Electronic Supplementary Material (ESI) for Chemical Communications

Supporting Information

Synthetic and structural exploration of disulfide bridged [2^n]pillararene like molecules

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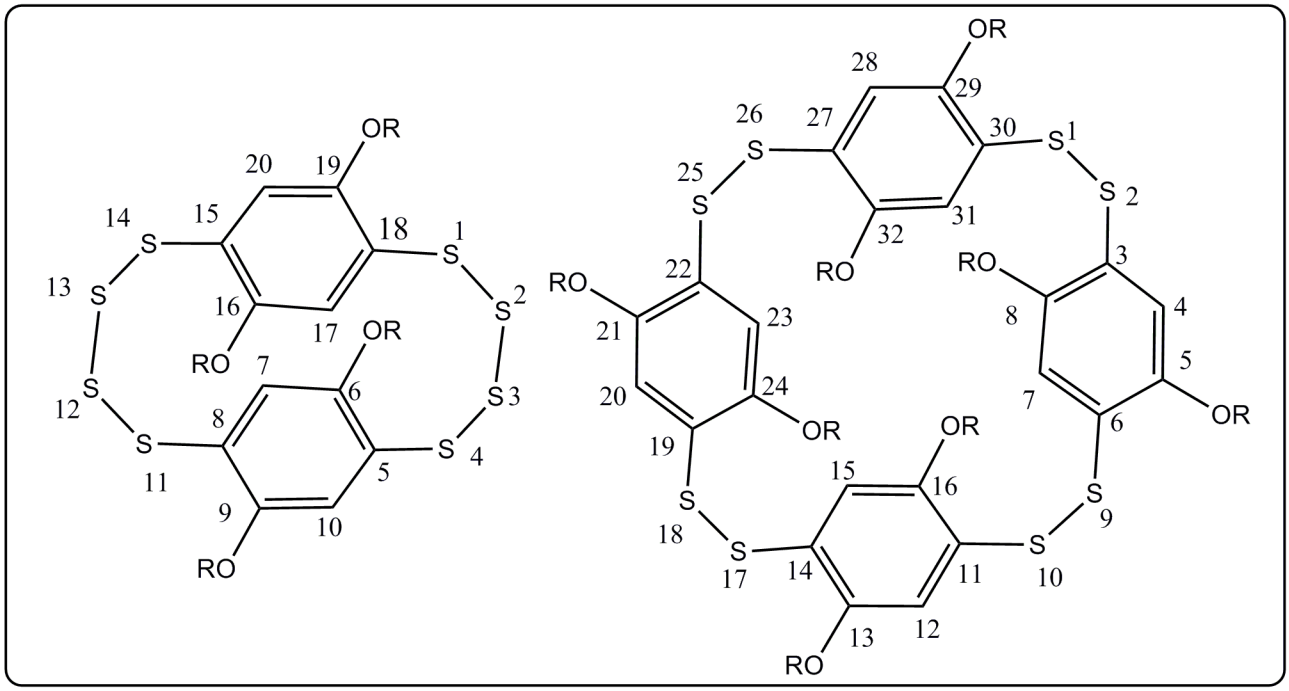


Fig 1. Numbering scheme for Disulfide bridged macrocycle

EXPERIMENTAL SECTION

1. General experimental methods

NMR spectra were acquired on commercial instruments, and chemical shifts (δ) are reported in parts per million (ppm) referenced to tetramethylsilane (^{1}H) or the internal (NMR) solvent signals (^{13}C).[1] Exact mass measurements were acquired in the EI (at a resolution of 10000) or ESI (at a resolution of 60000) mode. Melting points were determined by using a Reichert Thermovar apparatus and were not corrected. For column chromatography, 70–230 mesh silica 60 was used as the stationary phase. Chemicals received from commercial sources were used without further purification.

[1] H. E Gottlieb, V. Kotlyar, A. Nudelman, *J. Org. Chem.* 1997, **62**, 7512.

2. Experimental and characterization data

1,4-bis(bromomethyl)-2,5-dimethoxybenzene: The compound was synthesized according to the reported procedure,[2] the identity of the compound was confirmed by ^{1}H, ^{13}C and Mass spectroscopy.

6, 9, 16, 19-Tetramethoxy-[4,4]-1, 2, 3, 4, 11, 12, 13, 14-octathiathiaparacyclophane (2a) :1,4-Dimethoxybenzene (5 g, 36.18 mmol), aluminium trichloride (482 mg, 3.6 mmol) was dissolved in methylene dichloride (100 mL) cooled to 0° C and sulfur monochloride (4.88 g, 36.14 mmol) was added dropwise. During addition of sulfur monochloride copious evolution of chlorine gas was observed and solution turned green. After 15 -20 min the HCl liberation gradually ceased, the solution was then mechanically stirred and refluxed, After refluxing for 16 hrs it was filtered hot through the Buchner funnel thereby removing any unreacted starting material soluble in solvent. The orange crystalline filtrate contaminated with catalyst weighed 5.2 g. This material is extremely insoluble and was removed from catalyst by Soxhlet extraction with toluene to give an orange solid yielding 4.8 g, (50%). mp: 209 – 211° C; (literature 210 – 212° C)[3] MS (ESI+) *m/z* 567 [MH+K]; HRMS (ESI+) calcd for $C_{16}H_{16}O_4S_8$: 527.8814 [M]; found: *m/z* 527.8817; (extremely low solubility of this compound precluded further spectral analysis)

6, 9, 16, 19-Tetraethoxy-[4,4]-1, 2, 3, 4, 11, 12, 13, 14-octathiathiaparacyclophane (2b) : 1, 4-Diethoxybenzene (1 g, 6.01 mmol), aluminium trichloride (80 mg, 0.6 mmol) was dissolved in methylene dichloride (2 mL) and sulfur monochloride (811 mg, 6.01 mmol) was added drop wise to the solution at 0° C. During addition of sulfur monochloride copious evolution of chlorine gas was observed and reaction became

[2] K. A. White, D. A. Chengelis, M. Zeller, S. J. Geib, J. Szakos, S. Petoud, N. L. Rosi, *Chem. Commun.* 2009, **30**, 4506
[3] Z. S. Ariyan, R. L. Martin, *J. Chem. Soc., Perkin Trans. 1*, 1972, 1687

exothermic. The solution was gradually warmed to room temperature and mechanically stirred for 16 h, after which it was heated to 40° C for one hour, then cooled down to room temperature. Filtration gave yellow crystals along with catalyst. Extraction with chloroform yielded a yellow crystalline compound. Yield: 55% (980 mg); mp: 186 – 188° C; MS (ESI+) *m/z* 623 [M+K]; HRMS (ESI+) calcd for $C_{20}H_{25}O_4S_8$: 584.9518 [M+H]; found: 584.9517 *m/z*; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (s, 4H; Ph), 4.17−4.10 (m, 4H; CH_2), 4.04−3.97 (*m*, 4H; CH_2), 1.44 (t, 12H; *J* = 6 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.4 (C), 122.1 (C; Ph), 109.8 (CH; Ph), 64.83 (CH_2), 14.9 (CH_3)

