Electronic Supplementary Information

Catalytic Activation of a Single C-F bond in Trifluoromethyl Arenes

Hester Dang, Aaron M. Whittaker, Gojko Lalic*

correspondence to: lalic@chem.washington.edu

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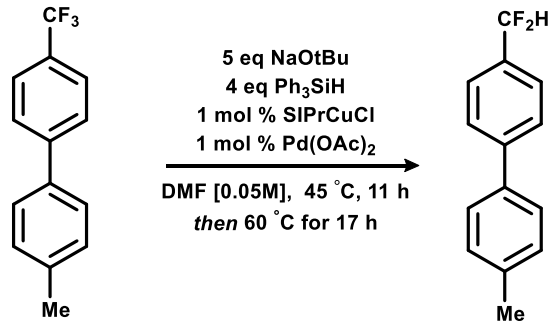
1. *General Information*

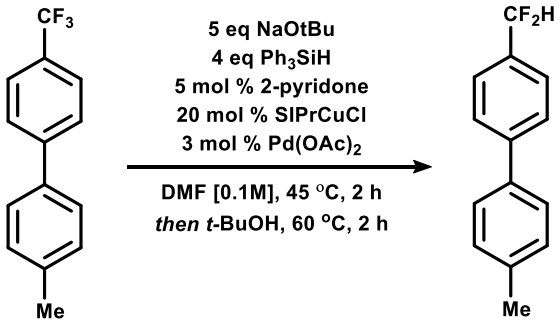
All reactions were performed in a nitrogen-filled glovebox (Nexus II from Vacuum Atmospheres). Column chromatography was performed using a Biotage Iso-1SV flash purification system with silica gel from Agela Technologies Inc. (60Å, 40-60 μm, 230-400 mesh) or activated alumina purchased from Sigma Aldrich (CAS# 344-28-1). ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker AV-300 or AV-500 spectrometer. ^{1}H NMR chemical shifts (δ) are reported in parts per million (ppm) downfield of TMS and are referenced relative to the residual solvent peak ($CDCl_3$ (7.26 ppm), C_6D_6 (7.16 ppm), or CD_2Cl_2 (5.32 ppm)). ^{13}C chemical shifts are reported in parts per million downfield of TMS and are referenced to the carbon resonance of the solvent ($CDCl_3$: δ 77.2 ppm, C_6D_6: δ 128.1 ppm, CD_2Cl_2: δ 54.0 ppm). Data are represented as follows: chemical shift, multiplicity (s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, p = pentet, h = heptet m = multiplet), integration, and coupling constants in Hertz (Hz). Mass spectra were collected on a JEOL HX-110 Mass Spectrometer, a Bruker Esquire 1100 Liquid Chromatograph – Ion Trap Mass Spectrometer, or a Hewlett Packard 5971A gas chromatograph Mass Spectrometer. GC analysis was performed on a Shimadzu GC-2010 instrument with a flame ionization detector and a SHRXI-5MS column (15 m, 0.25 mm inner diameter, 0.25 μm film thickness). The following temperature program was used: 2 min @ 60 °C, 13 °C/min to 160 °C, 30 °C/min to 250 °C, 5.5 min @ 250 °C. Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum RX I spectrometer. IR peak absorbencies are represented as follows: s = strong, m = medium, w = weak, br = broad.

Materials: DriSolv™ DMF (EMD Millipore) was stored over activated 3Å molecular sieves in the glovebox and used without any further purification. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. Common commercial reagents such as triphenylsilane, sodium *tert*-butoxide, potassium trimethylsilanoate, palladium(II) acetate, and copper (II) fluoride were purchased from Sigma-Aldrich Co., VWR International, LLC., TCI America, Gelest, or STREM Chemicals, Inc and was used without further purification.

2. *Reaction Development*



Procedure A (General procedure used in experiments shown in Table 1, entries 2 and 3): In a glovebox, a dram vial was charged with a stir bar, sodium *t*-butoxide (24.0 mg, 0.25 mmol, 5.0 equiv), triphenylsilane (52.1 mg, 0.20 mmol, 4.0 equiv), trifluoromethyl arene **1** (11.8 mg, 0.05 mmol, 1.0 equiv), and internal standard (dodecane, 4.3 mg, 0.025 mmol, 0.05 equiv). 500 µL of DMF was added and reaction was allowed to stir at 25°C for 5 minutes. SIPrCuCl (when applicable, 0.2 mg, 0.001 mmol, 0.01 equiv from a 0.1 M stock solution) and palladium(II) acetate (when applicable, 0.1 mg, 0.001 mmol, 0.01 equiv. from a 0.1 M stock solution) was then deposited into a separate vial and diluted to a total volume of 500 µL with DMF and transferred into the reaction vessel. The reaction vessel was then sealed and temperature was elevated and maintained at 45 °C until full conversion of substrate was observed by GC analysis. When conversion of starting substrate was observed to have stopped or was completed, the temperature was increased to 60 °C and the progress of the reaction was monitored using GC analysis.



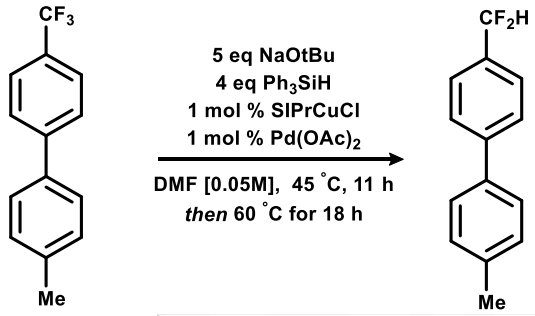
Procedure B (General procedure used in experiments shown in Table 1 (entries 4 and 5), Table 2, and Figs. 2 and 3): In a glovebox, a dram vial was charged with a stir bar, sodium *t*-butoxide (24.0 mg, 0.25 mmol, 5.0 equiv), trifluoromethyl arene **1** (11.8 mg, 0.05 mmol, 1.0 equiv), internal standard (dodecane, 4.3 mg, 0.025 mmol, 0.05 equiv), 2-pyridone (where applicable, 0.2 mg, 0.003 mmol, 0.05 equiv from a 0.15 M stock solution), SIPrCuCl (4.9 mg, 0.010 mmol, 0.20 equiv) and palladium(II) acetate (0.3 mg, 0.002 mmol, 0.03 equiv. from a 0.17

M stock solution), and 168 µL DMF. After allowing the mixture to stir vigorously at 45 °C for 2 minutes, triphenylsilane (52.1 mg diluted up to 300 µL of solvent, 0.200 mmol, 4.0 equiv.) was added slowly (due to evolution of gas) to the stirring reaction mixture. The reaction vessel was then sealed and temperature was maintained at 45 °C until full conversion of substrate was observed with ^{19}F NMR analysis. *t*-BuOH (when applicable, 3.7 mg, 1.0 mmol, 1.0 equiv) was then added and the reaction temperature was increased to 60 °C. GC analysis was used to monitor reaction until completion. **Note* Pressure build up from gas production occurs as the starting substrate gets consumed in the reaction. When scaling up reaction, venting is necessary.*

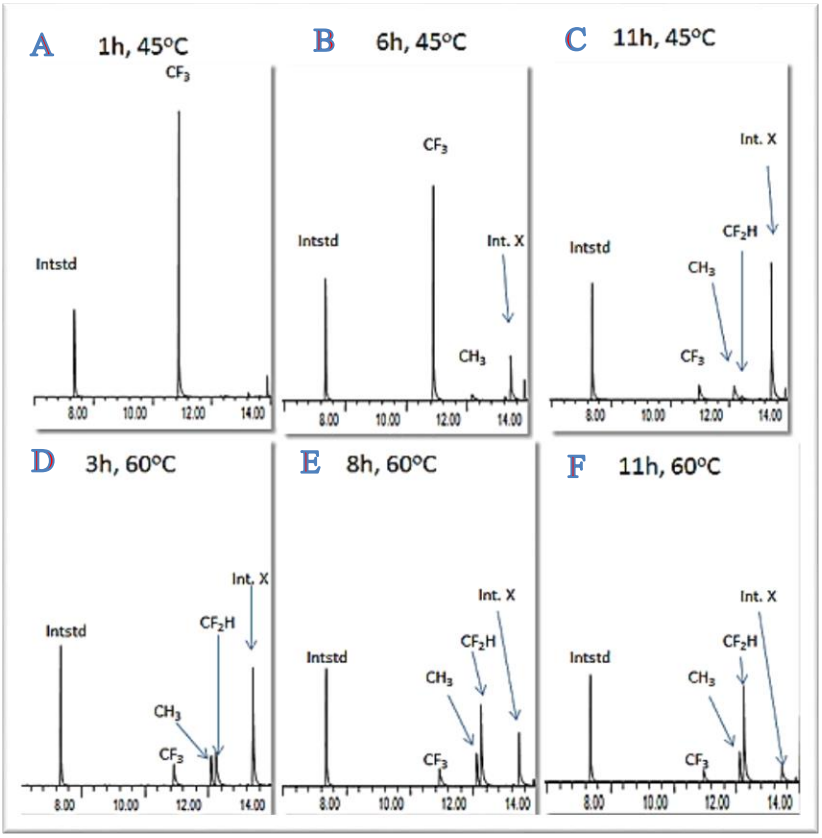
3. *Reaction Time Course*

Procedure A (as described in the Reaction Development Section) was used to set up the experiment shown in Figure S1. Reaction progress was monitored by taking aliquots for GC analysis every hour.

Figure S1 Time course experiment without addition of *t*-BuOH. Shown are results and GC traces of the reaction progress at selected time points. Abbreviations: Instd (Internal Standard), Int.X (Intermediate X.)

