Supporting information

Configurational stability of bis-*ortho*-methyl Tröger's base: The methylene bridge substitution with retention of stereochemistry

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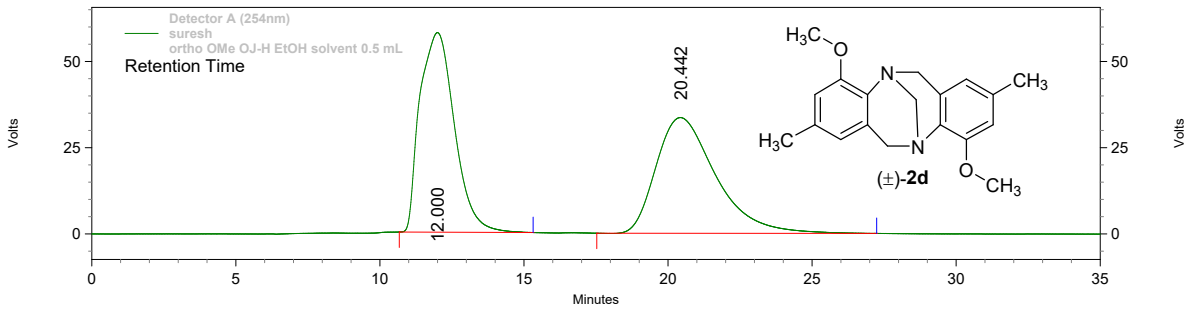
1. Copies of HPLC profiles

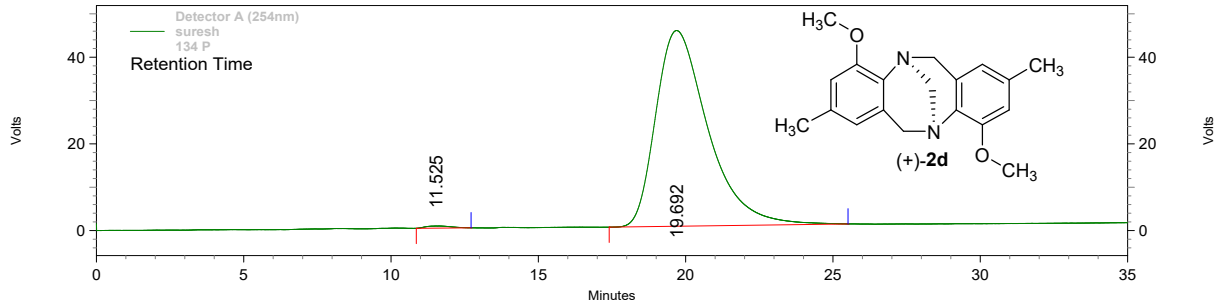
HPLC Profile of (±)-2d: chiral column Chiralcel OJ-H, EtOH; flow rate 0.5 mL/min



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	12.000	4828779	50.003	57869	63.297
2	20.442	4828171	49.997	33555	36.703
Totals		9656950	100.000	91424	100.000

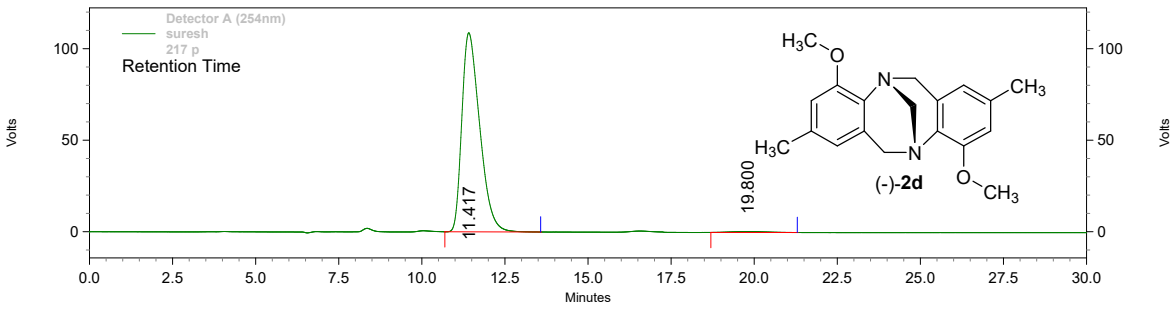
HPLC Profile of (+)-2d: chiral column Chiralcel OJ-H, EtOH; flow rate 0.5 mL/min



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	11.525	28894	0.517	485	1.062
2	19.692	5557610	99.483	45165	98.938
Totals		5586504	100.000	45650	100.000

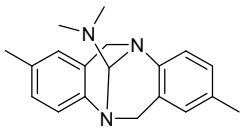
HPLC Profile of (-)-2d: chiral column Chiralcel OJ-H, EtOH; flow rate 0.5 mL/min

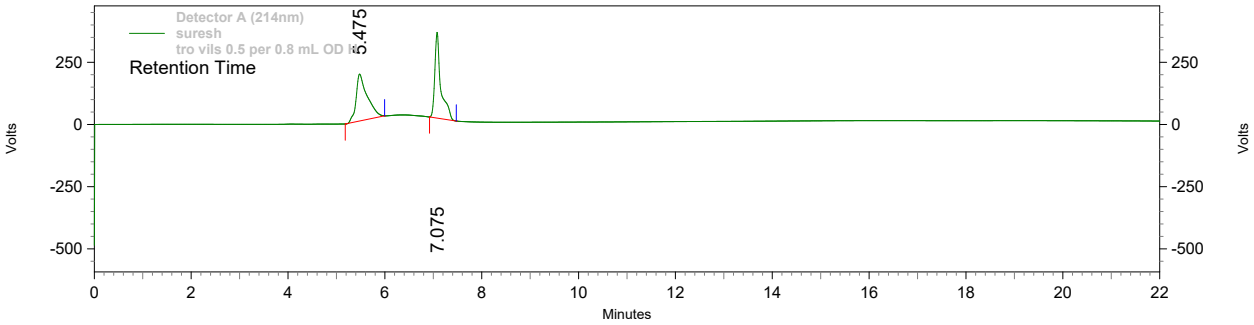


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	11.417	4060149	99.160	108718	99.548
2	19.800	34399	0.840	494	0.452
Totals		4094548	100.000	109212	100.000

HPLC Profile of (±)-6aa: chiral column Chiralcel OD-H, hexanes:i-PrOH/99.5:0.5; flow rate 0.8 mL/min

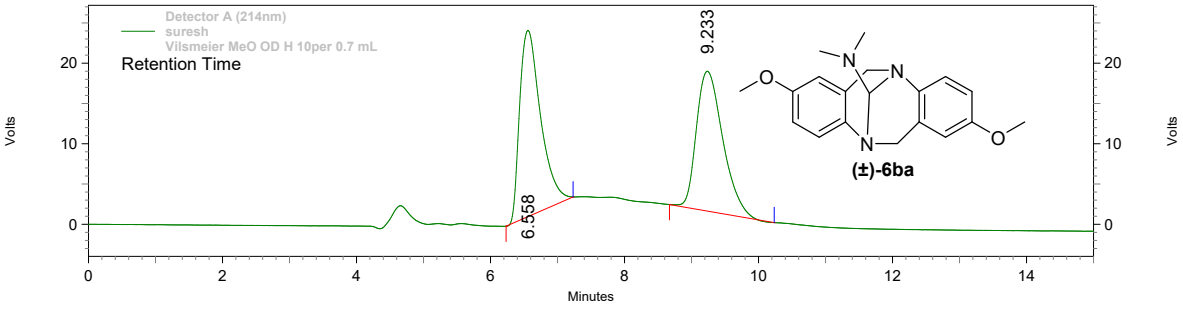




Detector A (214nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	5.475	3005344	50.070	188510	35.387
2	7.075	2996998	49.930	344193	64.613
Total		6002342	100.000	532703	100.000

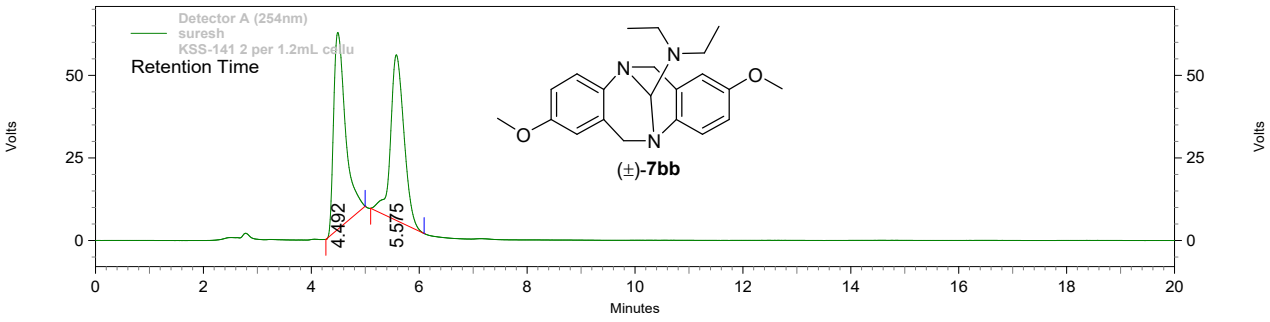
HPLC Profile of (±)-6ba: chiral column Chiralcel OD-H, hexanes:i-PrOH/90:10; flow rate 0.7 mL/min



Detector A (214nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	6.558	501812	51.329	23127	57.133
2	9.233	475821	48.671	17352	42.867
Total		977633	100.000	40479	100.000

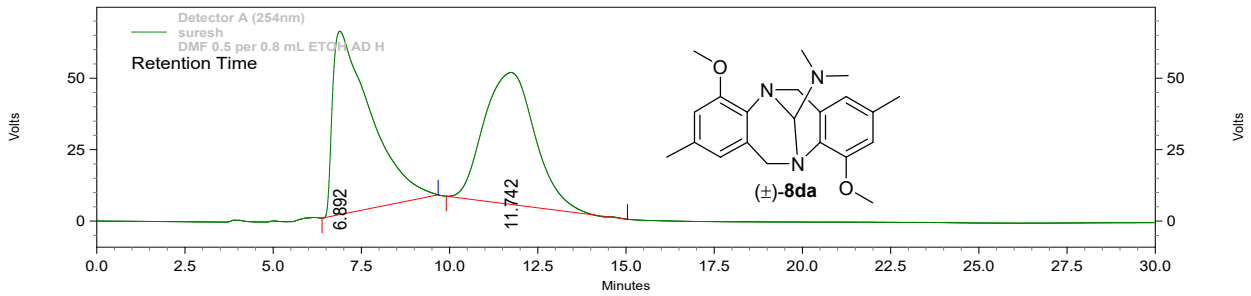
HPLC Profile of (±)-7bb: chiral column Chiralcel phenomenex cellulose-1, hexanes:i-PrOH/98:2; flow rate 1.2 mL/min



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	4.492	910303	51.042	59596	54.313
2	5.575	873144	48.958	50131	45.687
Total		1783447	100.000	109727	100.000

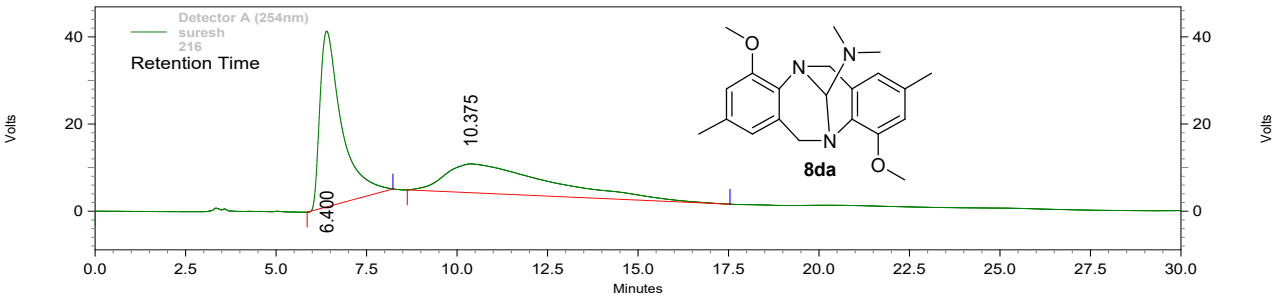
HPLC Profile of (±)-8da: chiral column Chiralcel AD-H, hexanes:EtOH/99.5:0.5; flow rate 0.8 mL/min



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	6.892	4819146	50.908	64144	58.149
2	11.742	4647204	49.092	46165	41.851
Total		9466350	100.000	110309	100.000

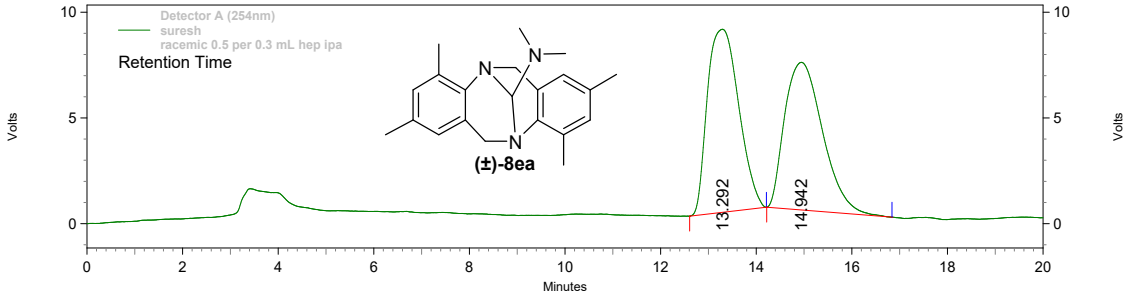
HPLC Profile of 8da: chiral column Chiralcel AD-H hexanes:EtOH/99.5:0.5; flow rate 0.8 mL/min



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	6.400	1677063	55.170	40317	85.922
2	10.375	1362728	44.830	6606	14.078
Total		3039791	100.000	46923	100.000