5,8,13,16,21,24,29,32-Octamethoxy-[2,2,2,2]-1,2,9,10,17,18,25,26-octathiaparacyclophane (3a): Compound **2a** (560 mg, 1.06 mmol) was suspended in methylene dichloride (50 mL) and to this suspension was added sodium borohydride (280 mg, 7.40 mmol) dissolved in ethanol (20 mL). The resulting solution was mechanically stirred and refluxed under argon atmosphere for one hour, then it was cooled to room temperature and potassium carbonate (586 mg, 4.24 mmol) dissolved in distilled water (20 mL) was added to the solution and stirred at room temperature for 16 h in presence of air. Then the solution was filtered through a Buchner funnel, washed with ample distilled water and dried. Flash column chromatography (silica, eluent; methylene dichloride) afforded pure compound **4,** yield 84 % (360 mg) mp: 255 – 257° C; MS (ESI+) *m/z* 801 [M+H]; HRMS (ESI+) calcd for $C_{32}H_{36}NO_8S_8$: 818.0207 [M+NH_4]; found: *m/z* 818.0202; ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.16 (s, 8H; Ph), 3.66 (s, 24H; OMe); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 152.0 (C), 125.6 (C; Ph), 113.57 (CH; Ph), 56.98 (CH_3; OMe).

5,8,13,16,21,24,29,32-Octaethoxy-[2,2,2,2]-1,2,9,10,17,18,25,26-octathiaparacyclophane (3b): Cyclic bi(2,5-bis-dithio-1,4-diethoxybenzene) **2b** (200 mg, 0.342 mmol) was dissolved in THF (30 mL), to this solution was added sodium borohydride (90 mg, 2.38 mmol) dissolved in ethanol (20 mL), and refluxed under argon

atmosphere for 1h. The solution was cooled to room temperature and potassium carbonate (189 mg, 1.36 mmol) dissolved in water (20 mL) was added, and the resulting solution was mechanically stirred in oxygen atmosphere. After 16h THF was removed using rotatory evaporator and the precipittate was filtered using a Buchner funnel, and washed with distilled water. Purification by flash column chromatography (silica, eluent; methylene dichloride – Pet.ether 80:20) afforded pure compound **3b**. Yield: 81% (127 mg); mp: 193 – 194° C; MS (ESI+) *m/z* 951 [M+K]; HRMS (ESI+) calcd for $C_{40}H_{48}O_8S_8$: 951.0752 [M+K]; found: 951.0743 *m/z*; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19 (s, 8H; Ph), 3.99−3.92 (q, 16H; J = 6.9 Hz, CH_2), 1.26−1.22 (t, 24H, J=6Hz, CH_3); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 151.1 (C), 125.9 (C; Ph), 114.8 (CH; Ph), 65.7 (CH_2), 14.5 (CH_3)

5,8,13,16,21,24,29,32-Octamethoxy-[2,2,2,2]-1,10,17,26-tetrathiaparacyclophane (4a)

Compound **3a** (100 mg, 0.124 mmol) was dissolved in 1,4-dioxane (50 mL) and was well degassed by purging argon gas. To this solution was added sodium borohydride (38 mg, 1 mmol) dissolved in ethanol (10 mL). The resulting solution was mechanically stirred under argon atmosphere for one hour at 50° C. After 1h a solution of 1,4-bis(bromomethyl)-2,5-dimethoxybenzene (161 mg, 0.5 mmol) in 1,4-dioxane (10mL) was well degassed, and added to the thiol solution *via* the aid of a syringe pump over the period of 20 h. After 20 h, the mixture was further stirred for 4 days at 50°C. The solvent was then evaporated, extraction was done with ethyl acetate, the organic layer was separated, dried over $MgSO_4$, filtered and evaporated to dryness to afford the crude product. Purification by column chromatography (silica, eluent; heptane – ethyl acetate 70:30) gave 13% (24 mg) of compound **4a** together with compound **4b**. mp: 238 – 240° C; MS (ESI+) *m/z* 751[M+Na]; HRMS (ESI+) calcd for $C_{36}H_{41}O_8S_4$: 729.1684 [M+H]; found: *m/z* 729.1682; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.72 (s, 4H; Ph), 6.54 (s, 4H; Ph), δ 4.02 (s, 8H; CH_2), 3.62 (s, 12H; OMe), 3.36 (s, 12H; OMe); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 152.4 (C), 150.8 (C), 126.9 (C), 122.6 (C),114.9 (CH; Ph), 112.8 (CH; Ph), 56.5 (CH_3; OMe), 55.9 (CH3; OMe), 30.1 (CH_2).

5,8,13,16,21,24,29,32,37,40,45,48-Dodecamethoxy-[2,2,2,2,2,2]-1,10,17,26,33,42-hexathiaparacyclophane (4b): Yield: 8% (14 mg); mp: 235 – 236° C; MS (ESI+) *m/z* 1116 [M+Na]; HRMS (ESI+) calcd for $C_{54}H_{64}NO_{12}S_6$: 1110.2752 [M+NH_4]; found: 1110.2653 *m/z*; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.70 (s, 6H; Ph), 6.64 (s, 6H; Ph), δ 4.03 (s, 12H; CH_2), 3.63 (s, 18H; OMe), 3.58 (s, 18H; OMe); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3 (C), 151.0 (C), 125.7 (C), 123.2 (C),114.4 (CH; Ph), 113.1 (CH; Ph), 56.6 (CH_3; OMe), 56.2(CH_3; OMe), 31.6 (CH_2).

13,16,29,32-tetramethoxy-[2,2,2,2]-1,10,17,26-Tetrathiaparacyclophane (4c): Compound **3a** (100 mg, 0.124 mmol) was dissolved in 1,4-dioxane (50 mL) and was well degassed by purging argon gas. To this solution was added sodium borohydride (38 mg, 1 mmol) dissolved in ethanol (10 mL). The resulting solution was mechanically stirred under argon atmosphere for one hour at 50° C. After 1h the solution of 1,4-bis(bromomethyl)benzene (131 mg, 0.5 mmol) in 1,4-dioxane (10 mL) was well degassed, and added to the thiol solution *via* the aid of a syringe pump over the period of 20h. After 20h, the mixture was further stirred for 4 days at 50° C. The solvent was then evaporated, and extraction was done with ethyl acetate, organic layer was separated, dried over $MgSO_4$, filtered and evaporated to dryness to afford the crude product. Purification by column chromatography (silica, eluent; heptane – ethyl acetate 70:30) yielded 18 % (26 mg) of compound **4c**; mp: 229 – 230° C; MS (ESI+) *m/z* 609 [M+H]; HRMS (ESI+) calcd for $C_{32}H_{33}O_4S_4$: 609.1262 [M+H]; found: 609.1253 *m/z*; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.76 (s, 8H; Ph), 6.60 (s, 4H; Ph), δ 3.92 (s, 8H; CH_2), 3.60 (s, 12H; OMe); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.0 (C), 138.1 (C), 128.2 (CH), 122.6 (C), 118.5 (CH; Ph), 56.6 (CH_3; OMe), 37.5 (CH_2).

