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Assembly of annulated 1,3-diazapyrenes by consecutive cross-coupling and cyclodehydrogenation of (het)arene moieties

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Experimental Section

General Information. All reagents and solvents were obtained from commercial sources and dried by using the standard procedures before use. 5-Bromopyrimidine and all (het)arylboronic acids were purchased from Sigma-Aldrich. 1,4-Dioxane and CH_2Cl_2 were deoxygenated by bubbling argon for 1 h.

The ^1H and ^{13}C NMR spectra were recorded on a Bruker AVANCE-500 and AVANCE-600 instruments using Me_4Si as an internal standard. Elemental analysis was carried on a Eurovector EA 3000 automated analyzer. High resolution mass spectrometry was performed using a Bruker maXis Impact HD spectrometer. Melting points were determined on Boetius combined heating stages and were not corrected.

Column chromatography was carried out using Alfa Aesar silica gel 0.040-0.063 mm (230–400 mesh). The progress of reactions and the purity of compounds were checked by TLC on Sorbfil plates (Russia), in which the spots were visualized with UV light (λ 254 or 365 nm).

UV/vis spectra were recorded for a 1×10^{-5} M solutions on Shimadzu UV-2600 spectrophotometer. Photoluminescent spectra were recorded for a 1×10^{-5} M solutions on a Varian Cary Eclipse fluorescence spectrophotometer. UV/vis and fluorescence spectra were recorded using standard 1 cm quartz cells at room temperature.

Microwave experiments were carried out in a Discover SP unimodal microwave system (CEM, USA) with a working frequency of 2.45 GHz and the power of microwave radiation ranged from 0 to 300W. The reactions were carried out in a 35 ml reaction tube with the hermetic silicone cork. The temperature of the reaction was monitored using an inserted IR sensor by the external surface of the reaction vessel.

Cyclic voltammetry was carried out on a Metrohm Autolab PGSTAT128N potentiostat with a standard three-electrode configuration. Typically, a three electrodes cell equipped with a glass carbon working electrode, a $Ag/AgNO_3$ (0.01 M) reference electrode, and a glass carbon rod counter electrode was employed. The measurements were done in CH_2Cl_2 with

tetrabutylammonium hexafluorophosphate (0.1 M) as the supporting electrolyte under an argon atmosphere at a scan rate of 100 mV s^{-1}. The potential of reference electrode was calibrated by using the ferrocene/ferrocenium redox couple (Fc/Fc^+), which has a known oxidation potential of +5.1 eV *vs*. vacuum for ferrocene as reported [Cardona, C. M.; Li, W.; Kaifer, A. E.; Stockdale, D.; Bazan, G. C. *Adv. Mater*. **2011**, *23*, 2367]. The HOMO energy values were estimated from the onset potentials (E_{ox}^{onset}) of the first oxidation event according to the following equations:

$$E_{HOMO}\ (eV) = -\ [E_{ox}^{onset} - E_{1/2}(Fc/Fc^+) + 5.1]$$

where $E_{1/2}(Fc/Fc^+)$ is the half-wave potential of the Fc/Fc^+ couple against the $Ag/AgNO_3$ electrode.

Geometry optimization and energy calculation for polycycles **5a-c** were performed by using density-functional theory at the B3LYP/6-31G* level with the ORCA 4.0.3 program[Neese F. The ORCA program system. *Wiley Interdiscip Rev. Comput. Mol. Sci*. **2012**, 2, 73].

5-(3,4,5-Trimethoxyphenyl)pyrimidine (2). A mixture of 5-bromopyrimidine (**1**) (1.75 g, 11.0 mmol), 3,4,5-trimethoxyphenylboronic acid (**2**) (2.12 g, 10.0 mmol), $Pd(PPh_3)_4$ (578 mg, 5 mol %) and K_3PO_4(4.25 g, 20.0 mmol) was dissolved in 1,4-dioxane 20 mL. The resulting mixture was irradiated in a microwave apparatus at 165 °C (250 W) for 30 min. After that, 50 mL water was added and extracted with ethyl acetate. The combined organic layer was washed with water, brine, and dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The crude product was purified by column chromatography on silica gel with EtOAc/hexane (1:1, v/v) as an eluent to give **2** (2.22 g, 90 %) as a pale white solid, mp 93-94 °C. ^{1}H NMR (500 MHz, DMSO-d_6) 9.19 (s, 2H), 9.17 (s, 1H), 7.10 (s, 2H), 3.88 (s, 6H), 3.71 (s, 3H) [Cf. lit. data: C. B. Toney, S. Q. Smith, *Journal of Undergraduate Chemistry Research* **2005**, *4(1)*, 15-18].

5-(2,6-Dibromo-3,4,5-trimethoxyphenyl)pyrimidine (3). *N*-Bromosuccinimide (318 mg, 10.0 mmol) was added to a solution of 5-(3,4,5-trimethoxyphenyl)pyrimidine (**2**) (493 mg, 2.0 mmol) in DMF (10 ml). The obtained solution was stirred overnight at room temperature. The reaction mixture was diluted with water. The formed precipitate was filtered off, washed with water, dried, and purified by silica gel column chromatography with EtOAc/hexane (1:1, v/v) as an eluent to afford the desired product **3** as a pale yellow solid, mp 167-169 °C. ^{1}H NMR (500 MHz, $CDCl_3$) 9.26 (s, 1H), 8.62 (s, 2H), 4.01 (s, 3H), 3.95 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) 157.7, 157.3, 151.2, 148.2, 135.1, 131.7, 114.7, 61.4, 61.1. Anal. Calcd for $C_{13}H_{12}Br_2N_2O_3$ (404.06): C, 38.64; H, 2.99; N, 6.93. Found: C, 38.74; H, 3.17; N, 6.66.

General procedure for the synthesis of 5-{2,6-di[(het)aryl]-3,4,5-trimethoxyphenyl}pyrimidines (4a-c). A mixture of 5-(2,6-dibromo-3,4,5-trimethoxyphenyl)pyrimidine (**3**) (202 mg, 0.5 mmol), phenyl-, 3-thienyl- or 3-furylboronic acid (3.0 mmol), $Pd(PPh_3)_4$ (58 mg, 10 mol %) and K_3PO_4 (531 mg, 2.5 mmol) was dissolved in 1,4-dioxane (10 ml). The mixture was irradiated in a microwave apparatus at 165 °C (250 W) for 30 min. After that, water (20 ml) was added, and the mixture was extracted with ethyl acetate. The combined organic layer was washed with water, brine, and dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The crude product was purified by column chromatography on silica gel (eluent EtOAc–hexane, gradient from 1:3 to 1:1, v/v) to afford the desired products **4a-c**.

5-(4',5',6'-Trimethoxy-[1,1':3',1''-terphenyl]-2'-yl)pyrimidine (**4a)**: Yield 120 mg (60%); pale yellow solid, mp 275-276 °C. ^{1}H NMR (500 MHz, DMSO-d_6) 8.63 (s, 1H), 8.16 (s, 2H), 7.20 (dd, J = 8.1, 6.5 Hz, 4H), 7.17–7.13 (m, 2H), 7.10–7.07 (m, 4H), 3.97 (s, 3H), 3.61 (s, 6H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 157.6, 155.4, 150.5, 146.2, 135.7, 134.3, 133.0, 132.1, 130.6, 127.6, 126.8, 60.7 (2OCH_3). Anal. Calcd for $C_{25}H_{22}N_2O_3$ (398.46): C, 75.36; H, 5.57; N, 7.03. Found: C, 75.31; H, 5.46; N, 7.06.

5-[3,4,5-Trimethoxy-2,6-di(thiophen-3-yl)phenyl]pyrimidine (**4b)**: Yield 107 mg (52%); off-white solid, mp 248-250 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.74 (s, 1H), 8.20 (s, 2H), 7.38 (dd, J = 4.9, 2.9 Hz, 2H), 7.16 (dd, J = 2.9, 1.3 Hz, 2H), 6.82 (dd, J = 4.9, 1.3 Hz, 2H), 3.94 (s, 3H), 3.63 (s, 6H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 157.1, 155.6, 151.1, 146.3, 135.2, 133.1, 130.4, 129.8, 127.1, 125.2, 125.1, 60.76, 60.72. HRMS (ESI): *m/z* calcd for $C_{21}H_{19}N_2O_3S_2$: 411.0832 $[M+H]^+$; found: 411.0833.

5-[2,6-Di(furan-3-yl)-3,4,5-trimethoxyphenyl]pyrimidine (**4c)**: Yield 95 mg (50%); colorless solid, mp 221-223 °C. ^{1}H NMR (500 MHz, $CDCl_3$) 8.96 (s, 1H), 8.30 (s, 2H), 7.28 (d, J = 1.7 Hz, 2H), 7.10 (d, J = 1.5 Hz, 2H), 6.03–6.01 (m, 2H), 4.04 (s, 3H), 3.75 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.8, 156.4, 151.8, 147.3, 142.4, 141.8, 133.8, 129.8, 123.3, 119.0, 112.4, 61.03, 60.99. HRMS (APCI): *m/z* calcd for $C_{21}H_{19}N_2O_5$: 379.1288 $[M+H]^+$; found: 379.1290.

General procedure for the synthesis of 1,3-diazapyrene derivatives (5a-c). The corresponding precursor **4a-c** (0.5 mmol) was dissolved in dry $CHCl_3$ (5 ml). The air in the flask was replaced with argon. Then, iron(III) chloride (324 mg, 2.0 mmol) was added to this solution. The resulting mixture was stirred at room temperature for 24 h, and the solvent was evaporated. The residue was diluted with aqueous ammonia (10 ml), the precipitate formed and was filtered off, washed with water and air-dried. The residue was purified by flash column chromatography (eluent EtOAc–hexane, gradient from 1:3 to 1:1, v/v) to afford products **5a-c**.

