with chloroform and the combined organic layers were washed with water, saturated brine, and dried ($MgSO_4$). The solvent was removed under reduced pressure. The residue and DBU (2 equiv) were refluxed together in benzene under nitrogen for 3 h. The mixture became black and formed a thick precipitate. The reaction mixture was cooled to 20 °C and poured onto excess dilute HCl and the layers separated. The aqueous layer was extracted with ether and the combined organic layers were washed with water and saturated brine and dried ($MgSO_4$). Solvent was removed under reduced pressure, and the residual oils were purified by preparative TLC to give, as the major or only product, the para-substituted product, as shown by NMR comparison with known compounds. Compound **9a** gave **12a** in 68% yield. Compounds **13a** and **13b** both gave **14a** in 58% yield. Compound **9c** gave **12c** in 53% yield.

General Procedure for Aromatization of Trisubstituted Diene Diels–Alder Adducts. The dienone **15** (1 equiv) and DBU (1 equiv) were refluxed together in benzene under nitrogen for 3 h. The reaction became black and formed a thick precipitate. The mixture was cooled to 20 °C and poured onto excess dilute HCl. The layers were separated and the aqueous layer was extracted with ether. The combined organic layers were washed with water and saturated brine and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the residual oil was purified by preparative TLC to give as the major, or only aromatic product, the para-substituted aromatic as shown by NMR comparison with known compounds. Compounds **15a** and **15b** both gave **12a** in 100% yields. Compounds **15 g** and **15 h** gave **14** in 70% and 100% yields, respectively. Compounds **15c** and **15d** gave **12c** in 40% and 100% yields, respectively. Compound **15e** gave **12e** in 88% yield. Compound **15f** gave **12f** in undetermined yield (due to the presence of MVK dimer).

***p*-(Phenylseleno)acetophenone (12c).** Acetyl chloride (0.13 mL, 1.8 mmol) was added dropwise to a stirring solution of diphenyl selenide (0.41 g, 1.8 mmol) and anhydrous aluminum chloride (0.29 g, 2.2 mmol) in carbon disulfide (5 mL) at 20 °C under nitrogen. There was a violent exothermic reaction, and the mixture was stirred for 1.5 h after the addition was completed. The reaction was quenched by pouring onto water (10 mL) and the layers were separated. The aqueous layer was extracted with ether (2 × 10 mL). The combined organic layers were washed with water (10 mL) and saturated brine (10 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure to yield a yellow oil which was purified by preparative TLC eluting with 10% ethyl acetate/hexane to give **13c** (0.14 g, 28%). Recrystallization from 95% EtOH gave yellow crystals: mp 47.5–49 °C. Anal. Calcd for $C_{14}H_{12}OSe$: C, 61.10; H, 4.29. Found: C, 61.17; H, 4.33. ^1H NMR δ 7.76 (2 H, half of AB quartet, J = 9 Hz, C2 aromatics), 7.4–7.7 (5 H, m, PhSe), 7.20 (2 H, half of AB quartet, J = 9 Hz, aromatics), 2.52 (3 H, s, methyl ketone); IR (KBr pellet) 1680, 1585, 1395, 1270, 955, 825, 750, 695 cm^{-1}.

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Registry No. **3a**, 85972-06-1; **3b**, 85972-07-2; **3c**, 85972-08-3; **3d**, 85972-09-4; **3e**, 85415-22-1; **3f**, 85972-10-7; **4a**, 85972-11-8; **4b**, 85972-12-9; **4c**, 85972-13-0; **4d**, 85972-14-1; **5a**, 85972-15-2; **5b**, 85972-16-3; **5c**, 85972-17-4; **5d**, 85972-18-5; **5e**, 85972-19-6; **5f**, 85972-20-9; **9a**, 85972-21-0; **9b**, 85895-55-2; **9c**, 85972-22-1; **9d**, 85972-32-3; **10a**, 85972-29-8; **10b**, 85972-30-1; **10c**, 85972-31-2; **10d**, 85972-33-4; **12c**, 85972-34-5; **13a**, 90606-71-6; **13b**, 90606-72-7; **15a**, 85972-23-2; **15b**, 85972-24-3; **15c**, 85972-25-4; **15d**, 85972-26-5; **15e**, 85972-27-6; **15f**, 85972-28-7; **15g**, 90606-73-8; **15h**, 90606-74-9; MVK, 78-94-4; $ClCH_2C{\equiv}CCH_2Cl$, 821-10-3; PhSCl, 931-59-9; PhSBr, 28074-23-9; PhSeCl, 5707-04-0; PhSeBr, 34837-55-3; Br_2, 7726-95-6; I_2, 7553-56-2; acrolein, 107-02-8.

Syntheses, Conformational Studies, and Reactions of Heteromacrocycles. Bis(2-pyridyl) Ketone Derivatives[1]

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A new series of spiromacrocycles were prepared by nucleophilic displacement of bromide from bis(6′-bromo-2′-pyridyl)-1,3-dioxolane; nucleophiles employed included the dianions of $HO(CH_2CH_2O)_nH$, n = 1–6, $HS(CH_2CH_2S)_nH$, n = 1,2, and $(HSCH_2CH_2)_2O$. Single-crystal X-ray diffraction studies on the 1:1 diethylene and 1:1 tetraethylene glycol ketal coronands showed them to have conformations dominated by the requirements of the pyridyl ketal unit (pyridine N anti to ketal O) and an inherent imidate moiety (N–C–O–C torsion angle near 0°). Besides the 1:1 coronands, isolated from most of the reactions, the higher oligomers and acyclic products were also obtained and characterized. ^1H NMR and elemental analytical data indicate that several of these macrocycles sequester $CHCl_3$. All of the 1:1 ketal crown ethers, and several of the 2:2 macrocycles, were hydrolyzed to the corresponding ketonic macrocycles. X-ray diffraction analysis indicated that the hexaethylene glycol ketonic coronand formed a neutral component complex with a water molecule, whereas the smaller tetraethylene glycol coronand did not. Reduction of the ketonic coronands with $NaBH_4$ produced the corresponding carbinol macrocycles, all of which were oils that were slowly transformed back to the corresponding ketone via air oxidation.

Introduction

Modified crown ether macrocycles containing a 2,6-pyridinediyl or 2,2′-bipyridine-6,6′-diyl subunit exhibit a penchant for the formation of neutral component complexes.[2] X-ray diffraction experiments confirm that **20e** and **1** bind a water molecule in the polyethylene portion of their structures,[2-4] whereas no evidence for this sort of neutral host–guest interaction is displayed by either **20c**

(1) (a) Part 98 in the Chemistry of Heterocyclic Compounds Series. (b) Taken from the PhD dissertation of HCRT, LSU, 1983.

(2) Newkome, G. R.; Taylor, H. C. R.; Fronczek, F. R.; Delord, T. J.; Kohli, D. K.; Vögtle, F. *J. Am. Chem. Soc.* **1981**, *103*, 7376.

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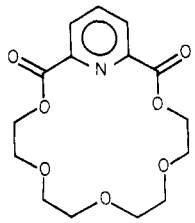

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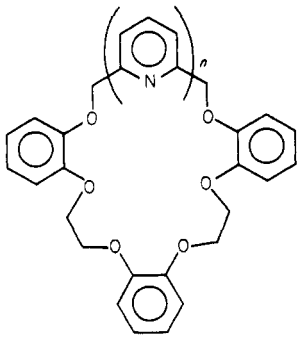
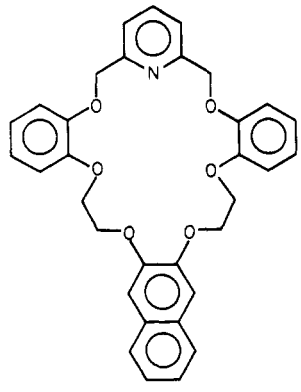
or 18-crown-6 (2). Coronands 3 and 4 have been shown



3, $n = 1$
4, $n = 2$



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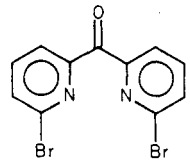
to exhibit remarkable discrimination between simple alcohols.[5] Most notably, methanol is selectively retrieved from ethanol by 3 and the converse by 4; neigher strongly bind isopropyl or larger alcohols. Slightly less specificity is manifested by 5, although it shows a strong preference for isopropyl alcohol and produces a neutral component complex of strict 2:1 (guest:host) stoichiometry. In an attempt to refine our understanding of the structural and conformational requirements of neutral component complexes, we have investigated a series of spiro ketal macrocycles and their corresponding ketones and carbinols. We report herein the syntheses, spectral studies, and selected X-ray data of coronands that possess a 2,2-bis(′-pyridyl)-1,3-dioxolane, 2,2-bis(2′-pyridyl) ketone, or 2,2-bis(2′-pyridyl)carbinol subunit connected by carbon–oxygen and/or sulfur linkages.

Results and Discussion

I. Ketal Macrocycles [2,2-Bis(2′-pyridyl)-1,3-dioxolane Subunit]. A. Preparation and Structure of 2,2-Bis(6′-bromo-2′-pyridyl)-1,3-dioxolane (7). Because pyridyl ketones can decarbonylate under mild, basic conditions,[6] protection of the carbonyl moiety of bis(6-bromo-2-pyridyl) ketone (6) was a necessary extra step,



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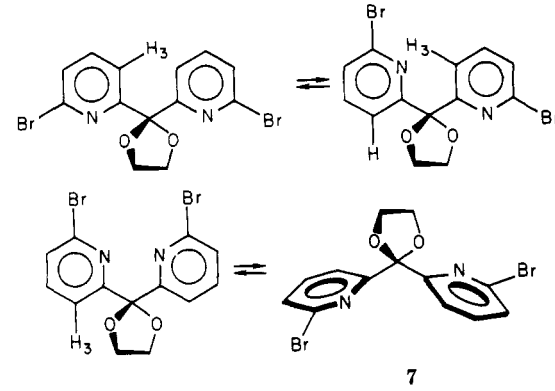
prior to macrocycle formation by our standard procedures.[7] Base-catalyzed ketalization of 6 by means of 2-chloro- or 2-bromoethanol afforded reasonable yields (48% and 85%, respectively) of 7,[8] but complicated isolation procedures

Scheme I



7

(to remove final traces of the halo alcohol and other side products) suggested that more traditional routes would be preferable. Ketalization was accomplished (98%) with freshly distilled ethylene glycol and a catalytic amount of concentrated H_2SO_4 in dry toluene; the solution was refluxed gently for five days. As a bonus, colorless prisms of ketal 7 crystallized upon in vacuo concentration of the solution.

The NMR spectrum of 7 exhibits an ABX pattern (three doublets of doublets) at δ 7.37, 7.56, and 7.79 for H-5, H-4, and H-3, respectively. The significant downfield shift ($\Delta\delta$ = 0.3) of ketone vs. ketal H-3 suggests that the pyridine rings adopt a conformation as close to anti (i.e., 7 in Scheme I) as can be accommodated with the investigation of the dioxolane ring. In this conformation, the proximity of H-3 to the N electrons on the adjacent pyridine ring subjects this proton to considerable deshielding effects derived from diamagnetic anisotropy and dipole fields effects.[9] The IR spectrum of 7, which lacks the characteristic carbonyl absorption at 1690 cm^{-1}, also substantiates the transformation of ketone to ketal.

