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Electronic Supplementary Information

Nickel-catalyzed dimerization of pyrrolidinoindoline scaffolds: Systematic access to chimonanthines, folicanthines and (+)-WIN 64821

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General Methods

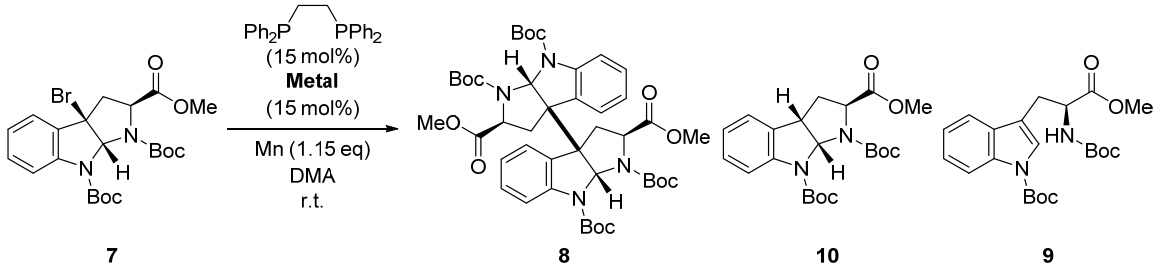
All reactions were performed under a nitrogen atmosphere unless otherwise specified. NMR spectra were recorded on JEOL α400, JNM-ECX 400 (^{1}H/400 MHz, ^{13}C/100 MHz), and Bulker VSP 500 (^{1}H/500 MHz, ^{13}C/125 MHz) spectrometers. Chemical shifts are reported in δ (ppm) using chloroform as an internal standard of δ 7.26, and 77.16, acetonitrile as an internal standard of δ 1.94, and 118.26, methanol as an internal standard of δ 3.31, and 49.00, and dimethyl sulfoxide as an internal standard of δ 2.50, and 39.52 for ^{1}H and ^{13}C NMR, respectively. Data for ^{1}H NMR are reported as follows: chemical shift (number of hydrogens, multiplicity, coupling constant). Multiplicity is abbreviated as follows: s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), m (multiplet), br (broad). ESI-Mass spectra were recorded on JEOL The AccuTOF LC-Plus JMS-T100. Optical rotations were recorded on JASCO DIP-360 digital polarimeter. The medium pressure liquid chromatography (MPLC) purifications were performed on a YAMAZEN YFLC-AI-580. Where necessary, solvents were distilled from appropriate drying agents prior to use. Reactions were monitored by thin layer chromatography using Merck Millipore TLC Silica gel F_{254} plates (0.25 mm) which were visualized using UV light, *p*-anisaldehyde stain, and PMS stain. Flash column chromatography was performed using Kanto Silica Gel 60N or Amino silica-gel [Kanto Silica Gel 60 (spherical) NH_2].

Materials

$NiCl_2$ was purchased from Wako Pure Chemical Industries, Ltd. and used after vacuuming for 5 h. $NiCl_2 \cdot 6H_2O$, $NiF_2 \cdot 4H_2O$, $NiBr_2$, $CuCl_2$, $FeCl_3$, and $CoCl_2$ were purchased from Wako Pure Chemical Industries, Ltd. and used as received. NiI_2 was purchased from Alfa Aesar and used as received. $NiI_2 \cdot 6H_2O$ was purchased from Nacalai Tesque, Inc. and used as received. Manganese and $InCl_3$ were purchased from Aldrich Chemical Co. and used as received. The ligands (SciOPP and TMS-SciOPP)[1] were provided through the generous gift by Prof. Masaharu Nakamura (Kyoto Univ.) and Prof. Takuji Hatakeyama (Kwansei Gakuin Univ.).

Synthetic procedures

Screening of catalyst for reductive dimerization of **7** (*exo*)



General procedure

To a mixture of metal catalyst (0.120 mmol, 15 mol%) and DPPE (47.8 mg, 0.120 mmol, 15 mol%) in DMA (650 μL) was added bromide **7** (398 mg, 0.800 mmol), and resulting mixture was purged with nitrogen. After treatment with Mn (50.5 mg, 0.920 mmol, 1.15 eq), the resulting suspension was immediately purged again with nitrogen and stirred at room temperature for 12 h. The mixture was diluted with AcOEt and treated with 1 N HCl. After separation of aqueous phase, organic layer was washed with H_2O x2, 1 N HCl, saturated aqueous solution of Na_2SO_3, and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to isolate dimer **8**,[2] byproducts (**9** and **10**) and recovered substrate **7**.

Procedure with pretreatment of anhydrous metal catalyst with H_2O

Anhydrous metal catalyst (0.120 mmol, 15 mol%) and H_2O (0.720 mmol, 90 mol%) were premixed, and then DMA (650 μL) was added. To a resulting mixture of metal catalyst in DMA were added DPPE (47.8 mg, 0.120 mmol, 15 mol%) and bromide **7** (398 mg, 0.800 mmol), and resulting mixture was purged with nitrogen. After addition of Mn (50.5 mg, 0.920 mmol, 1.15 eq), the resulting suspension was immediately purged again with nitrogen and stirred at room temperature for 12 h. The mixture was diluted with AcOEt and treated with 1 N HCl. After separation of aqueous phase, organic layer was washed with H_2O x2, 1 N HCl, saturated aqueous solution of Na_2SO_3, and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to isolate dimer **8**, byproducts (**9** and **10**) and recovered substrate **7**.

Table S1: Screening of catalyst for reductive dimerization of **7** (*exo*)

Entry	Metal	**8** [%][a] (C_2-dimer)	**10** [%][a] (reduced)	**9** [%][a] (cleaved)	**7** [%][a] (recovery)
1	$CuCl_2$	trace	trace	77	0
2	$FeCl_3$	trace	14	64	0
3	$InCl_3$	12	<5	74	0
4	$CoCl_2$	46	18	<5	0
5	$NiCl_2{\cdot}6H_2O$	60	17	8	0
6	$NiCl_2$	trace	trace	7	75
7	$NiCl_2 + 6H_2O$	52	13	5	0
8	$NiF_2{\cdot}4H_2O$	trace	<5	trace	83
9	$NiBr_2{+}6H_2O$	58	14	<5	0
10	$NiI_2 + 6H_2O$	70	8	6	0
11	$NiI_2{\cdot}6H_2O$	74	<5	13	0

a) Isolated yields, average of two trials.

Effects of ligand on nickel-catalyzed dimerization of **7** (*exo*)

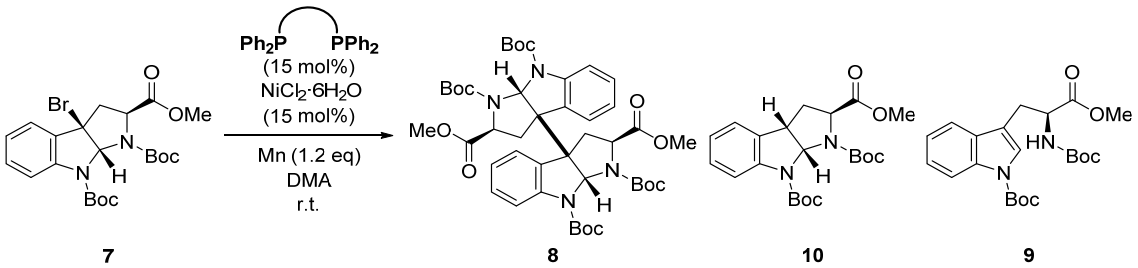


Table S2: Screening of optimum ligands for nickel-catalyzed reductive dimerization of **7** (*exo*)

Entry	Metal	Ligand	Solvent	**8** [%][a] (C_2-dimer)	**10** [%][a] (reduced)	**9** [%][a] (cleaved)	**7** [%][a] (recovery)
1	$NiCl_2{\cdot}6H_2O$	PPh_3[b]	DMA	11	10	19	36
2		DPPF		28	17	20	<5
3		DPPB		46	14	<5	<10
4		DPPP		56	<5	<5	<5
5		DPPBz		55	19	trace	<5
6		DPPE		60	17	8	0

a) Isolated yields, average of two trials. *b*) 30 mol%.

Effects of solvent on nickel-catalyzed dimerization of **7** (*exo*)

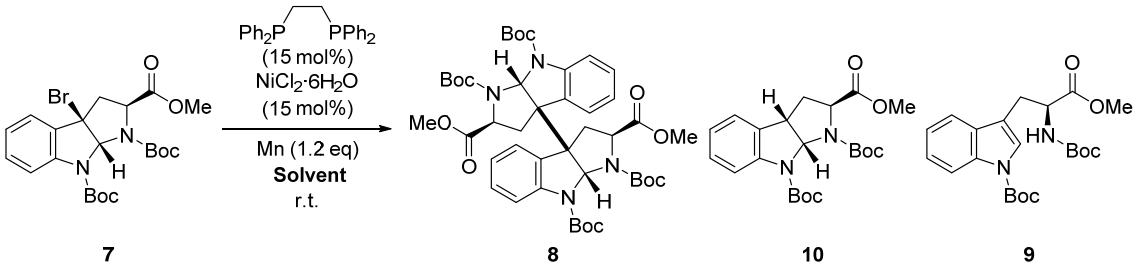


Table S3: Screening of optimum solvents for nickel-catalyzed reductive dimerization of **7** (*exo*)

Entry	Metal	Ligand	Solvent	**8** [%][a] (C_2-dimer)	**10** [%][a] (reduced)	**9** [%][a] (cleaved)	**7** [%][a] (recovery)
1	$NiCl_2·6H_2O$	DPPE	toluene	trace	<5	trace	82
2			CH_3CN	41	10	9	0
3			THF	24	23	16	0
4			DMSO	41	11	trace	<5
5			DMPU	23	31	28	0
6			NMP	51	19	14	0
7			DMF	60	5	10	0
8			DMA	60	17	8	0

a) Isolated yields, average of two trials.

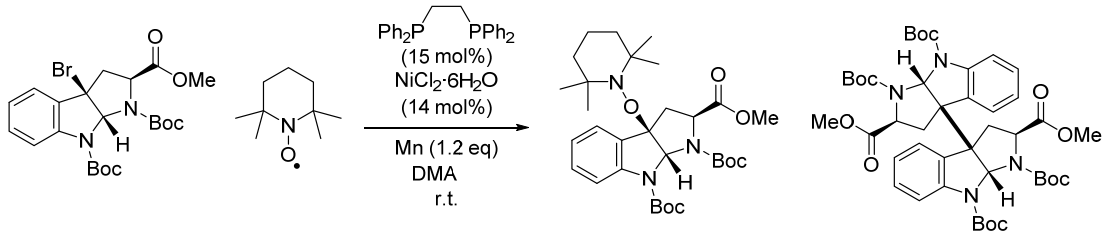
Control experiments and reactions in the presence of either excess amounts of water or TEMPO

Table S4: Control experiments and reactions with water or TEMPO

Entry	Metal	Reductant	Additive/ Conditions	**8** [%][a] (C_2-dimer)	**10** [%][a] (reduced)	**9** [%][a] (cleaved)	**7** [%][a] (recovery)
1	$NiCl_2·6H_2O$	-	-	-	-	-	95
2	-	Mn	-	-	-	n.d.[b]	93
3[c]	$NiI_2·6H_2O$	Mn	under air	n.d.[b]	n.d.[b]	n.d.[b]	83
4[d]	$NiCl_2·6H_2O$	Mn	H_2O (10 eq. to **7**)	19	45	trace	12
5[e]	$NiCl_2·6H_2O$	Mn	TEMPO (47 mol%)	-	-	-	91

a) Isolated yields. *b*) Analyzed by HPLC. n.d. (not determined). *c*) Average of two trials. *d*) H_2O (144 µL, 10 eq. based on **7**) and DMA (600 µL) were used. *e*) A trace amount of TEMPO-adduct **14** (<2%) was obtained (see following scheme).

An attempt for nickel-catalyzed dimerization of **7** in the presence of TEMPO

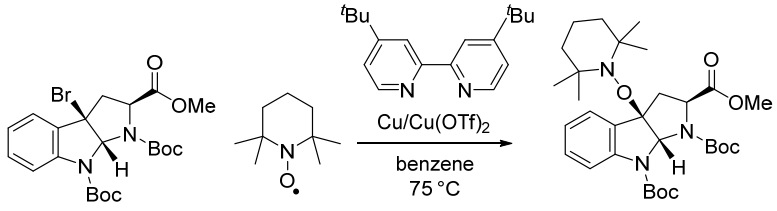


7 TEMPO (47 mol%) **14** (<2%) **8** (not obtained)

To a mixture of $NiCl_2$•$6H_2O$ (26.5 mg, 0.111 mmol, 14 mol%) and DPPE (48.2 mmol, 0.121 mmol, 15 mol%) in DMA (650 µL) was added bromide **7** (396 mg, 0.796 mmol), and resulting mixture was purged with nitrogen. After treatment with TEMPO (58.2 mg, 0.372 mmol, 47 mol%) and Mn (54.1 mg, 0.985 mmol, 1.2 eq.), the resulting suspension was immediately purged again with nitrogen and stirred at room temperature for 12 h. The mixture was diluted with AcOEt and treated with 1 N HCl. After separation of aqueous phase, organic layer was washed with H_2O x2, 1 N HCl, and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to afford a trace amount of **14** (7.7 mg, 0.013 mmol, <2%) and recovered substrate **7** (363 mg, recovery 91%).

14: R_f = 0.61 (Hex:AcOEt = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$, 45 °C): δ 7.54 (1H, br-s), 7.37 (1H, d, *J* = 7.5 Hz), 7.28 (1H, m), 7.07 (1H, t, *J* = 7.4 Hz), 6.61 (1H, s), 3.81 (1H, m), 3.72 (3H, d, *J* = 1.6 Hz), 2.76-2.64 (2H, m), 1.56 (9H, s), 1.40 (9H, s), 1.44-1.31 (5H, m), 1.29-1.21 (1H, m), 1.08-0.98 (6H, m), 0.94-0.70 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$, 45 °C): δ 172.56, 152.63, 144.42, 132.86, 130.11, 125.57, 123.39, 117.96, 91.89, 81.39, 80.89, 79.67, 77.36, 60.66, 59.82, 59.64, 52.10, 41.16, 40.69, 40.61, 33.91, 33.14, 28.48, 28.41, 20.78, 20.71, 17.22; HR-MS (ESI): calcd. $C_{31}H_{48}N_3O_7$ $[M+H]^+$ 574.3487, found 574.3515; $[\alpha]_D^{27}$ -116 (*c* 1.0, $CHCl_3$).

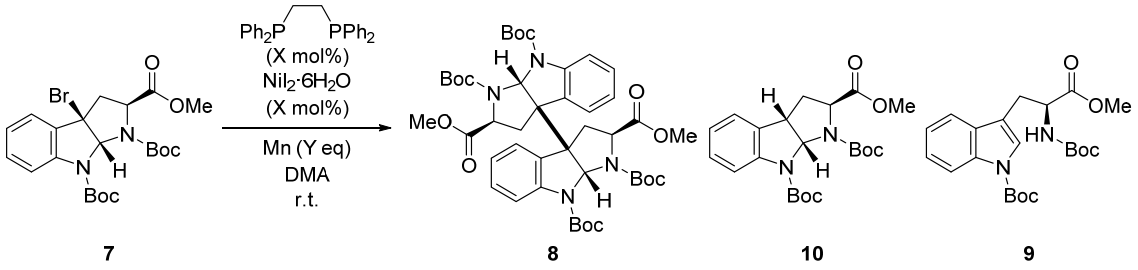
Synthesis of authentic **14**



7 TEMPO **14**

By adapting the protocol reported by Matyjaszewski,[3] a mixture of bromide **7** (499 mg, 1.00 mmol), TEMPO (180 mg, 1.15 mmol), cupper shot (955 mg, 15.0 mmol), $Cu(OTf)_2$ (37.9 mg, 0.105 mmol, 11 mol%) and (4,4'-di-*tert*-butyl)-2,2-bipyridine (116 mg, 0.432 mmol, 43 mol%) were suspended in benzene (6 mL) under nitrogen atmosphere. Resulting suspension was heated at 75 °C and stirred for 20 h. After being cooled to room temperature, suspension was filtered through a pad of Celite, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to afford **14** (481 mg, 0.838 mmol, 84%) as a white amorphous.

Effect of catalyst loading on NiI_2-catalyzed dimerization of **7** (*exo*)



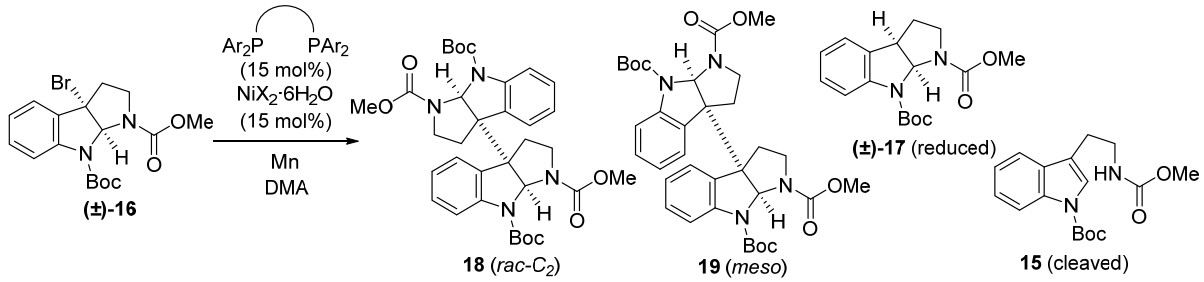
To a solution of $NiI_2 \cdot 6H_2O$ (X mol%) and DPPE (X mol%) in DMA (650 μL) was added bromide **7** (398 mg, 0.800 mmol), and resulting mixture was purged with nitrogen. After treatment with Mn (Y eq.), the resulting suspension was immediately purged again with nitrogen and stirred at room temperature for 12−24 h as shown in Table S5. The mixture was diluted with AcOEt and treated with 1 N HCl. After separation of aqueous phase, organic layer was washed with H_2O x2, 1 N HCl, saturated aqueous solution of Na_2SO_3, and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to isolate dimer **8**, byproducts (**9** and **10**).

Table S5: Effect of catalyst loading on NiI_2-catalyzed dimerization of **7** (*exo*)

Entry	Metal X [mol%]	Ligand X [mol%]	Mn Y [eq.]	Reaction Time [h]	**8** [%][a] (C_2-dimer)	**10** [%][a] (reduced)	**9** [%][a] (cleaved)	**7** [%][a] (recovery)
1	15	15	1.15	12	74	trace	13	0
2	4	4	1.1	14.5	67	11	3	0
3	2.5	2.5	1.05	24	63	17	<5	0

a) Isolated yields, average of two trials.

Nickel-catalyzed dimerization of **16** with modification of catalyst and reaction conditions



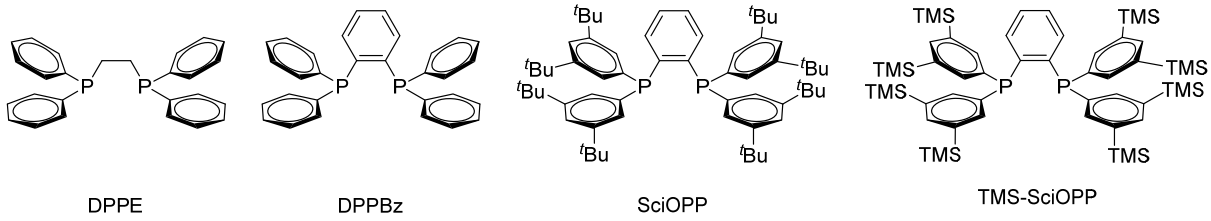
To a mixture of $NiX_2 \cdot 6H_2O$ (0.12 mmol, 15 mol%) and ligand (0.12 mmol, 15 mol%) in DMA (1000 μL) was added **16** (318 mg, 0.800 mmol), and resulting mixture was purged with nitrogen. After treatment with Mn (65.9 mg, 1.20 mmol, 1.5 eq.), the resulting suspension was immediately purged again with nitrogen and stirred at either room temperature or 4 °C for 12−24 h as shown in Table S6. The mixture was diluted with AcOEt and treated with 1 N HCl. After separation of aqueous phase, organic layer was washed with H_2O x2, 1 N HCl, saturated aqueous solution of Na_2SO_3, and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to isolate dimers (*C*$_2$-**18** and *meso*-**19**), byproducts (**15** and **17**) and recovered substrate **16**.

Table S6: Nickel-catalyzed dimerization of **16** with modification of catalyst and reaction conditions

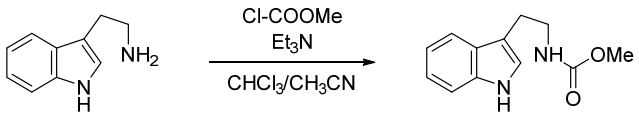
Entry	Ni(II)	Ligand	Temp. [°C]	Time [h]	**18** [%]^b (*rac*-*C*$_2$)	**19** [%]^b (*meso*)	**17** [%] (reduced)	**15** [%] (cleaved)	**16** [%] (recovery)
1^{a,c}	$NiI_2 \cdot 6H_2O$	DPPE	r.t.	12	8	8	11	9	35
2^c				17	13	18	17	15	0
3^c		DPPBz		17	17	20	11	12	0
4^c			4	19	18	22	11	8	trace
5^c	$NiCl_2 \cdot 6H_2O$	DPPBz	4	20	25	30	11	7	trace
6^d	$NiCl_2 \cdot 6H_2O$	SciOPP	25	25	16	22	23^b	7^b	-
7^d			40	24	16	20	40^b	2^b	-
8^d		TMS-SciOPP	40	19	9	17	25^b	10^b	3^b
9^d			60	12	15	20	29^b	6^b	-

a) Mn (1.2 eq.). *b*) Calculated yields based on ^{1}H NMR. *c*) Average of two trials. *d*) 10 mol% of catalyst and ligand.

Structure of phosphine ligands[1] employed



Synthesis of methyl (2-(1*H*-indol-3-yl)ethyl)carbamate **S-1**.

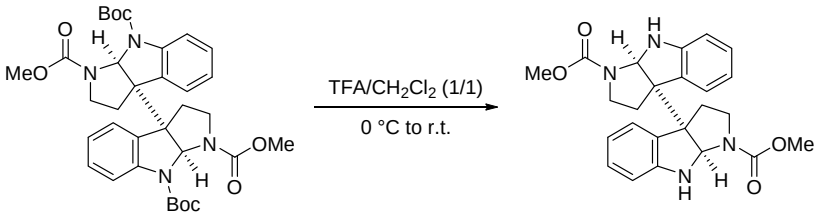


tryptamine **S-1**

A solution of tryptamine (4.01 g, 25.1 mmol) and triethyl amine (10.4 mL, 75.0 mmol) in 1:1 mixture of chloroform and acetonitrile (170 mL) was added methyl chloroformate (2.30 mL, 30.0 mmol) at 0 °C and stirred for 15 min. The solution was then heated to 35 °C and stirred for 1.5 h. After being cooled to 0 °C, the resulting reaction mixture was diluted with chloroform and treated with 1 N HCl. The combined chloroform extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to afford **S-1** (4.29 g, 19.6 mmol, 78%) as a light brown amorphous.

S-1: R_f = 0.64 ($CHCl_3$:MeOH = 7:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10 (1H, br-s), 7.61 (1H, d, *J* = 7.8 Hz), 7.37 (1H, dd, *J* = 8.1, 0.9 Hz), 7.21 (1H, m), 7.13 (1H, m), 7.03 (1H, s), 4.77 (1H, br-s), 3.67 (3H, s), 3.52 (2H, m), 2.98 (2H, t, *J* = 6.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.23, 136.57, 127.45, 122.35, 122.18, 119.64, 118.88, 113.10, 111.36, 52.16, 41.42, 25.94; HR-MS (ESI): calcd. $C_{12}H_{14}N_2O_2Na$ $[M+Na]^+$ 241.0947, found 241.0954.

