Supporting Information

Catalytic α-Selective Deuteration of Styrene Derivatives

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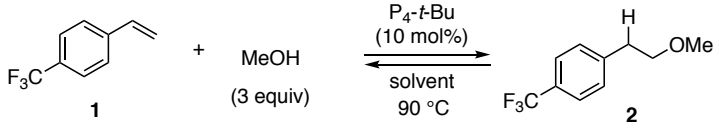
I. General Information

General Reagent Information: All reactions to prepare α-deuterated styrenes were performed under a nitrogen atmosphere. DMSO-d_6 was purchased from Cambridge Isotopes Inc. and was stored over activated 4Å molecular sieves. Potassium *tert*-butoxide (KO-*t*-Bu) was purchased from Acros (product #192860) and used as purchased. Anhydrous methanol was purchased from Sigma-Aldrich and used as purchased. DMSO-d_6, KO-*t*-Bu, and MeOH were stored in a nitrogen filled glovebox and used immediately if brought outside the glovebox. Tetrahydrofuran and dichloromethane were deoxygenated and dried by passage over packed columns of neutral alumina and copper (II) oxide under positive pressure of nitrogen or argon. NaH was purchased from Acros as a 60% dispersion in mineral oil and was stored in a desiccator with $CaSO_4$ as the desiccant. 1-*tert*-Butyl-4,4,4-tris(dimethylamino)-2,2-bis[tris(dimethylamino)-phosphoranylidenamino]-2λ^5,4λ^5-catenadi(phosphazene) (P_4-*t*-Bu) was purchased from a Sigma-Aldrich as a 0.8M solution in hexanes and was stored in a -30 °C freezer inside a nitrogen filled glovebox. Before use, the P_4-*t*-Bu solution was allowed to warm to room temperature and homogenize if any solid was evident. AD-mix-β was purchased from Sigma-Aldrich and used as received. (*S*)-DTBM-SEGPHOS was purchased from Strem Chemicals and stored in a nitrogen filled glovebox. (*R*)-DTBM-SEGPHOS was purchased from Sigma-Aldrich and stored inside a nitrogen filled glovebox. $Cu(OAc)_2$ was purchased from Aldrich and used as received. PPh_3 was purchased from Combi-Blocks and used as received. (*S*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride was purchased from Matrix Scientific and used as received. All other solvents and reagents were purchased from Sigma-Aldrich, Combi-Blocks, TCI, Acros Organics, Matrix, or Alfa-Aesar and used as received unless otherwise noted. Flash Chromatography was performed on 40-63 μm silica gel (SiliaFlash® F60 from Silicycle).

General Analytical Information: All reported compounds were characterized by ^{1}H, ^{2}H, ^{13}C and ^{19}F (as appropriate) NMR spectroscopy, FTIR spectroscopy and mass spectrometry. Melting point analysis was conducted if the compound was solid. Optical rotation analysis was conducted if the compound was chiral. Enantiomeric excess of compounds **24** and **25** was determined by chiral HPLC on a Shimadzu Prominence UFLC instrument using the given conditions. ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were obtained on a Bruker Advanced NEO or Varian Inova 400 spectrometer. ^{1}H NMR data is reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, m = multiplet), coupling constant (Hz), and integration. ^{13}C NMR data is reported as follows: chemical shift (δ ppm), multiplicity (if applicable, q = quartet, T = 1:1:1 triplet). All ^{1}H NMR signals are reported as chemical shifts (δ ppm) relative to residual $CHCl_3$, CH_2Cl_2, or DMSO at 7.26 ppm, 5.32 ppm, or 2.50 ppm respectively. ^{13}C NMR signals are reported as chemical shifts (δ ppm) relative to $CDCl_3$, CD_2Cl_2, or DMSO-d_6 at 77.23 ppm, 53.84 ppm, or 39.52 ppm respectively. α,α,α-Trifluorotoluene (δ -63.72 ppm) internal standard was added to all ^{19}F NMR samples. Chemical shifts for ^{2}H NMR are reported as chemical shifts (δ ppm) relative to residual CD_3CN (1.94 ppm). High resolution mass spectra (HRMS) were recorded on an Agilent 6210 TOF interfaced to a DART 100 or APCI source provided by Colorado State University Central Instrumentation Facility. If the substrate would not ionize using LC-MS methods, a GC-MS method was used on an Agilent 5977A GC/MSD system. IR spectra were recorded using a Thermo Scientific Nicolet iS-50 FTIR Spectrometer and reported as frequency of absorption (cm^{-1}). Melting point analyses were conducted using a Mel-Temp capillary melting point apparatus. The specific rotation of chiral

molecules was measured using a Rudolph Research Analytical Autopol III polarimeter. Thin-layer chromatography analysis was performed on silica gel 60Å F_{254} plates (250 µm, SiliaPlate from Silicycle, #TLG-R10014B-323) and interpreted using UV light (254 nm) or $KMnO_4$ stain.

II. Equilibrium Studies and K_{eq} Calculations



General Process: The equilibrium constant (K_{eq}) for the above reaction was calculated in both DMSO and *m*-xylene. To do so, the reaction was run in both the forward (starting from **1**) and reverse (starting from **2**) directions until both reactions converged to the same yields of styrene **1** and the corresponding methyl ether (**2**). The yields of the styrene and methyl ether were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as the internal standard. The final concentration of methanol was calculated by subtracting the final concentration of **2** from the starting concentration of methanol. The K_{eq} of the reaction was calculated using the following equation:

$$K_{eq} = \frac{[\mathbf{2}]}{[\mathbf{1}]\,[\mathrm{MeOH}]}$$

Forward reaction general procedure: In a nitrogen filled glovebox, 1-(trifluoromethyl)-4-vinylbenzene (**1**) (43.0 mg, 0.25 mmol, 1 eq) was weighed into an oven-dried 4 mL vial (ThermoFisher, C4015-1). The appropriate solvent (DMSO or *m*-xylene, 0.5 mL), anhydrous MeOH (30 µl, 0.75 mmol, 3 eq) and P_4-*t*-Bu (31 µl of a 0.8M solution in hexanes, 0.025 mmol, 0.1 eq) was then added in that order. The vial was capped with a screw top PTFE-lined cap (ThermoFisher, C4015-1A), removed from the glovebox and placed in a preheated 90 °C aluminum reaction block for 6 h (DMSO) or 3 h (*m*-xylene). After the indicated time, the reaction was immediately quenched with acetic acid while at 90 °C. 1,3,5-Trimethoxybenzene was weighed into each vial and used to calculate the equilibrium quantities of **1** and **2**.

Reverse reaction general procedure: In a nitrogen filled glovebox, 1-(2-methoxyethyl)-4-(trifluoromethyl)benzene (**2**) (51.0 mg, 0.25 mmol, 1 eq) was weighed into an oven-dried 4 mL vial (ThermoFisher, C4015-1) and constituted in the appropriate solvent (DMSO or *m*-xylene, 0.5 mL). Anhydrous MeOH (20 µl, 0.5 mmol, 2 eq) and P_4-*t*-Bu (31 µl of 0.8M solution in hexanes, 0.025 mmol, 0.1 eq) was then added in that order. The vial was capped with a PTFE-lined screw cap (ThermoFisher, C4015-1A), removed from the glovebox and placed in a preheated 90 °C aluminum reaction block for 6 h (DMSO) or 3 h (*m*-xylene). After the indicated time, each reaction was immediately quenched with acetic acid while at 90°C. 1,3,5-Trimethoxybenzene was weighed into each vial and used to calculate the equilibrium quantities of **1** and **2**.

Example spectra: Provided below are example spectra used to calculate K_{eq} for a reaction run in the forward and reverse direction in DMSO and *m*-xylene.

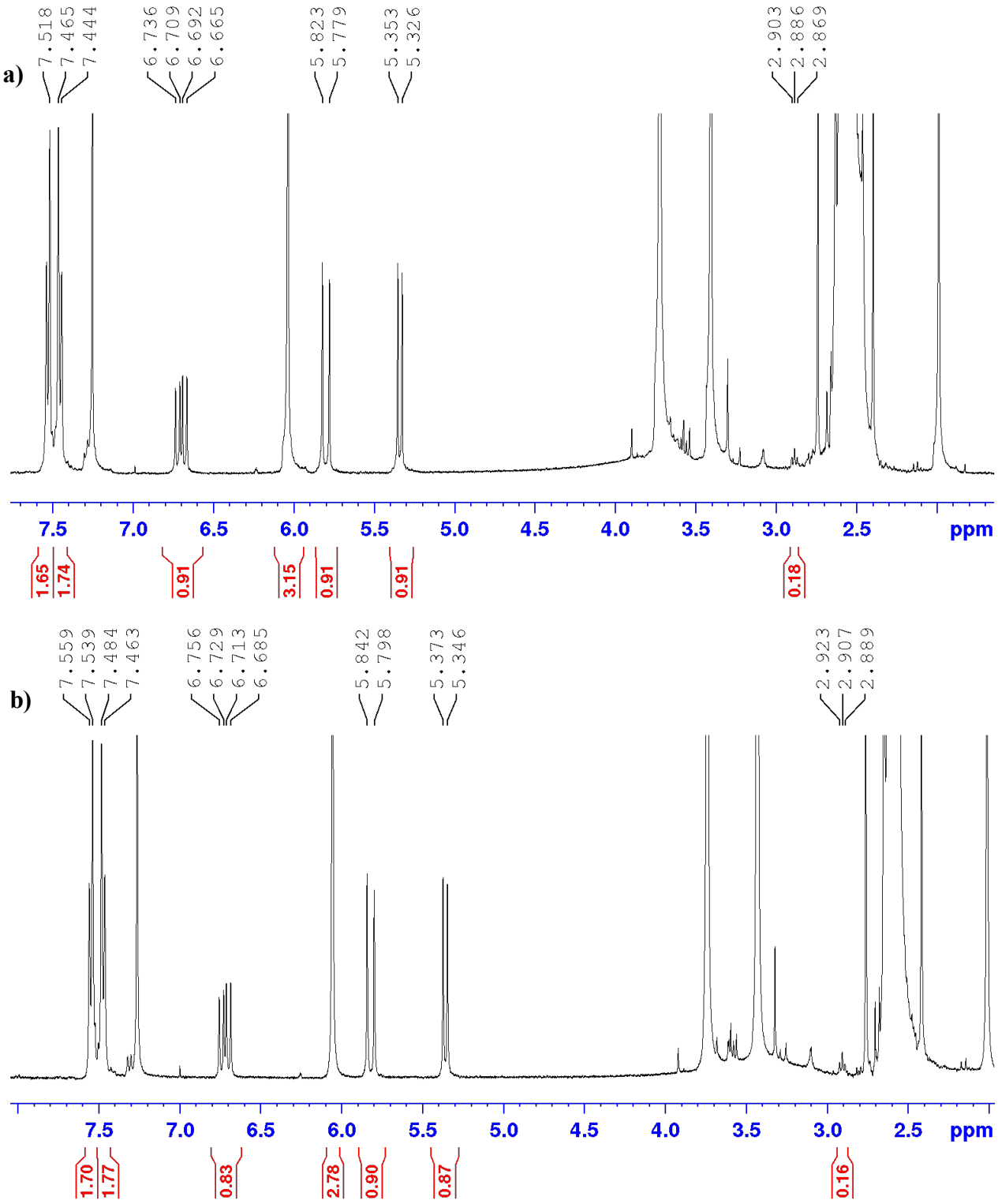


Figure S1: In DMSO **(a)**: Forward reaction (0.25 mmol scale and 0.26 mmol 1,3,5-trimethoxybenzene (TMB) as internal standard, 91% yield of **1**, 9% yield of **2**. **(b)**: Reverse reaction (0.25 mmol scale and 0.23 mmol TMB as internal standard, 90% yield of **1**, 8% yield of **2**.

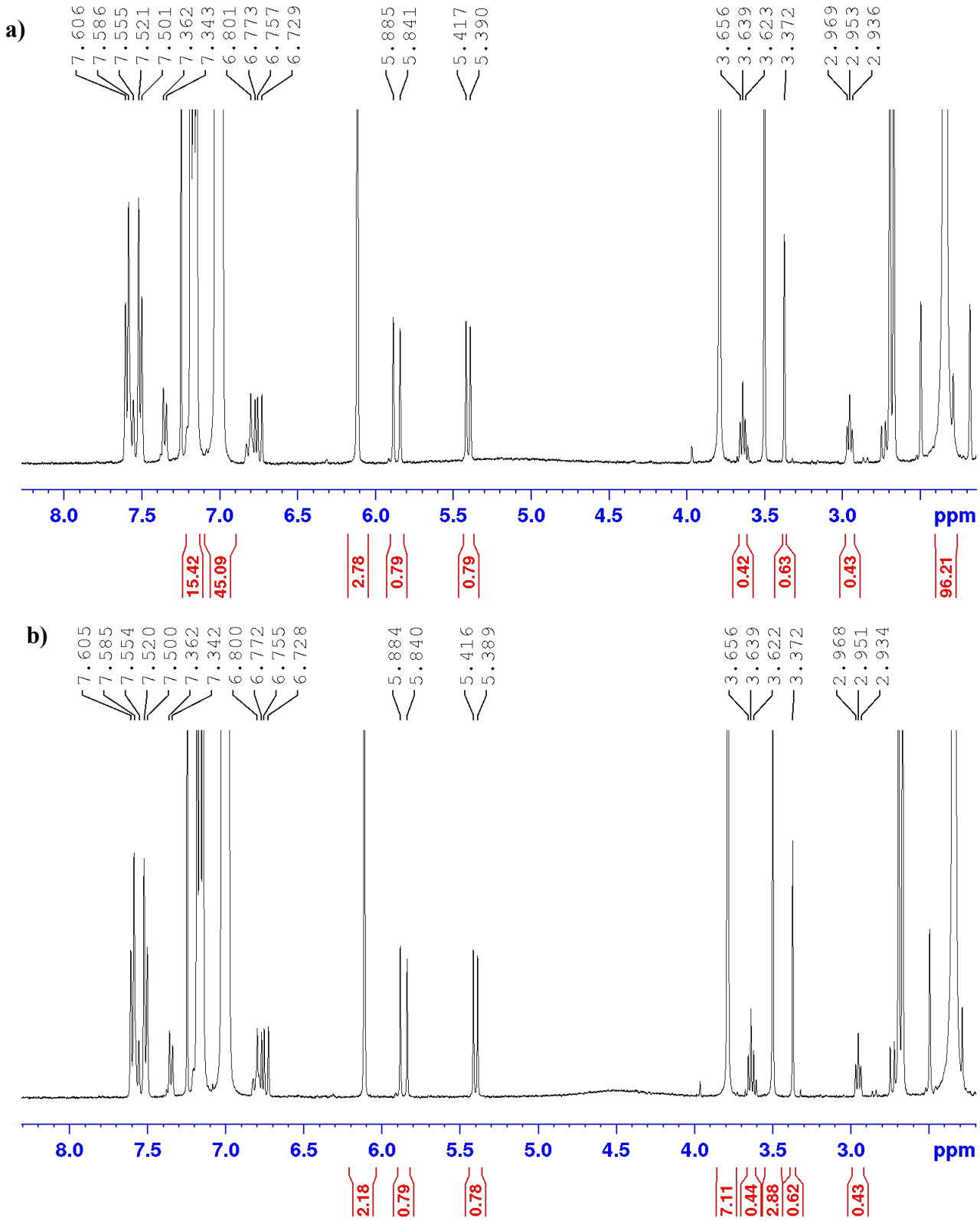


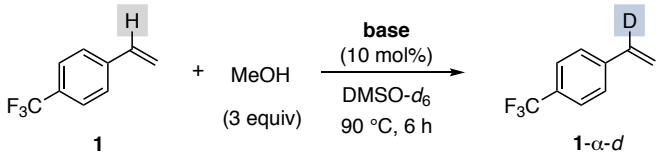
Figure S2: In *m*-xylene **(a)**: Forward reaction (0.25 mmol scale and 0.23 mmol 1,3,5-trimethoxybenzene (TMB) as internal standard, 79% yield of **1**, 21% yield of **2**. **(b)**: Reverse

reaction (0.25 mmol scale and 0.18 mmol TMB as internal standard, 79% yield of **1**, 21% yield of **2**.

	forward		backward		K_{eq}
solvent	styrene (%)	ether (%)	styrene (%)	ether (%)	
m-xylene	79	21	79	21	0.20
DMSO	91	9	90	8	0.07

Table S1: Equilibrium proportions of **1** (styrene) and **2** (ether) and K_{eq} value for the addition of methanol to 1-(trifluoromethyl)-4-vinylbenzene in DMSO and *m*-xylene.

III. Initial α-Deuteration Discovery



Procedure: 1-(trifluoromethyl)-4-vinylbenzene (**1**) (43.0 mg, 0.25 mmol, 1 eq) was weighed into an oven dried 4 mL vial (ThermoFisher, C4015-1) in a nitrogen filled glovebox. MeOH (30 µl, 0.75 mmol, 3 eq), DMSO-d_6 (0.5 mL), and either KO-*t*-Bu (2.8 mg, 0.025 mmol, 0.1 eq) or P_4-*t*-Bu (31 µl, 0.025 mmol, 0.1 eq) were then added in that order. The vial was sealed with a PTFE-lined screw cap (ThermoFisher, C4015-1A), removed from the glovebox, and placed into a pre-heated 90 °C silicon oil bath. The reaction solution was stirred for 6 h and then was quenched with acetic acid while at 90 °C. 1,3,5-Trimethoxybenzene internal standard was then weighed into each vial and a ^{1}H NMR (400 MHz, $CDCl_3$) spectrum was taken to determine the yield and α-deuterium incorporation in each reaction. For full characterization of **1**-α-*d* see Section V.

Note: Provided below are example ^{1}H NMR spectra of starting styrene (**1**) and the crude reaction mixture containing α-deuterated product **1**-α-*d*. The chemical shift of the α-proton for 4-trifluoromethyl styrene (**1**) is 6.75 ppm.

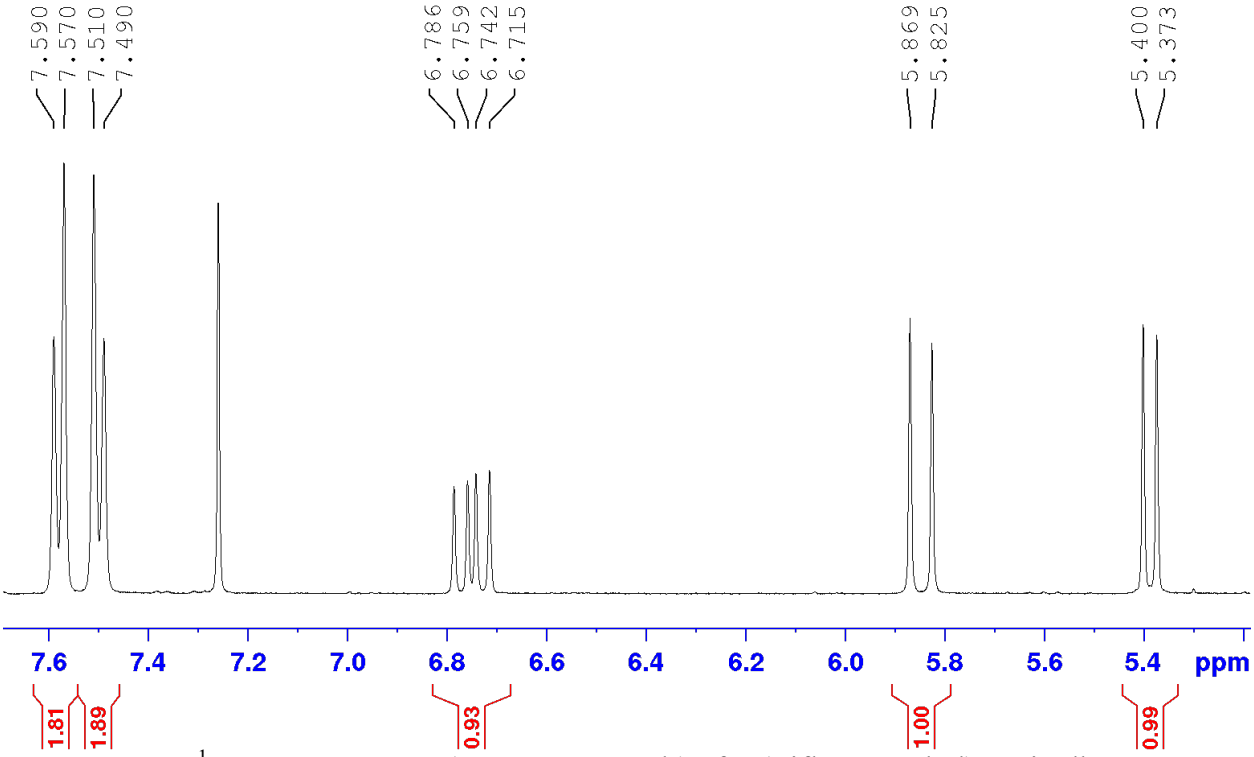


Figure S3 (a): ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 1-(trifluoromethyl)-4-vinylbenzene.

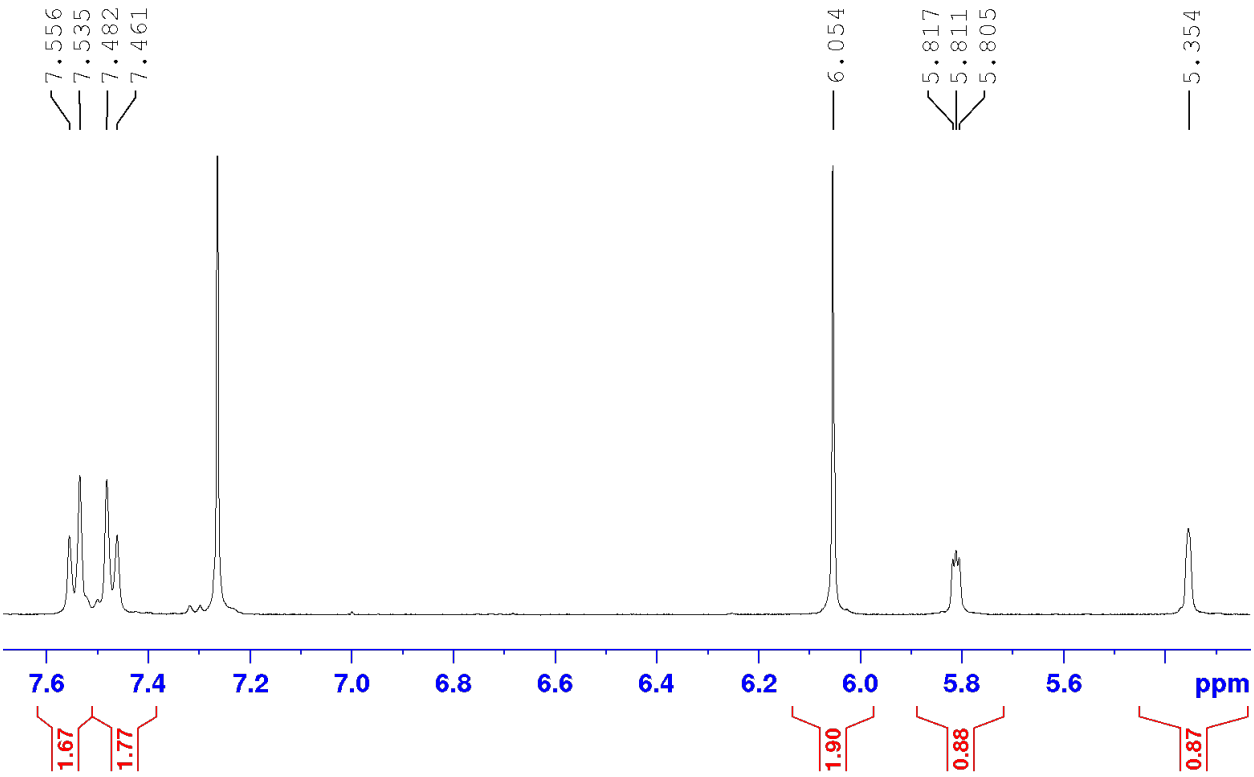


Figure S3 (b): Preliminary α-deuteration reaction of 1-(trifluoromethyl)-4-vinylbenzene with P_4-*t*-Bu as the base (0.25 mmol scale; 1,3,5-trimethoxybenzene (26.7 mg, 0.16 mmol) used as internal standard, 88% ^{1}H NMR yield, >99% α-deuteration).

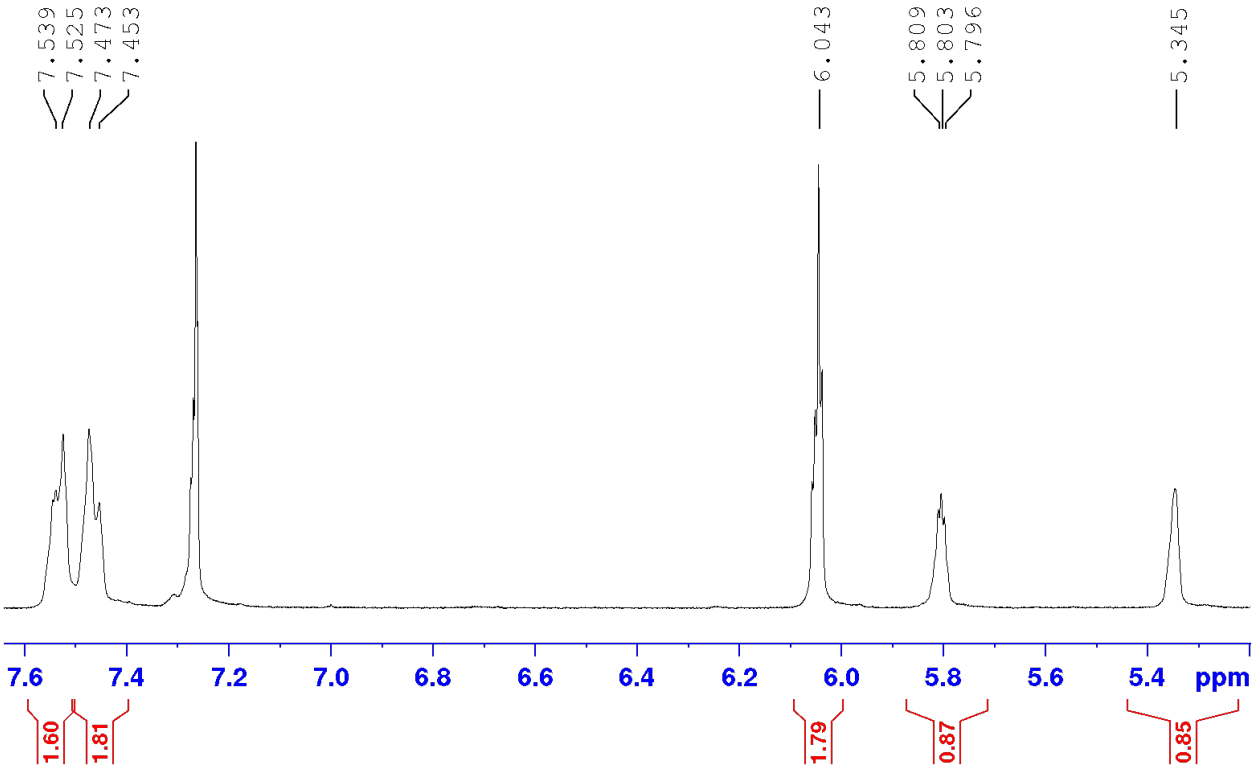
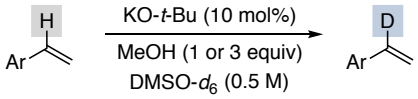


Figure S3 (c): Preliminary α-deuteration reaction of 1-(trifluoromethyl)-4-vinylbenzene with KO-*t*-Bu as the base (0.25 mmol scale; 1,3,5-trimethoxybenzene (25.1 mg, 0.15 mmol) used as internal standard, 87% ^{1}H NMR yield, >99% α-deuteration).

IV. General Procedure for Preparation of *α*-Deuterated Styrenes



General procedure for 1 mmol scale reactions: KO-*t*-Bu, methanol and DMSO-d_6 were stored in a nitrogen filled glovebox until use. Outside of the glovebox, an oven-dried 4 mL vial (ThermoFisher, C4015-1) was charged with a magnetic stir bar and KO-*t*-Bu (11.2 mg, 0.1 mmol, 0.1 eq) and sealed with a PTFE-lined screw cap (ThermoFisher, C4015-1A). The vial was then evacuated and backfilled with nitrogen three times and left under positive pressure with a nitrogen balloon after the third cycle. A separate vial was then charged with the appropriate vinyl arene (1 mmol, 1 eq), methanol (1 or 3 mmol, 1 or 3 eq), and DMSO-d_6 (2.0 mL). This solution was sparged with nitrogen for three minutes, and then transferred to the vial containing KO-*t*-Bu via syringe. The cap was then parafilmed, and the vessel was placed into a preheated silicon oil bath. The reactions were monitored by observing the disappearance of the *α*-proton by ^{1}H NMR spectroscopy (**Note:** the reactions were observed to be air sensitive and care should be taken to not introduce air to the system while taking aliquots). After the indicated time, the reaction solution was quenched with acetic acid before allowing to cool to rt. The crude reaction mixture was washed with H_2O (30 mL), extracted with EtOAc (3 x 30 mL), dried over Na_2SO_4, and

concentrated *in vacuo* unless otherwise noted. All substrates were purified by silica gel chromatography using the given conditions. The percentage of deuterium incorporation into the α-position was determined by integrating one terminal vinyl peak assumed to have a value of 1.0, to the residual α-proton signal. The percentage of deuterium incorporation into other positions was determined by integrating ^{2}H NMR signals to the calibrated α-deuterium signal (value determined by ^{1}H NMR). For example, α-deuteration of compound **11-α-*d*** was determined to be 97% by ^{1}H NMR; the integration of the α-deuterium signal was thus set to 0.97 in the ^{2}H NMR and integration of an additional signal (value = 0.04) indicated 4% amount of additional deuteration. **Note:** ^{1}H NMR experiments with relaxation delays of 1 s and 5 s (45° pulse width in both cases) were taken to ensure that delay was not a factor in the depleted integration of the α-proton signal for all substrates. Both experiments showed the same percentage of α-deuterium incorporation.

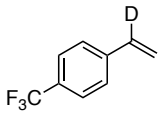
Safety note: DMSO can undergo autocatalytic decomposition at temperatures near its boiling point (189 °C). The reactions described in this manuscript are typically run below 100 °C and no decomposition was observed. For a discussion of DMSO safety and proper protocols for scaling reactions in this solvent, see reference 1.

Note on process used for identification of reaction conditions for each styrene substrate: Suitable conditions for preparative scale reactions could generally be found by testing 1 or 3 equiv of MeOH at varying temperatures on a 0.1 mmol scale. For relatively electron-deficient substrates, a lower temperature (e.g. **15** was originally tested at 40 °C) was initially tested and suitable conditions could be identified from there. For relatively electron-rich substrates, a higher temperature (e.g. **11** was originally tested at 120 °C) was initially tested and suitable reaction conditions could be identified from there. If aromatic deuteration was an issue, it was found that lower temperatures and extended reactions times generally improved α-positional selectivity. If the corresponding methyl ether comprised a significant amount of the mass balance, it was found that increasing the temperature generally improved the yield of the styrene.

V. Characterization Data for α-Deuterated Styrenes

Note on nomenclature: The names provided for the structures below were obtained from ChemDraw Professional 16.0.

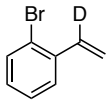
1-(trifluoromethyl)-4-(vinyl-1-*d*)benzene (**1**-α-*d*)



1-(trifluoromethyl)-4-(vinyl-1-*d*)benzene was prepared according to the general procedure using 1-(trifluoromethyl)-4-vinylbenzene (172.2 mg, 1 mmol, 1 eq), MeOH (40 µl, 1 mmol, 1 eq), KO-*t*-Bu (11.2 mg, 0.1 mmol, 0.1 eq), and DMSO-d_6 (2.0 mL). The solution was stirred at 90 °C for 1.5 h. 1,3,5-Trimethoxybenzene internal standard (61.2 mg, 0.36 mmol) was added to the solution prior to purification to determine the ^{1}H NMR yield (86% yield). The crude reaction mixture was loaded directly onto a silica gel column and eluted with hexanes to afford the title compound as a clear oil (89.9 mg, 52% isolated yield, 99% α-deuteration, 1% other deuteration). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.2 Hz, 2H), 7.50 (d, J = 8.2 Hz, 2H), 6.75 (dd, J_1 = 11.0 Hz, J_2 = 17.6 Hz, 0.01H), 5.84 (m, 1H), 5.39 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.1, 135.6 (T, J = 23.8 Hz), 129.9 (q, J = 32.6 Hz),

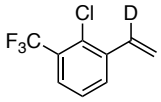
126.6, 125.8 (q, J = 3.9 Hz), 123.1, 116.6. **^{2}H NMR** (62 MHz, CH_3CN) δ 7.66 (0.01D), 6.83 (0.99D). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.5 (3F). **HRMS** (APCI) $[M+H]^+$ calcd. for $[C_9H_7DF_3]^+$ 174.0641, 174.0633 found. **IR** (neat, cm^{-1}) 3094, 2936, 2241, 1618, 1401, 1321, 1164, 1113, 1065, 1016, 918, 845.

1-bromo-2-(vinyl-1-*d*)benzene (**4**-α-*d*)



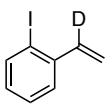
1-bromo-2-(vinyl-1-*d*)benzene was prepared according to the general procedure on a 2 mmol scale using 1-bromo-2-vinylbenzene (366.1 mg, 2 mmol, 1 eq), MeOH (64.1 mg, 2 mmol. 1 eq), KO-*t*-Bu (22.4 mg, 0.2 mmol, 0.1 eq), and DMSO-d_6 (4.0 mL). The solution was stirred at 70 °C for 2 h. The crude reaction mixture was loaded directly onto a silica gel column and eluted with hexanes to afford the title compound as a clear oil (330.4 mg, 90% yield, 97% α-deuteration, 0% other deuteration). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.56 (m, 2H), 7.29 (t, J = 7.6 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H), 7.07 (dd, 0.03H), 5.71 (m, 1H), 5.37 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.7, 135.7 (T, J = 24.4 Hz), 133.1, 129.3, 127.7, 127.0, 123.8, 116.7. **^{2}H NMR** (62 MHz, CH_3CN) δ 7.10 (0.97D). **HRMS** (APCI) $[M+H]^+$ calcd. for $[C_8H_7DBr]^+$ 183.9872, 183.9881 found. **IR** (neat, cm^{-1}) 3057, 2924, 2853, 2253, 1612, 1587, 1560, 1467, 1431, 1402, 1025, 916, 832, 756, 727, 660. Note: The α-deuterium incorporation was determined by ^{1}H NMR with DMSO-d_6 as the solvent. In $CDCl_3$ the α-proton overlaps with aromatic protons.

2-chloro-1-(trifluoromethyl)-3-(vinyl-1-*d*)benzene (**5**-α-*d*)



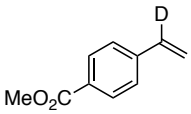
2-chloro-1-(trifluoromethyl)-3-(vinyl-1-*d*)benzene was prepared according to the general procedure using 2-chloro-1-(trifluoromethyl)-3-vinylbenzene (206.6 mg, 1 mmol, 1 eq), MeOH (40 µl, 1 mmol, 1 eq), KO-*t*-Bu (11.2 mg, 0.1 mmol, 0.1 eq), and DMSO-d_6 (2.0 mL). The solution was stirred at 70 °C for 10 min. The crude reaction mixture was loaded directly onto a silica gel column and eluted with hexanes to afford the title compound as a clear oil (144.2 mg, 70% yield, 97% α-deuteration, 0% other deuteration). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, J = 7.9 Hz, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.34 (t, J = 7.9 Hz, 1H), 7.18 (dd, J_1 = 11.0 Hz, J_2 = 17.4 Hz, 0.03H), 5.76 (m, 1H), 5.49 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.4, 132.5 (T, J = 24.7 Hz), 131.1, 130.3, 129.3 (q, J = 30.9 Hz), 127.0 (q, J = 5.5 Hz), 126.7, 123.1 (q, J = 274.4 Hz), 118.3. **^{2}H NMR** (62 MHz, CH_3CN) δ 7.21 (0.98D). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.5 (3F). **GCMS** calcd. for $[C_9HDClF_3]^+$ 207.0, 207.0 found. **IR** (neat, cm^{-1}) 3093, 2918, 2360, 2341, 1581, 1428, 1399, 1316, 1170, 1125, 1086, 1049, 924, 802, 733.

