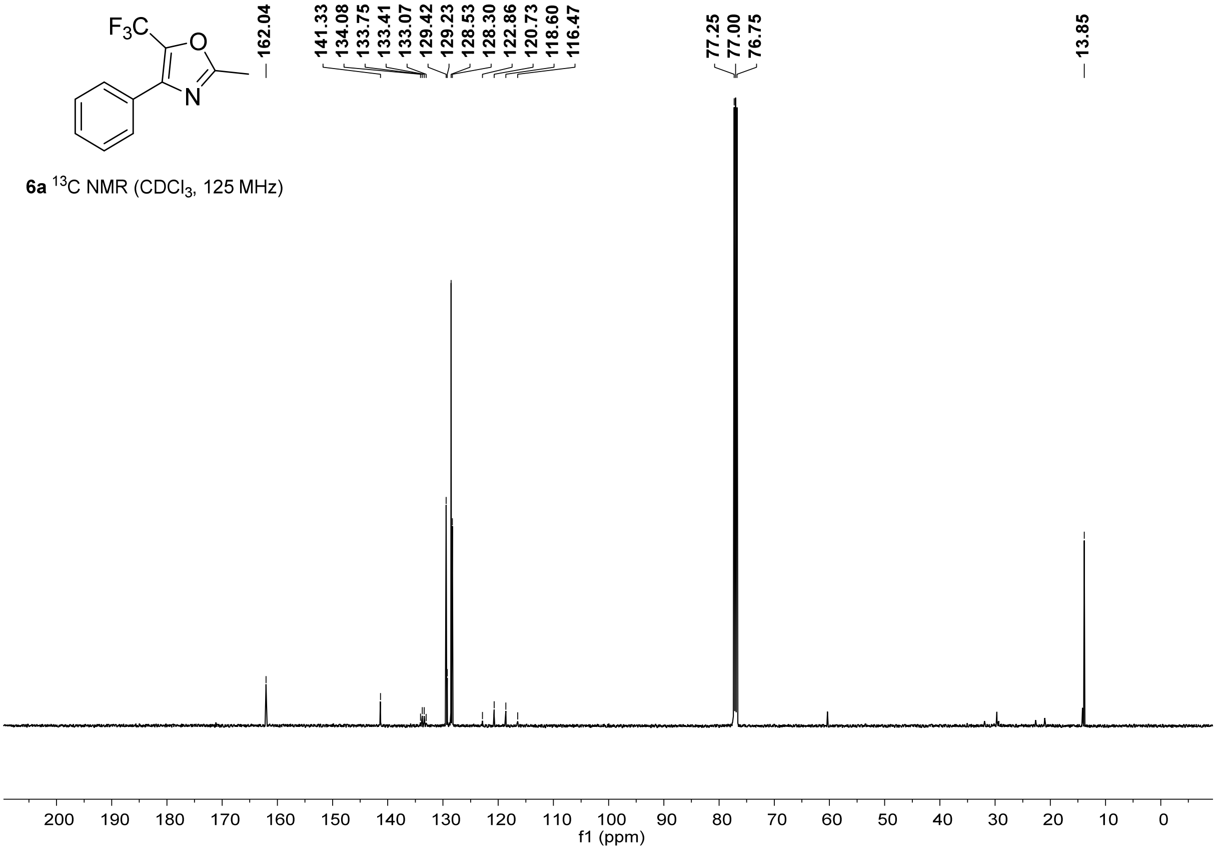
5a ^{13}C NMR ($CDCl_3$, 100 MHz)