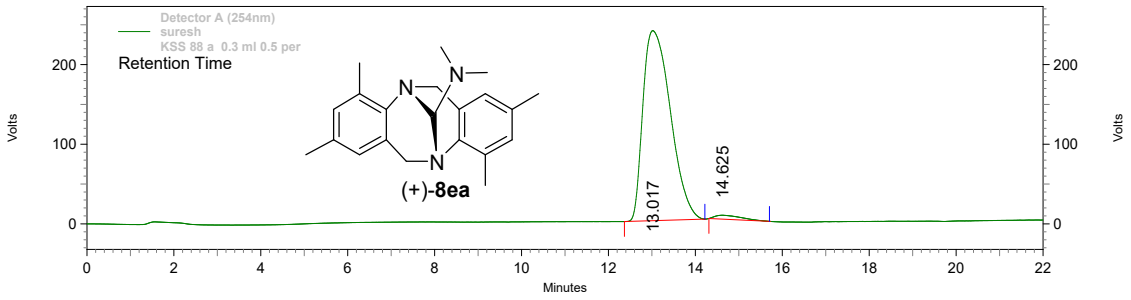
HPLC Profile of (±)-8ea: chiral column Chiralcel phenomenex cellulose-1, hexanes:i-PrOH/99.5:0.5; flow rate 0.3 mL/min



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	13.292	395629	50.663	8658	55.358
2	14.942	385273	49.337	6982	44.642
Total		780902	100.000	15640	100.000

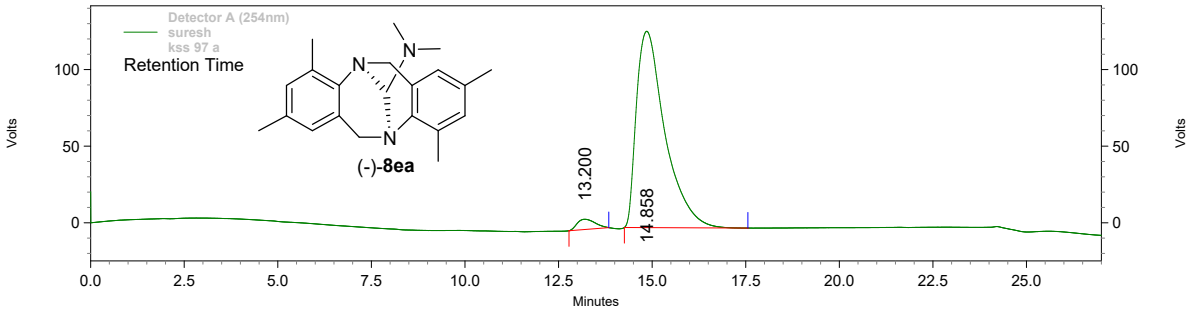
HPLC Profile of (+)-8ea: chiral column Chiralcel phenomenex cellulose-1, hexanes:i-PrOH/99.5:0.5; flow rate 0.3 mL/min



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	13.017	10514135	98.021	238563	97.966
2	14.625	212297	1.979	4952	2.034
Total		10726432	100.000	243515	100.000

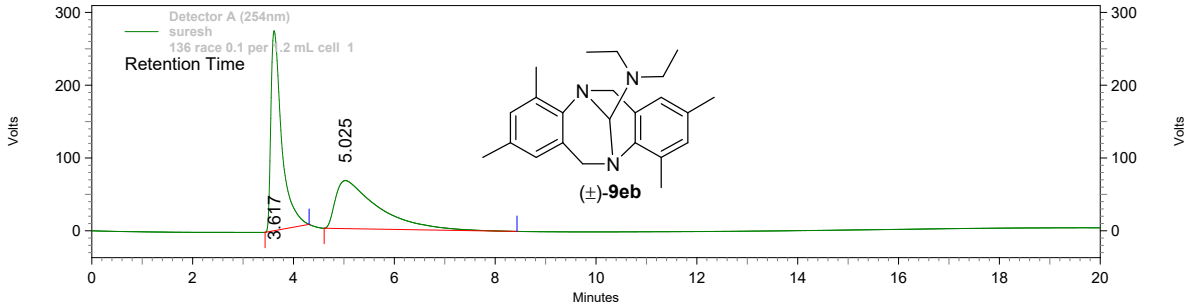
HPLC Profile of (–)-8ea: chiral column Chiralcel phenomenex cellulose-1, hexanes:i-PrOH/99.5:0.5; flow rate 0.3 mL/min



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	13.200	222250	3.167	6677	4.952
2	14.858	6795584	96.833	128165	95.048
Total		7017834	100.000	134842	100.000

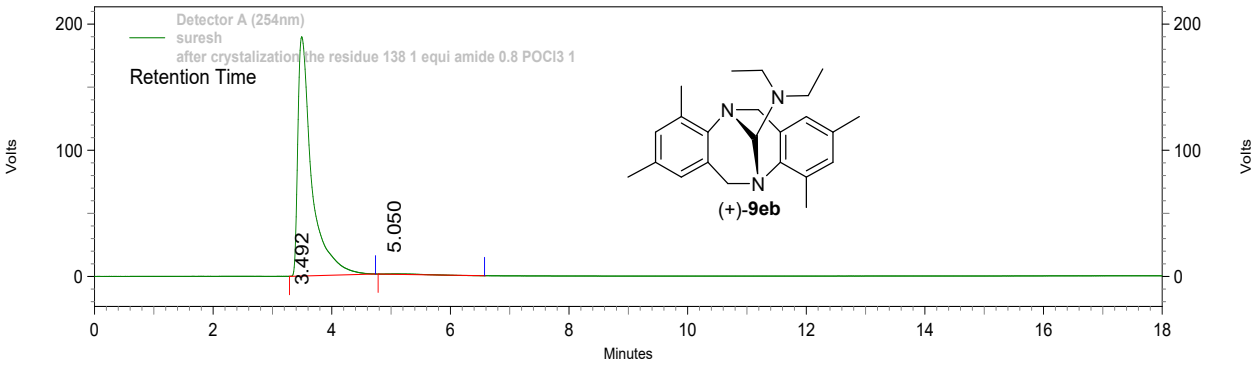
HPLC Profile of (±)-9eb: chiral column Chiralcel phenomenex cellulose-1, hexanes:i-PrOH/99.9:0.1; flow rate 1.2 mL/min



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	3.617	4086581	51.506	274704	80.629
2	5.025	3847551	48.494	65998	19.371
Total		7934132	100.000	340702	100.000

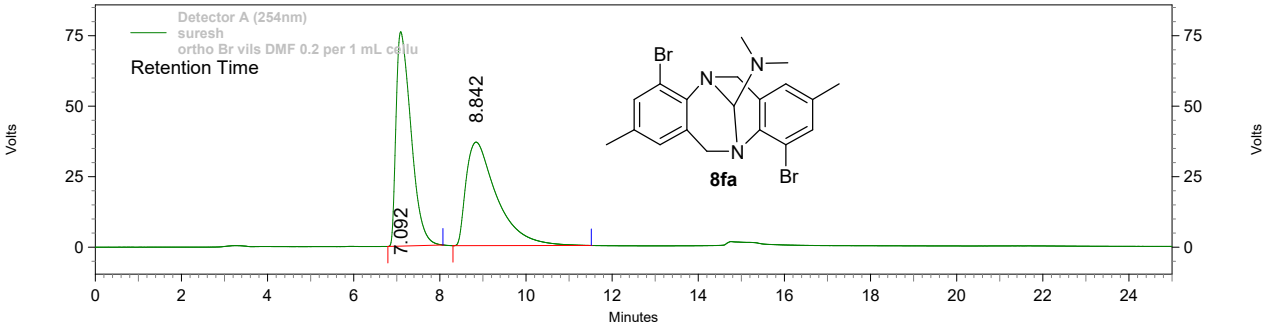
HPLC Profile of (+)-9eb: chiral column Chiralcel phenomenex cellulose-1, hexanes:i-PrOH/99.9:0.1; flow rate 1.2 mL/min



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	3.492	3082453	99.635	189631	99.845
2	5.050	11286	0.365	294	0.155
Total		3093739	100.000	189925	100.000

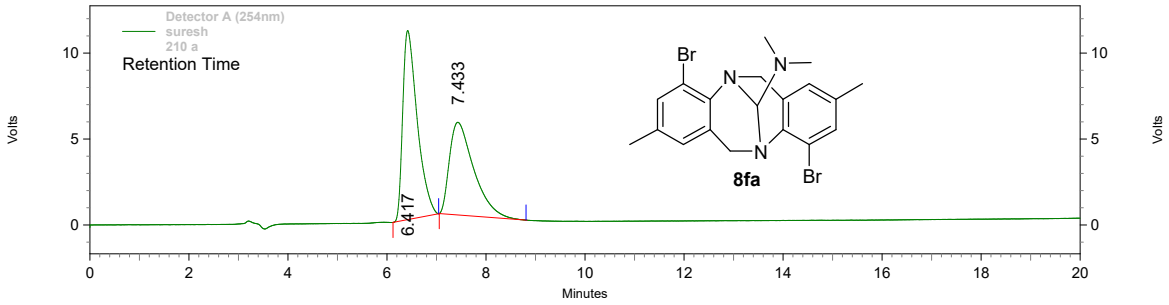
HPLC Profile of (±)-8fa: chiral column Chiralcel phenomenex cellulose-1, hexanes:i-PrOH/99.8:0.2; flow rate 1.0 mL/min



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	7.092	1837338	50.287	76026	67.434
2	8.842	1816368	49.713	36715	32.566
Total		3653706	100.000	112741	100.000

HPLC Profile of 8fa: chiral column Chiralcel phenomenex cellulose-1, hexanes:i-PrOH/99.8:0.2; flow rate 1.0 mL/min

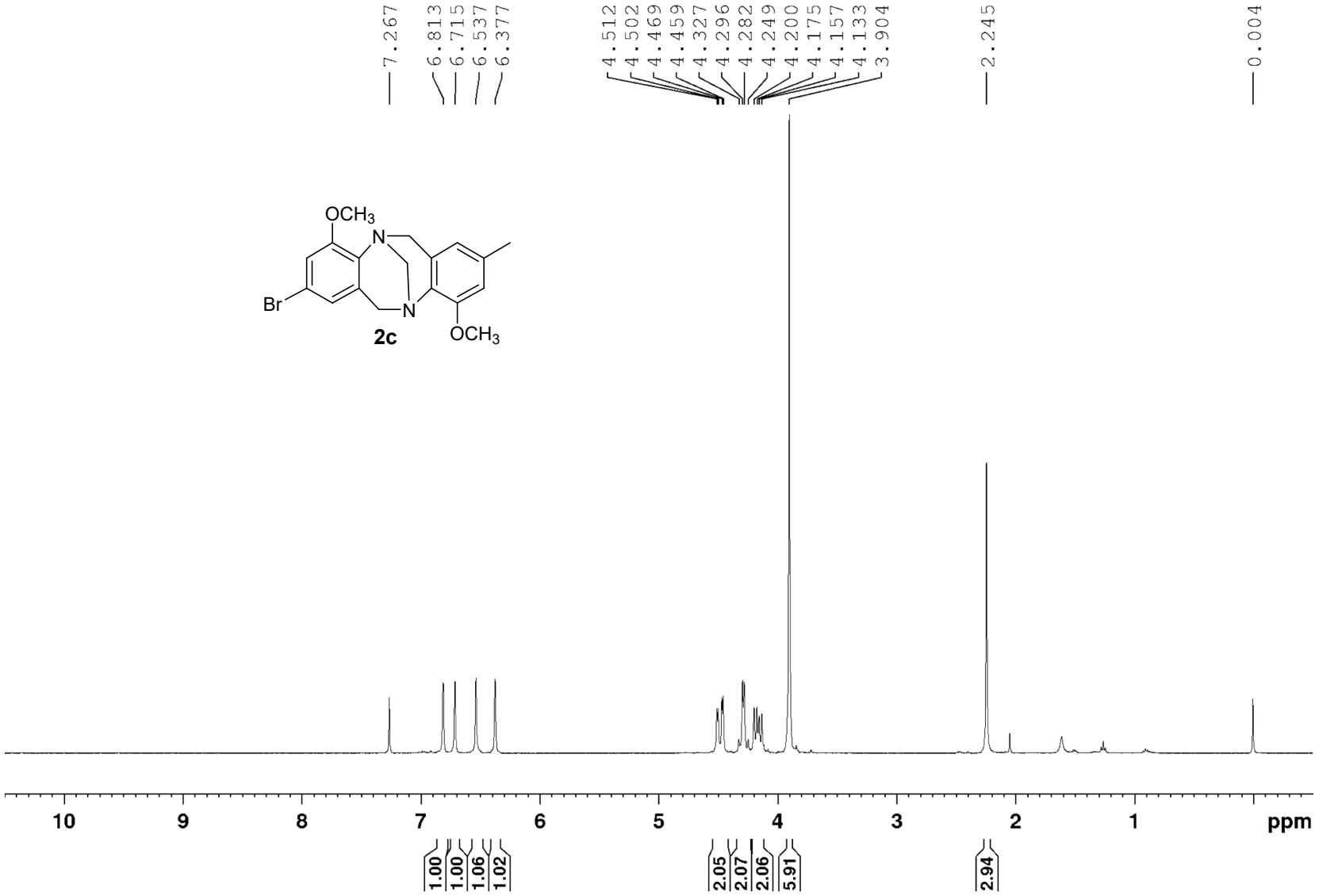


Detector A (254nm)

