Cyclophanes with Sharp Corners: Synthesis of Macrocycles Containing One or Two 1,5,2,4,6,8-Dithiatetrazocine Rings

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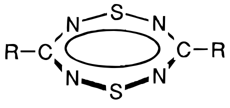
Several cyclophanes have been prepared which contain one or two of the bent 3,7-diamino-1,5,2,4,6,8-dithiatetrazocine (DTTA) ring systems linked by polymethylene chains: 1,8-dimethyl-1,8-diaza[8](3,7)(1,5,2,4,6,8-dithiatetrazocinophane) (**6**), 1,6,15,20-tetramethyl-1,6,15,20-tetraaza[6.6](3,7)(1,5,2,4,6,8-dithiatetrazocinophane) (**8**), and 1,5,14,18-tetramethyl-1,5,14,18-tetraaza[5.5](3,7)(1,5,2,4,6,8-dithiatetrazocinophane) (**9**). In each synthesis, an *N,N*′-dimethyl-α,ω-diamine was converted to the corresponding bis(guanidinium hydrobromide), which was then treated with sulfur dichloride in the presence of DBU under conditions of moderate dilution to form the cyclophane in low yield (0.1−0.7%). When *N,N*′-dimethylhexanediamine was used, a cyclophane containing a single DTTA ring bridged by the polymethylene chain was formed (**6**), but with the corresponding butane- and propanediamines, dimeric cyclophanes containing a pair of DTTA rings resulted (**8** and **9**). When *N,N*′-dimethylpentanediamine was used, a monomeric phane, 1,7-dimethyl-1,7-diaza[7](3,7)(1,5,2,4,6,8-dithiatetrazocinophane) (**7**), appeared to be formed, but it was not isolated as a pure material. Compounds **6**, **8**, and **9** were characterized by X-ray crystallography. Crystallographic data: for **6**, $C_{10}H_{18}N_6S_2$, monoclinic $P2_1/c$, $Z = 4$, $a = 8.356(1)$ Å, $b = 12.991(2)$ Å, $c = 13.298(2)$ Å, $\beta = 111.705(9)°$; for **8**, $C_{16}H_{28}N_{12}S_4{\cdot}0.69CH_2Cl_2$, triclinic, $P\bar{1}$, $Z = 2$, $a = 9.6095(8)$ Å, $b = 11.7085(11)$ Å, $c = 13.2683(10)$ Å, $\alpha = 66.243(7)°$, $\beta = 82.340(6)°$, $\gamma = 73.989(7)°$; for **9**, $C_{14}H_{24}N_{12}S_4$, triclinic $P\bar{1}$, $Z = 2$, $a = 6.304(1)$ Å, $b = 8.366(1)$ Å, $c = 21.357(3)$ Å, $\alpha = 91.03(1)°$, $\beta = 92.26(1)°$, $\gamma = 110.56(1)°$. The dimeric cyclophanes **8** and **9** were observed to form roughly rectangular troughs enclosing a small cavity, with the DTTA rings at two of the corners. The DTTA ring of the monomeric phane **6** was observed to be significantly distorted when compared with the structures of less constrained DTTA's, and ab initio calculations indicated that the phane **7**, which has a shorter bridge, but for which there is no X-ray structure, is even more highly strained.

Introduction

The 1,5,2,4,6,8-dithiatetrazocines (DTTA's) were first prepared by the Woodward group in 1981, and they exhibit a curious structural dichotomy.[1] In most derivatives, the heterocycle is planar and is best understood as a 10-π-electron aromatic system (**1**),[1−3] but when one[3] or both[1] of the R groups is a dimethylamino group, the heterocycle is sharply folded (**2**). In the bent forms, the S−S distance is only 2.4−2.5 Å and may represent a weak bond.[4]



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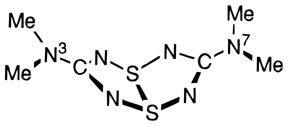

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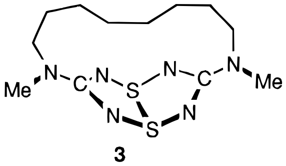

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These bent bis(dialkylamino)-DTTA's appear to be well suited for the construction of molecular cavities. They are relatively rigid molecules, with a barrier to ring inversion of 17−18 kcal/mol,[5] and they may be synthesized from a variety of dialkylamines in only two steps, although the yields are variable.[1,3] Indeed, in order to test for the presence of a ring current in the bent DTTA's, we easily prepared cyclophane **3**.[6] Although the heterocycle induced no unusual shifts in the ^{1}H NMR resonances of the bridging methylenes of **3**, its synthesis demonstrated that relatively complex molecules containing the DTTA ring could be prepared. We felt that the "corner-enforcing" conformation of the DTTA's could be used to form molecular troughs of varied dimensions, and we now report a systematic investigation of the synthesis of DTTA-containing cyclophanes from a series of α,ω-diamines and the effects of cyclophane-induced strain on the structures of these unusual heterocycles.