Synthesis of C_2-dianiline **S-2**



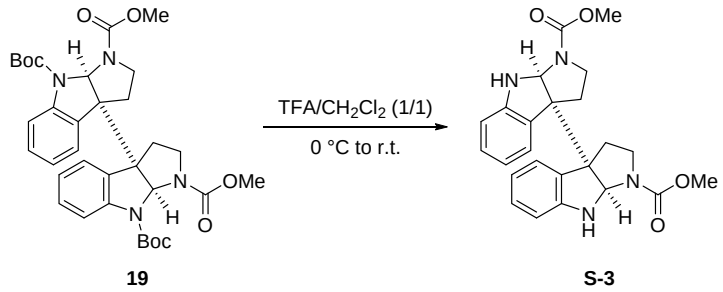
18 **S-2**

Trifluoroacetic acid (TFA, 3.7 mL) was slowly added to a stirred solution of C_2-dimer **18** (236 mg, 0.372 mmol) in dichloromethane (3.7 mL) at 0 °C. The mixture was stirred for 15 min at 0 °C and then warm up to room temperature. After being stirred for 2 h, the resulting mixture was concentrated under reduced pressure. The residue was diluted with chloroform and then treated with saturated aqueous solution of $NaHCO_3$. The combined chloroform extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to afford **S-2** (131 mg, 0.301 mmol, 81%) as a white solid. The NMR spectra were identical to the literature data.[4]

S-2: R_f = 0.49 (Hex:AcOEt = 1:1); ^{1}H NMR (400 MHz, DMSO, 95 °C): δ 7.23 (2H, d, *J* = 7.4 Hz), 7.02 (2H, t, *J* = 7.5 Hz), 6.64 (2H, t, *J* = 7.4 Hz), 6.59 (2H, d, *J* = 7.8 Hz), 4.91 (2H, s), 3.61-3.45 (8H, m), 2.75 (2H, td,

J = 10.8, 5.9 Hz), 2.52 (2H, m), 2.12 (2H, dd, *J* = 12.4, 5.8 Hz); ^{13}C NMR(100 MHz, DMSO, 95 °C): δ 153.48, 150.45, 128.14, 128.01, 124.05, 116.98, 108.29, 77.48, 60.94, 51.34, 44.28, 31.78; HR-MS (ESI): calcd. for $C_{24}H_{26}N_4O_4Na$ $[M+Na]^+$ 457.1846, found 457.1853.

Synthesis of *meso*-dianiline **S-3**

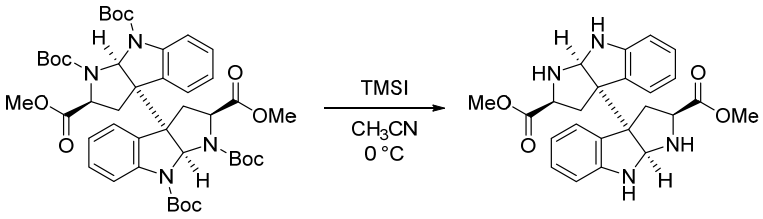


19 **S-3**

Trifluoroacetic acid (TFA, 7 mL) was slowly added to a stirred solution of *meso*-dimer **19** (442 mg, 0.696 mmol) in dichloromethane (7 mL) at 0 °C. The mixture was stirred for 10 min at 0 °C and then warm up to room temperature. After being stirred for 1.5 h, the resulting mixture was concentrated under reduced pressure. The residue was diluted with chloroform and then treated with saturated aqueous solution of $NaHCO_3$. The combined chloroform extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to afford **S-3** (245 mg, 0.563 mmol, 81%) as a pale yellow amorphous. The NMR spectra were identical to the literature data.[5]

S-3: R_f = 0.32 (Hex:AcOEt = 1:1); ^{1}H NMR (400 MHz, DMSO, 100 °C): δ 6.97 (2H, t, *J* = 7.7 Hz), 6.60 (2H, m), 6.52-6.44 (4H, m), 6.01 (2H, s), 5.32 (2H, s), 3.70-3.59 (8H, m), 2.83 (2H, m), 2.34-2.16 (4H, m); ^{13}C NMR (100 MHz, DMSO, 100 °C): δ 153.60, 150.32, 128.47, 127.92, 127.88, 123.20, 116.74, 107.80, 76.48, 61.46, 51.38, 44.27, 33.31; HR-MS (ESI): calcd. $C_{24}H_{26}N_4O_4Na$ $[M+Na]^+$ 457.1846, found 457.1853.

Synthesis of tetra-amine **S-4**[2]



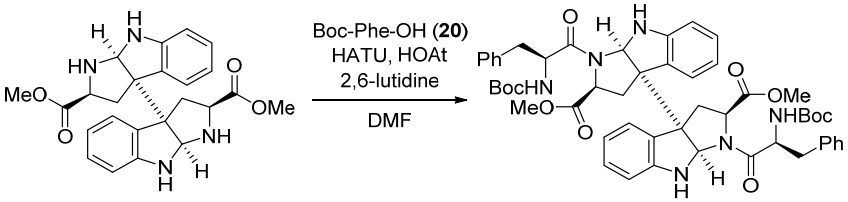
12 **S-4**

Iodotrimethylsilane (220 μL, 1.62 mmol, 10.6 eq.) was added dropwisely to a solution of the C_2-dimer **12** (128 mg, 0.153 mmol) in acetonitrile (3.1 mL) at 0 ºC. The resulting solution was stirred at 0 ºC for 90 min and then treated with saturated aqueous solution of Na_2SO_3. The resulting mixture was extracted with chloroform 4-5 times. Combined extracts were dried over Na_2SO_4, filtered, and concentrated under reduced

pressure to afford crude tetra-amine **S-4** (81.7 mg) as a yellow amorphous. The crude tetra-amine **S-4** was subjected to the next reaction without further purification.

S-4: R_f = 0.41 ($CHCl_3$:MeOH = 9:1); ^{1}H NMR (500 MHz, CD_3OD): δ 7.19 (2H, d, *J* = 7.6 Hz), 7.03 (2H, td, *J* = 7.6, 0.9 Hz), 6.67 (2H, td, *J* = 7.5, 0.9 Hz), 6.55 (2H, d, *J* = 7.8 Hz), 4.65 (2H, s), 3.74 (2H, dd, *J* = 8.0, 2.8 Hz), 3.26 (6H, s), 2.83 (2H, dd, *J* = 13.0, 8.0 Hz), 2.53 (2H, dd, *J* = 13.0, 2.8 Hz); ^{13}C NMR (125 MHz, CD_3OD): δ 175.15, 152.84, 130.81, 130.11, 127.15, 119.13, 110.81, 81.85, 63.11, 60.86, 52.40, 39.29; HR-MS (ESI): calcd. for $C_{24}H_{27}N_4O_4$ $[M+H]^+$ 435.2027, found 435.2046.

Synthesis of dipeptide **S-5**



S-4 **S-5**

To a solution of Boc-Phe-OH (126 mg, 0.475 mmol, 3.1 eq.), HOAt (73 mg, 0.536 mmol, 3.5 eq.), HATU (195 mg, 0.514 mmol, 3.4 eq.), and 2,6-lutidine (260 μL, 2.23 mmol, 14.6 eq.) in DMF (1.3 mL) was added the solution of the crude tetra-amine **S-4** (81.7 mg) in DMF (2 mL) at 0 °C. After being warmed up to room temperature, the mixture was stirred for 7 h. The solution was diluted with AcOEt and treated with saturated aqueous solution of NH_4Cl. After separation of organic layer, the aqueous phase was extracted with AcOEt. Combined organic extracts were washed with saturated aqueous solution of $NaHCO_3$, H_2O x3, and brine. The extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to afford dipeptide **S-5** (108 mg, 0.116 mmol, 76% for 2 steps).

S-5: R_f = 0.92 (CH_2Cl_3:CH_3CN = 4:1); NMR spectra were difficult to be characterized due to broadening of signals even at elevated temperature; HR-MS (ESI): calcd. for $C_{52}H_{60}N_6O_{10}Na$ $[M+Na]^+$ 951.4263, found 951.4252; $[\alpha]_D^{30}$ +249 (*c* 1.0, $CHCl_3$).

References

[1] (a) T. Hatakeyama, T. Hashimoto, Y. Kondo, Y. Fujiwara, H. Seike, H. Takaya, Y. Tamada, T. Ono and M. Nakamura, *J. Am. Chem. Soc.*, 2010, **132**, 10674-10676; (b) T. Hatakeyama, Y. Okada, Y. Yoshimoto and M. Nakamura, *Angew. Chem. Int. Ed.*, 2011, **50**, 10973-10976; (c) M. Jin and M. Nakamura, *Chem. Lett.*, 2011, **40**, 1012-1014; (d) T. Hatakeyama, Y. Fujiwara, Y. Okada, T. Itoh, T. Hashimoto, S. Kawamura, K. Ogata, H. Takaya and M. Nakamura, *Chem. Lett.*, 2011, **40**, 1030-1032; (e) T. Hashimoto, T. Hatakeyama and M. Nakamura, *J. Org. Chem.*, 2012, **77**, 1168-1173; (f) S. Kawamura and M. Nakamura, *Chem. Lett.*, 2013, **42**, 183-185.

[2] (a) C. Pérez-Balado and Á. R. de Lera, *Org. Lett.*, 2008, **10**, 3701-3704; (b) C. Pérez-Balado, P. Rodríguez-Graña and Á. R. de Lera, *Chem. Eur. J.*, 2009, **15**, 9928-9937.

[3] K. Matyjaszewski, B. E. Woodworth, X. Zhang, S. G. Gaynor and Z. Metzner, *Macromolecules*, 1998, **31**, 5955-5957.

[4] (a) M. Movassaghi and M. A. Schmidt, *Angew. Chem. Int. Ed.*, 2007, **46**, 3725-3728; (b) H. Mitsunuma, M. Shibasaki, M. Kanai and S. Matsunaga, *Angew. Chem. Int. Ed.*, 2012, **51**, 5217-5221.

[5] R. H. Snell, R. L. Woodward and M. C. Willis, *Angew. Chem. Int. Ed.*, 2011, **50**, 9116-9119.

