Cyclic Ketones via the Reaction of Dithiols with 1,3-Dichloroacetone. An Unexpected Base-Catalyzed Rearrangement of α,α'-Dithia Ketones

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Received October 5, 1992

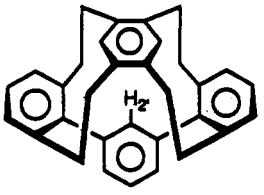
The reaction of dithiols with 1,3-dichloroacetone under high dilution and catalyzed by cesium carbonate in DMF affords macrocyclic ketones in good yield. Examples of functionalized cyclophanes prepared in this way include **10**, **15**, **16**, **19**, **21**, and **24**. With NaOMe/MeOH as the base, dithiol **14** gave ring-contracted ketone **17** in low yield, in addition to the expected **15** and **16**. Ketone **17** was the sole product, in good yield, from **14** and 1,1-dichloroacetone. NaOMe/MeOH also brought about the novel ring contraction of **10** to **11** and **11** to **12**. X-ray structures of **10**, **12**, **16**, **19**, and **21** are briefly described. Possible mechanisms for the formation of **17** from **14** and for the rearrangement of **10** → **11** → **12** are discussed.

We accidentally discovered an unexpected and, as far as we are aware, unprecedented base-catalyzed conversion of an α,α'-dithia ketone **1** to a dithiaketal **2** through extrusion of the elements of ketene. Unfortunately, the

$$\underset{\mathbf{1}}{\mathrm{RSCH_2C(O)CH_2SR}} \xrightarrow{\mathrm{NaOMe}} \underset{\mathbf{2}}{\mathrm{RSCH_2SR}} \qquad (1)$$

reaction so far seems to be unique to rather special R structures. To explain how the reaction was discovered it is necessary to describe what we were trying to do, and what actually happened.

We recently described a series of cappedophanes[1] based on the easily assembled[2] *m*-terphenyl framework. These compounds have some interesting structural features. For example, aryl proton $H_{2'}$ in cappedophane **3** appears at δ 3.77, strongly shielded by the capping aryl ring. We wanted



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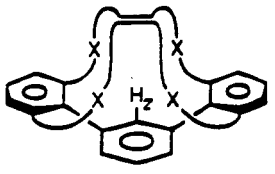
to use this type of system to probe the electron density of a carbon–carbon double bond (and later, of the corresponding epoxides and cyclopropanes), oriented either as in **4** or **5**, using in each case the chemical shift of $H_{2'}$.



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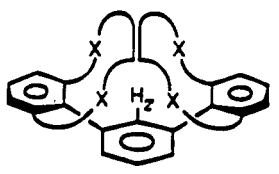

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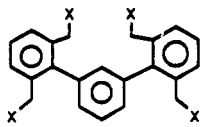
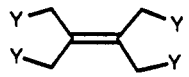
Unfortunately, direct approaches to **4** and **5** have so far failed. For example, the reaction of tetrabromide **6**[1b] with tetrathiol **7**,[3] or of tetrathiol **8**[1b] with tetrabromide **9**[4] failed to give isolable yields of the desired cappedophanes.[5]



6 (X = Br)
8 (X = SH)

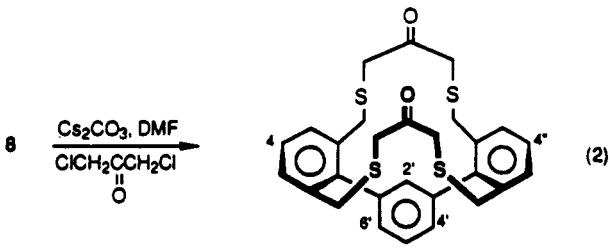


7 (Y = SH)
9 (Y = Br)

We next sought an indirect route to **5** through diketone **10**, hoping that the carbonyl carbons could subsequently be connected via a McMurry or other type of reduction. It was during the synthesis of diketone **10** that we discovered the unexpected and novel rearrangement in eq 1.

Results and Discussion

Treatment of tetrathiol **8** with 1,3-dichloroacetone in a suspension of cesium carbonate in dimethylformamide (DMF)[6] gave the desired diketone **10** in 66% yield. The



(2)

10 (66%)

† To whom inquiries regarding X-ray structures should be directed.

(1) (a) Vinod, T. K.; Hart, H. *J. Am. Chem. Soc.* **1988**, *110*, 6574–6575. (b) Vinod, T. K.; Hart, H. *J. Org. Chem.* **1990**, *55*, 881. (c) Vinod, T. K.; Hart, H. *Ibid.* **1991**, *56*, 5630–5640.

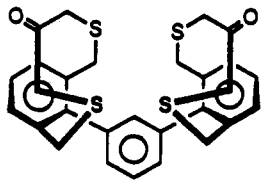
(2) Du, C.-J. F.; Hart, H.; Ng, K.-K. D. *J. Org. Chem.* **1986**, *51*, 3162–3165. Du, C.-J. F.; Hart, H. *Ibid.* **1987**, *52*, 4311–4314. Hart, H,; Ghosh, T. *Tetrahedron Lett.* **1988**, *29*, 881–884. Vinod, T. K.; Hart, H. *Ibid.* **1988**, *29*, 885–888.

(3) Prepared in 62% yield from 2,3-bis(bromomethyl)-1,4-dibromo-2-butene **9** via the tetrakis-isothiouronium salt and base: mp 65–68 °C; ^{1}H NMR δ 1.71 (t, *J* = 7.4 Hz, 4 H, –S*H*), 3.37 (d, *J* = 7.4 Hz, 8 H, –CH_2); ^{13}C NMR δ 24.25, 135.52. Tetrathiol **7** is referred to only once in the literature [Schriver, G. W.; Thomas, T. A. *J. Am. Chem. Soc.* **1987**, *109*, 4121], and although this paper describes its very interesting reaction with **9**, no description of its preparation or properties are given. We found it difficult to purify, and did not obtain an elemental analysis (unpublished results with R. S. Grewal and J.-J. Chiu).

(4) Cope, A. C.; Kagan, F. *J. Am. Chem. Soc.* **1958**, *80*, 5499–5502.

