b]furan-6,11-dione, 93404-27-4; 4-phenylanthra[2,1-b]-thiophene-6,11-dione, 64747-11-1; 5-(2-thienyl)benz[a]-anthracene-7,12-dione, 64747-12-2; 3-methyl-4-phenyl-3H-naphth[2,3-e]indole-6,11-dione, 66643-69-4; 8-phenylanthra[2,1-d]thiophene-8,13-dione, 75488-33-4; 5-(2-benzo[b]thienyl)benz-[a]anthracene-7,12-dione, 75488-34-5; 5-methyl-6-phenyl-5H-naphtho[2,3-c]carbazole-8,13-dione, 66643-67-2; 5-(3-pyridyl)-benz[a]anthracene-7,12-dione, 75488-37-8; 5-(4-pyridyl)benz[a]-anthracene-7,12-dione, 75488-38-9; 2-methoxy-3-(2-methoxy-1-propenyl)-1,4-naphthoquinone, 93404-28-5; 2-bromo-3-(2-methoxy-1-propenyl)-1,4-naphthoquinone, 93404-29-6; 2-acetonyl-3-methoxy-1,4-naphthoquinone, 91406-82-5; 2-acetonyl-3-bromo-1,4-naphthoquinone, 91406-81-4; 6-methoxy-5,8-quinoxalinedione, 56369-10-9.

A Novel Hexacyclic Ring System from Glycoluril

William L. Mock,* T. Manimaran, Wade A. Freeman,* Robert M. Kuksuk, John E. Maggio,[1] and Dudley H. Williams[1]

Department of Chemistry, University of Illinois at Chicago, Chicago, Illinois 60680

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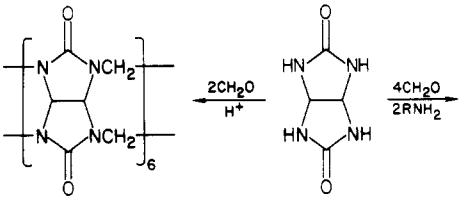
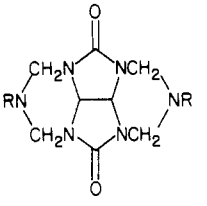
Condensation of 2 equiv of an alkanediamine (ethane–butane) with 6 equiv of formaldehyde and 1 equiv of glycoluril (or a simple derivative thereof) yields a new hexacyclic ring system. Seven examples are described (**4–10**). An X-ray crystallographic structure determination is provided.

Glycoluril (**1**) has proven to be a versatile progenitor of polycyclic ring systems. When allowed to react with formaldehyde under strongly acidic conditions, **1** yields the novel nonadecacyclic cage structure of cucurbituril (**2**).[2]



2 **1**



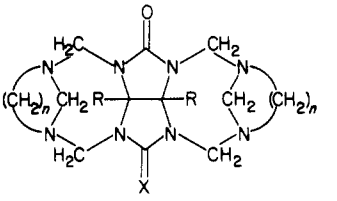
3

Under less stringent conditions **1** condenses with formaldehyde in the presence of aliphatic amines to yield **3**.[3] In attempting to carry out this latter reaction with certain alkanediamines, we have encountered yet another novel ring system, the subject of this report.

Results

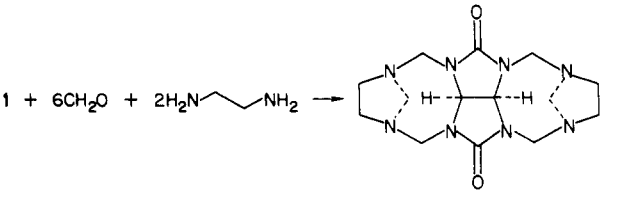
Synthesis. Slow addition of 1,2-ethanediamine to a refluxing mixture of **1** and formaldehyde in methanol yielded a high-melting crystalline substance **4**. The stoichiometry of the reaction was indicated to be $1 + 6CH_2O + 2H_2NCH_2CH_2NH_2 \rightarrow C_{14}H_{22}N_8O_2 + 6H_2O$ by mass spectral and NMR analyses of the product. An initially puzzling feature of the characterization of **4** was the clear indication that the six formaldehyde moieties had entered into two different and unique environments, according to NMR data (^1H, ^{13}C). However, elements of symmetry appeared to be present in the structure of **4**, since chemically equivalent carbons of the glycoluril and ethanediamine reactants retained magnetic equivalence in the product **4**. The spectral properties were eventually reconciled by the following equation.