The ^{1}H, ^{13}C NMR spectra of synthetic compounds

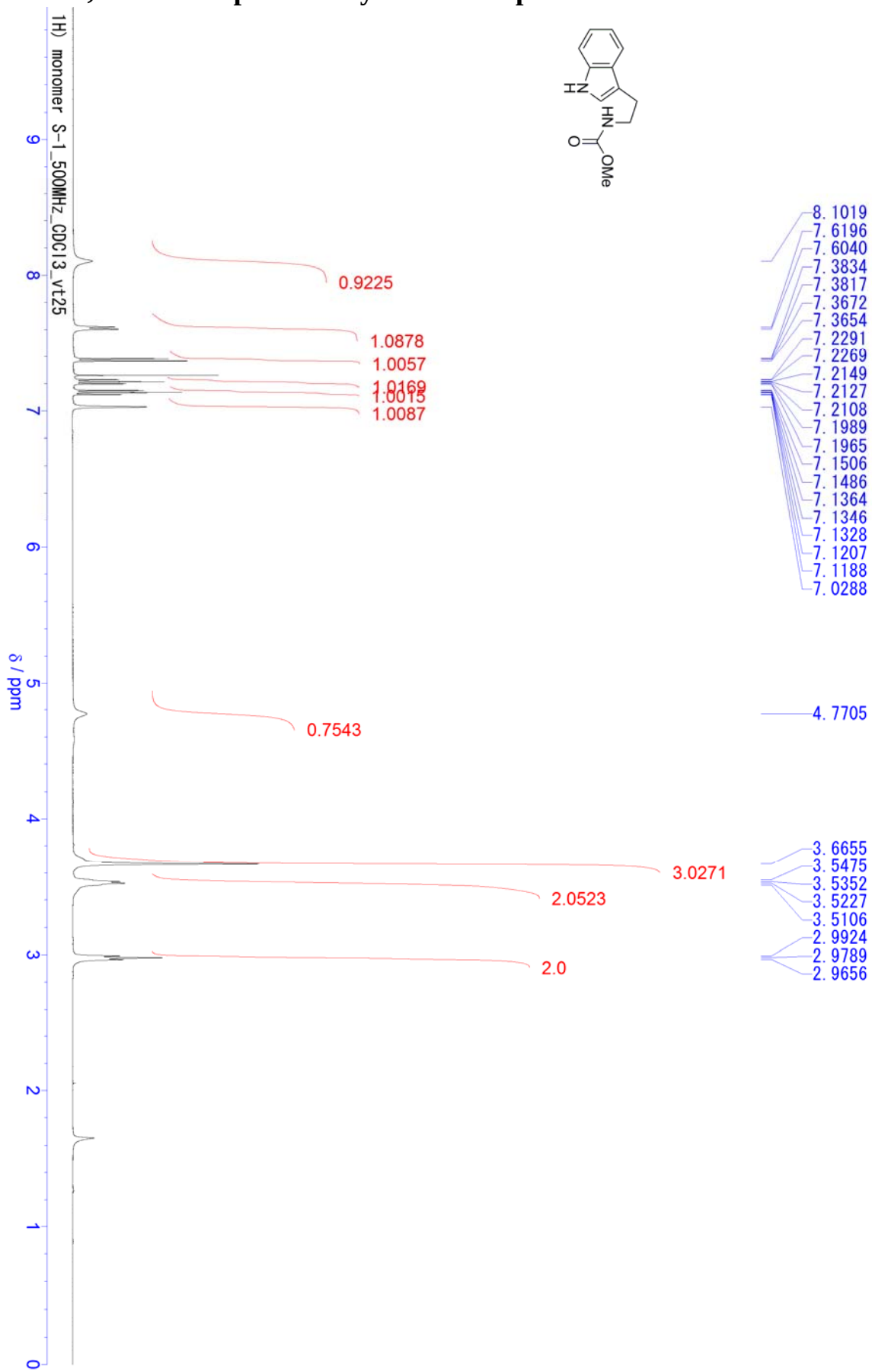


Figure S1. A ^{1}H-NMR spectrum of **S-1** in $CDCl_3$

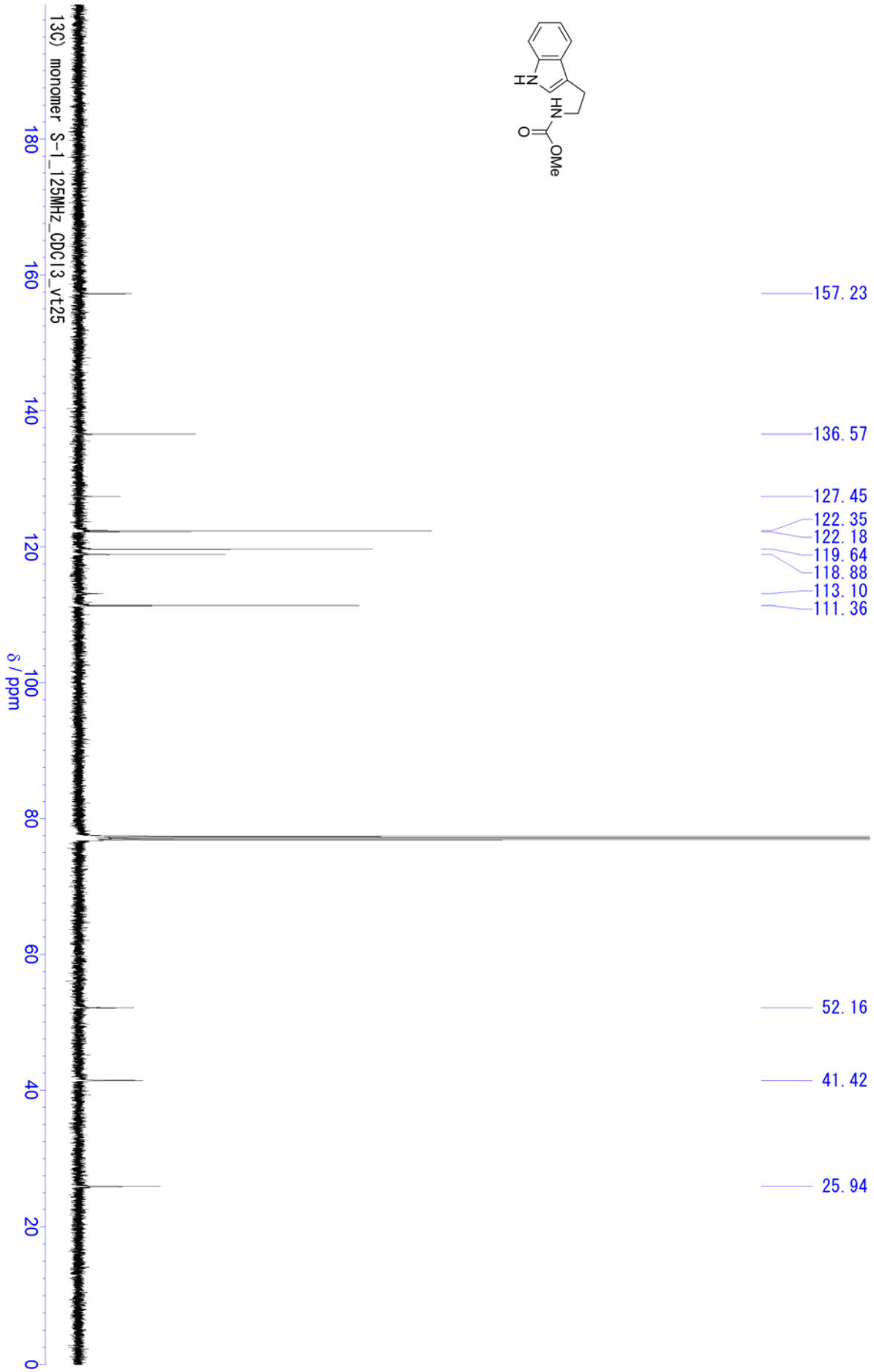


Figure S2. A ^{13}C-NMR spectrum of **S-1** in $CDCl_3$

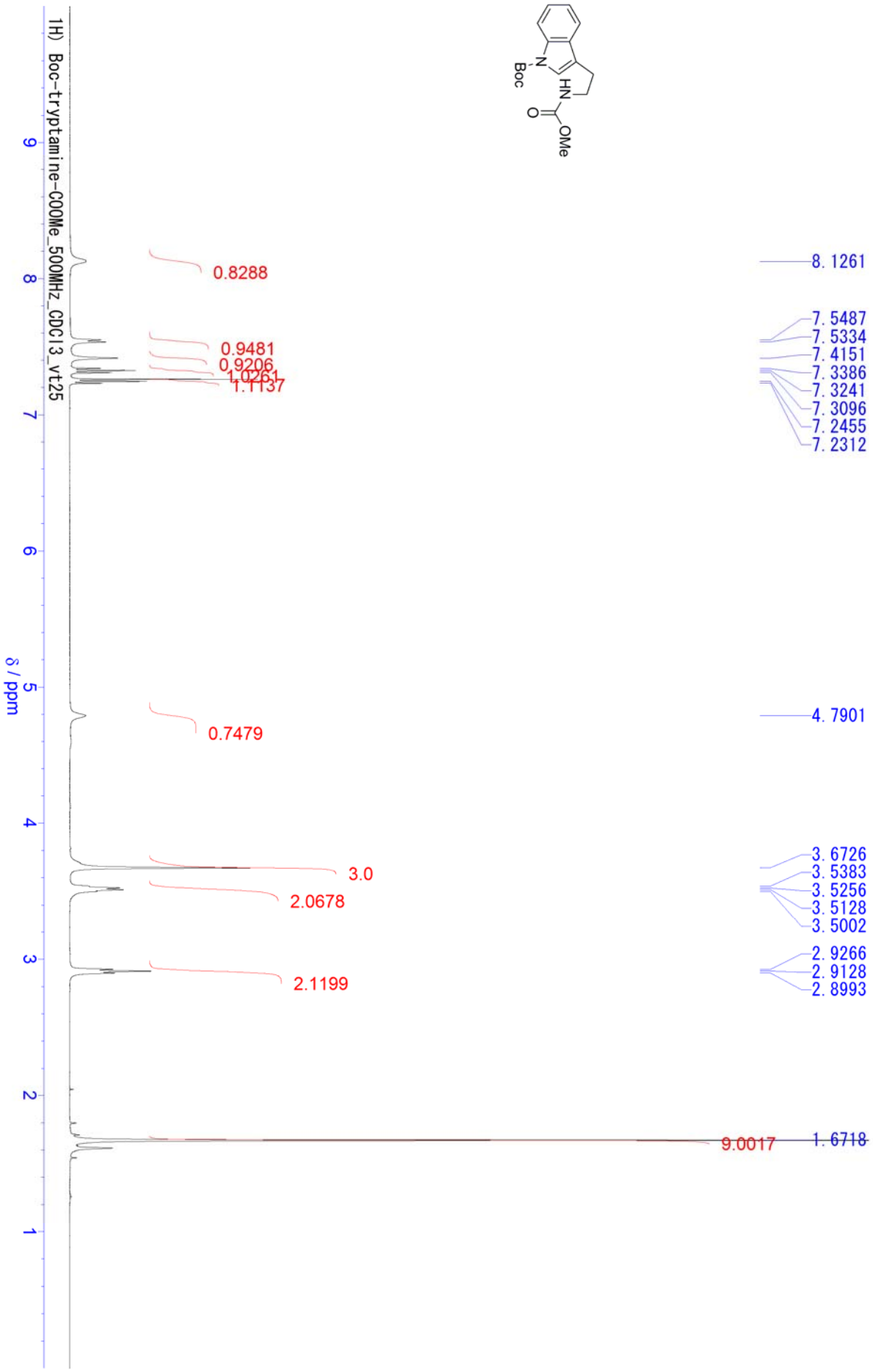


Figure S3. A ^{1}H-NMR spectrum of **15** in $CDCl_3$

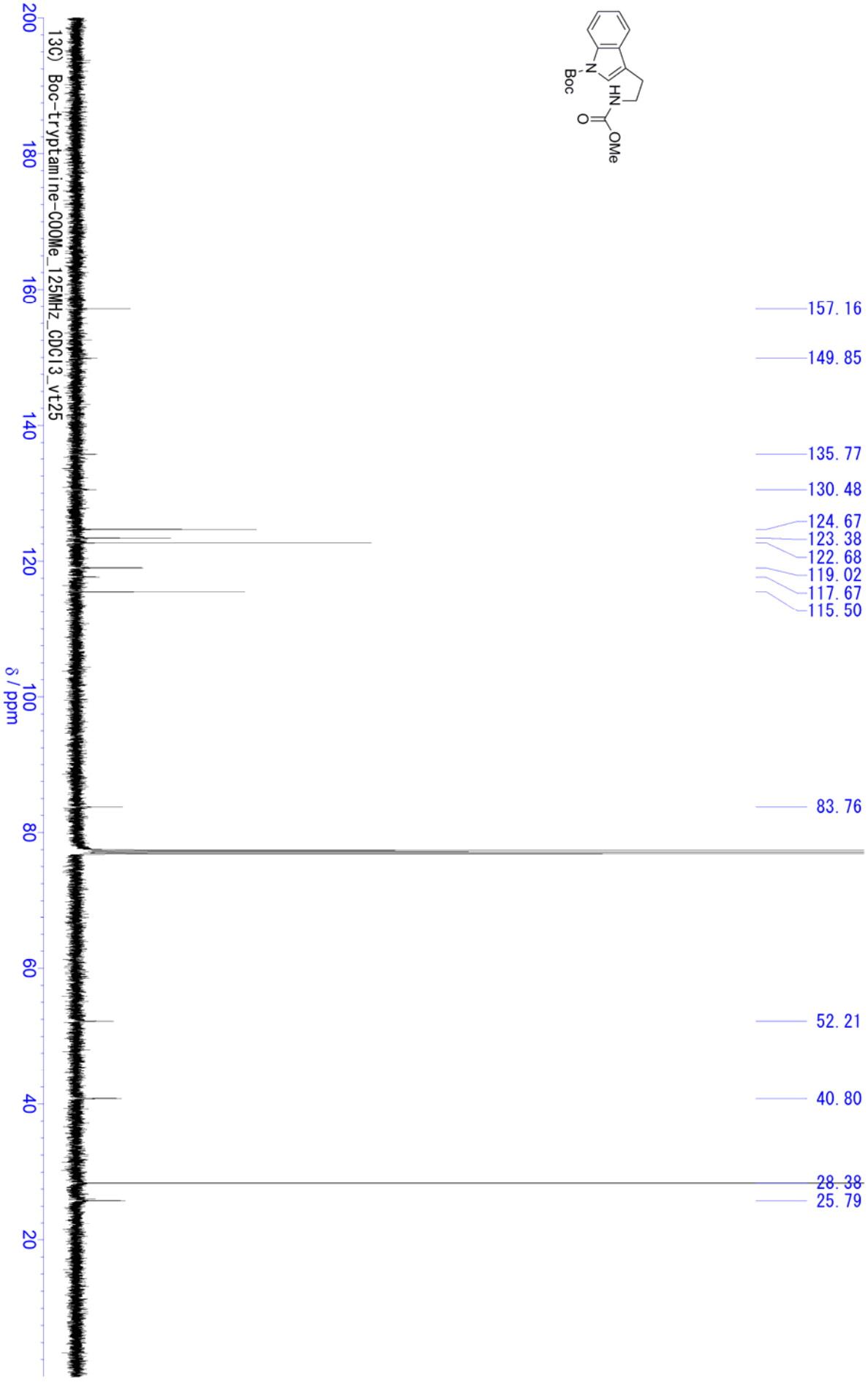


Figure S4. A ^{13}C-NMR spectrum of **15** in $CDCl_3$

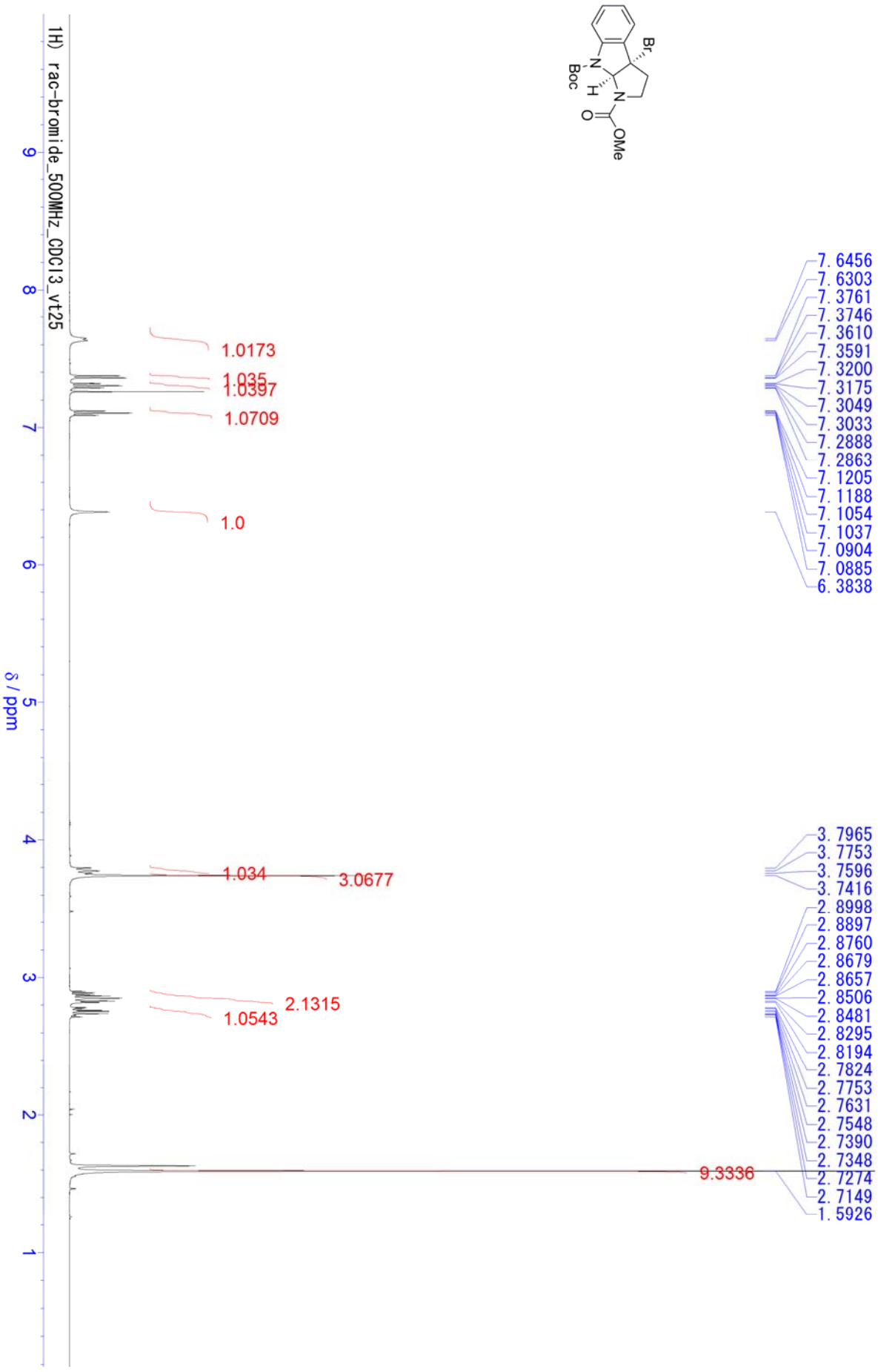


Figure S5. A ^{1}H-NMR spectrum of **16** in $CDCl_3$

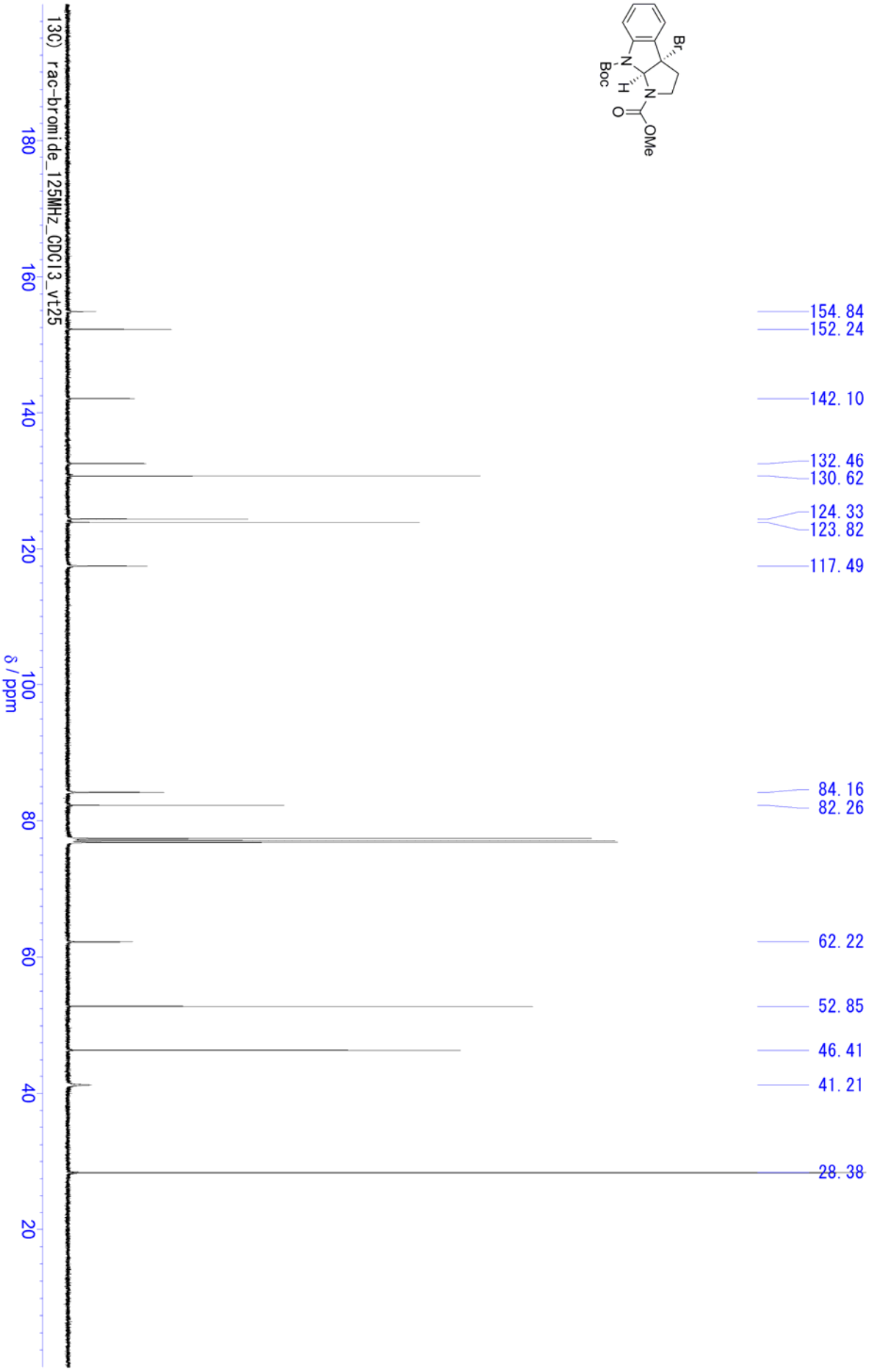


Figure S6. A ^{13}C-NMR spectrum of **16** in $CDCl_3$

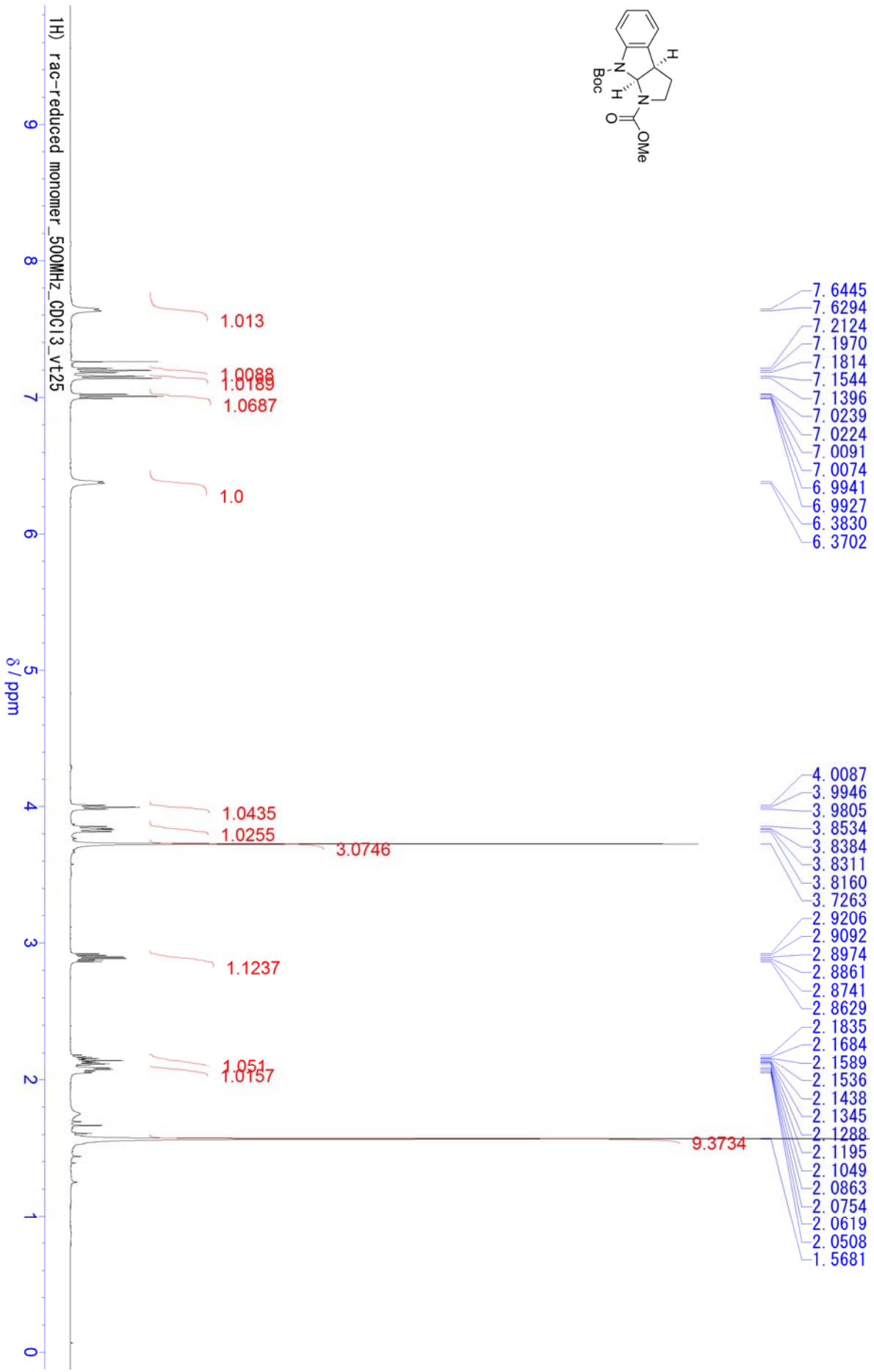


Figure S7. A ^{1}H-NMR spectrum of **17** in $CDCl_3$

