Electronic Supplementary Material (ESI) for ChemComm.

N-Aryltrifluoromethanesulfonimides as new trifluoromethylating agents for the (photo)catalyst-free functionalization of (hetero)aromatics.

Edoardo Torti, Stefano Protti, Maurizio Fagnoni[*]

PhotoGreen Lab, Department of Chemistry, University of Pavia,
Viale Taramelli 12, 27100 Pavia, Italy

SUPPORTING INFORMATION

Table of Contents:

1 General information.

All the chemicals and solvents used for the synthesis of **1** and **1′** were commercially available and used as received. The solvents used for the irradiations (GC or HPLC grade purity), as well as Cs_2CO_3 and $K_2S_2O_8$, were likewise commercially available and used as received (except for diethyl ether, which was passed through alumina and distilled prior to use). Dichloromethane (GC grade purity) was previously dried on $CaCl_2$.

^1H and ^{13}C NMR spectra were recorded on a 300 MHz spectrometer. Attributions were made on the basis of ^1H and ^{13}C NMR, as well as distortionless enhancement by polarization transfer (DEPT)-135 experiments; chemical shifts are reported in ppm downfield from tetramethylsilane (TMS). Photochemical reactions were carried out by using nitrogen- or oxygen purged solutions in quartz tubes. Irradiations were performed in a multilamp reactor fitted with 10×15 W phosphor-coated Hg lamps (emission centered at 310 nm) for irradiation. In selected cases the process have been also performed by exposing a Pyrex vessel containing the reaction mixture (see Fig. S1)[S1,S2] to solar light (in July 2017) on a window ledge of the Department of Chemistry of the University of Pavia.

Flow photochemical reactions were performed in a photochemical flow reactor (see Fig. S1) equipped with a water-cooled 500 W medium pressure mercury lamp. All the tubing used in this work are made of Fluorinated Ethylene Propylene (FEP, outer diameter: 3.18 mm; inner diameter: 2.1 mm; reactor volume: 50 mL). Injection of the solutions and flow rate control were achieved by a syringe pump.[S3]

The reaction course was monitored by gas chromatographic (GC) analyses and thin-layer chromatography (TLC). GC analyses were carried out by means of a gas chromatograph equipped with a FID detector. A 30 m × 0.25 mm × 0.25 μm capillary column was used for analytes separation with nitrogen as carrier gas at 1 mL min^{-1}. The injection in the GC system was performed in split mode and the injector temperature was 250 °C. The GC oven temperature was held at 50 °C for 2 min, increased to 250 °C by a temperature ramp of 10 °C min^{-1} and held for 20 min.

GC-MS analysis were carried out using a single quadrupole GC/MS system. A 30 m × 0.25 mm × 0.25 μm capillary column was used for analytes separation with helium as carrier gas at 1 mL min^{-1}. The injection in the GC system was performed in split mode and the injector temperature was 250 °C. The GC oven temperature was held at 50 °C for 2 min, increased to 250 °C by a temperature ramp of 10 °C min^{-1} and held for 20 min. The transfer line temperature was 270 °C and the ion source temperature 250 °C. Mass spectral analysis was carried out in full scan mode.

The formation of fluoroform (CHF_3) when irradiating **1** in the presence (or in the absence) of benzene was detected by FT-IR measurements on the head-space of the solution performed in a chamber with NaCl windows (see Section 5).

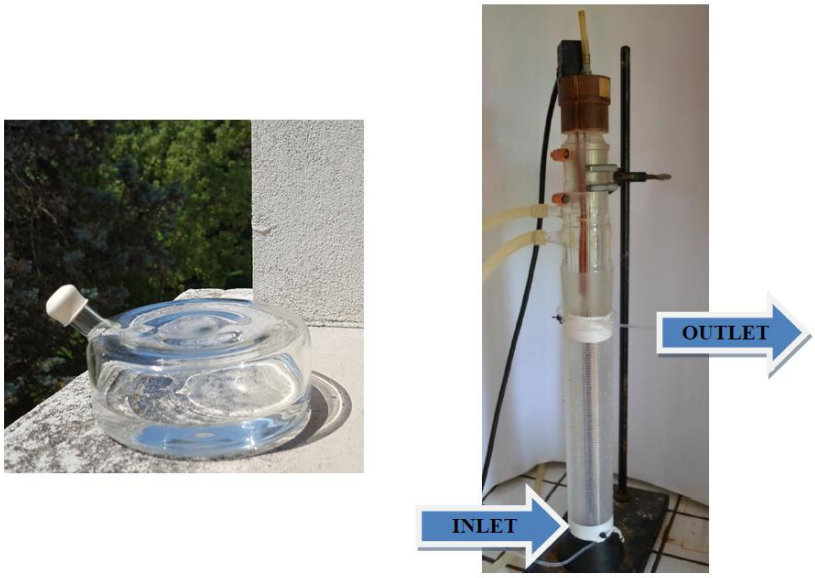
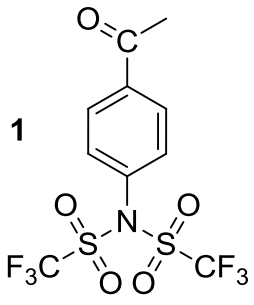


Fig. S1. Pyrex vessel used for solar irradiations (left) and flow photoreactor experimental setup (right).

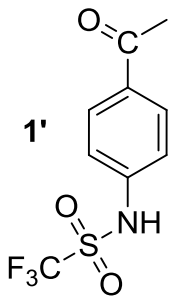
2 Syntheses of trifluoromethylating agents 1, 1′ and 1-CN.

Synthesis of *N*-(4-acetylphenyl)-1,1,1-trifluoro-*N*-[(trifluoromethyl)sulfonyl]methanesulfonamide (1).



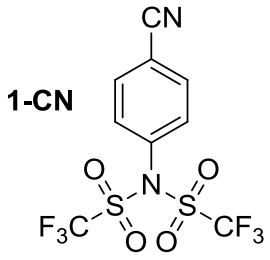
Compound **1** was synthesized by following a known procedure.[S4] To a cooled solution (-78 °C) of 4′-aminoacetophenone **1′′** and triethylamine (3.0 equiv.) in dry dichloromethane, trifluoromethanesulfonic anhydride (2.1 equiv.) was added dropwise under nitrogen atmosphere. The mixture was kept under stirring at -78 °C for 1 h, allowed to warm to room temperature and then further stirred for another hour. The resulting mixture was treated with aqueous saturated $NaHCO_3$ and the crude residue was purified by column chromatography, to afford **1** as a white solid (83% yield, m.p. = 87-89°C).[S4] Spectroscopic data of **1** were in accordance with the literature.[S4] Anal. Calcd for $C_{10}H_7F_6NO_5S_2$: C, 30.08; H, 1.77; N, 3.51. Found: C, 30.3; H, 1.8; N, 3.5.

Synthesis of *N*-(4-acetylphenyl)-1,1,1-trifluoromethanesulfonamide (1′).



Compound **1′** was synthesized by following a known procedure.[S4] To a cooled solution (-78 °C) of 4'-aminoacetophenone **1′′** and triethylamine (1.1 equiv.) in dry CH_2Cl_2, trifluoromethanesulfonic anhydride (1.1 equiv.) was added dropwise under nitrogen atmosphere. The mixture was stirred at -78 °C for 2 h and then allowed to warm to room temperature. The obtained mixture was transferred in a separatory funnel and quenched with water. The aqueous layer was extracted with CH_2Cl_2 and the reunited organic phases were washed with aqueous NaOH. The resulting aqueous phase was then acidified at 0 °C to pH 2.0 (by adding aqueous HCl 18%) until **1′** precipitated as a white solid (70% yield, m.p. = 139-142°C).[S4] No further purification was needed. Spectroscopic data of **1′** were in accordance with the literature.[S4] Anal. Calcd for $C_9H_8F_3NO_3S$: C, 40.45; H, 3.02; N, 5.24. Found: C, 40.4; H, 3.1; N, 5.1.

Synthesis of *N*-(4-cyanophenyl)-1,1,1-trifluoro-*N*-[(trifluoromethyl)sulfonyl]methanesulfonamide (1-CN).



Compound **1** was synthesized following the same procedure employed for the synthesis of **1**.[S4] To a cooled solution (-78 °C) of 4-aminobenzonitrile (1.18 g, 10 mmol), triethylamine (4.0 mL, 30 mmol) in dry CH_2Cl_2 (35 mL) under nitrogen atmosphere, trifluoromethanesulfonic anhydride (3.6 mL, 21 mmol), was added dropwise. The mixture was kept under stirring at -78 °C for 1 hour, allowed to warm to room temperature and then further stirred for another hour. The resulting mixture was diluted with 80 mL of dichloromethane and washed with saturated aqueous $NaHCO_3$ (3×30 mL) and brine (3×30 mL). The organic layer was then dried over Na_2SO_4 and the solvent was evaporated. The crude residue was thus purified by column chromatography (eluant: cyclohexane/ethyl acetate, 95:5), affording **1-CN** as a white solid (1.91 g, 50% yield, m.p. = 64-65 °C). ^{1}H NMR ($CDCl_3$) δ: 7.90-7.50 (AA′BB′ system, 4H). ^{13}C NMR ($CDCl_3$) δ: 135.7, 133.8 (CH), 132.1 (CH), 118.6 (q, CF_3, J = 323 Hz), 117.3, 116.6. IR (KBr, ν/cm^{-1}): 2926, 2231, 1493, 1223, 958. Anal. Calcd for $C_9H_4F_6N_2O_4S_2$: C, 28.28; H, 1.05; N, 7.33. Found: C, 28.3; H, 1.1; N, 7.4.

3 UV-visible absorption spectra.

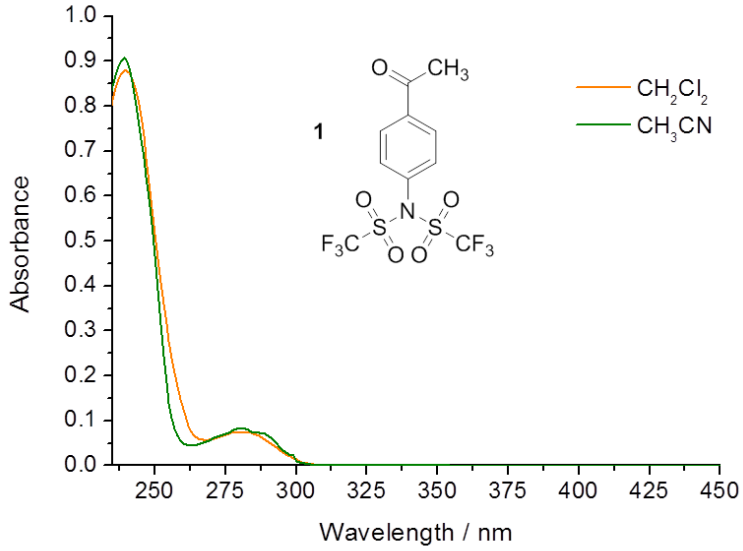


Fig. S2. UV-visible spectra of sulfonimide **1** (5.0×10^{-5} M) in dry dichloromethane and dry acetonitrile.

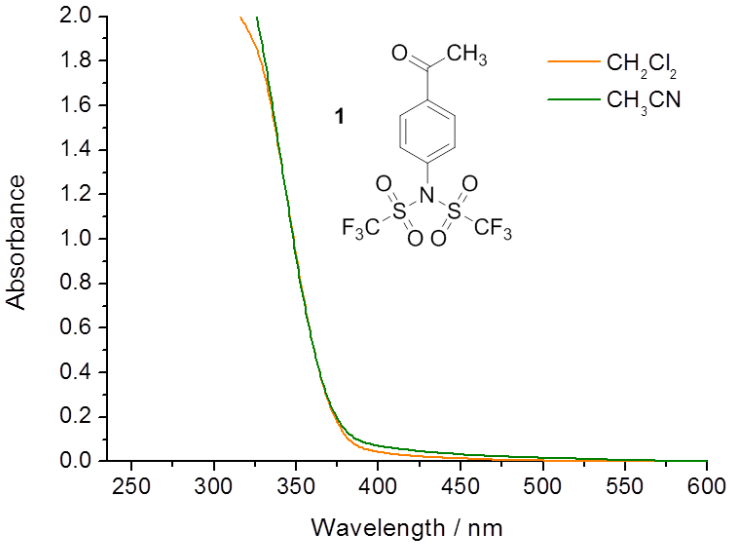


Fig. S3. UV-visible spectra of sulfonimide **1** (2.4×10^{-2} M) in dry dichloromethane and dry acetonitrile.

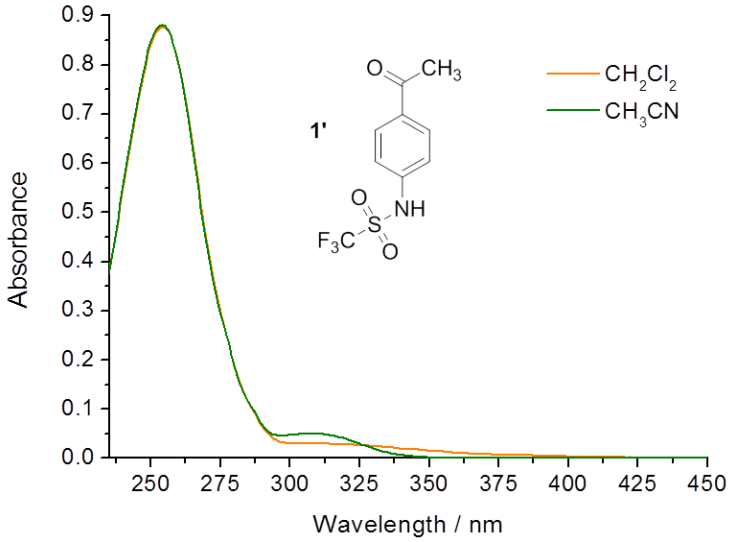


Fig. S4. UV-visible spectra of sulfonamide **1′** (5.0×10^{-5}M) in dry dichloromethane and dry acetonitrile.

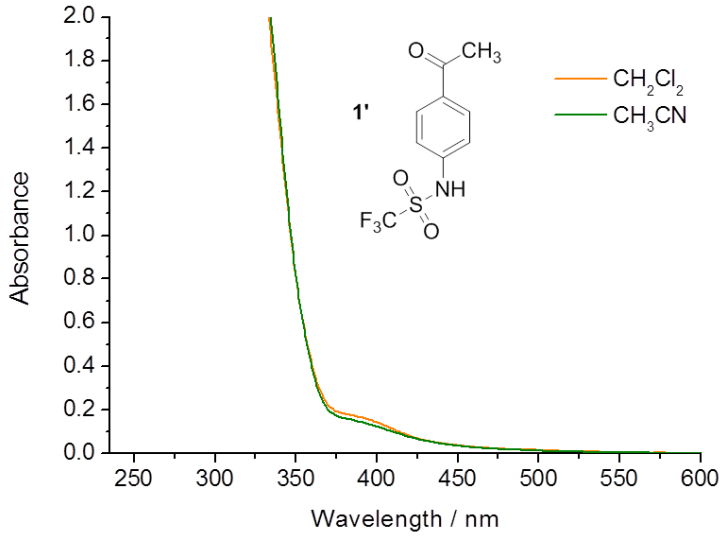


Fig. S5. UV-visible spectra of sulfonamide **1′** (2.4×10^{-2} M) in dry dichloromethane and dry acetonitrile.

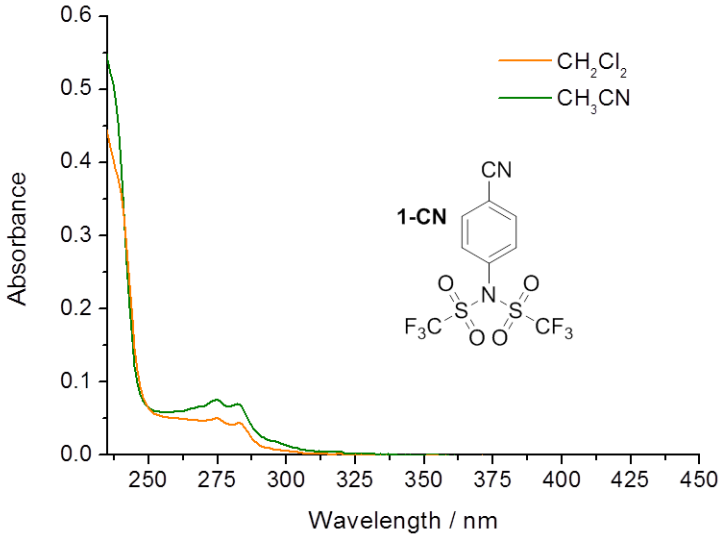


Fig. S6. UV-visible spectra of sulfonimide **1-CN** (5.0×10^{-5}M) in dry dichloromethane and dry acetonitrile.

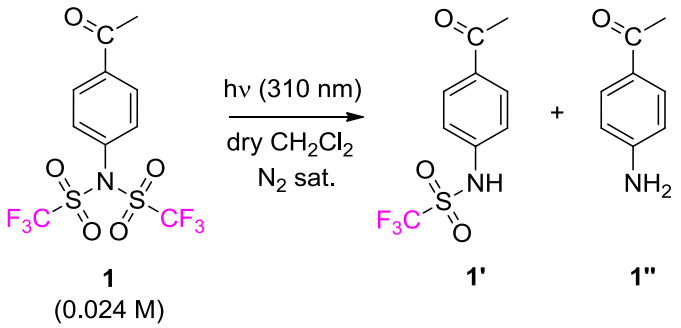
Table S1. UV-visible absorption maxima (with the corresponding molar extinction coefficients) for compounds **1**, **1′** and **1-CN**.

Compound	Solvent	λ_{MAX} / nm	ε / M^{-1} cm^{-1}
1	dry CH_2Cl_2	240 281	17685 1492
	dry CH_3CN	239 280	18126 1652
1′	dry CH_2Cl_2	254 310	17612 592
	dry CH_3CN	254 309	17681 1011
1-CN	dry CH_2Cl_2	274 283	1007 874
	dry CH_3CN	275 282	1508 1407

4 Irradiation of 1 in dry dichloromethane.

A 0.024 M solution of sulfonimide **1** in deaerated dry dichloromethane was irradiated for increasing times in a quartz tube in a multi-lamp reactor equipped with 10×15 W phosphor-coated lamps (emission centered at 310 nm). After irradiation, the distribution of photoproducts was examined by GC analysis (α,α,α-Trifluorotoluene was used as internal standard). This experiment was performed to evaluate the time needed to have total consumption of **1** and **1′** (see Table S2).

Table S2. Irradiation of sulfonimide **1** in neat dry dichloromethane.[a]



Irradiation time / h	Consumption of **1** [%][b]	**1′** yield [%][b]	**1″** yield [%][b]
2	49	29	10
4	75	33	25
8	100	23	48
12	100	0	64

[a] Sulfonimide **1** was dissolved in 3.0 mL of nitrogen satured dry dichloromethane and irradiated in a quartz tube. [b] Gas Chromatography (GC) yields referred to the initial amount of **1**. α,α,α-Trifluorotoluene was used as internal standard.

5 Headspace FT-IR analysis.

10 mL of a solution of sulfonimide **1** (0.024 M) and benzene **2e** (0.030 M) in deaerated dry dichloromethane was irradiated for 12 h in a sealed 15 mL quartz tube in a multi-lamp reactor equipped with 10×15 W phosphor-coated lamps (emission centered at 310 nm). After irradiation the head-space of the sample was examined by means of FT-IR analysis. In detail the gaseous phase was driven by a cannula in a sealed chamber with NaCl windows. Then a FT-IR spectrum was measured across this chamber and the revealed peaks that were attributed to CHF_3 and SO_2 (Fig. S7).[S4,S5]

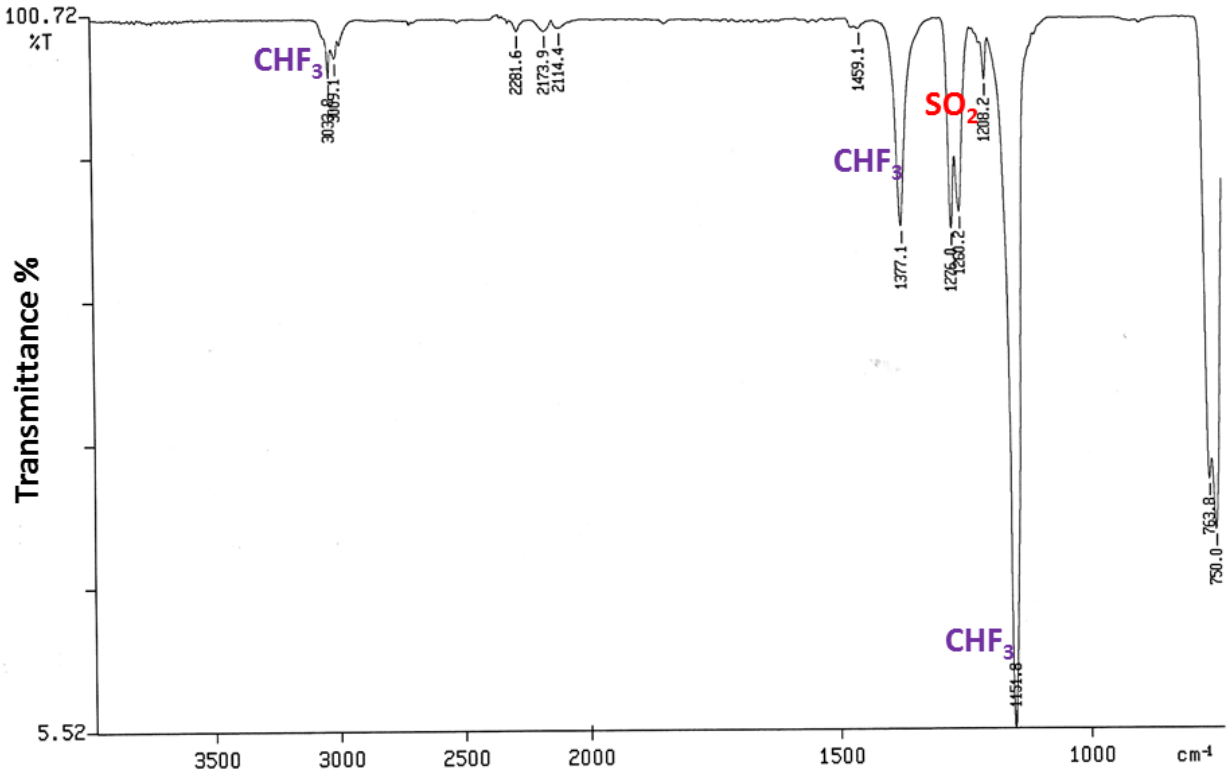
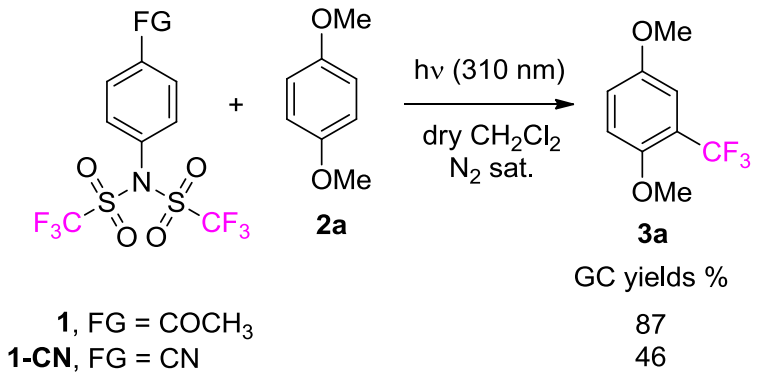


Fig. S7. FT-IR spectrum of the headspace of an irradiated solution of **1** (0.024 M) and benzene **2e** (0.030 M) in dry dichloromethane.

