Supporting Information

Mild Deuteration Method of Terminal Alkynes in Heavy Water using Reusable Basic Resin

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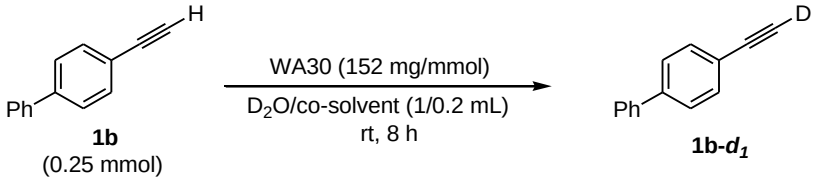
Contents

1. General

DIAION WA30 was obtained from Mitsubishi Chemical Corporation, Japan. D_2O (>99.8% D atom) was purchased from Kanto Chemical Co., Inc. ^1H and ^2H NMR spectra were recorded by a JEOL AL-400, EX-400 (^1H: 400 MHz) or ECA-500 spectrometer (^1H: 500 MHz, ^2H: 61 MHz). Chemical shifts (δ) are expressed in ppm and are internally referenced (7.26 ppm for $CDCl_3$ for ^1H and ^2H NMR, 0.00 ppm for tetramethylsilane for ^1H NMR or 3.31 ppm for CD_3OD-d_4 for ^1H NMR). The deuterium content was also assigned by the ^2H NMR. Flash column chromatography was performed with Silica Gel 60 N (Kanto Chemical Co., Inc., 63–210 μm spherical, neutral). Substrates (**1a-e** and **1g-m**) were purchasable and used without further purification. The substrate (**1f**) was prepared according to the reference 1.

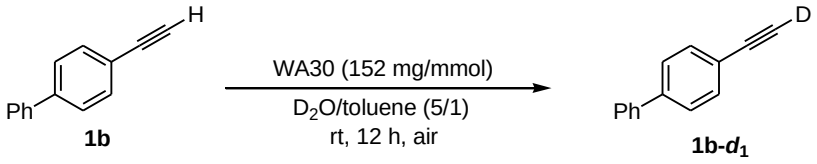
2. Effect of co-solvent in deuteration of 4-phenylethynylbenzene (1b)



Entry	Co-solvent	D content (%)	Yield (%)
1	AcOEt	45	Quant.
2	Et_2O	28	84
3	*n*-Hexane	28	96
4	*c*-Hexane	41	Quant.
5	Toluene	80	Quant.
6[a]	Toluene	99	99

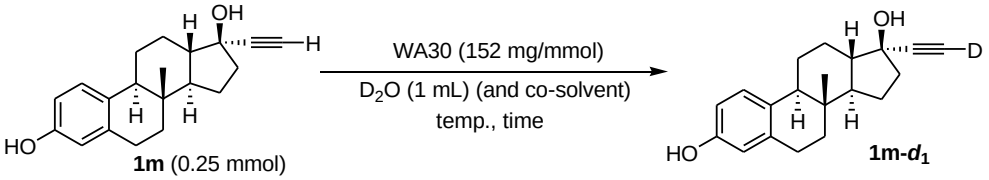
[a]For 12 h.

3. Reuse test of WA30 in D_2O-toluene mixed solvent



Try	D content (%)	Yield (%)	Recovery yield of WA30 (%)
1st	99	Quant.	99
2nd	94	95	Quant.
3rd	94	96	94

4. Effect of co-solvent in deuteration of 1m



co-solvent	Temp. (°C)	Time (h)	D content (% D)	Yield (%)
–	rt	8	19	84
Toluene (0.5 mL)	rt	12	28	89
EtOAc (0.5 mL)	rt	12	43	89
EtOAc (0.5 mL)	rt	24	49	94
EtOAc (0.5 mL)	50	24	93	94

5. Procedures for deuteration of terminal alkynes

5-1. Typical procedure for deuteration of terminal alkynes in D_2O

A suspension of WA30 (38 mg) and an alkyne (0.25 mmol) in D_2O (1 mL) in a round bottom flask was stirred at room temperature or 50 ^oC under atmospheric conditions. After stirring for adequate time, the reaction mixture was filtrated to remove WA30. The filtrate was extracted with Et_2O (10 mL) and H_2O (5 mL), and then the aqueous layer was further extracted with Et_2O (10 mL x 3). The combined organic layers were dried over anhydrous $MgSO_4$, filtrated and concentrated in vacuo to give the deuterated alkyne (alkyne-d_1).

5-2. Typical Procedure for deuteration of terminal alkynes in D_2O-toluene mixed solvent

A suspension of WA30 (38 mg) and an alkyne (0.25 mmol) in D_2O (1 mL) and toluene (0.2 mL) in a round bottom flask was stirred at room temperature under atmospheric conditions. After stirring for adequate time, the reaction mixture was filtrated to remove WA30. The filtrate was extracted with Et_2O (10 mL) and H_2O (5 mL), and then the aqueous layer was further extracted with Et_2O (10 mL x 3). The combined organic layers were dried over anhydrous $MgSO_4$, filtrated and concentrated in vacuo to give the deuterated alkyne (alkyne-d_1).

6. Reuse test of WA30 in D_2O (Tabl 3)

A suspension of WA30 (152 mg) and **1a** (1.00 mmol) in D_2O (4 mL) in a round bottom flask was stirred at room temperature under atmospheric conditions. After stirring for 8 h, the mixture was filtrated to collect WA30. The filtrate was extracted with Et_2O (20 mL) and H_2O (10 mL), and then the aqueous layer was further extracted with Et_2O (20 mL x 3). The combined organic layers were dried over anhydrous $MgSO_4$, filtrated and concentrated in vacuo to give deuterated alkyne (**1a-d_1)**. The collected WA30 was washed with H_2O (20 mL) and Et_2O (20 mL) and dried in vacuo for 24 h. The recovered WA30 was reused in the next reaction.

7. Spectroscopic data of deuterated terminal alkynes

1-(Ethynyl-2-*d*)-4-methoxybenzene (**1a-d_1; Table 1, entry 1**) : **1a-d_1** (31.1 mg, 233 μmol) was obtained in 93% as a colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, *J* = 9.2 Hz, 2H), 6.85 (d, *J* = 9.2 Hz, 2H), 3.81 (s, 3H), 3.00 (s, 0.01H); ^{2}H NMR (61 MHz,

$CHCl_3$): δ 3.01 (s).

1-(Ethynyl-2-*d*)-4-phenylbenzene (**1b-d_1; eq. 1**) : **1b-d_1** (44.5 mg, 248 μmol) was obtained in 99% as a colorless solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58–7.53 (m, 6H), 7.43 (t, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.0 Hz, 1H) 3.12 (s, 0.01H); ^{2}H NMR (61 MHz, $CHCl_3$): δ 3.16 (s).

1-(Ethynyl-2-*d*)-2-methoxybenzene (**1c-d_1; Table 4, entry 1**) : After the purification by silica gel chromatography (eluent; Et_2O/pentanes 1/40), **1b-d_1** (31.5 mg, 237 μmol) was obtained in 95% as a colorless oil, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.32 (ddd, *J* = 9.0, 7.8, 1.5 Hz, 1H), 6.91 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.89 (d, *J* = 9.0 Hz, 1H), 3.89 (S, 3H), 3.32 (s, 0.04H); ^{2}H NMR (61 MHz, $CHCl_3$): δ 3.32 (s).

1-(Ethynyl-2-*d*)-2-trifluoromethylbenzene-d_1 (**1d-d_1; Table 4, entry 2**) : After the purification by silica gel chromatography (eluent; Et_2O/pentanes 1/40), **1d-d_1** (25.3 mg, 148 μmol) was obtained in 59% as a colorless oil, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67 (d, *J* = 7.5 Hz, 1H), 7.65 (d, *J* = 7.0 Hz, 1H), 7.51 (dd, *J* = 7.5, 7.0 Hz, 1H), 7.45 (dd, *J* = 7.5, 7.5 Hz, 1H), 3.37 (m, 0.01H); ^{2}H NMR (61 MHz, $CHCl_3$): δ 3.39 (s).

2-(Propynyl-3-*d*)-benzoate (**1e-d_1; Table 4, entry 3**) : **1e-d_1** (36.8 mg, 250 μmol) was obtained in 100% as a colorless oil, ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.07 (dd, *J* = 8.5, 1.5 Hz, 2H), 7.58 (tt, *J* = 7.5, 1.5 Hz, 1H), 7.45 (dd, *J* = 8.5, 7.5 Hz, 2H), 4.93 (s, 2H), 2.53 (brs, 0.01H); ^{2}H NMR (61 MHz, $CHCl_3$): δ 2.51 (brs).

[2-(Propynyl-3-*d*-oxy)methyl]-benzene (**1f-d_1; Table 4, entry 4**) : After the purification by silica gel chromatography (eluent; Et_2O/pentanes 1/40), **1f-d_1** (33.0 mg, 225 μmol) was obtained in 90% as a colorless oil, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38–7.30 (m, 5H), 4.63 (s, 2H), 4.19 (s, 2H), 2.48 (s, 0.01H); ^{2}H NMR (61 MHz, $CHCl_3$): δ 2.47 (s).

1-Phenylthio-2-propyne-3-*d* (**1g-d_1; Table 4, entry 5**) : **1g-d_1** (34.6 mg, 248 μmol) was obtained in 99% as a colorless oil, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45 (dd, *J* = 8.0, 2.0, Hz, 2H), 7.32 (dd, *J* = 8.0, 7.5 Hz, 2H), 7.24 (tt, *J* = 7.5, 2.0 Hz, 1H), 3.60 (s, 2H), 2.23 (brs, 0.05H); ^{2}H NMR (61 MHz, $CHCl_3$): δ 2.24 (brs).

1-Dodecyne-1-*d* (**1h-d_1; Table 4, entry 6**) : **1h-d_1** (27.3 mg, 163 μmol) was obtained in 65% as a colorless oil, ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.18 (t, *J* = 7.5 Hz, 2H), 1.93 (brs, 0.03H), 1.52 (tt, *J* = 7.5, 7.5 Hz, 2H), 1.39–1.26 (m, 14H), 0.88 (t, *J* = 7.0 Hz, 3H); ^{2}H NMR (61 MHz, $CHCl_3$): δ 1.92 (brs).

1-Amino-4-(ethynyl-2-*d*)-benzene (**1i-*d*$_1$; Table 4, entry 7**) : **1i-*d*$_1$;** 91% (26.7 mg, 228 μmol) as a yellow solid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (d, *J* = 9.0 Hz, 2H), 6.59 (d, *J* = 9.0 Hz, 2H), 3.82 (brs, 2H), 2.97 (s, 0.85H); ^{2}H NMR (61 MHz, $CHCl_3$): δ 2.98 (brs).

1-Amino-4-(ethynyl-2-*d*)-benzene (**1i-*d*$_1$; Table 4, entry 8**) : **1i-*d*$_1$** (28.7 mg, 243 μmol) was obtained in 97% as a yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.8 Hz, 2H), 6.58 (d, *J* = 8.8 Hz, 2H), 3.80 (brs, 2H), 2.96 (s, 0.03H); ^{2}H NMR (61 MHz, $CHCl_3$): δ 2.98 (brs).

1-(ethynyl-2-*d*)-4-nitrobenzene (**1j-*d*$_1$; Table 4, entry 9**) : **1j-*d*$_1$** (34.6 mg, 235 μmol) was obtained in 94% as a yellow solid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19 (d, *J* = 8.5 Hz, 2H), 7.63 (d, *J* = 8.5 Hz, 2H), 3.36 (s, 0.18H); ^{2}H NMR (61 MHz, $CHCl_3$): δ 3.37 (brs).

1-(Ethynyl-2-*d*)-4-nitrobenzene (**1j-*d*$_1$; Table 4, entry 10**) : **1j-*d*$_1$** (36.0 mg, 243 μmol) was obtained in 97% as an yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, *J* = 8.2 Hz, 2H), 7.64 (d, *J* = 8.2 Hz, 2H), 3.64 (s, 0.06H); ^{2}H NMR (61 MHz, $CHCl_3$): δ 3.33 (brs).

6-(Ethynyl-2-*d*)-2-methoxynaphthalene (**1k-*d*$_1$; Table 4, entry 11**) : **1k-*d*$_1$** (44.7 mg, 245 μmol) was obtained in 98% as a colorless solid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 (s, 1H), 7.67–7.63 (m, 2H), 7.48 (dd, *J* = 10.0, 1.5 Hz, 1H), 7.14 (dd, *J* = 9.0, 2.0 Hz, 1H), 7.07 (d, *J* = 1.5 Hz, 1H), 3.89 (s, 3H), 3.10 (s, 0.81H); ^{2}H NMR (61 MHz, $CHCl_3$): δ 3.15 (brs).

6-(Ethynyl-2-*d*)-2-methoxynaphthalene (**1k-*d*$_1$; Table 4, entry 12**) : **1k-*d*$_1$** (45.8 mg, 250 μmol) was obtained in 100% as a colorless solid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 (s, 1H), 7.71–7.67 (m, 2H), 7.51 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.18 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.10 (d, *J* = 2.0 Hz, 1H) , 3.92 (s, 3H) , 3.14 (s, 0.04H); ^{2}H NMR (61 MHz, $CHCl_3$): δ 3.12 (brs).

***N*-[2-(Propynyl-3-*d*-oxy)]-phthalimide** (**1l-*d*$_1$; Table 4, entry 13**) : **1l-*d*$_1$** (43.2 mg, 215 μmol) was obtained in 86% as a colorless solid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85–7.83 (m, 2H), 7.77–7.74 (m, 2H), 4.86 (d, *J* = 2.0 Hz, 2H), 2.59 (t, *J* = 2.0 Hz, 0.81H); ^{2}H NMR (61 MHz, $CHCl_3$): δ 2.59 (brs).

***N*-[2-(Propynyl-3-*d*-oxy)]-phthalimide** (**1l-*d*$_1$; Table 4, entry 14**) : **1l-*d*$_1$** (44.6 mg, 223

μmol) was obtained in 89% as a colorless solid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85–7.82 (m, 2H), 7.78–7.40 (m, 2H), 4.86 (d, *J* = 1.0 Hz, 2H), 2.59 (t, *J* = 1.0 Hz, 0.64H); ^{2}H NMR (61 MHz, $CHCl_3$): δ 2.59 (m).