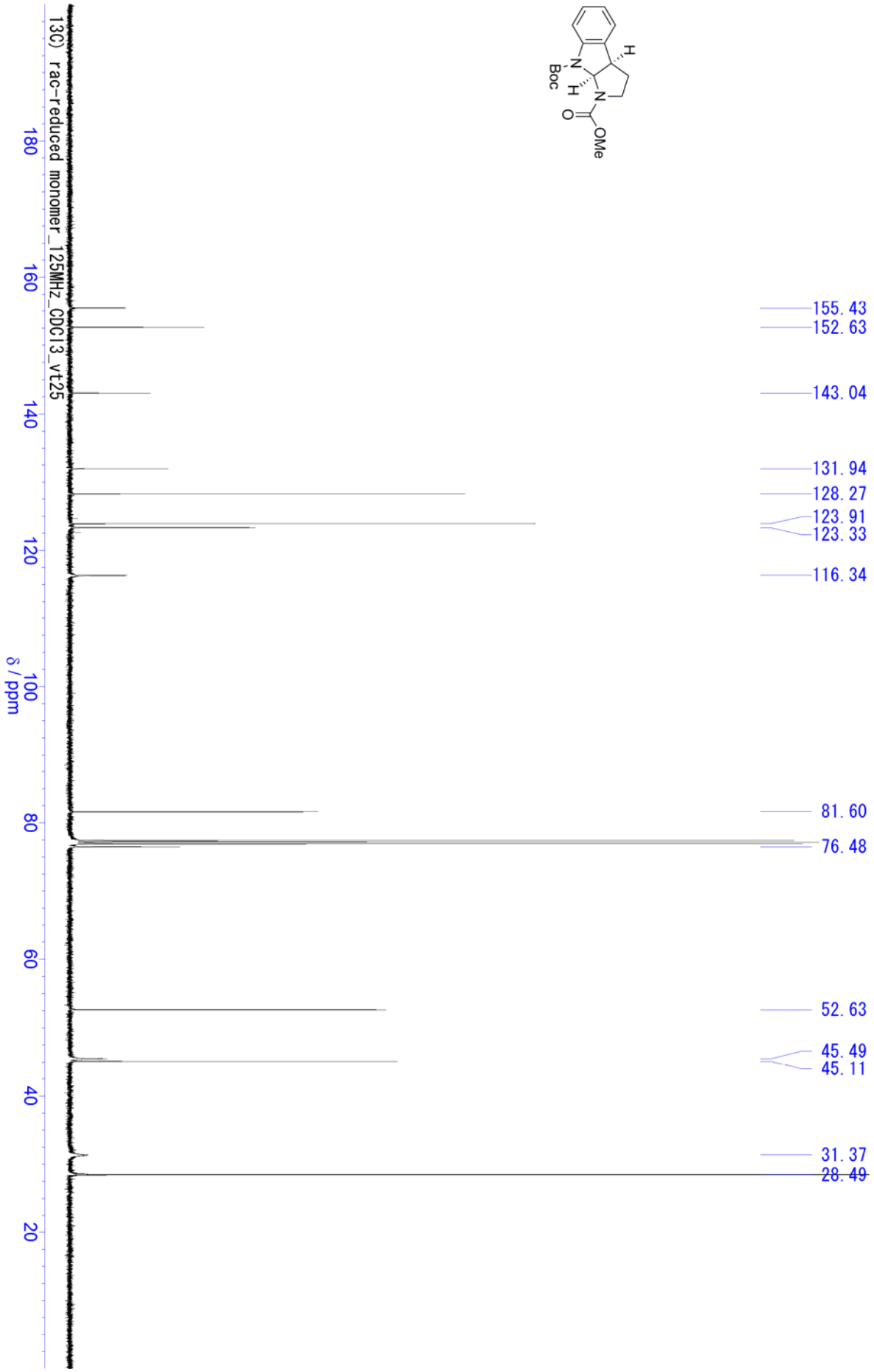


Figure S8. A ^{13}C-NMR spectrum of **17** in $CDCl_3$

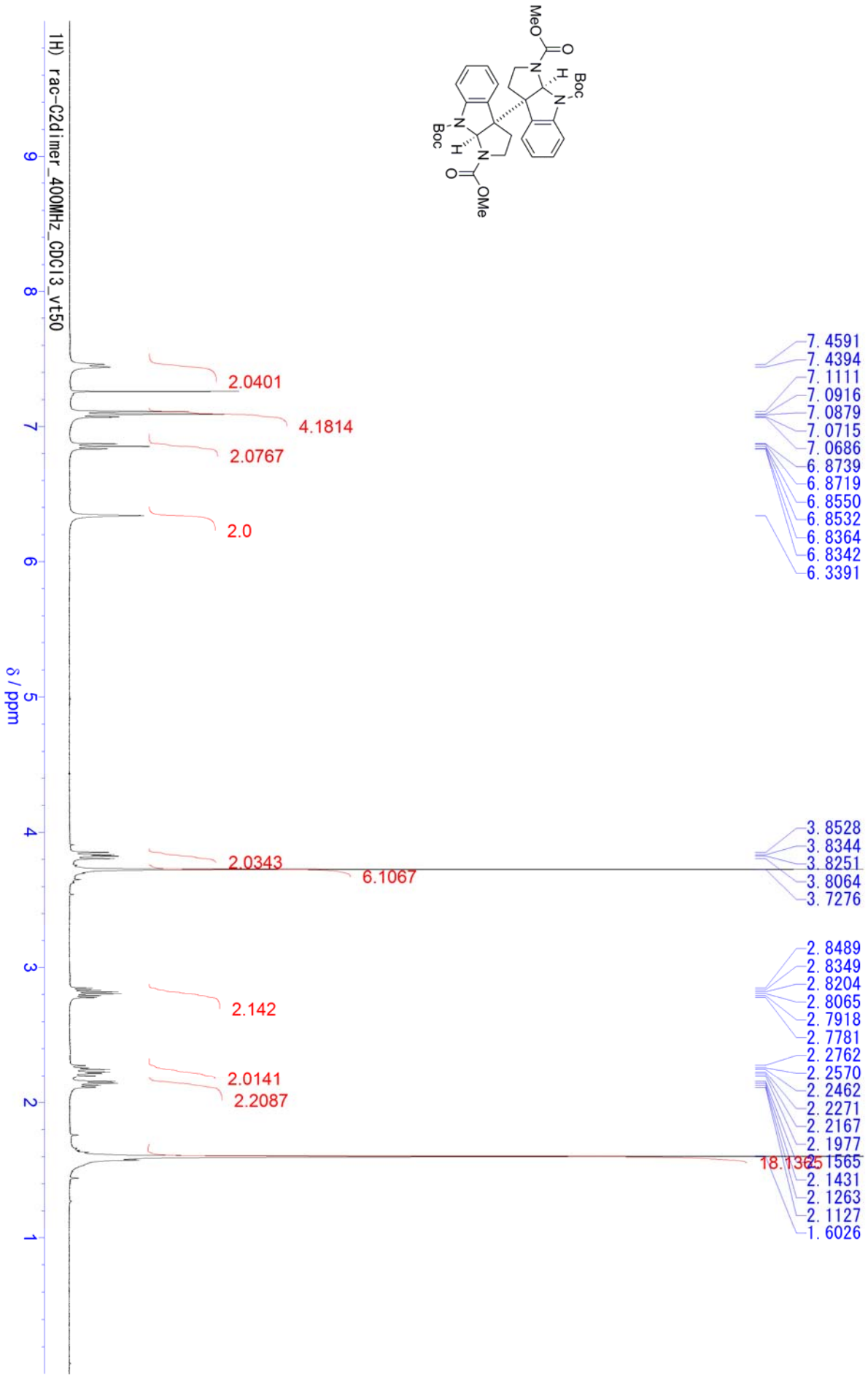


Figure S9. A ^{1}H-NMR spectrum of **18** in $CDCl_3$

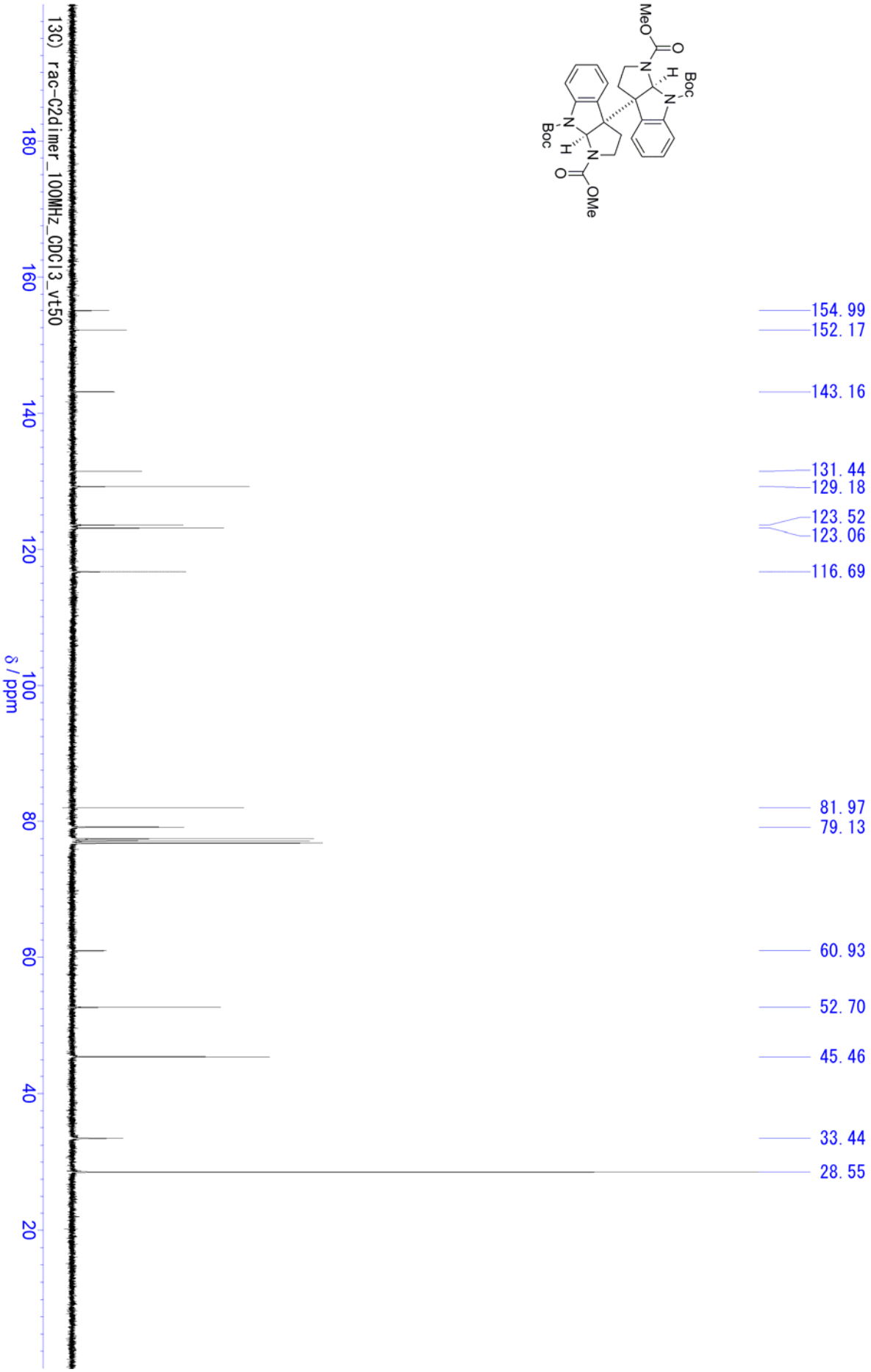


Figure S10. A ^{13}C-NMR spectrum of **18** in $CDCl_3$

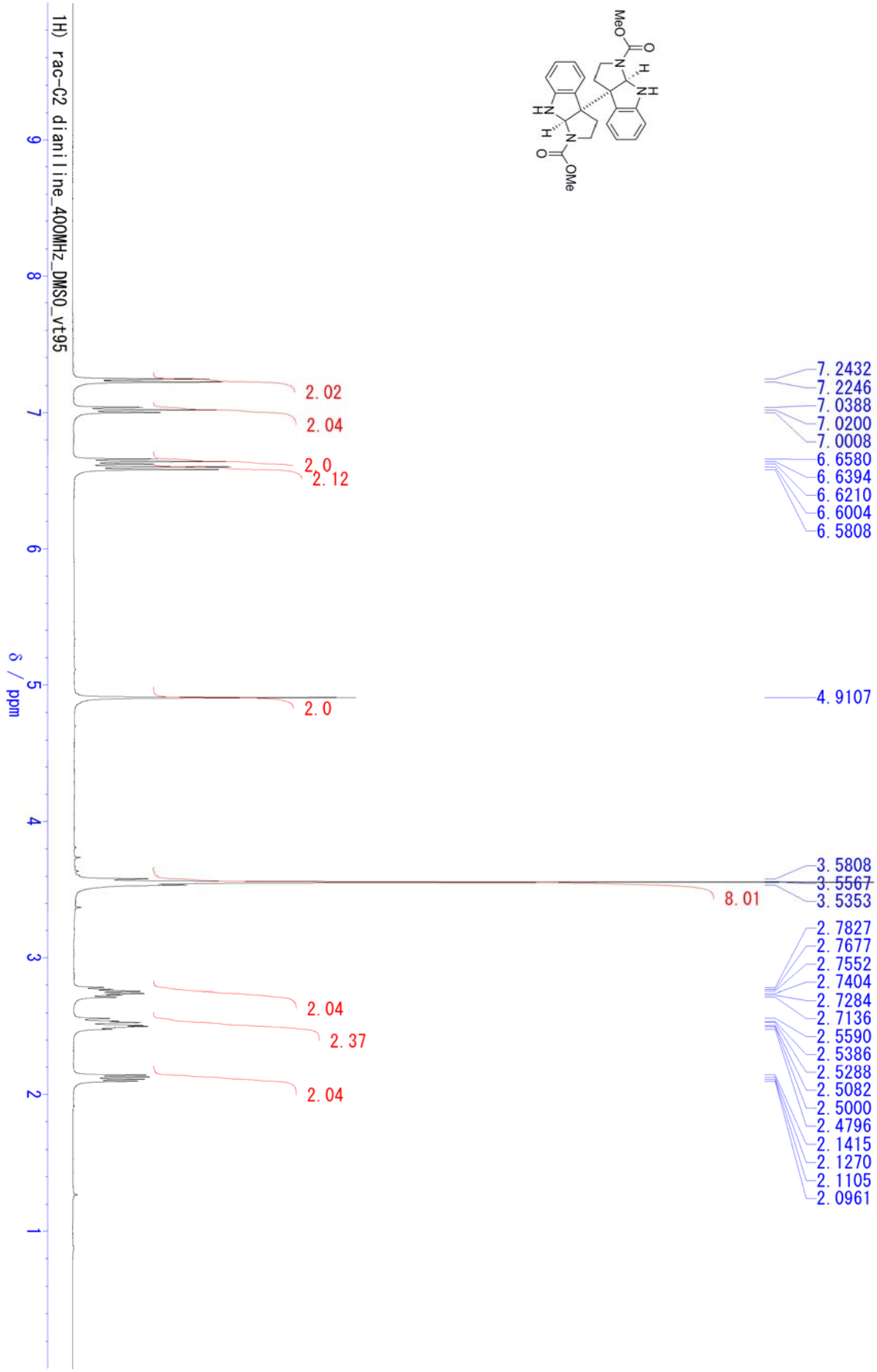


Figure S11. A ^{1}H-NMR spectrum of **S-2** in DMSO

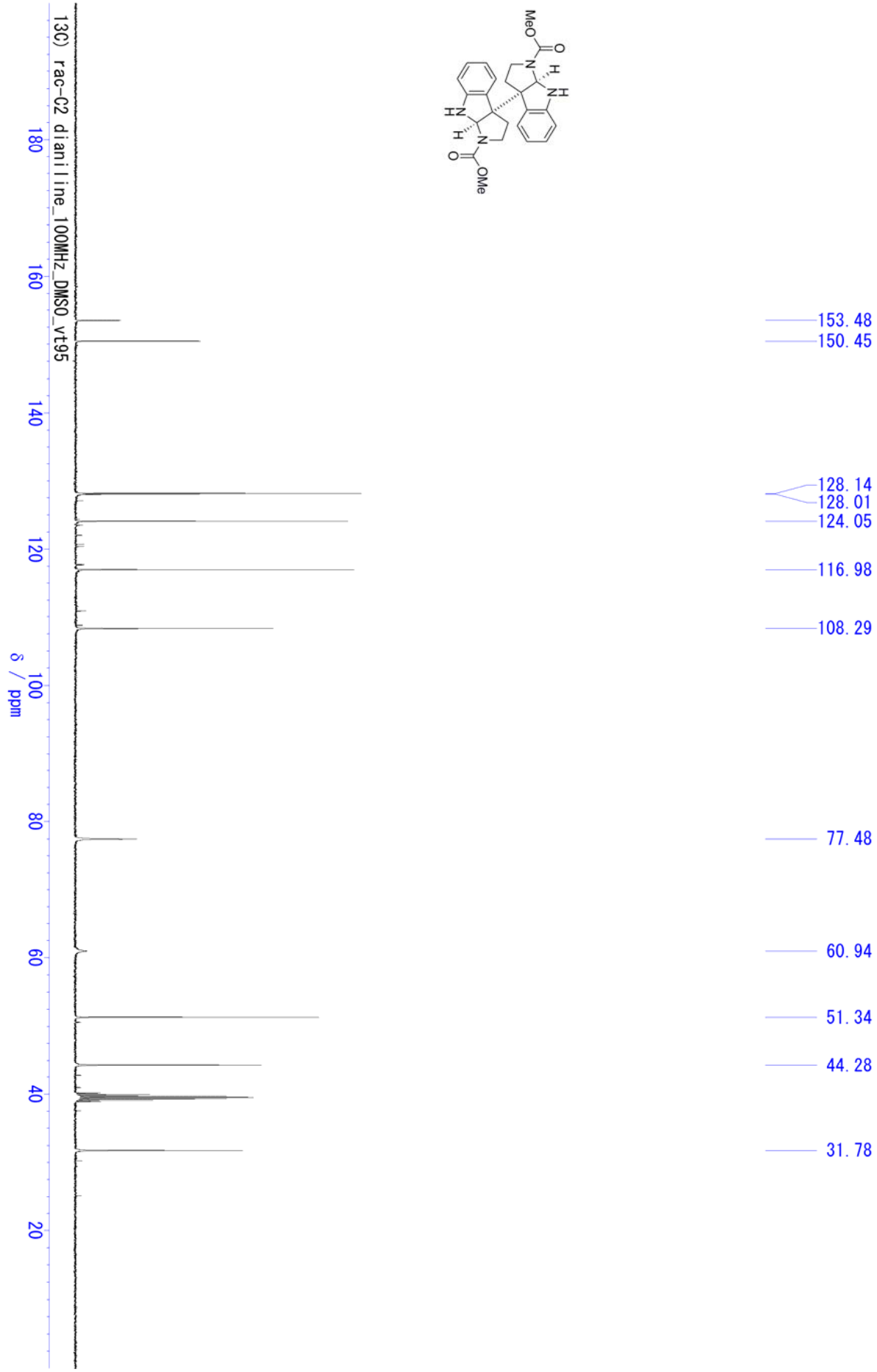


Figure S12. A ^{13}C-NMR spectrum of **S-2** in DMSO

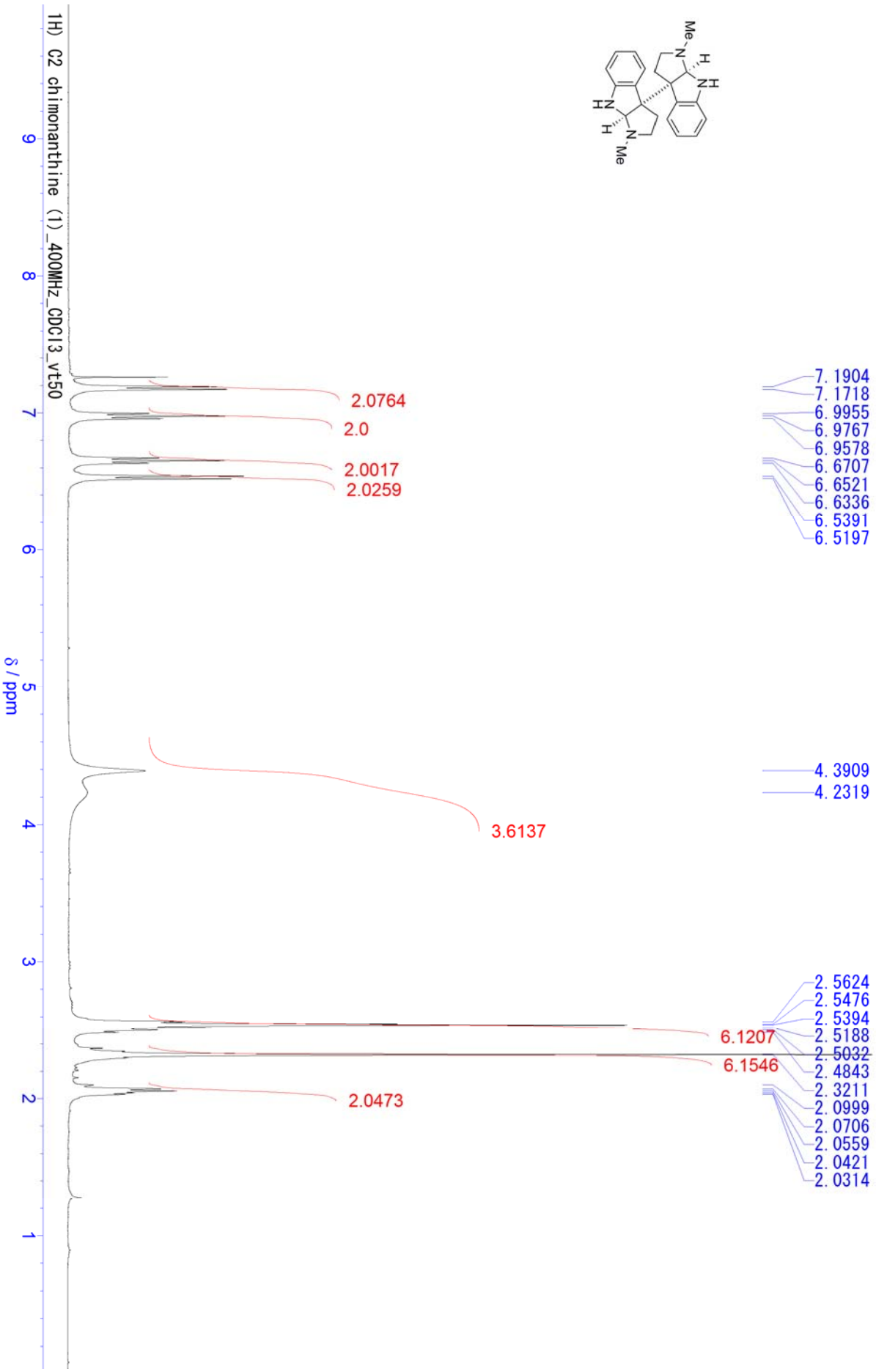


Figure S13. A ^{1}H-NMR spectrum of (±)-chimonanthine (±)-**1** in $CDCl_3$

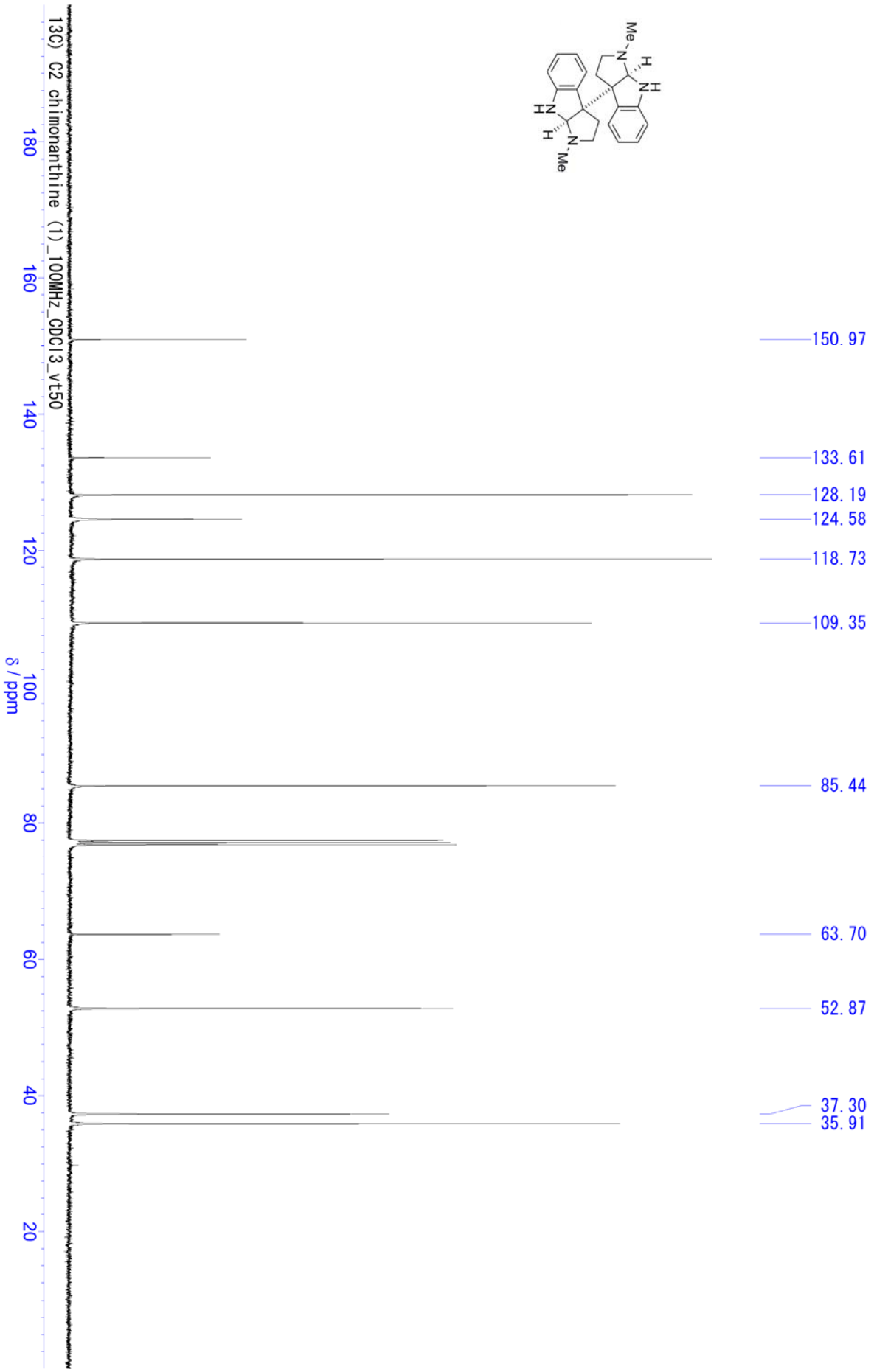


Figure S14. A ^{13}C-NMR spectrum of (±)-chimonanthine (±)-**1** in $CDCl_3$