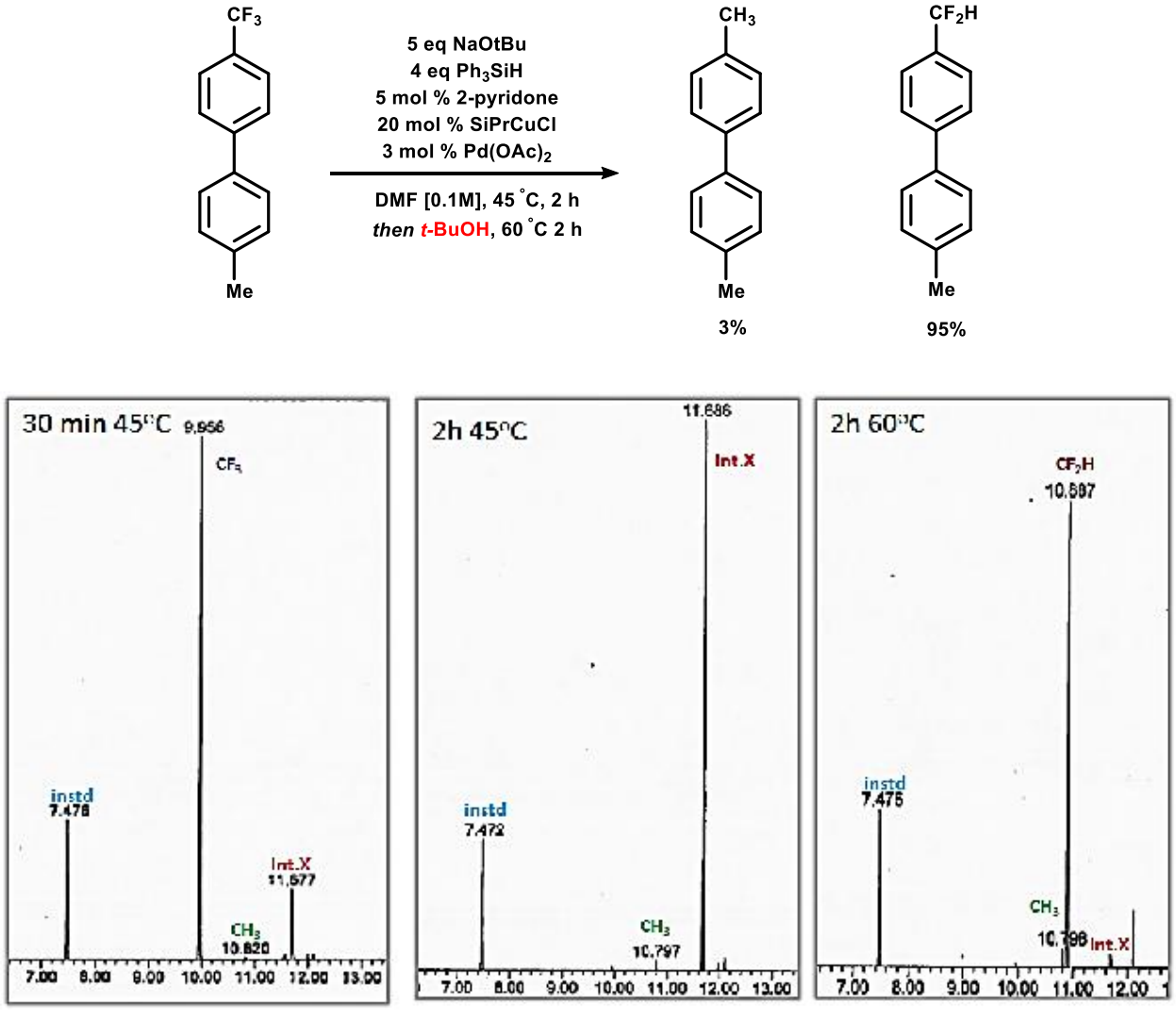


	Yield	
	11 h, 45 °C	18 h, 60 °C
Ar—CF_3 1	10%	10%
Ar—CH_3 2	11%	12%
Ar—CF_2H 3	4%	52%



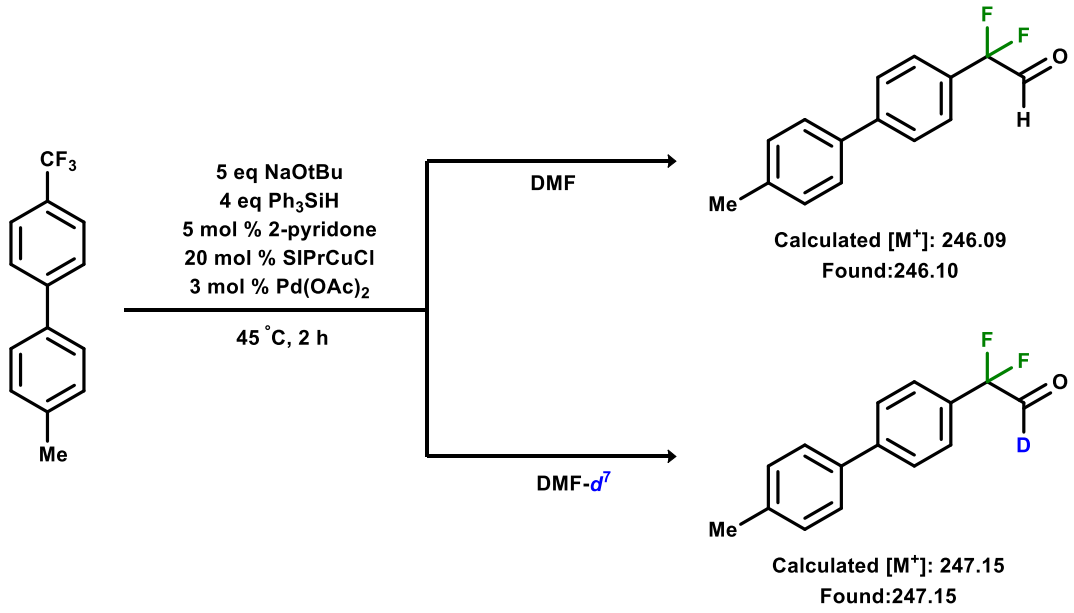
Procedure B (from Reaction Development Section) was used to set up the experiment shown in Figure S2. Reaction progress was monitored by taking aliquots for GC analysis.

Figure S2 Optimized reaction profile with addition of *t*-BuOH. Shown are the GC results of the reaction progress at selected time points.



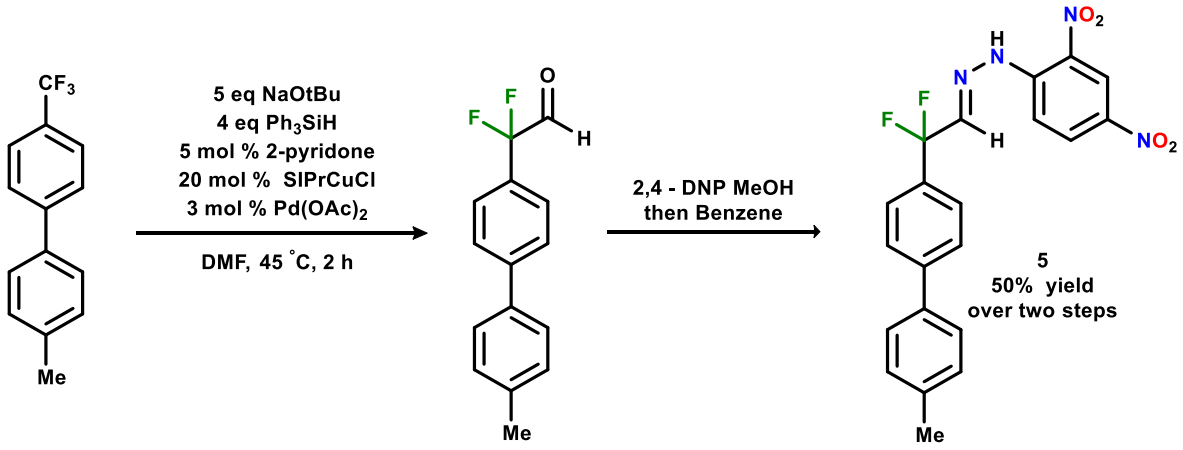
4. *Intermediate X: Observations, Isolation, 2, 4 – DNP derivative (5), and X-Ray data*

Figure S3 GC-MS observations on Intermediate X.



Isolation of Intermediate X.

Figure S4 Isolation and 2, 4 – DNP derivative of Intermediate X (0.50 mmol scale).

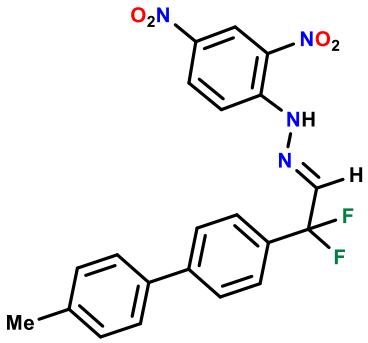


In a glovebox, a scintillation vial was charged with a stir bar, sodium *t*-butoxide (240.0 mg, 0.25 mmol, 5.0 equiv), trifluoromethyl arene **1** (118 mg, 0.50 mmol, 1.0 equiv), internal standard (dodecane, 43 mg, 0.25 mmol, 0.05 equiv), 2-pyridone (2.4 mg, 0.025 mmol, 0.05 equiv from a 0.1 M stock solution), SiPrCuCl (49.1 mg, 0.10 mmol, 0.20 equiv from a 0.1 M stock solution),palladium(II) acetate (3.0 mg, 0.015 mmol, 0.03 equiv from a 0.1 M stock solution), and

1680 µL DMF. After allowing the mixture to stir vigorously at 45 °C for 2 minutes, triphenylsilane (520.8 mg dissolved in 3000 µL of solvent, 0.20 mmol, 4.0 equiv) was added slowly (due to evolution of gas) to the stirring reaction mixture. The reaction vessel was then sealed and temperature was maintained at 45 °C until full conversion of substrate was observed by ^{19}F NMR analysis. Pressure builds up over time in the reaction vessel, and it was necessary to vent the vessel intermittently during the substrate conversion phase. Temperature was maintained at 45 °C until full conversion of substrate was observed. At this point, the reaction mixture was loaded directly onto a 100 g silica column and flushed with 0-35% diethyl ether in hexanes. GC analysis was used to determine the fractions that contained Intermediate X. Concentrated combined fractions down until 2 mL of solvent remained.

Synthesis of 2, 4-Dinitrophenylhydrazine (2, 4- DNP) derivative of Intermediate X.

To the 2 mL solution of intermediate X obtained after the column chromatography (see above) in a scintillation vial, was added 3 mL of freshly prepared 2, 4- DNP solution. 5 mL of benzene was then layered over the reaction mixture and allowed to sit overnight. The resulting orange crystals were collected via Buchner funnel filtration and washed with small portions of cold benzene. The final product was then dried under reduced pressure. *(Preparation of 2, 4-DNP solution: Suspend 2.0 g of 2, 4-dinitrophenylhydrazine in 100 mL of methanol. Cool mixture to 0 °C, and cautiously add 4.0 mL of concentrated sulphuric acid).*



(E)-1-{2,2-difluoro-2-[4-(4-methylphenyl)phenyl]ethylidene}-2-(2,4-dinitrophenyl)hydrazine (5): Compound **5** was isolated as an orange crystal, 107 mg, 50% overall yield from two steps shown in figure S4. ^{1}H NMR (300 MHz, C_6D_6) δ 10.29 (s, 1H), 8.67 (d, J = 2.5 Hz, 1H), 7.98 – 7.20 (m, 7H), 7.07 (t, J = 8.6 Hz, 3H), 6.32 (td, J = 5.0, 1.1 Hz, 1H), 2.15 (s, 3H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 145.1, 144.0, 140.1, 138.7, 137.4, 131.1, 130.7, 130.2, 127.5, 127.5, 126.8, 126.8, 126.7, 123.5, 118.2 (t, J = 37.7 Hz), 117.5, 108.9 (t, J = 26.6 Hz), 93.9 (t, J = 239.8 Hz), 21.4. ^{19}F NMR (282 MHz, C_6D6) δ -94.9 (d, J = 5.0 Hz).

