Supporting Information

Palladium(0)-Lithium Iodide-Cocatalyzed Asymmetric Hydroalkylation of Conjugated Enynes with Pronucleophiles Leading to 1,3-Disubstituted Allenes

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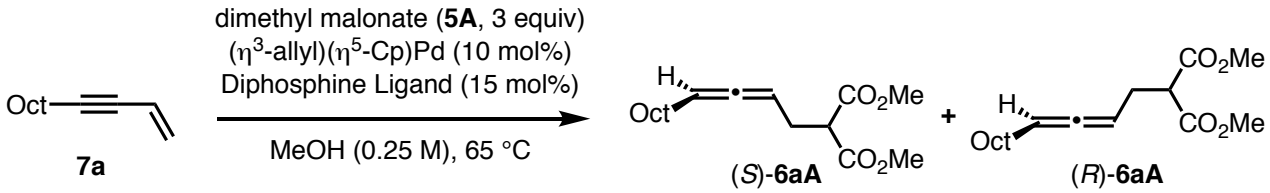
Experimental Procedures

General Techniques. All commercially available reagents and anhydrous solvents including tetrahydrofuran (THF), dichloromethane (DCM), and xylene were purchased and used without further purification. Anhydrous *N*, *N*-dimethylformamide (DMF), methanol, and toluene were obtained by distillation from calcium hydride, magnesium, and sodium, respectively. All reactions were monitored by thin layer chromatography (TLC) performed on 0.25 mm silica gel glassplates (60 F_{254}) using UV light and ethanolic *p*-anisaldehyde-sulfuric acid, ethanolic molybdatophosphoric acid, aqueous cerium sulfate-hexaammonium heptamolybdate-sulfuric acid, or aqueous potassium permanganate-potassium carbonate-sodium hydroxide solutions as visualizing agents. Flash column chromatography was carried out with silica gel (spherical, neutral, 63-210 μm grade). Preparative thin layer chromatography was performed on 0.75 mm Wakogel® B-5F PLC plates. Yields refer to chromatographically and spectroscopically homogenous materials. Melting points were measured on a melting point apparatus and were uncorrected. Only the strongest and/or structurally important absorptions of infrared (IR) spectra are reported in reciprocal centimeters (cm^{-1}). ^1H NMR spectra (400 MHz and 600 MHz) and $^{13}C\{^1H\}$NMR spectra (100 MHz and 151 MHz) were recorded in the indicated solvent. Chemical shifts (δ) are reported in delta (δ) units, parts per million (ppm). Chemical shifts for ^1H NMR spectra are given relative to signals for internal tetramethylsilane (0 ppm) or residual nondeuterated solvents, i.e., chloroform (7.26 ppm). Chemical shifts for ^{13}C NMR spectra are given relative to the signal for chloroform-*d* (77.0 ppm). Chemical shifts for ^{31}P NMR spectra are given relative to the signal for external 85% phosphoric acid (0 ppm). Multiplicities are reported by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). Coupling constants (*J*) are represented in hertz (Hz). ^1H and ^{13}C NMR chemical shifts were assigned using a combination of COSY, NOESY, HMQC, and HMBC. Low and high-resolution mass spectra were measured on TOF-MS with EI, FAB, or ESI probe. Analytical HPLC was performed using Daicel Chiralpak Daicel Chiralpak AD-H, OD-H or AS-H. Optical rotations ($[\alpha]_D$) were measured on JASCO P-1010 polarimeter.

Enynes **7a**–**d** were prepared according to the literature procedures.[1]

General procedure for optimization of the hydroalkylation of 7a with 5A (Table S1)



Scheme S1. Optimization of the reaction conditions.

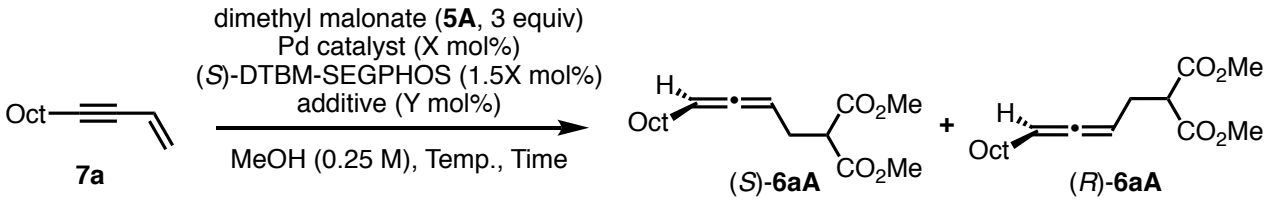
To a test tube containing enyne **7a** (1 equiv), (η^3-allyl)(η^5-Cp)Pd (10 mol%), and diphosphine ligand (15 mol%) were added anhydrous MeOH (0.25 M) and dimethyl malonate (**5A**, 3 equiv) under argon. The resulting mixture was sealed with a screw cap and stirred at 65 °C for the time described in Table S1. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. NMR yield of **6aA** was determined by ^1H NMR analysis of the crude product using 1,1,2,2-tetrachloroethane as an internal standard. The residue was purified by preparative TLC eluting with 20% EtOAc/hexane to give **6aA**. The enantiomeric ratio (*er*) of **6aA** was determined by HPLC analysis with chiral stationary phase column (Daicel Chiralpak OD-H, hexane/*i*-propanol = 397/3, 0.5 mL/min, λ = 210 nm, t_R(*S*) = 13.9 min, t_R(*R*) = 14.7 min). Since it was reported that (*R*)-**6aA** exhibited levorotatory, the retention time of each enantiomer was assigned by that of a dextrorotatory 85:15 mixture of (*S*)- and (*R*)-**6aA** obtained in Table S2, Entry 12.

Table S1. Optimization of the reaction conditions.

Entry	Diphosphine ligand (mg)	(η^3-allyl)(η^5-Cp)Pd (mg)[b]	**7a** (mg)	Time (h)	**6aA** (%)[a]	*Er* (*S*:*R*)
1	$Ph_2PCH_2PPh_2$, 7.2	3.3	19.7	19	0	—
2	$Ph_2P(CH_2)_2PPh_2$, 7.8	3.0	19.9	19	11	—
3	$Ph_2P(CH_2)_3PPh_2$, 8.0	2.5	20.2	19	52	—
4	$Ph_2P(CH_2)_4PPh_2$, 7.8	2.8	20.4	9.5	42	—
5	$Ph_2P(CH_2)_6PPh_2$, 8.5	2.8	19.9	9.5	59	—
6	$Cy_2P(CH_2)_4PCy_2$, 8.8	2.8	19.6	1.5	61	—
7	Xantphos[b], 10.8	2.8	19.7	24	34	—
8	DPEphos[c], 10.3	2.8	19.8	24	57	—
9	dppf[d], 10.0	2.5	20.1	9.5	52	—
10[e]	dppf[d], 8.4	2.1	16.5	24	5	—
11	(*S*)-BINAP, 11.4	2.7	19.8	5	69	45:55
12	(*S*)-H_8-BINAP, 11.6	2.6	20.0	2.5	63	42:58
13	(*S*)-MeO-BIPHEP, 8.7	2.1	16.5	12	80 (75)	54:46
14	(*S*)-SEGPHOS, 11.6	2.7	19.8	18.5	74	56:44
15	(*S*)-Tol-BINAP, 12.8	2.7	19.9	1.5	71	49:51
16	(*S*)-DTBM-BINAP, 21.8	2.5	19.8	0.67	(90)	36:64
17	(*S*)-DTBM-MeO-BIPHEP, 21.0	2.6	20.0	0.67	(92)	32:68
18	(*S*)-DTBM-SEGPHOS, 22.4	2.6	20.0	0.83	(81)	29:71

[a] NMR yields were determined by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard. Isolated yields are shown in parentheses. [b] 4,5-Bis(diphenylphophino)-9,9-dimethylxanthene. [c] Bis[2-(diphenylphosphino)phenyl] ether. [d] 1,1′-Bis(diphenylphosphino)ferrocene. [e] Reaction in THF instead of MeOH.

General procedure for optimization of the asymmetric hydroalkylation of 7a with 5A (Table 1 and S2)



Scheme S2. Optimization of the asymmetric hydroalkylation of **7a** with **5A**.

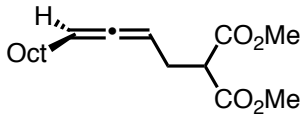
To a test tube containing enyne **7a** (1 equiv), Pd catalyst (X mol%), (*S*)-DTBM-SEGPHOS (1.5X mol%), and additive (Y mol%) were added anhydrous MeOH (0.25 M) and dimethyl malonate (**5A**, 3 equiv) under argon. The resulting mixture was sealed with a screw cap and stirred at 65 °C (entries 1–8), 50 °C (entries 9–11, 13) or rt (entry 12) for the time described in Table S2. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. NMR yield of **6aA** was determined by ^{1}H NMR analysis of the crude product using 1,1,2,2-tetrachloroethane as an internal standard. The residue was purified by preparative TLC eluting with 20% EtOAc/hexane to give **6aA**. The enantiomeric ratio (*er*) of **6aA** was determined by HPLC analysis with chiral stationary phase column (Daicel Chiralpak OD-H, hexane/*i*-propanol = 397/3, 0.5 mL/min, λ = 210 nm, t_R(*S*) = 13.9 min, t_R(*R*) = 14.7 min).

Table S2. Optimization of the asymmetric hydroalkylation of **7a** with **5A**.

Entry	Pd catalyst (mg, mol%)	Additive (mg, mol%)	**7a** (mg)	(*S*)-DTBM-SEGPHOS (mg, mol%)	Temp (°C)	Time (h)	**6aA** (%)[a]	*Er* (*S*:*R*)
1	(η^3-allyl)(η^5-Cp)Pd, 2.6, 10	none	20.0	22.4, 15	65	0.83	(81)	29:71
2	$Pd_2dba_3 \cdot CHCl_3$, 6.9, 5	none	19.9	21.4, 15	65	24	(83)	33:67
3	$Pd(dba)_2$, 7.0, 10	none	20.2	21.8, 15	65	0.83	(quant)	28:72
4	(η^3-allyl)(η^5-Cp)Pd, 2.1, 10	LiOAc, 2.7, 30	16.5	17.6, 15	65	0.25	94 (78)	28:72
5	(η^3-allyl)(η^5-Cp)Pd, 2.2, 10	KOAc, 4.5, 30	16.5	17.6, 15	65	0.25	100 (78)	25:75
6	(η^3-allyl)(η^5-Cp)Pd, 2.0, 10	LiCl, 1.7, 30	16.5	17.3, 15	65	0.25	95 (77)	68:32
7	(η^3-allyl)(η^5-Cp)Pd, 2.1, 10	LiBr, 3.2, 30	16.5	18.2, 15	65	0.25	93 (81)	76:24
8	(η^3-allyl)(η^5-Cp)Pd, 2.8, 10	LiI, 5.3, 30	20.2	21.8, 15	65	4.7	(90)	78:22
9	(η^3-allyl)(η^5-Cp)Pd, 2.2, 10	LiI, 5.5, 30	16.6	17.5, 15	50	0.67	94	83:17
10	(η^3-allyl)(η^5-Cp)Pd, 1.1, 5	LiI, 4.0, 30	16.5	8.9, 7.5	50	0.5	99	86:14
11	(η^3-allyl)(η^5-Cp)Pd, 1.1, 5	LiI, 2.0, 15	16.3	8.9, 7.5	50	0.5	quant	84:16
12	(η^3-allyl)(η^5-Cp)Pd, 1.0, 5	LiI, 2.1, 15	16.4	8.9, 7.5	rt	1	quant	86:14
13	(η^3-allyl)(η^5-Cp)Pd, 1.2, 5	LiI, 1.0, 5	16.6	8.9, 7.5	50	0.5	98 (84)	85:15

[a] NMR yields were determined by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard. Isolated yields are shown in parentheses.

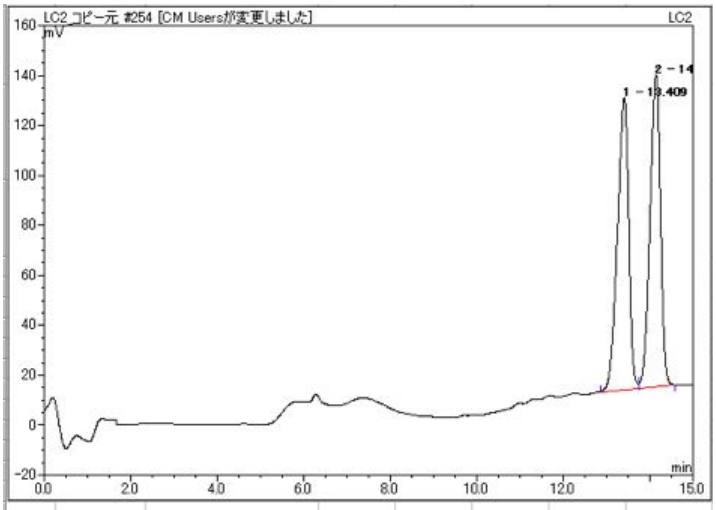
Dimethyl (*S*)-2-(5-oxododeca-2,3-dien-1-yl)malonate (**6aA**)[2, 3]



Yellow oil. Rf = 0.49 (17% EtOAc/hexane). $[\alpha]^{22}_D$ +43 (*c* 0.76 in hexane) (Table 2, Entry 11). IR (neat): 2954, 2926, 2855, 1964, 1756, 1739, 1436, 1262, 1231, 1152, 1042 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.20–5.04 (m, 2H), 3.74 (s, 6H), 3.51 (t, *J* = 7.6 Hz, 1H), 2.58 (ddd, *J* = 7.6, 6.1, 3.2 Hz, 2H), 1.95 (ddt, *J* = 3.0, 6.8, 6.8 Hz, 2H), 1.46–1.15 (m, 12H), 0.88 (d, *J* = 6.9 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 203.9, 169.4, 169.3, 93.0, 87.3, 52.5, 51.2, 31.8, 29.4, 29.2, 29.1, 29.0, 28.8, 28.0, 22.6, 14.0 (one carbon is missing due to overlap). LRMS m/z (relative intensity) 296 $[M]^+$ (6), 233 (7), 198 (41), 166 (33), 138 (100). HRMS (EI) calcd for $C_{17}H_{28}O_4$ 296.1988, found 296.1982 $[M]^+$.

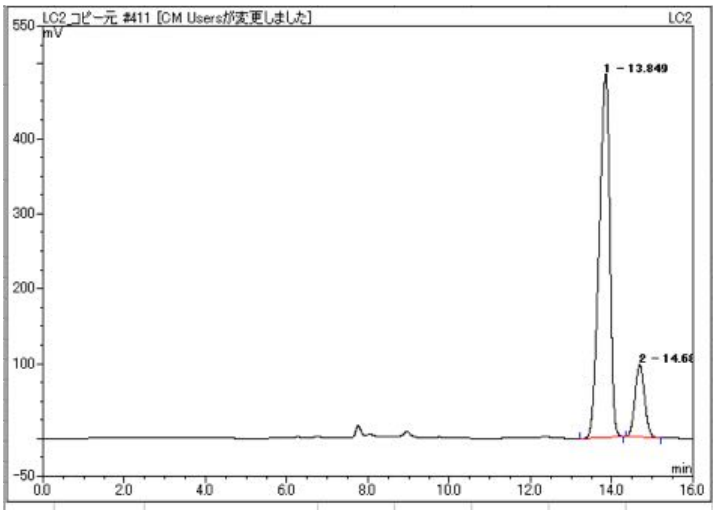
HPLC chromatograms of **6aA**

(±)-**6aA**



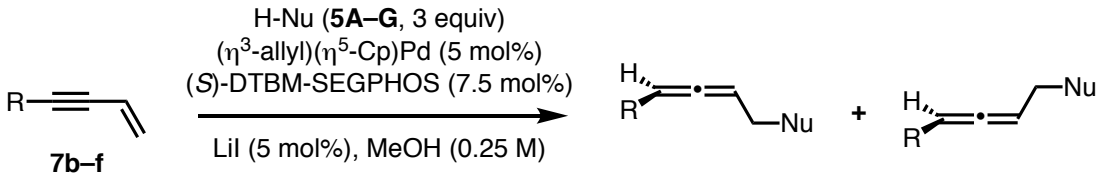
番号	保持時間 分	ピーク名	高さ mV	面積 mV× 分	相対面積 %	含有量 n.a.	タイプ
1	13.41	n.a.	116.684	35.229	50.18	n.a.	BM *
2	14.14	n.a.	124.896	34.970	49.82	n.a.	MB*
合計:			241.580	70.199	100.00	0.000	

6aA (Table 2, Entry 11)



番号	保持時間 分	ピーク名	高さ mV	面積 mV× 分	相対面積 %	含有量 n.a.	タイプ
1	13.85	n.a.	484.811	146.884	84.68	n.a.	BMB*
2	14.68	n.a.	96.862	26.582	15.32	n.a.	BMB*
合計:			581.673	173.465	100.00	0.000	

General procedure for scope of conjugated enynes 7b–d and pronucleophiles 5A–G (Figure 1)



7b: R = Cy
7c: R = Ph
7d: R = ^{t}Bu

5A: $CH_2(CO_2Me)_2$
5B: $CHMe(CO_2Me)_2$
5C: $CHPh(CO_2Me)_2$
5D: $CH(NHAc)(CO_2Me)_2$
5E: $CH_2(SO_2Ph)_2$
5F: $CH_2(COMe)_2$
5G: $CH_2(CN)_2$

Scheme S3. The scope of conjugated enynes **7b–d** and pronucleophiles **5A–G** investigated in the hydroalkylation reaction.

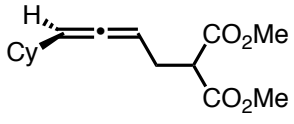
To a test tube containing enyne **7b**–**d** (1 equiv), (η^3-allyl)(η^5-Cp)Pd (5 mol%), (*S*)-DTBM-SEGPHOS (7.5 mol%) and LiI (5 mol%) were added anhydrous MeOH (0.25 M) and pronucleophile (**5A–G**, 3 equiv) under argon. The resulting mixture was sealed with a screw cap and stirred at the temperature and for the time described in Table S3. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The residue was purified by preparative TLC or silica gel column chromatography to give **6(b–d)(A–G)**. The authentic racemic mixture was obtained by the similar procedure using *rac*-MeO-BIPHEP instead of (*S*)-DTBM-SEGPHOS without LiI. The absolute configuration of **6(b–d)(A–G)** were determined by the sign of the optical rotation of literature known compounds or deduced by the Lowe-Brewster rule.[4]

Table S3. The scope of conjugated enynes **7b–d** and pronucleophiles **5A–G** investigated in the hydroalkylation reaction.

Entry	**7** (mg)	**5** (mg or μL)	(η^3-allyl)(η^5-Cp)Pd (mg)	(*S*)-DTBM-SEG-PHOS (mg)	LiI (mg)	Temp. (°C) Time (h)	Isolated yield of **6** (mg, %)	*Er* (*S*:*R*)
1	**7b**, 13.2	**5A**, 34.5 μL	1.1	8.7	0.8	50 °C, 5 h	**6bA**: 26.5, quant	86:14
2	**7c**, 12.6	**5A**, 34.5 μL	1.1	9.1	1.0	rt , 19 h	**6cA**: 20.9, 82	96:4
3	**7d**, 10.9 (66% purity)[a]	**5A**, 34.5 μL	1.1	9.0	1.8	80 °C, 8 h	**6dA**: 15.2, 96	98:2
4	**7d**, 10.8 (81% purity)[a]	**5B**, 45.3 mg	1.1	9.3	0.8	80 °C, 6 h	**6bB**: 11.0, 54	94:6
5	**7d**, 10.8 (81% purity)[a]	**5C**, 64.2 mg	1.1	9.0	0.8	80 °C, 6 h	**6dC**: 16.7, 65	96:4
6	**7d**, 10.8 (81% purity)[a]	**5D**, 56.5 mg	1.0	9.3	1.0	80 °C, 6 h	**6dD**: 16.0, 65	95:5
7	**7b**, 13.2	**5E**, 90.0 mg	1.0	9.0	0.6	50 °C, 24 h	**6bE**: 39.7, 94	88:12
8	**7d**, 11.0 (81% purity)[a]	**5E**, 88.6 mg	1.3	9.2	1.2	80 °C, 3 h	**6dE**: 16.8, 51	94:6
9	**7b**, 13.3	**5F**, 30.8 μL	1.2	9.0	1.2	50 °C, 2 h; 65 °C, 11 h; 80 °C, 8 h	**6bF**: 11.3, 49	78:22
10	**7b**, 13.2	**5G**, 18.9 μL	1.1	9.0	1.4	50 °C, 24 h; 65 °C, 8 h	**6bG**: 5.1, 26	75:25

[a] THF was contained.

Dimethyl (*S*)-2-(4-cyclohexylbuta-2,3-dien-1-yl)malonate (**6bA**)[5]



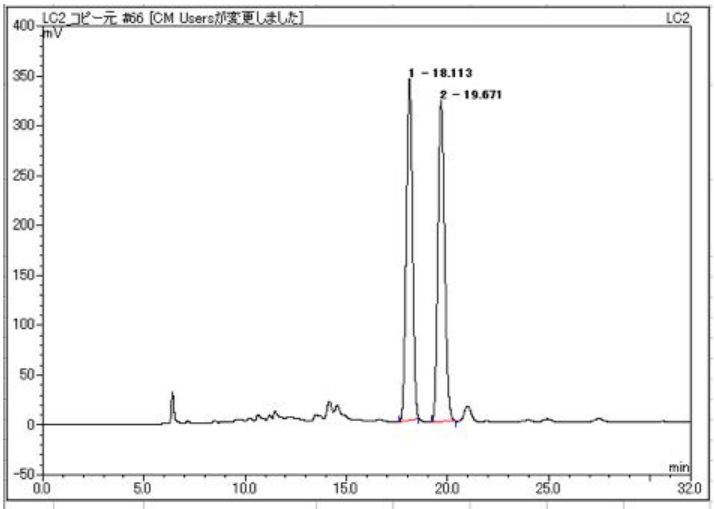
Isolated by preparative TLC eluting with 20% EtOAc/hexane. Yellow oil. Rf = 0.29 (17% EtOAc/hexane). $[\alpha]^{21}_D$ +50 (*c* 1.04 in $CHCl_3$). IR (neat): 2925, 2850, 1962, 1755, 1738, 1435, 1342, 1250, 1154, 1036 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.19–5.09

(m, 2H), 3.74 (s, 6H), 3.51 (t, *J* = 7.4 Hz, 1H), 2.62–2.54 (m, 2H), 1.98–1.85 (m, 1H), 1.80–1.50 (m, 4H), 1.45–0.96 (m, 6H).^{13}C-NMR (100 MHz, $CDCl_3$): δ 202.8, 169.4, 169.3, 99.0, 88.3, 52.50, 52.48, 51.2, 37.2, 32.9, 32.8, 28.1, 26.1, 26.0. LRMS m/z (relative intensity) 266 $[M]^+$ (15), 203 (26), 174 (15), 147 (27), 134 (100). HRMS (EI) calcd for $C_{15}H_{22}O_4$ 266.1518, found 266.1506 $[M]^+$.

Chiral HPLC: (Daicel Chiralpak OD-H, hexane/*i*-propanol = 397/3, 0.5 mL/min, λ = 210 nm): t_R(*S*) = 18.5 min (major enantiomer), t_R(*R*) = 20.2 min (minor enantiomer).

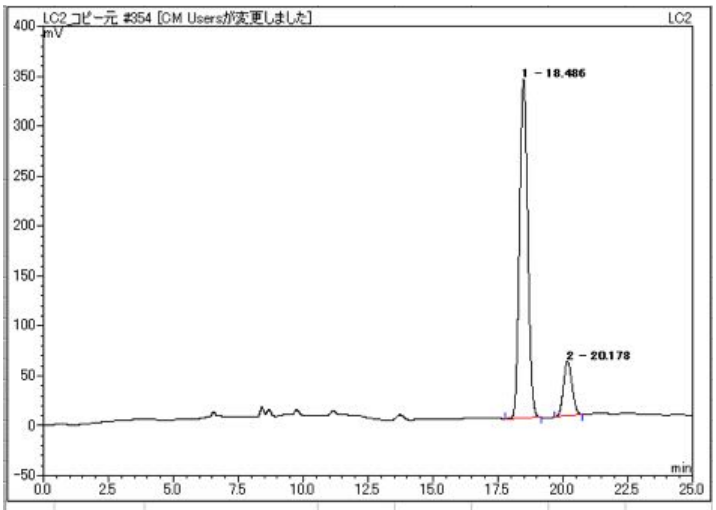
HPLC chromatograms of **6bA**

(±)-**6bA**



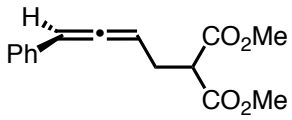
番号	保持時間 分	ピーク名	高さ mV	面積 mV×分	相対面積 %	含有量 n.a.	タイプ
1	18.11	n.a.	341.923	120.960	49.45	n.a.	BMB*
2	19.67	n.a.	321.290	123.634	50.55	n.a.	BMB*
合計:			663.213	244.595	100.00	0.000	

6bA



番号	保持時間 分	ピーク名	高さ mV	面積 mV×分	相対面積 %	含有量 n.a.	タイプ
1	18.49	n.a.	339.687	124.647	85.55	n.a.	BMB*
2	20.18	n.a.	54.954	21.054	14.45	n.a.	BMB*
合計:			394.641	145.701	100.00	0.000	

Dimethyl (*S*)-2-(4-phenylbuta-2,3-dien-1-yl)malonate (**6cA**)[3]

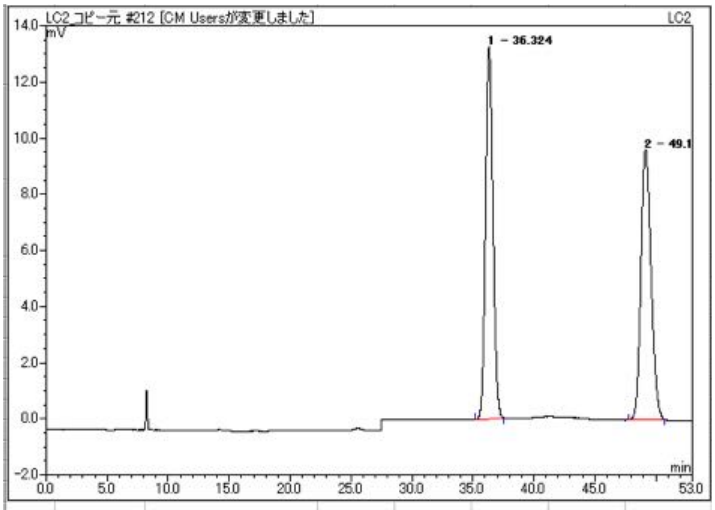


Isolated by preparative TLC eluting with 20% EtOAc/hexane. Yellow oil. Rf = 0.34 (17% EtOAc/hexane). $[\alpha]^{22}_{D}$ +118 (*c* 0.97 in $CHCl_3$). IR (neat): 2954, 2360, 2341, 1952, 1736, 1437, 1235, 1155, 1029, 695 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.34–7.15 (m, 5H), 6.20 (dt, *J* = 6.4, 3.2 Hz, 1H), 5.62 (dt, *J* = 6.4, 6.4 Hz, 1H), 3.73 (s, 3H), 3.59 (t, *J* = 7.4 Hz, 1H), 3.58 (s, 3H), 2.84–2.62 (m, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 205.1, 169.3, 169.1, 134.0, 128.5, 127.1, 126.8, 96.5, 91.7, 52.6, 52.5, 50.9, 27.8. LRMS m/z (relative intensity) 260 $[M]^+$ (42), 201 (14), 169 (23), 160 (48), 128 (100). HRMS (EI) calcd for $C_{15}H_{16}O_4$ 260.1049, found 260.1051 $[M]^+$.

Chiral HPLC: (Daicel Chiralpak AD-H, hexane/*i*-propanol = 50/1, 1.0 mL/min, λ = 254 nm): t_R(*S*) = 30.9 min (major enantiomer), t_R(*R*) = 42.8 min (minor enantiomer).

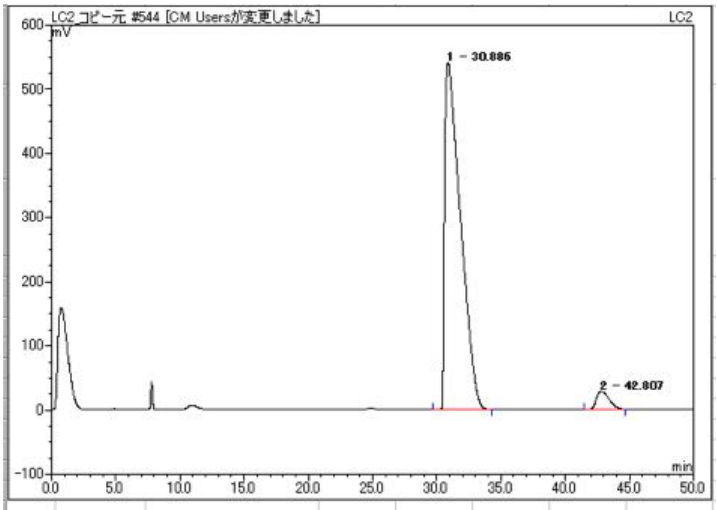
HPLC chromatograms of **6cA**

(±)-**6cA**



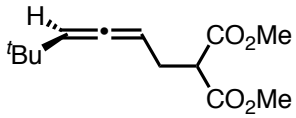
番号	保持時間 分	ピーク名	高さ mV	面積 mV×分	相対面積 %	含有量 n.a.	タイプ
1	36.32	n.a.	13.272	9.387	50.23	n.a.	BMB*
2	49.16	n.a.	9.646	9.300	49.77	n.a.	BMB*
合計:			22.918	18.686	100.00	0.000	

6cA



番号	保持時間	ピーク名	高さ	面積	相対面積	含有量	タイプ
	分		mV	mV×分	%	n.a.	
1	30.89	n.a.	541.121	773.985	95.94	n.a.	BMB*
2	42.81	n.a.	27.929	32.732	4.06	n.a.	BMB*
合計:			569.050	806.717	100.00	0.000	

Dimethyl (*S*)-2-(5,5-dimethylhexa-2,3-dien-1-yl)malonate (**6dA**)[6, 7]

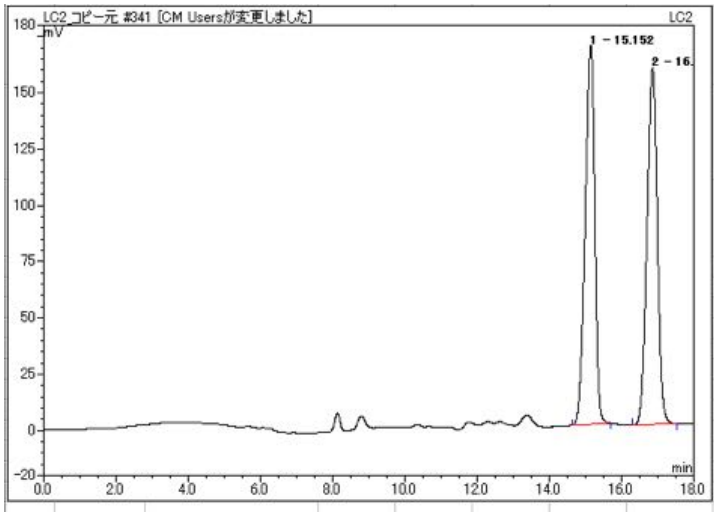


Isolated by silica gel column chromatography eluting with 3% EtOAc/hexane. Colorless oil. Rf = 0.40 (17% EtOAc/hexane). $[\alpha]^{26}_{D}$ +68.6 (*c* 0.51 in $CHCl_3$). IR (neat): 2959, 1964, 1737, 1457, 1246, 1201, 1111, 877 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.21–5.11 (m, 2H), 3.74 (s, 3H), 3.74 (s, 3H), 3.49 (t, *J* = 7.4 Hz, 1H), 2.60 (ddd, *J* = 7.4, 5.9, 3.2 Hz, 2H), 1.01 (s, 9H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 201.2, 169.41, 169.37, 104.9, 89.2, 52.6, 52.5, 51.3, 31.7, 30.0, 28.3. LRMS m/z (relative intensity) 240 $[M]^+$ (52), 225 (7), 177 (32), 165 (18), 132 (100). HRMS (EI) calcd for $C_{13}H_{20}O_4$ 240.1362, found 240.1372 $[M]^+$.

Chiral HPLC: (Daicel Chiralpak OD-H, hexane/*i*-propanol = 397/3, 0.5 mL/min, λ = 210 nm): t_R(*S*) = 15.3 min (major enantiomer), t_R(*R*) = 16.8 min (minor enantiomer).

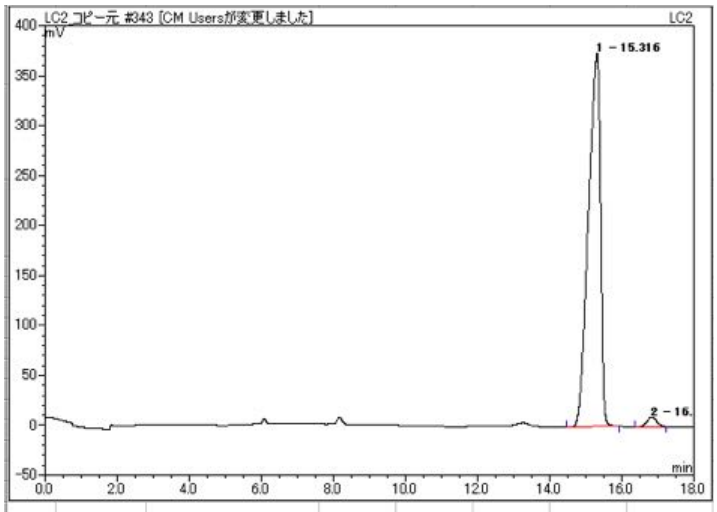
HPLC chromatograms of **6dA**

(±)-**6dA**



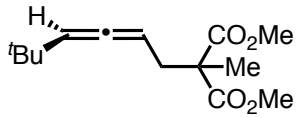
番号	保持時間 分	ピーク名	高さ mV	面積 mV× 分	相対面積 %	含有量 n.a.	タイプ
1	15.15	n.a.	168.365	52.204	49.76	n.a.	BMB*
2	16.86	n.a.	158.702	52.714	50.24	n.a.	BMB*
合計:			327.066	104.918	100.00	0.000	

6dA



番号	保持時間 分	ピーク名	高さ mV	面積 mV× 分	相対面積 %	含有量 n.a.	タイプ
1	15.32	n.a.	373.122	144.840	97.98	n.a.	BMB*
2	16.83	n.a.	9.680	2.991	2.02	n.a.	BMB*
合計:			382.802	147.831	100.00	0.000	

Dimethyl (*S*)-2-(5,5-dimethylhexa-2,3-dien-1-yl)-2-methylmalonate (**6dB**)[6–8]

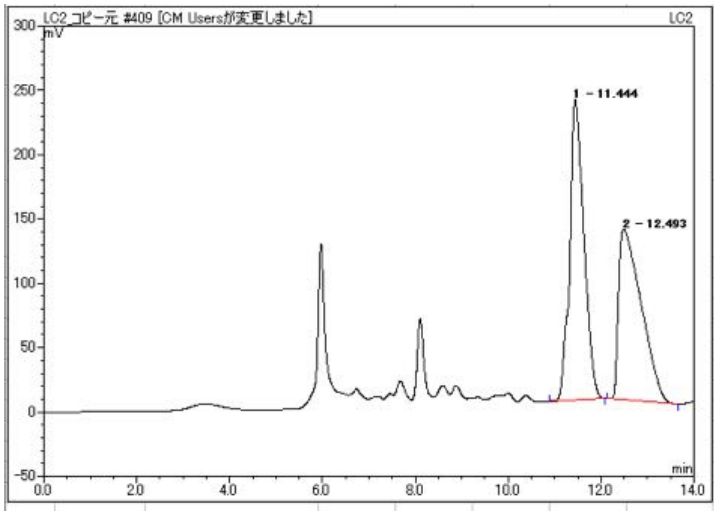


Isolated by silica gel column chromatography eluting with 3% EtOAc/hexane. Yellow oil. Rf = 0.55 (17% EtOAc/hexane). $[\alpha]^{18}_{D}$ +30.3 (*c* 0.23 in $CHCl_3$). IR (neat): 2959, 1964, 1737, 1457, 1246, 1201, 1111, 877 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.10 (dt, *J* = 6.3, 2.4 Hz, 1H), 5.00 (dt, *J* = 6.3, 7.6 Hz, 1H), 3.72 (s, 6H), 2.61–2.56 (m, 2H), 1.45 (s, 3H), 1.02 (s, 9H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 203.2, 172.4, 172.3, 102.9, 86.9, 53.8, 52.52, 52.47, 36.3, 31.7, 30.1, 19.9. HRMS (ESI) calcd for $C_{14}H_{23}O_4$ 255.1596, found 255.1587 $[M+H]^+$.

Chiral HPLC: (Daicel Chiralpak AD-H, hexane/*i*-propanol = 397/3, 0.5 mL/min, λ = 210 nm): t_R(*R*) = 11.4 min (minor enantiomer), t_R(*S*) = 12.1 min (major enantiomer).

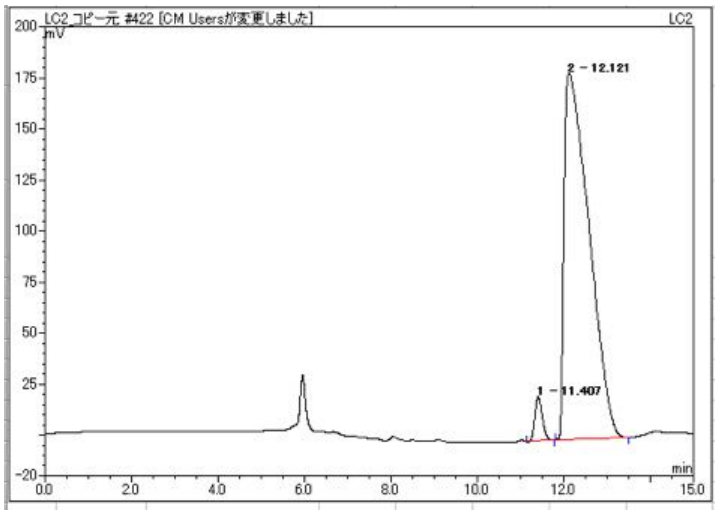
HPLC chromatograms of **6dB**

(±)-**6dB**



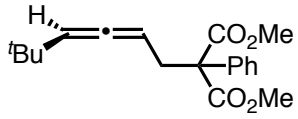
番号	保持時間 分	ピーク名	高さ mV	面積 mV×分	相対面積 %	含有量 n.a.	タイプ
1	11.44	n.a.	233.813	82.569	52.41	n.a.	BMB*
2	12.49	n.a.	132.691	74.976	47.59	n.a.	BMB*
合計:			366.503	157.545	100.00	0.000	

6dB



番号	保持時間 分	ピーク名	高さ mV	面積 mV×分	相対面積 %	含有量 n.a.	タイプ
1	11.41	n.a.	21.560	4.280	3.47	n.a.	BMB*
2	12.12	n.a.	179.447	118.944	96.53	n.a.	BMB*
合計:			201.007	123.223	100.00	0.000	

Dimethyl (*S*)-2-(5,5-dimethylhexa-2,3-dien-1-yl)-2-phenylmalonate (**6dC**)[6]

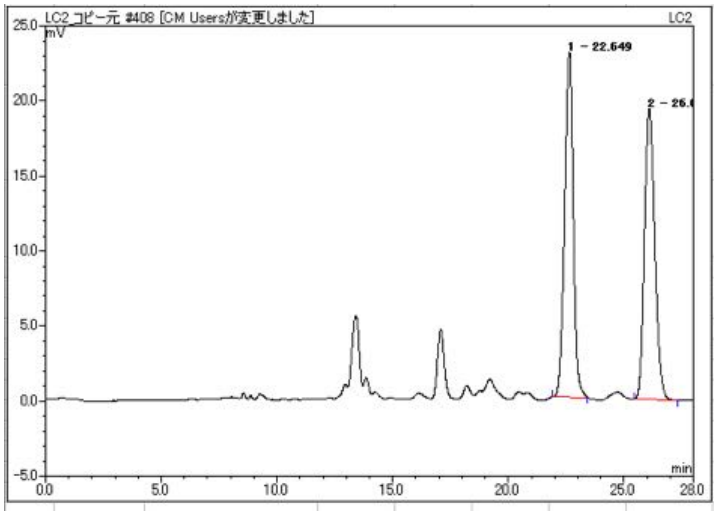


Isolated by preparative TLC eluting with 20% EtOAc/hexane. Yellow oil. Rf = 0.47 (17% EtOAc/hexane). $[\alpha]^{19}_{D}$ +40.8 (*c* 0.79 in $CHCl_3$). IR (neat): 2956, 2864, 1961, 1737, 1499, 1435, 1362, 1233, 1175, 1074, 878, 730, 696 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.46–7.37 (m, 2H), 7.37–7.23 (m, 3H), 5.12–4.99 (m, 2H), 3.75 (s, 6H), 3.07–3.03 (m, 2H), 0.96 (s, 9H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 202.9, 170.8, 170.7, 136.5, 128.2, 128.1, 127.6, 102.9, 87.4, 62.9, 52.7, 36.4, 31.6, 30.1 (one carbon is missing due to overlap). HRMS (ESI) calcd for $C_{19}H_{25}O_4$ 317.1753, found 317.1741 $[M+H]^+$.

