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SYNTHESIS AND CHARACTERIZATION OF OXYGEN AND SULFUR BRIDGED AROMATIC MACROCYCLES

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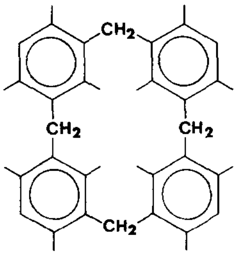
Abstract—The synthesis of nine 16-18-20-22-membered, oxygen and sulfur bridged aromatic macrocycles is reported, and reaction pathways to macrocycles formation are described. Molecular characterization of the nine compounds has been achieved by their mass spectra. Due to the cyclic nature of the compounds analyzed, the mass spectra are of particular interest. The 16-18-membered macrocycles, containing single oxygen and sulfur bridges, display very strong molecular ion intensities, while the 20-22-membered macrocycles, containing double bridges, show lower stability to electron-impact, and the molecular ion intensities are lower. Some of the salient features of the electron fragmentation processes are briefly discussed in the text.

INTRODUCTION

The synthesis of two hydrocarbon aromatic macrocycles, **1** and **2**, has been previously reported.[1]



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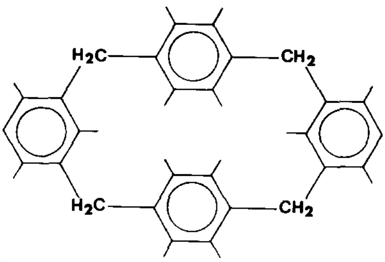


/ = CH_3

2

Because of the general interest[2] in macrocyclic compounds containing oxygen and sulfur heteroatoms, and also because the general lack of information[3] about macrocycles of types **1** and **2**, we became interested in the synthesis and characterization of some oxygen and sulfur bridged aromatic macrocycles. In fact, macrocyclic compounds recently proved very useful for metal complexation work[4,5] and have recently found use in organic chemistry to study certain chemical reactions by solvolyzing cationic species.[6]

We report here the synthesis of a series of aromatic macrocycles containing oxygen and sulfur single and/or double bridges (Schemes 1–3).

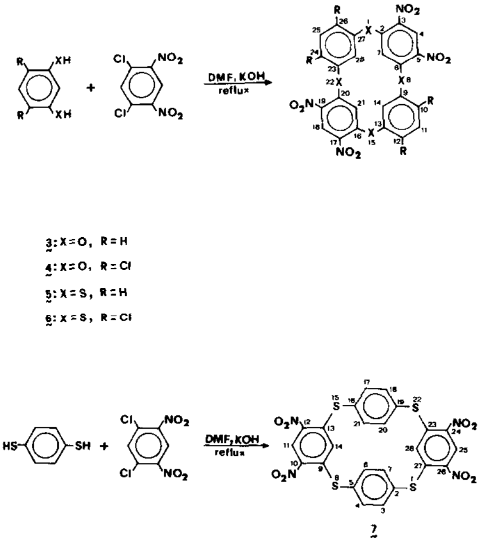
As easily recognized from the inspection of these schemes, the molecular design of these macrocycles was directed to provide 16-18-20-22-membered macrocycles with the purpose to obtain different sizes and shapes of the central complexing hole. Further studies in this laboratory will deal with the complexation properties of this novel class of compounds.

The molecular characterization of the nine macrocycles has been achieved by their mass spectra.

Due to the cyclic nature of these compounds, the mass spectra are of particular interest. The 16- and 18-membered macrocycles containing single oxygen and sulfur bridges display strong molecular ion intensities, while the 20- and 22-membered macrocycles, containing double bridges show lower stability to electron impact and the molecular ion intensities are lower. This behaviour parallels the lower thermal stabilities of the latter macrocycles with respect to the single bridged ones.

RESULTS AND DISCUSSION

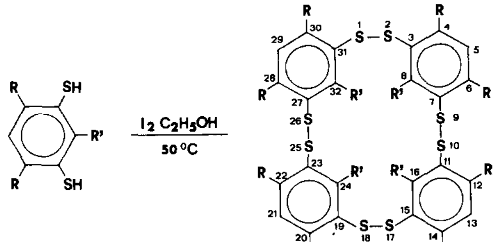
Syntheses. The synthesis of compounds **3**–**7** was achieved by reacting in dilute solution equimolecular amounts of 1,3-dichloro-4,6-dinitrobenzene with opportune diols and dithiols, as shown in Scheme 1.