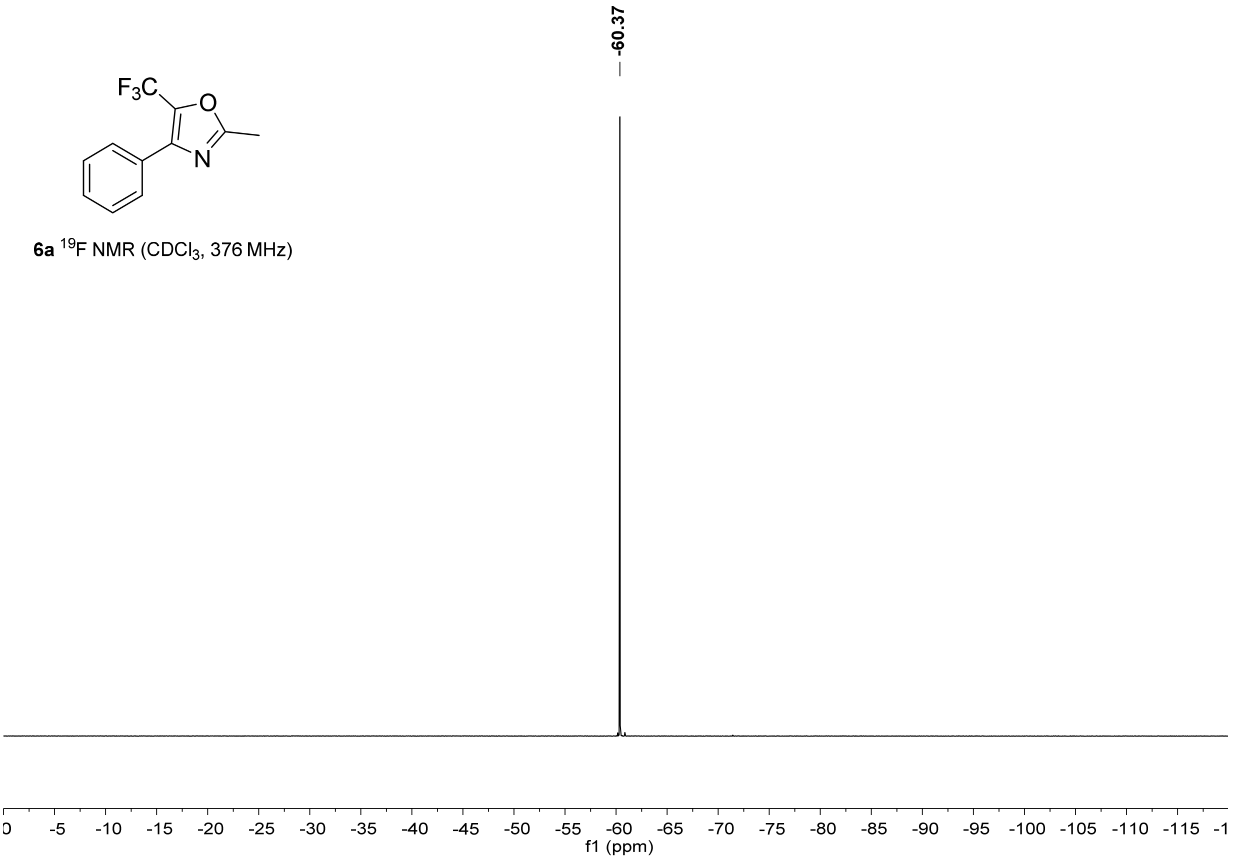
5a ^{19}F NMR ($CDCl_3$, 376 MHz)



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



6a ^{13}C NMR (CDCl$_3$, 125 MHz)



6a ^{19}F NMR ($CDCl_3$, 376 MHz)

4. References

1. Ke, J.; Tang, Y.; Yi, H.; Li, Y.; Cheng, Y.; Liu, C.; Lei, A., *Angew. Chem. Int. Ed.* **2015**, *54*, 6604.
2. Too, P. C.; Wang, Y.-F.; Chiba, S., *Org. Lett.* **2010**, *12*, 5688.
3. Novák, P.; Lishchynskyi, A.; Grushin, V. V., *J. Am. Chem. Soc.* **2012**, *134*, 16167.
4. Wang, Y.-F.; Lonca, G. H.; Chiba, S., *Angew. Chem. Int. Ed.* **2014**, *53*, 1067.
5. Deb, A.; Manna, S.; Modak, A.; Patra, T.; Maity, S.; Maiti, D., *Angew. Chem. Int. Ed.* **2013**, *52*, 9747.
6. Feng, C.; Loh, T.-P., *Chem. Sci.* **2012**, *3*, 3458.
7. Tanaka, K.; Ishiguro, Y.; Mitsuhashi, K., *Bull. Chem. Soc. Jpn.* **1993**, *66*, 661.