Chiral HPLC: (Daicel Chiralpak AD-H, hexane/*i*-propanol = 397/3, 0.5 mL/min, λ = 210 nm): t_R(*R*) = 23.2 min (minor enantiomer), t_R(*S*) = 27.1 min (major enantiomer).

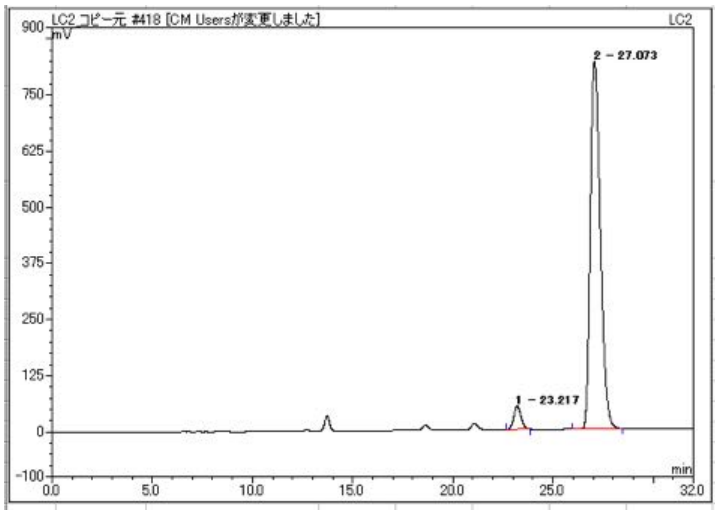
HPLC chromatograms of **6dC**

(±)-**6dC**



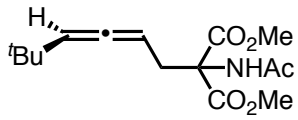
番号	保持時間 分	ピーク名	高さ mV	面積 mV×分	相対面積 %	含有量 n.a.	タイプ
1	22.65	n.a.	23.017	9.993	49.97	n.a.	BMB*
2	26.09	n.a.	19.346	10.007	50.03	n.a.	BMB*
合計:			42.363	20.000	100.00	0.000	

6dC



番号	保持時間 分	ピーク名	高さ mV	面積 mV×分	相対面積 %	含有量 n.a.	タイプ
1	23.22	n.a.	51.808	21.930	4.42	n.a.	BMB*
2	27.07	n.a.	817.207	474.429	95.58	n.a.	BMB*
合計:			869.016	496.358	100.00	0.000	

Dimethyl (*S*)-2-acetamido-2-(5,5-dimethylhexa-2,3-dien-1-yl)malonate (**6dD**)

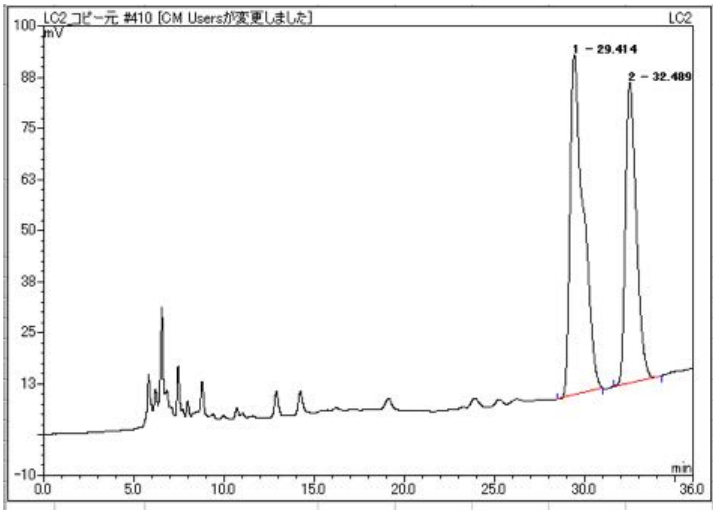


Isolated by silica gel column chromatography eluting with 33% EtOAc/hexane. Colorless oil. Rf = 0.41 (50% EtOAc/hexane). $[\alpha]^{20}_{D}$ +24.1 (*c* 0.66 in $CHCl_3$). IR (neat): 3297, 2959, 1961, 1748, 1683, 1506, 1437, 1305, 1214, 1065, 979, 886 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.78 (s, 1H), 5.52 (dt, *J* = 7.6, 2.2 Hz, 1H), 4.89 (dt, *J* = 7.6, 7.6 Hz, 1H), 3.78 (s, 6H), 3.03 (dd, *J* = 7.6, 2.2 Hz, 2H), 2.03 (s, 3H), 1.00 (s, 9H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 203.2, 169.0, 168.2, 168.1, 103.2, 85.5, 66.3, 53.5, 53.4, 33.2, 31.5, 30.0, 23.0. HRMS (ESI) calcd for $C_{15}H_{24}NO_5$ 298.1654, found 298.1642 $[M+H]^+$.

Chiral HPLC: (Daicel Chiralpak AD-H, hexane/*i*-propanol = 19/1, 0.5 mL/min, λ = 210 nm): t_R(*R*) = 29.9 min (minor enantiomer), t_R(*S*) = 32.8 min (major enantiomer).

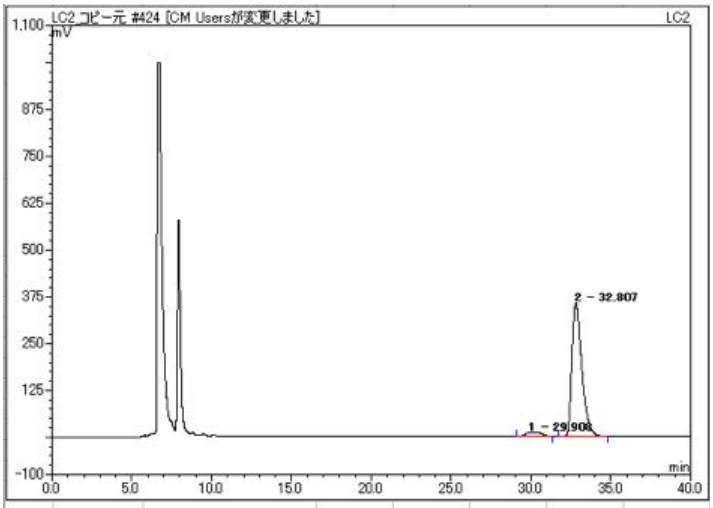
HPLC chromatograms of **6dD**

(±)-**6dD**



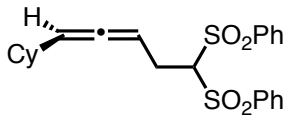
番号	保持時間 分	ピーク名	高さ mV	面積 mV×分	相対面積 %	含有量 n.a.	タイプ
1	29.41	n.a.	83.307	71.121	58.14	n.a.	BMB*
2	32.49	n.a.	73.376	51.201	41.86	n.a.	BMB*
合計:			156.683	122.322	100.00	0.000	

6dD



番号	保持時間 分	ピーク名	高さ mV	面積 mV×分	相対面積 %	含有量 n.a.	タイプ
1	29.91	n.a.	10.831	12.137	4.51	n.a.	BMB*
2	32.81	n.a.	356.101	257.170	95.49	n.a.	BMB*
合計:			366.931	269.307	100.00	0.000	

(*S*)-(5-Cyclohexylpenta-3,4-diene-1,1-diyldisulfonyl)dibenzene (**6bE**)

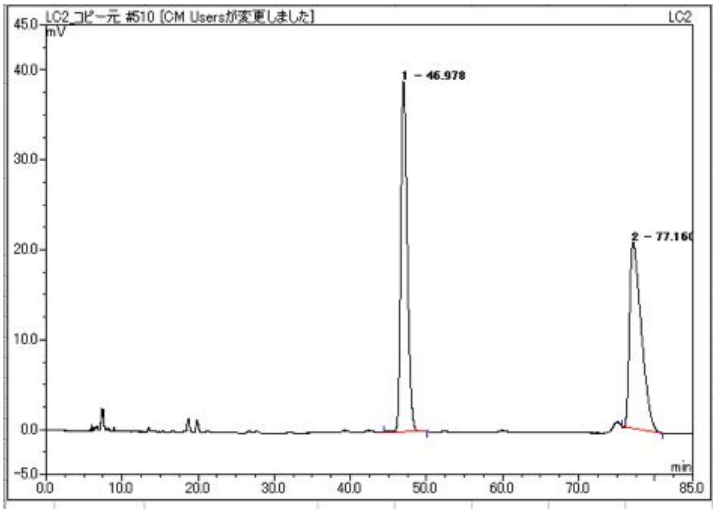


Isolated by preparative TLC eluting with 40% EtOAc/hexane. Yellow oil. Rf = 0.13 (17% EtOAc/hexane). $[\alpha]^{25}_{D}$ +71.8 (*c* 1.80 in $CHCl_3$). IR (neat): 3065, 2924, 2850, 2358, 2343, 1961, 1583, 1447, 1331, 1312, 1156, 1079, 1023, 999, 892, 738, 724, 687 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.01–7.89 (m, 4H), 7.75–7.65 (m, 2H), 7.65–7.52 (m, 4H), 5.19 (ddt, *J* = 6.2, 3.0, 6.2 Hz, 1H), 5.12 (ddt, *J* = 6.2, 6.2, 3.0 Hz, 1H), 4.57 (t, *J* = 6.2 Hz, 1H), 2.88 (dddd, *J* = 6.2, 6.2, 3.0, 1.0 Hz, 2H), 1.96–1.83 (m, 1H), 1.74–1.58 (m, 4H), 1.36–1.15 (m, 4H), 0.99–0.96 (m, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 202.7, 138.2, 138.0, 134.6, 134.5, 129.6, 129.5, 129.1, 100.5, 87.9, 83.0, 37.0, 32.92, 32.89, 25.95, 25.87, 25.86, 25.3. HRMS (ESI) calcd for $C_{23}H_{27}O_4S_2$ 431.1351, found 431.1334 $[M+H]^+$.

Chiral HPLC: (Daicel Chiralpak AD-H, hexane/*i*-propanol = 9/1, 0.5 mL/min, λ = 254 nm): t_R(*R*) = 47.0 min (minor enantiomer), t_R(*S*) = 77.2 min (major enantiomer).

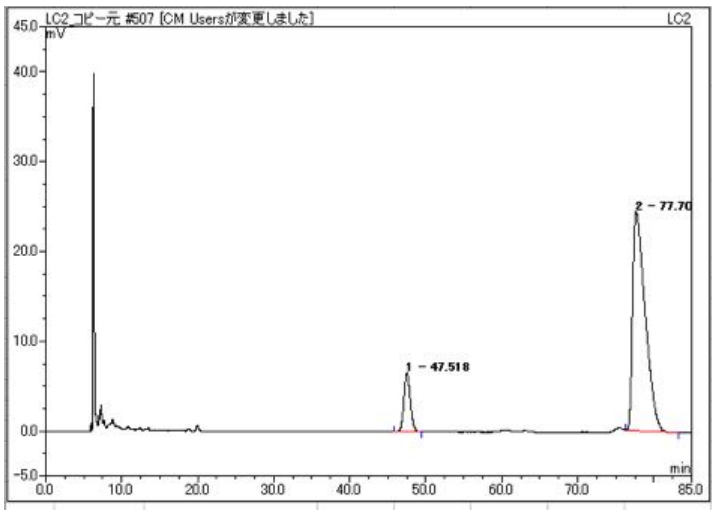
HPLC chromatograms of **6bE**

(±)-**6bE**



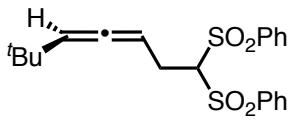
番号	保持時間 分	ピーク名	高さ mV	面積 mV×分	相対面積 %	含有量 n.a.	タイプ
1	46.98	n.a.	38.982	38.276	51.07	n.a.	BMB*
2	77.16	n.a.	20.625	36.672	48.93	n.a.	BMB*
合計:			59.607	74.948	100.00	0.000	

6bE



番号	保持時間 分	ピーク名	高さ mV	面積 mV×分	相対面積 %	含有量 n.a.	タイプ
1	47.52	n.a.	6.537	6.347	11.98	n.a.	BMB*
2	77.70	n.a.	24.439	46.626	88.02	n.a.	BMB*
合計:			30.976	52.973	100.00	0.000	

(*S*)-(6,6-Dimethylhepta-3,4-diene-1,1-diyldisulfonyl)dibenzene (**6dE**)

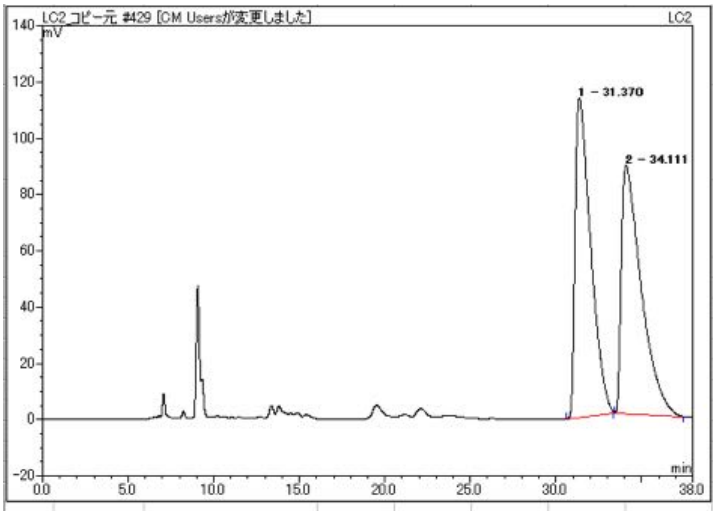


Isolated by preparative TLC eluting with 50% EtOAc/hexane. Yellow oil. Rf = 0.17 (17% EtOAc/hexane). $[\alpha]^{24}_{D}$ +74.8 (c 0.75 in $CHCl_3$). IR (neat): 3066, 2959, 2866, 1962, 1584, 1447, 1332, 1156, 1079, 743, 724, 687 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.02–7.88 (m, 4H), 7.75–7.64 (m, 2H), 7.64–7.55 (m, 4H), 5.23 (dt, *J* = 6.1, 6.1 Hz, 1H), 5.14 (dt, *J* = 6.1, 3.0 Hz, 1H), 4.55 (t, *J* = 6.1 Hz, 1H), 2.88 (ddd, J = 6.1, 6.1, 3.0 Hz, 2H), 0.97 (s, 9H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 201.2, 139.0, 138.3, 137.9, 134.6, 134.5, 129.7, 129.5, 129.1, 106.4, 88.9, 83.1, 31.9, 30.0, 25.5. HRMS (ESI) calcd for $C_{21}H_{25}O_4S_2$ 405.1194, found 405.1180 $[M+H]^+$.

Chiral HPLC: (Daicel Chiralpak OD-H, hexane/*i*-propanol = 9/1, 0.5 mL/min, λ = 254 nm): t_R(*S*) = 31.6 min (major enantiomer), t_R(*R*) = 35.2 min (minor enantiomer).

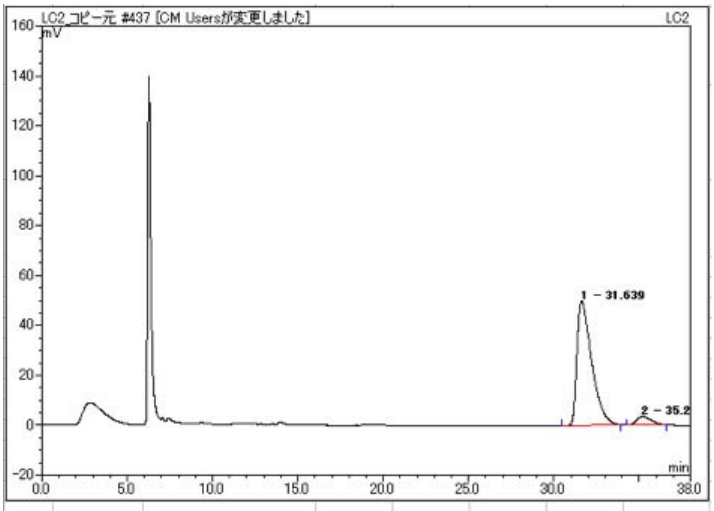
HPLC chromatograms of **6dE**

(±)-**6dE**



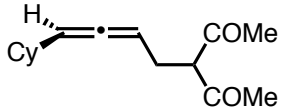
番号	保持時間 分	ピーク名	高さ mV	面積 mV×分	相対面積 %	含有量 n.a.	タイプ
1	31.37	n.a.	113.738	119.649	50.13	n.a.	BMB*
2	34.11	n.a.	88.446	119.017	49.87	n.a.	BMB*
合計:			202.184	238.666	100.00	0.000	

6dE



番号	保持時間 分	ピーク名	高さ mV	面積 mV×分	相対面積 %	含有量 n.a.	タイプ
1	31.64	n.a.	49.717	49.564	93.65	n.a.	BMB*
2	35.20	n.a.	3.330	3.360	6.35	n.a.	BMB*
合計:			53.047	52.924	100.00	0.000	

(*S*)-3-(4-Cyclohexylbuta-2,3-dien-1-yl)pentane-2,4-dione (**6bF**)



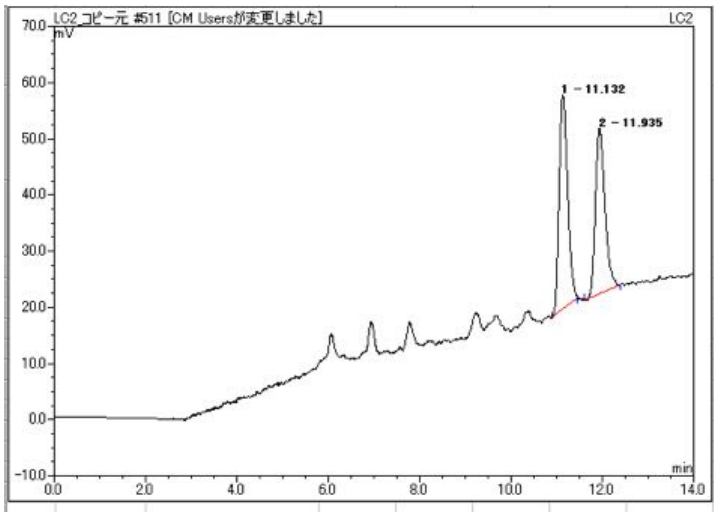
Isolated by silica gel column chromatography eluting with 3% EtOAc/hexane. Yellow oil. Rf = 0.50 (17% EtOAc/hexane). $[\alpha]^{24}_D$ +81.4 (c 0.57 in $CHCl_3$). IR (neat): 2925, 2851, 1961, 1755, 1738, 1437, 1341, 1258, 1231, 1152, 1034, 891 cm^{-1}. ^{1}H-NMR (400

MHz, $CDCl_3$): δ 5.24–5.02 (m, 2H), 2.92 (t, *J* = 4.5 Hz, 1H), 2.58–2.47 (m, 1H), 2.33–2.02 (m, 7H), 2.02–1.83 (m, 1H), 1.83–1.51 (m, 4H), 1.36–0.91 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 203.8, 203.7, 202.9, 202.8, 191.3, 99.33, 99.25, 90.5, 88.5, 67.9, 37.4, 37.2, 33.1, 33.03, 33.00, 32.8, 29.2, 29.1, 27.3, 27.0, 26.14, 26.08, 26.07, 26.01, 25.99, 25.96, 25.94, 22.8 (as a tautomeric mixture of the keto and enol forms). LRMS m/z (relative intensity) 234 $[M]^+$ (9), 191 (81), 134 (47), 121 (100). HRMS (EI) calcd for $C_{15}H_{22}O_2$ 234.1620, found 234.1615 $[M]^+$.

Chiral HPLC: (Daicel Chiralpak AD-H, hexane/*i*-propanol =397/3, 0.5 mL/min, λ = 190 nm): t_R(*R*) = 11.2 min (minor enantiomer), t_R(*S*) = 12.0 min (minor enantiomer).

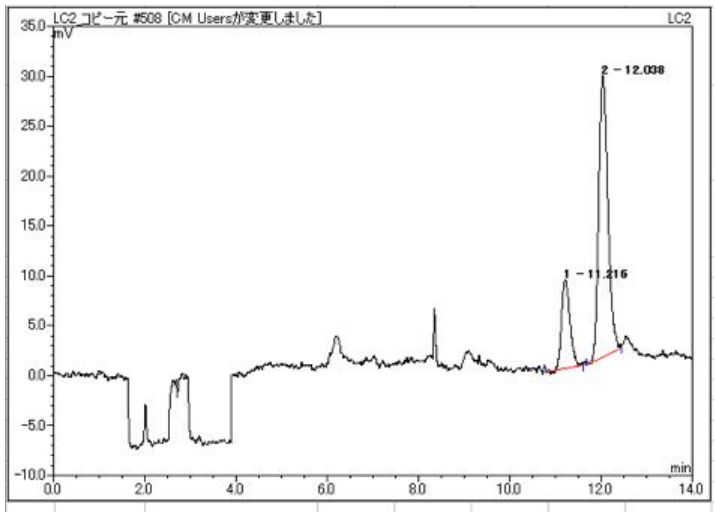
HPLC chromatograms of **6bF**

(±)-**6bF**



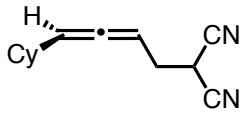
番号	保持時間 分	ピーク名	高さ mV	面積 mV× 分	相対面積 %	含有量 n.a.	タイプ
1	11.13	n.a.	38.203	8.263	53.83	n.a.	BMB*
2	11.94	n.a.	29.360	7.088	46.17	n.a.	BMB*
合計:			67.562	15.351	100.00	0.000	

6bF



番号	保持時間 分	ピーク名	高さ mV	面積 mV× 分	相対面積 %	含有量 n.a.	タイプ
1	11.22	n.a.	8.934	1.904	22.47	n.a.	BMB*
2	12.04	n.a.	28.158	6.570	77.53	n.a.	BMB*
合計:			37.092	8.474	100.00	0.000	

(*S*)-2-(4-Cyclohexylbuta-2,3-dien-1-yl)malononitrile (**6bG**)[9]

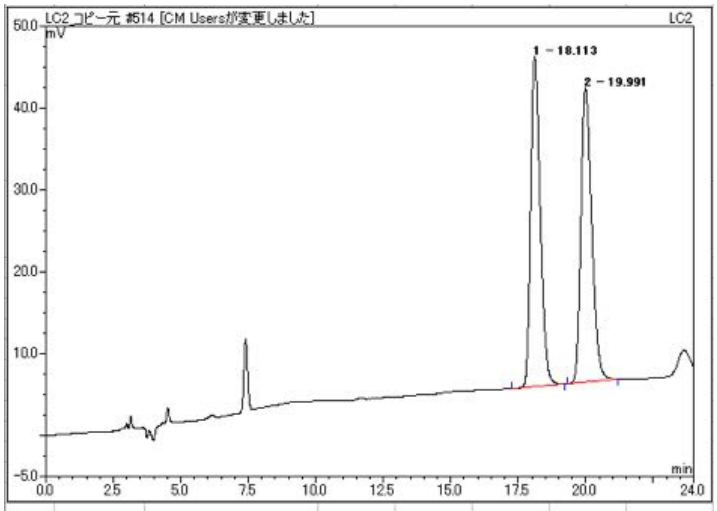


Isolated by silica gel column chromatography eluting with 3% EtOAc/hexane. Yellow solid. Mp = 48.3–49.9 °C. Rf = 0.50 (17% EtOAc/hexane). $[\alpha]^{25}_{D}$ +45.3 (*c* 0.28 in $CHCl_3$). IR (neat): 2925, 2851, 2256, 1963, 1962, 1725, 1448, 1260, 891, 868, 722 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.40 (ddt, *J* = 6.4, 6.4, 3.1 Hz, 1H), 5.23 (ddt, *J* = 3.0, 6.4, 6.4 Hz, 1H), 3.77 (t, *J* = 7.0 Hz, 1H), 2.73–2.64 (m, 2H), 2.13–1.99 (m, 1H), 1.85–1.60 (m, 4H), 1.38–1.02 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 203.8, 112.38, 112.35, 101.5, 85.0, 37.1, 32.9, 32.8, 30.5, 26.0, 25.9, 22.4. LRMS m/z (relative intensity) 200 $[M]^+$ (10), 135 (100), 93 (85), 81 (86). HRMS (EI) calcd for $C_{13}H_{16}N_2$ 200.1313, found 200.1311 $[M]^+$.

Chiral HPLC: (Daicel Chiralpak OD-H, hexane/*i*-propanol = 50/1, 1.0 mL/min, λ = 214 nm): t_R(*S*) = 18.3 min (major enantiomer), t_R(*R*) = 20.4 min (minor enantiomer).

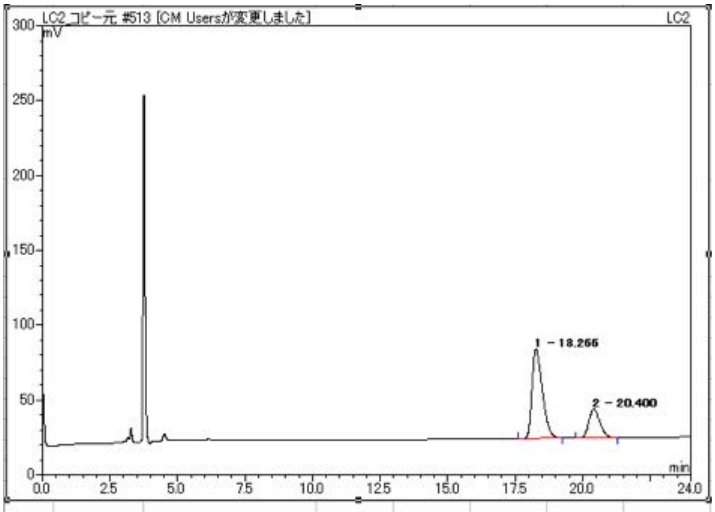
HPLC chromatograms of **6bG**

(±)-**6bG**



番号	保持時間 分	ピーク名	高さ mV	面積 mV× 分	相対面積 %	含有量 n.a.	タイプ
1	18.11	n.a.	40.340	16.576	49.89	n.a.	BMB*
2	19.99	n.a.	35.898	16.648	50.11	n.a.	BMB*
合計:			76.238	33.224	100.00	0.000	

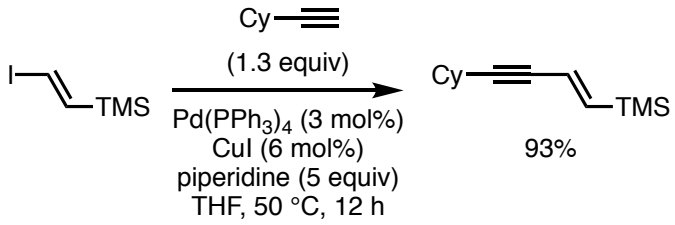
6bG



番号	保持時間 分	ピーク名	高さ mV	面積 mV×分	相対面積 %	含有量 n.a.	タイプ
1	18.27	n.a.	59.874	26.423	74.50	n.a.	BMB*
2	20.40	n.a.	19.114	9.042	25.50	n.a.	BMB*
合計:			78.987	35.464	100.00	0.000	

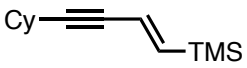
Preparation of 7b-*d*

Preparation of (*E*)-(4-cyclohexylbut-1-en-3-yn-1-yl)trimethylsilane



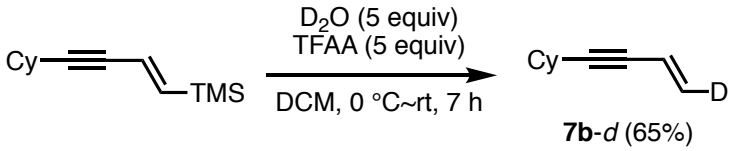
Scheme S4. Preparation of (*E*)-(4-cyclohexylbut-1-en-3-yn-1-yl)trimethylsilane.

To a mixture of ethynylcyclohexane (4.13 g, 38.2 mmol), $Pd(PPh_3)_4$ (1.02 g, 0.882 mmol), and CuI (336 mg, 1.76 mmol) in anhydrous THF (29 mL) were added piperidine (14.5 mL, 147 mmol) and a solution of alkenyl iodide[10] (6.64 g, 29.4 mmol) in anhydrous THF (30 mL) at 0 °C under argon. The mixture was allowed to warm up to room temperature, stirred at 50 °C for 12 h, and then treated with water. The aqueous layer was extracted with Et_2O three times. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was diluted with hexane, filtered through a pad of SiO_2 and concentrated *in vacuo* to give (*E*)-(4-cyclohexylbut-1-en-3-yn-1-yl)trimethylsilane (5.62 g, 93%) as a red-black oil. The oil was pure enough for analysis.



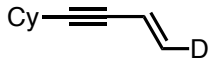
Rf = 0.51 (hexane). IR (neat): 2931, 2854, 2359, 2342, 2208, 1574, 1448, 1249, 975, 865, 839 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.32 (d, *J* = 19.3 Hz, 1H), 5.96 (dd, *J* = 19.3, 1.9 Hz, 1H), 2.53–2.43 (m, 1H), 1.87–1.76 (m, 2H), 1.76–1.64 (m, 2H), 1.64–1.21 (m, 6H), 0.07 (s, 9H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 143.4, 124.1, 95.2, 80.9, 32.7, 29.7, 25.9, 24.9, –1.6. LRMS m/z (relative intensity) 206 $[M]^+$ (24), 191 (100), 125 (44), 109 (28). HRMS (EI) calcd for $C_{13}H_{22}Si$ 206.1491, found 206.1517 $[M]^+$.

Preparation of (*E*)-(but-3-en-1-yn-1-yl-4-*d*)cyclohexane (**7b**-*d*)



Scheme S5. Preparation of (*E*)-(but-3-en-1-yn-1-yl-4-*d*)cyclohexane (**7b**-*d*).

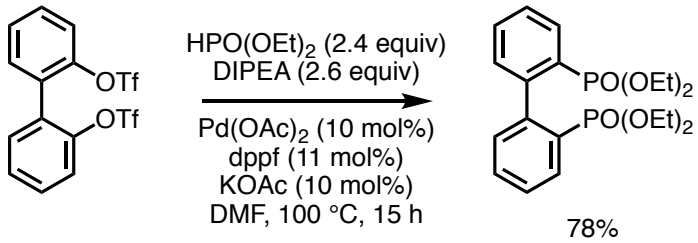
To a solution of (*E*)-(4-cyclohexylbut-1-en-3-yn-1-yl)trimethylsilane (5.62 g, 27.2 mmol) in anhydrous DCM (109 mL) were added D_2O (2.45 mL, 136 mmol) and TFAA (18.9 mL, 136 mmol) at 0 °C under argon.[11] The mixture was allowed to warm up to room temperature, stirred for 7 h, and then treated with saturated aqueous $NaHCO_3$ slowly at 0 °C. The aqueous layer was extracted with DCM three times. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was diluted with hexane and filtered through a pad of SiO_2 (thoroughly washed with hexane). The filtrate was concentrated *in vacuo* and then purified by bulb-to-bulb distillation (120 °C/40 mmHg) to give **7b**-*d* (2.38 g, 65%) as a pale yellow oil.



Rf = 0.56 (hexane).^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.79 (d, *J* = 17.4 Hz, 1H), 5.52 (d, *J* = 17.4 Hz, 1H), 5.36 (dd, *J* = 10.9, 2.0 Hz, 0.08 H), 2.57–2.34 (m, 1H), 1.92–1.61 (m, 4H), 1.61–1.06 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 124.9 (t, *J* = 24.5 Hz), 117.6, 95.1, 79.2, 32.6, 29.6, 25.9, 24.9 (additional small peak at 125.2 ppm due to undeuterated olefinic carbon). LRMS m/z (relative intensity) 135 $[M]^+$ (34), 120 (16), 106 (35), 92 (100). HRMS (EI) calcd for $C_{10}H_{13}D$ 135.1158, found 135.1159 $[M]^+$.

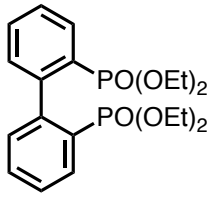
Preparation of 8

Preparation of tetraethyl [1,1'-biphenyl]-2,2'-diylbis(phosphonate)



Scheme S6. Preparation of tetraethyl [1,1'-biphenyl]-2,2'-diylbis(phosphonate).

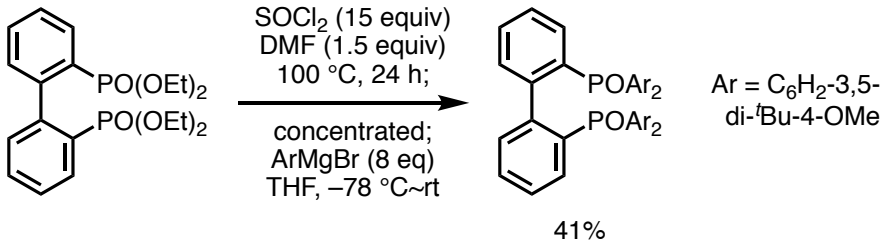
To a 200 mL two-necked flask containing $Pd(OAc)_2$ (397 mg, 1.77 mmol), dppf (1.07 g, 1.93 mmol), and KOAc (172 mg, 1.75 mmol) was added anhydrous DMF (9 mL) under argon. The resulting mixture was stirred at 60 °C for 30 min and cooled to room temperature. Then the mixture was treated with DIPEA (7.80 mL, 45.6 mmol) and $HPO(OEt)_2$ (5.45 mL, 42.2 mmol) and stirred at room temperature for 15 min.[12] A solution of [1,1'-biphenyl]-2,2'-diyl bis(trifluoromethanesulfonate)[13] (7.92 g, 17.6 mmol) in anhydrous DMF (30 mL + 6 mL) was added to the mixture. The mixture was stirred at 100 °C for 15 h and cooled to room temperature. Then, the resulting mixture was diluted with EtOAc (180 mL) and filtered through a pad of Celite (thoroughly washed with EtOAc). The filtrate was washed with water (90 mL x 1, 45 mL x 1) and brine (45 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography eluting with 10% EtOH/EtOAc to give tetraethyl [1,1'-biphenyl]-2,2'-diylbis(phosphonate) (5.82 g, 78%) as a black solid. The analytical sample was obtained as a pale yellow oil after purification using silica gel column chromatography eluting with 3% MeOH/$CHCl_3$.



Rf = 0.64 (10% $CHCl_3$/MeOH). IR (neat): 3670–3120 (br), 2983, 1660, 1589, 1430, 1392, 1231, 1141, 1055, 1025, 971, 765 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10–7.97 (m, 2H), 7.52 (t, *J* = 7.3 Hz, 2H), 7.50–7.39 (m, 4H), 4.08–3.87 (m, 6H), 3.85–3.72 (m, 1H), 1.15 (t, *J* = 7.2 Hz, 6H), 1.10 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 144.0 (dd, *J* = 9.2, 4.2 Hz), 133.0 (d, *J* = 9.8 Hz), 131.7 (d, *J* = 13.7 Hz), 130.8 (d, *J* = 2.9 Hz), 127.7 (d, *J* = 190 Hz), 127.2 (d, *J* = 14.8 Hz), 61.8 (d, *J* = 6.1 Hz), 61.6 (dd, *J* =

6.1 Hz), 16.2 (d, *J* = 6.5 Hz), 16.1 (dd, *J* = 6.5 Hz). ^{31}P-NMR (243 MHz, $CDCl_3$): δ 18.0. HRMS (ESI) calcd for $C_{20}H_{28}NaO_6P_2$ 449.1253, found 449.1247 $(M+Na)^+$.

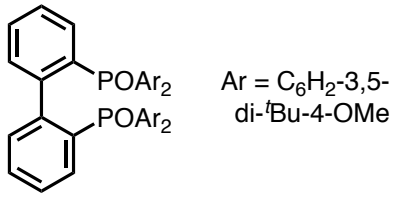
Preparation of [1,1'-biphenyl]-2,2'-diylbis(bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphine oxide)



Scheme S7. Preparation of [1,1'-biphenyl]-2,2'-diylbis(bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphine oxide).

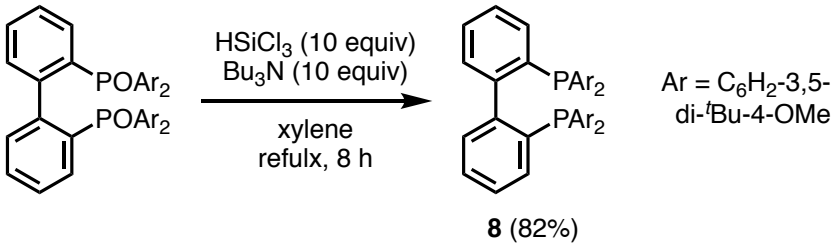
To a 50 mL recovery flask containing tetraethyl [1,1'-biphenyl]-2,2'-diylbis(phosphonate) (2.03 g, 4.76 mmol) were added $SOCl_2$ (5.2 mL, 72 mmol) and anhydrous DMF (0.55 mL, 7.1 mmol) under argon. The resulting mixture was stirred at 100 °C for 24 h and cooled to room temperature. Then the mixture was concentrated *in vacuo* and evaporated with toluene (10 mL x 3) azeotropically to give a crude [1,1'-biphenyl]-2,2'-diylbis(phosphonic dichloride), which was used for the next reaction without further purification.

0.63 M Grignard solution in THF prepared from Mg (1.15 g, 47.3 matom), bromoarene[14] (11.4 g, 38.1 mmol), anhydrous THF 60 mL, and 1,2-dibromoethene (0.33 mL, 3.8 mmol) was treated with a solution of the crude [1,1'-biphenyl]-2,2'-diylbis(phosphonic dichloride) in THF (20 mL + 2 mL) at –78 °C. The resulting mixture was allowed to warm up to room temperature over 12 h. The mixture was cooled to –78 °C and treated with sat. aq. NH_4Cl (80 mL). The aqueous layer was extracted with EtOAc two times. The combined organic layers were washed with brine (40 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography eluting with 16% EtOAc/hexane to give [1,1'-biphenyl]-2,2'-diylbis(bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphine oxide) (2.22 g, 41%) as a white solid.