0022-3263/93/1958-1553$04.00/0

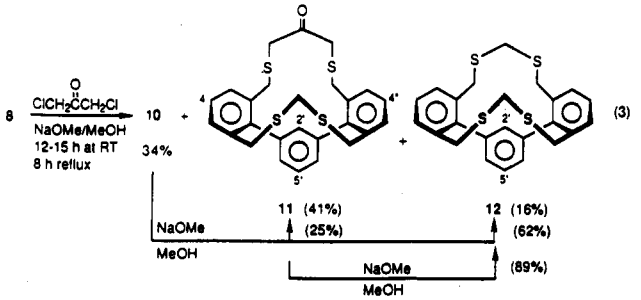
C_{2v} symmetry of **10** was clear from its ^1H NMR spectrum, which showed four four-proton doublets for the four sets of geminally coupled methylene protons, as well as a two-proton doublet of doublets at δ 7.15 for $H_{4',6'}$ and a one-proton meta-coupled triplet at δ 7.41 for $H_{2'}$. The ^{13}C NMR spectrum of **10** showed only two aliphatic carbon peaks (δ 34.9, 40.0) and one carbonyl carbon peak (δ 199.6). The alternate but highly strained and hence unlikely structure **10'**, which has the same symmetry as **10** and



10'

could be formed by the alternative mode of sulfur bridging, was ruled out by an X-ray structure determination and by further transformations (vide infra).

The surprise came when we used sodium methoxide in methanol in place of Cs_2CO_3/DMF to couple **8** with 1,3-dichloroacetone. Two other products, **11** and **12**, were obtained in addition to **10**. Their structures were deduced from their NMR spectra.



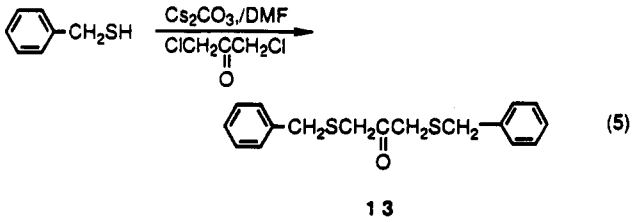
Ketone **11** ($\nu_{C=O}$ 1713 cm^{-1}) showed, in its ^1H NMR spectrum, three four-proton AB quartets and one two-proton AB quartet as required by its C_s symmetry. Consistent with this assignment, the aryl protons occur in four two-proton and two one-proton sets. The ^{13}C NMR spectrum of **11** showed four methylene carbon signals, one carbonyl carbon signal, and 10 signals for the aryl carbons, as required.

Bis-thioketal **12**, which like **10** has C_{2v} symmetry, showed in its ^1H NMR spectrum one four-proton and one eight-proton AB quartet for the two sets of methylene protons and in its ^{13}C NMR spectrum two aliphatic and eight aromatic carbon signals, as required. The structure of **12** was unequivocally established by its independent synthesis from tetrathiol **8** and formaldehyde (eq 4),[7] and by an X-ray structure (vide infra).

$$8 \xrightarrow[\substack{CHCl_3,\ HCl\\ -20\ ^\circ C\ to\ rt}]{1,3,5\text{-trioxane}} \mathbf{12}\ (69\%) \qquad (4)$$

Separate treatment of **10** with CH_3ONa/CH_3OH gave **11** (25%) and **12** (62%), and **11** was similarly converted to **12** (89%). Therefore, these products are formed sequentially by the base-catalyzed rearrangement of ketones **10** and **11**.

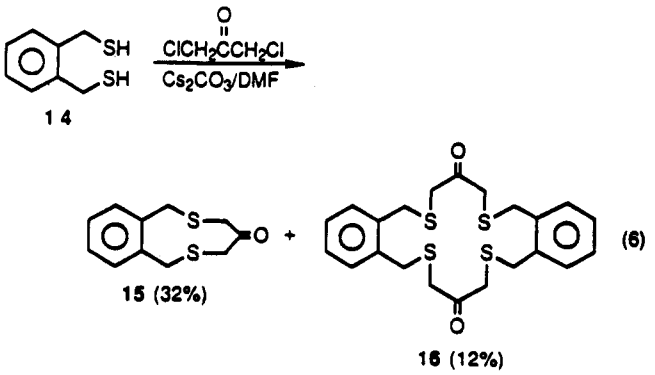
Test of Generality. As the first model for **10** (or **11**), to test the generality of the rearrangement, we chose 1,3-bis(benzylthio)acetone (**13**), prepared from benzylmercaptan and 1,3-dichloroacetone as shown. However, treat-



13

ment of **13** with $NaOCH_3/CH_3OH$ either at room temperature or at reflux gave only recovered starting material, and no evidence of formaldehyde bis(benzylthio)ketal.

Thinking that perhaps a cyclic structure might be required, we studied the reactions of *o*-, *m*-, and *p*-xylylenedithiols with 1,3-dichloroacetone. Reaction of the ortho-isomer **14**, using Cs_2CO_3/DMF, gave monoketone **15** and the macrocyclic diketone **16** in the yields shown.



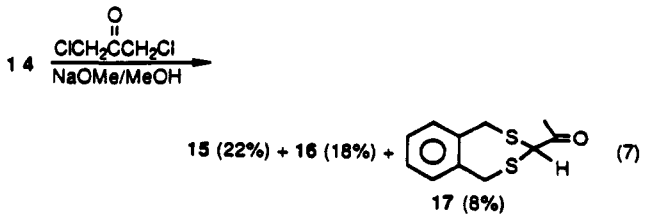
14

15 (32%)

16 (12%)

The symmetry of both products was clear from their NMR spectra (see Experimental Section) and an X-ray structure confirmed the macrocyclic nature of **16**.

When the same condensation was carried out using sodium methoxide in methanol, a third product **17** was obtained. The structure of **17** was evident from its NMR



17 (8%)

spectra. The methyl and methine protons appeared as singlets (δ 2.40 and 4.51, respectively), and the benzylic methylene protons, which in **15** gave a sharp singlet at δ 3.88, now appeared as two geminally coupled doublets at δ 3.61 and δ 4.76 (J = 15 Hz). The IR and ^{13}C spectra both showed the presence of a carbonyl group. Finally, inde-

(5) The reaction of **7** and **8** gave mainly polymer, but traces of a product with a single proton at δ 5.66 (t, J = 1.5 Hz) which may be the aryl proton at $C_{2'}$ of the *m*-terphenyl moiety of **4** or **5**, shielded by the capping double bond. Unfortunately, we were unable to obtain sufficient amounts for full characterization (unpublished results with R. S. Grewal).

(6) Klieser, B.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 618–619.

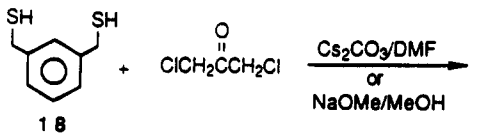
(7) Surprisingly, similar reactions with acetaldehyde or benzaldehyde failed to give the corresponding bis-thioketals.