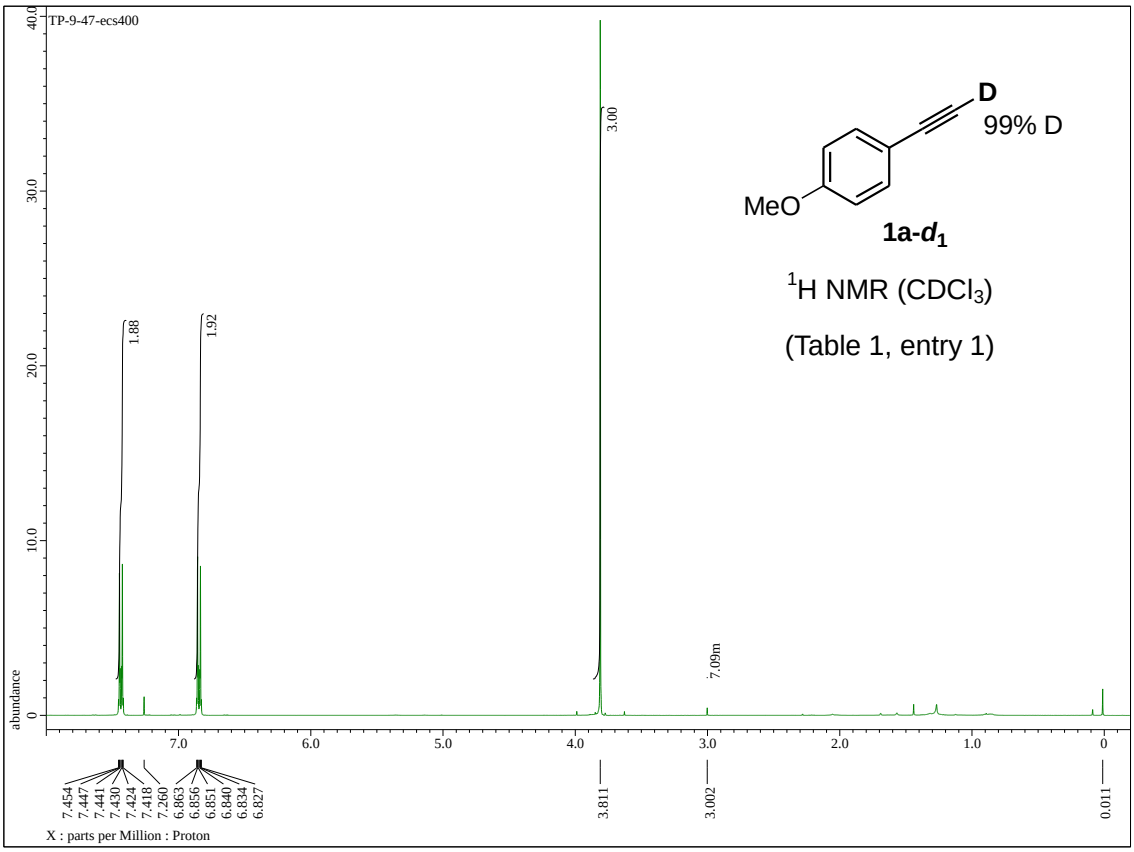
(8S,9S,13S,14R,17S)-17-(ethynyl-2-*d*)-8-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene-3,17-diol (**1m-d_1; Table 4, entry 16**) : **1m-d_1** (69.5 mg, 235 μmol) was obtained in 94% as a colorless solid, ^{1}H NMR (500 MHz, CD_3OD): δ 7.06 (d, *J* = 8.0 Hz, 1H), 6.54 (dd, *J* = 8.0, 2.5 Hz, 1H), 6.47 (d, *J* = 2.5 Hz, 1H), 2.86 (s, 0.07H), 2.80–2.70 (m, 2H), 2.32–2.22 (m, 2H), 2.12–2.08 (m, 1H), 2.00–1.90 (m, 2H), 1.85–1.82 (m, 1H), 1.77–1.70 (m, 2H), 1.44–1.22 (m, 4H), 0.84 (s, 3H); ^{2}H NMR (61 MHz, CH_3OH): δ 2.83 (brs).

8. Reference

1) D. Farran, A. M. Z. Slawin, P. Kirsch and D. O'Hagan, *J. Org. Chem.*, 2009, **74**, 7168–7171.

9. ^{1}H and ^{2}H NMR spectra of deuterated terminal alkynes

^{1}H NMR of 1a-d_1



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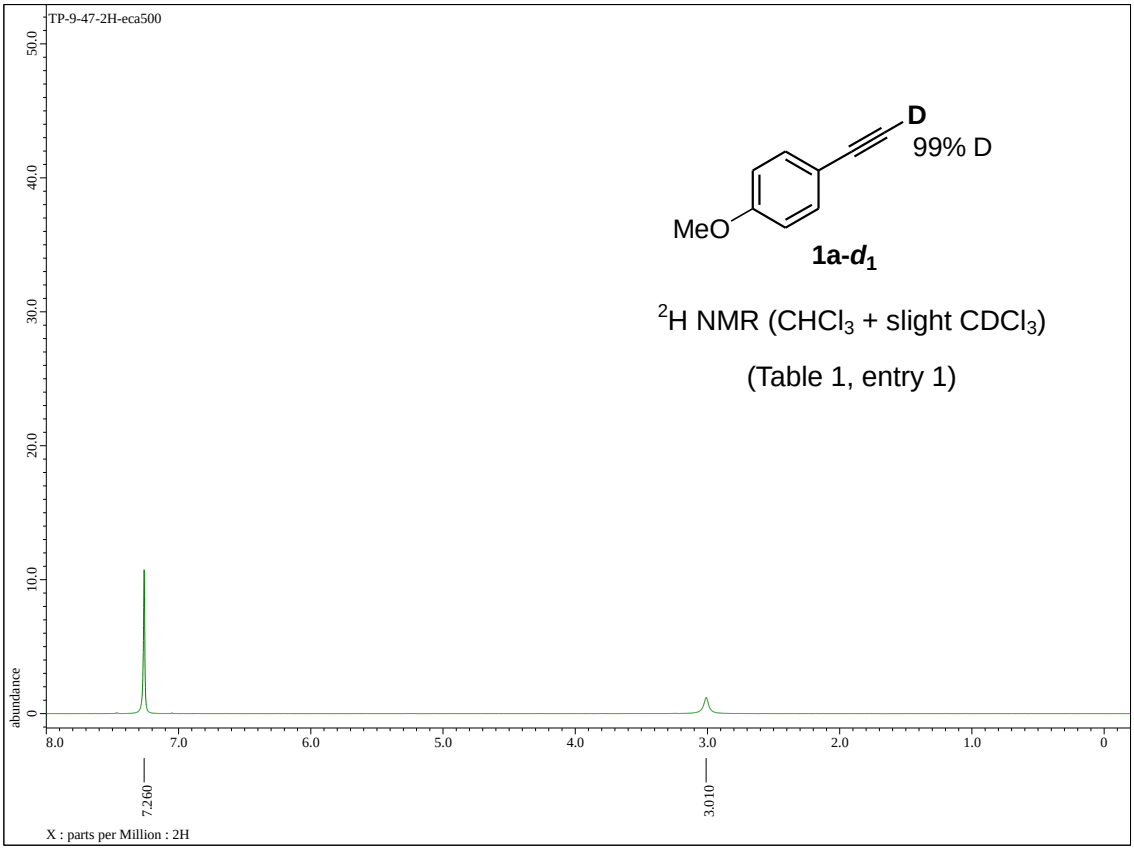

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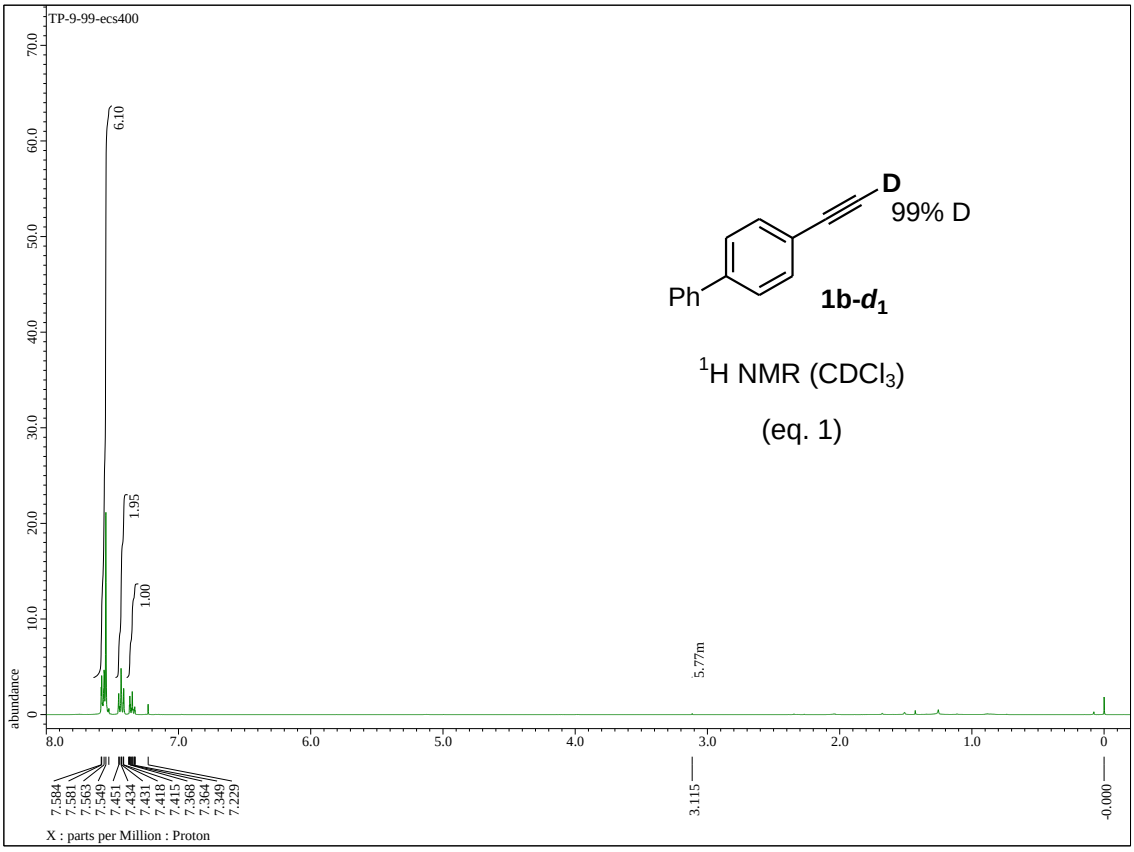

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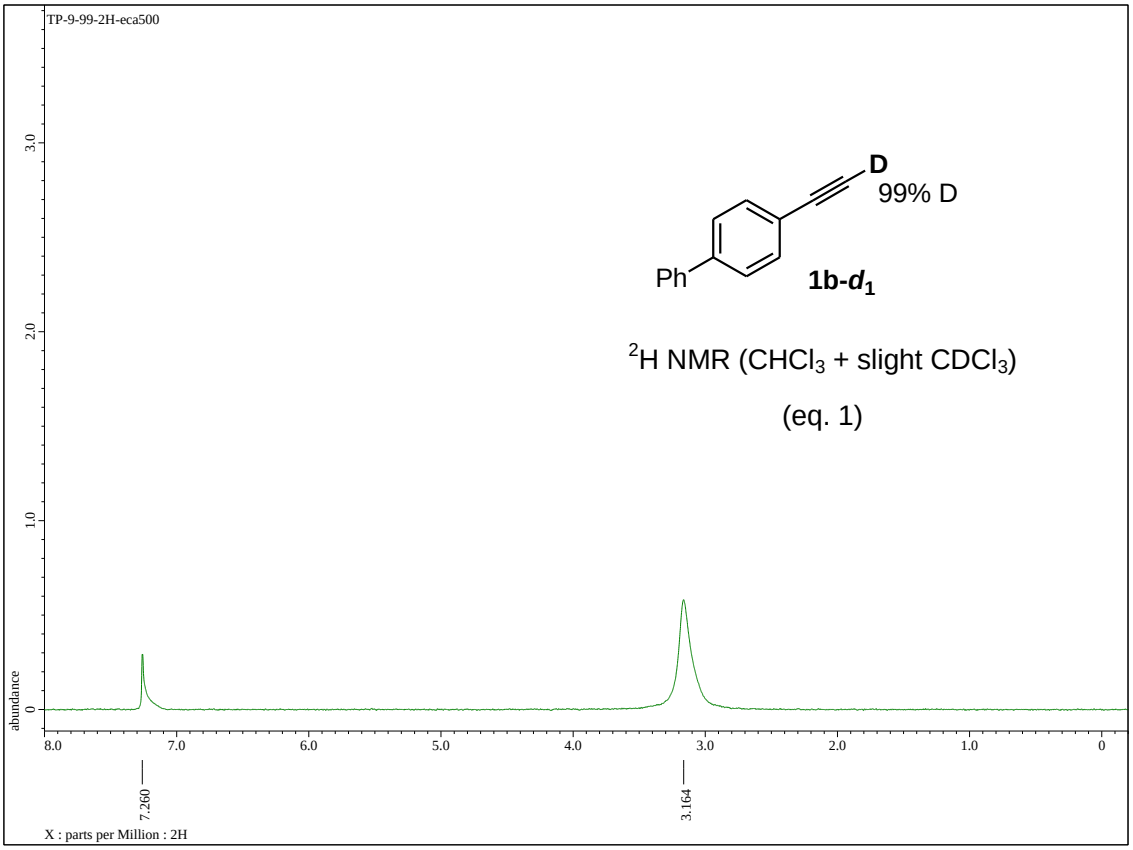

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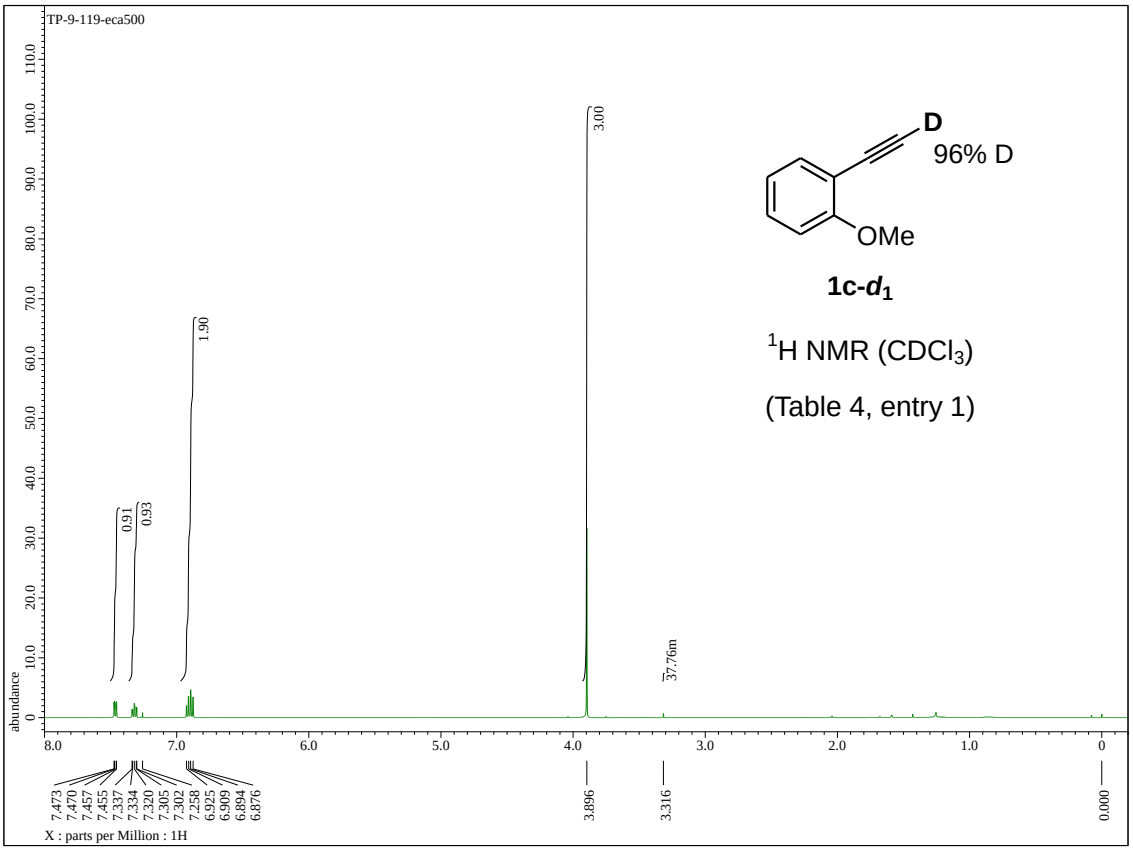