6 Comparison between sulfonimides 1 and 1-CN.

With the aim to find alternative electron-poor sulfonimides for the trifluoromethylation of aromatics we compare the efficiency of **1** or **1-CN** in the trifluoromethylation of **2a**. We used the same experimental condition described in Table 1, entry 7 (the optimized conditions). Thus 0.024 M solutions of sulfonimides **1** and **1-CN** in deaerated dry dichloromethane were irradiated for 12 h in a quartz tube in a multi-lamp reactor equipped with 10×15 W phosphor-coated lamps (emission centered at 310 nm) in the presence of 1,4-dimethoxybenzene **2a** (0.030 M). After irradiation, the yield of trifluoromethylated **3a** was determined by GC analysis (α,α,α-trifluorotoluene was used as internal standard). The experiments showed that, in the optimized experimental conditions, **1** performed better than the cyano derivative **1-CN** (see Scheme S1).



Scheme S1. Trifluoromethylation of **2a** to **3a** by sulfonimides **1** and **1-CN**.

7 Optimization of flow photoreactions conditions.

General procedure.

The optimization of the flow conditions was performed by investigating the reaction between **1** and **2a** to give the trifluoromethylated **3a** as the model reaction. We considered dry acetonitrile and dry dichloromethane as the solvents since these media gave the best results under batch conditions (see Table 1). In the case of reactions performed in acetonitrile, the solvent was removed under reduced pressure from the photolyzed solution. Then, in both cases dichloromethane was added to the obtained sample (20 mL for reactions done in dichloromethane, 30 mL when acetonitrile was employed). The resulting solution was washed sequentially with saturated aqueous $NaHCO_3$ (3×10 mL), water (10 mL) and brine (2×10 mL). The organic layer was then dried over Na_2SO_4 and the solvent evaporated under reduced pressure. The crude product purified by silica-gel column chromatography (eluant: hexane/ethyl acetate 95:5). The obtained isolated yields of **3a** are resumed in Table S3.

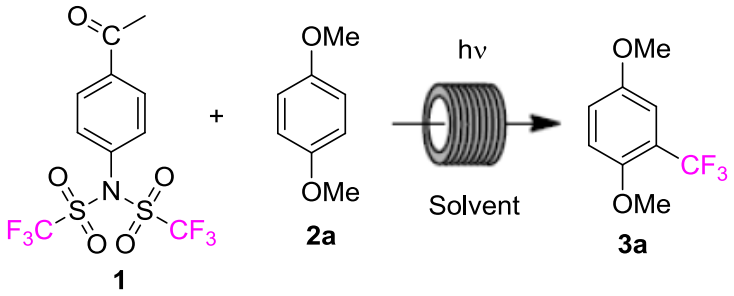
As concerning the optimization of the reaction conditions, we initially modified the concentration of **2a** keeping constant the molar ratio **1**/**2a** to 0.8. However, when increasing the concentration from 0.03 M to 0.06 M in dichloromethane, trifluoromethylating agents **1** and **1′** were not completely consumed and conversion of **2a** was only the 74%. A similar experiment could not be performed in acetonitrile due to the lower solubility of **1** and **2a** in this solvent.

We then compared the yields of **3a** obtained from the irradiations in acetonitrile and dichloromethane, (**2a** = 0.03 M was used in both cases). We observed that functionalization of **2a** took place in a more efficient way in acetonitrile rather than in dichloromethane, thus the former solvent was used for the following reactions.

No improvement of the process was observed when we modified the chosen flow rate from 10 mL/hour to 20 mL/hour since we detected significant amounts of unreacted **1** and **1′** after the photolysis.

Thus, the conditions highlighted in bold in Table S3 were chosen.

Table S3. Optimization of the reaction conditions for the trifluoromethylation of 1,4-dimethoxybenzene **2a** under flow conditions.[a]



Solvent	Conc. **2a**[b] / M	Flow rate / mL h^{-1}	**1** Conversion [%][c]	**2a** Conversion [%][d]	**3a** yield [%][e]	**1′** and **1″**, yield [%][c]
dry CH_2Cl_2	0.03	10	100	93	77	**1″**, 77
dry CH_2Cl_2	0.06	10	80	74	62	**1′**, 11; **1″**, 53
dry CH_3CN	**0.03**	**10**	**100**	**100**	**84**	**1″, 80%**
dry CH_3CN	0.03	15	89	75	66	**1′**, 10; **1″**, 62
dry CH_3CN	0.03	20	83	72	60	**1′**, 12; **1″**, 54

[a] Irradiated volume: 10 mL. Irradiation performed in a FEP photoreactor equipped with 500 W medium pressure mercury lamp (total volume: 50 mL). [b] Molar ratio between **1** and **2a** = 0.8. [c] Gas Chromatography (GC) yields referred to the initial amount of **1**. α,α,α-Trifluorotoluene was used as internal standard. [d] Gas Chromatography (GC) yields referred to the initial amount of **2a**. [e] Isolated yield after column chromatography purification.

8 Photochemical trifluoromethylating reactions.

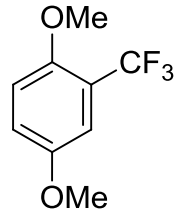
General Procedure for the batch photochemical trifluoromethylation of aromatics and heteroaromatics.

A dry dichloromethane solution (15 mL) of compound **1** (144 mg, 0.36 mmol, 0.024 M) and the chosen aromatic (**2a-m**; 0.45 mmol, 0.03 M) was poured in a quartz tube, capped with a septum and purged for 5 min with nitrogen. The tube was then irradiated for 12 h in a multi-lamp apparatus fitted with 10×15 W phosphor-coated lamps (emission centered at 310 nm), until the complete consumption of both **1** and **1′**. In selected cases the irradiation was also performed by exposing a Pyrex vessel containing the reaction mixture to solar light (in July 2017) on a window ledge of the Department of Chemistry (Pavia). In each case, the photolyzed solution was then diluted with 20 mL of dichloromethane and washed sequentially with saturated aqueous $NaHCO_3$ (3×10 mL), water (10 mL) and brine (2×10 mL). The organic layer was then dried over Na_2SO_4 and the solvent was evaporated under reduced pressure (being careful of volatile products). The crude residue was thus purified by silica-gel column chromatography or by distillation.

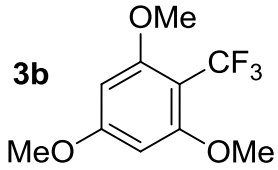
General Procedure for the flow photochemical trifluoromethylation of aromatics and heteroaromatics.

A solution of the compound **1** (96 mg, 0.24 mmol, 0.024 M) and the chosen aromatic (**2a, 2d, 2j, 2l**; 0.30 mmol, 0.03 M) in dry acetonitrile (10 mL) was charged in a polypropylene syringe and pumped through the flow irradiating apparatus with a flow rate of 10.0 mL/h. The solvent was then removed under reduced pressure from the photolyzed solution. 30 mL of dichloromethane were added to the obtained residue and the resulting solution was washed sequentially with saturated aqueous $NaHCO_3$ (3×10 mL), water (10 mL) and brine (2×10 mL). The organic layer was then dried over Na_2SO_4 and the solvent evaporated under reduced pressure (being careful of volatile products). The crude product was then purified by column chromatography (eluant: hexane/ethyl acetate mixtures).

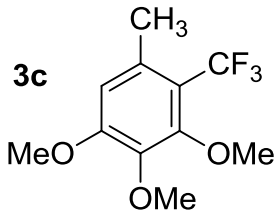
Compounds synthesized by photochemical trifluoromethylations.

3a 

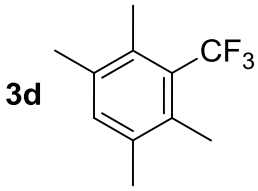
1,4-Dimethoxy-2-(trifluoromethyl)benzene (3a). From 62 mg of 1,4-dimethoxybenzene (**2a**). Purification of the residue by column chromatography (eluant: hexane/ethyl acetate 95:5) afforded 75 mg of **3a** as a colorless liquid in 81% yield (using 310 nm radiation source). The same reaction carried out upon sunlight exposure (6 h × 3 days) and under continuous flow conditions gave **3a** in 79% and 87% yield, respectively. ^{1}H-NMR ($CDCl_3$)[S6] δ: 7.12 (d, 1H, *J* = 3 Hz), 7.02 (dd, 1H, *J* = 3 and 9 Hz), 6.93 (d, 1H, *J* = 9 Hz), 3.86 (s, 3H), 3.80 (s, 3H). ^{13}C-NMR ($CDCl_3$)[S6] δ: 153.1, 151.7, 123.6 (q, CF_3, *J* = 271 Hz), 119.6 (q, *J* = 31 Hz), 118.3 (CH), 113.8 (CH), 113.0 (q, CH, *J* = 5 Hz), 56.8 (CH_3), 56.1 (CH_3). IR (KBr, ν/cm^{-1}): 2938, 1505, 1130, 1053, 728. Anal. Calcd for $C_9H_9F_3O_2$: C, 52.43; H, 4.40. Found: C, 52.5; H, 4.3.

3b 

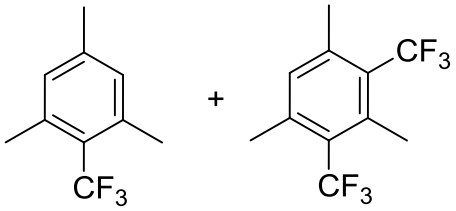
1,3,5-Trimethoxy-2-(trifluoromethyl)benzene (3b). From 76 mg of 1,3,5-trimethoxybenzene (**2b**). Purification of the residue by column chromatography (eluant: hexane/ethyl acetate 9:1) afforded 90 mg of **3b** as a white solid (85% yield, m.p. = 58-60°C, lit. = 51-53°C).[S7] ^{1}H-NMR ($CDCl_3$)[S7] δ: 6.12 (s, 2H), 3.83 (s, 9H). ^{13}C-NMR ($CDCl_3$)[S7] δ: 163.6, 160.5, 124.5 (q, CF_3, *J* = 272 Hz), 100.4 (q, *J* = 29 Hz), 91.3 (CH), 56.3 (CH_3), 55.5 (CH_3). IR (KBr, ν/cm^{-1}): 2956, 1610, 1108, 1026, 817. Anal. Calcd for $C_{10}H_{11}F_3O_3$: C, 50.85; H, 4.69. Found: C, 50.8; H, 4.7.

3c 

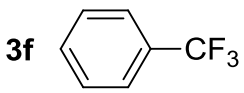
1,3,5-Trimethoxy-5-methyl-4-(trifluoromethyl)benzene (3c). From 82 mg of 3,4,5-trimethoxytoluene (**2c**). Purification of the residue by column chromatography (eluant: hexane/ethyl acetate 9:1) afforded 89 mg of **3c** as a colorless liquid in 85% yield. ^{1}H-NMR ($CDCl_3$)[S8] δ: 6.49 (s, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.84 (s, 3H), 2.40 (q, 3H, *J* = 3 Hz). ^{13}C-NMR ($CDCl_3$)[S8] δ: 156.3, 153.5 (q, *J* = 2 Hz),141.0, 133.2 (q, *J* = 2 Hz), 125.0 (q, CF_3, *J* = 272 Hz), 115.5 (q, *J* = 29 Hz),110.8 (CH), 61.8 (CH_3), 60.8 (CH_3), 56.0 (CH_3), 125.0 (q, CH_3, *J* = 4 Hz). IR (KBr, ν/cm^{-1}):[S8] 2944, 1598, 1305, 1111, 1014, 840. Anal. Calcd for $C_{11}H_{13}F_3O_3$: C, 52.80; H, 5.24. Found: C, 52.7; H, 5.2.



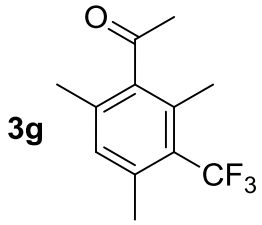
1,2,4,5-Tetramethyl-3-(trifluoromethyl)benzene (3d). From 60 mg of durene (**2d**). Purification of the residue by column chromatography (eluant: hexane) afforded 55 mg of **3d** as a white solid, using 310 nm radiation source (61% yield, m.p. = 37-40°C, lit. = 35-36°C).[S9] The same reaction carried out upon sunlight exposure (6 h × 3 days) and under continuous flow conditions gave **3d** in 62% and 80% yield, respectively. ^{1}H-NMR ($CDCl_3$)[S9] δ: 7.09 (s, 1H), 2.32 (q, 6H, *J* = 3 Hz), 2.26 (s, 6H). ^{13}C-NMR ($CDCl_3$) δ: 135.2, 134.7 (CH), 133.6 (q, *J* = 2 Hz), 128.2 (q, *J* = 27 Hz), 126.5 (q, CF_3, *J* = 274 Hz), 20.7 (CH_3), 16.8 (q, CH_3, *J* = 5 Hz). IR (KBr, ν/cm^{-1}): 2924, 1317, 1104, 1016, 720. Anal. Calcd for $C_{11}H_{13}F_3$: C, 65.33; H, 6.48. Found: C, 65.5; H, 6.6.



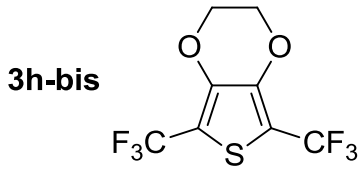
1,3,5-Trimethyl-2-(trifluoromethyl)benzene (3e) and 1,3,5-trimethyl-2,4-bis(trifluoromethyl)benzene (3e-bis). From 63 μL (54 mg) of mesitylene (**2e**). Purification of the residue by distillation at reduced pressure (25 torr, 80 °C) afforded 65 mg of a colorless liquid containing 1,3,5-trimethyl-2-(trifluoromethyl)benzene (**3e**, 51 mg, 60% yield) and 2,4-bis(trifluoromethyl)-1,3,5-trimethylbenzene (**3e-bis**, 14 mg, 12% yield). **3e**: ^{1}H-NMR (from the mixture, $CDCl_3$)[S10] δ: 6.90 (s, 2H), 2.44 (q, 6H, *J* = 3 Hz), 2.30 (s, 3H). ^{13}C-NMR (from the mixture, $CDCl_3$)[S10] δ: 141.0, 137.4 (q, *J* = 2 Hz), 131.0 (CH), 126.4 (q, CF_3, *J* = 274 Hz), 124.9 (q, *J* = 28 Hz), 21.4 (q, CH_3, *J* = 4 Hz), 21.0 (CH_3). **3e-bis**: ^{1}H-NMR (from the mixture, $CDCl_3$)[S11] δ: 6.99 (s, 1H), 2.55-2.45 (m, 9H). ^{13}C-NMR (from the mixture, $CDCl_3$)[S11] δ: 140.3, 138.9-138.8 (m), 134.6 (CH), 127.9 (q, *J* = 28 Hz), 125.6 (q, CF_3, *J* = 274 Hz), 22.2 (q, CH_3, *J* = 5 Hz), 17.58-17.36 (m, CH_3). IR of the mixture (KBr, ν/cm^{-1}): 2982, 1612, 1295, 1111, 1040, 853.



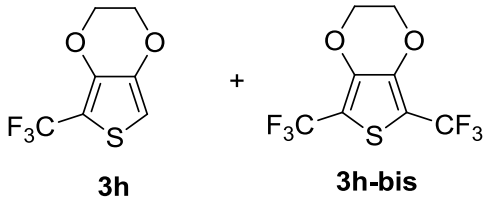
(Trifluoromethyl)benzene (3f). From 40 μL (35 mg) of benzene (**2f**). After the basic work-up the dichloromethane solution containing **3f** was directly analyzed by gas chromatography and **3f** was quantified by comparison with an authentic commercial sample (dodecane was added to this solution as an internal standard). GC yield: 73%.



1-[2,4,6-trimethyl-3-(trifluoromethyl)phenyl]ethanone (3g). From 287 mg (0.72 mmol, 0.048 M) of **1** and 75 μL (73 mg) of 2′,4′,6′-trimethylacetophenone (**2g**). Irradiation lasted 42 h until total consumption of **1**/**1′** and **2g**. Column chromatography of the obtained crude residue (eluant: hexane/ethyl acetate 95:5) afforded 77 mg of **3g** as a colorless liquid in 74% yield. ^{1}H-NMR ($CDCl_3$)[S8] δ: 6.94 (s, 1H), 2.46 (s, 3H), 2.44 (q, 3H, *J* = 3 Hz), 2.32 (q, 3H, *J* = 3 Hz), 2.21 (s, 3H). ^{13}C-NMR ($CDCl_3$)[S8] δ: 207.8, 142.7, 137.7 (q, *J* = 2 Hz), 135.4, 132.4 (CH), 132.1 (q, *J* = 2 Hz),126.0 (q, *J* = 28 Hz), 125.9 (q, CF_3, *J* = 274 Hz), 32.6 (CH_3), 21.8 (q, CH_3, *J* = 5 Hz), 19.1 (CH_3), 17.5 (q, CH_3, *J* = 4 Hz). IR (KBr, ν/cm^{-1}):[S8] 2929, 1702, 1301, 1254, 1113, 1070. Anal. Calcd for $C_{12}H_{13}F_3O$: C, 62.60; H, 5.69. Found: C, 62.8; H, 5.5.

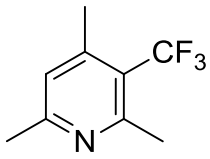


3,4-Ethylenedioxy-2,5-bis(trifluoromethyl)thiophene (3h-bis). From 48 μL (64 mg) of 3,4-ethylenedioxythiophene (**2h**). Purification of the residue (eluant: hexane/ethyl acetate 95:5) afforded 74 mg of **3h-bis** as a colorless liquid in 59% yield. ^{1}H-NMR ($CDCl_3$) δ: 4.36 (s, 4H). ^{13}C-NMR $CDCl_3$) δ: 141.6-141.4 (m), 121.6 (q, CF_3, *J* = 268 Hz), 106.9 (q, *J* = 40 Hz), 64.8 (CH_2). ^{19}F-NMR ($CDCl_3$) δ: -59.3 (s, 6F). IR (KBr, ν/cm^{-1}): 1536, 1314, 1142, 1053, 924. Anal. Calcd for $C_8H_4F_6O_2S$: C, 34.54; H, 1.45. Found: C, 34.5; H, 1.6.

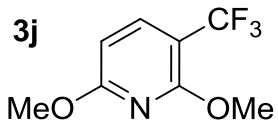


3,4-Ethylenedioxy-2-(trifluoromethyl)thiophene (3h) and 3,4-ethylenedioxy-2,5-bis(trifluoromethyl)thiophene (3h-bis). From 90 mg (0.22 mmol, 0.015 M) of **1** and 48 μL (64 mg) of 3,4-ethylenedioxythiophene (**2h**). Irradiation lasted 6 h until total consumption of **1** and **1′**. Purification of the crude residue (eluant: hexane/ethyl acetate 95:5) afforded 47 mg of a colorless liquid containing 3,4-ethylenedioxy-2-(trifluoromethyl)thiophene (**3h**, 25 mg, 26% yield) and 3,4-ethylenedioxy-2,5-bis(trifluoromethyl)thiophene (**3h-bis**, 22 mg, 18% yield). **3h**:^{1}H-NMR (from the mixture, $CDCl_3$)[S12] δ: 6.49 (s, 1H), 4.31-4.29 (m, 2H), 4.24-4.21 (m, 2H). ^{13}C-NMR (from the mixture, $CDCl_3$)[S12] δ: 142.1 (q, *J* = 4 Hz), 141.5, 122.4 (q, CF_3, *J* = 266 Hz), 104.5 (q, *J* = 39 Hz), 102.2 (CH), 65.1 (CH_2), 64.4 (CH_2). ^{19}F-NMR (form the mixture, $CDCl_3$) δ: -58.5 (s, 3F). IR of the mixture (KBr, ν/cm^{-1}): 1506, 1445, 1314, 1177, 1073, 940, 910. GC-MS of the mixture revealed two peaks, one belonging to **3h** and one to

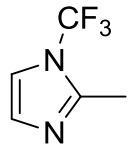
3h-bis. **3h** (m/z): 210 (M^+, 88), 195 (20), 181 (7), 164 (45), 113 (17), 85 (12), 69 (27), 45 (36), 28 (100). **3h-bis** (m/z): 278 (M^+, 100), 259 (26), 232 (49), 212 (16), 184 (22), 137 (31), 122 (28), 113 (73), 94 (33), 69 (20).