(8) Vinod, T. K.; Hart, H. *J. Org. Chem.* **1990**, *55*, 5461–5466.

pendent synthesis via the reaction of 14 with 1,1-dichloroacetone gave 17 in good yield.

$$14 + CH_3C(O)CHCl_2 \xrightarrow[\text{or NaOMe/MeOH}]{Cs_2CO_3/DMF} 17\ (61\text{–}85\%) \quad (8)$$

In contrast with *o*-xylylenedithiol, the meta- and para-isomers gave only the macrocyclic diketones 19 and 21, respectively, regardless of whether the base was cesium carbonate or sodium methoxide. IR and NMR spectra were consistent with the assigned structures, which were confirmed by X-ray structure determinations.



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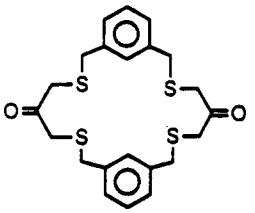
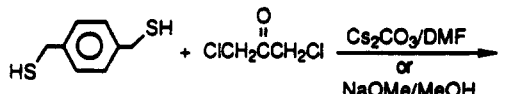


19 (50-55 %) (9)



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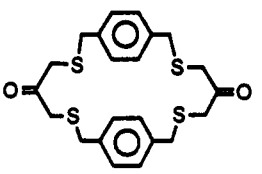
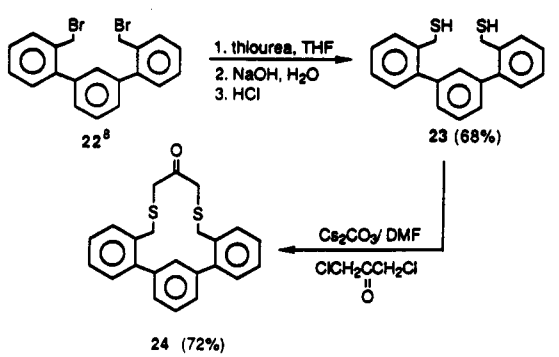


21 (45-55%) (10)

Finally, the monocyclic analogue of 10 (i.e., 24) was synthesized from bis(bromomethyl)terphenyl 22 as shown. The ^1H NMR spectrum of 24 showed two four-



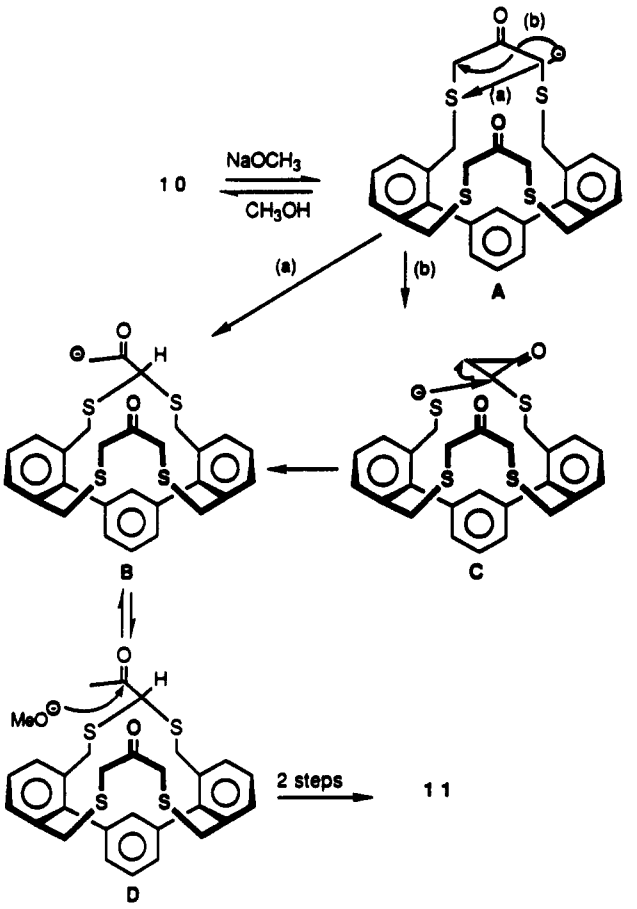
22[8] 23 (68%) (11)

24 (72%)

proton singlets for the two sets of methylene protons, and the ^{13}C NMR spectrum showed 13 signals as required. It seems quite remarkable that despite the close structural similarity of 24 to 10, it did not undergo ring contraction when treated with NaOMe/MeOH, either at room temperature or at reflux.

Mechanisms. The base-catalyzed rearrangement of 10 → 11 and 11 → 12 (eq 3) appears to be unique, and at this stage we can only speculate briefly about the mechanism. Two possibilities are shown in Scheme I. Removal

Scheme I



of an α-proton by the base should give anion **A**,[9] which might then displace directly on sulfur to give **B** (path a) or arrive at **B** via a Favorskii-type intermediate **C** (path b), although there seems to be no special advantage to the latter route. Intermediate **B** might eliminate ketene to give the anion of 11 directly or more likely accept a proton to give **D** which might then be cleaved by methoxide attack at the carbonyl group.[10]

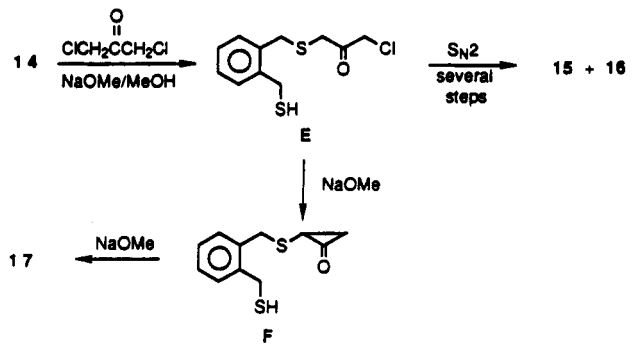
The formation of 17 in the methoxide-catalyzed reaction of dithiol 14 with 1,3-dichloroacetone (eq 7) appeared to support the mechanisms in Scheme I, since 17 is an analogue of the proposed intermediate **D**. However, further study showed that the reactions are only superficially related. For example, separate treatment of 15 with NaOMe/MeOH failed to bring about ring contraction to 17; the starting 15 was recovered (94%). Furthermore, treatment of ketone 17 with either NaOMe/MeOH or *t*-BuOK/EtOH at room temperature or reflux did not cleave the acetyl group, thus failing to provide an analogy for the final mechanistic step (**D** → 11).