B. Synthesis of Carbon–Oxygen Macrocycles. In general, treatment of dioxolane 7 with sodium (poly)-ethylene glycolate (generated from the appropriate glycol and 2.2 equiv of NaH) in toluene resulted in the formation of both spiromacrocyclic 8 and 9 (Scheme II) as well as numerous acyclic compounds.

In particular, reaction of 7 with ethylene glycolate in refluxing toluene afforded **9a** as the only macrocyclic product isolated. Inspection of a Corey–Pauling–Koltun (CPK) molecular model of **8a** indicated that although ethylene glycol is of sufficient length to bridge a 1:1 coronand, cyclization would require essentially complete overlap of the neighboring N electrons. Use of diethylene through hexaethylene glycols in this procedure under similar conditions generated the 1:1 **8b–f** and 2:2 **9b–g** spiromacrocycles. The 3:3 products (**10a,b**) were obtained from the reactions of diethylene (**a**) and hexaethylene (**b**) glycols, and even the 4:4 macrocycle (**11**) was isolated when hexaethylene glycol was employed. Numerous uncyclized compounds were also isolated and characterized. Both fragmentation and oligomerization processes are quite common for the polyethylene glycols, but these side reactions are generally minimized when the temperature is maintained below 140 °C.[7] For this reason, several of the reactions were repeated in refluxing (110 °C) or warm (70

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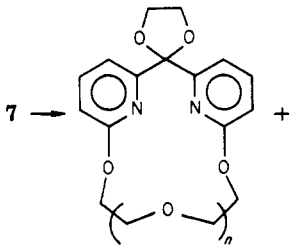
Table I. Physical Data for Ketal Macrocycles 8 and 9

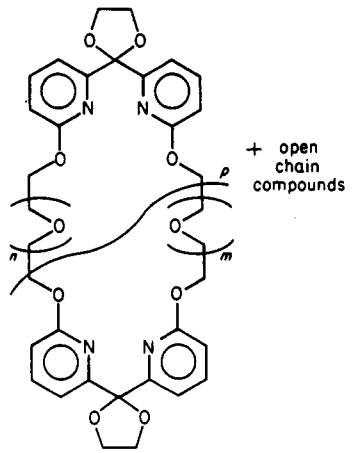
compd	NMR chem shift δ (J = Hz) 4-py H[a]	3-py H[b]	5-py H[c]	CH_2[d]	α ($J_{\alpha\beta}$)	β	γ (δ, ε, ξ)	mp, °C	IR[e]
8b	7.55	7.23	6.60	4.12	4.37 (5.7)	3.60		123–123.5	1592, 1455
8c	7.64	7.36	6.69	4.19	4.38 (4.5)	3.44	3.44 (m)	119.5–120	1593, 1455
8d	7.60	7.35	6.69	4.18	4.36 (4.6)	3.53	3.47 (m)	71–72	1591, 1457
8e	7.60	7.33	6.69	4.16	4.31 (4.9)	3.57	3.57 (m)	101.5–102	1592, 1456
8f	7.60	7.33	6.69	4.16	4.29 (4.9)	3.5 (m)	3.5 (m)	oil	1593, 1455
9a	7.50	7.24	6.55	4.16	4.34[d]			oil	1591, 1455
9b	7.57	7.30	6.63	4.15	4.25 (4.9)	3.46		oil	1587, 1458
9c	7.57	7.29	6.65	4.16	4.40 (4.9)	3.54	3.46 (m)	oil	1589, 1460
9d	7.57	7.29	6.66	4.16	4.30 (5.1)	3.62	3.51 (m)	oil	1592, 1458
9e	7.56	7.29	6.66	4.16	4.30 (4.9)	3.65	3.57 (m)	oil	1597, 1456
9f	7.56	7.28	6.67	4.16	4.31 (4.9)	3.68	3.62 (m)	oil	1598, 1458
9g	7.56	7.29	6.67	4.16	4.31 (4.9)	3.67	3.60 (m)	oil	1592, 1460

[a] J = 7.9, 7.3 Hz. [b] J = 7.3, 1.2 Hz. [c] J = 7.9, 1.2 Hz. [d] Broad singlet. [e] Pyridine frequencies in cm^{-1}.

Scheme II



8a, $n = 0$
b, $n = 1$
c, $n = 2$
d, $n = 3$
e, $n = 4$
f, $n = 5$



9a, $n = m = 0, p = 1$
b, $n = m = 1, p = 1$
c, $n = m = 2, p = 1$
d, $n = m = 3, p = 1$
e, $n = m = 4, p = 1$
f, $n = m = 5, p = 1$
g, $n = 4, m = 5, p = 1$

10a, $n = m = 1, p = 2$
b, $n = m = 5, p = 2$

11, $n = m = 5, p = 3$

°C) toluene in an effort to favor formation of the desired macrocycle. Unfortunately, utilization of toluene as the solvent necessitated extended reaction times and seemed to promote formation of the 2:2 and larger macrocycles at the expense of the desired 1:1 coronands.

In general, as the polyethylene glycols increased in length, the yield of the desired 1:1 spiromacrocycles **8** decreased. This observation is in accord with reports of enhanced fragmentation of these higher oligomers[10,11] and with the results of Monte Carlo calculations performed to determine the feasibility of cyclization of similar pyridyl crowns.[12] Although yields generally decreased as bridge length increased, the related dipyridine systems displayed the opposite trend: the yields *increased* with increased glycol length. The rationale for this phenomenon will be considered in detail elsewhere.

C. Structures of C,O Macrocycles. The ^1H NMR resonance frequencies (Table I) for the aromatic protons of the 1:1 **8b–f** and 2:2 spiromacrocycles **9a–g** form two internally consistent sets; chemical shifts for only the smallest member of each series deviate appreciably from those of the larger members. With the exception of **8b**, all macrocycles **8** and **9** commonly exhibit three doublets of doublets at approximately δ 6.65, 7.30, and 7.60 for H-5, H-3, and H-4, respectively. The strained 1:1 macrocycle **8b** exhibits a shift ($\Delta\delta$ = 0.1) of the aromatic region as a result of restricted conformational rotation to a more syn-type orientation. The ketal methylene protons of all of the spiromacrocycles resonate as a broad singlet very near δ 4.16 and likewise the α-methylene protons of the glycol bridges resonate at δ 4.3–4.4. The significant upfield shift of H-5 with respect to its position in **7**, the appearance of a broad singlet for the ketal methylene group, and the integration of the region for the α-methylene protons all substantiate the symmetrical nature of these macrocycles, in which an oxygen is attached *directly* to the pyridine ring. That H-3 becomes considerably more shielded than in the parent dioxolane indicates a diminished diamagnetic anisotropy, probably as a result of partial rotation of each pyridine ring away from the N electrons of the other.[13,14] The lack of discrimination among the β-through ξ-methylene protons is evidence that in solution the glycol bridge is, on the average, well removed from the vicinity of the heteroaromatic ring currents;[15] in other words the bridge is not confined to span the pyridine π-face. This is certainly the conformation adopted in the solid state, as proven by the X-ray crystal structure determination.

Although the 2:2 macrocycle **9a** has not been induced to crystallize, a reasonable estimate of its conformation can be derived by imposition of the several dioxolane macrocycle constraints discerned from the X-ray data of **8b** and **8d** (described below). Construction of a CPK model of **9a** that incorporates (a) a dihedral angle of approximately 90° between the pyridines flanking the two dioxolanes, (b)

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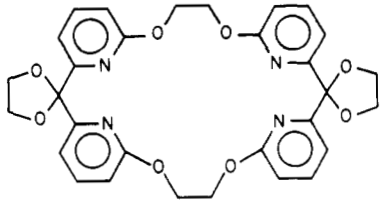


9a

the concomitant anti orientation of each pyridine with a dioxolane oxygen (a torsion angle of 180° for O–C–C–N), and (c) a torsion angle of nearly 0° associated with the imidate moiety results in a helical molecule which possesses D_2 symmetry. That these constraints are operative in solution, at least in the range 220–365 K, is evidenced by the results of variable temperature (VT) ^{1}H NMR studies.

Systematic changes in the VT NMR spectra of **9a** in toluene-d_8 from −53 to 27 °C result from a combination of temperature effects and solvent shifts. At 27 °C, a change of solvent from $CDCl_3$ to toluene-d_8 results in an upfield shift ($\Delta\delta$ = 0.4) of the H-4 signal. Resonance frequencies of the other heteroaromatic protons are basically unaltered by solvent changes. The conformation of **9a** must therefore permit interactions of H-4 with the ring current of the aromatic solvent while protecting H-3 and H-5 from its effect. As the temperature is decreased, the only change in the spectrum is the slow diamagnetic shift of H-4. The low-temperature contraction of polyethylene glycols is documented[12] and in **9a** there must be a concurrent torsion which acts to "tighten" the helix in order to accomodate the decreased length of the bridge. This molecular motion is represented by a clockwise twist of the upper portion of the molecule which brings each H-4 nearer the bridgeO electrons. The spectrum of **9a** retains a first-order aromatic region even at diminished temperature (−53 °C): the H-4 proton must therefore be magnetically equivalent. The D_2 symmetry proposed for **9a** also accounts for the extreme simplicity of the aliphatic region and the uniform appearance of the spectra throughout the observed temperature range. Corresponding changes in the low-temperature NMR spectra of **8b,f** indicate that the relative orientations of the pyridine rings, dioxolane ring, and α-oxygens must be similar in all of these molecules.

At higher temperatures (27–92 °C), however, a dramatic change in the heteroaromatic region is observed. The VT NMR spectra of **8b** are virtually identical with those of **8f**. In both cases, the ABX pattern observed at 27 °C is converted, at 92 °C, to one doublet at ca. δ 7.23 for H-3 and H-4 and a 5-line signal at ca. δ 6.50 for H-5. Resonances for the aliphatic protons shift slightly downfield but the pattern remains unchanged. This dependence of chemical shift on temperature arises primarily from the influence of sample density on the bulk magnetic susceptibility.[14] For **8b**, the resulting decrease in $\Delta\delta$ for H-3 and H-4 induces mixing of the corresponding wave functions, which in turn affects the transition frequencies and intensities.[15] Gradual variation of the AB chemical shifts as a function of temperature accounts for the progressive changes in appearance of both the AB and X regions. At 92 °C, fortuitous degeneracy of the H-3 and H-4 resonances leads not only to complete coalescence of the central two lines in the X spectrum, but also to the emergence of combination lines at the periphery of this pattern.[16]

The mass spectra of all of these macrocycles (**8** and **9**) are similar. Scheme SI (supplementary material) depicts the general fragmentation pattern of **8**; the relative abundances of important fragments are compiled in Table SI for **8** and in Table SII for **9**. A parent peak is observed for all 1:1 macrocycles **8**. Prominent in each spectrum is a peak due to loss of fragment m/e 43 ($C_2H_3O\cdot$) from the molecular ion; this is envisioned to arise from a McLafferty rearrangement, followed by fragmentation. The base peaks of macrocycles **8** and **9** results from the product of a double McLafferty rearrangement, i.e., a *bis*(pyridinonyl)dioxolane or fragment thereof.