Table I. Alkanediamine–Formaldehyde Condensation Products from Glycolurils



no.	X	R	n	M_r,[a] (MH^+)	yield, %
4	O	H	2	335	62
5	O	H	3	363	54
6	O	CH_3	2	363	28
7	O	CH_3	3	391	70
8	O	CH_3	4	419	40
9	O	C_6H_5	3		28
10	S	H	3	379	20

[a] FAB mass spectral molecular weight (Kratos MS-50, samples dissolved in glycerol–1% acetic acid on Cu probe, bombarded with 6 keV xenon atoms at 10^{-5} torr).



4

The new synthesis appears to have some generality. As may be seen in Table I, an analogous structure (**5**) was obtained employing 1,3-propanediamine and formaldehyde with **1**. The reaction succeeded equally well with substituted derivatives of the diurea component. Dimethylglycoluril and formaldehyde gave **6**, **7**, and **8** with 1,2-ethanediamine, 1,3-propanediamine, and 1,4-butanediamine, respectively. Diphenylglycoluril formed **9** with

(1) University Chemistry Laboratory, Cambridge, U.K.
(2) Freeman, W. A.; Mock, W. L.; Shih, N.-Y. *J. Am. Chem. Soc.* **1981**, *103*, 7367.
(3) Savostianoff, D. Fr. Demande 2 291 203; *Chem. Abstr.* **1977**, *86*, 121377n.

0022-3263/85/1950-0060$01.50/0

Table II. Crystallographic Data for Glycoluril Derivatives

no.	crystal system; cell constants[a]	density[b]	Z[c]	space group
4	monoclinic;[d] a = 10.81, b = 6.74, c = 11.43, γ = 97.7, V = 825	1.46	2	$P2_1$ or $P2_1/m$
5	orthorhombic; a = 11.87, b = 26.37, c = 11.60, V = 3631	1.36	8	$Pbm2$ or $Pb2_1m$ or $Pbmm$
6	orthorhombic; a = 7.14, b = 13.33 c = 18.55, V = 1766	1.34	4	$Pc2_1b$ or $Pcmb$
7	orthorhombic; a = 7.43, b = 13.86, c = 18.21, v = 1875	1.33	4	$Pc2_1b$ or $Pcmb$
10	monoclinic;[e] a = 7.275(5), b = 13.052(7), c = 9.726(7), β = 104.92, V = 892.4	1.43	2	$P2_1$
	monoclinic;[f] a = 7.23, b = 14.88, c = 17.54, a = 107.2, V = 1803	1.39	4	$P2_1/c$

[a] Dimensions: Å, degrees, and Å^3; nonconventional cells chosen for the sake of comparison. [b] By flotation, g cm^{-3}. [c] No. molecules per unit cell. [d] Obtained with 1 CH_3COCH_3 (solvent) per unit cell. [e] From CH_3OH solution. [f] From CH_2Cl_2 solution.

1,3-propanediamine and formaldehyde. The reaction was also successfully carried out with (mono)thioglycoluril, yielding **10** with 1,3-propanediamine and formaldehyde. An attempt was made to extend the reaction to higher aliphatic diamines than those reported in Table I. However, in such cases analogous molecules were not obtained, but oligomeric structures corresponding to **3** appear to be produced instead. These results will be reported separately.

The structures proposed (Table I) are entirely supported by spectral evidence provided in the Experimental Section Furthermore, these substances were demonstrated to be homologous by NMR induced-shift studies (^{1}H, ^{13}C), in which nuclei in analogous positions showed similar spectral perturbations in the presence of europium or ytterbium shift reagents. However, since certain alternative structures could not be rigorously excluded, and because configurational features were not spectrally discernible, a crystallographic determination of one member of the series (**10**) was undertaken.

Crystal Structures. Preliminary crystallographic information was obtained on several of the new substances. Comparison of the crystal data in Table II strongly suggests that all of the compounds examined in this way have a similar geometry. With respect to the unit cell, in every case $|\vec{b}|$ is approximately 1,2, or 4 times 6.8 Å, and $|\vec{a} \times \vec{c}|$ is likewise an integral multiple of 66 Å^2. In addition, the space groups are related. Crystals of the sulfur-containing substance **10** chosen for detailed study were obtained from methanol in the monoclinic system (Table II). Solution and refinement of the structure succeeded in the space group $P2_1$. The structure was solved by direct methods (ACSHELX)[4] and was refined to R = 0.0787 and R_w = 0.0929 based on 1562 diffractometer-measured data with $F > 3.0\sigma(F)$. A perspective view of the molecule is given in Figure 1.