Indeed, these results raise another mechanistic question, how is 17 formed (eq 7)? Since neither 15 nor 16 are converted to 17 by NaOMe/MeOH the latter must be formed directly. One possibility is shown in Scheme II. Following monoalkylation, methoxide may cause 1,3-elimination in intermediate **E** to give cyclopropanone intermediate **F** which can then undergo cyclization to 17. Apparently methoxide (but not cesium carbonate) allows

(9) 10 contains two different sets of α-protons, and it is not known whether proton removal is stereoselective.

(10) There is ample precedent for the cleavage of α,α-disulfenylated ketones, particularly if strained. See, for example: Trost, B. M. *Chem. Rev.* **1978**, *78*, 363–382.

Scheme II



a path such as this to compete with the S_N2 displacements that furnish the main products, **15** and **16**.[11]

X-ray Studies. To confirm structures and also to study conformations which might in some way rationalize the propensity of **10** (and **11**) to ring-contract with base, single-crystal X-ray structures were determined for **10**, **12**, **16**, **19**, and **21**.[12] In each case the structures assigned on the basis of spectral data were confirmed (Figures 1–5).

The structure of **10** is unusual in that one of the two dithia ketone arms (from S6 through C11) that connect the outer rings of the *m*-terphenyl moiety is disordered (Figure 1). The structure was solved and refined (R = 0.041) with an occupancy ratio of 0.5/0.5 for the two partial occupancy sets of atoms; these two sets can most easily be compared in the ORTEP figure of the superimposed conformers.

If the rearrangement of **10** → **11** were to follow path (a) in Scheme I, the $-S-CH_2-C(O)-CH_2-$ dihedral angles might be pertinent, because they could determine whether a carbanion formed on one side of the carbonyl group could approach the sulfur atom on the other side of the carbonyl group. In one conformer these atoms are nearly colinear (i.e., the dihedral angles S6′–C7′–C8′–C9′ and S10′–C9′–C8′–C7′ are 172°) and approach of C9′ to S6′ to C7′ to S10′ is impossible. However in the other conformer, one of these dihedral angles is 90° (S10–C9–C8–C7); the other, S6–C7–C8–C9, is 173°. Also, in the fixed arm, one of these angles (S23–C24–C25–C26) is 85° whereas the other (S27–C26–C25–C24) is 147°. The approximately 90° angles may allow some carbanion–sulfur 1,4-interaction.

Although this idea gained some credence from the X-ray structure of **16**, where both pertinent dihedral angles are 170–171° and no rearrangement occurs, it lost ground with the structures of **19** and **21**, where small dihedral angles are present. And of course **13**, which is acyclic and flexible, also failed to rearrange. At this stage, then, a rationale for the rearrangments of **10** → **11** and **11** → **12** remains obscure.[11]

Conclusions. The base-catalyzed reaction of 1,3-dichloroacetone with bis-thiols (or in the case of **8**, a tetrathiol) provides a useful synthetic approach to macrocyclic cyclophanes (examples are **10**, **15**, **16**, **19**, and **21**). Since the sulfurs and carbonyl groups may be broadly manipulated, this promises to be a useful approach to functionalized macrocycles. Cesium carbonate/DMF is the medium of choice for these syntheses. When sodium methoxide/methanol was used, some novel rearrangements were observed, as in the conversion of **10** → **11** → **12** and the formation of **17** from **14**. The mechanisms of these rearrangements are, at this stage, speculative.

Experimental Section

General Procedures. ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, in $CDCl_3$ unless otherwise mentioned. Mass spectra were recorded at 70 eV and were obtained at the Michigan State University Mass Spectrometry Facility, supported in part by a grant (DRR-00480) from the Biotechnology Resources Branch, National Institutes of Health. FTIR spectra were recorded using KBr pellets. Melting points are uncorrected. Anhydrous $MgSO_4$ was the drying agent throughout, and silica gel for chromatography was 230–400 mesh.

***7H,8H,9H,11H*-1,15-(Methanothiopropanothiomethano)-16,20-metheno-5*H*-dibenzo[*g,n*](1,5)dithiacyclohexadecin-8,25-dione (10).** A 1-L three-necked flask was equipped with two addition funnels that could be regulated for slow addition, a stirrer, and an Ar gas line. To a well-stirred suspension of anhydrous Cs_2CO_3 (3.18 g, 9.75 mmol) in 500 mL of DMF at 45–50 °C were added simultaneously over 12–15 h a solution of tetrathiol **8** (1.0 g, 2.41 mmol) in 100 mL of DMF and 1,3-dichloroacetone (0.615 g, 4.84 mmol) in 100 mL of DMF. After addition was complete, the mixture was heated at reflux for 8 h and then concentrated under vacuum. The residue was extracted with CH_2Cl_2, and the extract was washed with water and dried. Removal of the solvent afforded a solid which was chromatographed over silica gel using CH_2Cl_2–hexanes (2:1, v/v) as eluent to give 0.83 g (66%) of **10**, mp 263 °C: ^1H NMR δ 3.10 (d, J = 15.4 Hz, 4 H), 3.36 (d, J = 15.4 Hz, 4 H), 3.51 (d, J = 12.3 Hz, 4 H), 3.61 (d, J = 12.3 Hz, 4 H), 7.15 (dd, J = 7.6, 1.7 Hz, 2 H, $H_{4',6'}$), 7.33–7.40 (m, 2 H, $H_{4,4''}$), 7.41 (t, J = 1.7 Hz, 1 H, $H_{2'}$), 7.46–7.55 (m, 5 H); ^{13}C NMR δ 34.9, 40.0, 128.4, 129.61, 129.64, 130.2, 135.4, 137.7, 142.1, 199.6 (one signal overlapped); IR $\nu_{C=O}$ 1713 cm^{-1}; mass spectrum (FAB, *m*-nitrobenzyl alcohol matrix) 523 (MH^+); HRMS calcd for $C_{28}H_{27}O_2S_4$ (MH^+) 523.0894, found 523.0883. Anal. Calcd for $C_{28}H_{26}O_2S_4$: C, 64.33; H, 5.01. Found: C, 64.23; H, 5.12.