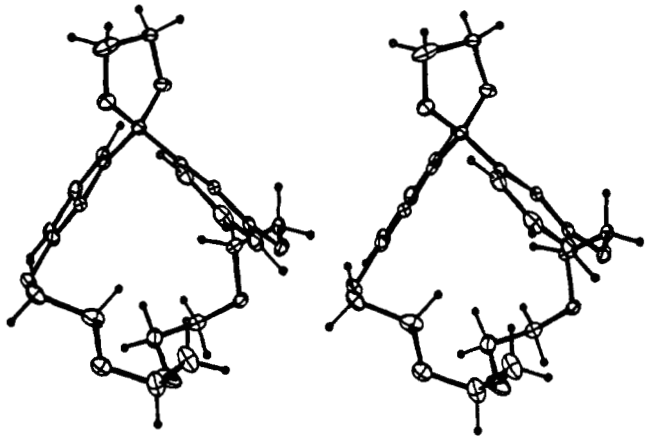


Figure 1. ORTEP stereopair of **8d**.

Several of these spiromacrocycles, especially **8b**, **9b**, **9f**, and **10b**, *tenaciously hold $CHCl_3$ even at the GC/MS probe temperature (200 °C, 4 × 10^{-7} mm)*. Concentration in vacuo of $CHCl_3$ solutions of these products and subsequent dissolution in toluene-d_8 affords samples that exhibits a resonance at δ 7.26 in the NMR spectra. Prolonged warming of the $CHCl_3$ solution at a pressure of 2.5 mm results in a material that lacks a $CHCl_3$ resonance. The possibility that these spiromacrocycles represent further examples of neutral component complexes[2] has prompted X-ray diffraction studies on those compounds from which suitable single crystals have been obtained.

Molecule **8d** is illustrated in Figure 1. It crystallizes without solvent complexation, and has approximate symmetry C_2. The major features of its solid state conformation are described by several key torsion angles. In both cases, the pyridine rings are turned with respect to the dioxolane ring such that nitrogen atoms are essentially anti to oxygen. Descriptive torsion angles of N1–C5–C6–O1 and N2–C7–C6–O7 and −179.9° and −178.1°, respectively; the pyridine rings thus form a dihedral angle of 97.2°. The imidate moiety is in both cases essentially syn to nitrogen: torsion angles N1–C1–O6–C19 and N2–C11–O2–C12 are −6.4° and 7.1°, respectively. The 13-atom polyether chain is sufficiently long and flexible to link the bis(pyridyl) ketal unit into the macrocycle framework in this unstrained, undistorted conformation. The dioxolane ring is nonplanar: the sum of the five intraannular torsion angle magnitudes is 61°. The largest of these, 18.8°, is about the C–C bond. Average lengths for various bond types are 1.331 Å C–N, 1.379 Å for aromatic C–C, 1.488 Å for aliphatic C–C, and 1.408 Å for C(sp^3)–O. The pyridine rings are planar to within 0.015 Å. Crystal data and non-hydrogen atom coordinates are compiled in Table SIII; bond lengths and angles are listed in Table SIV.

Molecule **8b** also crystallizes without complexed solvent. It is asymmetric and is illustrated in Figure 2. The much shorter polyether linkage does not allow the molecule to assume the unstrained C_2 symmetric conformation of **8d**. The near zero torsion angles of the pyridine–ether linkages are retained at the expense of rotation of one of the pyr-

(16) Freeman, R.; Bhacca, N. H. *J. Chem. Phys.* **1966**, *45*, 3795.

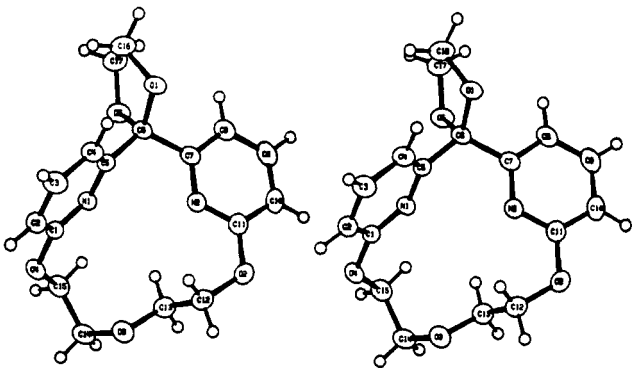


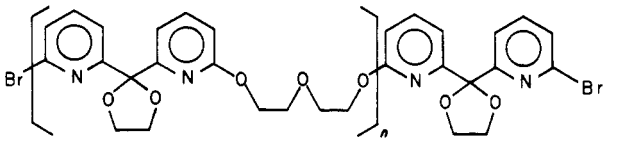
Figure 2. ORTEP stereopair of **8b**.

idine rings with respect to the dioxolane ring. Torsion angles N1–C1–O4–C15 (15.8°), N2–C11–O2–C12 (4.5°), and N1–C5–C6–O1 (172.1°) are analogous to those in the unstrained **8d**; however, the second pyridine ring is rotated away from the position anti to O5. Torsion angles N2–C7–C6–O5 (−122.4°) and N2–C7–C6–O1 (123.0°) indicate that this pyyridine ring is staggered between the two dioxolane oxygen atoms. The two pyridine rings thus form a dihedral angle of 66.8°. The dioxolane ring itself deviates much more from planarity than does that of **8d**: the sum of intraannular torsion angle magnitudes is 103°. The conformation of the five-membered ring is an approximate envelope in which C16 is at the flap. Average lengths for various bond types are 1.332 Å for C–N, 1.378 Å for aromatic C–C, 1.493 Å for aliphatic C–C, and 1.426 Å for C(sp^3)–O. The pyridine rings are planar to within 0.016 Å. Crystal data and non-hydrogen atom coordinates are compiled in Table SV; bond lengths and bond angles are listed in Table SVI.

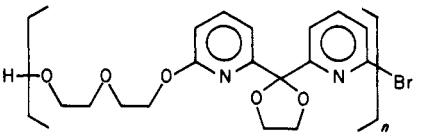
D. Structures of Acyclic Polyethylene Glycol Compounds. Sequential displacement of bromide and the slow rate of heteroaromatic nucleophilic substitution, even at elevated temperatures (140 °C), result in the isolation of numerous open chain substances irrespective of glycol used.[17] Several compounds obtained from treatment of **7** with the disodium salt of diethylene glycol were fully characterized; other acyclic materials were identified solely by their characteristic ^{1}H NMR spectra and were not dealt with further.

The ^{1}H NMR spectra of acyclic pyridyl ketals that possess at least one set of unsymmetrically substituted pyridine rings (**12–14**) are quite distinctive: two or more groups of first-order heteroaromatic patterns are observed. The first pattern corresponds to a pyridine substituted with a 6-oxygen atom (H-4 farthest downfield) and the second, shifted downfield with respect to the first, is essentially identical to the spectrum of **7** (H-3 farthest downfield). Furthermore, the ketal signal exists as a complicated multiplet, whereas in the symmetrically substituted compounds it appears as a broad singlet. Yet another diagnostic feature is provided by the presence of a terminal glycol, as in **13** and **14**, the various methylenes of which resonate at different frequencies and integrate for only two protons each. For **14**, symmetrical substitution renders the ketal signal a broad singlet; however, upfield resonances for the terminal glycols are quite conclusive.

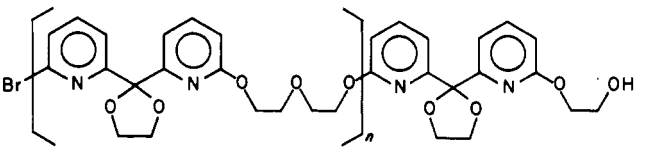
Bromo substitution is evidenced in the mass spectral data by the characteristic molecular fragments and isotopic abundance patterns. When a molecular ion is observed,



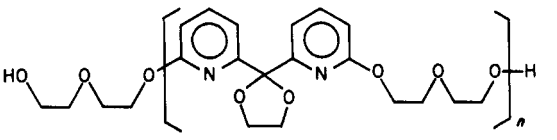
12a, $n = 1$
b, $n = 2$



13a, $n = 1$
b, $n = 2$
c, $n = 3$
d, $n = 4$



14, $n = 2$

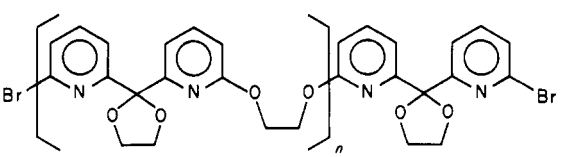


15a, $n = 1$
b, $n = 2$

determination of the number of bromines is facilitated and serves to corroborate the NMR data. Finally, the IR spectra of **11–13** exhibit a band at approximately 800 cm^{-1} that is associated with a C–Br stretch.

As is the case for several of the other macrocycles, **14** also sequesters and retains $CHCl_3$ even at 200 °C (GC/MS).

Ketal **7** when treated with purified ethylene glycolate afforded only low yields of acyclic **16a** and **16b** and cyclic **9a** products, all which were characterized as described above.



16a, $n = 0$
b, $n = 1$

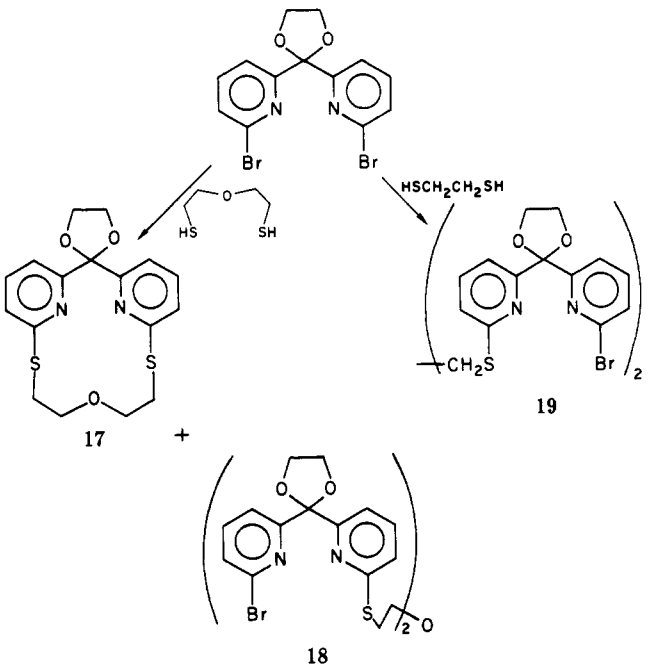
E. Synthesis of Carbon–Sulfur and Carbon–Oxygen–Sulfur Macrocycles. Attempts to prepare thioether analogues of C–O–C and **9** have met with minimal success: the only macrocycle that has been isolated (1%) is **17**, from reaction of **7** with bis(2-mercaptoethyl) ether. Dioxolane **7** is recovered *quantitatively* from the reaction with bis(2-mercaptoethyl) sulfide and constitutes the major fraction isolated from reactions with bis(2-merceptoethyl) ether (14%) and 1,2-ethanediol (22%) (Scheme III). Open chain compounds possessing terminal bromines [bis(pyridyl)dioxolanes:dithiol (2:1)] are the only other products obtained. Several acyclic disulfides have been identified by ^{1}H NMR, but these arise from air oxidation during purification[18] and have not been fully characterized.