8,9,10-Trimethoxytribenzo[*e,gh,j*]perimidine (**5a)**: Yield 128 mg (65%); yellow solid, mp 200-202 °C. ^{1}H NMR (600 MHz, $CDCl_3$) 9.76 (s, 1H), 9.74 (ddd, J = 8.5, 1.2, 0.6 Hz, 2H), 9.52 (ddd, J = 8.0, 1.6, 0.6 Hz, 2H), 7.93 (ddd, J = 8.5, 6.9, 1.6 Hz, 2H), 7.83 (ddd, J = 8.0, 6.9, 1.2 Hz, 2H), 4.28 (s, 3H), 4.15 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) 155.1, 153.4, 152.8, 148.3, 132.8, 131.3, 129.1, 127.8, 127.5, 125.5, 120.6, 119.0, 114.7, 61.7, 61.0. HRMS (ESI): *m/z* calcd for $C_{25}H_{19}N_2O_3$: 395.1390 $[M+H]^+$; found: 395.1389.

7,8,9-Trimethoxybenzo[*gh*]dithieno[2,3-*e*:3',2'-*j*]perimidine (**5b)**: Yield 175 mg (86%); pale yellow solid, mp 265-267 °C. ^{1}H NMR (600 MHz, $CDCl_3$) 9.61 (s, 1H), 8.72 (d, J = 5.3 Hz, 2H), 7.99 (d, J = 5.3 Hz, 2H), 4.29 (s, 6H), 4.26 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.5, 151.5, 150.1, 146.8, 139.1, 135.8, 131.0, 128.0, 118.8, 118.6, 112.2, 61.5, 61.4. HRMS (APCI): *m/z* calcd for $C_{21}H_{15}N_2O_3S_2$: 407.0519 $[M+H]^+$; found: 407.0521.

7,8,9-Trimethoxybenzo[*gh*]difuro[2,3-*e*:3',2'-*j*]perimidine (**5c)**: Yield 82 mg (44%); pale brown solid, mp 225-227 °C. ^{1}H NMR (600 MHz, $CDCl_3$) 9.75 (s, 1H), 8.16 (d, J = 1.9 Hz, 2H), 7.84 (d, J = 1.9 Hz, 2H), 4.32 (s, 6H), 4.25 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) 155.9, 151.1, 147.6, 146.4, 146.3, 143.1, 127.0, 116.5, 116.0, 113.5, 110.5, 61.6 (2OCH_3). HRMS (ESI): *m/z* calcd for $C_{21}H_{15}N_2O_5$: 375.0975 $[M+H]^+$; found: 375.0975.

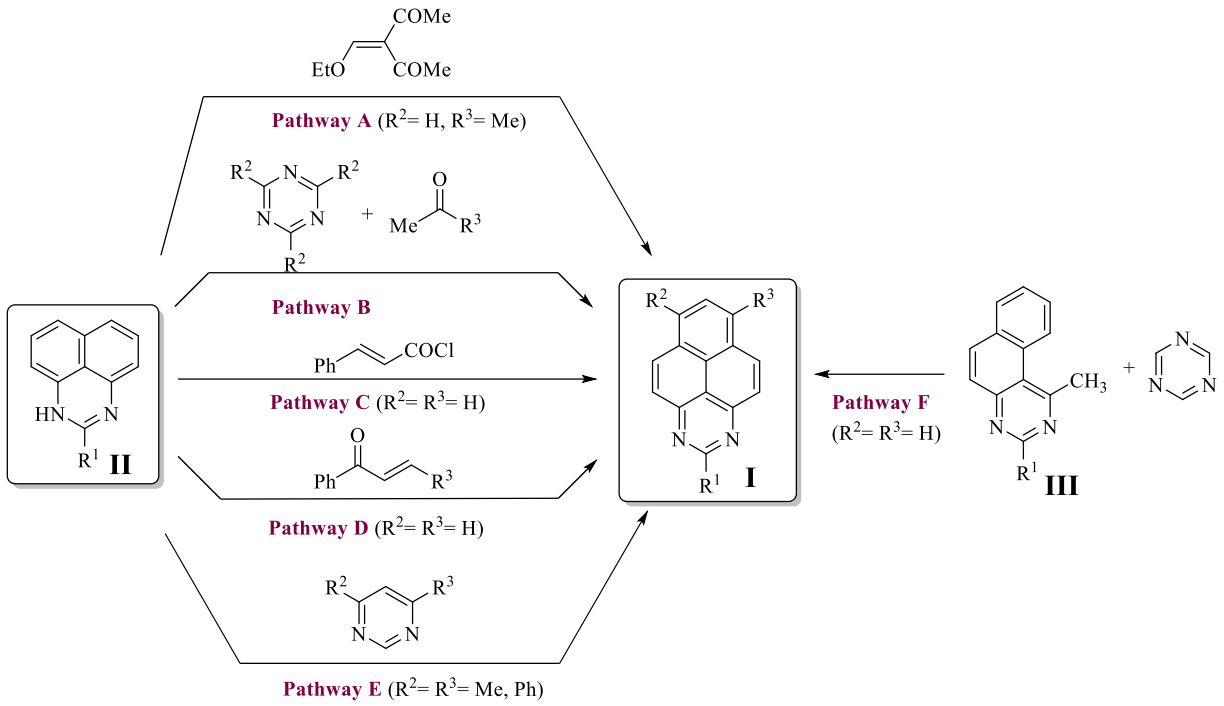


Figure S1 Synthetic approaches towards 1,3-diazapyrenes.

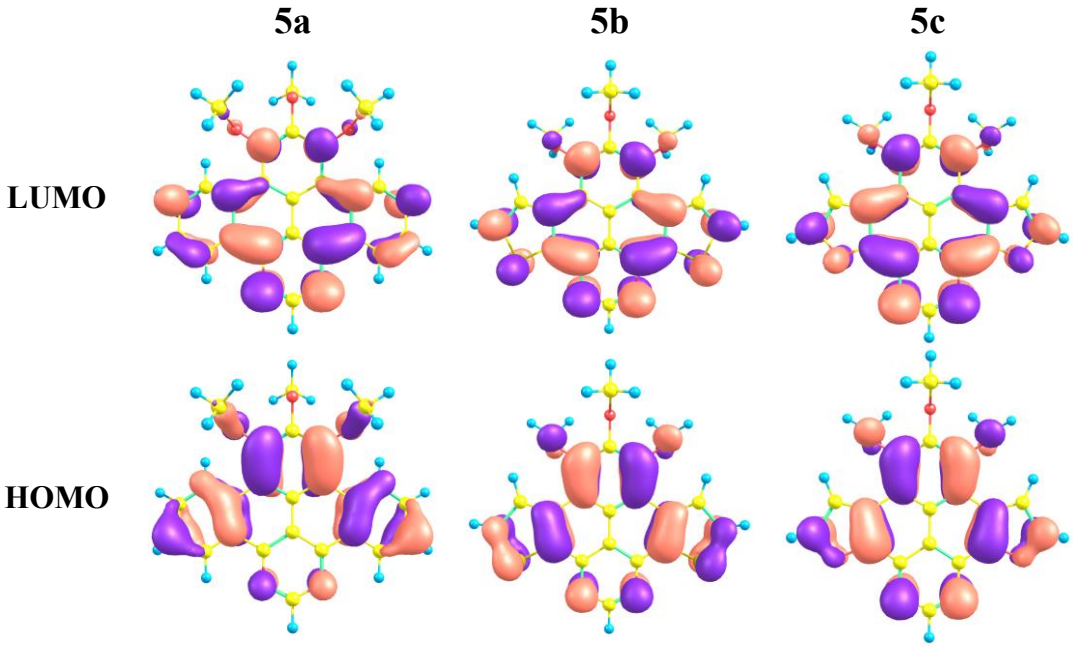


Figure S2 Molecular orbital diagrams for the LUMO and HOMO of compounds **5a-c** from TD-DFT calculation.

Compound 5a

0 imaginary frequencies

Final Energy -1298.20495038 Eh

Final Gibbs free enthalpy -1297.88002290 Eh

N	-3.46151361052467	1.20751349817124	-0.44272755679380
C	-2.65569916734146	2.25985334807298	-0.53682942911805
N	-1.33353663041169	2.27598683951267	-0.40566743200557
C	-0.73581736826830	1.09597505028335	-0.17159851958693
C	-1.47750714525039	-0.10242250946707	-0.08019044266015
C	-2.87861785535084	0.02006978704897	-0.20897663511286
C	-0.83748589603439	-1.38267093269275	0.08244180999715
C	-1.65364281792971	-2.55872801445585	0.10182672565752
C	-3.12211307051946	-2.42586524116938	0.14801328703417
C	-3.71856777228114	-1.15431766637967	-0.05105690512059
C	0.70275305019049	1.06572732713623	0.02631492248881
C	1.36075186481553	-0.17486912692547	0.22718806761987
C	0.59212039590477	-1.43119127788642	0.14171598131486
C	1.19152542914303	-2.70713253101254	0.10566922105107
C	0.40747180898217	-3.86125876376048	0.05097220223668
C	-0.98737842954923	-3.80092965439182	0.06625729433144
O	-1.65570162941046	-5.00175521297639	0.06166171931270
O	1.02420573615341	-5.08440368796166	-0.05534478203909
O	2.55317694678241	-2.88810221740864	0.13946736643961
C	3.15771431128128	-3.18407015785312	-1.12896337703512
C	1.30635689338552	-5.71565271607083	1.20153738565846
C	-1.74522146099976	-5.63973551643659	-1.22168077003778
C	-3.99585925523147	-3.50738544469613	0.41342379343796
C	-5.36990566257198	-3.34044571255252	0.42660976651482
C	-5.94308934324981	-2.08882184583955	0.17482387952779
C	-5.11784859896921	-1.00642961026535	-0.05245258229620
C	1.41934341295132	2.27614809570763	0.06154141585971
C	2.77337747130267	2.28832514721706	0.32739219003397
C	3.42775177096577	1.07767526345078	0.58149395242087
C	2.74196012538600	-0.12371795183517	0.53257063017041
H	-3.13253075407401	3.21648960163406	-0.73815544683077
H	4.22495766288452	-3.29042369432447	-0.93622827099135
H	2.99382721609517	-2.36400522149184	-1.83476405803848