Coupling of Tetrathiol 8 with 1,3-Dichloroacetone Using Sodium Methoxide/Methanol. Using the same apparatus as described above, there were added simultaneously over 12–15 h at rt to a solution of anhydrous $NaOCH_3$ (0.461 g, 8.54 mmol) in 500 mL of methanol solutions of tetrathiol **8** (0.737 g, 1.78 mmol) and 1,3-dichloroacetone (0.461 g, 3.63 mmol), each dissolved in 150 mL of MeOH. After addition was complete, the mixture was heated at reflux for 8 h. Workup as above gave, after chromatography using hexanes–CH_2Cl_2 (3:1 v/v) as eluent, 0.32 g (34%) of diketone **10**, 0.35 g (41%) of 7*H*,8*H*,9*H*,11*H*-1,15-(methanothiomethanothiomethano)-16,20-metheno-5*H*-dibenzo[*g,n*](1,5)dithiacyclohexadecin-8-one (**11**) and 0.13 g (16%) of 7*H*,9*H*-1,13-(methanothiomethanothiomethano)-14,18-metheno-5*H*-dibenzo[*e,l*](1,3)dithiacyclotetradecin (**12**). For **11**: mp 288 °C; ^1H NMR δ 3.05, 3.32 (AB q, J = 16.2 Hz, 4 H), 3.47, 4.24 (AB q, J = 11.4 Hz, 4 H), 3.46, 3.57 (AB q, J = 14.4 Hz, 2 H, CH_2 between two sulfurs), 3.64, 3.97 (AB q, J = 12.6 Hz, 4 H), 7.07 (dd, J = 7.6, 1.7 Hz, 2 H), 7.24 (dd, J = 7.6, 1.5 Hz, 2 H), 7.31 (t, J = 7.6 Hz, 2 H, $H_{4,4''}$), 7.46 (dd, J = 7.6, 1.4 Hz, 2 H), 7.48 (t, J = 7.6 Hz, 1 H, $H_{5'}$), 7.59 (t, J = 1.6 Hz, 1 H, $H_{2'}$); ^{13}C NMR δ 33.2, 34.3, 38.2, 39.2, 127.7, 127.8, 128.6, 128.9, 129.0, 129.5, 135.0, 135.8,

(11) These novel reactions are clearly worthy of a more detailed study. Due to retirement (H.H.) we are unable to continue this research, and invite others to do so.

(12) The authors have deposited atomic coordinates for these structures with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

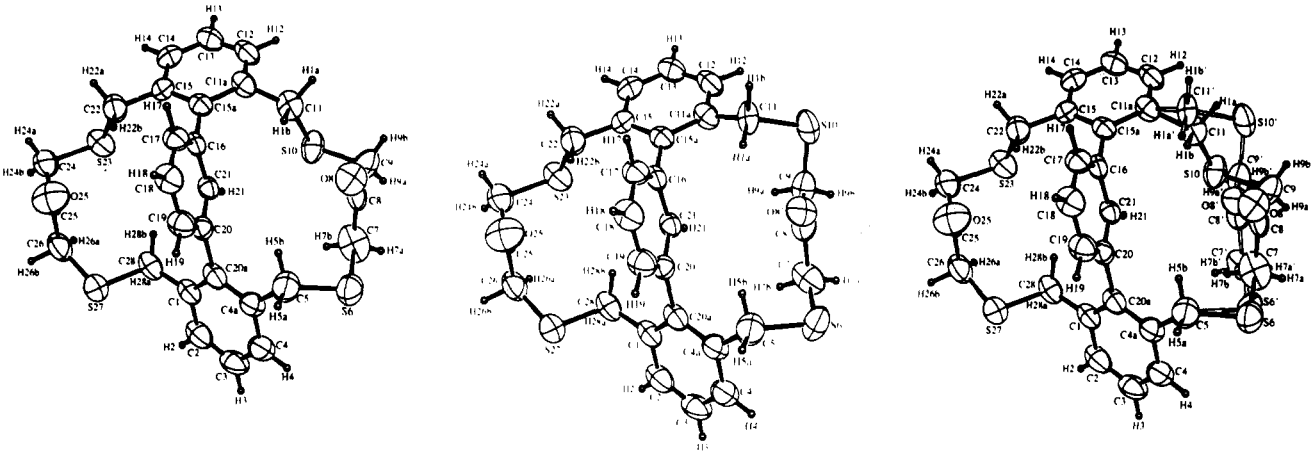


Figure 1. Ortep drawings of the two conformations of **10** (left and center) and superimposed (right). Note from the latter that only the conformations of the "right" arm differ.

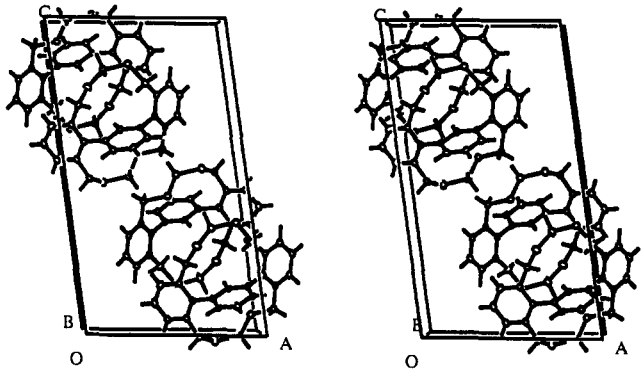


Figure 2. Stereoview of the unit cell of **12**.

137.7, 141.0, 200.0; IR $\nu_{C=O}$ 1713 cm^{-1}; mass spectrum (*m/e*) 480 (M^+). Anal. Calcd for $C_{26}H_{24}OS_4$: C, 64.96; H, 5.03. Found: C, 64.95; H, 5.06. For **12**: mp 304 °C; ^{1}H NMR δ 2.52, 3.89 (AB q, J = 11.7 Hz, 4 H, CH_2 between the sulfurs), 3.54, 4.03 (AB q, J = 12.9 Hz, 8 H, benzylic CH_2), 7.13–7.23 (m, 8 H), 7.58 (t, J = 7.5 Hz, 1 H, $H_{5'}$), 7.99 (t, J = 1.6 Hz, 1 H, $H_{2'}$); ^{13}C NMR δ 37.1, 40.1, 126.6, 127.3, 128.2, 128.3, 133.7, 137.2, 138.2, 141.3; mass spectrum (*m/e*) 438 (M^+). Anal. Calcd for $C_{24}H_{22}S_4$: C, 65.71; H, 5.05. Found: C, 65.79; H, 5.08.