Experimental Section

General Procedures. 2-Ethyl-2-thiopseudourea hydrobromide, sulfur dichloride, DBU, *N,N*′-dimethyl-1,6-hexanediamine, and *N,N*′-dimethyl-1,3-propanediamine were purchased from Aldrich Chemical Co. and used without further purification. *N,N*′-Dimethyl-1,5-pentanediamine[7] and *N,N*′-dimethyl-1,4-butanediamine[8] were prepared by literature procedures. CH_2Cl_2 was distilled from P_2O_5 before use. ^{1}H NMR spectra were recorded on JEOL GSX270 and General Electric QE300 NMR spectrometers operating at 270 and 300 MHz, respectively; resonances are listed in ppm downfield from tetramethylsilane. IR spectra were obtained with a Nicolet Model 730 FTIR spectrometer.

⊗ Abstract published in *Advance ACS Abstracts,* May 1, 1996.

(1) Ernest, I.; Holick, W.; Rihs, G.; Schomburg, D.; Shoham, G.; Wenkert, D.; Woodward, R. B. *J. Am. Chem. Soc.* **1981**, *103,* 1540.

(2) Gleiter, R.; Bartetzko, R.; Cremer, D. *J. Am. Chem. Soc.* **1984**, *106,* 3437.

(3) Amin, M.; Rees, C. W. *J. Chem. Soc., Perkin Trans. 1* **1989**, 2495.

(4) For a review of experimental and theoretical studies of the heterocyclic thiazenes, see: Oakley, R. T. *Prog. Inorg. Chem.* **1988**, *36,* 299.

(5) Pascal, R. A., Jr.; L'Esperance, R. P. *J. Am. Chem. Soc.* **1994**, *116,* 5167.

(6) (a) Pascal, R. A., Jr. *Pure Appl. Chem.* **1993**, *65,* 105. (b) Ho, D. M.; Pascal, R. A., Jr. *Acta Crystallogr., Sect. C* **1994**, *50,* 108.

(7) Devinsky, F.; Lacko, I.; Krasnec, L. *Synthesis* **1980**, 303.

(8) Boon, W. R. *J. Chem. Soc.* **1947**, 307.

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Melting points were recorded on an Electrothermal digital melting point apparatus and are uncorrected. The widely adopted nomenclature of Schubert et al.[9] has been used for the naming of cyclophanes **6**−**9**.

1,8-Dimethyl-1,8-diaza[8](3,7)(1,5,2,4,6,8-dithiatetrazocinophane) (6). A solution of *N*,*N*′-dimethyl-1,6-hexanediamine (4.61 g, 32 mmol) and 2-ethyl-2-thiopseudourea hydrobromide (10.38 g, 56 mmol) in water (50 mL) was heated overnight at 80 °C. The solvent was evaporated, and residual water was removed by azeotropic distillation with toluene and ethanol. The resulting bis(guanidine hydrobromide), a colorless oil, was further dried under vacuum over P_2O_5. This material (9.78 g, 25 mmol), DBU (30.5 g, 201 mmol), and CH_2Cl_2 (725 mL) were mixed and cooled in an ice bath. A solution of sulfur dichloride (4.78 mL, ∼75 mmol) in CH_2Cl_2 (20 mL) was added dropwise. The reaction mixture turned dark purple during the addition, and stirring was continued overnight with the reaction warming to room temperature. The solution was washed with water (5 × 700 mL), and the resulting dark orange organic phase was dried over Na_2SO_4 and concentrated under vacuum. This dark material was chromatographed on a column of silica gel (23 cm × 5 cm), eluting first with toluene and then 2:1 toluene−ethyl acetate. A compound exhibiting $R_f = 0.57$ on analytical silica gel TLC (solvent: 2:1 toluene−ethyl acetate) was isolated, and it was further purified by preparative TLC in the same solvent to give cyclophane **6** (47.3 mg, 0.165 mmol; 0.7% yield based on the bis(guanidine)). Mp behavior: 81 °C begins to darken, 169−172 °C melts with decomposition. ^1H NMR ($CDCl_3$): δ 0.97 (m, 2H), 1.27 (m, 2H), 1.61 (m, 4H), 3.00 and 3.04 [overlapping s (6H) and m (2H)], 4.53 (ddd, 2H, $J = 13, 13, 3$ Hz). IR (KBr): ν_{max} 721, 782, 838, 902, 1142, 1182, 1233, 1243, 1337, 1406, 1531, 1560, 2848, 2866, 2901, 2923, 2939 cm^{-1}. MS: *m/z* 286 (M^+, 100), 245 ($M - CH_3NC$, 44), 240 (M − SN, 65), 147 ($S_2N_2CNCH_3(CH_2)^+$, 63); exact mass 286.1040, calculated for $C_{10}H_{18}N_6S_2$ 286.1034. Crystals of **6** suitable for X-ray analysis were obtained by the slow evaporation of a solution of **6** in 1:1 CH_2Cl_2−acetone.

Attempted Synthesis of 1,7-Dimethyl-1,7-diaza[7](3,7)(1,5,2,4,6,8-dithiatetrazocinophane) (7). Several attempts were made to prepare compound **7** from *N*,*N*′-dimethyl-1,5-pentanediamine[7] by procedures similar to that successfully employed for cyclophane **6**. Small amounts of a yellow material were isolated which exhibited mass spectral data consistent with those expected for compound **7**, but no crystals of this material were obtained. The material was inhomogeneous by ^1H NMR analysis, and the mass spectrum showed signifcant contamination by S_8. MS: *m/z* 272 (M^+, 32), 226 (M − SN, 31), 147 ($S_2N_2CNCH_3(CH_2)^+$, 28), 69 (100); exact mass 272.0880, calculated for $C_9H_{16}N_6S_2$ 272.0878.