3. X-ray Crystallography Data.

Single crystals of **3a**, suitable for X-ray diffraction were obtained by slow evaporation from dichloromethane solution at room temperature. X-ray intensity data were collected at 100K on an Agilent Supernova diffractometer, equipped with an Atlas CCD detector, using Mo Kα radiation (λ = 0.7107 Å). The images were interpreted and integrated with the CrysAlisPro software from Agilent Technologies[4]. Using Olex2[5], the structure was solved with the ShelxS[6] structure solution program using Direct Methods and refined with the ShelxL refinement package using full-matrix least squares minimization on F^2. Non hydrogen atoms were anisotropically refined and the hydrogen atoms in the riding mode with isotropic temperature factors were fixed at 1.2 times $U_{eq}$of the parent atoms (1.5 for methyl groups). Dichloromethane is disordered over two positions. CCDC 934188 contains the supplementary crystallographic data for this paper can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033; or deposit@ccdc.cam.ac.uk).

Single crystals of **4a**, suitable for X-ray diffraction were obtained by slow evaporation from an acetonitrile solution at room temperature. X-ray intensity data were collected at 100K on an Agilent Supernova diffractometer, equipped with an Atlas CCD detector, using Mo Kα radiation (λ = 0.7107 Å). The images were interpreted and integrated with the CrysAlisPro software from Agilent Technologies. Using Olex2, the structure was solved with the ShelxS structure solution program using Direct Methods and refined with the ShelxL refinement

[4]CrysAlis PRO (2012). Agilent Technologies UK Ltd, Yarnton,Oxfordshire, England.

[5] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, OLEX2: a complete structure solution, refinement and analysis program. *J. Appl. Cryst.* 2009,.**42**, 339

[6] G.M. Sheldrick, *ActaCryst*. 2008, **A64**, 112

package using full-matrix least squares minimization on F^2. The crystal was twinned and solved using a HKLF5 refinement. Non-hydrogen atoms were anisotropically refined and the hydrogen atoms in the riding mode with isotropic temperature factors were fixed at 1.2 times U_{eq} of the parent atoms (1.5 for methyl groups). CCDC 934190 contains the supplementary crystallographic data for this paper and can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033; or deposit@ccdc.cam.ac.uk).

Single crystals of **2b**, suitable for X-ray diffraction were obtained by slow evaporation from an dichloromethane solution at room temperature. X-ray intensity data were collected at 100K on an Agilent Supernova diffractometer, equipped with an Atlas CCD detector, using Mo Kα radiation (λ = 0.7107 Å). The images were interpreted and integrated with the CrysAlisPro software from Agilent Technologies. Using Olex2, the structure was solved with the ShelxS structure solution program using Direct Methods and refined with the ShelxL refinement package using full-matrix least squares minimization on F^2. Non hydrogen atoms were anisotropically refined and the hydrogen atoms in the riding mode with isotropic temperature factors were fixed at 1.2 times U_{eq} of the parent atoms (1.5 for methyl groups). The structure, measured on room temperature is known in the Cambridge Structural Database[7] with ref codes: TEOSHE01[7] and TEOSHE10[8]. Because we were unable to access these papers, the structure was remeasured at 100K. CCDC 934189 contains the supplementary crystallographic data for this paper and can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data

[7] Z. S. Ariyan, R.L. Martin (1969) *J. Chem. Soc. D*, 847
[8] J. S. Ricci Junior, I. Bernal (1971) *J. Chem. Soc. B, 1928*
[7]F. H. Allen, *ActaCryst*, 2002, **B58**, 380, "The Cambridge Structural Database: a quarter of a million crystal structures and rising"
[DOI: 10.1107/S0108768102003890]

Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033; or deposit@ccdc.cam.ac.uk).

Compound **2b** crystallizes into the monoclinic space group $P2_1/n$. The conformation of the compound at 100K does not change in correspondence to those measured at room temperature: the box is formed as such that there is an intermolecular π-π interaction between *Cg1* and *Cg*2 with a distance of 3.4273(15) Å (*Cg1* and *Cg2* are the centroids of respectively the aromatic rings C1-C6 and C11-C16).

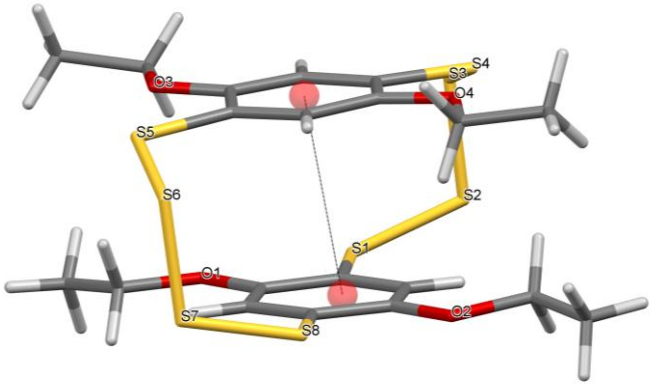


Fig. 2 Asymmetric unit of compound **2b**. Intermolecular interactions are represented by dotted lines.