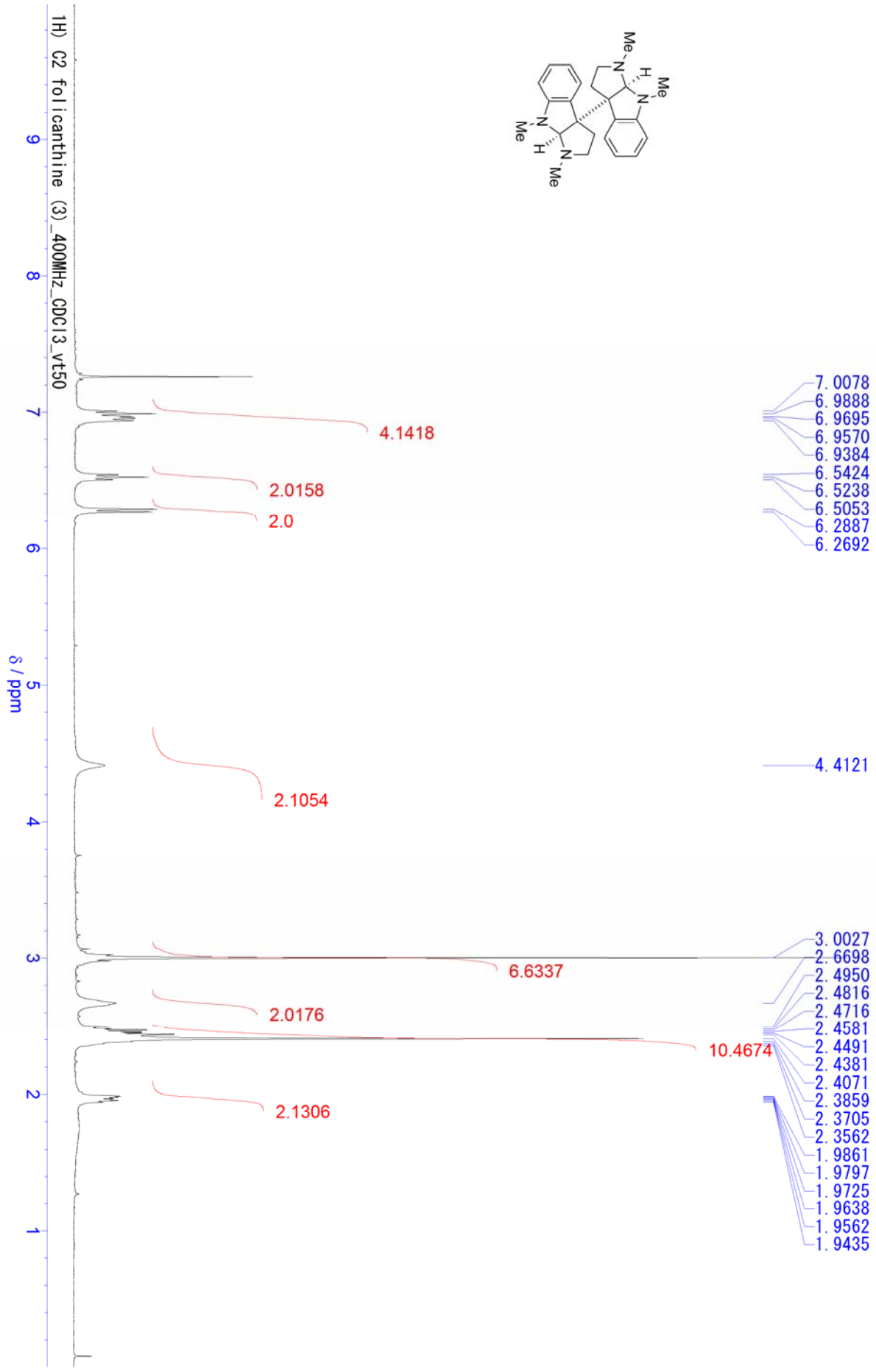


Figure S15. A ^{1}H-NMR spectrum of (±)-folicanthine (±)-**3** in $CDCl_3$

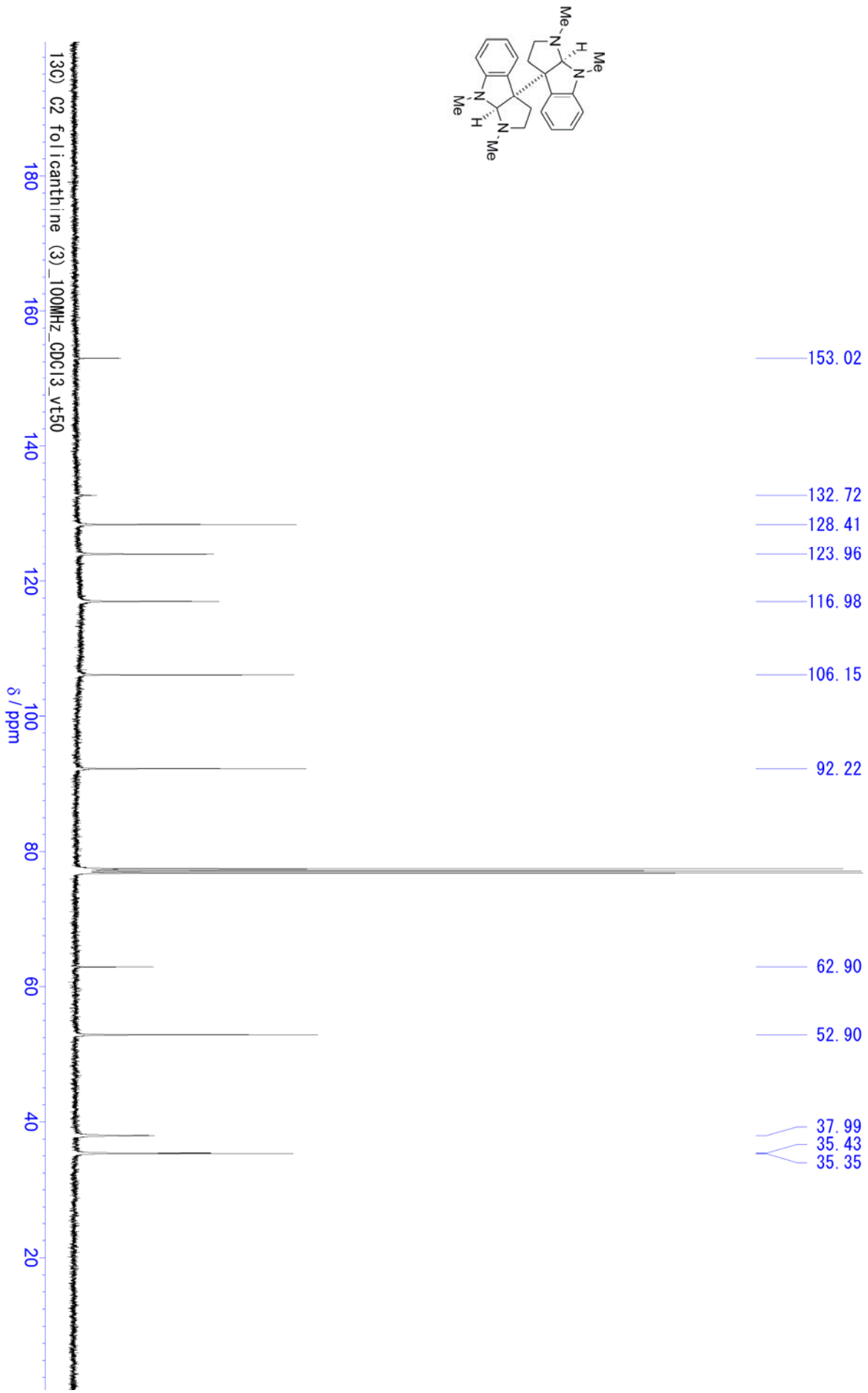


Figure S16. A ^{13}C-NMR spectrum of (±)-folicanthine (±)-**3** in $CDCl_3$

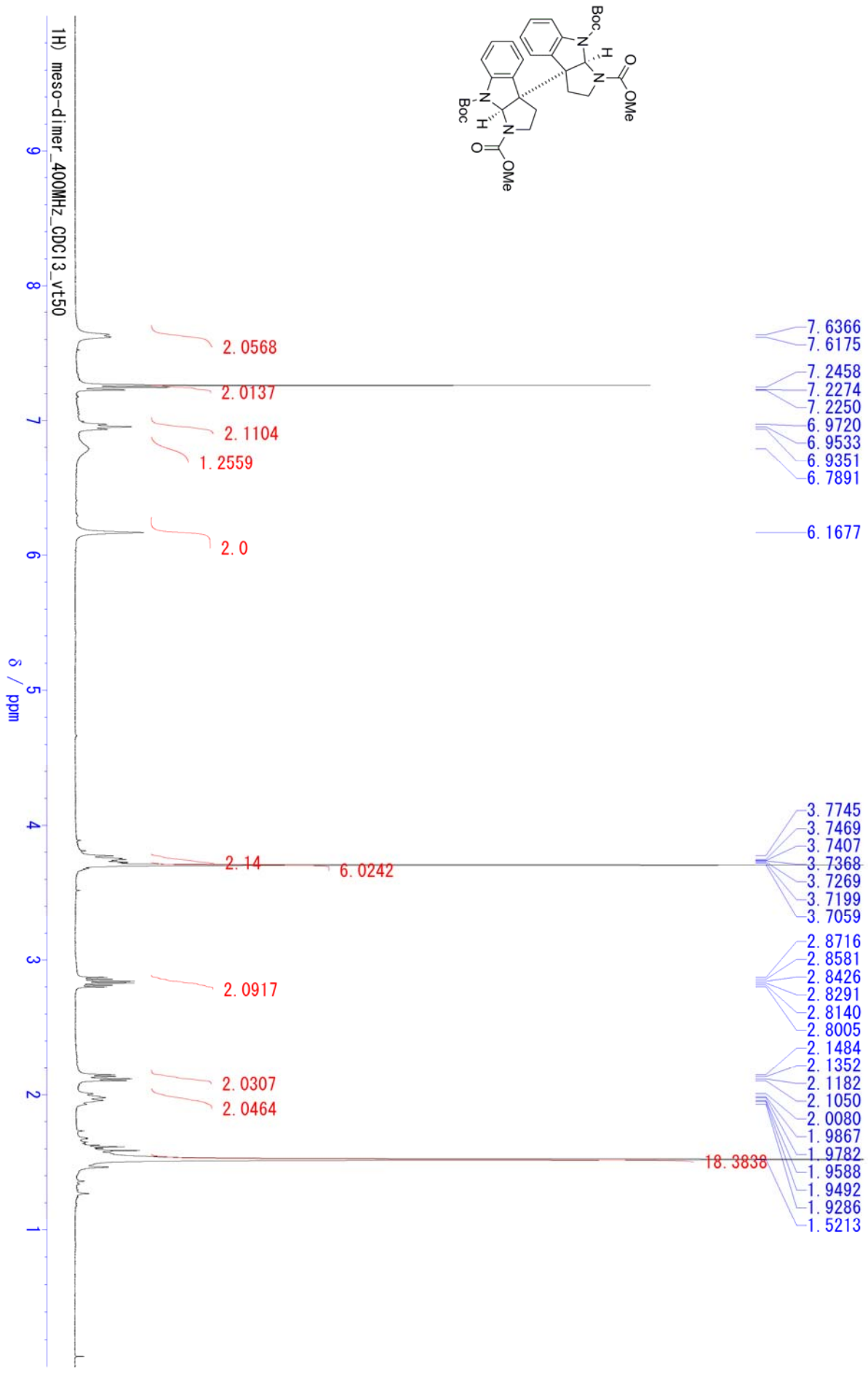


Figure S17. A ^{1}H-NMR spectrum of **19** in $CDCl_3$

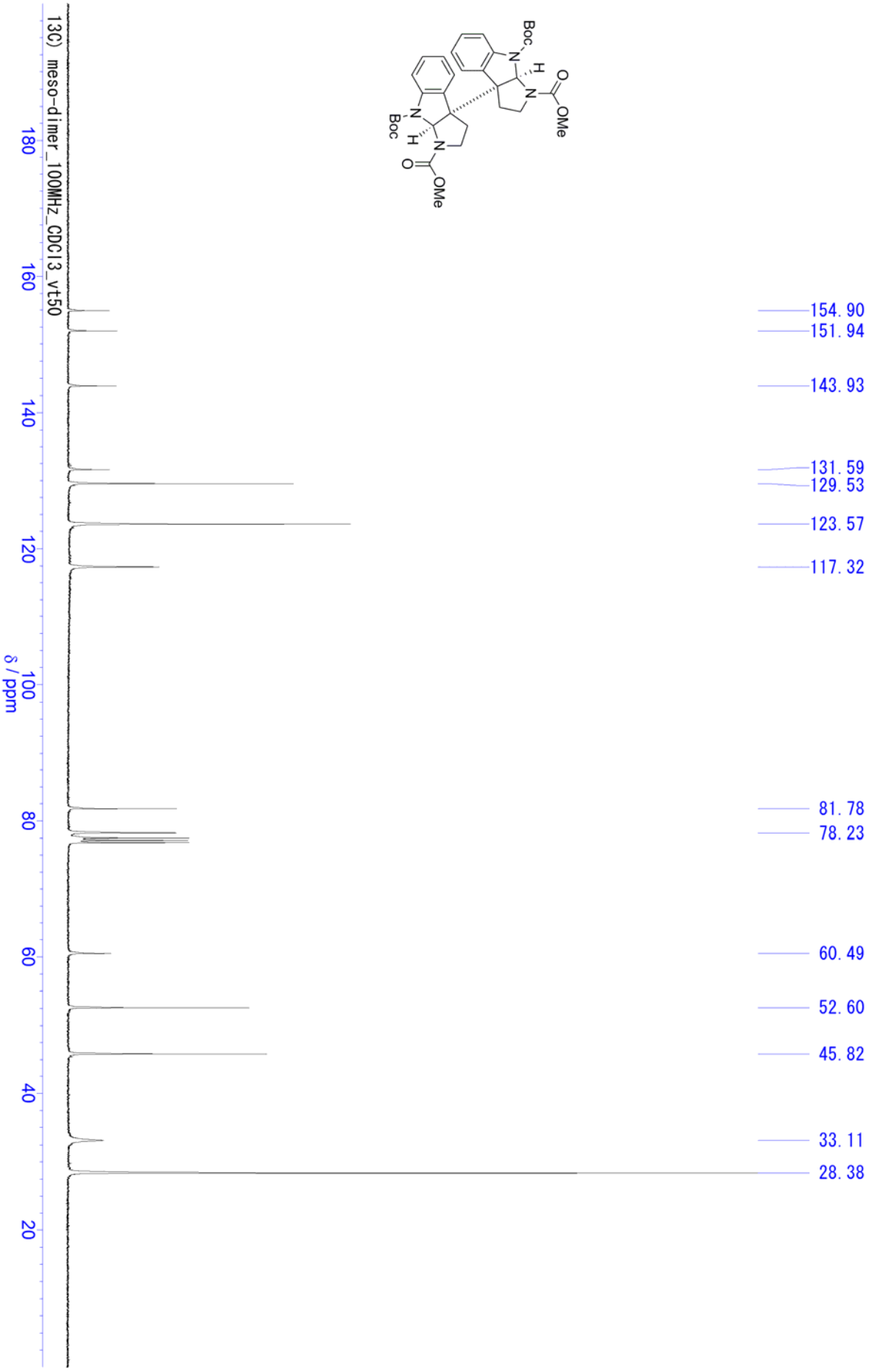


Figure S18. A ^{13}C-NMR spectrum of **19** in $CDCl_3$

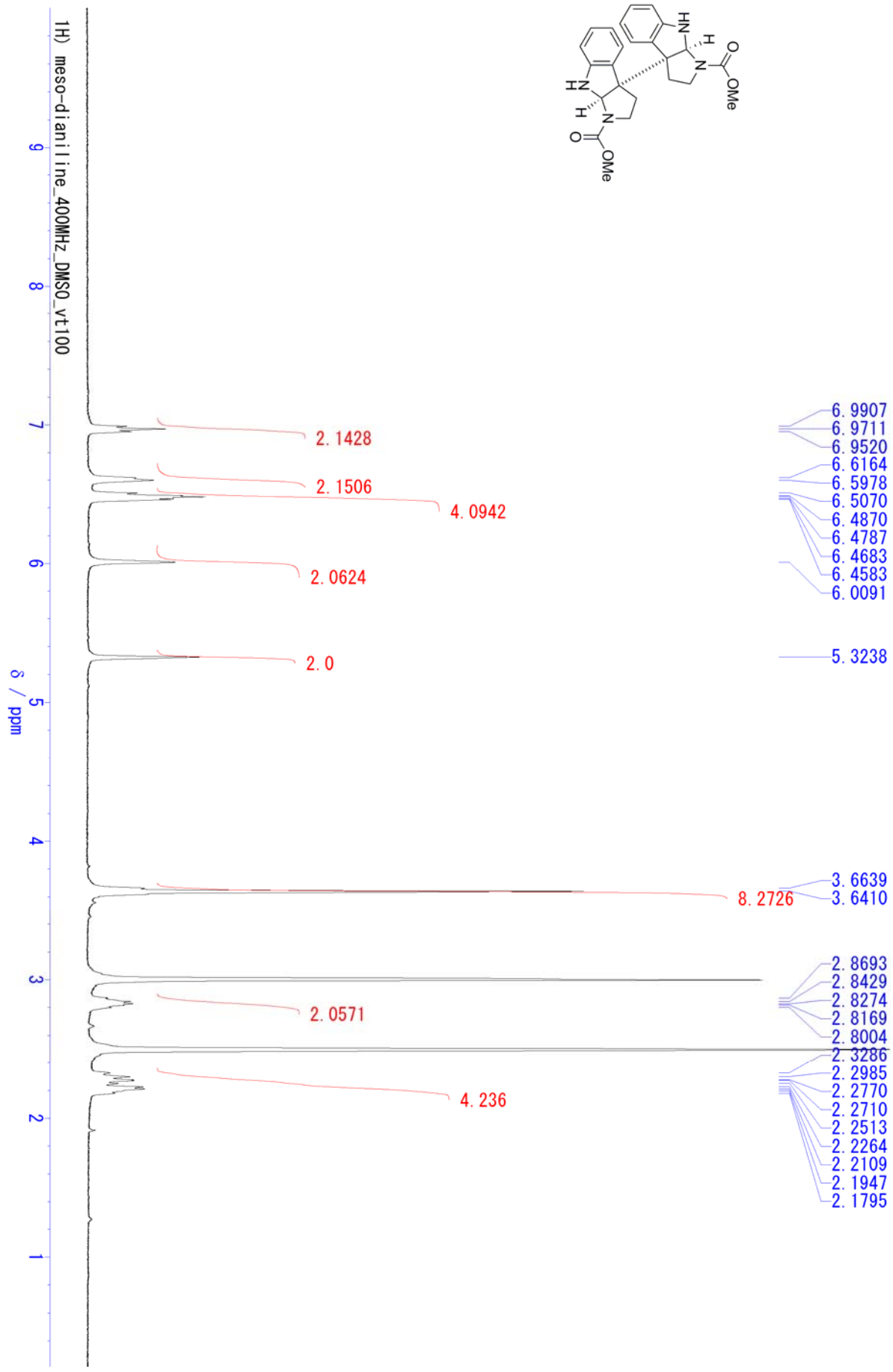


Figure S19. A ^{1}H-NMR spectrum of **S-3** in DMSO

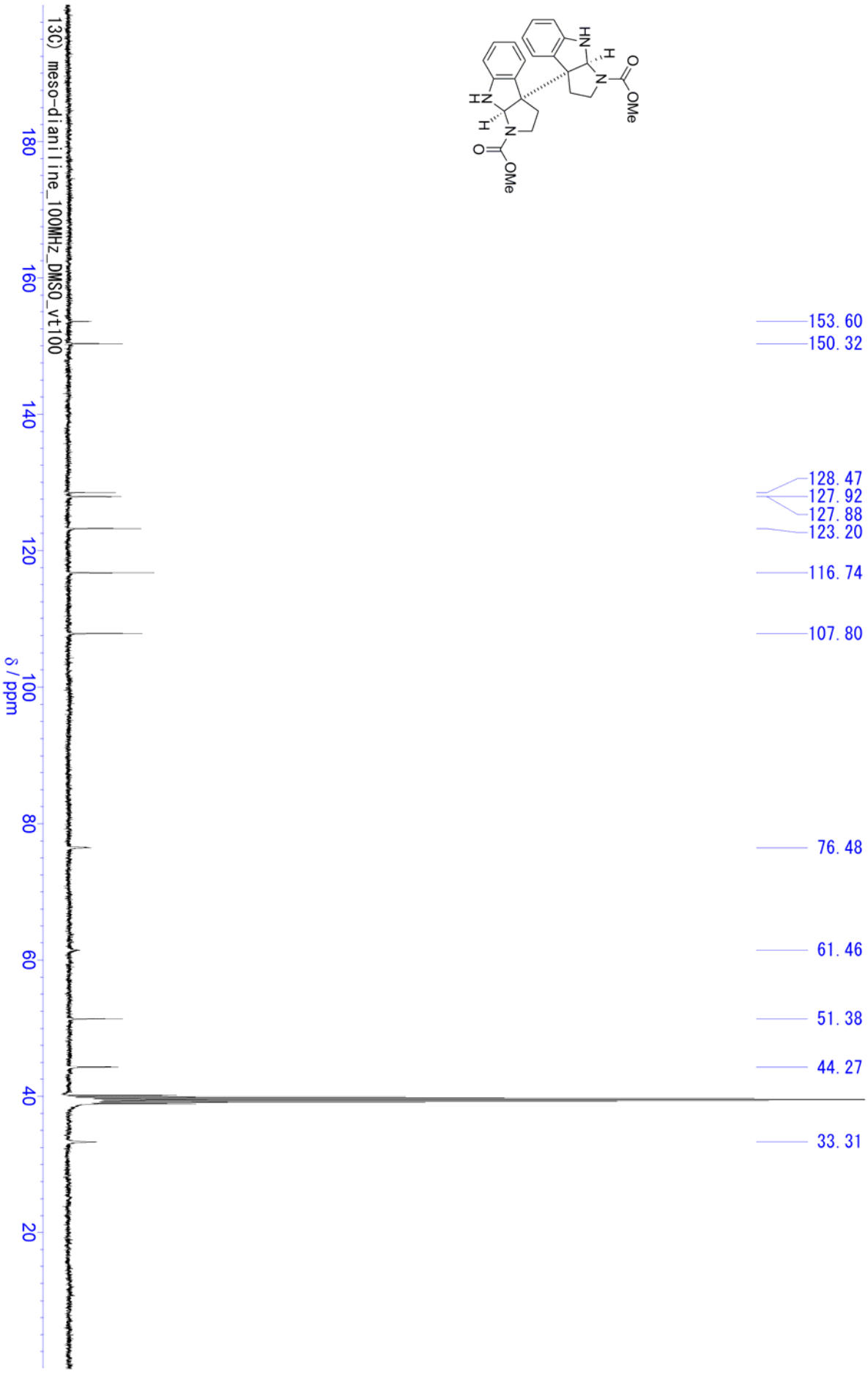


Figure S20. A ^{13}C-NMR spectrum of **S-3** in DMSO

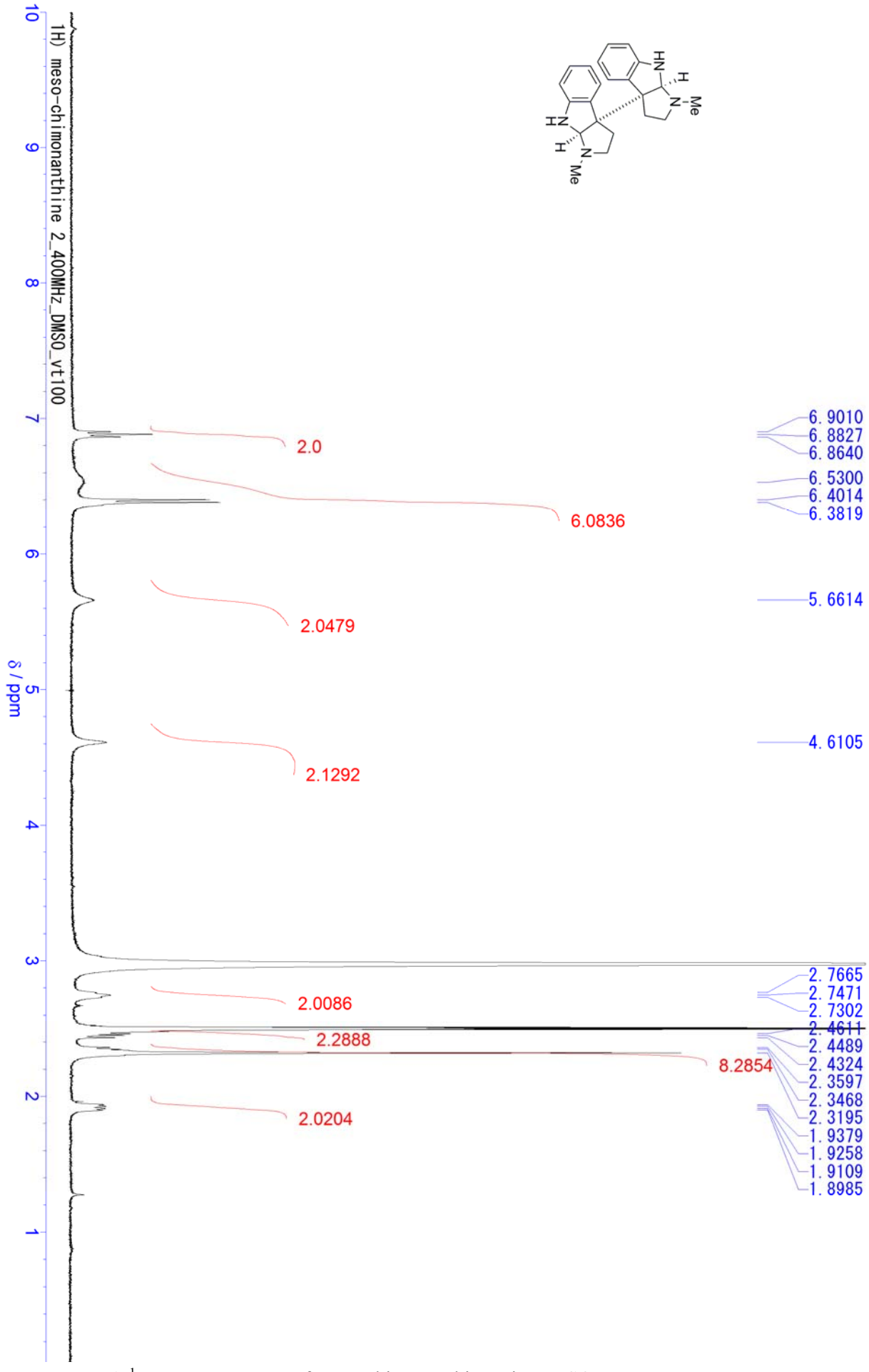