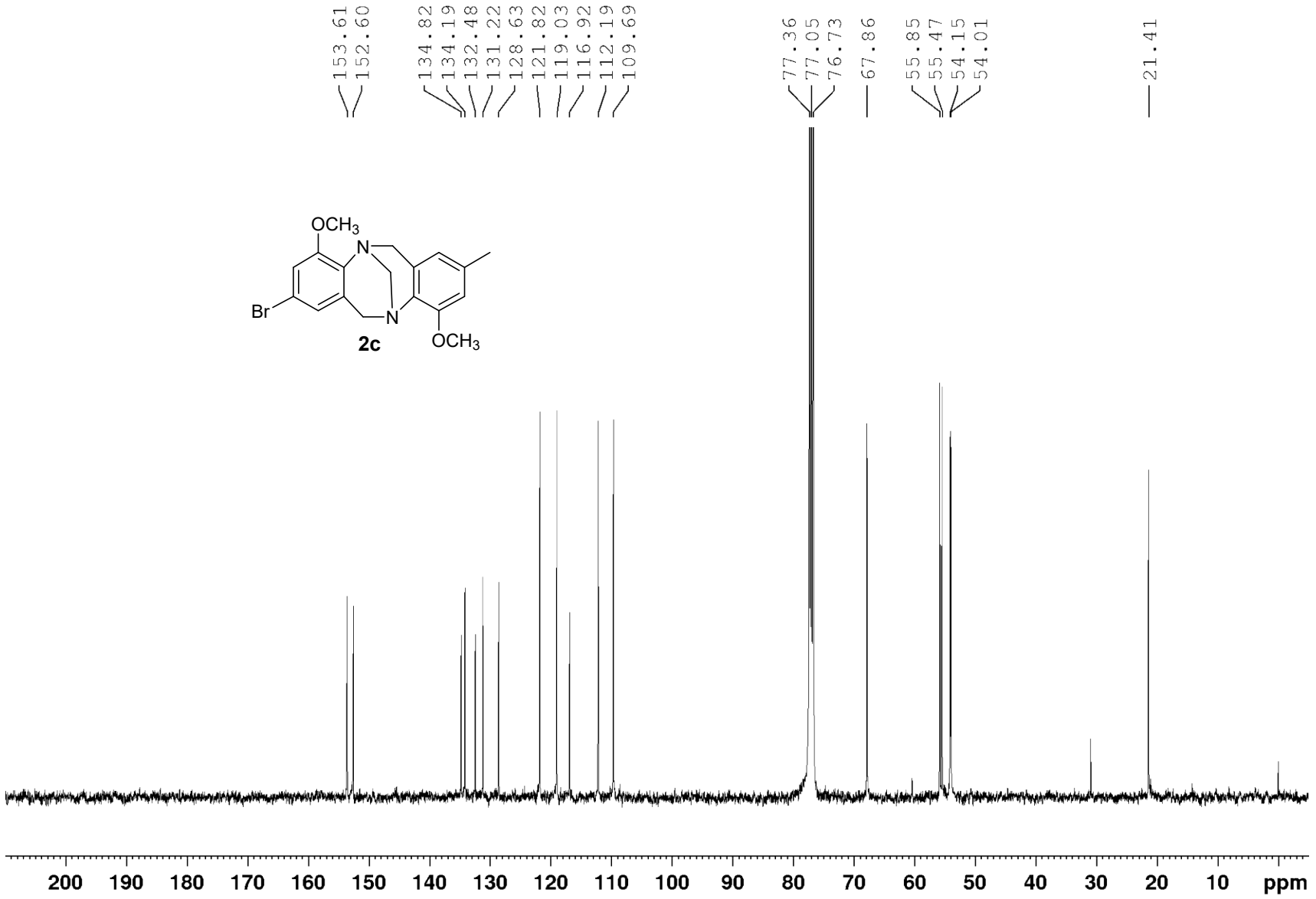
Pk #	Retention Time	Area	Area %	Height	Height %
1	6.417	223873	54.918	11003	67.120
2	7.433	183775	45.082	5390	32.880
Total		407648	100.000	16393	100.000