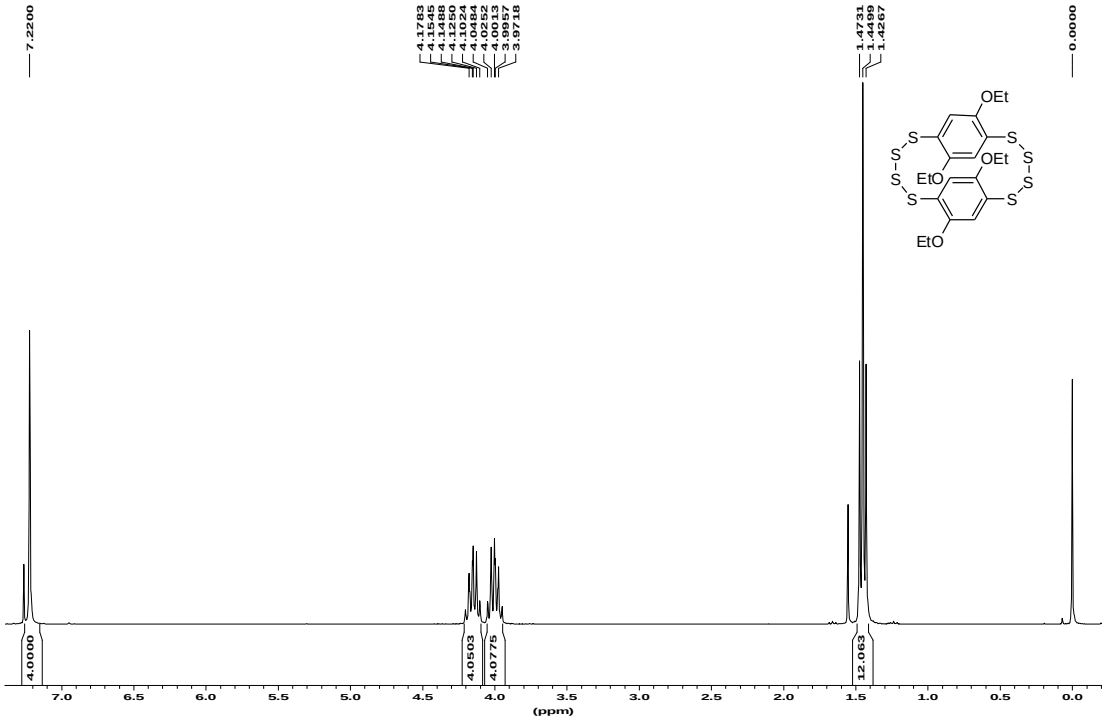
Crystallographic data

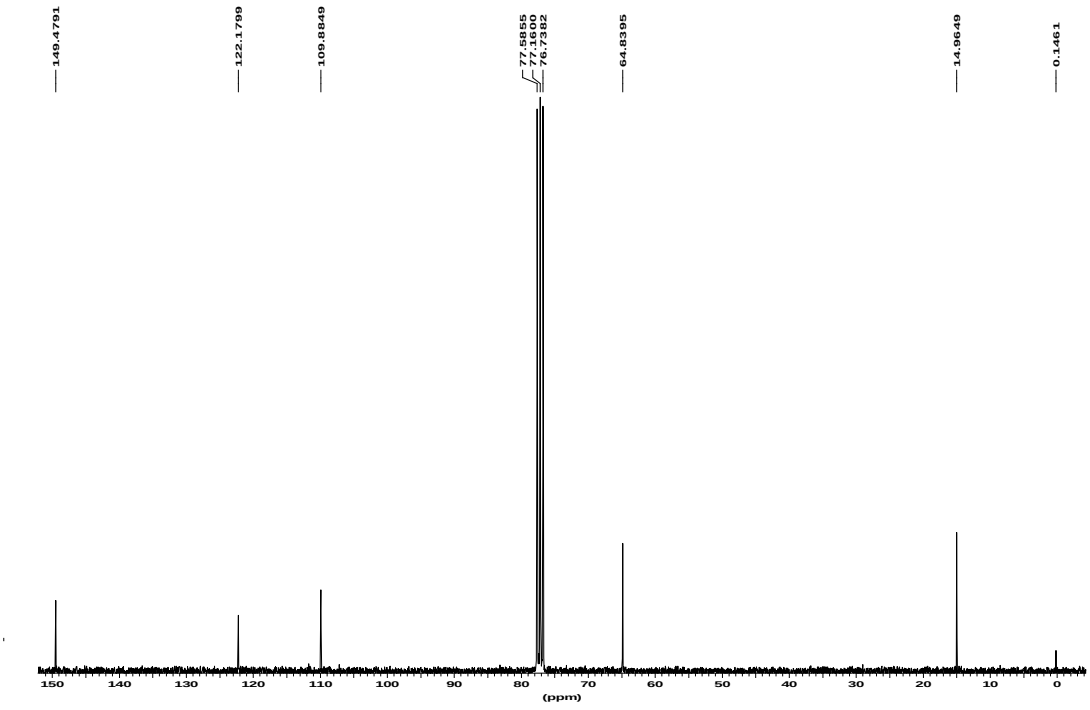
	3a	**4a**	**2b**
Formula	$C_{33}H_{34}Cl_2O_8S_8$	$C_{38}H_{43}NO_8S_4$	$C_{20}H_{24}O_4S_8$
M (g/mol)	885.99	769.97	584.87
Space group	P-1 (no. 2)	C2/c (no. 15)	$P2_1/n$ (no. 14)
a(Å)	12.2168(4)	19.8050(10)	10.1833(5)

b(Å)	14.4704(5)	16.8099(6)	9.4106(4)
c(Å)	23.0473(9)	11.1767(5)	26.6809(12)
α (°)	74.053(3)	90.0	90.0
β (°)	77.801(3)	102.785(5)	95.174(4)
γ (°)	86.239(3)	90.0	90.0
V ($Å^3$)	3829.0(2)	3628.7(3)	2546.4(2)
Z	4	4	4
T (K)	100.00(10)	100.0(2)	100.0(3)
ρ_{calcd}(g cm^{-3})	1.537	1.409	1.526
μ(Mo Kα) (mm^{-1})	0.655	0.317	0.727
F(000)	1832	1624	1216
crystal size (mm^3)	0.2 x 0.1 x 0.1	0.2 x 0.1 x 0.1	0.2 x 0.2 x 0.1
reflections measured	17402	4231	5210
Unique reflections	14749	3679	4593
R(int)	0.0192	0.0000 (twin)	0.0393
wR_2(all data)	0.0843	0.1164	0.0985
R_1 (>2sigma(I))	0.0337	0.0420	0.0391

4. ^{1}H, and ^{13}C NMR spectra.

2b.