1,6,15,20-Tetramethyl-1,6,15,20-tetraaza[6.6](3,7)(1,5,2,4,6,8-dithiatetrazocinophane) (8). A solution of *N*,*N*′-dimethyl-1,4-butanediamine[8] (5.45 g, 47 mmol) and 2-ethyl-2-thiopseudourea hydrobromide (15.24 g, 82 mmol) in water (50 mL) was heated overnight at 80 °C. The solvent was evaporated, and residual water was removed by azeotropic distillation with toluene and ethanol. The resulting bis(guanidine hydrobromide), a colorless oil, was further dried under vacuum over P_2O_5. This material (12.1 g, 33 mmol), DBU (40.5 g, 266 mmol), and CH_2Cl_2 (800 mL) were mixed and cooled in an ice bath. A solution of sulfur dichloride (6.30 mL, ∼100 mmol) in CH_2Cl_2 (20 mL) was added dropwise. The reaction mixture turned dark purple during the addition, and stirring was continued overnight with the mixture warming to room temperature. The solution was washed with water (4 × 700 mL), and the resulting orange organic phase was dried over Na_2SO_4 and concentrated under vacuum. This material was chromatographed on a column of silica gel (23 cm × 5 cm), eluting first with toluene and then 2:1 toluene−ethyl acetate. A compound exhibiting $R_f = 0.37$ on silica gel TLC (solvent: 2:1 toluene−ethyl acetate) was isolated, and it was further purified by preparative TLC in the same solvent to give cyclophane **8** (8.3 mg, 0.016 mmol; 0.1% yield based on the bis(guanidine)). Mp behavior: 83 °C begins to darken, 236−240 °C dark material melts with gas evolution. ^1H NMR ($CDCl_3$): δ 1.40 (m, 8H), 2.99 (m, 4H), 3.11 (s, 12H), 4.28 (m, 4H). IR (KBr): ν_{max} 713, 778, 887, 901, 1079, 1092, 1186, 1228, 1259, 1286, 1361, 1406, 1457, 1593, 2856, 2922 cm^{-1}. MS: *m/z* 516 (M^+, 38), 474 ($M - CH_3NCH$, 19), 402 ($M - CH_3N(CH_2)_4NCH_3$, 9), 391 ($M - N_2CN(CH_3)(CH_2)_4$, 15), 147 ($S_2N_2CNCH_3(CH_2)^+$, 40), 69 (100); exact mass 516.1452, calculated for $C_{16}H_{28}N_{12}S_4$ 516.1442. Crystals of the methylene chloride solvate of **8** suitable for X-ray analysis were obtained by the slow evaporation of a solution of **8** in 2:1 CH_2Cl_2−CH_3OH. NMR analysis of a part of the batch of crystals employed for X-ray analysis indicated the presence of approximately 0.4 CH_2Cl_2 molecule per molecule of **8**, and the refinement of the X-ray structure, in which the occupancy of the solvent was allowed to vary, yielded a value of 0.69 CH_2Cl_2 per molecule of **8**.

1,5,14,18-Tetramethyl-1,5,14,18-tetraaza[5.5](3,7)(1,5,2,4,6,8-dithiatetrazocinophane) (9). A solution of *N*,*N*′-dimethyl-1,3-propanediamine (5.11 g, 50 mmol) and 2-ethyl-2-thiopseudourea hydrobromide (16.24 g, 88 mmol) in water (50 mL) was heated overnight at 80 °C. The solvent was evaporated, and residual water was removed by azeotropic distillation with toluene and ethanol. The resulting bis(guanidine hydrobromide), a white powder, was further dried under vacuum over P_2O_5. A portion of this material (6.03 g, 17 mmol), DBU (21.0 g, 139 mmol), and CH_2Cl_2 (500 mL) were mixed and cooled in an ice bath. A solution of sulfur dichloride (3.30 mL, ∼52 mmol) in CH_2Cl_2 (30 mL) was added dropwise. The reaction mixture turned dark purple during the addition, and stirring was continued overnight with the mixture warming to room temperature. The solution was washed with water (4 × 500 mL), and the resulting dark orange organic phase was dried over Na_2SO_4 and concentrated under vacuum. This dark material was chromatographed on a column of silica gel (23 cm × 4 cm), eluting first with toluene and then 2:1 toluene−ethyl acetate. A compound exhibiting $R_f = 0.26$ on analytical silica gel TLC (solvent: 2:1 toluene−ethyl acetate) was isolated, and it was further purified by preparative TLC in the same solvent to give cyclophane **9** (12.8 mg, 0.026 mmol; 0.3% yield based on the bis(guanidine)). Mp behavior: 73 °C begins to darken, 188−195 °C dark material melts with gas evolution. ^1H NMR ($CDCl_3$): δ 1.75 (m, 4H), 2.90 (ddd, 4H, $J = 14, 12, 4$ Hz), 3.12 (s, 12H), 4.03 (ddd, 4H, $J = 14, 12, 6$ Hz). IR (KBr): ν_{max} 720, 780, 879, 909, 957, 980, 1079, 1118, 1182, 1239, 1265, 1316, 1355, 1405, 1437, 1528, 1642, 1678, 2850, 2918 cm^{-1}. MS: *m/z* 488 (M^+, 54), 377 ($M - N_2CN(CH_3)(CH_2)_3$, 48), 322 ($M - N_2CN(CH_3)(CH_2)_3N(CH_3)CN$, 72), 147 ($S_2N_2CNCH_3(CH_2)^+$, 80), 69 (100); exact mass 488.1132, calculated for $C_{14}H_{24}N_{12}S_4$ 488.1129. Crystals of **9** suitable for X-ray analysis were obtained by the slow evaporation of a solution of **9** in 2:1 CH_2Cl_2−CH_3OH.