1-iodo-2-(vinyl-1-*d*)benzene (**6**-α-*d*)



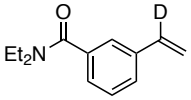
1-iodo-2-(vinyl-1-*d*)benzene was prepared according to the general procedure using 1-iodo-2-vinylbenzene (230 mg, 1 mmol, 1 eq), MeOH (120 µl, 3 mmol, 3 eq), KO-*t*-Bu (11.2 mg, 0.1 mmol, 0.1 eq), and DMSO-d_6 (2.0 mL). The solution was stirred at 100 °C for 2 h. Silica gel chromatography (2% EtOAc/hexanes) yielded the title compound as a clear oil (177.9 mg, 77% yield, 99% α-deuteration, 1% other deuteration). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (d, J = 7.9 Hz, 1H), 7.52 (d, J = 7.8 Hz, 1H), 7.32 (t, J = 7.5 Hz, 1H), 6.95 (t, J = 7.6 Hz, 1H), 6.91 (dd, 0.01H), 5.63 (m, 1H), 5.33 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.9, 140.5 (T, J = 24.3 Hz), 139.7, 129.5, 128.6, 126.6, 116.9, 99.9. **^{2}H NMR** (62 MHz, CH_3CN) δ 7.92 (0.01D), 6.93 (0.99D). **HRMS** (APCI) $[M+H]^+$ calcd. for $[C_8H_7DI]^+$ 231.9733, 231.9722 found. **IR** (neat, cm^{-1}) 3052, 2922, 2245, 1610, 1583, 1555, 1462, 1430, 1400, 1010, 916, 756, 646.

methyl 4-(vinyl-1-*d*)benzoate (**7**-α-*d*)



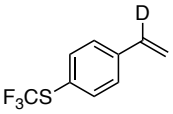
Methyl 4-(vinyl-1-*d*)benzoate was prepared according to the general procedure using methyl 4-vinylbenzoate (162.2 mg, 1 mmol, 1eq), MeOH (40 µl, 1 mmol, 1 eq), KO-*t*-Bu (11.2 mg, 0.1 mmol, 0.1 eq), and DMSO-d_6 (2.0 mL). The solution was stirred at 50 °C for 12 h. Silica gel chromatography (15% EtOAc/hexanes) yielded the title compound as a white solid (103.0 mg, 63% yield, 99% α-deuteration, 0% other deuteration). **Melting Point**: 33-34 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.2 Hz, 2H), 7.45 (d, J = 8.2 Hz, 2H), 6.74 (dd, J_1 = 10.8 Hz, J_2 = 17.6 Hz, 0.01H), 5.84 (s, 1H), 5.36 (s, 1H), 3.90 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.9, 141.9, 135.7 (T, J = 24.0 Hz), 129.9, 129.3, 126.1, 116.3, 52.2. **^{2}H NMR** (62 MHz, CH_3CN) δ 6.80 (0.99D). **HRMS** (DART) $[M+H]^+$ calcd. for $[C_{10}H_{10}DO_2]^+$ 164.0822, 164.0820 found. **IR** (neat, cm^{-1}) 2949, 2848, 2230, 1713, 1606, 1436, 1275, 1180, 1102, 1015, 962, 931, 861, 779, 710.

***N*,*N*-diethyl-3-(vinyl-1-*d*)benzamide** (**8**-α-*d*)



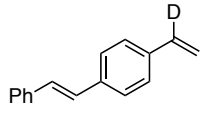
N,*N*-diethyl-3-(vinyl-1-*d*)benzamide was prepared according to the general procedure using *N*,*N*-diethyl-3-vinylbenzamide (203.3 mg, 1 mmol, 1 eq), MeOH (40 µl, 1 mmol, 1 eq), KO-*t*-Bu (11.2 mg, 0.1 mmol, 0.1 eq), and DMSO-d_6 (2.0 mL). The solution was stirred at 100 °C for 24 h. Silica gel chromatography (50% EtOAc/hexanes) yielded the title compound as a viscous clear oil (151.7 mg, 74% yield, 98% α-deuteration, 0% other deuteration). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41-7.43 (m, 2H), 7.34 (t, J = 7.5 Hz, 1H), 7.23-7.25 (m, 1H), 6.71 (dd, J_1 = 11.1 Hz, J_2 = 17.7 Hz, 0.02H), 5.77 (s, 1H), 5.29 (s, 1H), 3.27-3.56 (m, 4H), 1.12-1.26 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.1, 137.8, 137.6, 135.9 (T, J = 23.7 Hz), 128.6, 126.9, 125.6, 124.1, 114.6, 43.3, 39.2, 14.3, 12.9. **^{2}H NMR** (62 MHz, CH_3CN) δ 6.82 (0.98D). **HRMS** (DART) $[M+H]^+$ calcd. for $[C_{13}H_{17}DNO]^+$ 205.1451, 205.1458 found. **IR** (neat, cm^{-1}) 2972, 2934, 2234, 1626, 1433, 1290, 1098, 909, 802, 707.

(trifluoromethyl)(4-(vinyl-1-*d*)phenyl)sulfane (**9**-α-*d*)



(trifluoromethyl)(4-(vinyl-1-*d*)phenyl)sulfane was prepared according to the general procedure using (trifluoromethyl)(4-vinylphenyl)sulfane (204.2 mg, 1 mmol, 1 eq), MeOH (121 µl, 3 mmol, 3 eq), KO-*t*-Bu (11.2 mg, 0.1 mmol, 0.1 eq), and DMSO-d_6 (2.0 mL). The solution was stirred at 80 °C for 3 h. The crude reaction mixture was loaded directly onto a silica gel column and eluted with hexanes to afford the title compound as a clear oil (102.4 mg, 50% yield, 95% α-deuteration, 0% other deuteration). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.2, 2H), 7.45 (d, J = 8.2, 2H), 6.73 (dd, J_1 = 10.9 Hz, J_2 = 17.6 Hz, 0.05H), 5.84 (m, 1H), 5.38 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.2, 136.7, 135.5 (T, J = 23.8 Hz), 129.7 (q, J = 309.4 Hz), 127.3, 123.5, 116.4. **^{2}H NMR** (62 MHz, CH_3CN) δ 6.84 (0.95D). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -43.83 (3F). **HRMS** (APCI) $[M + H]^+$ calcd. for $[C_9H_7DF_3S]$ 206.0362, 206.0358 found. **IR** (neat, cm^{-1}) 3092, 2926, 2359, 2239, 1491, 1396, 1118, 1102, 1014, 916, 839.

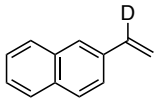
(*E*)-1-styryl-4-(vinyl-1-*d*)benzene (**10**-α-*d*)



(E)-1-styryl-4-(vinyl-1-*d*)benzene was prepared using a modified procedure. (*E*)-1-styryl-4-vinylbenzene (206.3 mg, 1.0 mmol, 1.0 eq) and NaH (60% dispersion, 8.0 mg, 0.2 mmol, 0.2 eq) was weighed into a 4 mL oven-dried vial (ThermoFisher, C4015-1). The vial was sealed with a PTFE lined screw cap

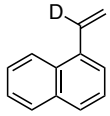
(ThermoFisher, C4015-1A) and parafilmed. The vial was evacuated and backfilled three time with N_2 using a nitrogen balloon and left under positive pressure after the third cycle. MeOH (121 µl, 3 mmol, 3 eq) and DMSO-d_6 (2.0 mL) was measured into a separate vial, sparged with N_2 for three min, and then added to the NaH/alkene mixture via syringe. The rest of the procedure was carried out in accordance with the general procedure. The solution was stirred at 90 °C for 24 h. Silica gel chromatography (3% EtOAc/hexanes) yielded the title compound as a pale yellow solid (192.5 mg, 93% yield, 97% α-deuteration, 0% other deuteration). **Melting Point**: 159-162 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48-7.53 (m, 4H), 7.34-7.42 (m, 4H), 7.24-7.28 (m, 1H), 7.11 (s, 2H), 6.72 (dd, J_1 = 10.8 Hz, J_2 = 17.5 Hz, 0.03H), 5.76 (s, 1H), 5.25 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.3, 137.1, 137.0, 136.2 (T, J = 23.7 Hz), 128.7, 128.6, 128.3, 127.7, 126.7, 126.6, 126.5, 113.6. **^{2}H NMR** (62 MHz, CH_3CN) δ 6.80 (0.97D). **HRMS** (APCI) $[M+H]^+$ calcd. for $[C_{16}H_{14}D]$ 208.1237, 208.1227 found. **IR** (neat, cm^{-1}) 3080, 3053, 3021, 2923, 2360, 2341, 2226, 1607, 1508, 1389, 1448, 1401, 966, 903, 828, 757, 733, 690.

2-(vinyl-1-*d*)naphthalene (**11**-α-*d*)



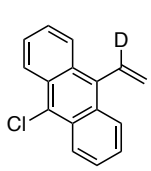
2-(vinyl-1-*d*)naphthalene was prepared according to the general procedure using 2-vinylnaphthalene (154.2 mg, 1 mmol, 1 eq), MeOH (121µl, 3 mmol, 3 eq), KO-*t*-Bu (11.2 mg, 0.1 mmol, 0.1 eq), and DMSO-d_6 (2.0 mL). The solution was stirred at 130 °C for 4 h. Silica gel chromatography (hexanes) yielded the title compound as a white powder (133.0 mg, 86% yield, 97% α-deuteration, 4% other deuteration). **Melting Point**: 64-65 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80-7.84 (m, 3H), 7.77 (s, 1H), 7.66 (dd, J_1 = 8.6 Hz, J_2 = 1.7 Hz, 1H), 7.44-7.50 (m, 2H), 6.91 (dd, J_1 = 10.8 Hz, J_2 = 17.6 Hz, 0.03H), 5.89 (m, 1H), 5.36 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 136.8 (T, J = 23.6 Hz), 135.2, 133.8, 133.5, 128.3, 128.2, 127.9, 126.5, 126.4, 126.1, 123.3, 114.2. **^{2}H NMR** (62 MHz, CH_3CN) δ 7.85 (0.04D), 6.93 (0.97D). **HRMS** (APCI) $[M+H]^+$ calcd. for $[C_{12}H_9D]^+$ 156.0924, 156.0886 found. **IR** (neat, cm^{-1}) 3053, 2922, 2852, 2361, 2341, 1613, 1590, 1571, 1505, 1185, 894, 861, 820, 749.

1-(vinyl-1-*d*)naphthalene (**12**-α-*d*)



1-(vinyl-1-*d*)naphthalene was prepared according to the general procedure using 1-vinylnapthalene (154.2 mg, 1 mmol, 1 eq), MeOH (121 µl, 3 mmol, 3 eq), KO-*t*-Bu (11.2 mg, 0.1 mmol, 0.1 eq), and DMSO-d_6 (2.0 mL). The solution was stirred at 130 °C for 4 h. Silica gel chromatography (hexanes eluent) yielded the title compound as a clear oil (122.2 mg, 79% yield, 99% α-deuteration, 0% other deuteration). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15 (d, J = 8.2 Hz, 1H), 7.88 (d, J = 8.1 Hz, 1H), 7.82 (d, J = 8.2 Hz, 1H), 7.66 (d, J = 7.1 Hz, 1H), 7.46-7.56 (m, 3H), 5.82 (m, 1H), 5.51 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 135.7, 134.3 (T, J = 23.7 Hz), 133.8, 131.1, 128.7, 128.3, 126.3, 125.9, 125.8, 123.9, 123.8, 117.1. **^{2}H NMR** (62 MHz, CH_3CN) δ 7.57 (0.99D). **HRMS** (APCI) $[M+H]^+$ calcd. for $[C_{12}H_{10}D]^+$ 156.0924, 156.0952 found. **IR** (neat, cm^{-1}) 3045, 2924, 2852, 2242, 1609, 1590, 1409, 1337, 914, 797, 773.

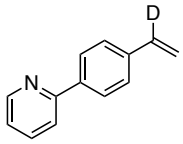
9-chloro-10-(vinyl-1-*d*)anthracene (**13**-α-*d*)



9-chloro-10-(vinyl-1-*d*)anthracene was prepared according to the general procedure using 9-chloro-10-vinylanthracene (238.7 mg, 1 mmol, 1 eq), MeOH (40 µl, 1 mmol, 1 eq), KO-*t*-Bu (11.2 mg, 0.1 mmol, 0.1 eq), and DMSO-d_6 (2.0 mL). The solution was stirred at 70 °C for 45 min. Silica gel chromatography (hexanes) yielded the title compound as a yellow solid (199.6 mg, 83% yield, 99% α-deuteration, 0% other deuteration). **Melting Point**: 111-114 °C. **^{1}H NMR** (400 MHz, CD_2Cl_2) δ 8.54 (d, J = 8.8 Hz, 2H),

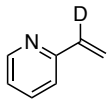
8.37 (d, J = 8.8 Hz, 2H), 7.61-7.65 (m, 2H), 7.52-7.56 (m, 2H), 6.06 (s, 1H), 5.61 (s, 1H). **^{13}C NMR** (101 MHz, CD_2Cl_2) δ 134.0, 133.3 (T, J = 24.2 Hz), 130.1, 128.9, 128.4, 127.1, 126.8, 126.0, 125.2, 123.8. **^{2}H NMR** (62 MHz, CH_3CN) δ 7.54 (0.99D). **HRMS** (APCI) $[M+H]^+$ calcd. for $[C_{16}H_{11}DCl]^+$ 240.0690, 240.0661 found. **IR** (neat, cm^{-1}) 3078, 3038, 2981, 2921, 2222, 1619, 1439, 1420, 1327, 1258, 925, 757.

2-(4-(vinyl-1-*d*)phenyl)pyridine (**14**-α-*d*)



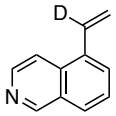
2-(4-(vinyl-1-*d*)phenyl)pyridine was prepared according to the general procedure using 2-(4-vinylphenyl)pyridine (181.2 mg, 1 mmol, 1 eq), MeOH (40 µl, 1 mmol, 1 eq), KO-*t*-Bu (11.2 mg, 0.1 mmol, 0.1 eq), and DMSO-d_6 (2.0 mL). The solution was stirred at 70 °C for 24 h. Silica gel chromatography (30% EtOAc/hexanes) yielded the title compound as a pale yellow oil (151.6 mg, 83% yield, 97% α-deuteration, 4% other deuteration). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.69 (d, J = 4.6 Hz, 1H), 7.98 (d, J = 8.2 Hz, 2H), δ 7.71-7.76 (m, 2H), 7.52 (d, J = 8.2 Hz, 2H), 7.22 (m, 1H), 6.77 (dd, J_1 = 11.0 Hz, J_2 = 17.7 Hz, 0.03H), 5.82 (s, 1H), 5.30 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) 157.2, 149.9, 139.9, 138.4, 136.9, 136.3 (T, J = 23.8 Hz), 127.2, 126.8, 122.3, 120.6, 114.5. **^{2}H NMR** (62 MHz, CH_3CN) δ 7.85 (0.04D), 6.84 (0.97D). **HRMS** (DART) $[M+H]^+$ calcd. for $[C_{13}H_{11}DN]^+$ 183.1033, 183.1041 found. **IR** (neat, cm^{-1}) 3083, 3049, 3007, 2232, 1612, 1587, 1572, 1465, 1433, 908, 850, 783, 739.

2-(vinyl-1-*d*)pyridine (**15**-α-*d*)



2-(vinyl-1-*d*)pyridine was prepared according to the general procedure using 2-vinylpyridine (105.1 mg, 1 mmol, 1 eq), MeOH (20 µl, 0.5 mmol, 0.5 eq), KO-*t*-Bu (11.2 mg, 0.1 mmol, 0.1 eq), and DMSO-d_6 (2.0 mL). The solution was stirred at 50 °C for 12 h. 1,3,5-Trimethoxybenzene internal standard (79.3 mg, 0.47 mmol) was added to the solution prior to purification to determine the ^{1}H NMR yield (78% yield). The crude reaction mixture was loaded directly onto a silica gel column and eluted with a gradient of hexanes to 20% Et_2O/hexanes to afford the title compound as a clear oil (65.2 mg, 61% isolated yield, >99% α-deuteration, 0% other deuteration). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.58 (d, J = 4.6 Hz, 1H), δ 7.64 (td, J_1 = 7.7 Hz, J_2 = 1.8 Hz, 1H), 7.34 (d, J = 7.8 Hz, 1H), 7.15 (m, 1H), 6.82 (dd, J_1 = 11.0 Hz, J_2 = 17.6 Hz, 0.01H), 6.20 (s, 1H), 5.48 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.9, 149.7, 136.8 (T, J = 24.1 Hz), 136.6, 122.6, 121.4, 118.2. **^{2}H NMR** (62 MHz, $CDCl_3$) δ 6.83 (0.99D). **HRMS** (DART) $[M+H]^+$ calcd. for $[C_7H_7DN]$ 107.0720, 107.0735 found. **IR** (neat, cm^{-1}) 3077, 3005, 2926, 2218, 1586, 1563, 1470, 1432, 1150, 925, 796, 730.

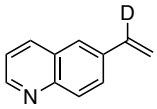
5-(vinyl-1-*d*)isoquinoline (**16**-α-*d*)



5-(vinyl-1-*d*)isoquinoline was prepared according to the general procedure using 5-vinylisoquinoline (155.2 mg, 1 mmol, 1 eq), MeOH (40 µl, 1 mmol, 1 eq), KO-*t*-Bu (11.2 mg, 0.1 mmol, 0.1 eq), and DMSO-d_6 (2.0 mL). The solution was stirred at 60 °C for 6 h. Silica gel chromatography (30% EtOAc/hexanes) yielded the title compound as a pale yellow oil (118.1 mg, 76% yield, 97% α-deuteration, 0% other deuteration). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.24 (s. 1H), 8.54 (d, J = 6.0 Hz, 1H), 7.82-7.90 (m, 3H), 7.57 (t, J = 7.4 Hz, 1H), 7.36 (dd, J_1 = 11.0 Hz, J_2 = 17.4 Hz, 0.03H), 5.83 (s, 1H), 5.53 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.3, 143.5, 134.6, 133.8, 132.5 (T, J = 23.9 Hz), 129.0, 127.7, 127.5, 127.2, 118.2, 116.8. **^{2}H NMR** (62 MHz, CH_3CN) δ 7.49 (0.97D). **HRMS** (APCI) $[M+H]^+$ calcd. for $[C_{11}H_9DN]^+$

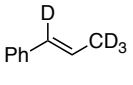
157.0876, 157.0871 found. **IR** (neat, cm^{-1}) 3055, 3026, 2923, 2851, 1616, 1584, 1487, 1367, 915, 809, 755, 686.

6-(vinyl-1-*d*)quinoline (**17**-α-*d*)



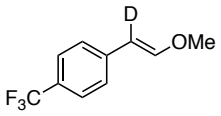
6-(vinyl-1-*d*)quinoline was prepared according to the general procedure using 6-vinylquinoline (155.2 mg, 1 mmol, 1 eq), MeOH (40 µl, 1 mmol, 1 eq), KO-*t*-Bu (11.2 mg, 0.1 mmol, 0.1 eq), and DMSO-d_6 (2.0 mL). The solution was stirred at 60 °C for 13 h. Silica gel chromatography (40% EtOAc/hexanes) yielded the title compound as a pale yellow oil (131.5 mg, 84% yield, 95% α-deuteration, 4% other deuteration). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.86 (d, J = 4.3 Hz, 1H), 8.04-8.11 (m, 2H), 7.86 (d, J = 8.9 Hz, 1H), 7.70 (s, 1H), 7.37 (dd, J_1 = 4.2 Hz, J_2 = 8.2 Hz, 1H), 6.88 (dd, J_1 = 10.9 Hz, J_2 = 17.6 Hz, 0.05H), 5.89 (m, 1H), 5.39 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.2, 148.2, 136.1 (T, J value could not be determined due to signal overlap), 136.0, 135.8, 135.6, 129.7, 128.4, 125.8, 121.4, 115.2. **^{2}H NMR** (62 MHz, CH_3CN) δ 8.19 (0.04D), 6.91 (0.95D). **HRMS** (DART) $[M+H]^+$ calcd. for $[C_{11}H_9DN]^+$ 157.0876, 157.0880 found. **IR** (neat, cm^{-1}) 3016, 2923, 2233, 1585, 1498, 908, 888, 837, 795, 775.

prop-1-en-1-yl-1,3,3,3-*d*$_4$ benzene (**18**-d_4)



Prop-1-en-1-yl-1,3,3,3-d_4 benzene was prepared according to the general procedure using (*Z*)-prop-1-en-1-ylbenzene (118.2 mg, 1 mmol, 1 eq), MeOH (40 µl, 1 mmol, 1 eq), KO-*t*-Bu (11.2 mg, 0.1 mmol, 1 eq), and DMSO-d_6 (2.0 mL). The solution was stirred at 70 °C for 22 h. The crude reaction mixture was loaded directly onto a silica gel column and eluted with hexanes to afford an isomeric mixture (*E*/*Z* approximately 97:3) of the title compound as a clear oil (81.6 mg, 67% yield, 97% β-methyl deuteration, 95% α-deuteration, 0% other deuteration). Note: "*" denotes minor isomer. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28-7.35 (m, 4H), 7.20 (t, J = 7.1 Hz, 1H), 6.41 (d, J = 15.8 Hz, 0.05H), 6.23 (m, 1H), 5.79* (m, 0.03H), 1.86 (m, 0.10H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.1, 131.0 (T, J = 23.1 Hz), 129.0, 128.7, 126.9, 125.6, 17.9 (m). **^{2}H NMR** (62 MHz, CH_3CN) δ 6.47 (1D), 1.82 (3D). **GCMS** calcd. for $[C_9H_6D_4]^+$ 122.1, 122.1 found. **IR** (neat, cm^{-1}) 3080, 3058, 3023, 2924, 2223, 2110, 1494, 1446, 930, 769, 692.

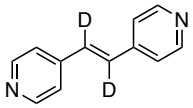
1-(2-methoxyvinyl-1-*d*)-4-(trifluoromethyl)benzene (**19**-α-*d*)



1-(2-methoxyvinyl-1-*d*)-4-(trifluoromethyl)benzene was prepared using a slightly modified procedure. Inside a nitrogen filled glovebox, 1-(2-methoxyvinyl)-4-(trifluoromethyl)benzene (101.0 mg, 0.5 mmol, 1 eq), MeOH (20 µl, 0.5 mmol, 1 eq), KO-*t*-Bu (5.6 mg, 0.05 mmol, 0.1 eq) and DMSO-d_6 (1.0 mL) were added to an oven-dried 4 mL vial (ThermoFisher, C4015-1). The vial was sealed with a PTFE lined screw cap (ThermoFisher, C4015-1A) and then removed from the glovebox. The solution was placed into a preheated 100 °C aluminum reaction block for 26 h. The reaction solution was quenched with acetic acid before allowing to cool to rt. The crude reaction mixture was washed with H_2O (20 mL), extracted with EtOAc (3 x 20 mL), dried with Na_2SO_4 and concentrated *in vacuo*. Silica gel chromatography (1% EtOAc/hexanes) yielded an isomeric mixture (*E/Z* approximately 2:1) of the title compound as a clear oil (65.8 mg, 65% yield, 97% α-deuteration, 0% other deuteration). Note: "*" denotes minor isomer. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65* (d, J = 8.1 Hz, 1H), 7.49-7.53 (m, 3H), 7.31 (d, J = 8.0 Hz, 2H), 7.13 (s, 1H), 6.24* (s, 1H), 5.82 (d, J = 12.9 Hz, 0.01H), 5.25* (d, J = 7.0 Hz, 0.01H), 3.82* (s, 3H), 3.72 (s, 3H). **^{13}C**

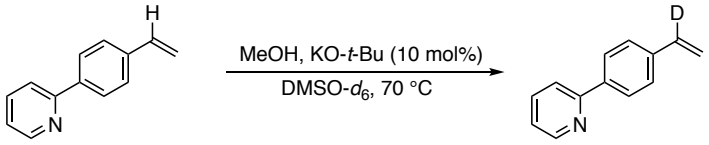
NMR (101 MHz, $CDCl_3$) δ 150.6, 149.8, 140.2, 139.4, 128.1, 127.6, 127.4, 127.3, 127.1, 125.8 (q, J = 3.9 Hz), 125.0 (q, J = 3.9 Hz), 124.9, 123.1, 123.0, 103.9, 103.7, 103.3, 61.0, 56.7. **^{2}H NMR** (62 MHz, CH_3CN) δ 5.95 (1D), 5.35* (1D). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.29 (3F), -63.31* (3F). **IR** (neat, cm^{-1}) 3011, 2937, 1641, 1613, 1321, 1104, 1065, 841. **HRMS** (APCI) $[M+H]^+$ calcd. for $[C_{10}H_9DF_3O]^+$ 204.0747, 204.0737 found. A HMBC 2D-NMR was acquired to confirm that the α-position (and not the β-position) was deuterated. The 3-bond correlation between the $-OCH_3$ carbon and the β-proton (see section XII) is consistent with the signal that disappears due to incorporation of deuterium and does not correspond to the β-proton.

(*E*)-1,2-di(pyridin-4-yl)ethene-1,2-d_2 (20-d_2)



(*E*)-1,2-di(pyridin-4-yl)ethene-1,2-d_2 was prepared according to the general procedure using (*E*)-1,2-di(pyridin-4-yl)ethene (182.2 mg, 1 mmol, 1 eq), MeOH (202 µl, 5 mmol, 5 eq), KO-*t*-Bu (11.2 mg, 0.1 mmol, 0.1 eq), and DMSO-d_6 (2.0 mL). The solution was stirred at 60 °C for 72 h. Silica gel chromatography (10% $MeOH/CH_2Cl_2$) yielded the title compound as a yellow solid (144.0 mg, 79% yield, 95% α-deuteration, 0% other deuteration). **Melting Point**: 151-152 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.61 (d, J = 6.0 Hz, 4H), 7.62 (d, J = 6.0 Hz, 4H), 7.54 (s, 0.09 H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.4, 143.3, 130.1 (T, J = 23.6 Hz), 121.1. **^{2}H NMR** (62 MHz, CH_3CN) δ 7.43 (1.90D). **HRMS** (DART) $[M+H]^+$ calcd. for $[C_{12}H_9N_2D_2]^+$ 185.1048, 185.1048 found. **IR** (neat, cm^{-1}) 3020, 2923, 2362, 2341, 1594, 1409, 819, 542.

VI. Influence of MeOH on Reaction Kinetics and Mass Balance



General Procedure: Outside of the glovebox, 2-(4-vinylphenyl)pyridine (**14**) (181.2 mg, 1 mmol, 1 eq) was weighed to three oven-dried 4 mL vial (ThermoFisher, C4015-1). Inside of a nitrogen filled glovebox, the appropriate quantity of MeOH (40 µl, 1 mmol, 1 eq; 20 µl, 0.5 mmol, 0.5 eq; or 10 µl, 0.25 mmol, 0.25 eq) and DMSO-d_6 (2.0 mL) were added to each vial. The solutions were then added to an oven-dried 4 mL vial (ThermoFisher, C4015-1) containing KO-*t*-Bu (11.2 mg, 0.1 mmol, 0.1 eq) and approximately 0.35 mmol of 1,3,5-trimethoxybenzene. The solution was agitated until homogenous and then divided into eight separate 0.25 mL portions into eight oven-dried 4 mL vials (ThermoFisher, C4015-1) and sealed with PTFE lined screw cap (ThermoFisher, C4015-1A). The solutions were removed from the glovebox and placed into a preheated 70 °C aluminum reaction block. For each reaction time point in the tables below, a separate reaction solution was quenched with acetic acid at 70 °C and an ^{1}H NMR spectrum was acquired. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum was used to determine the percentage of deuterium incorporation into the α-position and the overall quantity of styrene (indicated as NMR yield below).

Time (min)	α-deuteration (%)	NMR Yield (%)
15	16	99
60	45	99
90	53	99
180	80	99
300	90	98.5
360	93	98.5
600	100	97

Table S2 (a): Results of α-deuteration reaction of **14** using 1 equiv MeOH.

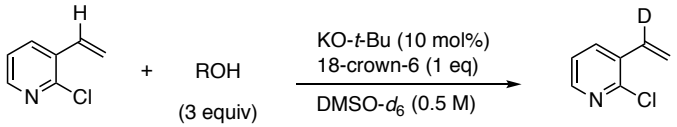
Time (min)	α-deuteration (%)	NMR Yield (%)
10	15	99
20	23	99
30	30	99
40	40	98
80	61	97
170	89	91
210	93	89
300	100	75

Table S2 (b): Results of α-deuteration reaction of **14** using 0.5 equiv MeOH.

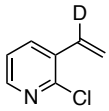
Time (min)	α-deuteration (%)	NMR Yield (%)
10	26	90
20	38	85
30	46	77
50	63	65
70	72	48
100	79	30
110	81	22

Table S2 (c): Results of α-deuteration reaction of **14** using 0.25 equiv MeOH.

VII. Overcoming S_NAr for 2-chloro-3-vinylpyridine



2-chloro-3-(vinyl-1-*d*)pyridine (**21**-α-*d*)



2-chloro-3-vinyl pyridine (69.8 mg, 0.5 mmol, 1 eq) was weighed into an oven-dried 4 mL vial (ThermoFisher, C4015-1). The vial was sealed and brought into a nitrogen filled glovebox where 1-cyclopropyl ethanol (147 µl, 1.5 mmol, 3 eq) or anhydrous MeOH (61 µl, 1.5 mmol, 3 eq) was added followed by DMSO-d_6 (1.0 mL), 18-crown-6 ether (132.2 mg, 0.5 mmol, 1 eq), and KO-*t*-Bu (11.2 mg, 1 mmol, 1 eq). The vials were capped, removed from glovebox and placed into a pre-heated 40 °C silicon oil bath and stirred for 1 h. The reaction solutions were quenched with acetic acid after 1 h while at 40 °C. The reaction solutions were then washed with H_2O (20 mL) and extracted with EtOAc (3 x 20 mL), dried over Na_2SO_4, and concentrated *in vacuo*. Silica gel chromatography (2% EtOAc/hexanes) yielded the title compound as a light yellow oil. **Note**: provided below are regions of the isolated alkene ^{1}H NMR spectra using both alcohols for comparison of the degree of deuterium incorporation.

Using MeOH: (30.1 mg, 43% yield, 21% α-deuteration, 0% other deuteration).
Using 1-cyclopropylethanol: (44.1 mg, 63% yield, 96% α-deuteration, 0% other deuteration)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (dd, J_1 = 4.7 Hz, J_2 = 1.8 Hz, 1H), 7.87 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.23 (dd, J_1 = 7.8 Hz, J_2 = 4.7 Hz, 1H), 7.03 (dd, J_1 = 17.5 Hz, J_2 = 11.0 Hz, 0.04H),

5.78 (m, 1H), 5.49 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.2, 148.8, 135.1, 132.5, 131.9 (T, J = 24.8 Hz), 122.9, 118.7. **^{2}H NMR** (CH_3CN, 62 MHz) δ 7.01 (0.96D). **HRMS** (APCI): $[M+H]^+$ calcd. for $[C_7H_6DClN]^+$ 141.0330, 141.0334 found. **IR** (neat, cm^{-1}) 3090, 3045, 2926, 2853, 1555, 1381, 1134, 1063, 922, 803, 682.

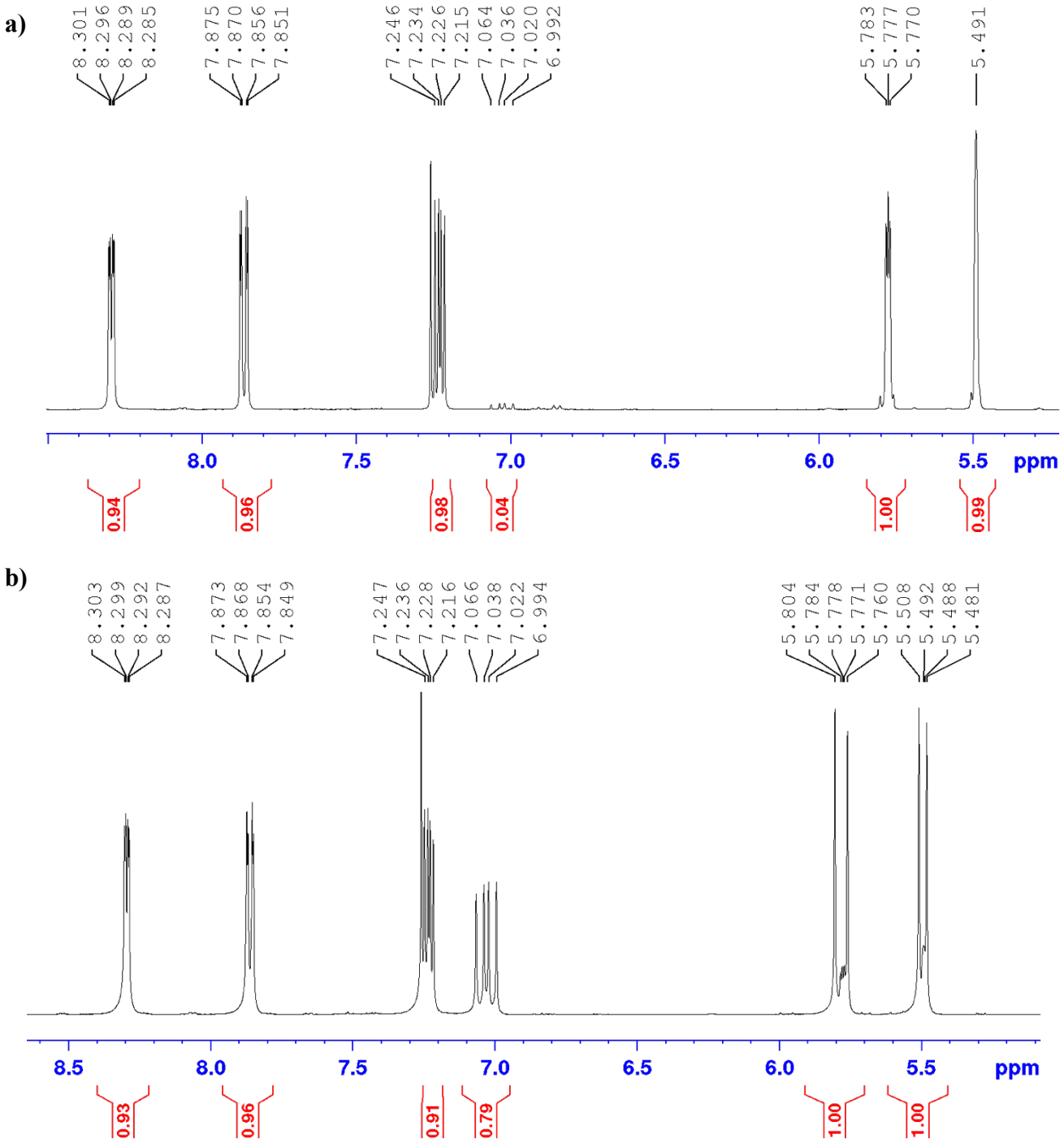
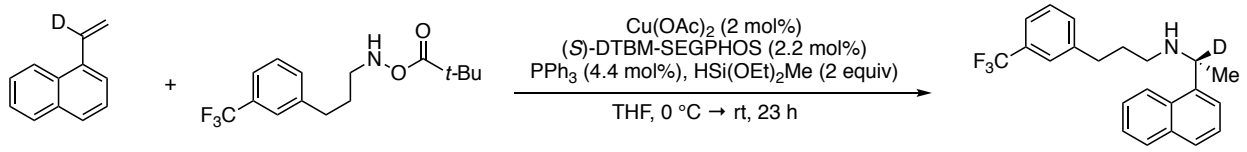
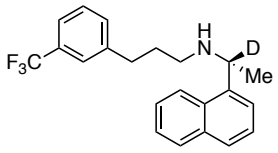


Figure S4: ^{1}H NMR spectra of 1-cyclopropylethanol **(a)** and MeOH **(b)** conditions.

VIII. Enantioselective Derivatization of α-Deuterated Styrenes



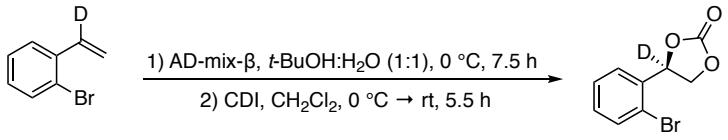
(*R*)-*N*-(1-(naphthalen-1-yl)ethyl-1-*d*)-3-(3-(trifluoromethyl)phenyl)propan-1-amine (23)



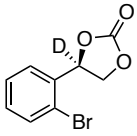
This procedure was adopted from a literature report.[2] Inside a nitrogen filled glovebox, $Cu(OAc)_2$ (3.7 mg, 0.02 mmol), (*S*)-DTBM-SEGPHOS (26.0 mg, 0.022 mmol), PPh_3 (11.5 mg, 0.044 mmol) and THF (1.0 mL) were added to an oven-dried 4 mL vial (ThermoFisher, C4015-1). The vial was sealed with a screw cap lined with a PTFE septum (ThermoFisher, C4015-1A), removed from the glovebox, and stirred under ambient conditions until the solution was homogenous. The solution was then taken back into the glovebox and $HSi(OEt)_2Me$ (320 µl, 2.0 mmol) was added. This solution (0.5 mL, corresponding to 2 mol% L*CuH and 2.0 equiv of silane) was taken up into an air tight syringe, removed from the glovebox and transferred to a solution of 1-(vinyl-1-*d*)naphthalene (77.6 mg, 0.5 mmol, 1 eq), *O*-pivaloyl-*N*-(3-(3-(trifluoromethyl)phenyl)propyl)hydroxylamine (182.0 mg, 0.6 mmol, 1.2 eq), and THF (0.5 mL) under an N_2 atmosphere at 0 °C. The reaction was stirred at 0 °C for 9 h and then rt for 14 h. The reaction solution was then diluted with CH_2Cl_2 and washed with 3M K_2CO_3 (*aq*, 3 x 30 mL). The organic layer was dried over Na_2SO_4 and then concentrated *in vacuo*. Silica gel chromatography (30% EtOAc/hexanes to 50% EtOAc/hexanes) yielded the title compound as a light yellow oil (149.7 mg, 84% yield, 94% ee). Benzylic deuteration was measured to be >99%, consistent with that of the 1-(vinyl-1-*d*)naphthalene starting material. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.2 Hz, 1H), 7.88 (m, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.64 (d, J = 7.2 Hz, 1H),7.46-7.54 (m, 3H), 7.42-7.44 (m, 2H), 7.30-7.37 (m, 2H), 2.56-2.77 (m, 4H), 1.80-1.88 (m, 2H), 1.49 (s, 3H), 1.40 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.3, 141.3, 134.2, 132.0, 131.5, 130.8 (q, J = 32.0 Hz), 129.2, 128.9, 127.4, 126.0, 125.9, 125.5, 125.2 (q, J = 3.7 Hz), 123.1, 122.8, 53.5 (T, J = 20.9 Hz), 47.4, 33.7, 32.1, 23.7. **^{2}H NMR** (62 MHz, CH_3CN) δ 4.56 (0.97D). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.5 (3F). **HRMS** (DART) $[M+H]^+$ calcd. for $[C_{22}H_{22}DF_3N]^+$ 359.1845, 359.1850 found. **IR** (neat, cm^{-1}) 3047, 2927, 2859, 1449, 1326, 1159, 1119, 1072, 797, 776, 702. **Specific Rotation**: $[\alpha]_D^{22} = +22.5°$.