Mp = 107–108 °C. Rf = 0.40 (33% EtOAc/hexane). IR (neat): 3398 (br), 2964, 2871, 1585, 1448, 1411, 1395, 1362, 1265, 1200, 1148, 1118, 1011, 887, 811, 793, 761, 714, 617 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.70 (d, *J* = 12.4 Hz, 4H), 7.42 (d, *J* = 12.0 Hz, 4H), 7.28–7.22 (m, 2H), 7.20 (dd, *J* = 7.2 , 7.6 Hz, 2H), 7.12 (dd, *J* = 7.6, 7.6 Hz, 4H), 6.80–6.74 (m, 2H), 3.69 (s, 6H), 3.68 (s, 6H), 1.35 (s, 36H), 1.33 (s, 36H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ 161.92 (d, *J* = 3.1 Hz), 161.89 (d, *J* = 3.3 Hz), 145.7 (dd, *J* = 6.6, 3.7 Hz), 143.2 (d, *J* = 11.9 Hz), 143.1 (d, *J* = 12.3 Hz), 132.6 (d, *J* = 102.2 Hz), 132.4 (d, *J* = 12.3 Hz), 131.9 (d, *J* = 11.6 Hz), 131.0 (d, *J* = 9.8 Hz), 130.6 (d, *J* = 10.8 Hz), 129.19 (d, *J* = 104.9 Hz), 129.18 (d, *J* = 2.3 Hz), 128.1 (d, *J* = 108.2 Hz), 126.1 (d, *J* = 12.5 Hz), 64.4, 64.2, 35.93, 35.87, 31.99, 31.97. ^{31}P-NMR (243 MHz, $CDCl_3$): δ 27.4. HRMS (ESI) calcd for $C_{72}H_{101}O_6P_2$ 1123.7068, found 1123.7035 $[M+H]^+$.

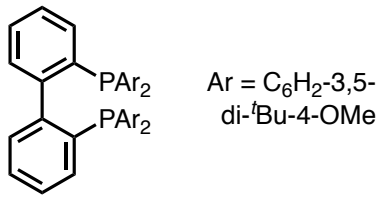
Preparation of 2,2'-bis(bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphaneyl)-1,1'-biphenyl (**8**)



Scheme S8. Preparation of 2,2'-bis(bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphaneyl)-1,1'-biphenyl (**8**).

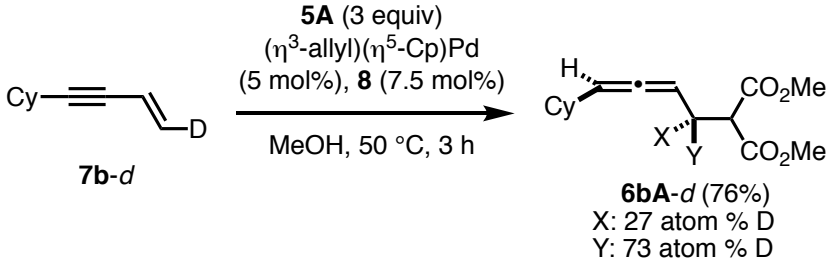
To a 50 mL recovery flask containing [1,1'-biphenyl]-2,2'-diylbis(bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphine oxide) (1.12 g, 0.997 mmol) were added anhydrous xylene (10 mL) and tributylamine (2.4 mL, 10 mmol) under argon. The resulting mixture was stirred at 0 °C and treated with $HSiCl_3$ (1.0 mL, 9.9 mmol).[15] The mixture was stirred at 0 °C for 15 min, refluxed for 8 h, cooled to

0 °C, and treated with 7.5 M aqueous NaOH (15 mL). The immiscible mixture was stirred at 60 °C for 2 h, cooled to room temperature, and extracted with toluene. The organic phase was washed with water (10 mL), 1 M aqueous HCl (15 mL), water (10 mL), and brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography eluting with 4% EtOAc/hexane to give **8** (894 mg, 82%) as a white solid. The analytical sample was obtained by recrystallization from MeOH.



Mp = 116–117 °C. Rf = 0.50 (10% EtOAc/hexane). IR (neat): 2962, 2870, 1578, 1447, 1409, 1361, 1263, 1223, 1140, 1117, 885, 754 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.31 (dd, *J* = 3.6, 3.6 Hz, 4H), 7.19 (ddd, *J* = 7.6, 7.6, 1.4 Hz, 2H), 7.06 (dd, *J* = 7.6, 1.0 Hz, 2H), 7.03 (ddd, *J* = 7.2 , 7.6, 1.0 Hz, 2H), 7.00 (dd, *J* = 3.6, 3.6 Hz, 4H), 6.66 (d, *J* = 7.2 Hz, 2H), 3.68 (s, 6H), 3.63 (s, 6H), 1.32 (s, 36H), 1.29 (s, 36H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ 159.9, 159.4, 147.1 (t, *J* = 17.5 Hz), 142.8 (t, *J* = 3.1 Hz), 142.6 (t, *J* = 3.8 Hz), 139.0 (dd, *J* = 6.1, 5.8 Hz), 133.0, 132.8 (t, *J* = 11.5 Hz), 132.3 (t, *J* = 11.5 Hz), 132.0 (dd, *J* = 6.8, 6.5 Hz), 131.4 (dd, *J* = 6.3, 5.0 Hz), 130.3 (t, *J* = 3.7 Hz), 64.2, 64.1, 35.8, 35.7, 32.2, 32.0. ^{31}P-NMR (243 MHz, $CDCl_3$): δ −13.9. HRMS (ESI) calcd for $C_{72}H_{101}O_4P_2$ 1092.7203, found 1092.7174 $[M+H]^+$.

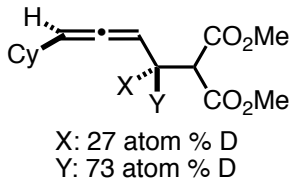
Hydroalkylation of 7b-*d* with 5A under the catalysis of Pd-achiral diphosphine 8 (Scheme 2)



Scheme S9. Hydroalkylation of **7b**-*d* with **5A** under the catalysis of Pd-achiral diphosphine **8**.

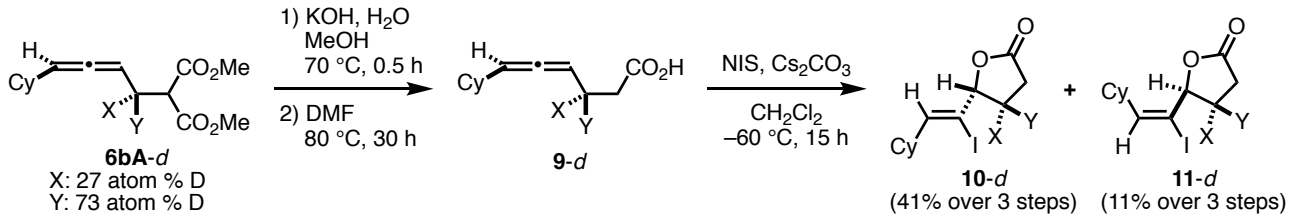
To a test tube containing enyne **7b**-*d* (84.9 mg, 0.628 mmol), (η^3-allyl)(η^5-Cp)Pd (6.7 mg, 0.031 mmol), and diphosphine **8** (51.4 mg, 0.0471 mmol) were added anhydrous MeOH (2.5 mL) and dimethyl malonate (216 μL, 1.88 mmol) under argon. The resulting mixture was sealed with a screw cap and stirred at 50 °C for 3 h. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The residue was purified by silica gel column chromatography eluting with 3% EtOAc/hexane and preparative TLC eluting with 20% EtOAc/hexane to give **6bA**-*d* (128 mg, 76%) as a pale yellow oil. The diastereomeric ratio and stereochemistry of **6bA**-*d* were determined using NMR analysis of γ-lactone **10**-*d* prepared according to the following procedure.

Dimethyl 2-(4-cyclohexylbuta-2,3-dien-1-yl-1-*d*)malonate (**6bA**-*d*) as a 73:27 diastereomeric mixture



Rf = 0.29 (17% EtOAc/hexane). IR (neat): 2925, 2850, 1962, 1737, 1435, 1250, 1153, 1030, 891 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.15–5.12 (m, 2H), 3.740 (s, 3H), 3.737 (s, 3H), 3.50 (d, *J* = 7.3 Hz, 1H), 2.62–2.51 (m, 1H), 1.99–1.86 (m, 1H), 1.79–1.58 (m, 4H), 1.34–0.96 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 202.8, 169.4, 169.3, 98.9, 88.2, 52.5, 52.4, 51.2, 37.1, 32.9, 32.8, 27.8 (t, *J* = 20.2 Hz), 26.1, 26.0 (additional small peak at 28.1 ppm due to undeuterated allylic carbon). HRMS (ESI) calcd for $C_{15}H_{22}DO_4$ 268.1659, found 268.1649 $[M+H]^+$.

Conversion of 6bA-*d* into stereodefined iodolactone 10-*d* and 11-*d* (Scheme 2)



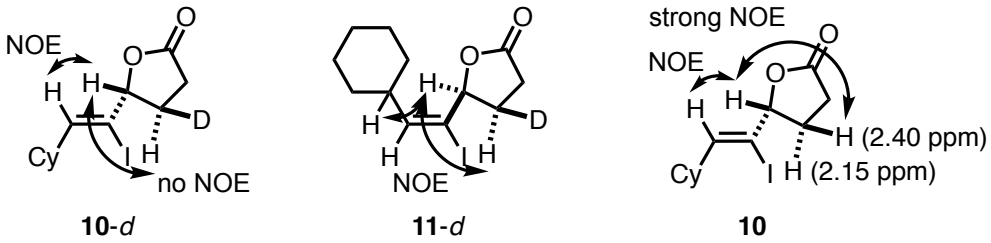
Scheme S10. Conversion of **6bA**-*d* into stereodefined iodolactone **10**-*d* and **10**-*d*.

To a solution of **6bA**-*d* (62.9 mg, 0.235 mmol) in anhydrous MeOH (0.9 mL) were added KOH (56.7 mg, 0.940 mmol) and H_2O (24 μL).[2] The resulting mixture was stirred at 70 °C for 30 min, and then treated with aqueous 3 M HCl. The aqueous layer was extracted with EtOAc twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude dicarboxylic acid, which was used for the next reaction without further purification.

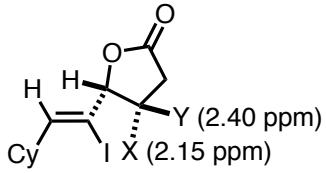
A solution of the crude dicarboxylic acid in anhydrous DMF (0.5 mL) was sealed with a screw cap and stirred at 80 °C for 30 h.[16] The reaction mixture was cooled to room temperature and concentrated *in vacuo* to give a crude monocarboxylic acid **9**-*d*, which was used for the next reaction without further purification.

To a solution of the crude acid **9**-*d* in anhydrous DCM (2.8 mL) was added Cs_2CO_3 (115 mg, 0.323 mmol) under argon. The resulting mixture was stirred at room temperature for 1.5 h, cooled to –60 °C, and then treated with NIS (159 mg, 0.705 mmol).[17] The reaction mixture was stirred at the same temperature for 15 h, and then treated with water and saturated aqueous $Na_2S_2O_3$. The aqueous layer was extracted with Et_2O three times. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography eluting with 7–10% EtOAc/hexane and then HPLC (eluent: hexane/*i*-propanol = 95/5, flow rate: 2 mL/min, t_R = 14.5 min (minor **11**-*d*) and t_R = 16.0 min (major **10**-*d*)) to give **11**-*d* (8.5 mg, 11%) and **10**-*d* (30.7 mg, 41%) as a white solid and a white solid, respectively.

The stereochemistries of **10**-*d* and **11**-*d* were established by their NOESY spectra. While the methine proton at γ-position in **10**-*d* had NOE with vinyl proton and no NOE with major residual proton as X at β-position, the γ-proton in **11**-*d* had NOE with major residual proton as X and no NOE with vinyl proton. The chemical shifts of geminal protons at β-position in **10**-*d* and **11**-*d* also agreed with those reported for γ-vinyl-γ-butyrolactone, where the vinyl group shielded and deshielded *cis*- and *trans*-protons, respectively.[18] The shielded X and deshielded Y were also observed after reductive deiodination of **10**-*d* (vide infra). The corresponding undeuterated iodolactone **10** was also prepared from **6bA** by the same procedure described above and its NOESY spectrum showed a strong NOE between the methine δ-proton and β-proton located trans to the adjacent alkenyl group at 2.40 ppm.



(4*R**,5*R**)-5-((*Z*)-2-Cyclohexyl-1-iodovinyl)dihydrofuran-2(3*H*)-one-4-*d* (**10**-*d*)

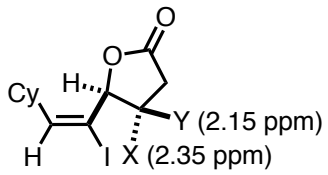


10-*d*
X: 27 atom % D
Y: 73 atom % D

White solid. Mp = 101 °C. Rf = 0.24 (17% EtOAc/hexane). IR (neat): 2924, 2849, 1781, 1635, 1447, 1317, 1258, 1165, 1006, 965, 896, 661 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.85 (d, *J* = 8.5 Hz, 1H), 4.76 (d, *J* = 6.8 Hz, 1H), 2.66 (dd, *J* = 18.0, 10.0, 1H), 2.53 (dd, *J* = 10.0, 8.8 Hz, 1H), 2.45–2.36 (m, 0.27H), 2.36–2.24 (m, 1H), 2.22–2.09 (m, 0.73H), 1.82–1.60 (m, 4H), 1.41–1.04 (m, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 176.4, 143.0, 104.3, 84.2, 44.6, 31.31, 31.29, 28.4 (t, *J* = 13.9 Hz), 28.0, 25.8, 25.5 (additional small peak at 28.7 ppm due to undeuterated homoallylic carbon). LRMS m/z (relative intensity) 321 $[M]^+$ (46), 240 (49), 194 (100), 152 (65). HRMS (EI) calcd for $C_{12}H_{16}DIO_2$ 321.0336 found 321.0333 $[M]^+$.

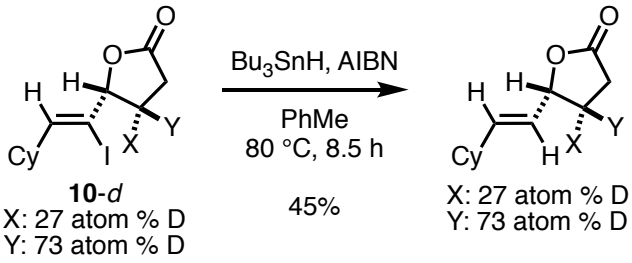
(4*R**,5*S**)-5-((*E*)-2-Cyclohexyl-1-iodovinyl)dihydrofuran-2(3*H*)-one-4-*d* (**11**-*d*)



11-*d*
X: 28 atom % D
Y: 72 atom % D

White solid. Rf = 0.24 (17% EtOAc/hexane). IR (neat): 2924, 2850, 1783, 1541, 1448, 1418, 1363, 1318, 1263, 1197, 1156, 1010, 961, 899, 802, 740, 697, 657 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.33 (d, *J* = 9.6 Hz, 1H), 5.90 (d, *J* = 7.2 Hz, 1H), 2.79–2.71 (m, 1H), 2.59 (dd, *J* = 18.6, 10.2, 1H), 2.49–2.39 (m, 1H), 2.39–2.30 (m, 0.72H), 2.20–2.10 (m, 0.28H), 1.80–1.55 (m, 4H), 1.35–1.12 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 176.2, 151.8, 101.5, 77.2, 41.1, 33.1, 32.7, 28.5 (t, *J* = 20.9 Hz), 28.3, 25.53, 25.50, 25.38 (additional small peak at 28.8 ppm due to undeuterated homoallylic carbon). HRMS (ESI) calcd for $C_{12}H_{17}DIO_2$ 322.0414 found 322.0409 $[M+H]^+$.

Reductive Deiodination of 10-*d*



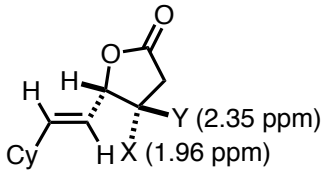
10-*d*
X: 27 atom % D
Y: 73 atom % D

X: 27 atom % D
Y: 73 atom % D

Scheme S11. Conversion of **6bA**-*d* into stereodefined iodolactone **10**-*d* and **10**-*d*.

To a solution of **10**-*d* (22.0 mg, 0.0687 mmol) in anhydrous PhMe (1.3 mL) were added Bu_3SnH (66.7 μL, 0.412 mmol) and AIBN (4.3 mg, 0.026 mmol) under argon. The mixture was stirred at 80 °C for 8.5 h. The reaction mixture was cooled to room temperature and concentrated in *vacuo*. The residue was purified by silica gel column chromatography eluting with 7–10% EtOAc/hexane and then HPLC (eluent: 5% i-PrOH/hexane, flow rate: 2 mL/min) to give **12** (6.1 mg, 45%) as a colorless oil.

(4*R**,5*R**)-5-((*E*)-2-Cyclohexylvinyl)dihydrofuran-2(3*H*)-one-4-*d*

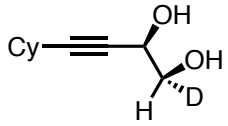


X: 27 atom % D
Y: 73 atom % D

Rf = 0.44 (25% EtOAc/PhMe). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 5.75 (dd, *J* = 15.6, 6.5 Hz, 1H), 5.44 (dd, *J* = 15.6, 7.2 Hz, 1H), 4.88 (dd, *J* = 7.2, 7.2 Hz, 1H), 2.57–2.46 (m, 2H), 2.37–2.31 (m, 0.3H), 2.02–1.91 (1.7H), 1.78–1.59 (m, 4H), 1.37–1.00 (m, 6H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ 177.1, 141.3, 125.0, 81.3, 40.3, 32.6, 32.6, 29.8, 29.4, 29.0, 28.8, 28.7, 28.7, 28.5, 26.1, 26.0. LRMS m/z (relative intensity) 195 $[M]^+$ (27), 135 (48), 121 (39), 112 (100). HRMS (EI) calcd for $C_{12}H_{17}DO_2$ 195.1370 found 195.1375 $[M]^+$.

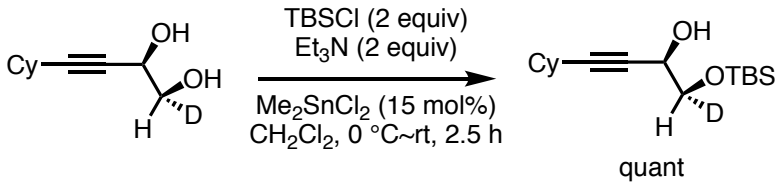
Preparation of (*S*a, *S*)-2b-*d*

(1*R*, 2*R*)-4-Cyclohexylbut-3-yne-1-*d*-1,2-diol was prepared by asymmetric dihydroxylation of **7b**-*d* according to the literature procedure.[19]



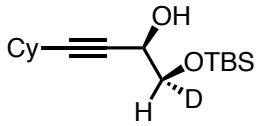
White solid. Mp = 42.6 °C. Rf = 0.53 (67% EtOAc/hexane). $[\alpha]^{24}_{D}$ −13.6 (*c* 1.00 in $CHCl_3$). IR (neat): 3353 (br), 2929, 2853, 2656, 2361, 2332, 2227, 1450, 1444, 1087, 1048, 1030, 889, 865 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.45 (d, *J* = 6.6 Hz, 1H), 3.61 (d, *J* = 6.6 Hz, 1H), 2.60–2.11 (br, 3H), 1.86–1.59 (m, 4H), 1.59–1.04 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 91.3, 77.5, 66.5 (t, *J* = 20.0 Hz), 63.4, 32.5, 29.0, 25.7, 24.8 (additional small peak at 66.9 ppm due to undeuterated homopropargylic carbon). LRMS m/z (relative intensity) 169 $[M]^+$ (0.4), 137 (100), 119 (11), 91 (33). HRMS (EI) calcd for $C_{10}H_{15}DO_2$ 169.1213, found 169.1213 $[M]^+$.

(1*R*, 2*R*)-1-((*tert*-Butyldimethylsilyl)oxy)-4-cyclohexylbut-3-yn-1-*d*-2-ol



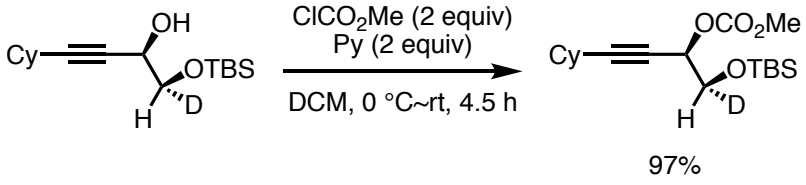
Scheme S12. Monosilylation of diol.

To a solution of diol (846 mg, 5.00 mmol) in anhydrous DCM (30 mL) were added Et_3N (1.4 mL, 10.0 mmol), Me_2SnCl_2 (165 mg, 0.750 mmol), and TBSCl (1.09 g, 10.0 mmol) at 0 °C under argon.[20] The mixture was allowed to warm to room temperature and stirred for 2.5 h, and then treated with water. The aqueous layer was extracted with DCM three times. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography eluting with 2–3% EtOAc/hexane to give TBS ether (1.43 g, quant) as a colorless oil.



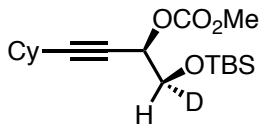
Rf = 0.56 (17% EtOAc/hexane). $[\alpha]^{24}_{D}$ −12.3 (*c* 0.98 in $CHCl_3$). IR (neat): 2930, 2856, 2361, 2342, 2231, 2151, 1254, 1125, 1050, 837, 777, 668 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.39 (ddd, *J* = 7.3, 4.4, 1.6 Hz, 1H), 3.58 (d, *J* = 7.3 Hz, 1H), 2.53 (d, *J* = 4.4 Hz, 1H), 2.43–2.31 (m, 1H), 1.85–1.61 (m, 4H), 1.61–1.20 (m, 6H), 0.91 (s, 9H), 0.10 (s, 3H), 0.90 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 90.2, 77.7, 67.0 (t, *J* = 20.0 Hz), 63.2, 32.5, 29.0, 25.82, 25.80, 24.9, 18.3, −5.35, −5.39 (additional small peak at 67.4 ppm due to undeuterated homopropargylic carbon). LRMS m/z (relative intensity) 283 $[M]^+$ (2), 251 (10), 226 (100), 134 (40). HRMS (EI) calcd for $C_{16}H_{29}DO_2Si$ 283.2078, found 283.2084 $[M]^+$.

(1*R*, 2*R*)-1-((*tert*-Butyldimethylsilyl)oxy)-4-cyclohexylbut-3-yn-2-yl-1-*d* methyl carbonate



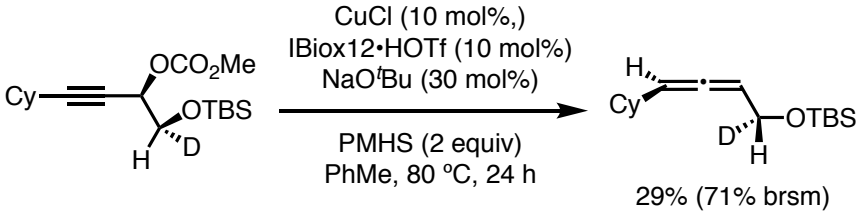
Scheme S13. Introduction of leaving group.

To a solution of the alcohol (140 mg, 0.494 mmol) in anhydrous DCM (0.8 mL) were added pyridine (63 µL, 0.78 mmol) and methyl chloroformate (61 µL, 0.78 mmol) at 0 °C under argon. The mixture was stirred at room temperature for 4.5 h, and then treated with water. The aqueous layer was extracted with Et_2O twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo.* The residue was purified by preparative TLC eluting with 6% EtOAc/hexane to give carbonate (164 mg, 97%) as a colorless oil.



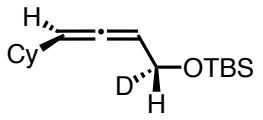
Rf = 0.68 (17% EtOAc/hexane). $[\alpha]^{18}_{D}$ −41.7 (*c* 1.21 in $CHCl_3$). IR (neat): 2931, 2856, 2239, 2158, 1757, 1577, 1472, 1463, 1443, 1409, 1389, 1362, 1340, 1268, 1140, 1106, 1084, 1007, 986, 939, 890, 873, 838, 815, 778, 740, 667 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.33 (dd, *J* = 8.0, 1.7 Hz, 1H), 3.98–3.75 (m, 1H), 3.79 (s, 3H), 2.47–2.33 (m, 1H), 1.86–1.25 (m, 10H), 0.88 (s, 9H), 0.08 (s, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 155.2, 92.1, 74.3, 69.4, 65.0 (t, *J* = 22.0 Hz), 54.8, 32.3, 29.0, 25.8, 25.7, 24.7, 18.2, –5.4 (additional small peak at 65.3 ppm due to undeuterated homopropargylic carbon). LRMS m/z (relative intensity) 341 $[M]^+$ (0.04), 310 (0.3), 284 (3), 240 (10), 133 (100). HRMS (EI) calcd for $C_{18}H_{31}DO_4Si$ 341.2133 found 341.2138 $[M]^+$.

***tert*-Butyl(((1*R*, 3*S*)-4-cyclohexylbuta-2,3-dien-1-yl-1-*d*)oxy)dimethylsilane**



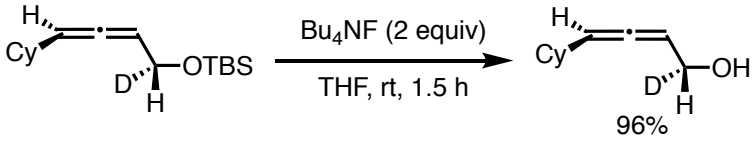
Scheme S14. SN2' anti reduction of propargyl carbonate.

To a test tube containing CuCl (7.0 mg, 0.0707 mmol), IBiox12·HOTf (42.5 mg, 0.0700 mmol), and NaO^{t}Bu (20.2 mg, 0.210 mmol) was added anhydrous PhMe (2.8 mL) under argon.[21] The mixture was stirred at 40 °C for 1 h, treated with PMHS (23.7 μL, 1.40 mmol), and stirred at room temperature for 5 min. To the resulting mixture was added carbonate (239 mg, 0.700 mmol). The mixture was stirred at 80 °C for 24 h and cooled to room temperature. The mixture was poured into saturated aqueous Na_2CO_3 and Et_2O, and was stirred for 1 h. The aqueous layer was extracted with Et_2O twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by preparative TLC eluting with 2% EtOAc/hexane to give allene (54.7 mg, 29%) as a colorless oil and the recovered substrate (140 mg, 59%).



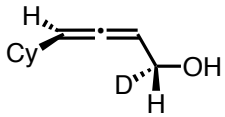
Rf = 0.16 (hexane). $[\alpha]^{23}_{D}$ +48.6 (*c* 1.08 in $CHCl_3$). IR (neat): 2927, 2854, 2363, 2141, 1962, 1471, 1448, 1361, 1254, 1095, 1006, 951, 836, 775, 704 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.23 (ddd, *J* = 6.1, 6.1, 2.7 Hz, 1H), 5.16 (ddd, *J* = 6.1, 6.1, 2.7 Hz, 1H), 4.19–4.14 (m, 1H), 2.05–1.92 (m, 1H), 1.80–1.53 (m, 4H), 1.34–1.01 (m, 6H), 0.90 (s, 9H), 0.08 (s, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 202.4, 98.3, 92.5, 61.9 (t, *J* = 22.5 Hz), 37.1, 33.12, 33.10, 26.2, 26.0, 18.4, −5.06, −5.08 (additional small peak at 62.2 ppm due to undeuterated allylic carbon). LRMS m/z (relative intensity) 267 $[M]^+$ (0.3), 210 (100), 209 (33), 128 (62). HRMS (EI) calcd for $C_{16}H_{29}DOSi$ 267.2129 found 267.2123 $[M]^+$.

(1*R*, 3*S*)-4-Cyclohexylbuta-2,3-dien-1-*d*-1-ol



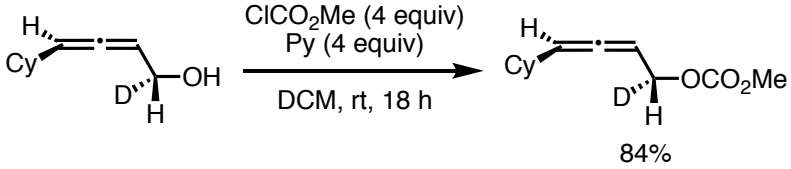
Scheme S15. Removal of TBS group.

To a test tube containing substrate (54.7 mg, 0.204 mmol) were added anhydrous THF (0.8 mL) and 1 M Bu_4NF solution in THF (408 μL, 0.41 mmol) under argon. The resulting mixture was sealed with a screw cap, stirred at room temperature for 1.5 h, and then treated with saturated aqueous NH_4Cl. The aqueous layer was extracted with Et_2O twice. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo.* The residue was purified by preparative TLC eluting with 20% EtOAc/hexane to give allenic alcohol (30.1 mg, 96%) as a colorless oil. The enantiomeric ratio (*er*) of **6aA** was (1*R*, 3*S*):(1*S*, 3*R*) = 84:16, which was determined by HPLC analysis with chiral stationary phase column (Daicel Chiralpak AS-H, hexane/*i*-propanol = 50/1, 0.6 mL/min, λ = 214 nm, t_R(1*S*, 3*R* - minor enantiomer) = 14.9 min, t_R(1*R*, 3*S* - major enantiomer) = 16.1 min).[22]



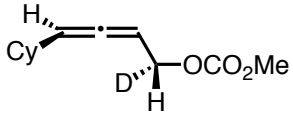
Rf = 0.30 (17% EtOAc/hexane). $[\alpha]^{27}_{D}$ +43.8 (*c* 0.69 in $CHCl_3$). IR (neat): 3341 (br), 2924, 2850, 2158, 1961, 1448, 1290, 1066, 1046, 1017, 890 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.45–5.12 (m, 2H), 4.22–4.00 (m, 1H), 2.09–1.84 (m, 1H), 1.84–1.47 (m, 4H), 1.38–0.98 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 201.9, 100.0, 92.6, 60.5 (t, *J* = 22.5 Hz), 37.0, 33.04, 32.98, 26.0, 25.92, 25.91 (additional small peak at 60.8 ppm due to undeuterated allylic carbon). LRMS m/z (relative intensity) 153 $[M]^+$ (4), 137 (27), 121 (36), 108 (100). HRMS (EI) calcd for $C_{10}H_{15}DO$ 153.1264 found 153.1246 $[M]^+$.

(1*R*, 3*S*)-4-Cyclohexylbuta-2,3-dien-1-yl-1-*d* methyl carbonate ((*Sa*, *R*)-2b-*d*)



Scheme S16. Formation of methyl carbonate (*Sa*, *R*)-**2b**-*d*.

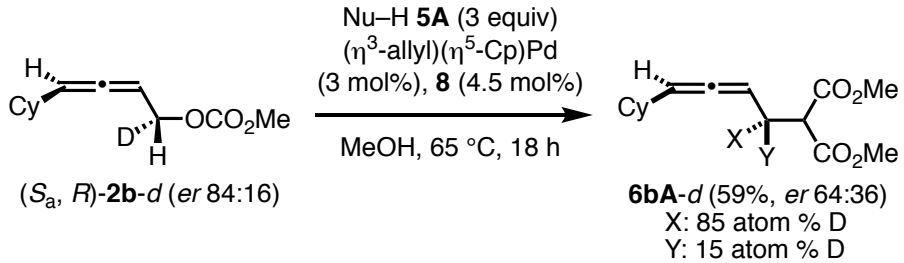
To a solution of the allenic alcohol (30.1 mg, 0.196 mmol) in anhydrous DCM (0.8 mL) were added pyridine (63 μL, 0.78 mmol) and methyl chloroformate (61 μL, 0.78 mmol) under argon. The mixture was stirred at room temperature for 18 h and then treated with water. The aqueous layer was extracted with Et_2O twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo.* The residue was purified by preparative TLC eluting with 10% EtOAc/hexane to give allenic carbonate (34.9 mg, 84%) as a colorless oil.



Rf = 0.68 (17% EtOAc/hexane). $[\alpha]^{23}_{D}$ +31.0 (*c* 1.06 in $CHCl_3$). IR (neat): 2925, 2851, 1964, 1750, 1444, 1340, 1265, 946, 791 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.36–5.19 (m, 2H), 4.63–4.50 (m, 1H), 3.79 (s, 3H), 2.05–1.93 (m, 1H), 1.79–1.51 (m, 6H), 1.40–0.96 (m, 4H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 204.7, 155.6, 99.0, 87.2, 66.1 (t, *J* = 23.0 Hz), 54.7, 36.8, 32.8, 26.0, 25.90, 25.88 (additional small peak at 66.4 ppm due to undeuterated allylic carbon). LRMS m/z (relative intensity) 136 $[M-OCO_2Me]^+$ (3), 119 (15), 107 (43), 92 (43), 83 (100). HRMS (EI) calcd for $C_{10}H_{14}D$ 136.1237 found 136.1235 $[M-OCO_2Me]^+$.

Substitution reaction of (*Sa*, *R*)-2b-*d* with 5A under the catalysis of Pd-diphosphine 8 in the absence or presence of LiI

In the absence of LiI

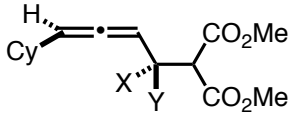


Scheme S17. Substitution reaction of (*Sa*, *R*)-**2b**-*d* with **5A** under the catalysis of Pd-diphosphine **8** in the absence of LiI.

To a test tube containing (*Sa*, *R*)-**2b**-*d* (25.0 mg, 0.118 mmol), (η^3-allyl)(η^5-Cp)Pd (0.8 mg, 0.004 mmol), and **8** (5.8 mg, 0.0053 mmol) were added anhydrous MeOH (1.2 mL) and dimethyl malonate (41 μL, 0.354 mmol) under argon. The resulting mixture was sealed with a screw cap and stirred at 65 °C for 18 h. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The residue was purified by preparative TLC eluting with 10% EtOAc/hexane to give **6bA**-*d* (18.5 mg, 59%) as a colorless oil. The enantiomeric ratio (*er*) of **6bA**-*d* was (1*R*, 3*S*):(1*S*, 3*R*) = 64:36, which was determined by HPLC analysis with chiral stationary phase column (Daicel Chiralpak OD-H, hexane/*i*-propanol = 397/3, 0.5 mL/min, λ = 210 nm, t_R(3*S* -

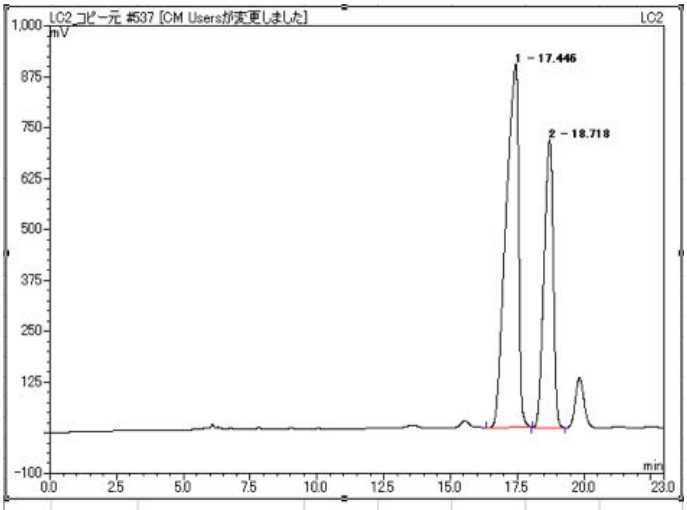
major enantiomer) = 17.5 min, t_R(3*R* - minor enantiomer) = 18.7 min). The diastereomeric ratio and stereochemistry of **6bA**-*d* were determined using NMR analysis of γ-lactone **10**-*d* prepared according to the following procedure.

Dimethyl 2-((1*R*,3*S*)-4-cyclohexylbuta-2,3-dien-1-yl-1-*d*)malonate (**6bA**-*d*)



X: 85 atom % D
Y: 15 atom % D

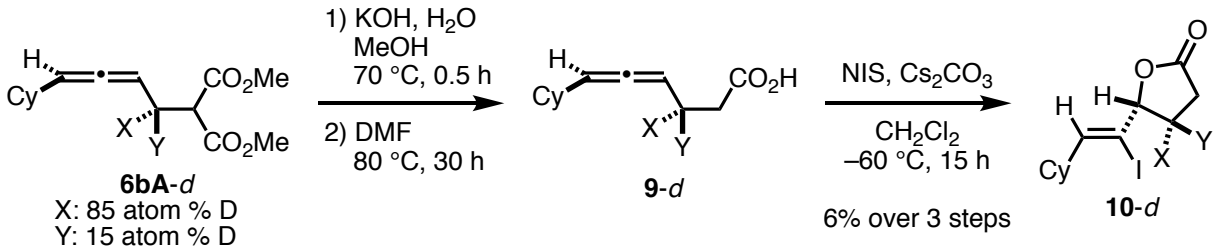
Rf = 0.29 (17% EtOAc/hexane). $[\alpha]^{23}_D$ +33.4 (*c* 0.50 in $CHCl_3$). IR (neat): 2925, 2851, 1961, 1755, 1738, 1436, 1262, 1154, 1038, 892 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.14 (m, 2H), 3.74 (s, 6H), 3.50 (d, *J* = 7.6 Hz, 1H), 2.66–2.52 (m, 1H), 2.02–1.81 (m, 1H), 1.81–1.58 (m, 4H), 1.34–0.95 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 202.9, 169.42, 169.37, 99.0, 88.2, 52.49, 52.47, 51.2, 37.2, 32.94, 32.88, 27.9 (t, *J* = 20.5 Hz), 26.1, 26.0 (additional small peak at 28.1 ppm due to undeuterated allylic carbon). HRMS (ESI) calcd for $C_{15}H_{22}DO_4$ 268.1659, found 268.1649 $[M+H]^+$.



番号	保持時間 分	ピーク名	高さ mV	面積 mV×分	相対面積 %	含有量 n.a.	タイプ
1	17.45	n.a.	892.451	489.217	63.52	n.a.	BMB*
2	18.72	n.a.	707.386	280.980	36.48	n.a.	BMB*
合計:			1599.837	770.197	100.00	0.000	

6bA-*d* obtained from (*Sa*, *R*)-**2b**-*d* was also converted into iodolactone **10**-*d* (6% over 3 steps) and overall retention of the stereoselectivity in the substitution reaction of (*Sa*, *R*)-**2b**-*d* with **5A** was confirmed.

Conversion of 6bA-*d* into stereodefined iodolactone 10-*d*



6bA-*d*
X: 85 atom % D
Y: 15 atom % D

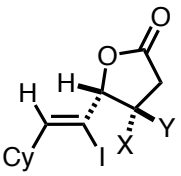
9-*d*

6% over 3 steps

10-*d*

Scheme S18. Conversion of **6bA**-*d* into stereodefined iodolactone **10**-*d*.

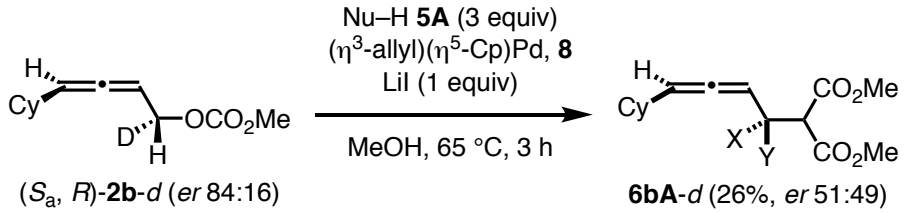
(4*S*, 5*R*)-5-((*Z*)-2-Cyclohexyl-1-iodovinyl)dihydrofuran-2(3H)-one-4-*d* (**10**-*d*)



X: 85 atom % D
Y: 15 atom % D

White solid. Rf = 0.24 (17% EtOAc/hexane). IR (neat): 2923, 2849, 1780, 1450, 1317, 1165, 1009 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.85 (d, *J* = 8.8 Hz, 1H), 4.76 (d, *J* = 7.6 Hz, 1H), 2.82–2.60 (m, 1H), 2.60–2.47 (m, 1H), 2.47–2.37 (m, 0.85H), 2.37–2.23 (m, 1H), 2.23–2.10 (m, 0.15H) 1.60 (m, 4H), 1.20 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 176.5, 143.1, 104.3, 84.2, 44.6, 31.3, 31.2, 28.4 (t, *J* = 21.0 Hz), 28.0, 25.7, 25.4 (additional small peak at 28.7 ppm due to undeuterated homoallylic carbon). LRMS m/z (relative intensity) 321 $[M]^+$ (37), 240 (35), 194 (100), 152 (50). HRMS (EI) calcd for $C_{12}H_{16}DIO_2$ 321.0336 found 321.0329 $[M]^+$.