3i 

2,4,6-Trimethyl-3-(trifluoromethyl)pyridine (3i). From 59 μL (54 mg) of 2,4,6-trimethylpyridine (**2i**). In the present case the photolyzed solution was washed using saturated aqueous Na_2CO_3 (3×10 mL) instead of $NaHCO_3$. Purification of the residue by column chromatography (eluant: hexane/ethyl acetate 9:1) afforded 50 mg of **3i** as a colorless liquid in 59% yield. ^{1}H-NMR ($CDCl_3$) δ: 6.88 (s, 1H), 2.87 (q, 3H, *J* = 3 Hz), 2.50 (s, 3H), 2.44 (q, 3H, *J* = 3 Hz). ^{13}C-NMR $CDCl_3$) δ: 159.8, 156.4, 146.7, 125.5 (q, CF_3, *J* = 273 Hz), 124.1 (CH), 120.7 (q, *J* = 30 Hz), 24.3 (q, CH_3, *J* = 4 Hz), 24.0 (CH_3), 20.8 (q, CH_3, *J* = 4 Hz). ^{19}F-NMR ($CDCl_3$) δ: -58.4 (s, 3F). IR (KBr, ν/cm^{-1}): 2928, 1598, 1296, 1116, 1038. Anal. Calcd for $C_9H_{10}F_3N$: C, 57.14; H, 5.33; N, 7.40. Found: C, 57.0; H, 5.4; N, 7.3.

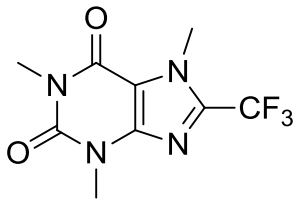
3j 

2,6-Dimethoxy-3-(trifluoromethyl)pyridine (3j). From 59 μL (62 mg) of 2,6-dimethoxypyridine (**2j**). In the present case the photolyzed solution was washed using saturated aqueous Na_2CO_3 (3×10 mL) instead of $NaHCO_3$. Purification of the residue by column chromatography (eluant: hexane/ethyl acetate 95:5) afforded 59mg of **3j** as a colorless liquid in 64% yield (using 310 nm radiation source). The same reaction carried out upon sunlight exposure (6 h × 3 days) and under continuous flow conditions gave **3j** in 60% and 82% yield, respectively. ^{1}H-NMR ($CDCl_3$)[S8] δ: 7.72 (d, 1H, *J* = 9 Hz), 6.32 (d, 1H, *J* = 9 Hz), 4.02 (s, 3H), 3.96 (s, 3H). ^{13}C-NMR ($CDCl_3$)[S8] δ: 165.3, 160.6, 138.9 (q, CH, *J* = 4 Hz), 123.9 (q, CF_3, *J* = 268 Hz), 104.5 (q, *J* = 34 Hz), 100.9 (CH), 54.0 (CH_3), 53.9 (CH_3). IR (KBr, ν/cm^{-1}): 2956, 1606, 1473, 1314, 1027, 817. Anal. Calcd for $C_8H_8F_3NO_2$: C, 46.38; H, 3.89; N, 6.76. Found: C, 46.3; H, 3.7; N, 6.8.

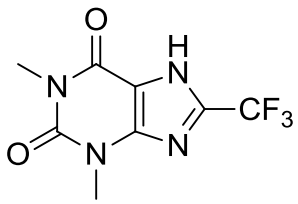
3k 

2-Methyl-1-(trifluoromethyl)-1*H*-imidazole (3k). From 37 mg of 2-methylimidazole (**2k**). In the present case the photolyzed solution was washed using saturated aqueous Na_2CO_3 (3×10 mL) instead of $NaHCO_3$. Purification of the residue by distillation at reduced pressure (25 torr, 85 °C) afforded 47mg of **3k** as a colorless liquid in 69% yield. ^{1}H-NMR ($CDCl_3$) δ: 7.28 (d, 1H, *J* = 3 Hz), 7.04 (d, 1H, *J* = 3 Hz), 2.64 (s, 3H). ^{13}C-NMR

$CDCl_3$) δ: 146.1, 129.7 (CH), 120.4 (CH), 119.3 (q, CF_3, J = 321 Hz), 15.2 (CH_3). ^{19}F-NMR ($CDCl_3$) δ: -78.7 (s, 3F). IR (KBr, ν/cm^{-1}): 1565, 1425, 1393, 1233, 1041, 982, 736. Anal. Calcd for $C_5H_5F_3N_2$: C, 40.01; H, 3.36; N, 18.66. Found: C, 40.0; H, 3.3; N, 18.8.

3l 

1,3,7-Trimethyl-8-(trifluoromethyl)-3,7-dihydro-1*H*-purine-2,6-dione (3l). From 87 mg of caffeine (**2l**). In the present case the photolyzed solution was washed using 10% aqueous NaOH (3×10 mL) instead of $NaHCO_3$. Purification of the residue by column chromatography (eluant: hexane/ethyl acetate 9:1) afforded 68 mg of **3l** as a white solid, using 310 nm radiation source (58% yield, m.p. = 126-128 °C, lit. = 131-133°C).[S13] The same reaction carried out upon sunlight exposure (6 h × 4 days) and under continuous flow conditions gave **3l** in 57% and 75% yield, respectively. ^{1}H-NMR ($CDCl_3$)[S14] δ: 4.16 (q, 3H, J = 1 Hz),3.59 (s, 3H), 3.42 (s, 3H). ^{13}C-NMR ($CDCl_3$)[S14] δ: 155.6, 151.5, 146.7, 139.1 (q, J = 40 Hz), 118.3 (q, CF_3, J = 269 Hz), 109.8, 33.3 (q, CH_3, J = 2 Hz), 30.0 (CH_3), 28.3 (CH_3). IR (KBr, ν/cm^{-1}): 1710, 1667, 1179, 1147, 745. Anal. Calcd for $C_9H_9F_3N_4O_2$: C, 41.23; H, 3.46; N, 21.37. Found: C, 41.1; H, 3.3; N, 21.4.

3m 

1,3-Dimethyl-8-(trifluoromethyl)-3,7-dihydro-1*H*-purine-2,6-dione (3m). From 81 mg of theophylline (**2m**). In the present case the irradiation was performed in an acetonitrile/water 5:1 mixture and the solvent was removed from the photolyzed solution by reduced pressure directly, without work-up. Purification of the residue by column chromatography (eluant: hexane/ethyl acetate 8:2) afforded 75 mg of **3m** as a white solid (67% yield, m.p. = 270-273 °C, lit. = 266-268 °C).[S15] ^{1}H-NMR (DMSO-d_6)[S16] δ: 3.43 (s, 3H), 3.24 (s, 3H), 2.92 (brs, 1H). ^{13}C-NMR (DMSO-d_6)[S16] δ: 154.6, 151.0, 146.8, 137.3 (q, J = 40 Hz), 118.2 (q, CF_3, J = 268 Hz), 109.2, 29.9 (CH_3), 27.9 (CH_3). IR (KBr, ν/cm^{-1}):[S15] 1642, 1559, 1152, 745. Anal. Calcd for $C_8H_7F_3N_4O_2$: C, 38.72; H, 2.84; N, 22.58. Found: C, 38.7; H, 2.9; N, 22.7.

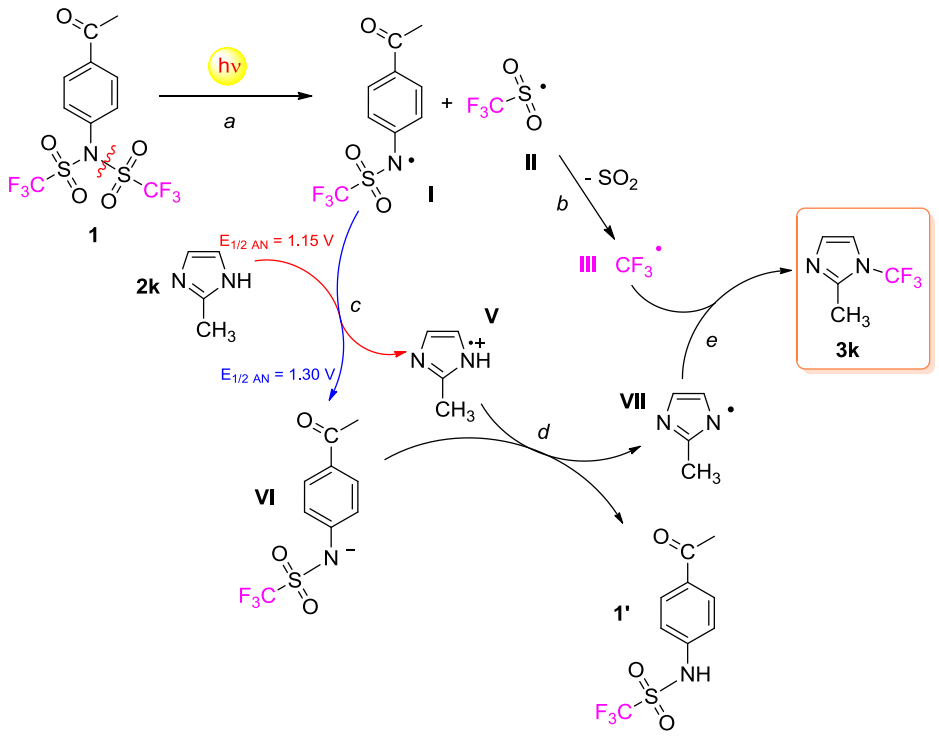
9 Mechanism for the formation of *N*-CF_3 derivative 3k.

Mechanistic proposal. As pointed out in the main text, the trifluoromethylation of 2-methylimidazole **2k** cannot be explained by the general mechanism described in Scheme 3. Indeed, to the best of our knowledge, radical trifluoromethylation of imidazoles (including **2k**) results in the formation of C-CF_3 bonds.[S8,S17]

An alternative suggested mechanism for the formation of **3k** has been resumed in Scheme S2. After photo-homolysis of the C-S bond (*path a*) radicals **I** and **II** are formed and the latter loose SO_2 to produce $F_3C^{\bullet}$ radical **III** (*path b*). Then radical **I** oxidizes imidazole **2k** (*path c*), giving radical cation **V** and sulfonamide anion **VI**.

To support the proposed mechanism we measured the redox potentials for the oxidation of **2k** and **VI** ($E_{1/2\ AN}$) by cyclic voltammetry experiments. The obtained values clearly indicate that the former is easier to be oxidized than the latter (Scheme S2 and Table S4), thus supporting the feasibility of the proposed redox process.

Once intermediates **V** and **VI** are formed, a proton transfer takes place (*path d*). Finally, recombination of $F_3C^{\bullet}$ radical **III** and **VII** gives **3k** (*path e*). A similar reactivity, where oxidation of azoles followed by radical coupling occurred, have already been recently reported in the literature.[S18]



Scheme S2. Proposed mechanism for the photochemical reaction between **1** and imidazole **2k**.

Electrochemical measurements.

Electrochemical measurements (cyclic voltammetry) were performed on 10^{-3} M solutions of the chosen compounds (**2k**, **3k**, **1′** and **VI**) in a three-electrode cell (volume 10 mL, tetrabutylammonium perchlorate 0.1 M in *N*,*N*-dimethylformamide as the supporting electrolyte). A glassy carbon electrode (diameter 2 mm) was chosen as the working electrode, Pt wire as the auxiliary electrode, and Ag/AgCl (3 M NaCl) as the reference electrode. Scan speed was 100 mV s^{-1}. The potential range investigated was between 0.0 V and 2.0 V (vs. Ag/AgCl, 3 M NaCl). No iR-compensation was performed.

Prior to each experiment the electrodes were washed with *N*,*N*-dimethylformamide and the working electrode was further cleaned using a polishing alumina slurry. Furthermore, the electrolyte solution was checked by conducting a cyclic voltammetry across the whole potential range.

The electrolyte solutions containing the different compounds were purged with nitrogen for 5-10 minutes before every measurements.

The potentials measured are anodic peak potentials ($E_{1/2\ AN}$) and are referred to Ag/AgCl (3 M NaCl). In all cases an irreversible redox behavior was observed, except for derivative **3k**, for which no oxidation could be detected in the potential range investigated.

To confirm the mechanism shown in Scheme S2 we performed cyclic voltammetry experiments. Compound **2k** has an $E_{1/2\ AN}$ = 1.15 V (Fig. S8), whereas two anodic peaks were observed when analyzing a solution of sulfonamide **1′** (ca. 10^{-3} M) in the presence of an equimolar amount of tetrabutylammonium hydroxide (TBAOH) (Fig. S8). The first peak ($E_{1/2\ AN}$ = 1.30 V) may be safely assigned to anion **VI** whereas the second peak ($E_{1/2\ AN}$ = 1.30 V) is due to some **1′** still present in the solution (compare Fig. S9 and Fig. S10). The trifluoromethylation of **2k** made it more difficult to be oxidized ($E_{1/2\ AN}$ > 2.0 V for **3k**, Fig. S11).

Table S4. Half-wave oxidation potentials measured in *N*,*N*-dimethylformamide (vs. Ag/AgCl, 3 M NaCl).

Compound	$E_{1/2\ AN}$ / V
2k	1.15
VI	1.30
1′	1.50
3k	> 2.0[a]

[a] No anodic peak was observed.

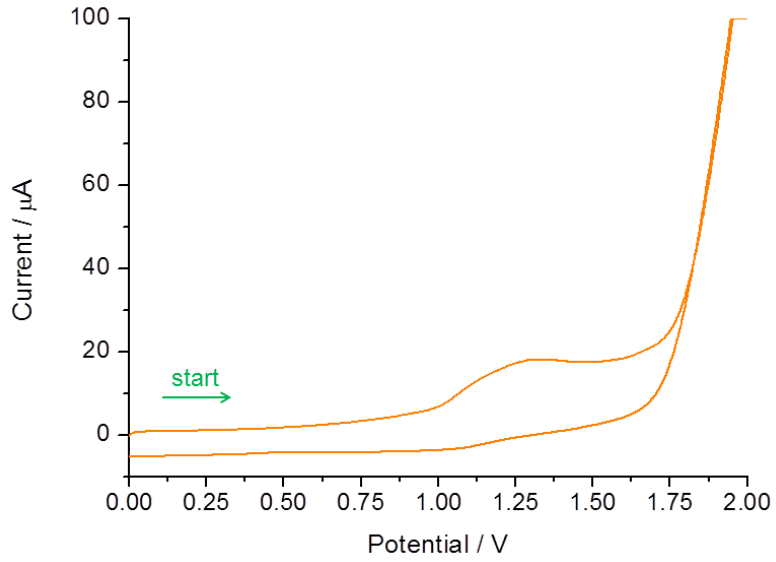


Fig. S8. Cyclic voltammogram obtained for **2k** in *N*,*N*-dimethylformamide (potential referred to Ag/AgCl, 3 M NaCl).

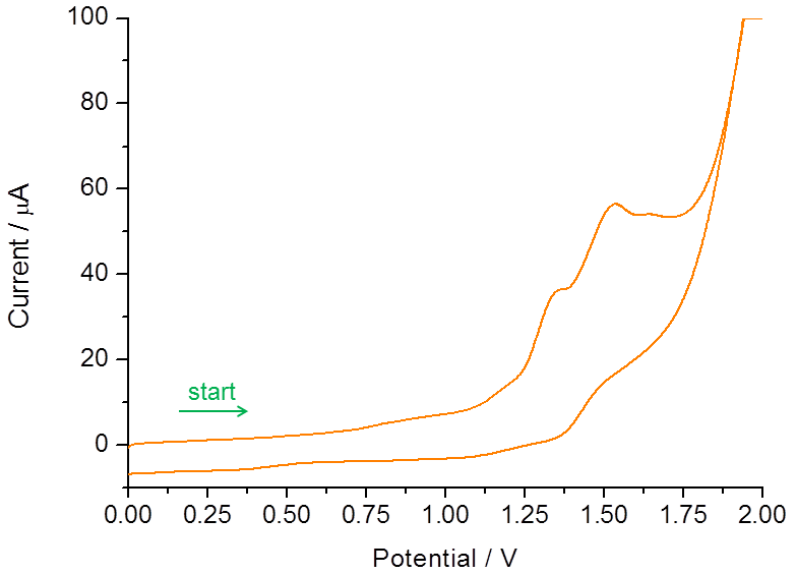


Fig. S9. Cyclic voltammogram obtained for **VI** (**1′** + TBAOH) in *N*,*N*-dimethylformamide (potential referred to Ag/AgCl, 3 M NaCl).

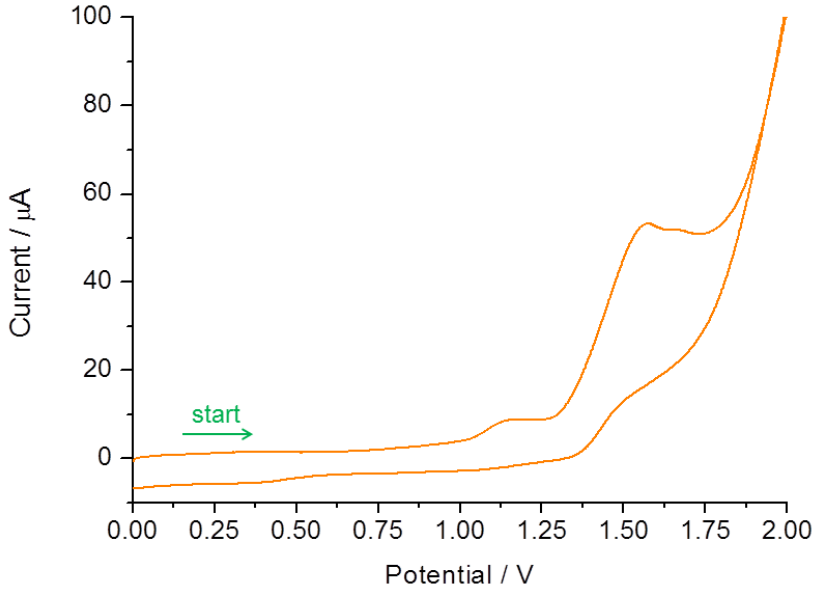


Fig. S10. Cyclic voltammogram obtained for **1′** in *N*,*N*-dimethylformamide (potential referred to Ag/AgCl, 3 M NaCl).

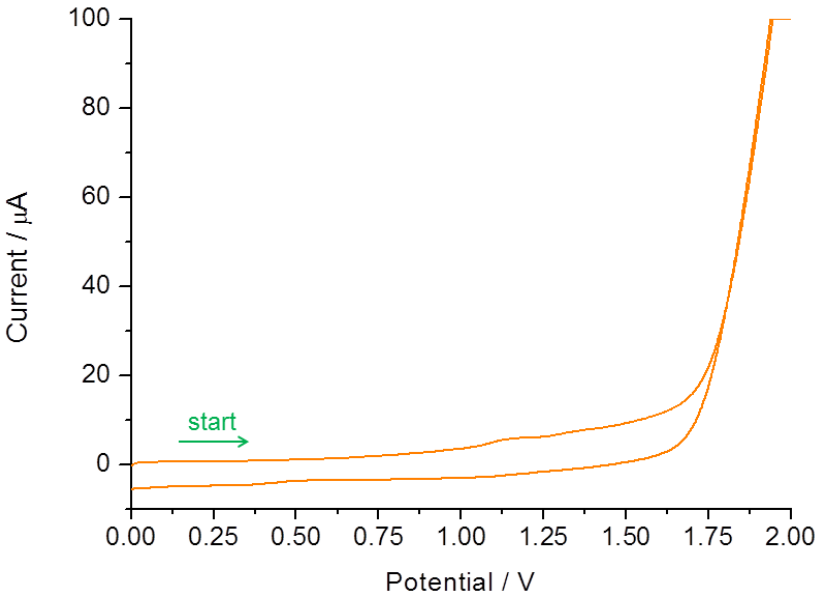


Fig. S11. Cyclic voltammogram obtained for **3k** in *N*,*N*-dimethylformamide (potential referred to Ag/AgCl, 3 M NaCl).

10 References.

S1 S. Protti, D. Ravelli, M. Fagnoni and A. Albini, *Chem. Commun.*, 2009, 7351–7353.

S2 D. Ravelli, S. Protti and M. Fagnoni, *Acc. Chem. Res.*, 2016, **49**, 2232–2242.

S3 M. Bergami, S. Protti, D. Ravelli and M. Fagnoni, *Adv. Synth. Catal.*, 2016, **358**, 1164-1172.

S4 E. Torti, S. Protti, D. Merli, D. Dondi and M. Fagnoni, *Chem. Eur. J.*, 2016, **22**, 16998-17005.

S5 (*a*) M. Terpolilli, D. Merli, S. Protti, V. Dichiarante, M. Fagnoni and A. Albini, *Photochem. Photobiol. Sci.*, 2011, **10**, 123-127; (*b*) R. A. Levine and W. B. Person, *J. Phys. Chem.*, 1977, **81**, 1118-1119.

S6 Y. Ye, S. H. Lee and M. S. Sanford, *Org. Lett.*, 2011, **13**, 5464-5467.

S7 D. Wang, G.-J. Deng, S. Chen and H. Gong, *Green Chem.*, 2016, **18**, 5967-5970.

S8 L. Li, X. Mu, W. Liu, Y. Wang, Z. Mi and C.-J. Li, *J. Am. Chem. Soc.*, 2016, **138**, 5809-5812.

S9 N. V. Kirij, A. A. Filatov, G. Yu. Khrapach and Y. L. Yagupolskii, *Chem.Commun.*, 2017, **53**, 2146-2149.

S10 S. Mizuta, I. S. R. Stenhagen, M. O'Duill, J. Wolstenhulme, A. K. Kirjavainen, S. J. Forsback, M. Tredwell, G. Sandford, P. R. Moore, M. Huiban, S. K. Luthra, J. Passchier, O. Solin and V. Gouverneur, *Org. Lett.*, 2013, **15**, 2648–2651.

S11 T. Kino, Y. Nagase, Y. Ohtsuka, K. Yamamoto, D. Uraguchi, K. Tokuhisa and T. Yamakawa, *J. Fluorine Chem.*, 2010, **131**, 98-105.

S12 Y. Wu, H.-R. Zhang, R.-X. Jin, Q. Lan and X.-S. Wang, *Adv. Synth. Catal.*, 2016, **358**, 3528-3533.