Figure S21. A ^{1}H-NMR spectrum of *meso*-chimonanthine **2** in DMSO

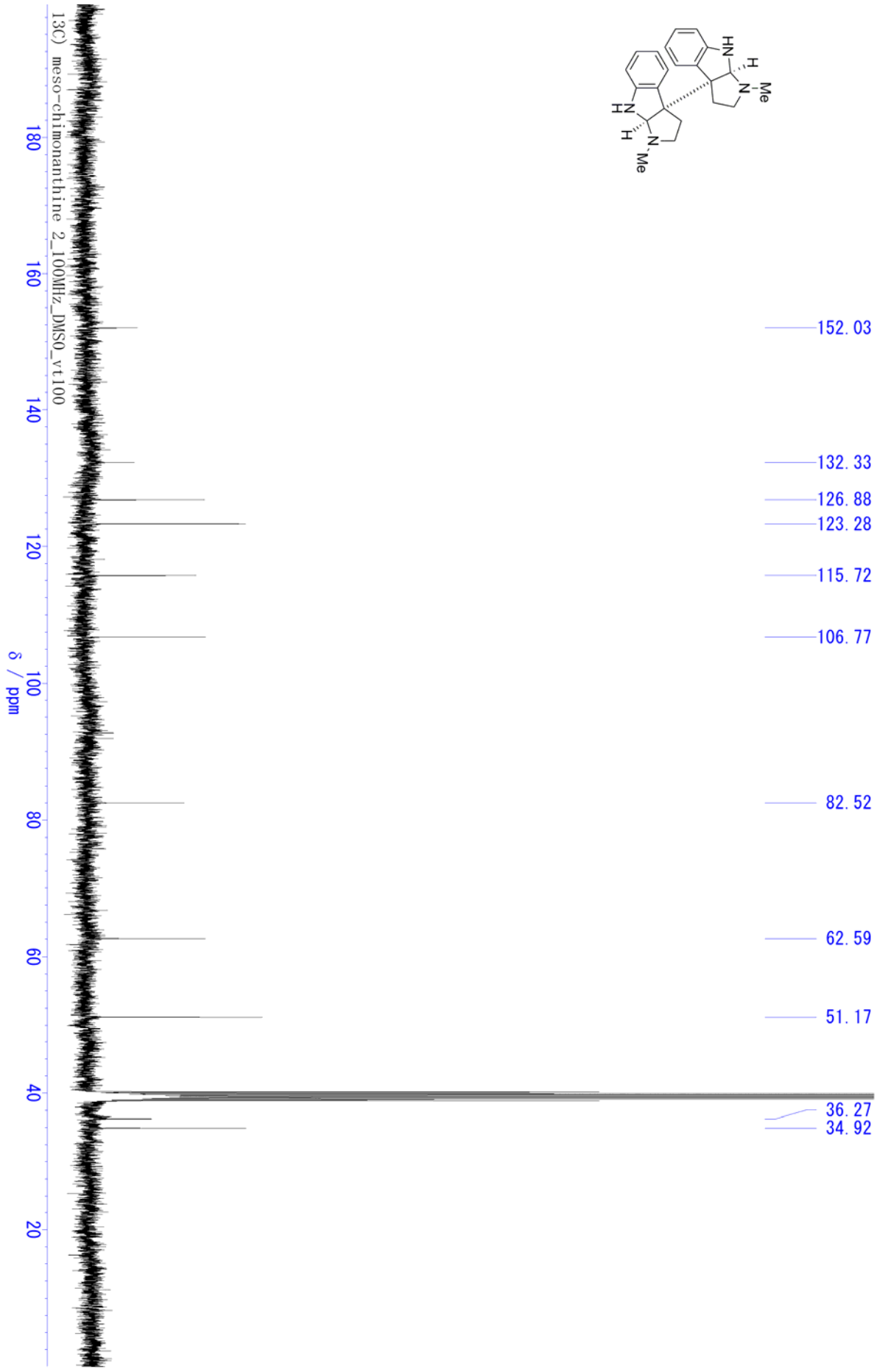


Figure S22. A ^{13}C-NMR spectrum of *meso*-chimonanthine **2** in DMSO

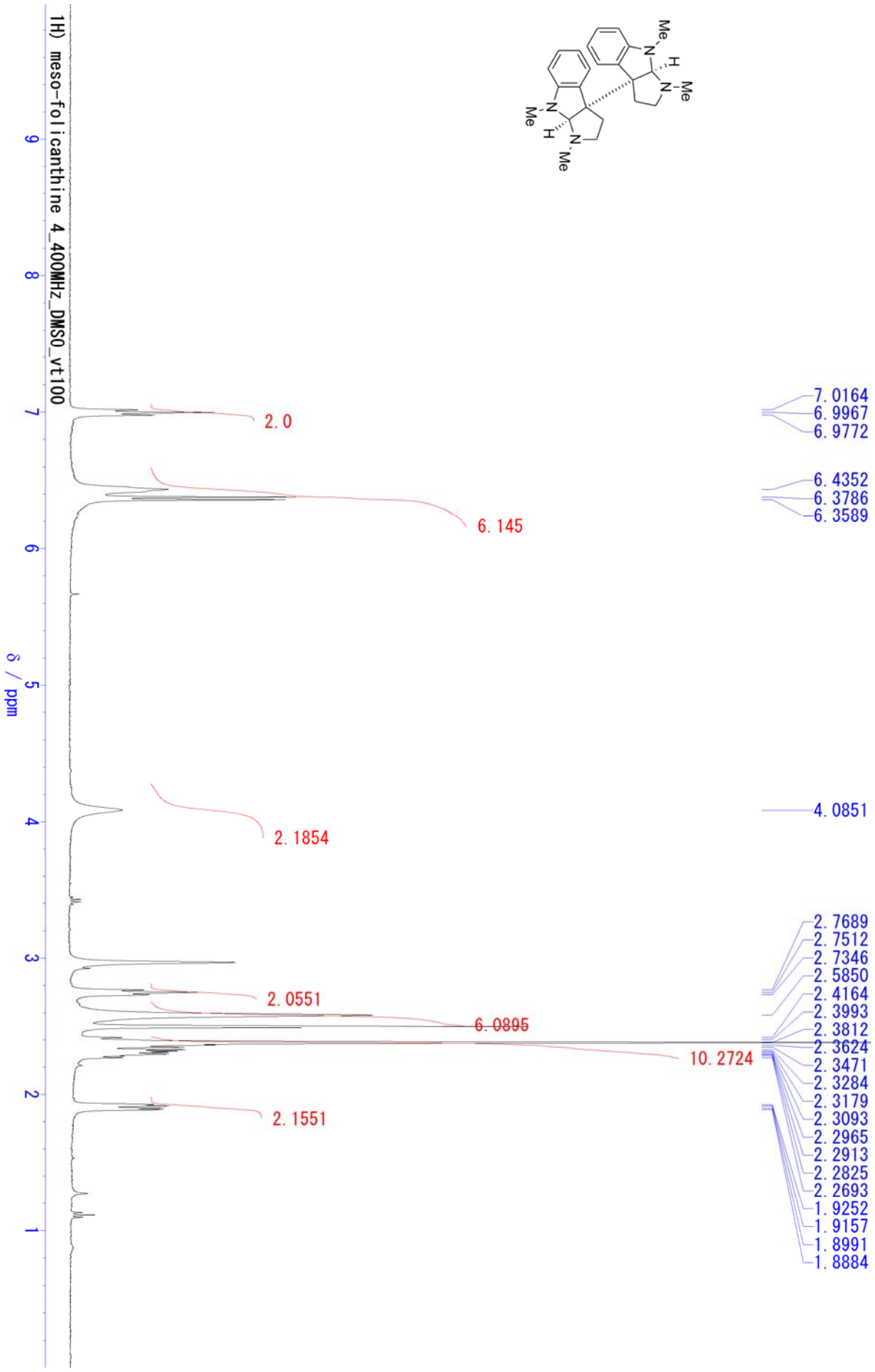


Figure S23. A ^{1}H-NMR spectrum of *meso*-folicanthine **4** in DMSO

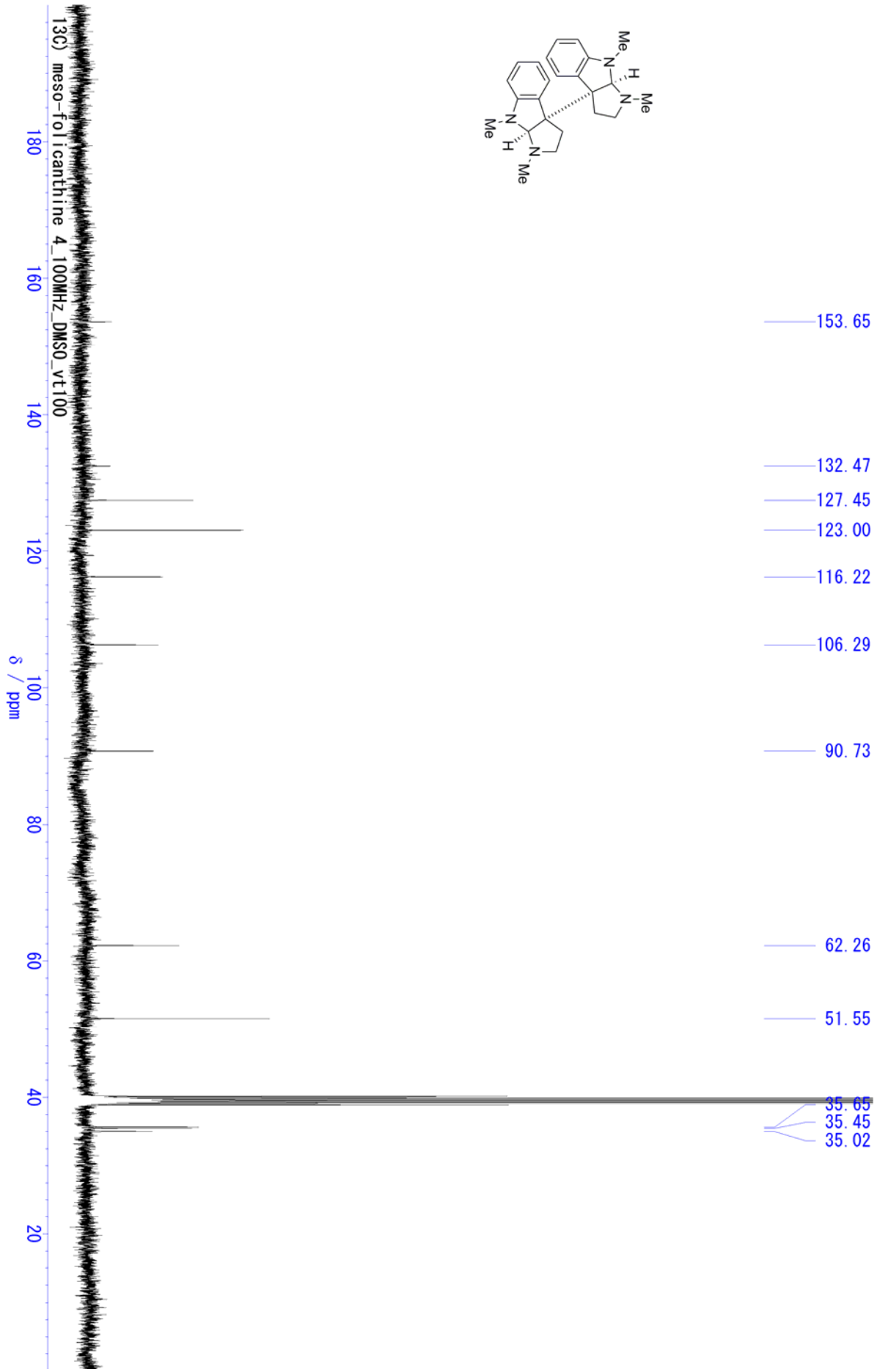


Figure S24. A ^{13}C-NMR spectrum of *meso*-folicanthine **4** in DMSO

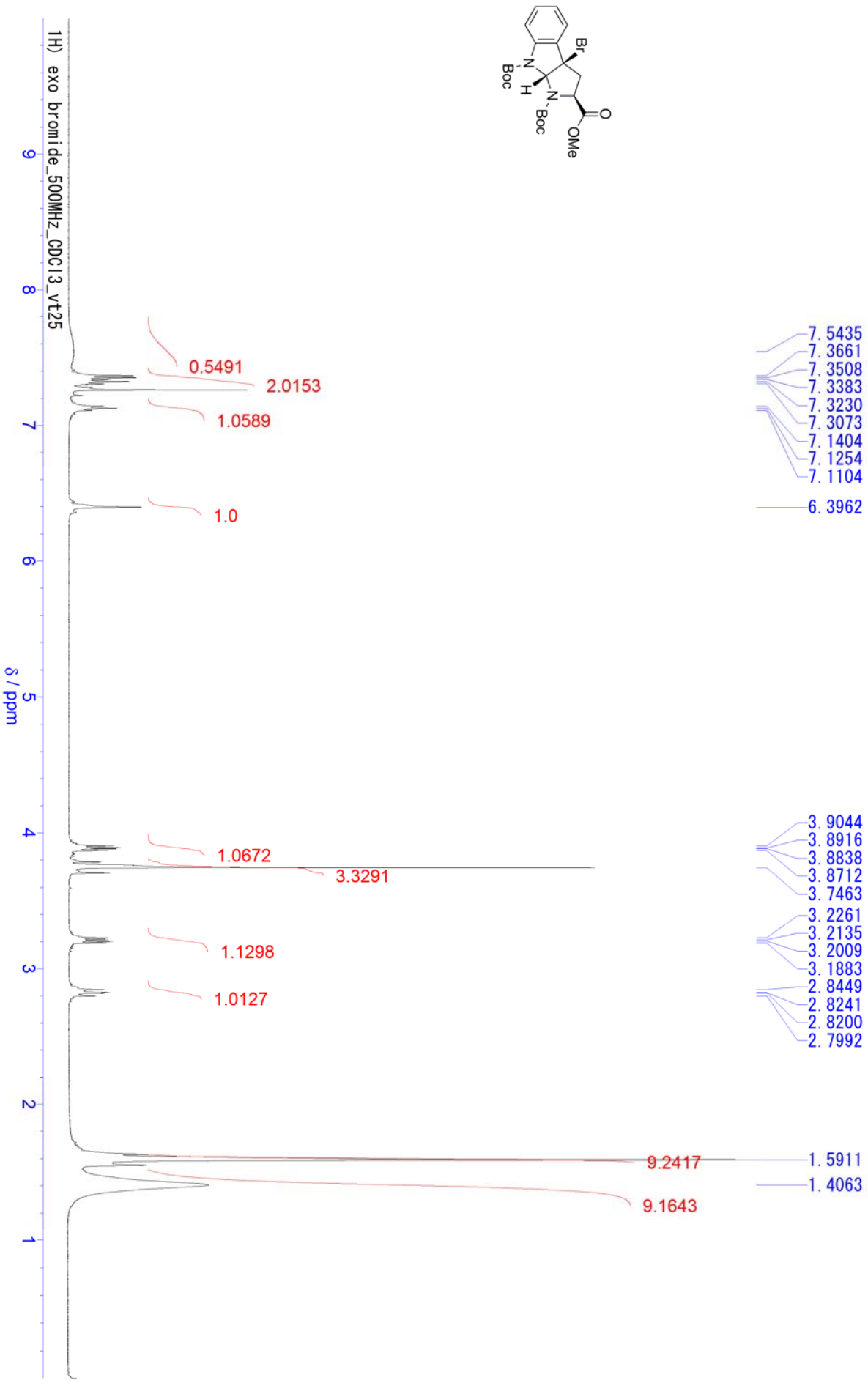


Figure S25. A ^{1}H-NMR spectrum of **7** in $CDCl_3$

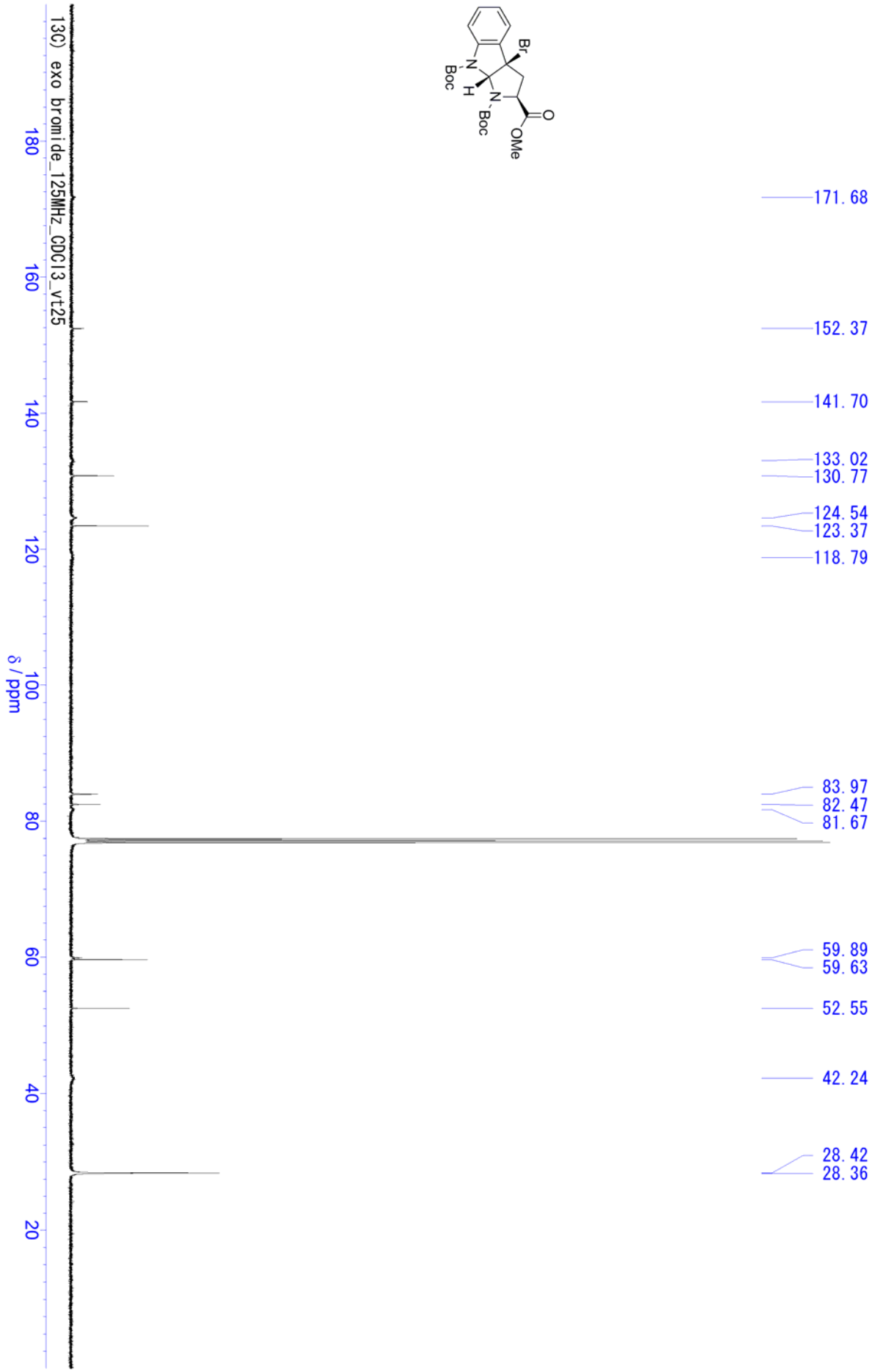


Figure S26. A ^{13}C-NMR spectrum of **7** in $CDCl_3$

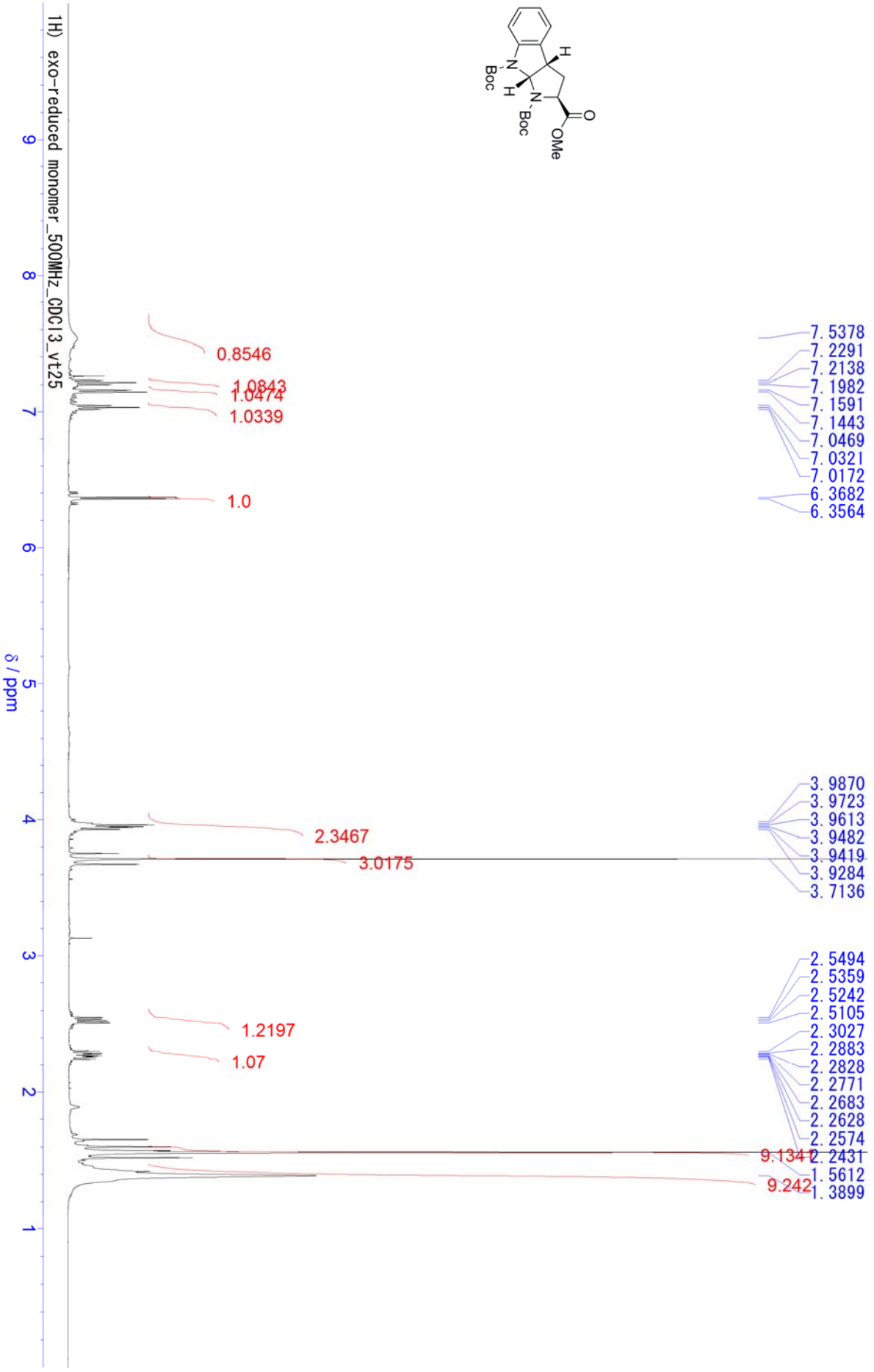


Figure S27. A ^{1}H-NMR spectrum of **10** in $CDCl_3$

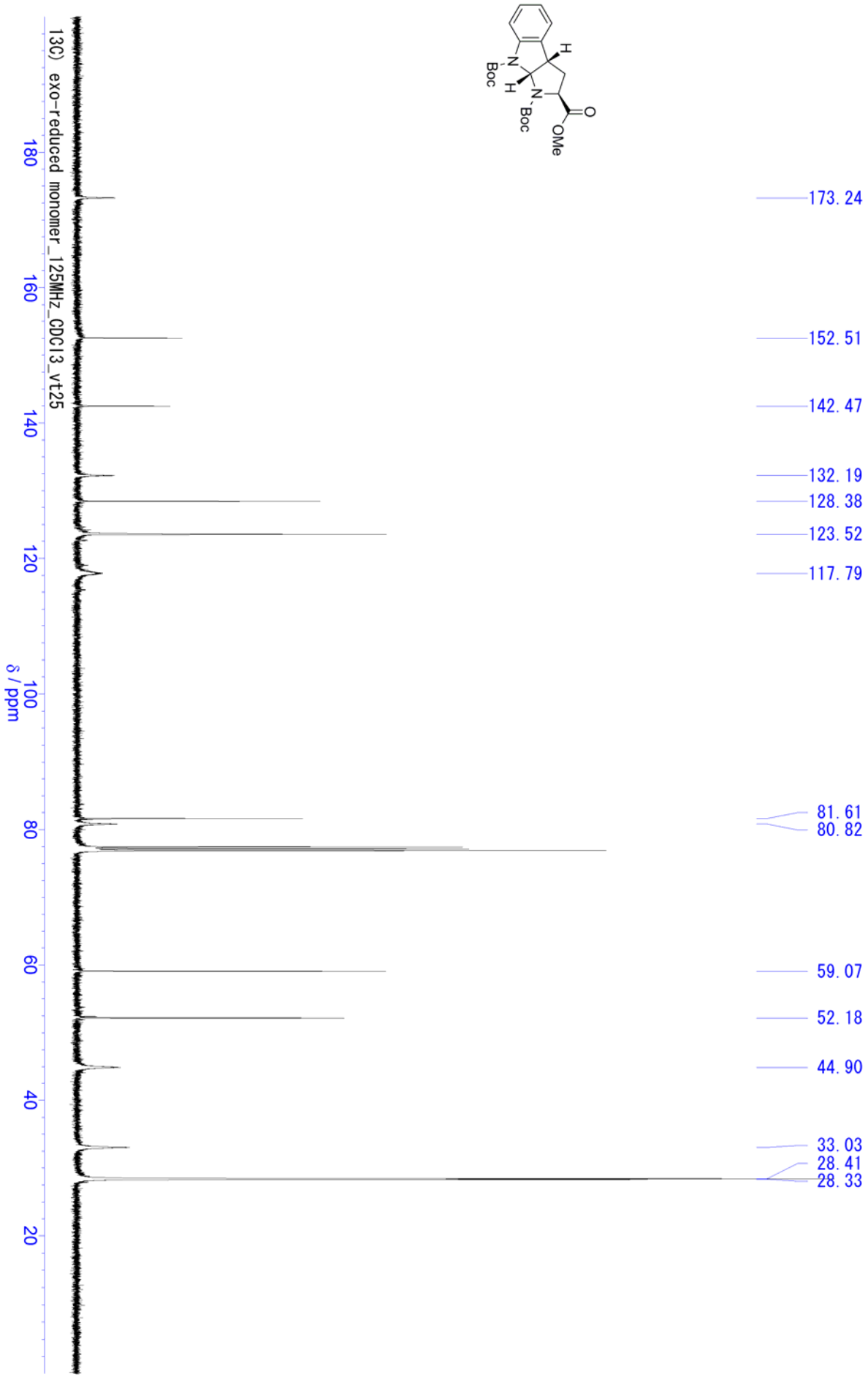