Procedure for ee determination of 23: isolated compound **23** was subsequently acylated with (*S*)-2-chloro-2-methoxy-2-phenylacetyl chloride to determine the enantiomeric excess. All procedural steps were conducted open to air. (*R*)-*N*-(1-(naphthalen-1-yl)ethyl-1-*d*)-3-(3-(trifluoromethyl)phenyl)propan-1-amine (35.8 mg, 0.1 mmol, 1 eq) was weighed into an oven-dried 4 mL vial and constituted in dry CH_2Cl_2 (1.0 mL). (*S*)-2-chloro-2-methoxy-2-phenylacetyl chloride (21 µl, 0.12 mmol, 1.2 eq) was added followed by triethylamine (21 µl, 0.15 mmol, 1.5 eq). The solution was stirred at rt for 14 h. The reaction solution was diluted with CH_2Cl_2 (40 mL) and washed once with H_2O (30 mL), once with saturated aqueous $NaHCO_3$ (30 mL) and then dried over Na_2SO_4. The organic solution was concentrated *in vacuo*. The ee (%) was determined by ^{1}H NMR spectroscopy using the relative integration of the (-OMe) peaks of the diastereomers

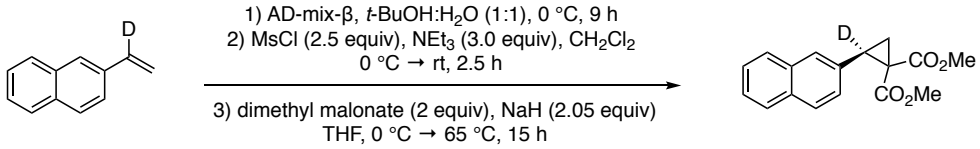
compared to a racemic sample of acylated **25** (See section XII). The observed ee value (94%) is similar to that reported by Buchwald.[2]



(*R*)-4-(2-bromophenyl)-1,3-dioxolan-2-one-4-*d* (24)



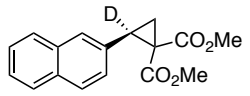
AD-mix-β (700 mg) was weighed into a 25 mL round bottom flask and constituted in *t*-BuOH (2.0 mL) and H_2O (2.5 mL). The slurry was cooled to 0 °C and 1-bromo-2-(vinyl-1-*d*)benzene (92.1 mg, 0.5 mmol, 1 eq in 0.5 mL *t*-BuOH) was added. The reaction mixture was stirred at 0 °C for 7.5 h. Na_2SO_3 (about 30 mg) was then added, and the solution was allowed to stir an additional 30 min at rt. The solution was then washed with H_2O (30 mL) and extracted with EtOAc (3 x 30 mL). The organic layer was washed once with brine (20 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was then transferred into an oven-dried 10 mL round bottom flask, constituted in dry CH_2Cl_2 (2.0 mL) and cooled to 0 °C. Next, 1,1'-carbonyldiimidazole (162.2 mg, 1.0 mmol, 2 eq) was added over 3 min. The solution was allowed to warm to rt and stirred for 5.5 h. The reaction solution was directly loaded onto a silica gel column and eluted with 10% EtOAc/hexanes to afford the title compound as a clear oil (89.9 mg, 74% yield, 98% ee). Benzylic deuteration was measured to be 97%, consistent with that of the 1-bromo-2-(vinyl-1-*d*)benzene starting material. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.9 Hz, 1H), 7.50 (d, J = 7.9 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.28 (t, J = 7.7 Hz, 1H), 5.95 (t, J = 7.9 Hz, 0.03H), 4.98 (d, J = 8.6 Hz, 1H), 4.24 (d, J = 8.6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.8, 136.4, 133.3, 130.8, 128.4, 126.2, 120.4, 76.4 (T, J = 24.4 Hz), 70.7. **^{2}H NMR** (62 MHz, CH_3CN) δ 5.99. **HRMS** (DART) $[M+NH_4]^+$ calcd. for $[C_9H_9DBrNO_3]^+$ 260.9985, 260.9991 found. **IR** (neat) 3067, 2918, 1797, 1470, 1198, 1058, 752. **Specific Rotation**: $[\alpha]_D^{23}$ = -54.1°. **HPLC** analysis: Chiralcel AD-3 (Hex/EtOH = 90/10, 0.6 mL/min, 210 nm, 50 °C), 14.7 min (major), 15.5 min (minor), 98% ee.



Step 1: AD-mix-β (1.40 g) was weighed into a 50 mL round bottom flask and constituted in *t*-BuOH/H_2O (10 mL of a 1:1 ratio). The slurry was cooled to 0 °C and 2-vinylnaphthalene-α-d_1 (155.2 mg, 1.0 mmol, 1 eq) was added. The reaction solution was stirred at 0 °C for 9 h. Na_2SO_3 (about 30 mg) was then added, and the solution was allowed to stir an additional 30 min at rt. The solution was then washed with H_2O (30 mL) and extracted with EtOAc (3 x 30 mL). The organic layer was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Silica gel chromatography (60% EtOAc/hexanes to 100% EtOAc) yielded (*R*)-1-(naphthalen-2-yl)ethane-1-*d*-1,2-diol as a white solid (186 mg, 98% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83-7.86 (m, 4H), 7.46-7.52 (m, 3H), 3.87 (dd, J_1 = 7.4 Hz, J_2 = 11.2 Hz, 1H), 3.77 (dd, J_1 = 4.7 Hz, J_2 = 11.2 Hz, 1H), 2.54 (s, 1H), 1.99 (dd, J_1 = 4.7 Hz, J_2 = 7.4 Hz, 1H).

Step 2: (*R*)-1-(naphthalen-2-yl)ethane-1-*d*-1,2-diol (186 mg, 0.98 mmol, 1 eq) was weighed into an oven-dried 10 mL round bottom flask and constituted in dry CH_2Cl_2 (5.0 mL). The solution was cooled to 0 °C and triethylamine (410 µl, 2.94 mmol, 3.0 eq) was added followed by a solution of methanesulfonyl chloride (190 µl, 2.45 mmol, 2.5 eq in 1.3 mL of CH_2Cl_2). The solution was stirred at 0 °C for 1 h, warmed to rt, and stirred for an additional 1.5 h. The reaction solution was then poured into 1M HCl (30 mL) and extracted CH_2Cl_2 (3 x 30 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (30 mL) and brine (20 mL). The organic layer was then dried over Na_2SO_4 and concentrated *in vacuo*. Silica gel chromatography (30% EtOAc/hexanes to 40% EtOAc/hexanes) yield (*R*)-1-(naphthalen-2-yl)ethane-1,2-diyl-1-*d* dimethanesulfonate as a white solid (295.3 mg, 86% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86-7.94 (m, 4H), 7.54-7.59 (m, 2H), 7.50 (dd, J_1 = 1.8 Hz, J_2 = 8.5 Hz, 1H), 4.64 (1H), 4.48 (1H), 3.11 (s, 3H), 2.87 (s, 3H).

dimethyl (*R*)-2-(naphthalen-2-yl)cyclopropane-1,1-dicarboxylate-2-*d* (25)[3]



Step 3: A 60% dispersion of NaH (70.2 mg, 1.8 mmol, 2.05 eq) was weighed into an oven-dried 50 mL round bottom flask and sealed with a septum. The flask was evacuated and backfilled 3 times with N_2 gas and left under positive pressure. Dry THF (5.0 mL) was added via syringe and the slurry was cooled to 0 °C. Dimethyl malonate (195 µl, 1.7 mmol, 2 eq) was then added slowly. The solution was allowed to stir for 30 min at 0 °C. (*R*)-1-(naphthalen-2-yl)ethane-1,2-diyl-1-*d* dimethanesulfonate (295.3 mg, 0.86 mmol, 1 eq in 8.0 mL of THF) was then added dropwise to the NaH solution. The reaction mixture was allowed to warm to rt and was then placed in a pre-heated 65 °C silicon oil bath and stirred for 15 h. The reaction solution was quenched with H_2O (30 mL) and extracted EtOAc (3 x 30 mL). The organic layer was washed with 1.0M NaOH (30 mL) and brine (20 mL), dried over Na_2SO_4, and then concentrated *in vacuo*. Silica gel chromatography (5% EtOAc/hexanes to 10% EtOAc/hexanes) yielded the title compound as a white solid (186.1 mg, 76% yield for the step, 65% yield overall, 96% ee). Benzylic deuteration was assumed to be 97%, corresponding to that of the 2-(vinyl-1-*d*)naphthalene starting material. **Melting Point**: 84-86 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74-7.80 (m, 3H), 7.64 (s, 1H), 7.43-7.47 (m, 2H), 7.33 (dd, J_1 = 8.5 Hz, J_2 = 1.8 Hz, 1H), 3.82 (s, 3H), 3.30 (s, 3H), 2.33 (d, J = 5.2 Hz, 1H), 1.83 (d, J = 5.2 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.4, 167.2, 133.3, 132.8, 132.2, 128.0, 127.9, 127.8, 127.3, 126.8, 126.3, 126.1, 53.0, 52.4, 37.5, 32.7 (T, J = 25.5 Hz), 19.4. **^{2}H NMR** (62 MHz, CH_3CN) δ 3.30 (0.97D). **HRMS** (APCI) $[M+H]^+$ calcd. for $[C_{17}H_{16}DO_4]^+$ 286.1190, 286.1162 found. **IR** (neat, cm^{-1}) 3059, 2951, 2846, 1739, 1712, 1435, 1336, 1264, 1121, 750. **Specific Rotation**: $[\alpha]_D^{23}$ = +191.4°. **HPLC** analysis: Chiralcel OJ-3 (Hex/EtOH = 80/20, 0.8 mL/min, 210 nm, 50 °C), 10.2 min (minor), 11.2 min (major), 96% ee.

IX. Additional Examples of Styrene α-Deuteration

During the course of the development of the reported substrate scope, we found additional examples of styrene derivatives that underwent highly α-selective deuteration. We also discovered that electron-rich styrenes fail to undergo any α-deuteration. These findings, along with examples of vinyl arenes that undergo competitive side deuteration, are reported in Figure S5 below. The reported values were obtained following the general procedure provided in Section IV.

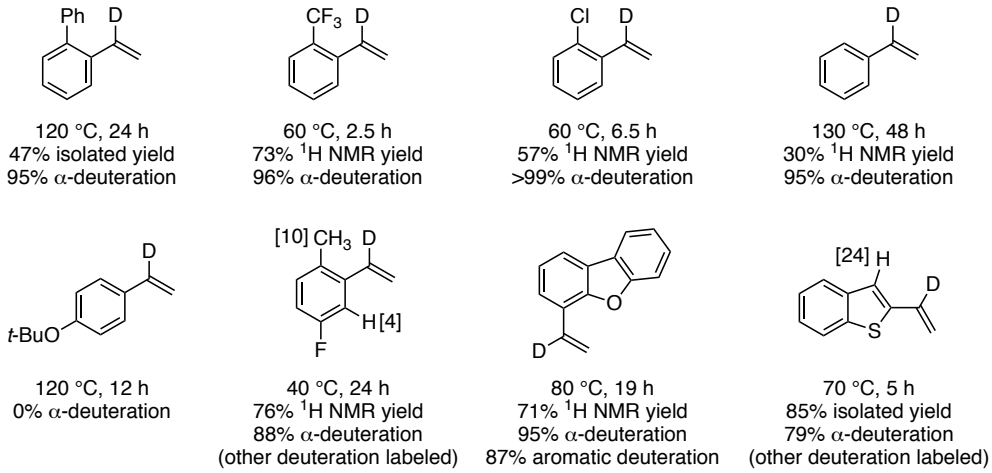


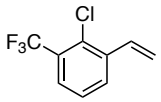
Figure S5: Additional examples of styrene α-deuteration. Yield determined by isolation or ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.

X. Preparation of Aryl Alkene Substrates

1-Bromo-2-vinylbenzene, 2-vinylpyridine, and (*E*)-1,2-di(pyridin-4-yl)ethene were purchased from Combi-Blocks and used as received. (*Z*)-prop-1-en-1-ylbenzene was purchased from TCI and used as received. (*E*)-1-styryl-4-vinylbenzene[4], 1-iodo-2-vinylbenzene[5], methyl 4-vinylbenzoate[6], (trifluoromethyl)(4-vinylphenyl)sulfane[7], 4-vinyl-1,1'-biphenyl[8], 1-(trifluoromethyl)-4-vinylbenzene[9], 2-(4-vinylphenyl)pyridine[10], 1-vinylnaphthalene[11], 9-chloro-10-vinylanthracene[12], 6-vinylquinoline[13], 5-vinylisoquinoline[14] and 2-chloro-3-vinylpyridine[15] were prepared according to the general procedure below unless otherwise noted. 1-(2-Methoxyethenyl)-4-trifluoromethylbenzene[16] was made according to the general procedure below with methoxymethyltriphenylphosphonium chloride as the ylide precursor. Characterization of the aryl alkenes matched reported literature data.

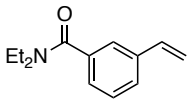
General procedure for styrene preparation: Methyltriphenylphosphonium bromide (1.2-1.5 eq) was added to an oven or flame-dried round bottom flask (methyltriphenylphosphonium bromide was dried for at least 1 hour *in vacuo* at 100 °C prior to use). The flask was then evacuated and backfilled with N_2 gas (3 times). Anhydrous THF (20 mL per 1 g of aldehyde) was added via syringe and the solution was cooled to 0 °C. KO-*t*-Bu (1.2-1.5 eq) constituted in anhydrous THF or *n*-butyl lithium (1.6M in hexanes, 1.2-1.5 eq) was then added via syringe, forming the observed yellow phosphonium ylide. The solution was stirred for 15 min at 0 °C and then the appropriate aldehyde (1M in THF) was added dropwise. The reaction was allowed to stir at 0 °C until all of the aldehyde was consumed as indicated by TLC analysis (approximately 15 to 30 min). The reaction solution was quenched with H_2O and extracted with ethyl acetate (3 x reaction volume). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo.* Silica gel chromatography was used to purify all substrates.

2-chloro-1-(trifluoromethyl)-3-vinylbenzene (5)



2-chloro-1-(trifluoromethyl)-3-vinylbenzene was made according to the general procedure with 2-chloro-3-trifluoromethylbenzaldehyde (2.00 g, 9.6 mmol, 1 eq), methyltriphenylphosphonium bromide (4.45 g, 12.5 mmol, 1.3 eq), and KO-*t*-Bu (1.51 g, 13.4 mmol, 1.4 eq) and THF (50 mL). Purification by silica gel chromatography (hexanes) yielded the title compound as a clear oil (971 mg, 49% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, J = 7.8 Hz, 1H), 7.62 (d, J = 7.7 Hz, 1H), 7.34 (t, J = 7.8 Hz, 1H), 7.18 (dd, J_1 = 11.0 Hz, J_2 = 17.4 Hz, 1H), 5.76 (d, J = 17.4 Hz, 1H), 5.49 (d, J = 11.0 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.5, 132.9, 131.1, 130.4, 129.3 (q, J = 31.0 Hz), 127.0 (q, J = 5.6 Hz), 126.7, 123.0 (q, J = 274.5 Hz), 118.6. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.5 (3F). **GCMS** calcd. for $[C_9H_6ClF_3]^+$ 206.0, 206.0 found. **IR** (neat, cm^{-1}): 3094, 3025, 2992, 1435, 1404, 1318, 1129, 1096, 1049, 805.

***N,N*-diethyl-3-vinylbenzamide (8)**



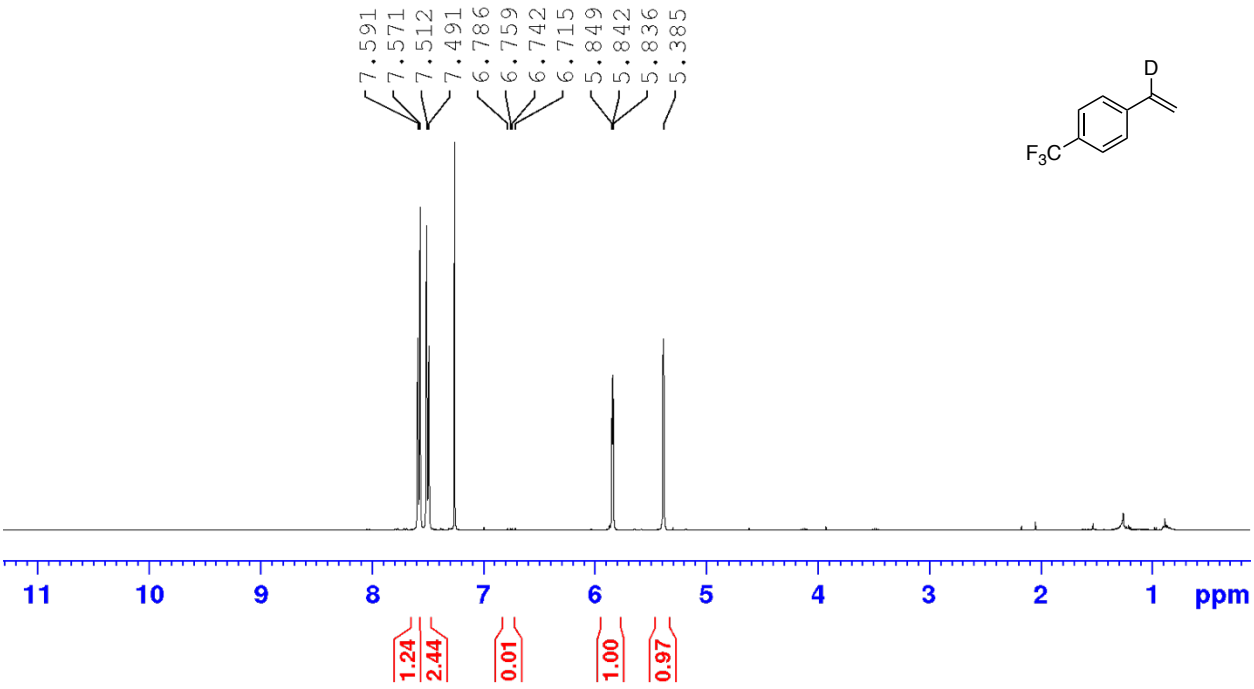
3-Vinylbenzoic acid (2.0 g, 13.5 mmol, 1 eq), *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (3.88 g, 20.3 mmol, 1.5 eq), and 1-hydroxybenzotriazole hydrate were added to a round bottom flask and constituted in CH_2Cl_2 (30 mL). The solution was cooled to 0 °C and *N*,*N*-diethylamine (1.8 mL, 17.6 mmol, 1.3 eq) and triethylamine (2.8 mL, 20.3 mmol, 1.5 eq) were added via syringe. The reaction solution was allowed to warm to rt and stirred for 23 h. The mixture was washed with H_2O and extracted CH_2Cl_2 (3 x 50 mL). The organic layer was dried over Na_2SO_4 and then concentrated *in vacuo*. Silica gel chromatography yielded the title compound as a viscous clear oil (2.48 g, 90% yield). Spectroscopic characterization matched that of reported literature.[15]

XI. References

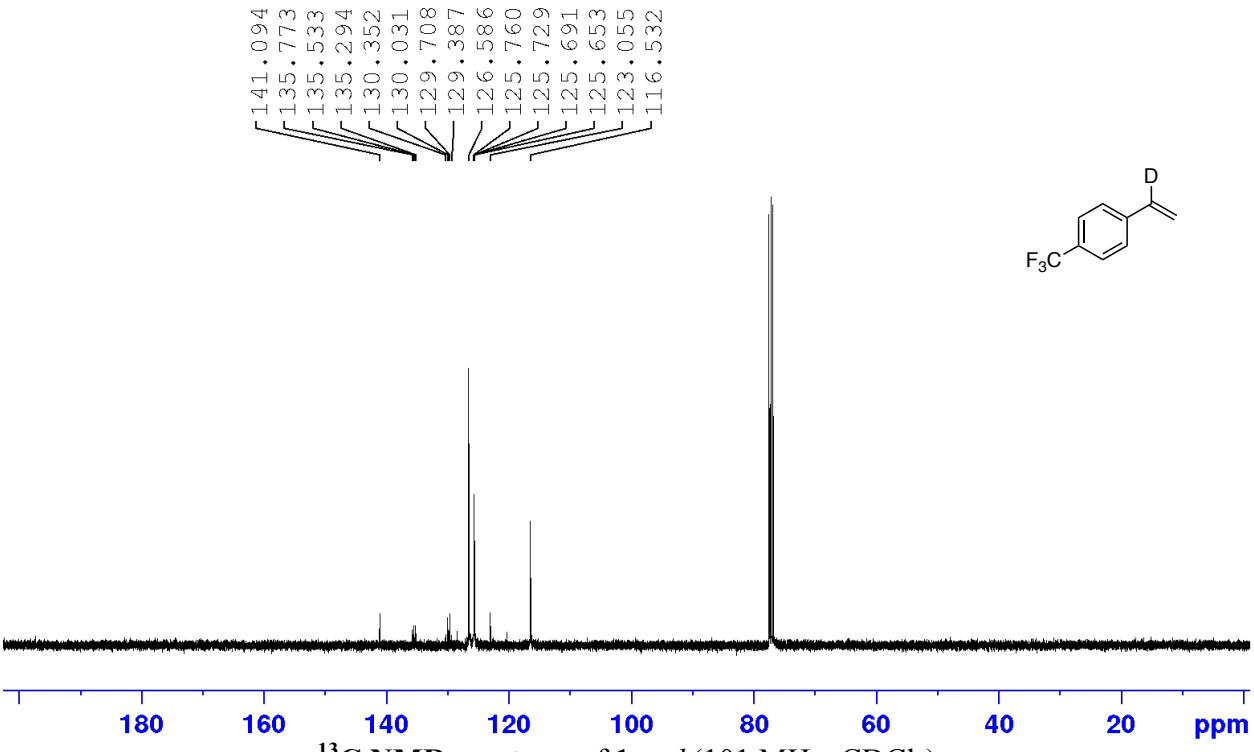
1) Wang, Z.; Richter, S. M.; Gates, B. D.; Grieme, T. A. *Org. Process Res. Dev.* **2012**, *16*, 1994.
2) Niu, D.; Buchwald, S. L. *J. Am. Chem Soc.* **2015**, *137*, 9716.
3) (a) Sapeta, K.; Kerr, M. A. *J. Org. Chem.* **2007**, *72*, 8597. (b) Chu, Z.-Y.; Liang, D.; Li, Z.-H.; Zheng, Y.-S.; Liu, J.-K. *Tetrahedron Lett.* **2018**, *59*, 715.
4) Bezou, P.; Hilberer, A.; Hadziioannou, G. *Synthesis* **1996**, 449.
5) Acheson, R. M.; Lee, G. C. M. *J. Chem. Soc. Perkin Trans. I*, **1987**, 2321.
6) Yokoyama, A.; Maruyama, T.; Tagami, K.; Masu, H.; Katagiri, K.; Azumaya, I.; Yokozawa, T. *Org. Lett.* **2008**, *10*, 3207.
7) Shao, X.; Wang, X.; Yang, T.; Lu, L.; Shen, Q. *Angew. Chem. Int. Ed.* **2013**, *52*, 3457.
8) Bejot, R.; He, A.; Falck, J. R.; Mioskowski, C. *Angew. Chem. Int. Ed.* **2007**, *46*, 1719.
9) Molander, G. A.; Brown, A. R. *J. Org. Chem.* **2006**, *71*, 9681.
10) Mizuno, H.; Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc.* **2011**, *133*, 1251.
11) Khan, Z. A.; Iwaoka, M.; Wirth, T. *Tetrahedron* **2010**, *66*, 6639.
12) Gülak, S.; Gieshoff, T. N.; von Wangelin, A. J. *Adv. Synth. Catal.* **2013**, *355*, 2197.
13) Cong, F.; Wei, Y.; Tang, P. *Chem. Commun.* **2018**, *54*, 4473.
14) Chen, D.; Xu, G.; Zhou, Q.; Chung, L. W.; Tang, W. *J. Am. Chem. Soc.* **2017**, *139*, 9767.
15) Lafaye, K.; Nicolas, L.; Guérinot, A.; Reymond, S.; Cossy, J. *Org. Lett.* **2014**, *16*, 4972.

16) Kondo, M.; Kochi, T.; Kakiuchi, F. *J. Am. Chem. Soc.* **2011**, *133*, 32.
17) Wang, Y.-M.; Buchwald, S. L. *J. Am. Chem. Soc.* **2016**, *138*, 5024.

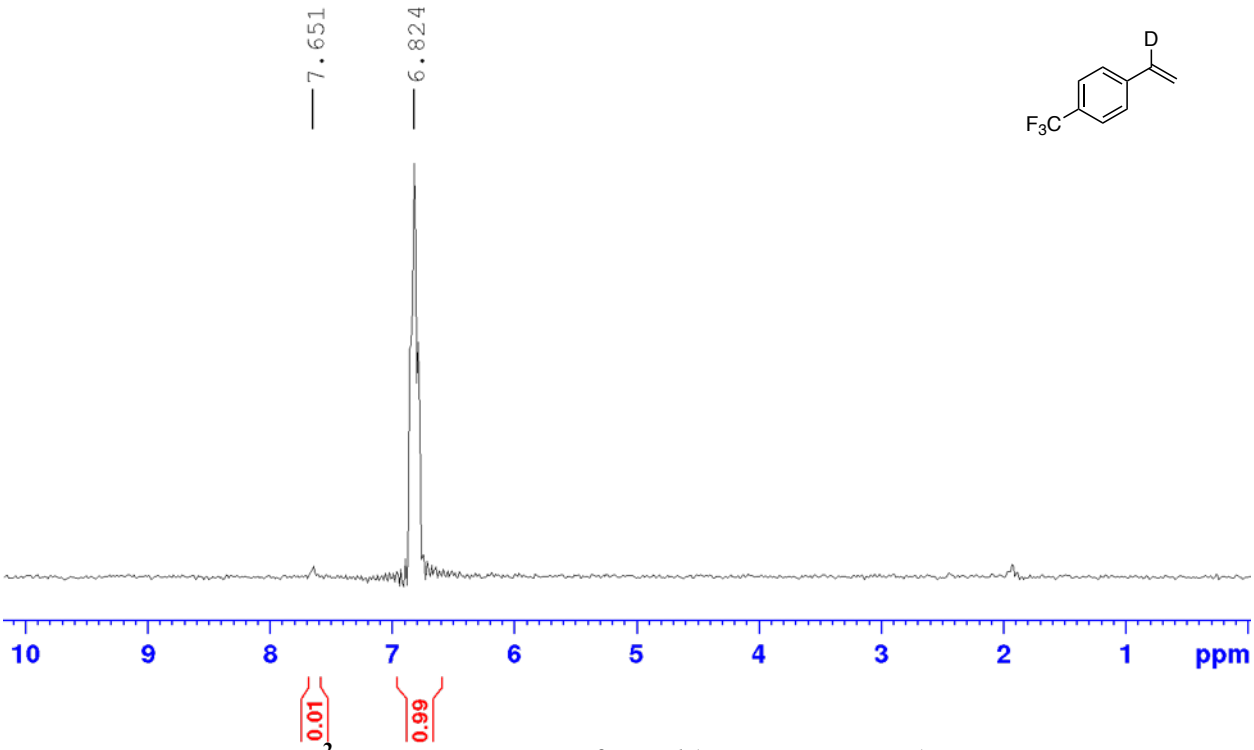
XII. Copies of NMR Spectra



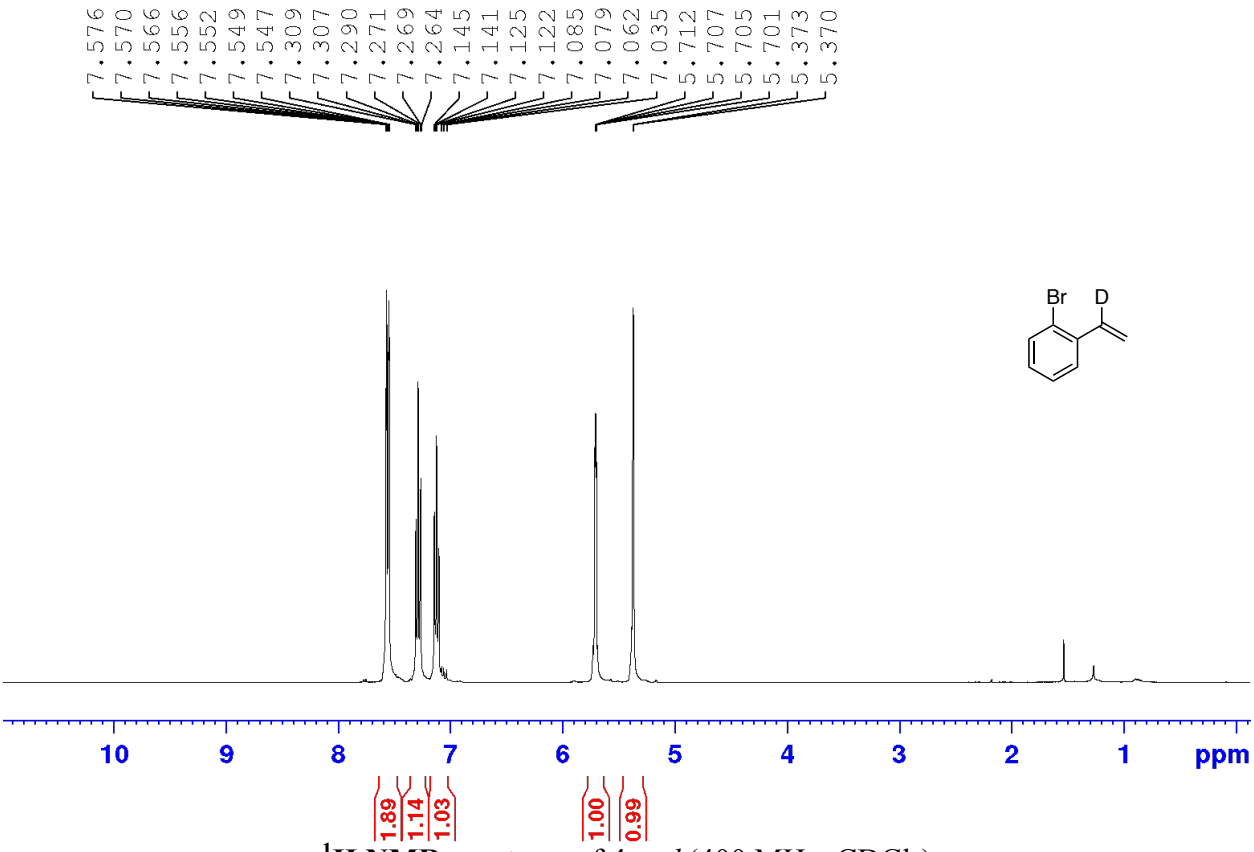
^{1}H NMR spectrum of **1**-α-*d* (400 MHz, $CDCl_3$)



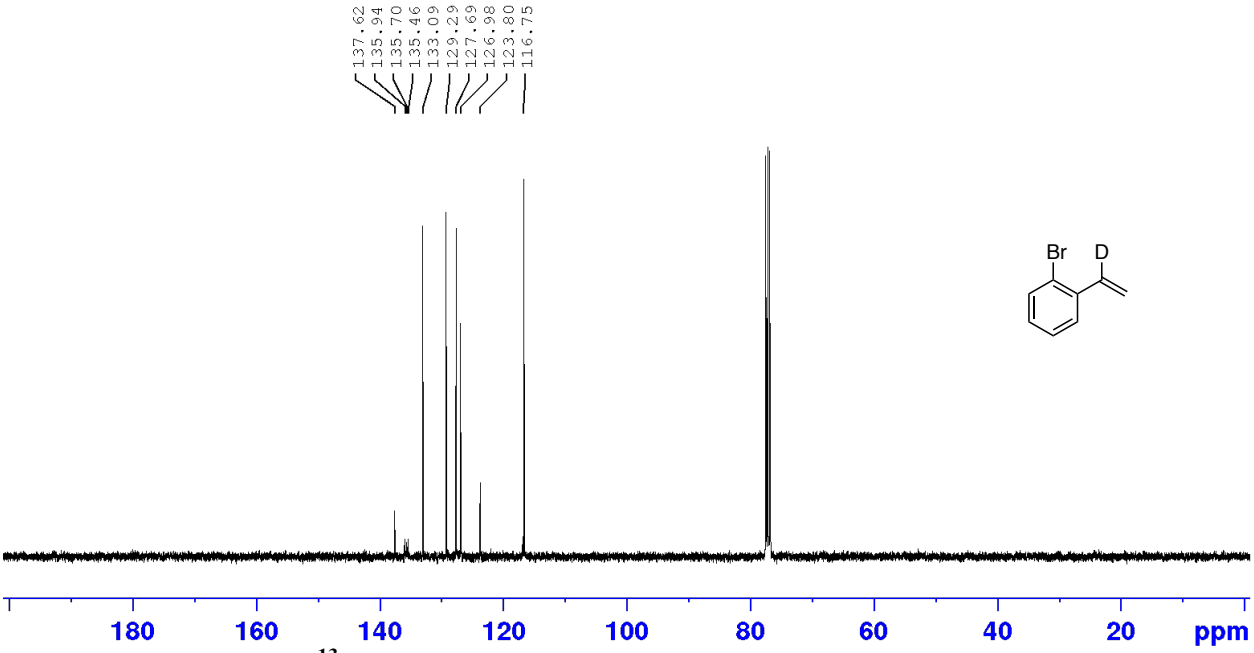
^{13}C NMR spectrum of **1**-α-*d* (101 MHz, $CDCl_3$)



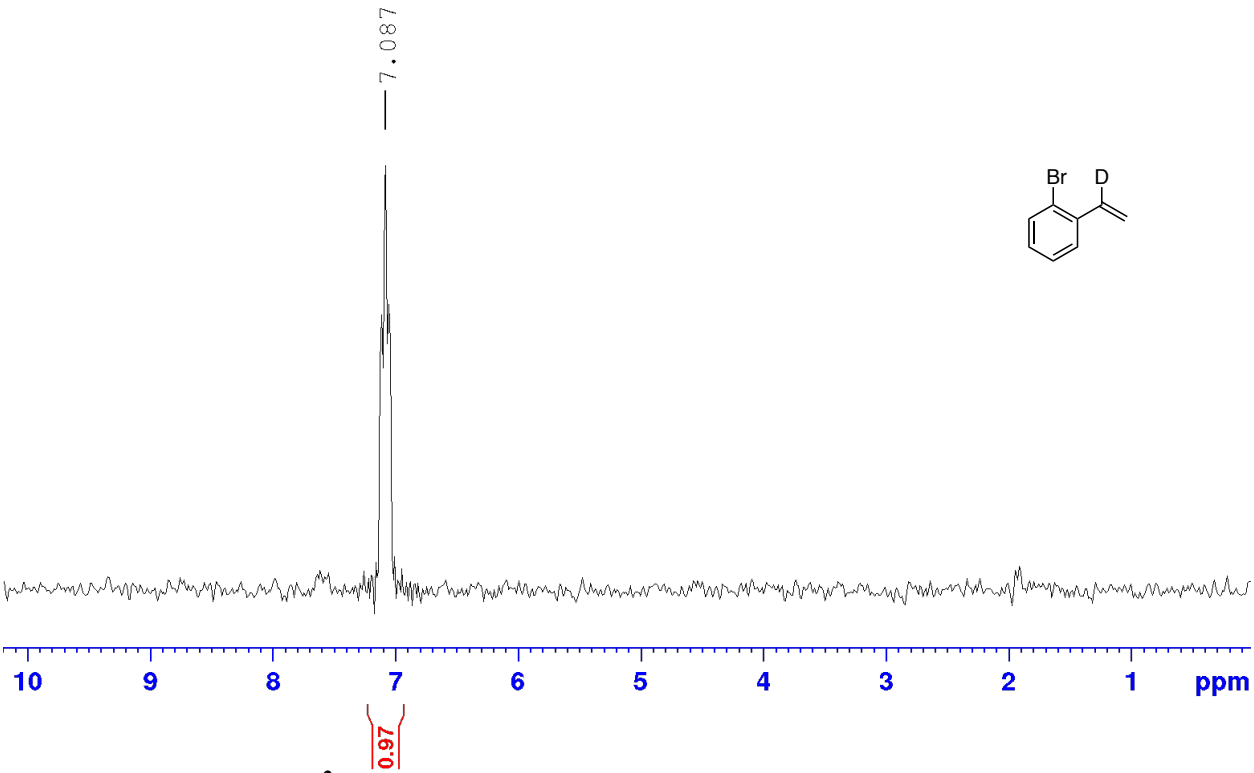
^{2}H NMR spectrum of **1**-α-*d* (62 MHz, CH_3CN)