3: X = O, R = H
4: X = O, R = Cl
5: X = S, R = H
6: X = S, R = Cl

Scheme 1.

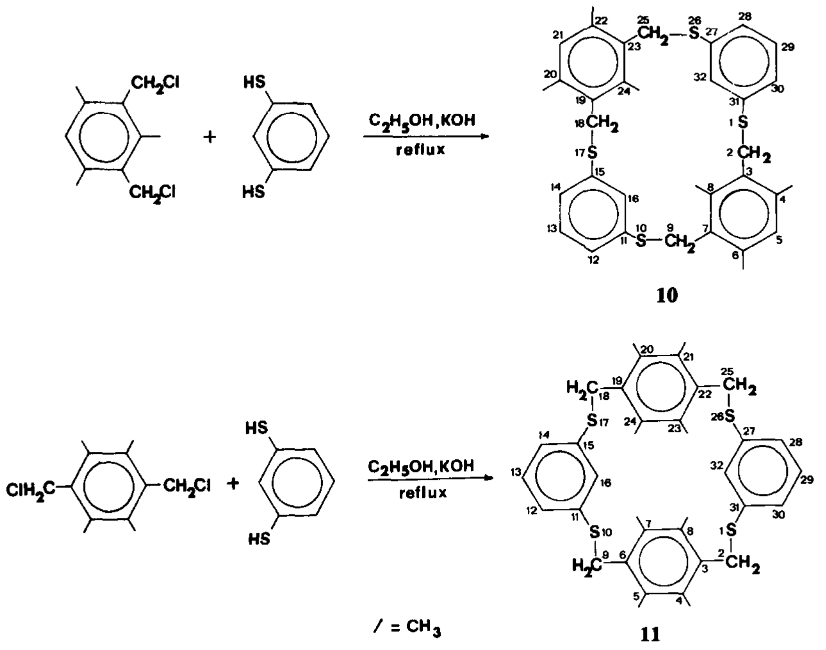
The synthesis of compounds **8** and **9** was achieved by mild oxidation of opportune dithioresorcinol derivatives, as shown in Scheme 2.



8: $R = R' = CH_3$;
9: $R = Cl$, $R' = H$;

Scheme 2.

Compounds **10** and **11** were obtained by reacting in dilute solution equimolecular amounts of dithioresorcinol with 2,4-bischloromethyl-mesitylene and 1,4-bischloromethyl-durene, respectively, as shown in Scheme 3.



10

11

Scheme 3.

The compounds are high melting and present, in general, low solubility in organic solvents. Single bridged oxigenated compounds **3** and **4** are more soluble with respect to sulfur containing ones (**5**–**11**), and dissolve in nitrobenzene, dimethylsulfoxide and tetrahydrofuran.

Due to their low solubility the characterization of the macrocycles synthetised was achieved by mass spectrometry.

Mass spectra. The mass spectrum of the compound **3** is shown in Fig. 1. The main feature of this spectrum, common also to the other single bridged compounds investigated, is that the molecular ion (*m/e* 548) is the base peak. This fact is in agreement with the proposed structure of our compounds, since it is well known that cyclic compounds of this type display strong molecular ion intensities.[7] From the molecular ion the peaks at *m/e* 532, 518 and 502 are formed by loss of O, NO and NO_2. Other fragments are present in the spectrum with lower intensities.

Neglecting peaks at lower masses, symmetrical fragmentation of the macrocyclic ring accounts for the formation of the peak at *m/e* 274.†

Loss of O, NO and NO_2 from the fragment at *m/e* 274 leads to peaks at *m/e* 258, 245 and 229.

The spectra of compounds **4**–**7** are presented in Table 1. The mass spectrum of the compound **4** exhibits a very strong molecular ion at *m/e* 684 accompanied by the characteristic isotopic patterns resulting from the presence of four Cl atoms in the molecule.

As above discussed, also here the peak at *m/e* 342 may be a double carged ion M^{2+} or a fragment $(M/2)^+$.

Loss of O, NO and NO_2 from the molecular ion and from the fragment at *m/e* 342, yields to fragments at *m/e* 670, 656, 640 and 326, 311, 297, respectively.

The mass spectra of the isomeric compounds **5** and **7** are essentially identical. Peaks at *m/e* 582 indicate loss of NO from the molecular ion (*m/e* 612).