Computational Studies. Geometries were fully optimized at the Hartree−Fock level of theory, in some cases under a constraint of symmetry or a selected bond distance or angle. All calculations were performed by using the SPARTAN 3.0 package of programs (Wavefunction, Inc.), and its built-in default thresholds for wave function and gradient convergence were employed. Frequency calculations were performed on all optimized equilibrium geometries. The atomic coordinates for each of the calculated geometries are contained in the Supporting Information.

Results and Discussion

Syntheses. The cyclophanes in this report were prepared in the most nearly direct fashion possible, and the syntheses are outlined below. In each case a known *N*,*N*′-dimethyl-α,*ω*-diamine (**4**) was converted to the corresponding bisguanidinium hydrobromide (**5**) by treatment with 2-ethyl-2-thiopseudourea hydrobromide in hot water. These guanidine salts were thoroughly dried but used without further purification. Treatment of the guanidines with sulfur dichloride in the presence of DBU under conditions of moderate dilution (30−50 mM) gave complex mixtures of products from which the cyclophanes were isolated by chromatography and crystallization.

N,*N*′-Dimethyl-α,*ω*-diamines containing six, five, four, three, and two methylene groups were used for cyclophane synthesis. Numerous fractions from each reaction mixture were screened by ^1H NMR and mass spectrometry for DTTA-containing macrocycles. As it happened, in each reaction no more than

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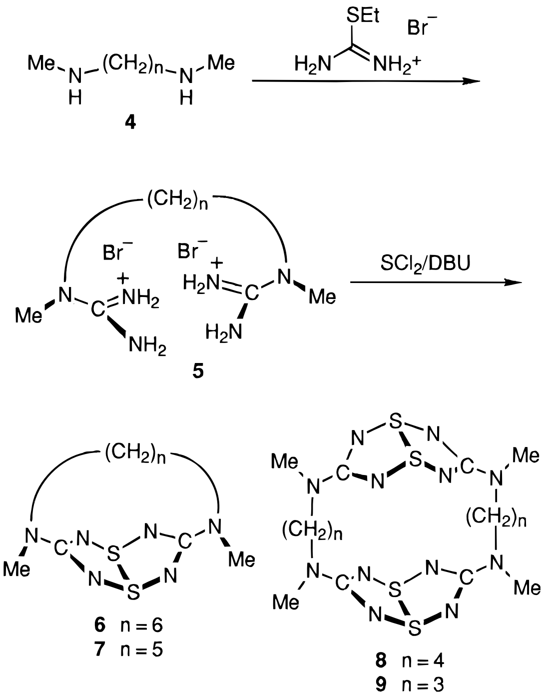
[9] Schubert, W. M.; Sweeney, W. A.; Latourette, H. K. *J. Am. Chem. Soc.* **1954**, *76*, 5462. See also: Vogtle, F. *Cyclophane Chemistry*; Wiley: Chichester, U.K., 1993; pp 11−16.



one type of cyclophane was found. The monomeric cyclophanes **6** and **7** were obtained from the dimethylhexane- and dimethylpentanediamines, respectively. Compound **6** was isolated in 0.7% overall yield, comparable to the 1.1% yield previously observed for the synthesis of **3** (which contains eight methylene groups). We were unable to obtain cyclophane **7** in pure form; it is more highly strained than **6** (see below), and it appeared to decompose partly with each chromatographic step. The shorter diamines gave no monomeric cyclophanes; instead, the dimeric macrocycles **8** and **9** were obtained in low yield from the dimethylbutane- and dimethylpropanediamines, respectively. No cyclophanes of any kind were observed, however, from reactions with *N*,*N′*-dimethylethylenediamine. In addition to syntheses with simple polymethylene-bridged precursors, the bis(guanidine) of piperazine was also prepared and subjected to the same macrocyclization conditions, but again no cyclophanes were found.

The low yields of the cyclophanes are not unexpected, for several reasons. First, the syntheses of even simple DTTA's are inefficient. The best is the 54% yield reported for the preparation of bis(dimethylamino)-DTTA (**2**) in the original Woodward study,[1] but the yields of other derivatives, synthesized in several laboratories, have not exceeded 20%.[1−3,5] Second, the formation of most cyclophanes is both entropically disfavored (with respect to oligomeric or polymeric products), since a particular conformation of the bridging chain is required to close the ring, and enthalpically disfavored, since the ring will be strained to some degree. Finally, the syntheses of the dimeric cyclophanes **8** and **9** are particularly difficult, since *two* DTTA rings must be formed to make the cyclophane.