H	2.76243357263859	-4.11662793245866	-1.53457864738175
H	1.78966613737007	-6.66293036642611	0.96344547781695
H	0.38150335708126	-5.90375651054036	1.75313410648848
H	1.98325120650360	-5.09812051328231	1.79792826072964
H	-2.29898306007368	-6.56429054872604	-1.06044046754047
H	-0.75039702833224	-5.86919541244715	-1.60665331812857
H	-2.28894385168657	-5.00669564121117	-1.92956784572806
H	-3.58442862990387	-4.47920123971355	0.62858762716385
H	-6.00390906076400	-4.19539461021113	0.64219387290394
H	-7.02150420358592	-1.96571226580667	0.17700610160839
H	-5.51923571778846	-0.01513506516263	-0.22094871484137
H	0.86881094685194	3.19242590531354	-0.11020263112279
H	3.31821050805410	3.22661146345332	0.35763925185437
H	4.48559473586560	1.07247277806757	0.82710156291219
H	3.26959345951347	-1.03698929122989	0.75043995982410

Compound 5b

0 imaginary frequencies

Final Energy -1939.73246024 Eh

Final Gibbs free enthalpy -1939.47450873 Eh

N	2.57458626235091	0.17072308829513	-0.14373904958667
C	3.18712691961758	-1.00915446184851	-0.22086564745718
N	2.62998628517846	-2.21852440520134	-0.20603410067601
C	1.28927859473124	-2.25431895097122	-0.10383667337871
C	0.50622368035650	-1.07656809389391	-0.01885800658562
C	1.23379918137856	0.13902312453377	-0.04154119480373
C	-0.92374015112807	-1.11224622504139	0.07588337555411
C	-1.65023682321957	0.12048396394499	0.13731413707536
C	-0.90639206223692	1.37114797597354	0.16222969902703
C	0.48467829516423	1.34542050244607	0.05864784008239
C	0.59692782205153	-3.49764983177474	-0.06751458767767
C	-0.79136091604931	-3.59321351379452	0.03297902021158
C	-1.59246716515404	-2.37873945924995	0.07237277533934
C	-2.99909868294315	-2.38190923838475	0.12135830702142
C	-3.71200403142310	-1.17960810464624	0.18010149583248
C	-3.05525356389195	0.05571461253458	0.18340316005917
C	-1.38347002206473	2.72116147225411	0.29000678696158

C	-0.37722647015828	3.63874998613628	0.26781039056088
S	1.19725198167640	2.93056834885394	0.09813534698784
S	1.38231901492324	-5.04788936447284	-0.11072889694372
C	-0.15724637510583	-5.83623571577494	0.02162215269197
C	-1.20502782577342	-4.96876537159931	0.08973472144623
O	-3.80874380711991	1.19785545111749	0.28246229377010
O	-5.08639512546247	-1.21262125331884	0.21669078237261
O	-3.69746053981849	-3.56165329329183	0.16296566952669
C	-4.43373223312044	-3.88625520573069	-1.02761994833855
C	-5.63640659186954	-1.23869714240797	1.54279500474225
C	-4.55362664133096	1.54900090320079	-0.89519388538608
H	4.27081691866490	-0.98182799811009	-0.30492409537125
H	-2.42106666015435	2.98145922737058	0.41941170595126
H	-0.47026069418916	4.71247824405766	0.35154765939624
H	-0.20021985366018	-6.91601041648657	0.04990938753890
H	-2.22917140971690	-5.28349306845101	0.20431556348783
H	-4.91430467597249	-4.84425290109429	-0.83061403584062
H	-3.75607377871653	-3.98573497190391	-1.88137031317384
H	-5.19124348495789	-3.12968242878005	-1.23395172821902
H	-6.71911316405478	-1.26154672919872	1.42172401395174
H	-5.34703498274677	-0.34160323212831	2.09632382878439
H	-5.30745155301848	-2.13362987341817	2.07765516048464
H	-5.08237134756540	2.47024767128831	-0.65175940429638
H	-5.27153716944314	0.76803870180753	-1.14750360214271
H	-3.87708715402730	1.72706797715927	-1.73694510898025

Compound 5c

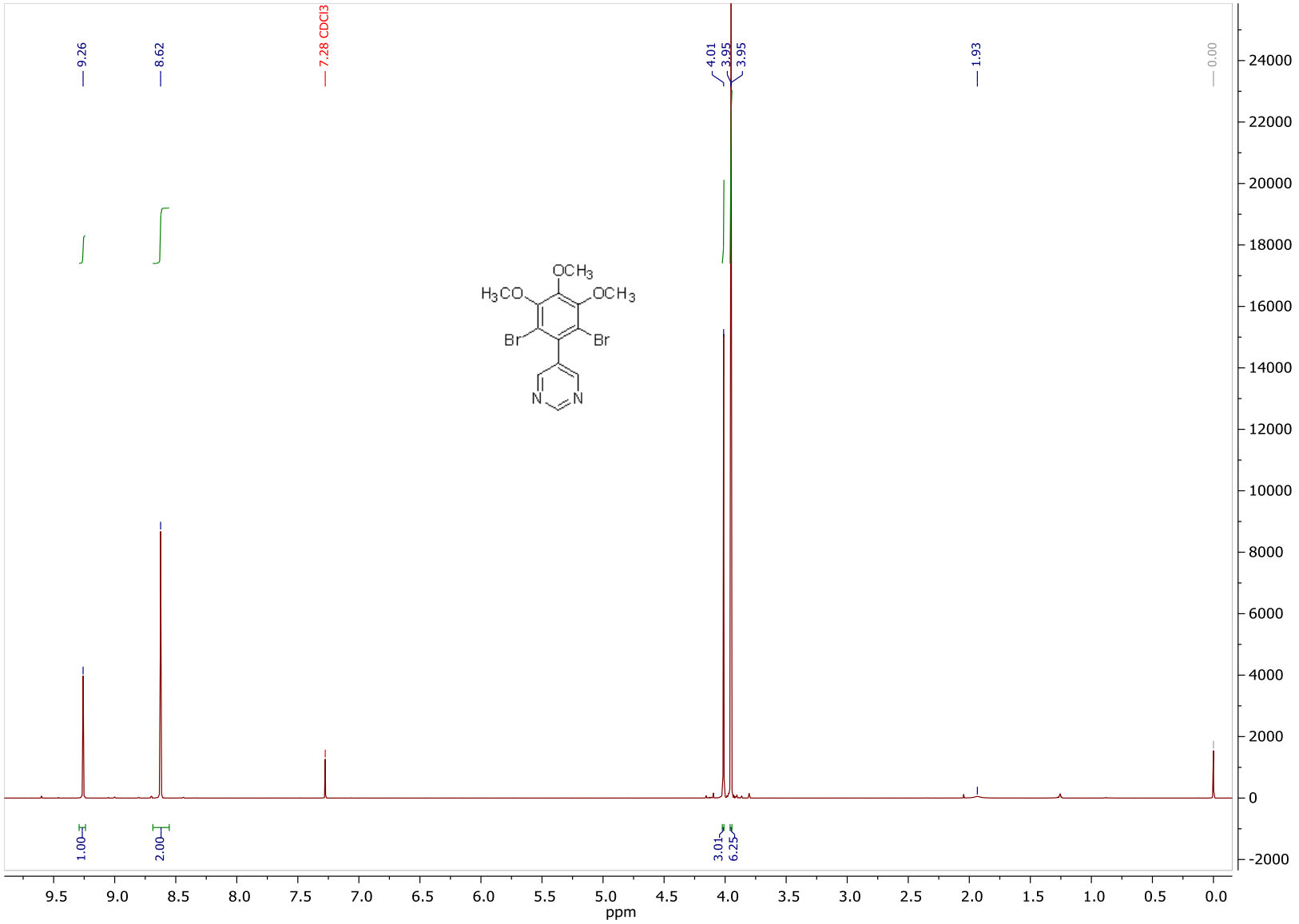
0 imaginary frequencies

Final Energy -1293.82007562 Eh

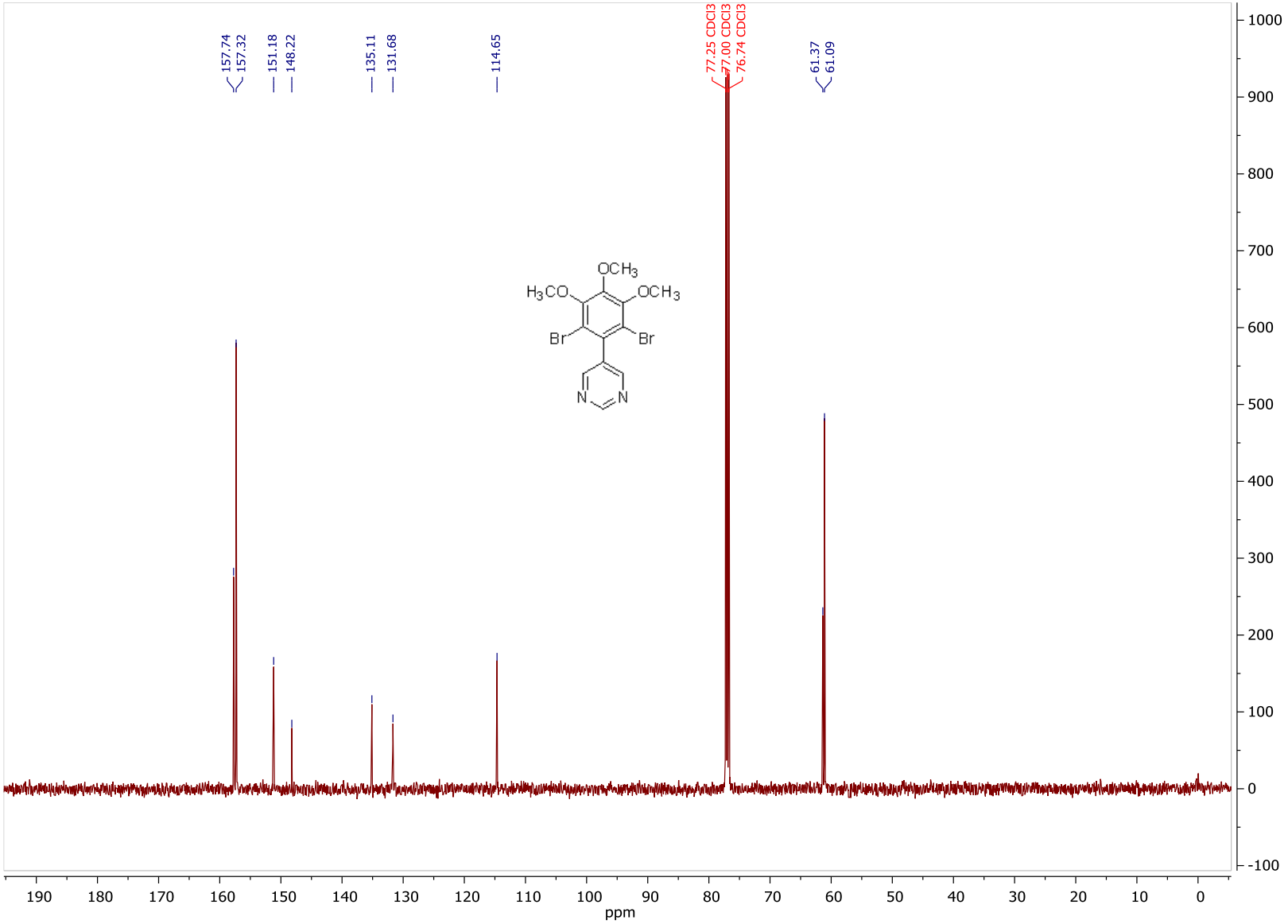
Final Gibbs free enthalpy -1293.55446135 Eh