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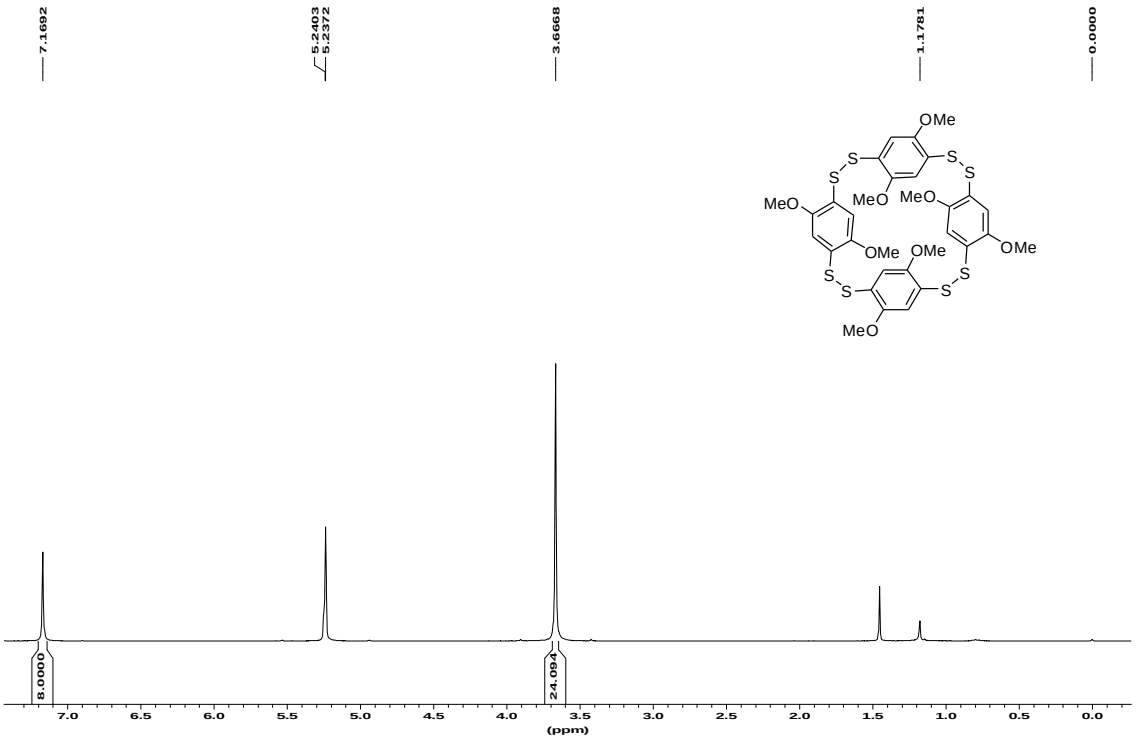
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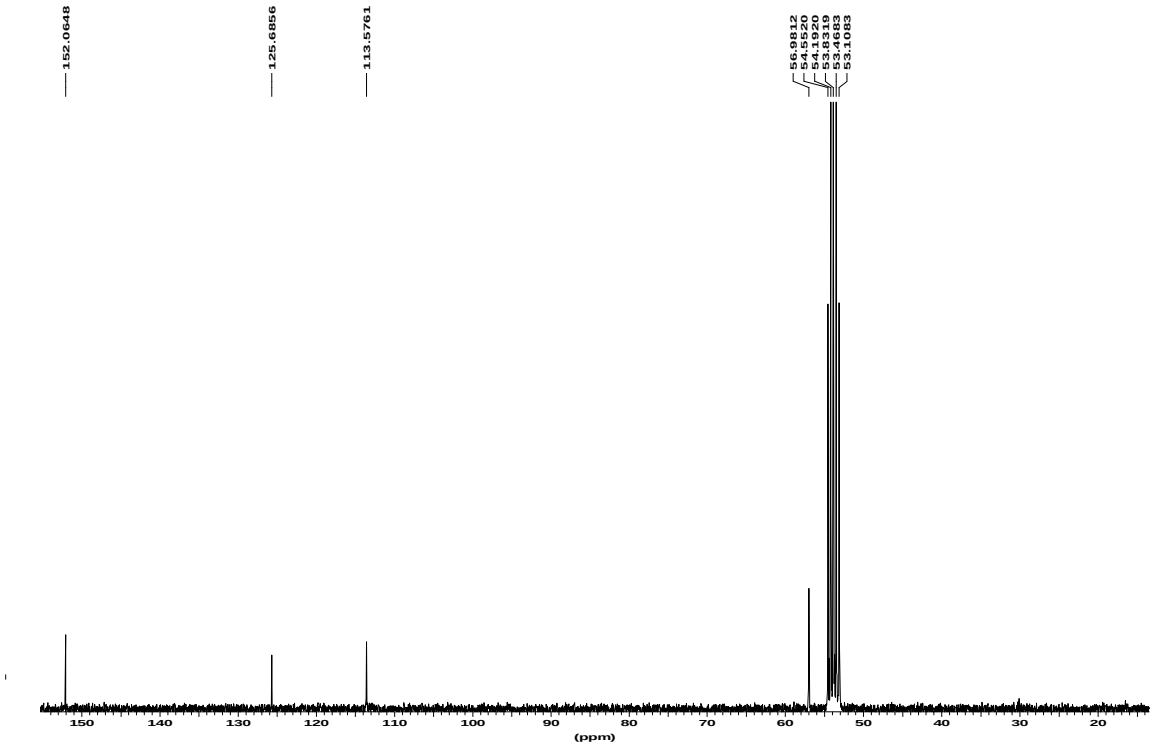
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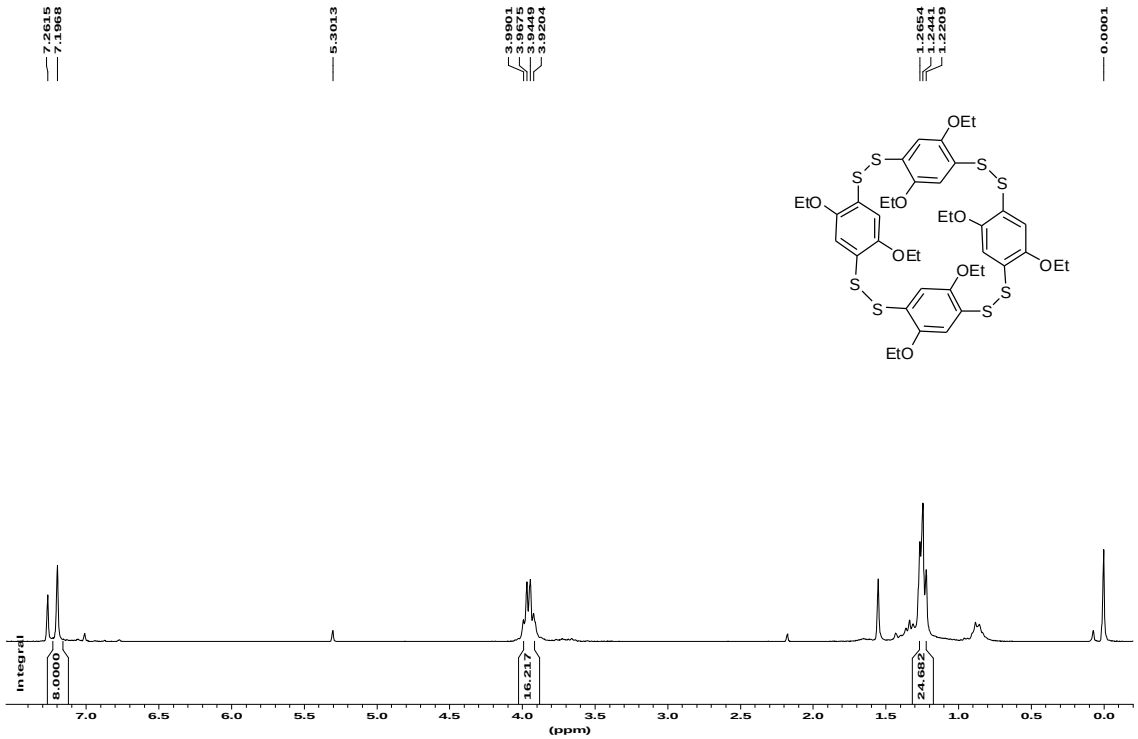