As demonstrated in the case of 2,6-pyridinediyl macrocycles,[18] RO^- must be a better nucleophile than RS^- under

(17) Newkome, G. R.; McClure, G. L.; Broussard-Simpson, J.; Danesh-Khoshboo, F. *J. Am. Chem. Soc.* **1975**, *97*, 3232.

(18) Newkome, G. R.; Danesh-Khoshboo, F.; Nayak, A.; Benton, W. H. *J. Org. Chem.* **1978**, *43*, 2685.

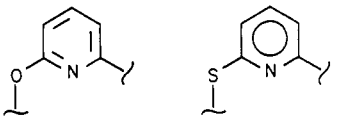
Scheme III



these reaction conditions, although studies performed in MeOH or HMPA indicate the reverse trend.[19] Whatever the cause of this effect, the result is certainly clear: polyether macrocycles are formed under the prevailing conditions whereas thioether macrocycles generally are not. Thus, although a smaller C–S–C vs. C–O–C bond angle should favor formation of the 14-membered ring of **17** over that of the corresponding C, O macrocycle, it is **8b** that is generated in the highest relative yield. [**8b** was isolated from reactions of triethylene and tetraethylene glycols, but not from that of diethylene glycol, which was conducted at higher concentration]. The reported yield (1%) is based on dioxolane; if based on the available diethylene glycol, which arose by fragmentation of the larger oligomer, the yield would be considerably greater. The yield reported for **17** is based on dioxolane as well, but in the presence of a slight excess of dithiol.

The best explanation for these results is in terms of the template effect.[20] Strong coordination of oxygens to alkali metal ions favorably organizes the various reacting species and so accounts for the relatively high yields of the polyethylene glycol macrocycles.[21-23] In contrast, thioethers coordinate alklai metal ions much more weakly, and the competition between macrocyclization and linear polymerization becomes dominated by statistical considerations.[24-26]

F. Structures of C, O, S and C, S Compounds. The ^{1}H NMR spectra of these sulfur analogues reflect the inherent differences in electronegativity, polarizability, and bonding character between sulfur and oxygen. Macrocycle **17** exhibits three doublets of doublets for its aromatic protons at δ 7.18, 7.40, and 7.52 for H-5, H-3, and H-4, respectively. The broad singlet for the ketal methylenes appears at δ 4.14 and the α- and β-protons appear as two doublets of doublets at δ 3.68 and 3.18, respectively. Thus, substitution of sulfur for oxygen adjacent to the pyridine

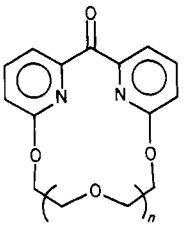


rings produces a significant downfield shift ($\Delta\delta$ = 0.5) for H-5 and a concomitant upfield shift ($\Delta\delta$ = 0.6) for the α-protons. The rigidity and bond localization engendered by imidate bonding[27] must be diminished when sulfur adjoins the pyridine ring. Similarly, the reduced electronegativity of sulfur compared to that of oxygen provides little deshielding at the α-methylene protons.

Completely analogous to the spectra of **12** and **16**, those for **18** and **19** show two sets of aromatic resonances and a multiplet for the ketal signal, indicative of asymmetry. Protons on the S-substituted rings resonate upfield from those on the Br-substituted rings and, whereas H-4 provides the lowest-field signal for the former group, H-3′ does so for the latter.

Limited data preclude assessment of general mass spectra trends, but selected comparisons with the oxygen systems can be made. (1) The molecular ion is observed for **17** but not for the acyclic compounds. (2) The base peak for **17**, inferred to be a bis(pyridinthionyl)dioxolane, can arise from a double McLafferty rearrangement. (3) In the spectra of **18** and **19**, peaks of roughly equal intensity separated by 2 mass units corroborate the presence of a bromine atom. (4) There is no evidence for the presence of sequestered $CHCl_3$.

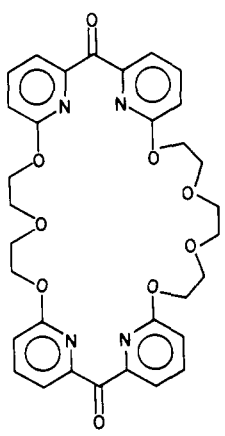
II. Ketone Macrocycles [Bis(2-pyridyl) Ketone Subunit]. A. Synthesis. Individual ketal coronands **8** are converted to the corresponding ketone coronands **20** upon treatment with a refluxing mixture of 1:1 MeOH and 6 M HCl for 72 h. The solution turns bright yellow during the reaction, but the identity of the trace yellow component has never been ascertained. When the crude product of the reaction of dioxolane **7** with triethylene glycol is hydrolyzed without isolation of the ketal coronands, **20a** and **20b**, two 2:2 diketone coronands (**21a** and **21b**) are obtained. As described in previous sections, the formation of 2:2 ketal macrocycles is quite common. Like **9g**, **21b** must arose from one glycol that has undergone fragmentation.[7]



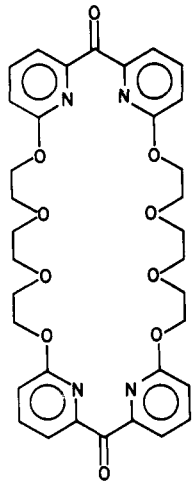
20a, n = 1
b, n = 2
c, n = 3
d, n = 4
e, n = 5

B. Structures of Ketone Macrocycles. The ^{1}H NMR spectra of the ketones are quite distinct from those of **8** and are summarized in Table II. With respect to their

(19) Abramovitch, R. A.; Newman, A. J. *J. Org. Chem.* **1974**, *39*, 2690.
(20) Gokel, G. W.; Durst, H. D. *Synthesis* **1976**, 168.
(21) (a) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 2495. (b) Pedersen, C. J. *Fed. Proc., Fed. Am. Soc. Ecp. Biol.* **1968**, *27*, 1305. (c) Pedersen, C. J. *J. Org. Chem.* **1971**, *36*, 254.
(22) Poonia, N. S. *J. Am. Chem. Soc.* **1974**, *96*, 1012.
(23) Down, J. L.; Lewis, J.; Moore, B.; Wilkinson, G. *J. Chem. Soc.* **1959**, 3764.
(24) Ochrymowycz, L. A.; Mak, C.-P.; Michna, J. D. *J. Org. Chem.* **1974**, *39*, 2079.
(25) Black, D. St.C.; McLean, I. A. *Tetrahedron Lett.* **1969**, 3961.
(26) Mattice, W. L. *J. Am. Chem. Soc.* **1980**, *102*, 2242.
(27) Newkome, G. R.; Nayak, A.; Sauer, J. D.; Mattschei, P. K.; Watkins, S. F.; Fronczek, F.; Benton, W. H. *J. Org. Chem.* **1979**, *44*, 3816.



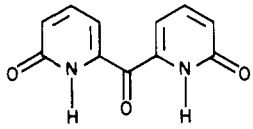
21a



21b

relative positions in the spectra of the ketals, the signals for H-3 and H-4 experience a downfield shift ($\Delta\delta$ = 0.2) to average values of δ 7.56 and 7.75, respectively. The H-5 proton is more strongly affected; it is shifted downfield ($\Delta\delta \simeq 0.3$) to an average value of δ 7.78. This general diamagnetic shift reflects the increased electron-withdrawing character of the pyridyl ketone group compared with that of a pyridyl ketal and is a consequence of the delocalization of π-electron density from the pyridine rings onto the carbonyl oxygen.

The mass spectra of **20** show molecular ions of substantial intensity (20–40%). For all but **20b**, the base peak



(m/e 216) has been assigned the structure of a bis(pyridinonyl)ketone, which is likely to arise from the same sort of double McLafferty rearrangement described for the corresponding ketals.

A useful diagnostic feature of these ketones is provided by their appearance in long wavelength UV light. When illuminated on a TLC plate at 366 nm, each of the compounds displays a characteristic greenish-brown color.

Anhydrous coronand **20e** is a viscous oil, but upon treatment with a mixture of Me_2CHOH and H_2O, it can be transformed into the crystalline monohydrate.[2] Complex **20e**·H_2O exists in the crystal in a conformation that approximates C_2 symmetry (Figure 3). The pyridine rings are twisted out of the carbonyl plane by an average of 34.6°, and the five ethereal oxygen atoms lie in a plane to within 0.6 Å. The water oxygen lies 1.34 Å out of this plane, making its closest contact (3.000 Å) with the *central bridge oxygen* and (3.19–3.61 Å) with all other ethereal oxygens, which is generally too long for hydrogen bonding. This water molecule is located in a well-defined position, has reasonable thermal parameters, and a residual electron density (0.12–0.20 e Å^{-3}) indicative of disorder of the hydrogen atoms.

In contrast, coronand **20c** crystallizes easily from a mixture of $CHCl_3$ and aqueous EtOH to afford large, colorless crystals that display no evidence of complexed water. This macrocycle also exists in the crystal in a conformation of approximate C_2 symmetry (Figure 4). The pyridine rings twist out of the carbonyl plane by an average of 30.1°, and the linkage of polyether to pyridine (imidate) is syn to nitrogen (average N–C–O–C torsion angle 5.0°) in both cases. The two nitrogen and five ether

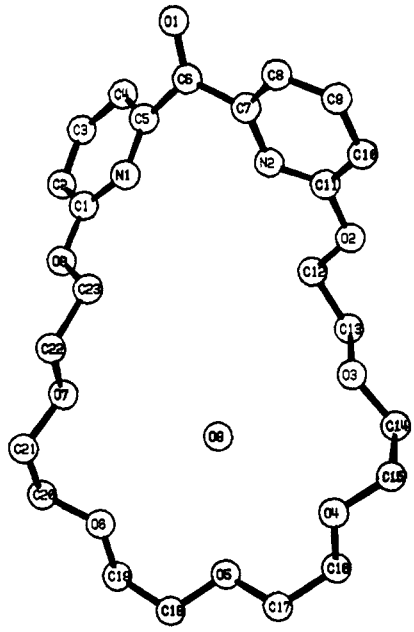


Figure 3. ORTEP **20e**·H_2O.

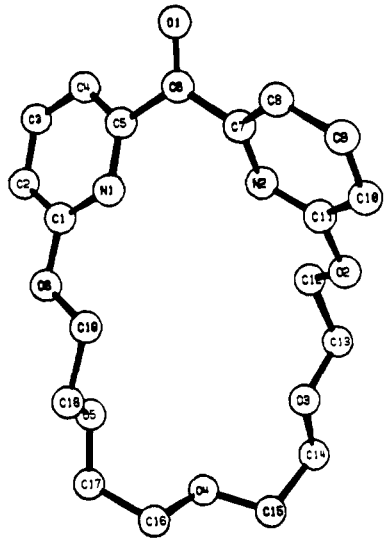


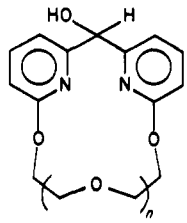
Figure 4. ORTEP of **20c**.

oxygen atoms are within 0.23 Å of their best plane.