X-Ray Crystallography Data

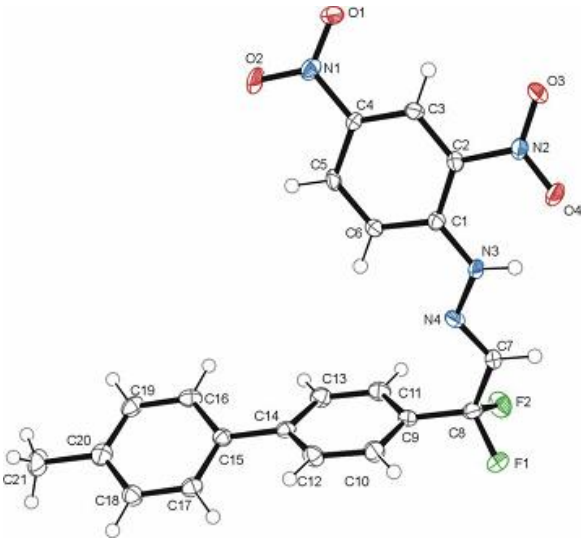
A yellow prism, measuring 0.32 x 0.03 x 0.03 mm^3 was mounted on a glass capillary with oil. Data was collected at -173°C on a Bruker APEX II single crystal X-ray diffractometer, Mo-radiation.

Crystal-to-detector distance was 40 mm and exposure time was 240 seconds per degree for all sets. The scan width was 1.0°. Data collection was 99.8% complete to 24.76°. A total of 37,909 (merged) reflections were collected covering the indices, h = -28 to 28, k = -7 to 7, l = -29 to 29. 3,300 reflections were symmetry independent and the R_{int} = 0.141 indicated that the data was less than average quality (average quality 0.07). Indexing and unit cell refinement indicated an orthorhombic lattice. The space group was found to be P b c a (No.61).

The data was integrated and scaled using SAINT, SADABS within the APEX2 software package by Bruker.[1]
Solution by direct methods (SHELXS[2], SIR97[3]) produced a complete heavy atom phasing model consistent with the proposed structure. The structure was completed by difference Fourier synthesis with SHELXL97.[4],[5] Scattering factors are from Waasmair and Kirfel.[6] Hydrogen atoms were placed in geometrically idealised positions and constrained to ride on their parent atoms with C---H distances in the range 0.95-1.00 Angstrom. Isotropic thermal parameters U_{eq} were fixed such that they were 1.2U_{eq} of their parent atom Ueq for CH's and 1.5U_{eq} of their parent atom U_{eq} in case of methyl groups. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares.

A close bond distance between O4 and itself related through symmetry of 2.60 Å is noticed. This is due to hydrogen bond interactions with the hydrogen of N3.

Figure S5 ORTEP of the structure with thermal ellipsoids at the 50% probability level.[7]



Crystal data and structure refinement for Intermediate X.

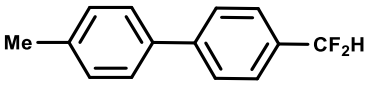
Identification code	hd_bam_0ma	
Empirical formula	C21 H16 F2 N4 O4	
Formula weight	426.38	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P b c a	
Unit cell dimensions	a = 24.4634(19) Å	□= 90°.
	b = 6.1982(4) Å	□= 90°.
	c = 25.443(2) Å	□ = 90°.
Volume	3857.8(5) $Å^3$	
Z	8	
Density (calculated)	1.468 Mg/m^3	
Absorption coefficient	0.117 mm^{-1}	
F(000)	1760	
Crystal size	0.32 x 0.03 x 0.03 mm^3	
Theta range for data collection	1.80 to 24.76°.	
Index ranges	-28<=h<=28, -7<=k<=7, -29<=l<=29	
Reflections collected	37909	
Independent reflections	3300 [R(int) = 0.1414]	
Completeness to theta = 24.76°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9965 and 0.9636	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3300 / 0 / 281	
Goodness-of-fit on F^2	1.003	
Final R indices [I>2sigma(I)]	R1 = 0.0487, wR2 = 0.0925	
R indices (all data)	R1 = 0.1047, wR2 = 0.1112	
Largest diff. peak and hole	0.283 and -0.254 $e.Å^{-3}$	

5. *Representative Procedure for Catalytic Mono-Defluorination (0.5 mmol scale)*

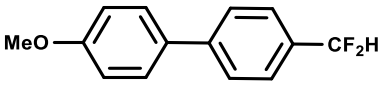
In a nitrogen filled glovebox, a scintillation vial was charged with a stir bar, potassium trimethyl siloxide (449.0 mg, 7.0 equiv 4.0 mmol), trifluoromethyl arene substrate **1** (118.2 mg, 0.5 mmol,

1.0 equiv), 2-pyridone (2.4 mg, 0.025 mmol 0.05 equiv), copper(II) fluoride (10.2 mg, 0.1 mmol, 0.2 equiv) and DMF was added to obtain a reaction volume of 2 mL. The resulting mixture was stirred at 45 °C until homogenized, and palladium acetate (3.4 mg, 0.015 mmol, 0.03 equiv) was added. After allowing the resulting mixture to stir vigorously at 45 °C for an additional 10 minutes, triphenylsilane (651 mg, 2.5 mmol, 5.0 equiv) dissolved in 3 mL of DMF was added slowly (evolution of a gas). Pressure builds over time in the reaction vessel, and it was necessary to vent the vessel intermittently during the substrate conversion phase. Temperature was maintained at 45 °C until full conversion of substrate was observed by ^{19}F NMR. When conversion of starting substrate was completed, *t*-BuOH (74.1mg, 2.0 equiv 1.0 mmol) was added. Reaction mixture was placed at 60 °C and progress of the reaction was monitored using GC analysis. When full conversion of the intermediate was observed, the reaction mixture was passed through a pad of silica gel using EtOAc as an eluent. The crude mixture was concentrated under reduced pressure and purified by column chromatography using silica gel.

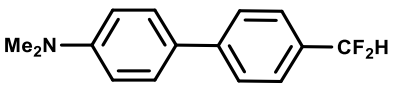
6. *Characterization Data for Difluoromethylarene Products*



1-[4-(difluoromethyl)phenyl]-4-methylbenzene (3): Isolated as a white solid (mp 129-131 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 – 7.26 (m, 8H), 6.69 (t, *J* = 56.6 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.7, 137.9, 137.4, 133.04 (t, *J* = 22.3 Hz), 129.8, 127.3, 127.2, 126.12 (t, *J* = 5.6 Hz), 114.94 (t, *J* = 238.5 Hz), 21.2. ^{19}F NMR (282 MHz, $CDCl_3$) δ -111.11 (d, *J* = 56.5 Hz). GC/MS calculated for $[M]^+$ 218.09, found 218.10. FTIR (neat, cm^{-1}): 3047 (m), 2906 (m), 1609 (w), 1495 (w), 1372 (m), 1264 (s), 1023 (s).

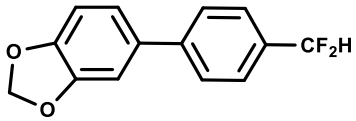


1-[4-(difluoromethyl)phenyl]-4-methoxybenzene (6): Isolated as a white solid (mp 113-114 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 – 7.47 (m, 6H), 7.00 (d, *J* = 8.3 Hz, 2H), 6.69 (t, *J* = 56.6 Hz, 1H), 3.87 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.7, 143.3, 132.6 (t, *J* = 22.4 Hz), 132.6, 128.3, 126.9, 126.0 (t, *J* = 6.0 Hz), 114.8 (t, *J* = 238.3 Hz), 114.4, 55.4. ^{19}F NMR (282 MHz, C_6D6) δ -110.08 (d, *J* = 56.4 Hz). GC/MS calculated for $[M]^+$ 234.09, found 234.10. FTIR (neat, cm^{-1}): 3000 (w), 2972 (s), 2883 (m), 1661 (w), 1467 (m), 1379 (s), 1309 (m), 1161 (s), 1130 (s).

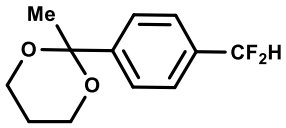


N,N-dimethyl-4-[4-(difluoromethyl)phenyl]aniline (7): Isolated as an off-white solid (mp 191-192 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 – 7.40 (m, 6H), 6.97 – 6.26 (m, 3H), 3.02 (s, 6H). ^{13}C NMR (126 MHz, THF) δ 151.6, 144.8 (t, *J* = 2.1 Hz), 133.2 (t, *J* = 22.4 Hz), 128.6, 128.4, 126.9 (t, *J* = 6.0 Hz), 126.9, 116.4 (t, *J* = 236.7 Hz), 113.6, 40.6. ^{19}F NMR (282 MHz, CD_3CN) δ -111.24 (d, *J* = 56.4 Hz). GC/MS calculated for $[M]^+$ 247.12, found

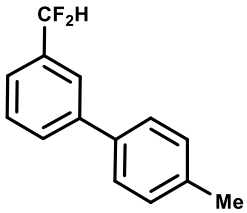
247.10. FTIR (neat, cm^{-1}): 3028 (w), 2972 (s), 2931 (m), 2884 (m), 1658 (w), 1465 (m), 1380 (s), 1162 (s), 1129 (s).



5-[4-(difluoromethyl)phenyl]-2H-1,3-benzodioxole (8): Isolated as a white solid (mp 77-79 °C). ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.7 – 7.4 (m, 4H), 7.2 – 7.0 (m, 2H), 6.9 – 6.9 (m, 1H), 6.7 (t, *J* = 56.5 Hz, 1H), 6.0 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.3, 147.6, 143.4, 134.5, 132.9 (t, *J* = 22.8 Hz), 127.1, 126.0 (t, *J* = 6.1 Hz), 120.9, 114.8 (t, *J* = 238.6 Hz), 108.7, 107.7, 101.3. ^{19}F NMR (282 MHz, C_6D6) δ -110.24 (d, *J* = 56.4 Hz). GC/MS calculated for $[M]^+$ 248.06, found 248.10. FTIR (neat, cm^{-1}): 3000 (w), 2971 (s), 2884 (m), 1656 (w), 1465 (m), 1379 (m), 1162 (s), 1129 (s).