Independent Synthesis of 12.[13] A solution of 1,3,5-trioxane (0.22 g, 2.44 mmol) and tetrathiol **8** (1.0 g, 2.41 mmol) in 300 mL of $CHCl_3$ was kept at rt for 1 h prior to cooling to −20 °C, after which dry HCl gas was passed through the solution for 10 min. The mixture was allowed to warm to rt and after 15 h was worked up by successively washing 3× each with water, 10% aqueous KOH and water, and dried. Evaporation of the solvent and chromatography over silica gel using hexanes–CH_2Cl_2 (3:1 v/v) as eluent gave 0.73 g (69%) of **12**, identical (mp, NMR) with material described above.

Conversion of 10 to 11 and 12. A solution of diketone **10** (0.52 g, 1 mmol) and $NaOCH_3$ (0.22 g, 4 mmol) in 100 mL of CH_3OH was stirred under Ar at rt for 24 h, and then heated at reflux for 8 h. The usual workup gave, after chromatography as above, 0.035 g (7%) of **10**, 0.12 g (25%) of **11**, and 0.27 g (62%) of **12**.

Conversion of 11 to 12. A solution of ketone **11** (0.48 g, 1 mmol) and $NaOCH_3$ (0.22 g, 4 mmol) in 100 mL of CH_3OH was allowed to react as described above for **10**. Workup and chromatography gave 0.39 g (89%) of **12**.

(13) Seebach, D.; Corey, E. J. *J. Org. Chem.* **1975**, *40*, 231–237.

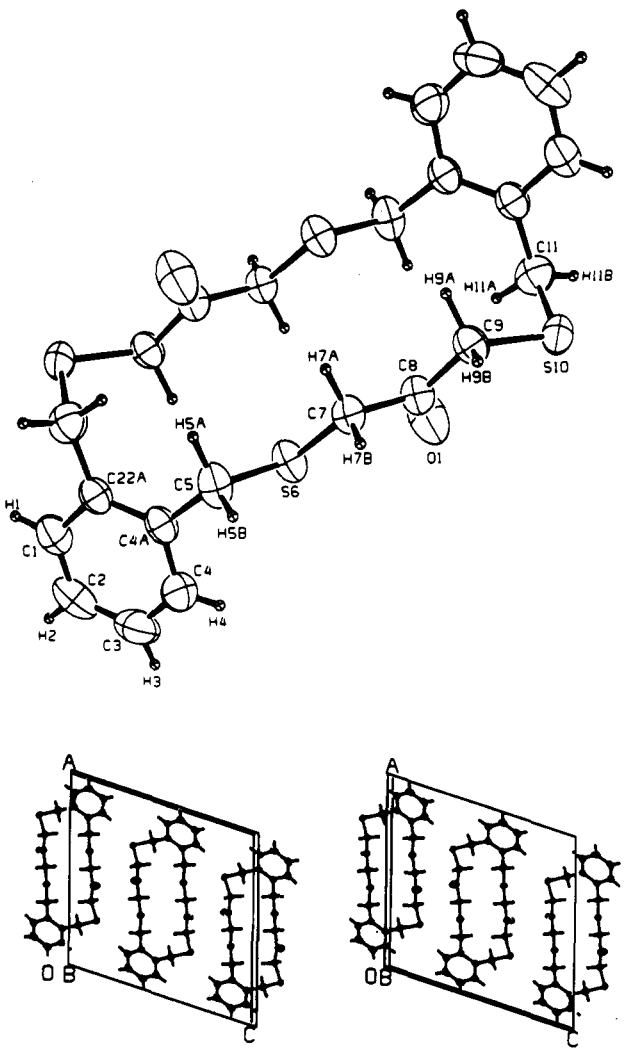


Figure 3. Ortep (top) and stereoview of **16**.

1,3-Bis[(phenylmethyl)thio]-2-propanone (13).[14] Using the procedure described for the preparation of **10**, from 6.48 g (20 mmol) of Cs_2CO_3 in 500 mL of DMF and solutions of benzylmercaptan (4.96 g, 40 mmol) and 1,3-dichloroacetone (2.54 g, 20 mmol), each in 200 mL of DMF, there was obtained after chromatography 4.66 (77%) of **13** as

(14) Fromm, E.; Kapeller, R.; Taubmann, I. *Chem. Ber.* **1928**, *61*, 1353–1358. Povalyaeva, O. S.; Rodionov, V. Ya.; Suvorov, N. M. *Zh. Org. Khim.* (Engl. trans.) **1984**, *20*, 773–782.

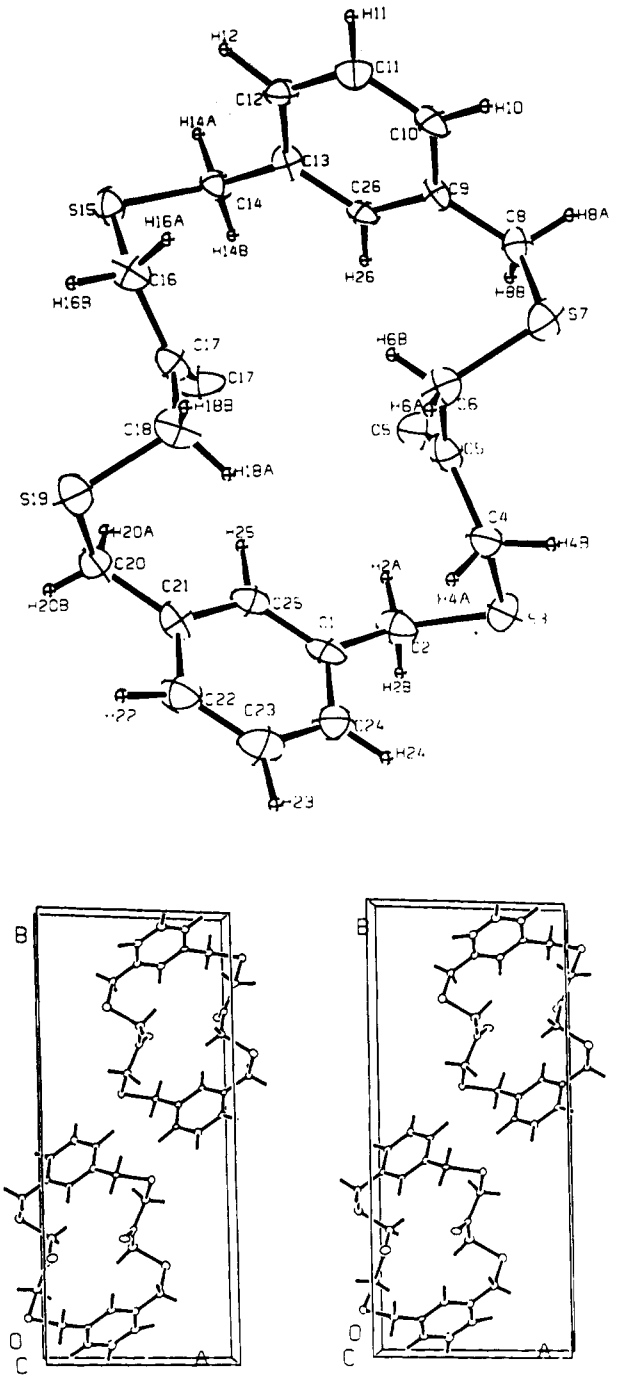


Figure 4. Ortep (top) and stereoview of 19.