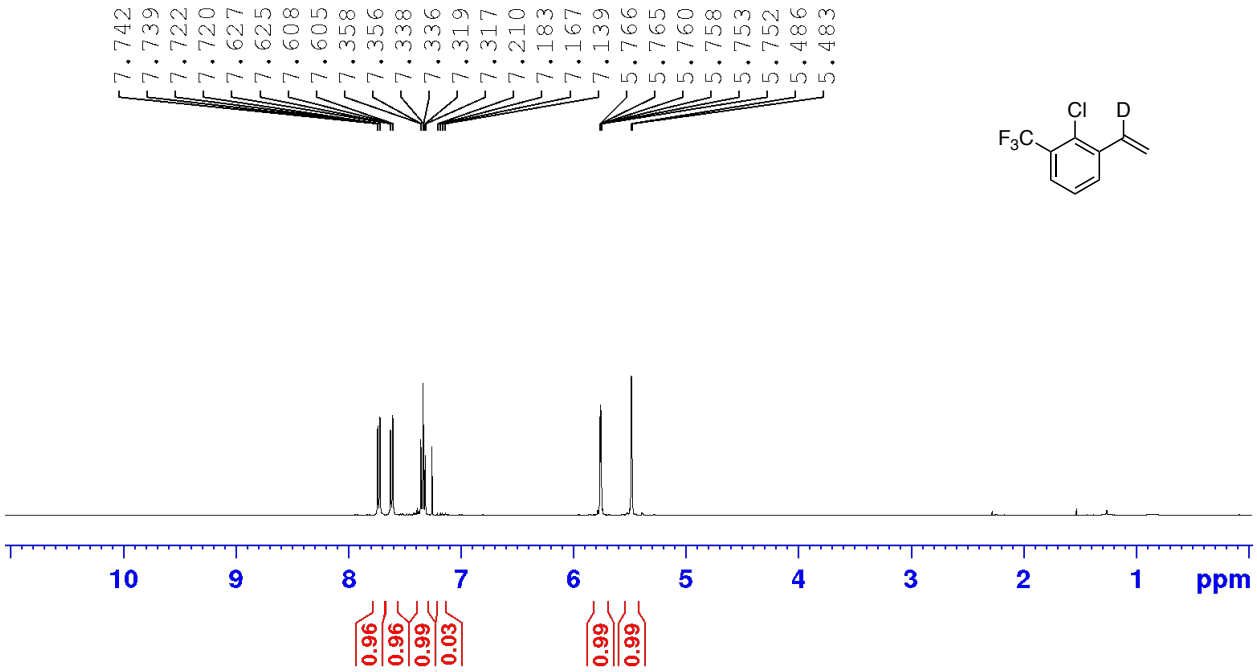
^{1}H NMR spectrum of **4**-α-*d* (400 MHz, $CDCl_3$)



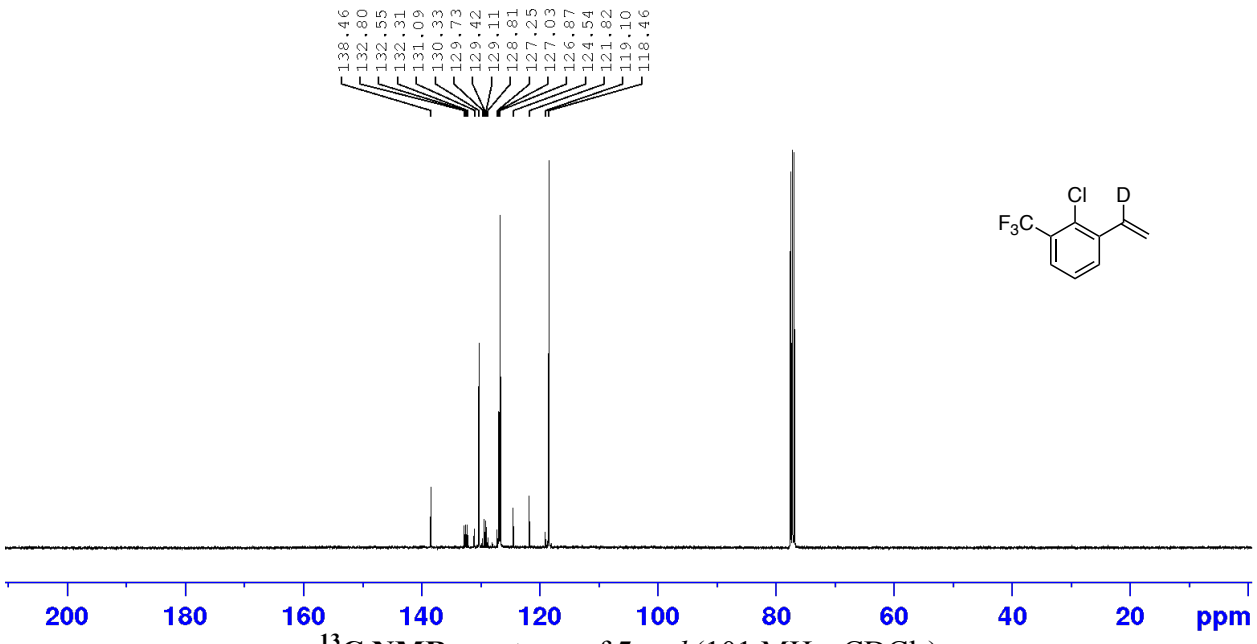
^{13}C NMR spectrum of **4**-α-*d* (101 MHz, $CDCl_3$)



^{2}H NMR spectrum of **4**-α-*d* (62 MHz, CH_3CN)



^{1}H NMR spectrum of **5**-α-*d* (400 MHz, $CDCl_3$)



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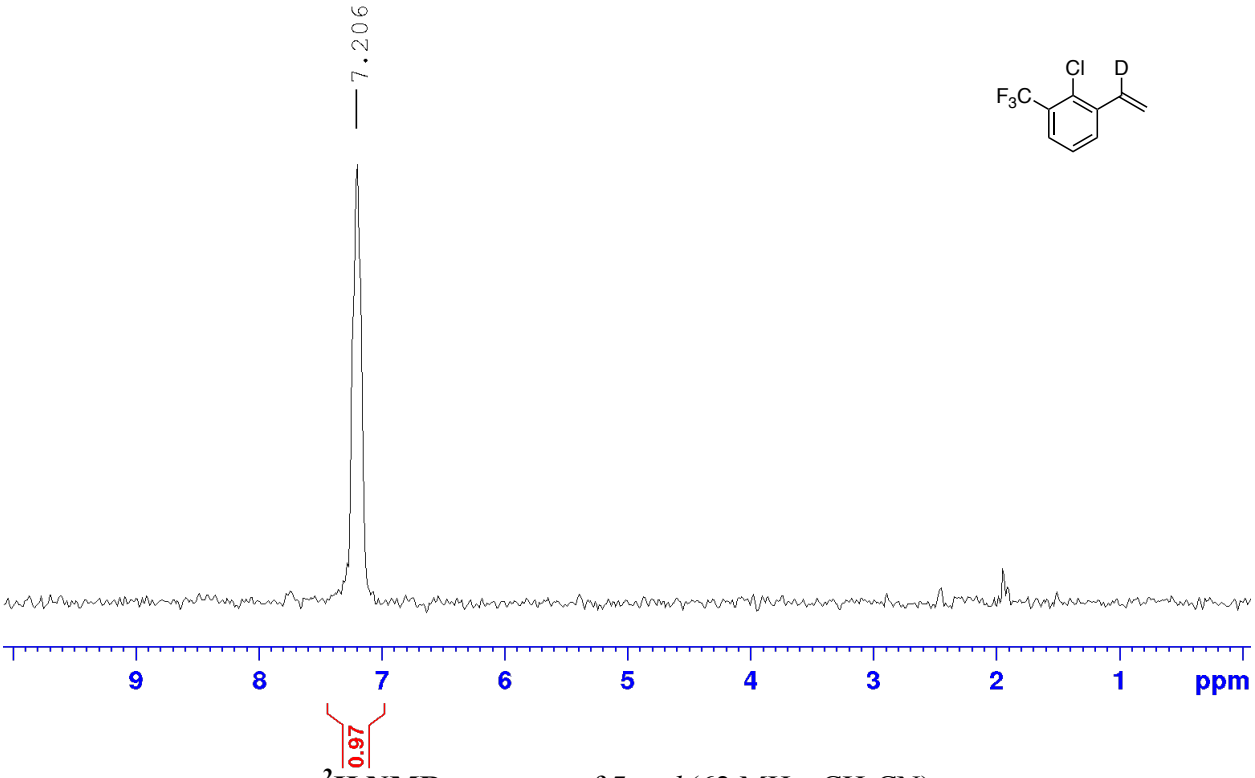

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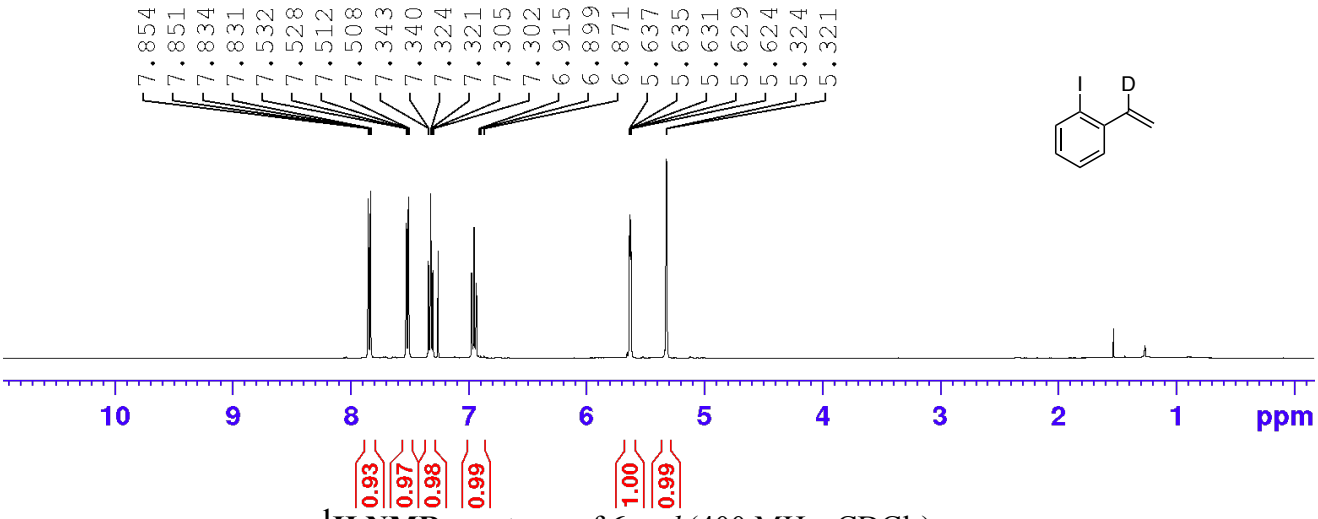

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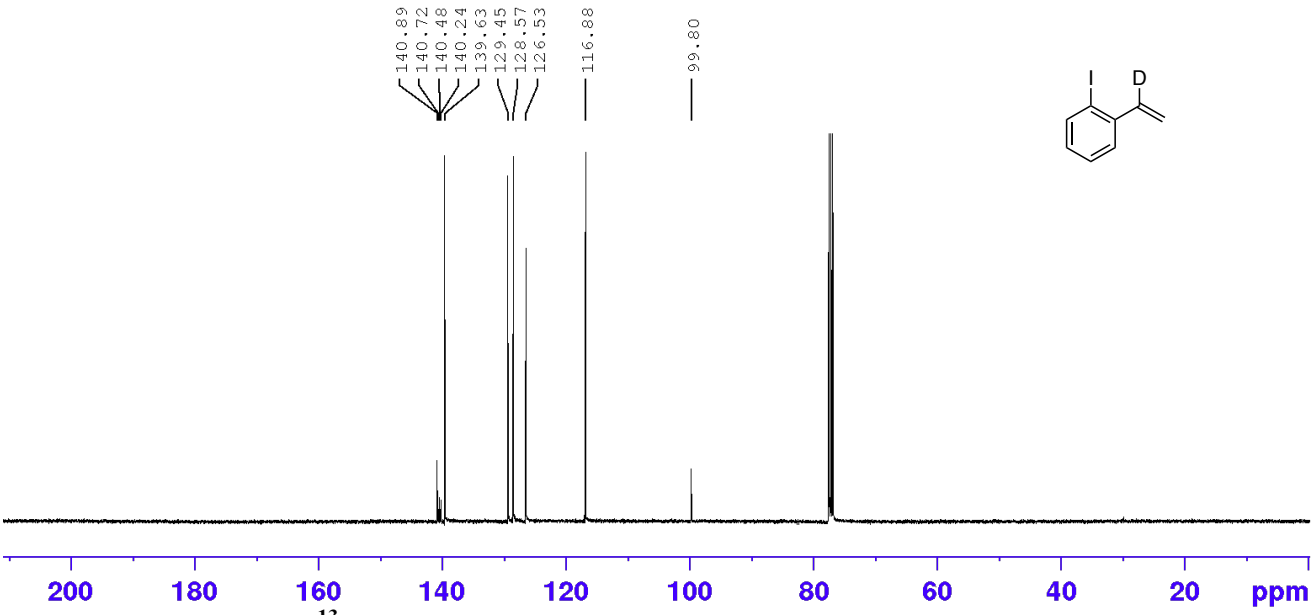

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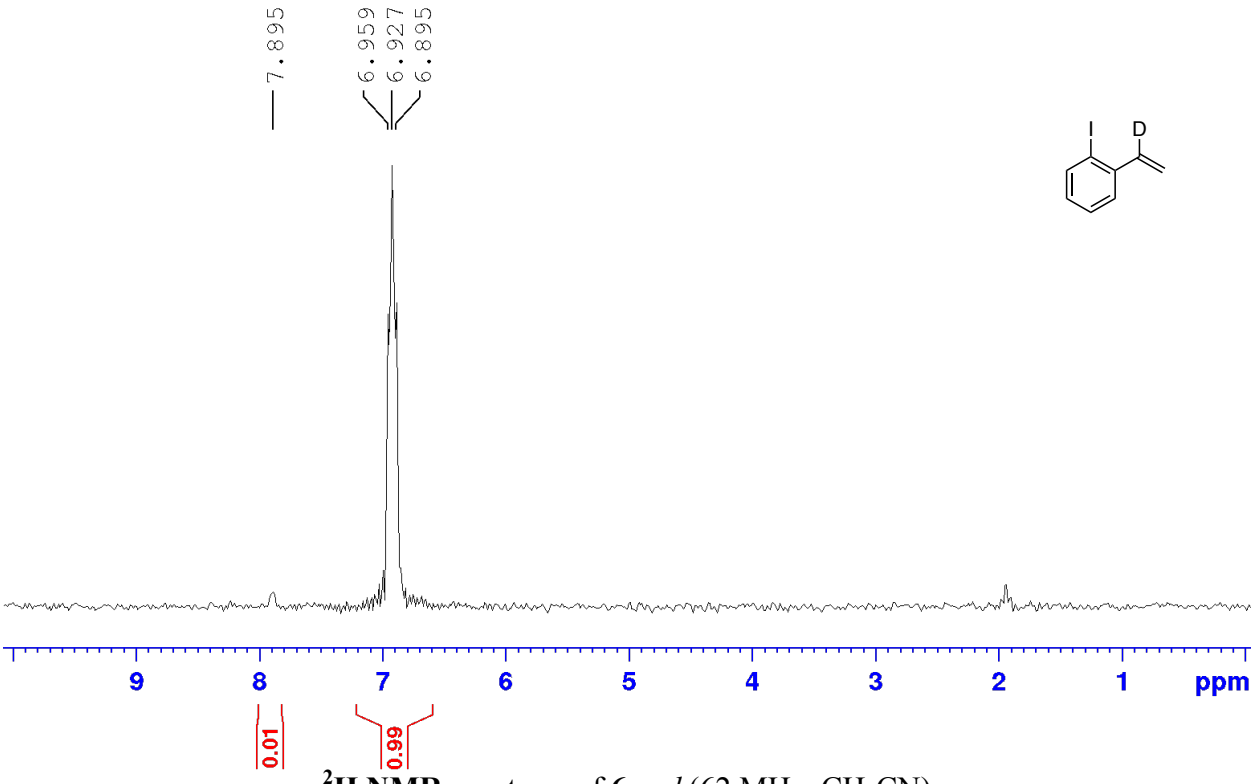

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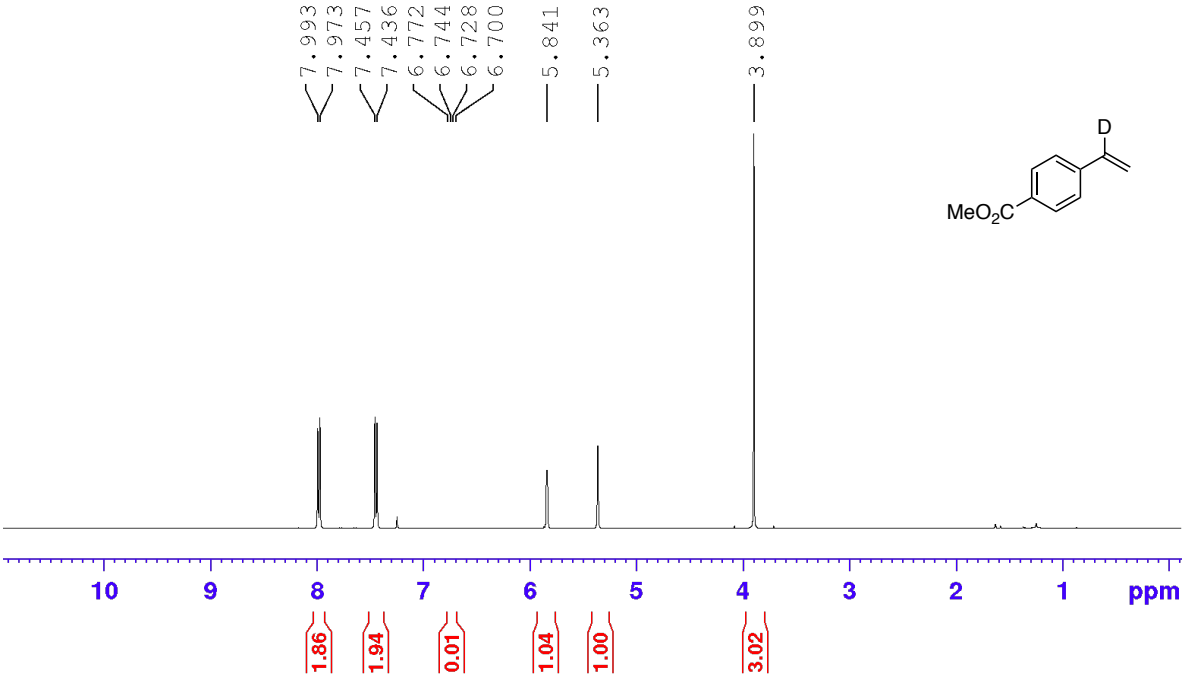

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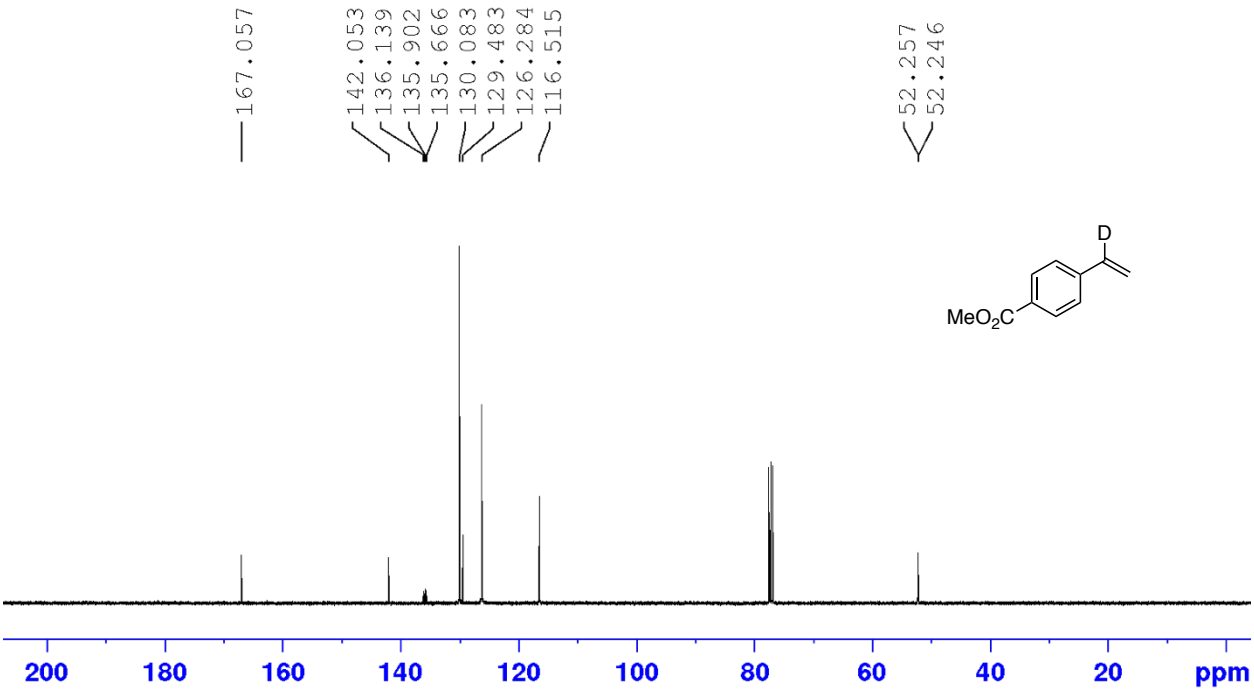
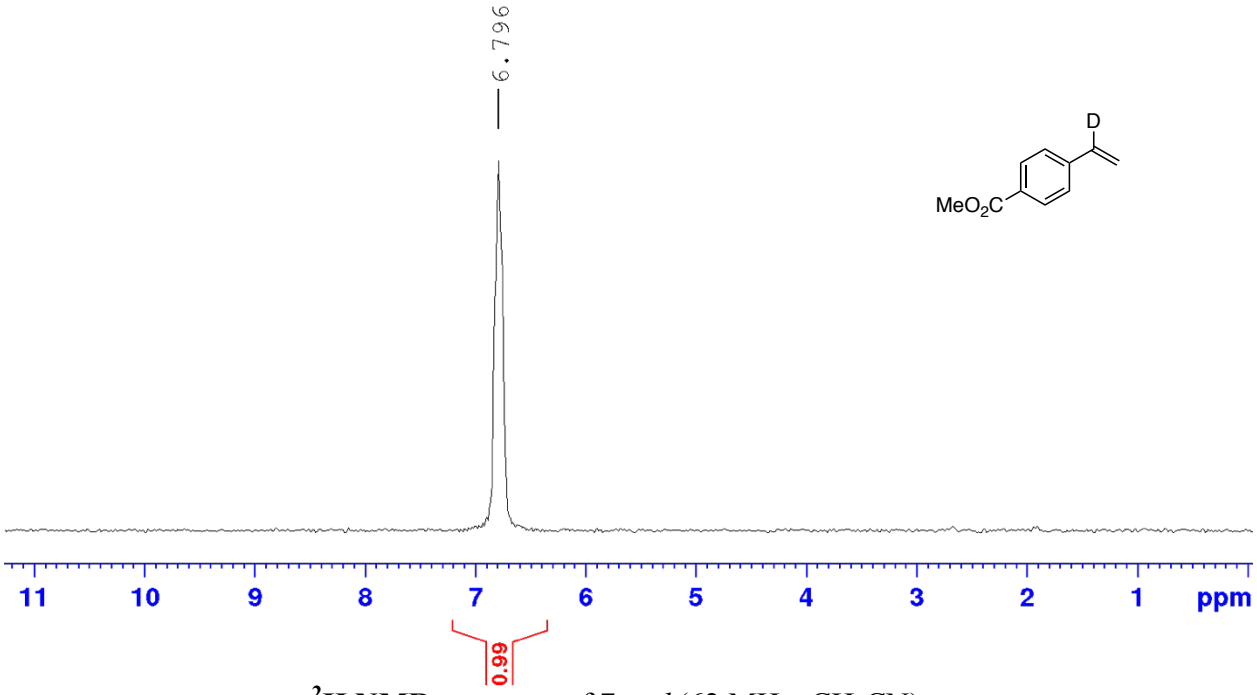
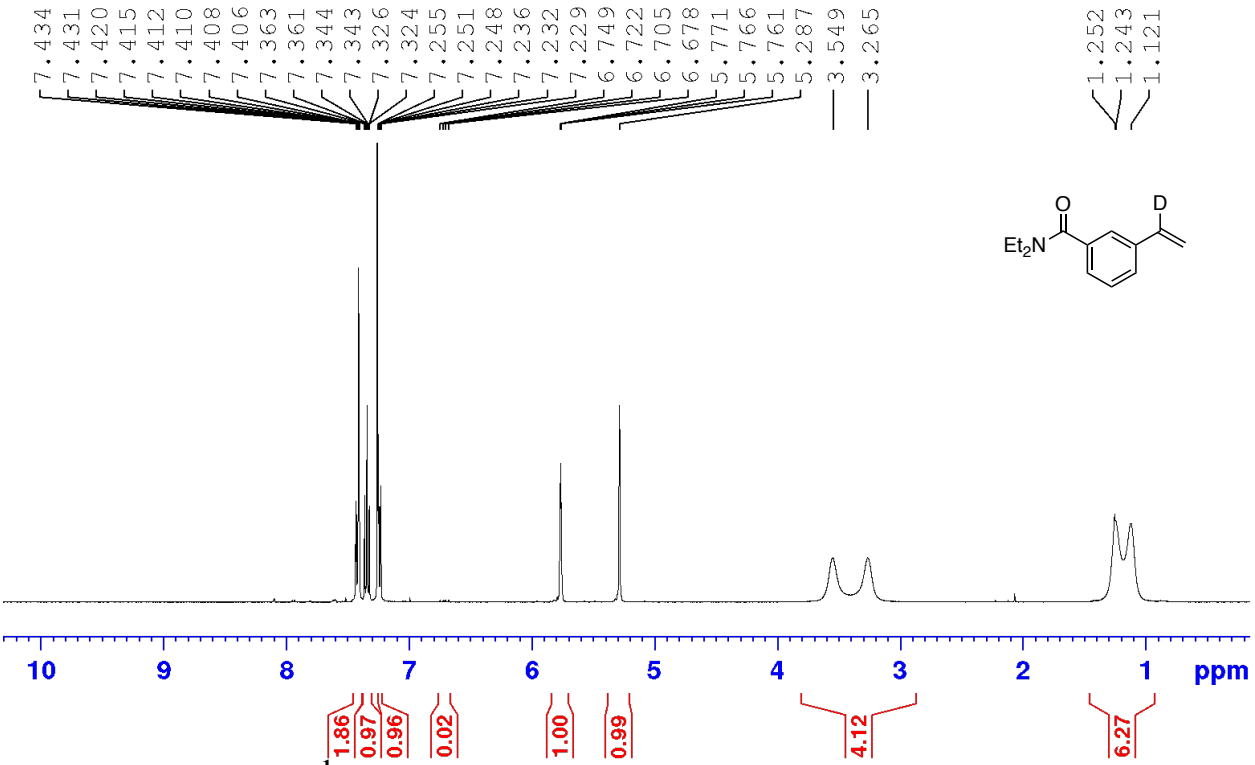


^{13}C NMR spectrum of **7**-α-*d* (101 MHz, $CDCl_3$)



^{2}H NMR spectrum of **7**-α-*d* (62 MHz, CH_3CN)



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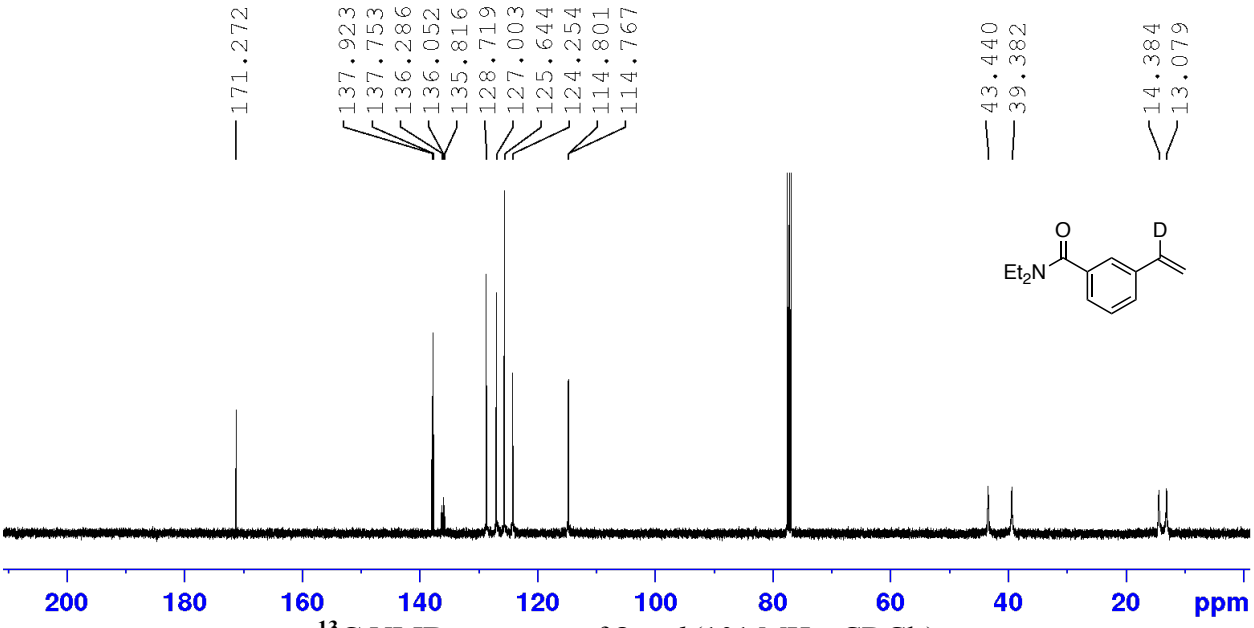

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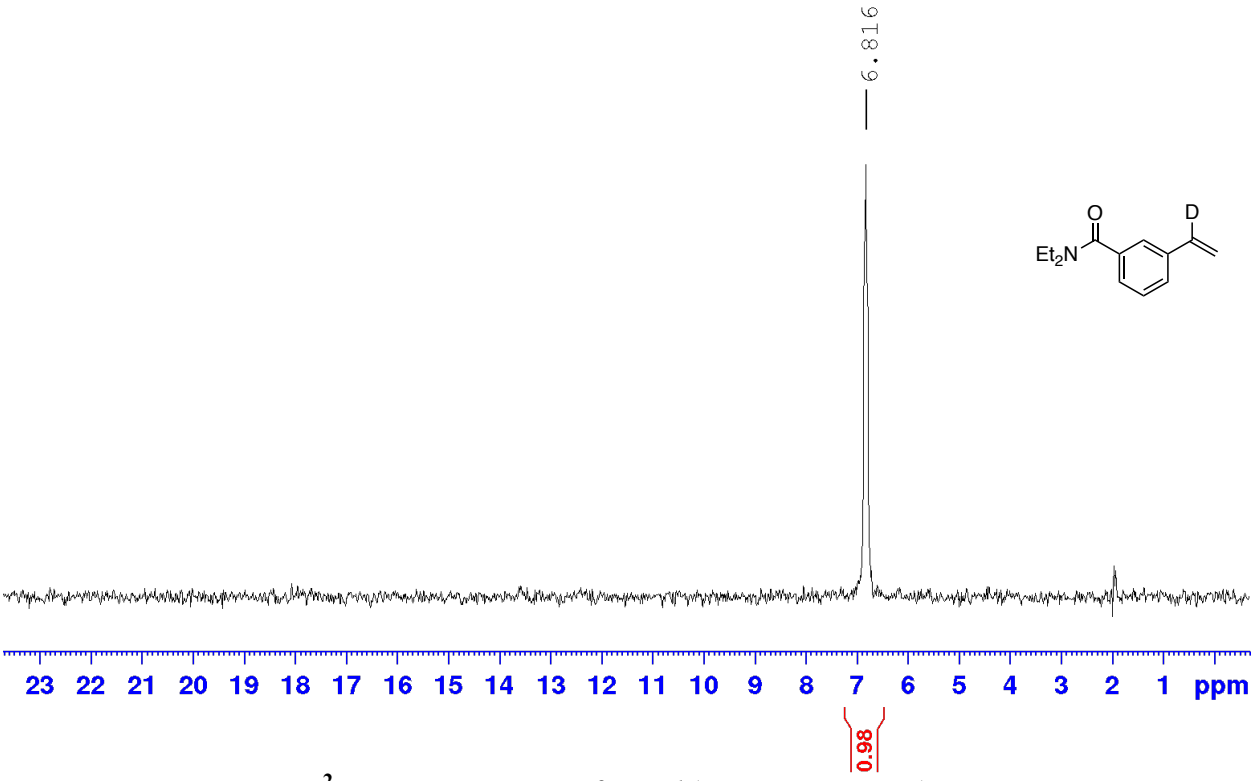

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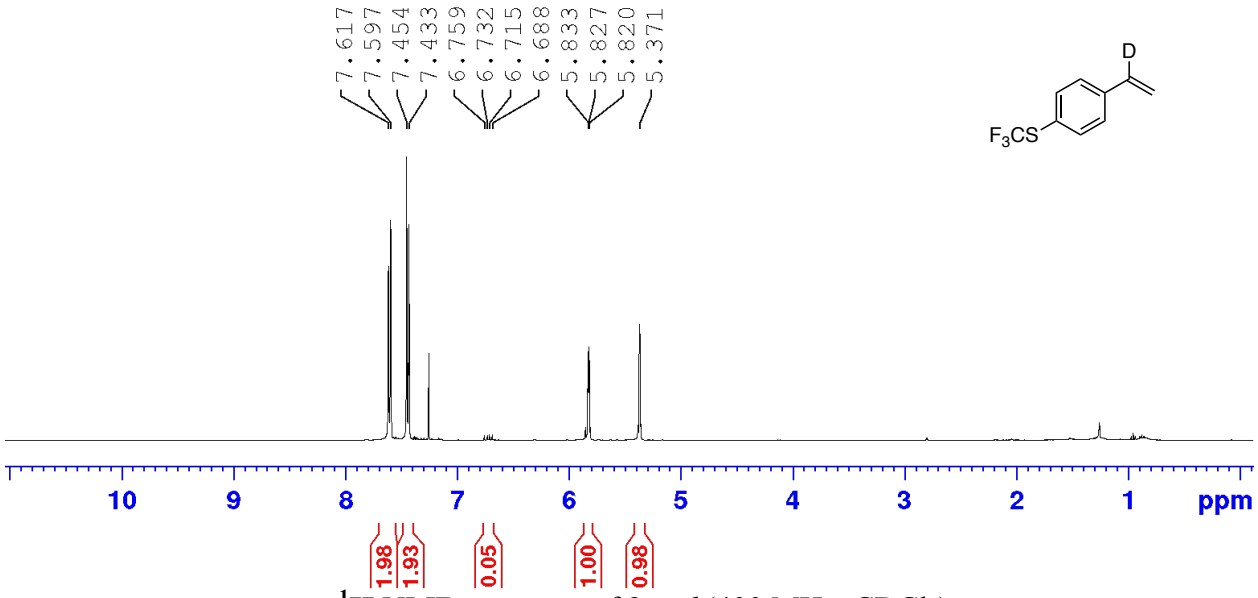
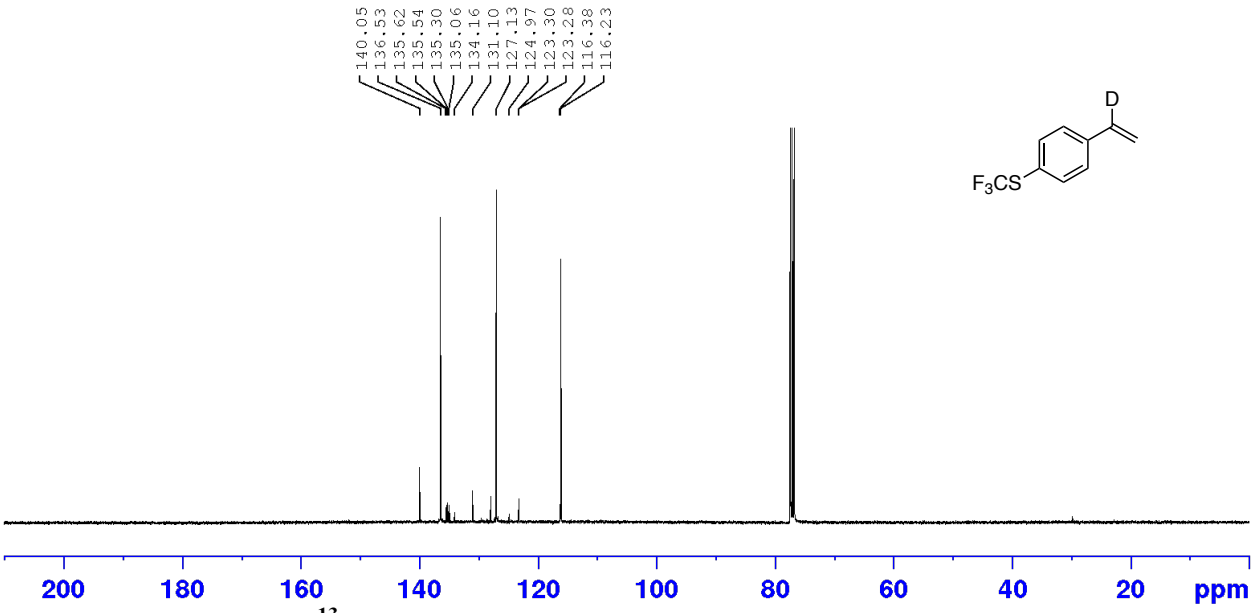