Figure S28. A ^{13}C-NMR spectrum of **10** in $CDCl_3$

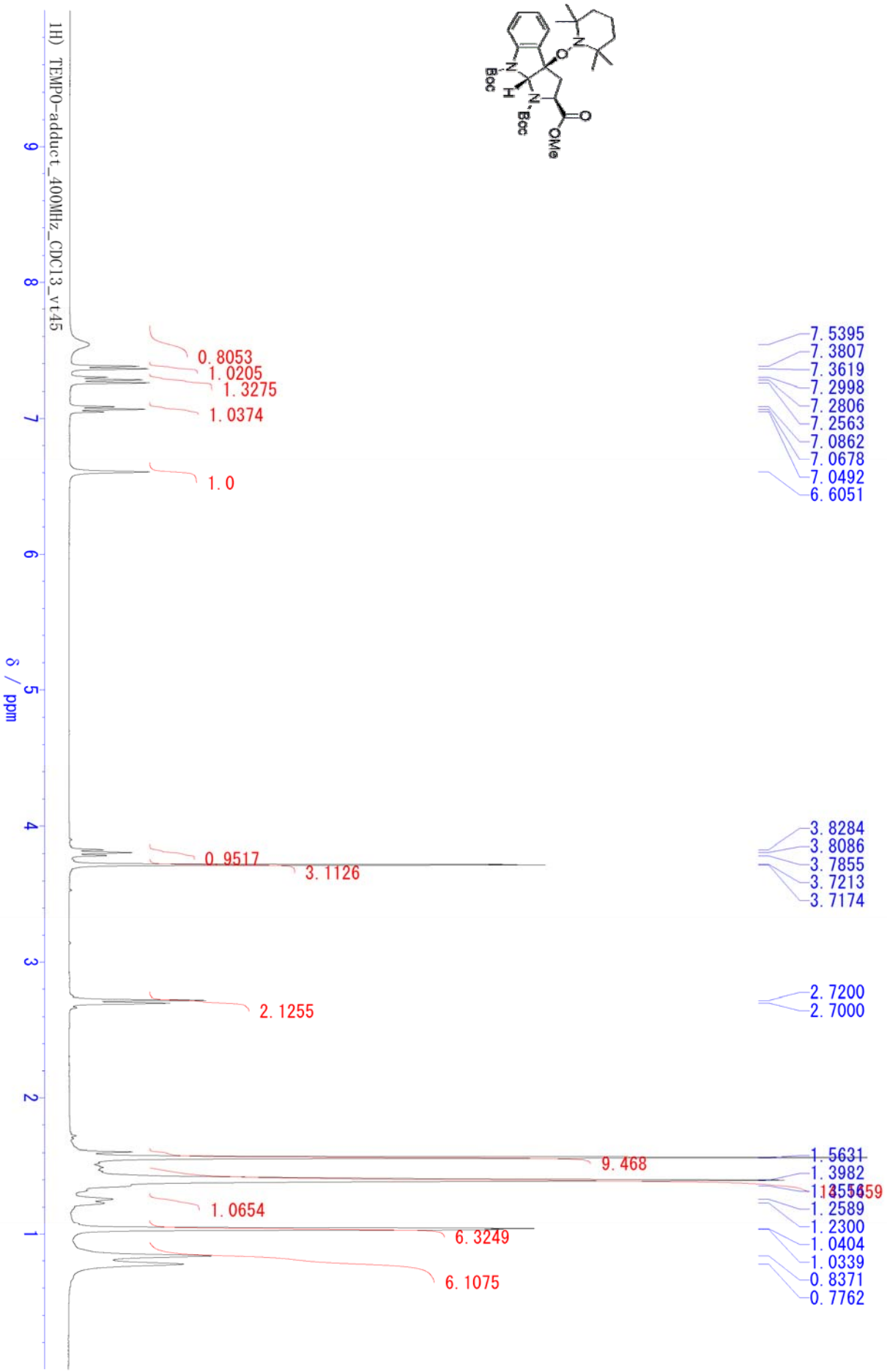


Figure S29. A ^{1}H-NMR spectrum of **14** in $CDCl_3$

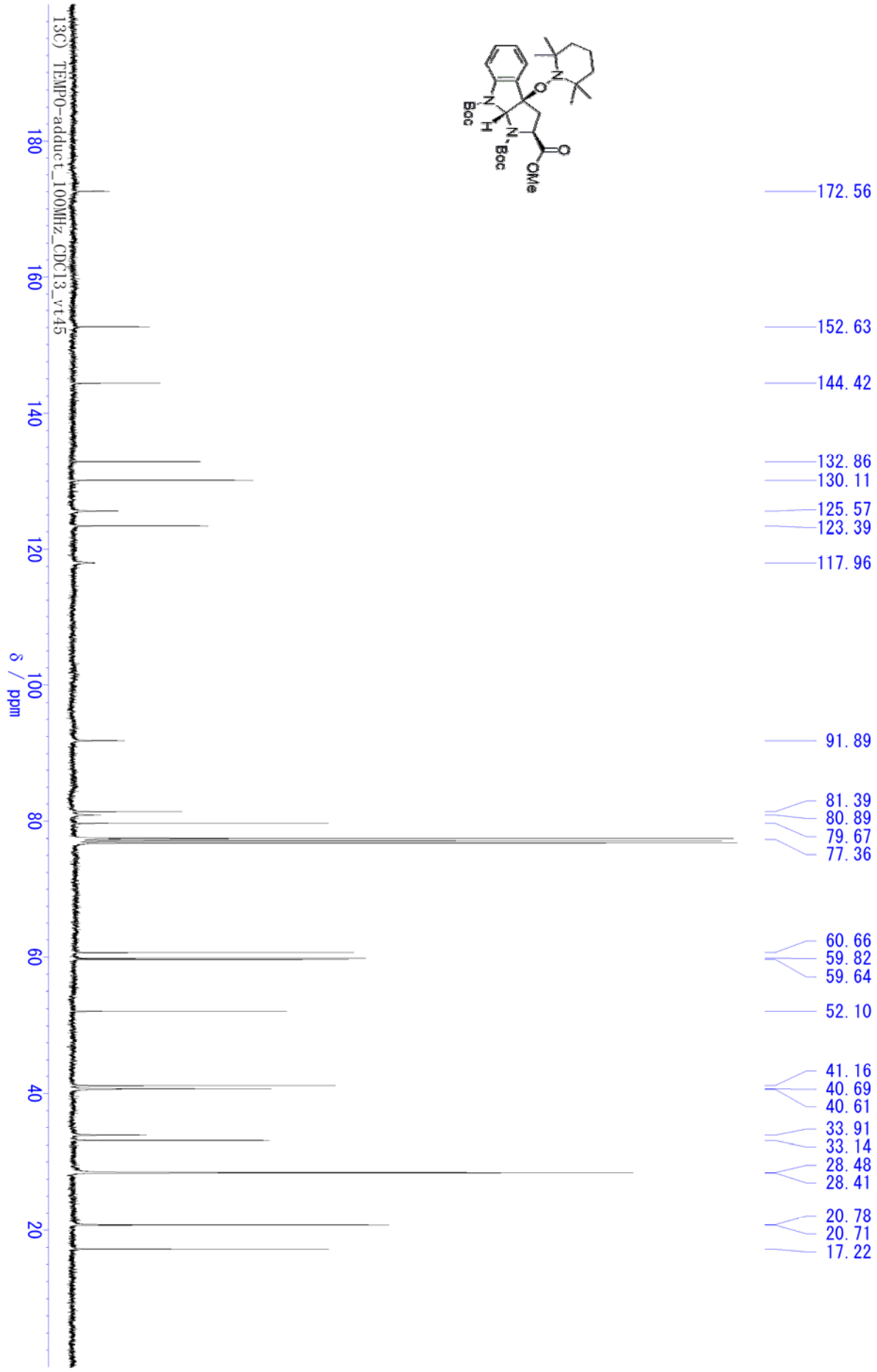


Figure S30. A ^{13}C-NMR spectrum of **14** in $CDCl_3$

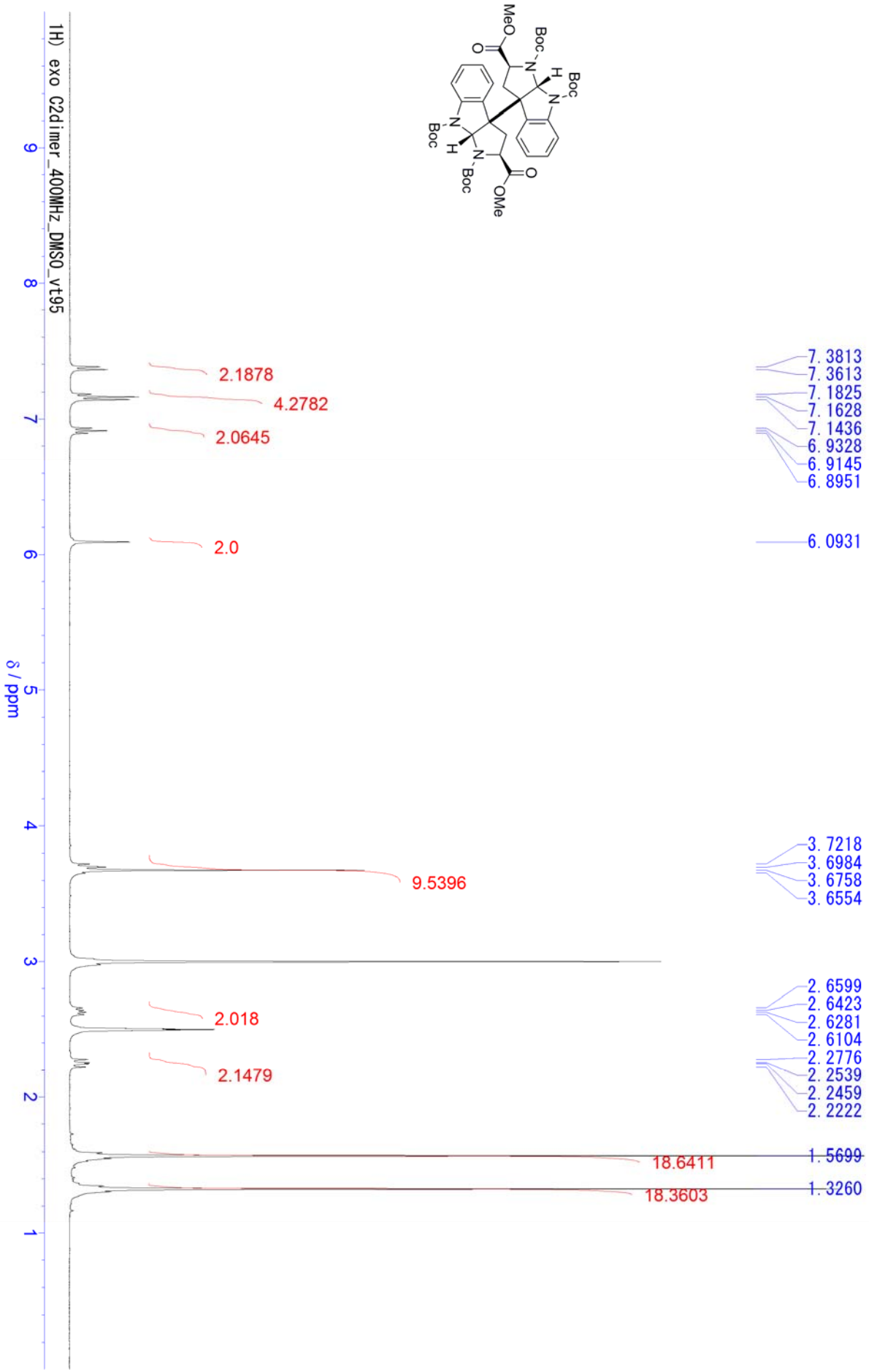


Figure S31. A ^{1}H-NMR spectrum of **8** in DMSO

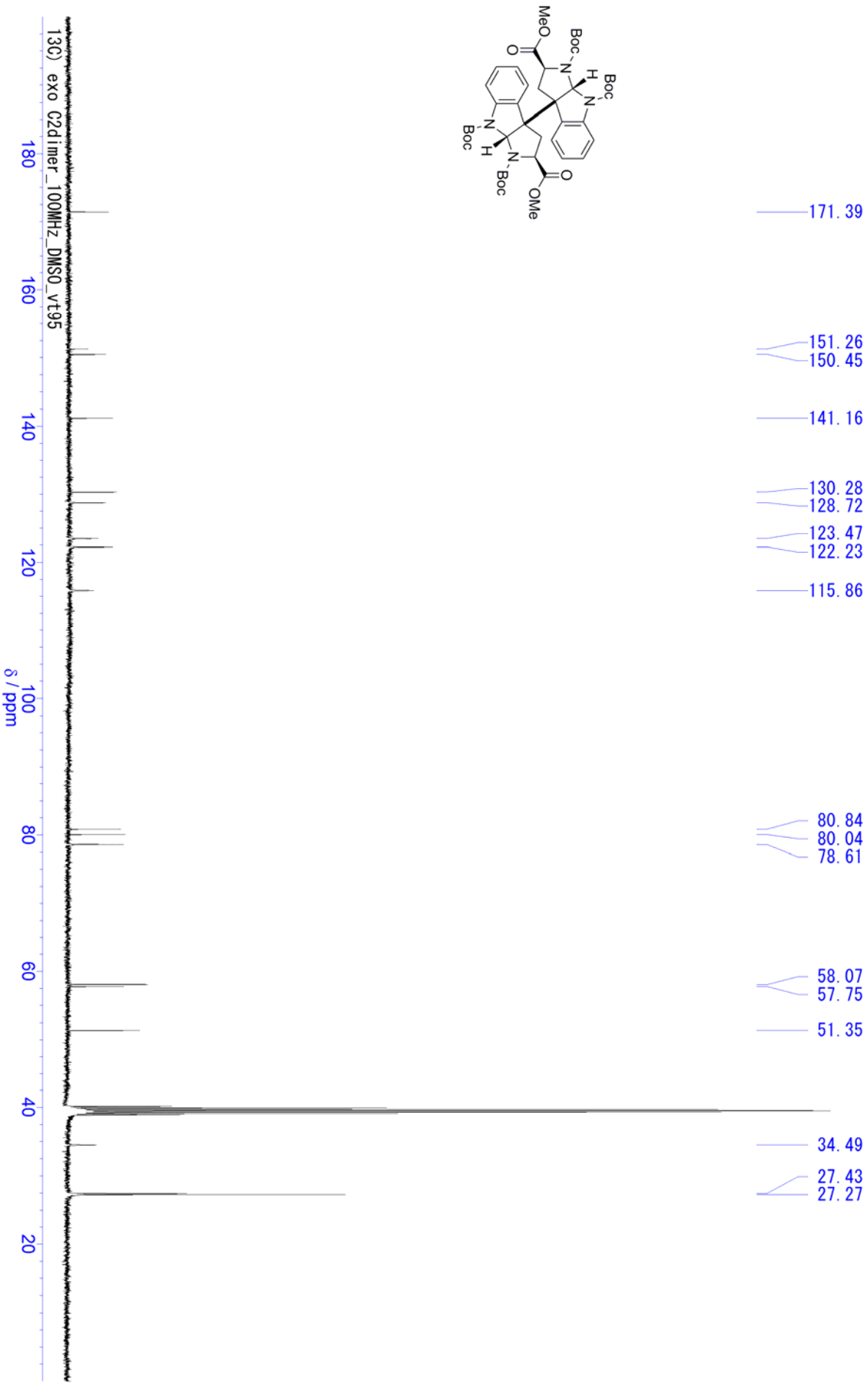


Figure S32. A ^{13}C-NMR spectrum of **8** in DMSO

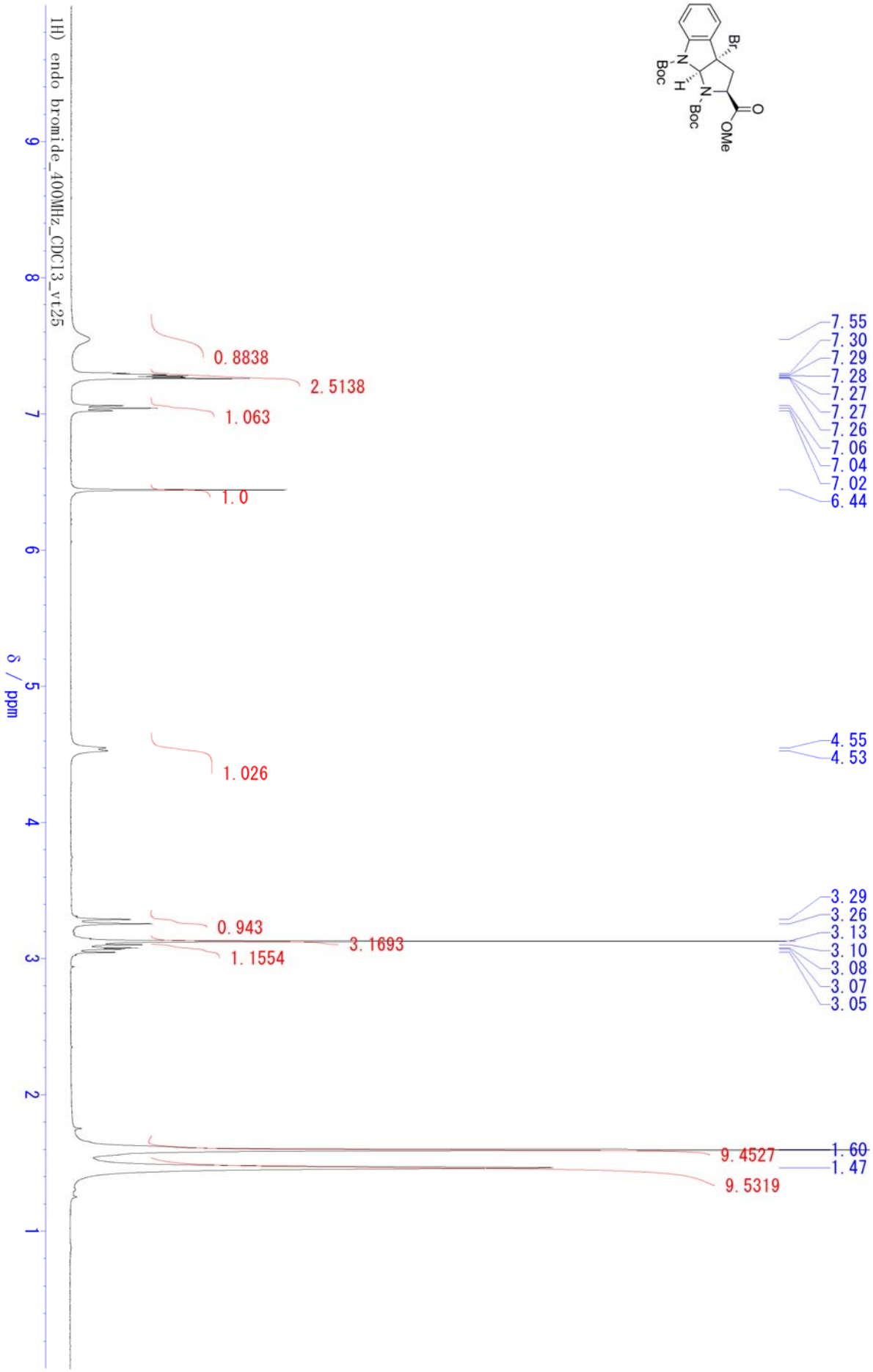


Figure S33. A ^{1}H-NMR spectrum of **11** in $CDCl_3$

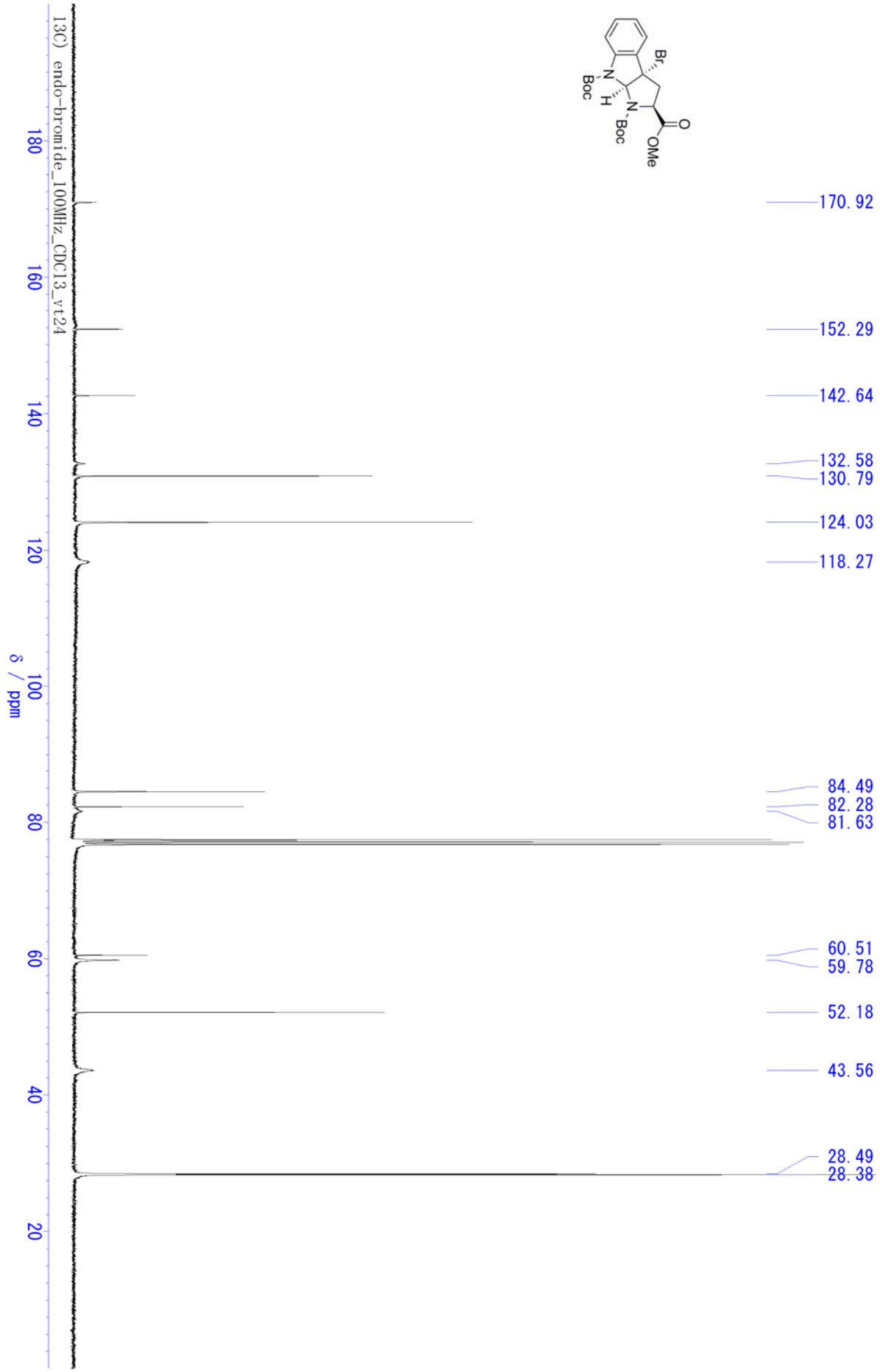


Figure S34. A ^{13}C-NMR spectrum of **11** in $CDCl_3$

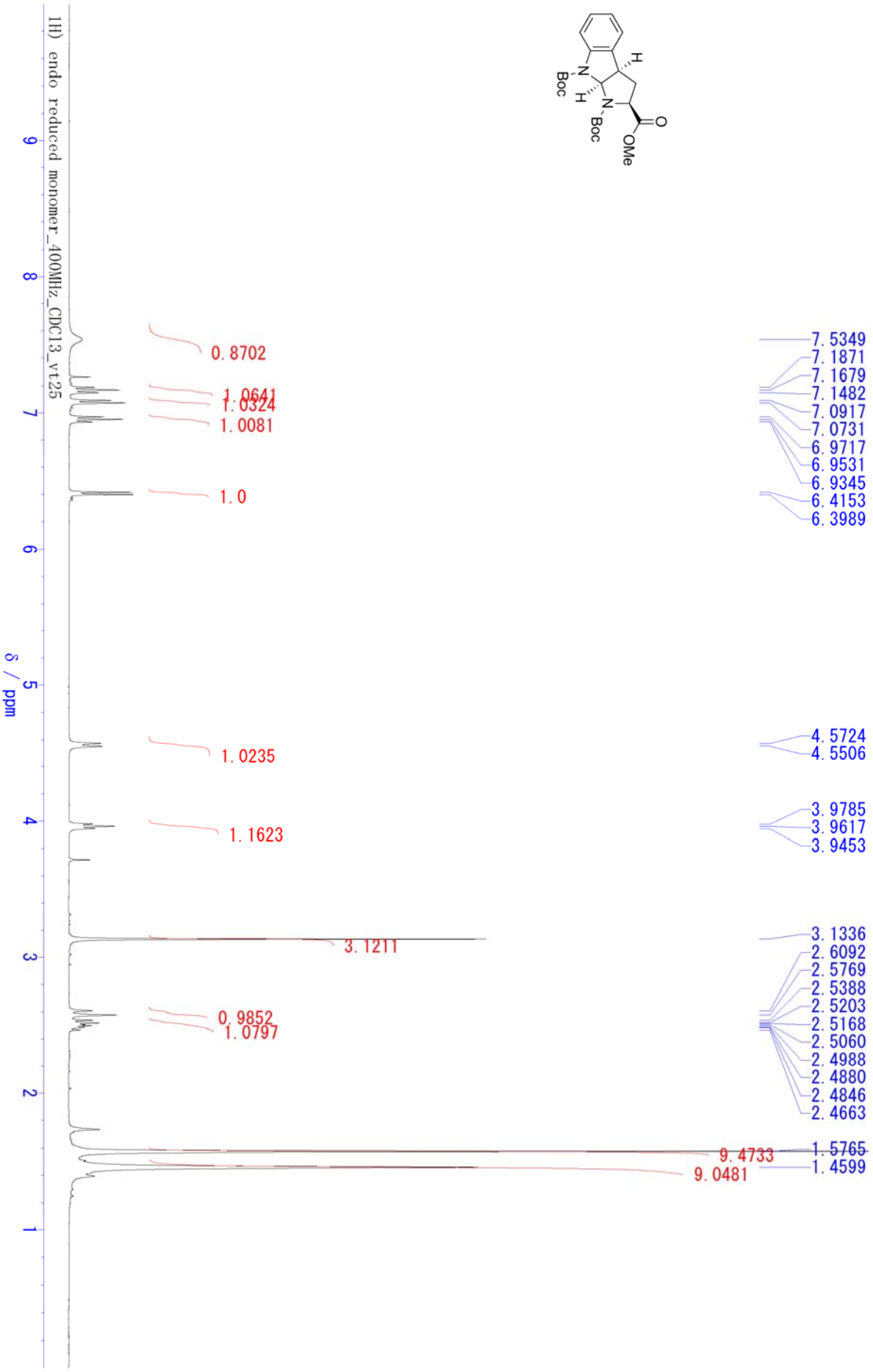


Figure S35. A ^{1}H-NMR spectrum of **13** in $CDCl_3$