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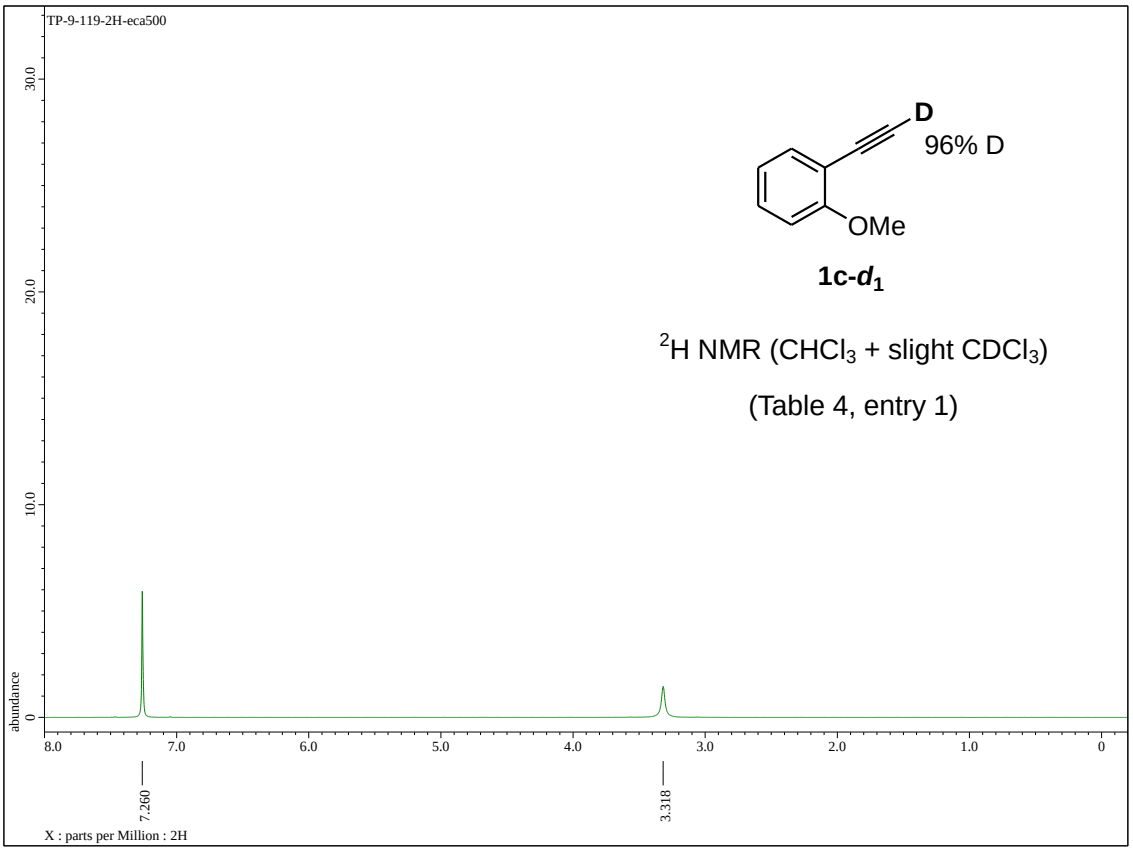

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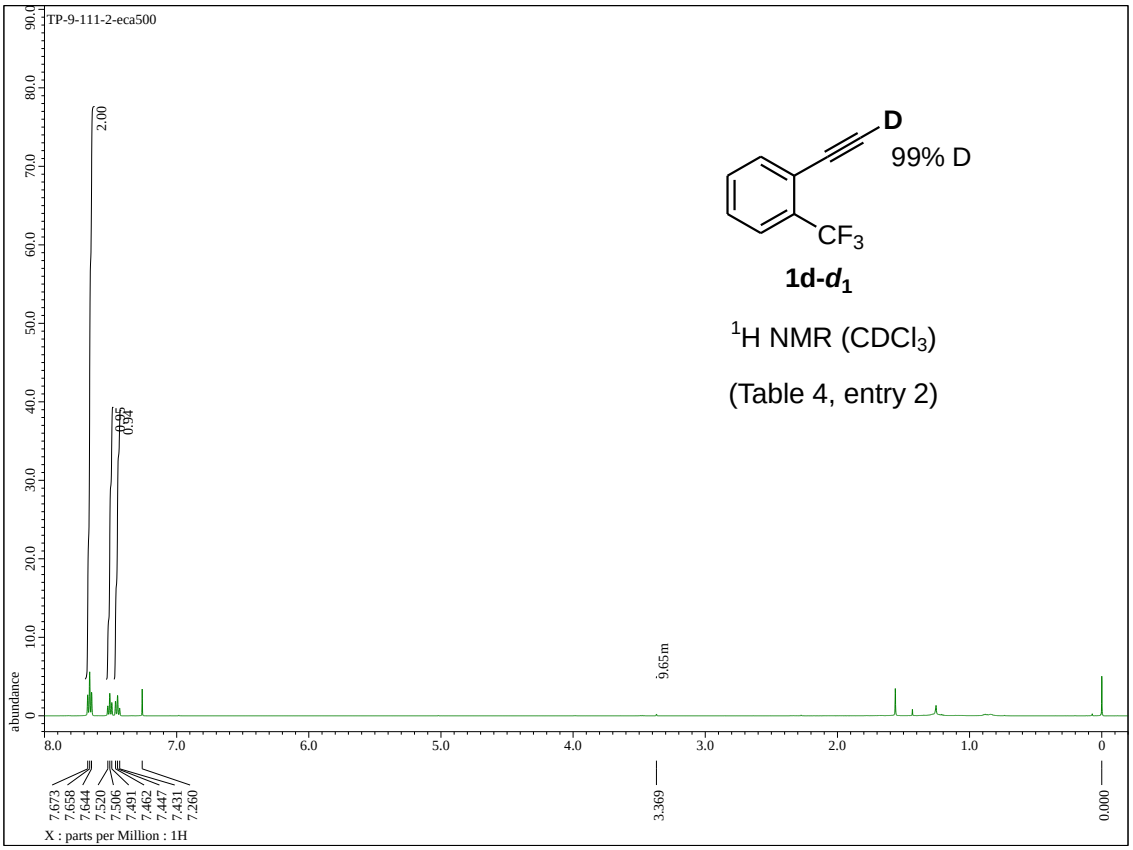

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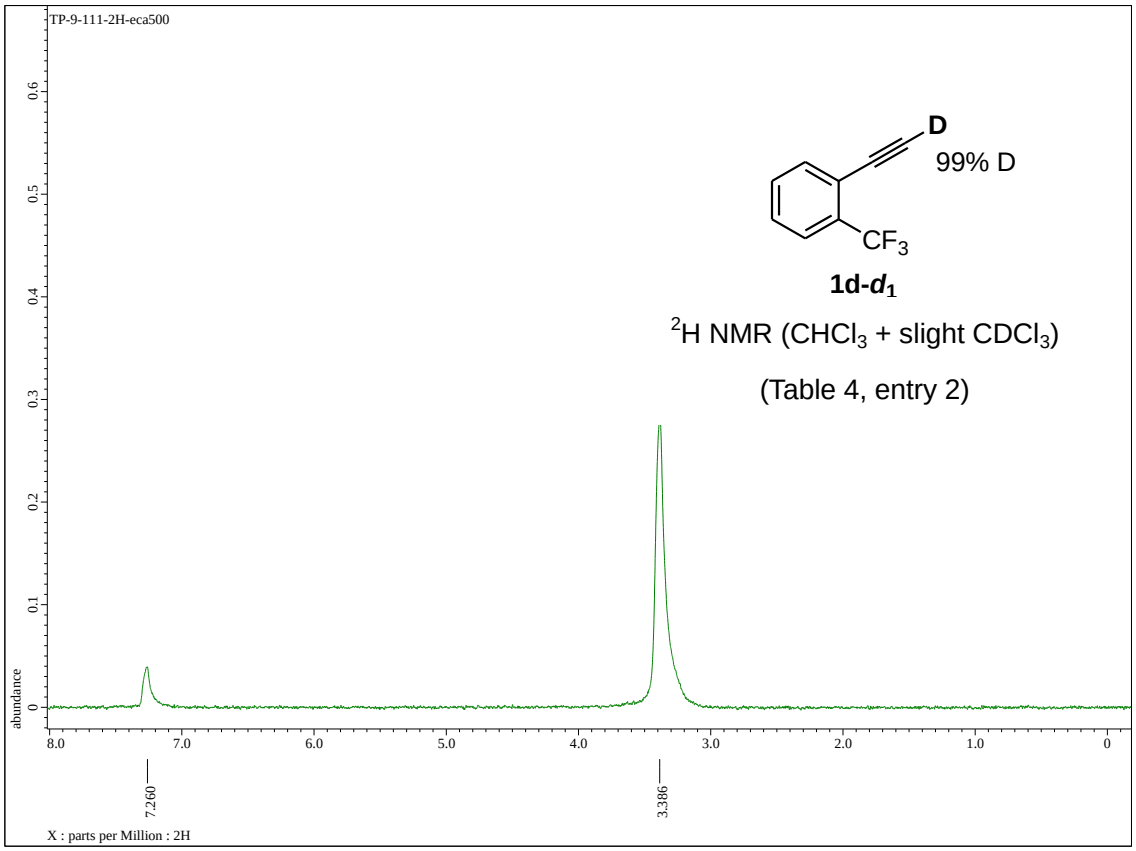

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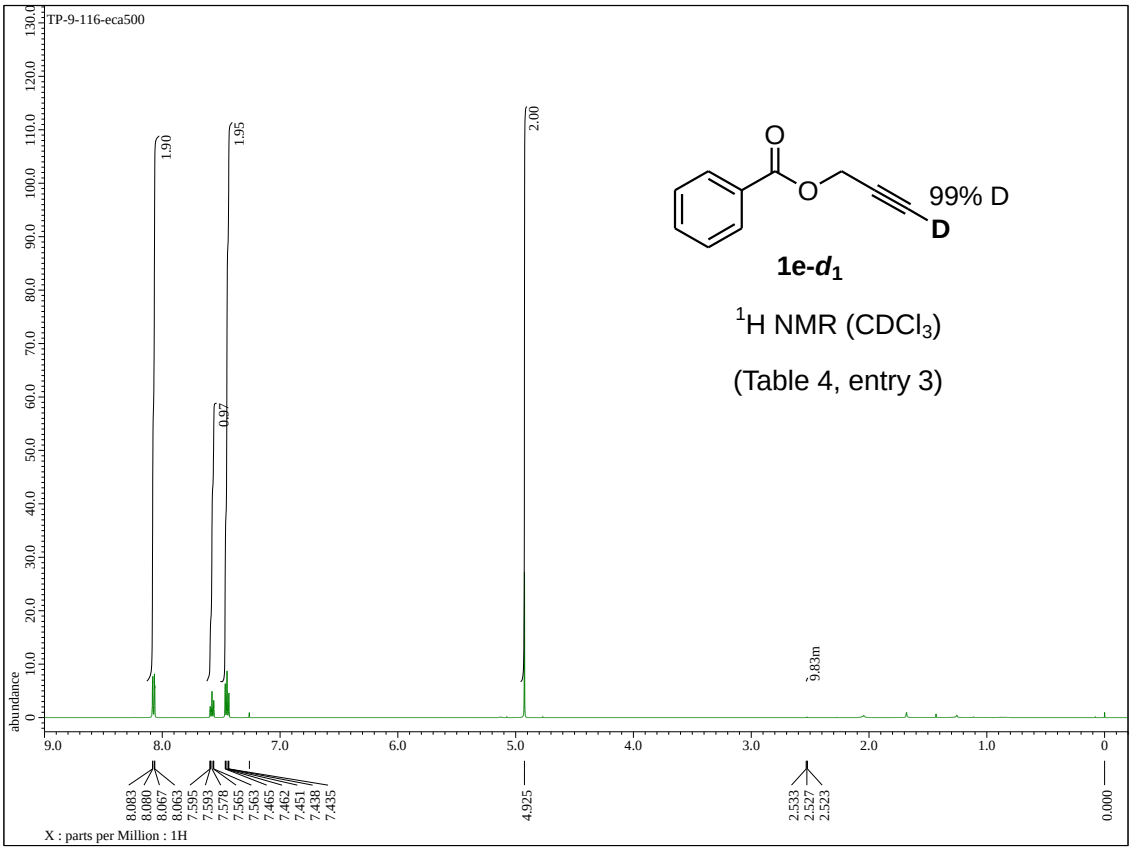