The change in products from monomeric to dimeric cyclophanes as the bridging polymethylene chain is shortened is easily understood: as the bridges shrink, the monomeric phanes are increasingly strained. The failure to prepare a piperazine-bridged dimeric phane (the monomeric phane is clearly much too strained to form) must be attributed to the fact that two piperazines would be required to adopt boat conformations in such a molecule. Further, the failure of the ethylenediamine-bridged phane to form is likely due to a preference for the *anti* conformation by its acyclic precursor, which has bulky methylguanidine groups attached to adjacent carbons.

Table 1. Crystallographic Data for Compounds **6**, **8**, and **9**

	6	**8**	**9**
empirical formula	$C_{10}H_{18}N_6S_2$	$C_{16}H_{28}N_{12}S_4{\cdot}0.69CH_2Cl_2$	$C_{14}H_{24}N_{12}S_4$
fw	286.4	575.2	488.7
space group	$P2_1/c$ (No. 14)	$P\bar{1}$ (No. 2)	$P\bar{1}$ (No. 2)
a, Å	8.356(1)	9.6095(8)	6.304(1)
b, Å	12.991(2)	11.7085(11)	8.366(1)
c, Å	13.298(2)	13.2683(10)	21.357(3)
α, deg		66.243(7)	91.03(1)
β, deg	111.705 (9)	82.340(6)	92.26(1)
γ, deg		73.989(7)	110.56(1)
V, Å^3	1341.2 (3)	1312.9(2)	1053.2(3)
Z	4	2	2
ρ_{calcd}, g/cm^3	1.418	1.455	1.541
μ, mm^{-1}	0.390	0.534	0.482
T, K	296	230	296
λ(Mo Kα), Å	0.710 73	0.710 73	0.710 73
$R(F)^a$	0.039	0.036	0.045
$R_w(F)^a$	0.051		0.044
$R_w(F^2)^a$		0.081	

[a] $R(F) = \sum||F_o| - |F_c||/\sum|F_o|$; $R_w(F) = [\sum w(|F_o| - |F_c|)^2/\sum w|F_o|^2]^{1/2}$; $R_w(F^2) = [\sum w(F_o^2 - F_c^2)^2/\sum w(F_o^2)^2]^{1/2}$.

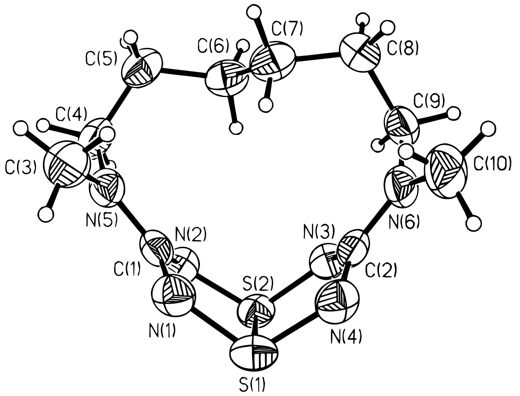


Figure 1. X-ray structure of the hexamethylene-bridged monomeric cyclophane **6**. Thermal ellipsoids are drawn at the 50% probability level.

In these syntheses, only cyclophanes containing one or two dithiatetrazocine rings were observed. Had trimeric phanes been formed, which might have been expected for the reactions which produced **8** and **9**, they should have been detected if produced in reasonable quantity. Higher cyclic oligomers might have been missed, since the masses of such molecules would exceed 1000, and the molecular ions would not have been observed in the course of routine mass spectrometric analysis. Much open-chain oligomeric material is formed in these reactions, but the very polar ends of the oligomers (presumably still guanidino groups) make them difficult to purify, and these compounds were not pursued.

Structural and Computational Studies. Although the gross structures of cyclophanes **6**−**9** are clear from their spectra, X-ray analyses were required to elucidate their conformations. The details of the X-ray structure determinations are summarized in Table 1; the molecular structures of compounds **6**, **8**, and **9** are illustrated in Figures 1−3, respectively; their atomic coordinates are listed in Tables 2−4, respectively; and selected geometric parameters for the heterocycles in these compounds, as well as those for the two previously reported bis(dialkylamino)-DTTA structures, are found in Table 5.

The structures of dimeric macrocycles **8** and **9** are superficially similar, each forming a roughly rectangular trough, with the DTTA rings at two of the corners, as expected. In compound **8**, however, the bridging tetramethylene chains are attached *trans* with respect to each other on both of the DTTA rings, with the result that the four *N*-methyl groups project alternately above and below the trough (Figure 2). In contrast,