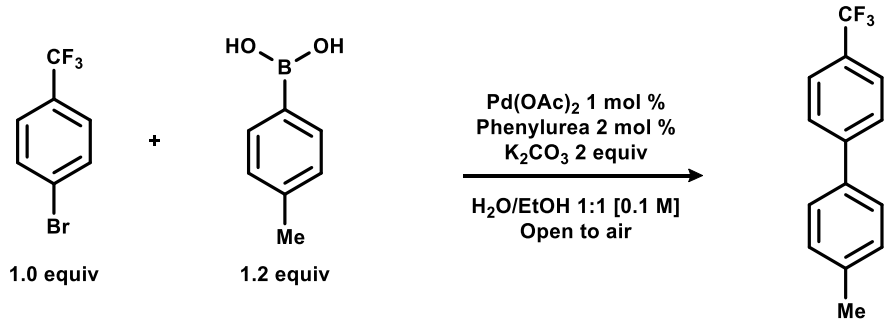
2-[4-(difluoromethyl)phenyl]-2-methyl-1,3-dioxane (9): Isolated as a colorless oil. ^{1}H NMR (300 MHz, Benzene-d_6) δ 7.48 – 7.23 (m, 4H), 6.19 (t, *J* = 56.4 Hz, 1H), 3.78 – 3.05 (m, 4H), 1.98 – 1.73 (m, 1H), 1.58 (s, 3H), 0.72 – 0.48 (m, 1H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 145.1, 134.0 (t, *J* = 22.4 Hz), 127.7, 126.3 (t, *J* = 6.0 Hz), 115.3 (t, *J* = 237.8 Hz), 100.4, 61.7, 32.4, 25.8. ^{19}F NMR (282 MHz, C_6D_6) δ -110.24 (d, *J* = 56.4 Hz). GC/MS calculated for $[M]^+$ 228.10, found 228.10. FTIR (neat, cm^{-1}): 3056 (w), 2963 (m), 2870 (m), 1617 (w), 1419(w), 1371 (s), 1240 (s), 1193 (s), 1146 (s), 1075 (s).



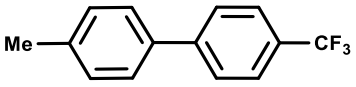
1-(difluoromethyl)-3-(4-methylphenyl)benzene (10): Isolated as a colorless oil. ^{1}H NMR (300 MHz, C_6D_6) δ 7.93 – 6.70 (m, 8H), 6.21 (t, *J* = 56.4, 56.4 Hz, 1H), 2.14 (s, 3H). ^{13}C NMR (126 MHz, CD_3CN) δ 142.40, 138.90, 137.87, 135.97 (t, *J* = 22.1 Hz), 130.6, 130.4, 130.2, 127.8, 125.1 (t, *J* = 6.0 Hz), 124.9 (t, *J* = 6.3 Hz), (peak which completes triplet with peaks 116.2 and 114.3 is hidden under solvent signal) 116.2, 114.3, 21.1. ^{19}F NMR (282 MHz, C_6D6) δ -110.58 (d, *J* = 56.1 Hz). GC/MS calculated for $[M]^+$ 218.19, found 218.10. FTIR (neat, cm^{-1}): 3028 (m), 2960 (m), 2923 (m), 1612 (w), 1518 (m), 1485 (s), 1369 (s), 1197 (s), 1030 (s).

7. *Synthesis of Trifluoromethyl Arenes*

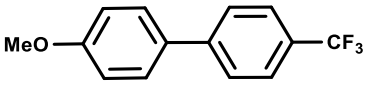
Figure S6 Suzuki coupling for the synthesis of trifluoromethyl arene substrates.



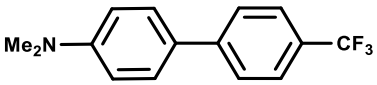
Syntheses of the following compounds were done according to a known literature procedure.[8]



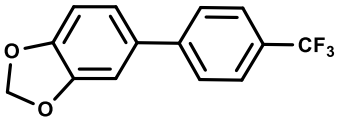
1-methyl-4-[4-(trifluoromethyl)phenyl]benzene (1): is a known compound and spectral data match the reported literature values.[9]



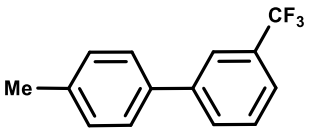
1-methoxy-4-[4-(trifluoromethyl)phenyl]benzene (S1): is a known compound and spectral data match the reported literature values.[45]



N,N-dimethyl-4-[4-(trifluoromethyl)phenyl]aniline (S2): is a known compound and spectral data match the reported literature values.[10]



5-[4-(trifluoromethyl)phenyl]-2H-1,3-benzodioxole (S3): is a known compound and spectral data match the reported literature values.[11]

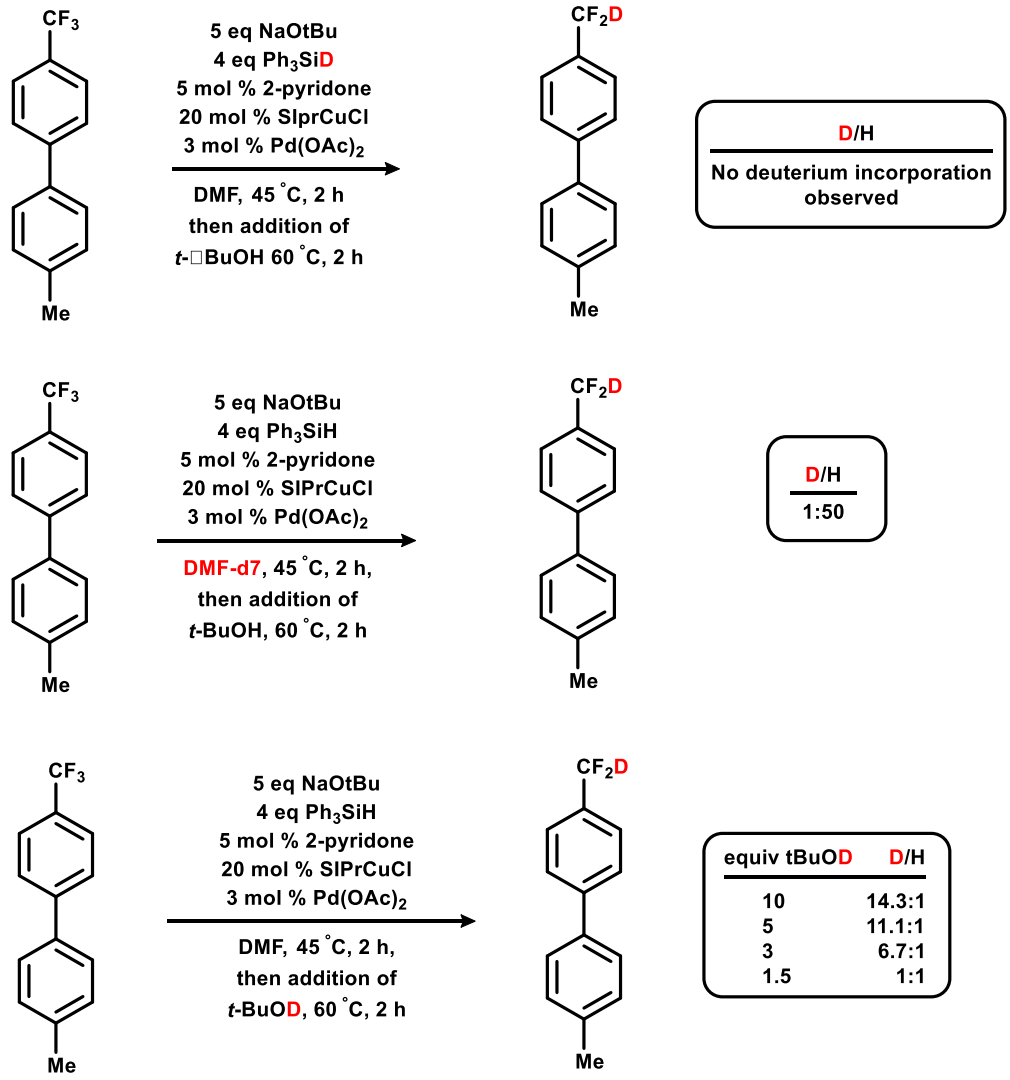


1-(4-methylphenyl)-3-(trifluoromethyl)benzene (S4): spectral data match the reported literature values.[12]

8. *Deuterium Incorporation Experiments, 0.05 mmol scale, 0.1 M.*

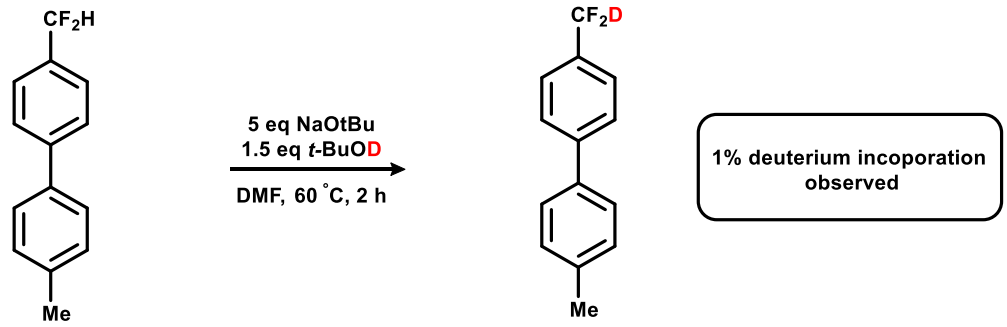
Procedure B (as a described in the reaction development section) was used to set up deuterium labeling experiments shown in Figure S7.

Figure S7 Deuterium incorporation using various deuterated reagents.



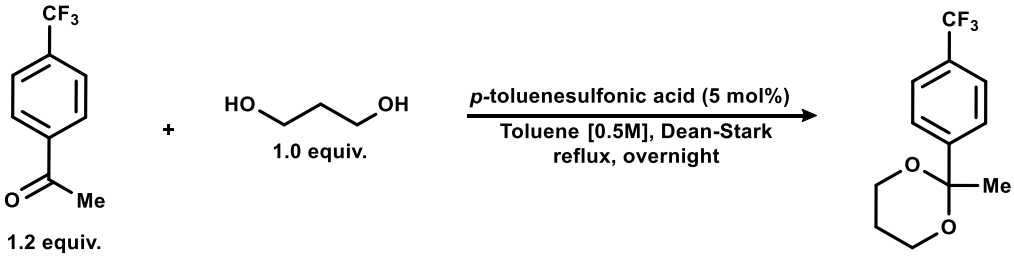
A control experiment, figure S8, was performed to eliminate the possibility that the deuterium incorporation was a result of the base induced H/D exchange after the formation of the product. The following procedure was used: In a glovebox, a dram vial was charged with a stir bar, sodium *t*-butoxide (24.0 mg, 0.25 mmol, 5.0 equiv.), difluoromethyl arene (10.9 mg, 0.05 mmol, 1.0 equiv.), *t*-BuOD (5.6 mg, 0.75 mmol, 1.5 equiv), and 500 µL of DMF. The reaction temperature was maintained at 60 °C for 2 hours. At 2 hours, a 100 µL aliquot was diluted with 400 µL dry C_6D_6 and transferred into a J. Young tube for ^{19}F NMR analysis.

Figure S8 Control reaction for deuterium exchange.

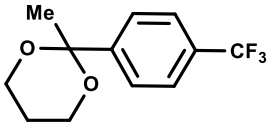


9. *Synthesis of 2-methyl-2-[4-(trifluoromethyl)phenyl]-1,3-dioxane and SIPrCuCl*

Figure S9 Synthesis of 2-methyl-2-[4-(trifluoromethyl)phenyl]-1,3-dioxane.