S13 K. A. Jacobson, D. Shi, C. Gallo-Rodriguez, M. Manning Jr., C. Müller, J. W. Daly, J. L. Neumeyer, L. Kiriasis and W. Pfleiderer, *J. Med. Chem.*, 1993, **36**, 2639-2644.

S14 J. Lin, Z. Li, J. Kan, S. Huang, W. Su and Y. Li, *Nat. Commun.*, 2017, **8**, 14353.

S15 K. Hirota, M. Sako and H. Sajiki, *Heterocycles*, 1997, **46**, 547-554.

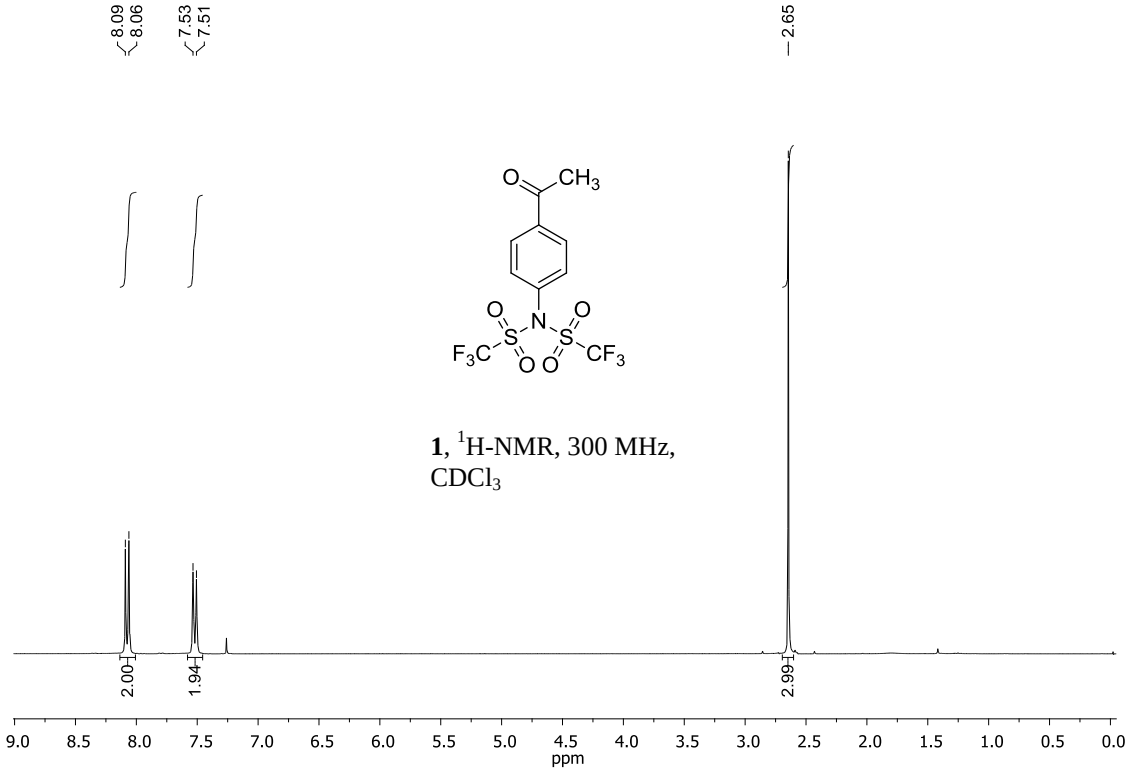
S16 K. Natte, R. V. Jagadeesh, L. He, J. Rabeah, J. Chen, C. Taeschler, S. Ellinger, F. Zaragoza, H. Neumann, A. Brückner and M. Beller, *Angew. Chem. Int. Ed.*, 2016, **55**, 2782-2786; *Angew. Chem.*, 2016, **128**, 2832–2836.

S17 (*a*) M. S. Wiehn, E. V. Vinogradova and A. Togni, *J. Fluorine Chem.*, 2010, **131**, 951-957; (*b*) M. Nishida, H. Kimoto, S. Fujii, Y. Hayakawa and L. A. Cohen, *Bull. Chem. Soc. Jpn.*, 1991, **64**, 2255-2259; (*c*) V. M. Labroo, R. B. Labroo and L. A. Cohen, *Tetrahedron Lett.*, 1990, **40**, 5705-5708; (*d*) H.

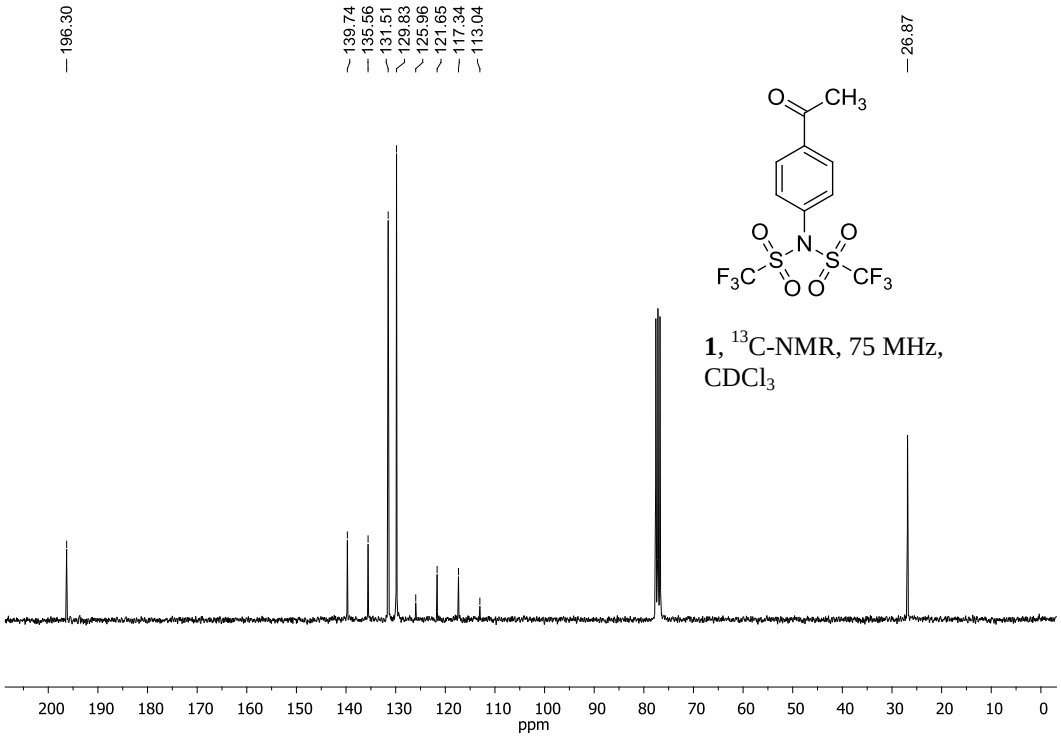
Kimoto, S. Fujii and L. A. Cohen, *J. Org. Chem.*, 1984, **49**, 1060-1064; (*e*) H. Kimoto, S. Fujii and L. A. Cohen, *J. Org. Chem.*, 1982, **47**, 2867-2872.

S18 For recent examples see: (*a*) L. Zhang, H. Yi, J. Wang and A. Lei, *J. Org. Chem.*, 2017, **82**, 10704-10709; (*b*) H. Aruri, U. Singh, M. Kumar, S. Sharma, S. K. Aithagani, V. K. Gupta, S. Mignani, R. A. Vishwakarma and P. P. Singh, *J. Org. Chem.*, 2017, **82**, 1000-1012; (*c*) J. Zhao, P. Li, C. Xia and F. Li, *Chem. Commun.*, 2014, **50**, 4751-4754.

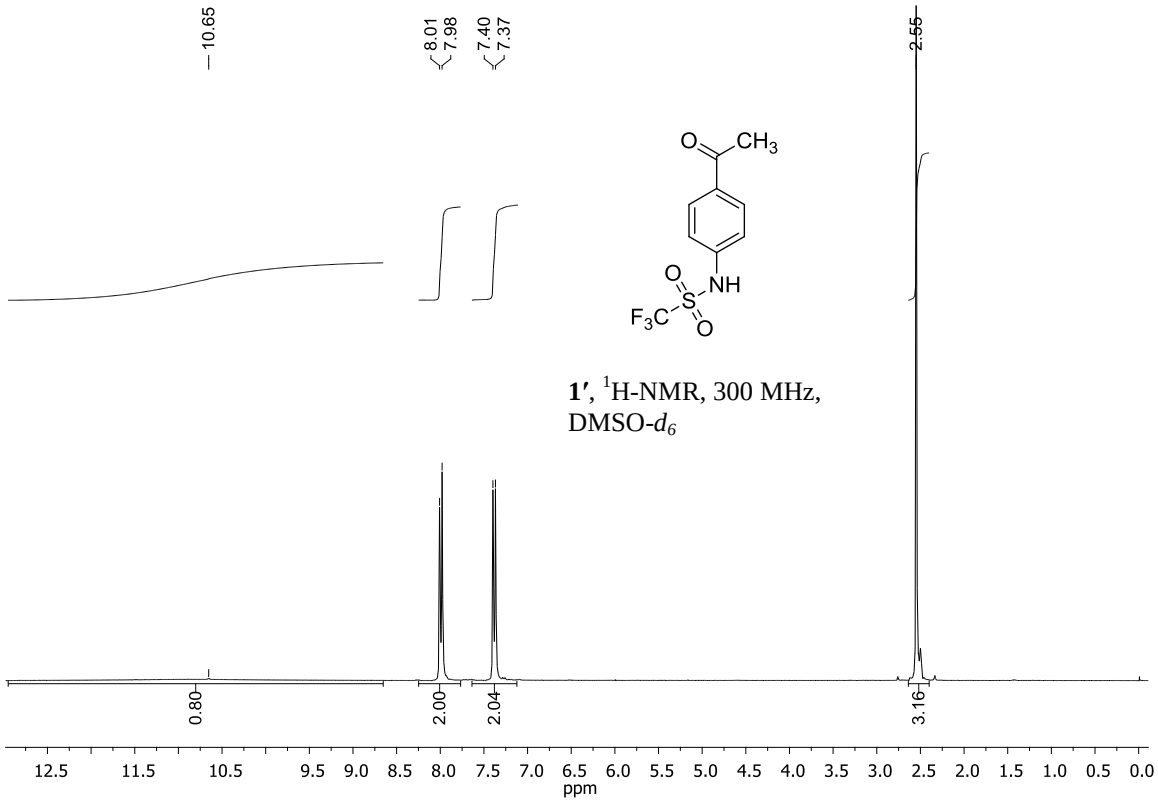
11 ^{1}H, ^{13}C and ^{19}F NMR spectra.