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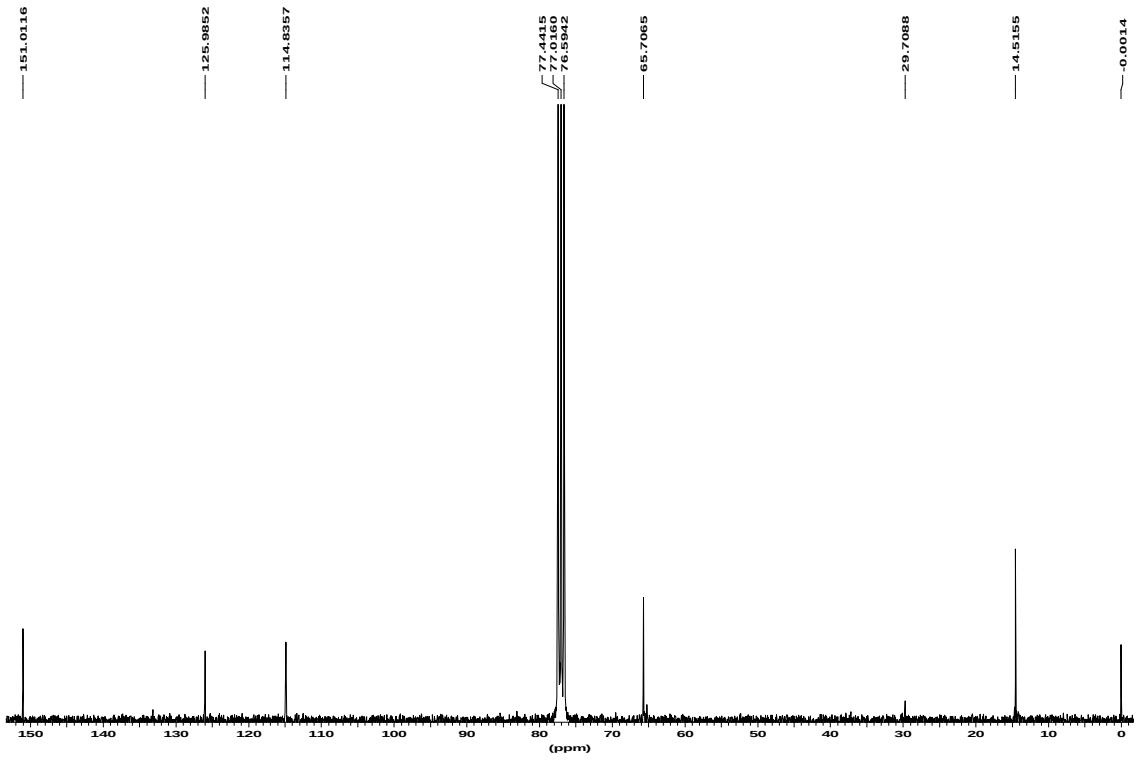
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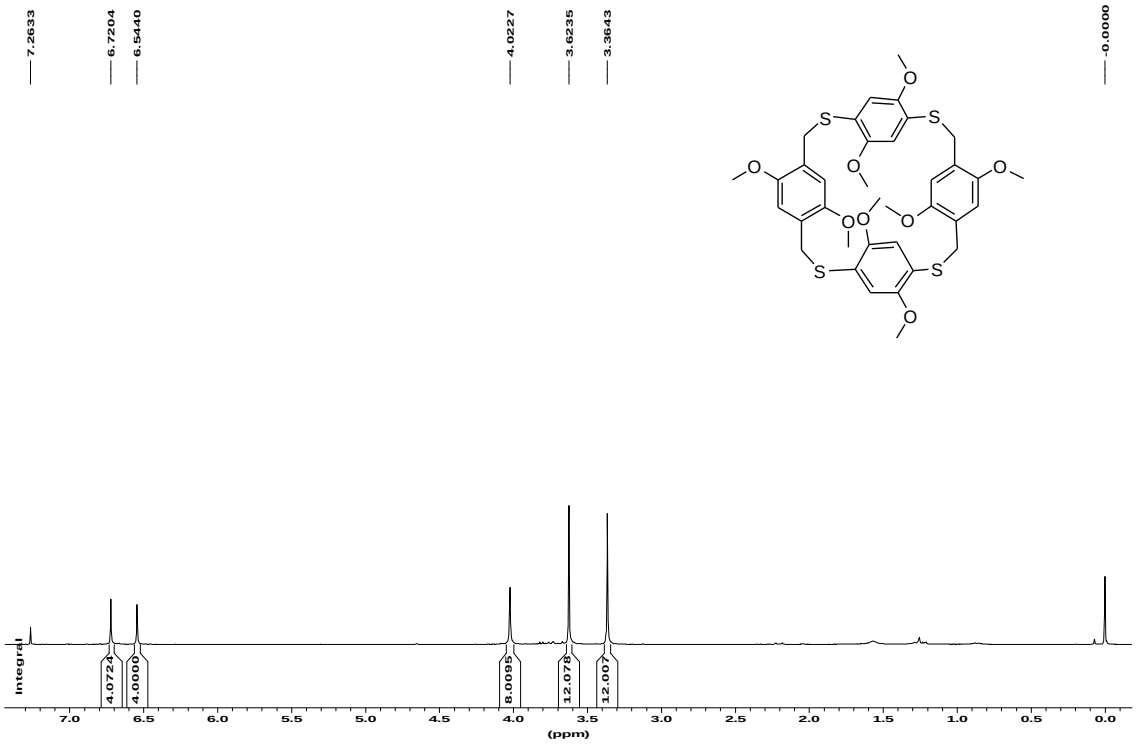
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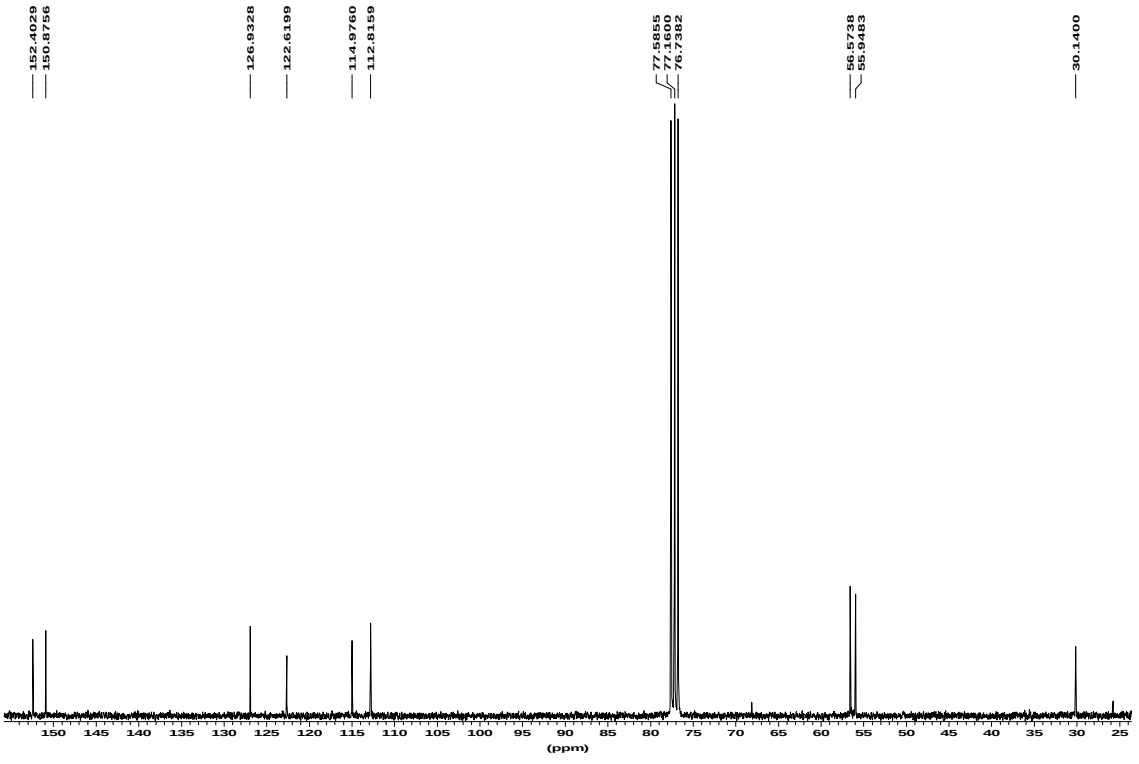