2. NMR Spectra Copies

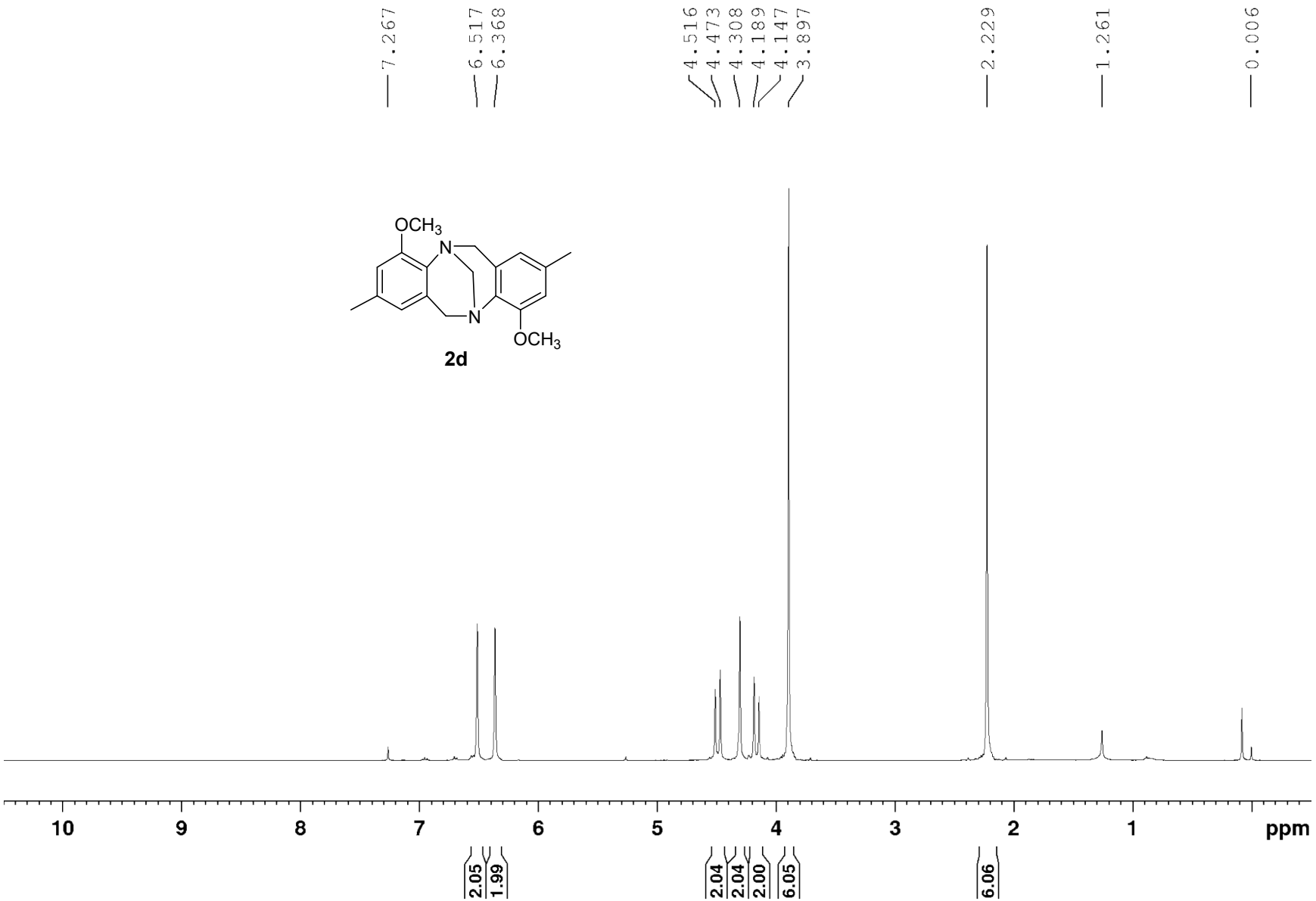
^{1}H NMR spectrum of compound **2c**



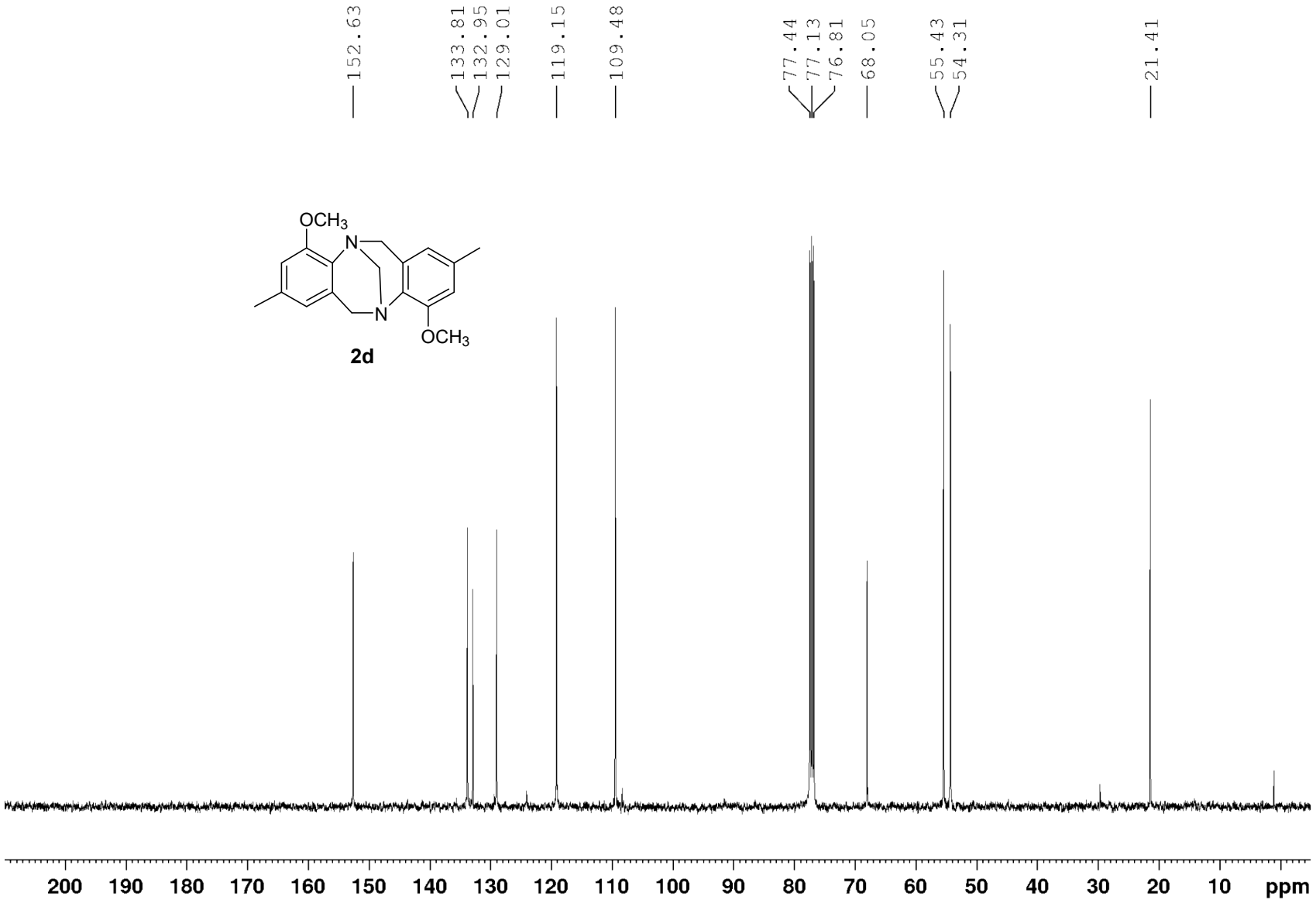
^{13}C NMR spectrum of compound **2c**



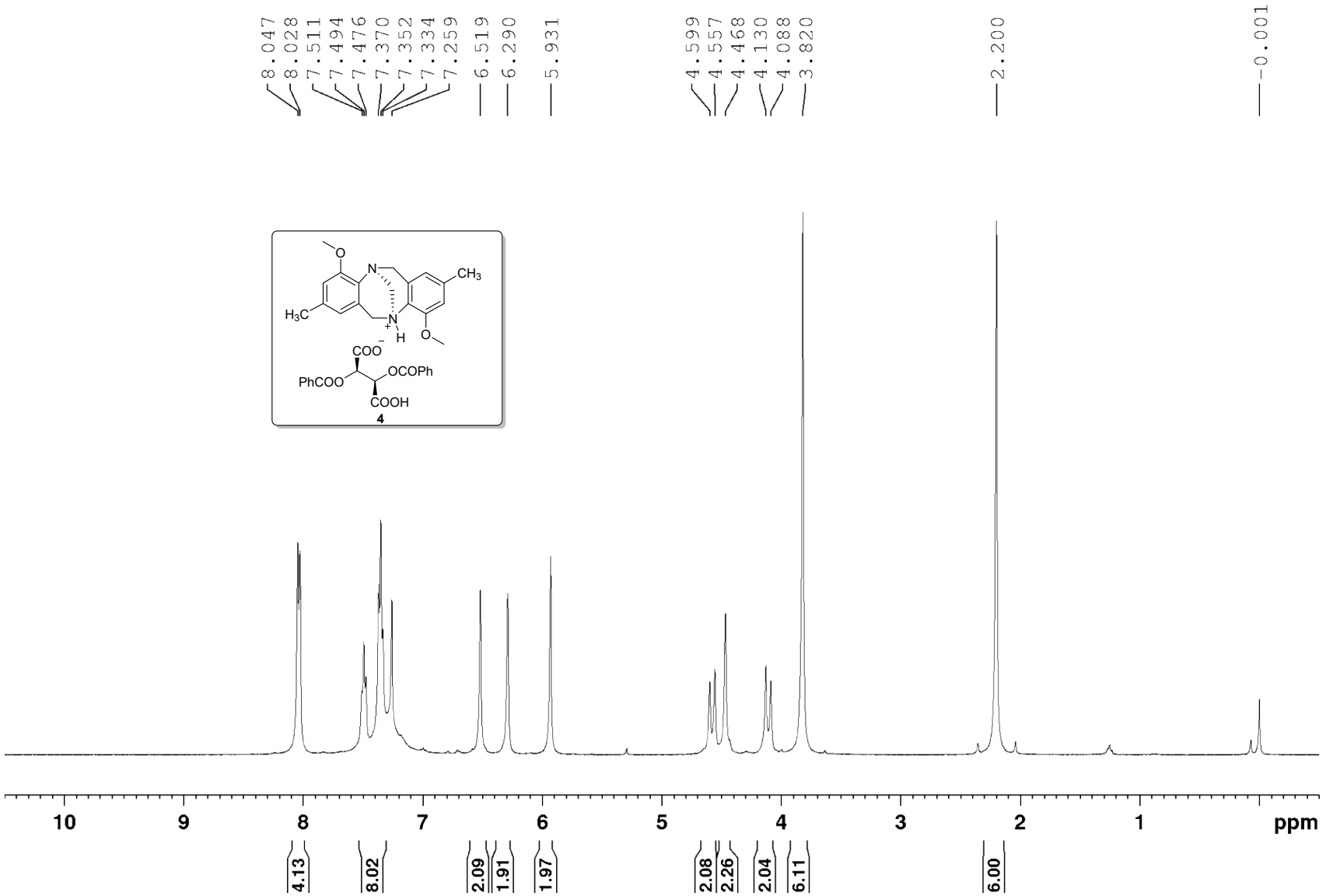
^{1}H NMR spectrum of compound **2d**



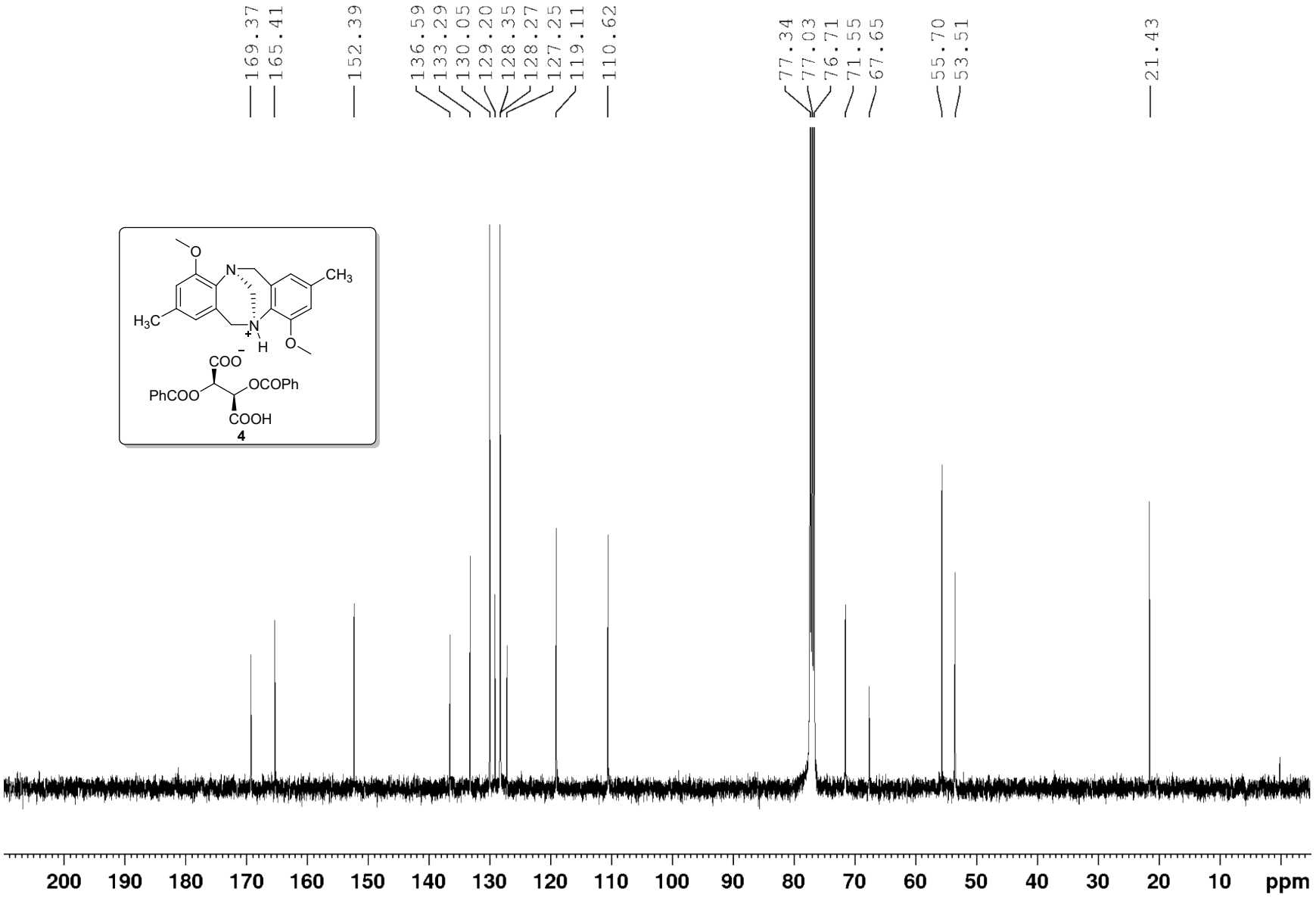
^{13}C NMR spectrum of compound **2d**



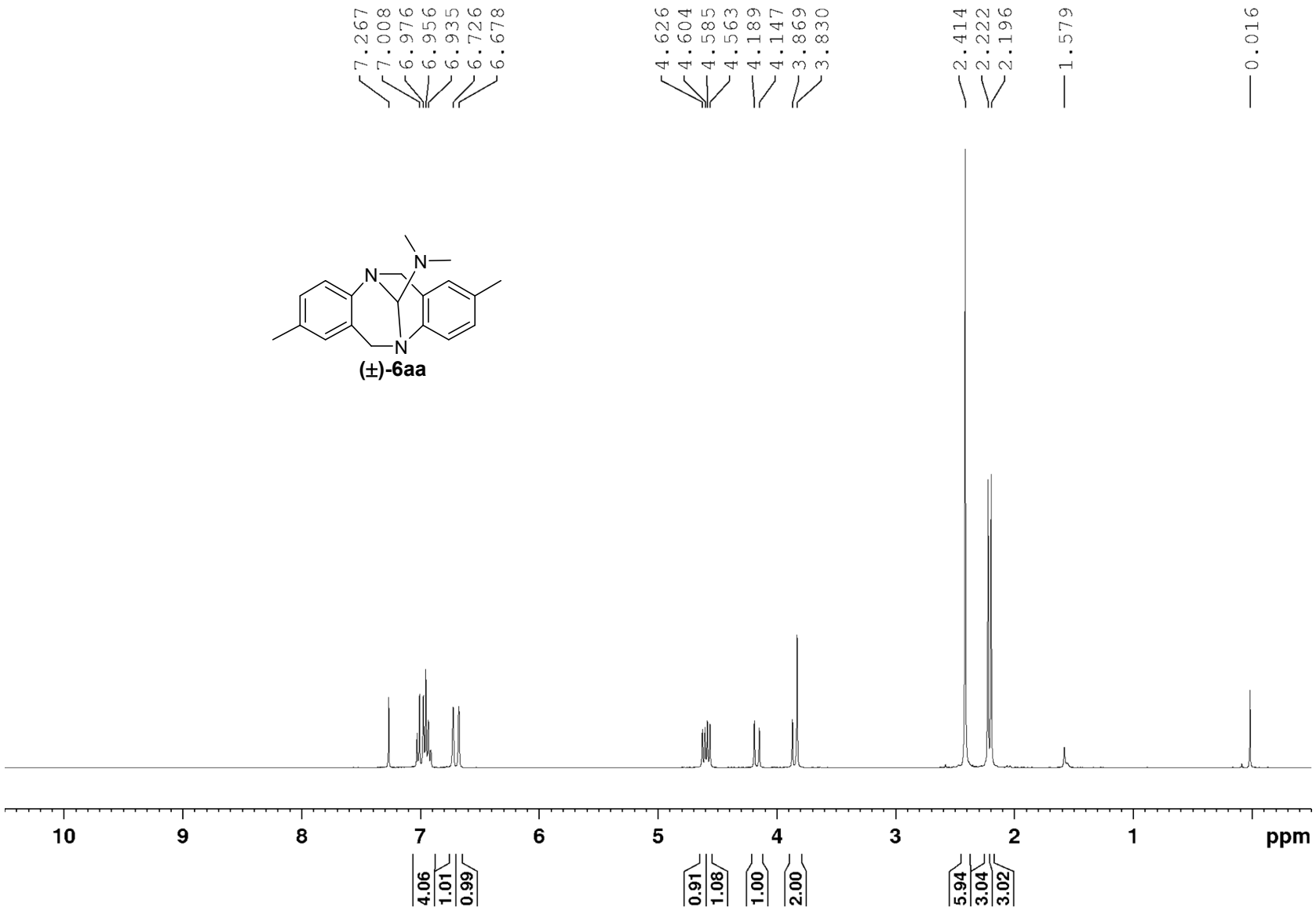
^{1}H NMR spectrum of diastereomeric salt **4**[(-)-DBTA•(+)-**2d**]



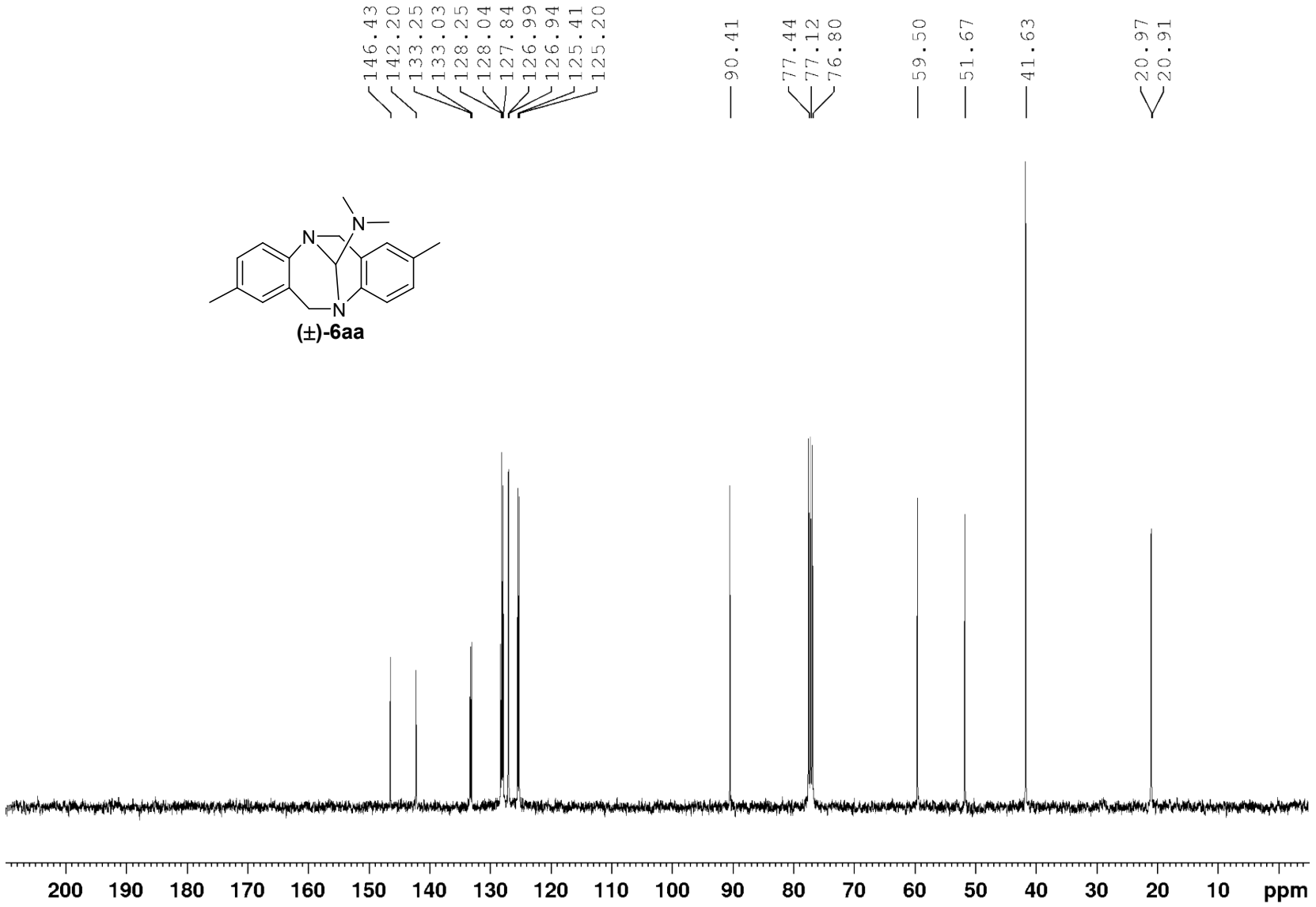
^{13}C NMR spectrum of diastereomeric salt **4**[(-)-DBTA•(+)-**2d**]