N	2.55866723003038	0.18964629975896	-0.05851128819952
C	3.17386493580736	-0.99197340876671	-0.09257846155317
N	2.62696848923632	-2.20707516991159	-0.07858029512052
C	1.28506645400712	-2.24595210217559	-0.02397750048672
C	0.48529604122138	-1.06946897464356	0.01448561071781
C	1.21678610110235	0.15112473090353	-0.00400445996184
C	-0.94999669051036	-1.11082614886162	0.06965908727548

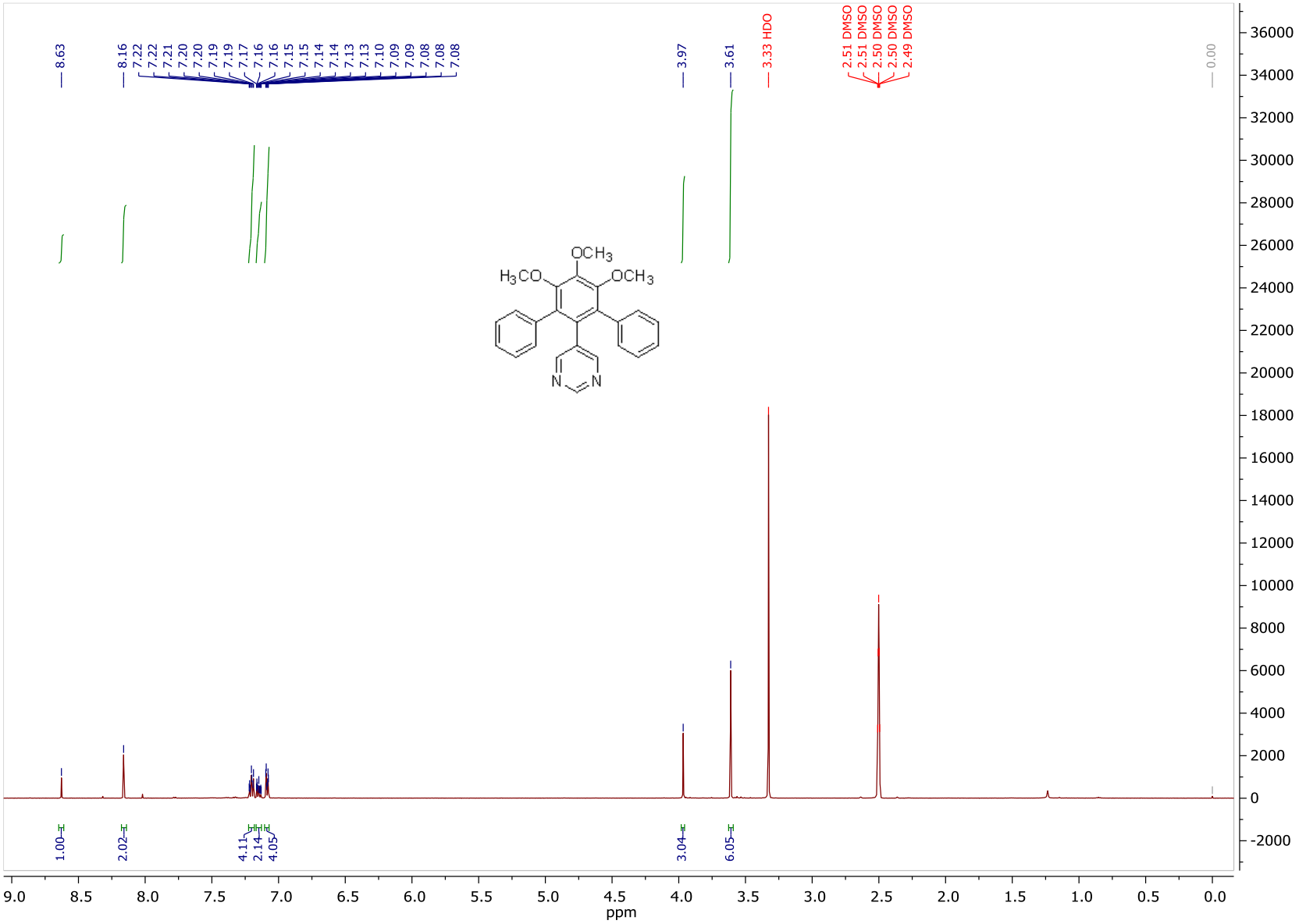
C	-1.69544576377656	0.10937011668814	0.09159896910564
C	-0.95622397273689	1.34856299416057	0.09924410501230
C	0.42777341816189	1.33229636822832	0.04300154783891
C	0.56460201677476	-3.47071110526768	0.00282038036062
C	-0.81623125757889	-3.56667563153950	0.05803972005898
C	-1.62484305016220	-2.37161625467753	0.07081872193326
C	-3.02873002098954	-2.38887669550048	0.10720551321978
C	-3.75396095765040	-1.19143983247947	0.14293993702493
C	-3.09783557055849	0.04574944954821	0.12683948371493
C	-1.31626712491990	2.74003961668862	0.15953515990292
C	-0.14543591043334	3.42767481326686	0.13142782541825
O	0.92993147829998	2.59459690132206	0.05880634621027
O	1.13782677041411	-4.70244580755805	-0.00279964259300
C	0.11167473611165	-5.59649590011053	0.05538890952018
C	-1.09639366476768	-4.97723019975465	0.09471267610283
O	-3.82781148408748	1.20450198179165	0.20475286770376
O	-5.12868121311821	-1.23094908136153	0.18401391866259
O	-3.69028099675662	-3.58882802151627	0.16676172887121
C	-4.45910185220024	-3.93381729436666	-0.99677100012901
C	-5.67229532916567	-1.24203868025056	1.51322949507802
C	-4.60999600390492	1.52493256538971	-0.95689832811967
H	4.26004066598384	-0.96063136862918	-0.13723254580174
H	-2.30562448485786	3.15617472591172	0.23775459637600
H	0.09073999501557	4.47960737565398	0.15881096131094
H	0.40736657124132	-6.63359060986421	0.06508706294549
H	-2.06039611945544	-5.45028556111456	0.16537815583801
H	-4.89436297210507	-4.91096724827292	-0.78877158403054
H	-3.81136440163960	-4.00197157129858	-1.87657219101069
H	-5.25200465198391	-3.20583540776238	-1.17051291983780
H	-5.38512499911607	-0.33616079944556	2.05361716057850
H	-5.33563717655328	-2.12746450857017	2.05909604871223
H	-6.75546718584081	-1.27244666639274	1.39800086461474
H	-5.10709175079734	2.46830939440467	-0.73218032980497
H	-5.35472370719346	0.75252794201723	-1.15111086365015
H	-3.96274659054783	1.65187877435801	-1.83052544380924



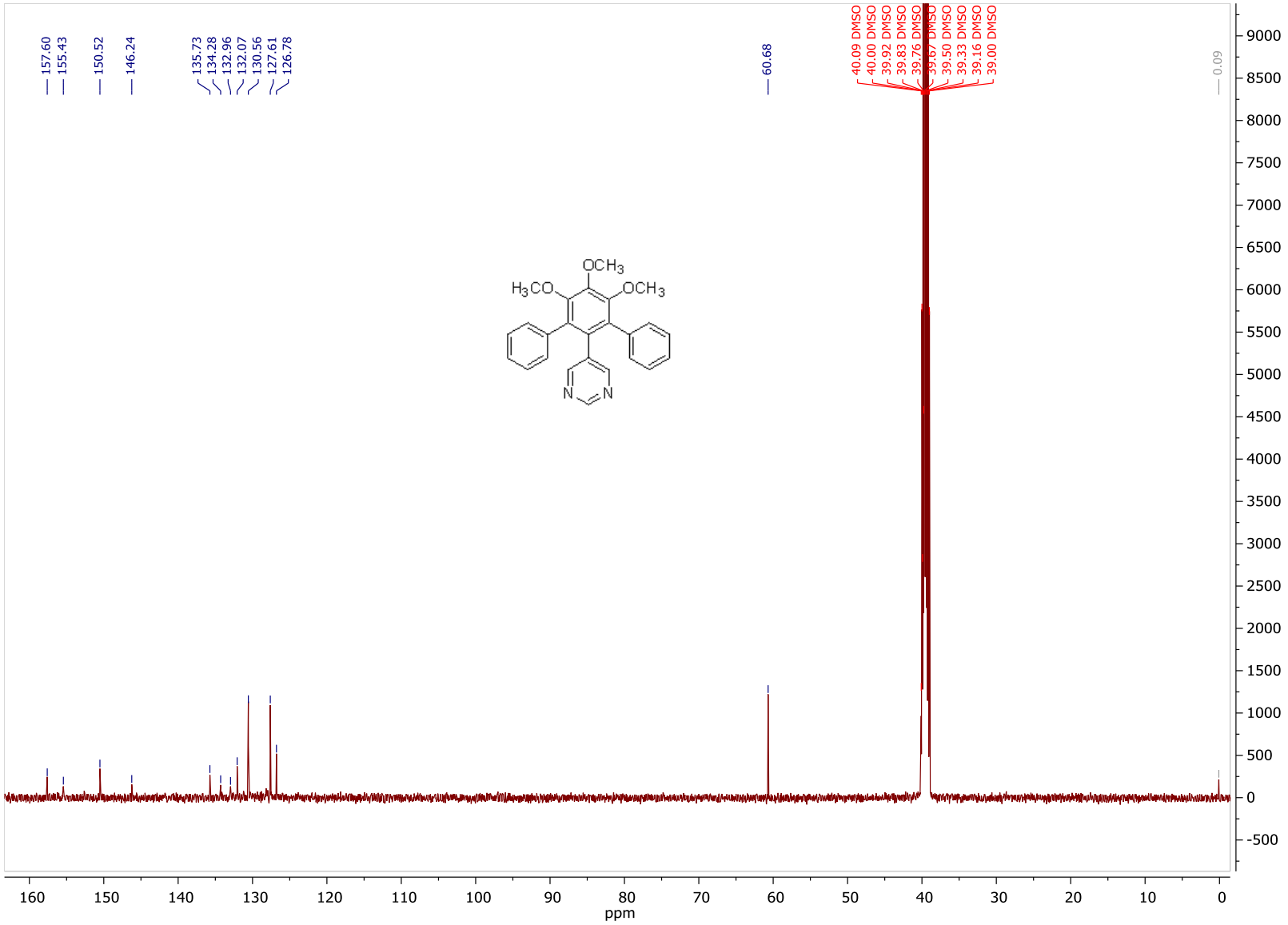
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **3**.