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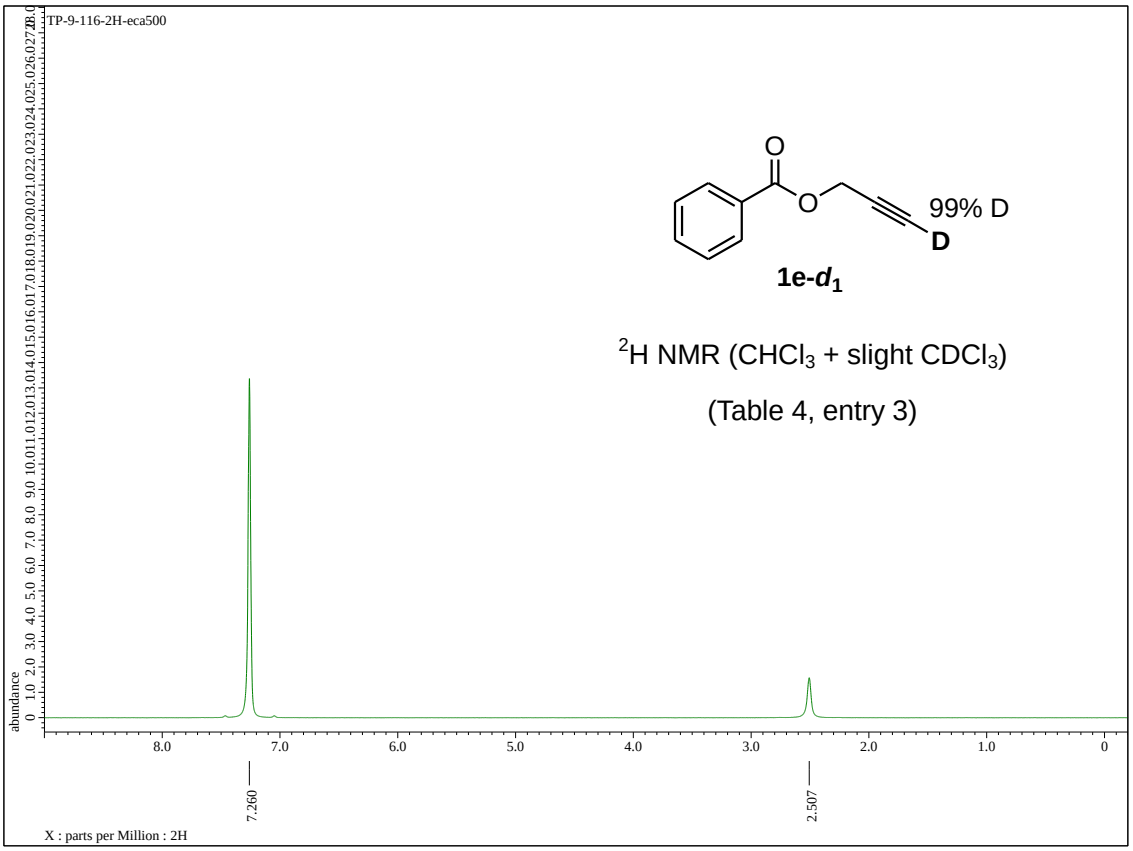

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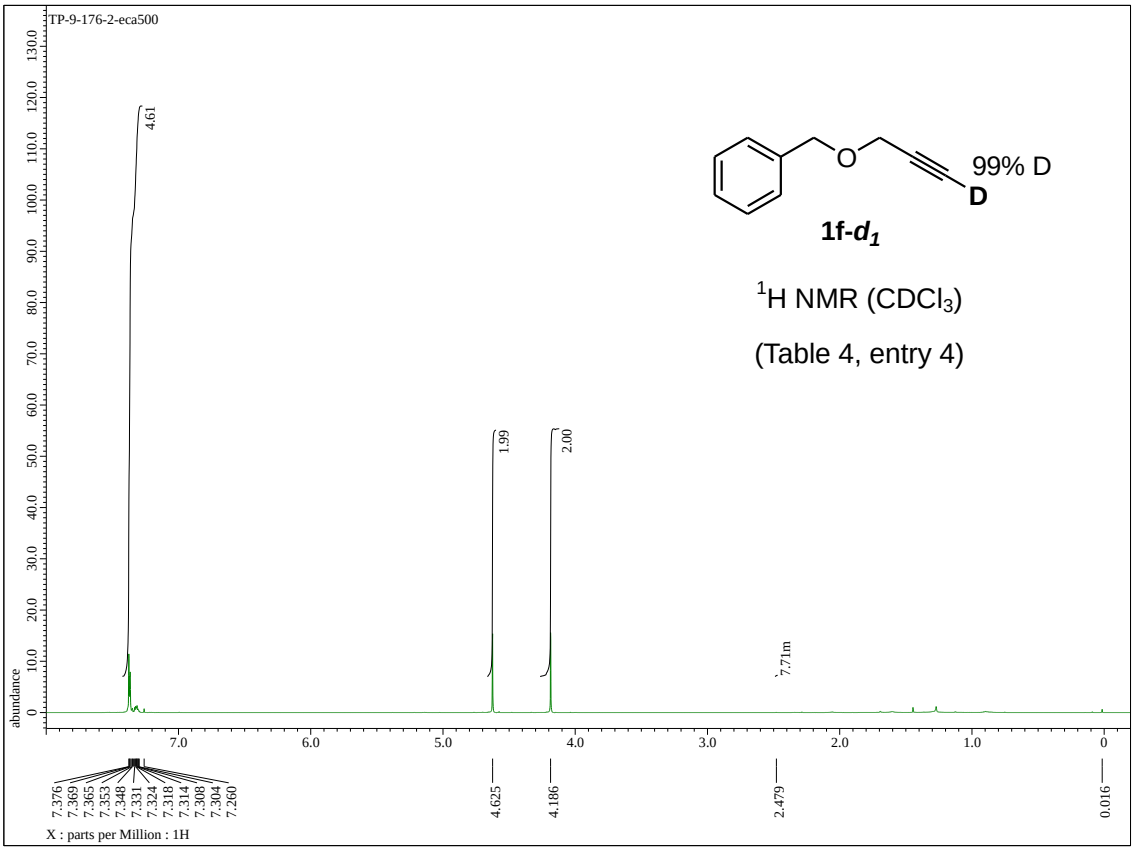

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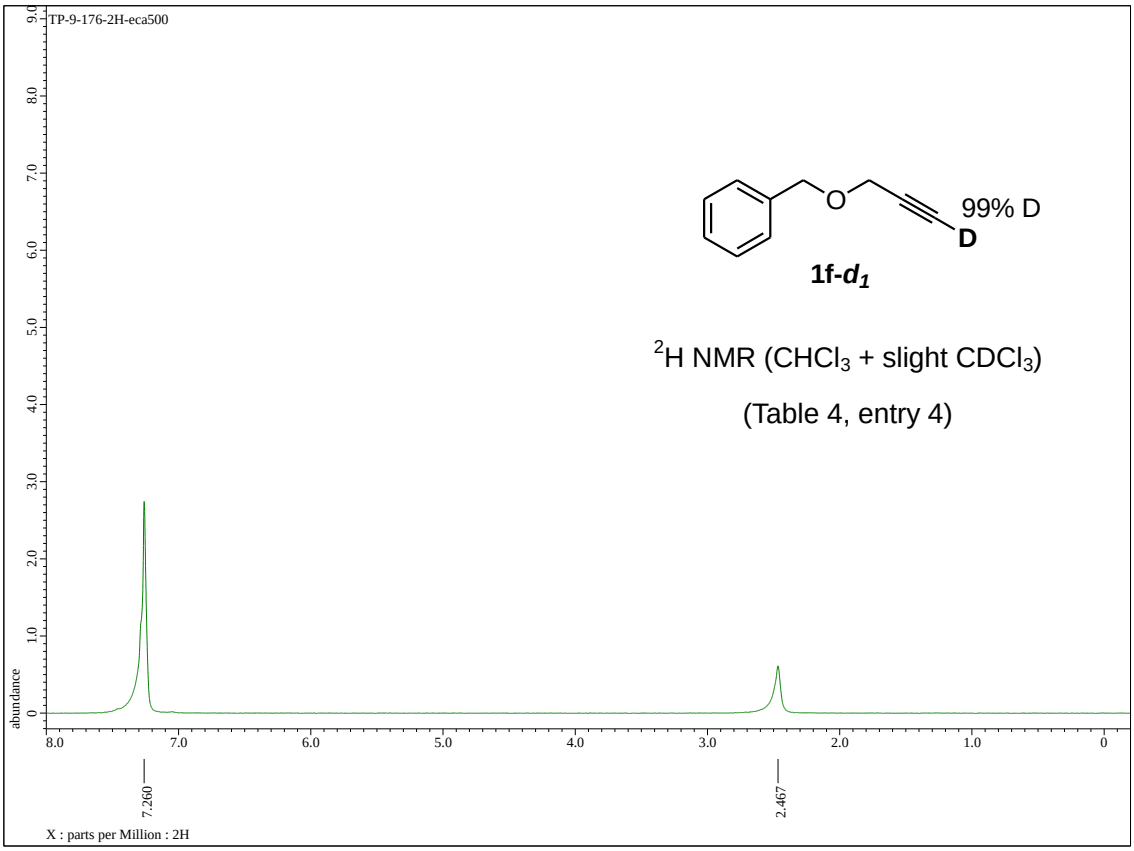

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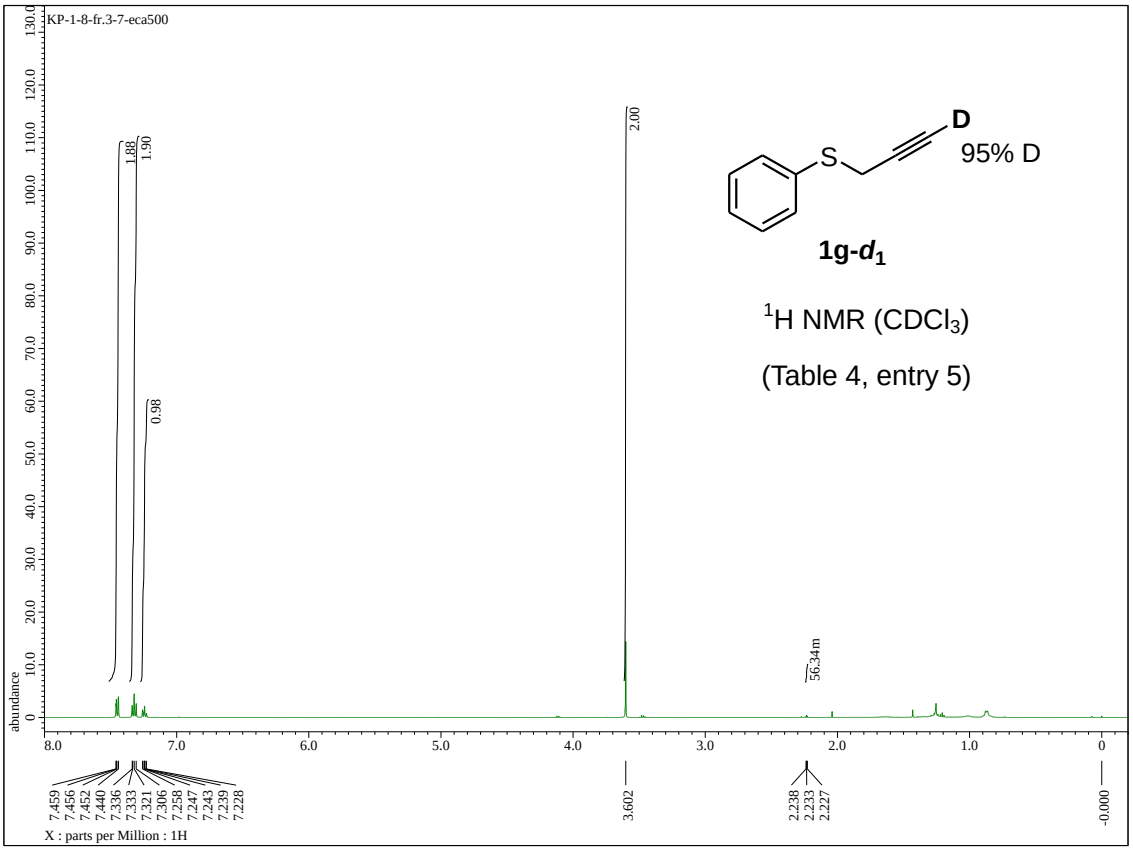

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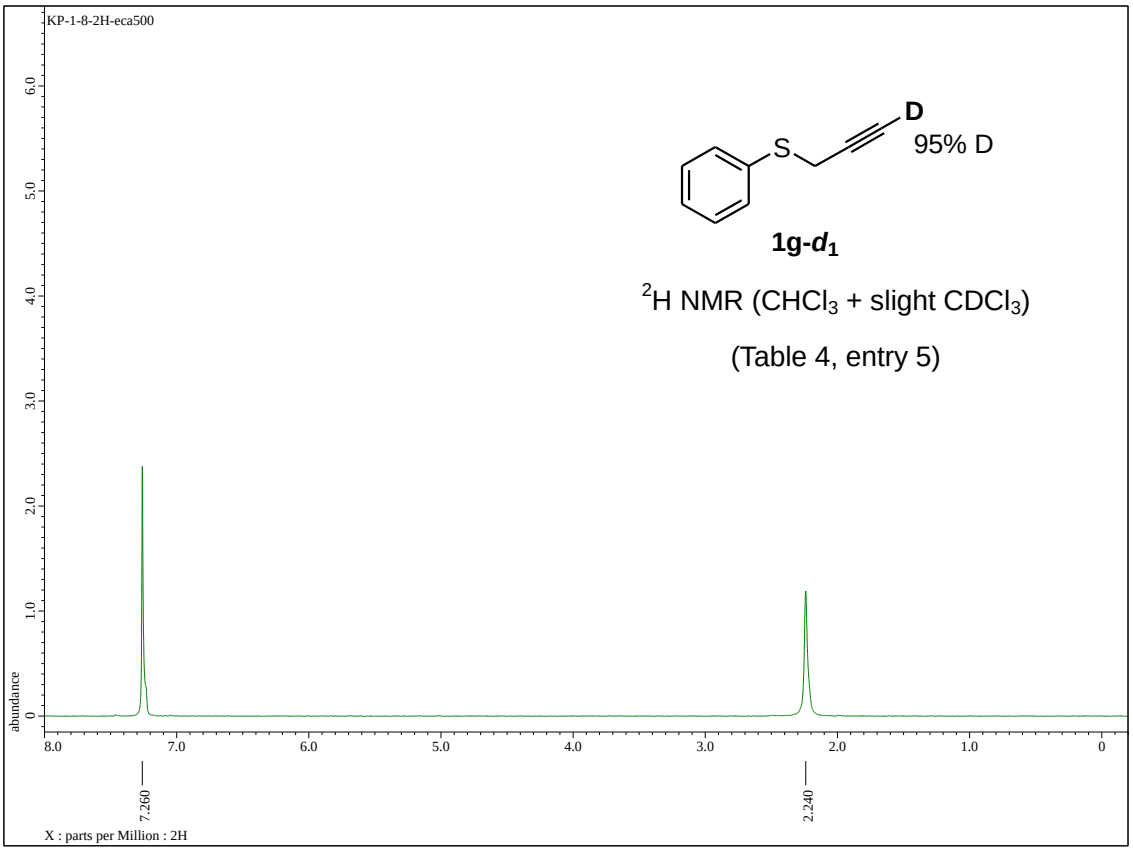