In the crystal the molecule half-surrounds a point in space equidistant from the sulfur atom (S), the oxygen atom (O), and the nominally equivalent nitrogen atom pairs N(3),N(3A) and N(4),N(4A) (Figure 1). The molecule is disordered about this point, as if it were a center of inversion, with site occupancies of (approximately) $^2/_3$ and $^1/_3$. Despite the complication, the X-ray study firmly establishes the molecule to be the diastereomer in which the methano bridges C(4) and C(9) are syn to the methine hydrogens of the thioglycoluril moiety. The distance from C(6) to C(11) is 4.42 Å, and the corresponding distance between hydrogen nuclei of these proximally located methylene units is 2.71 Å. The apprent sterically enforced separation between the two propano bridges of **10** is achieved by expanding the bond angles about N(3), N(3A), N(4), and N(4A) to an average of 116° (i.e., nitrogen bond angles enlarged from the pyramidal configuration expected for an aliphatic amine). The central portion of the molecule has a geometry comparable to that previously described for the glycoluril nucleus.[5] Additional information is provided as supplementary material.

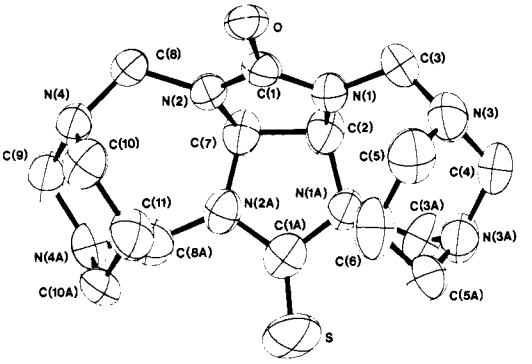


Figure 1. Perspective view of **10** as secured from crystallographic structure determination (hydrogen atoms deleted). Numbering corresponds to NMR spectral descriptions in Experimental Section.

Discussion

As for the details of the mechanism of assembly of **4–10**, some reasonable speculations are possible. Since aliphatic amino groups are rather more nucleophilic than are the urea nitrogens of **1**, we surmise that the intermediate **11** forms initially and subsequently condenses with the glycoluril (which only dissolves as the reaction proceeds) to yield the ultimate product. Intermediacy of **11** may also explain why ordinarily easily produced structures of type **3** are *not* formed with the lower aliphatic diamines (as our experience indicates).

$$H_2N(CH_2)_nNH_2 + 3CH_2O \xrightarrow{-H_2O} HOCH_2N\text{—}CH_2\text{—}NCH_2OH \rightarrow \textbf{4–10}$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\quad \llcorner(CH_2)_n\lrcorner$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad \textbf{11}$$

Considering the diversity of condensations which *might* occur between these reactants, obtention of a single, hexacyclic product in isolated yields of as much as 70% is remarkable. No fewer than 12 C–N bonds must spontaneously form sequentially (in several instances stereoselectively) in the synthesis of **4–10**. The extent to which kinetic and thermodynamic factors control the fate of the various intermediates is not known.

Experimental Section

General Methods. Synthesis and characterization of substances in Table I are described below. For purposes of recording crystallographic and NMR spectral data, C and N ring positions are numbered (superscript) as is Figure 1 (for NMR, $C^2 = C^7$, $C^3 = C^8$, etc.).

Preparation of 4. A suspension of 7.1 g of glycoluril (0.05 mol) in 24 mL of 37% aqueous formaldehyde (0.3 mol) and 150 mL of methanol in a 500-mL flask was brought to reflux in an oil bath

(4) G. Sheldrick, "Programs for Crystal Structure Determination", Cambridge, 1975.

(5) Freeman, W. *Acta. Crystallogr., Sect. B* **1984**, *B40*, 382. Himes, V. L.; Hubbard, C. R.; Mighell, A. D.; Fatiadi, A. J. *Acta. Crystallogr., Sect. B.* **1978**, *B34*, 3102.

with magnetic stirring. To this mixture was added slowly a solution of 6.0 g of ethanediamine (0.1 mol) in 200 mL of methanol dropwise, and refluxing was then continued overnight. The reaction mixture was cooled to room temperature, and unreacted glycoluril (0.93 g) was removed by filtration. The solution was concentrated and cooled to 5 °C. A precipitate was collected, washed with a little acetone, and dried, yielding 8.99 g of **4** (62%), which could be recrystallized from methanol, ethanol, or acetone: mp 256–258 °C; IR (KBr) 1690 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 4.99 (2 H, s, C^2H), 5.08 and 3.98 (4 H ea., reciprocal d, J = 14.4 Hz, C^3HaHb), 4.21 and 3.82 (2 H ea., reciprocal d, J = 11.7 Hz, C^4HaHb), and 2.82–3.14 (8H, m, C^5H); ^{13}C NMR ($CDCl_3$) δ 158.82 (C^1), 78.36 (C^3), 70.84 (C^2), 65.62 (C^4), 47.24 (C^5); mass spectrum, m/e 334. Anal. Calcd for $C_{14}H_{22}N_8O_2 \cdot 2H_2O$: C, 45.40; H, 7.08; N, 30.25. Found: C, 45.33; H, 7.08; N, 30.15. This material appeared rapidly to pick up atmospheric moisture after drying.