The serendipitous discovery that **20e** can encircle a neutral molecule of water, whereas **20c** and **2** (18-crown-6) do not, has prompted us to compare various solid-state structural parameters that might account for the disparity in behavior of these relatively similar molecules.[2] Analysis of the critical torsion angles and distances obtained from X-ray diffraction experiments indicate that the ability to sequester water is contingent upon the existence of a specific void area and a binding locus.

III. Carbinol Macrocycles [Bis(2-pyridyl)carbinol Subunit]. A. Synthesis. Reduction of **20** with $NaBH_4$ in refluxing MeOH affords carbinol macrocycles **23**. These viscous oils undergo rapid atmospheric oxidation back to the corresponding ketones.

B. Structures of Carbinol Macrocycles. The ^1H NMR spectra of the carbinols exhibit an aromatic region in which all of the resonances are moved upfield ($\Delta\delta \simeq 0.2$) with respect to their position in the parent ketal compounds. A broad singlet in the range δ 5.55–5.65 marks the methine hydrogen between the pyridine rings. As a consequence of the molecular dissymmetry, the α-methylene protons of **23a–c** are divided into two groups: δ 4.7



23a, n = 1
b, n = 2
c, n = 3
d, n = 4
e, n = 5

and δ 4.15–4.35. Complete ^{1}H NMR data are listed in Table III.

Experimental Section

General Comments. Melting point data were obtained from samples in capillary tubes with the aid of a Thomas-Hoover Unimelt apparatus and are uncorrected. IR spectra were measured on a Perkin-Elmer 621 Grating Spectrophotometer. NMR spectra were recorded on a Bruker WP-200 Spectrometer. Room temperature measurements were acquired from $CDCl_3$ solutions with Me_4Si as an internal standard (0 ppm), whereas variable temperature (VT) measurements were conducted on toluene-d_8 solutions (180–365 K). MS data were obtained at 70 eV by D. A. Patterson on a Hewlett-Packard Model 5985 GC/MS Spectrometer and reported herein as assignment, relative intensity. Preparative thick-layer chromatography (ThLC) was performed on 20 × 40 cm glass plates coated with a 2-mm layer of Brinkmann Silica Gel P/UV-254-366. Elemental analyses were performed in these laboratories by R. L. Seab.

Toluene and xylene were distilled from sodium wire under a nitrogen or argon atmosphere. Sodium hydride (57% oil dispersion) was washed with anhydrous petroleum ether (bp 30–60 °C) and dried in vacuo prior to the reaction. Ethylene glycol and diethylene, triethylene, and tetraethylene glycols were purchased from Aldrich Chemical Company. The pentaethylene and hexaethylene glycols[28] were acquired from Columbia Organic Chemicals, Inc.

X-ray Experimental Procedures. Intensity data were obtained on an Enraf-Nonius CAD4 diffractometer equipped with a graphite monochromator and Mo K_α (λ 0.71073 Å) or Cu K_α (λ 1.54184 Å) radiation. The $\omega - 2\theta$ scans were performed at variable speeds designed to yield $I \simeq n\sigma(I)$ for all significant data, where n = 50 for **8b**, n = 25 for **8d**, n = 25 for **20c**, and n = 20 for **20e**·H_2O. One quadrant of data was collected for each crystal (one hemisphere for **20e**·H_2O). Data reduction included corrections for background, Lorentz, polarization, decay (for **8d**), and absorption (for **8d**) effects. The absorption corrections were based upon ψ scans of reflections near χ = 90°. Structures were solved by direct methods (MULTAN)[29] and refined by a full-matrix least-squares treatment based upon F. C, N, and O atoms were refined anisotropically; H atoms were located from difference maps and included as fixed contributions. Only data for which $I > 3\sigma(I)$ were considered observed and used in refinements. Final R factors are included with the crystal data for each compound.

8d: $C_{21}H_{26}N_2O_7$, M_r 418.5, monoclinic space group $P2_1/c$, a = 9.051 (2) Å, b = 15.800 (3) Å, c = 14.662 (4) Å, β = 96.85 (2)°, Z = 4, D_c = 1.335 g cm^{-3}, μ(Cu K_α) = 8.51 cm^{-1}, R = 0.061 for 2411 observed data.

8b: $C_{17}H_{18}N_2O_5$, M_r 330.3, monoclinic space group $P2_1/n$, a = 8.919 (1) Å, b = 16.636 (3) Å, c = 10.397 (1) Å, β = 92.15 (1)°, Z = 4, D_c = 1.423 g cm^{-3}, μ(Mo K_α) = 0.99 cm^{-1}, R = 0.033 for 1771 observed data.

20e·H_2O: $C_{23}H_{30}N_2O_8$·H_2O, M_r 480.5, triclinic space group $P\bar{1}$, a = 10.265 (1) Å, b = 10.925 (1) Å, c = 11.633 (2) Å, α = 106.41 (1)°, β = 96.02 (1)°, γ = 97.14 (1)°, Z = 2, D_c = 1.299 g cm^{-3}, Mo K_α, R = 0.060 for 2330 observed data.

20c: $C_{19}H_{22}N_2O_6$, M_r 374.4, monoclinic space group $P2_1/c$, a = 10.238 (2) Å, b = 13.140 (2) Å, c = 14.540 (3) Å, β = 109.35 (2)°, Z = 4, D_c = 1.347 g cm^{-3}, Mo K_α, R = 0.044 for 1775 observed data.

Bis(6-bromo-2-pyridyl) ketone (6) was prepared by the procedure of Holm et al.[30] Recrystallization of the crude material from Me_2CHOH in $CHCl_3$ gave **6**, as colorless prisms: 13.67 g (53%); mp 155–156 °C (lit.[30] mp 155–156.5 °C); ^{1}H NMR δ 7.64 (dd, 5-py H, J = 7.9, 1.8 Hz), 7.76 (dd, 4-py H, J = 7.9, 7.9 Hz), 8.09 (dd, 3-py H, J = 7.9, 1.8 Hz).

2,2-Bis(6′-bromo-2′-pyridyl)-1,3-dioxolane (7). Method A. A slurry of **6** (3.0 g, 8.8 mmol), anhydrous Na_2CO_3 (30.0 g, 283 mmol), and 2-bromoethanol (80 mL, 141.0 g), as reactant and solvent, was refluxed gently for 5 h under N_2. Excess 2-bromoethanol was removed in vacuo and the cooled residue was poured into an aqueous solution of Na_2CO_3 (5%, 400 mL), which was then extracted with CH_2Cl_2 (4 × 75 mL). The combined organic extract was dried over $MgSO_4$, passed through a silica gel column (2.5 × 15 cm), and concentrated in vacuo to give a viscid, beige solid. The material was triturated with ice-cold EtOH, then recrystallized from EtOH/$CHCl_3$ to afford ketal **7**, as colorless rhombohedra: 2.87 g (85%); mp 146–148 °C (lit.[8] mp 146–148 °C); ^{1}H NMR δ 4.14 (bs, ketal CH_2), 7.37 (dd, 5-py H, J = 7.9, 1.8 Hz), 7.56 (dd, 4-py H, J = 7.9, 7.9 Hz), 7.79 (dd, 3-py H, J = 7.9, 1.8 Hz).

Method B.[8] Ketone **6** was treated according to Method A, except for the substitution of 2-chloroethanol (250 mL, 300.0 g) and a reflux period of three days, to give the ketal: 10.33 g (48%).

Method C.[31] A mixture of **6** (11.04 g, 32 mmol), freshly distilled ethylene glycol (20.0 g, 320 mmol), and concentrated H_2SO_4 (10 drops, 0.5 mL) in toluene (200 mL) was refluxed gently for five days. Water (ca. 15 mL) was removed by means of a Dean–Stark separator. Although large, colorless crystals has formed in the cooled mixture, it was concentrated in vacuo and extracted with water and $CHCl_3$ (4 × 75 mL); the combined organic phases were dried over $MgSO_4$ and evaporated in vacuo. The resulting yellowish solid was recrystallized from EtOH/$CHCl_3$ to afford **7**: 12.1 g (98%).

Reaction of 2,2-Bis(6′-bromo-2′-pyridyl)-1,3-dioxolane (7) with Hexaethylene Glycol. A General Macrocycle Preparation. Method A. A suspension of oil-free NaH (120 mg, 5 mmol) in anhydrous xylene (50 mL) was stirred under a N_2 atmosphere for 10 min. Addition of hexaethylene glycol (705 mg, 2.5 mmol) in xylene (25 mL) resulted in the formation of a viscous grey mass and vigorous evolution of hydrogen. After 30 min, all effervescence had ceased and solid **7** (960 mg, 2.5 mmol) was added, followed by xylene (25 mL). The mixture was refluxed for 24 h, *carefully* quenched with H_2O, and concentrated in vacuo. The aqueous slurry was extracted with CH_2Cl_2 (4 × 75 mL) and the organic phase was dried over anhydrous $MgSO_4$ and evaporated in vacuo to give a yellow oil, which was chromatographed (ThLC) on silica. Three elutions with EtOAc gave four major fractions.

Fraction A was recrystallized from a minimum of CH_2Cl_2 in EtOH to yield **8e**, as colorless massive crystals: 70 mg (6%); IR (KBr) 1455, 1594 cm^{-1}; MS, m/e 462 (M^+, 1.8), 166 ($C_8H_8NO_3$ 8 100). Anal. Calcd for $C_{23}H_{30}N_2O_8$·$^1/_2H_2O$: C, 58.60; H, 6.58; N, 5.94. Found: C, 58.79; H, 6.74; N, 5.84.

Fraction B afforded **8f**, as a colorless oil: 470 mg (37%). Anal. Calcd for $C_{25}H_{34}N_2O_9$: C, 59.29; H, 6.72; N, 5.53. Found: C, 59.03; H, 6.83; N, 5.79.

Fraction C gave the unsymmetrical **9g**, as a colorless oil: 170 mg (7%); ^{1}H NMR δ 3.61 (m, γ-ξ-CH_2), 3.69 (t, β-CH_2, J = 4.9 Hz), 4.16 (bs, ketal CH_2), 4.32 (t, α-, α'-CH_2, J = 4.9 Hz), 6.67 (dd, 5-py H, J = 7.9, 1.2 Hz), 7.28 (dd, 3-py H, J = 7.3, 1.2 Hz), 7.57 (dd, 4-py H, J = 7.9, 7.3 Hz); IR (neat) 1460, 1592 cm^{-1}; MS m/e 166 ($C_8H_8NO_3$, 100). Anal. Calcd for $C_{48}H_{84}N_4O_{17}$: C, 59.50; H, 6.61; N, 5.79. Found: C, 59.71; H, 6.43; N, 5.75.

Fraction D produced **9f**, as a light yellow oil: 430 mg (17%). Anal. Calcd for $C_{50}H_{68}N_4O_{18}$·$CHCl_3$: C, 54.09; H, 6.10; N, 4.95.