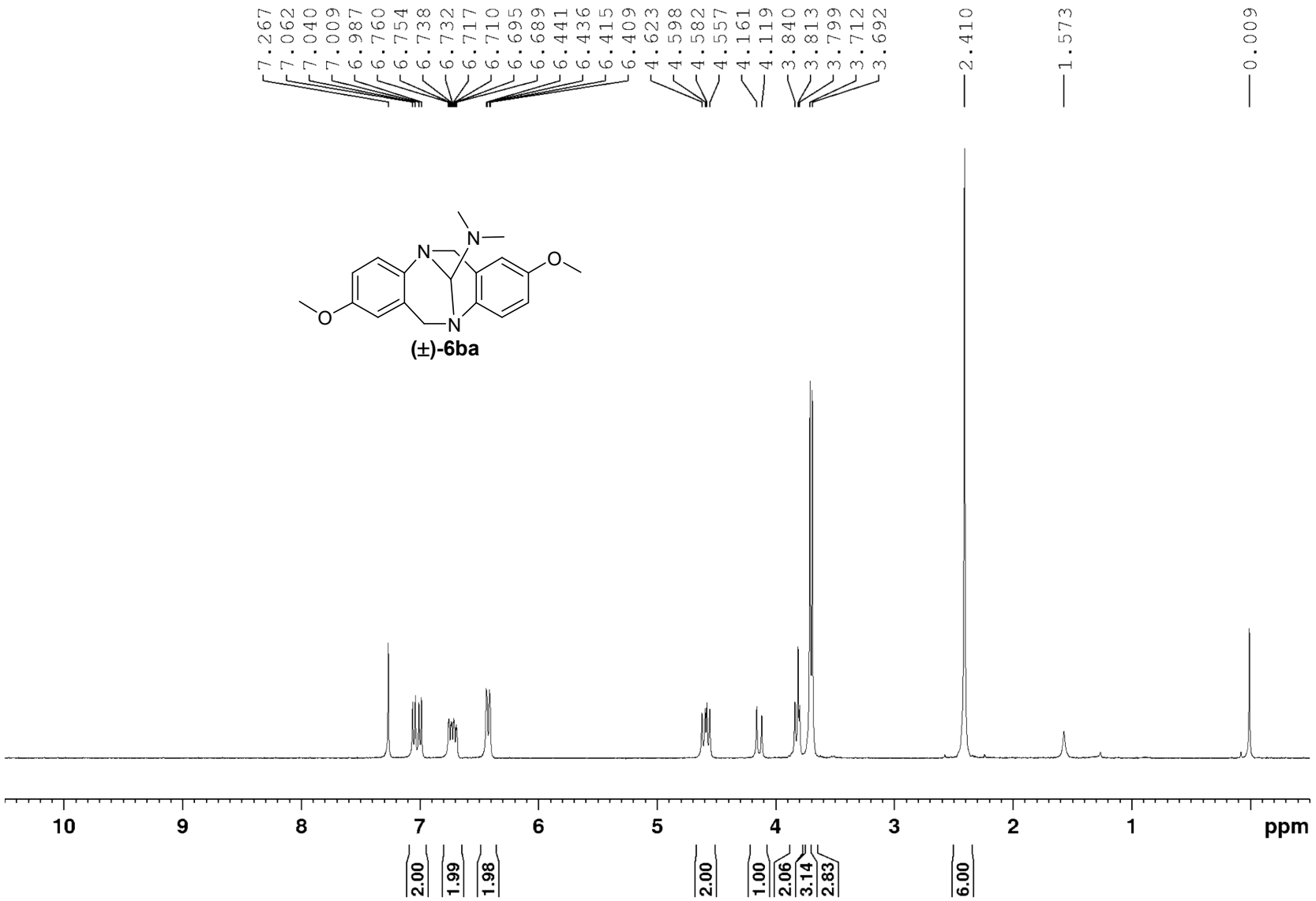
^{1}H NMR spectrum of compound **6aa**



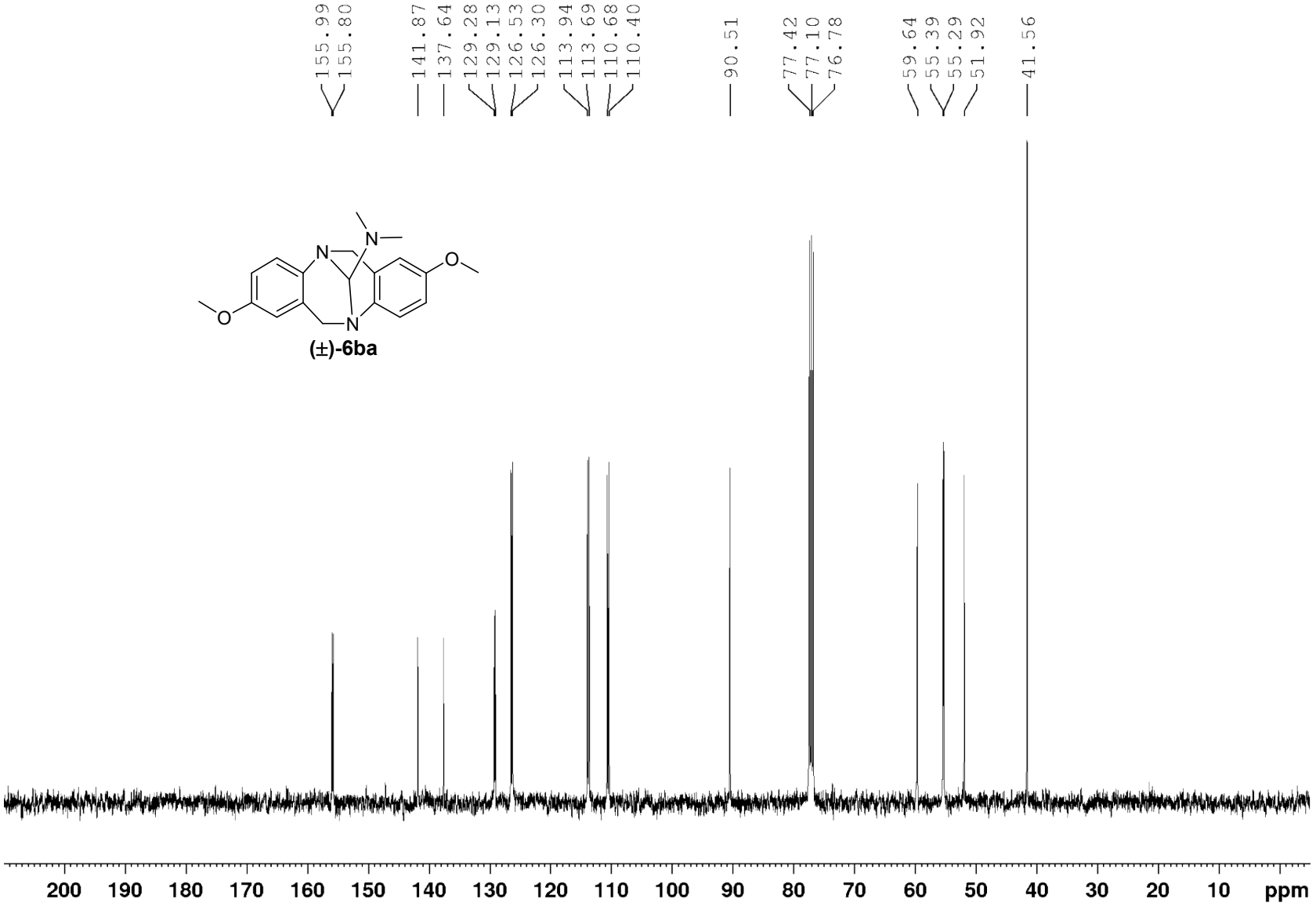
^{13}C NMR spectrum of compound **6aa**



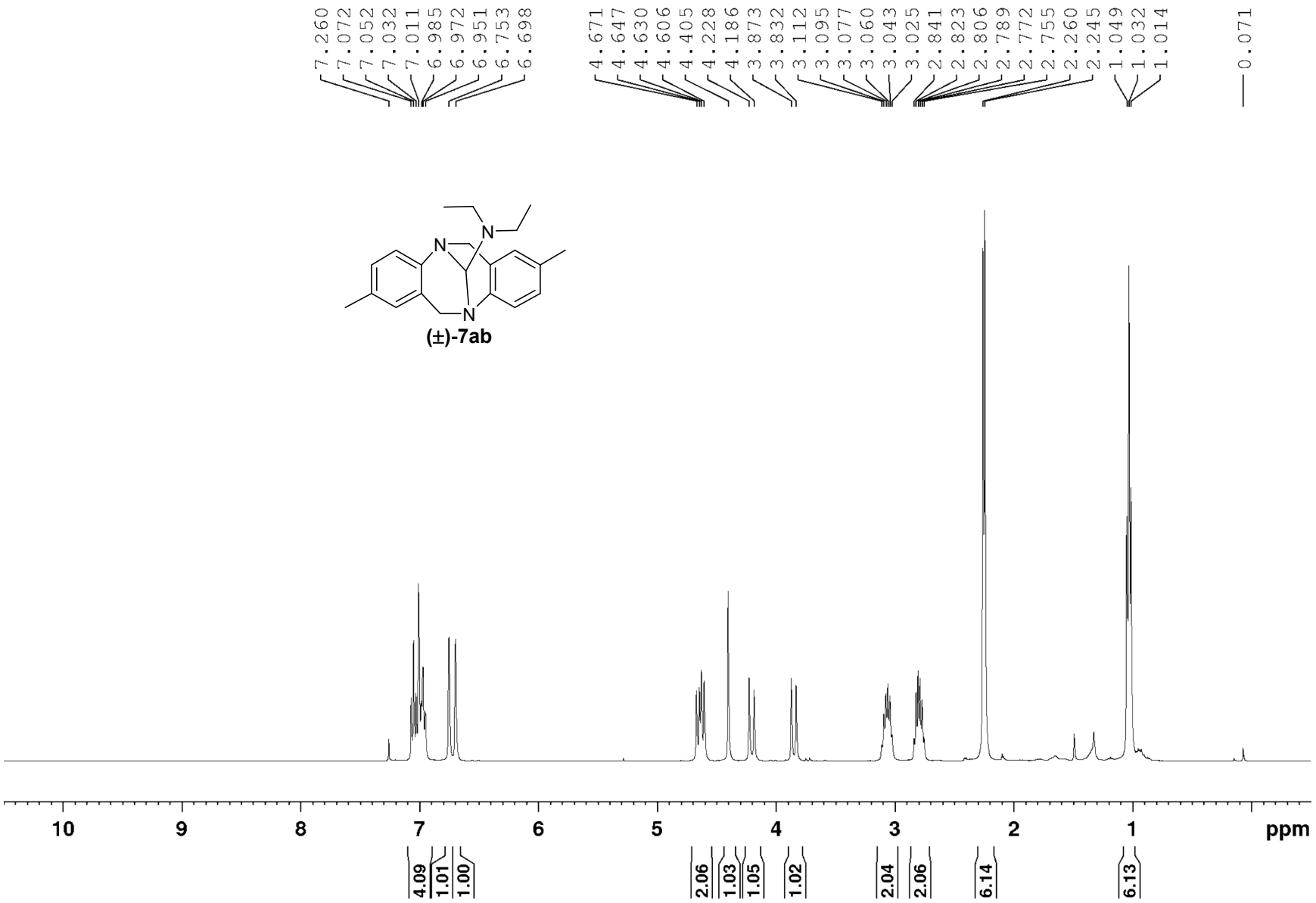
[1]H NMR spectrum of compound **6ba**



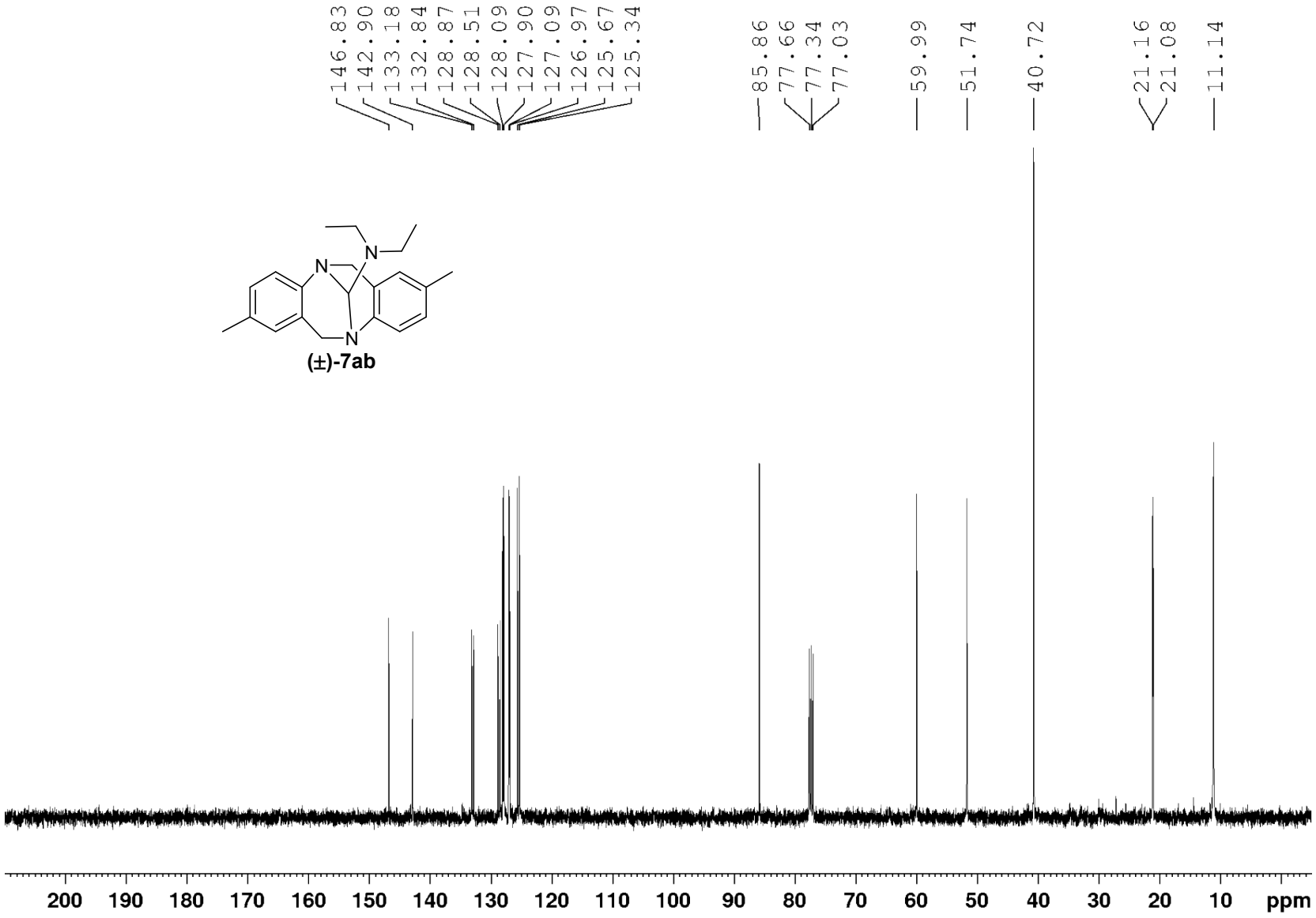
^{13}C NMR spectrum of compound **6ba**



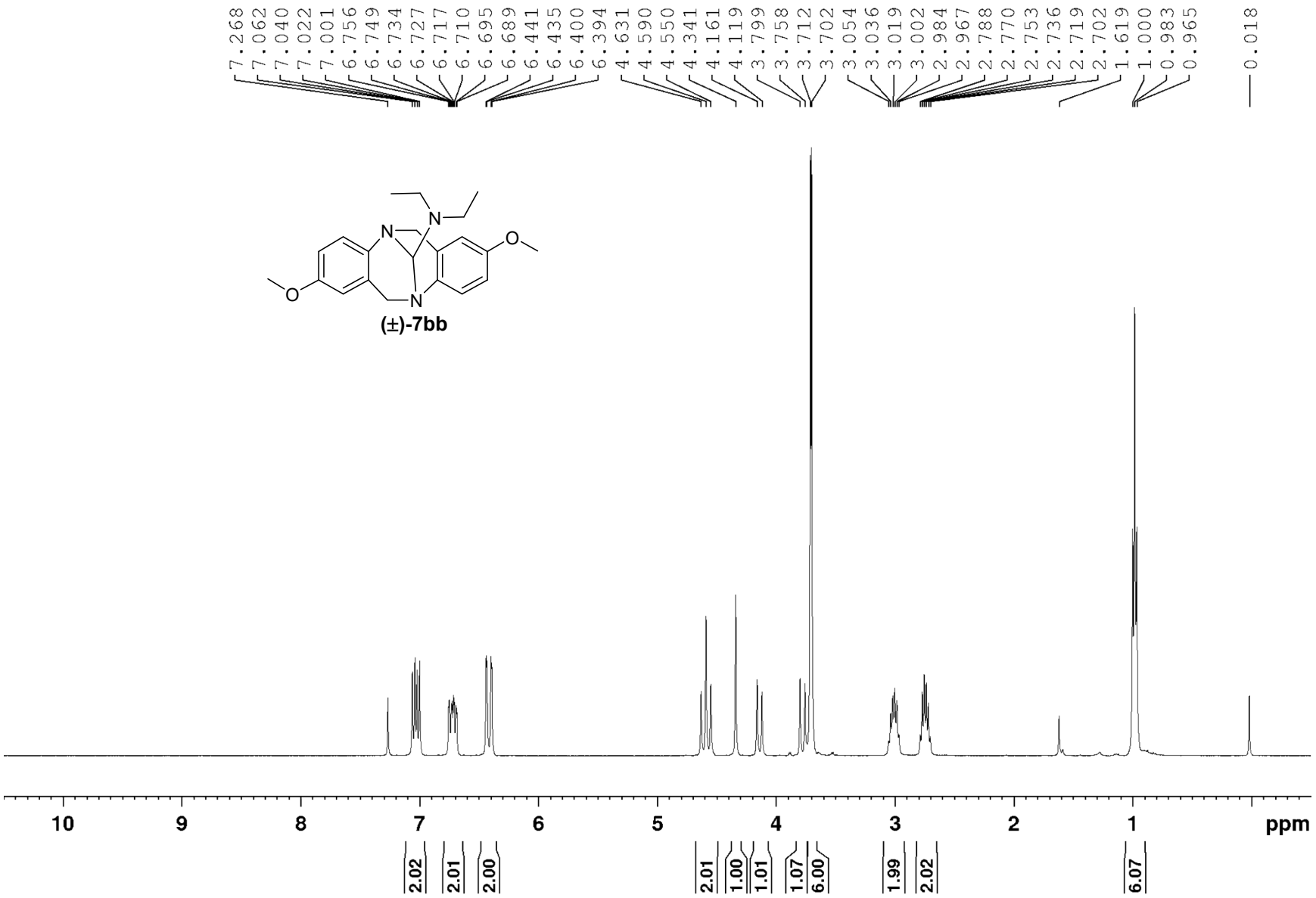
^{1}H NMR spectrum of compound **7ab**



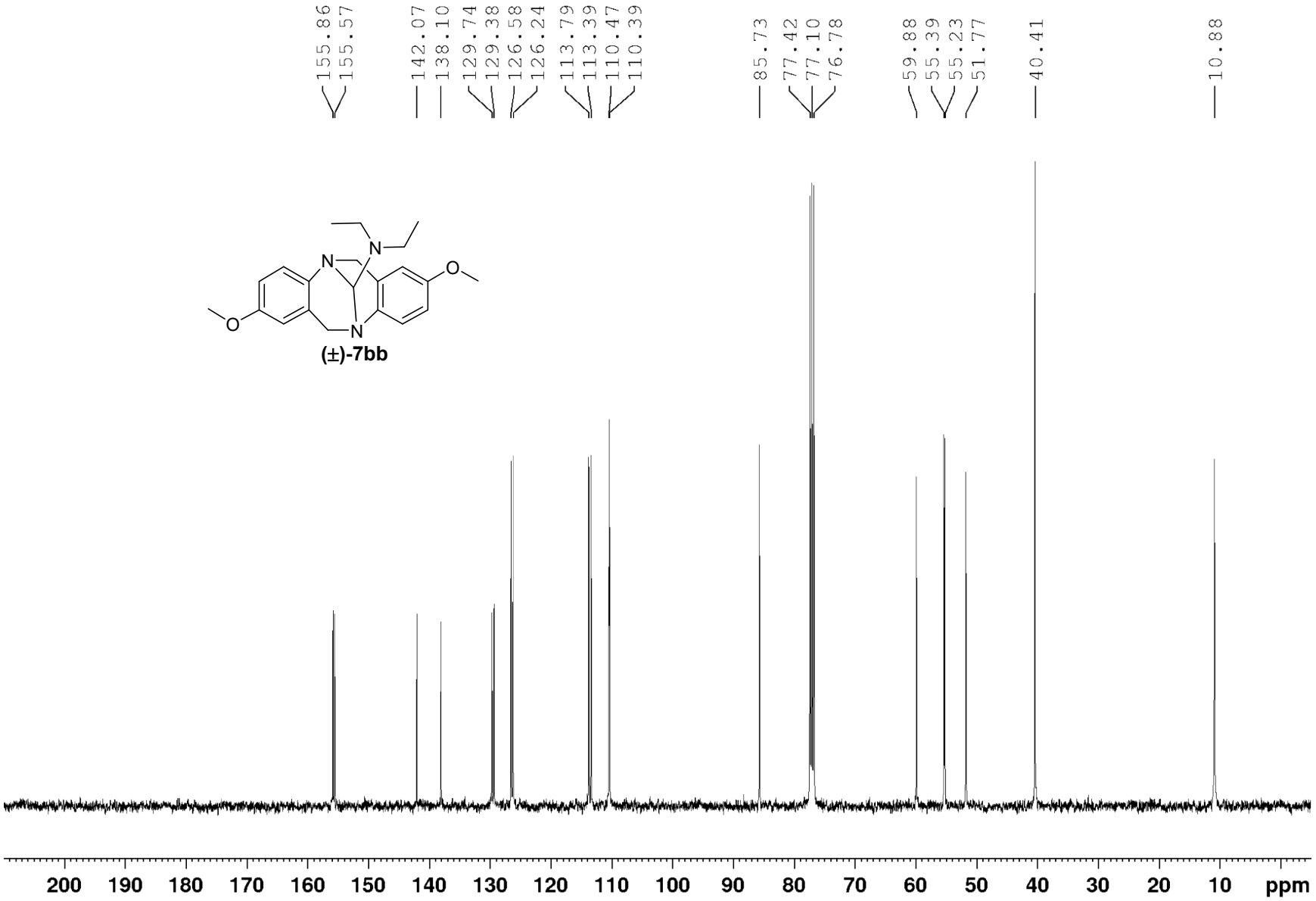
^{13}C NMR spectrum of compound **7ab**



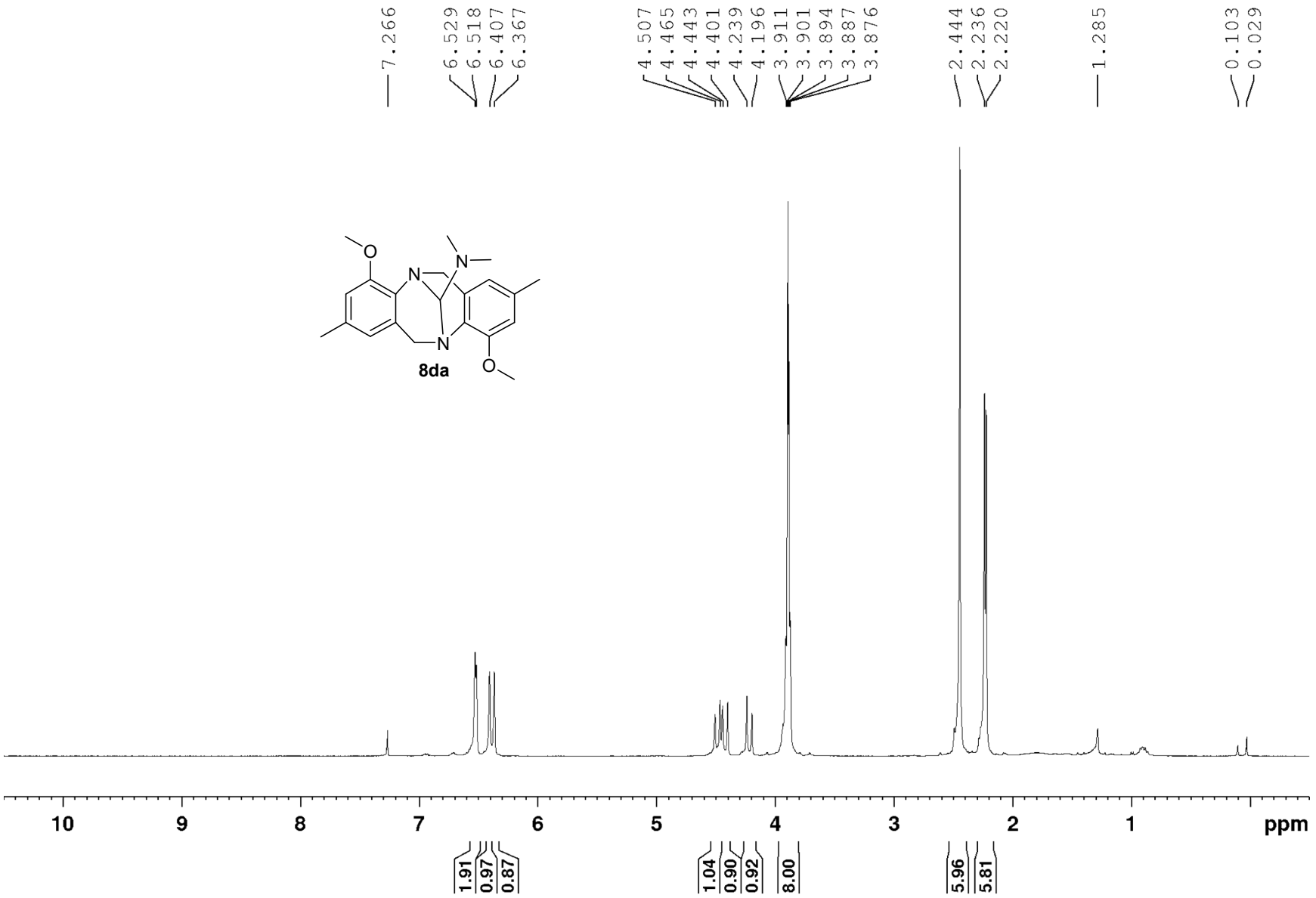
[1]H NMR spectrum of compound **7bb**



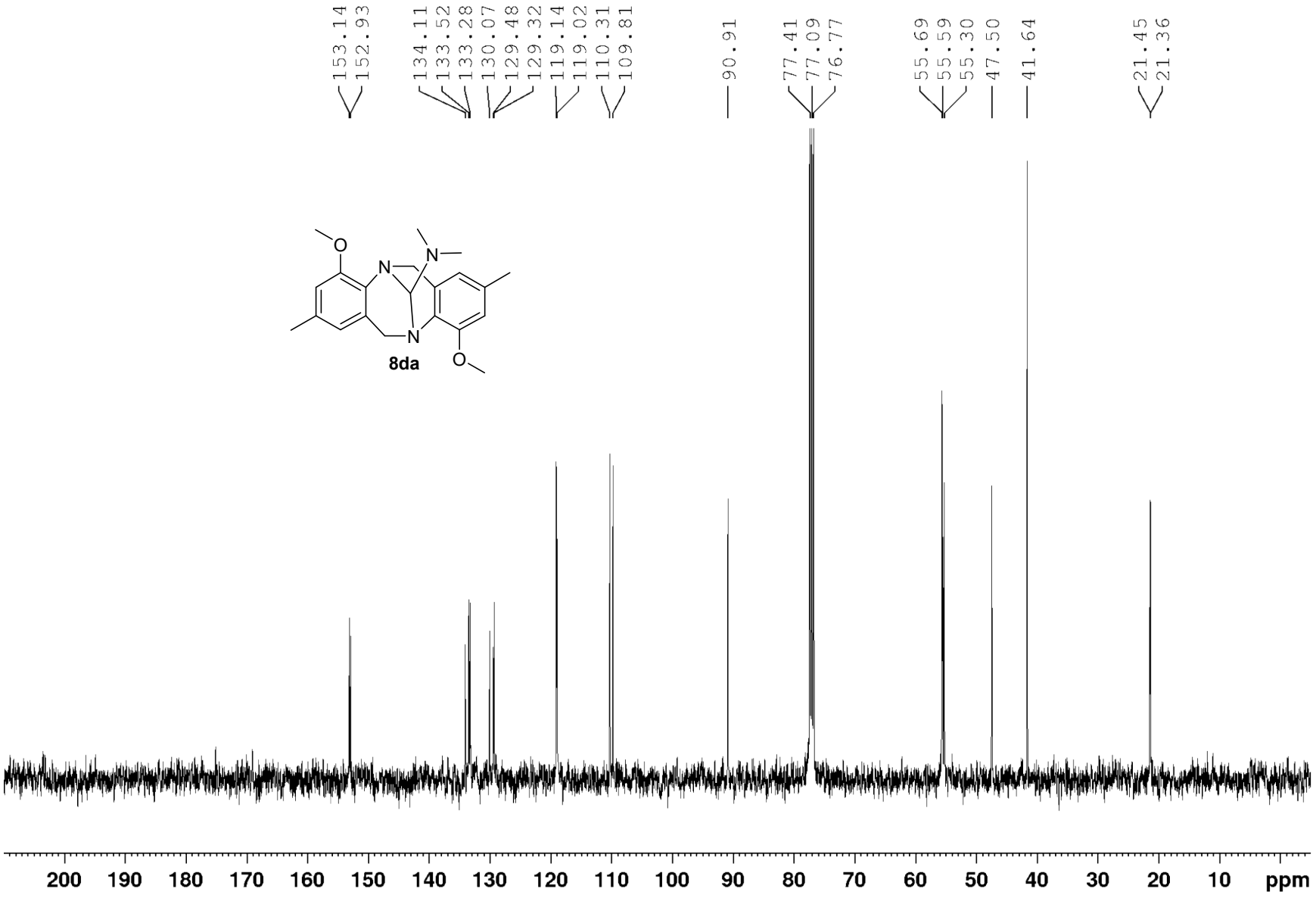
^{13}C NMR spectrum of compound **7bb**



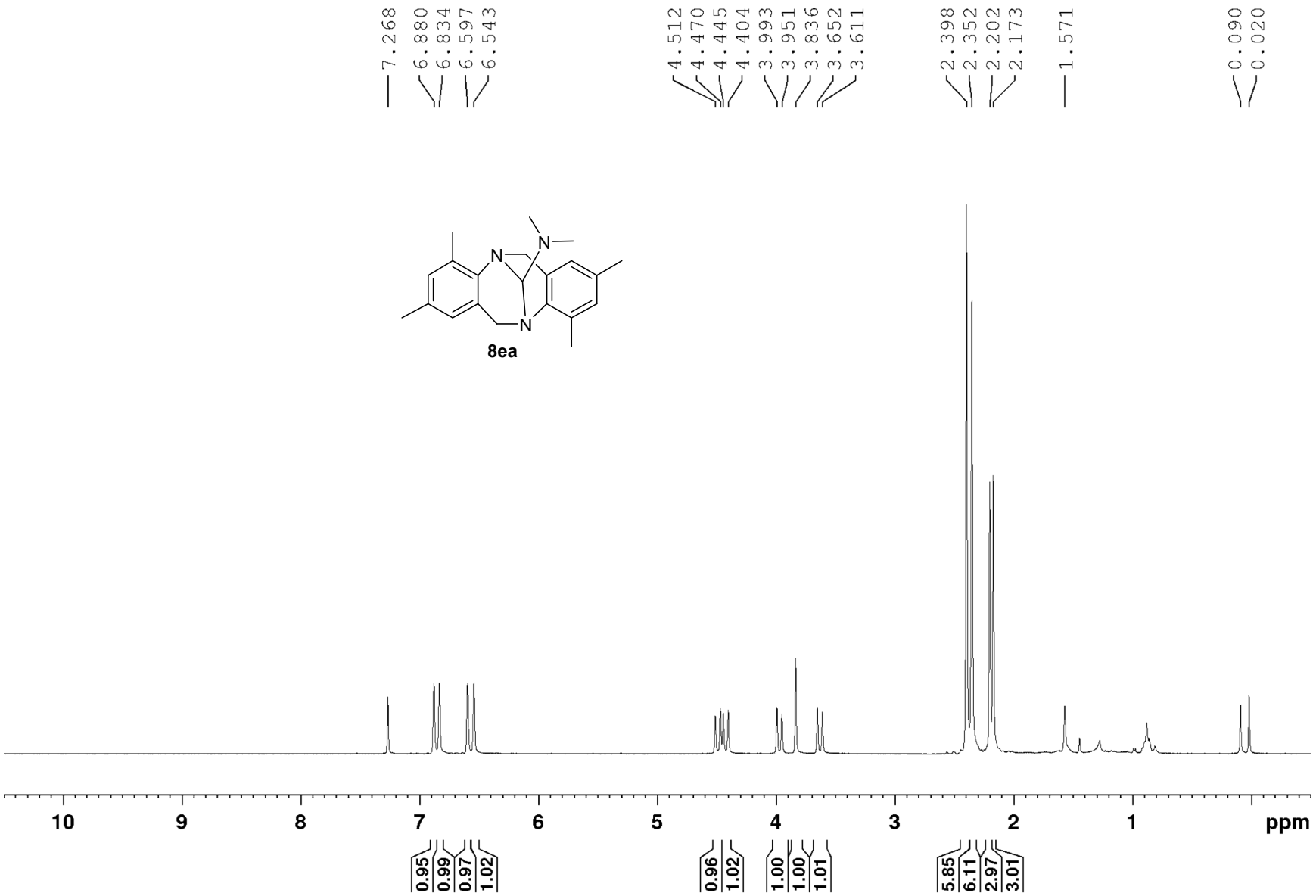
^{1}H NMR spectrum of compound **8da**



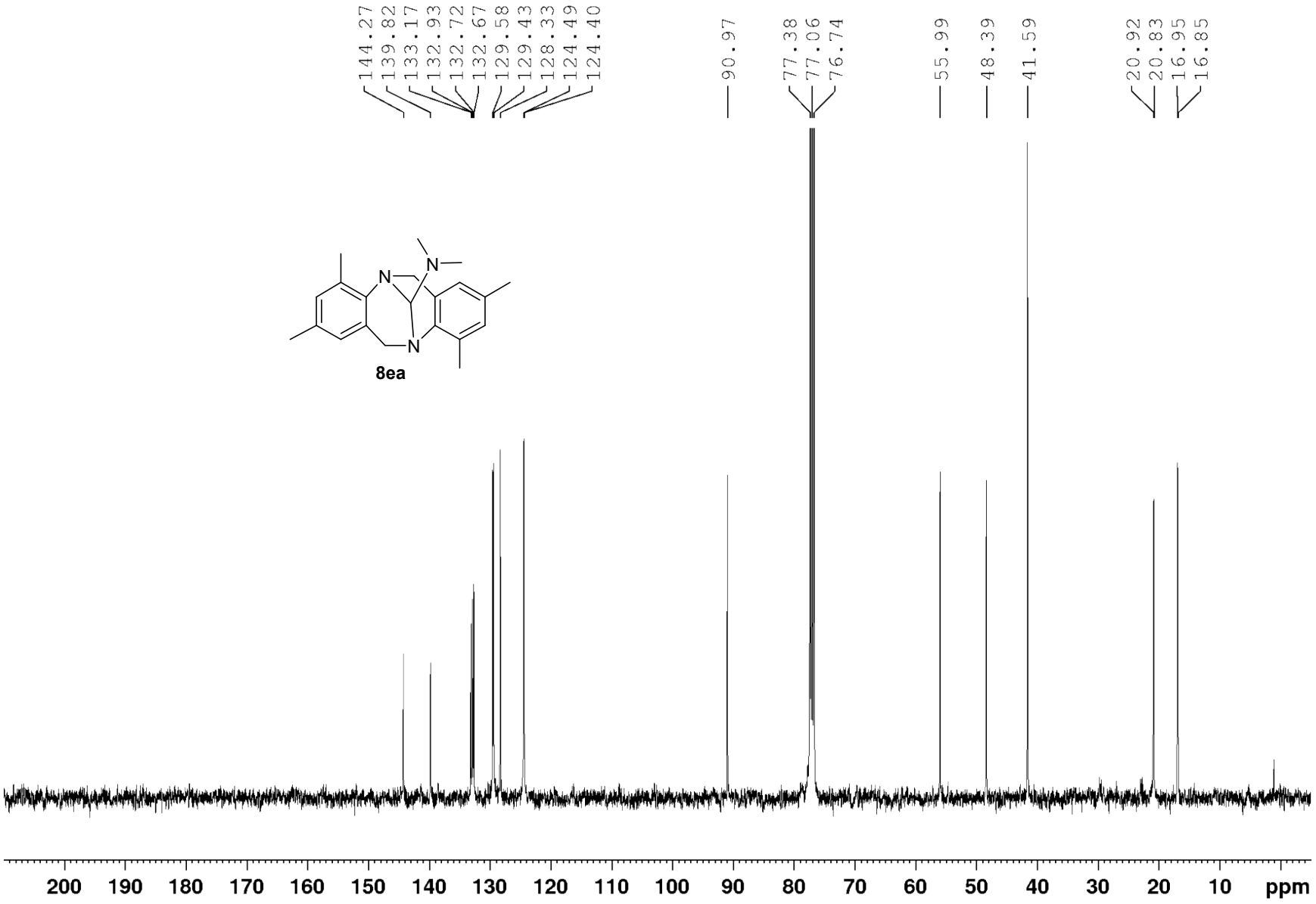
^{13}C NMR spectrum of compound **8da**



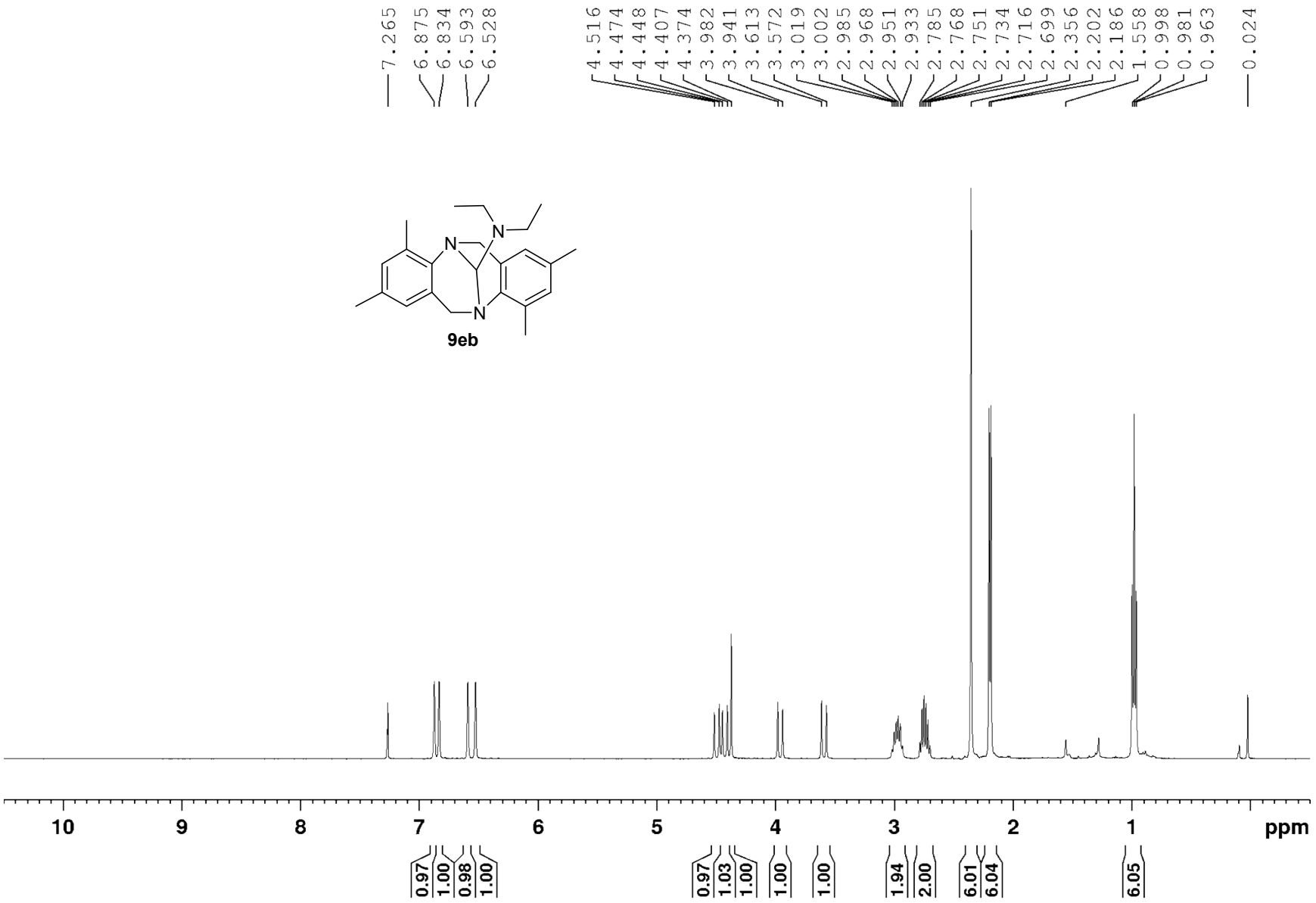
^{1}H NMR spectrum of compound **8ea**