Preparation of 5. From 7.1 g of glycoluril (0.05 mol) and 24 mL of aqueous formaldehyde (0.3 mol) in methanol with 7.4 g of 1,3-propanediamine (0.1 mol) there was obtained by the same procedure 9.77 g of **5** (54%); mp 273–275 °C; IR (KBr) 1690 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 5.11 (2 H, s, C^2H), 5.17 and 3.92 (4 H ea., reciprocal d, J = 14.6 Hz, C^3HaHb), 4.38 and 3.81 (2 H ea., reciprocal d, J = 14.6 Hz, C^4HaHb), 3.1–3.5 (8 H, m, C^5H), 1.7–2.0 and 1.0–1.2 (2 H ea., m, C^6HaHb); ^{13}C NMR ($CDCl_3$) δ 157.41 (C^1), 71.48 (C^4), 70.87 (C^2), 64.80 (C^3), 47.07 (C^5), 21.68 (C^6); mass spectrum, m/e 362. Anal. Calcd for $C_{16}H_{26}N_8O_2$: C, 53.02; H, 7.23; N, 30.92. Found: C, 52.81; H, 7.48; N, 30.90.

Preparation of 6. From 8.5 g of dimethylglycoluril (0.05 mol), 24 mL of aqueous formaldehyde, and 6.0 g of ethanediamine (0.1 mol) in 350 mL of refluxing methanol there was obtained 3.52 g of **6** (28%, based upon unrecovered dimethylglycoluril): mp 248–249 °C; IR (KBr) 1690 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 5.04 and 4.0, (4 H ea., reciprocal d, J = 15.1 Hz, C^3HaHb), 4.08 and 3.87 (2 H ea., reciprocal d, J = 12.0 Hz, C^4HaHb), 2.6–3.3 (8 H, m, C^5H), 1.58 (6 H, s, C^2CH_3); ^{13}C NMR ($CDCl_3$) δ 157.42 (C^1), 77.62 (C^4), 76.28 (C^2), 60.31 (C^3), 46.64 (C^5), 15.67 (C^2CH_3); mass spectrum, m/e 362. Anal. Calcd for $C_{16}H_{26}N_8O_2$: C, 53.02; H, 7.23; N, 30.92. Found: C, 52.77; H, 7.10; N, 30.32.

Preparation of 7. From 8.5 g of dimethylglycoluril (0.05 mol), 24 mL of aqueous formaldehyde solution, and 7.4 g of 1,3-propanediamine (0.1 mol) in refluxing methanol there was obtained 13.65 g of **7** (70%, most separating directly from the reaction mixture, with no recovery of dimethylglycoluril): mp 297–299 °C; IR (KBr) 1680 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 5.13 and 4.10 (4 H ea., reciprocal d, J = 15.1 Hz, C^3HaHb), 4.35 and 3.84 (2 H ea., reciprocal d, J = 14.6 Hz, C^4HaHb), 2.9–3.5 (8 H, C^5H), 1.7–2.0 and 0.9–1.1 (2 H ea., m, C^6H), 1.61 (6 H, s, C^2CH_3); ^{13}C NMR ($CDCl_3$) δ 157.06 (C^1), 76.40 (C^2), 71.06 (C^4), 60.01 (C^3), 47.68 (C^5), 22.41 (C^6), (C^2CH_3); mass spectrum, m/e 390. Anal. Calcd for $C_{18}H_{30}N_8O_2$: C, 55.37; H, 7.74; N, 28.70. Found: C, 55.09; H, 7.98; N, 28.50.