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Table II. Physical Data for Ketone Macrocycles 20 and 21

compd	NMR chem shift δ (J = Hz) 4-py H	3-py H	5-py H	α	β	γ (δ, ϵ, ξ)	yield, %	mp, °C	IR (C=O)	IR py	MS, m/e (rel int)
20a	7.76 (8.3, 7.3)	7.58 (7.3, 1.8)	6.8 (8.3, 1.8)	4.58 (5.5)	3.76 (5.5)		1	121.5–122	1669	1585, 1463	286 (20), 216 (100)
20b	7.68 (8.3, 7.3)	7.45 (7.3, 1.8)	6.57 (8.3, 1.8)	4.35 (m)	3.70 (m)	3.60 (s)	63	95.5–96.5	1682	1580, 1431	330 (20), 243 (100)
20c	7.82 (8.3, 7.3)	7.62 (7.3, 1.0)	7.00 (8.3, 1.0)	4.43 (m)	3.75 (m)	3.64 (m)	53	133–134	1666	1585, 1442	374 (32), 216 (100)
20d	7.74 (8.3, 7.3)	7.58 (7.3, 1.0)	6.97 (8.3, 1.0)	4.36 (m)	3.80 (m)	3.64 (m)	73	69–70.5	1667	1585, 1460	418 (34), 216 (100)
20e	7.74 (8.3, 7.3)	7.58 (7.3, 1.0)	6.97 (8.3, 1.0)	4.15 (m)	3.58 (m)	3.43 (m)	83	54.5–56	1666	1585, 1460	462 (35), 216 (100)
21a	7.72 (8.3, 7.3) 7.71 (8.3, 7.3)	7.57 (7.3, 1.0)	6.95 (8.3, 1.0) 6.93 (8.3, 1.0)	4.37 (m)	3.76 (m)	3.62 (s)	1	140–141	1673	1585, 1456	616 (38), 216 (100)
21b	7.76 (8.3, 7.3)	7.65 (7.3, 1.0)	6.83 (8.3, 1.0)	4.41 (m)	3.37 (m)		1	169.5–170	1676	1586, 1454	660 (36), 216 (100)

Table III. Physical Data for Carbinol Macrocycles 23

compd[a]	NMR chem shift δ (J = Hz) 4-py H	3-py H	5-py H	CHO	α	β	γ (δ, ϵ, ξ)	yield, %	IR (C=O)	IR Pyr	MS, m/e (rel int)
23a	7.38 (8.0, 7.2)	6.79 (7.2, 2.0)	6.42 (8.0, 2.0)	5.50 (bs)	4.70/4.15 (m)	3.75 (m)		79	1600	1460	288 (100), 232 (93)
23b[b]	7.45 (8.0, 7.2)	6.84 (7.2, 2.0)	6.54 (8.0, 2.0)	5.55 (bs)	4.73/4.16 (m)	3.58 (m)		81	1592	1456	332 (100), 232 (91)
23c	7.53 (8.5, 7.9)	6.91 (7.9, 2.0)	6.65 (8.5, 2.0)	5.62 (bs)	4.67/4.35 (m)	3.79 (m)	3.75 (m)	80	1595	1453	376 (100), 323 (89)
23d	7.53 (8.5, 7.9)	6.92 (7.9, 2.0)	6.65 (8.5, 2.0)	5.62 (bs)	4.49 (m)	3.82 (m)	3.0 (m)	77	1599	1459	420 (100), 232 (92)
23e	7.55 (8.5, 7.9)	6.99 (7.9, 2.0)	6.67 (8.5, 2.0)	5.65 (bs)	4.48 (m)	3.80 (m)	3.59 (m)	75	1600	1457	464 (100), 232 (84)

[a] All compounds were oils. [b] 4.62 (OH).

Found: C, 54.17; H, 5.92; N, 4.78.

Method B. To a stirred suspension of oil-free NaH (480 mg, 20 mmol) in anhydrous toluene (50 mL) under a N_2 atmosphere was added hexaethylene glycol (2.82 g, 10 mmol) in toluene (25 mL) slowly. The heterogeneous mixture was stirred at 25 °C for 30 min, at which time no further evolution of hydrogen was observed. Solid **7** (3.86 g, 10 mmol) was added, followed by the addition of toluene (25 mL). The mixture was stirred at 95 °C for 3 days. Water was *cautiously* added to the cooled solution in order to decompose any excess NaH and the organic solvent was removed in vacuo. The remaining aqueous slurry was extracted with CH_2Cl_2 (4 × 75 mL) and the combined organic extract was dried over anhydrous $MgSO_4$ and concentrated in vacuo to give a viscous yellowish oil that was chromatographed (ThLC) on silica. Elution with 5% EtOH in Et_2O afforded seven fractions that could be well characterized.

Fraction A was recrystallized from EtOH and H_2O to give **8d** as colorless prisms: 164 mg (0.4%). Anal. Calcd for $C_{21}H_{28}N_2O_7$: C, 60.29; H, 6.22; N, 6.70. Found: C, 60.13; H, 6.23; N, 6.71.

Fraction B was recrystallized from EtOH and H_2O to give **8e**, as evidenced by physical and spectral data: 30 mg (0.6%).

Fraction C had NMR and MS data consistent with that of **8f**: 80 mg (2%).

Fraction D exhibited spectral properties in accordance with those of **9g**: 62 mg (0.6%).

Fraction E gave **9f** according to TLC, NMR, and MS information: 97 mg (1%).

Fraction F yielded **10b**, as a brownish oil: 674 mg (4%); ^1H NMR δ 3.53 (m, γ–ξ-CH_2), 3.70 (t, β-CH_2, J = 4.9 Hz), 4.16 (bs, ketal CH_2), 4.33 (t, α-CH_2, J = 4.9 Hz), 6.67 (dd, 5-py H, J = 7.9, 1.2 Hz), 7.26 (dd, 3-py H, J = 7.3, 1.2 Hz), 7.56 (dd, 4-py H, J = 7.9, 7.3 Hz); IR (neat) 1454, 1592 cm^{-1}; MS, m/e 166 ($C_8H_8NO_3$, 100). Anal. Calcd for $C_{75}H_{102}N_6O_{27}\cdot CHCl_3$: C, 55.69; H, 6.29; N, 5.13. Found: C, 55.44; H, 6.40; N, 5.39.

Fraction G gave the 4:4 coronand **11**, as a brownish oil: 25 mg (0.1%); ^1H NMR δ 3.62 (m, γ–ξ-CH_2), 3.55 (t, β-CH_2, J = 4.9 Hz), 4.16 (bs, ketal CH_2), 4.33 (t, α-CH_2, J = 4.9 Hz), 6.67 (dd, 5-py H, J = 7.9, 1.2 Hz), 7.26 (dd, 3-py H, J = 7.3, 1.2 Hz), 7.56 (dd, 4-py H, J = 7.9, 7.3 Hz); IR (neat) 1456, 1597 cm^{-1}; MS, m/e 166 ($C_8H_8NO_3$, 100). Anal. Calcd for $C_{100}H_{136}N_8O_{36}$: C, 59.29; H, 6.72; N, 5.53. Found: C, 59.62; H, 6.98; N, 5.34.

Reaction of 2,2-Bis(6′-bromo-2′-pyridyl)-1,3-dioxolane (7) with Pentaethylene Glycol. The general procedure (Method A) was followed except for the substitution of pentaethylene glycol (595 mg, 2.5 mmol). Standard treatment of the mixture produced a yellowish oil that was chromatographed (ThLC) on silica. Elution with 5% EtOH/Et_2O gave four major components.

Fraction A was recrystallized from EtOH and H_2O to yield **8c**, as colorless needles: 9 mg (1%). Anal. Calcd for $C_{19}H_{22}N_2O_6$: C, 60.96; H, 5.88; N, 7.49. Found: C, 60.85; H, 5.92; N, 7.27.

Fraction B had physical and spectral properties consistent with those of **8d**: 59 mg (5.6%).

Fraction C was identical to **8e** according to TLC, NMR, and MS: 304 mg (26%).

Fraction D yielded **9e** as a colorless oil: 310 mg (13%). Anal. Calcd for $C_{46}H_{60}N_4O_{16}$: C, 59.74; H, 6.49; N, 6.06. Found: C, 59.47; H, 6.68; N, 6.32.

Reaction of 2,2-Bis(6′-bromo-2′-pyridyl)-1,3-dioxolane (7) with Tetraethylene Glycol. The reaction was conducted according to he General Procedure B except for the substitution of tetraethylene glycol (485 mg, 2.5 mmol). The resulting yellowish oil was chromatographed (ThLC) on silica. Two elutions with 5% EtOH/$CHCl_3$ produced four major components.

Fraction A was recrystallized from EtOH and H_2O to afford **8b** as colorless prisms: 10 mg (1%); mp 123–123.5 °C. Anal. Calcd for $C_{17}H_{18}N_2O_5$: C, 61.82; H, 5.45; N, 8.49. Found: C, 61.59; H, 5.53; N, 8.38.

Fraction B was identified as **8c** on the basis of physical and spectral data: 72 mg (7%).

Fraction C possessed melting point, NMR, and MS properties consistent with those of **8d**: 41 mg (39%).

Fraction D afforded **9d**, a colorless oil: 30 mg (14%). Anal. Calcd for $C_{42}H_{52}N_4O_{14}$: C, 60.29; H, 6.22; N, 6.70. Found: C, 60.54; H, 6.11; N, 6.92.

Reaction of 2,2-Bis(6′-bromo-2′-pyridyl)-1,3-dioxolane (7) with Triethylene Glycol. The general procedure B was used with NaH (105.6 mg, 4.4 mmol), triethylene glycol (330 mg, 2.2 mmol), and solid **7** (860 mg, 2.2 mmol). The mixture was stirred

at 70 °C for 15 days. The resulting yellowish semisolid was chromatographed (ThLC) on silica. Three elutions with Et_2O provided four major fractions.

Fraction A was **8b**, as evidenced by melting point, NMR, and MS data: 8 mg (1%).

Fraction B gave the starting ketal **7**: 200 mg (24%); mp 146–147 °C.

Fraction C afforded **8c**, based on physical and spectral information: 26 mg (27%).

Fraction D yielded **9c** as a colorless oil: 186 mg (11%). Anal. Calcd for $C_{38}H_{44}N_4O_{12}$: C, 60.96; H, 5.88; N, 7.49. Found: C, 60.65; H, 6.12; N, 7.63.

Several open chain fractions were also isolated but characterized only by ^1H NMR.

Reaction of 2,2-Bis(6′-bromo-2′-pyridyl)-1,3-dioxolane (7) with Diethylene Glycol. General procedure B was followed, except for the altered reagents: NaH (250 mg, 10 mmol), diethylene glycol (532 mg, 5 mmol), and solid **7** (1.93 g, 5 mmol). The mixture was stirred at 70 °C for 2 days, cooled, and treated in the manner described above. The yellowish semisolid was chromatographed (ThLC) on silica. Elution with Et_2O afforded numerous open chain compounds and several macrocycles.

Fraction A was unchanged starting material **7**: 152 mg (8%).