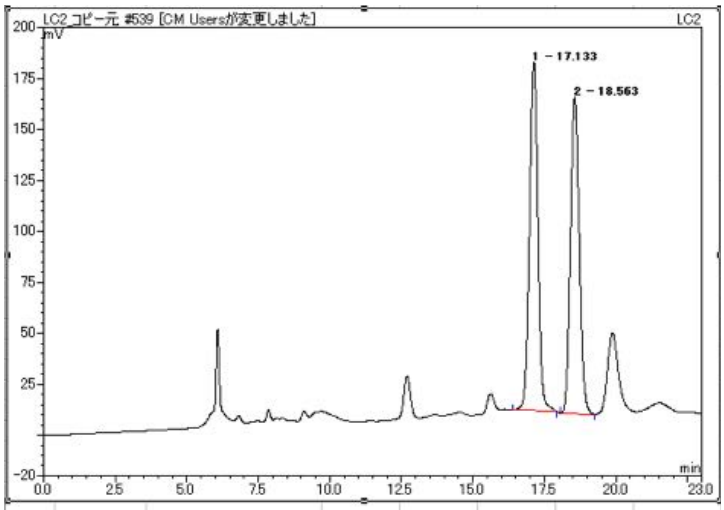
In the presence of LiI



(S_a, *R*)-**2b**-*d* (*er* 84:16) **6bA**-*d* (26%, *er* 51:49)

Scheme S19. Substitution reaction of (*Sa*, *R*)-**2b**-*d* with **5A** under the catalysis of Pd-diphosphine **8** in the presence of LiI.

To a test tube containing (*Sa*, *R*)-**2b**-*d* (0.9 mg, 4 μmol), (η^3-allyl)(η^5-Cp)Pd (0.2 mg, 0.9 μmol), **8** (0.3 mg, 0.3 μmol), and LiI (0.6 mg, 4 μmol) were added anhydrous MeOH (34 μL) and dimethyl malonate (1.5 μL, 13 μmol) under argon. The resulting mixture was sealed with a screw cap and stirred at 65 °C for 3 h. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The residue was purified by silica gel column chromatography eluting with 3% EtOAc/hexane to give **6bA**-*d* (0.3 mg, 26%) as a colorless oil. The enantiomeric ratio (*er*) of **6bA**-*d* was (1*R*, 3*S*):(1*S*, 3*R*) = 51:49, which was determined by HPLC analysis with chiral stationary phase column (Daicel Chiralpak OD-H, hexane/*i*-propanol = 397/3, 0.5 mL/min, λ = 210 nm, t_R(3*S* - major enantiomer) = 17.1 min, t_R(3*R* - minor enantiomer) = 18.6 min).



番号	保持時間 分	ピーク名	高さ mV	面積 mV×分	相対面積 %	含有量 n.a.	タイプ
1	17.13	n.a.	171.169	58.629	51.15	n.a.	BMB*
2	18.56	n.a.	155.258	55.993	48.85	n.a.	BMB*
合計:			326.427	114.622	100.00	0.000	

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16 We found that the similar two-step conversion of optically active malonate **6bA** (59% ee) into monocarboxylic acid followed by esterification (3 equiv. MeI, 3 equiv K_2CO_3, 0.25 M DMF, rt, 2.5 h) afforded the corresponding allenic acid methyl ester (57% ee). The two-step conversion involving hydrolysis and decarboxylation at 80 °C in DMF was required for the suppression of the racemization of allenic axial chirality. The reaction conditions were applied to the transformation of racemic **6bA**-*d*, where the epimerization could lower the diastereomeric ratio of iodolactone **10**-*d*.

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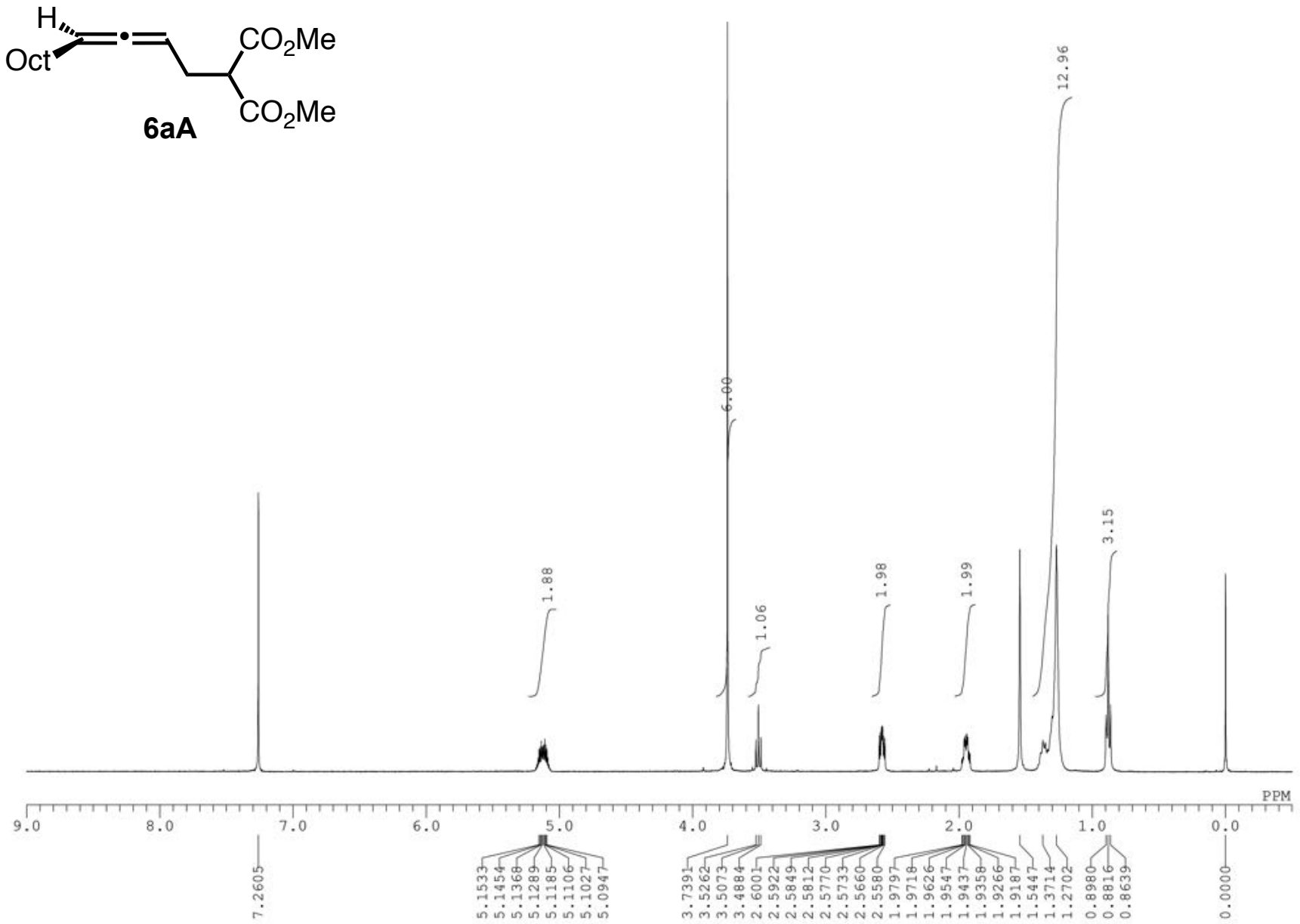
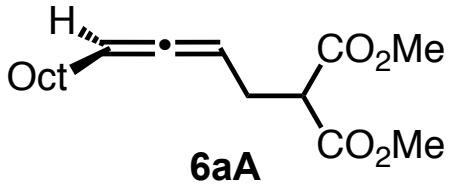
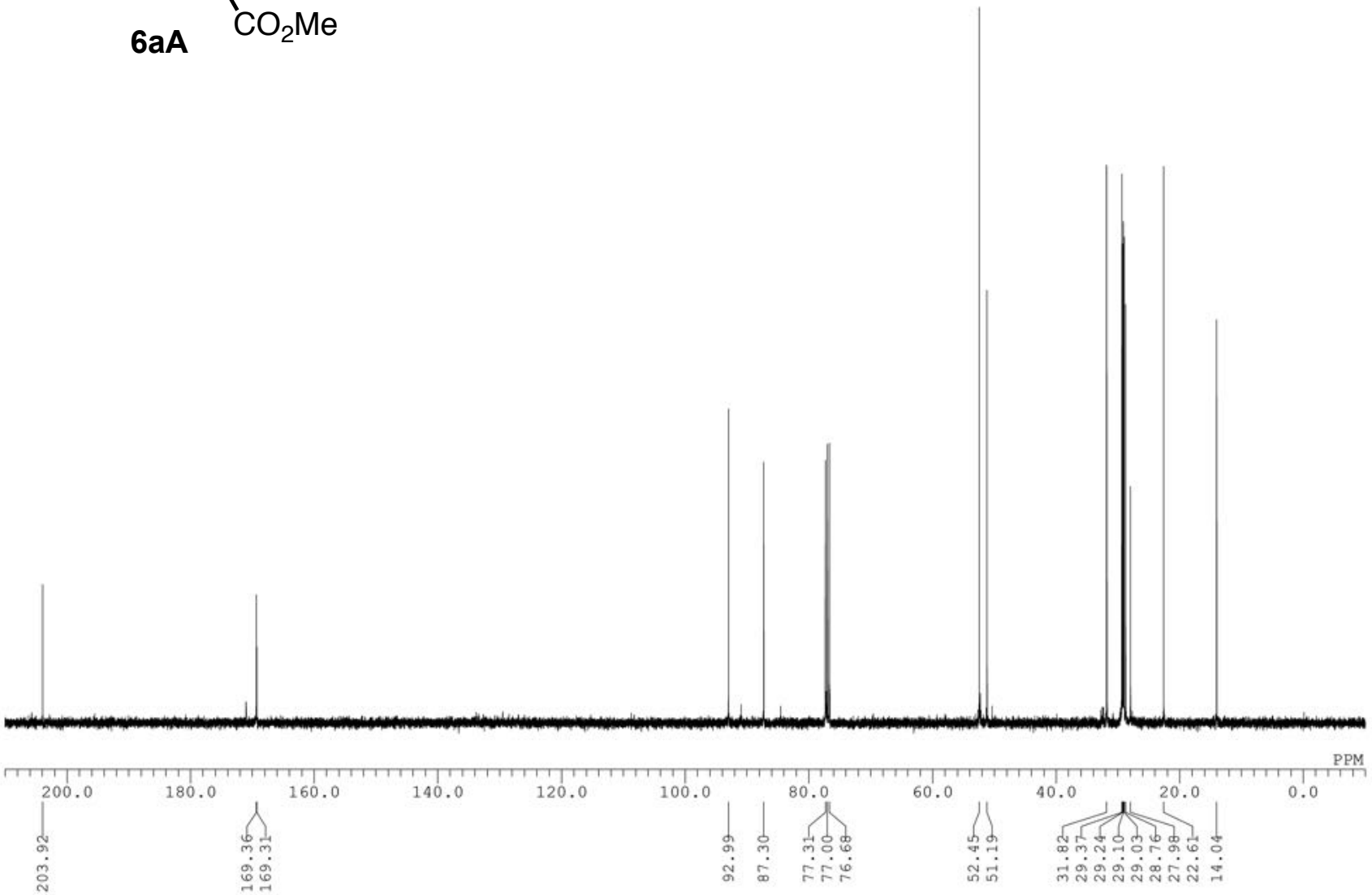
^{1}H NMR spectrum of **6aA**



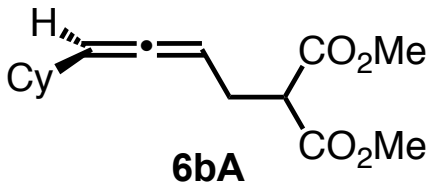
^{13}C NMR spectrum of **6aA**



6aA

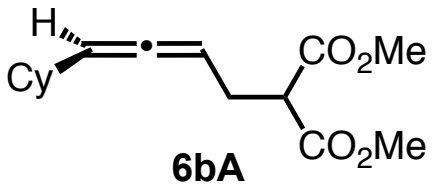


[1]H NMR spectrum of **6bA**

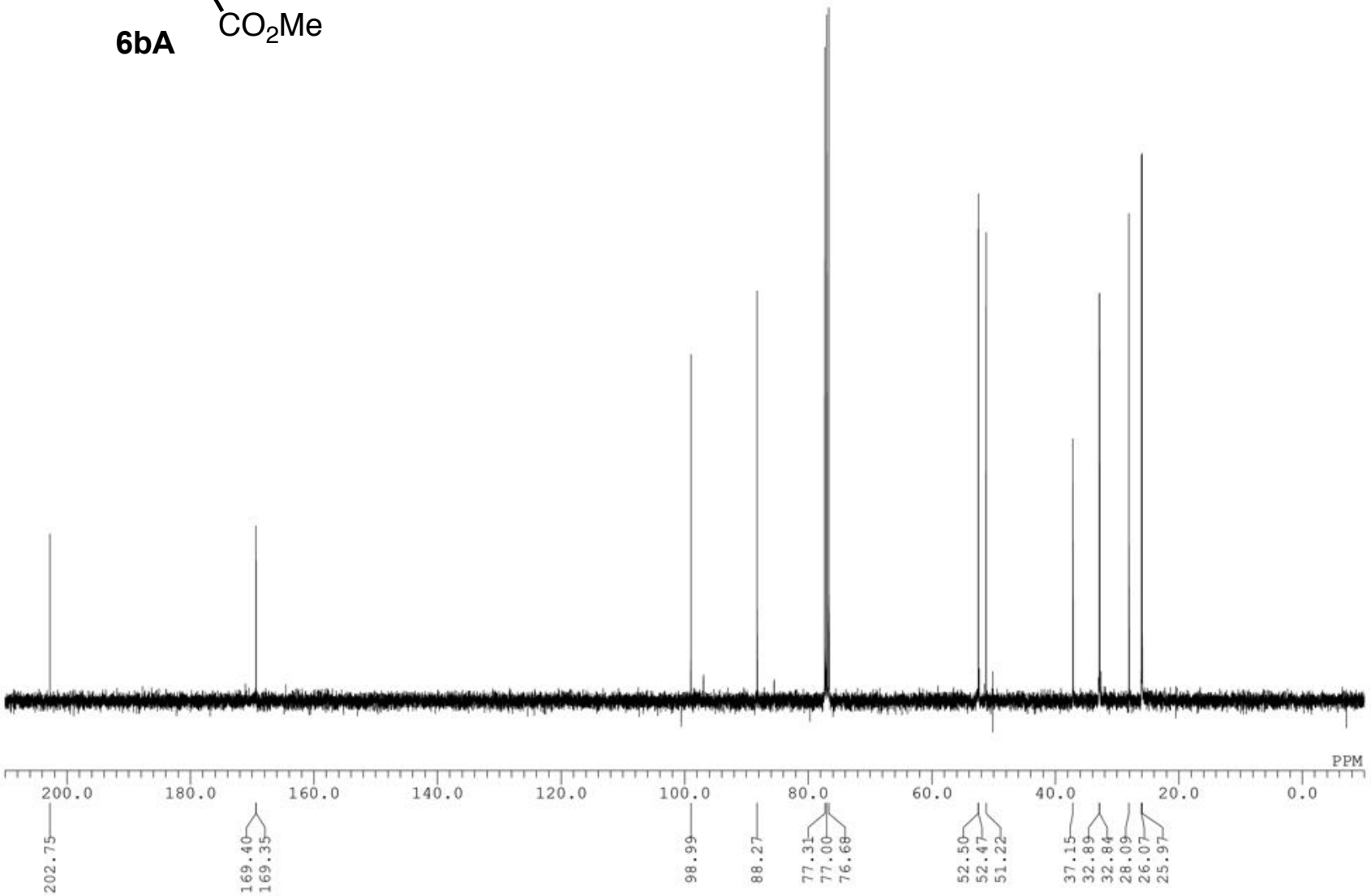


6bA

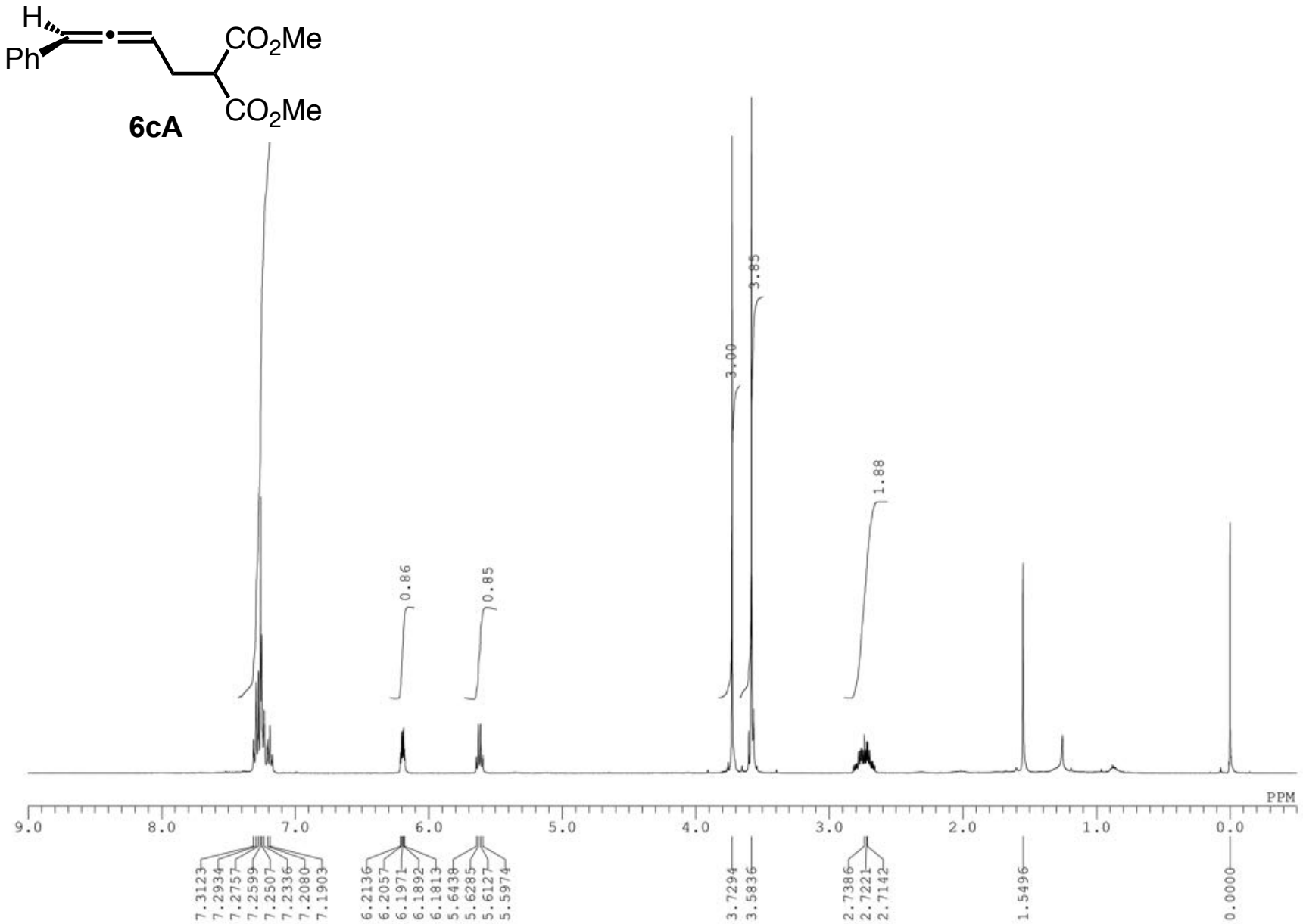
^{13}C NMR spectrum of **6bA**



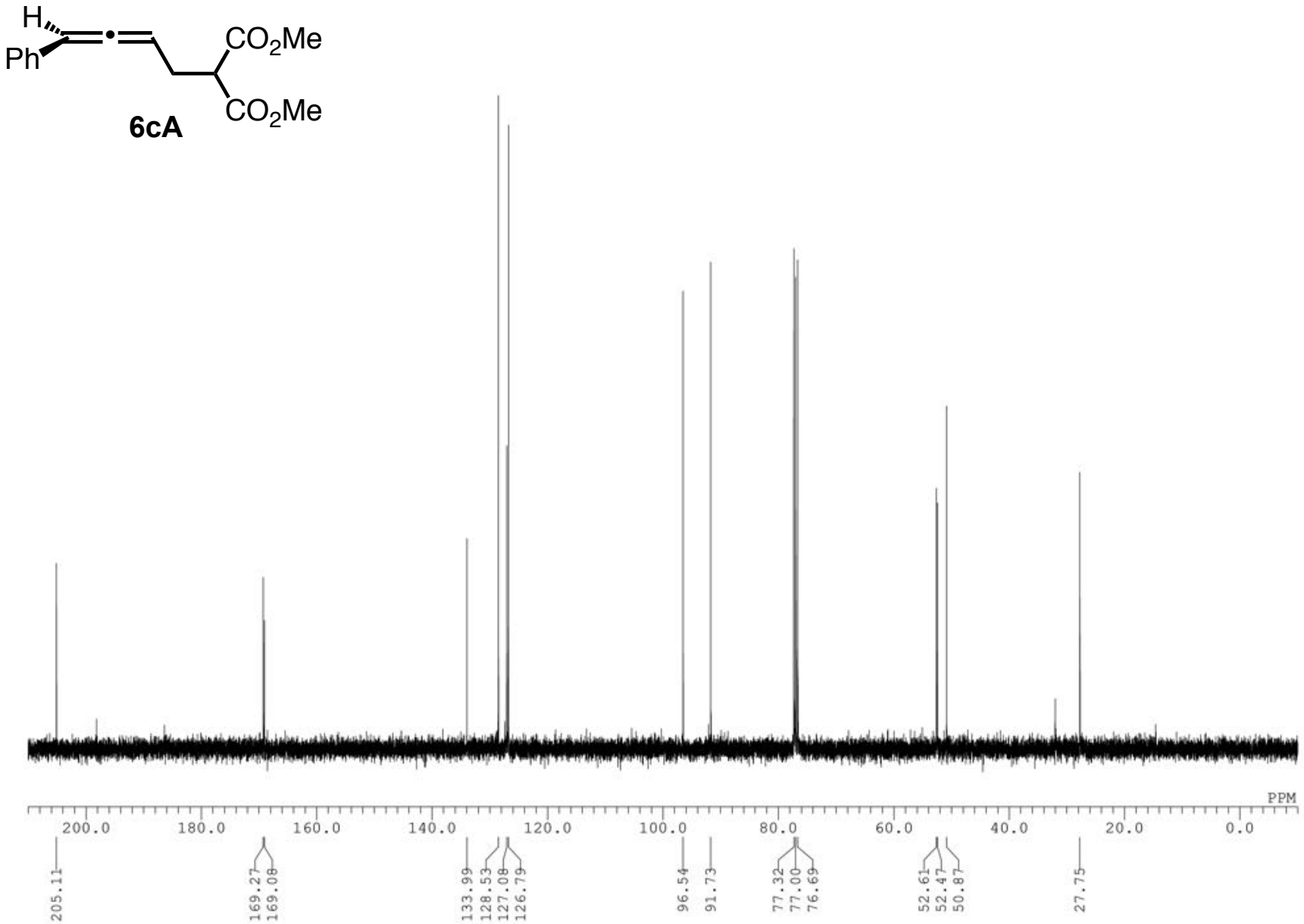
6bA



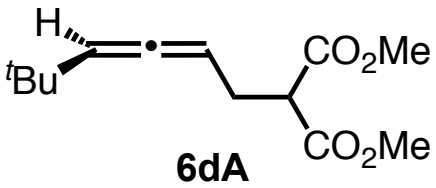
[1]H NMR spectrum of **6cA**



^{13}C NMR spectrum of **6cA**

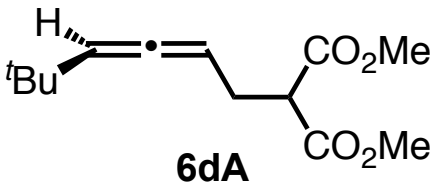


[1]H NMR spectrum of **6dA**

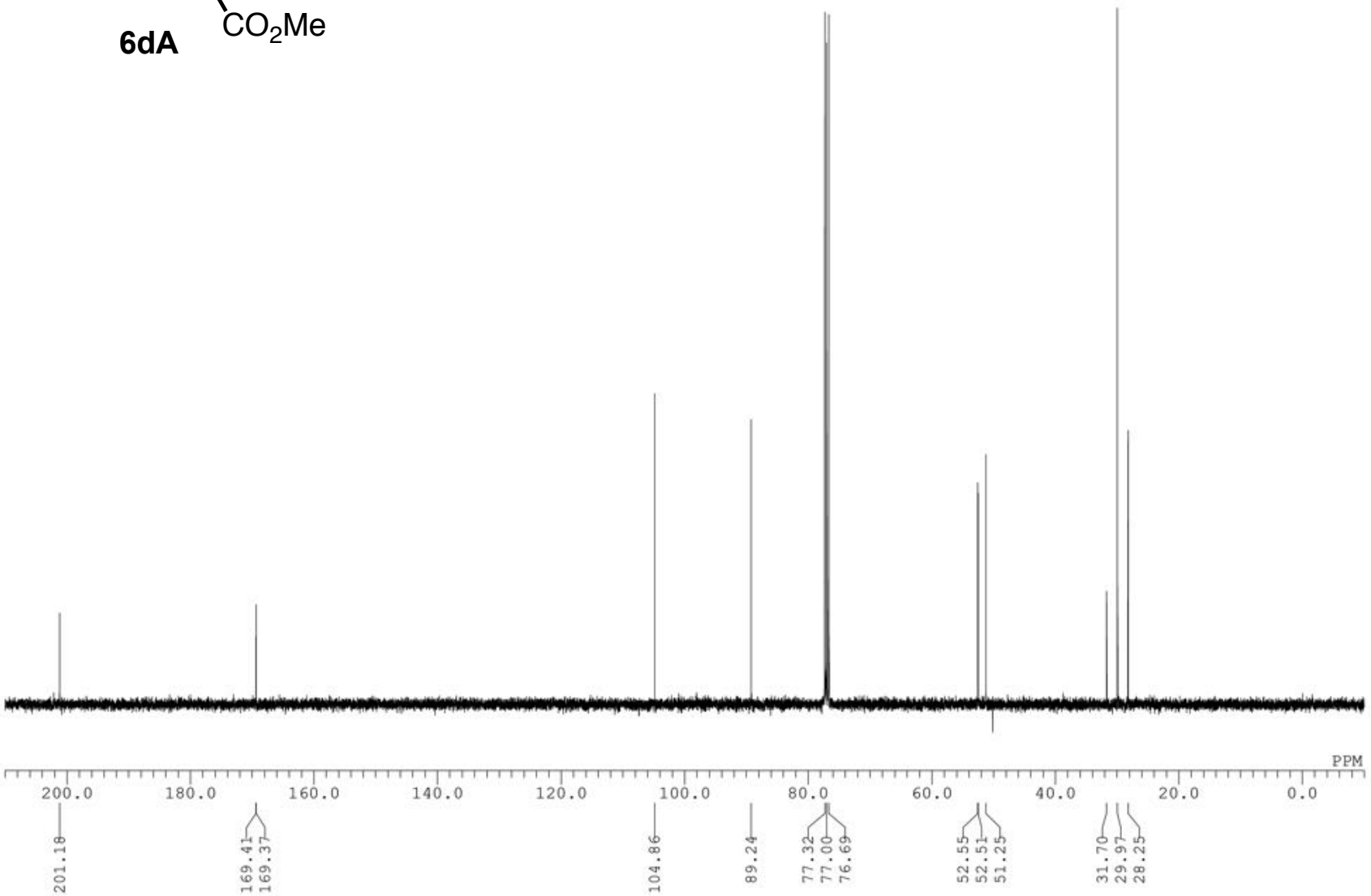


6dA

^{13}C NMR spectrum of **6dA**



6dA



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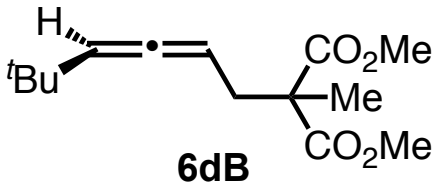
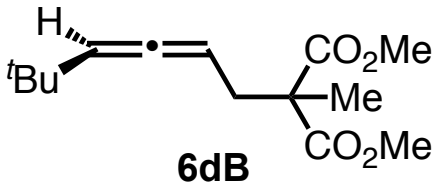
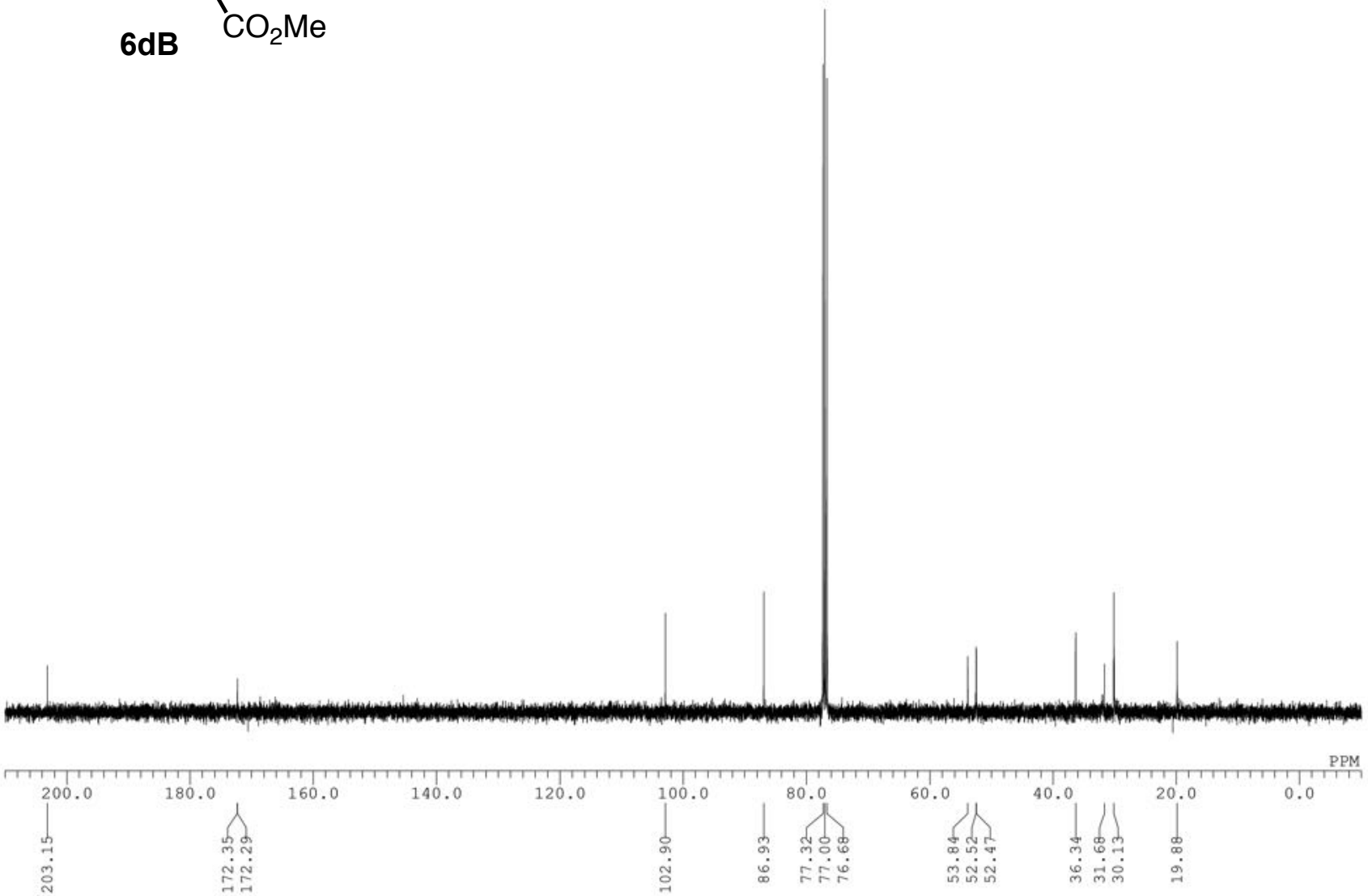