Peaks at *m/e* 290 and 276 are formed by loss of S and subsequent loss of NO from the peaks at *m/e* 306 [M^{2+} or $(M/2)^+$].

The spectrum of the compound **6** shows the molecular ion at *m/e* 748. Fragments due to the electron impact fragmentation process can be rationalized as already discussed in the preceding cases.

The proposed structure for the double bridged macrocycles is confirmed by the presence of the molecular ion in the spectra of all the products investigated. However, for these compounds the stability of the macrocycle to electron impact is lower with respect to the single bridged products, and the molecular ion is not the base peak. The preferred fragmentation process of the ring seems to be the cleavage of the S–S or CH_2–S bond.

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†However, this fragment could also be explained as due to a double carged ion.

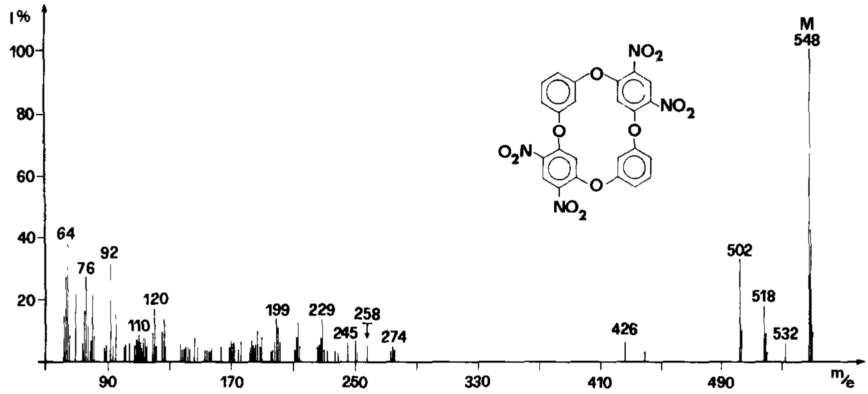

Fig. 1. Mass spectrum (70 eV) of the single bridged macrocycle 3.

Table 1. Mass spectra (70 eV) of compounds **4–7** and **9–11**

Compound	*M*/*e* (I%)
4	688 (56), 687 (30), 686 (100), 685 (24), 684 (85), 670 (4), 656 (6), 640 (13), 345 (5), 344 (4), 343 (6), 342 (5), 326 (4), 311 (5), 297 (5), 181 (12), 180 (7), 179(53), 178 (13), 177 (87), 165 (43), 151 (20), 150 (7), 149 (39), 148 (12), 147 (7), 146 (16), 120 (60), 119 (39), 97 (44), 92 (43), 77 (27).
5	612 (100), 582 (33), 552 (16), 380 (20), 338 (14), 320 (18), 306 (16), 290 (27), 277 (18), 276 (11), 245 (18), 229 (11), 169 (28), 141 (23), 108 (17); 93 (18), 77 (40).
6	752 (62), 751 (29), 750 (100), 749 (20), 748 (66), 720 (19), 715 (10), 604 (8), 511 (11), 494 (17), 464 (17), 392 (14), 230 (12), 212 (18), 203 (21), 168 (13), 120 (16), 106 (37), 93 (47), 76 (10).
7	612 (100), 596 (7), 582 (25), 552 (8), 382 (7), 338 (7), 306 (12), 290 (20), 277 (12), 276 (6), 245 (13), 230 (7), 169 (20), 141 (31), 110 (12), 93 (20), 77 (42).
9	840 (3), 838 (6), 837 (2), 836 (6), 834 (4), 832 (1), 630 (21), 628 (39), 626 (41), 624 (19), 596 (6), 594 (6), 564 (10), 562 (14), 560 (6), 420 (57), 418 (87), 416 (57), 386 (7), 384 (11), 382 (7), 352 (38), 350 (98), 348 (93), 320 (9), 318 (11), 316 (13), 210 (10), 208 (10), 175 (46), 173 (100), 148 (10), 146 (16), 138 (20), 129 (41), 93 (26), 69 (56).
10	572 (12), 431 (13), 286 (40), 271 (4), 253 (4), 177 (12), 145 (100), 133 (16), 119 (8), 105 (20), 91 (25), 77 (8).
11	600 (9), 461 (4), 442 (3), 331 (2), 300 (7), 191 (7), 160 (100), 145 (10), 119 (3), 105 (5), 91 (7), 77 (2).