^{1}H NMR spectrum of **9**-α-*d* (400 MHz, $CDCl_3$)



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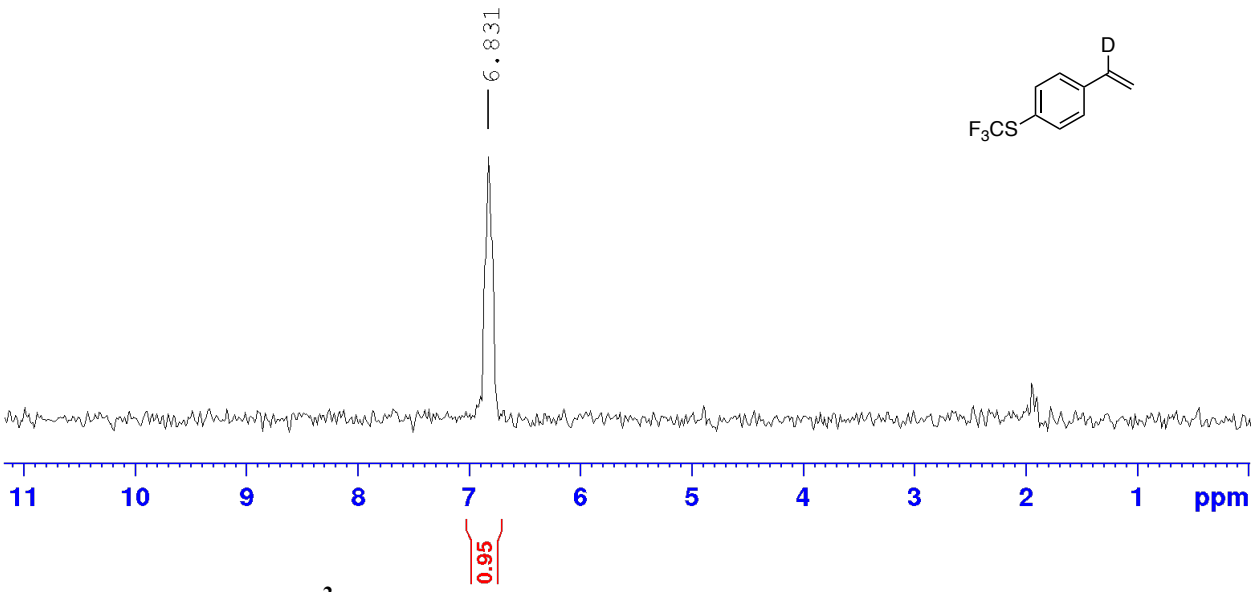

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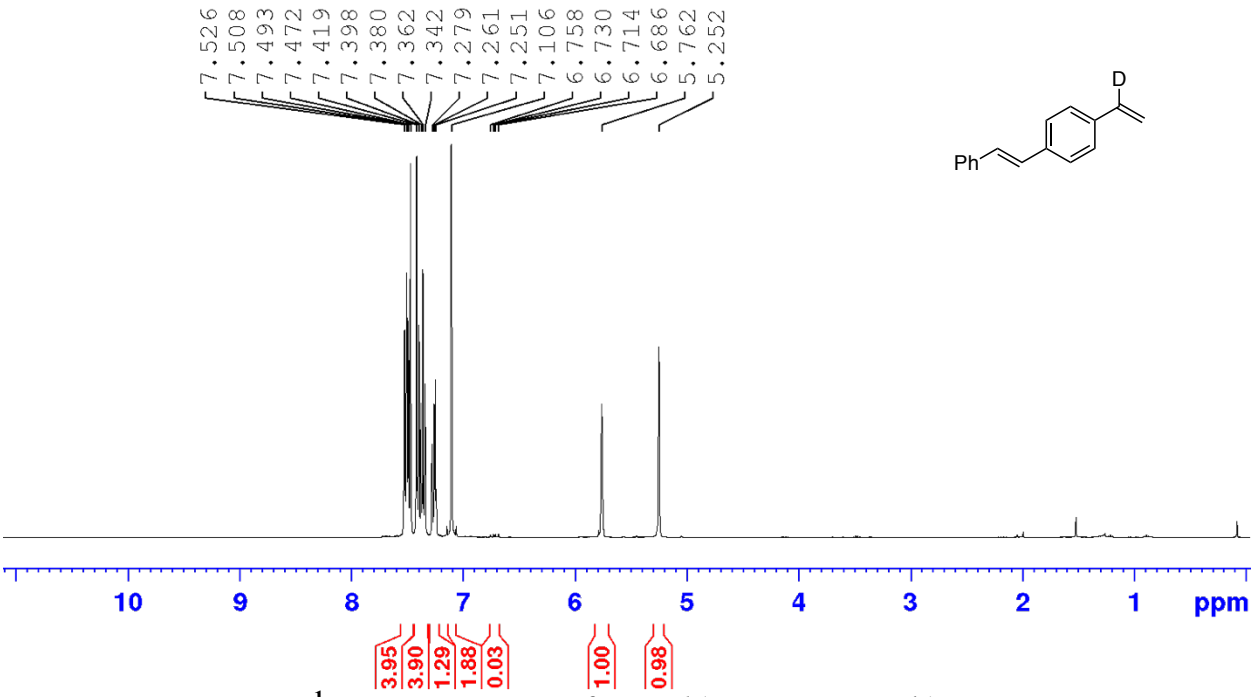

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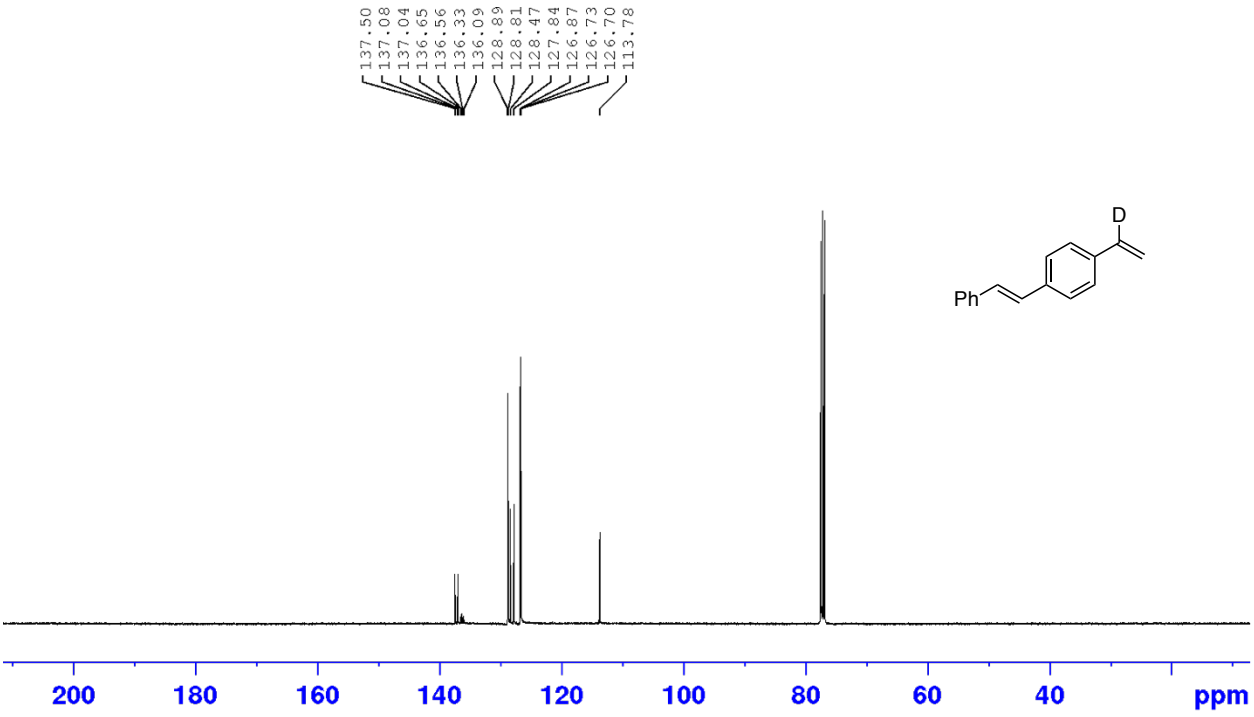

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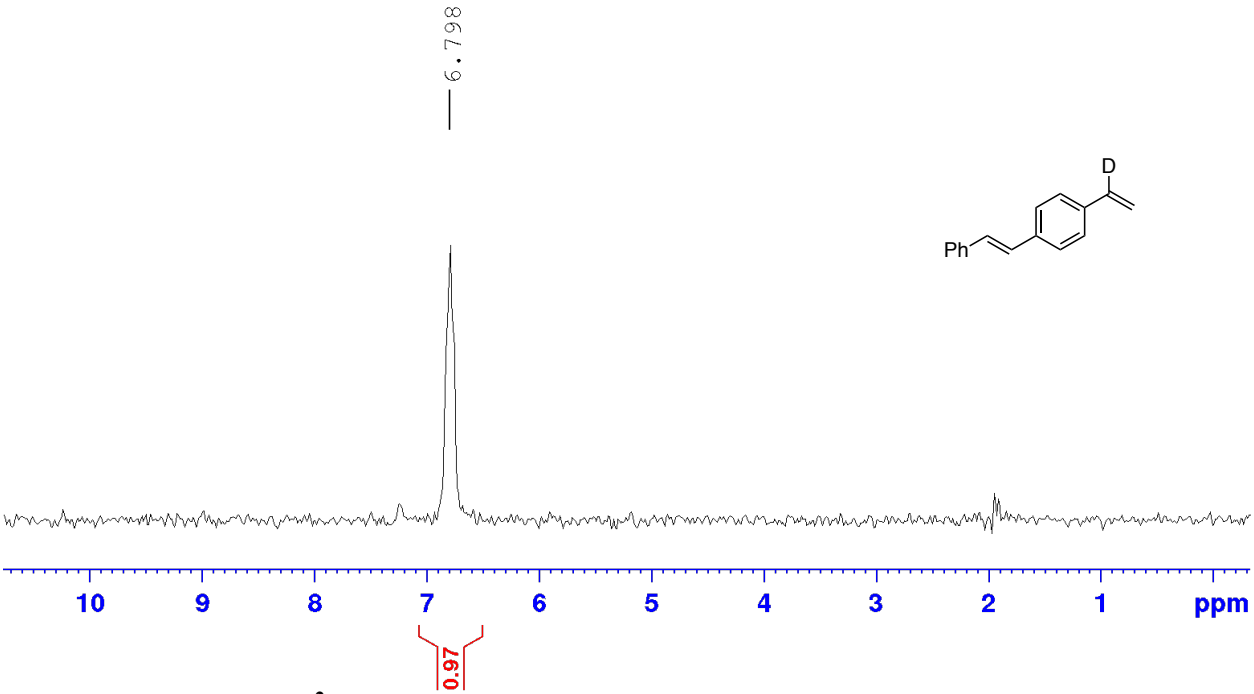

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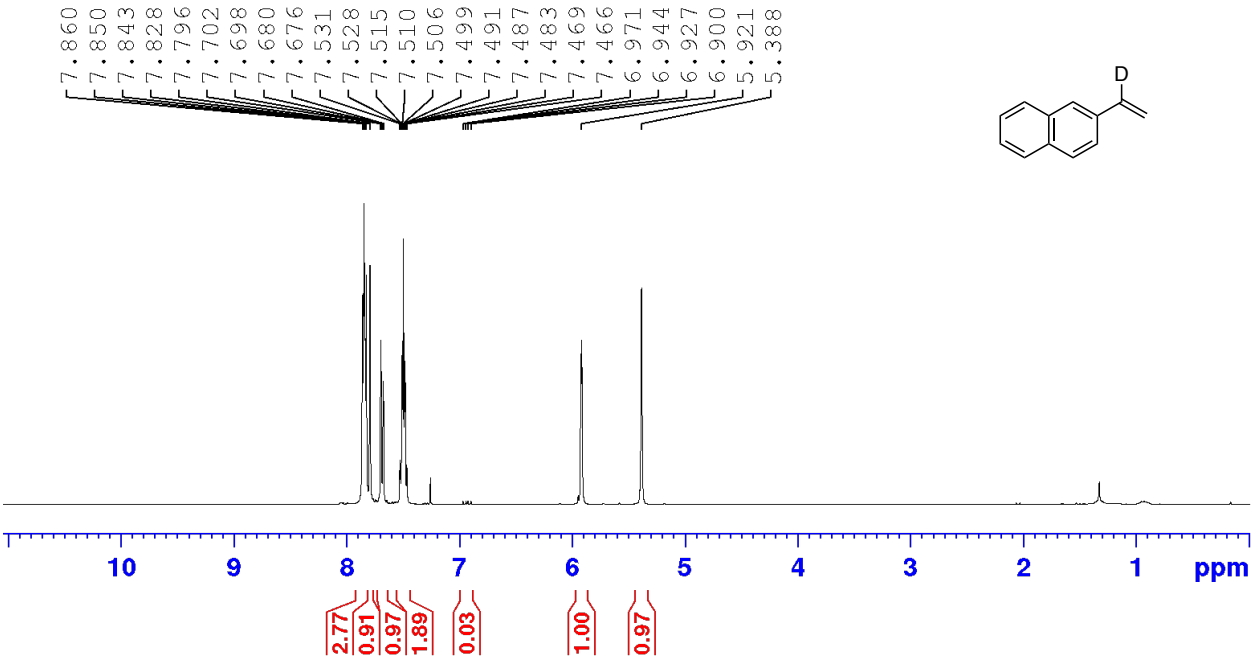
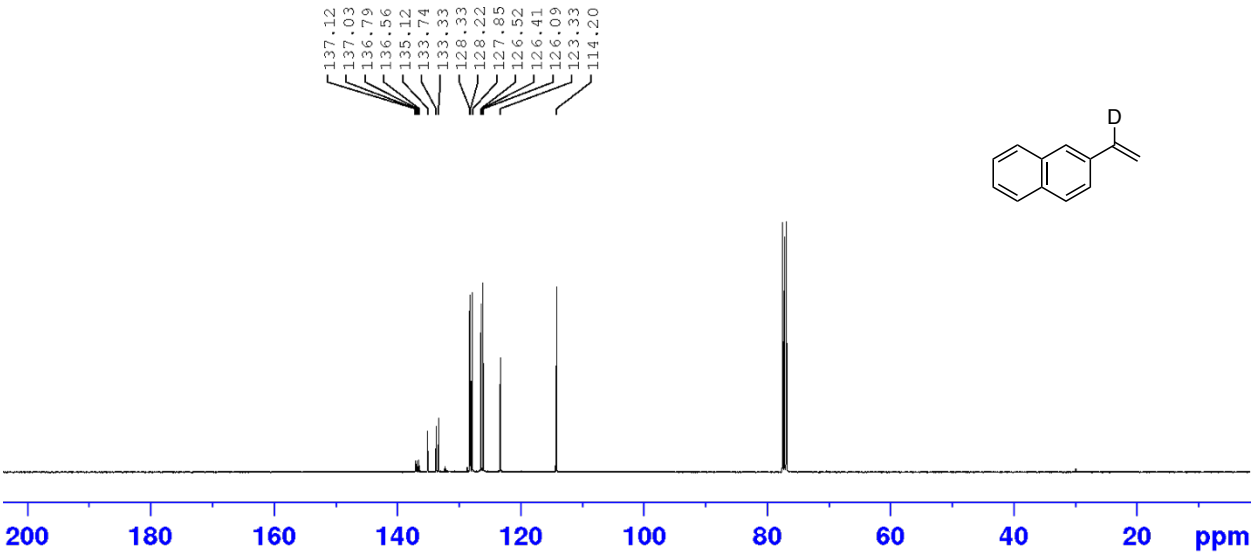


^{1}H NMR spectrum of **11**-α-*d* (400 MHz, $CDCl_3$)



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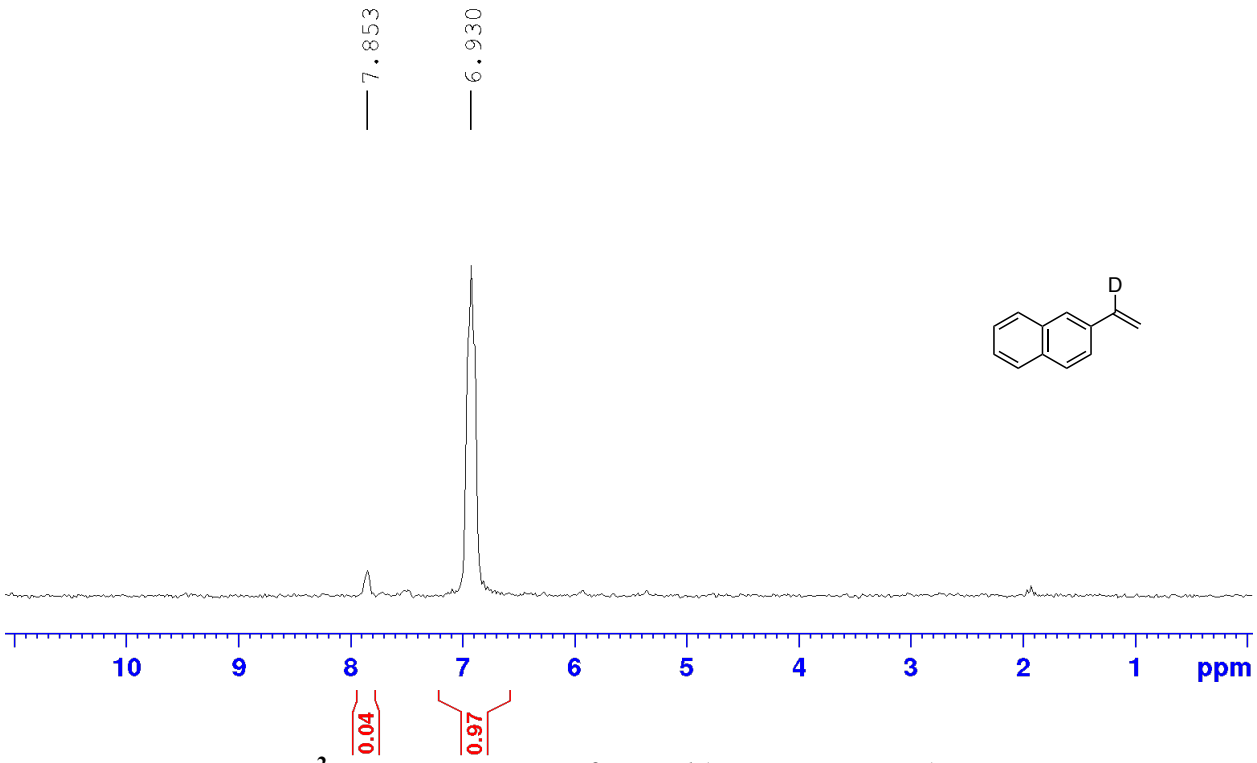

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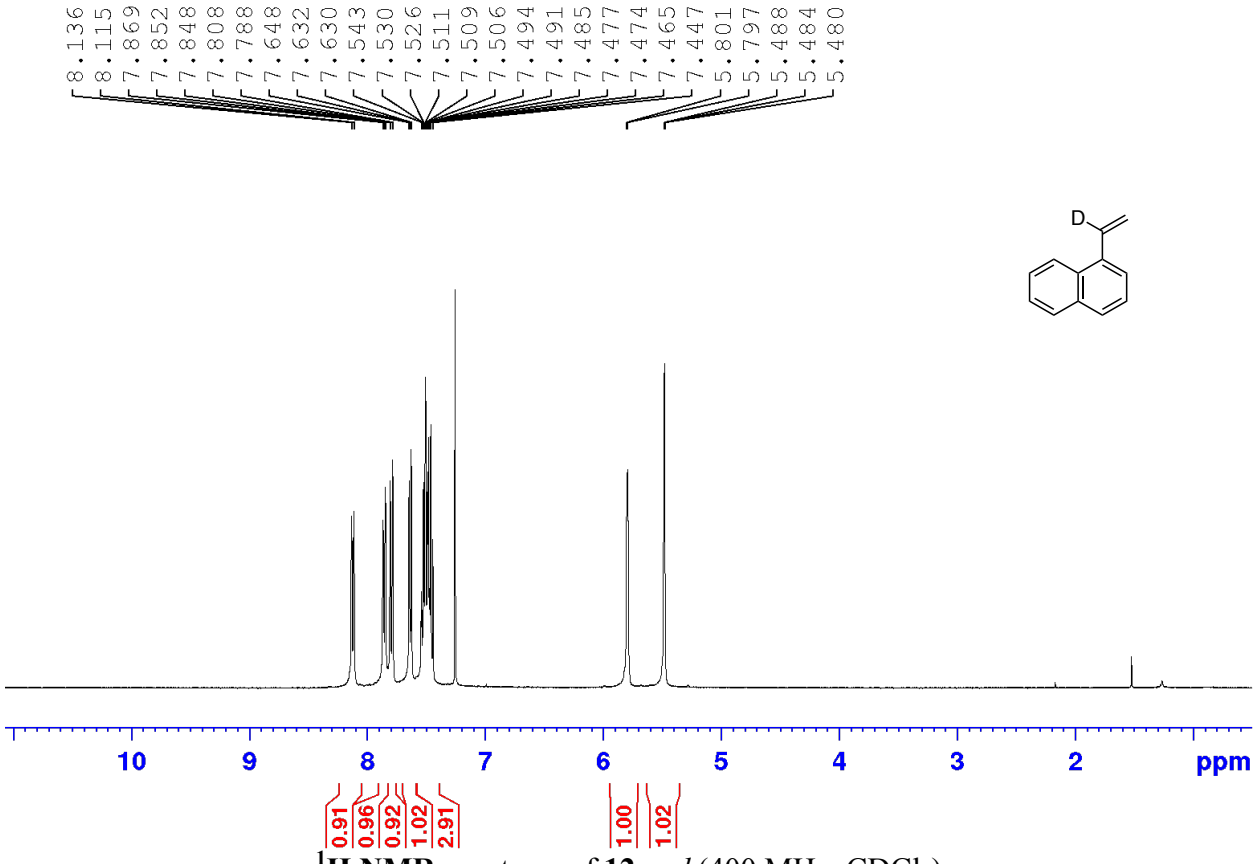
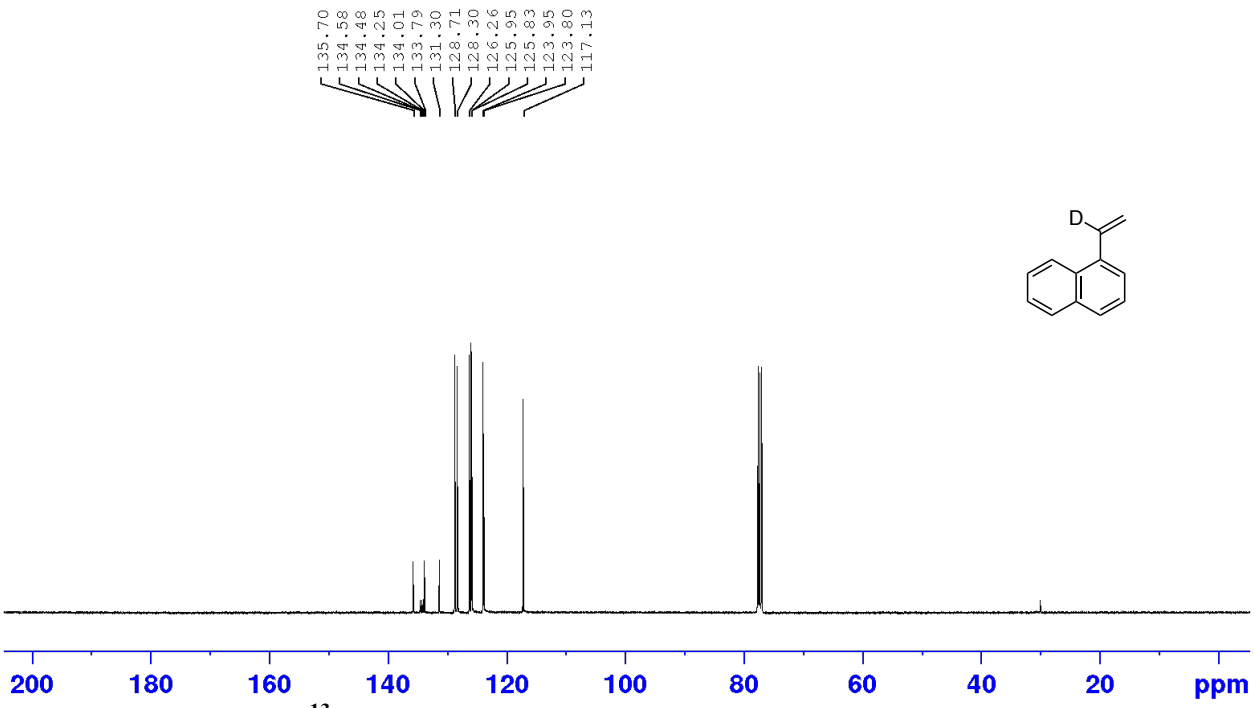
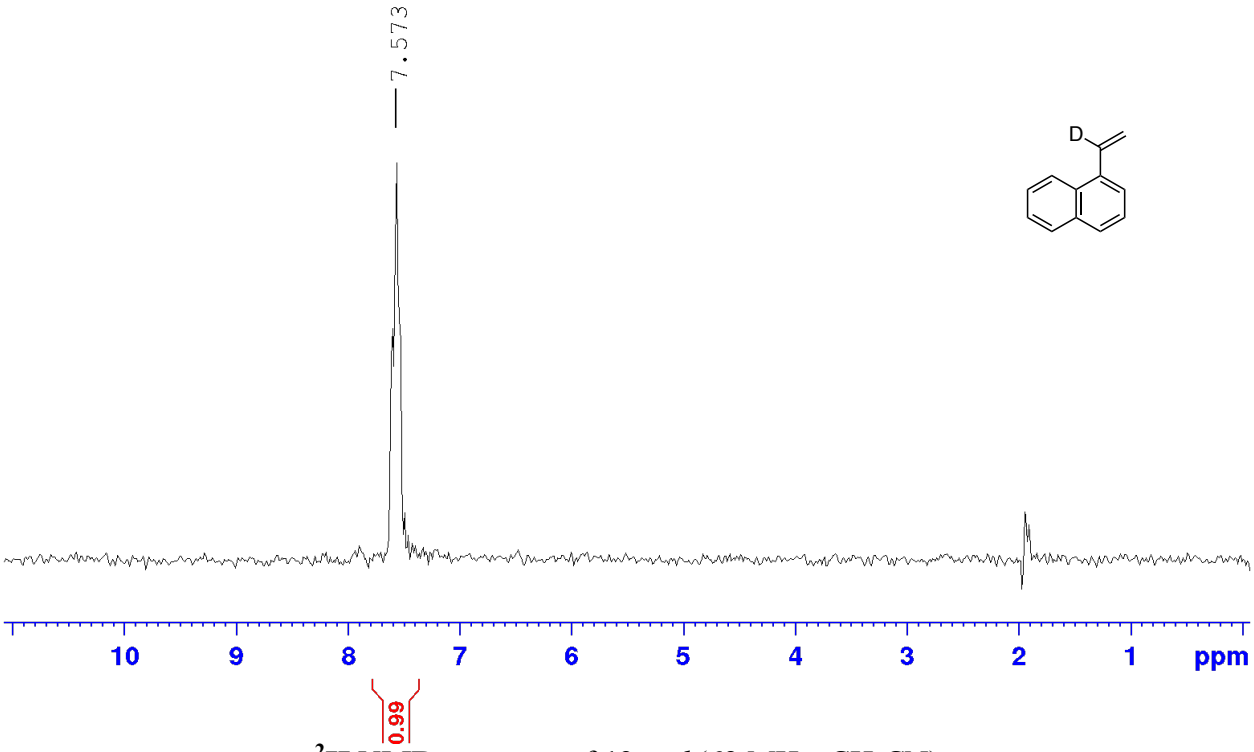


^{1}H NMR spectrum of **12**-α-*d* (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of **12**-α-*d* (101 MHz, $CDCl_3$)



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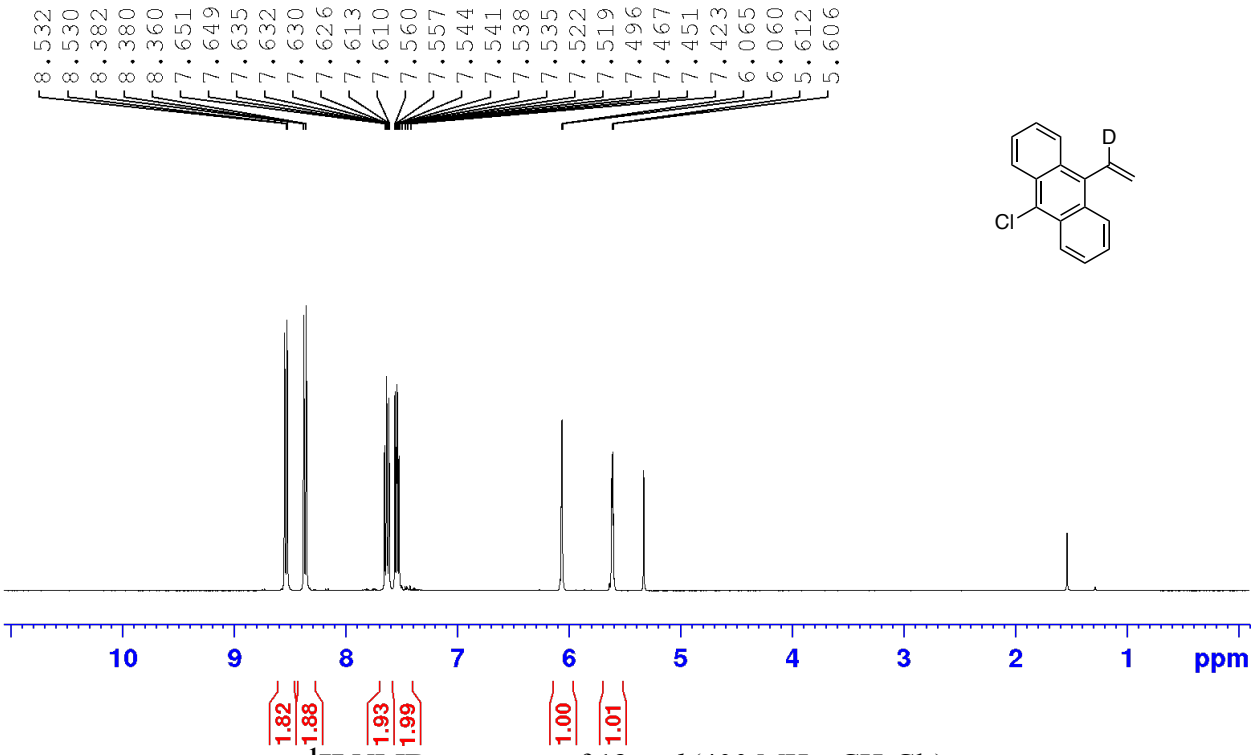

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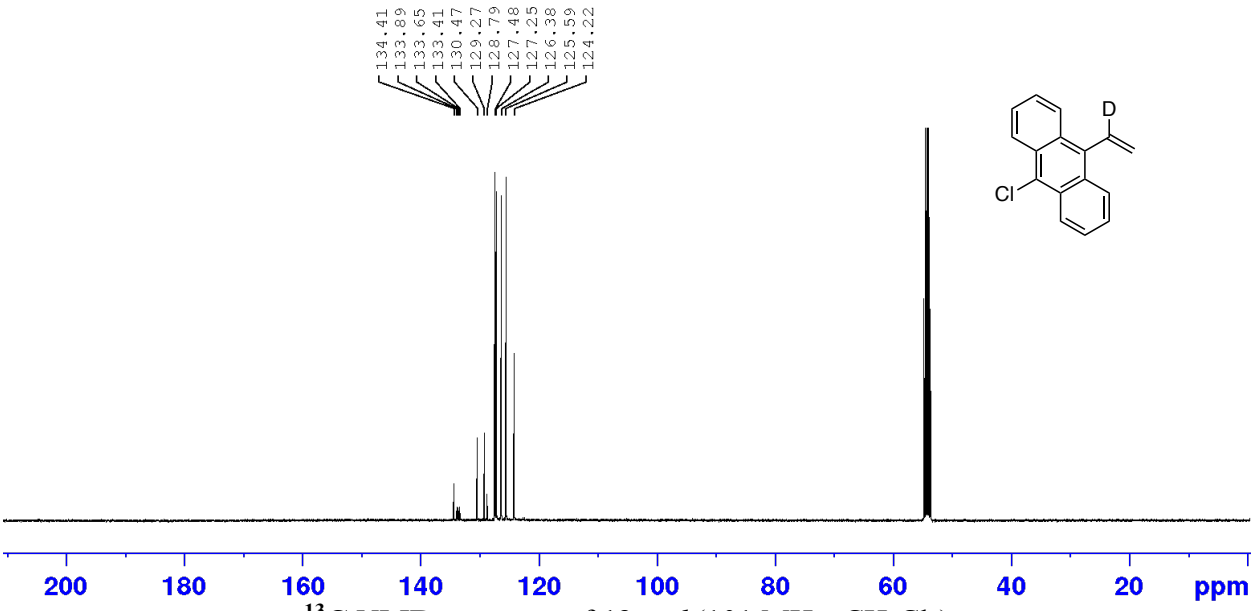

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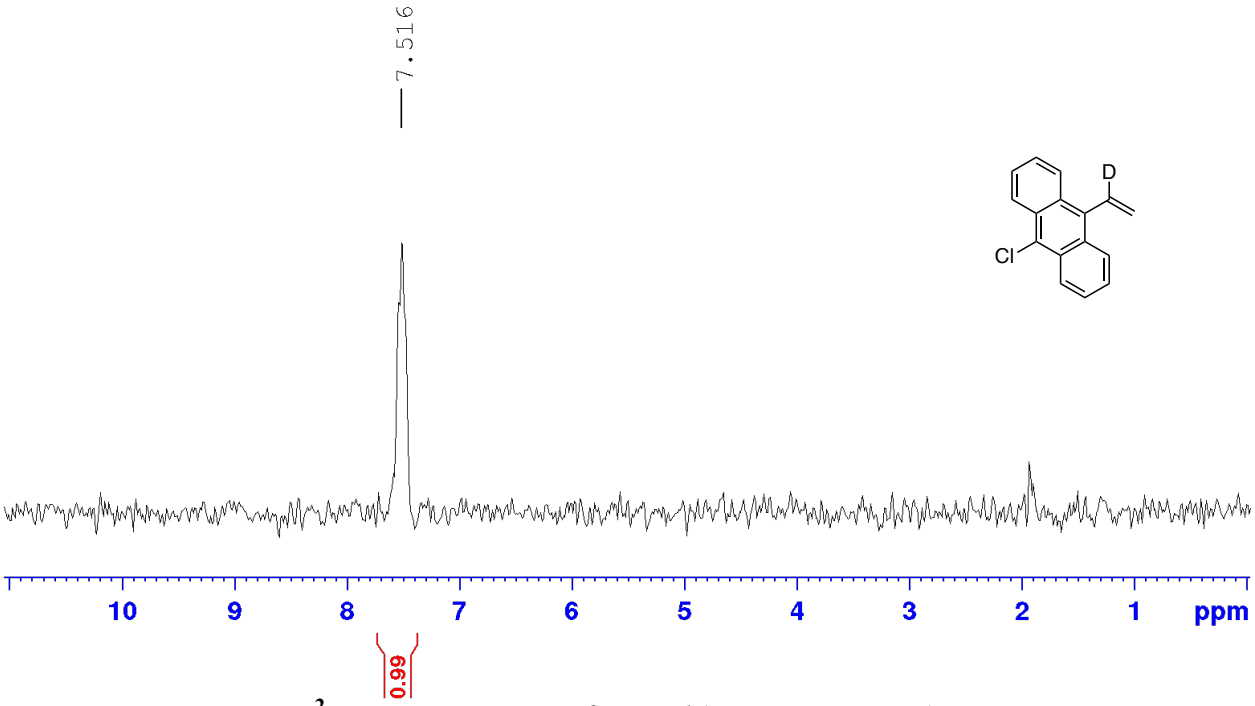