6dB

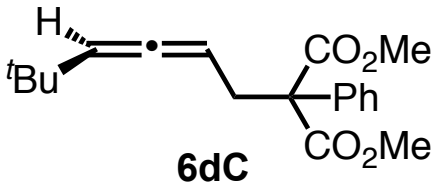
^{13}C NMR spectrum of **6dB**



6dB

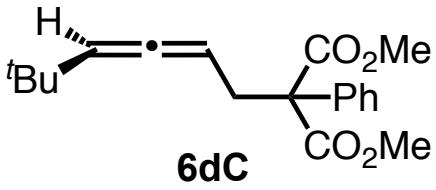


^{1}H NMR spectrum of **6dC**

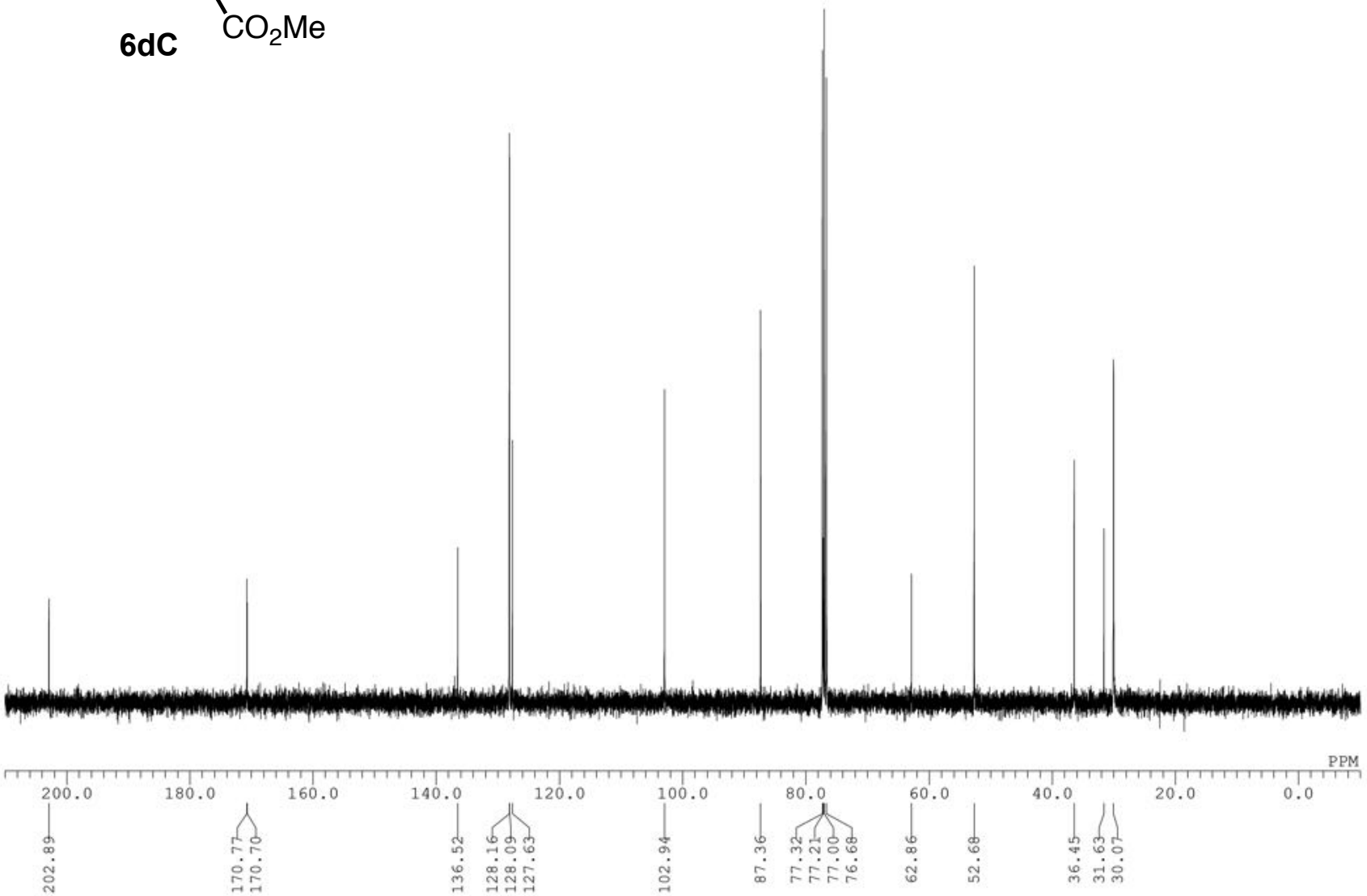


6dC

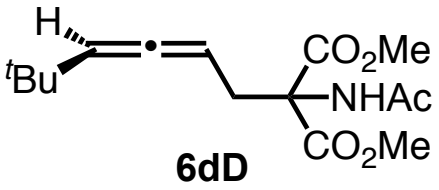
^{13}C NMR spectrum of **6dC**



6dC

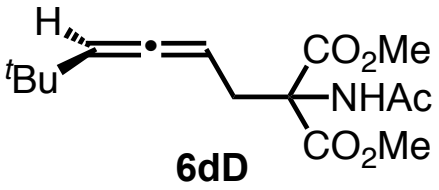


^{1}H NMR spectrum of **6dD**



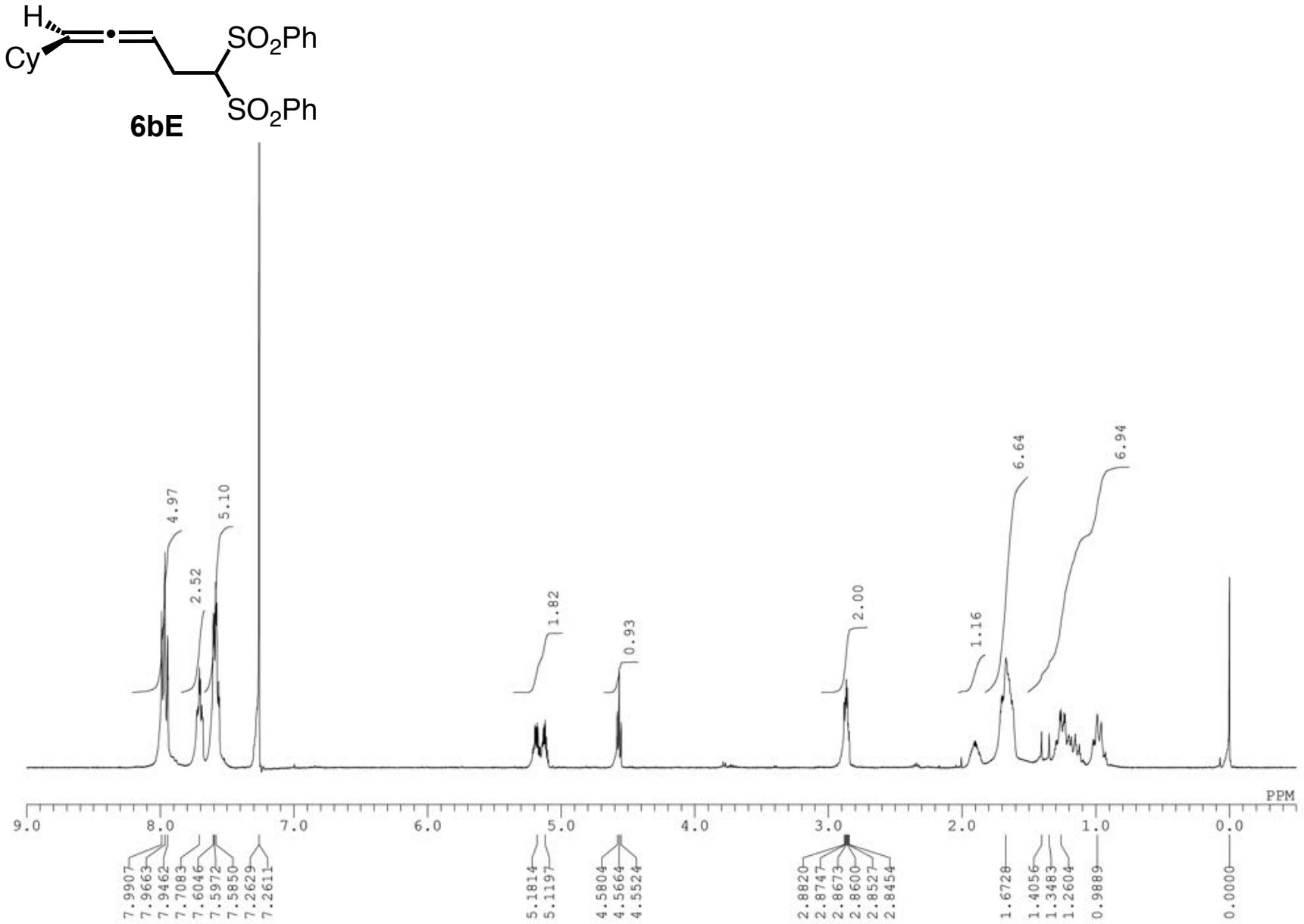
6dD

^{13}C NMR spectrum of **6dD**

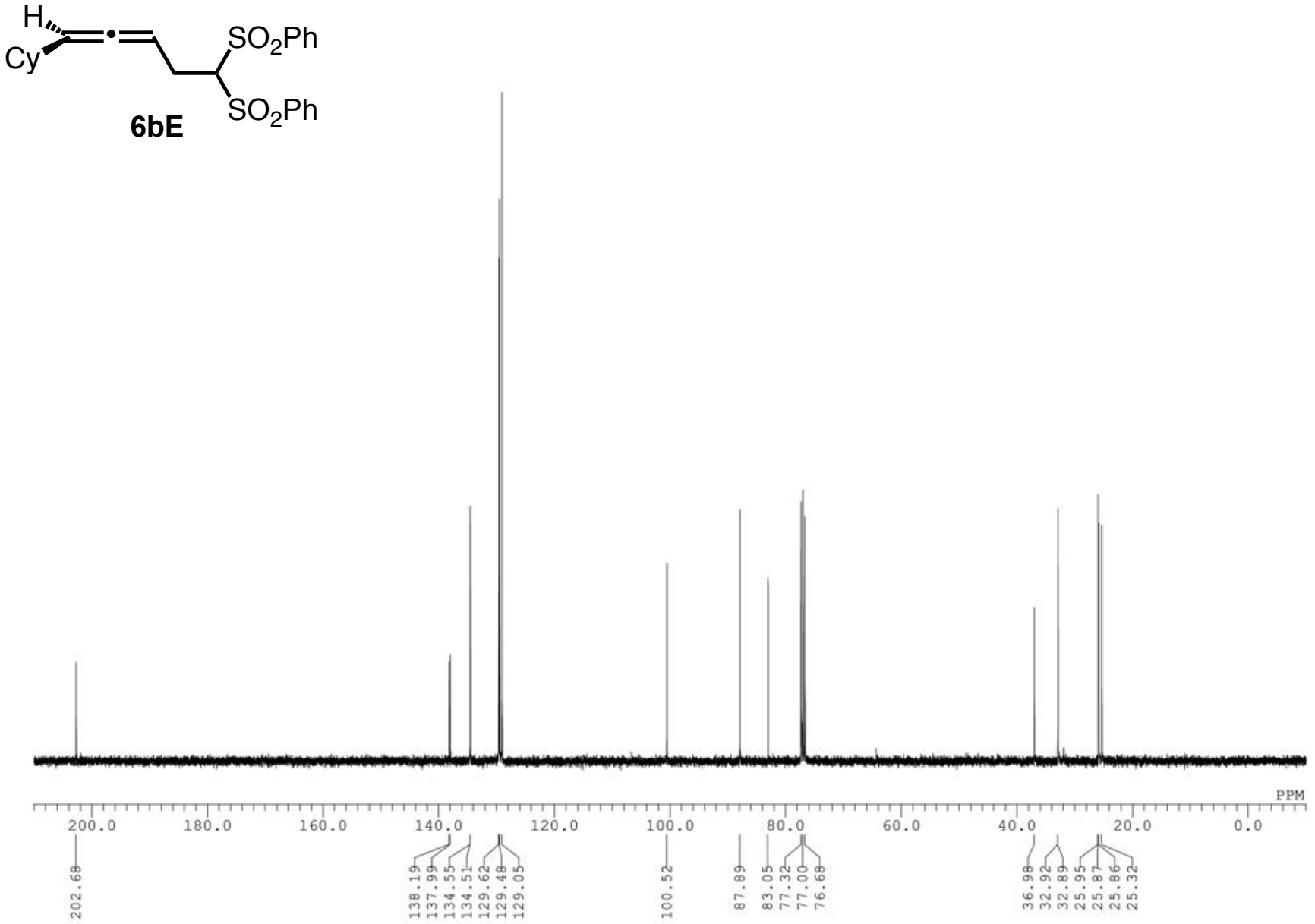


6dD

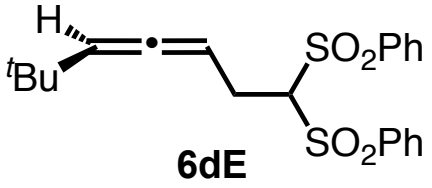
^{1}H NMR spectrum of **6bE**



^{13}C NMR spectrum of **6bE**

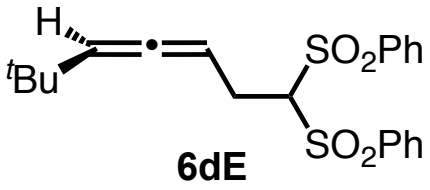


[1]H NMR spectrum of **6dE**

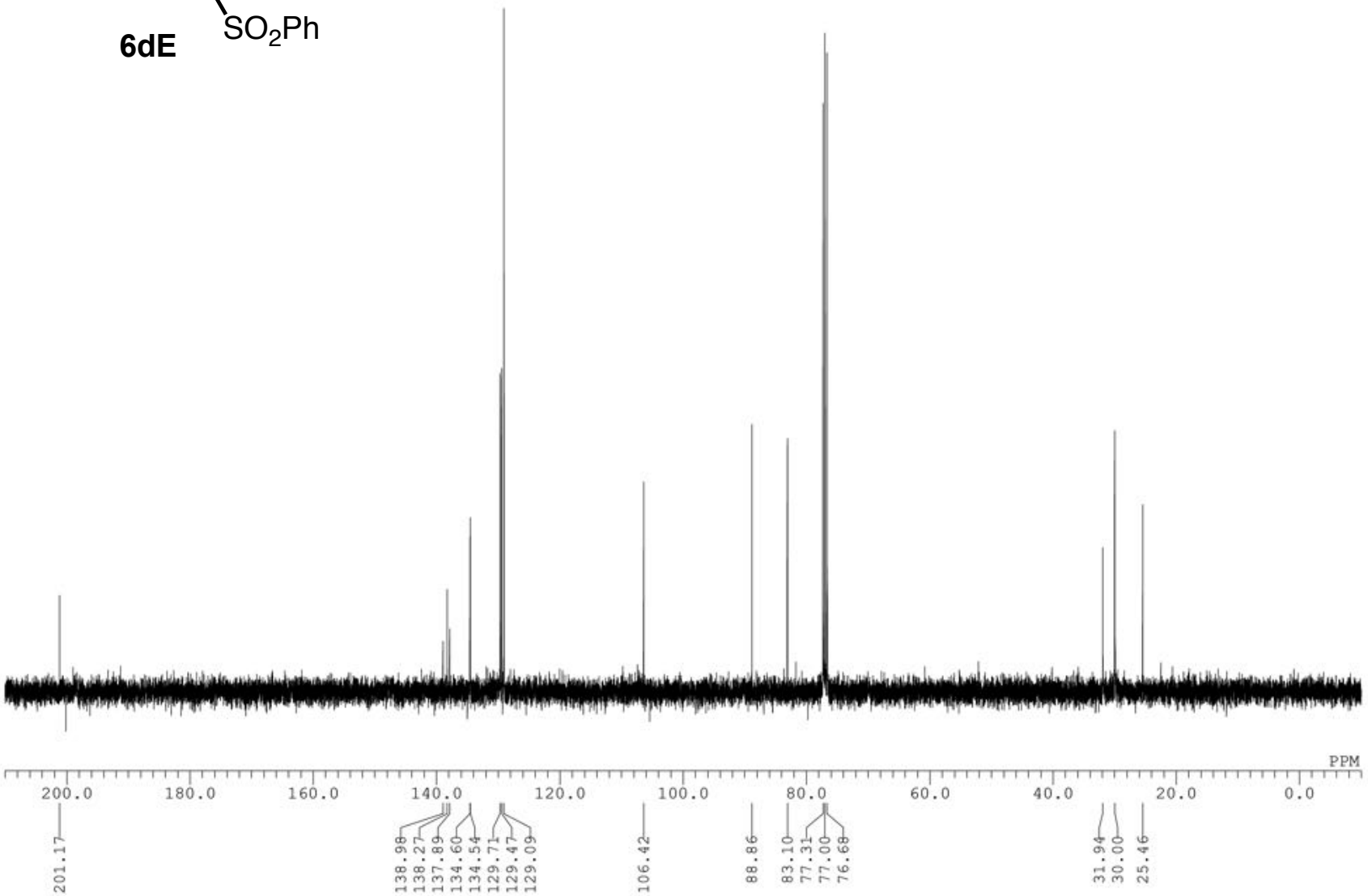


6dE

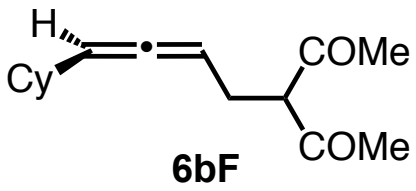
^{13}C NMR spectrum of **6dE**



6dE

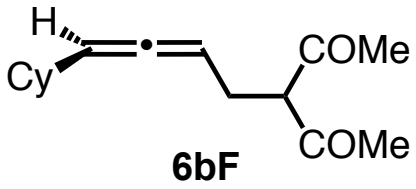


^{1}H NMR spectrum of **6bF**



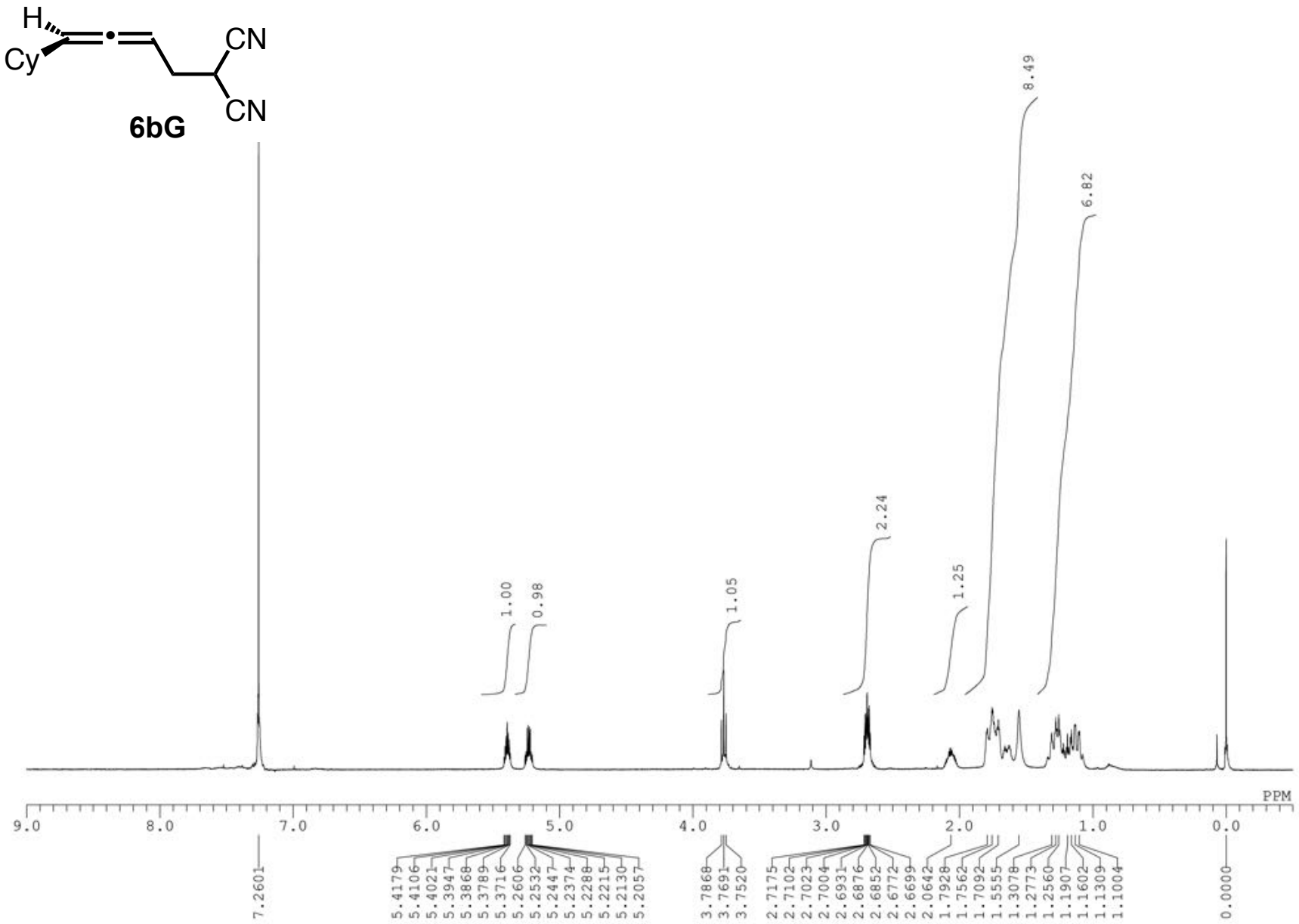
6bF

^{13}C NMR spectrum of **6bF**

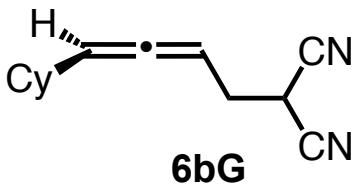


6bF

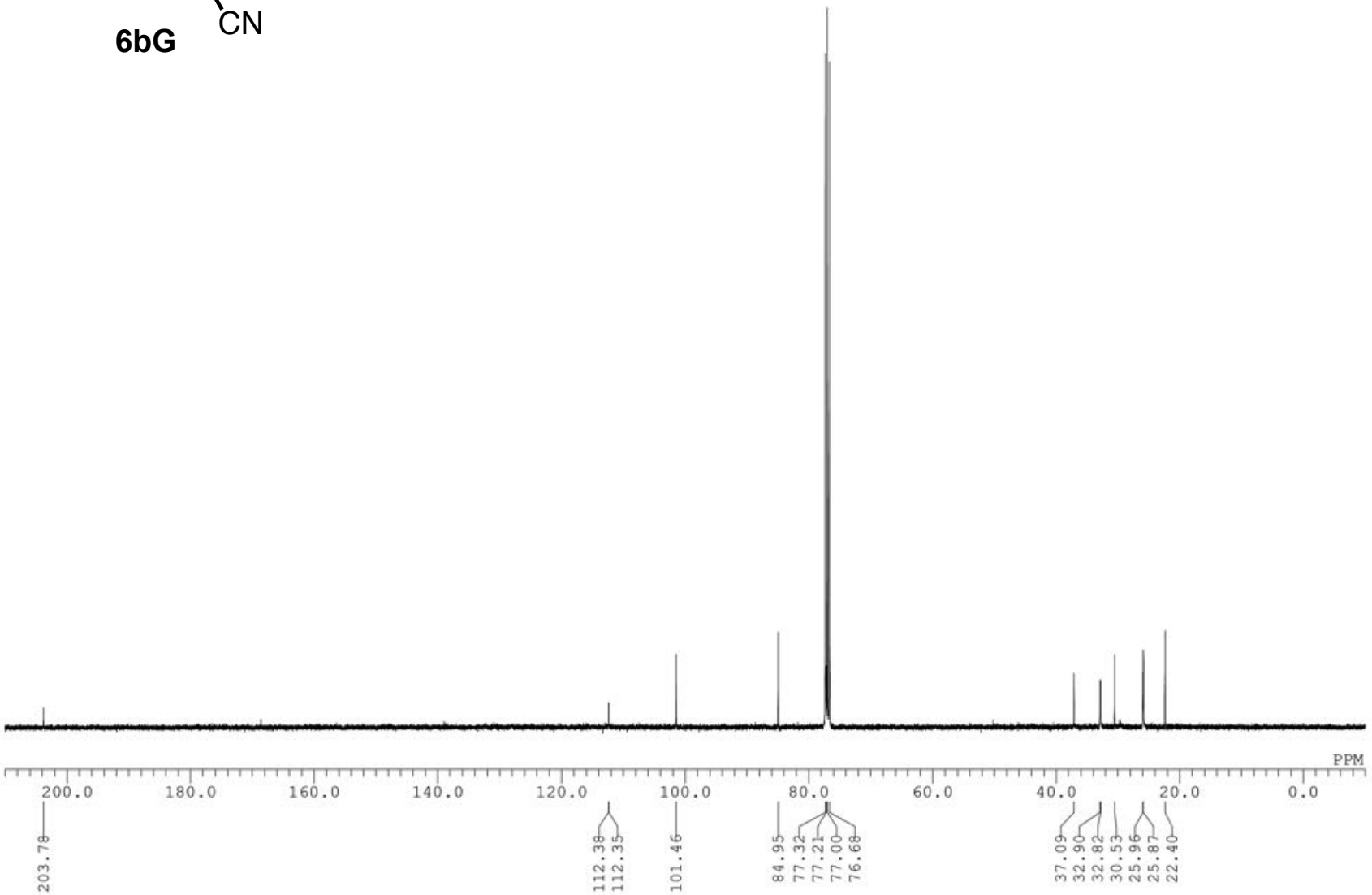
^{1}H NMR spectrum of **6bG**



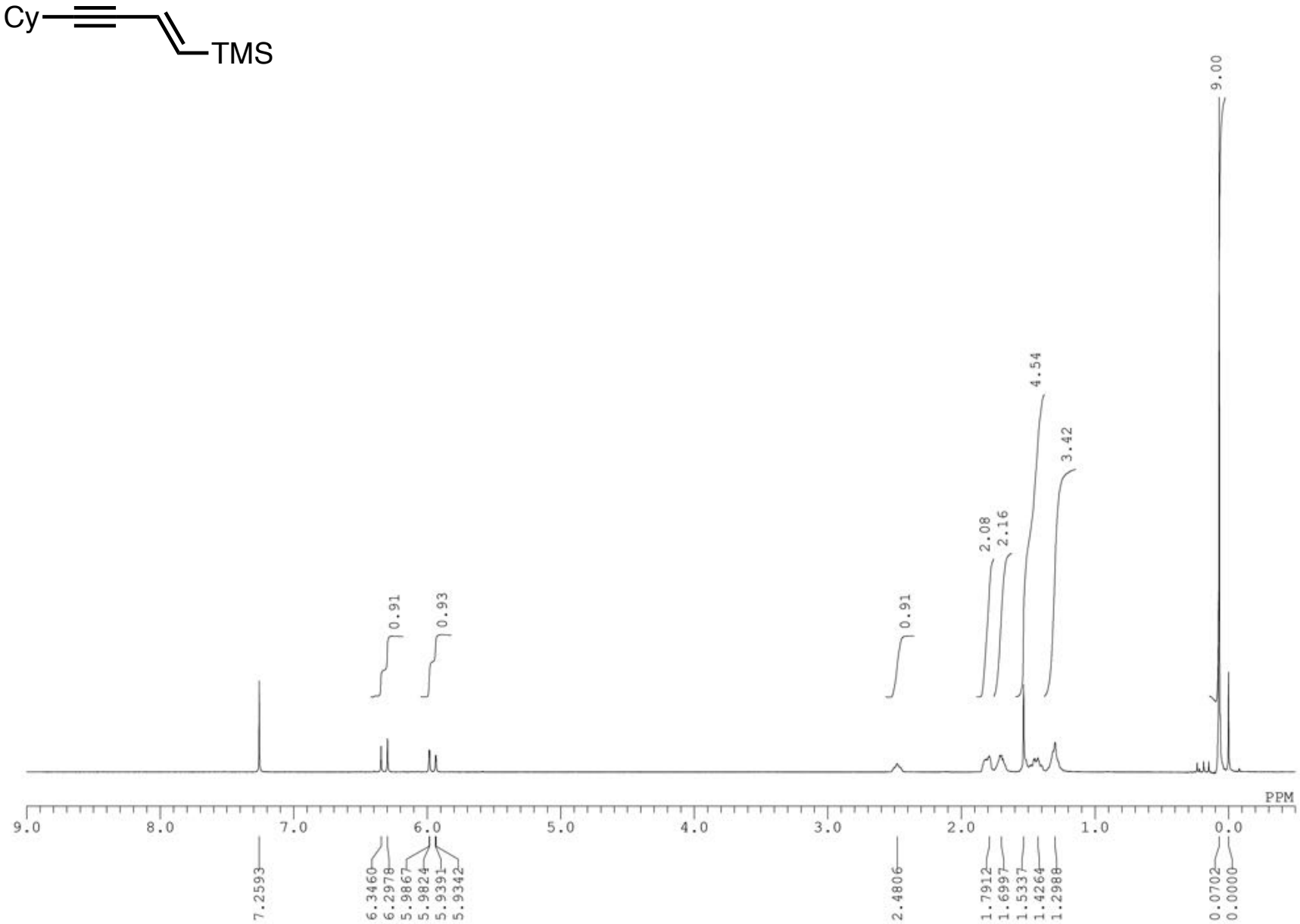
^{13}C NMR spectrum of **6bG**



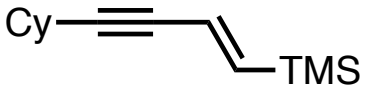
6bG

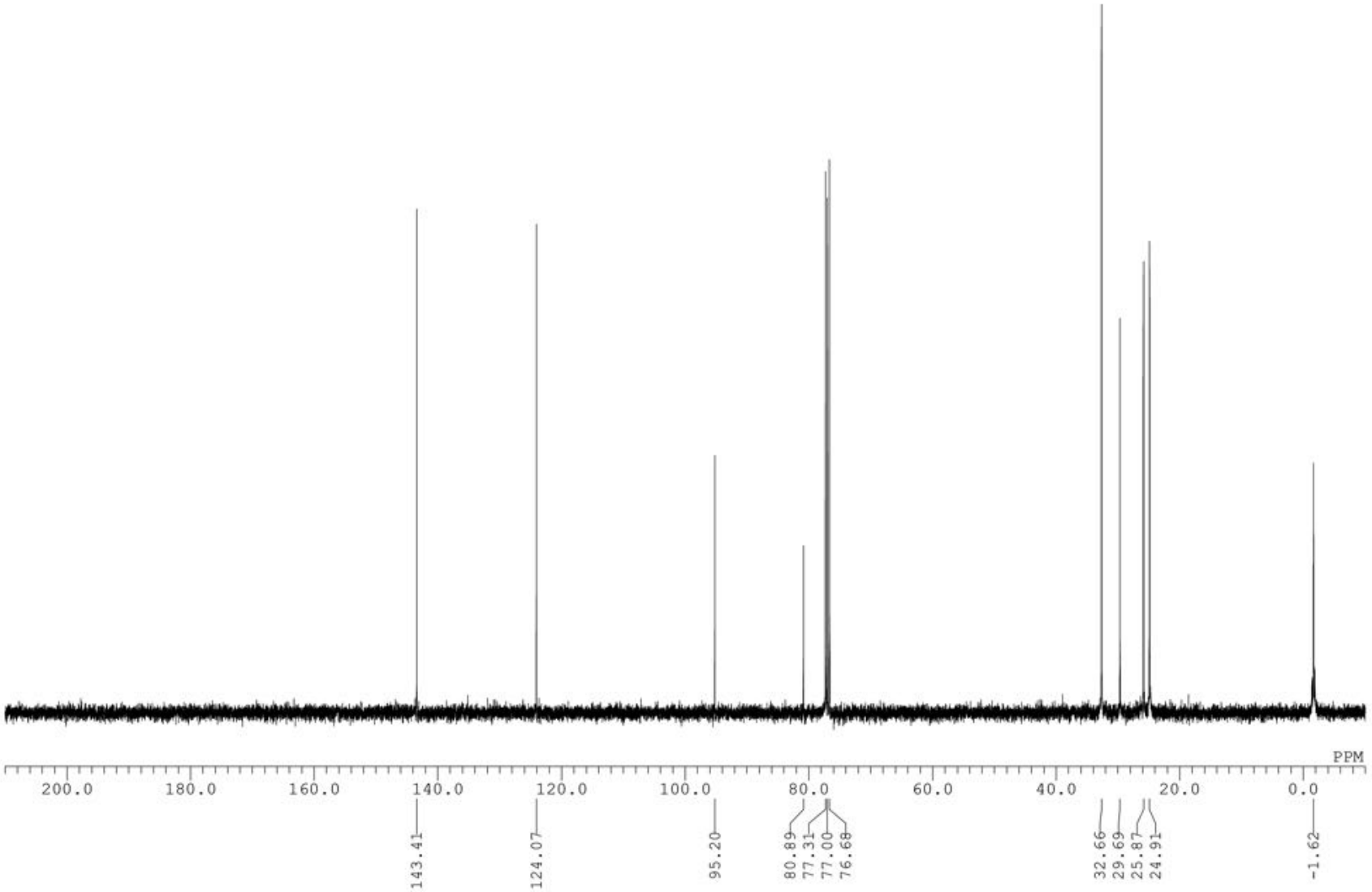


^{1}H NMR spectrum of (*E*)-(4-cyclohexylbut-1-en-3-yn-1-yl)trimethylsilane

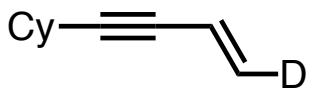


^{13}C NMR spectrum of (*E*)-(4-cyclohexylbut-1-en-3-yn-1-yl)trimethylsilane

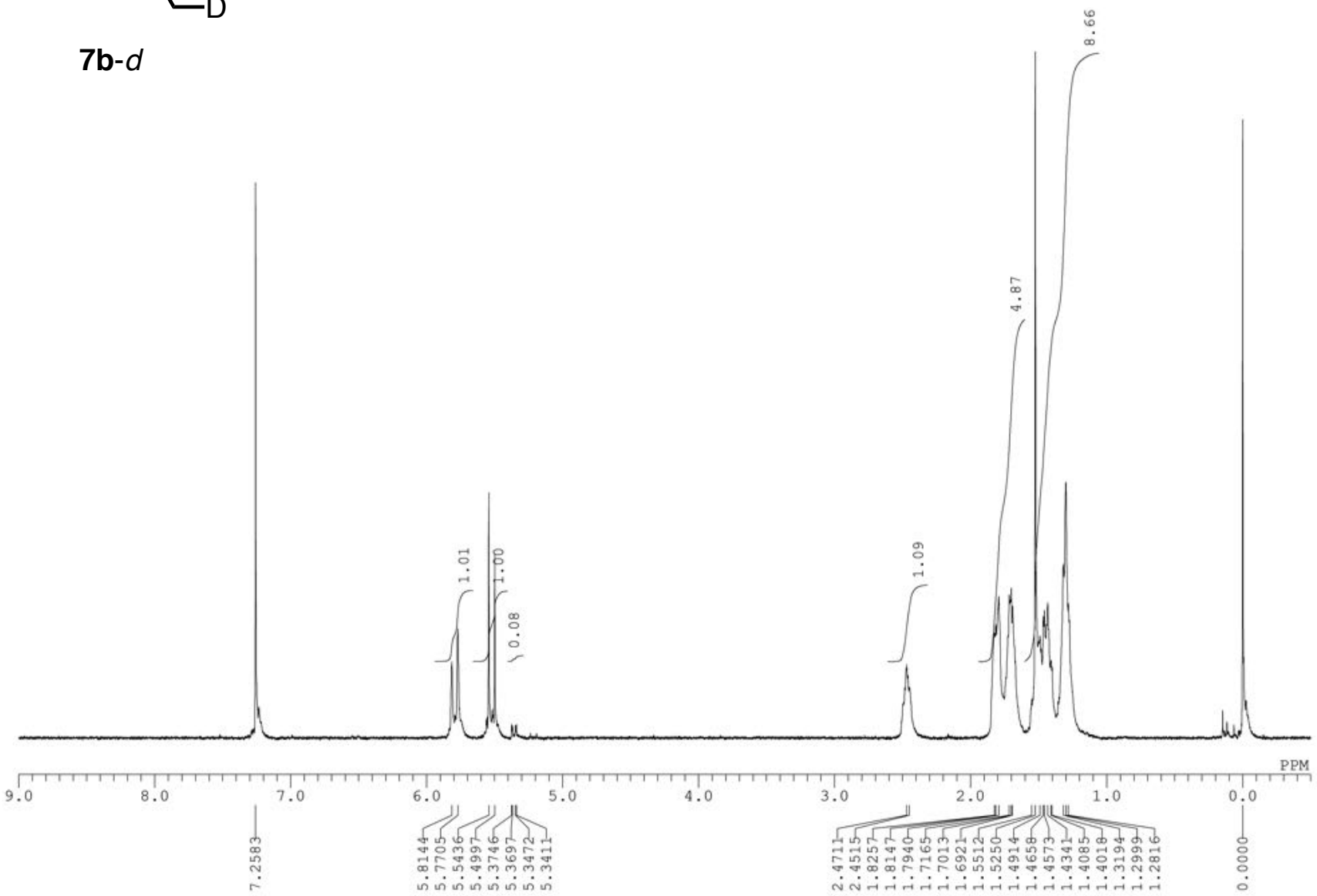




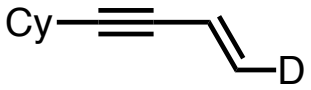
^{1}H NMR spectrum of **7b**-*d*



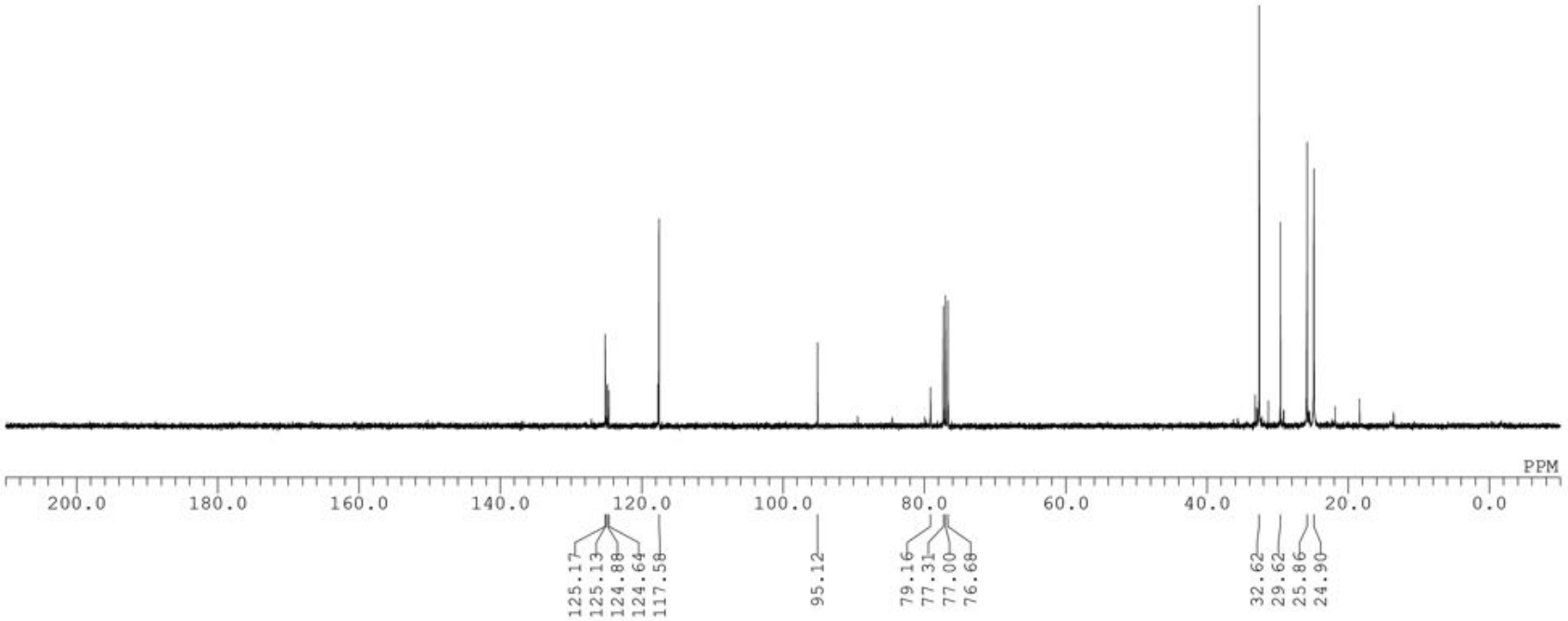
7b-*d*



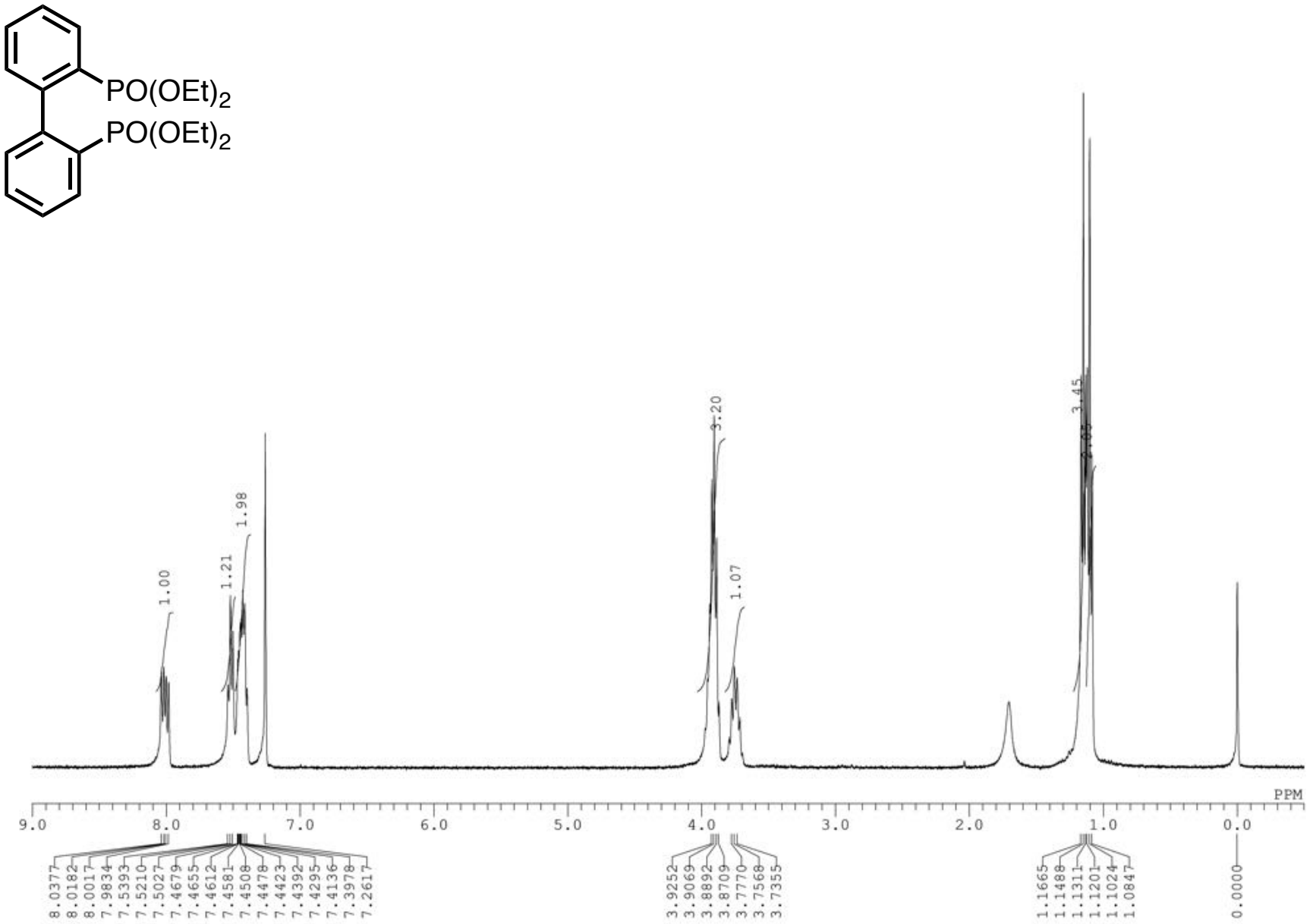
^{13}C NMR spectrum of **7b**-*d*



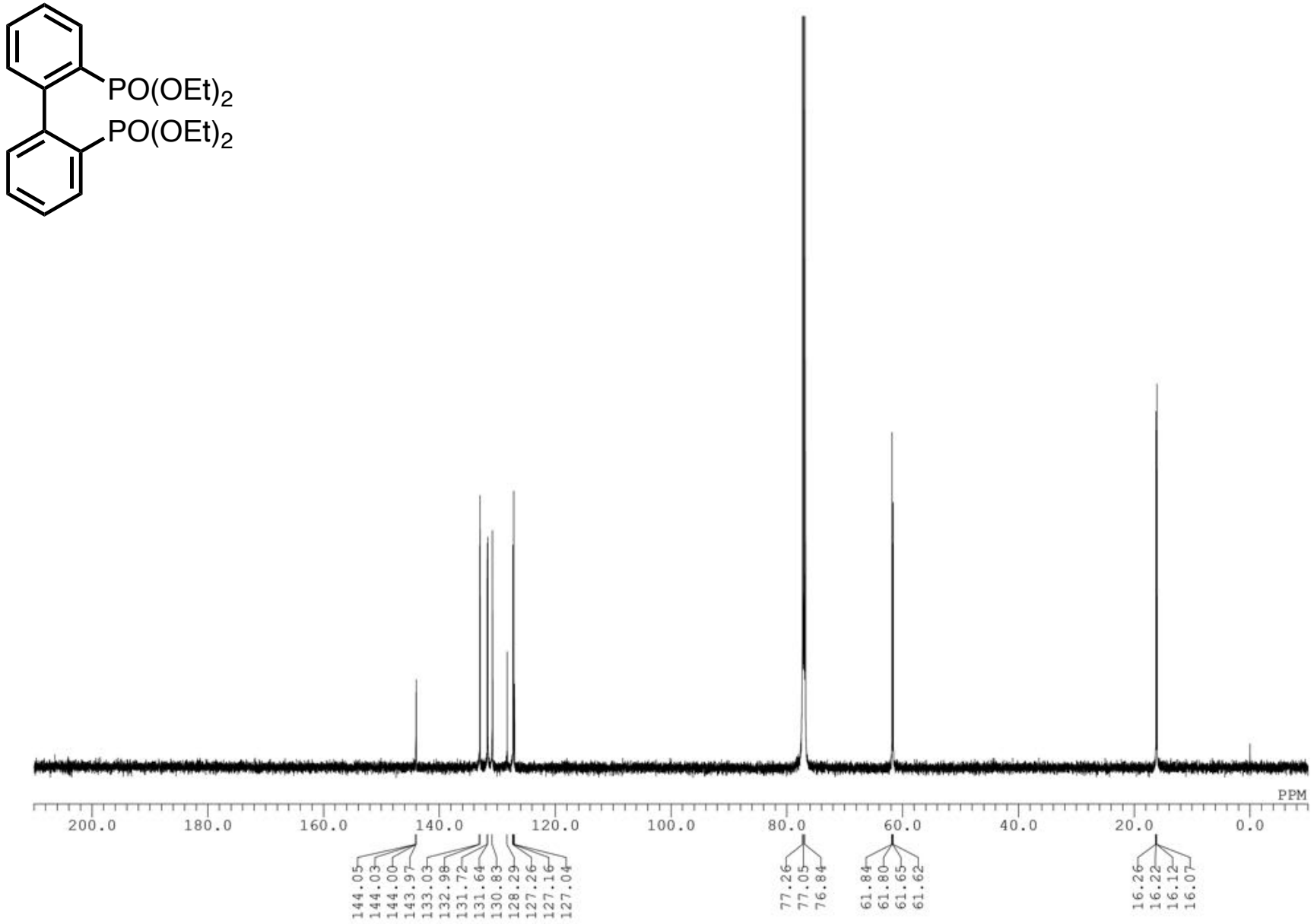
7b-*d*



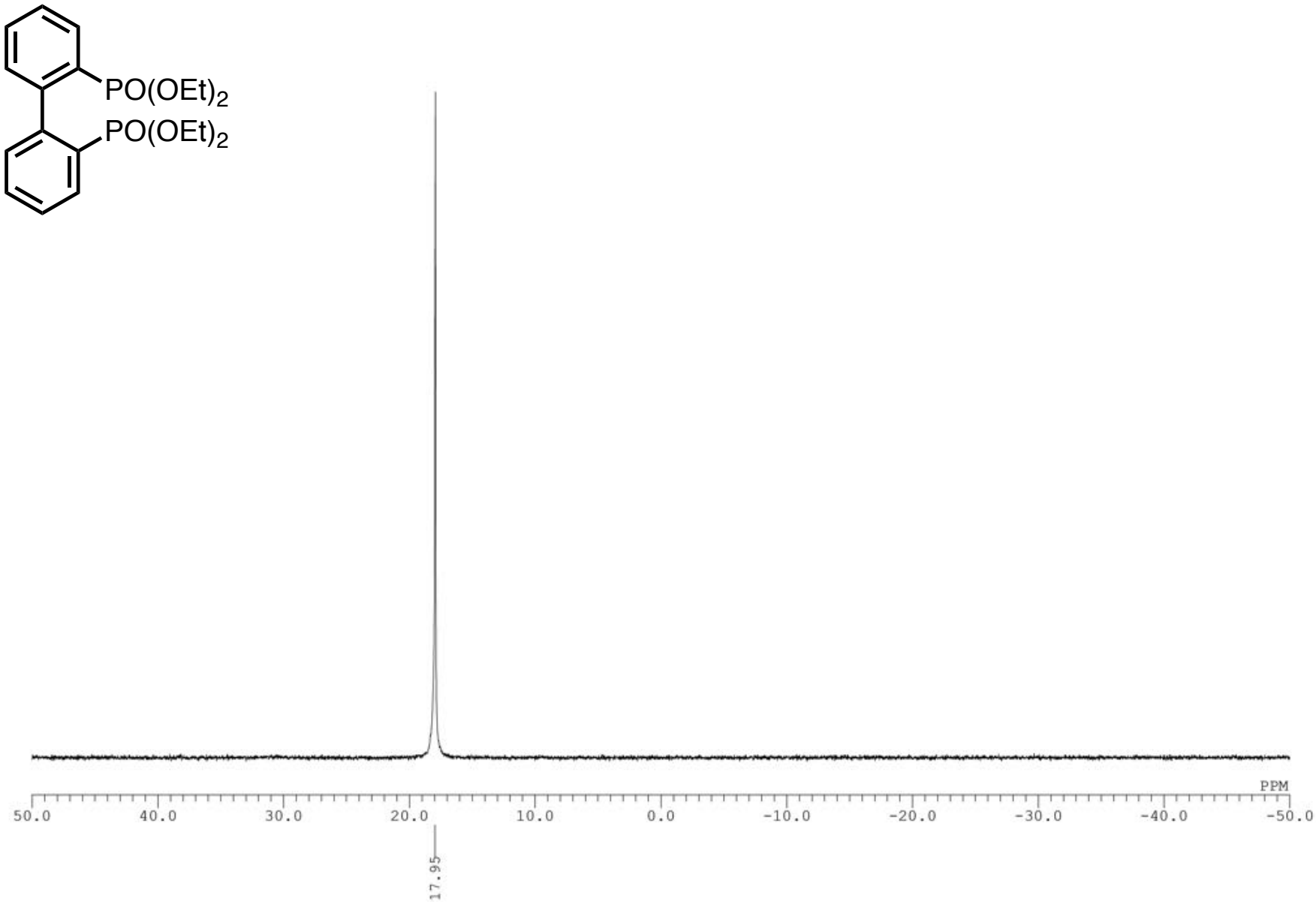
^{1}H NMR spectrum of tetraethyl [1,1'-biphenyl]-2,2'-diylbis(phosphonate)