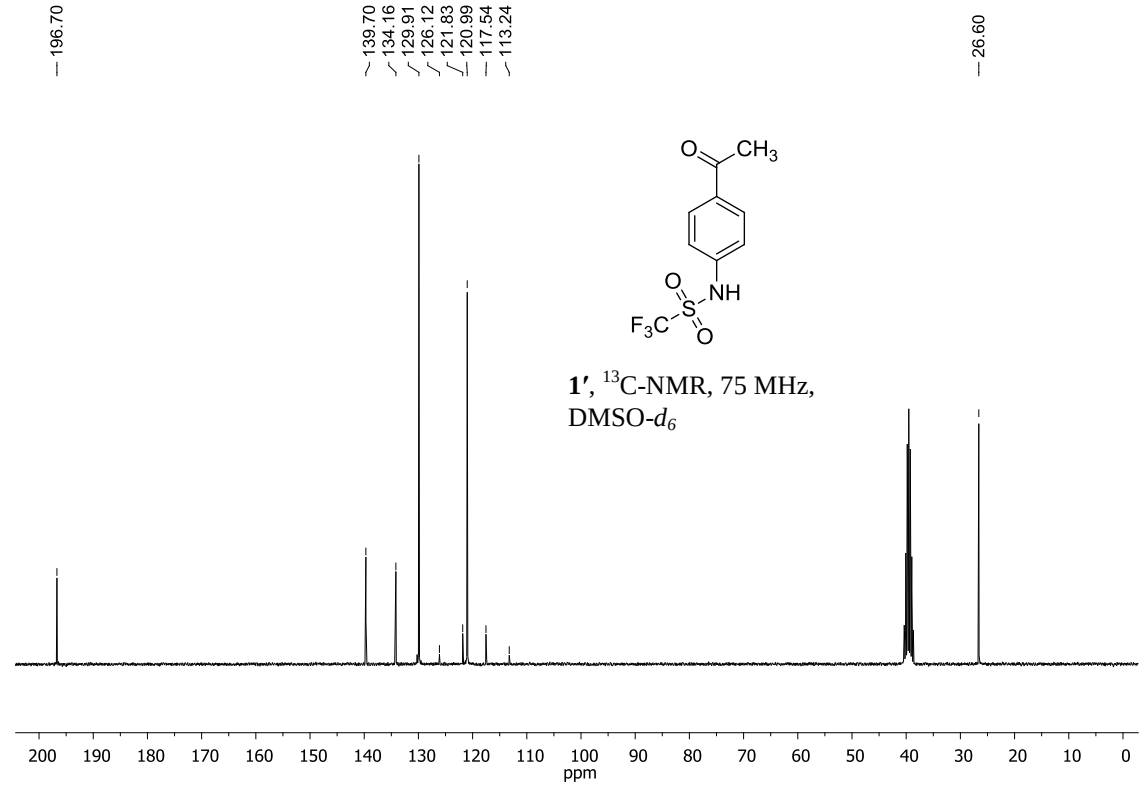
1, ^{1}H-NMR, 300 MHz, $CDCl_3$



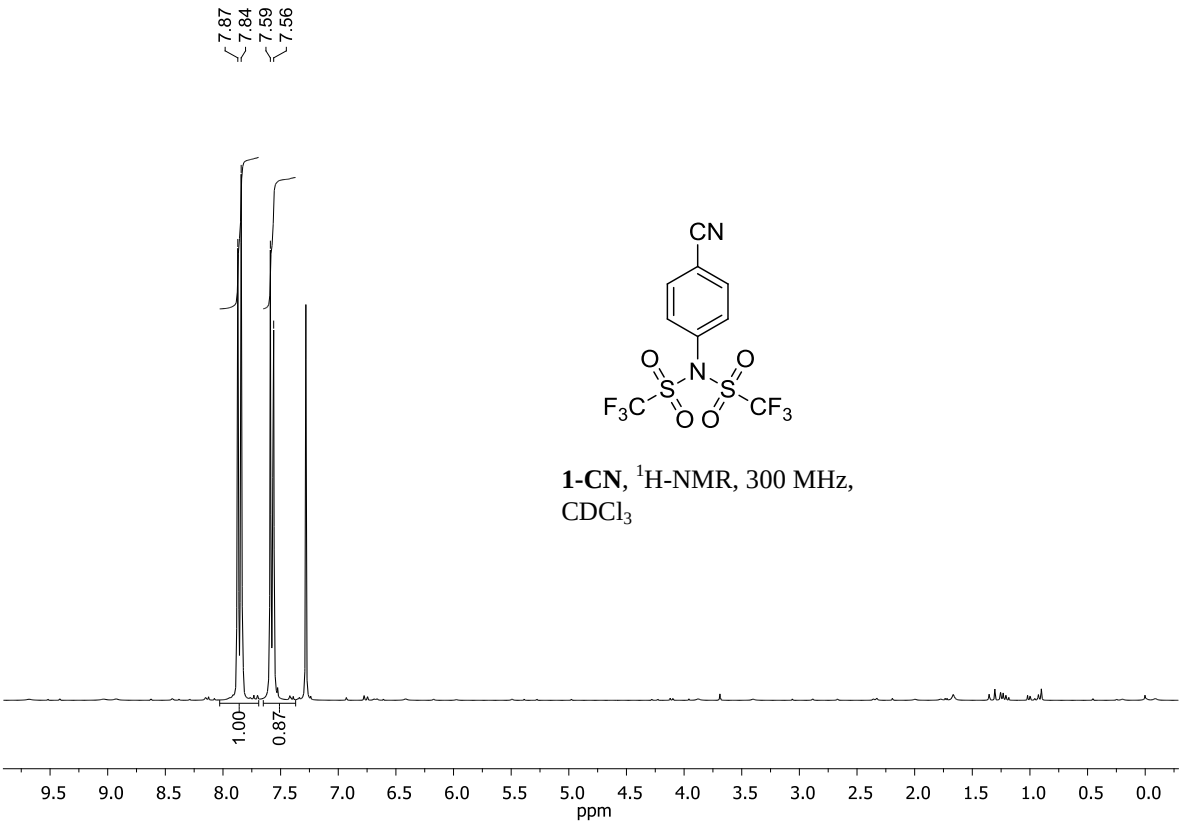
1, ^{13}C-NMR, 75 MHz, $CDCl_3$



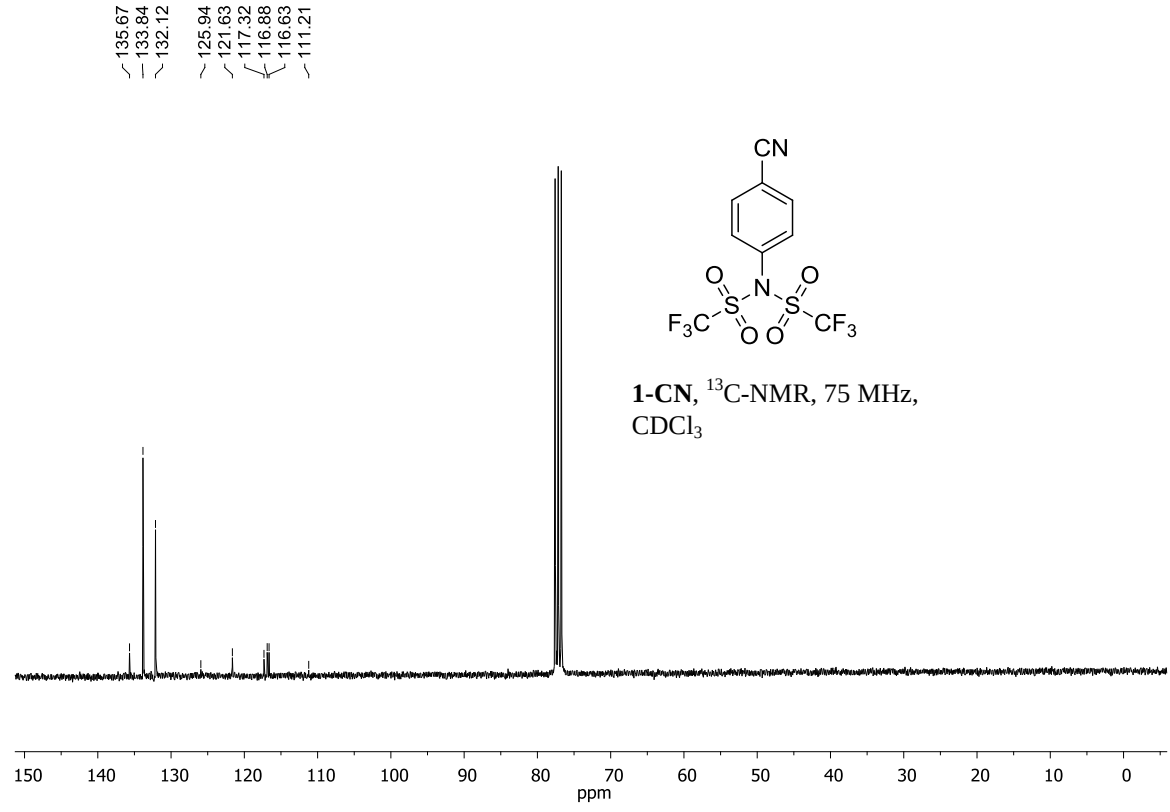
1′, ^{1}H-NMR, 300 MHz, DMSO-d_6



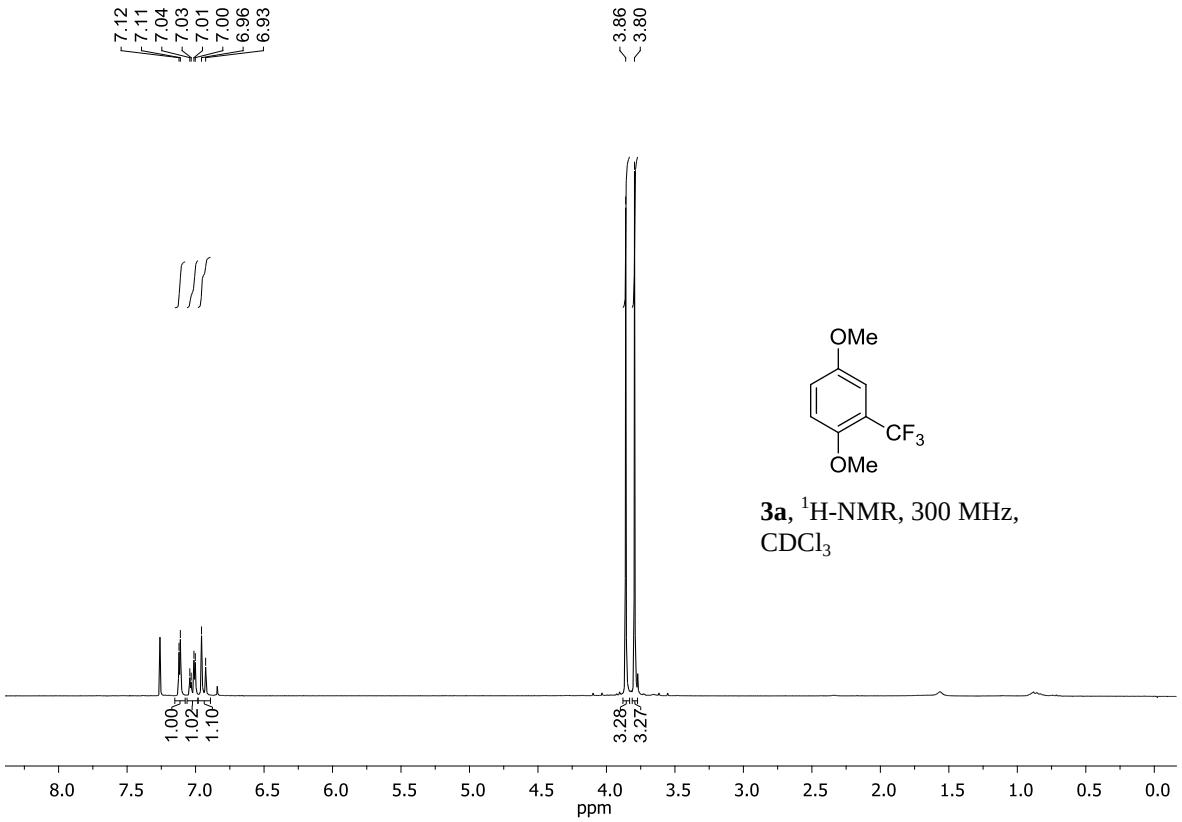
1′, ^{13}C-NMR, 75 MHz, DMSO-d_6



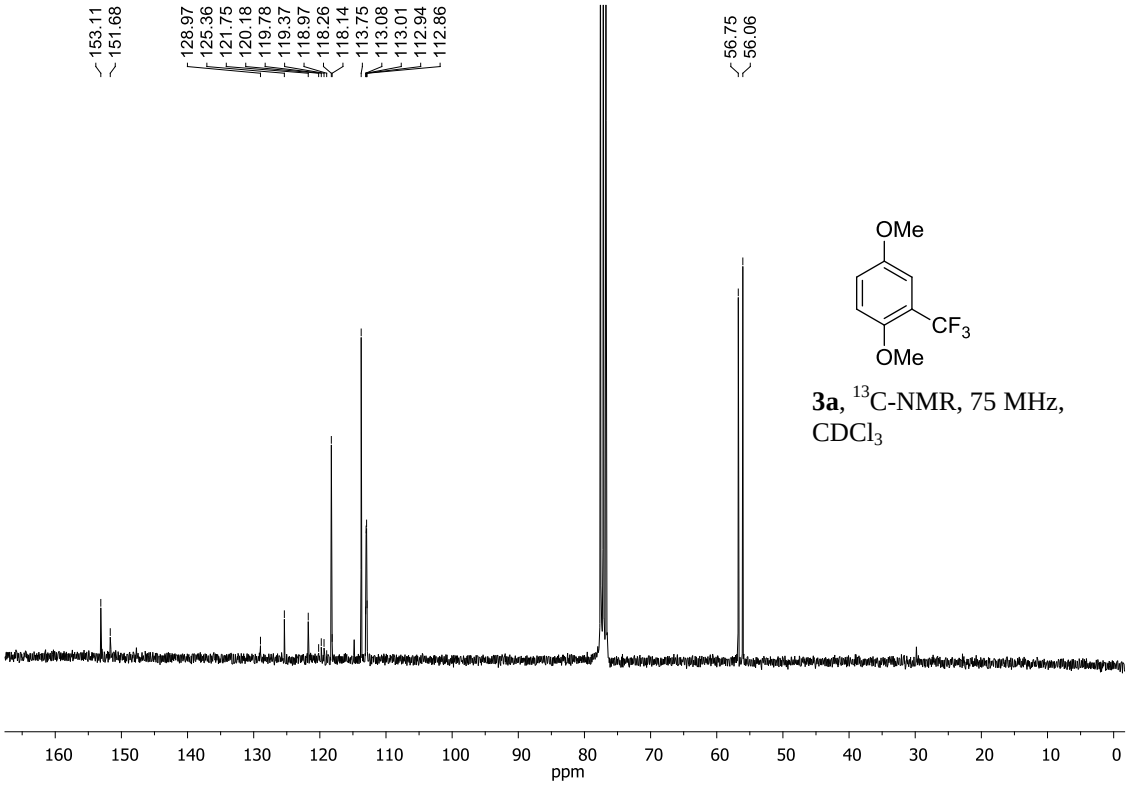
1-CN, ^{1}H-NMR, 300 MHz, $CDCl_3$



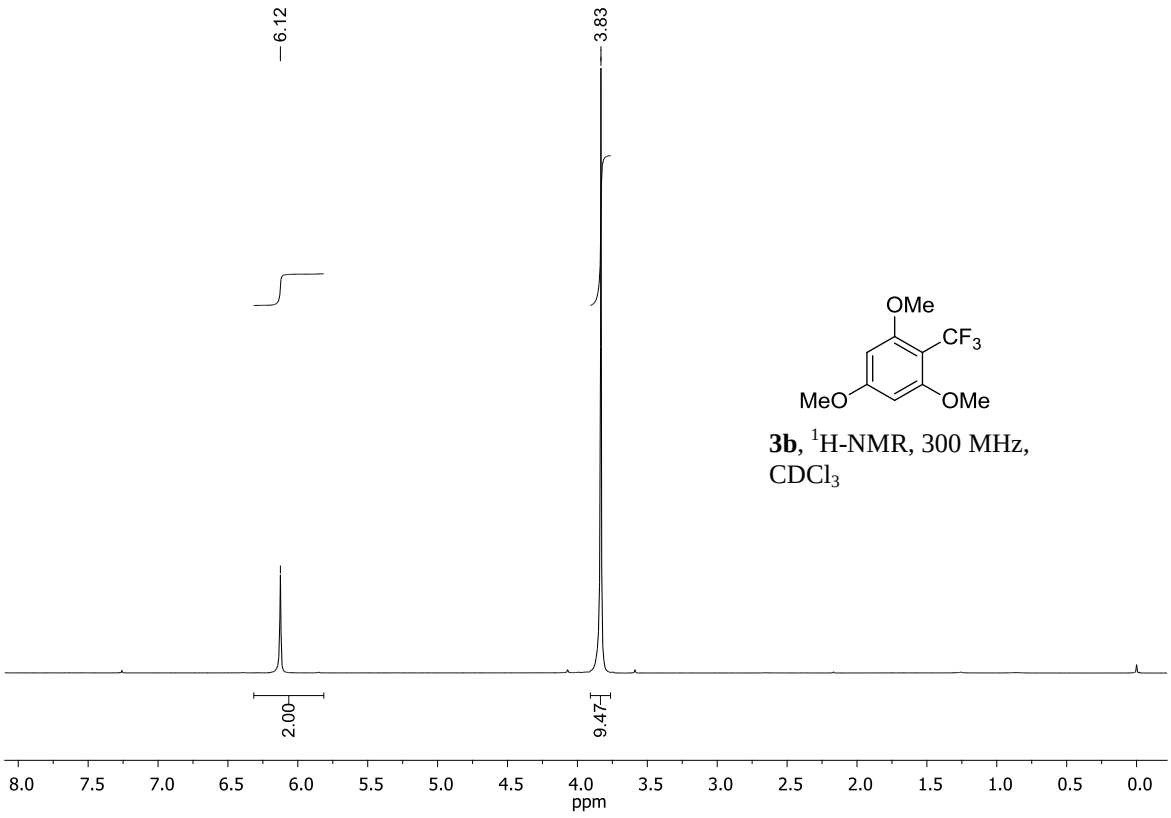
1-CN, ^{13}C-NMR, 75 MHz, $CDCl_3$



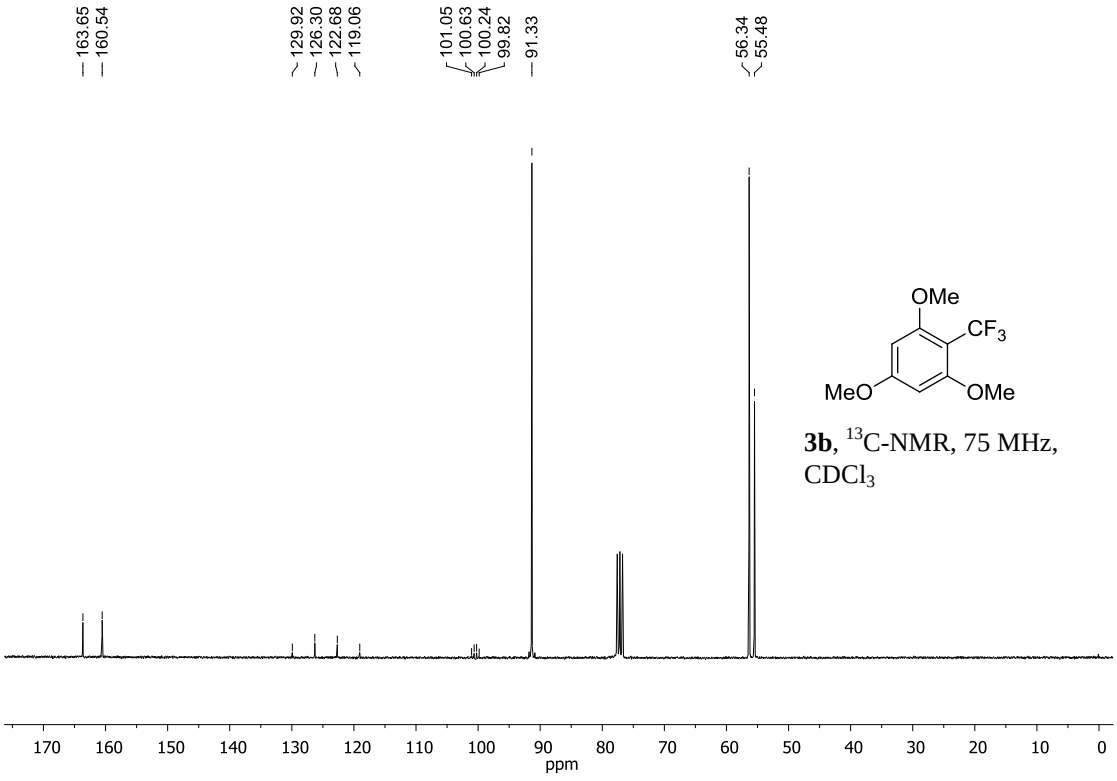
3a, ^{1}H-NMR, 300 MHz, $CDCl_3$



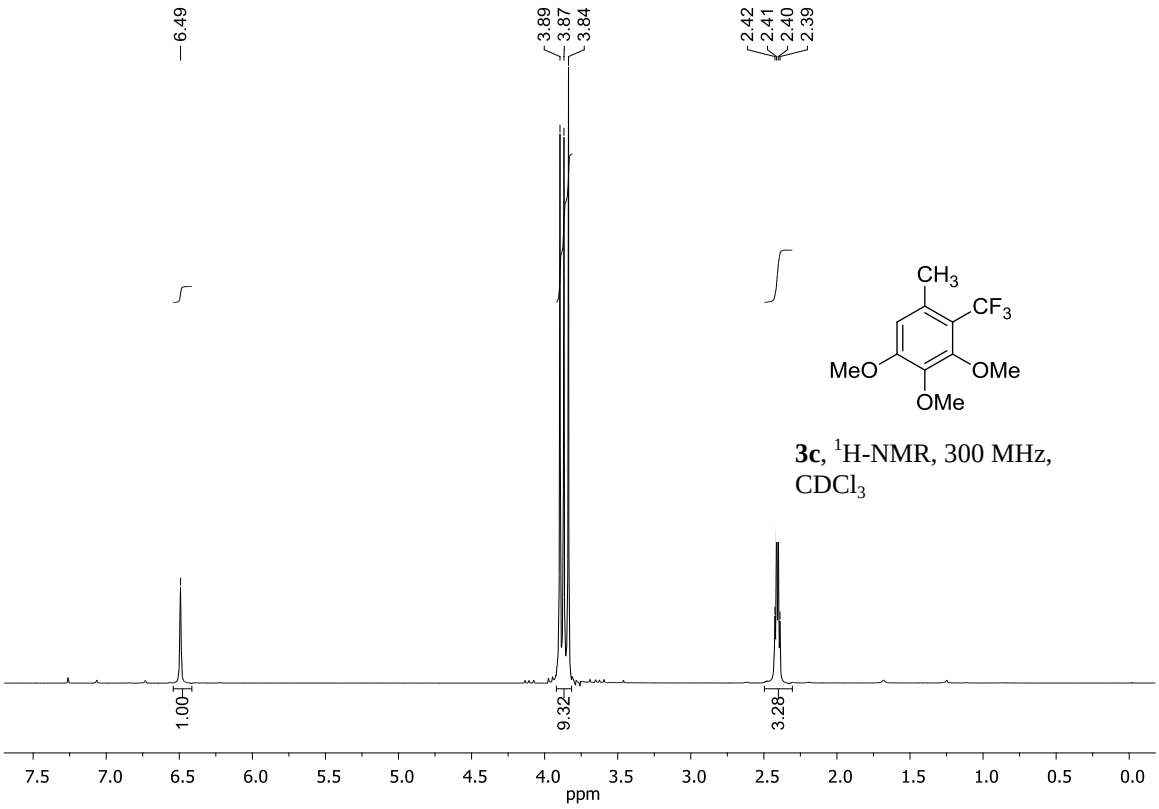
3a, ^{13}C-NMR, 75 MHz, $CDCl_3$