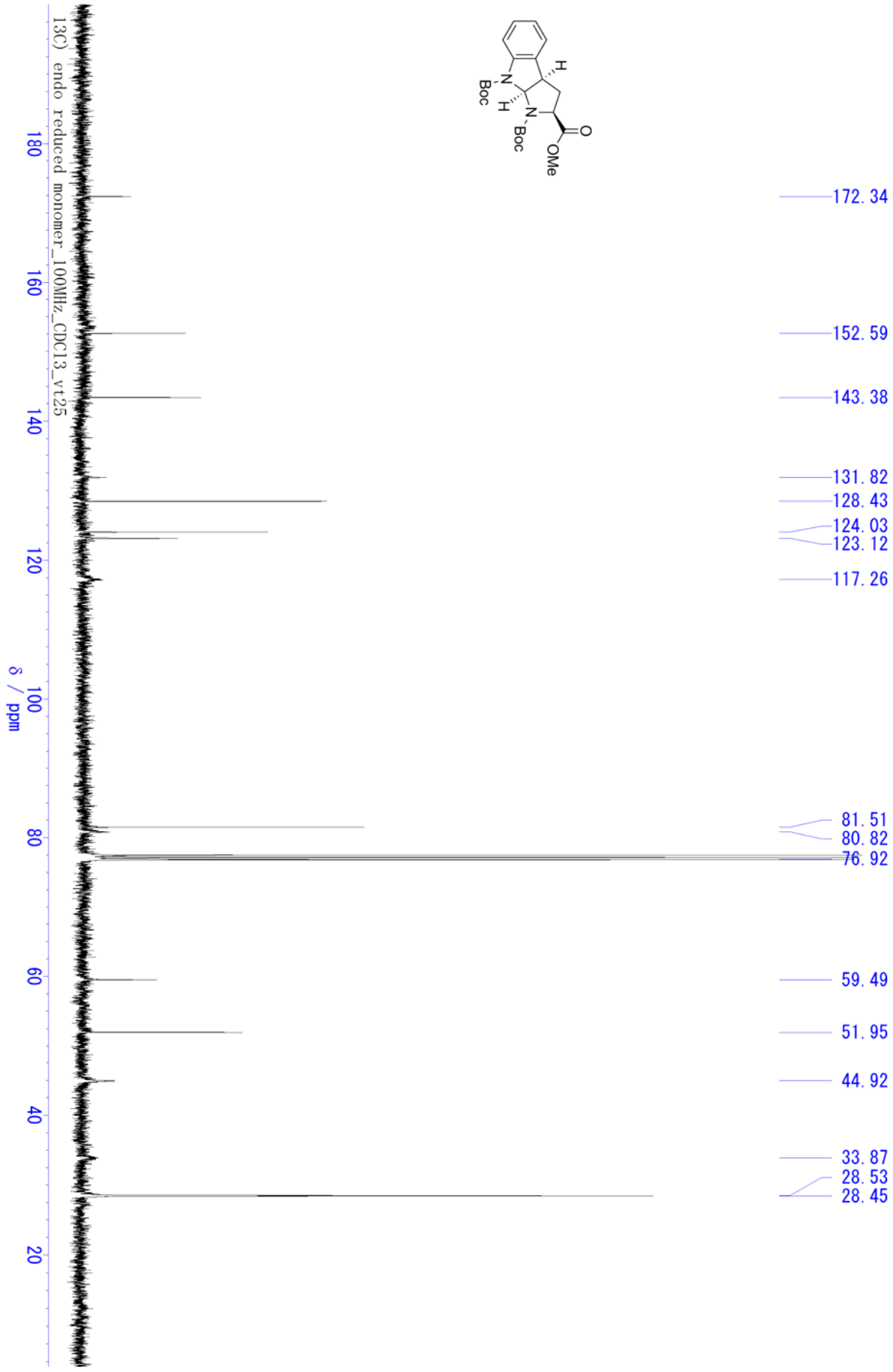


Figure S36. A ^{13}C-NMR spectrum of **13** in $CDCl_3$

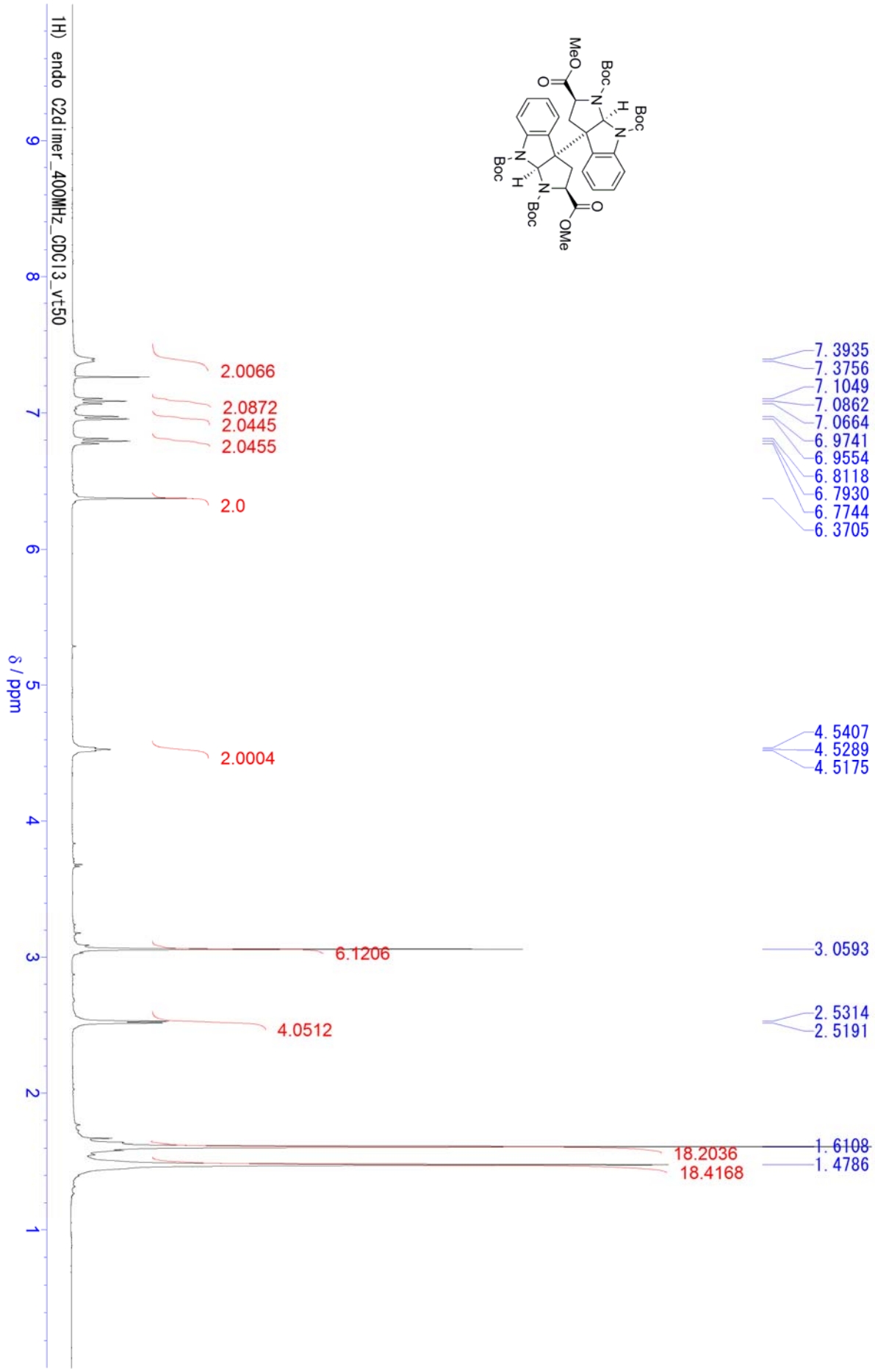


Figure S37. A ^{1}H-NMR spectrum of **12** in $CDCl_3$

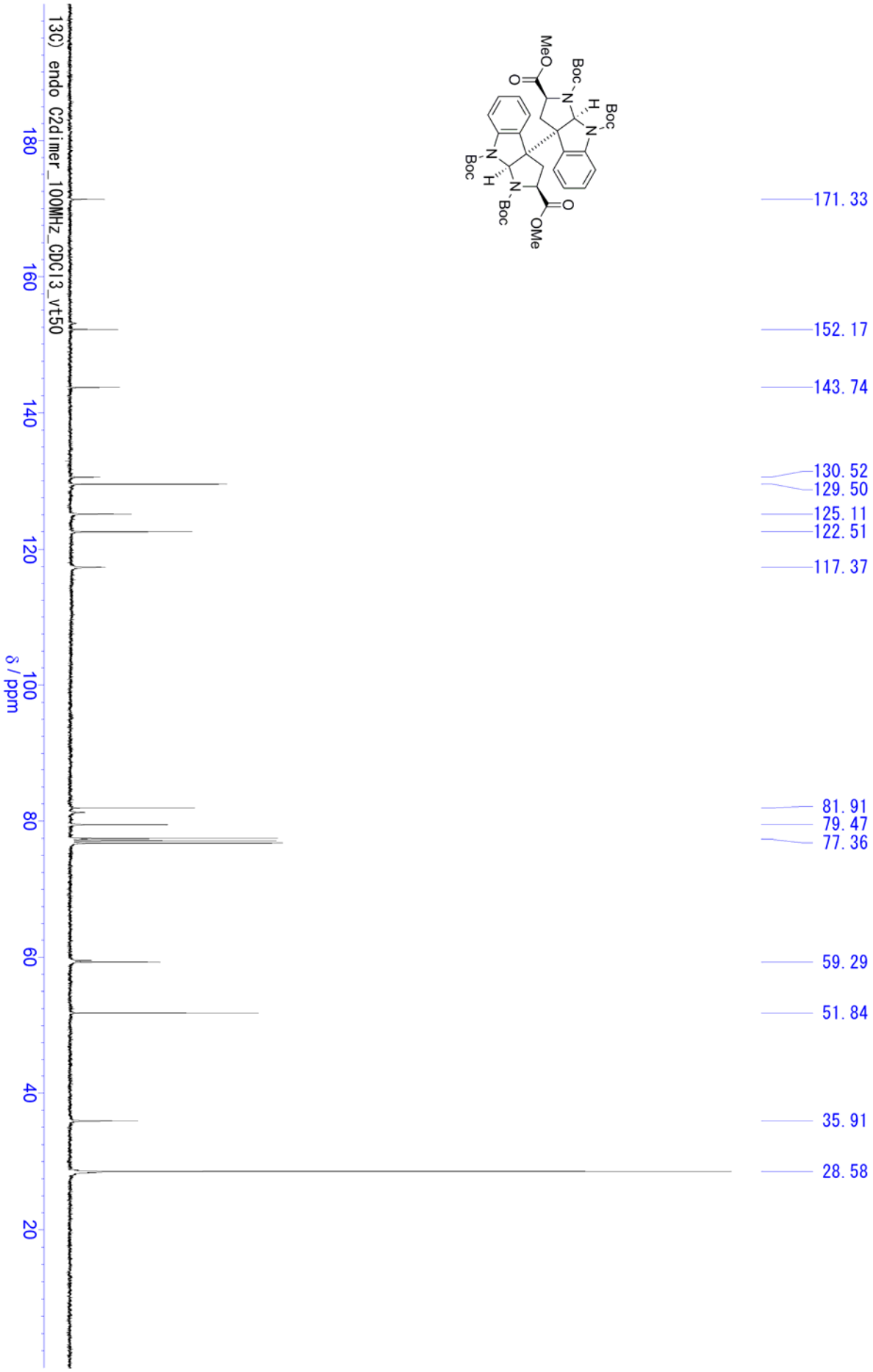


Figure S38. A ^{13}C-NMR spectrum of **12** in $CDCl_3$

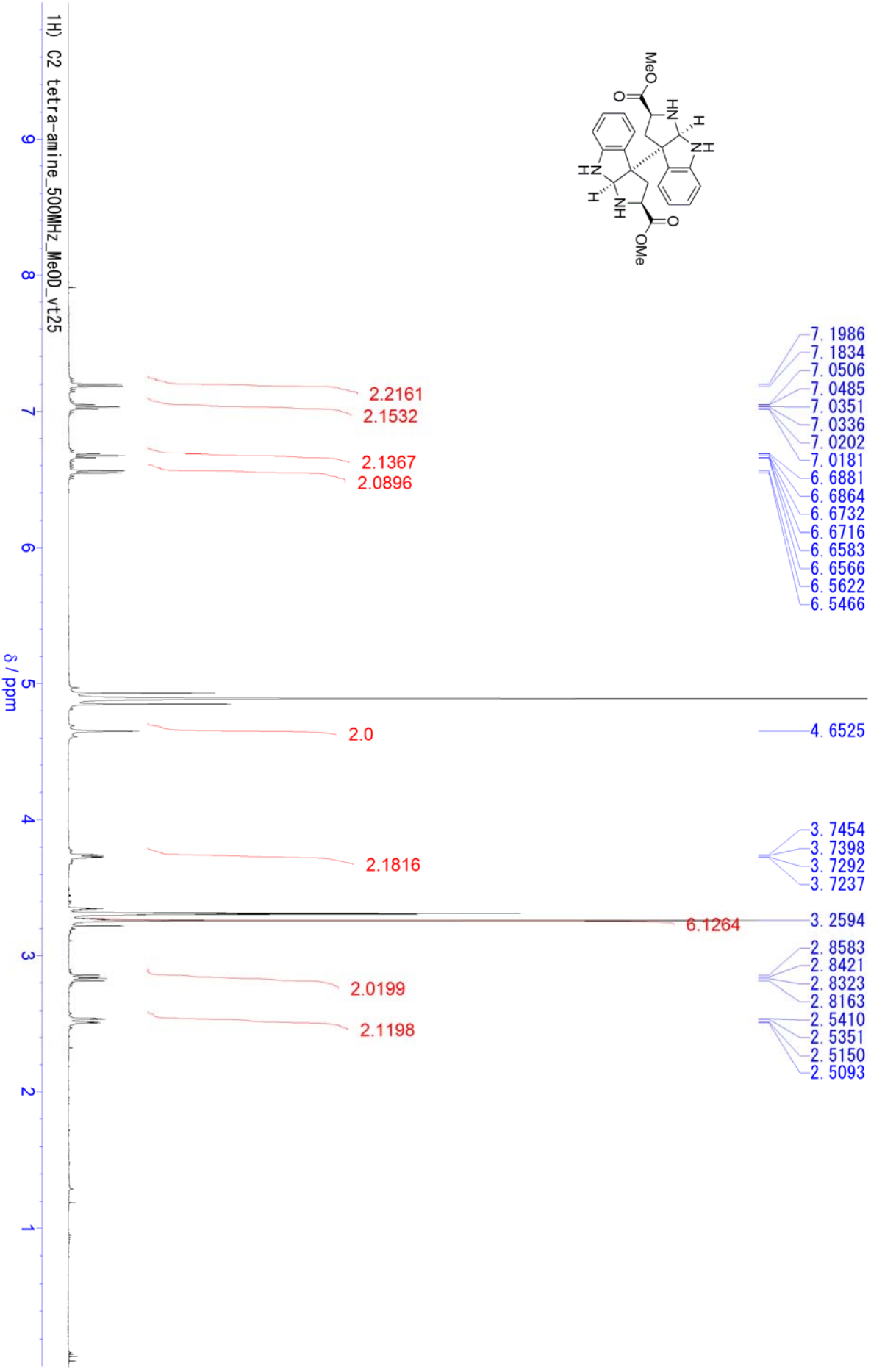


Figure S39. A ^{1}H-NMR spectrum of **S-4** in CD_3OD

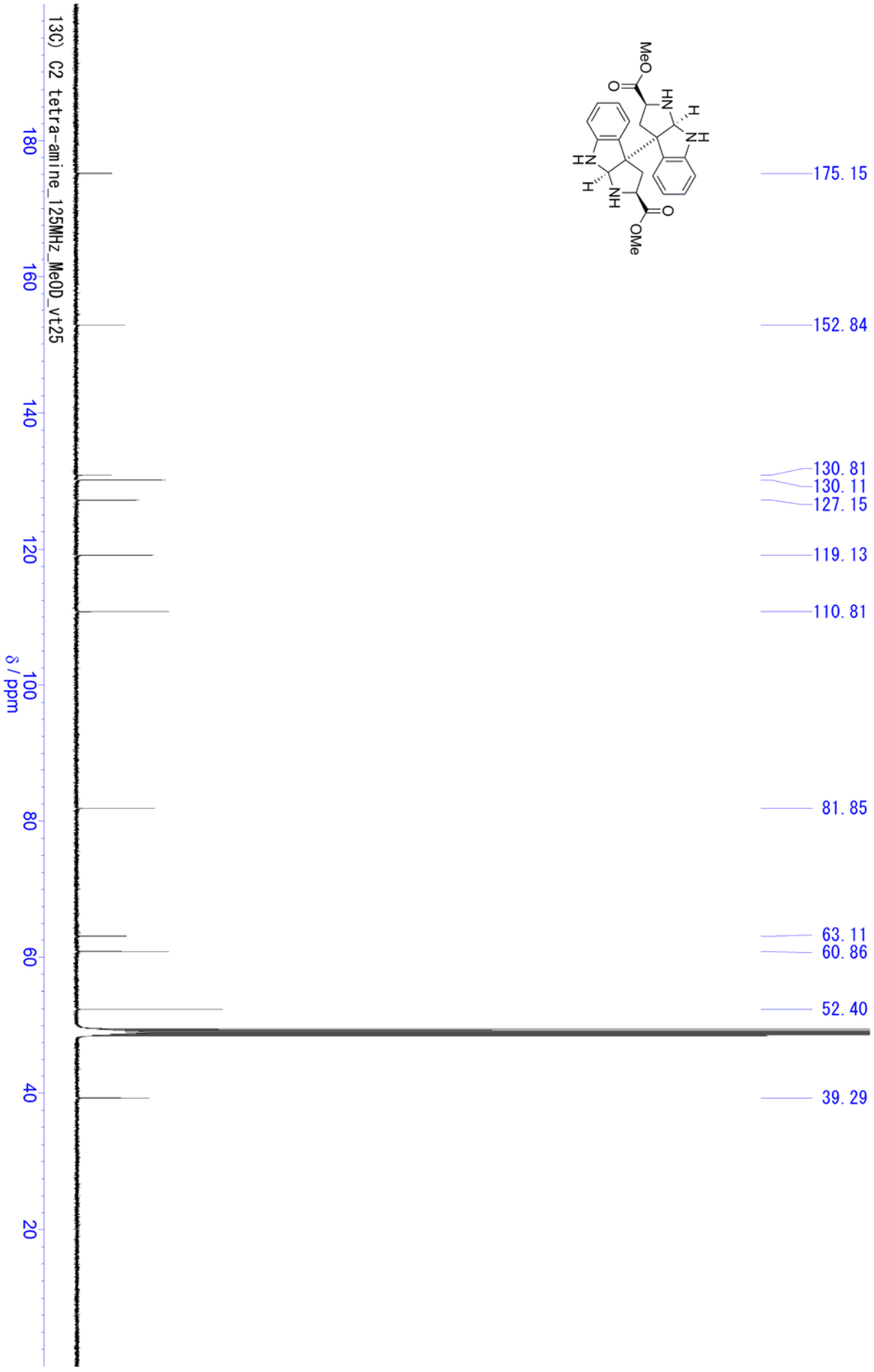


Figure S40. A ^{13}C-NMR spectrum of **S-4** in CD_3OD

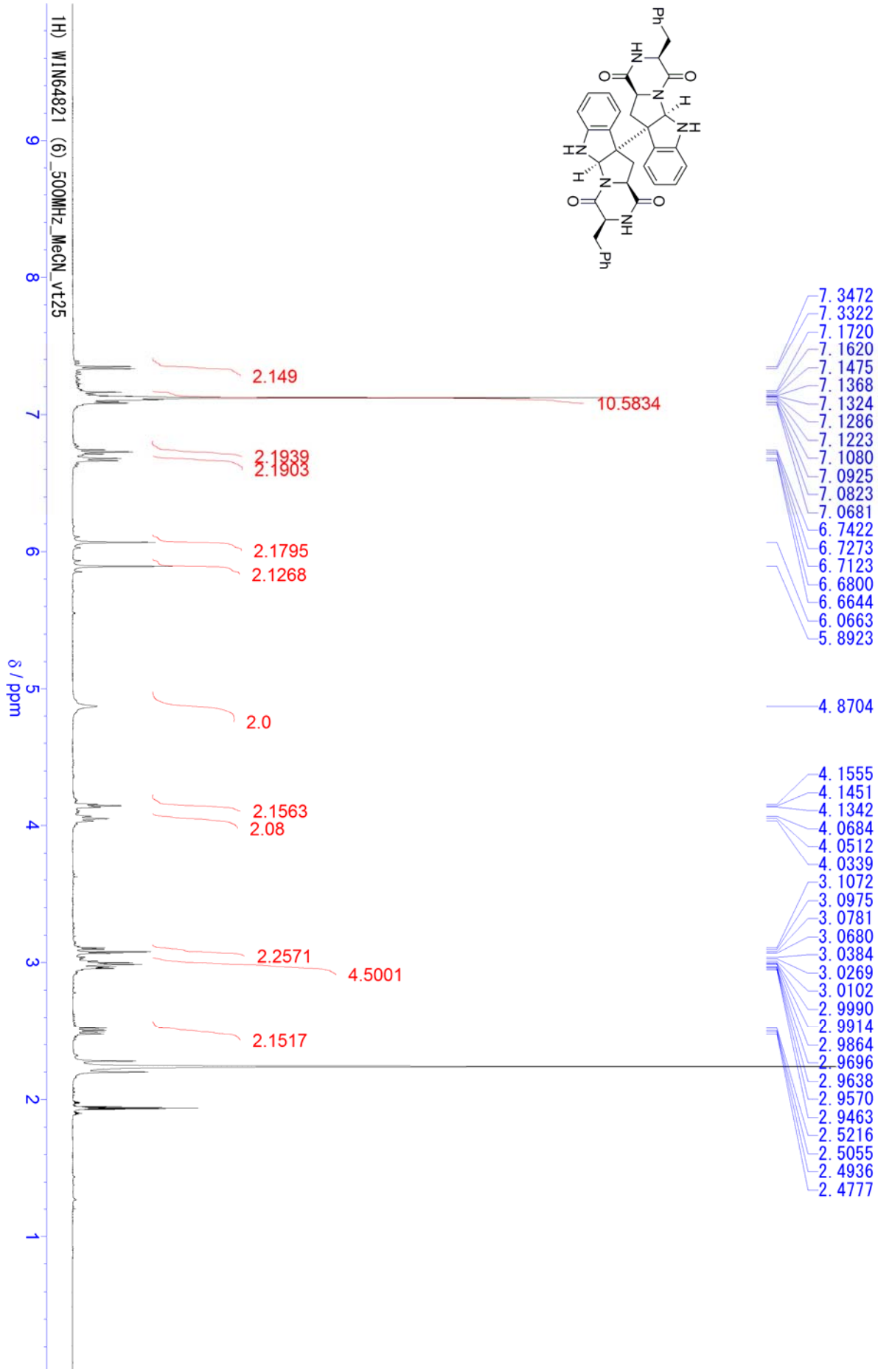


Figure S41. A ^{1}H-NMR spectrum of (+)-WIN 64821 (+)-**6** in CD_3CN

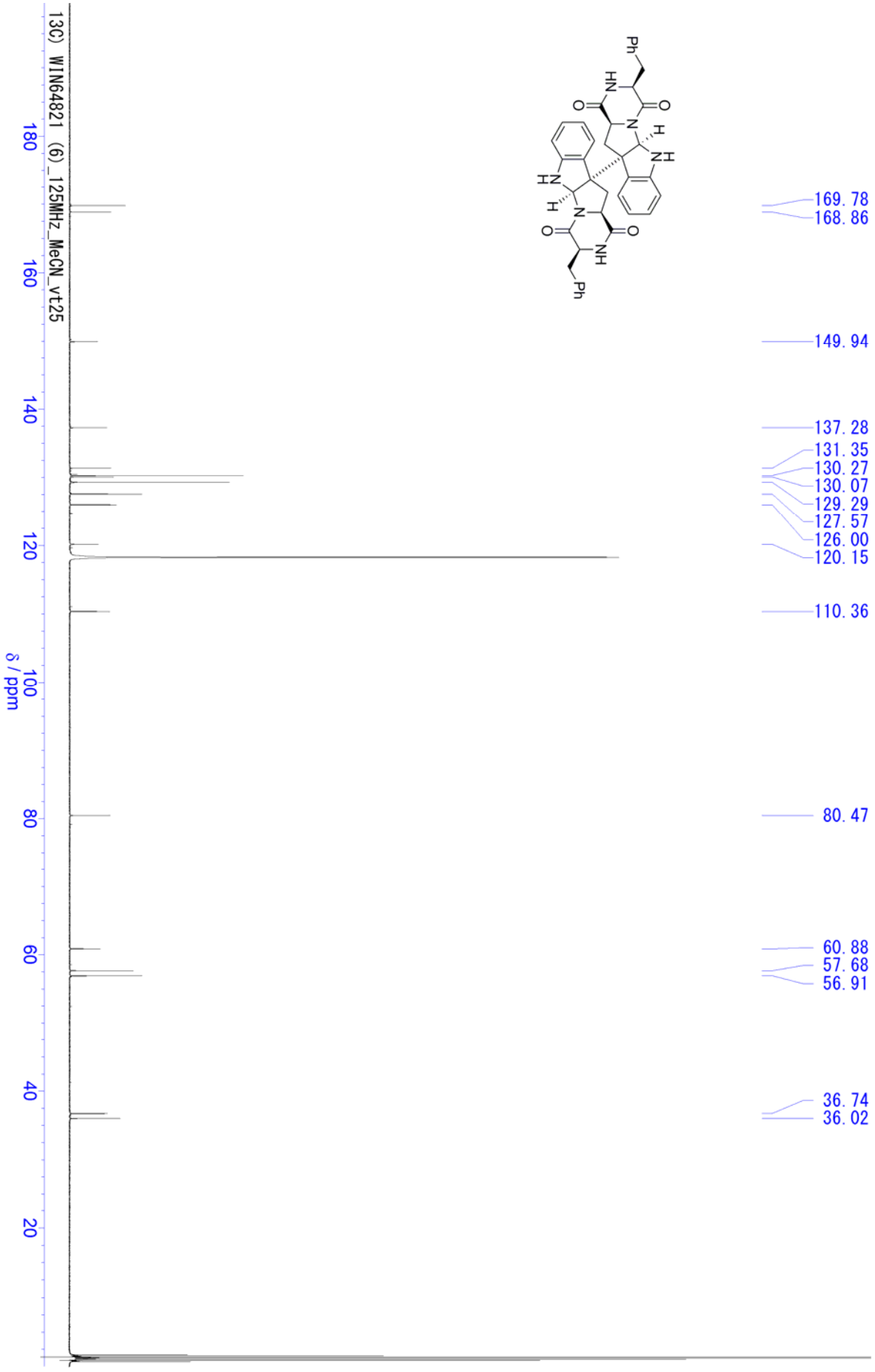


Figure S42. A ^{13}C-NMR spectrum of (+)-WIN 64821 (+)-**6** in CD_3CN