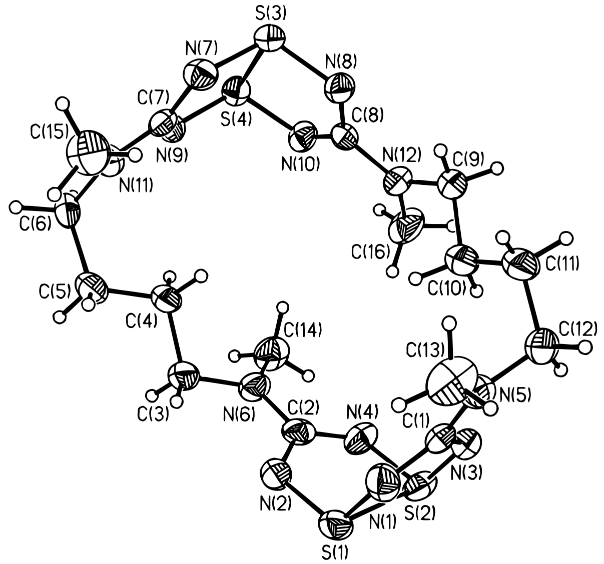


Figure 2. X-ray structure of the tetramethylene-bridged dimeric cyclophane **8**. Thermal ellipsoids are drawn at the 50% probability level, and the disordered molecule of methylene chloride found in the central cleft has been omitted for clarity.

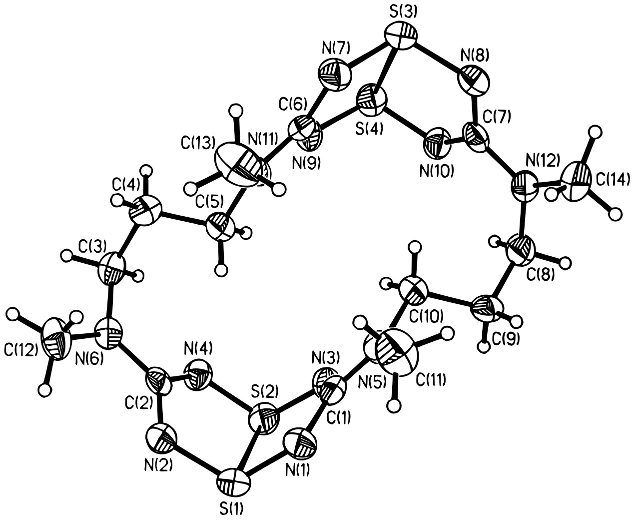


Figure 3. X-ray structure of the trimethylene-bridged dimeric cyclophane **9**. Thermal ellipsoids are drawn at the 50% probability level.

Table 2. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Coefficients ($Å^2 \times 10^3$) for Compound **6**[a]

	x	*y*	*z*	*U*(eq)
S(1)	6100(1)	3472(1)	−289(1)	51(1)
S(2)	7390(1)	1979(1)	836(1)	43(1)
N(1)	5009(3)	2689(2)	−1235(2)	49(1)
N(2)	6169(3)	1249(2)	−94(2)	44(1)
N(3)	9148(3)	2236(2)	673(2)	43(1)
N(4)	7929(3)	3735(2)	−358(2)	50(1)
N(5)	4860(2)	1057(2)	−1952(2)	44(1)
N(6)	10398(3)	2976(2)	−440(2)	48(1)
C(1)	5393(3)	1678(2)	−1093(2)	39(1)
C(2)	9122(3)	2970(2)	−67(2)	41(1)
C(3)	3910(4)	1467(3)	−3026(2)	62(1)
C(4)	5369(3)	−31(2)	−1863(2)	52(1)
C(5)	6875(3)	−237(2)	−2199(2)	56(1)
C(6)	8606(3)	258(2)	−1502(2)	52(1)
C(7)	9060(4)	1180(2)	−2017(2)	55(1)
C(8)	10952(4)	1531(3)	−1476(2)	61(1)
C(9)	11445(3)	2062(2)	−378(2)	53(1)
C(10)	10548(4)	3829(2)	−1122(3)	68(1)

[a] *U*(eq) is defined as one-third of the trace of the orthogonalized $\mathbf{U}_{ij}$ tensor.

Table 3. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Coefficients ($Å^2 \times 10^3$) for Compound **8**[a]

	x	*y*	*z*	*U*(eq)
S(1)	4136(1)	4485(1)	8193(1)	45(1)
S(2)	2540(1)	5847(1)	6713(1)	40(1)
S(3)	595(1)	−1354(1)	7166(1)	34(1)
S(4)	1912(1)	−617(1)	5491(1)	33(1)
N(1)	2782(2)	4121(2)	8980(2)	43(1)
N(2)	4817(2)	3549(2)	7548(2)	45(1)
N(3)	1192(2)	5469(2)	7500(2)	35(1)
N(4)	3215(2)	4912(2)	6070(2)	41(1)
N(5)	365(2)	4099(2)	9131(2)	41(1)
N(6)	4622(2)	2938(2)	6127(2)	40(1)
N(7)	2076(2)	−1971(2)	7833(2)	36(1)
N(8)	−127(2)	105(2)	7041(2)	36(1)
N(9)	3396(2)	−1200(2)	6146(2)	31(1)
N(10)	1168(2)	846(2)	5341(2)	36(1)
N(11)	4522(2)	−2104(2)	7817(2)	39(1)
N(12)	−155(2)	2263(2)	6116(2)	39(1)
C(1)	1473(3)	4537(2)	8517(2)	33(1)
C(2)	4180(3)	3793(3)	6605(2)	38(1)
C(3)	5680(3)	1714(2)	6634(2)	43(1)
C(4)	5168(3)	559(2)	6713(2)	40(1)
C(5)	6241(3)	−698(2)	7322(2)	43(1)
C(6)	5893(3)	−1866(3)	7266(2)	44(1)
C(7)	3305(3)	−1712(2)	7258(2)	31(1)
C(8)	334(3)	1050(2)	6192(2)	32(1)
C(9)	−1124(3)	2596(3)	6963(3)	50(1)
C(10)	−548(3)	3365(3)	7423(2)	48(1)
C(11)	−1524(3)	3626(3)	8348(3)	60(1)
C(12)	−1101(3)	4563(3)	8710(3)	53(1)
C(13)	585(4)	3113(3)	10245(2)	62(1)
C(14)	4169(3)	3244(3)	5025(2)	50(1)
C(15)	4513(4)	−2767(3)	9018(2)	60(1)
C(16)	210(3)	3330(2)	5175(2)	55(1)