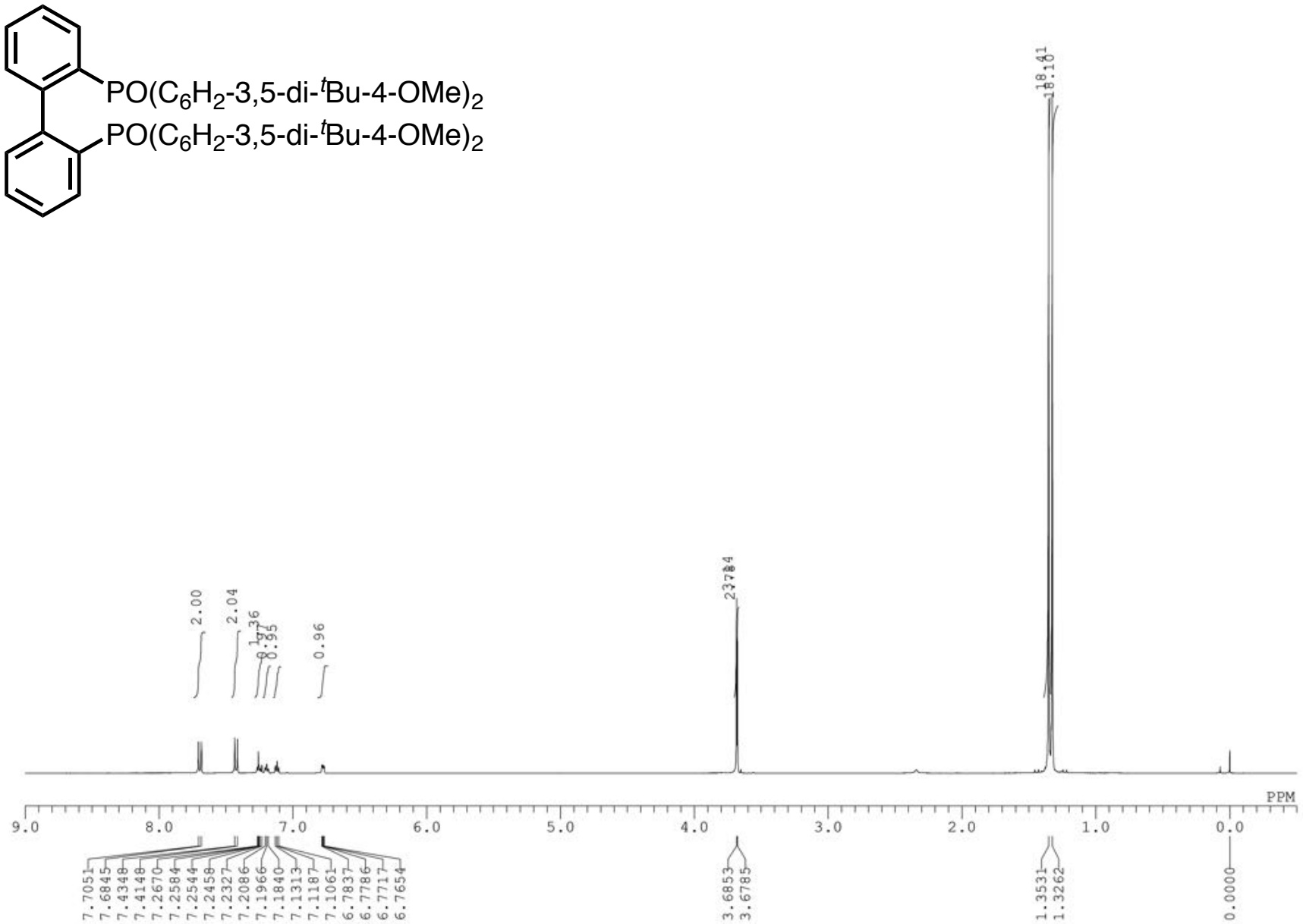
^{13}C NMR spectrum of tetraethyl [1,1'-biphenyl]-2,2'-diylbis(phosphonate



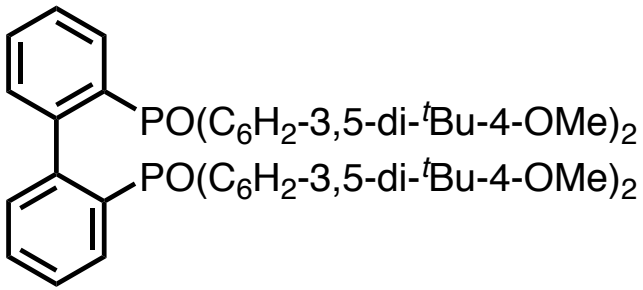
^{31}P NMR spectrum of tetraethyl [1,1'-biphenyl]-2,2'-diylbis(phosphonate



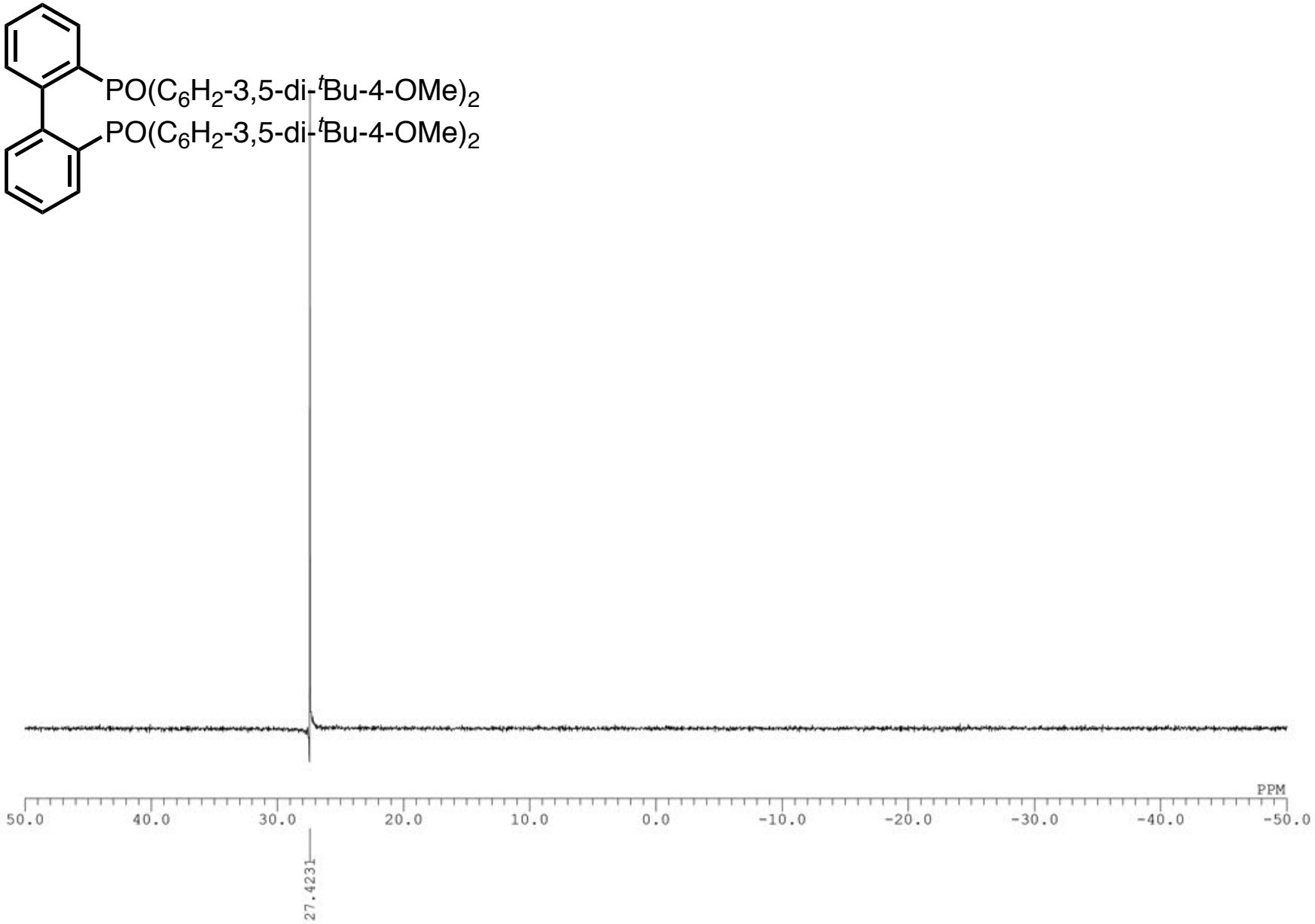
^{1}H NMR spectrum of [1,1'-biphenyl]-2,2'-diylbis(bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphine oxide)



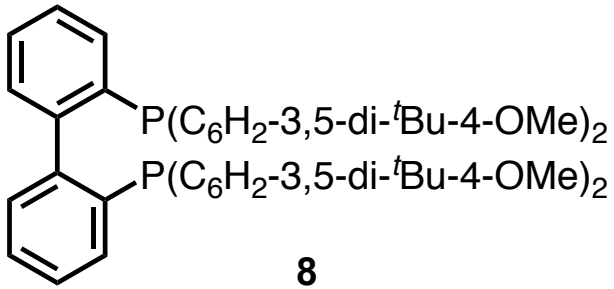
^{13}C NMR spectrum of [1,1'-biphenyl]-2,2'-diylbis(bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphine oxide)



^{31}P NMR spectrum of [1,1'-biphenyl]-2,2'-diylbis(bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphine oxide)

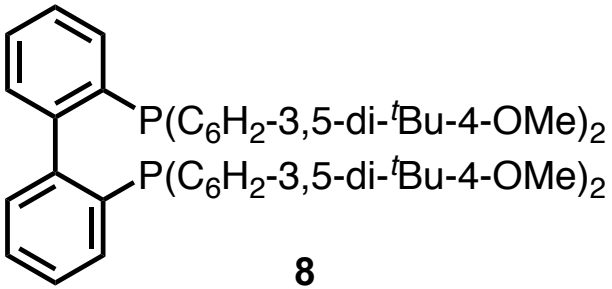


^{1}H NMR spectrum of **8**



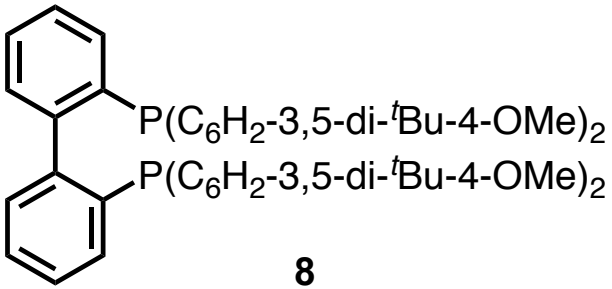
8

^{13}C NMR spectrum of **8**



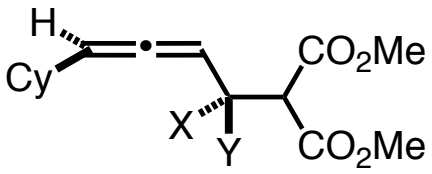
8

^{31}P NMR spectrum of **8**



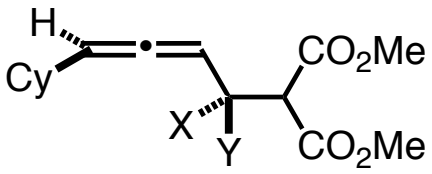
8

^{1}H NMR spectrum of **6bA**-*d* prepared from **7b**-*d*

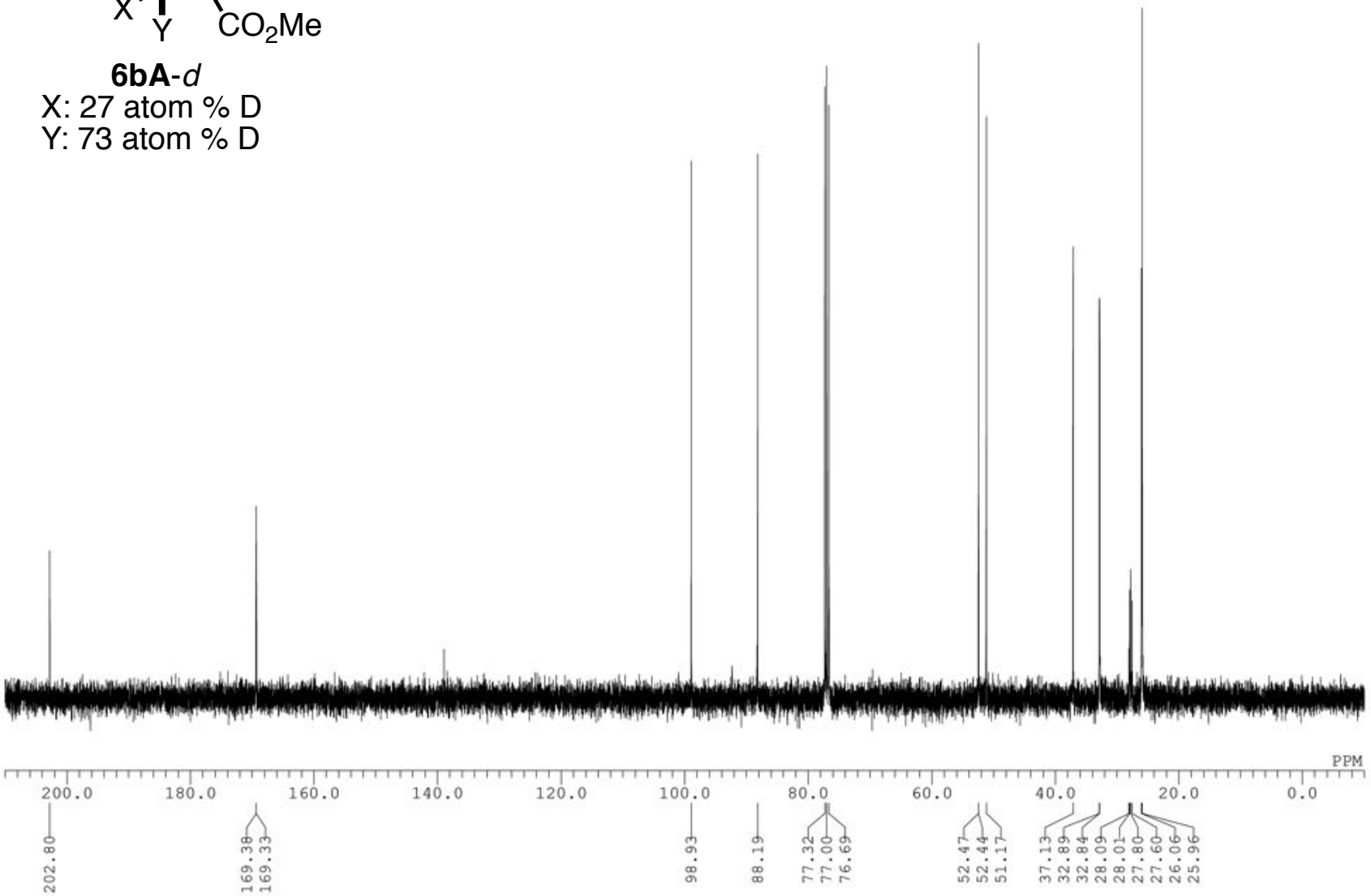


6bA-*d*
X: 27 atom % D
Y: 73 atom % D

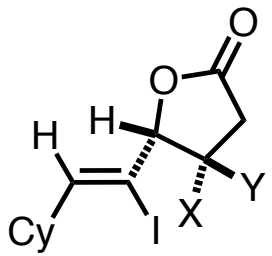
^{13}C NMR spectrum of **6bA**-*d* prepared from **7b**-*d*



6bA-*d*
X: 27 atom % D
Y: 73 atom % D

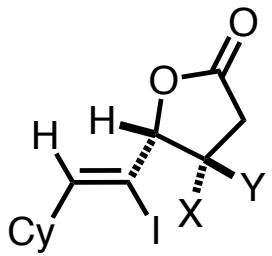


[1]H NMR spectrum of **10**-*d* prepared from **7b**-*d*

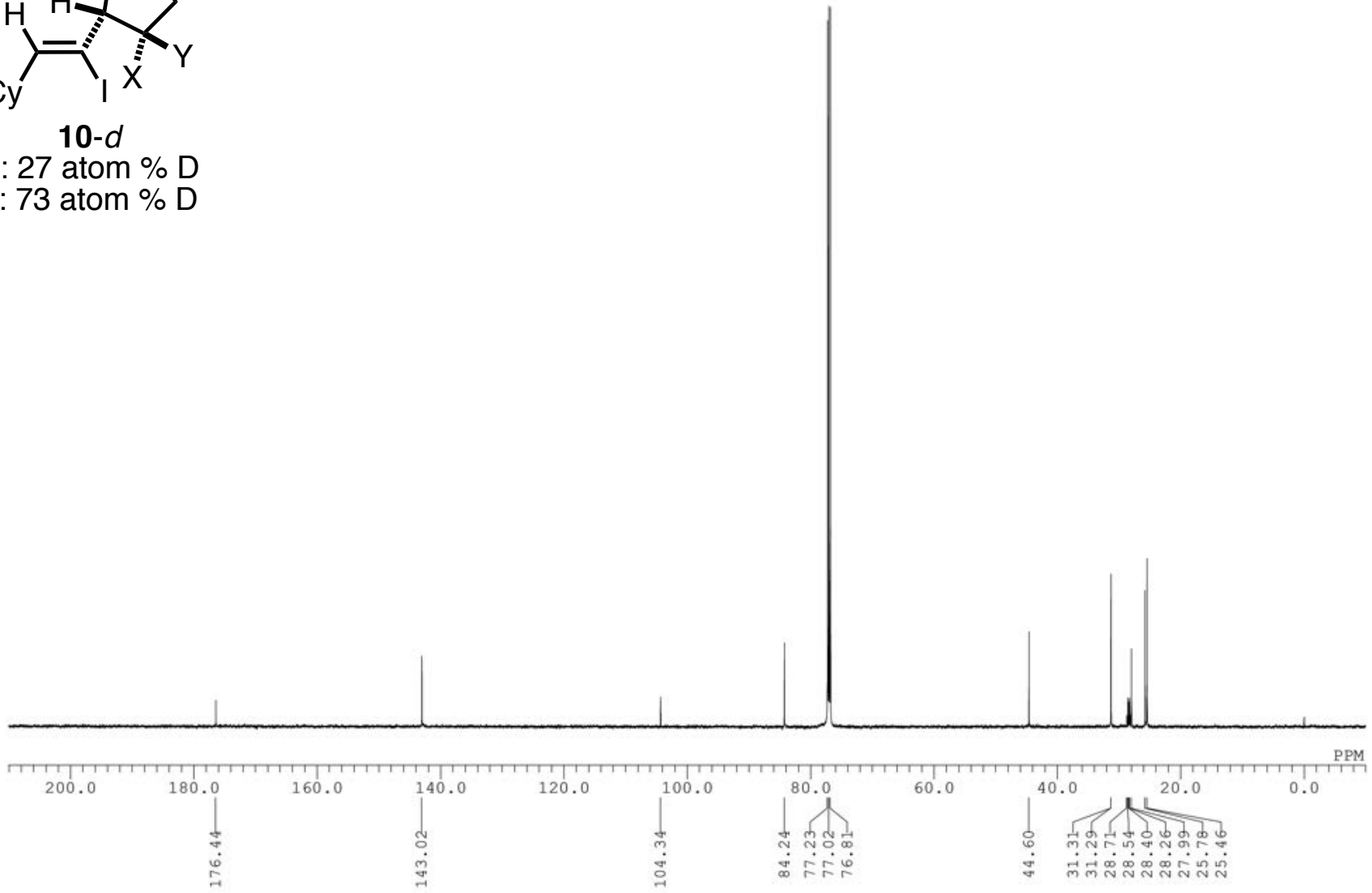


10-*d*
X: 27 atom % D
Y: 73 atom % D

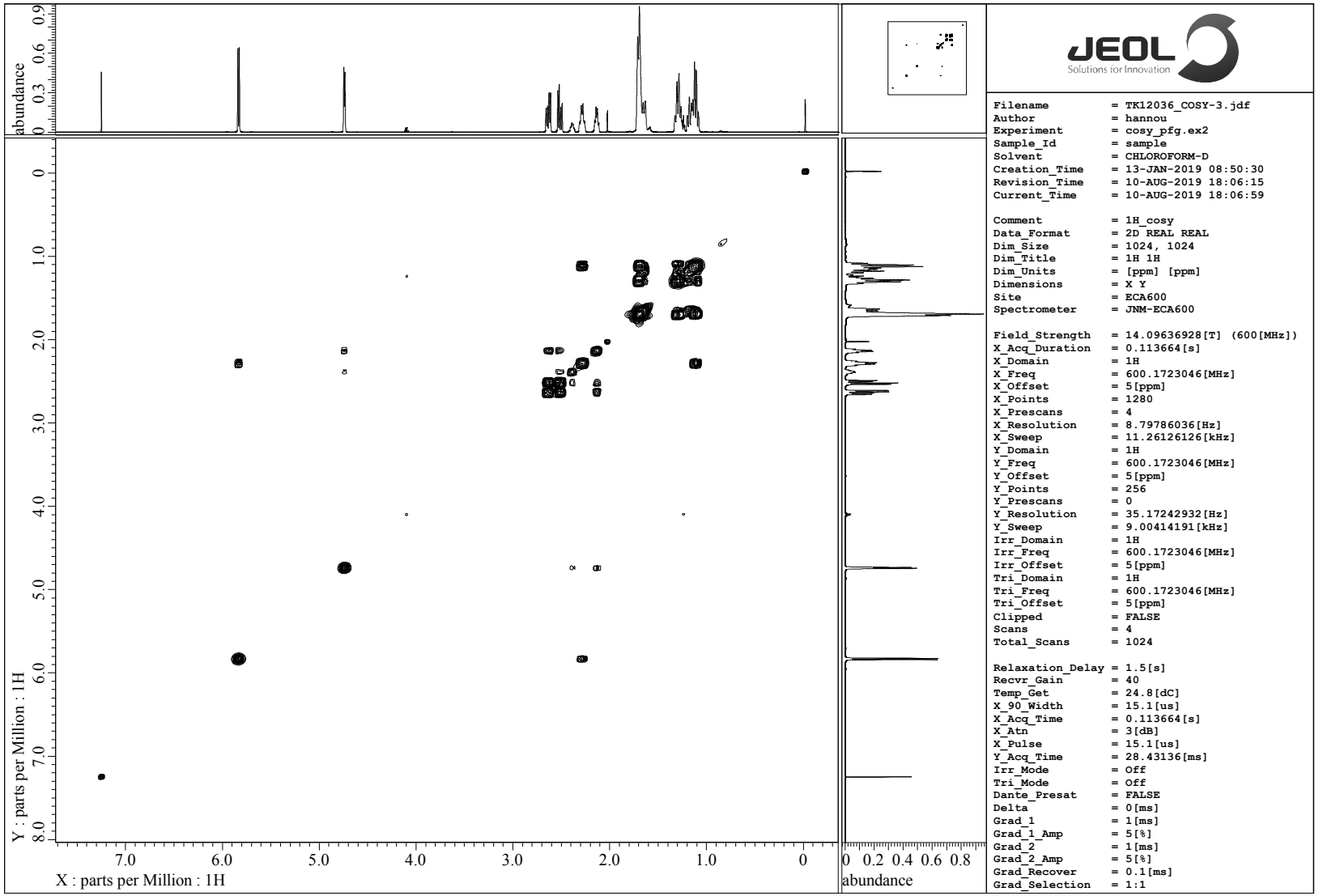
^{13}C NMR spectrum of **10**-*d* prepared from **7b**-*d*

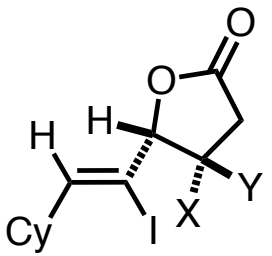


10-*d*
X: 27 atom % D
Y: 73 atom % D



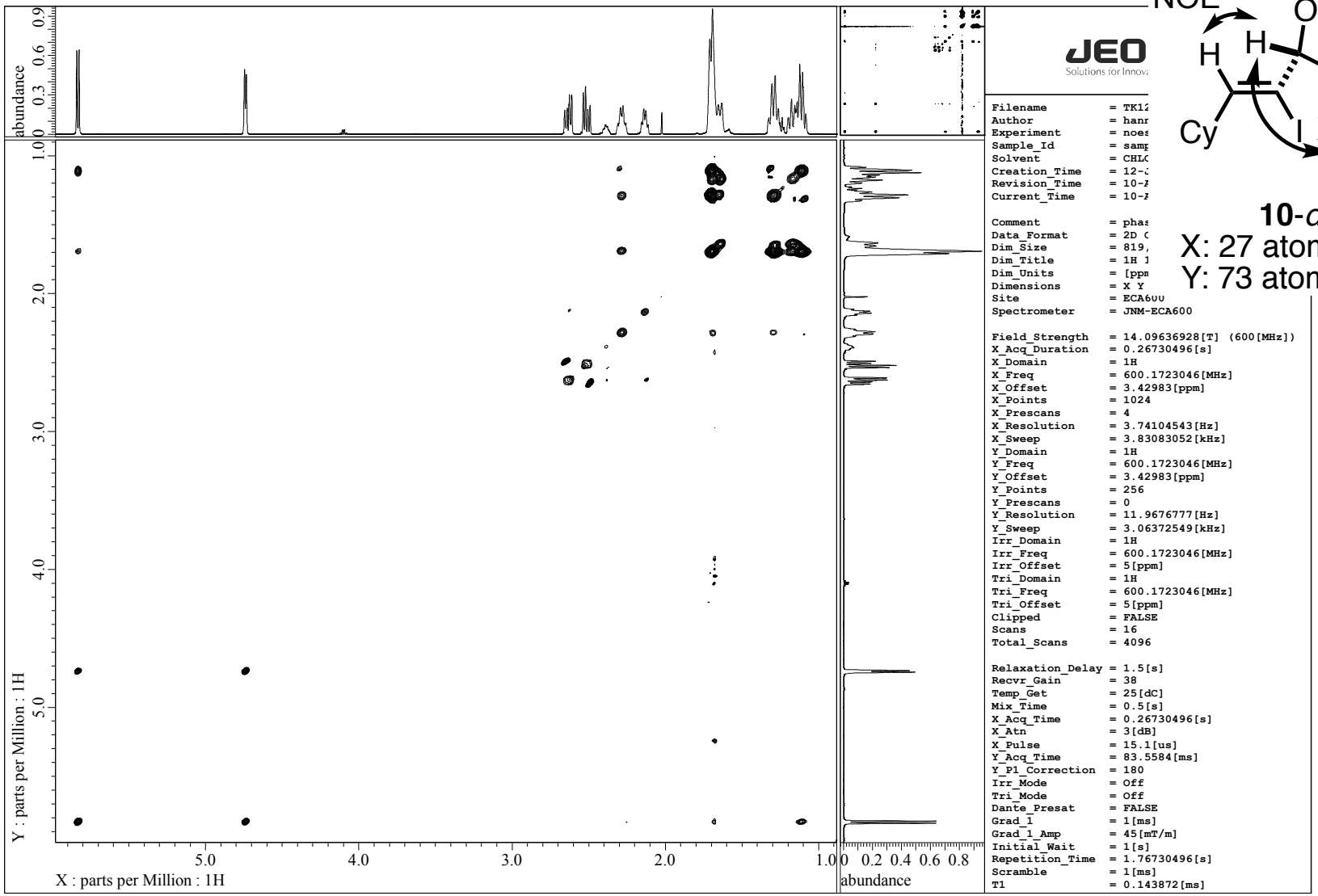
COSY spectrum of **10**-*d* prepared from **7b**-*d*

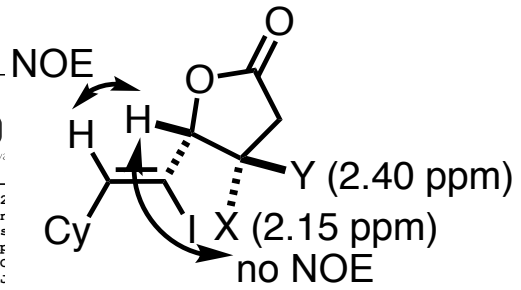




10-*d*
X: 27 atom % D
Y: 73 atom % D

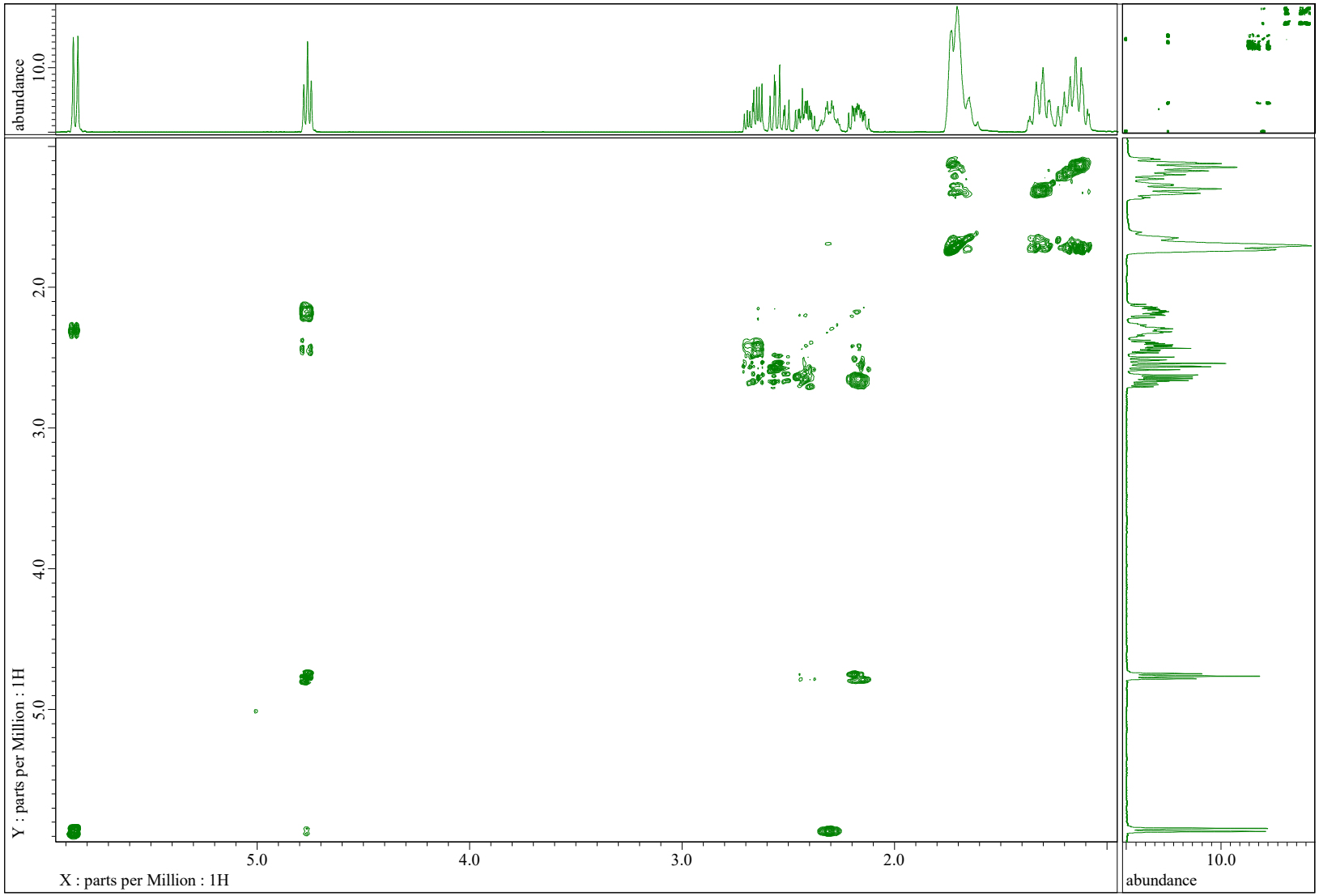
NOESY spectrum of **10**-*d* prepared from **7b**-*d*