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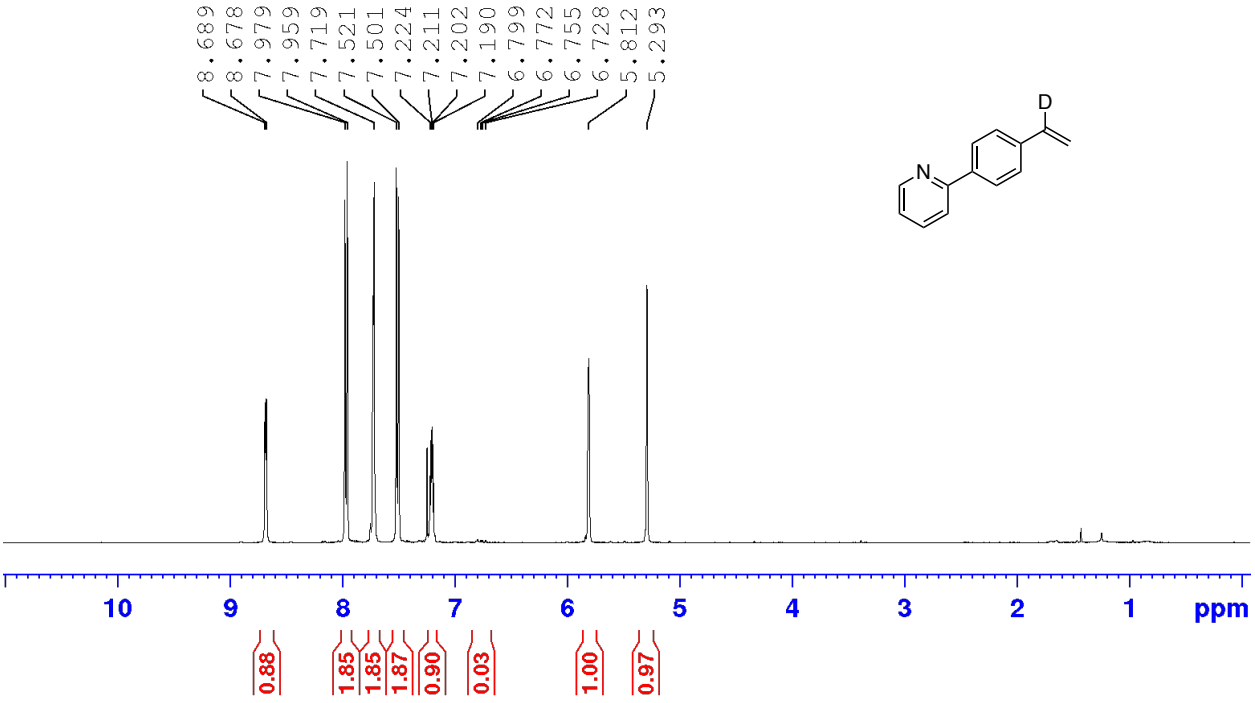

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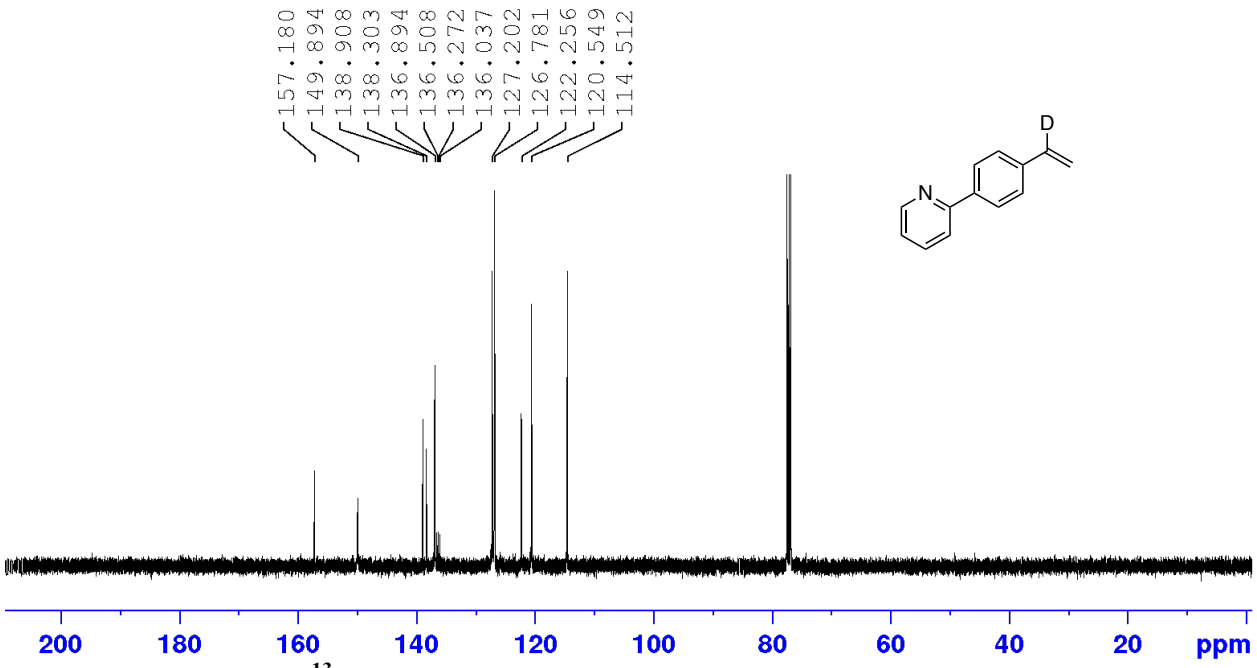

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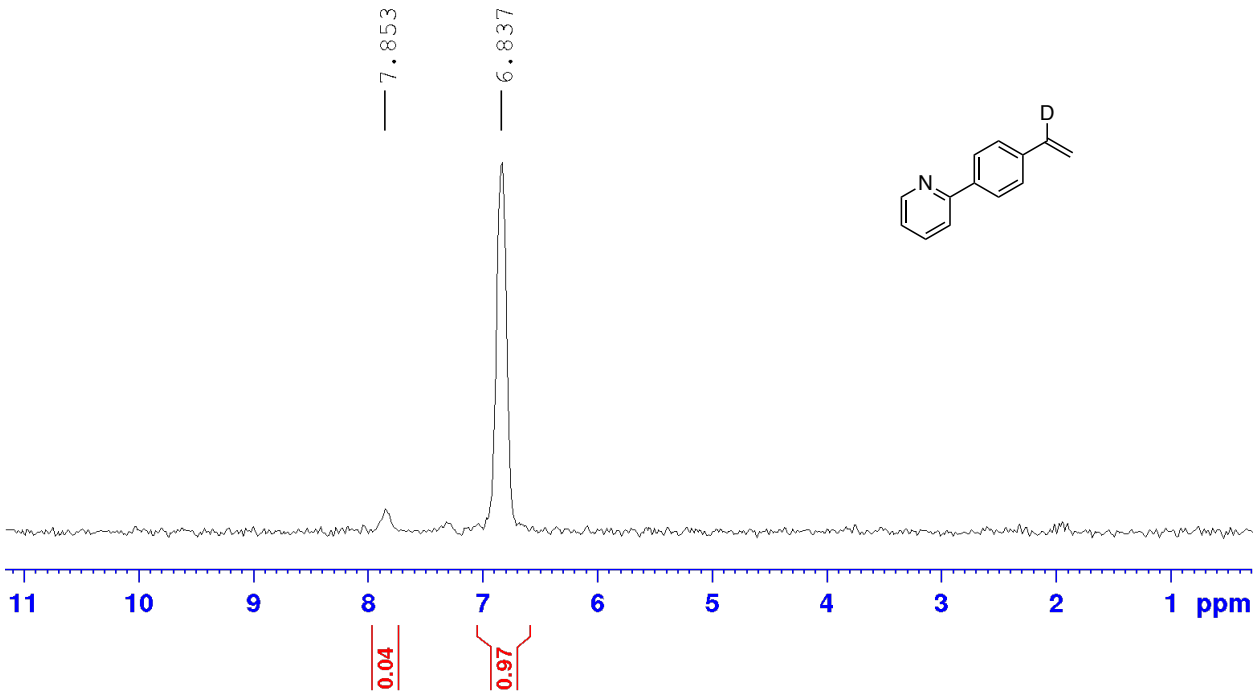

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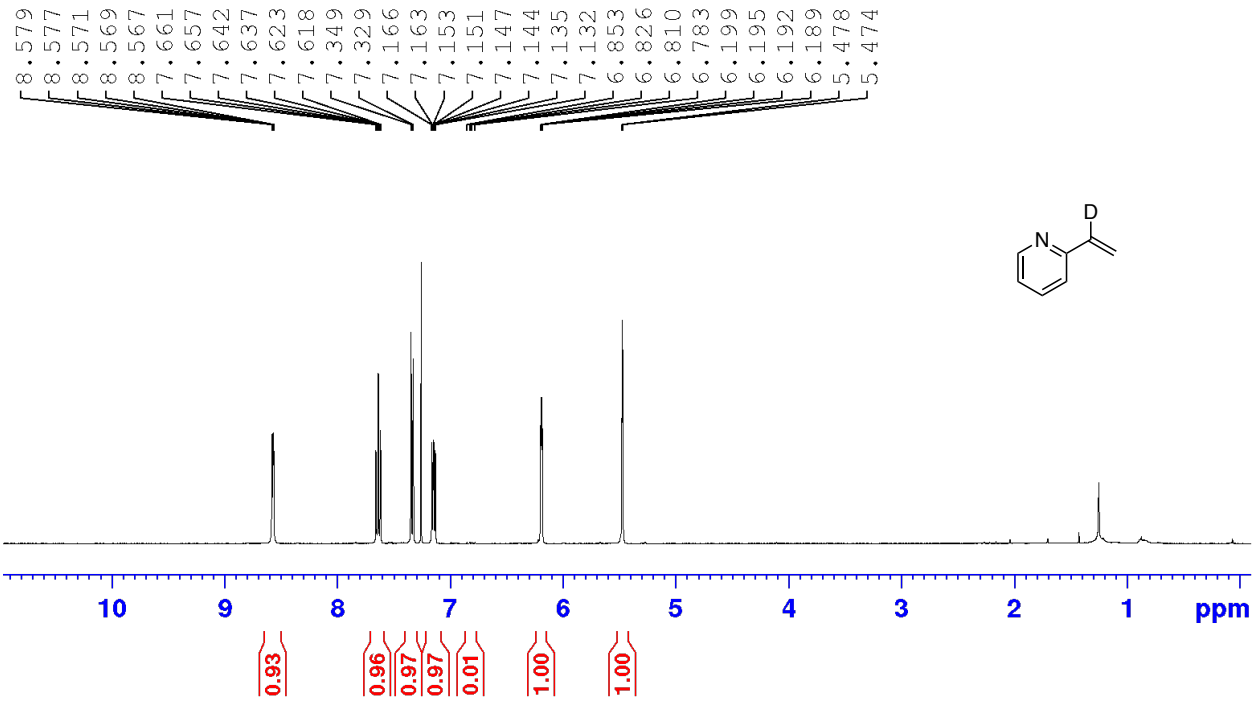

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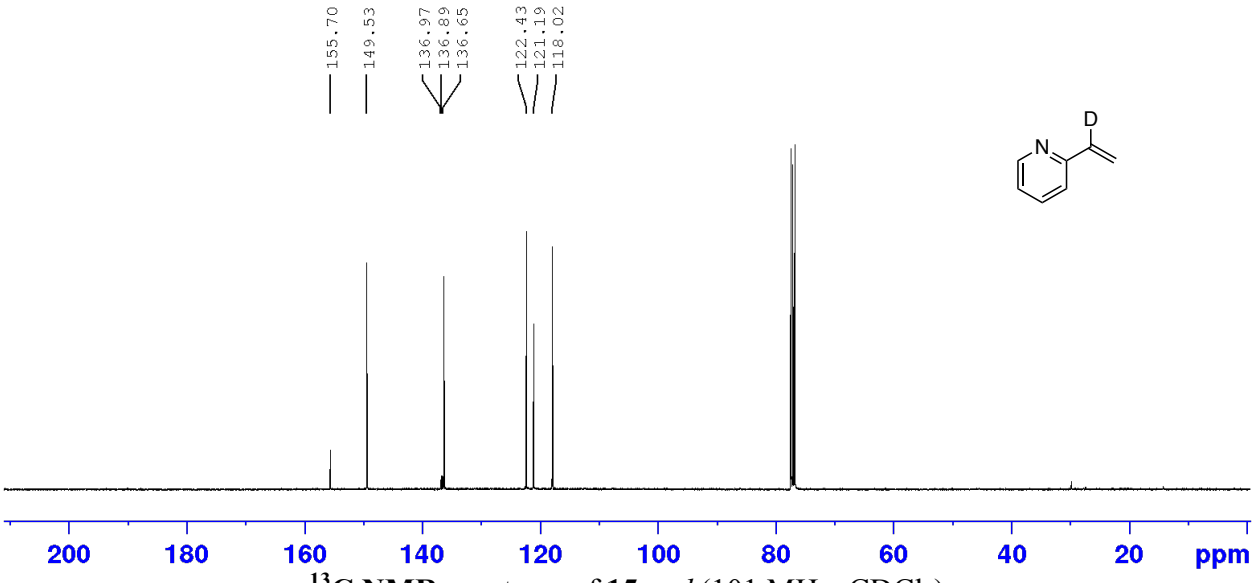
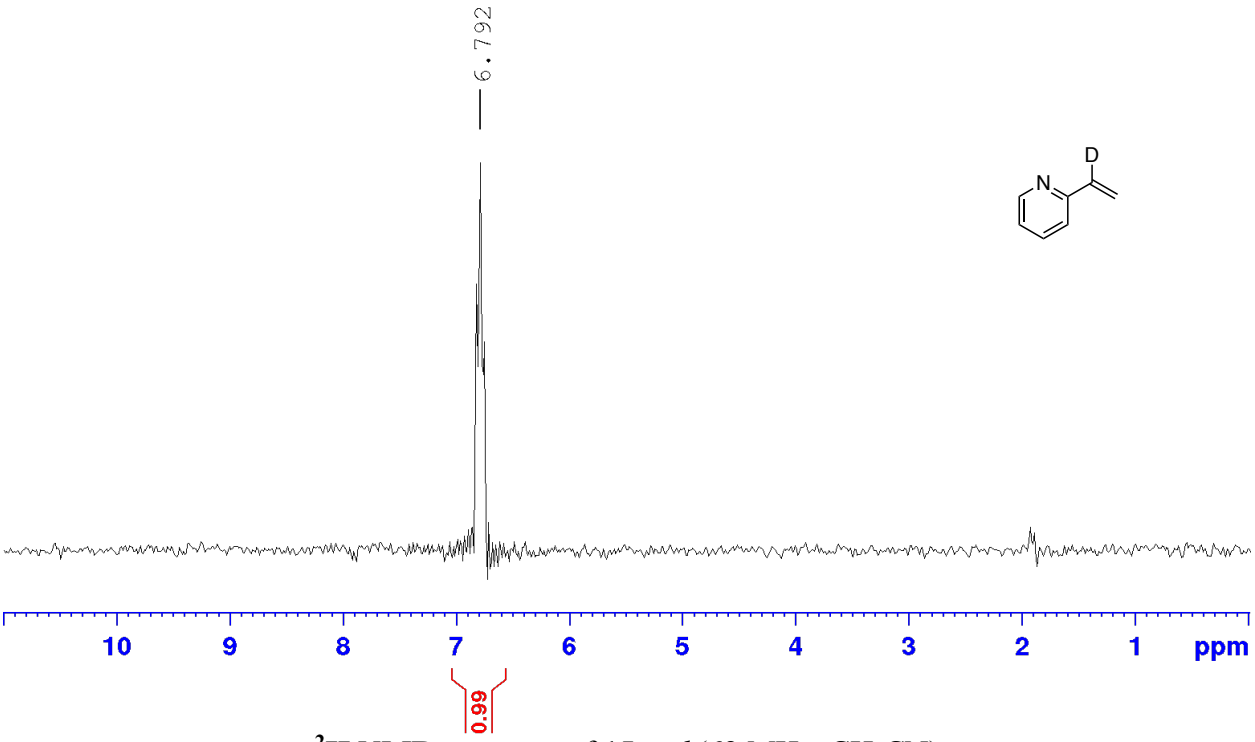
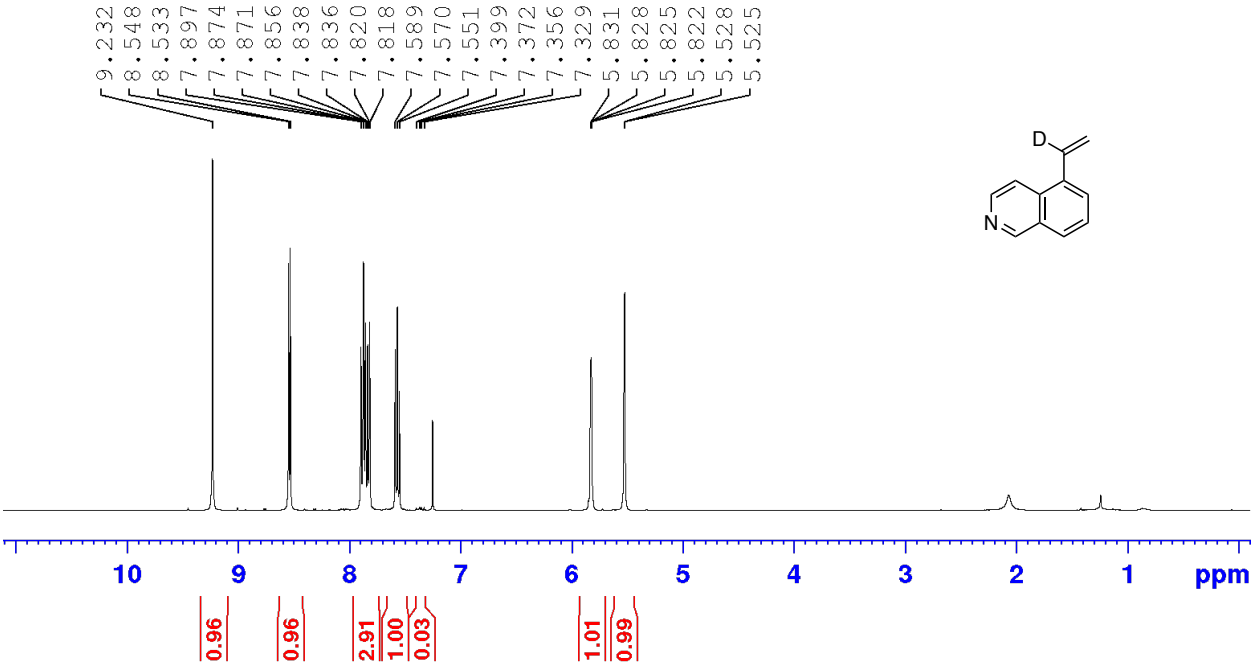


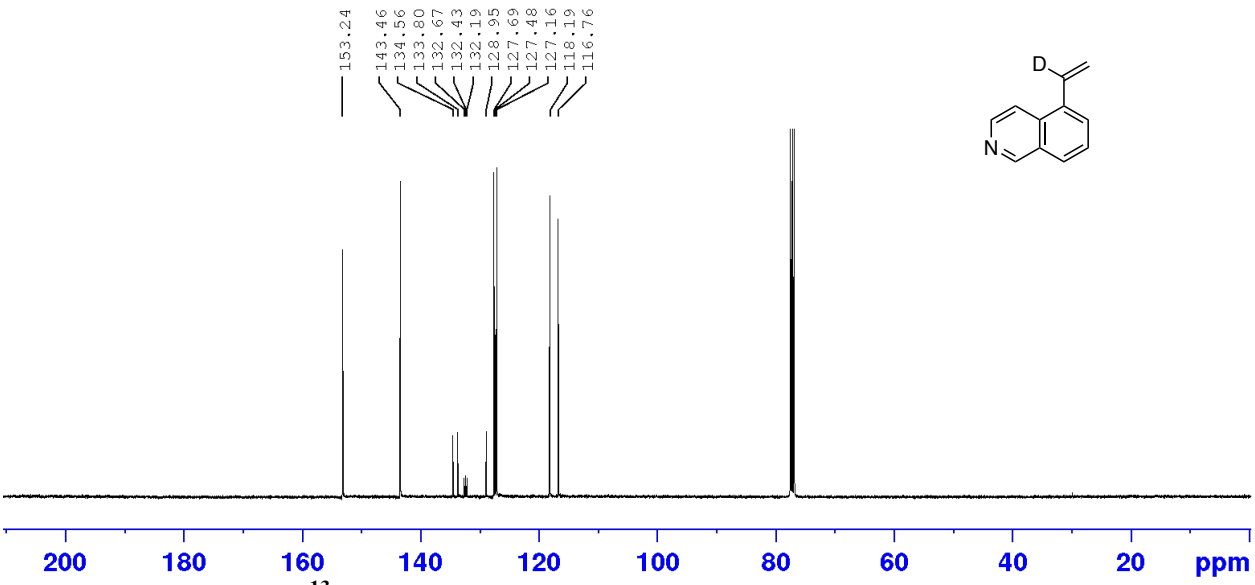
^{13}C NMR spectrum of **15**-α-*d* (101 MHz, $CDCl_3$)



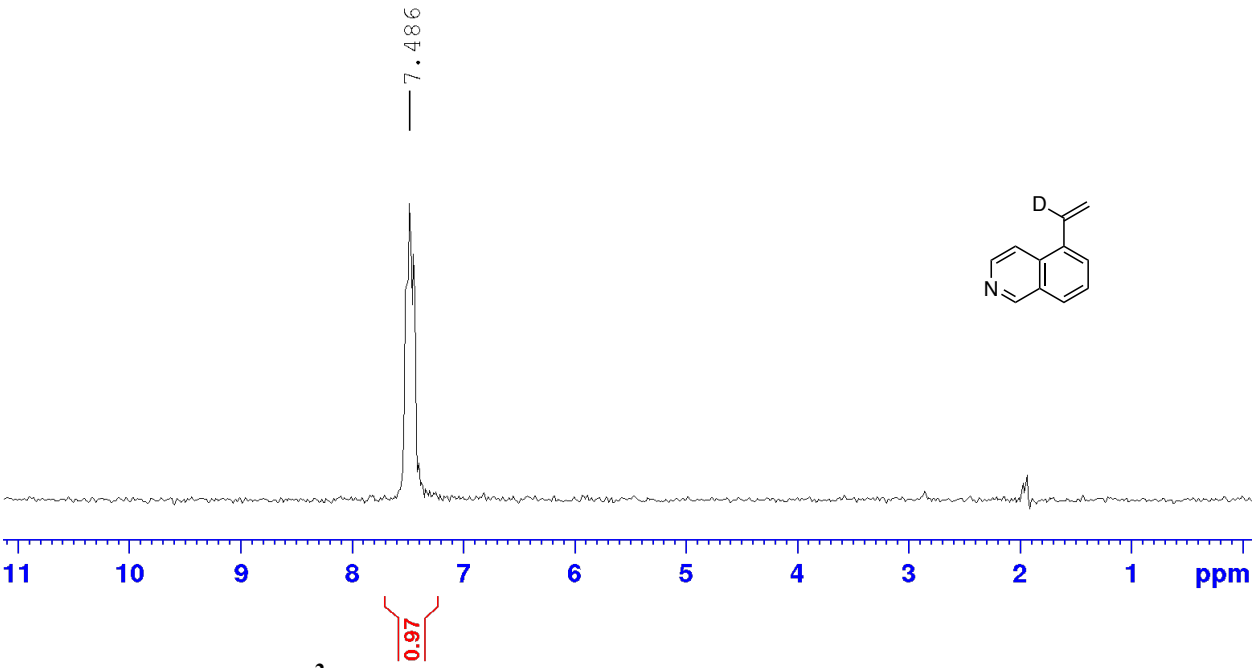
^{2}H NMR spectrum of **15**-α-*d* (62 MHz, CH_3CN)



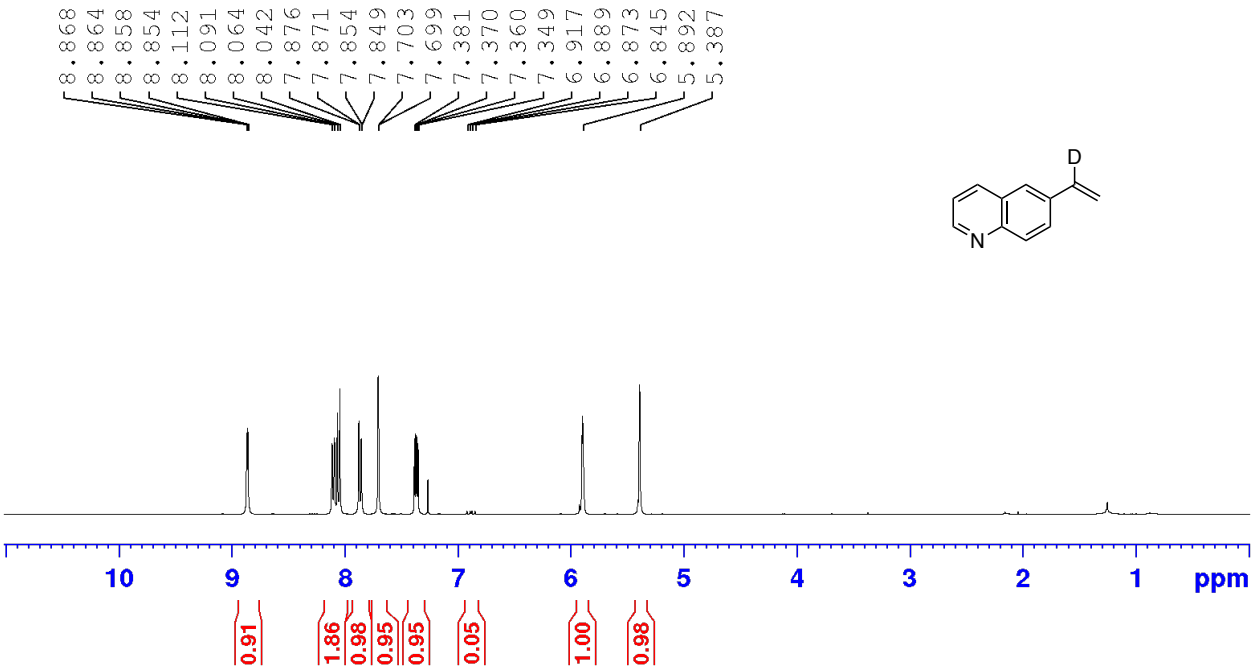
^{1}H NMR spectrum of **16**-α-*d* (400 MHz, $CDCl_3$)



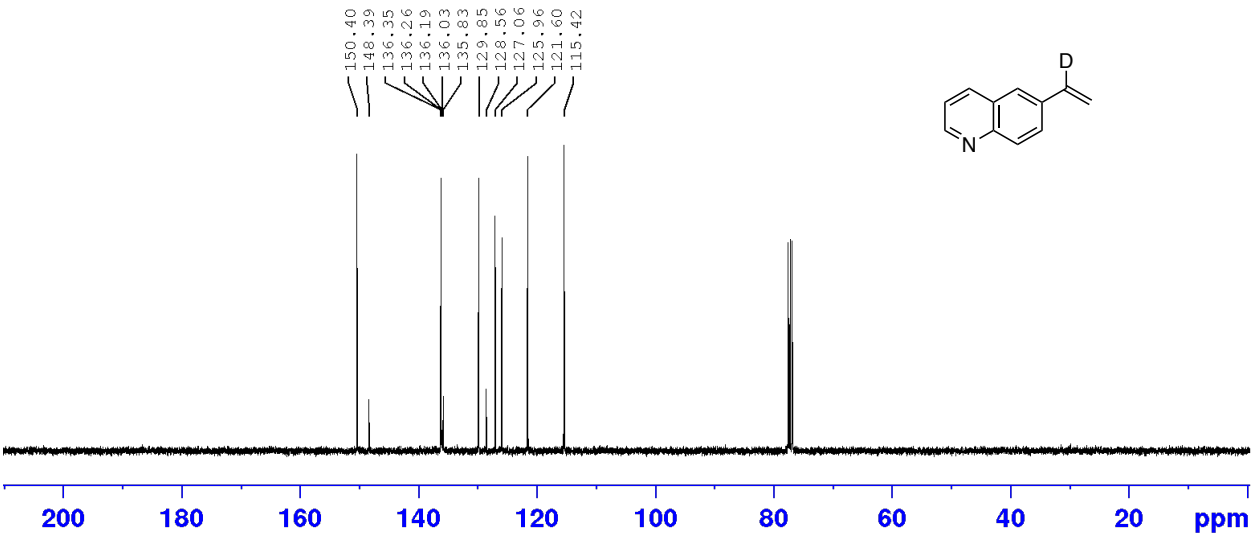
^{13}C NMR spectrum of **16**-α-*d* (101 MHz, $CDCl_3$)



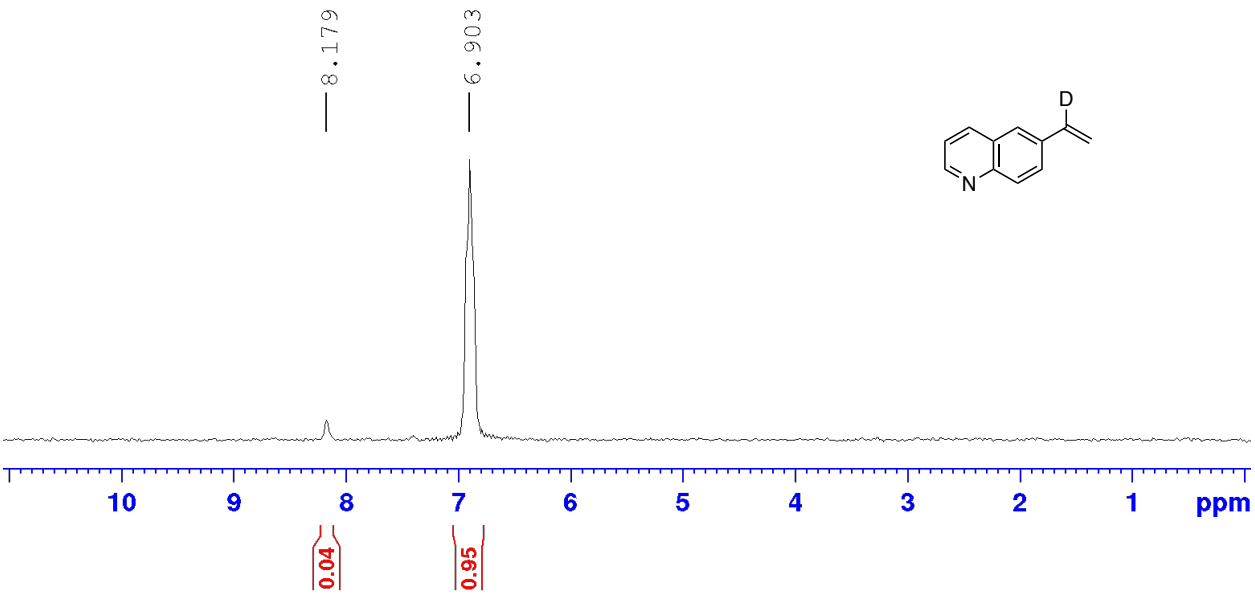
^{2}H NMR spectrum of **16**-α-*d* (62 MHz, CH_3CN)



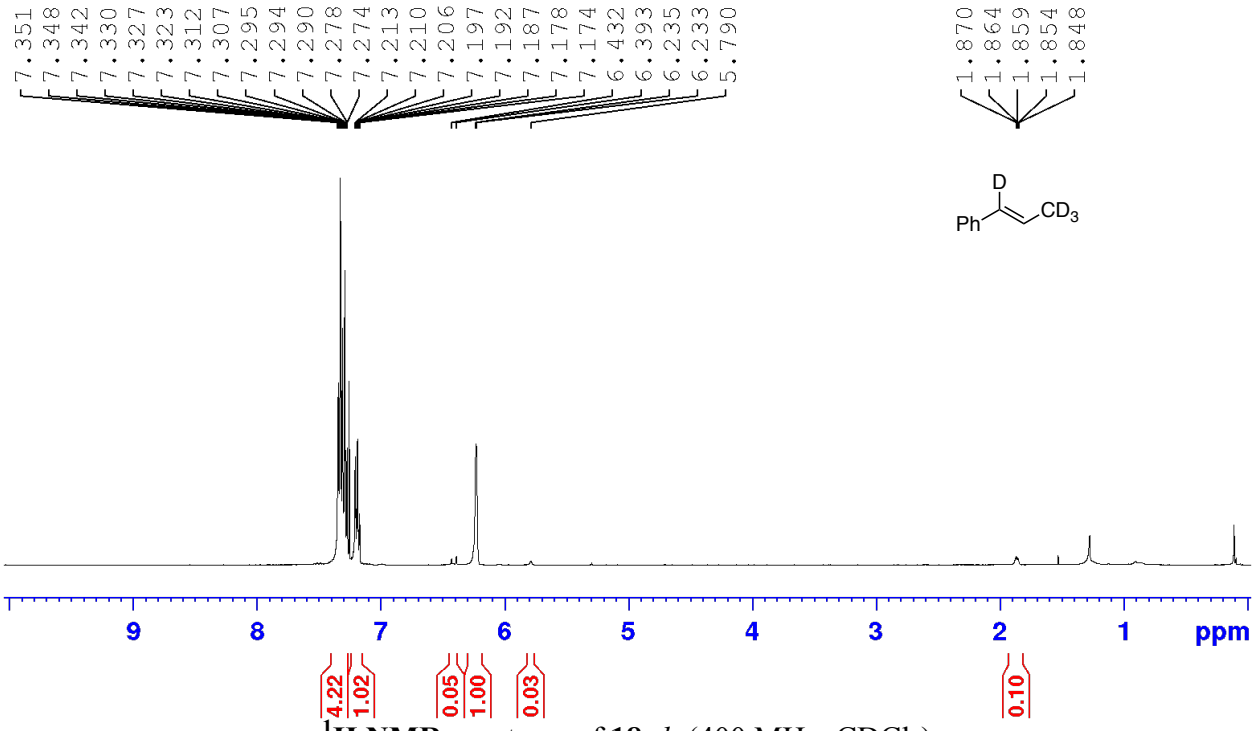
^{1}H NMR spectrum of **17**-α-*d* (400 MHz, $CDCl_3$)



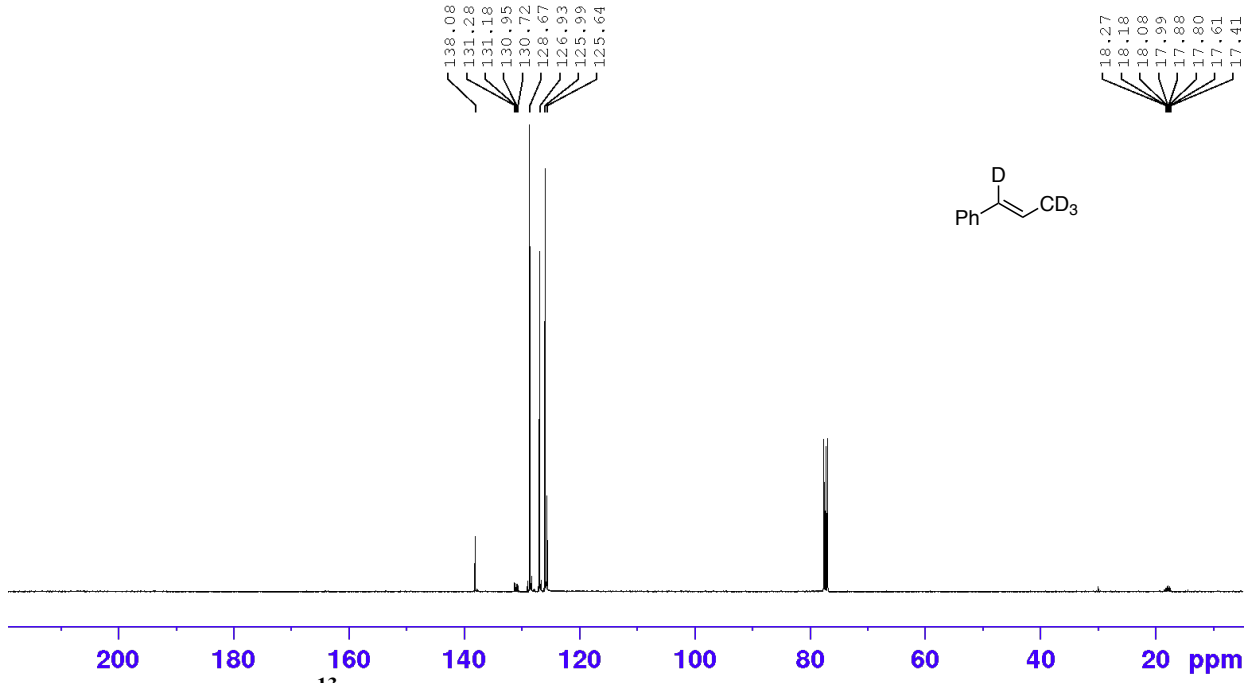
^{13}C NMR spectrum of **17**-α-*d* (101 MHz, $CDCl_3$)