Fraction B gave **9b** as a colorless oil: 26.5 mg (0.8%). Anal. Calcd for $C_{34}H_{36}N_4O_{10}$: C, 61.82; H, 5.45; N, 8.48. Found: C, 62.10; H, 5.32, N, 8.24.

Fraction C afforded **12a** as a colorless oil: 43 mg (1%); ^1H NMR δ 3.65 (t, β-CH_2, J = 4.8 Hz), 4.15 (m, keetal CH_2), 4.27 (t, α-CH_2, J = 4.8 Hz), 6.65 (dd, 5-py H, J = 7.9, 1.2 Hz), 7.35 (dd, 3-py H, J = 7.3, 1.2 Hz), 7.37 (dd, 5′-py H, J = 7.9, 1.2 Hz), 7.55 (m, 4,4′-py H), 7.70 (dd, 3′-py H, J = 7.3, 1.2 Hz); IR (neat) 1455, 1590, 806 cm^{-1}; MS, m/e 351 ($C_{15}H_{14}{}^{81}BrN_2O_3$, 100), 349 ($C_{15}H_{14}{}^{79}BrN_2O_3$, 96.8), 166 ($C_8H_8NO_3$, 43.4). Anal. Calcd for $C_{30}H_{28}Br_2N_4O_7 \cdot CH_2Cl_2$: C, 46.44; H, 3.74; N, 6.99. Found: C, 46.14; H, 3.72; N, 6.99.

Fraction D gave **13a**, as a colorless oil: 14 mg (0.7%); ^1H NMR δ 3.58 (m, δ-CH_2), 3.71 (m, β, γ-CH_2), 4.16 (m, ketal CH_2), 4.32 (m, α-CH_2), 6.69 (dd, 5-py H, J = 7.9, 1.2 Hz), 7.37 (dd, 3-py H, J = 7.3, 1.2 Hz), 7.40 (dd, 5′-py H, J = 7.9, 1.2 Hz), 7.56 (dd, 4-py H, J = 7.9, 7.3 Hz), 7.60 (dd, 4′-py H, J = 7.9, 7.3 Hz), 7.71 (dd, 3′-py H, J = 7.3, 1.2 Hz); IR (neat) 1456, 1586, 802 cm^{-1}; MS, m/e 412 (M^+, ^{81}Br, 0.1), 1.66 ($C_8H_8NO_3$, 100). Anal. Calcd for $C_{17}H_{18}BrN_2O_5$: C, 49.63; H, 4.62; N, 6.81. Found: C, 49.80; H, 4.84; N, 6.86.

Fraction E yielded **12b** as a colorless oil: 78 mg (1.5%); ^1H NMR δ 3.66 (m, β,β'-CH_2), 4.41 (m, ketal CH_2), 4.16 (bs, ketal CH_2), 4.29 (m, α,α' CH_2), 6.65 (dd, 5,5′-py H, J = 7.9, 1.2 Hz), 7.26 (dd, 3-py H, J = 7.3, 1.2 Hz), 7.34 (dd, 3′-py H, J = 7.3, 1.2 Hz), 7.36 (dd, 5″-py H, J = 7.9, 1.2 Hz), 7.55 (m, 7,7′,4″-py H), 7.70 (dd, 3″-py H, J = 7.3, 1.2 H); IR (neat) 1454, 1588, 804 cm^{-1}. Anal. Calcd for $C_{47}H_{46}Br_2N_6O_{12}$: C, 53.92; H, 4.40; N, 8.03. Found: C, 54.21; H, 4.19; N, 8.30.

Fraction F afforded **10a** as a colorless oil: 23 mg (0.5%); ^1H NMR δ 3.55 (t, β-CH_2, J = 4.9 Hz), 4.15 (bs, ketal CH.2), 4.25 (t, α-CH_2, J = 4.9 Hz), 6.60 (dd, 5-py H, J = 7.9, 1.2 Hz), 7.26 (dd, 3-py H, J = 7.3, 1.2 Hz), 7.52 (dd, 4-py H, J = 7.9, 7.3 Hz); IR (neat) 1457, 1591 cm^{-1}; MS, m/e 166 ($C_8H_8NO_3$, 100).

Fraction G provided **13b**, as colorless oil: 30.5 mg (1%); ^1H NMR δ 3.55 (m, δ-CH_2), 3.68 (m, β, γ-CH_2), 4.16 (m, ketal′ CH_2), 4.17 (bs, ketal CH_2), 4.31 (m, α-CH_2), 6.66 (dd, 5-py H, J = 7.9, 1.2 Hhz), 6.67 (dd, 5′-py H, J = 7.9, 1.2 Hz), 7.32 (m, 3,3′,5″-py H), 7.55 (m, 4, 4′, 4″-py H), 7.70 (dd, 3″-py H, J = 7.3, 1.2 Hz); IR (neat) 1456, 1591, 802 cm^{-1}; MS, m/e 166 ($C_8H_8NO_3$, 100). Anal. Calcd for $C_{34}H_{51}BrN_6O_{14}$: C, 5m.25; H, 4.97; N, 8.18. Found: C, 57.55; H, 4.75; N, 8.49.

Fraction H yielded **14** as a colorless oil: 124 mg (2%); ^1H NMR δ 3.65 (m, β-CH_2), 4.12 (m, ketal CH_2), 4.34 (m, α,α-CH_2), 6.64 (m, 5, 5′-py H), 7.25 (m, 3-py H), 7.33 (dd, 3′-py H, J = 7.3, 1.2 Hz), 7.36 (dd, 5″-py H, J = 7.9, 1.2 Hz), 7.48–7.60 (m, 4,4′,4″-py H), 7.69 (dd, 3″-py H, J = 7.3, 1.2 Hz); IR (neat) 1458, 1590, 800 cm^{-1}; MS, m/e 166 ($C_8H_8NO_3$, 16.7), 57 (C_3H_5O, 100). Anal. Caldd for $C_{49}H_{51}BrN_6O_{14}$: C, 57.25; H, 4.97; N, 8.18. Found: C, 57.35; H, 4.75; N, 8.19.

Fraction I afforded the symmetrical open chain compound **15a** as a colorless oil: 6 mg (0.3%); ^1H NMR δ 3.55 (m, δ-CH_2), 3.71 (m, β, γ-CH_2), 4.18 (bs, ketal CH_2), 4.35 (m, α-CH_2), 6.69 (dd, 5-py H, J = 7.9, 1.2 Hz), 7.30 (dd, 3-py H, J = 7.3, 1.2 Hz), 7.60 (dd, 4-py H, J = 7.9, 7.3 Hz); IR (neat) 1456, 1588 cm^{-1}; MS, m/e 436 (M^+, 0.5), 166 ($C_8H_8NO_3$, 100). Anal. Calcd for $C_{21}H_{28}N_2O_8$: C, 57.80; H, 6.42; N, 6.42. Found: C, 58.09; H, 6.26; N, 6.72.

Fraction J gave **13c** as colorless oil: 25 mg (0.5%); ^1H NMR δ 3.58 (m, δ-CH_2), 3.68 (m, β, γ-CH_2), 3.81 (m, β-CH_2), 4.15 (m, ketal CH_2), 4.30 (m, α,α'-CH_2), 6.65 (m, 5,5′-py H), 7.31 (m, 3,3′,5″-py H), 7.55 (m, 4,4′,4″-py H), 7.70 ndd, 3″-py H, J = 7.3, 1.2 Hz); IR (neat) 1461, 1590, 805 cm^{-1}; MS, m/e 166 ($C_8H_8NO_3$, 100). Anal. Calcd for $C_{51}H_{55}BrN_6O_{15}$: C, 57.14; H, 5.14; N, 7.84. Found: C, 56.99; H, 5.12; N, 7.67.

Fraction K was identified as the open chain **15b**, a colorless oil: 8 mg (0.2%); ^1H NMR δ 3.55 (m, δ-CH_2), 3.68 (m, β, γ-CH_2), 4.17 (bs, ketal CH_2), 4.38 (m, α, α'-CH_2), 6.67 (dd, 5-py H, J = 7.9, 1.2 Hz), 7.27 (dd, 3-py H, J = 7.3, 1.2 Hz), 7.57 (dd, 4-py H, J = 7.9, 7.3 Hz); IR (neat) 1457, 1592 cm^{-1}; MS, m/e 166 ($C_8H_8NO_3$, 100). Anal. Calcd for $C_{35}H_{46}N_4O_{13} \cdot EtOH$: C, 59.11; H, 6.40; N, 6.90. Found: C, 59.12; H, 6.29; N, 6.64.

Fraction L yielded **13d** as a colorless oil: 13 mg (0.2%); ^1H NMR δ 3.54 (m, δ-CH_2), 3.68 (m, β, γ-CH_2), 4.15 (m, ketal CH_2), 4.31 (m, α, α'-CH_2), 6.64 (m, 5,5′-py H), 7.24 (m, 3-py H), 7.34 (m, 3′,5″-py H), 7.55 (m, 4,4′,4″-py H), 7.69 (dd, 3″-py H, J = 7.3, 1.2 Hz); IR (neat) 1455, 1588, 802 cm^{-1}; MS, m/e 166 ($C_8H_8NO_3$, 100). Anal. Calcd for $C_{68}H_{73}BrN_8O_{20}$: C, 58.24; H, 5.21; N, 7.99. Found: C, 58.36; H, 5.08; N, 8.21.

Reaction of 2,2-Bis(6′-bromo-2′-pyridyl)-1,3-dioxolane (7) with Ethylene Glycol. General procedure B was followed, except for the following quantitites: oil-free NaH (250 mg, 10 mmol), ethylene glycol (159 mg, 1.5 mmol), and solid **7** (580 mg, 1.5 mmol). The mixture was refluxed for one week, cooled, and handled according to the standard procedure to produce a yellowish oil that was chromatographed (ThLC) on silica. Two elutions with Et_2O gave four major fractions:

Fraction A was recrystallized from $CHCl_3$ and EtOH to yield unchanged **7**: 39 mg (7%).

Fraction B afforded the open chain 2:1 compound **16a** as a colorless oil: 1.2 mg (0.1%); ^1H NMR δ 4.17 (m, ketal CH_2), 4.41 (bs, α-CH_2), 6.65 (dd, 5-py H, J = 7.9, 1.2 Hz), 7.26 (dd, 3-py H, J = 7.3, 1.2 Hz), 7.34 (dd, 5′-py H, J = 7.9, 1.2 Hz), 7.53 (m, 4,4′-py H), 7.70 (dd, 3′-py H, J = 7.3, 1.2 Hz); IR (neat) 1456, 1590, 803 cm^{-1}; MS, m/e 166 ($C_8H_8NO_3$, 100). Anal. Calcd for $C_{28}H_{24}Br_2N_4O_6$: C, 50.00; H, 3.57; N, 8.33. Found: C, 4..78; H, 3.73; N, 8.11.