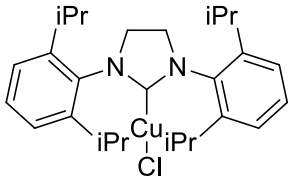
To a one neck 100 mL round bottom flask was added the ketone substrate (3.7 g, 1.2 equiv, 20 mmol) and diluted with 40 mL of toluene (0.50 M). After cooling to 0 °C, 1,3-propanediol (1.9 mL, 1.0 equiv, 16.7 mmol) and *p*-toluenesulfonic acid (0.16 g, 0.05 equiv, 0.83 mmol) was added and the reaction vessel was fitted with a dean-stark apparatus. Reaction mixture was heated to a reflux overnight. After completion of the reaction, the reaction mixture was filtered through a plug of deactivated silica gel (doped with triethylamine). Silica plug was eluted with 10% ethyl acetate in hexanes solvent mixture. The solvent was then removed under reduced pressure. Product purification by flash chromatography affords (3.6 g, 74%) pale yellow oil, which solidifies overtime into a translucent pale yellow solid.



2-methyl-2-[4-(trifluoromethyl)phenyl]-1,3-dioxane **(S5)**: Isolated as a translucent pale yellow solid. ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.22 (d, J = 8.1 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 3.67 – 2.97 (m, 4H), 1.81 – 1.46 (m, 1H), 0.85 – 0.77 (m, 1H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 146.9,130.4 (q, J = 32.2 Hz), 128.2, 126.4 (q, J = 3.8 Hz), 125.1 (q, J = 271.8 Hz), 100.7, 62.0, 32.6, 26.2. ^{19}F NMR (471 MHz, CD_2Cl_2) δ -62.86. GC/MS calculated for $[M]^+$ 246.09,

found 246.20. FTIR (neat, cm^{-1}): 3059 (w), 2967 (m), 2870 (m), 1618 (m), 1409 (m), 1327 (s), 1239 (s). 1125 (s).

Synthesis of SIPrCuCl:



SIPrCuCl (S6): In a nitrogen-filled glovebox, a 100-mL round bottom flask was charged with 1,3-bis(2,6-di-iso-propylphenyl)imidazolinium chloride (3.0g, 1.00 equiv, 7.0 mmol), sodium *t*-butoxide (682 mg, 1.01 equiv, 7.1 mmol), and 30 mL THF. The mixture was allowed to stir at 23 °C for 15 minutes then CuCl (696 mg, 1.00 equiv, 7.0 mmol) was added. After 16 hours, the reaction mixture was removed from the glovebox and concentrated under reduced pressure. The white-green solid was purified by silica plug filtration using dry DCM as an eluent. Upon removal of the solvent under reduced pressure, 2.8 g of SIPrCuCl was obtained as a white solid, 80% yield. This compound has been previously characterized.[13]

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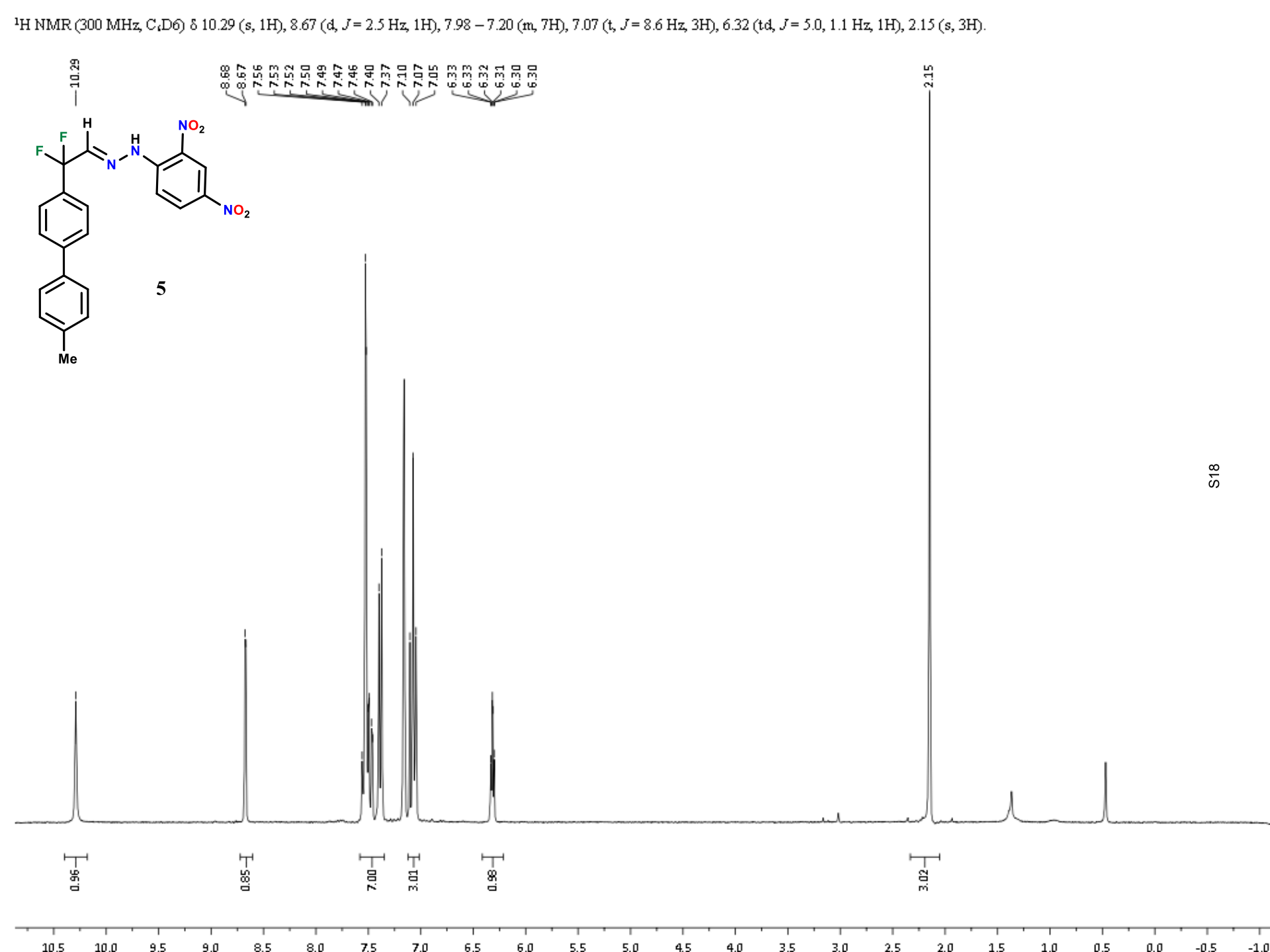
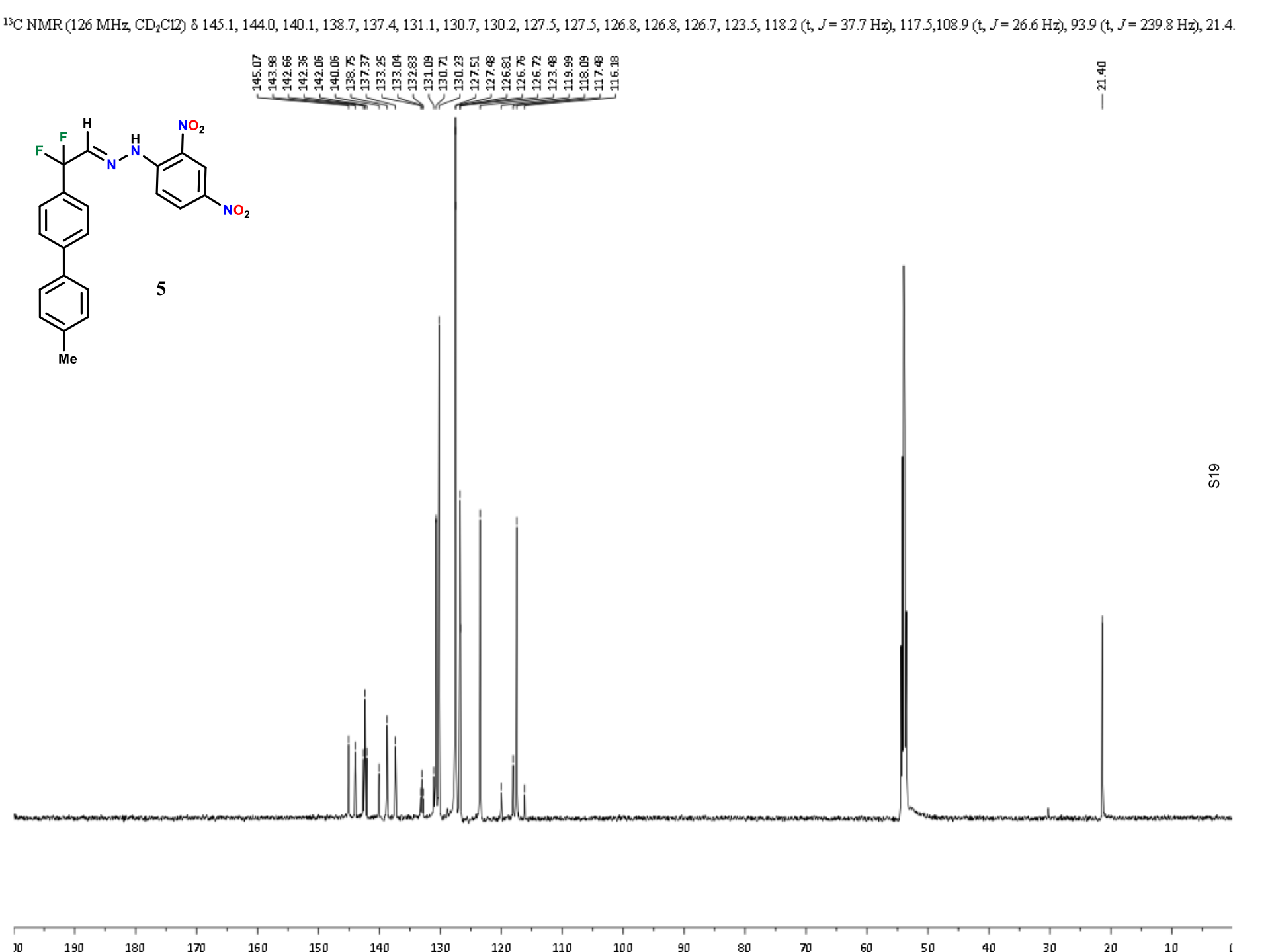
13. Thomson, J.E. et al., *J. Org. Chem.* **2008**, *73*, 2784-2791.

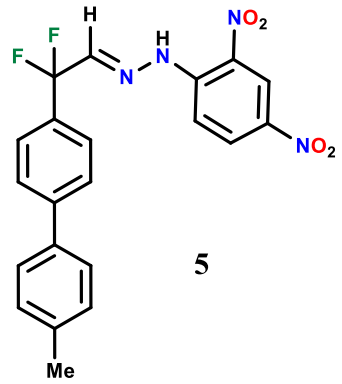
^{1}H NMR (300 MHz, C_6D_6) δ 10.29 (s, 1H), 8.67 (d, J = 2.5 Hz, 1H), 7.98 – 7.20 (m, 7H), 7.07 (t, J = 8.6 Hz, 3H), 6.32 (td, J = 5.0, 1.1 Hz, 1H), 2.15 (s, 3H).