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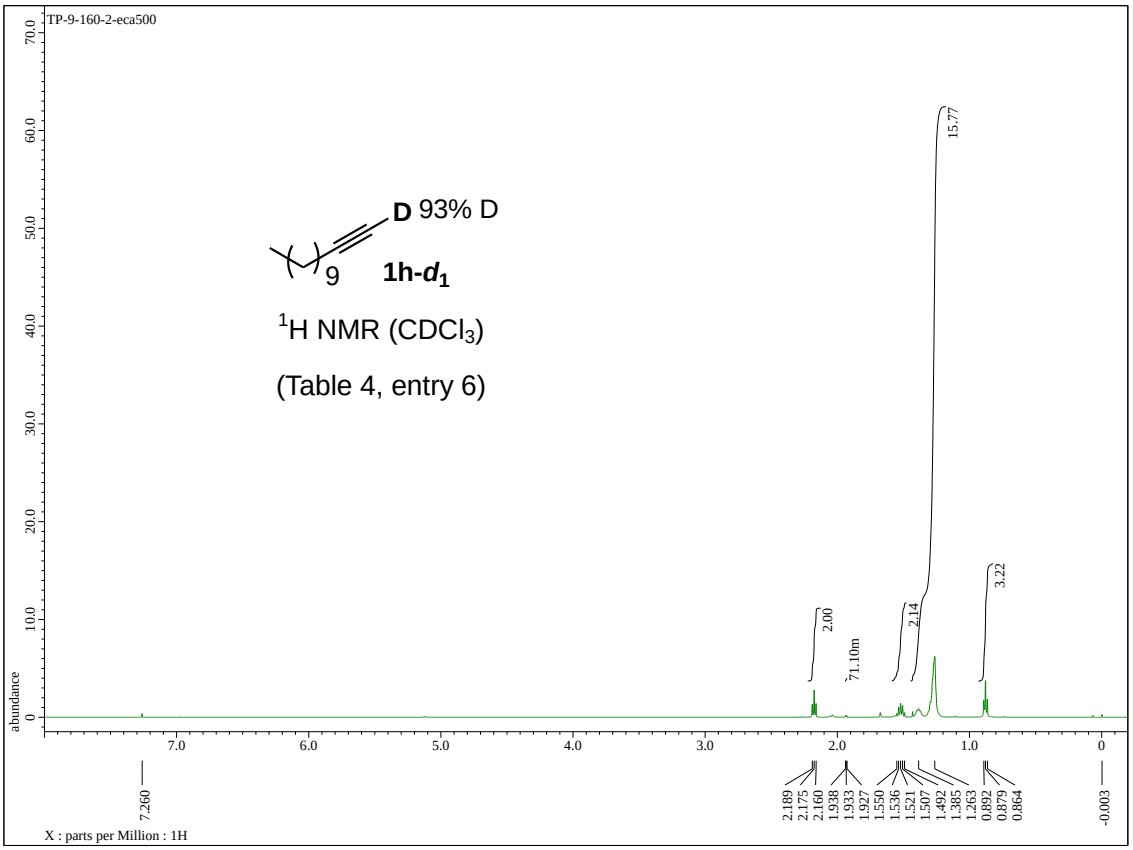

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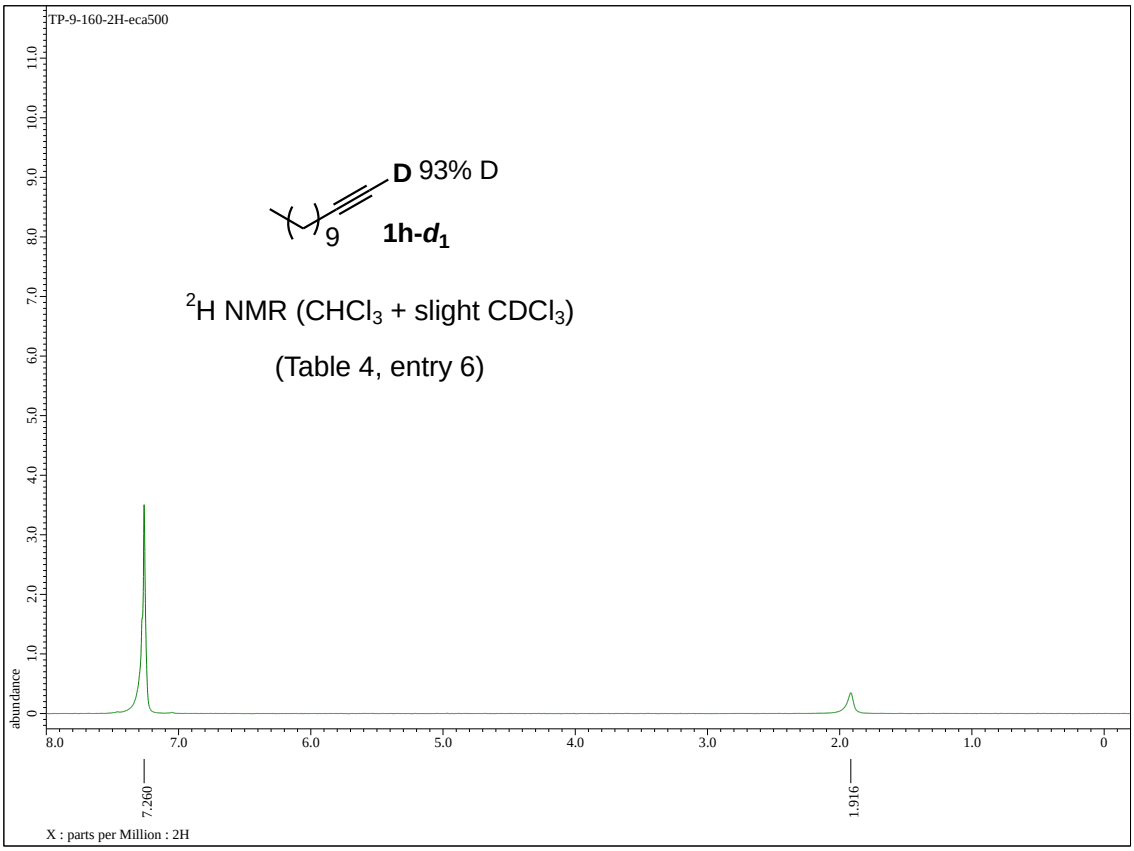

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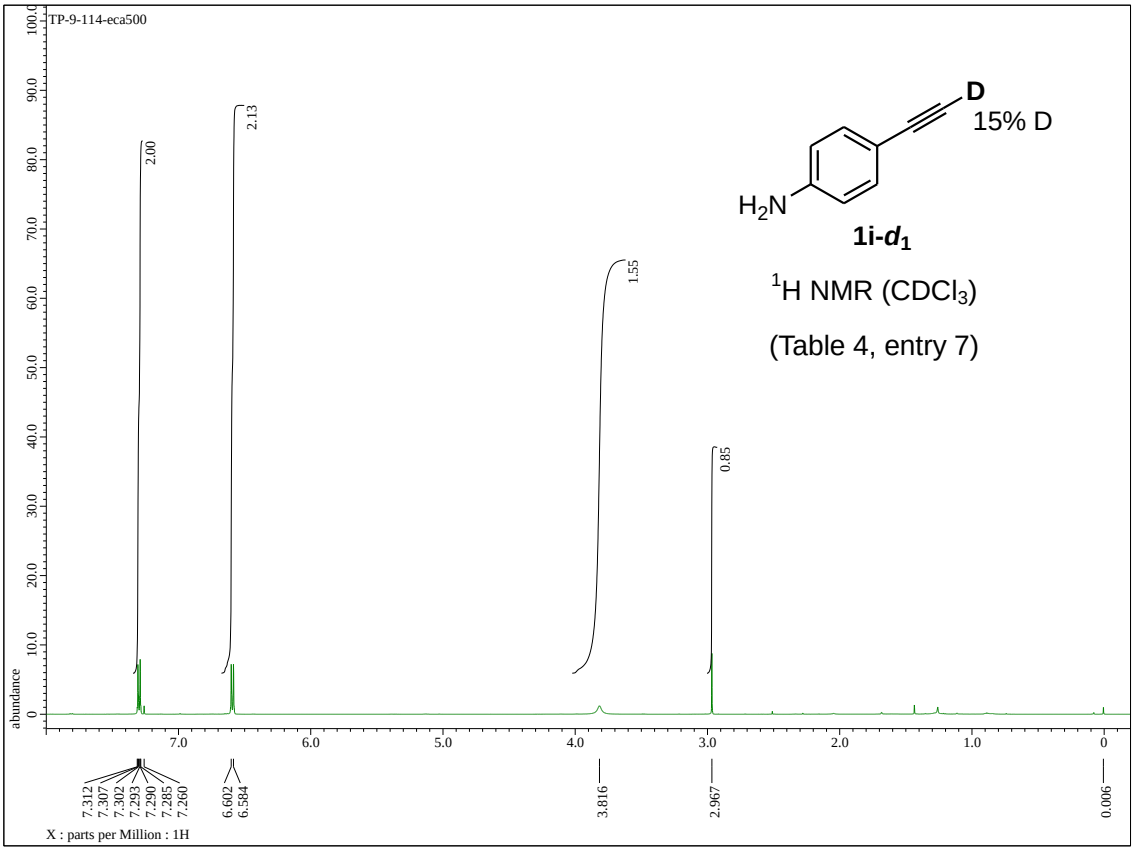

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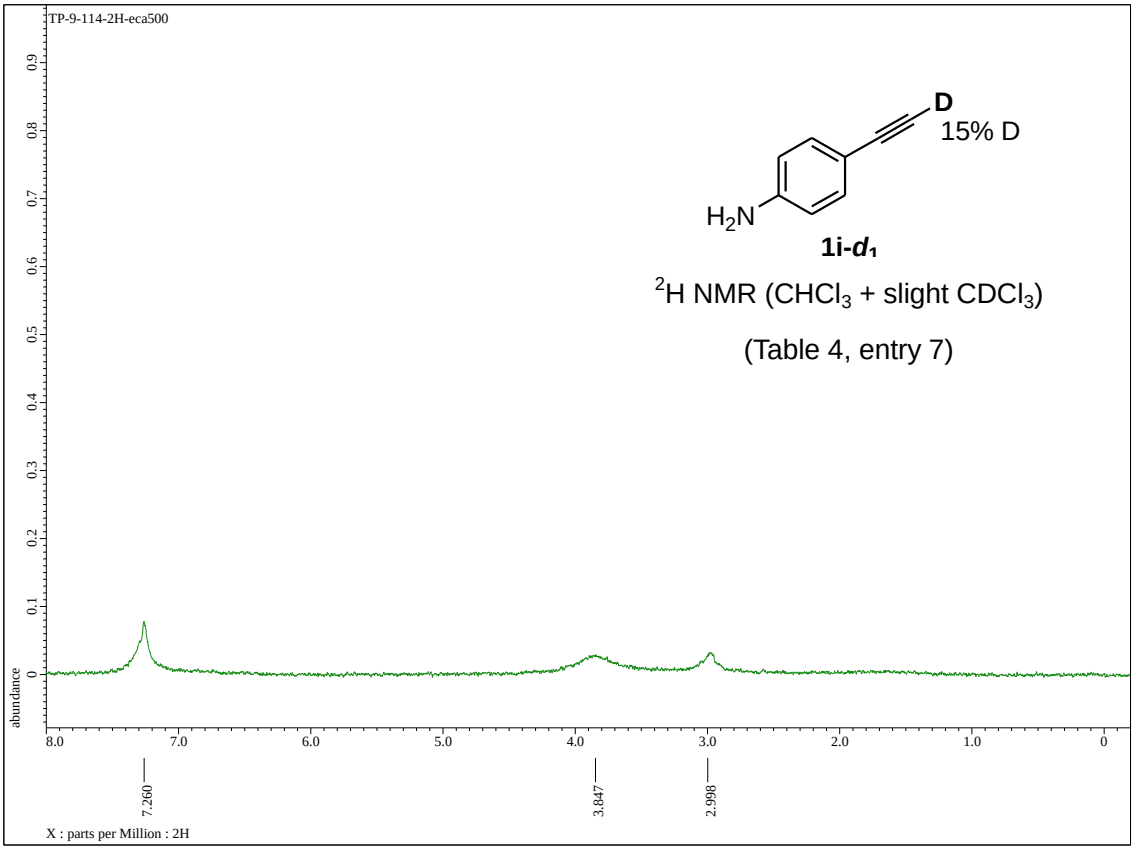
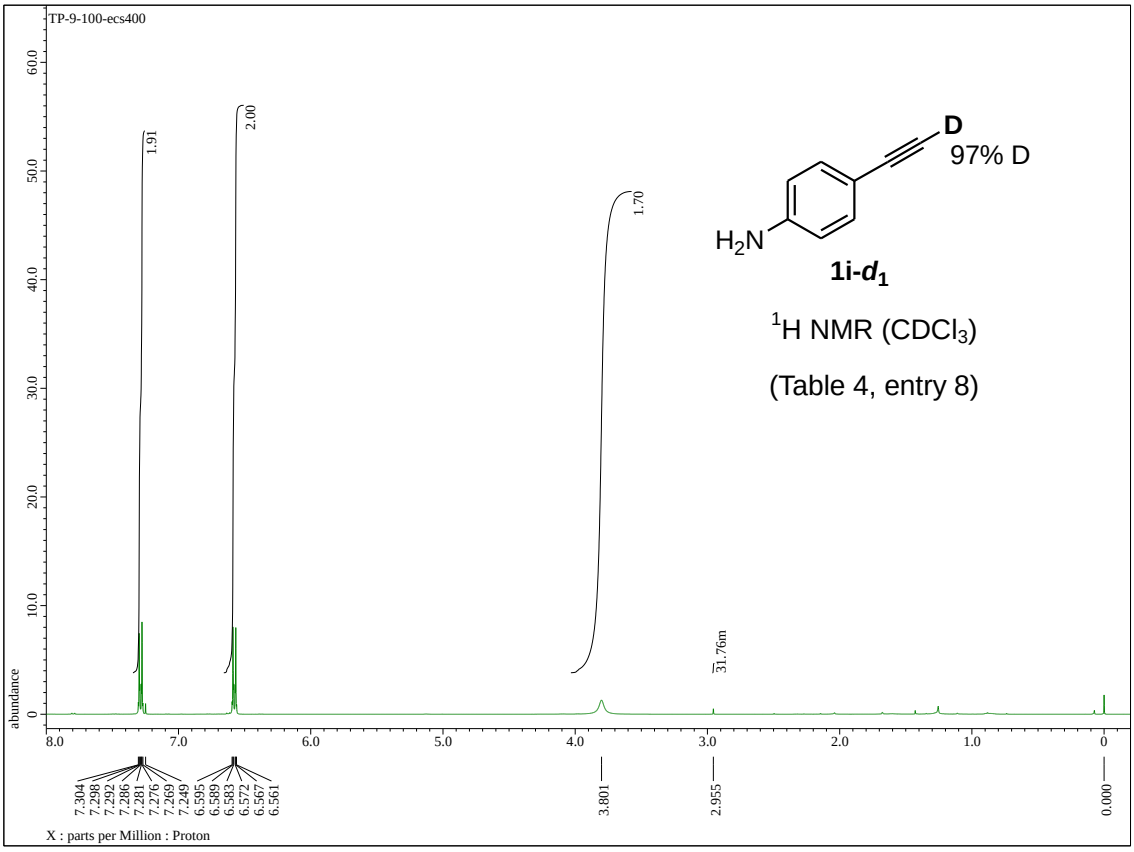
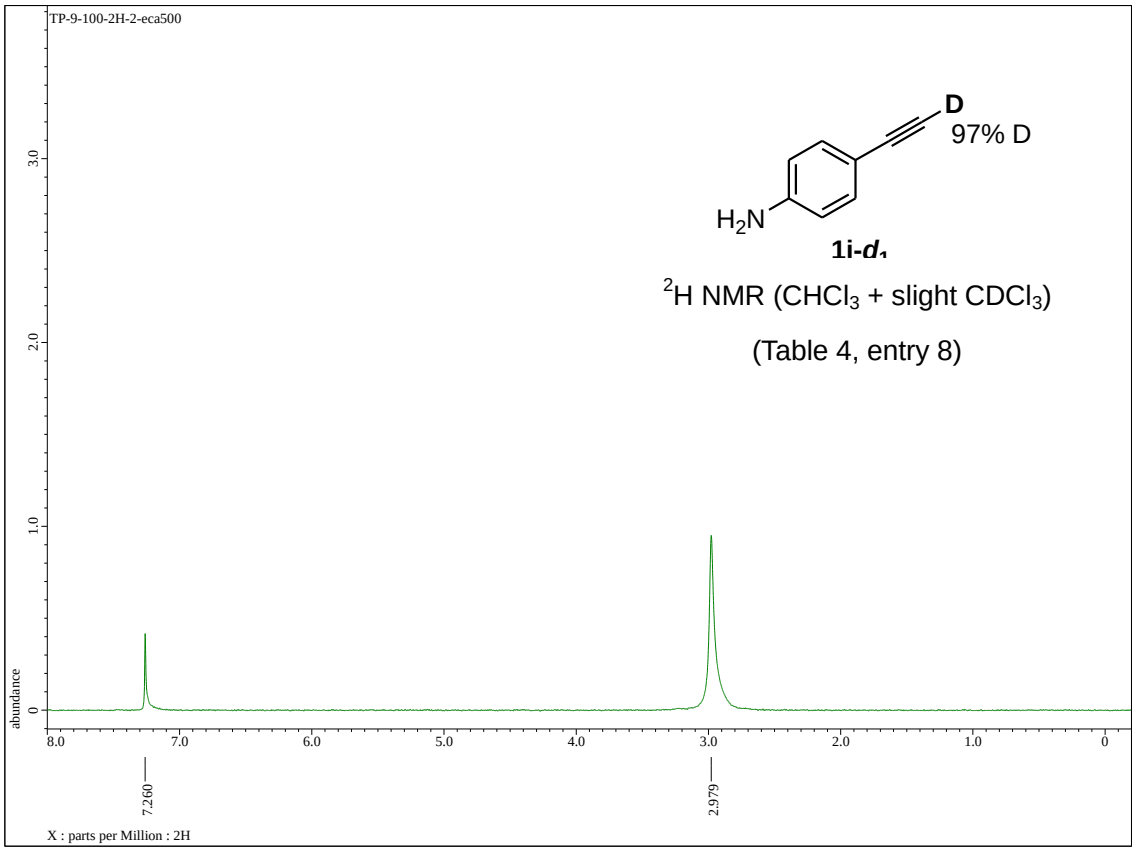