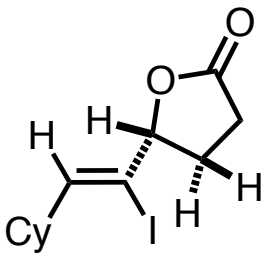




10-*d*
X: 27 atom % D
Y: 73 atom % D

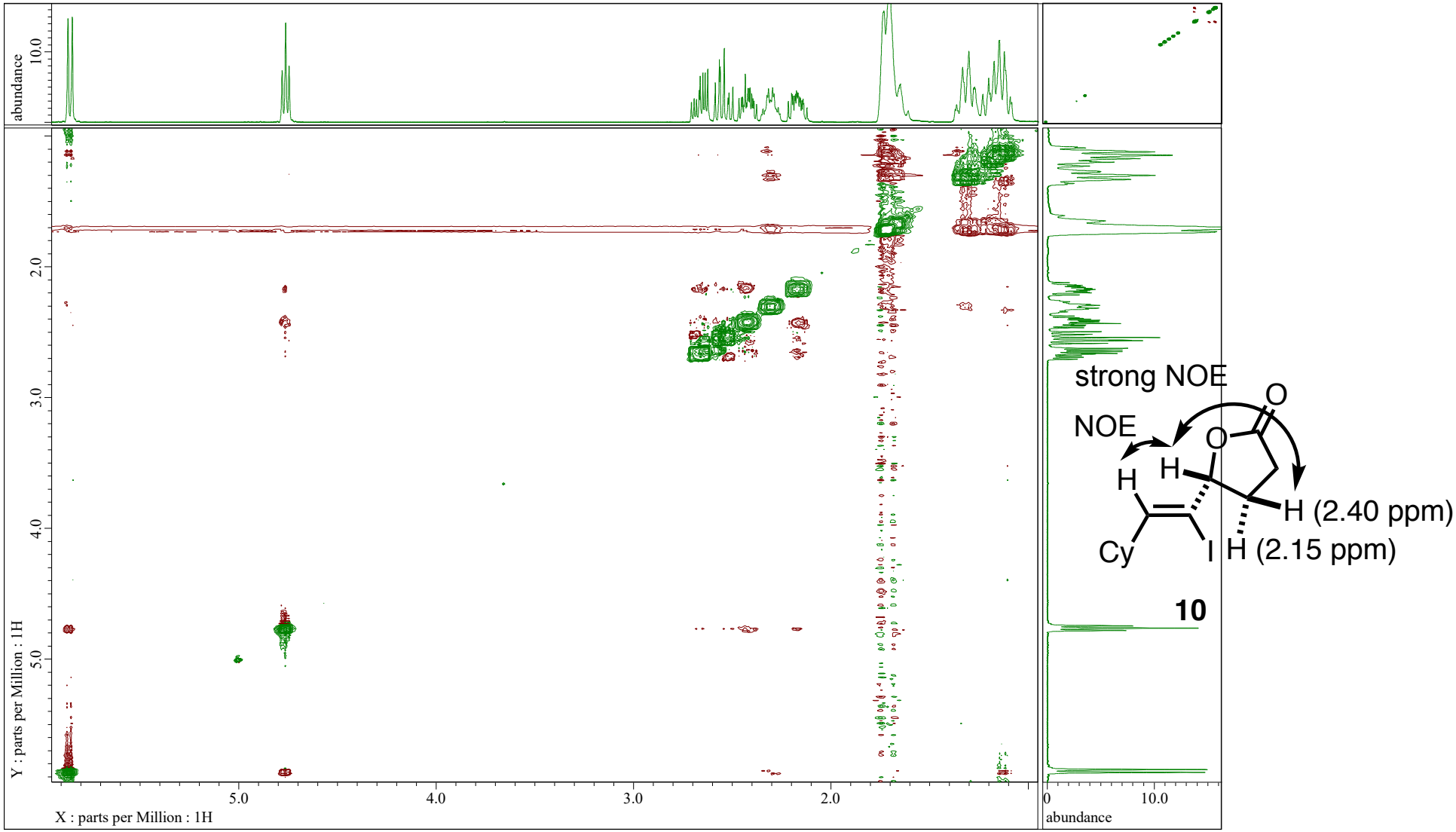
COSY spectrum of **10**



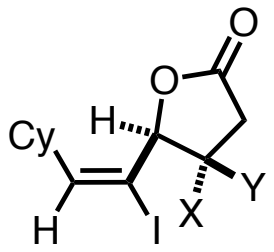


10

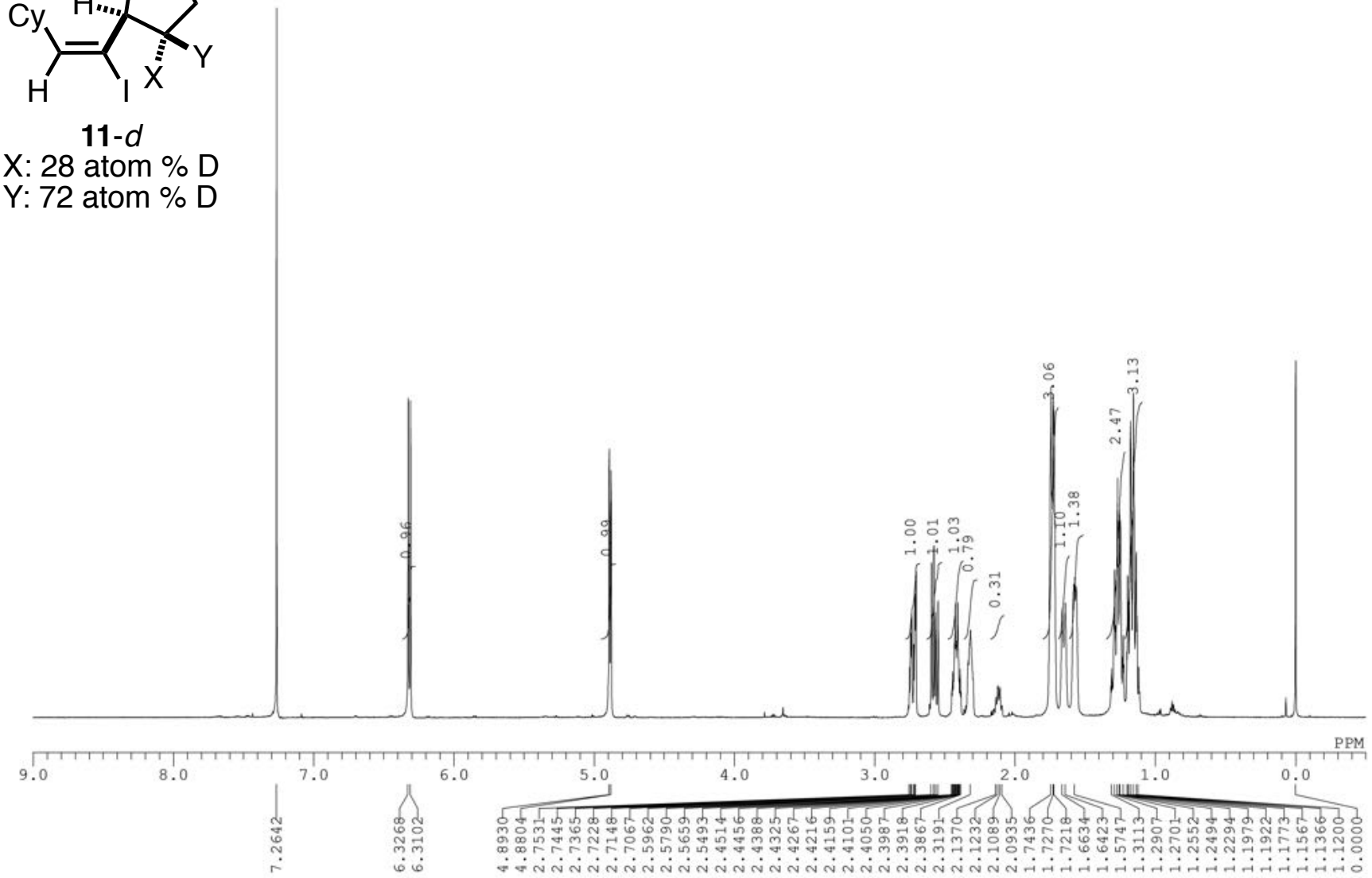
NOESY spectrum of **10**



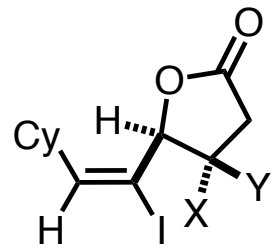
[1]H NMR spectrum of **11**-*d* prepared from **7b**-*d*



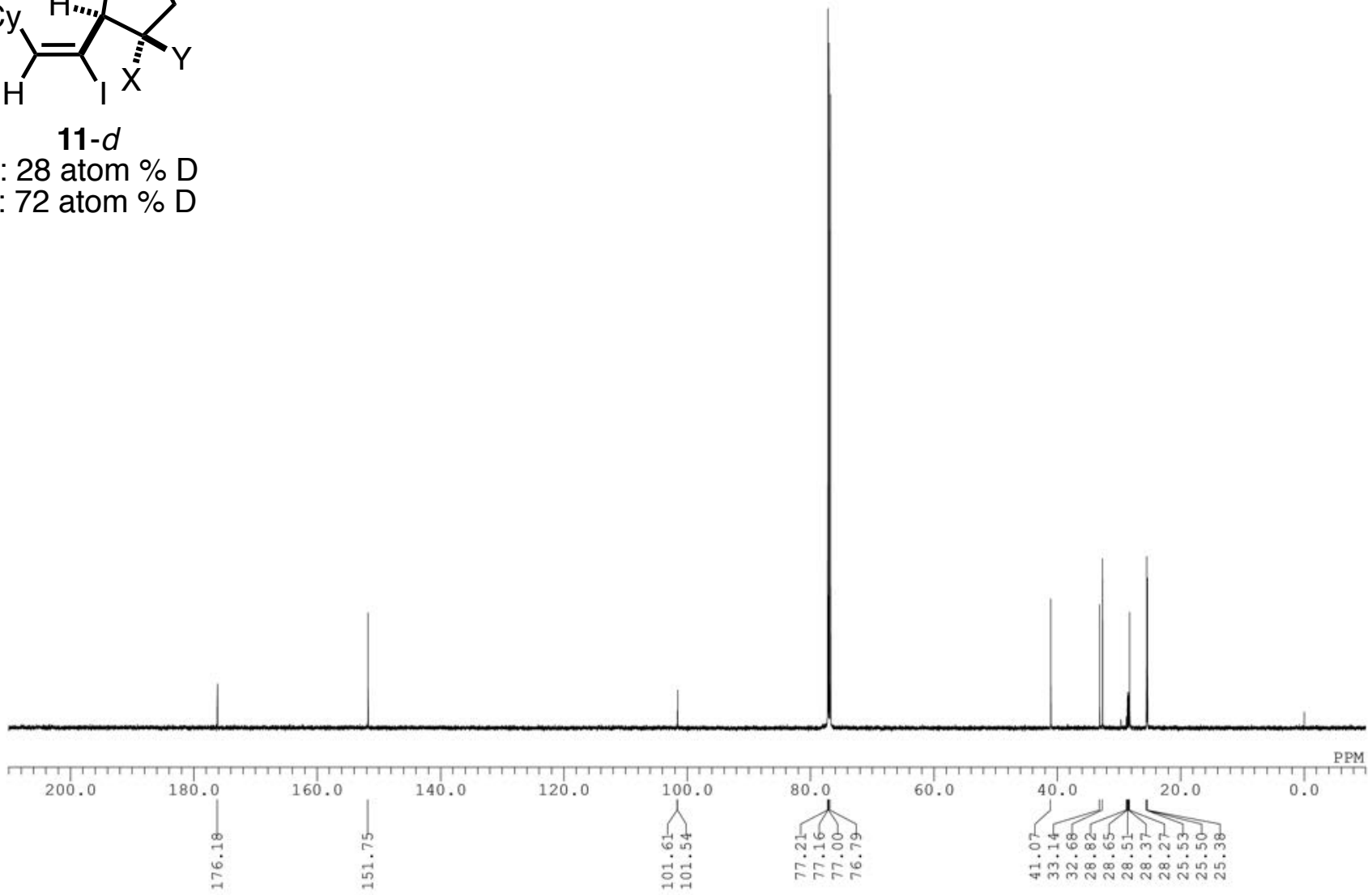
11-*d*
X: 28 atom % D
Y: 72 atom % D



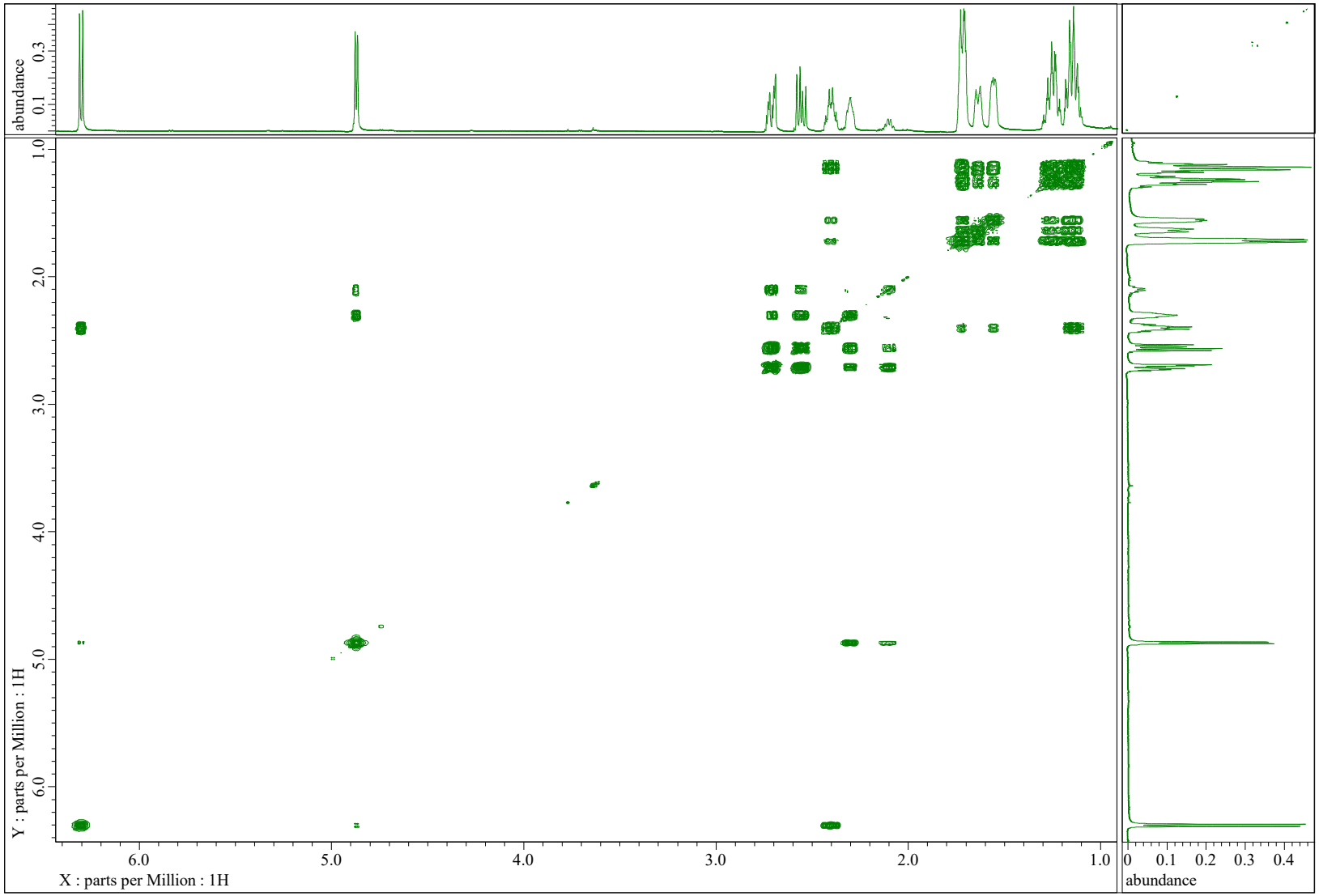
^{13}C NMR spectrum of **11**-*d* prepared from **7b**-*d*

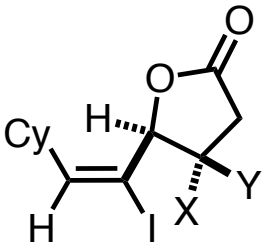


11-*d*
X: 28 atom % D
Y: 72 atom % D



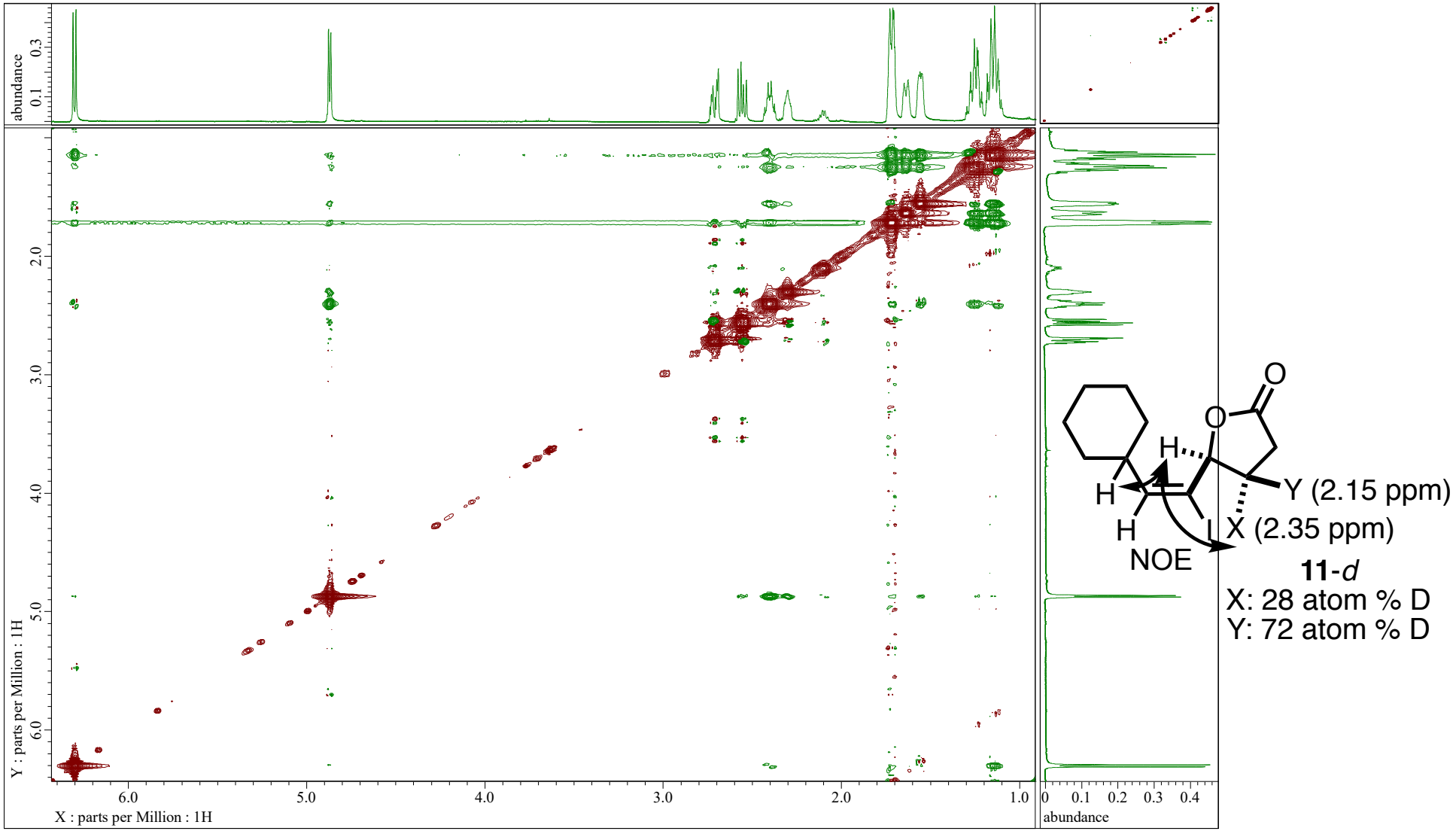
COSY spectrum of **11**-*d* prepared from **7b**-*d*



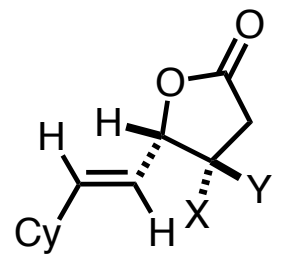


11-*d*
X: 28 atom % D
Y: 72 atom % D

NOESY spectrum of **11**-*d* prepared from **7b**-*d*

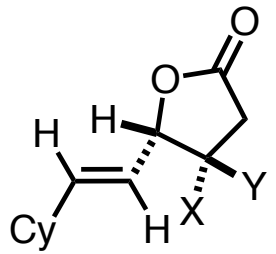


[1]H NMR spectrum of (4*R**,5*R**)-5-((*E*)-2-cyclohexylvinyl)dihydrofuran-2(3*H*)-one-4-*d*

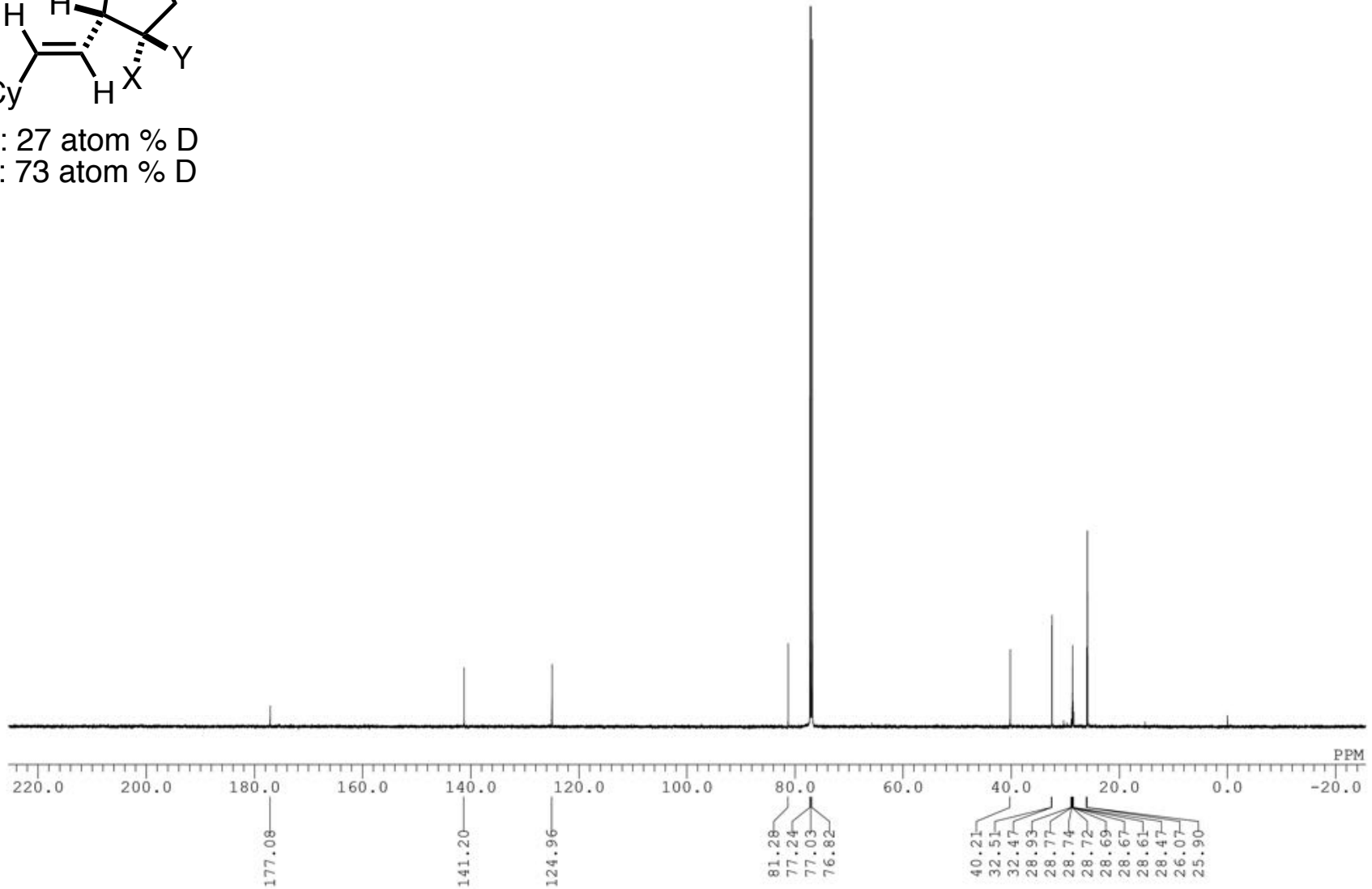


X: 27 atom % D
Y: 73 atom % D

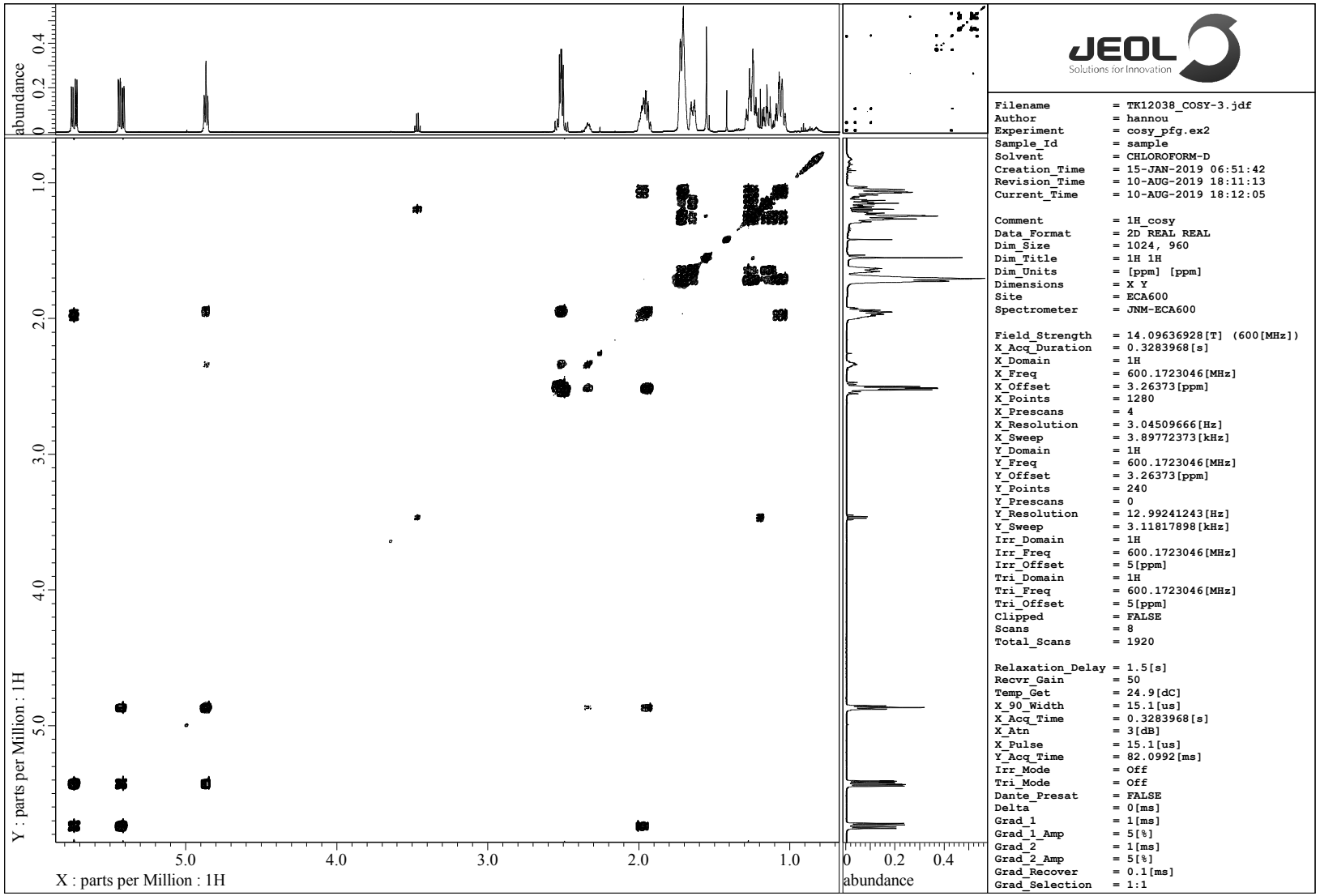
^{13}C NMR spectrum of (4*R**,5*R**)-5-((*E*)-2-cyclohexylvinyl)dihydrofuran-2(3*H*)-one-4-*d*

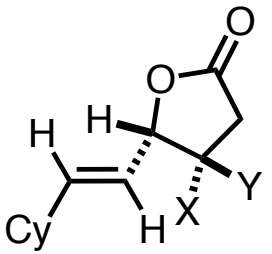


X: 27 atom % D
Y: 73 atom % D



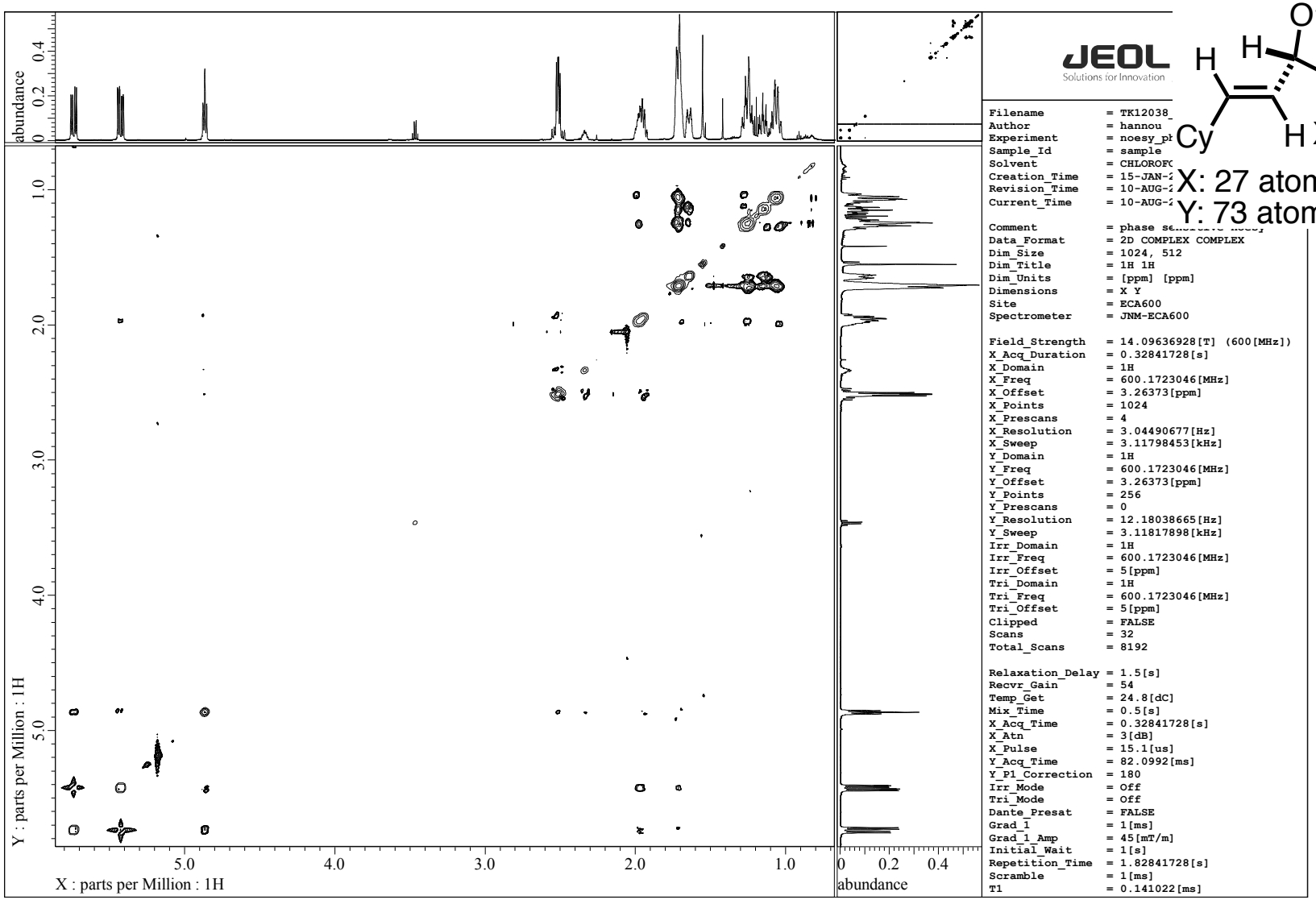
COSY spectrum of (4*R**,5*R**)-5-((*E*)-2-cyclohexylvinyl)dihydrofuran-2(3*H*)-one-4-*d*



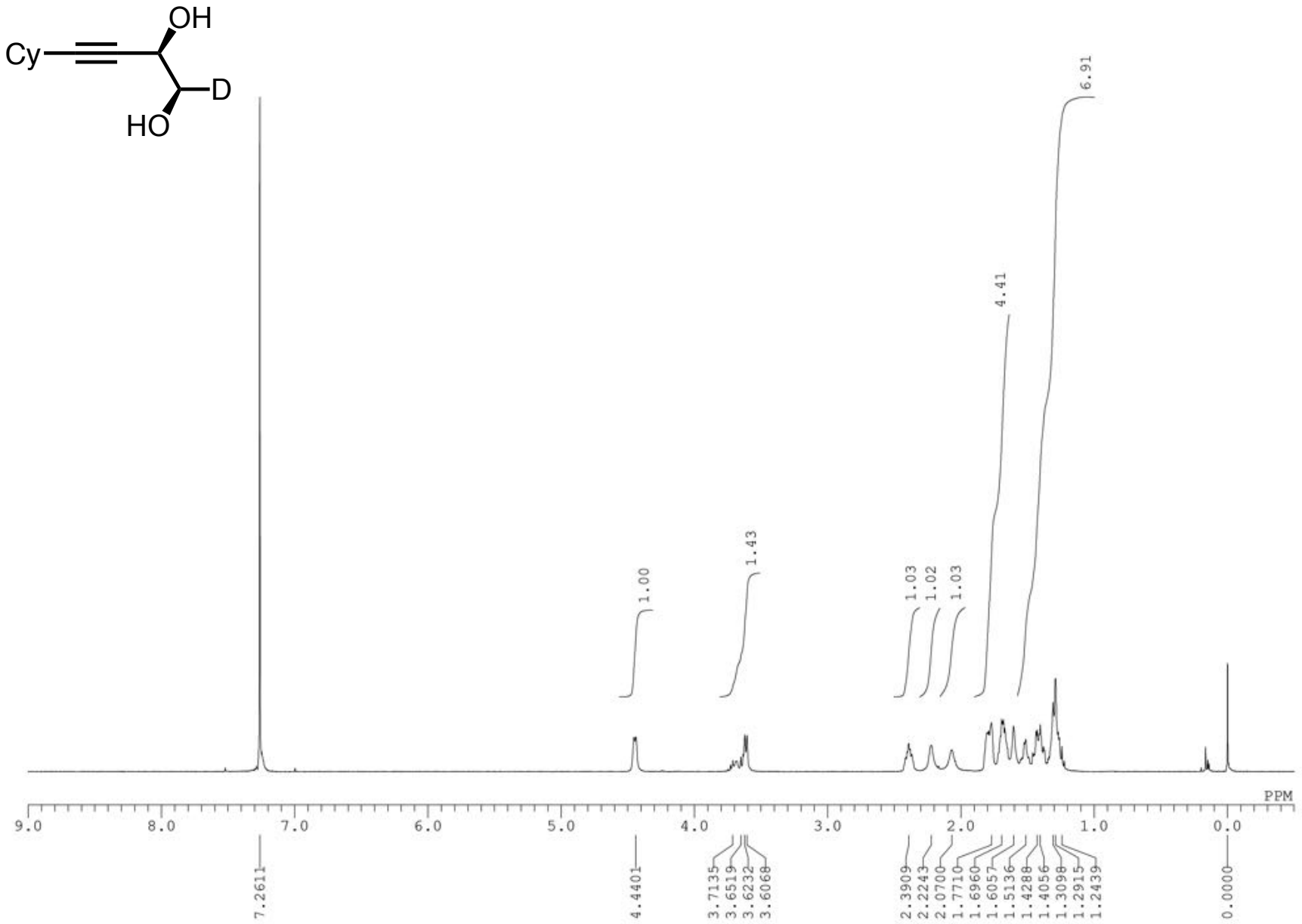


X: 27 atom % D
Y: 73 atom % D

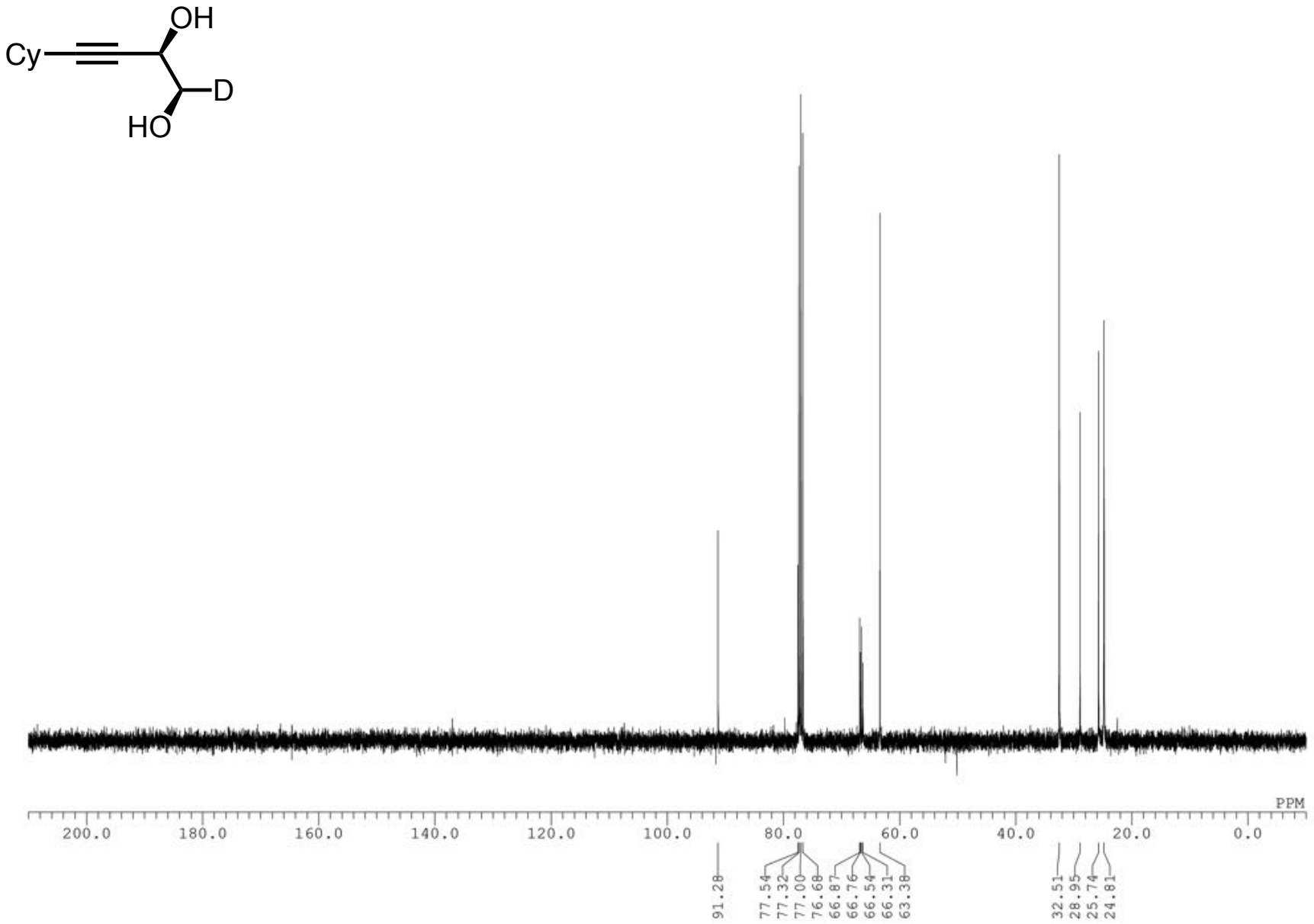
NOESY spectrum of (4*R**,5*R**)-5-((*E*)-2-cyclohexylvinyl)dihydrofuran-2(3*H*)-one-4-*d*



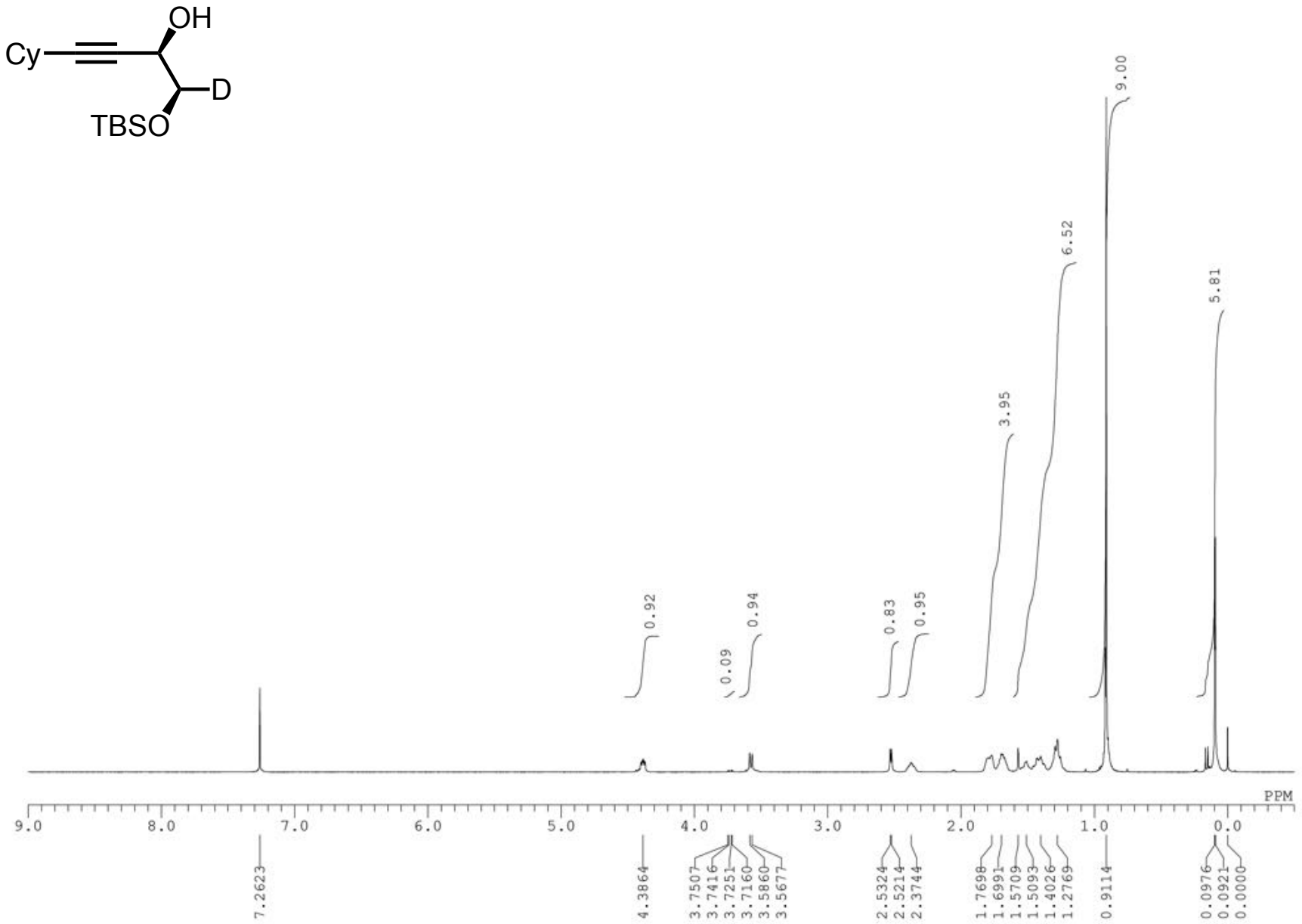
^{1}H NMR spectrum of (1*R*, 2*R*)-4-cyclohexylbut-3-yne-1-*d*-1,2-diol