Preparation of 8. From 8.5 g of dimethylglycoluril (0.05 mol), 24 mL of aqueous formaldehyde, and 8.8 g of 1,4-butanediamine in 350 mL of refluxing methanol there was obtained 8.3 g of **8** (40%, isolation as for **7**): mp 282–283 °C; IR (KBr) 1680 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 4.96 and 4.13 (4 H ea., reciprocal d, J = 15.1 Hz, C^3HaHb), 4.33 and 3.88 (2 H ea., reciprocal d, J = 15.6 Hz, C^4HaHb), 3.0 (8 H, br s, C^5H), 1.7 (8 H, br s, C^6H), 1.58 (6 H, s, C^2CH_3); ^{13}C NMR ($CDCl_3$) δ 157.36 (C^1), 76.46 (C^2), 71.24 (C^4), 59.76 (C^3), 51.02 (C^5), 29.04 (C^6), 17.43 (C^2CH_3); mass spectrum, m/e 418. Anal. Calcd for $C_{20}H_{34}N_8O_2$: C, 57.39; H, 8.19; N, 26.77. Found: C, 56.29; H, 8.13; N, 26.54.

Preparation of 9. From 7.4 g of diphenylglycoluril (0.025 mol), 12 mL of aqueous formaldehyde solution, and 3.7 g of 1,3-propanediamine (0.05 mol) there was obtained 3.67 g of **9** (28%): mp 270–272 °C; IR (KBr) 1680 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 6.5–7.1 (10 H, m, C_6H_5), 5.41 and 4.11 (4 H ea., reciprocal d, J = 14.9 Hz, C^3HaHb), 4.13 and 3.35 (2 H ea., reciprocal d, J = 14.3 Hz, C^4HaHb), 3.5–3.7 and 3.0–3.3 (8 H, m, C^5H), 2.0–2.4 and 0.9–1.4 (2 H ea., m, C^6H); ^{13}C NMR ($CDCl_3$) δ 159.54 (C^1), 85.57 (C^2), 71.61 (C^4), 61.83 (C^3), 46.83 (C^5), 21.93 (C^6), 131.73, 128.82, 128.27 (C_6H_5); mass spectrum, m/e 514. Anal. Calcd for $C_{28}H_{34}N_8O_2$: C, 65.35; H, 6.66; N, 21.77. Found: C, 65.08; H, 6.79; N, 21.54.

Preparation of 10. From 7.4 g of monothioglycoluril (0.05 mol), 24 mol of aqueous formaldehyde, and 7.4 g of 1,3-propanediamine (0.1 mol) in refluxing methanol there was obtained 3.8 g of **10** (20%) after chromatography on a silica column using chloroform as eluant: mp 242–243 °C; IR (KBr) 1680 cm^{-1} (C=O); ^1H NMR ($CDCl_3$), δ 6.05 and 4.04 (2 H ea., reciprocal d, J = 14.6 Hz, $C^{3A}HaHb$); 5.29 (2 H, s, C^2H), 5.19 and 3.96 (2 H ea., reciprocal d, J = 14.7 Hz, C^3HaHb), 4.37 and 3.86 (2 H ea., reciprocal d, 14.5 Hz, C^4HaHb), 3.0–3.8 (8 H, m, C^5H and $C^{5A}H$), 1.6–1.9 and 1.0–1.2 (2 H ea., m, C^6H); ^{13}C NMR ($CDCl_3$) δ 183.07 (C^{1A}), 157.32 (C^1), 74.72 (C^2), 72.20 (C^4), 68.55 (C^{3A}), 65.40 (C^3), 47.23 (C^5), 46.84 (C^{5A}), 21.72 (C^6); mass spectrum, m/e 378. Anal. Calcd for $C_{16}H_{26}N_8OS$: C, 50.54; H, 6.94; N, 29.36; S, 8.61. Found: C, 50.77; H, 6.92; N, 29.61; S, 8.47.

Acknowledgment. We thank the Dow Chemical Company Foundation for support (to W.L.M.) and Clifford Coon (Lawrence Livermore National Laboratory) for information and structural confirmations regarding **3**. We thank the University of Illinois at Chicago Computer Center for provision of computer time.

Registry No. **1**, 496-46-8; **4**, 93426-83-6; **5**, 93426-84-7; **6**, 93426-85-8; **7**, 93453-67-9; **8**, 93426-86-9; **9**, 93426-87-0; **10**, 93426-88-1; HCHO, 50-00-0; $NH_2(CH_2)_2NH_2$, 107-15-3; $NH_2(CH_2)_3NH_2$, 109-76-2; $NH_2(CH_2)_4NH_2$, 110-60-1; dimethylglycoluril, 28115-25-5; diphenylglycoluril, 5157-15-3; monothioglycoluril, 75371-25-4.

Supplementary Material Available: Experimental details of crystallographic structure determination for **10**; tables of bond distances and angles, atom coordinates, and anisotropic temperature factors (8 pages). Ordering information is given on any current masthead page.