^{13}C NMR (126 MHz, CD_2Cl_2) δ 145.1, 144.0, 140.1, 138.7, 137.4, 131.1, 130.7, 130.2, 127.5, 127.5, 126.8, 126.8, 126.7, 123.5, 118.2 (t, *J* = 37.7 Hz), 117.5,108.9 (t, *J* = 26.6 Hz), 93.9 (t, *J* = 239.8 Hz), 21.4.

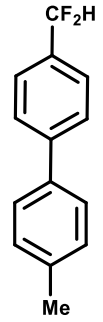


^{19}F NMR (282 MHz, C_6D_6) δ -94.9 (d, J = 5.0 Hz).



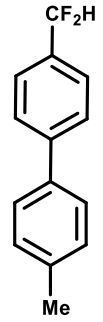
5

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 – 7.26 (m, 8H), 6.69 (t, J = 56.6 Hz, 1H), 2.41 (s, 3H).



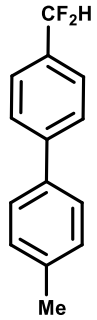
3

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.7, 137.9, 137.4, 133.04 (t, *J* = 22.3 Hz), 129.8, 127.3, 127.2,126.12 (t, *J* = 5.6 Hz),114.94 (t, *J* = 238.5 Hz), 21.2.



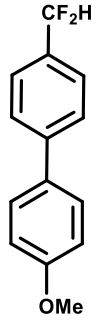
3

^{19}F NMR (282 MHz, $CDCl_3$) δ -111.11 (d, J = 56.5 Hz).



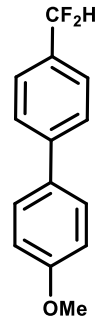
3

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 – 7.47 (m, 6H), 7.00 (d, *J* = 8.3 Hz, 2H), 6.69 (t, *J* = 56.6 Hz, 1H), 3.87 (s, 3H).



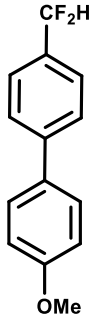
6

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.7, 143.3, 132.6 (t, J = 22.4 Hz), 132.6, 128.3, 126.9, 126.0 (t, J = 6.0 Hz), 114.8 (t, J = 238.3 Hz), 114.4, 55.4.



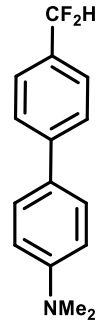
6

^{19}F NMR (282 MHz, C_6D_6) δ -110.08 (d, J = 56.4 Hz).



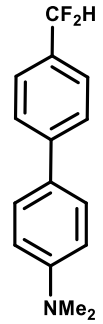
6

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 – 7.40 (m, 6H), 6.97 – 6.26 (m, 3H), 3.02 (s, 6H).



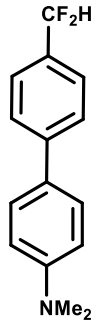
7

^{13}C NMR (126 MHz, THF) δ 151.6, 144.8 (t, J = 2.1 Hz), 133.2 (t, J = 22.4 Hz), 128.6, 128.4, 126.9 (t, J = 6.0 Hz), 126.9, 116.4 (t, J = 236.7 Hz), 113.6, 40.6.



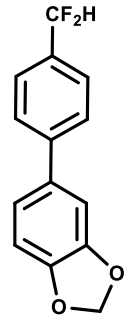
7

^{19}F NMR (282 MHz, CD_3CN) δ -111.24 (d, J = 56.4 Hz).



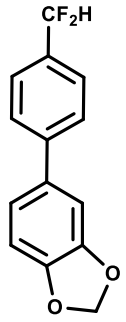
7

^{1}H NMR (500 MHz, CD_2Cl2) δ 7.7 – 7.4 (m, 4H), 7.2 – 7.0 (m, 2H), 6.9 – 6.9 (m, 1H), 6.7 (t, *J* = 56.5 Hz, 1H), 6.0 (s, 2H).



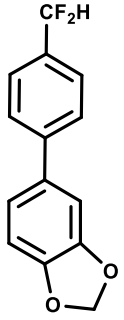
8

^{13}C NMR (126 MHz, $CDCl_3$) δ 148.3, 147.6, 143.4, 134.5, 132.9 (t, J = 22.8 Hz), 127.1, 126.0 (t, J = 6.1 Hz), 120.9, 114.8 (t, J = 238.6 Hz), 108.7, 107.7, 101.3.



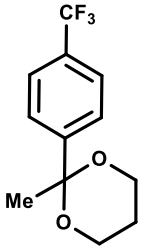
8

^{19}F NMR (282 MHz, C_6D_6) δ -110.24 (d, J = 56.4 Hz).



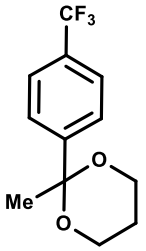
8

^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.22 (d, J = 8.1 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 3.67 – 2.97 (m, 4H), 1.81 – 1.46 (m, 1H), 0.85 – 0.77 (m, 1H).



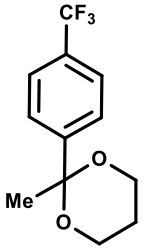
S5

^{13}C NMR (126 MHz, CD_2Cl2) δ 146.9,130.4 (q, J = 32.2 Hz), 128.2, 126.4 (q, J = 3.8 Hz), 125.1 (q, J = 271.8 Hz), 100.7, 62.0, 32.6, 26.2.



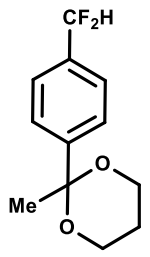
S5

^{19}F NMR (471 MHz, CD_2Cl_2) δ -62.86 .



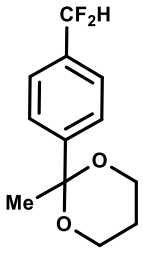
S5

^{1}H NMR (300 MHz, Benzene-d_6) δ 7.48 – 7.23 (m, 4H), 6.19 (t, J = 56.4 Hz, 1H), 3.78 – 3.05 (m, 4H), 1.98 – 1.73 (m, 1H), 1.58 (s, 3H), 0.72 – 0.48 (m, 1H).



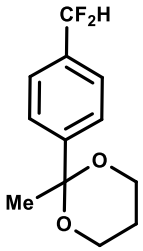
9

^{13}C NMR (126 MHz, CD_2Cl_2) δ 145.1, 134.0 (t, J = 22.4 Hz), 127.7, 126.3 (t, J = 6.0 Hz), 115.3 (t, J = 237.8 Hz), 100.4, 61.7, 32.4, 25.8.



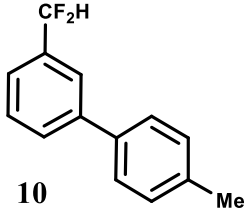
9

^{19}F NMR (282 MHz, C_6D_6) δ -110.24 (d, J = 56.4 Hz).



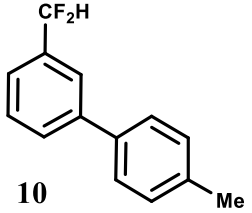
9

^{1}H NMR (300 MHz, C_6D_6) δ 7.93 – 6.70 (m, 8H), 6.21 (t, J = 56.4, 56.4 Hz, 1H), 2.14 (s, 3H).



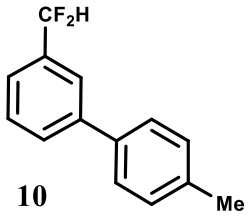
10

^{13}C NMR (126 MHz, CD_3CN) δ 142.40, 138.90, 137.87, 135.97 (t, J = 22.1 Hz), 130.6, 130.4, 130.2, 127.8, 125.1 (t, J = 6.0 Hz), 124.9 (t, J = 6.3 Hz), (peak that completes triplet with peaks 116.2 and 114.3 is hidden under solvent signal) 116.2, 114.3, 21.1.



10

^{19}F NMR (282 MHz, C_6D_6) δ -110.58 (d, J = 56.1 Hz).