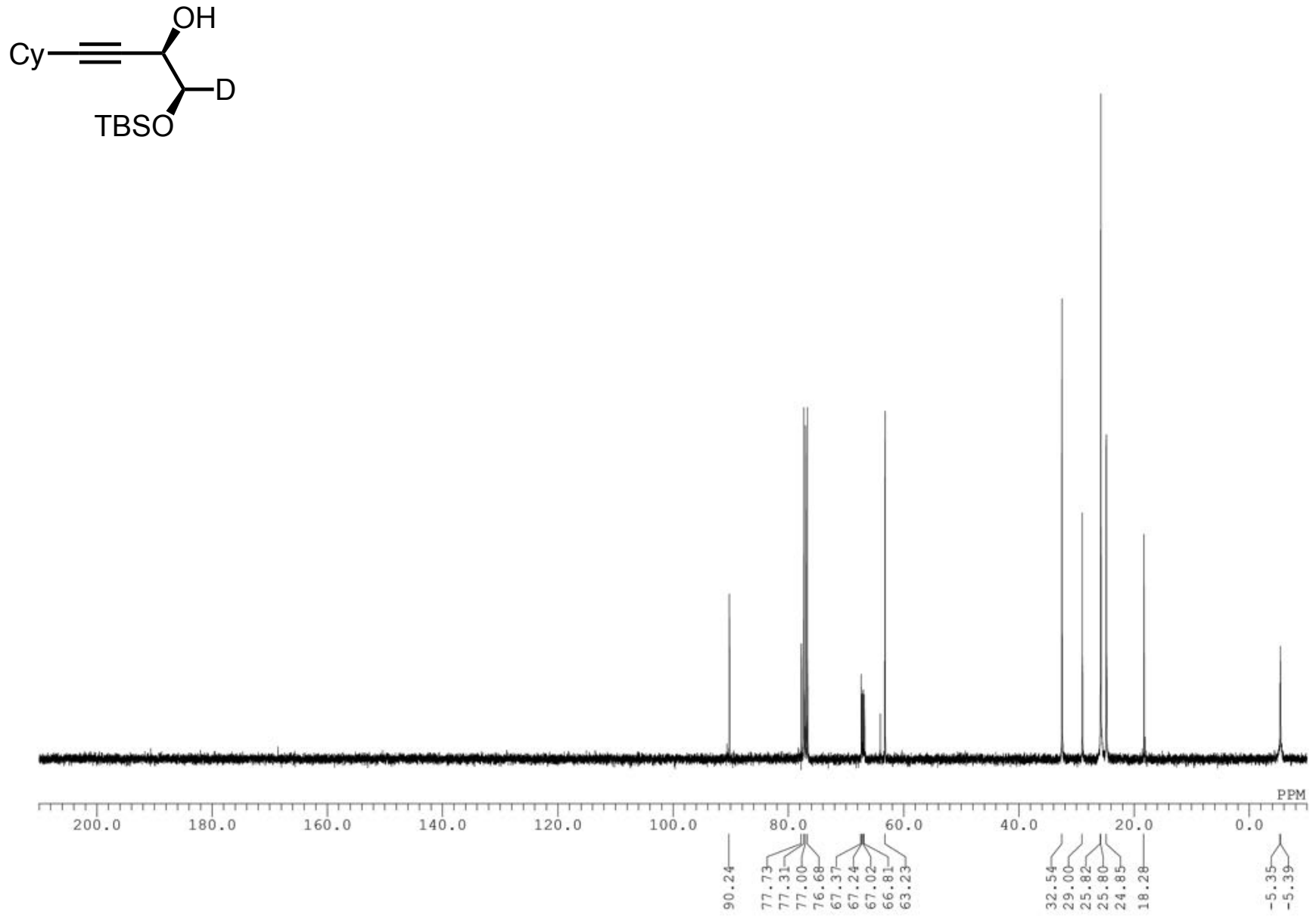
^{13}C NMR spectrum of (1*R*, 2*R*)-4-cyclohexylbut-3-yne-1-*d*-1,2-diol



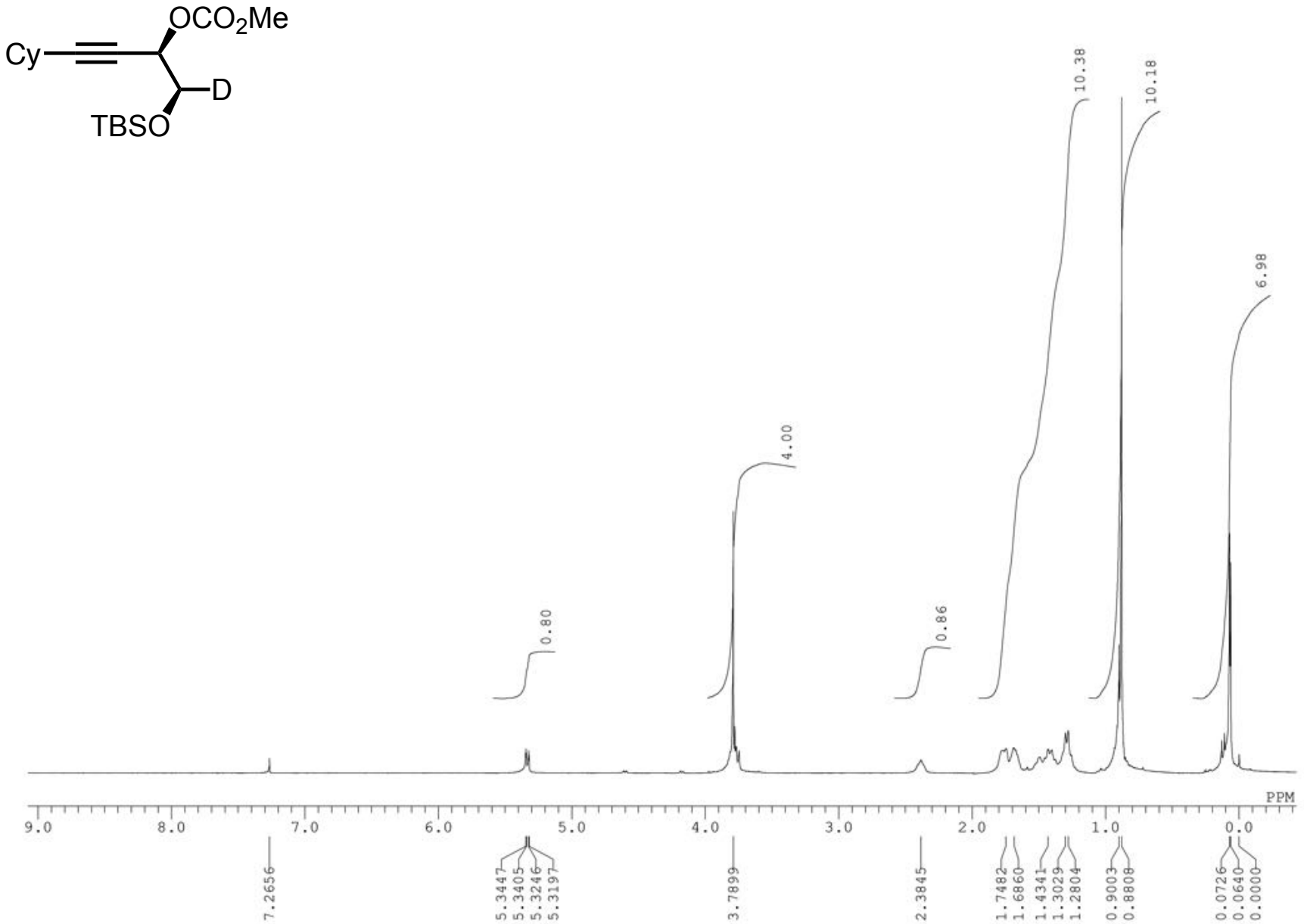
[1]H NMR spectrum of (1*R*, 2*R*)-1-((*tert*-butyldimethylsilyl)oxy)-4-cyclohexylbut-3-yn-1-*d*-2-ol



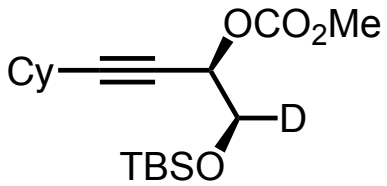
^{13}C NMR spectrum of (1*R*, 2*R*)-1-((*tert*-butyldimethylsilyl)oxy)-4-cyclohexylbut-3-yn-1-*d*-2-ol

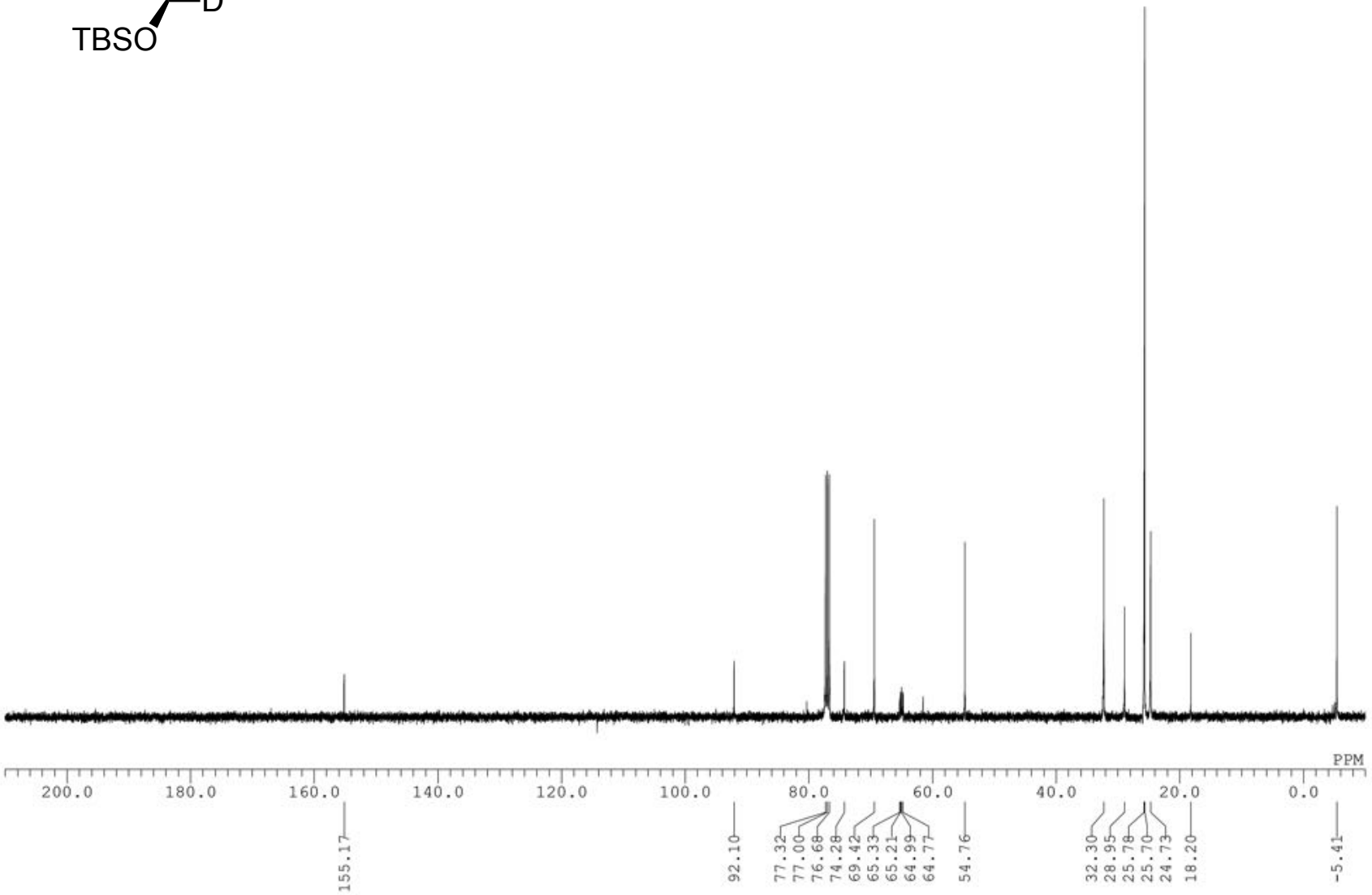


^{1}H NMR spectrum of (1*R*, 2*R*)-1-((*tert*-butyldimethylsilyl)oxy)-4-cyclohexylbut-3-yn-2-yl-1-*d* methyl carbonate

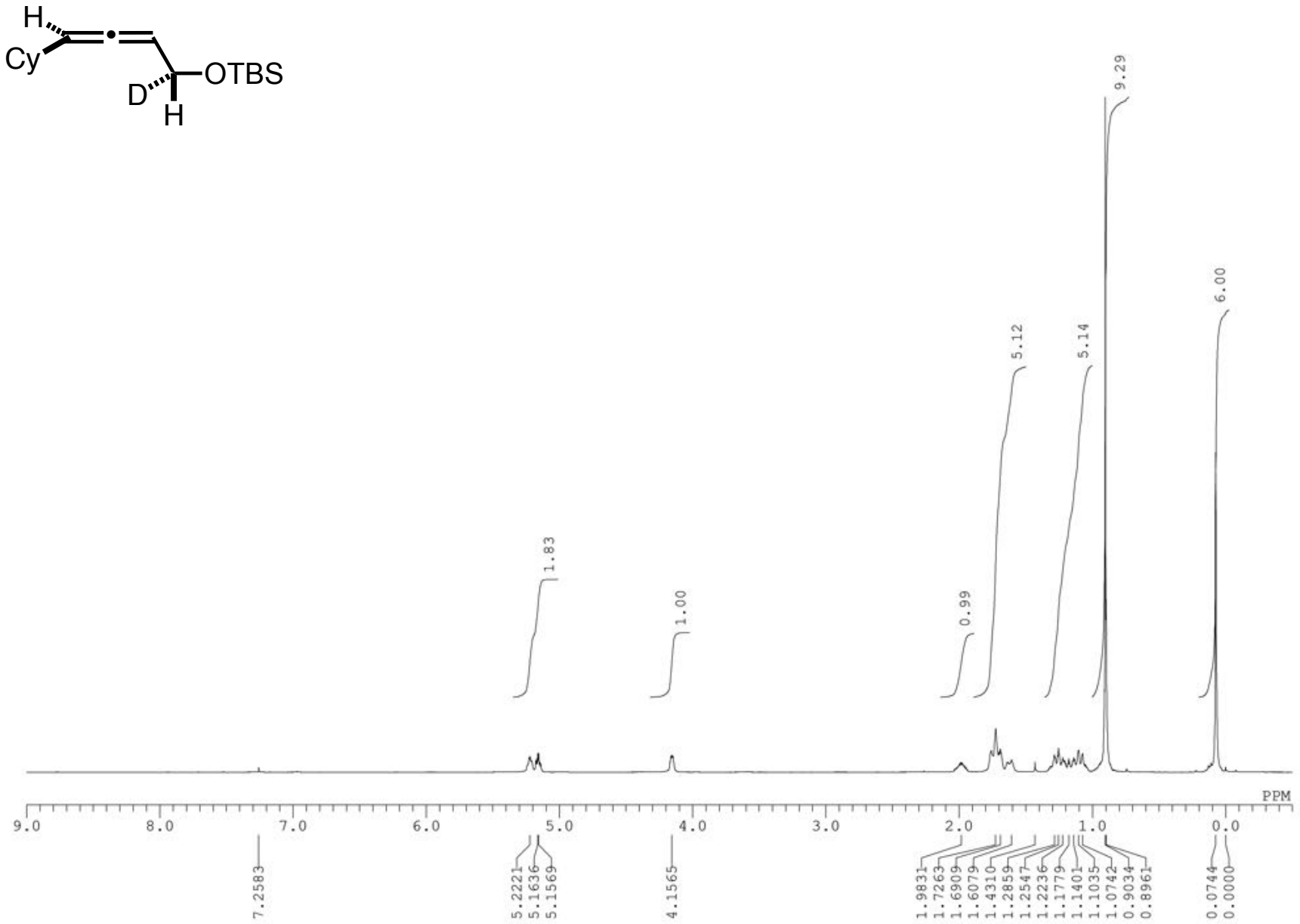


^{13}C NMR spectrum of (1*R*, 2*R*)-1-((*tert*-butyldimethylsilyl)oxy)-4-cyclohexylbut-3-yn-2-yl-1-*d* methyl carbonate

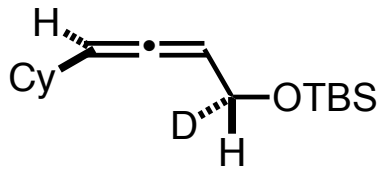


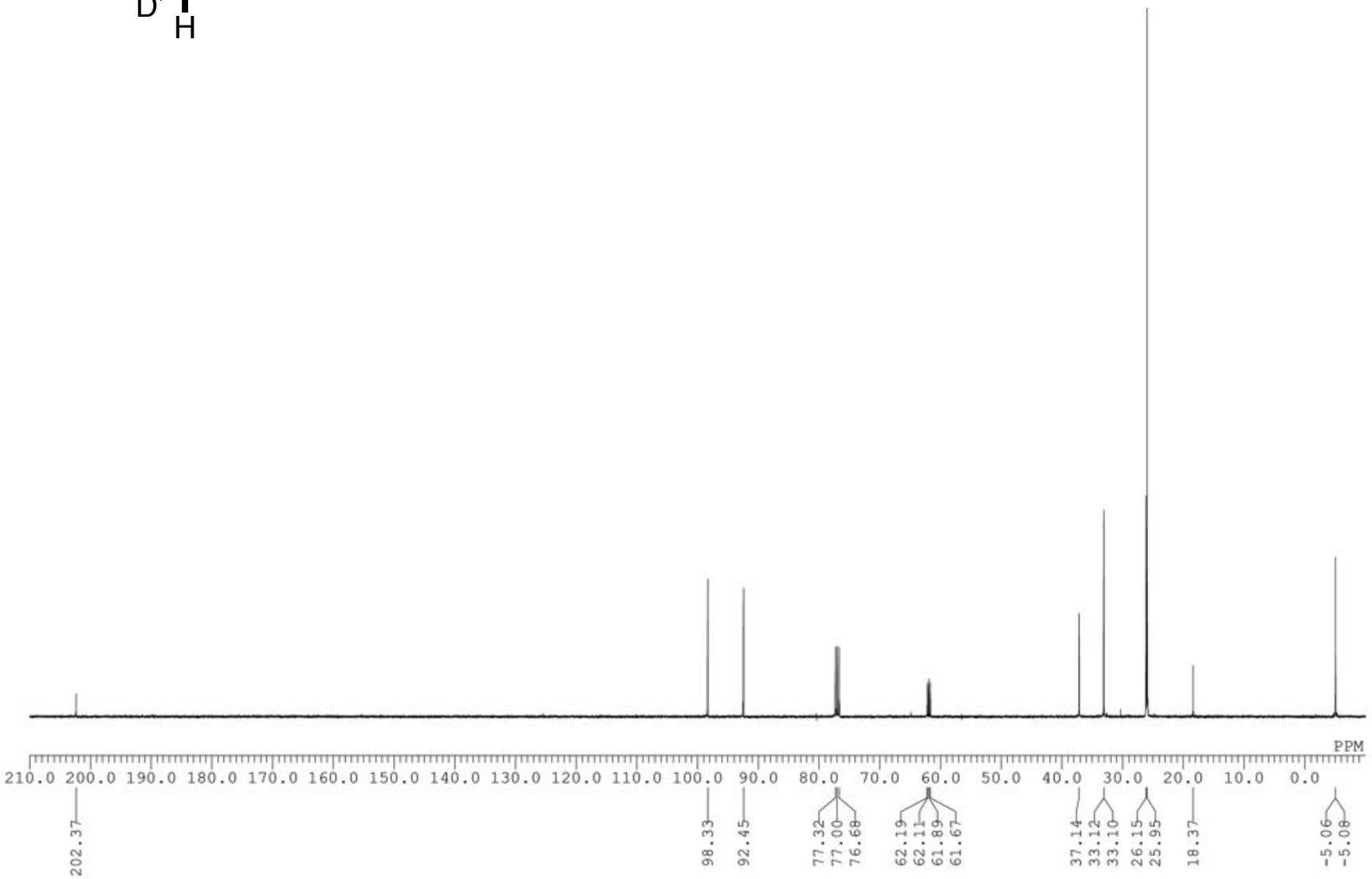


^{1}H NMR spectrum of *tert*-butyl(((1*R*, 3*S*)-4-cyclohexylbuta-2,3-dien-1-yl-1-*d*)oxy)dimethylsilane

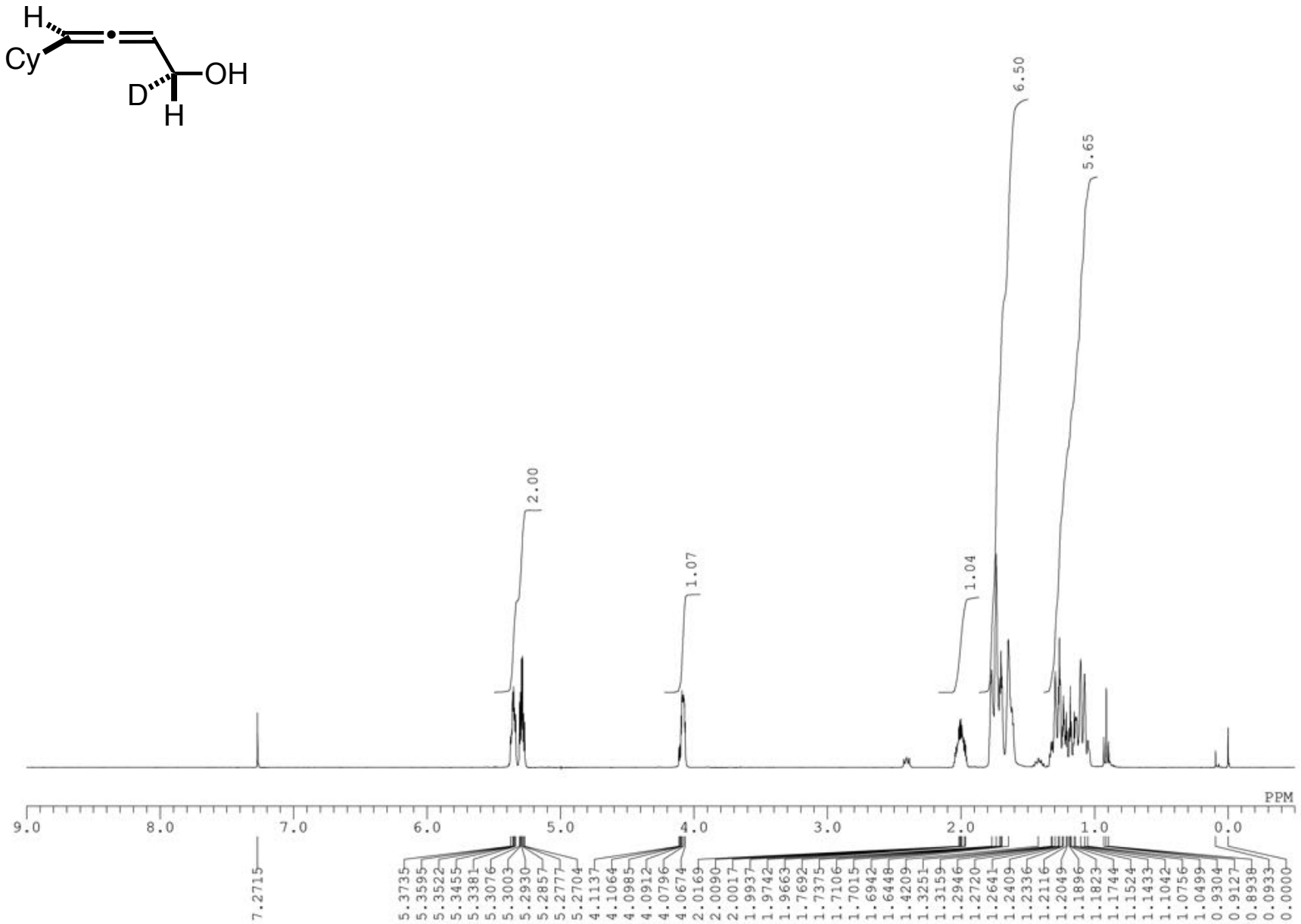


^{13}C NMR spectrum of *tert*-butyl(((1*R*, 3*S*)-4-cyclohexylbuta-2,3-dien-1-yl-1-*d*)oxy)dimethylsilane

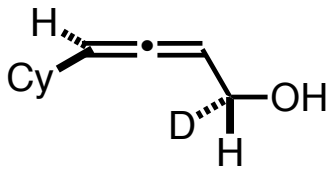


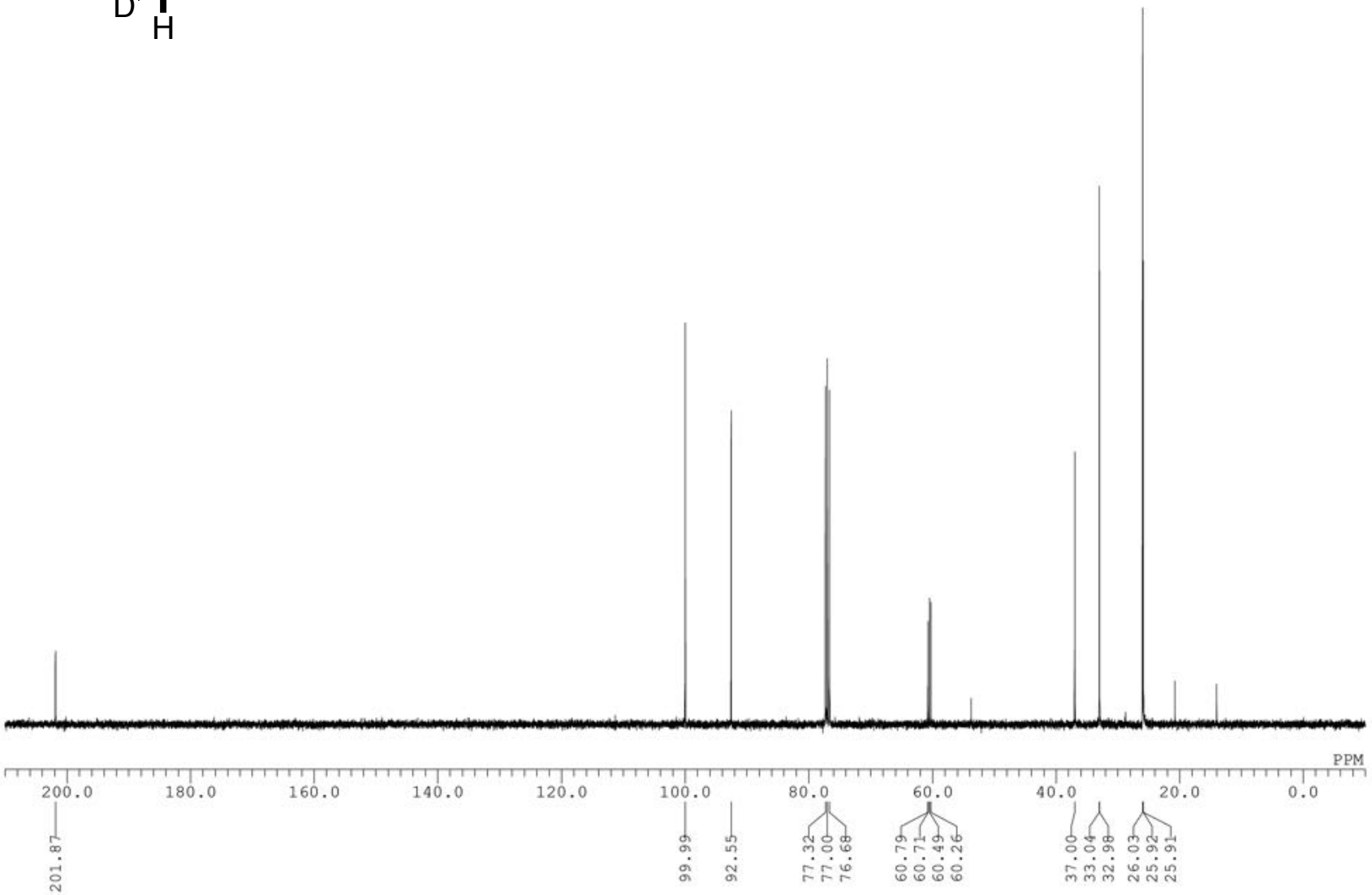


^{1}H NMR spectrum of (1*R*, 3*S*)-4-cyclohexylbuta-2,3-dien-1-*d*-1-ol

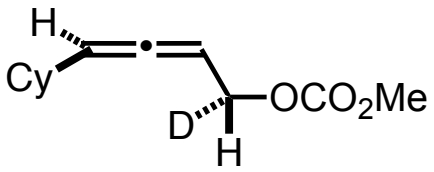


^{13}C NMR spectrum of (1*R*, 3*S*)-4-cyclohexylbuta-2,3-dien-1-*d*-1-ol



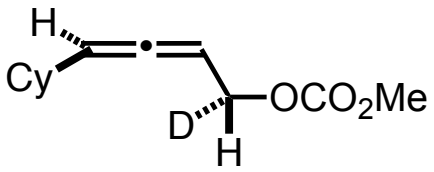


^{1}H NMR spectrum of (*S*a, *R*)-**2b**-*d*

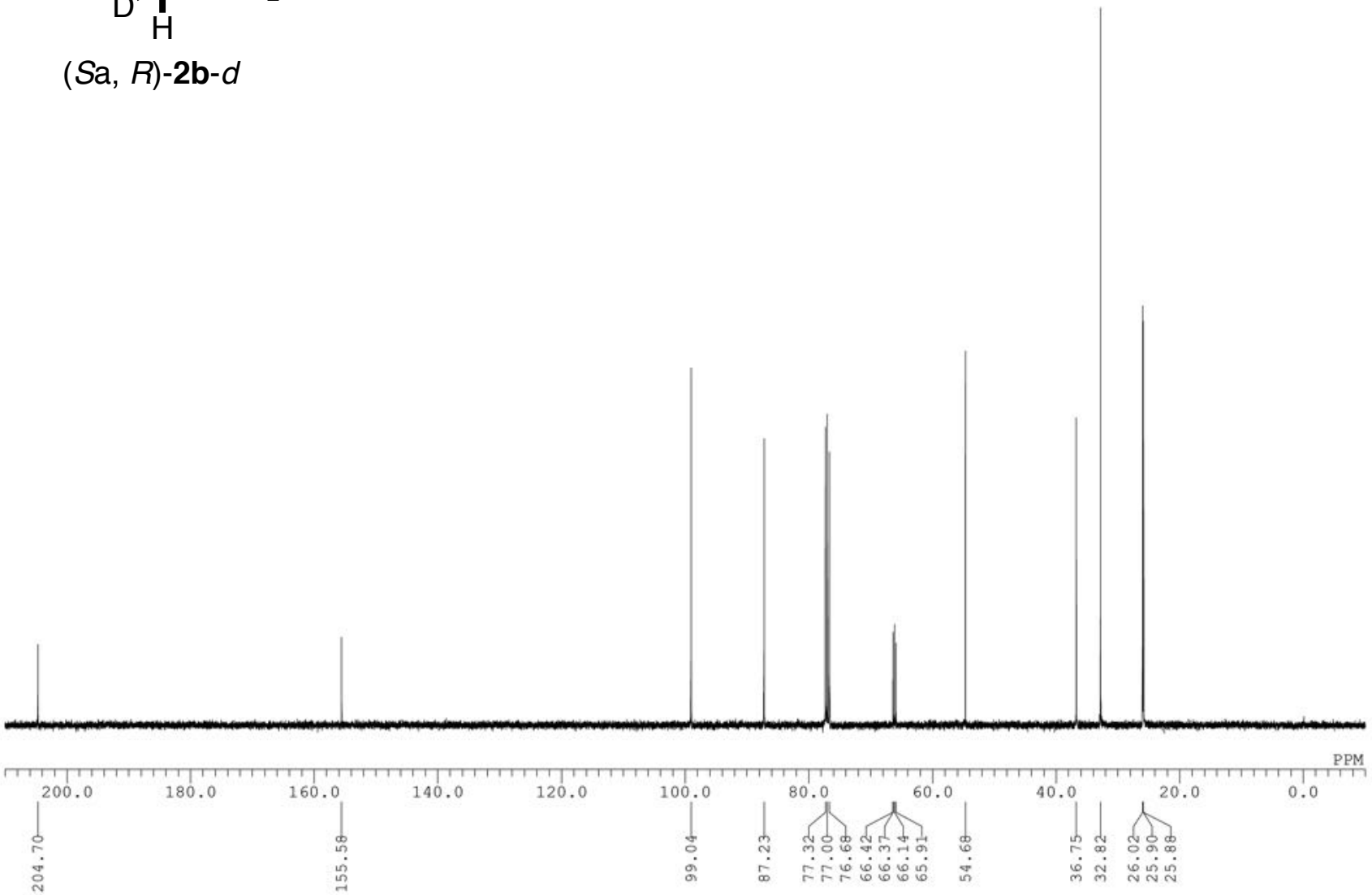


(*S*a, *R*)-**2b**-*d*

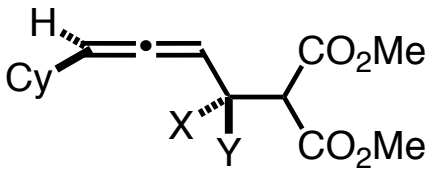
^{13}C NMR spectrum of (*S*a, *R*)-**2b**-*d*



(*S*a, *R*)-**2b**-*d*

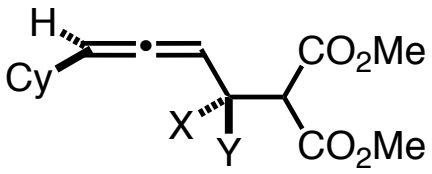


[1]H NMR spectrum of **6bA**-*d* prepared from (*S*a, *R*)-**2b**-*d*

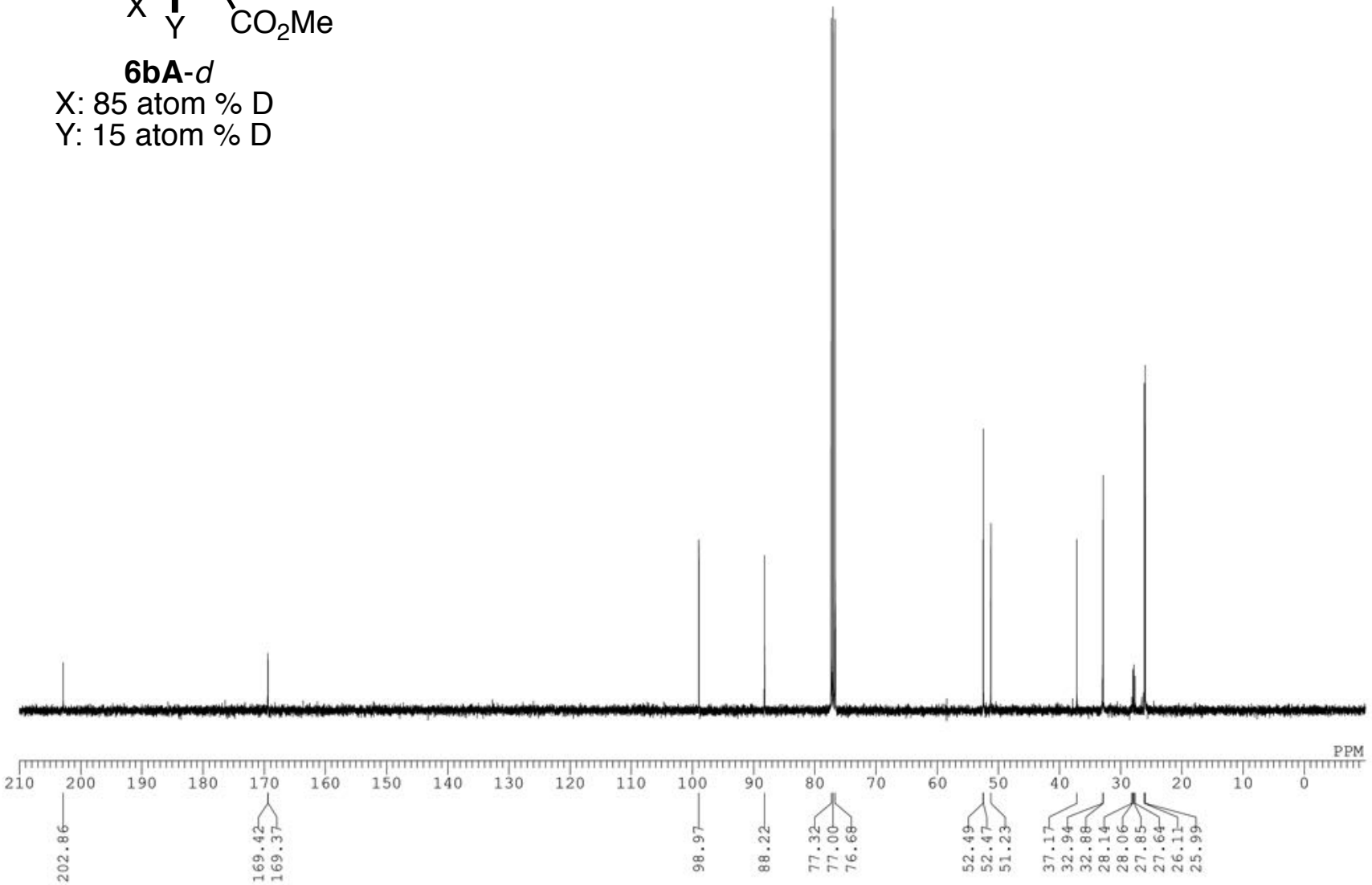


6bA-*d*
X: 85 atom % D
Y: 15 atom % D

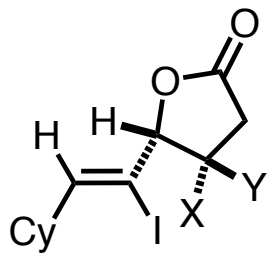
^{13}C NMR spectrum of **6bA**-*d* prepared from (*S*a, *R*)-**2b**-*d*



6bA-*d*
X: 85 atom % D
Y: 15 atom % D

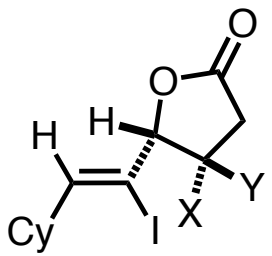


[1]H NMR spectrum of **10**-*d* prepared from (*S*a, *R*)-**2b**-*d*



10-*d*
X: 85 atom % D
Y: 15 atom % D

^{13}C NMR spectrum of **10**-*d* prepared from (*S*a, *R*)-**2b**-*d*



10-*d*
X: 85 atom % D
Y: 15 atom % D