For the compound **8** (Fig. 2) the spectrum shows the molecular ion at *m*/*e* 728 and the peaks at *m*/*e* 546 and *m*/*e* 364 arising from the cleavage of the S–S bond. The ions at *m*/*e* 151, 213 and 331 indicate cleavage of the C_{Ar}–S bond.

The mass spectra of compounds **9–11** are reported in Table 1. In the spectrum of the compound **9** besides the molecular ion at *m*/*e* 832, peaks at *m*/*e* 624, 416 and 208 are present, corresponding to cleavage of the S–S bond. The base peak (*m*/*e* 173) is formed by loss of Cl from the ion at *m*/*e* 416 and rearrangement of two H atoms.

In the spectra of compounds **10** and **11**, cleavage of the S-CH_2 bond accounts for formation of the more intense peaks.

In fact the spectrum of the compound **10** shows peaks at *m*/*e* 431 ($M^+ - C_6H_5S_2$), 286 $(M/2)^+$ and 145 $[C_6H(CH_3)_3(CH_2)_2]^+$ originating by cleavage of this type. The presence of the peaks with low relative abundance at *m*/*e* 177 and 253 results from the cleavage of the C_{Ar}–S bond. The peak at *m*/*e* 572 is the molecular ion.

As predictable, the fragmentation pattern for compound **11** is similar to that of the compound **10**. Also here are present a peak derived from molecular ion (*m*/*e* 600) by loss of $C_6H_4S_2$ and a peak at *m*/*e* 300 due to $(M/2)^+$. The base peak at *m*/*e* 160 is due to the fragment $[C_6(CH_3)_4(CH_2)_2]^+$. Other peaks with lower abundance at *m*/*e* 191 and 331 are formed by cleavage of the C_{Ar}–S bond.

EXPERIMENTAL

Materials and analytical procedures. All solvents and available organic materials were commercial products purified by standard procedures. 1,3-Dichloro-4,6-dinitrobenzene,[8] dithioresorcinol,[9] 1,4-benzenedithiol,[10] 4,6-dichloro-dithioresorcinol,[11] 2,4-

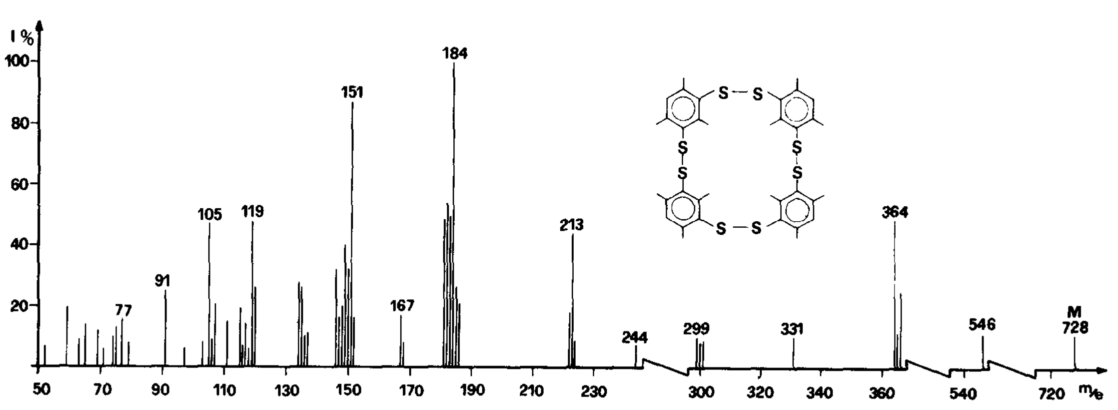

Fig. 2. Mass spectrum (70 eV) of the double bridged macrocycles **8**.

bischloromethylmesitylene[12] and 1,4-bischloromethyldurene[13] were prepared according to literature.

Mass spectra were obtained at 70 eV by direct insertion into the ion source of a Varian MAT CH-711 double focusing mass spectrometer coupled to a Varian 620 computer. The evaporation temps of the compounds investigated were 300–350°.

NMR spectra were recorded with a Varian EM 360 instrument with TMS as internal standard.

Elemental analyses were obtained commercially.