an oil: ^{1}H NMR δ 3.25 (s, 4 H), 3.69 (s, 4 H), 7.25–7.33 (m, 10 H); ^{13}C NMR δ 35.6, 37.1, 126.9, 128.1, 128.8, 136.7, 199.4; IR $\nu_{C=O}$ 1702 cm^{-1}; mass spectrum (m/e) 302 (M^+).

Treatment of 13 with CH_3ONa/CH_3OH. A solution of dithia ketone **13** (0.30 g, 1 mmol) and $NaOCH_3$ (0.22 g, 4 mmol) in 100 mL of CH_3OH was stirred under Ar at rt for 18 h. The usual workup gave, after chromatography using CH_2Cl_2–hexanes (1:2 v/v) as eluent, 0.28 g (93%) of recovered **13**. A similar reaction at reflux for 15 h gave 83% of recovered **13**.

Coupling of *o*-Xylylenedithiol with 1,3-Dichloroacetone Using Cesium Carbonate/DMF. To a well-stirred suspension of anhydrous cesium carbonate (4.21 g, 12.9 mmol) in 500 mL of DMF held at 45–50 °C under argon was added simultaneously from separate addition funnels over 15 h solutions of *o*-xylylenedithiol (**14**)[15] (2 g, 11.7 mmol) and 1,3-dichloroacetone (1.64 g, 12.9 mmol), each in 200 mL of DMF. After addition was complete, the mixture was heated at reflux for 8 h and then concentrated under vacuum. The residue was taken up in CH_2Cl_2, washed with water, and dried. Removal of the solvent and chromatography of the solid residue over silica gel using CH_2Cl_2/hexanes (3:1 v/v) as the eluent gave 0.32 g (12%) of **16** and 0.85 g (32%) of **15**. For **15**: mp 96 °C; ^{1}H NMR δ 3.31 (s, 4 H), 3.89 (s, 4 H), 7.28 (s, 4 H); ^{13}C NMR δ 33.0, 37.2, 128.0, 130.2, 136.2, 203.6; IR $\nu_{C=O}$ 1700 cm^{-1}; mass spectrum (m/e) 224 (M^+). Anal. Calcd for $C_{11}H_{12}OS_2$: C, 58.89; H, 5.39; S, 28.58. Found: C, 58.95; H, 5.37; S, 28.66. For **16**: mp 169 °C; ^{1}H NMR δ 3.56 (s, 8 H), 4.01 (s, 8 H), 7.23–7.27 (m, 4 H), 7.36–7.41 (m, 4 H); ^{13}C NMR δ 33.5, 40.0, 127.6, 130.1, 135.2, 200.0; IR $\nu_{C=O}$ 1701 cm^{-1}; mass spectrum (m/e) 448 (M^+).

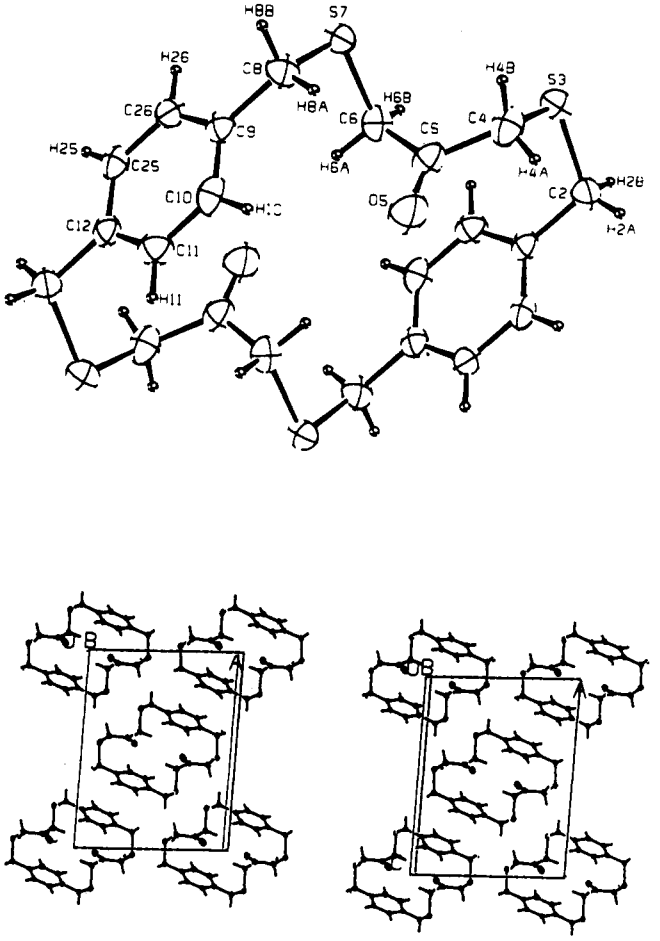


Figure 5. Ortep (top) and stereoview of 21.

Coupling of *o*-Xylylenedithiol with 1,3-Dichloroacetone Using NaOMe/MeOH. To a well-stirred solution of sodium methoxide (0.46 g, 8.52 mmol) in 500 mL of methano at rt under argon was added simultaneously from separate addition funnels over 15 h solutions of **14** (1.2 g, 7.05 mmol) and 1,3-dichloroacetone (0.98 g, 7.72 mmol), each in 200 mL of MeOH. Workup as above gave 0.28 g (18%) of **16**, 0.35 g (22%) of **15**, and 0.12 g (7.6%) of **17**: mp 89 °C; ^{1}H NMR δ 2.40 (s, 3 H, CH_3), 3.61 (d, J = 15 Hz, 2 H, methylene protons trans to acetyl), 4.51 (s, 1 H, methine), 4.76 (d, J = 15 Hz, 2 H, methylene protons cis to acetyl), 7.15–7.23 (m, 4 H); ^{13}C NMR δ 27.9, 33.3, 53.5, 127.5, 128.8, 139.0, 200.2; IR $\nu_{C=O}$ 1705 cm^{-1};

(15) Prepared from the corresponding xylylene dibromide via the bis(isothiouronium) salt; see: Urquhart, G. G.; Gates, J. W., Jr.; Connor, R. *Organic Synthesis*; Wiley: New York, 1955; Collect. Vol. III, 363–365.

mass spectrum (m/e) 224 (M^+). Anal. Calcd for $C_{11}H_{12}OS_2$: C, 58.89; H, 5.39; S, 28.58. Found: C, 58.93; H, 5.33; S, 28.50.