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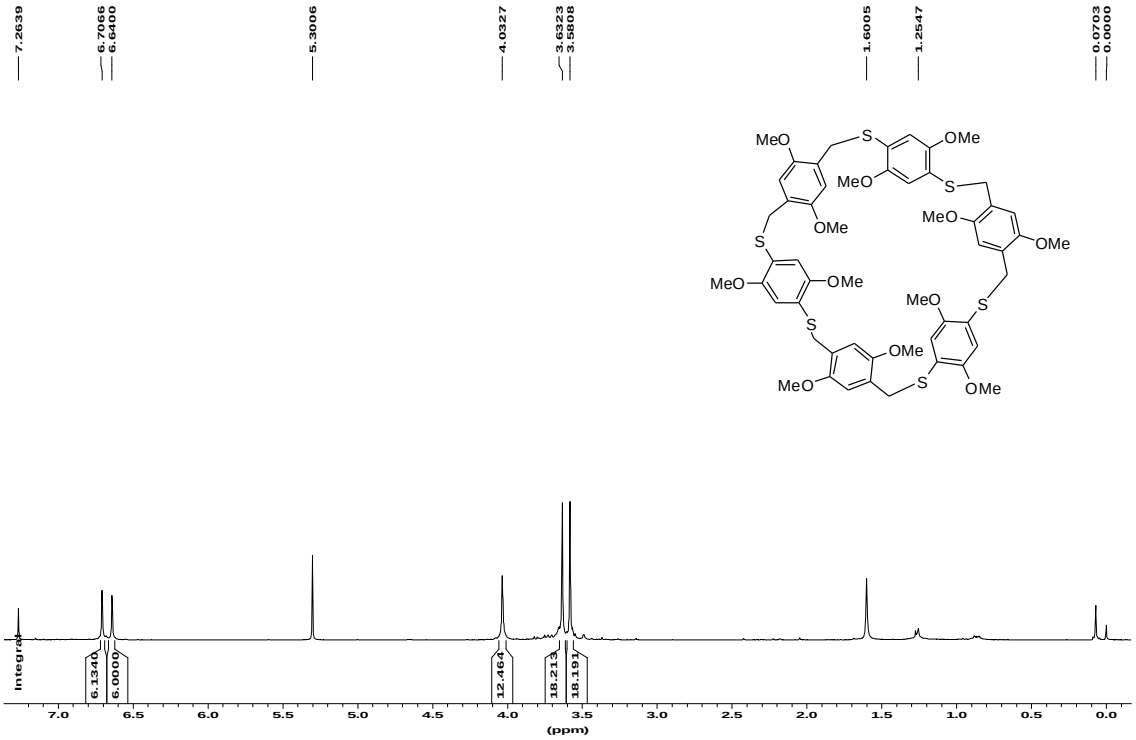
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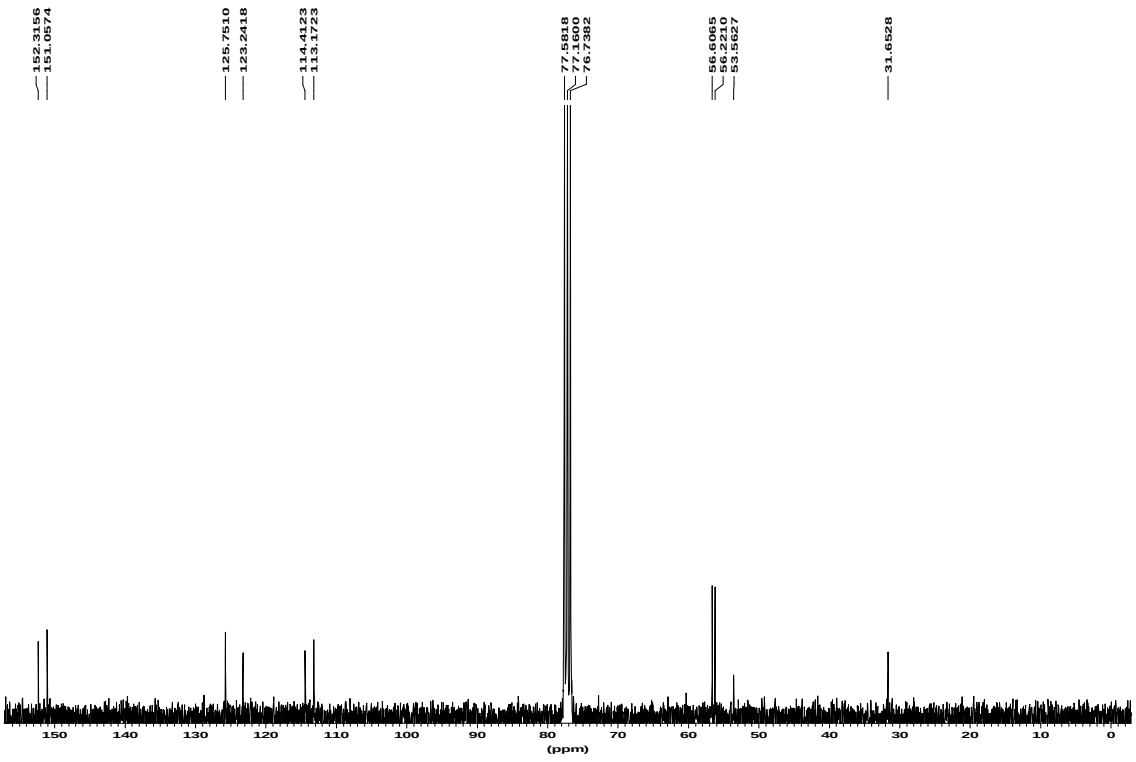
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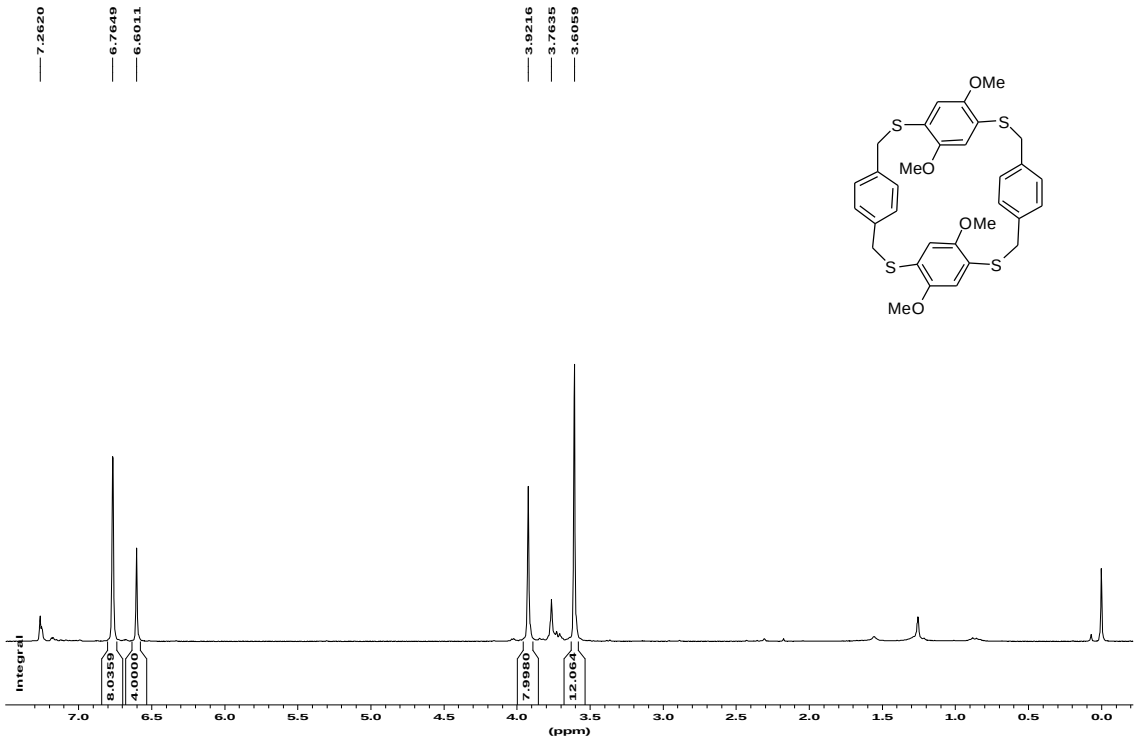
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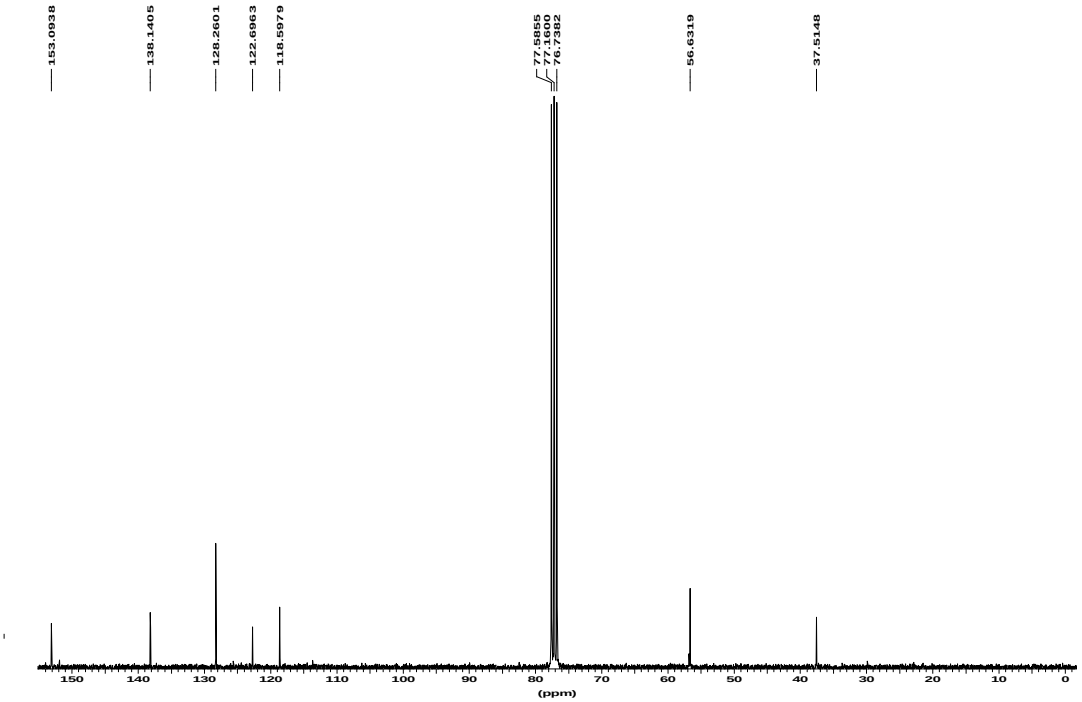