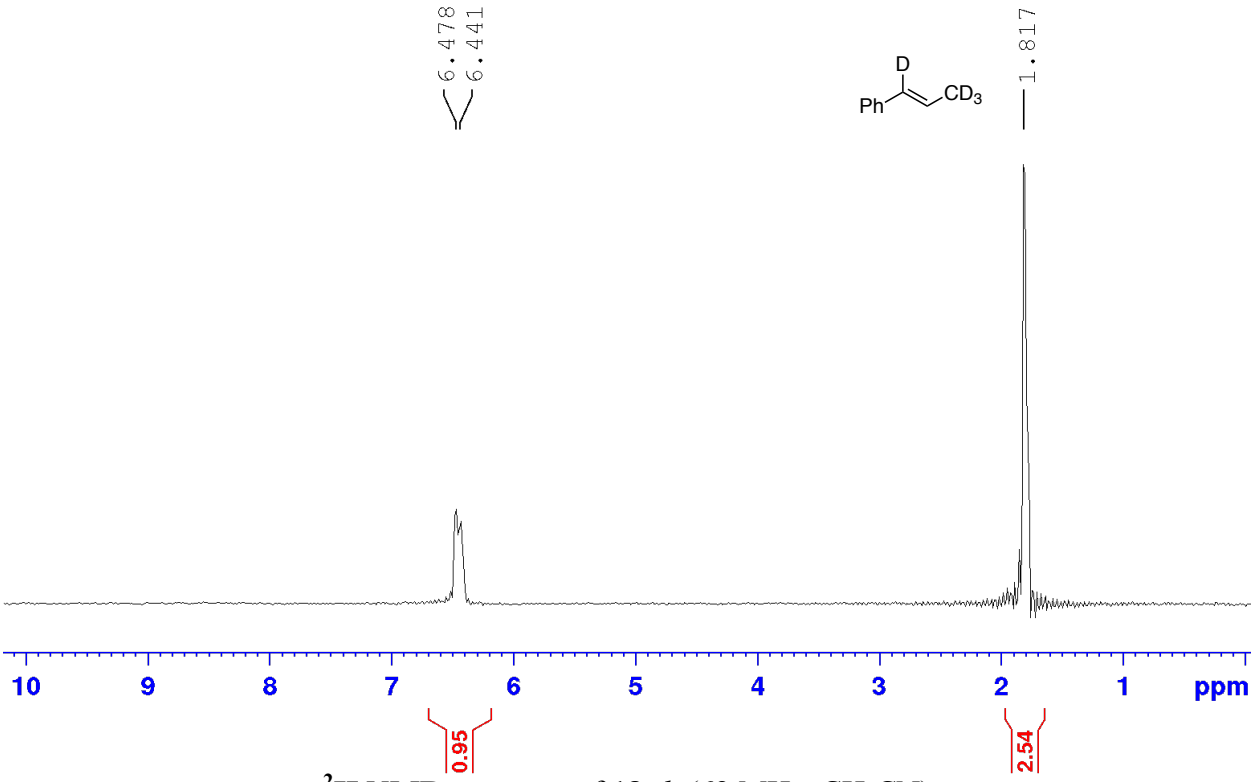
^{2}H NMR spectrum **17**-α-*d* (62 MHz, CH_3CN)



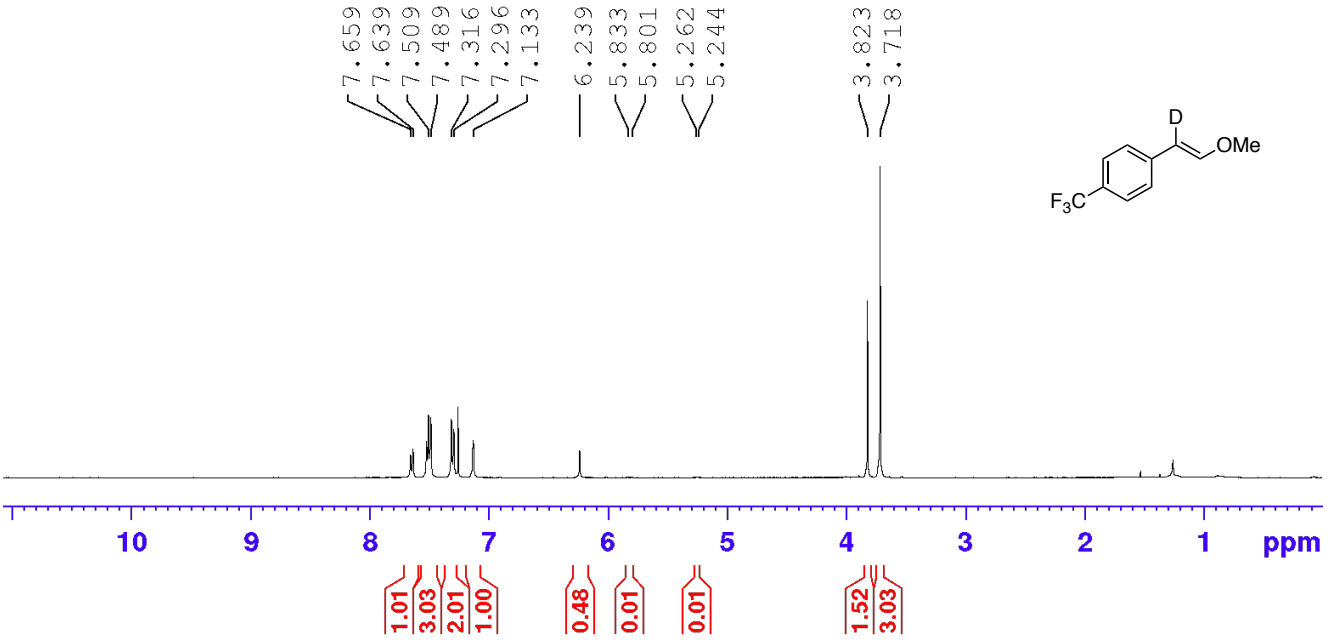
^{1}H NMR spectrum of **18**-d_4 (400 MHz, $CDCl_3$)



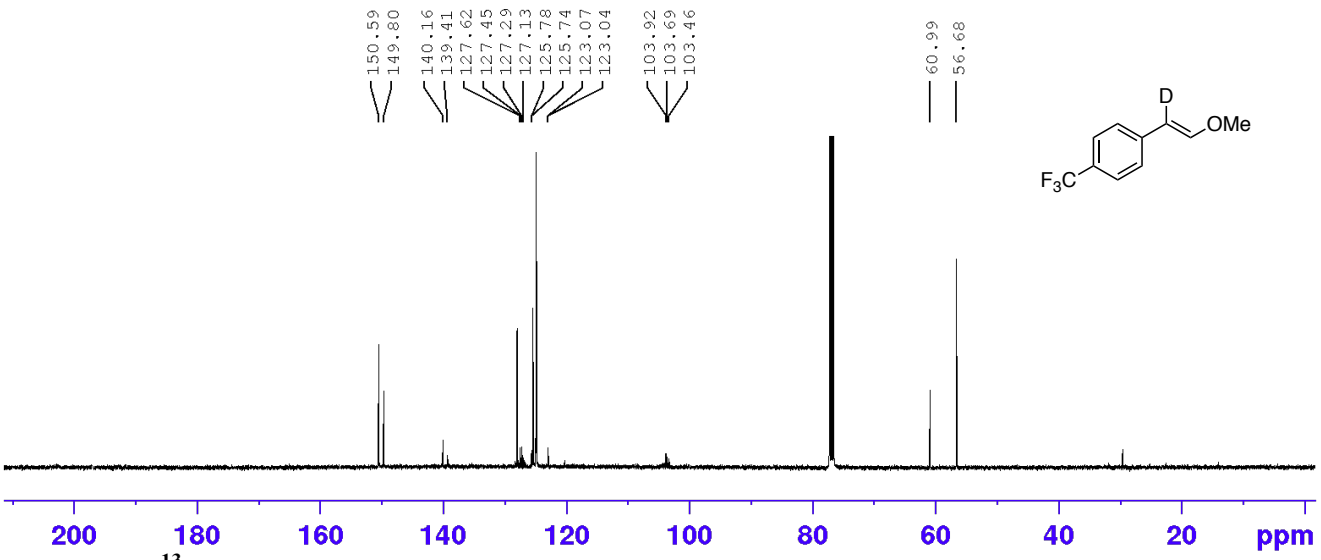
^{13}C NMR spectrum of **18**-d_4 (101 MHz, $CDCl_3$)



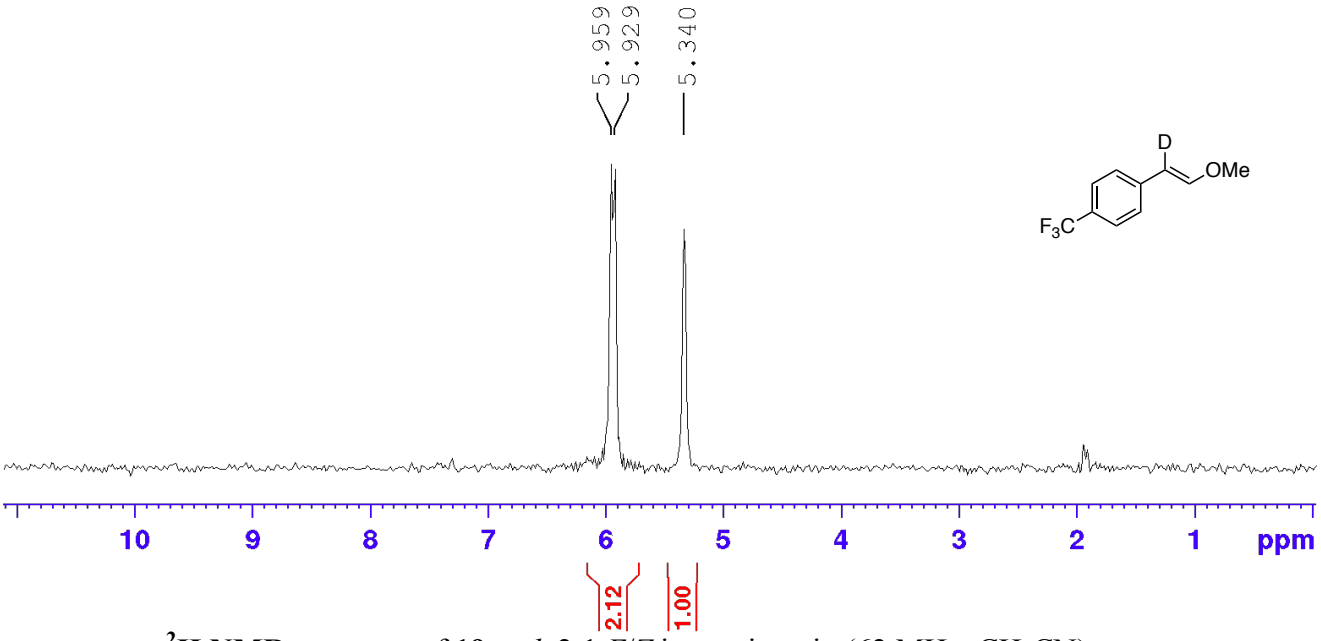
^{2}H NMR spectrum of **18**-d_4 (62 MHz, CH_3CN)



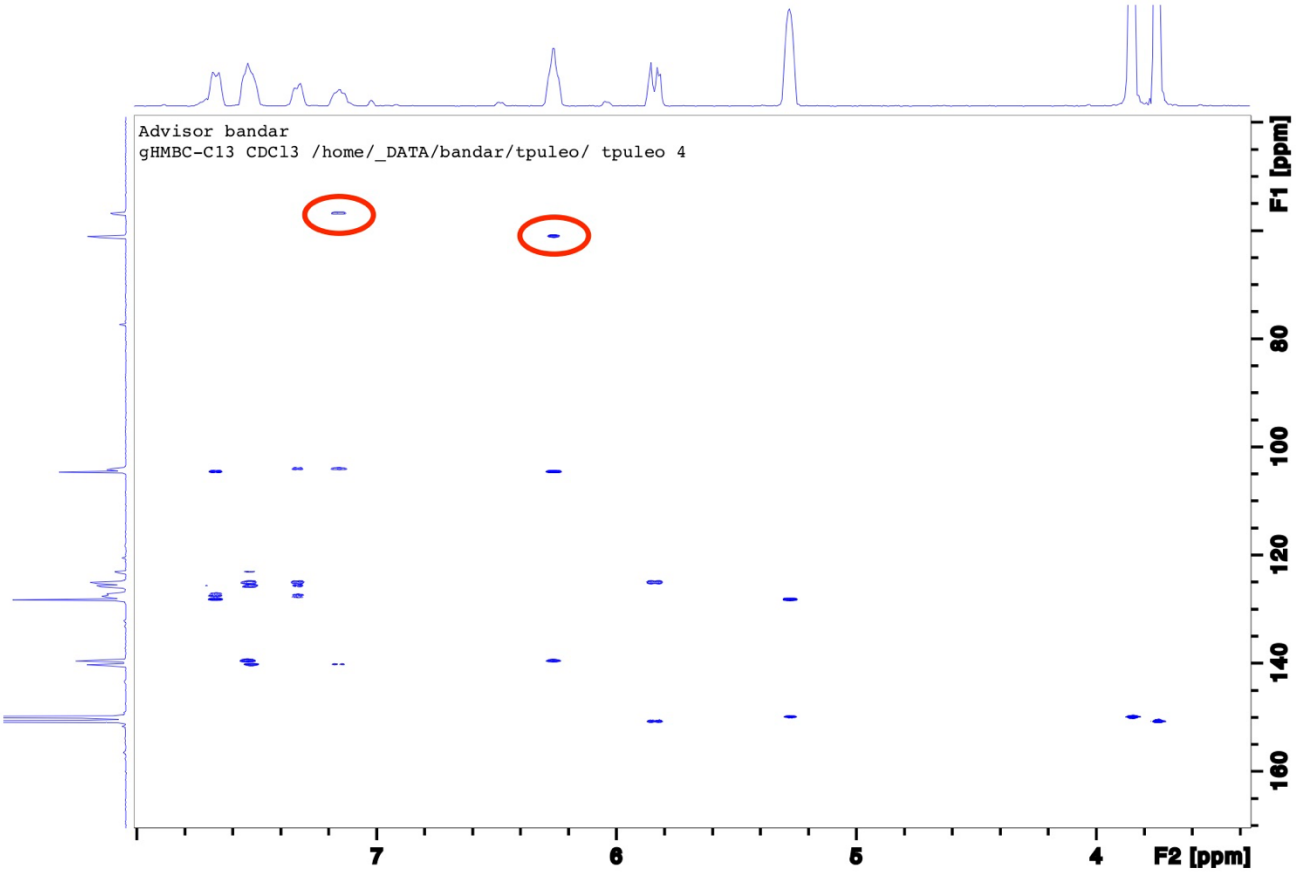
^{1}H NMR spectrum of **19**-α-*d*; 2:1 *E*/*Z* isomeric ratio (400 MHz, $CDCl_3$)



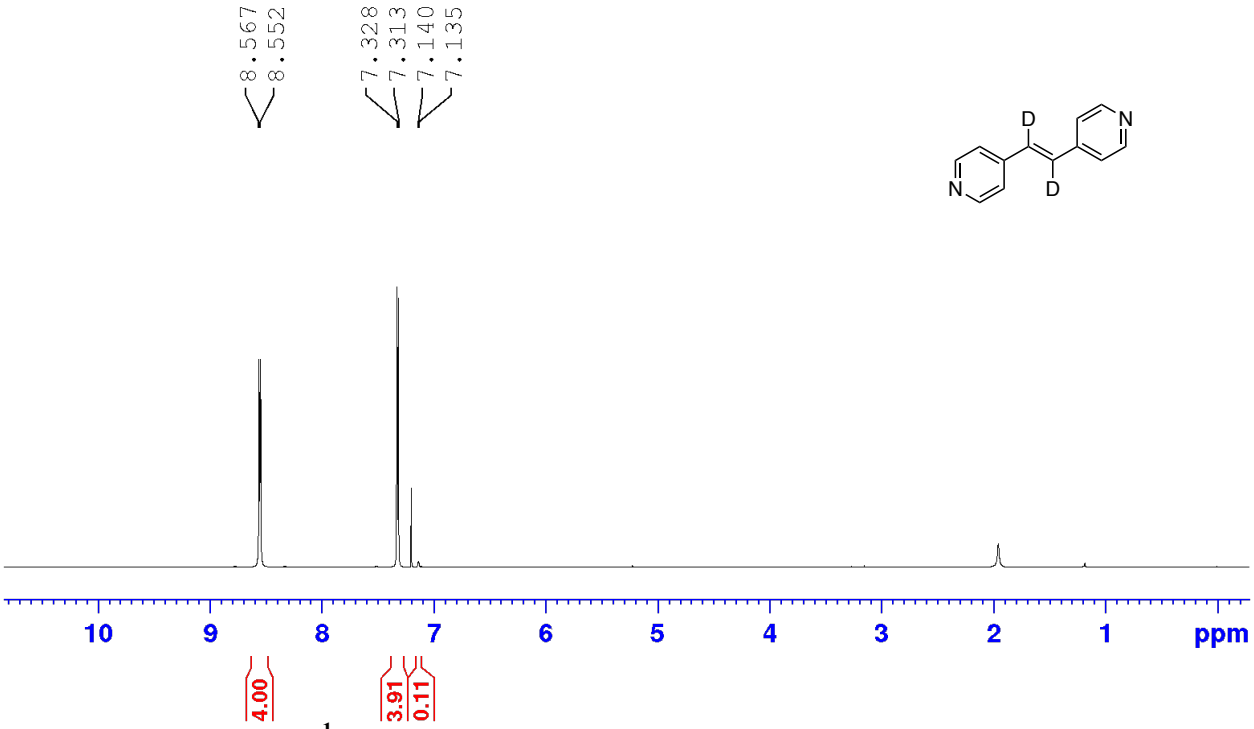
^{13}C NMR spectrum of **19**-α-*d*; 2:1 *E*/*Z* isomeric ratio (101 MHz, $CDCl_3$)



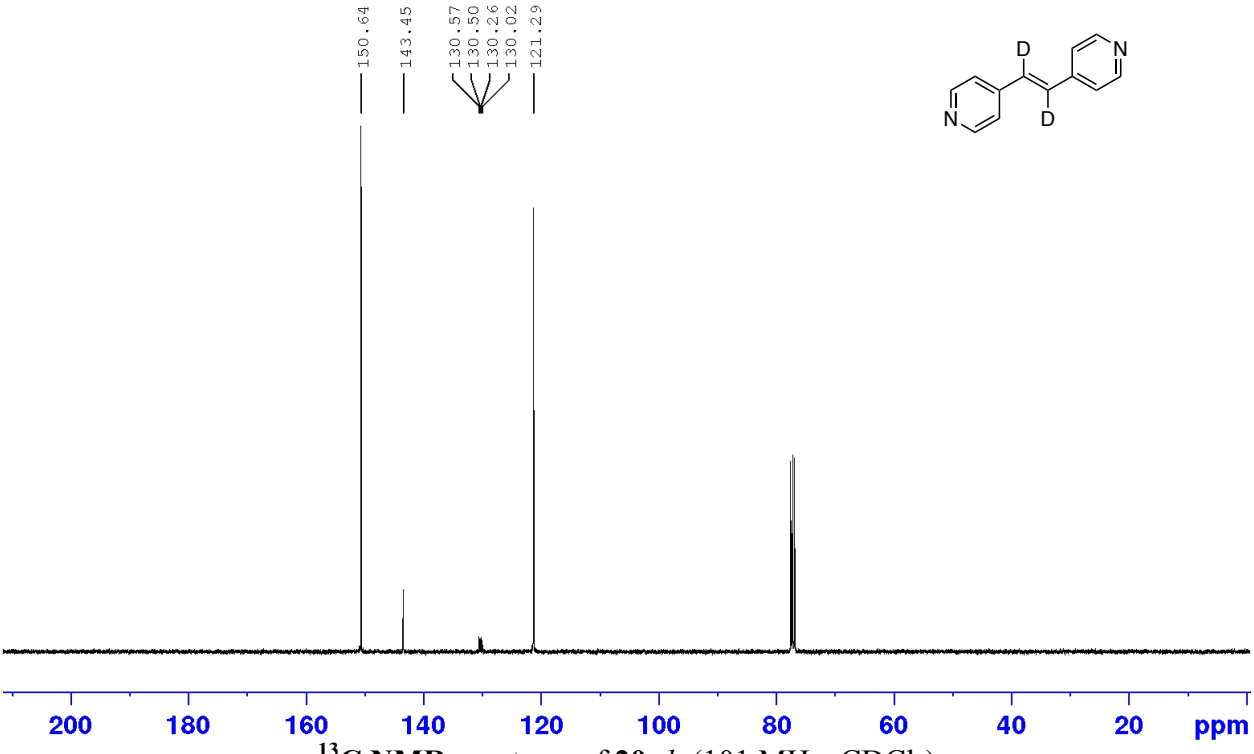
^{2}H NMR spectrum of **19**-α-*d*; 2:1 *E*/*Z* isomeric ratio (62 MHz, CH_3CN)



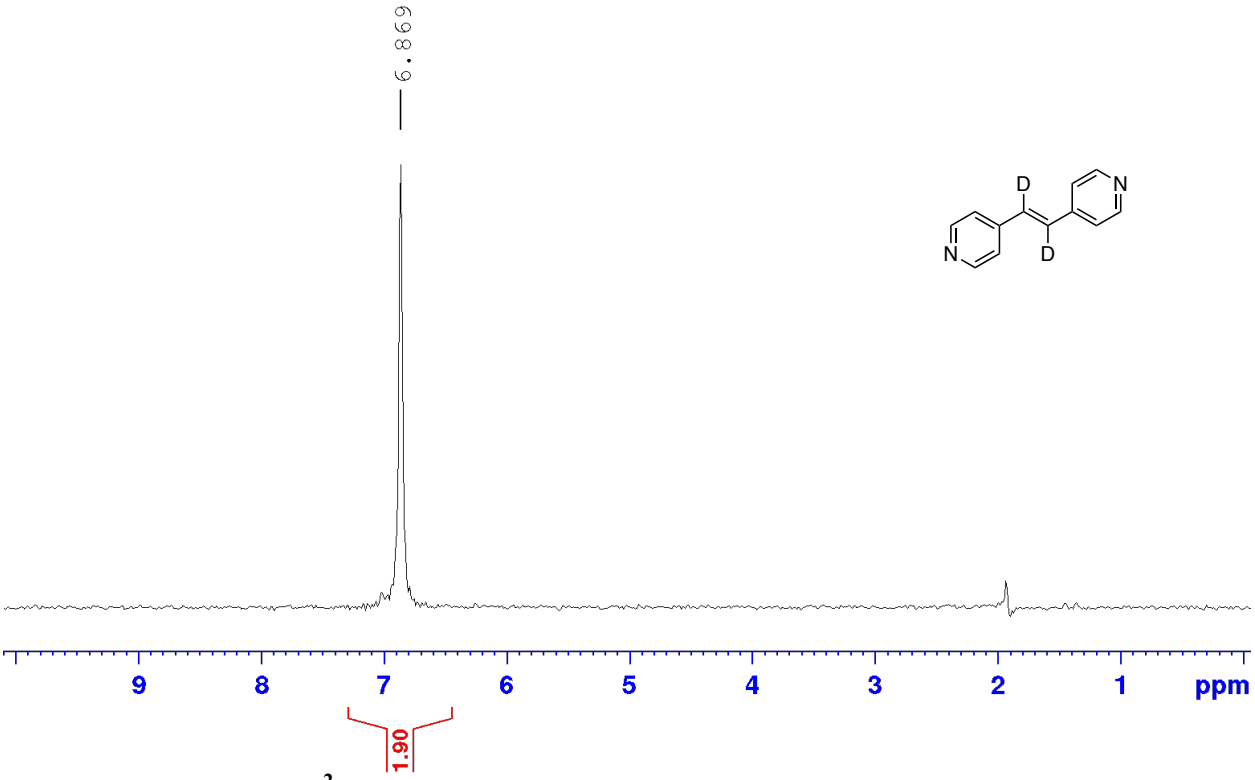
2D HMBC NMR spectrum of **19**. The circled signals correlate to the (-OMe) ^{13}C NMR and the β ^{1}H NMR 3-bond correlation.



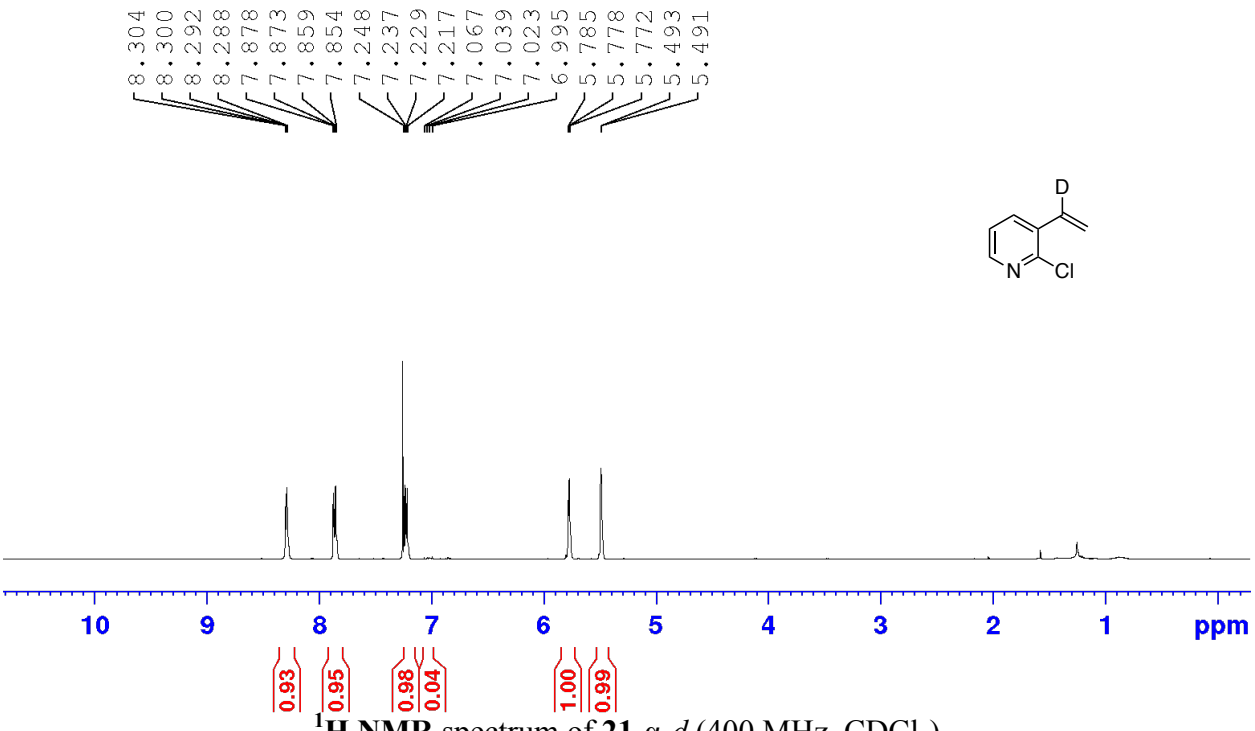
^{1}H NMR spectrum of **20**-d_2 (400 MHz, $CDCl_3$)



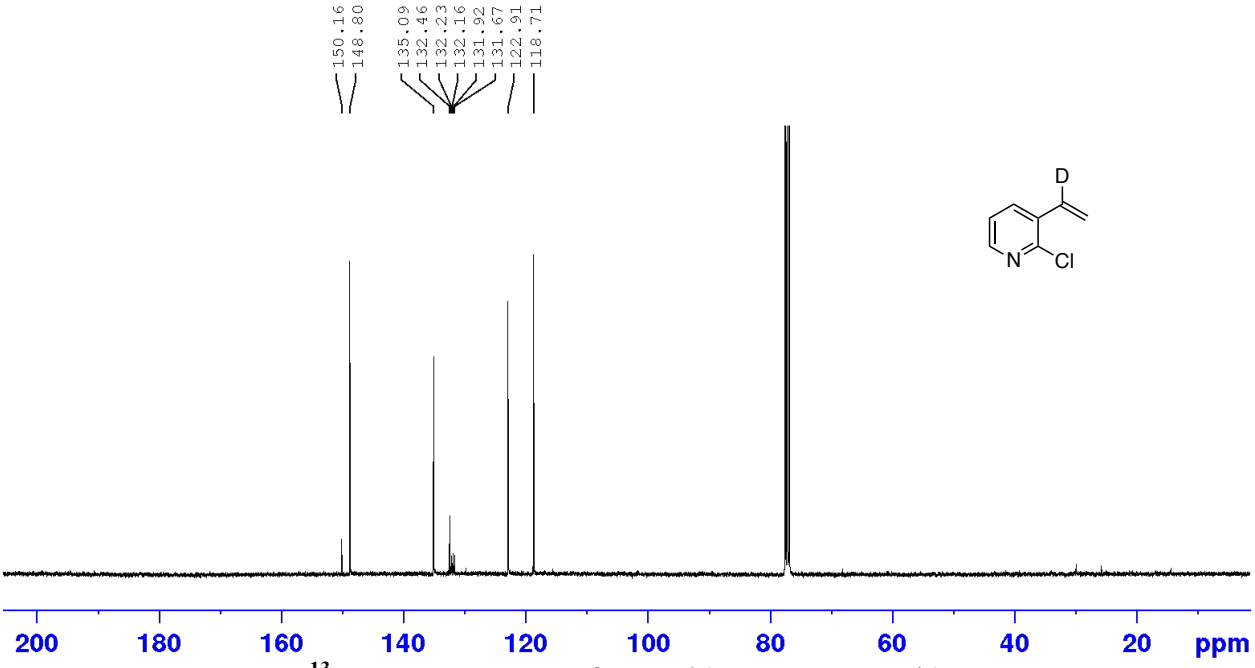
^{13}C NMR spectrum of **20**-d_2 (101 MHz, $CDCl_3$)



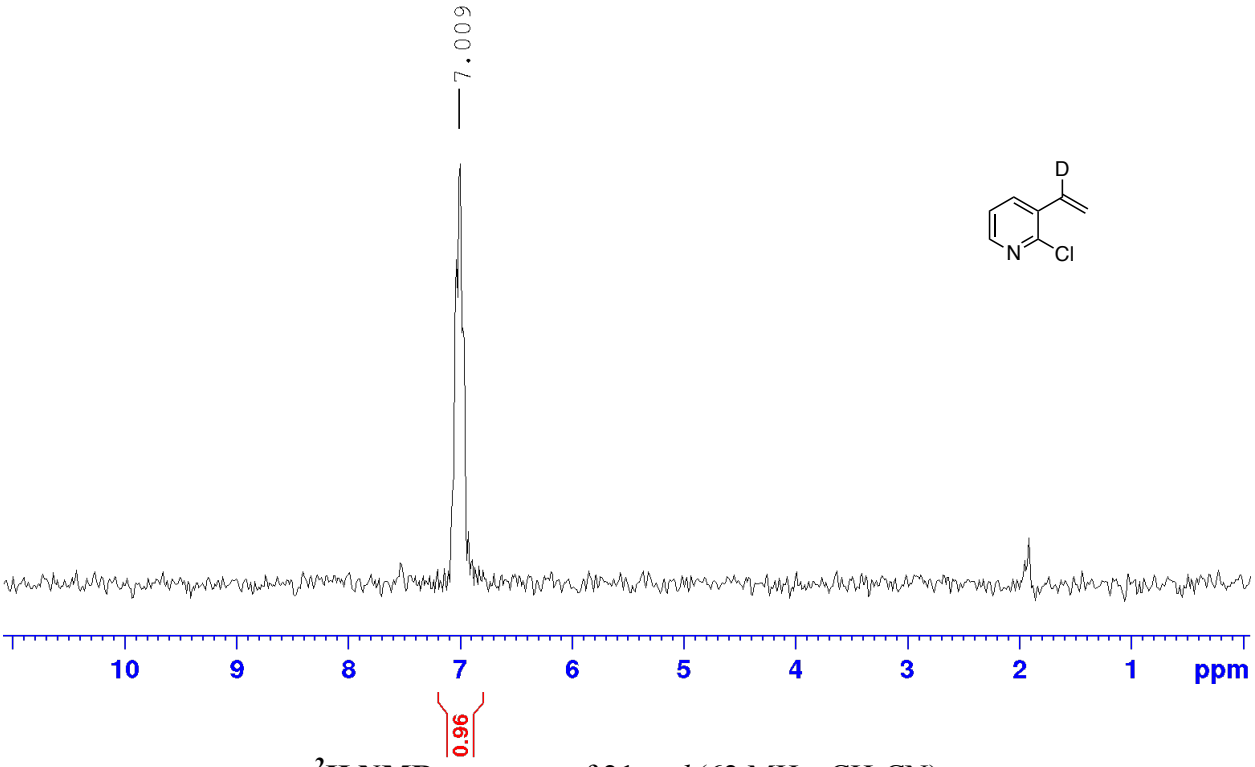
^{2}H NMR spectrum of **20**-d_2 (62 MHz, CH_3CN)



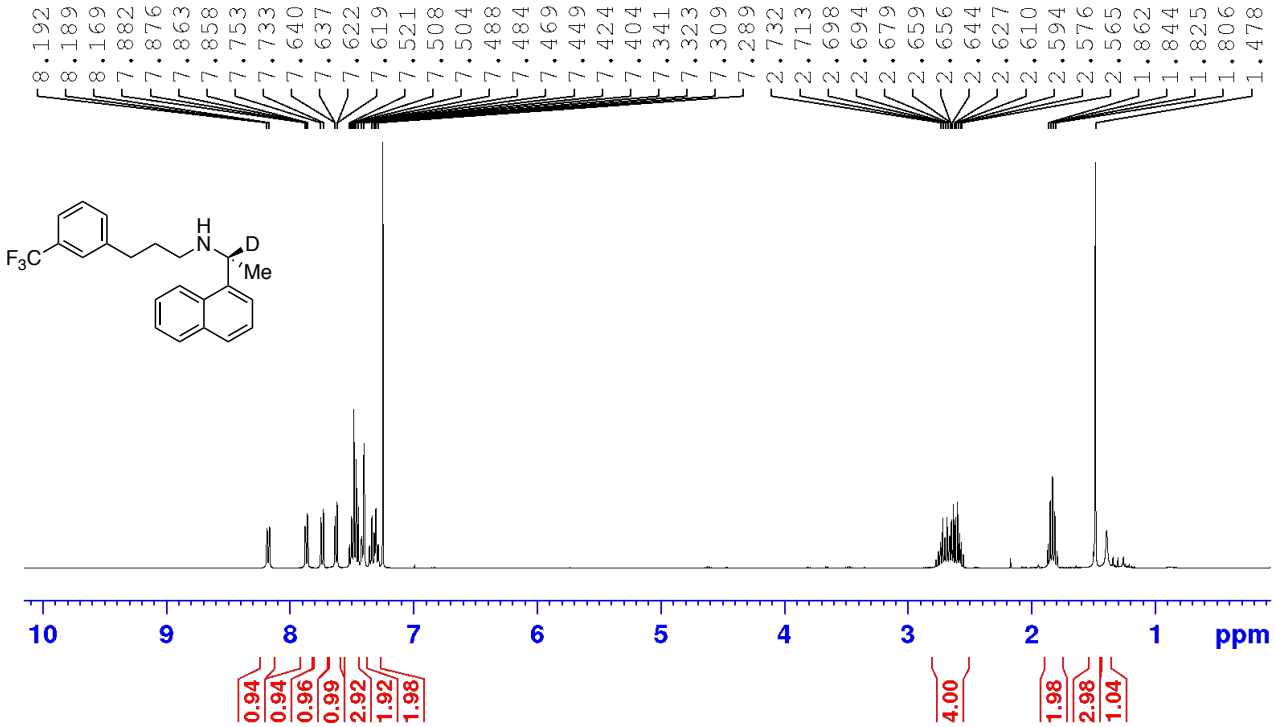
^{1}H NMR spectrum of **21**-α-*d* (400 MHz, $CDCl_3$)