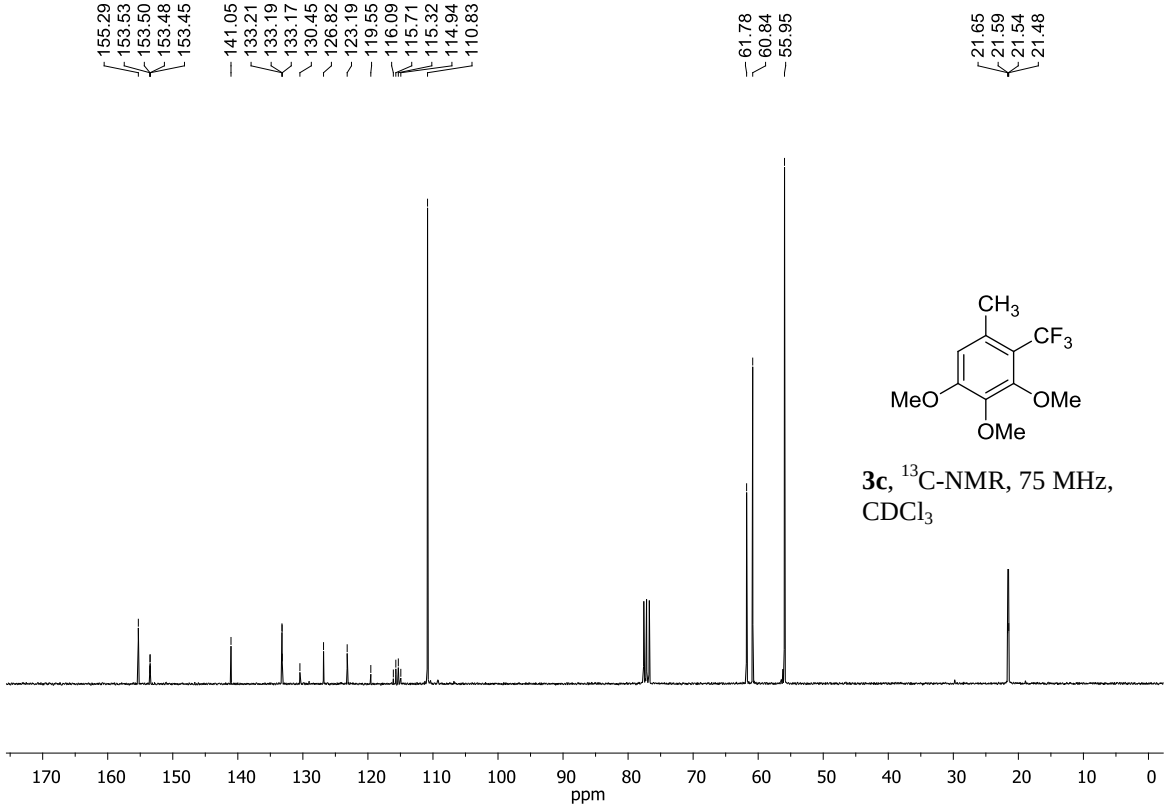
3b, ^{1}H-NMR, 300 MHz, $CDCl_3$



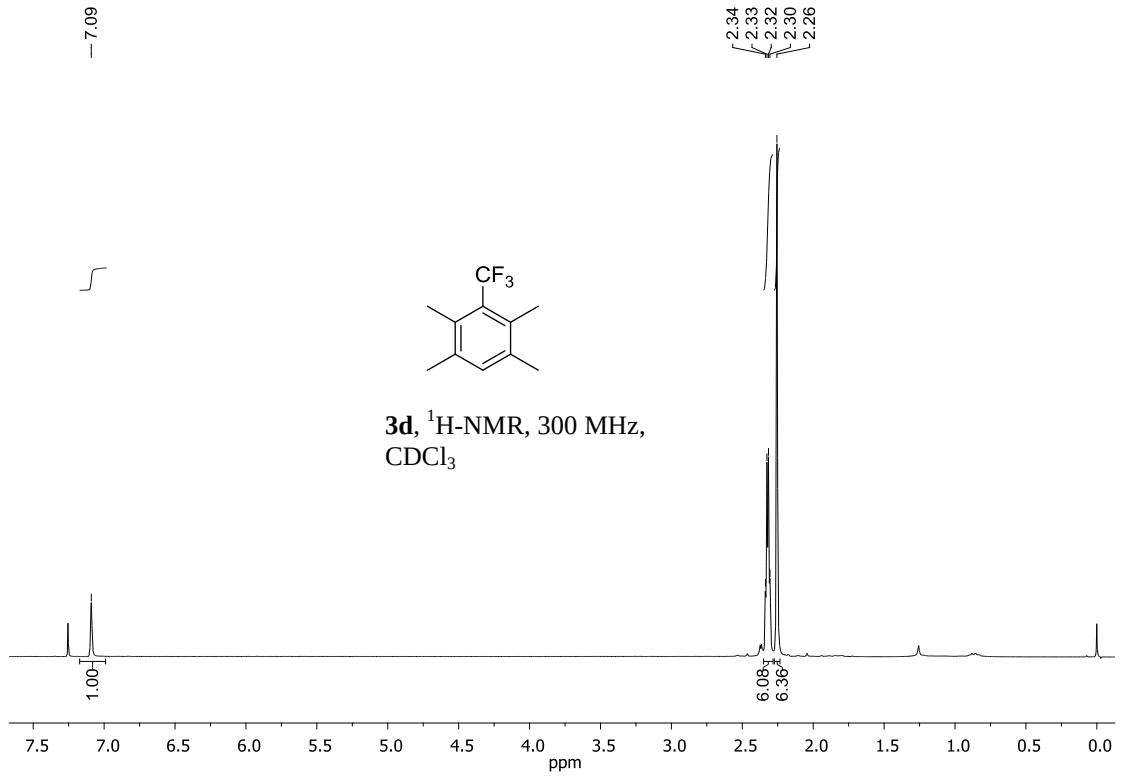
3b, ^{13}C-NMR, 75 MHz, $CDCl_3$



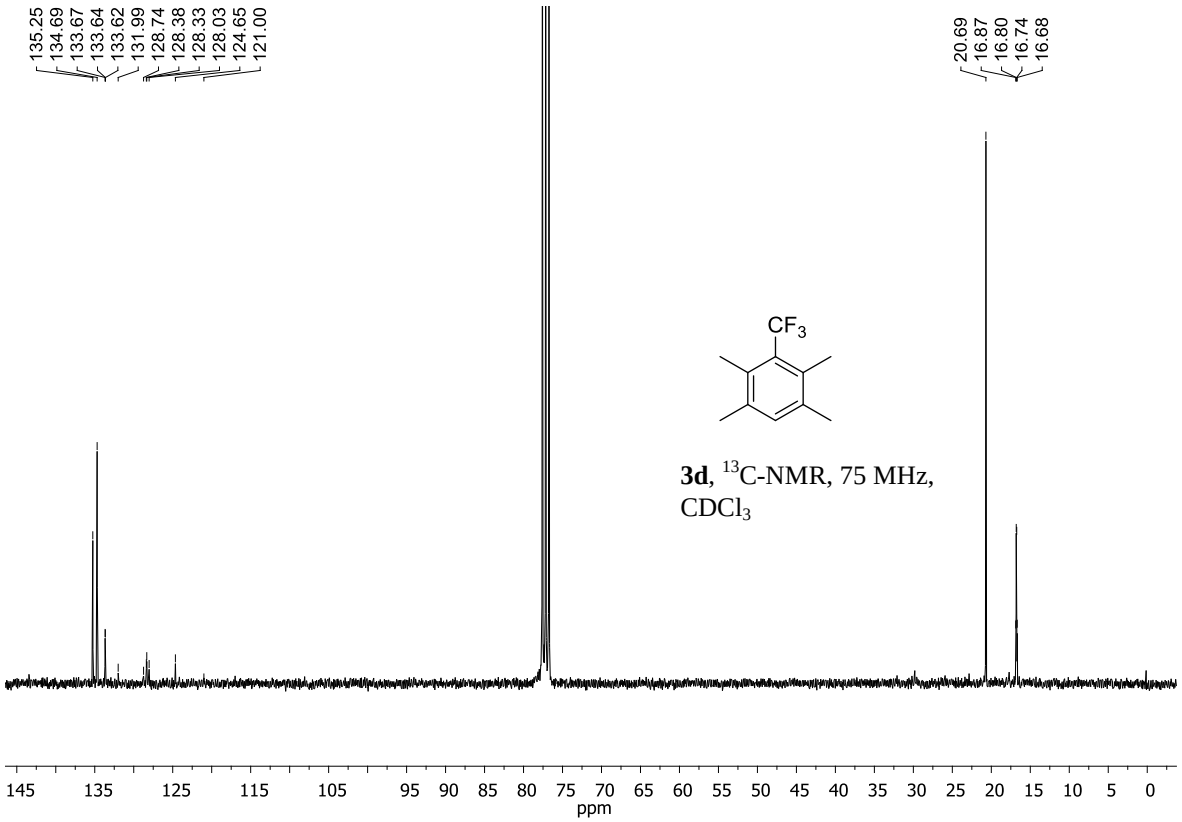
3c, ^{1}H-NMR, 300 MHz, $CDCl_3$



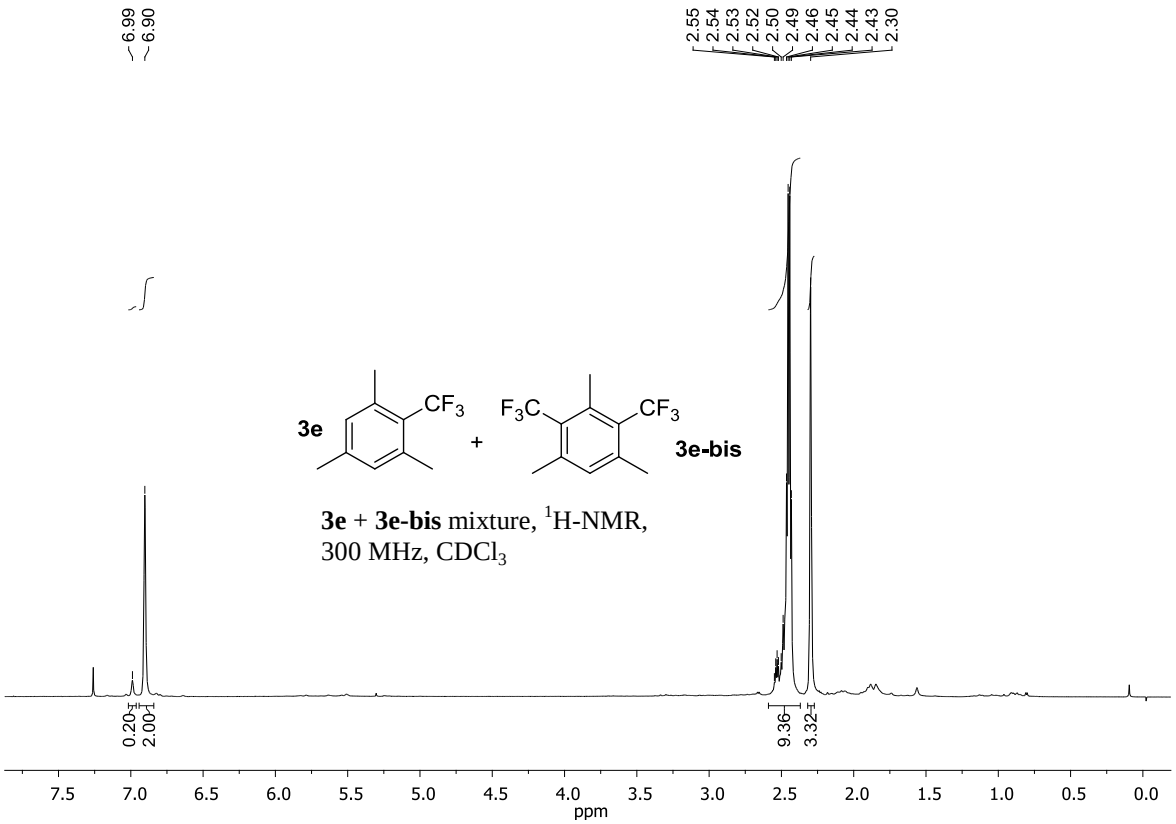
3c, ^{13}C-NMR, 75 MHz, $CDCl_3$



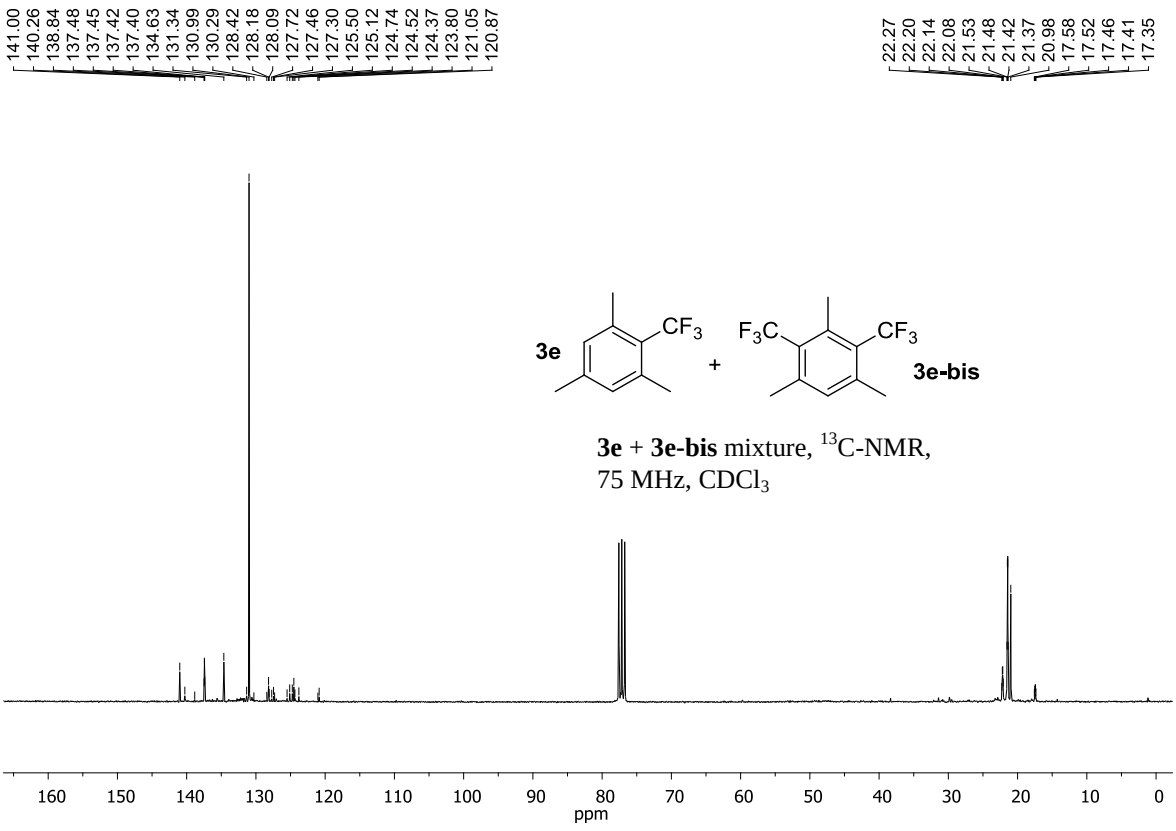
3d, ^{1}H-NMR, 300 MHz, $CDCl_3$



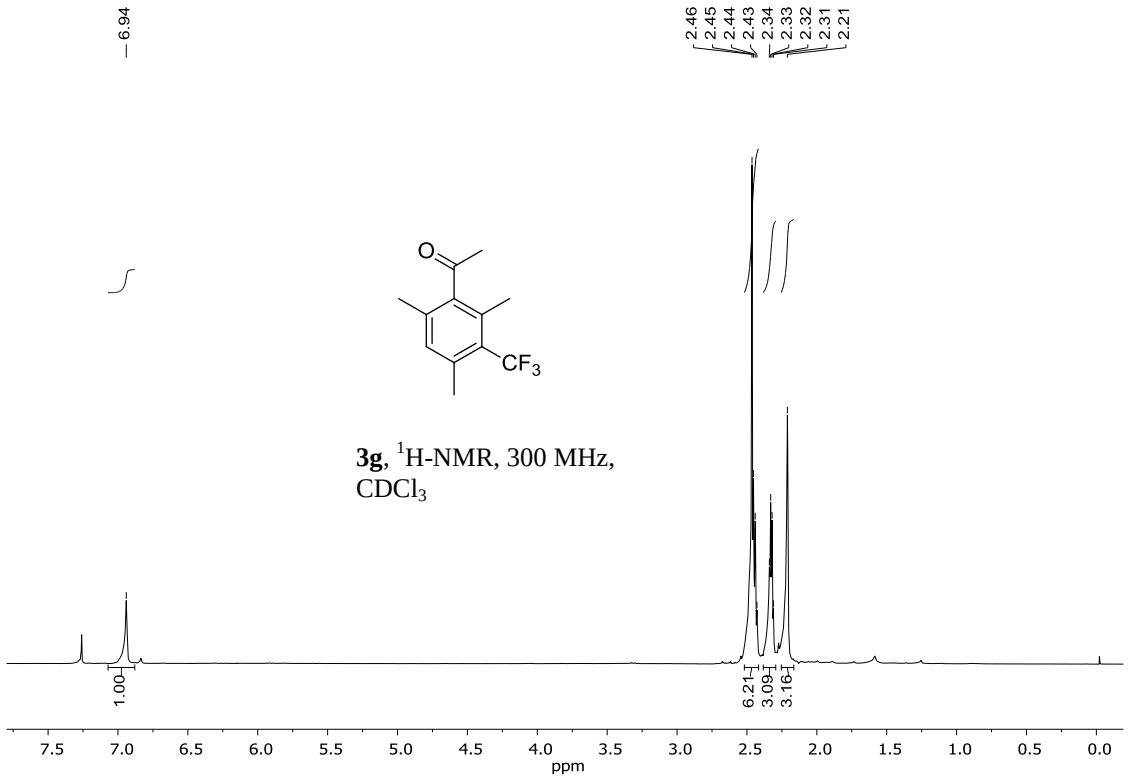
3d, ^{13}C-NMR, 75 MHz, $CDCl_3$



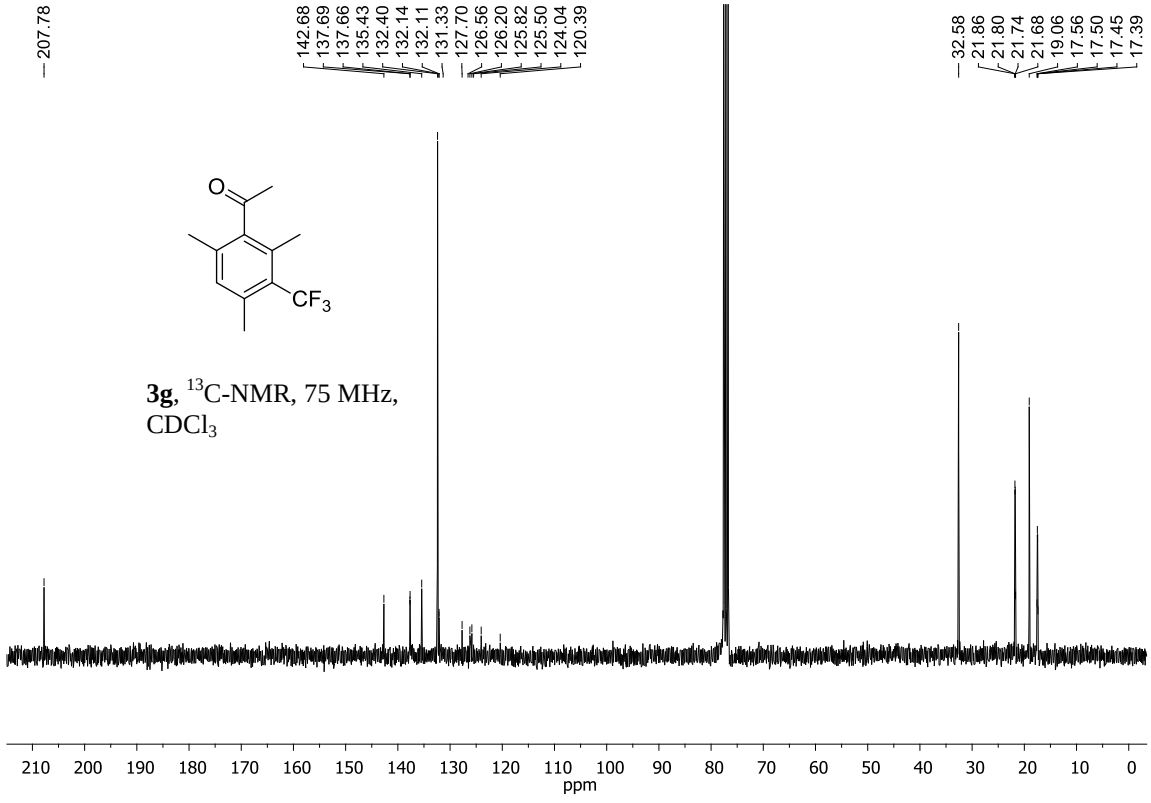
3e + **3e-bis** mixture, ^{1}H-NMR, 300 MHz, $CDCl_3$



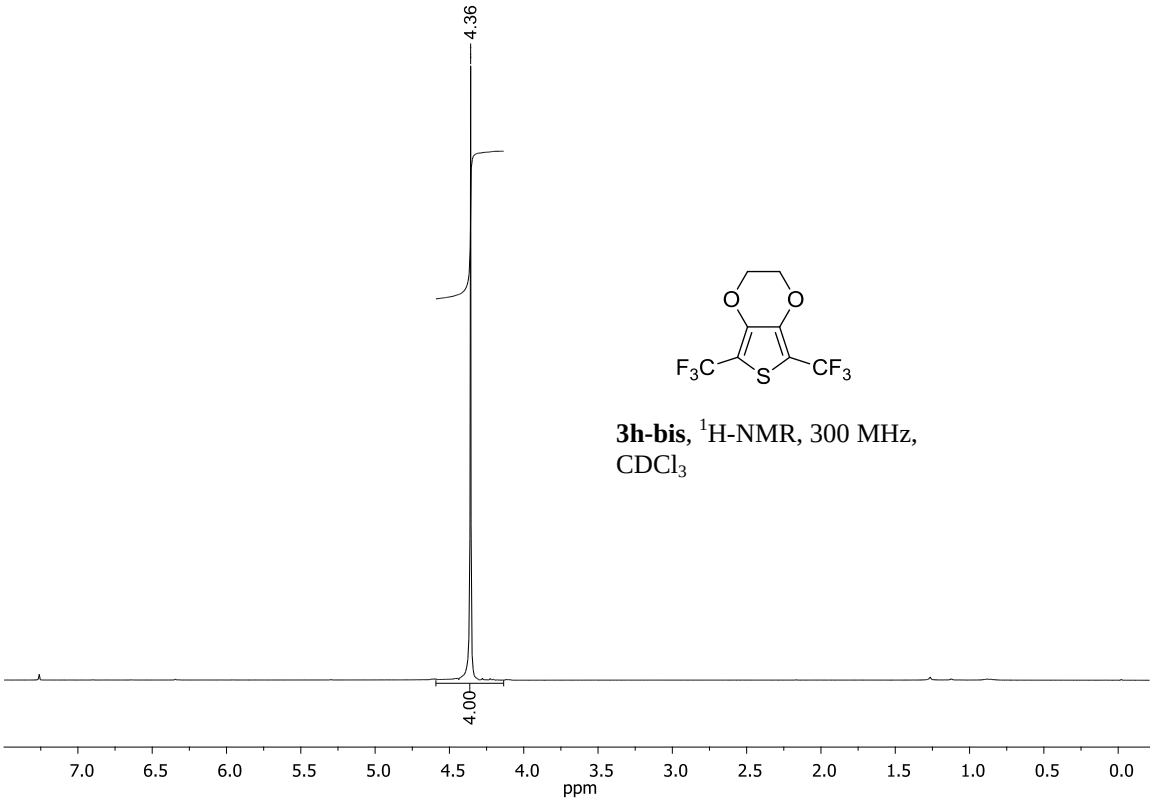
3e + **3e-bis** mixture, ^{13}C-NMR, 75 MHz, $CDCl_3$