Syntheses

Mesitylene-2,4-disulfochloride. To mesitylene, (30 g, 0.25 mole) cooled in ice bath, was added dropwise $ClSO_3H$ (160 g, 1.37 mole) with stirring. Half-addition produced solidification of reaction mass, that dissolved in additional $ClSO_3H$. After the addition of $ClSO_3H$ was complete, the mixture was allowed to stand at room temp. overnight, then poured into ice. The white product obtained was filtered, dried and washed with ethyl ether. The residue recrystallized from petroleum ether (b.p. 70–120°) as white needles: m.p. 123–24°. (Found: C, 34.52; H, 3.39; Cl, 22.51; S, 20.89. Calc. for $C_9H_{10}Cl_2O_4S_2$: C, 34.07; H, 3.18; Cl, 22.35; S, 20.22%.) NMR data (CS_2) gave δ values of 7.23 (1 H Ar), 3.07 (3H CH_3), 2.76 (6H CH_3).

Mesitylene-2,4-dithiol. To a well-stirred mixture of mesitylene-2,4-disulfochloride (30 g, 0.09 mole) and powdered Zn (50 g), cooled in ice bath, 37% HCl (100 ml) was added dropwise. When the addition was accomplished, the mixture was kept warm for 30 min, and then distilled in stream. Extraction with benzene, drying with Na_2SO_4 concentration *in vacuo* afforded white crystals: m.p. 63–64°. (Found: C, 58.82; H, 6.15; S, 35.01. Calc. for $C_9H_{12}S_2$: C, 58.64; H, 6.56; S, 34.79%). Mass spectrum (70 eV) m/e (rel. intensity) 184 (100). NMR data (CCl_4) gave δ values of 6.85 (1 H Ar), 3.01 (2H SH), 2.52 (3H CH_3), 2.28 (6H CH_3).

1,8,15,22 - *Tetraoxa*[1,1,1,1] - 3,5,17,19 - *tetranitro - metacyclophane* (**3**). To a boiling soln of 1,3-dichloro-4,6-dinitrobenzene (2.37 g; 0.01 mole) in 100 ml of N,N-dimethylformamide (DMF) was added dropwise with stirring a soln of resorcinol (1.1 g; 0.01 mole), containing KOH (1.12 g; 0.02 mole) in 50 ml DMF. When the addition was complete (1 hr), the mixture was boiled an additional hr, and then cooled and concentrated. A brownish solid separated when the residue was poured in 400 ml water. This was filtered off, washed with EtOH and ethyl ether and dried. The crude product recrystallized from 1,2-dichlorobenzene gave 0.68 g (yield 25%) of **3** as brownish microcrystals: m.p. > 350°. (Found: C, 53.02; H, 2.17; N, 10.07. Calc. for $C_{24}H_{12}N_4O_{12}$: C, 52.56; H, 2.20; N, 10.22%).

1,8,15,22 - *Tetraoxa* [1,1,1,1] - 3,5,17,19 - *tetranitro* - 10,12,24,26 - *tetrachloro-metacyclophane* (**4**). This compound was synthesized in the same way as **3**, from equimolecular amounts of 4,6-dichlororesorcinol and 1,3-dichloro-4,6-dinitrobenzene, and was obtained as light yellow microcrystals (yield 28%): m.p. >350°. (Found: C, 41.97; H, 1.22; Cl, 20.83; N, 8.28. Calc. for $C_{24}H_8Cl_4O_{12}$: C, 42.00; H, 1.18; Cl, 20.67; N, 8.16%).

1,8,15,22 - *Tetrathia*[1,1,1,1] - 3,5,17,19 - *tetranitro - metacyclophane* (**5**). To a boiling soln of 1,3-dichloro-4,6-dinitrobenzene (2.37 g; 0.01 mole) in 100 ml of DMF was added dropwise with stirring a soln of dithioresorcinol (1.42 g; 0.01 mole) containing KOH (1.12 g; 0.02 mole) in 50 ml of DMF. A yellow ppt was immediately obtained. The mixture was refluxed for 30 min. The product was filtered from the hot soln, washed with water, EtOH, ethyl ether and dried (yield 65%). Recrystallization from nitrobenzene afforded yellow crystals: m.p. >350°. (Found: C, 47.18; H, 2.20; N, 9.22; S; 21.02. Calc. for $C_{24}H_{12}N_4O_8S_4$: C, 47.06; H, 1.96; N, 9.16; S, 20.90%).