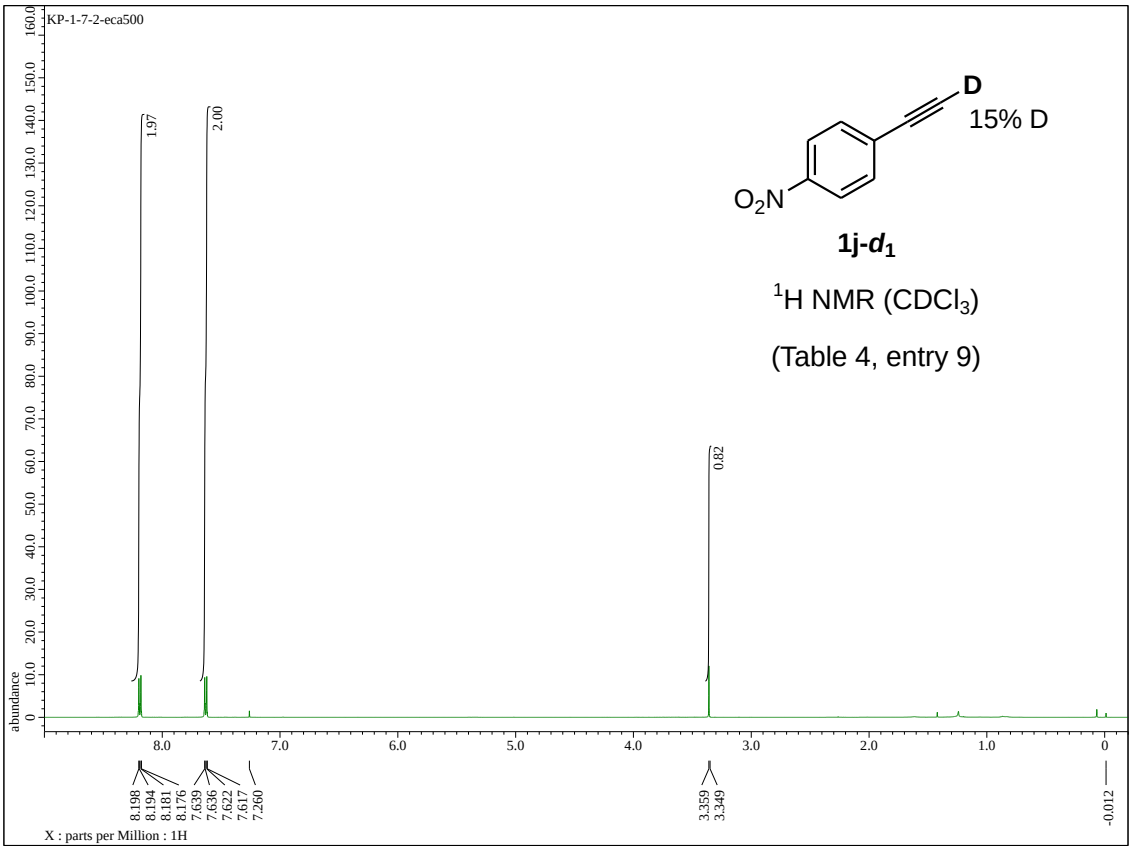
^{1}H NMR of 1i-d_1



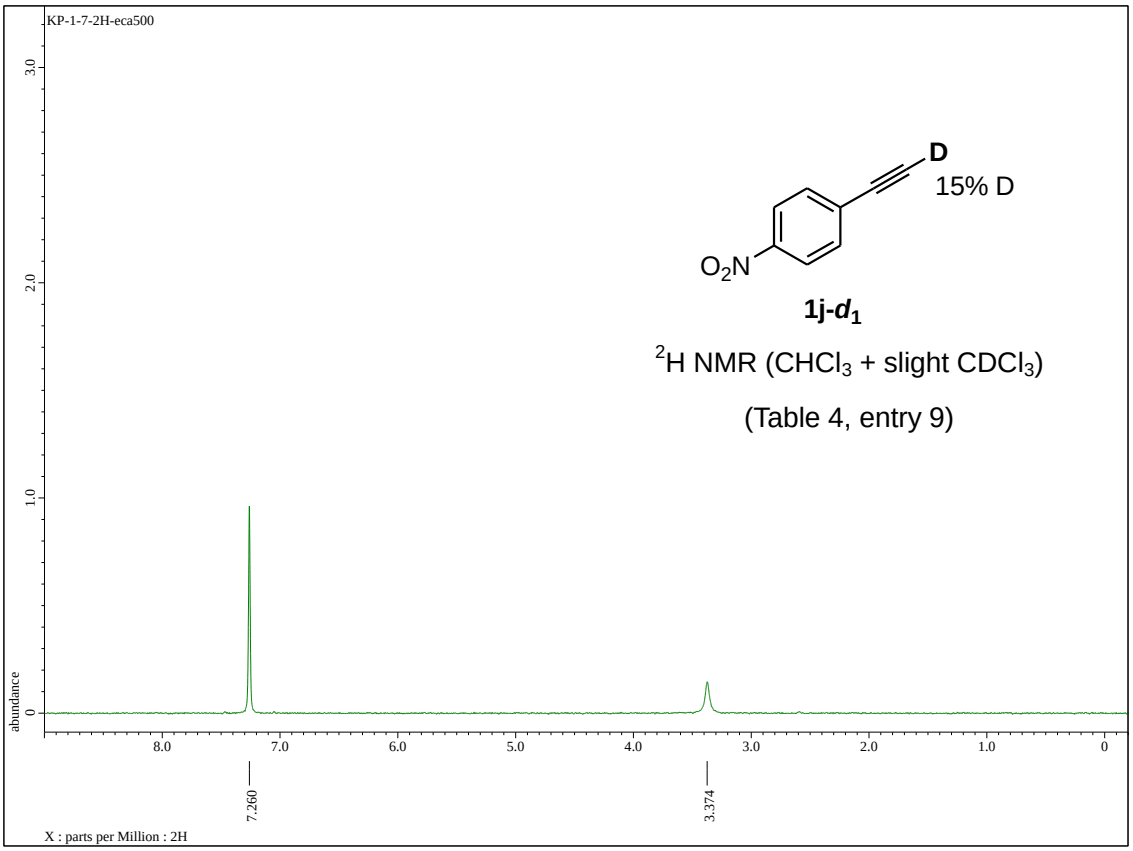
^{2}H NMR of 1i-d_1 (Using D_2O as a solvent)