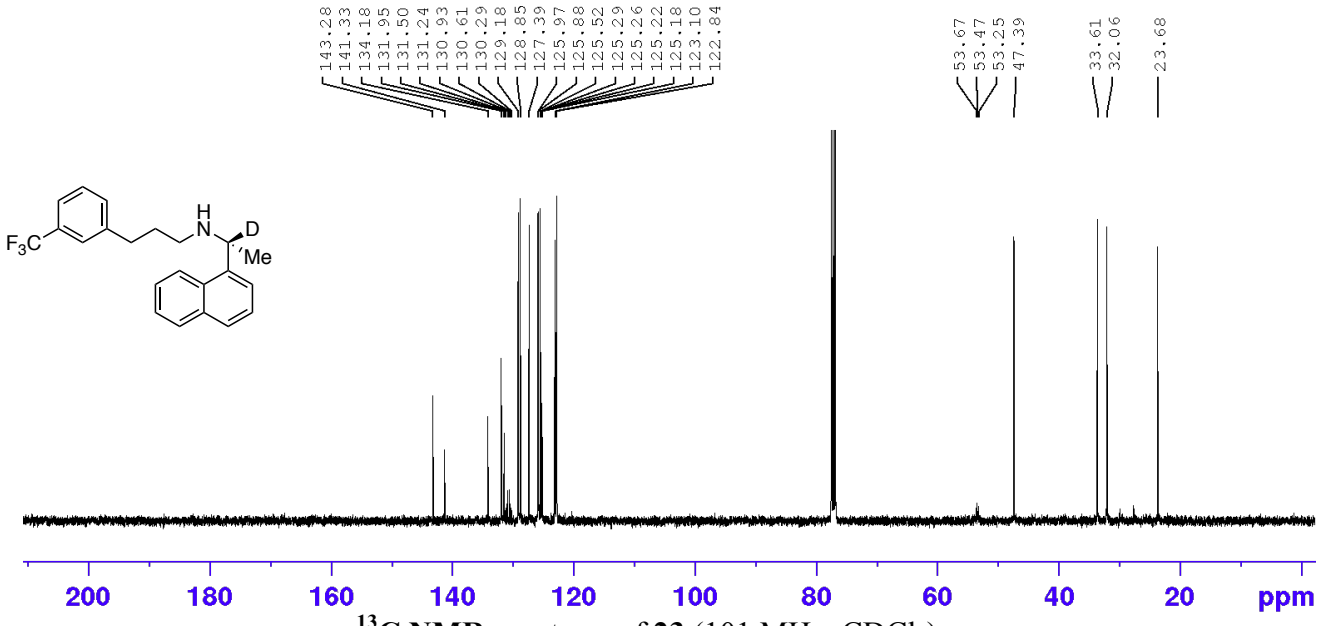
^{13}C NMR spectrum of **21**-α-*d* (101 MHz, $CDCl_3$)



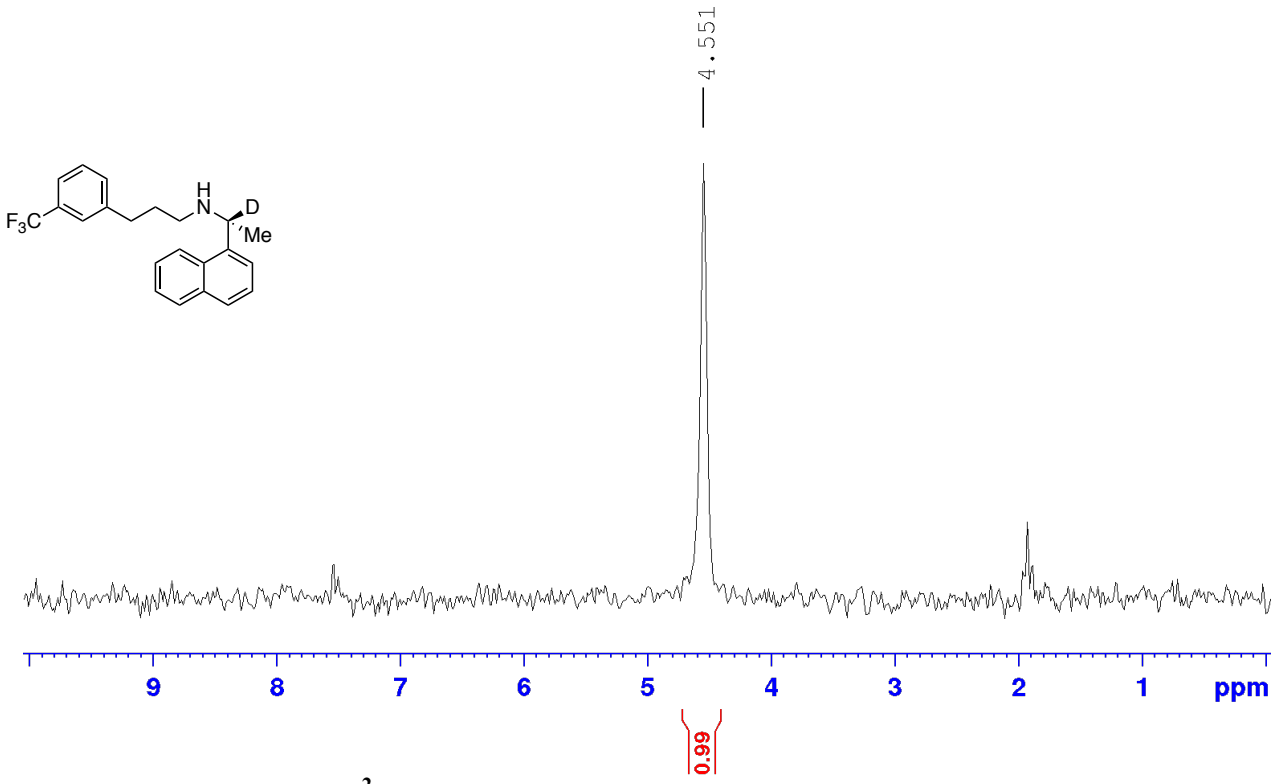
^{2}H NMR spectrum of **21**-α-*d* (62 MHz, CH_3CN)



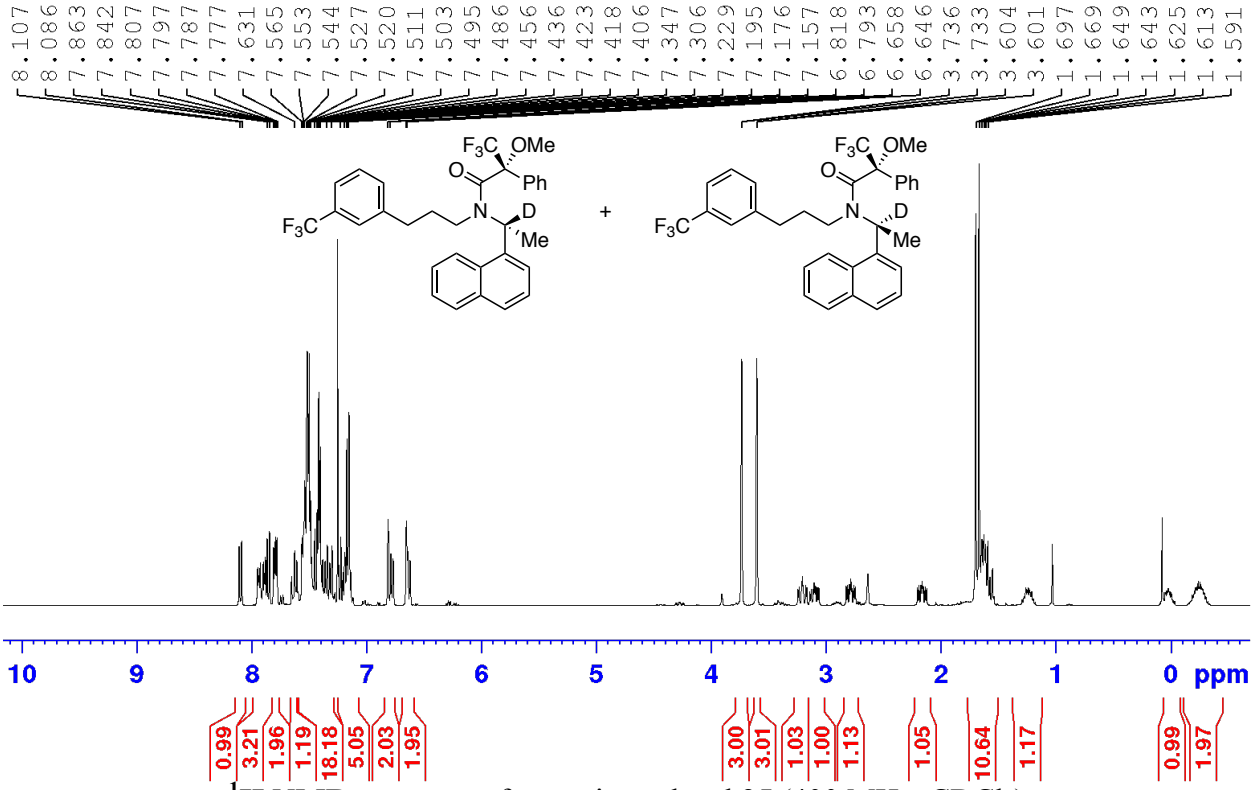
^{1}H NMR spectrum of **23** (400 MHz, $CDCl_3$)



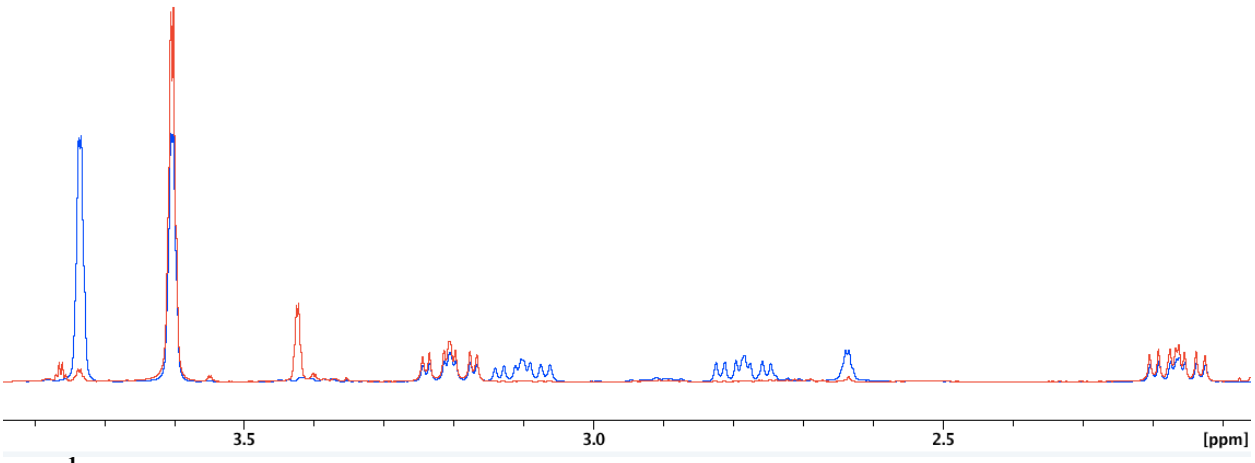
^{13}C NMR spectrum of **23** (101 MHz, $CDCl_3$)



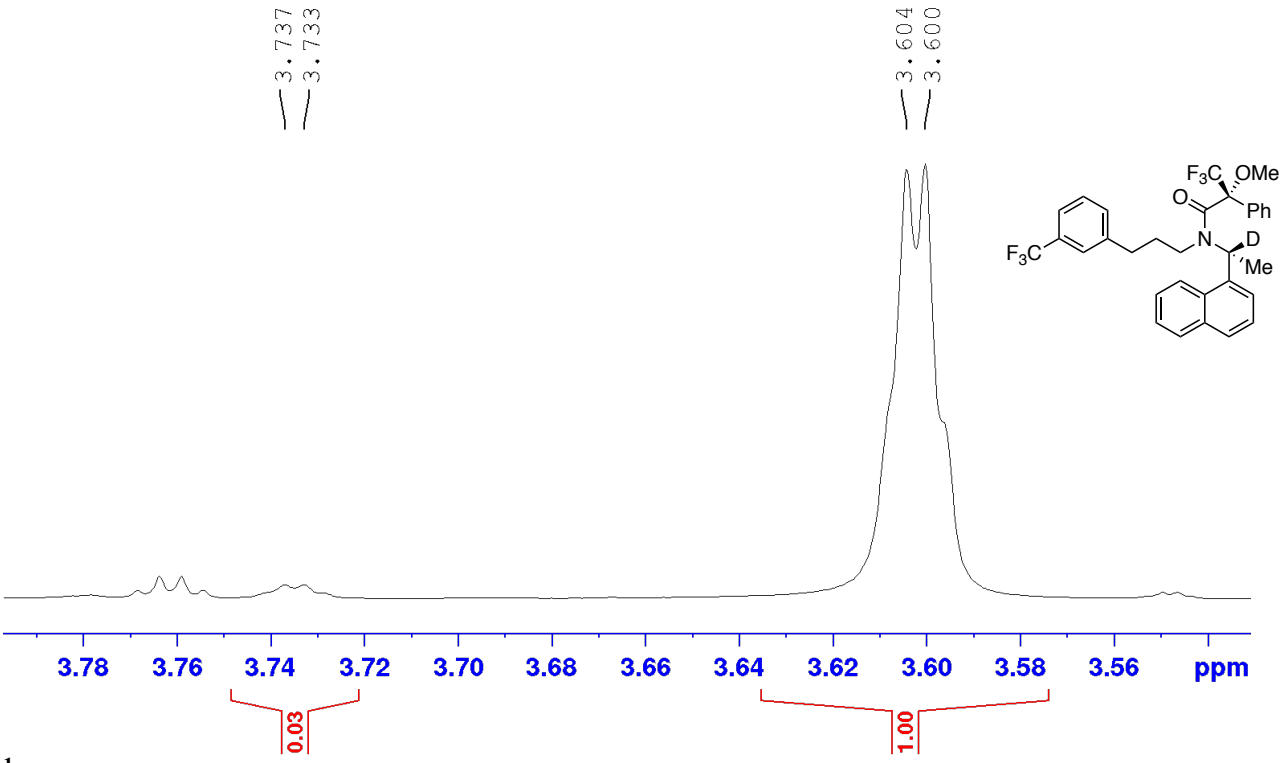
^{2}H NMR spectrum of **23** (62 MHz, CH_3CN)



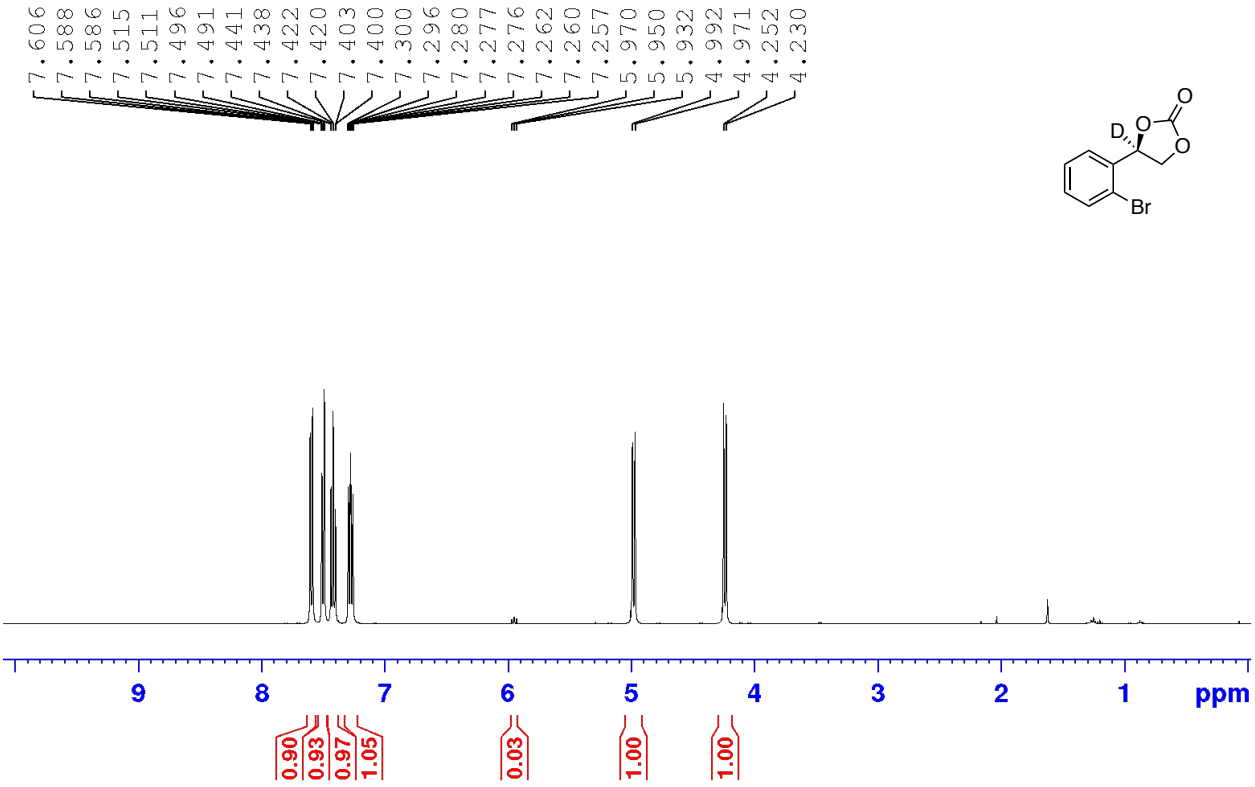
^{1}H NMR spectrum of racemic acylated **25** (400 MHz, $CDCl_3$)



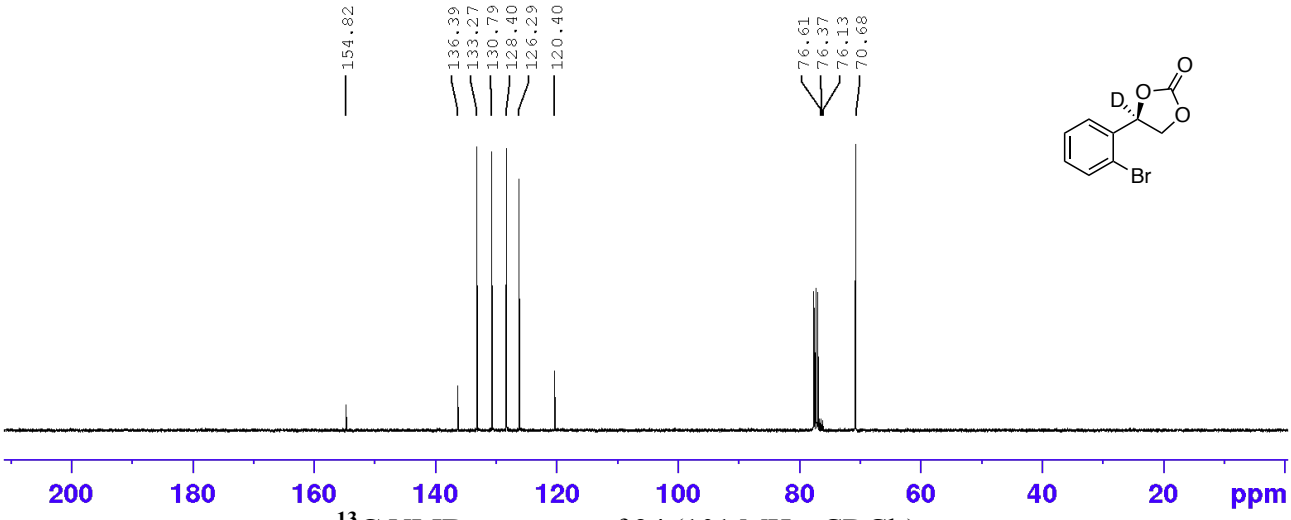
^{1}H NMR overlay of acylated **racemic 25** (blue) and **chiral 25** (red) (400 MHz, $CDCl_3$)



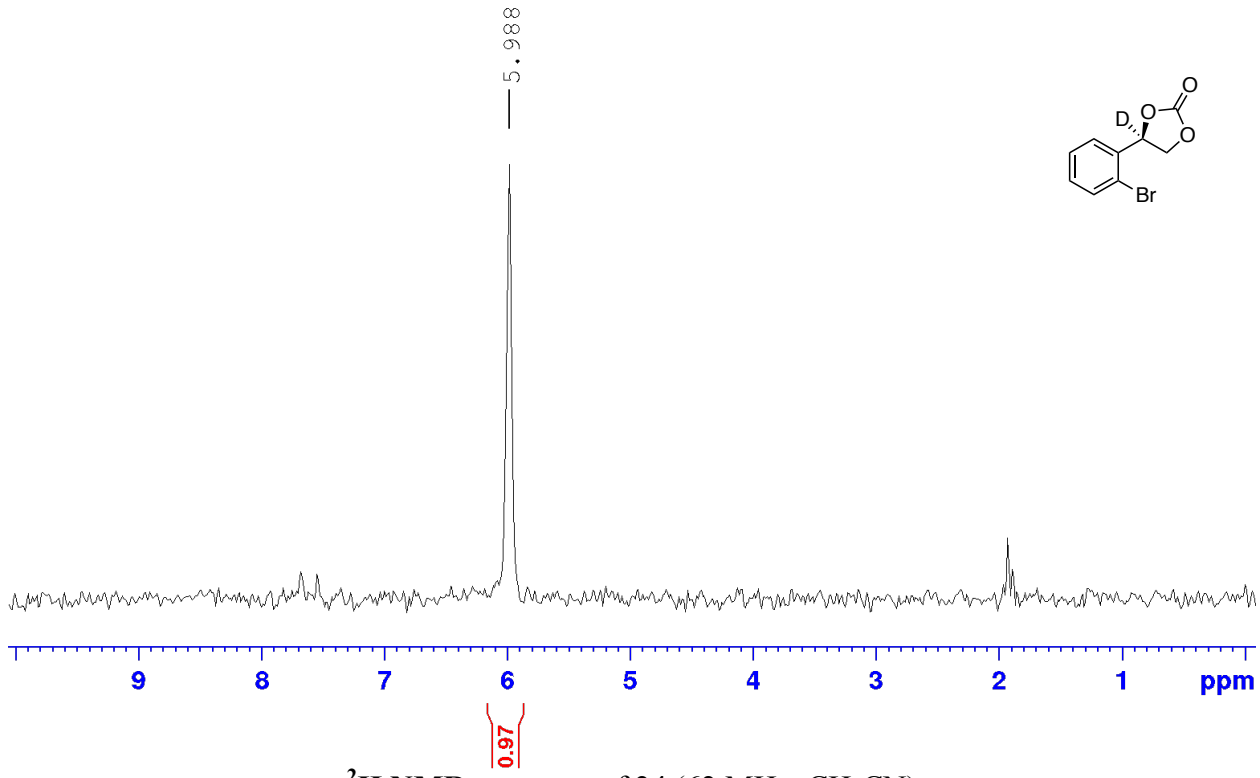
^{1}H NMR spectrum of -OMe signals for acylated chiral 25 used for ee determination (400 MHz, $CDCl_3$); see Section VIII for experimental details.



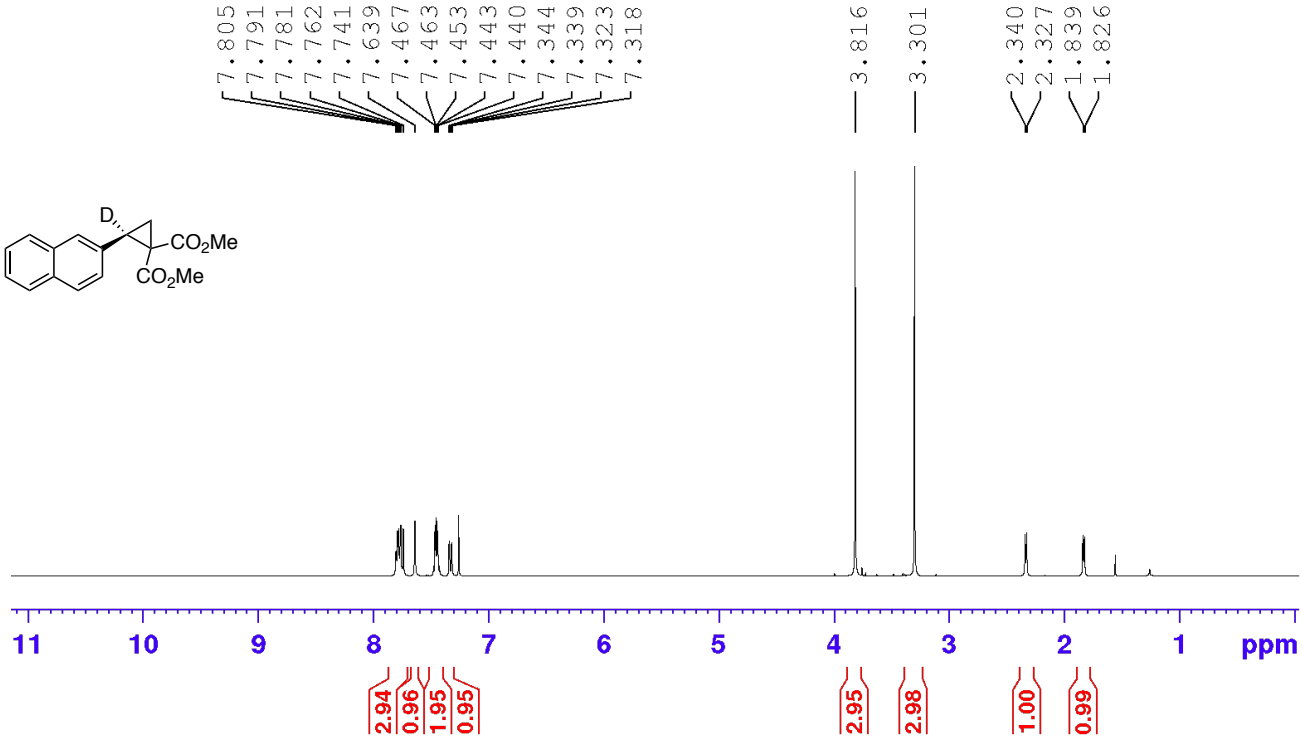
^{1}H NMR spectrum of **24** (400 MHz, $CDCl_3$)



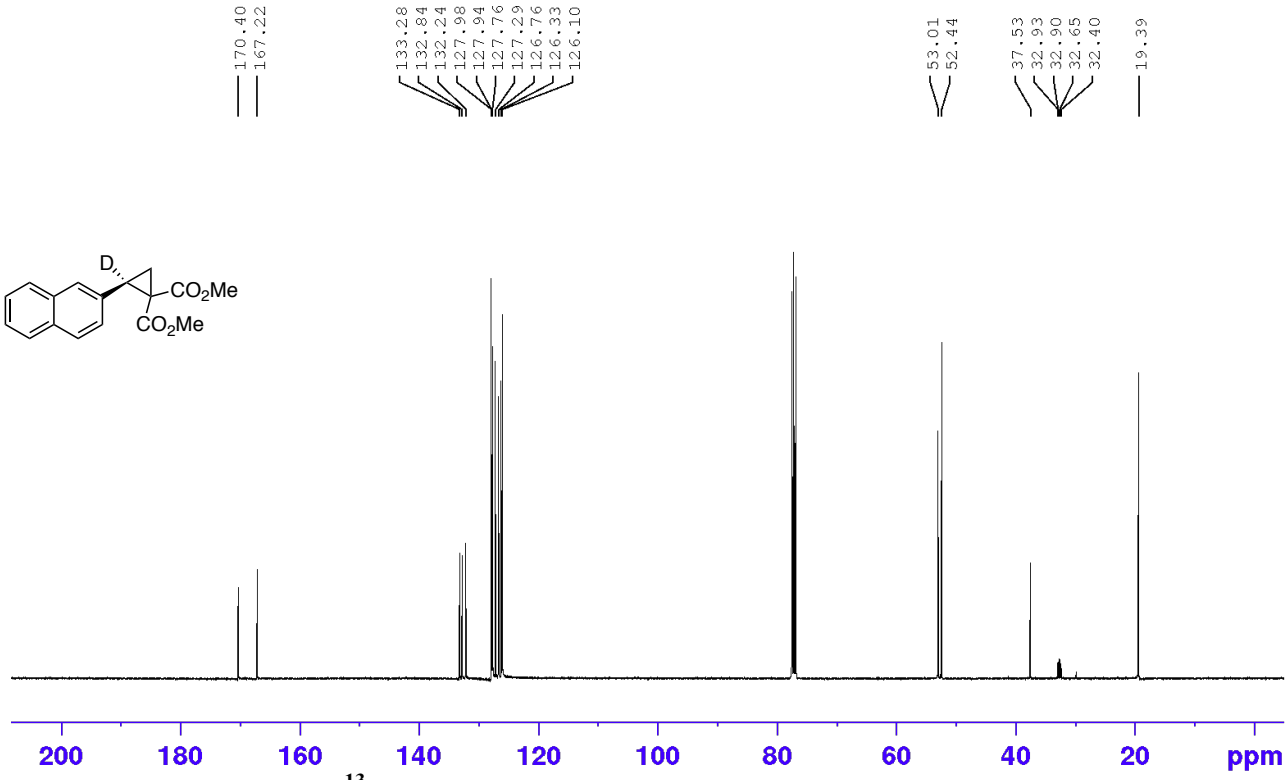
^{13}C NMR spectrum of **24** (101 MHz, $CDCl_3$)



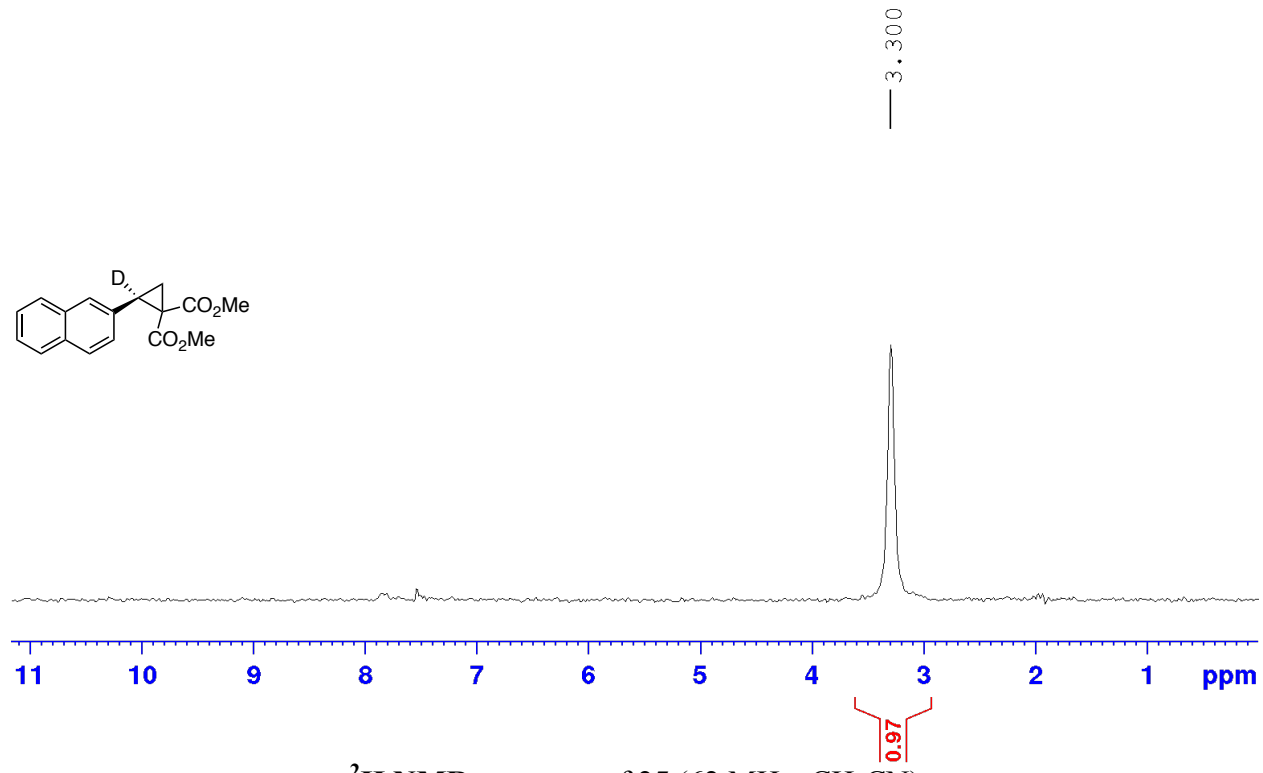
^{2}H NMR spectrum of **24** (62 MHz, CH_3CN)



^{1}H NMR spectrum of **25** (400 MHz, $CDCl_3$)



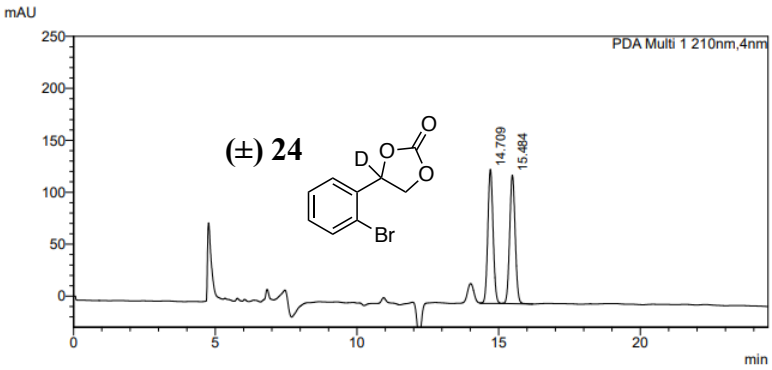
^{13}C NMR spectrum of **25** (101 MHz, $CDCl_3$)



^{2}H NMR spectrum of **25** (62 MHz, CH_3CN)

XIII. Copies of Chiral HPLC Chromatograms

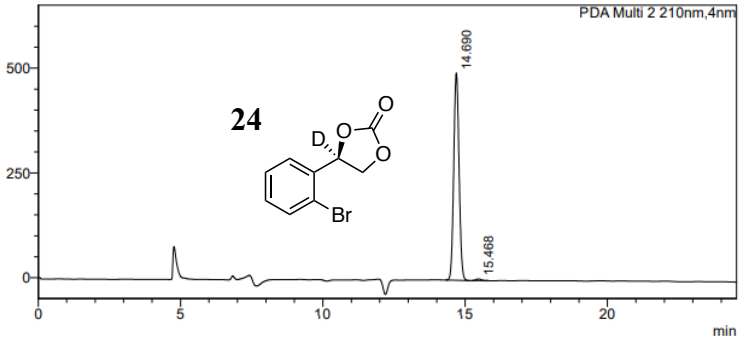
HPLC of racemic and chiral **24**. Hexanes/ethanol 90/10, 0.6 mL/min, 210 nm, Chiracel AD-3



<Peak Table>

PDA Ch1 210nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	14.709	1674699	129153	0.000			
2	15.484	1676379	123744	0.000			
Total		3351078	252898				

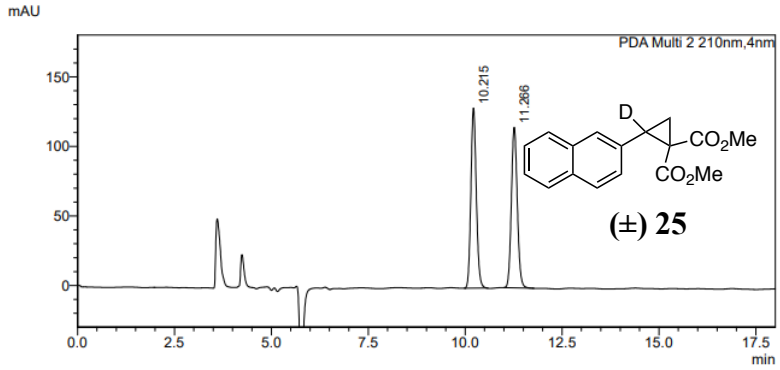


<Peak Table>

PDA Ch2 210nm

Peak#	Ret. Time	Conc.	ID#	Name	Area%
1	14.690	99.192			99.192
2	15.468	0.808			0.808
Total					100.000

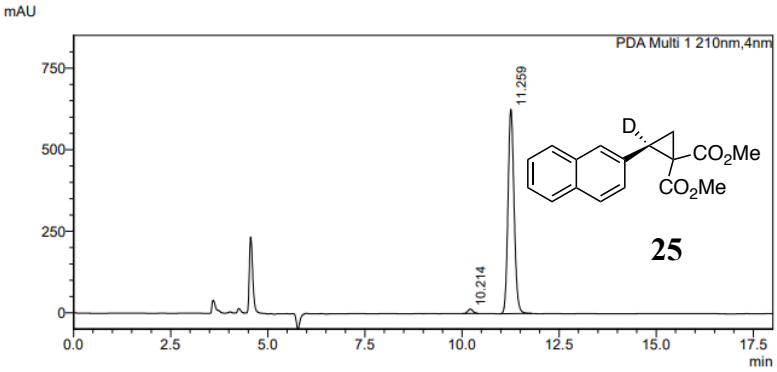
HPLC of racemic and chiral **25**. Hexanes/ethanol 80/20, 0.8 mL/min, 210 nm, Chiracel OJ-3



<Peak Table>

PDA Ch2 210nm

Peak#	Name	ID#	Area%
1			50.675
2			49.325
Total			100.000



<Peak Table>

PDA Ch1 210nm

Peak#	Ret. Time	Name	ID#	Area%
1	10.214			1.808
2	11.259			98.192
Total				100.000