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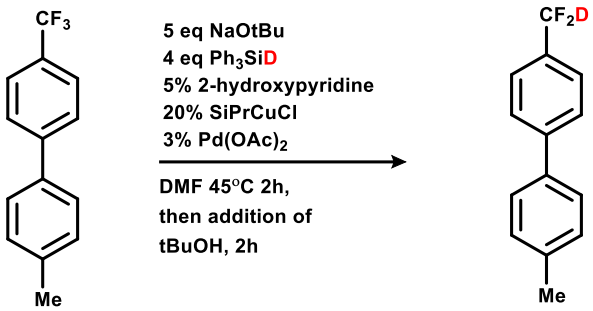
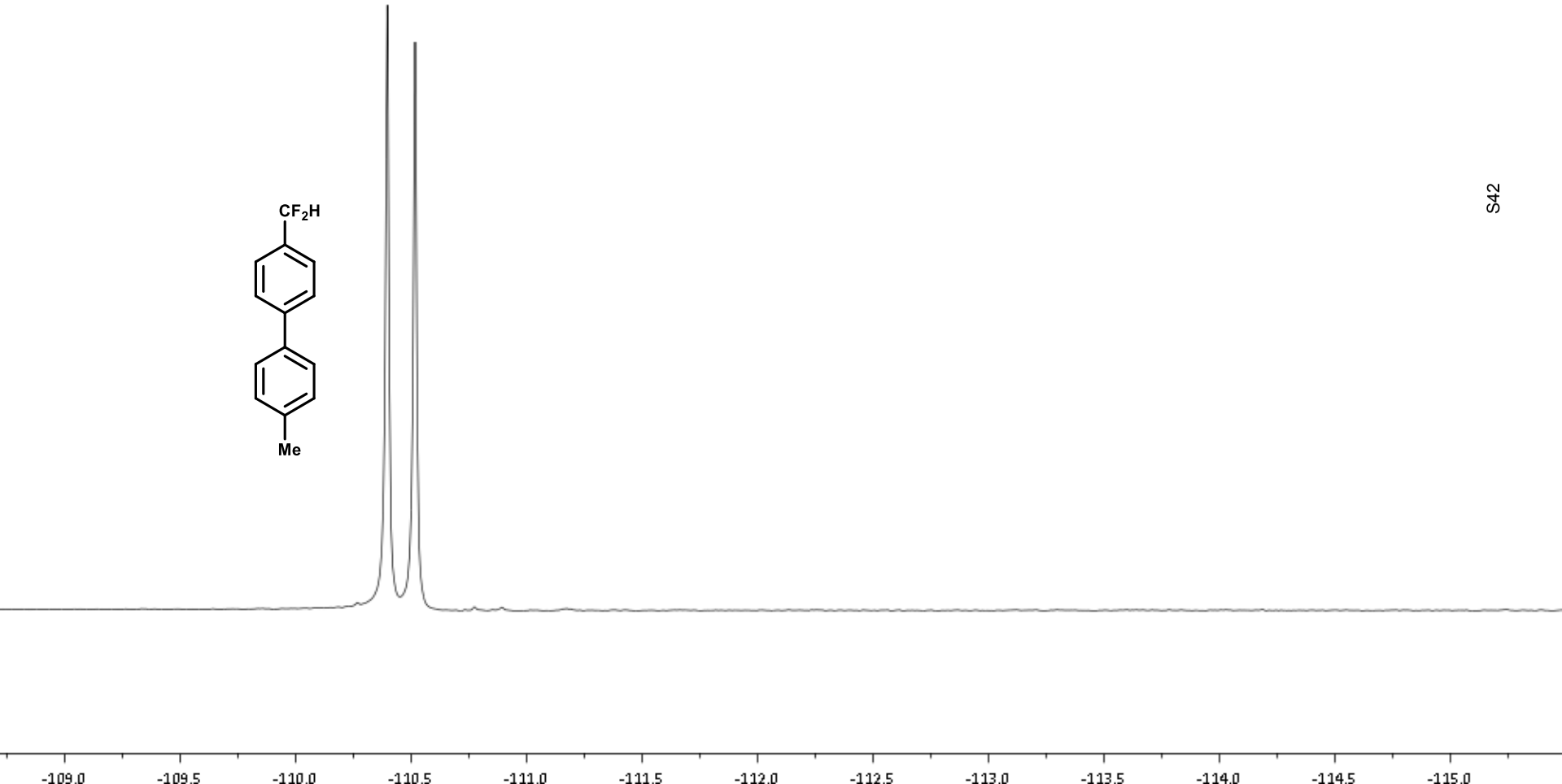
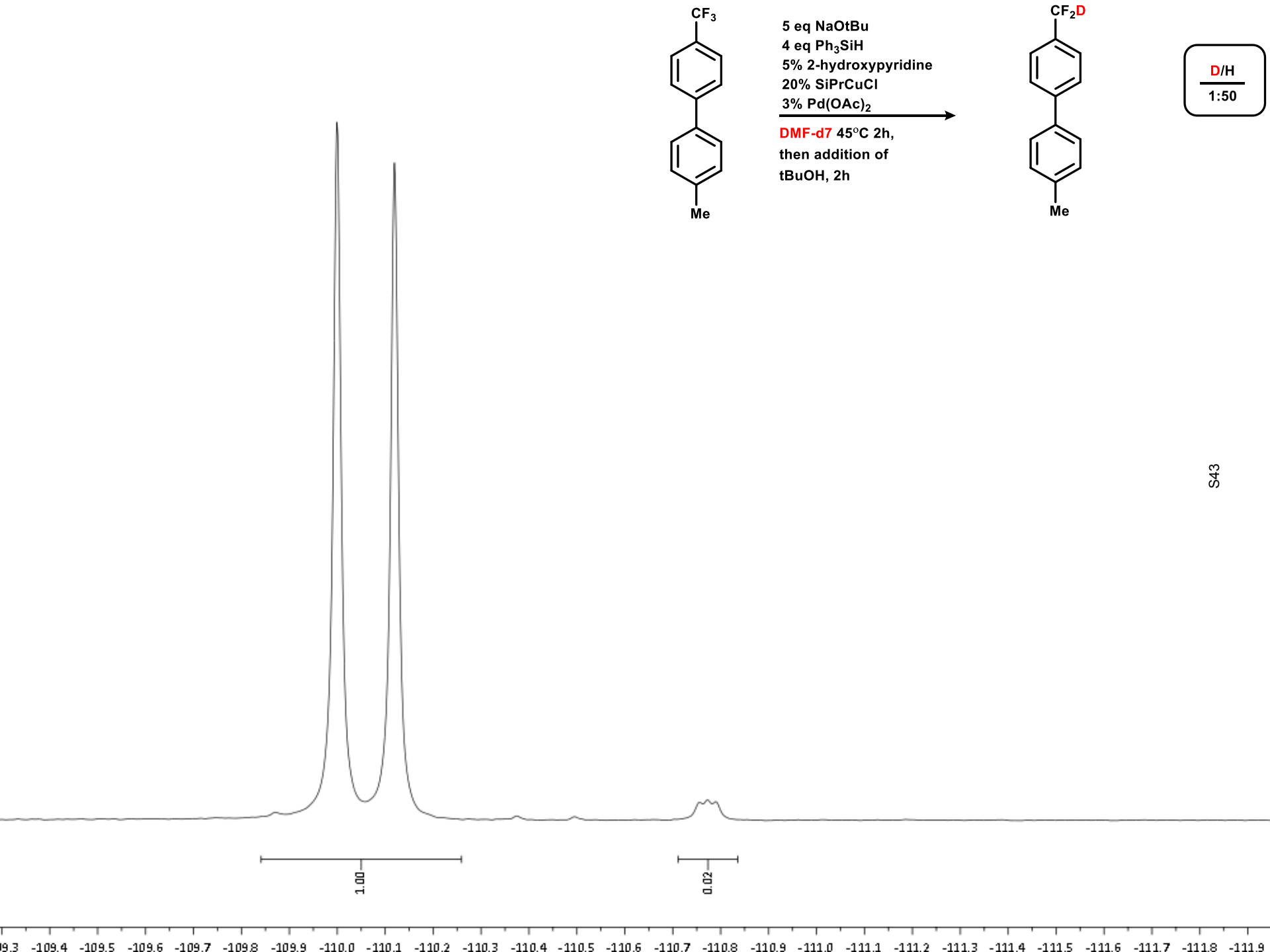
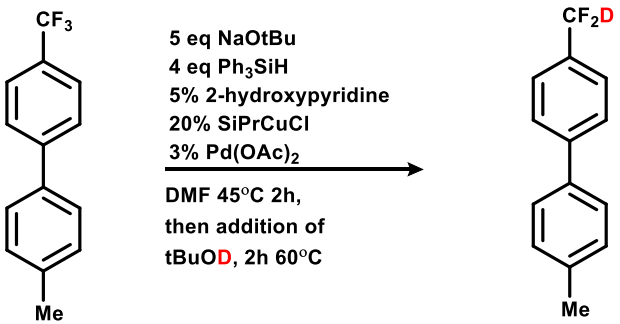


D/H
No deuterium incorporation observed



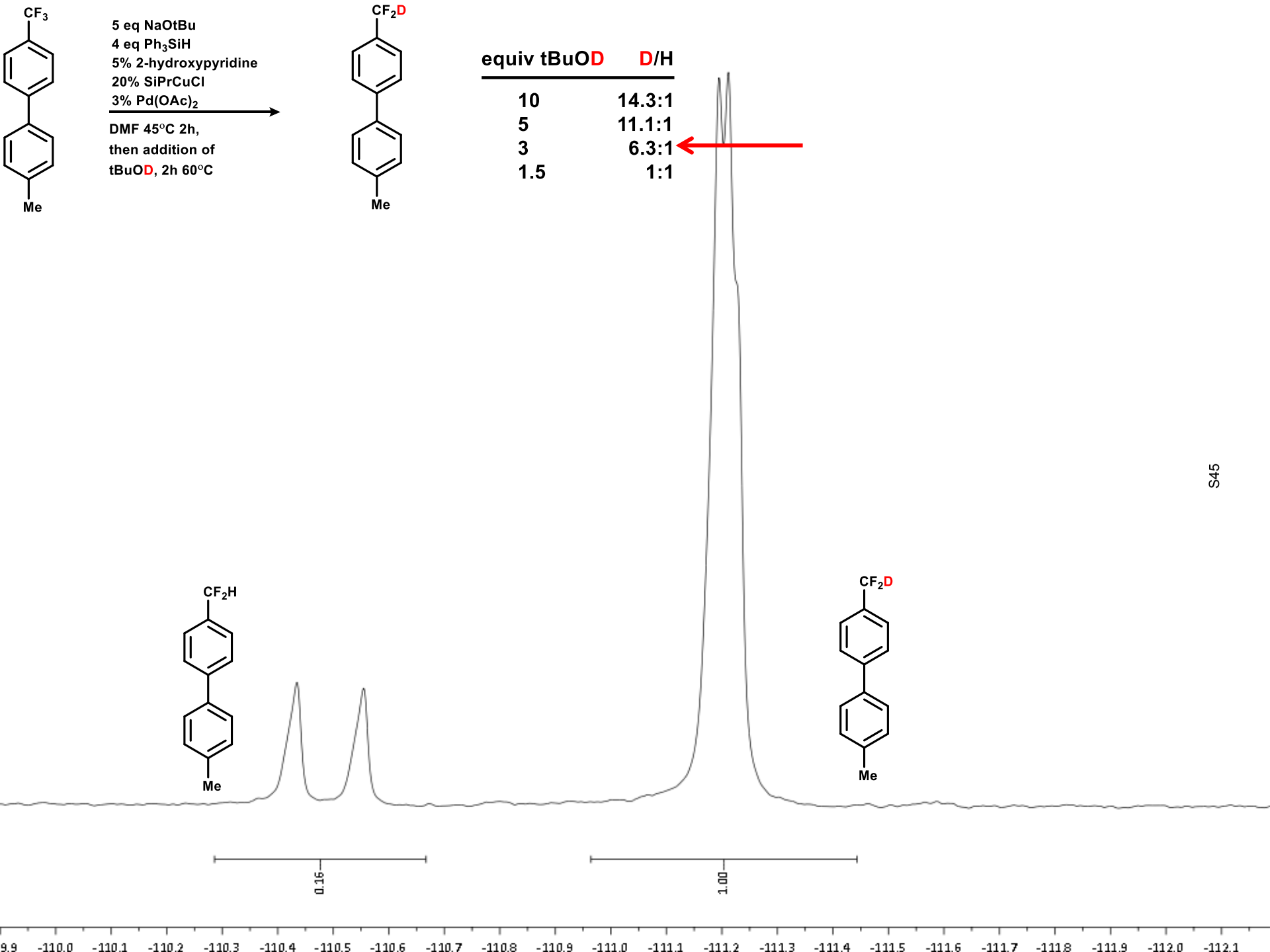

CF3
Me
5 eq NaOtBu
4 eq Ph3SiH
5% 2-hydroxypyridine
20% SiPrCuCl
3% Pd(OAc)2
DMF-d7 45°C 2h,
then addition of
tBuOH, 2h
CF2D
Me
D/H
1:50
S43
1.00
0.02
-109.3 -109.4 -109.5 -109.6 -109.7 -109.8 -109.9 -110.0 -110.1 -110.2 -110.3 -110.4 -110.5 -110.6 -110.7 -110.8 -110.9 -111.0 -111.1 -111.2 -111.3 -111.4 -111.5 -111.6 -111.7 -111.8 -111.9