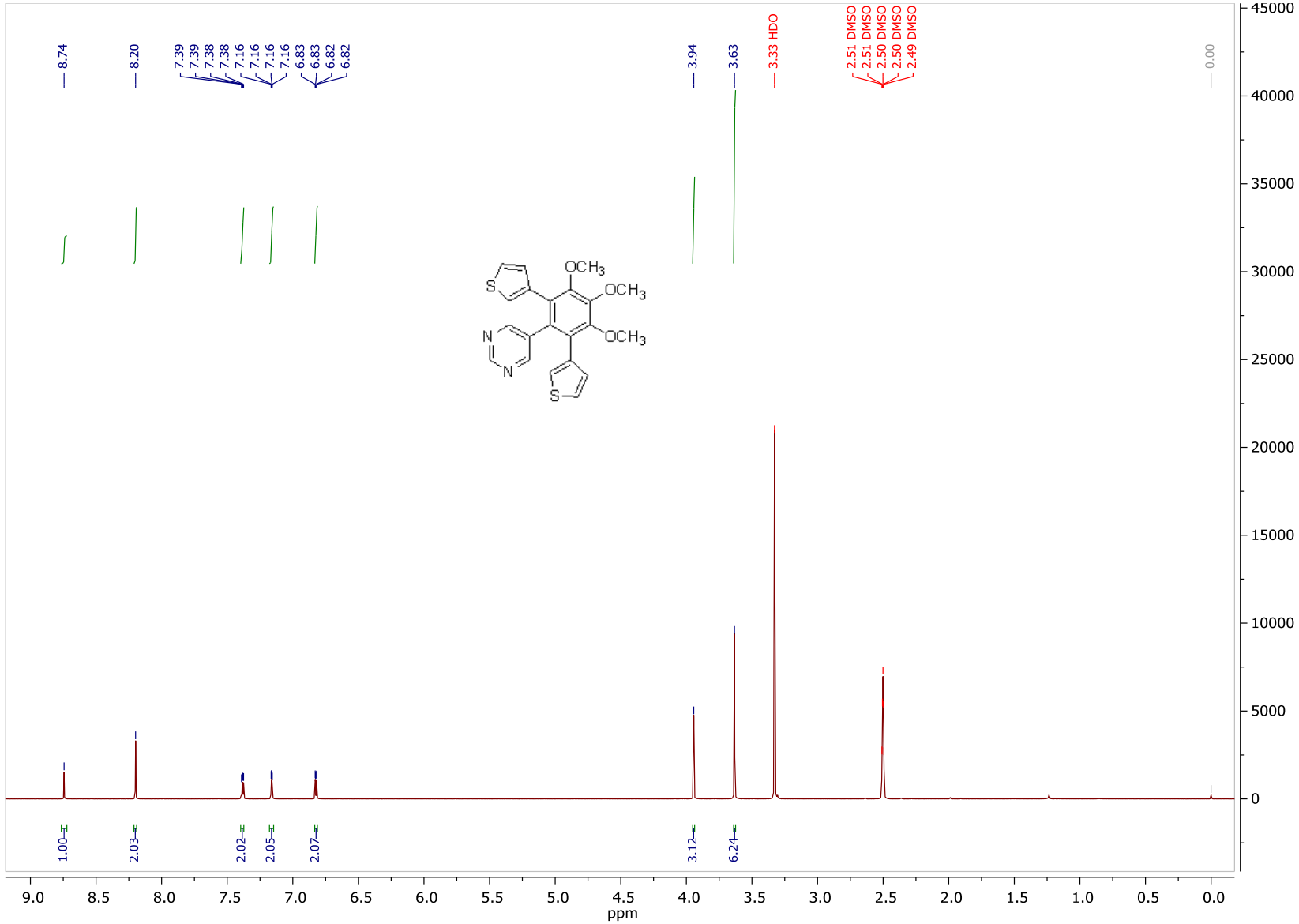
^{13}C NMR (126 MHz, $CDCl_3$) spectrum of **3**.



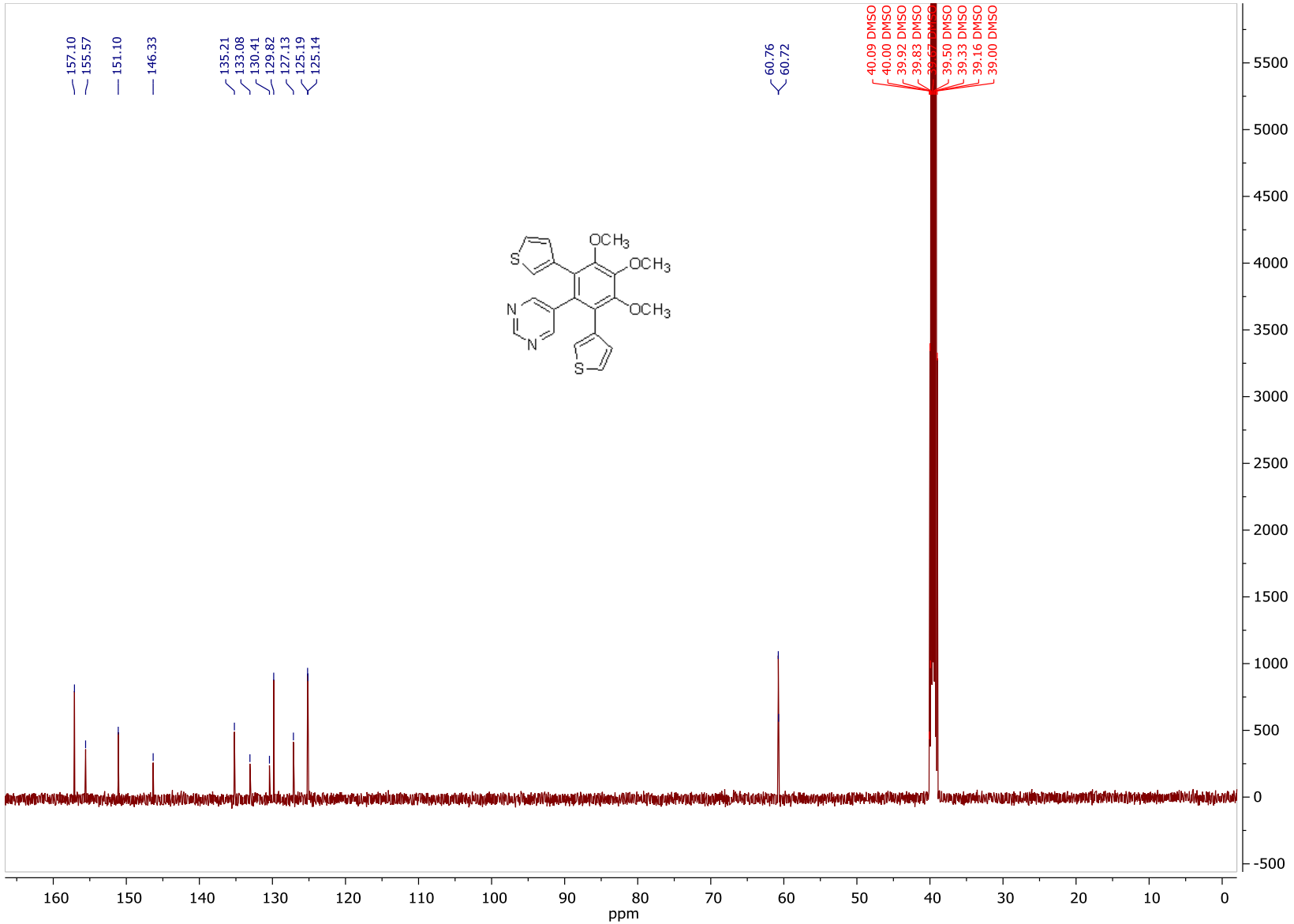
^{1}H NMR (500 MHz, DMSO-d_6) spectrum of **4a**.