1,8,15,22-*Tetrathia*[1,1,1,1] - 3,5,17,19 - *tetranitro* - 10,12,24,26 - *tetrachloro - metacyclophane* (**6**). This compound was synthesized in the same way as **5**, from equimolecular amounts of 4,6-dichloro-dithioresorcinol and 1,3-dichloro-4,6-dinitrobenzene, and was obtained as a yellow powder (yield 48%): m.p. > 350°. (Found: C, 38.37; H, 1.13; Cl, 19.10; N, 7.35; S, 17.30. Calc. for $C_{24}H_8Cl_4N_4O_8S_4$: C, 38.41; H, 1.07; Cl, 18.90; N, 7.46; S, 17.08%).

1,8,15,22 - *Tetrathia*[1,1,1,1] - 3,5,17,19 - *tetranitro - metapara - cyclophane* (**7**). This compound was synthesized in the same way as **5**, from equimolecular amounts of 1,4-benzenedithiol and 1,3-dichloro-4,6-dinitrobenzene. The product was obtained as yellow crystals (yield 70%) : m.p. >350°. (Found: C, 47.24; H, 2.30; N, 9.31; S, 20.93. Calc. for $C_{24}H_{12}N_4O_8S_4$: C, 47.06; H, 1.96; N, 9.16; S, 20.90%).

1,2,9,10,17,18,25,26 - *Octathia*[2,2,2,2] - 4,6,8,12,14,16,20,22, - 24,28,30,32 - *dodecamethyl - metacyclophane* (**8**). To a hot soln of mesitylene-2,4-dithiol in benzene, was added dropwise with stirring a N/10 solution of iodine until the brown colour of iodine was persistent. The yellowish ppt obtained was filtered off, washed with a dil soln of thiosulphate, then with water, EtOH and dried. The crude product recrystallized from 1,2-dichlorobenzene gave light yellow microcrystals in good yield: m.p. 315–16°. (Found: C, 59.72; H, 5.68; S, 35.82. Calc. for $C_{36}H_{40}S_8$: C, 59.30; H, 5.52; S, 35.18%).

1,2,9,10,17,18,25,26 - *Octathia*[2,2,2,2] - 4,6,12,14,20,22, - 28,30 - *octachloro-metacyclophane* (**9**). This compound was synthesized in the same way as **8**, from 4,6-dichloro-dithioresorcinol. The crude product recrystallized from 1,2-dichlorobenzene gave light yellow microcrystals in good yield: m.p. 338–39°. (Found: C, 34.75; H, 1.00; Cl, 33.82; S, 30.87. Calc. for $C_{24}H_8Cl_8S_8$: C, 34.46; H, 0.96; Cl, 33.91; S, 30.66%).

1,10,17,26 - *Tetrathia*[2,2,2,2] - 4,6,8,20,22,24 - *hexamethyl - metacyclophane* (**10**). To a boiling soln of 2,4 - bischloromethylmesitylene (2.17 g; 0.01 mole) in 150 ml EtOH, was added dropwise with stirring a soln of dithioresorcinol (1.42 g; 0.01 mole), containing KOH (1.12 g; 0.02 mole) in 50 ml EtOH. When the addition was complete (1 hr), the mixture was refluxed an additional hr. The white ppt was filtered off from the hot soln, washed with water and dried. The crude product recrystallized from tetraline as white crystals: m.p. 240–42°. (Found: C, 71.07; H, 6.38; S, 22.45. Calc. for $C_{34}H_{36}S_4$: C, 71.28; H, 6.33; S, 22.39%).

1,10,17,26 - *Tetrathia*[2,2,2,2] - 4,5,7,8,20,21,23,24 - *octamethyl - metapara - cyclophane* (**11**). To a boiling soln of dithioresorcinol (1.42 g; 0.01 mole), containing KOH (1.12 g; 0.02 mole), in 300 ml EtOH, was added dropwise with stirring a soln of 1,4-bischloromethyldurene (2.31 g; 0.01 mole) in 100 ml of ethanol-dioxane (4 : 1). When the addition was complete (2 hr), the mixture was refluxed an additional hr. The white ppt was filtered off from the hot soln, washed with water, and dried. The crude product recrystallized from tetraline as white crystals: m.p. 293–95°. (Found: C, 72.02; H, 6.78; S, 21.15. Calc. for $C_{36}H_{40}S_4$: C, 71.95; H, 6.70; S, 21.34%).

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