Fraction C gave the 3:2 compound **16b** as a colorless oil: 2.8 mg (0.2%); ^1H NMR δ 4.13 (m, ketal CH_2), 4.40 (m, α-CH_2), 6.64 (dd, 5,5′-py H, J = 7.9, 1.2 Hz), 7.27 (m, 3,3′-py H), 7.34 (dd, 5″-py H, J = 7.9, 1.2 Hz), 7.53 (m, 4,4′,4″-py H), 7.70 (dd, 3″-py H, J = 7.3, 1.2 Hz); IR (neat) 1458, 1587, 806 cm^{-1}; MS, m/e 166 ($C_8H_8NO_3$, 100). Anal. Calcd for $C_{43}H_{38}Br_2N_6O_{10}$: C, 53.86; H, 3.97; N, 8.77. Found: C, 53.56; H, 4.16; N, 8.93.

Fraction D provided the desired 2:2 macrocycle **9a** as a colorles oil: 30 mg (4%). Anal. Calcd for $C_{30}H_{28}N_4O_8$: C, 62.94; H, 4.90; N, 9.79. Found: C, 63.04; H, 4.76; N, 10.06.

Reaction of 2,2-Bis(6′-bromo-2′-pyridyl)-1,3-dioxolane (7) with Bis(2-mercaptoethyl) Ether. The general procedure B was followed except for the substitution of bis(2-mercaptoethyl) ether (345 mg, 2.5 mmol) and toluene as the solvent. Usual treatment of the cooled mixture resulted in a yellowish oil with a vile smell that was chromatographed (ThLC) on silica. Two elutions with Et_2O produced three maaor components; numerous trace products were characterized by NMR only.

Fraction A afforded the desired macrocycle **17** as a colorless oil: 11 mg (1.2%); ^1H NMR δ 3.18 (t, β-CH_2, J = 6.8 Hz), 3.68 (t, α-CH_2, J = 6.8 Hz), 4.14 (bs, ketal CH_2), 7.18 (dd, 5-py H, J = 7.9, 1.2 Hz), 7.40 (dd, 3-py H, J = 7.3, 1.2 Hz), 7.52 (dd, 4-py H, J = 7.9, 7.3 Hz); IR (neat) 1460, 1591 cm^{-1}; MS, m/e 362 (M^+, 0.3), 292 ($C_{13}H_{12}N_2O_2S_2$, 100), 136 ($C_6H_4N_2SO$, 21). Anal. Calcd for $C_{17}H_{18}N_2O_3S_2$: C, 56.35; H, 4.97;, N, 7.73. Found: C, 56.19; H, 5.12; N, 7.92.

Fraction B possessed the same physical and spectral properties as the starting **7**: 135 mg (14%).

Fraction C yielded the 2:1 compound **18** as a colorless oil: 51 mg (3%); ^1H NMR δ 3.11 (t, β-CH_2, J = 6.7 Hz), 3.37 (t, α-CH_2, J = 6.7 Hz), 4.14 (m, ketal CH_2), 7.08 (m, 5-py H), 7.36 (dd, 3-py H, J = 7.3, 1.2 Hz), 7.51 (m, 4,4′,5′-py H), 7.74 (dd, 3′-py H, J = 7.3, 1.2 Hz); IR (neat) 1458, 1587, 801 cm^{-1}; MS, m/e 367

($C_{15}H_{14}{}^{81}BrN_2O_2S$, 42), 365 ($C_{15}H_{14}{}^{79}BrN_2O_2S$, 43.9), 340 ($C_{13}H_{11}{}^{81}BrN_2O_2S$, 43.4), 338 ($C_{13}H_{11}{}^{79}BrN_2O_2S$, 45.3), 182 ($C_8H_8NO_2S$, 32.7), 158 ($C_5H_3{}^{81}BrN$, 62), 156 ($C_5H_3{}^{79}BrN$, 62.7), 136 ($C_7H_6NS$, 100). Anal. Calcd for $C_{30}H_{28}Br_2N_4O_5S_2$: C, 48.13; H, 3.74; N, 7.49. Found: C, 47.97; H, 3.55; N, 7.49.

Reaction of 2,2-Bis(6′-bromo-2′-pyridyl)-1,3-dioxolane (7) with Ethanedithiol. The general procedure B was followed except for the substitution of ethanedithiol (235 mg, 2.5 mmol) and toluene as the solvent; heating was continued for 21 days. The cooled mixture was handled according to the standard procedure to afford two major components.

Fraction A was unchanged **7**: 215 mg (22%).

Fraction B yielded the symmetrical open chain **19** as a yellow oil: 16 mg (1%); ^1H NMR δ 4.13 (m, ketal CH_2, SCH_2), 7.17 (dd, 5-py H, J = 7.9, 0.9 Hz), 7.38 (dd, 5′-py H, J = 7.9, 0.9 Hz), 7.52 ndd, 4,4′-py H, J = 7.9, 7.3 Hz), 7.62 (dd, 3-py H, J = 7.3, 0.9 Hz), 7.69 (dd, 3′-py H, J = 7.3, 0.9 Hz); IR (neat) 1458, 1590 cm^{-1}; MS, m/e 230 ($C_8H_7{}^{81}BrNO_2$, 100), 228 ($C_8H_7{}^{79}BrNO_2$, 96.8). Anal. Calcd for $C_{28}H_{24}Br_2N_4O_4S_2$: C, 47.73; H, 3.41; N, 7.95. Found: C, 47.47; H, 3.64; N, 8.25.

Reaction of 2,2-Bis(6′-bromo-2′-pyridyl)-1,3-dioxolane (7) with Bis(2-mercaptoethyl) Sulfide. Adherence to the general procedure except for the substitution of bis(2-mercaptoethyl) sulfide (385 mg, 2.5 mmol) and toluene as the solvent afforded only unchanged **7**.

Hydrolysis of Triethylene Glycol Ketal Macrocycle 8c. A General Procedure. A solution of **8c** (70 mg, 0.2 mmol), aqueous HCl (10 mL, 6 M), and MeOH (10 mL) was refluxed for 72 h. After concentration in vacuo, the acidic residue was neutralized carefully with aqueous Na_2CO_3 (10%) and extracted with $CHCl_3$ (4 × 50 mL). The combined organic extract was dried over $MgSO_4$ and concentrated to afford macrocyclic ketone **20b**, which was recrystallized from $CHCl_3$/EtOH to give colorless massive crystals. Pertinent data are shown in Table II.

Reduction of Diethylene Glycol Ketone Macrocycle (20a). A General Procedure. To an ice-cooled solution of **20a** (28 mg, 0.1 mmol) in MeOH (50 mL) was added solid $NaBH_4$ (380 mg, 10 mmol) at such a rate that the temperature did not rise above 10 °C. The mixture was stirred for 1 h at 20 °C, then refluxed for 12 h. After concentration in vacuo, an aqueous solution of Na_2CO_3 (20 mL, 10%) was added and the slurry was refluxed for 2 h. The cooled suspension was extracted with $CHCl_3$ (4 × 50 mL). The combined organic extract was dried over anhydrous $MgSO_4$ and concentrated to give a yellow oil, which was chromatographed (ThLC) on silica; elution with 3% MeOH/$CHCl_3$ afforded carbinol macrocycle **23a** as a colorless oil. See Table III for critical data.

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Registry No. **6**, 42772-87-2; **7**, 42772-88-3; **8b**, 90867-41-7; **8c**, 90867-42-8; **8d**, 70091-61-1; **8e**, 70091-62-2; **8f**, 70091-63-3; **9a**, 90867-43-9; **9b**, 90867-44-0; **9c**, 90867-45-1; **9d**, 90867-46-2; **9e**, 90867-47-3; **9f**, 90867-48-4; **9g**, 90867-49-5; **10a**, 90886-00-3; **10b**, 90867-58-6; **11**, 90885-99-7; **12a**, 90867-59-7; **12b**, 90867-61-1; **13a**, 90867-60-0; **13b**, 90867-62-2; **13c**, 90867-65-5; **13d**, 90867-67-7; **14**, 90867-63-3; **15a**, 90867-64-4; **15b**, 90867-66-6; **16a**, 42772-88-3; **16b**, 90867-68-8; **17**, 90867-69-9; **18**, 90867-70-2; **19**, 90867-71-3; **20a**, 90885-98-6; **20b**, 90867-50-8; **20c**, 70100-65-1; **20d**, 70091-64-4; **20e**, 70091-65-5; **21a**, 90867-51-9; **21b**, 90867-52-0; **23a**, 90867-53-1; **23b**, 90867-54-2; **23c**, 90867-55-3; **23d**, 90867-56-4; **23e**, 90867-57-5; $BrCH_2CH_2OH$, 540-51-2; $(HSCH_2CH_2)_2O$, 2150-02-9; $HSCH_2CH_2SH$, 540-63-6; $(HSCH_2CH_2)_2S$, 3570-55-6; hexaethylene glycol, 2615-15-8; pentaethylene glycol, 4792-15-8; tetraethylene glycol, 112-60-7; triethylene glycol, 112-27-6; diethylene glycol, 111-46-6; ethylene glycol, 107-21-1.

Supplementary Material Available: The general MS fragmentation scheme for **8**; tables of fragmentation data for **8** and **9**; coordinates of nonhydrogen atoms for **8d**, **8b**, **20e**·H_2O, **20c**; bond distances and angles for **8d**, **8b**, **20e**·H_2O, **20c**; coordinates assigned to hydrogen atoms for **8d**, **8b**, **20e**·H_2O, **20c**; anisotropic thermal parameters for **8d**, **8b**, **20e**·H_2O, **20c** (17 pages). Ordering information is given on any current masthead page.

Structures and Stabilities of $C_2H_4N^+$ Isomers: An ab Initio Molecular Orbital Study

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Structures and energies of seventeen $C_2H_4N^+$ isomers were determined by semiempirical (MNDO) and various ab initio methods in order to get information concerning stabilities and reactivities of these ions. Among the C–N–C topologues the nitrilium ion **5** is predicted to be lowest in energy, ca. 9 kcal/mol lower than the 2-azaallenium ion **1** (at MP2/6-31G*//4-31G, the highest calculational level used throughout in this study). The most stable of the C–C–N isomers is the nitrilium ion **6**, which is the best of all $C_2H_4N^+$ isomers. Among the cyclic structures the iminium ion **12** is favorable, whereas the nitrenium ion **14** is the most energy rich of all isomers considered here. Some of the ions also possess low lying triplet states: the β-aminovinyl cation **11t**, the cyclic ion **14t**, and the carbene type ion **16t**. The interconversion of the H_2C–N–CH_2^+ topologues **14**, **2**, **3**, and **1** was studied using the C–N–C bond angle as the reaction coordinate. **14** is, if at all, only a very shallow minimum; structures **2** and **3** correspond to the transition states. The only experimentally accessible ion is predicted to be the 2-azaallenium ion **1** with an estimated automerization barrier of ca. 42 kcal/mol. Formally all the $C_2H_4N^+$ ions can be derived from protonation reactions of seven C_2H_3N molecules. The heats of protonation are evaluated to determine the thermodynamic basicity of the different molecules and the different molecular sites.

Azacarbenium ions, synthetically useful intermediates in a great variety of chemical reactions,[1,2] are also interesting because of the different ways in which the nitrogen atom can interact with the electron deficient carbenium center.[3] Simple iminium salts of type $R_2C{=}NR_2^+X^-$

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