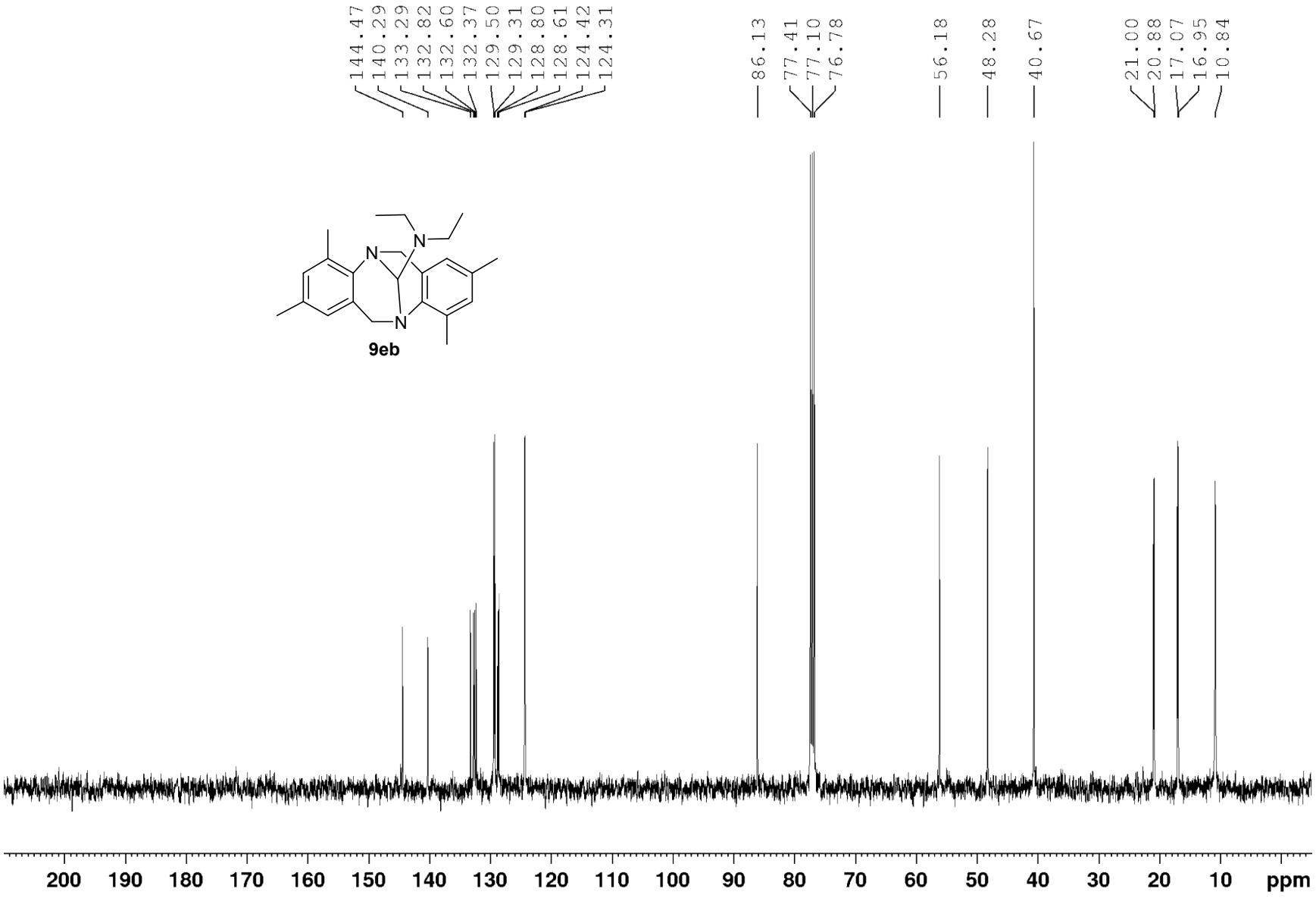
^{13}C NMR spectrum of compound **8ea**



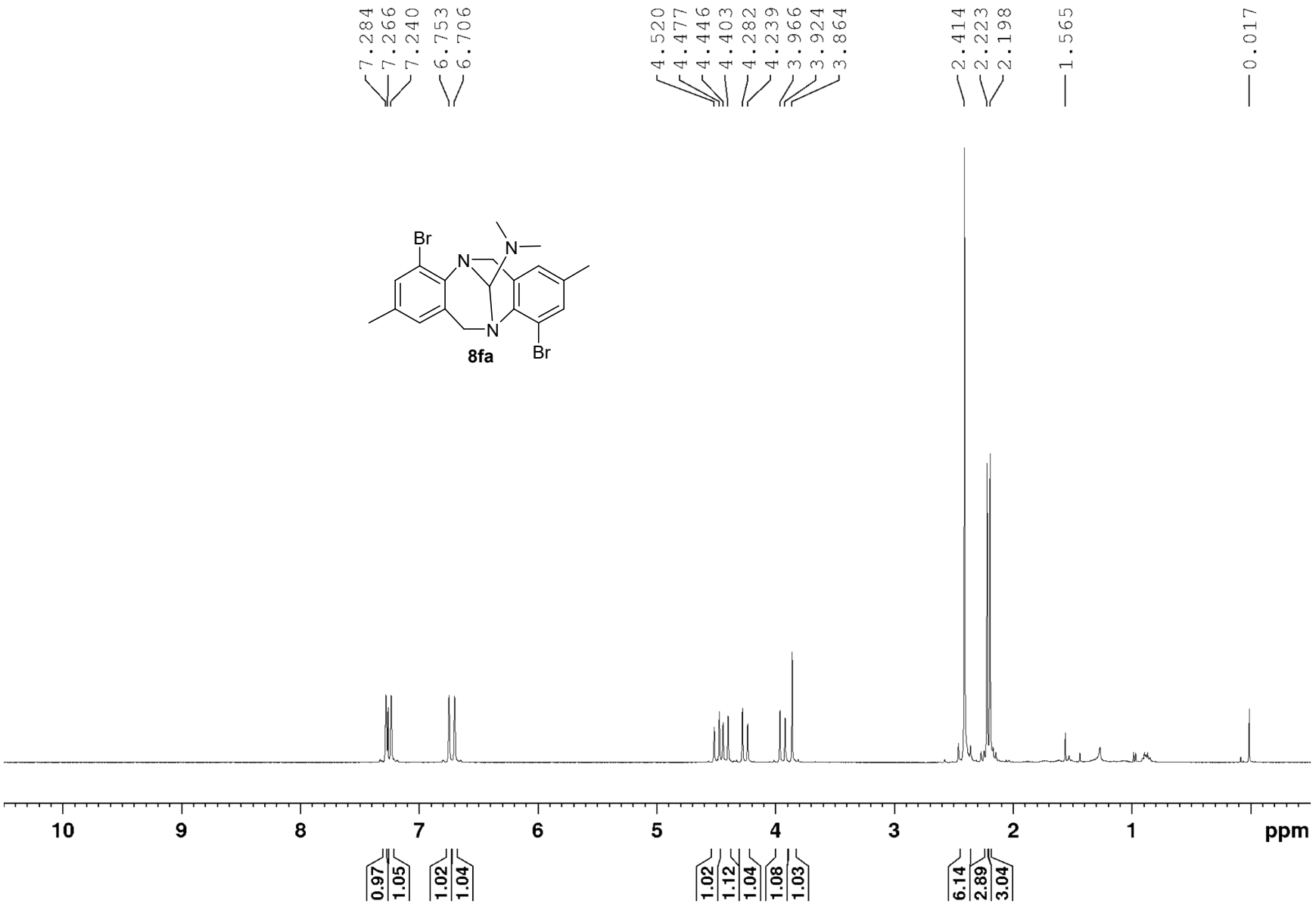
[1]H NMR spectrum of compound **9eb**



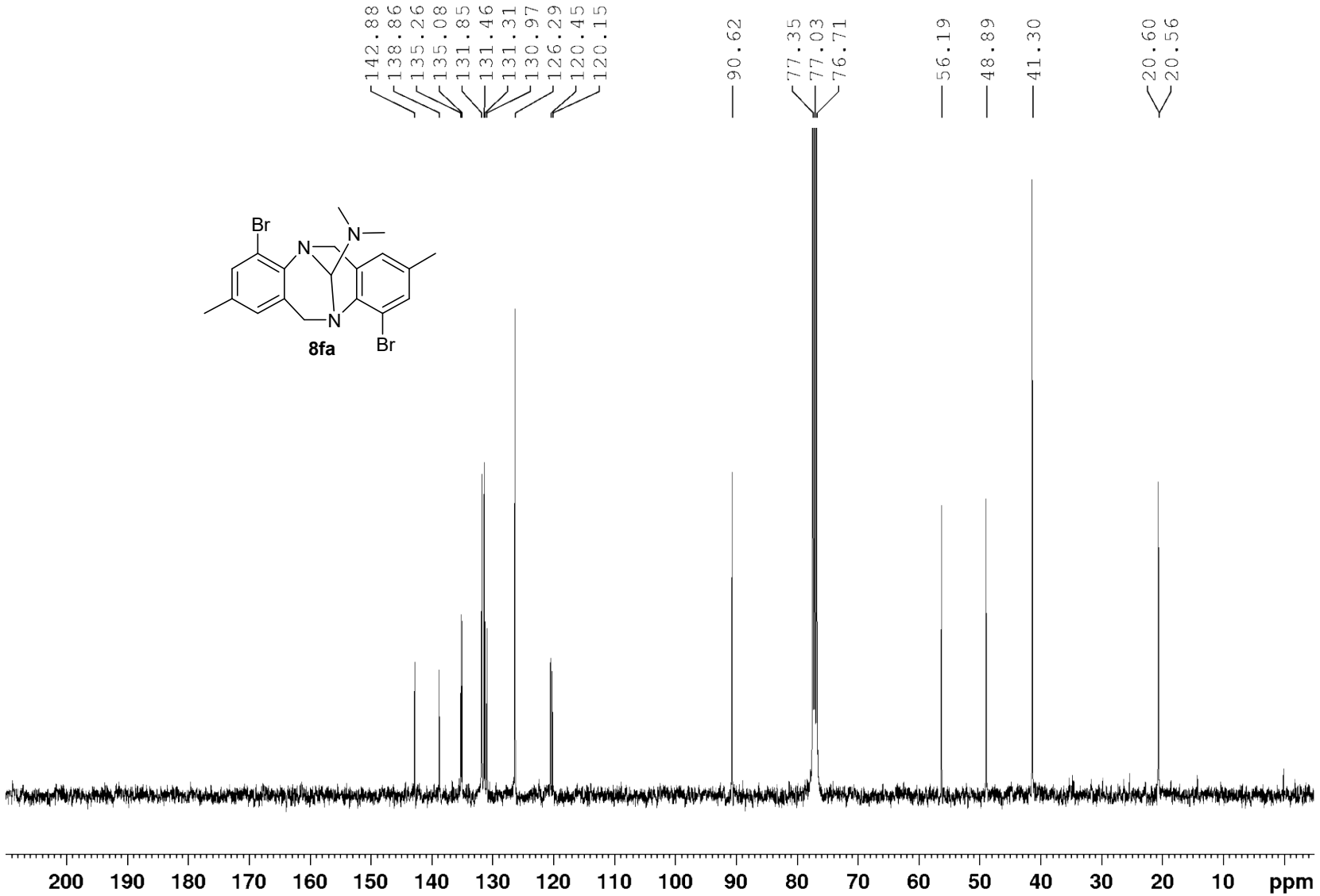
^{13}C NMR spectrum of compound **9eb**



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



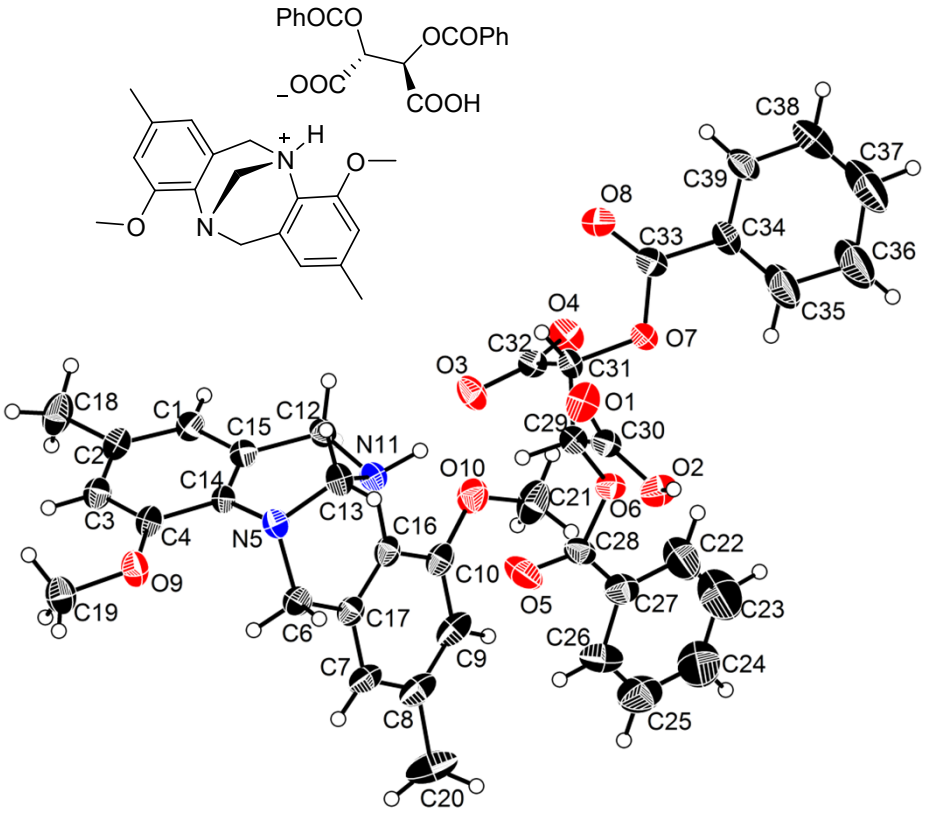
^{13}C NMR spectrum of compound **8fa**



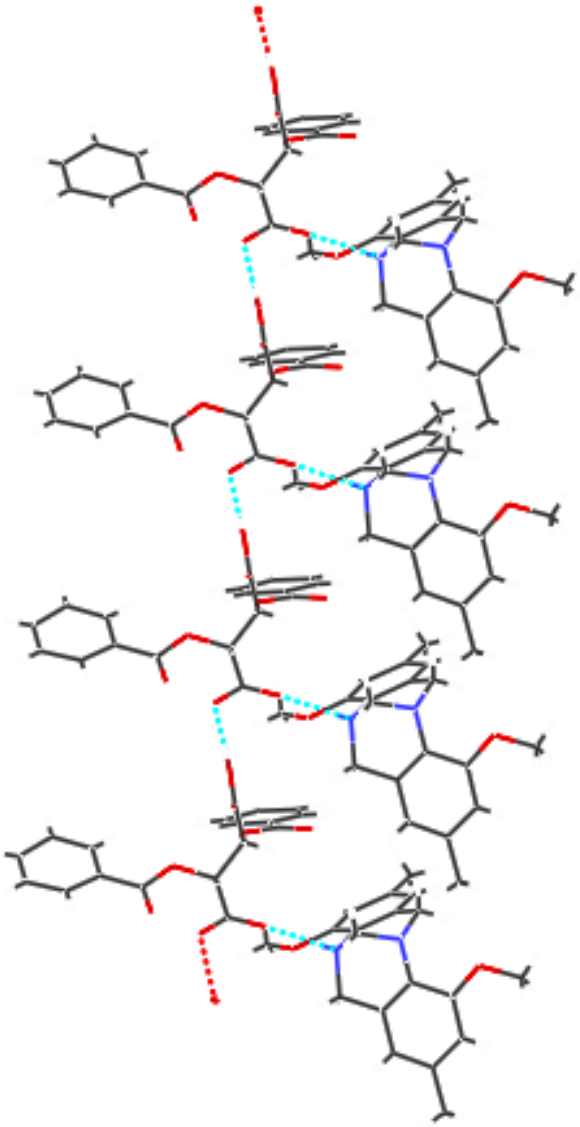
3. Single Crystal X-ray Analytical Data

Crystals suitable for X-ray analyses were obtained by a slow evaporation method using ethyl acetate as a solvent system. X-ray reflections were collected using Cu Kα X-radiation (λ = 1.54184 Å) on a single crystal at 293 (2) K using an Xcalibur, Eos, Gemini diffractometer. All the crystal structures were solved and refined using SHELX-2014. The details of crystal data collections and data refinement parameters are given in Table S1.