Separate treatment of **15** or **16** with NaOMe/MeOH under the above reaction conditions or at reflux afforded no **17**, only recovered starting material (94% for **15**, 89% for **16**). Attempted base-catalyzed cleavage of the acetyl group from **17** using *t*-BuOK/EtOH (reflux, 18 h) gave only recovered starting material (71%).

Independent Synthesis of 17. To a well-stirred solution of NaOMe (1.4 g, 26 mmol) in 1 L of MeOH at rt under argon was added simultaneously over 15 h solutions of **14** (2 g, 11.7 mmol) and 1,1-dichloroacetone (1.52 g, 12.0 mmol), each in 200 mL of methanol. After 8 h at reflux and workup as above there was obtained 2.23 g (85%) of **17**, identical (mp, NMR) with the product described above.

3,7,15,19-Tetrathiatricyclo[19.3.1.1^{9,13}]hexacosa-1(25),9,11,13(26),21,23-hexaene-5,17-dione (19). Following the procedure described for eq 6, from 2.6 g (8.0 mmol) of cesium carbonate suspended in 500 mL of DMF, 1.36 g (8.0 mmol) of *m*-xylylenedithiol,[15] and 1.014 g (8.0 mmol) of 1,3-dichloroacetone, each in 100 mL of DMF, there was obtained 0.98 g (54.7%) of **19**: mp 127 °C; ^{1}H NMR δ 3.15 (s, 8 H), 3.64 (s, 8 H), 7.13–7.28 (m, 8 H); ^{13}C NMR δ 35.7, 37.0, 127.7, 128.5, 129.8, 137.1, 200.4; IR $\nu_{C=O}$ 1707 cm^{-1}; mass spectrum (m/e) 448 (M^+). Using NaOMe/MeOH (see procedure for eq 7) the yield of **19** was 51%.

3,7,14,18-Tetrathiatricyclo[18.2.2.2^{9,12}]hexacosa-9,11,20,22,23,25-hexaene-5,16-dione (21). Following an analogous procedure as for **19**, from 4.21 g (12.9 mmol) of cesium carbonate suspended in 500 mL of DMF, 2.0 g (11.7 mmol) of *p*-xylylenedithiol,[15] and 1.64 g (12.9 mmol) of 1,3-dichloroacetone, each in 200 mL of DMF, there was obtained 1.45 g (55%) of **21**, mp 194 °C; ^{1}H NMR δ 2.96 (s, 8 H), 3.56 (s, 8 H), 7.14 (s, 8 H); ^{13}C NMR δ 35.6, 35.9, 129.0, 136.1, 201.2; IR $\nu_{C=O}$ 1700 cm^{-1}; mass spectrum (m/e) 448 (M^+). Using NaOMe/MeOH (see procedure for eq 7) the yield of **21** was 45%.

2,2′-Bis(mercaptomethyl)-1,1′:3′,1″-terphenyl (23). A solution of bis(bromomethyl)-*m*-terphenyl **22**[8] (8.32 g, 20 mmol) and thiourea (3.64 g, 48 mmol) in 300 mL of THF was stirred under Ar at rt overnight. Sodium hydroxide (300 mL, 10%) was added, and the mixture was stirred for 10 h and then acidified with ice and hydrochloric acid, the temperature being maintained at rt. The acidic solution was extracted with CH_2Cl_2, and the combined organic layers were dried. Solvent removal (rotavap) and chromatography of the residue on silica gel using CH_2Cl_2–hexanes (1:2 v/v) as eluent gave 4.37 g (68%) of bisthiol **23**: mp 44–45 °C; ^{1}H NMR δ 1.75 (t, J = 3.7 Hz, 2 H, –S*H*), 3.80 (d, J = 3.7 Hz, 4 H, –C*H*$_2$), 7.31–7.54 (m, 12 H); ^{13}C NMR δ 26.3, 126.7, 127.6, 127.9, 129.0, 129.5, 129.9, 138.2, 140.5, 140.6 (one overlapped); mass spectrum (m/e) 322 (M^+).

7*H*,8*H*,9*H*,11*H*-16,20-Metheno-5*H*-dibenzo[*g*,*n*]-(1,5)dithiacyclohexadecin-8-one (24). The coupling procedure described for **10** (eq 2) was used. From 3.26 g (10 mmol) of Cs_2CO_3 in 500 mL of DMF to which was added 3.0 g (9.3 mmol) of dithiol **23** and 1.27 g (10 mmol) of 1,3-dichloroacetone, each in 300 mL of DMF, there was obtained 2.53 g (72%) of dithia ketone **24**: mp 149 °C; ^{1}H NMR δ 3.24 (s, 4 H), 3.73 (s, 4 H), 7.22–7.49 (m, 10 H), 7.58 (dd, J = 7.6, 1.2 Hz, 2 H); ^{13}C NMR δ 33.7, 39.4, 126.8, 127.6, 127.7, 127.9, 129.2, 129.3, 130.1, 134.2, 140.1, 142.1, 199.8; IR $\nu_{C=O}$ 1713 cm^{-1}; mass spectrum (m/e) 376 (M^+). Anal. Calcd for $C_{23}H_{20}OS_2$: C, 73.37; H, 5.35; S, 17.03. Found: C, 73.32; H, 5.43; S, 17.10.

Treatment of 24 with CH_3ONa/CH_3OH. The procedures and amounts were as described for **13** above. Dithia ketone **24** was recovered unchanged after 24 h at room temperature (93%) or after 24 h at reflux (89%).

Acknowledgment. We are indebted to the National Science Foundation (CHE 90-08503) and the National Institutes of Health (GM 15997) for financial support of this research.

Supplementary Material Available: ^{1}H-NMR, ^{13}C-NMR, IR, and MS of **16**, **19**, and **21** and ^{1}H-NMR and ^{13}C-NMR of **23** (17 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.