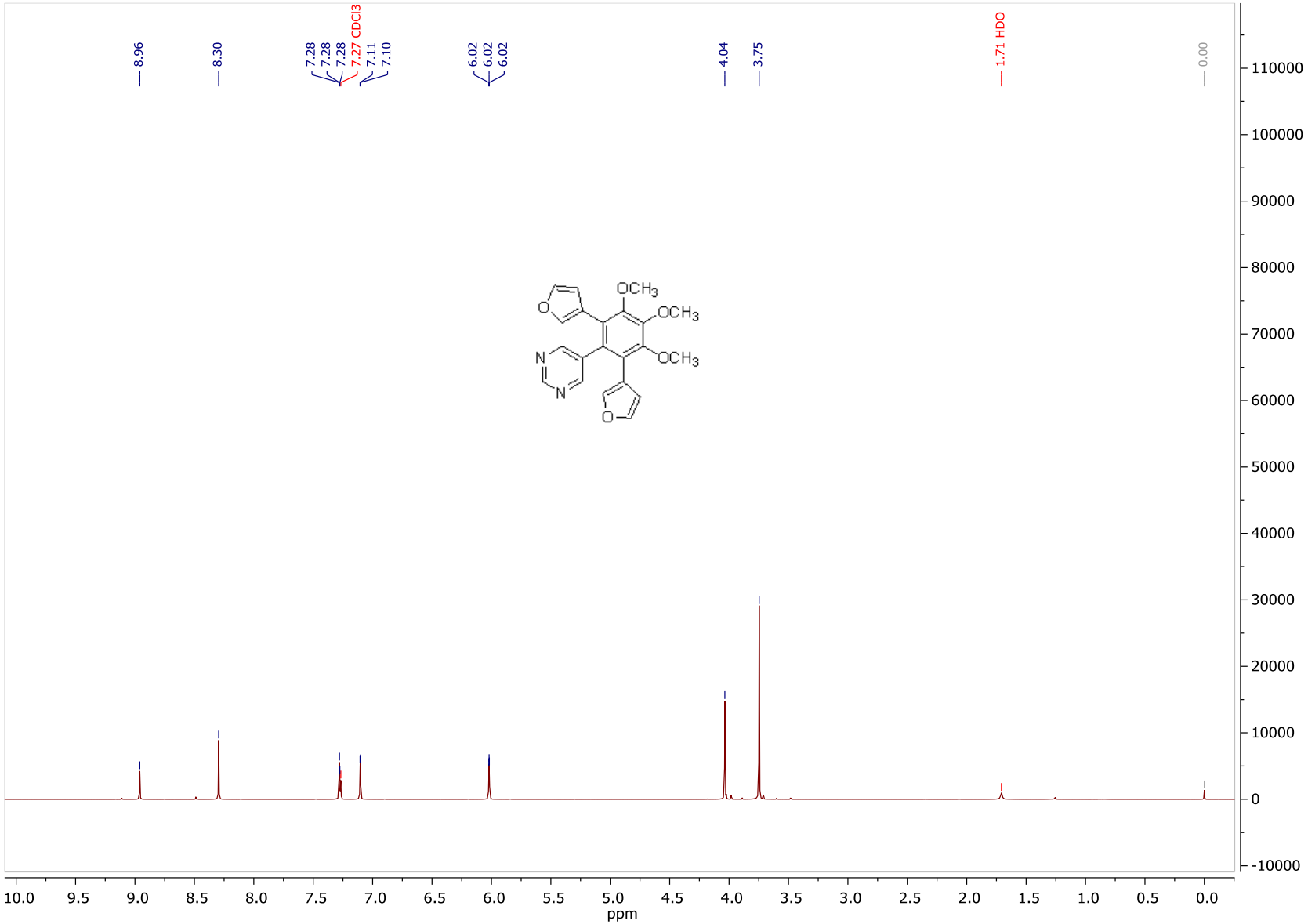
^{13}C NMR (126 MHz, DMSO-d_6) spectrum of **4a**.



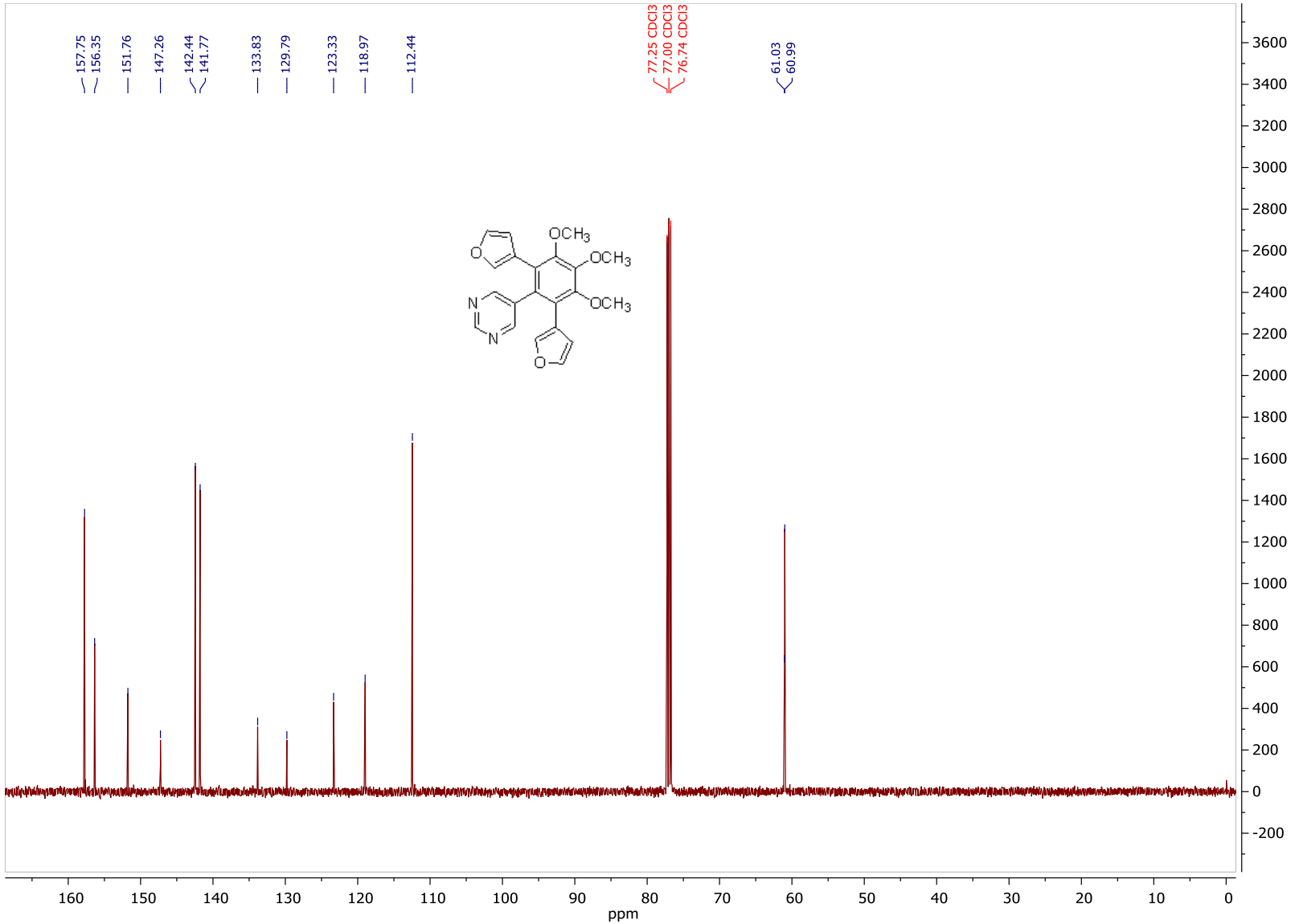
^{1}H NMR (500 MHz, DMSO-d_6) spectrum of **4b**.



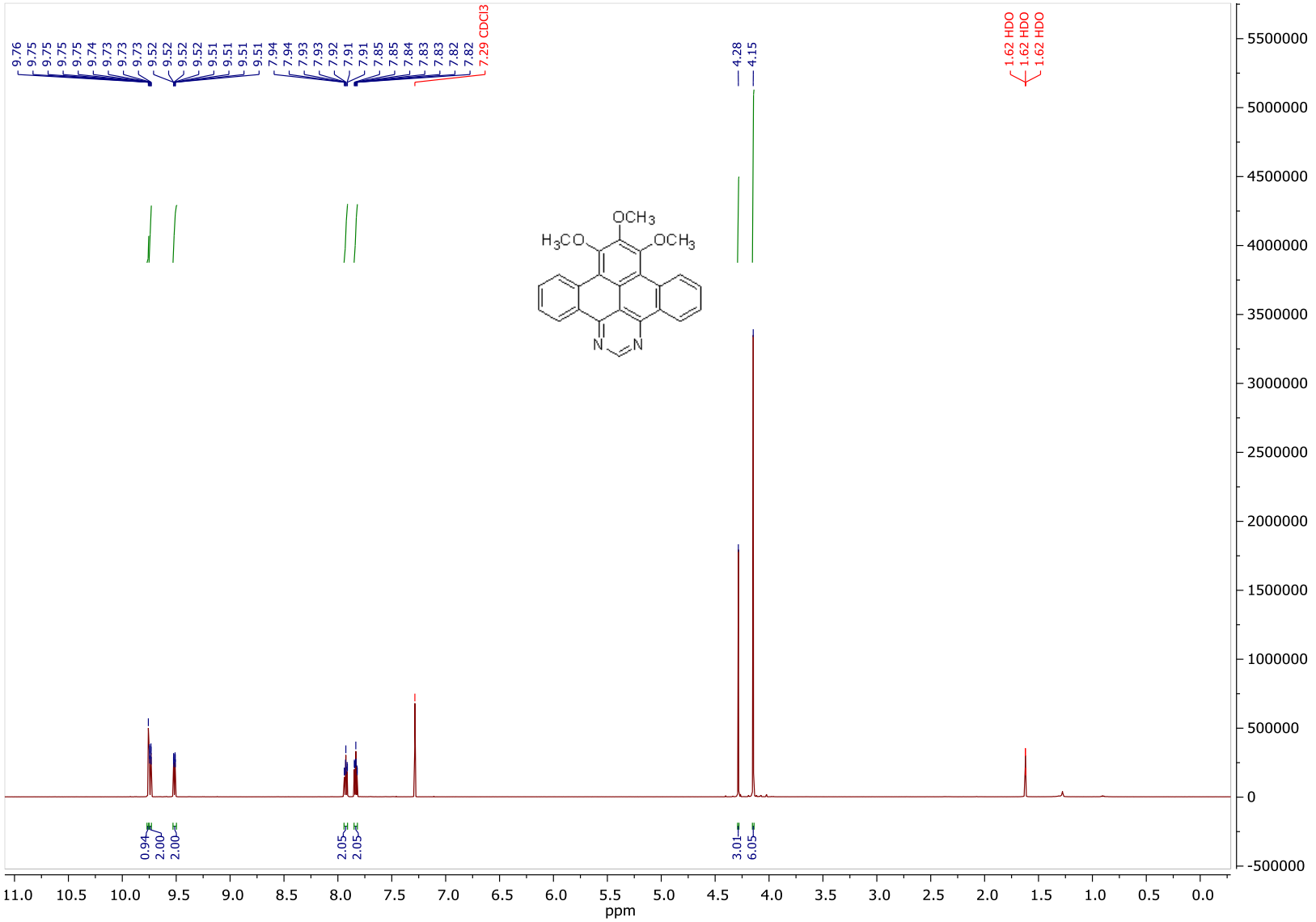
^{13}C NMR (126 MHz, DMSO-d_6) spectrum of **4b**.