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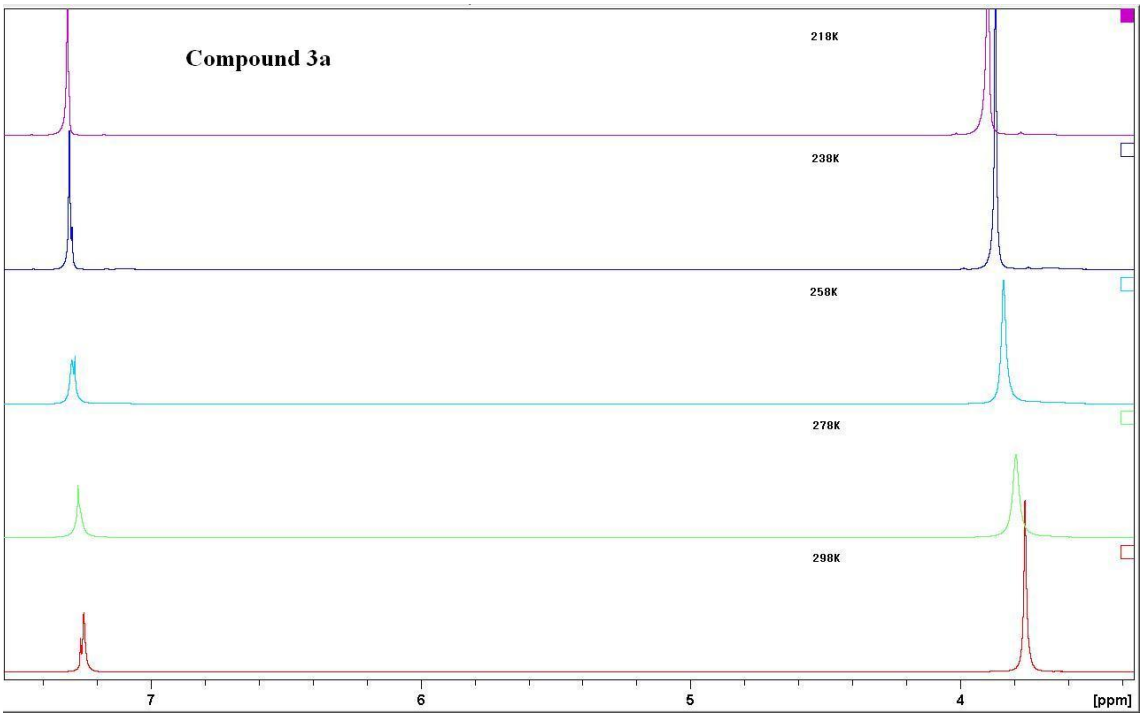
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

Compound **3a** Variable temperature measurement ^{1}H NMR data



Compound **4a** Variable temperature measurement ^{1}H NMR data