ORTEP (ellipsoid counter 25% probability) **diagram and crystal data of compound 4: CCDC Number 2529718**



Packing diagram of diastereomeric salt **4**[(-)-DBTA•(+)-**2d],** indicates the O-H···O and N-H···O hydrogen bonding interactions.



Structure **4** (CCDC 2529718): $C_{37}H_{36}N_2O_{10}$

PROBLEM: <Deprecated .res/.hkl Input Style SQUEEZE Job …! Note. >

RESPONSE: <Due to the crystals had large voids with badly disordered solvent molecules. The crystallographic refinement was completed with the solvent contribution subtracted from the data using SQUEEZE from the PLATON package of crystallographic software. Although attempts were made to solve this problem using different solvent systems, the problem couldn't be solved.

Table S1. Crystal data and structure refinement for **4**.

Identification code	shelx	
Empirical formula	$C_{37}H_{36}N_2O_{10}$	
Formula weight	668.68	
Temperature	293(2) K	
Wavelength	1.54184 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 2	
Unit cell dimensions	a = 23.8296(9) Å	α= 90°.
	b = 21.2588(9) Å	β= 90°.
	c = 7.8763(3) Å	γ = 90°.
Volume	3990.0(3) $Å^3$	
Z	4	
Density (calculated)	1.113 Mg/m^3	
Absorption coefficient	0.675 mm^{-1}	
F(000)	1408	
Crystal size	0.18 x 0.20 x 0.24 mm^3	
Theta range for data collection	2.785 to 71.739°.	
Index ranges	-29<=h<=28, -26<=k<=24, -9<=l<=7	
Reflections collected	9407	
Independent reflections	6283 [R(int) = 0.0785]	
Completeness to theta = 67.684°	99.9 %	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	6283 / 0 / 446	
Goodness-of-fit on F^2	0.907	
Final R indices [I>2sigma(I)]	R1 = 0.0699, wR2 = 0.1709	
R indices (all data)	R1 = 0.0985, wR2 = 0.1942	
Absolute structure parameter	-0.2(4)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.213 and -0.218 $e.Å^{-3}$	