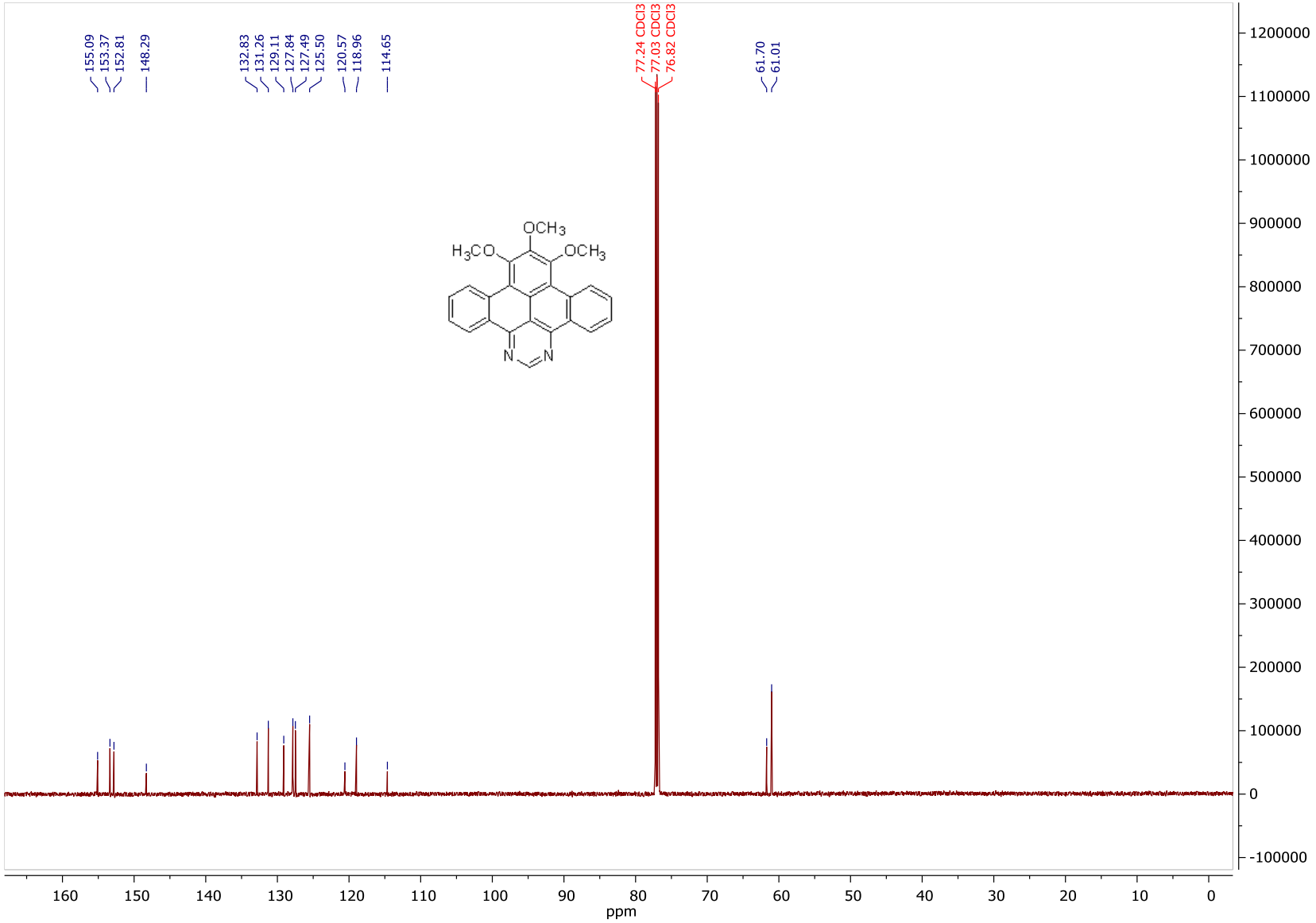
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **4c**.



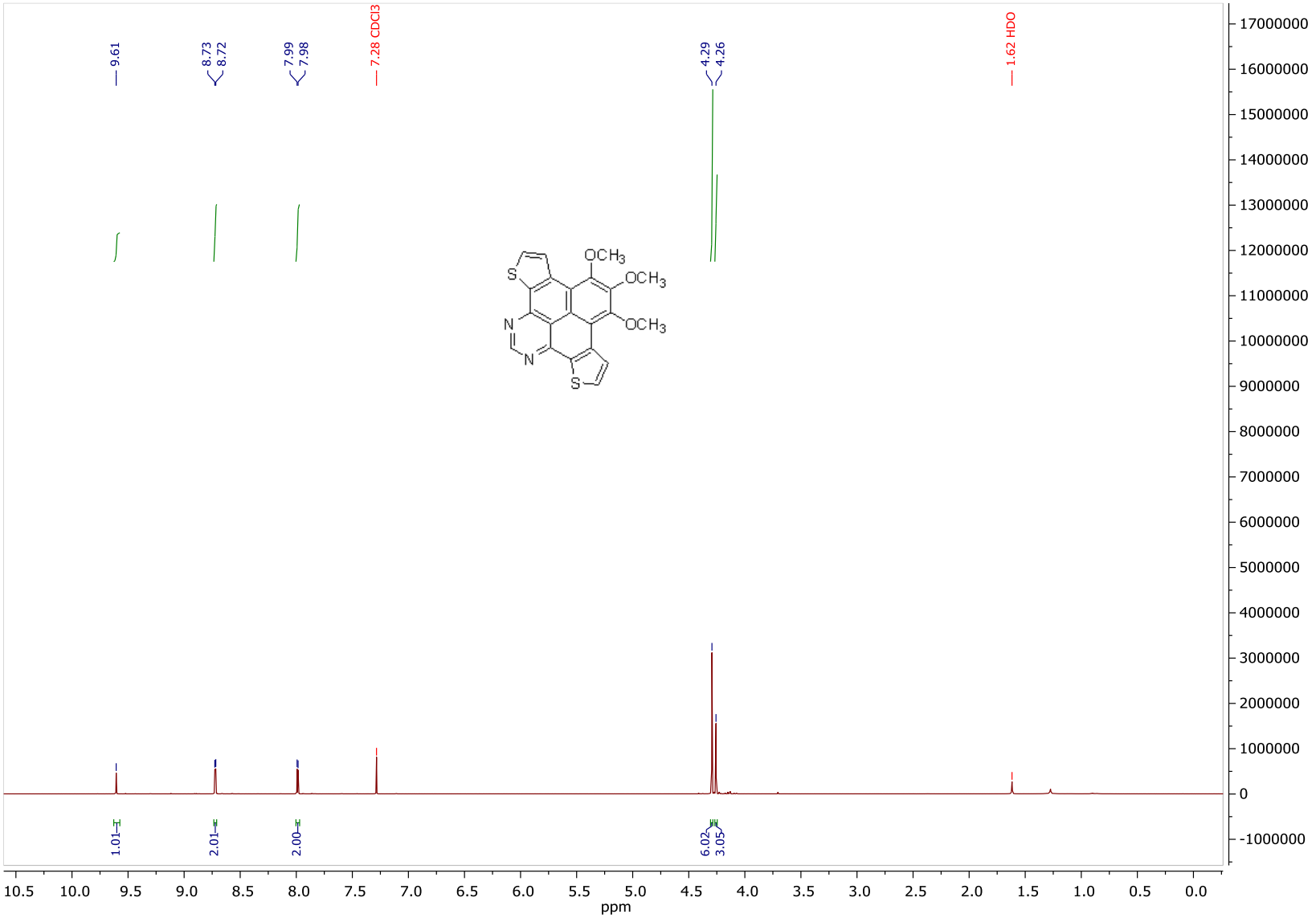
^{13}C NMR (126 MHz, $CDCl_3$) spectrum of **4c**.