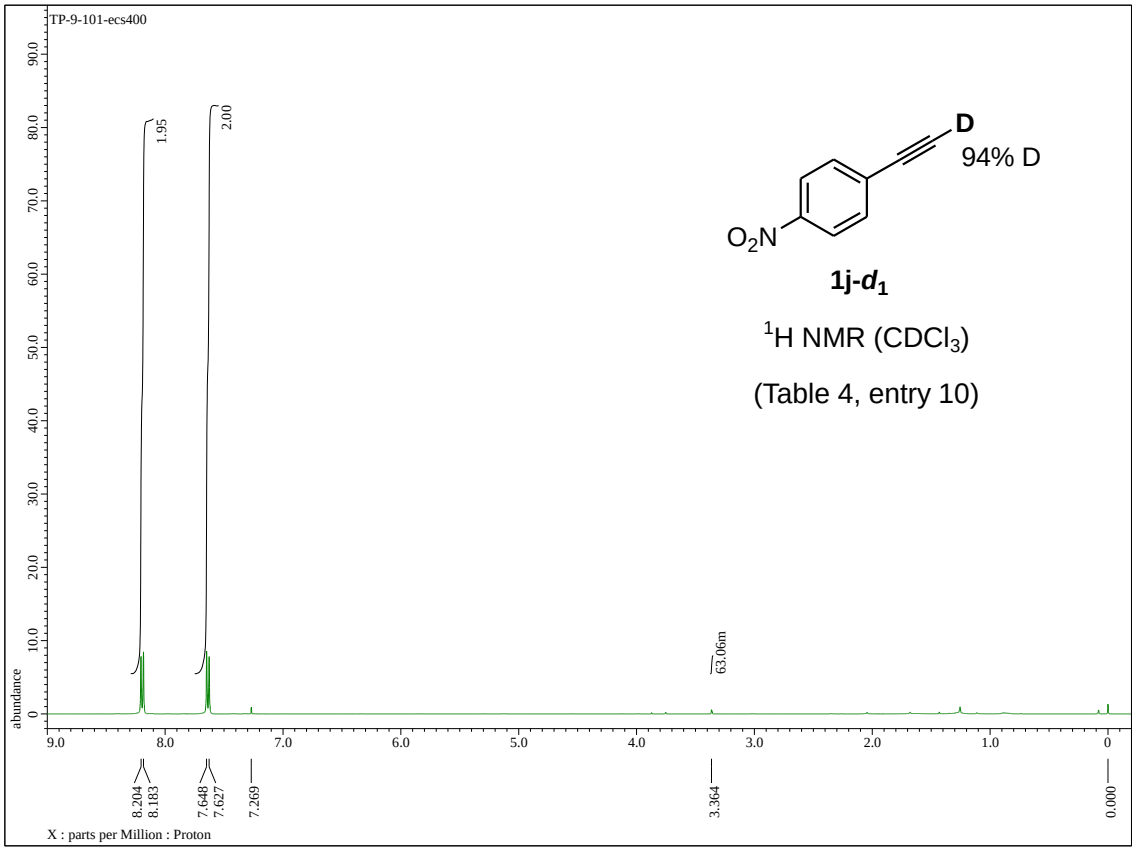
^{1}H NMR of 1j-d_1



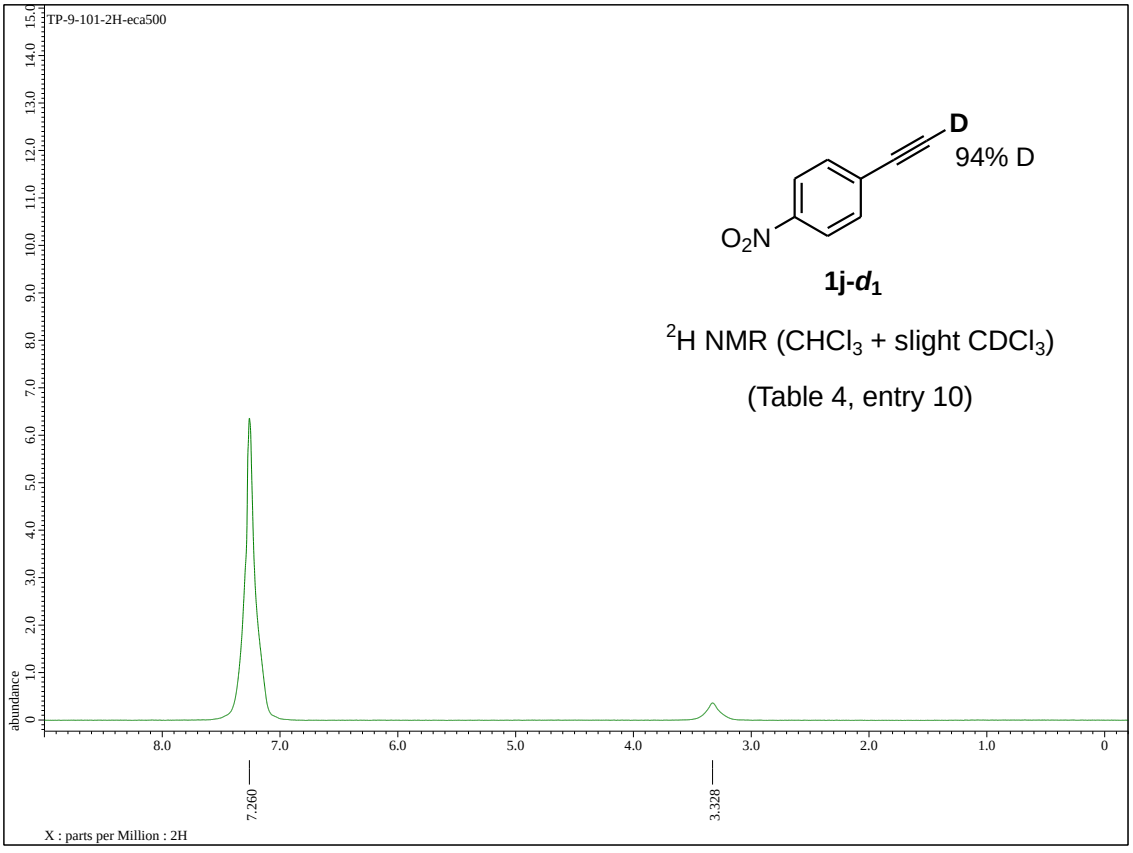
^{2}H NMR of 1j-d_1



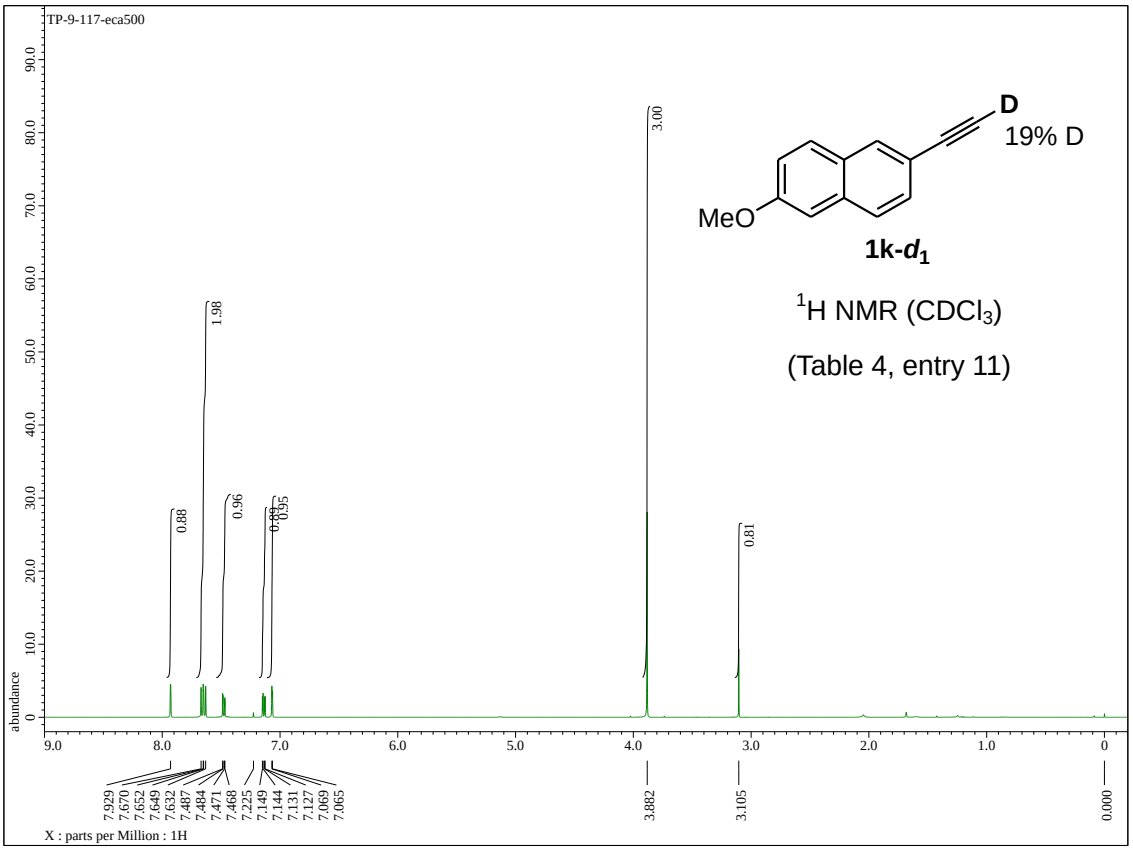
^{1}H NMR of 1j-d_1



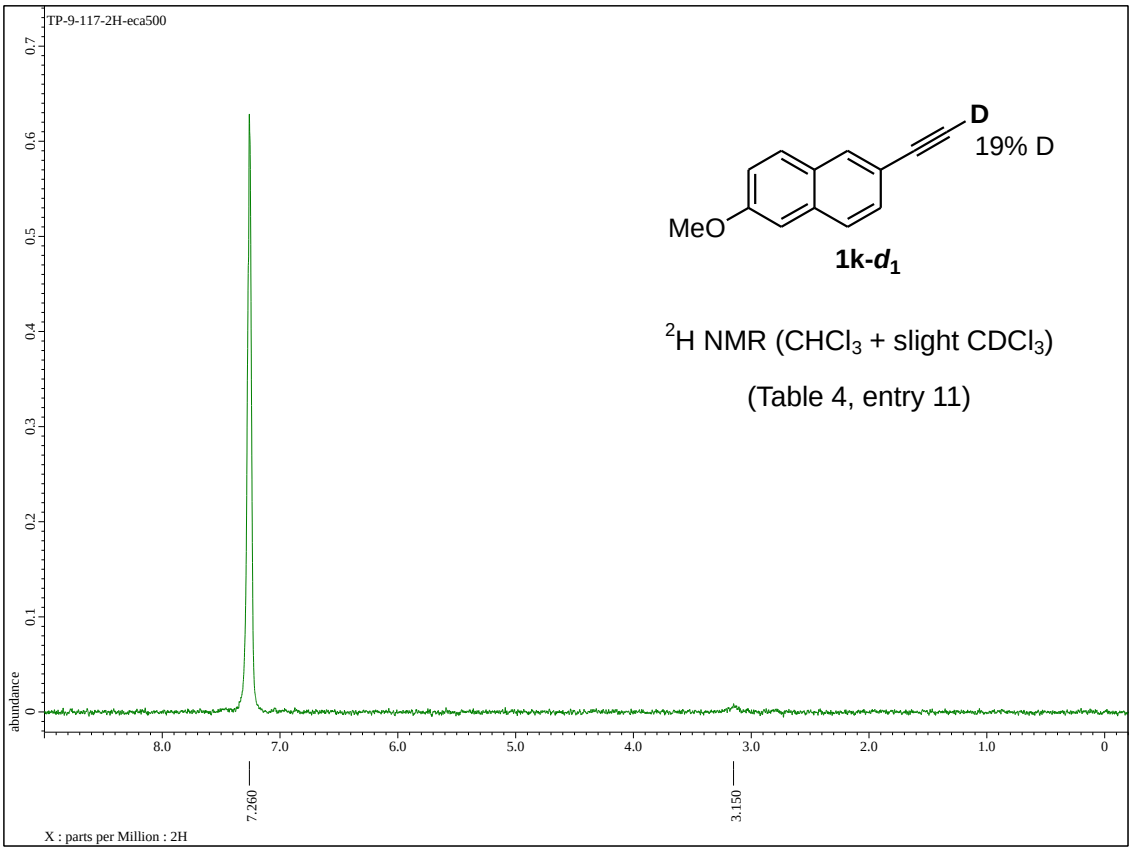
^{2}H NMR of 1j-d_1



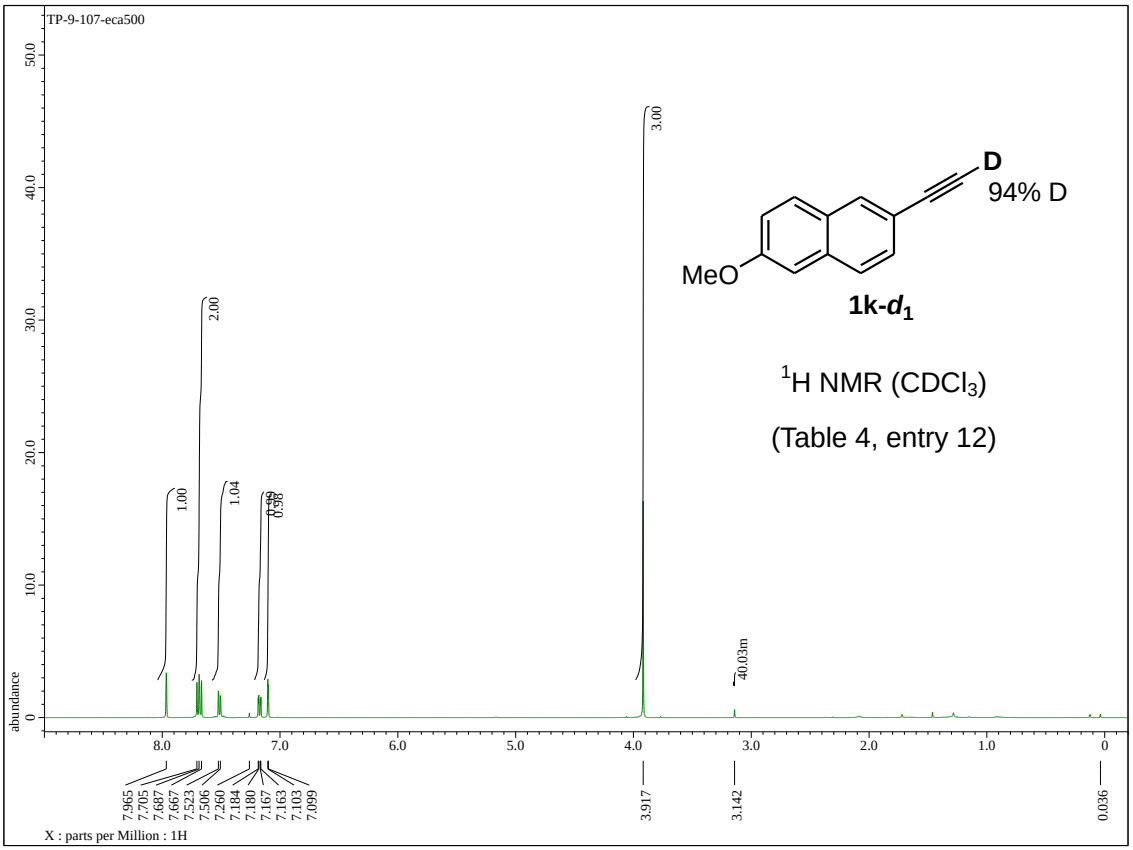
^{1}H NMR of 1k-d_1



^{2}H NMR of 1k-d_1



^{1}H NMR of 1k-d_1



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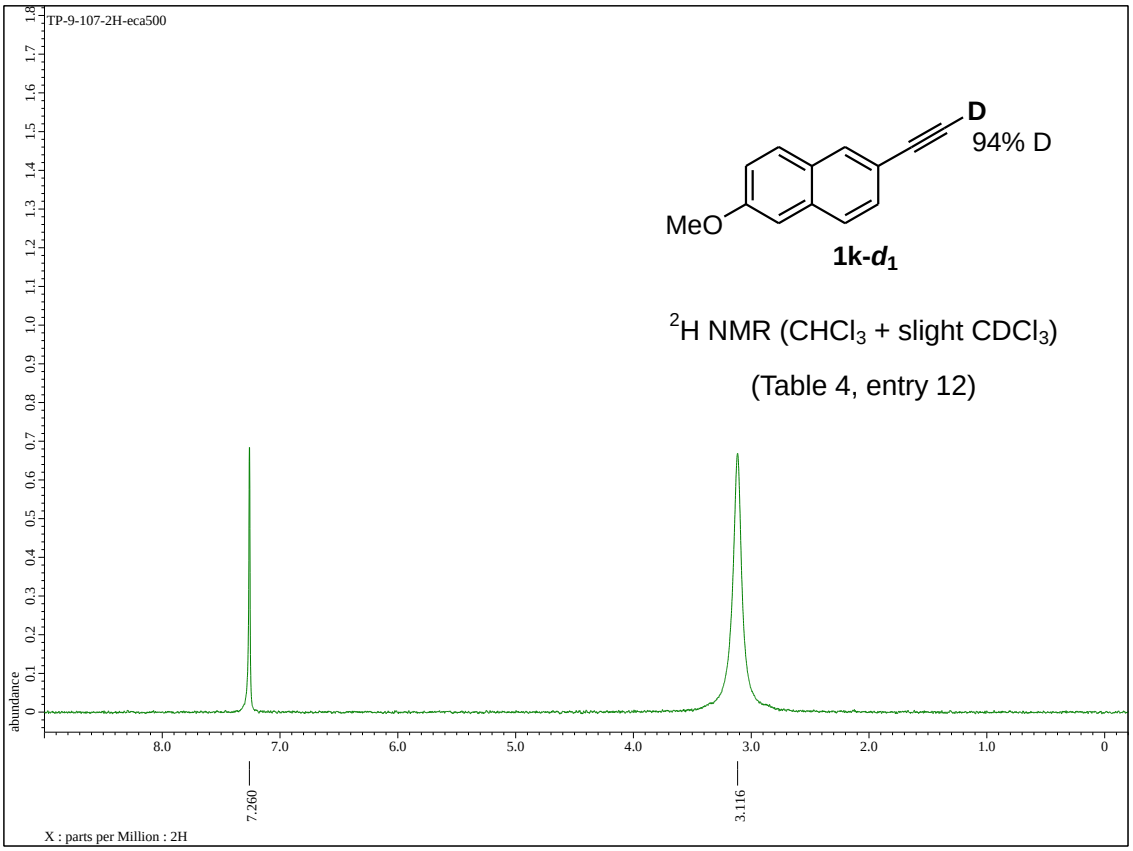
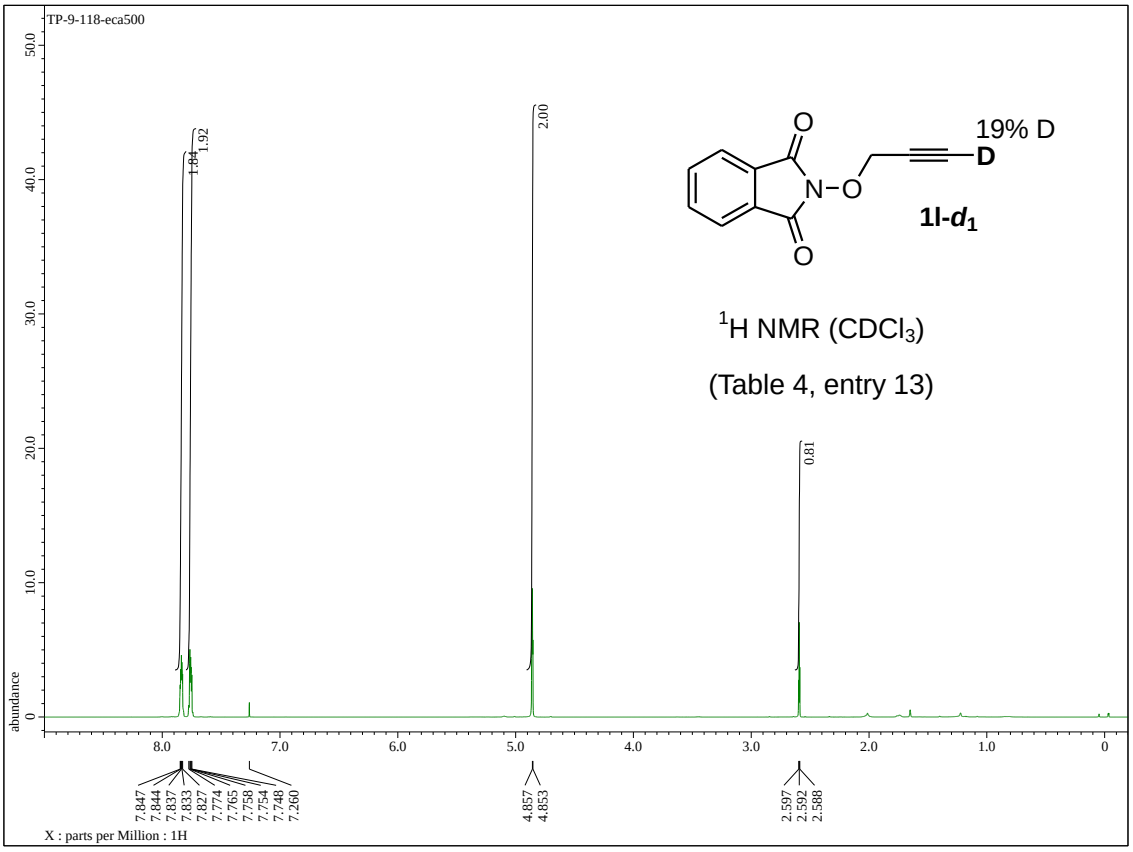