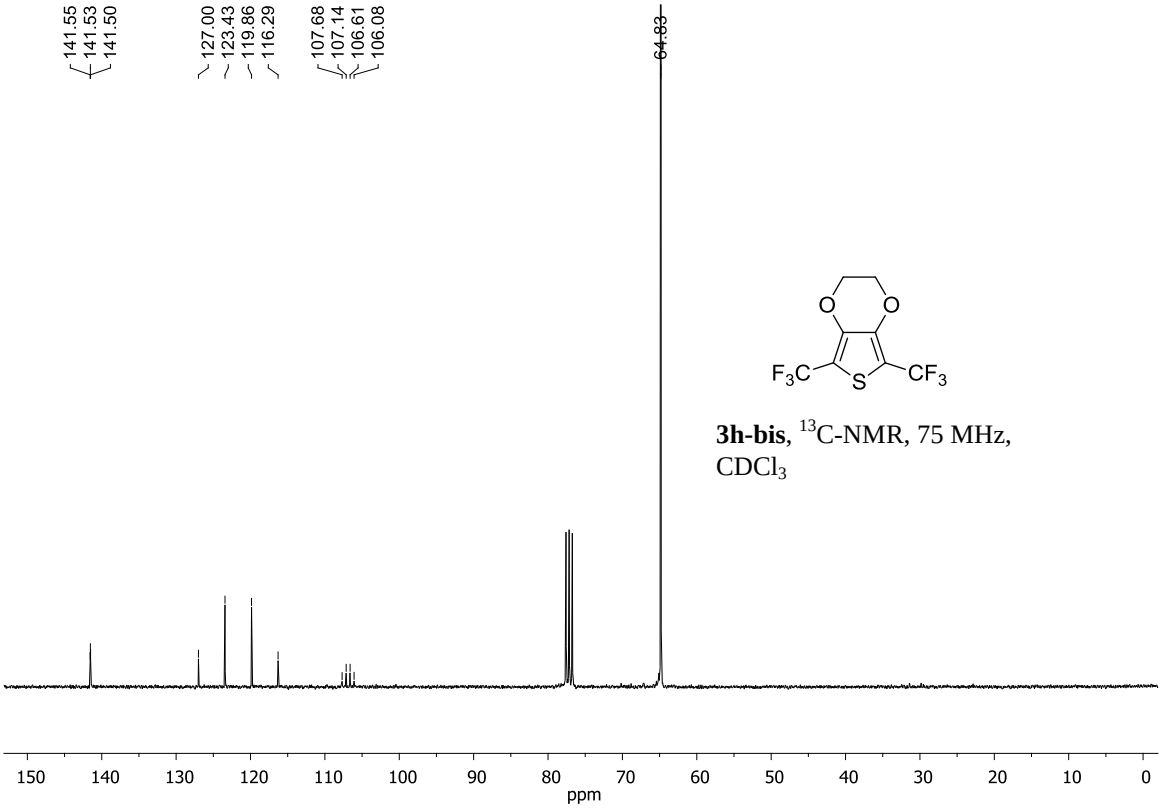
3g, ^{1}H-NMR, 300 MHz, $CDCl_3$



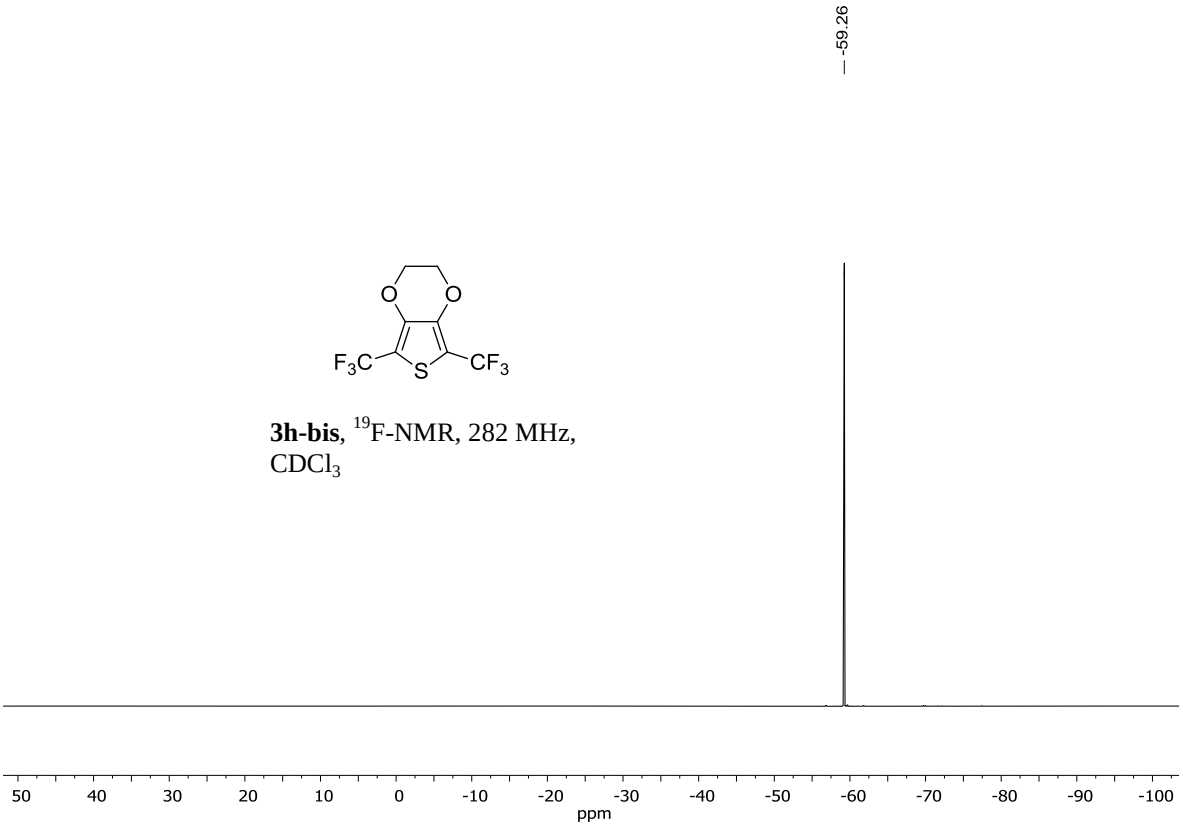
3g, ^{13}C-NMR, 75 MHz, $CDCl_3$



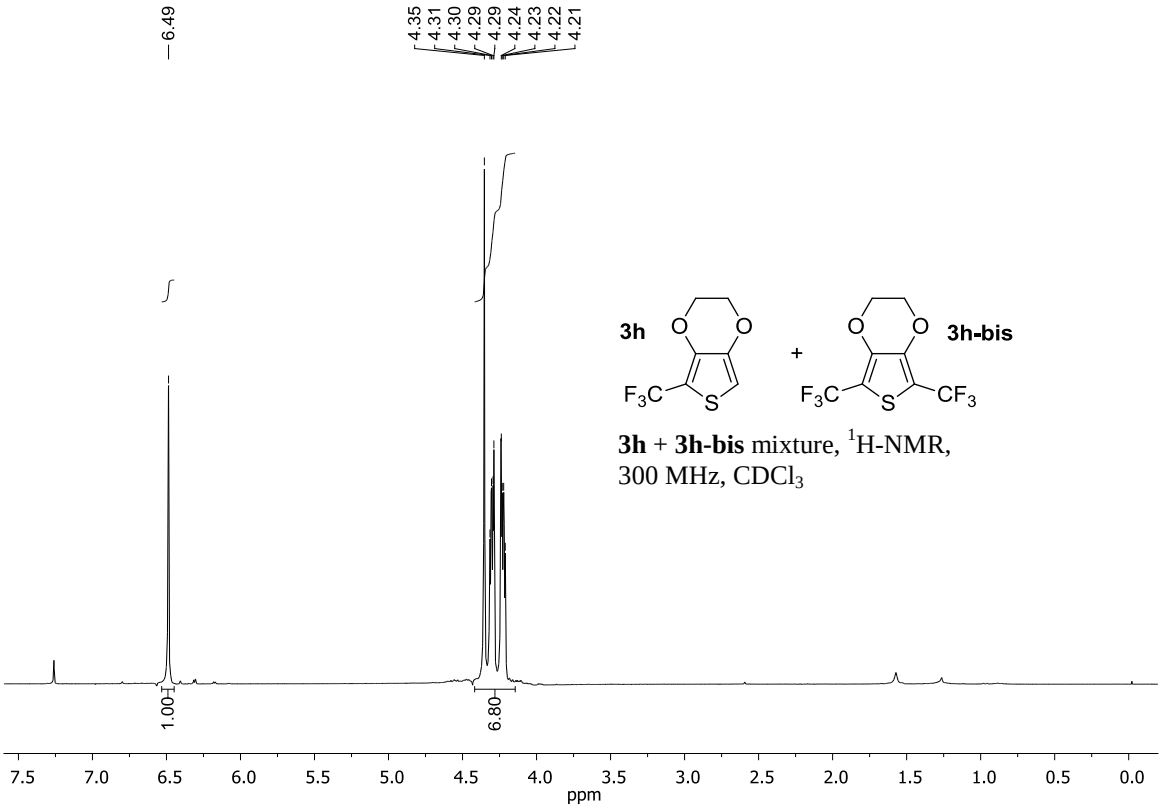
3h-bis, ^{1}H-NMR, 300 MHz, $CDCl_3$



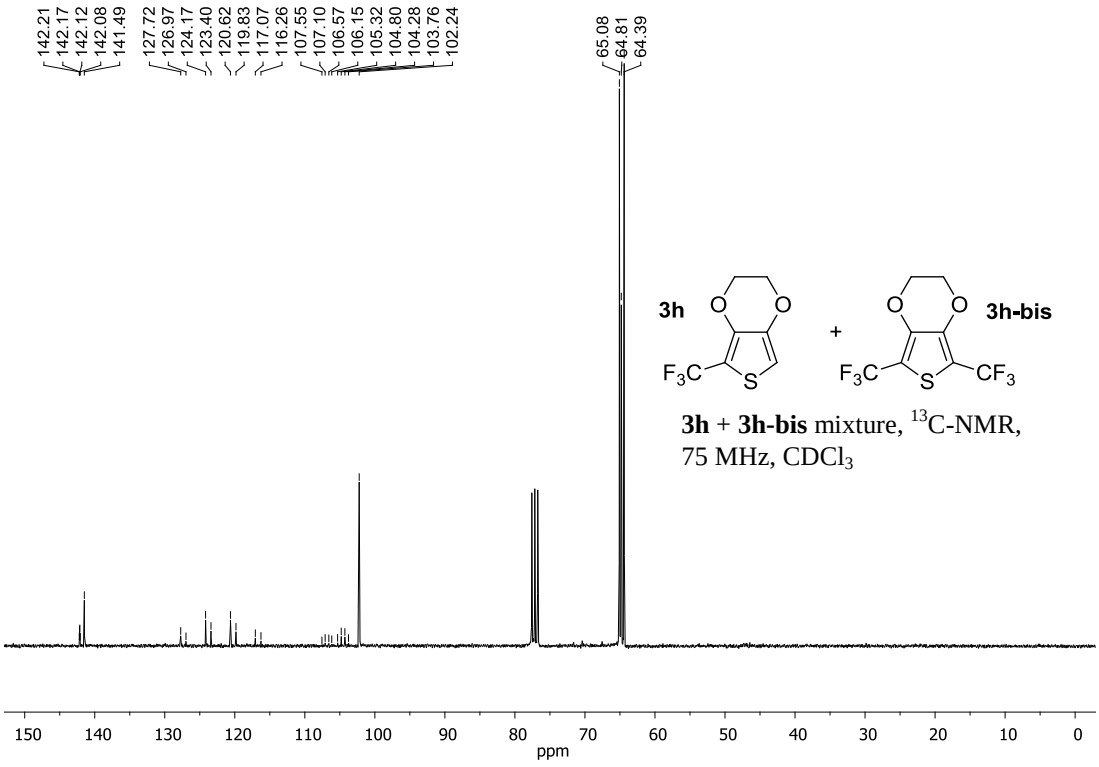
3h-bis, ^{13}C-NMR, 75 MHz, $CDCl_3$



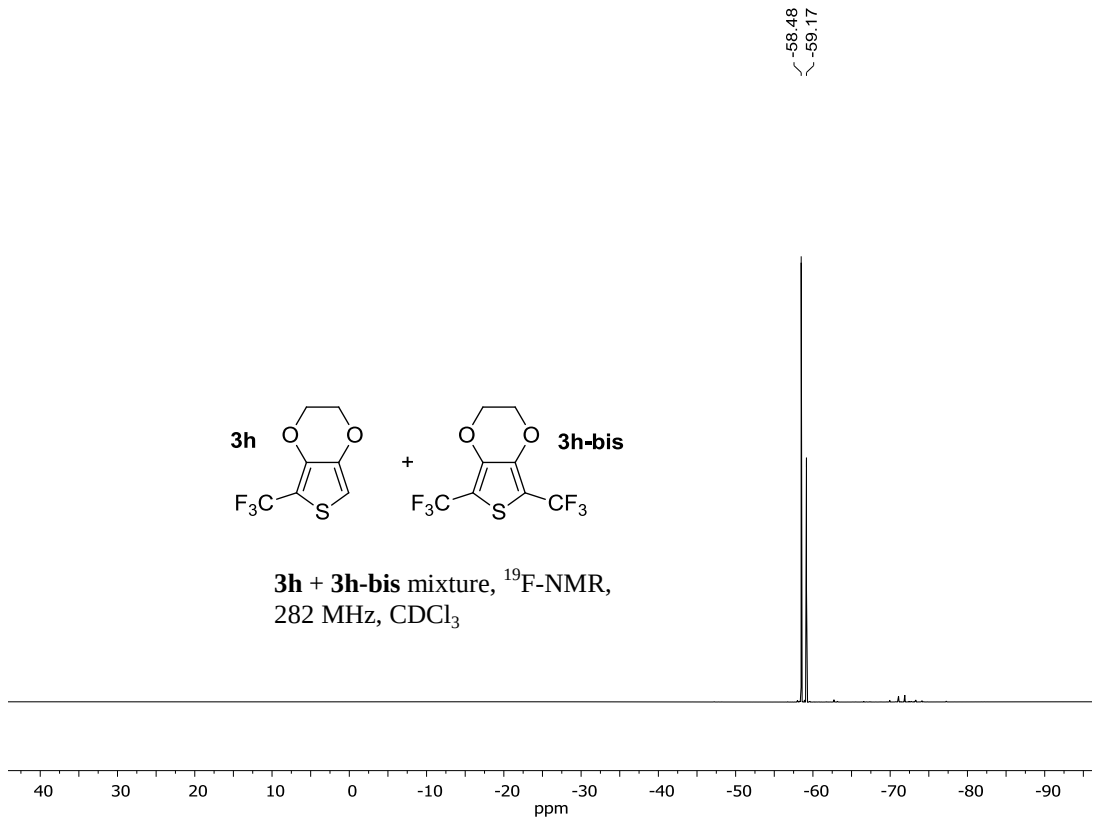
3h-bis, ^{19}F-NMR, 282 MHz, $CDCl_3$



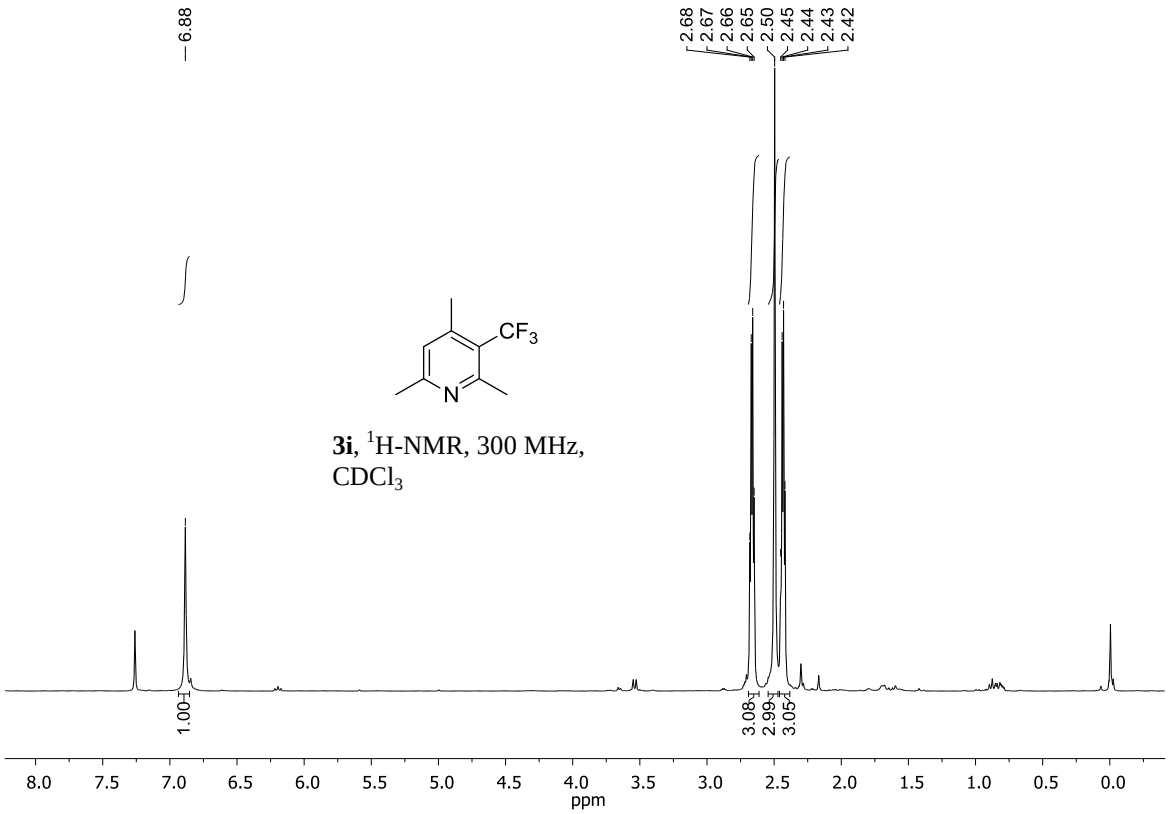
3h + **3h-bis** mixture, ^{1}H-NMR, 300 MHz, $CDCl_3$



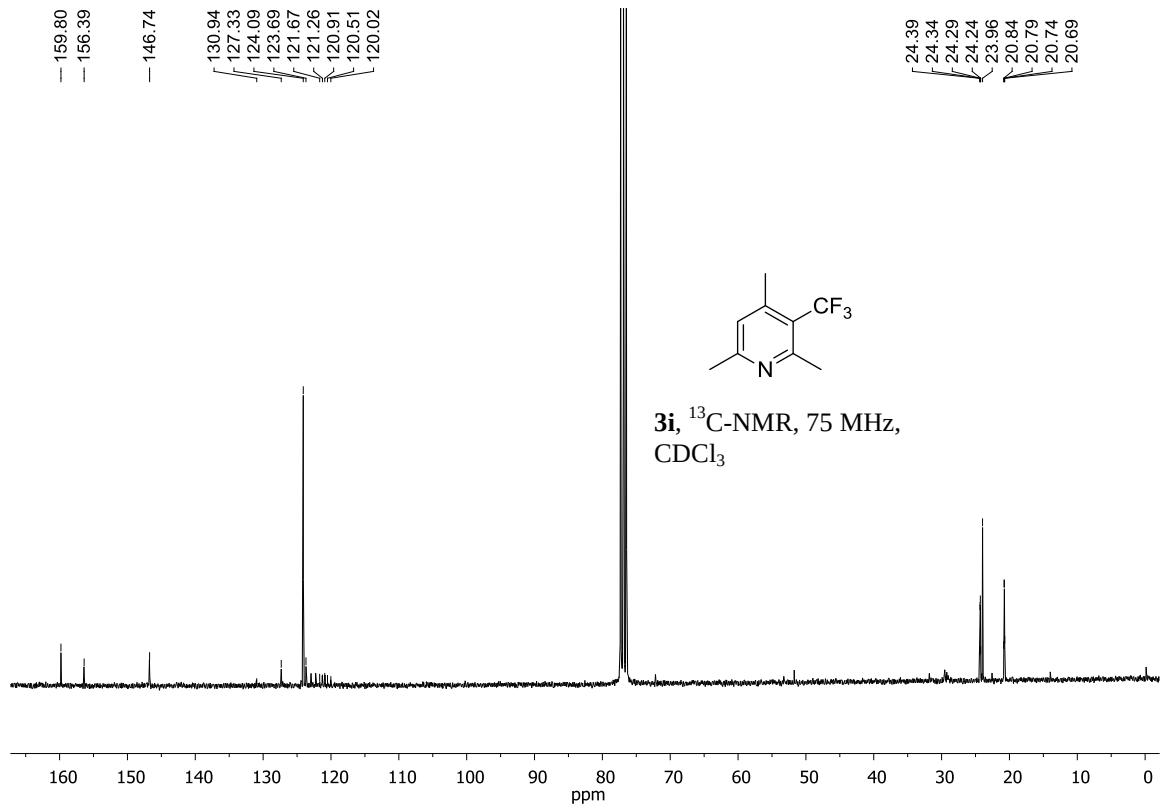
3h + **3h-bis** mixture, ^{13}C-NMR, 75 MHz, $CDCl_3$



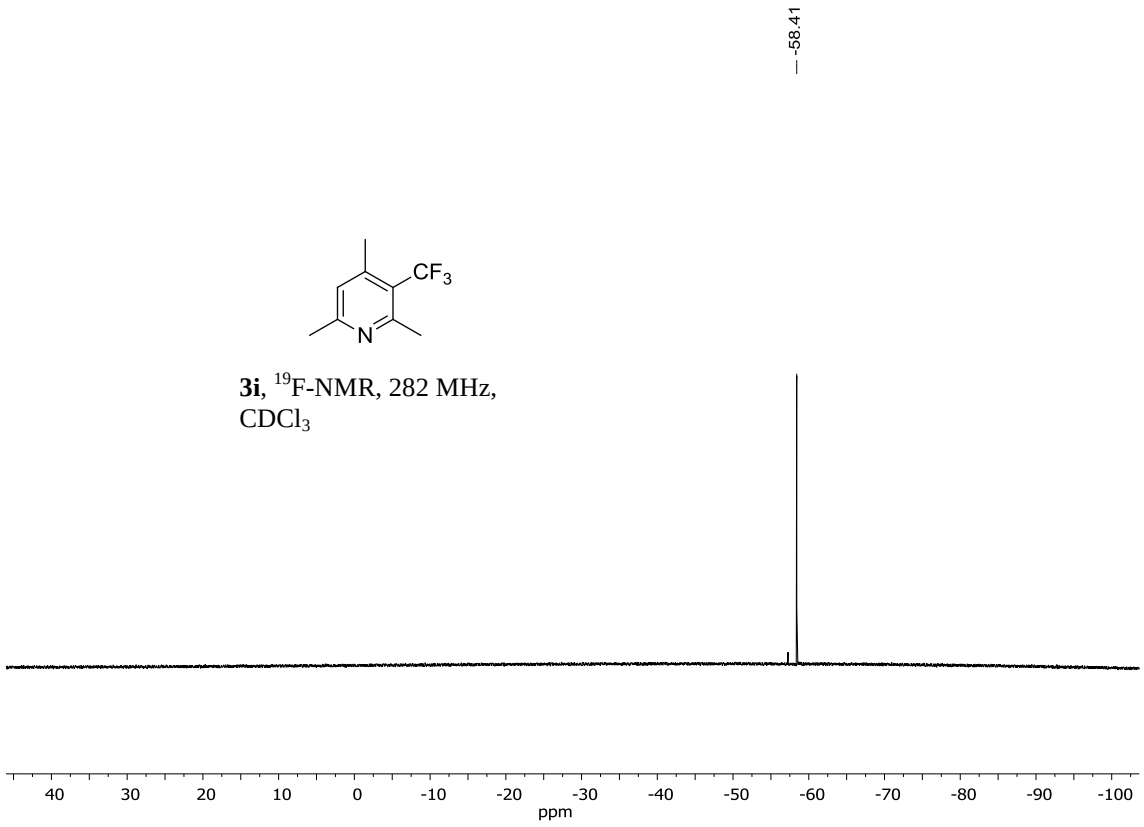
3h + **3h-bis** mixture, ^{19}F-NMR, 282 MHz, $CDCl_3$