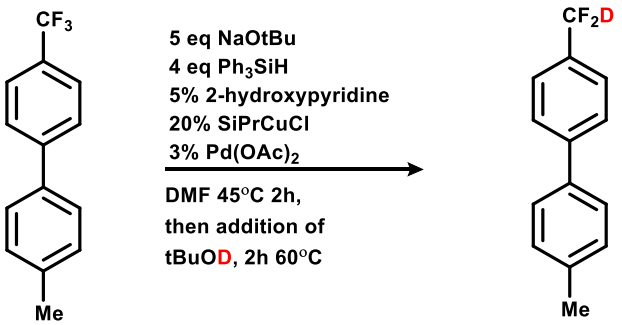


5 eq NaOtBu
4 eq Ph_3SiH
5% 2-hydroxypyridine
20% SiPrCuCl
3% $Pd(OAc)_2$

DMF 45°C 2h,
then addition of
tBuOD, 2h 60°C

equiv tBuOD	D/H
10	14.3:1
5	11.1:1
3	6.3:1
1.5	1:1

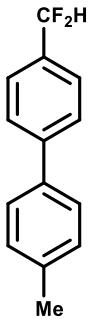

CF3
Me
5 eq NaOtBu
4 eq Ph3SiH
5% 2-hydroxypyridine
20% SiPrCuCl
3% Pd(OAc)2
DMF 45°C 2h,
then addition of
tBuOD, 2h 60°C
CF2D
Me
equiv tBuOD D/H
10 14.3:1
5 11.1:1
3 6.3:1
1.5 1:1
S45
CF2H
Me
CF2D
Me
0.16
1.00
-109.9 -110.0 -110.1 -110.2 -110.3 -110.4 -110.5 -110.6 -110.7 -110.8 -110.9 -111.0 -111.1 -111.2 -111.3 -111.4 -111.5 -111.6 -111.7 -111.8 -111.9 -112.0 -112.1

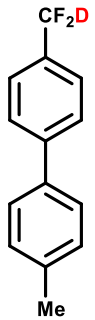


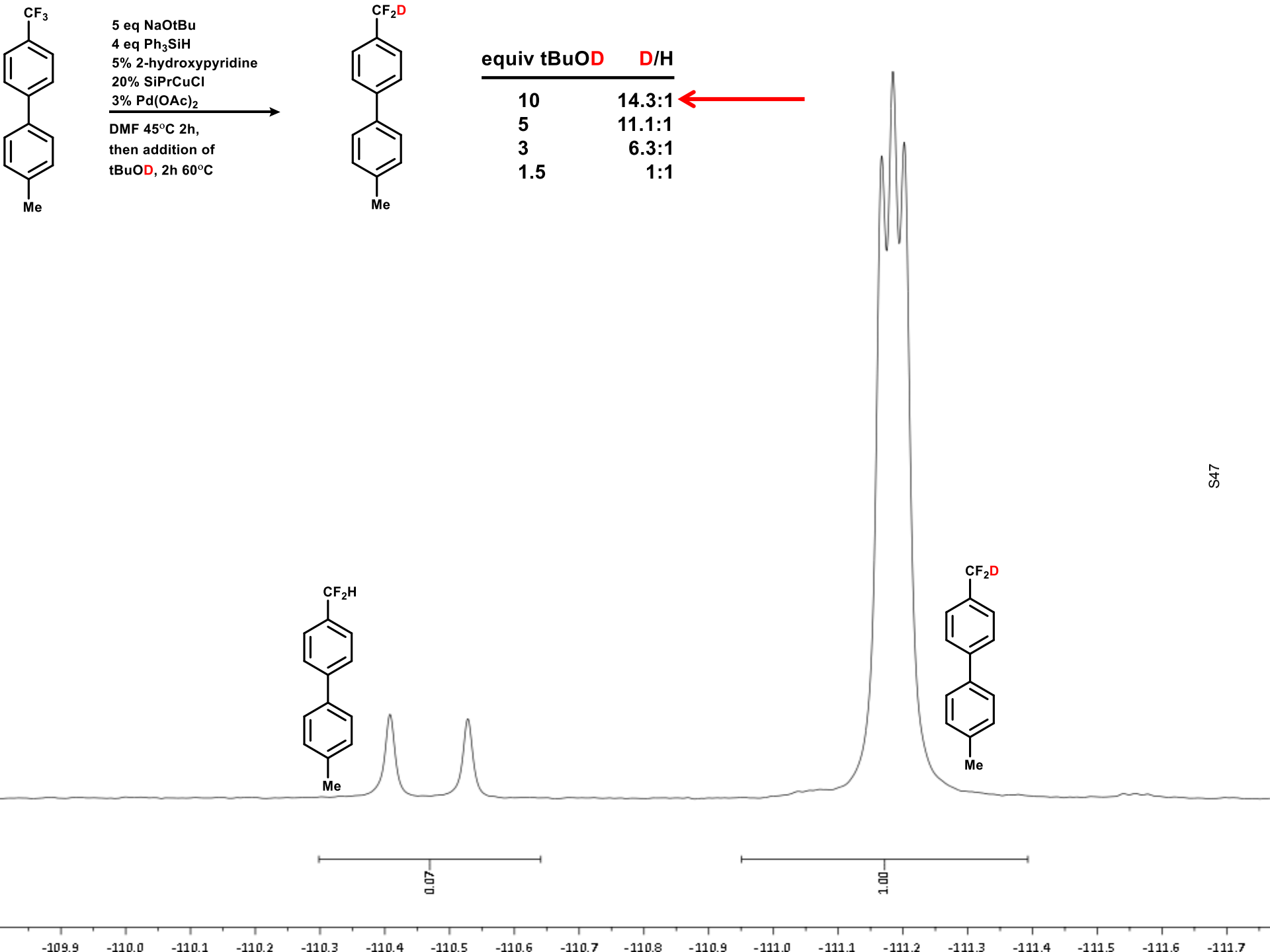
5 eq NaOtBu
4 eq Ph_3SiH
5% 2-hydroxypyridine
20% SiPrCuCl
3% $Pd(OAc)_2$

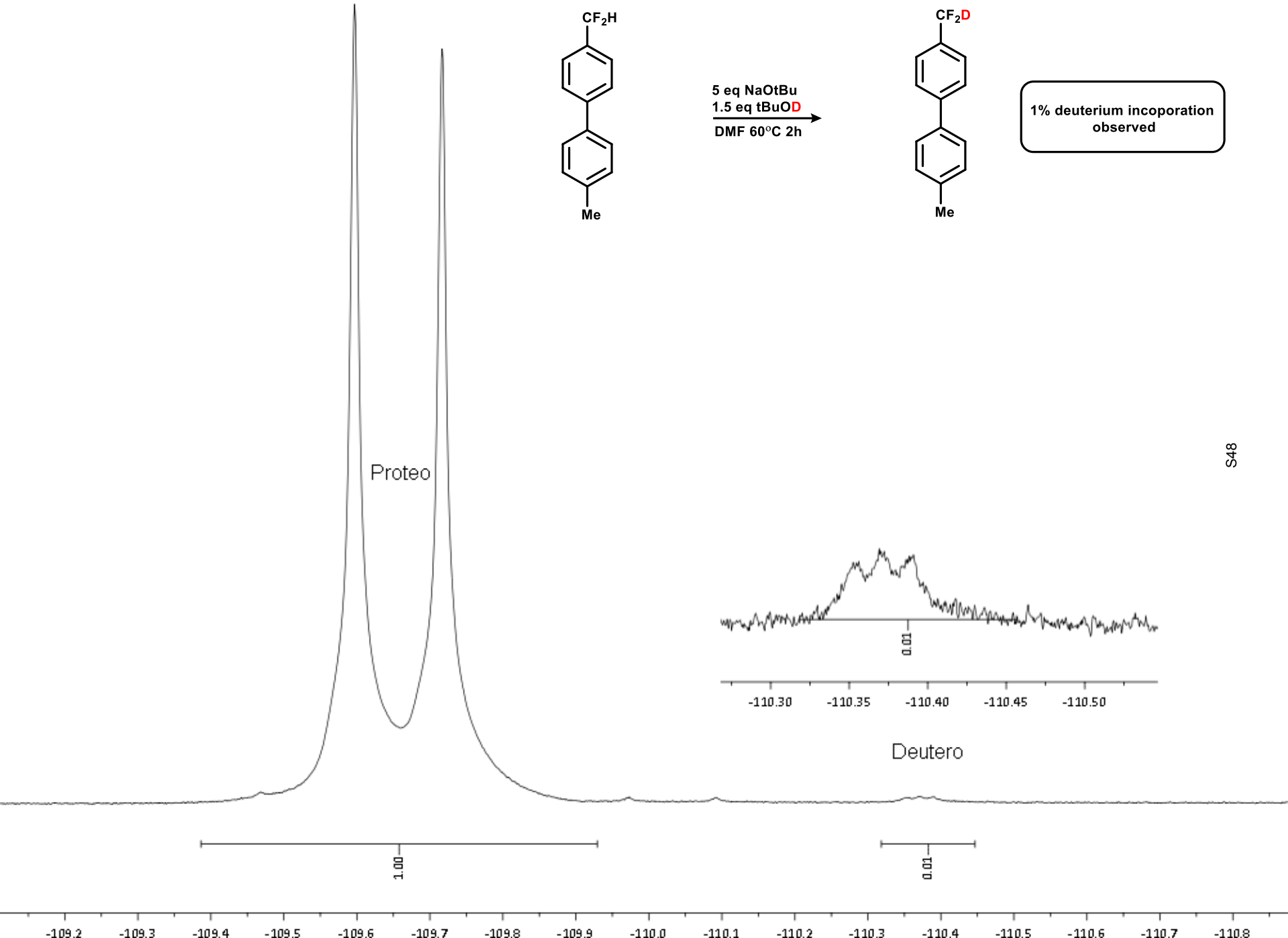
DMF 45°C 2h,
then addition of
tBuOD, 2h 60°C

equiv tBuOD	D/H
10	14.3:1
5	11.1:1
3	6.3:1
1.5	1:1






CF3
Me
5 eq NaOtBu
4 eq Ph3SiH
5% 2-hydroxypyridine
20% SiPrCuCl
3% Pd(OAc)2
DMF 45°C 2h,
then addition of
tBuOD, 2h 60°C
CF2D
Me
equiv tBuOD D/H
10 14.3:1
5 11.1:1
3 6.3:1
1.5 1:1
S47
CF2H
Me
CF2D
Me
0.07
1.00
-109.9 -110.0 -110.1 -110.2 -110.3 -110.4 -110.5 -110.6 -110.7 -110.8 -110.9 -111.0 -111.1 -111.2 -111.3 -111.4 -111.5 -111.6 -111.7


CF2H
Me
5 eq NaOtBu
1.5 eq tBuOD
DMF 60°C 2h
CF2D
Me
1% deuterium incoporation observed
Proteo
Deutero
1.00
0.01
0.01
-110.30
-110.35
-110.40
-110.45
-110.50
-109.2
-109.3
-109.4
-109.5
-109.6
-109.7
-109.8
-109.9
-110.0
-110.1
-110.2
-110.3
-110.4
-110.5
-110.6
-110.7
-110.8