^{1}H NMR of 1l-d_1



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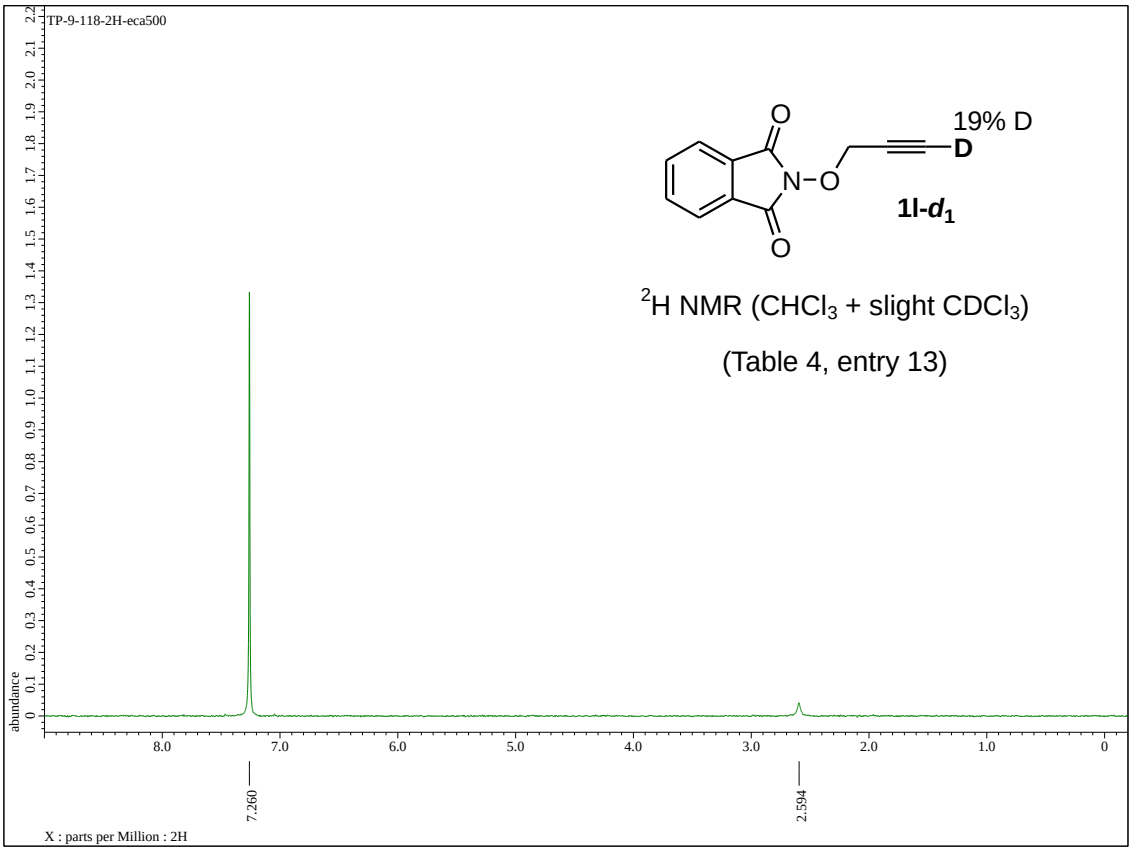

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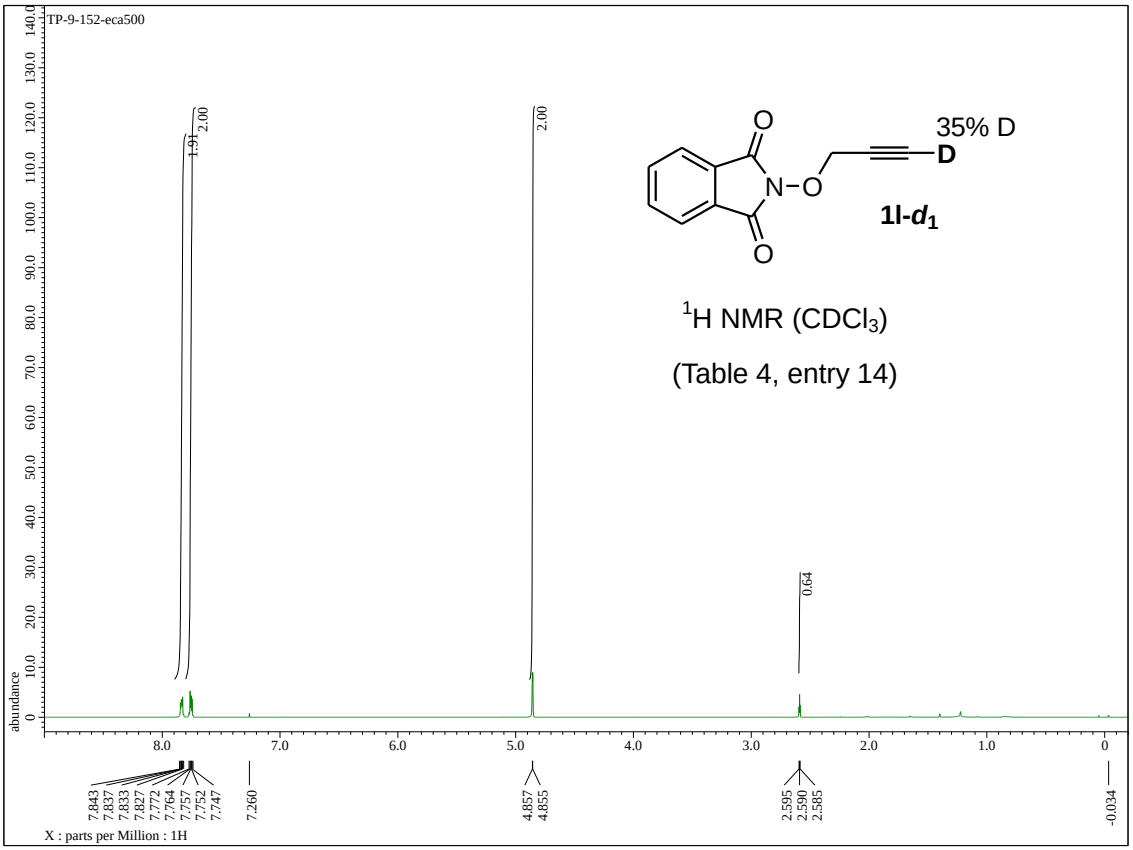

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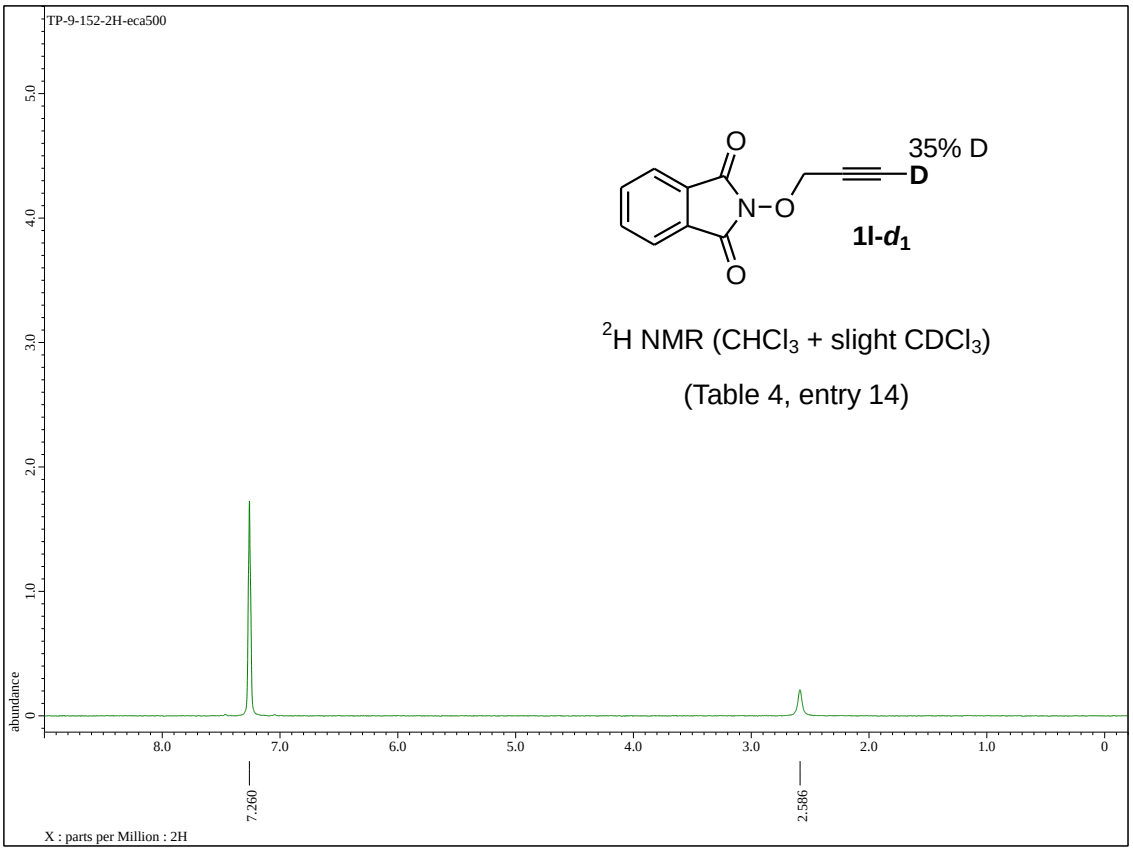

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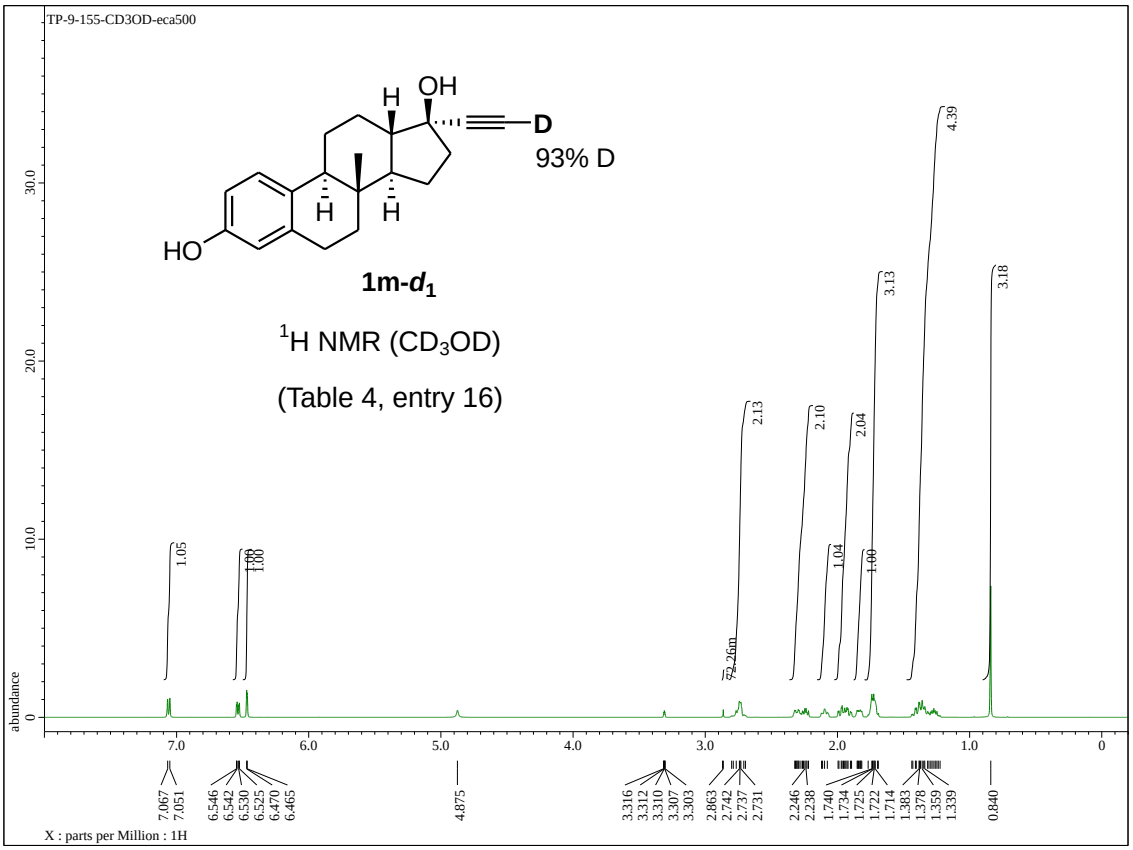

^{2}H NMR of 1m-d_1