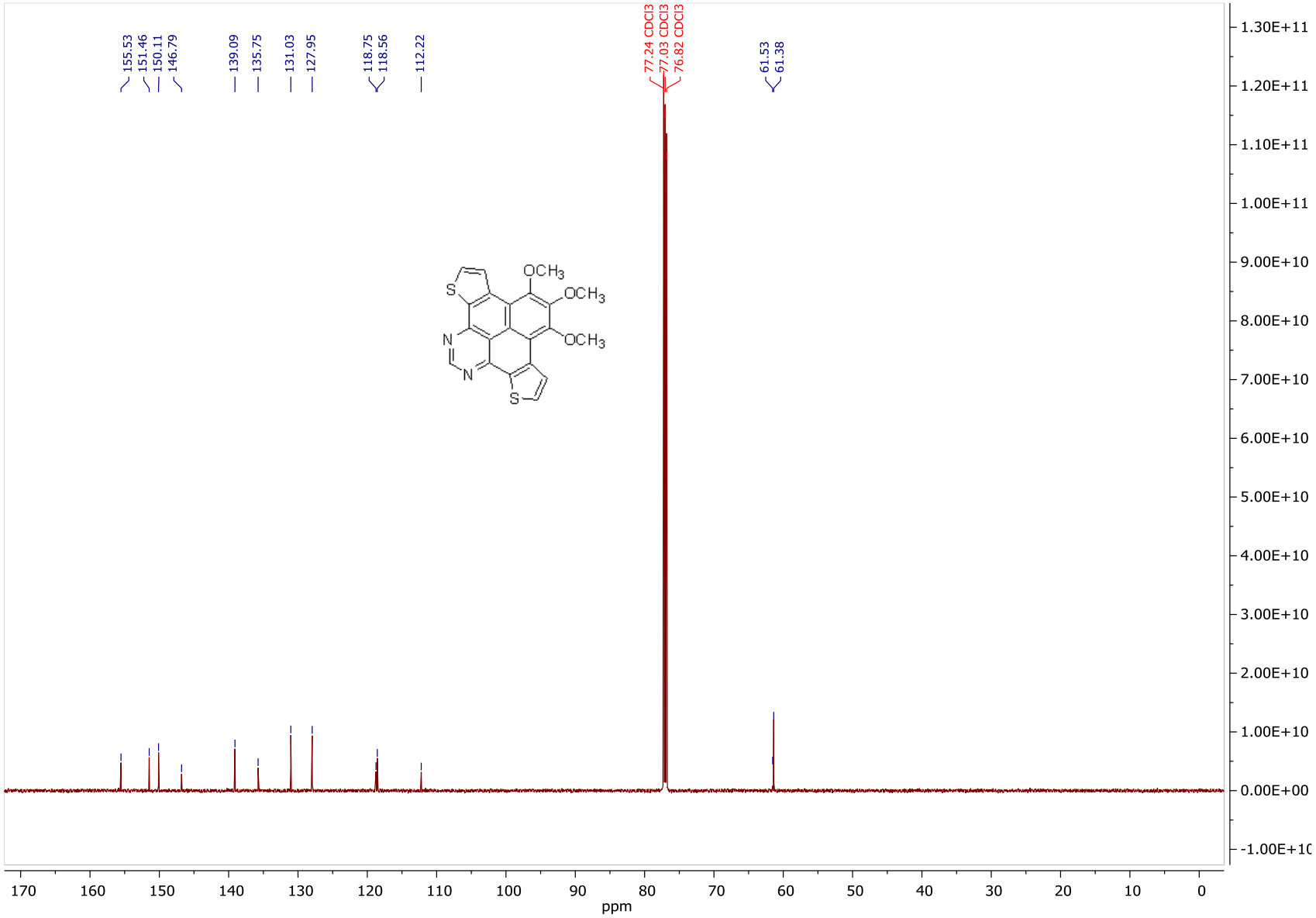
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of **5a**.



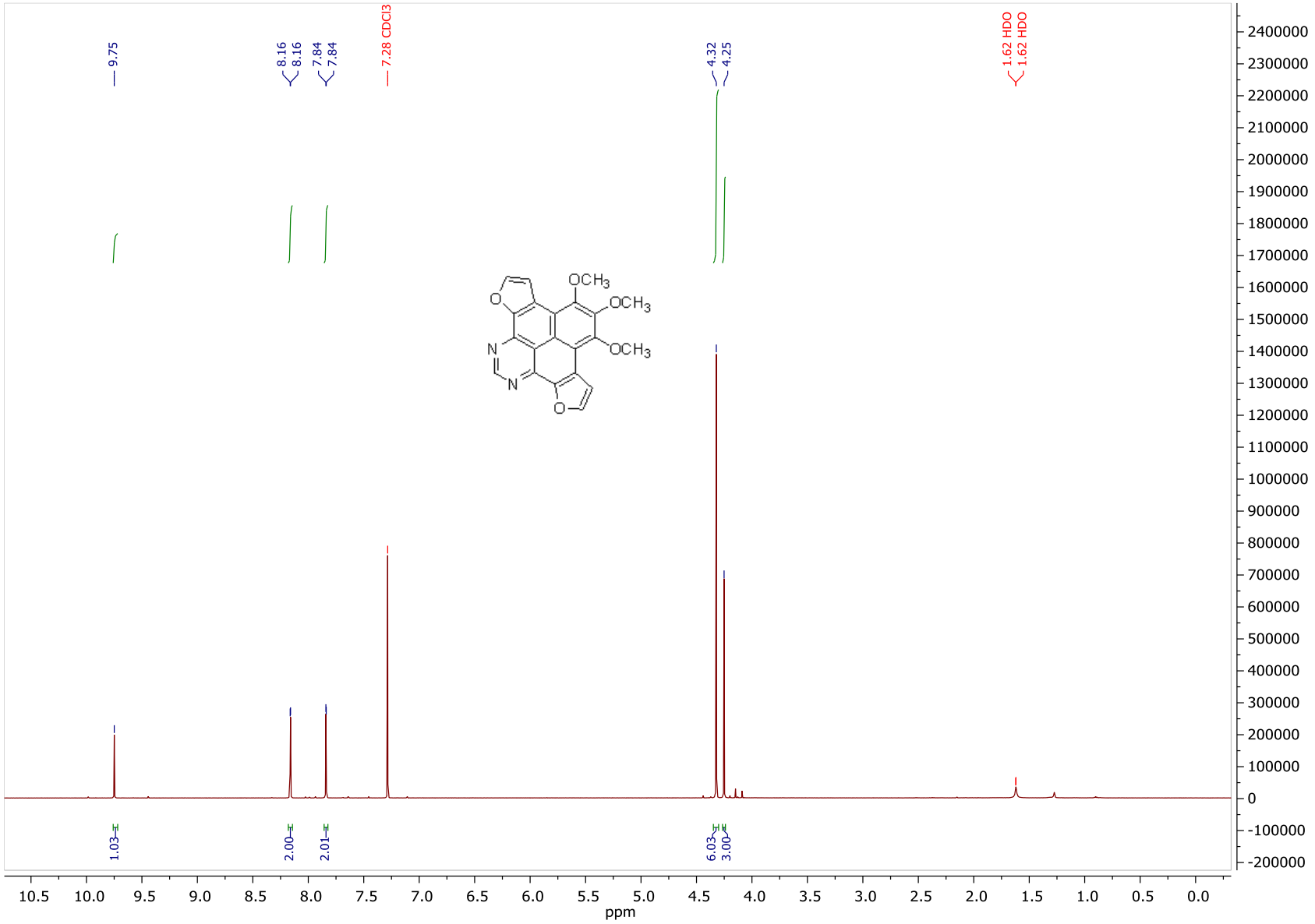
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of **5a**.



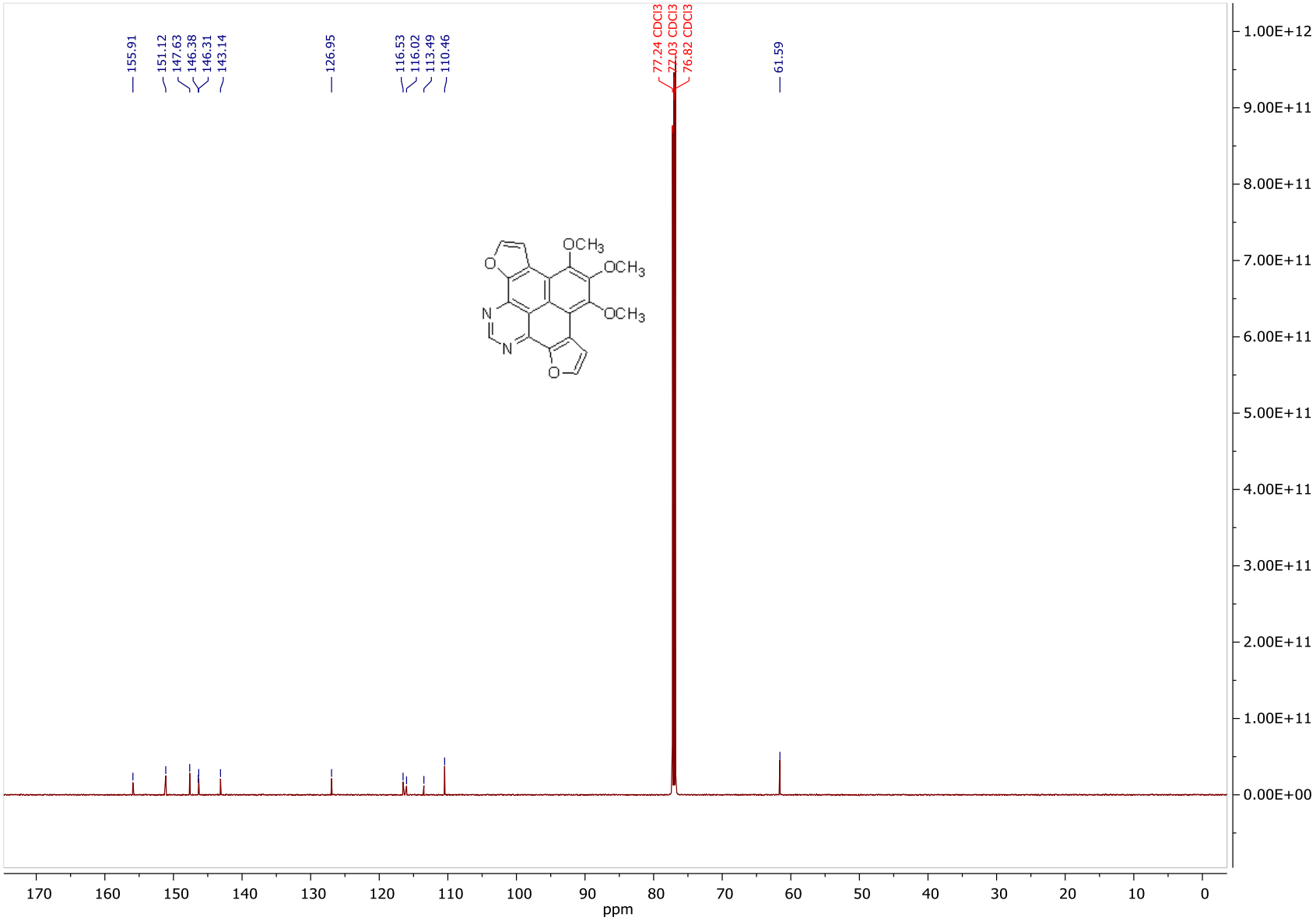
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of **5b**.



^{13}C NMR (151 MHz, $CDCl_3$) spectrum of **5b**.



^{1}H NMR (600 MHz, $CDCl_3$) spectrum of **5c**.



^{13}C NMR (151 MHz, $CDCl_3$) spectrum of **5c**.