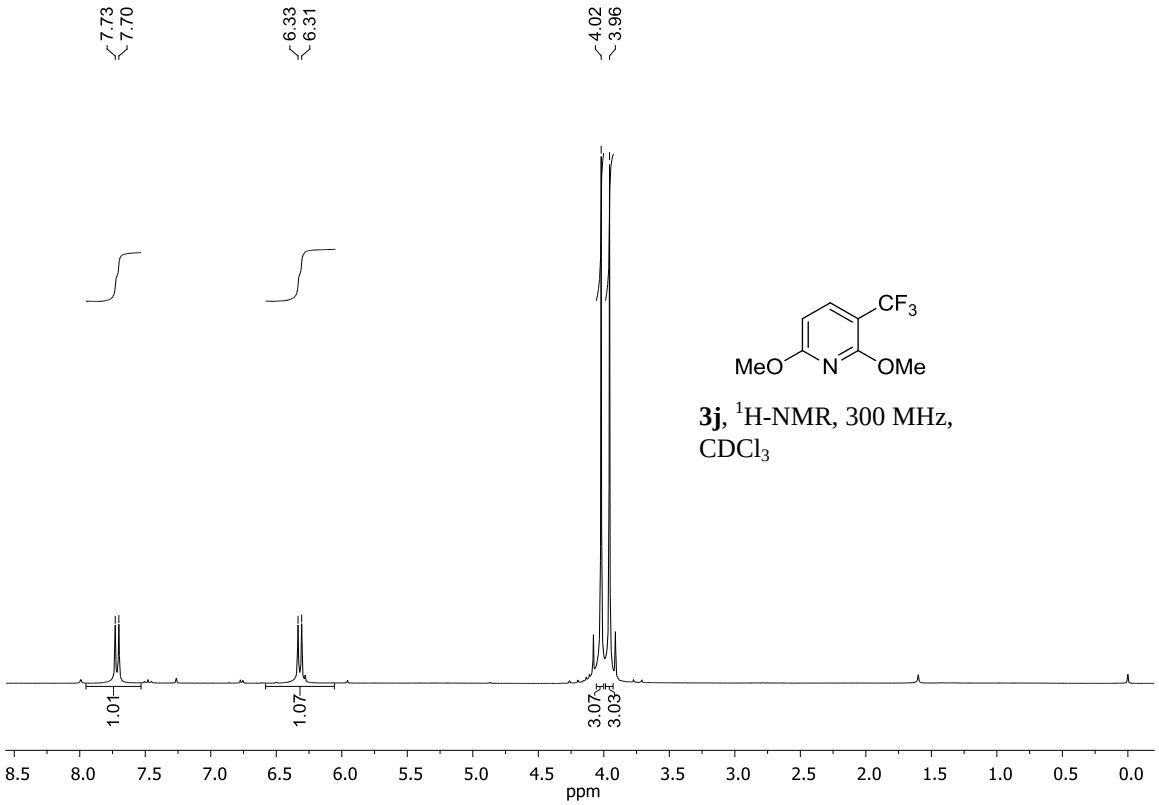
3i, ^{1}H-NMR, 300 MHz, $CDCl_3$



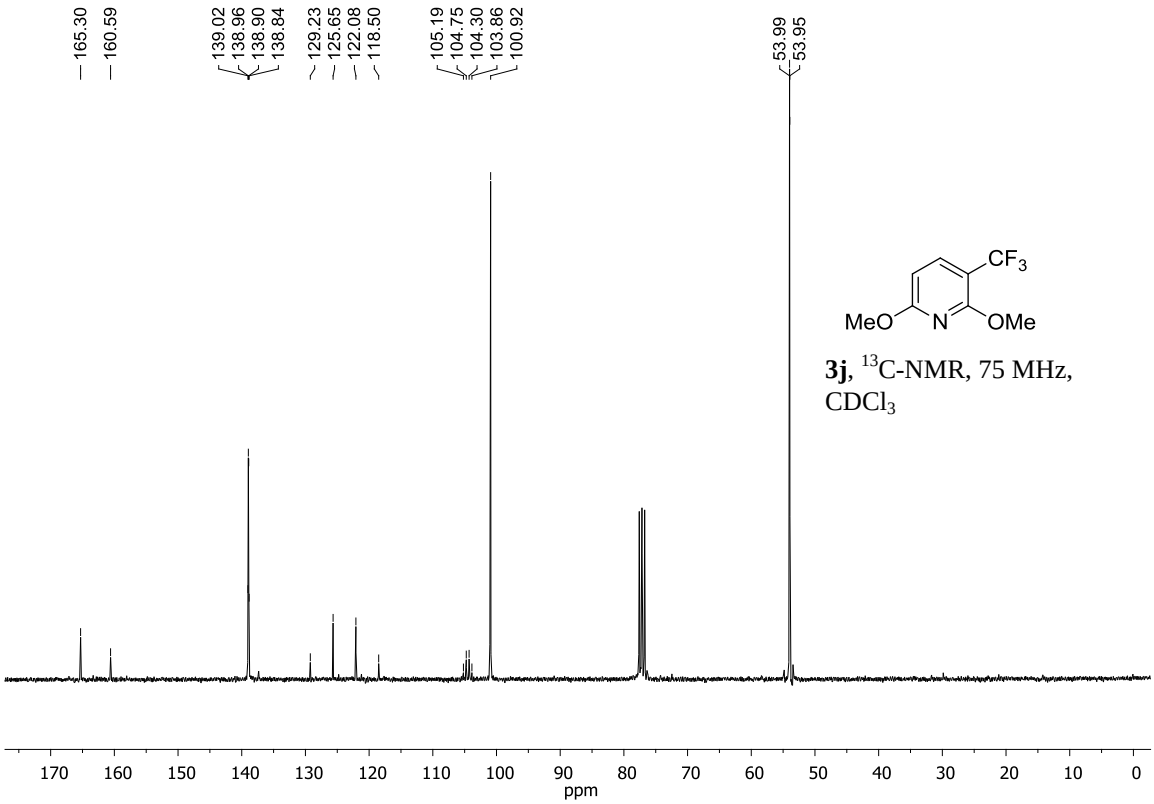
3i, ^{13}C-NMR, 75 MHz, $CDCl_3$



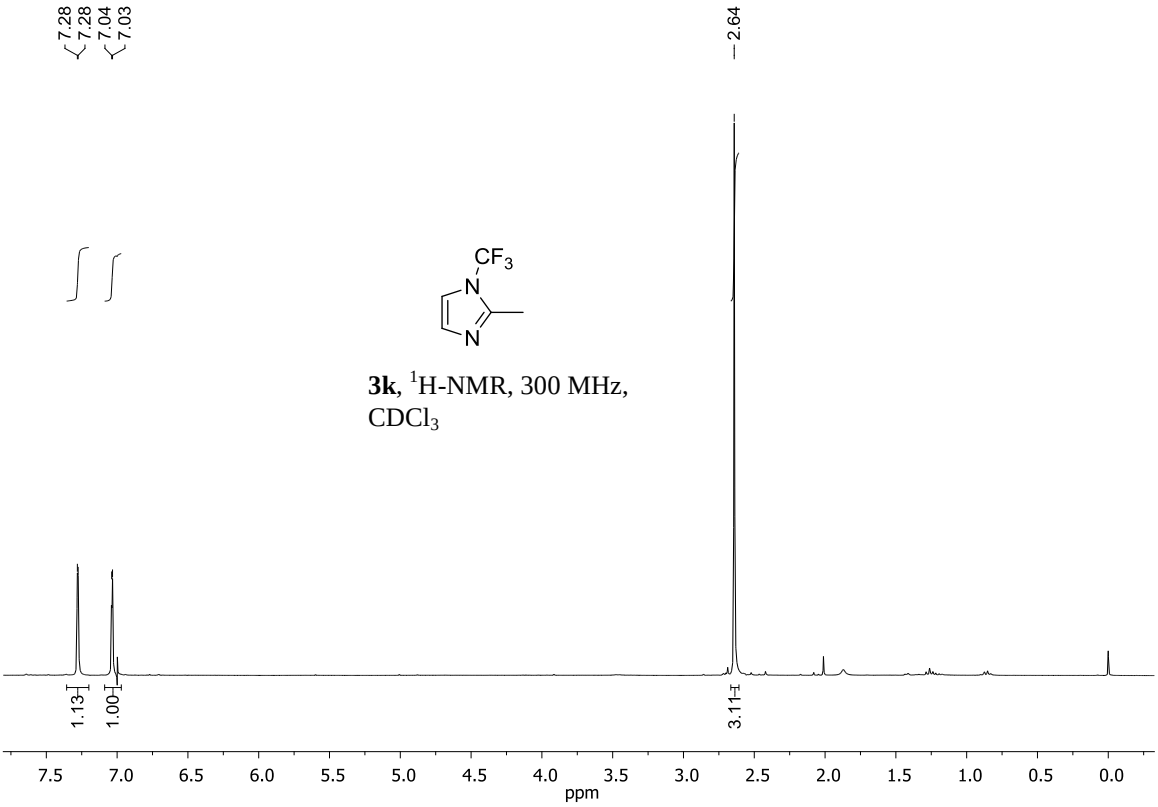
3i, ^{19}F-NMR, 282 MHz, $CDCl_3$



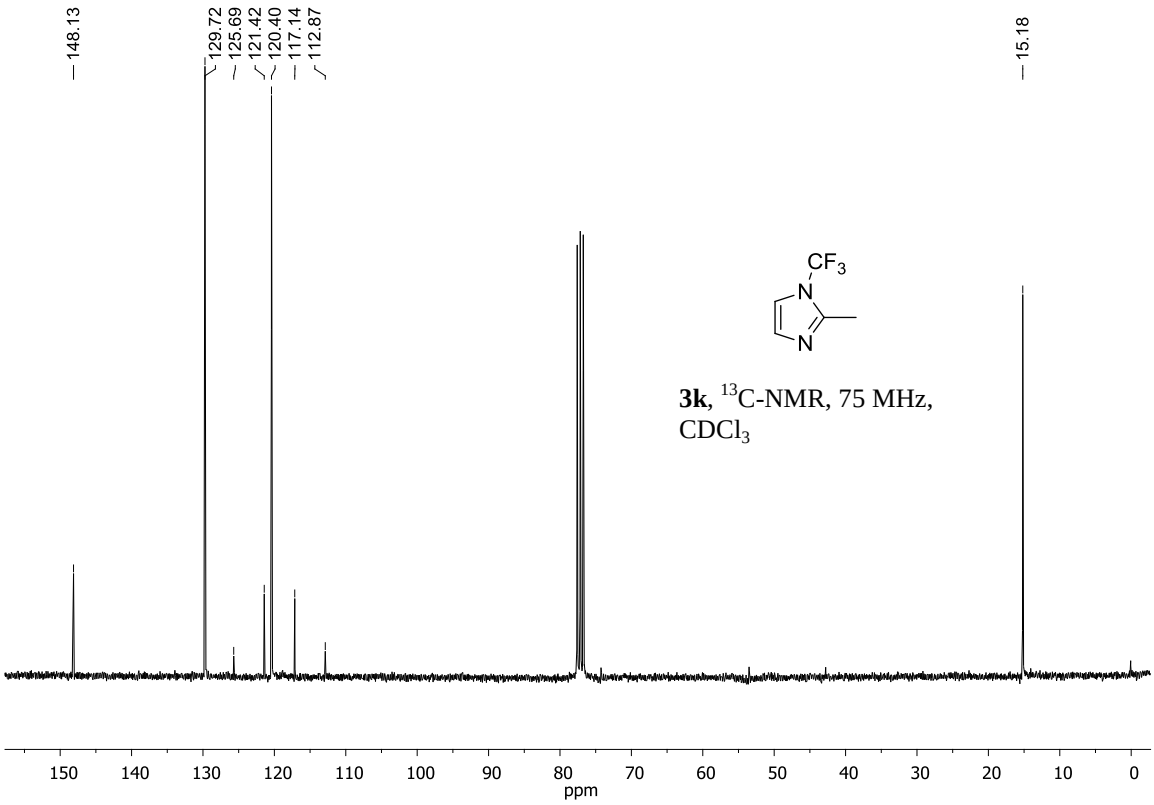
3j, ^{1}H-NMR, 300 MHz, $CDCl_3$



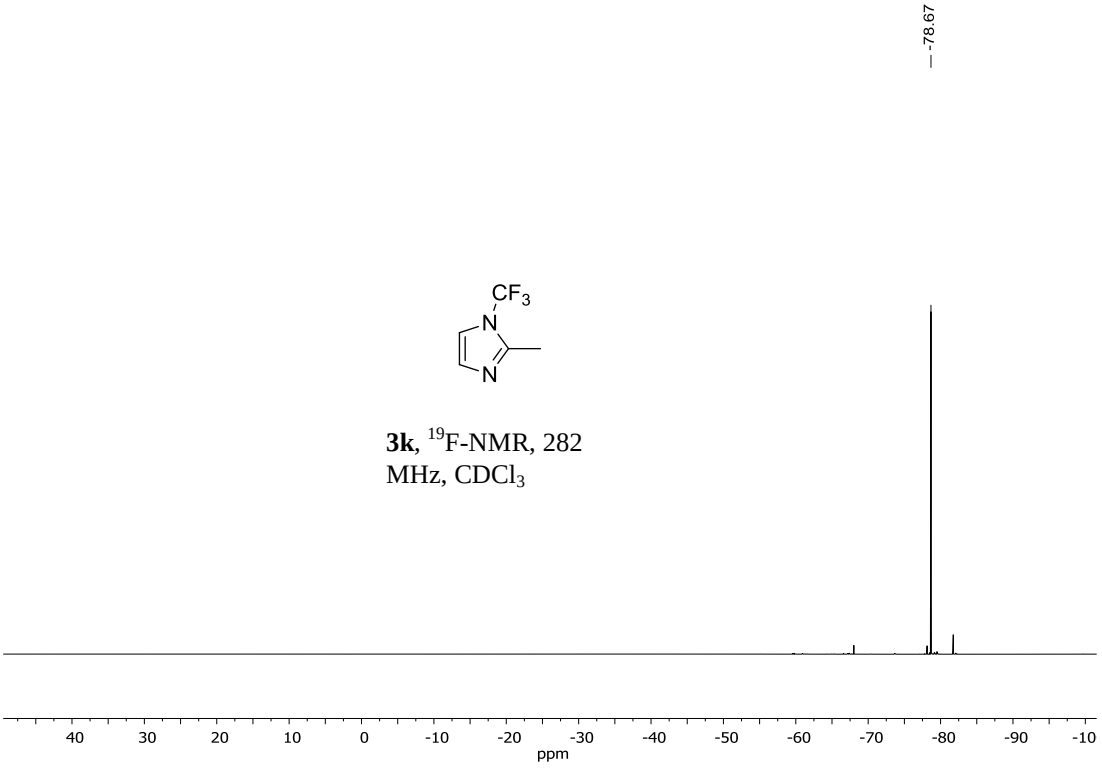
3j, ^{13}C-NMR, 75 MHz, $CDCl_3$



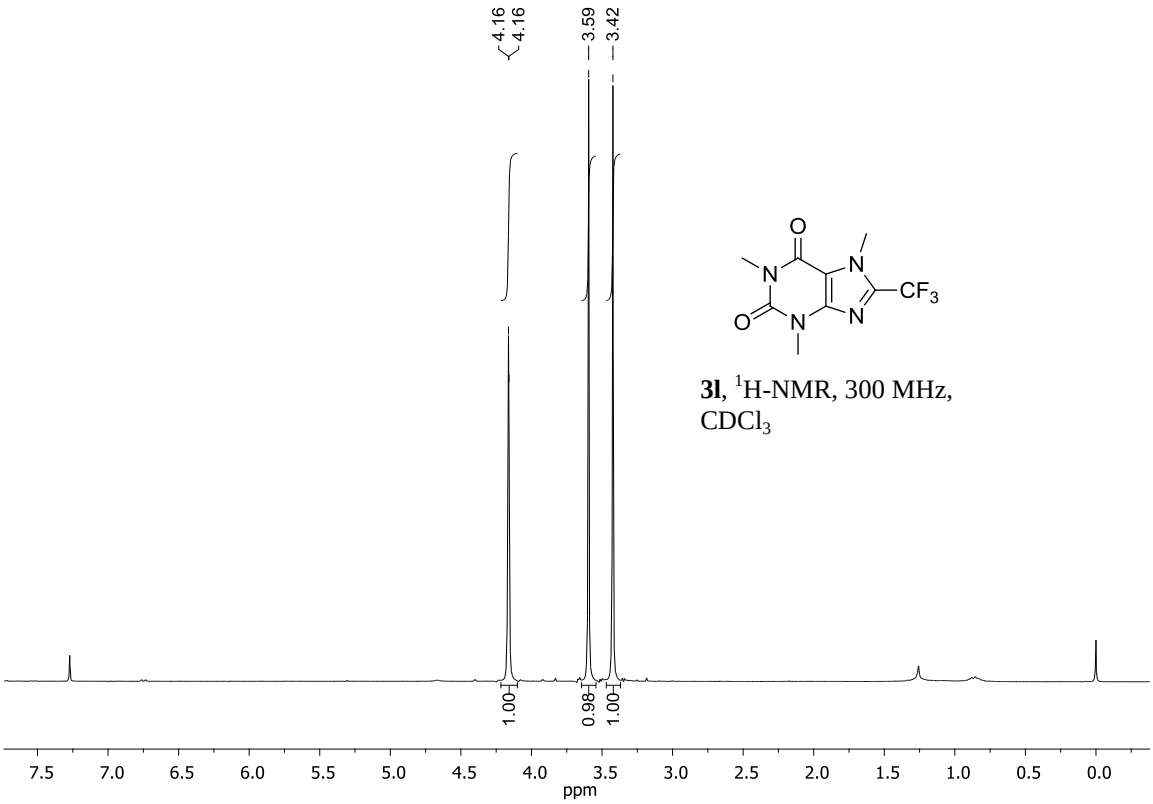
3k, ^{1}H-NMR, 300 MHz, $CDCl_3$



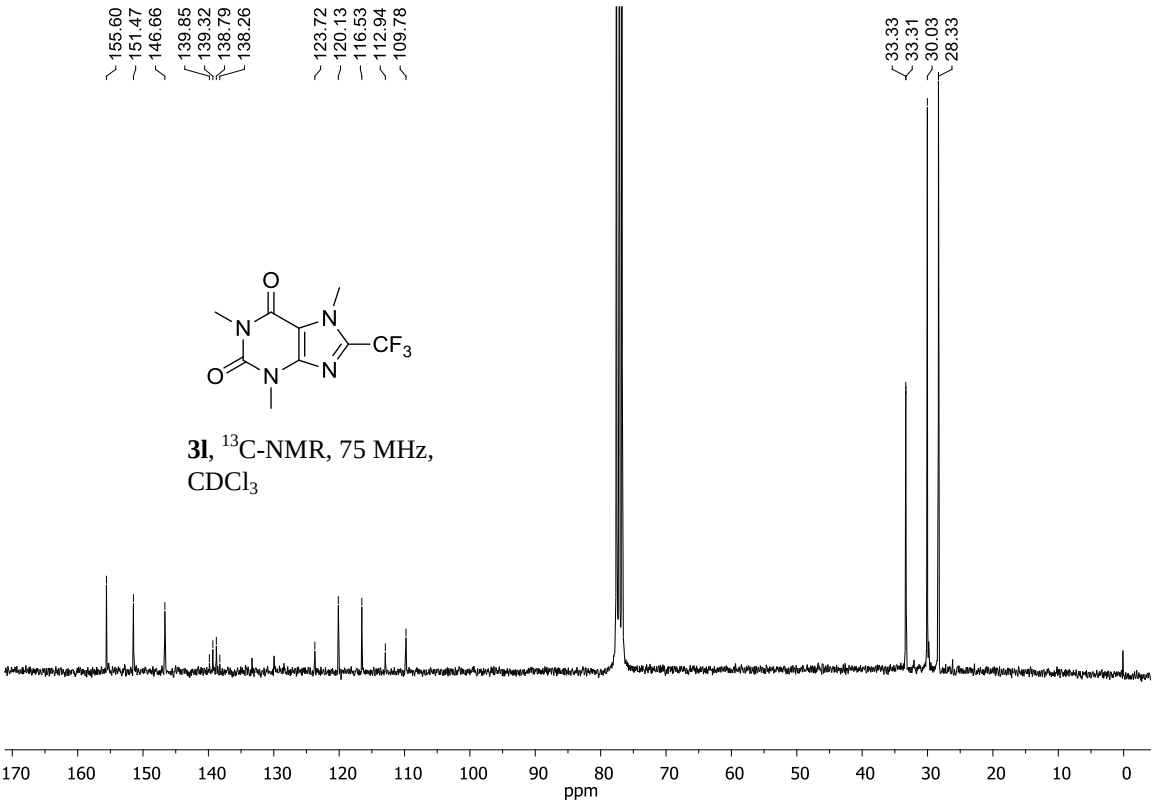
3k, ^{13}C-NMR, 75 MHz, $CDCl_3$



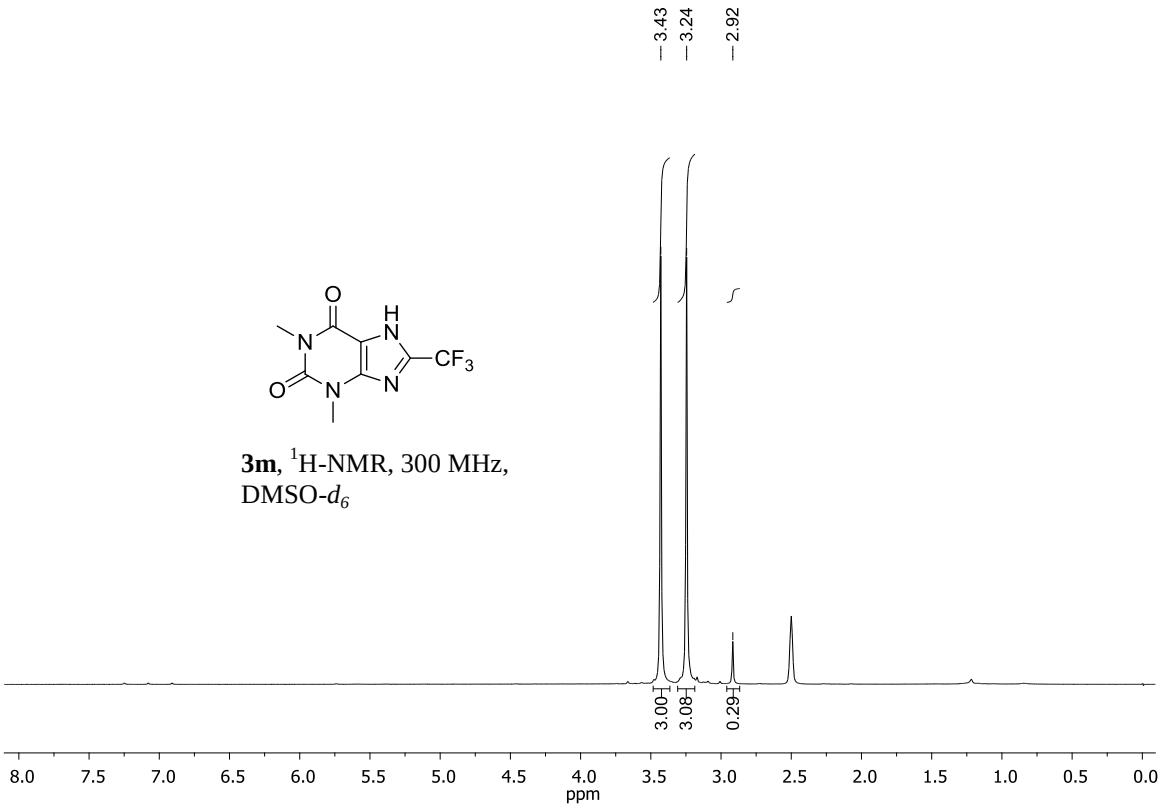
3k, ^{19}F-NMR, 282 MHz, $CDCl_3$



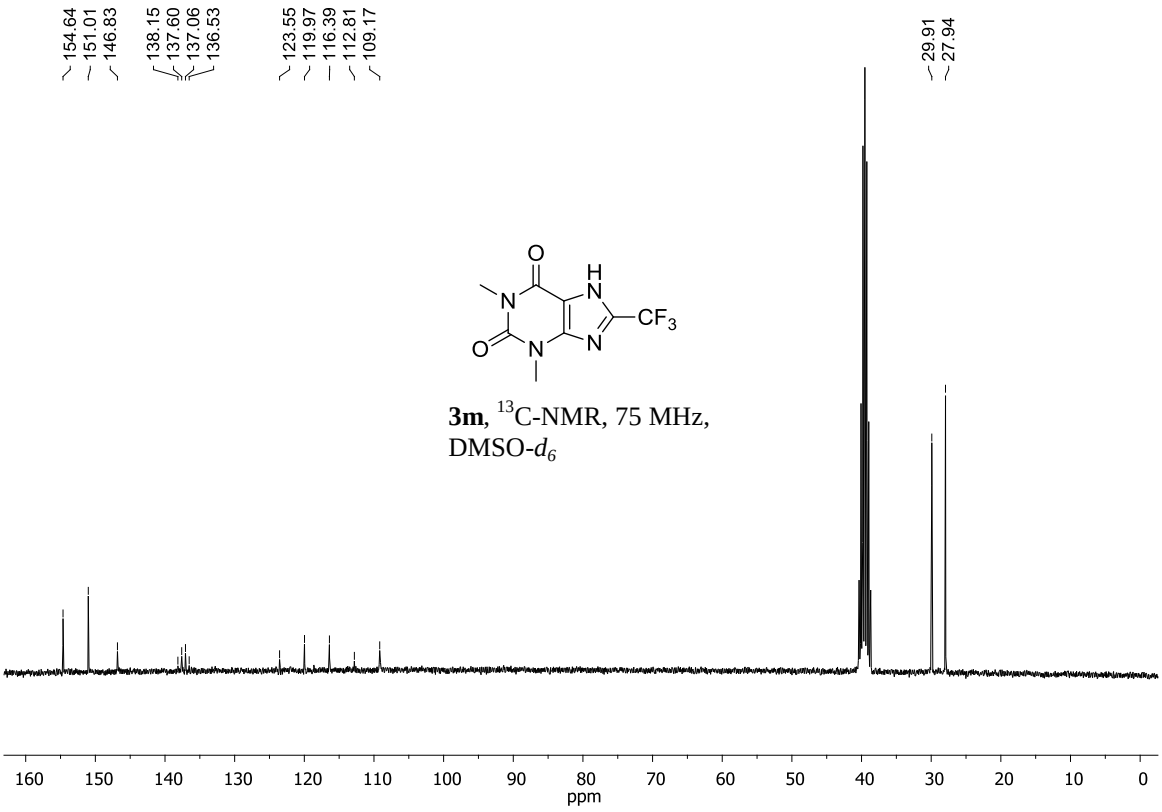
3l, ^{1}H-NMR, 300 MHz, $CDCl_3$



3l, ^{13}C-NMR, 75 MHz, $CDCl_3$



3m, ^{1}H-NMR, 300 MHz, DMSO-d_6



3m, ^{13}C-NMR, 75 MHz, DMSO-d_6