[a] *U*(eq) is defined as one-third of the trace of the orthogonalized $\mathbf{U}_{ij}$ tensor.

the trimethylene bridges of **9** are attached *cis* to one another on each of the heterocycles, and the four methyl groups project above the more open face of the trough, effectively blocking and filling this cleft (Figure 3). For this reason, it is only in **8** that the molecular cavity is sufficiently open to accommodate a solvent molecule (see Figure 4); in the crystal, this space is occupied by a disordered methylene chloride.

The geometries of the two DTTA rings in compound **8** are very similar to those of the unconstrained derivative **2** and the loosely-bridged cyclophane **3**. The small ranges of the observed transannular C−C distances (3.54−3.59 Å), N^3-N^7 distances (5.56−5.67 Å), and ring fold angles (105.7−106.6°) for the DTTA rings in these three molecules (see Table 4) suggest that they are relatively unstrained. Unexpectedly, the dimeric phane **9** appears to be slightly strained, with more acute ring folds (101.9 and 101.7°) and correspondingly shorter transannular distances. Significantly greater deviations from an "ideal" geometry are found in the structure of the monomeric phane **6**. Here the ring fold angle is only 98.3° and the N^3-N^7 distance is 4.98 Å, 0.6 Å shorter than the average for compounds **2**, **3**, and **8**. In addition, the bis(dialkylamino) groups of **6** are twisted with respect to the heterocycle: the torsional angles N(2)−C(1)−N(5)−C(4) and N(3)−C(2)−N(6)−C(9) (see Figure 1) are −11.3 and 20.9°, respectively.

As discussed above, the pentamethylene-bridged phane **7** appears to be formed in our macrocyclization reactions, but a pure sample was not obtained. The DTTA ring of **7** must be considerably more distorted than that of **6**, so we investigated the structure of this compound by means of ab initio calculations

Table 4. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Coefficients ($Å^2 \times 10^3$) for Compound **9**[a]

	x	*y*	*z*	*U*(eq)
S(1)	2769(3)	4531(2)	5570(1)	47(1)
S(2)	6471(3)	5897(2)	6101(1)	42(1)
S(3)	2913(3)	9170(2)	9381(1)	42(1)
S(4)	6602(3)	9663(2)	8951(1)	41(1)
N(1)	1738(8)	3917(5)	6235(2)	41(2)
N(2)	2744(8)	6362(5)	5393(2)	41(2)
N(3)	5398(8)	5218(5)	6754(2)	38(2)
N(4)	6291(7)	7719(5)	5951(2)	37(2)
N(5)	2151(8)	4296(5)	7313(2)	41(2)
N(6)	3946(7)	9236(5)	5683(2)	35(2)
N(7)	1909(7)	9264(5)	8685(2)	40(2)
N(8)	2771(8)	7274(5)	9552(2)	42(2)
N(9)	5554(8)	9823(5)	8269(2)	39(2)
N(10)	6301(8)	7721(5)	9093(2)	38(2)
N(11)	2300(8)	9097(5)	7625(2)	38(2)
N(12)	3872(8)	4998(5)	9276(2)	37(2)
C(1)	3104(10)	4534(6)	6758(3)	35(2)
C(2)	4292(9)	7733(7)	5692(2)	31(2)
C(3)	5275(9)	10669(6)	6097(2)	39(2)
C(4)	4061(9)	10716(6)	6700(2)	39(2)
C(5)	3586(10)	9107(7)	7072(2)	39(2)
C(6)	3267(10)	9346(6)	8201(2)	34(2)
C(7)	4287(9)	6698(7)	9292(2)	34(2)
C(8)	5208(10)	4272(7)	8900(2)	44(2)
C(9)	4036(10)	3611(6)	8263(2)	40(2)
C(10)	3500(10)	4976(6)	7895(2)	41(2)
C(11)	−289(10)	3478(8)	7354(3)	61(3)
C(12)	1890(9)	9327(7)	5380(3)	48(3)
C(13)	−149(10)	8674(9)	7524(3)	62(3)
C(14)	1742(10)	3846(7)	9512(3)	51(3)

[a] *U*(eq) is defined as one-third of the trace of the orthogonalized $\mathbf{U}_{ij}$ tensor.

Table 5. Selected Experimental and Calculated Geometric Parameters for Free and Cyclophane-Constrained 3,7-Bis(dialkylamino)-1,5,2,4,6,8-dithiatetrazocine Rings

compd	S−S, Å	C−C, Å	N^3-N^7, Å	ring fold angle,[a] deg
2 (X-ray)[b]	2.43	3.54	5.56	105.7
3 (X-ray)[c]	2.41	3.57	5.59	106.3
6 (X-ray)	2.44	3.35	4.98	98.3
8 (X-ray)	2.38	3.57	5.61	106.2
	2.37	3.59	5.67	106.6
9 (X-ray)	2.43	3.44	5.29	101.9
	2.44	3.44	5.26	101.7
2 (calcd)[d]	2.48	3.61	5.70	107.9
7 (calcd)[e]	2.47	3.30	4.78	96.2

[a] The ring fold angle is defined to be the angle formed by the two ring carbons and the midpoint between the two ring sulfur atoms. [b] Reference 1. [c] Reference 6b. [d] HF/3-21G(*) ab initio calculation fully optimized under the constraint of C_{2v} symmetry. [e] HF/3-21G(*) ab initio calculation fully optimized under the constraint of C_s symmetry.

at the HF/3-21G(*) level.[10] Selected geometric parameters for **2** and **7** from such calculations are also given in Table 5. From the data for **2**, which may be compared to the experimental values in the same table, it is seen that this method gives reasonable geometries but slightly overestimates the ring fold angle and transannular distances. Even so, the DTTA ring of **7** is calculated to have a fold angle of only 96.2°, fully 10° less than typical values for the unstrained heterocycles. The calculated structure of compound **7** is shown in Figure 5; all of the distortions present in **6** are exhibited to a greater degree in **7**.

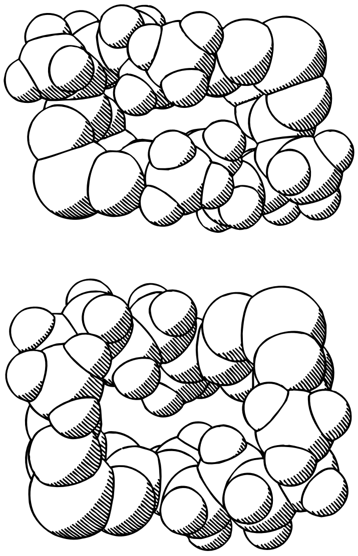


Figure 4. Space-filling drawings of compounds **9** (above) and **8** (below) which illustrate their rectangular shapes and central clefts.

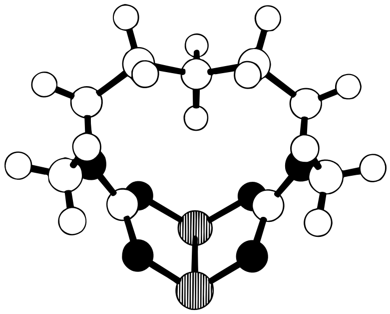
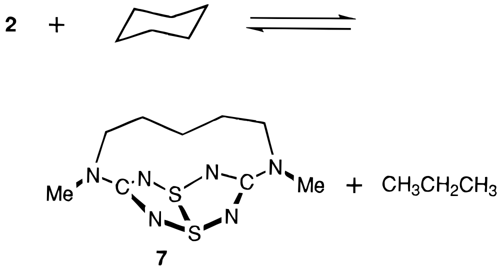


Figure 5. Perspective drawing of the calculated [HF/3-21G(*)] geometry for the pentamethylene-bridged monomeric cyclophane **7**.

These calculations also permit the estimation of the strain introduced by incorporation of the DTTA ring into cyclophane **7** from the calculated energy for the homodesmic reaction.



This is +18.0 kcal/mol, a reasonable, if not easily testable, value for the strain energy in compound **7**. Were the strain any higher, it is unlikely that the cyclophane could form under our mild reaction conditions, and of course, no monomeric phanes were found for bridges containing less than five methylene groups.

Conclusion

The syntheses of the cyclophanes reported here are extremely simple, and from a preparative standpoint, the very low yields are partly offset by the brevity of the syntheses. However, only relatively small macrocycles, containing one or two DTTA rings, were prepared. The DTTA's are certainly stable enough to be useful components of large host molecules or other organic structures, but if they are to be exploited in complex systems,

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(10) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; John Wiley & Sons: New York, 1986; pp 63−100.

a more efficient synthesis will be required. Amin and Rees[3] have shown that somewhat higher and more consistent yields for the synthesis of monomeric DTTA's can be achieved by the use of more exotic sulfurating reagents than SCl_2, but it remains to be seen if these methods will give much improvement in the synthesis of DTTA-containing cyclophanes. In addition, methods for the introduction of more than two DTTA's into a macrocycle will need to be developed if very large rings are required. Nevertheless, the unusual geometry of these molecules and the conformational preferences they induce in large rings should make such efforts worthwhile.

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Supporting Information Available: Crystal structure reports for compounds **6**, **8**, and **9**, including text describing the experimental work, tables of atomic coordinates, H atom coordinates, anisotropic thermal parameters, bond distances and angles, and torsion angles, and various molecular drawings; tables of atomic coordinates for the ab initio calculated geometries of compounds **2** and **7** (57 pages). Ordering information is given on any current masthead page.

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