worked up in the usual way and chromatographed, to give compound 15 (1.2 mg, 0.004 mmol): ^{1}H NMR δ 0.99 (d, J = 5.2 Hz, 3 H), 1.61 (s, 3 H), 1.69 (s, 3 H), 1.85 (s, 3 H), 3.95 (m, 1 H), 4.83 (s, 1 H), 4.87 (s, 1 H), 4.94 (m, 1 H), 5.11 (t, J = 7.1 Hz, 1 H), 5.43 (br s, 1 H).

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Registry No. 1, 132616-79-6; 2, 115890-56-7; 3, 115940-72-2; 4, 115890-57-8; 5, 61263-83-0; 6, 63908-63-4; 8, 132462-42-1; 9, 50299-47-3; 10, 132462-43-2; 11, 115890-64-7; 12, 132462-44-3; 13, 132490-52-9; 14, 132462-45-4; 15, 132462-46-5.

Preparation and Structural Properties of Large-Cavity Peraza Macrocycles Containing Pyridine, Phenanthroline, or Piperazine Subcyclic Units

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Ten large peraza macrocycles containing either two pyridine, two phenanthroline, or three, four, or six piperazine subcyclic groups have been prepared. Those containing pyridine or phenanthroline were prepared by reacting either 2,6-pyridinedicarbaldehyde or its dimethyl ketone analogue or 1,10-phenanthroline-2,9-dicarbaldehyde with the appropriate bisprimary amine to form the cyclic tetraSchiff base. Those macrocycles containing the piperazine units were prepared by the reaction of a crablike piperazine-containing bis(α-chloro amide) (formed from piperazine and 2 mol of chloroacetyl chloride) and piperazine to give tetrapiperazinoperaza-24-crown-8-tetramide, the 2:2 cyclization product, and hexapiperazinoperaza-36-crown-12-hexamide, the 3:3 cyclization product. The macrocyclic hexamide was fully reduced to form the hexapiperazino-36-crown-12 ligand. The reaction of equimolar amounts of the crablike piperazine-containing bis(α-chloro amide) and benzylamine gave N,N',N''-tribenzyltripiperazinoperaza-27-crown-9-hexamide. The structures of one of the diphenanthrolinoperaza-crowns and of the tetrapiperazinoperaza-24-crown-8-tetramide were determined by an X-ray crystallographic procedure. The diphenanthrolino-crowns contained water molecules as shown by their combustion analyses. These water molecules were replaced by solvent molecules as shown by two molecules of dimethylformamide in the solid-state structure of one phenanthrolino-crown. The dipyridinoperaza-crown formed a highly protonated ligand at neutral pH.

Introduction

Polyaza macrocycles with large cavities have received recent interest as inorganic and organic anion and cation receptors. The cyclic arrangement of a large number of donor atoms and the flexibility of these ligands make them good hosts for binuclear or even polynuclear metal ion complexes.[1-5] These complexes are potential candidates for supramolecular catalysts.[6] Macrocyclic and macropolycyclic polyaza ligands selectively form strong complexes with a variety of inorganic and organic anions.[7-9] This type of complexation with biologically important anions may allow these ligands to be used as model compounds for biological processes.[10-12]

A number of methods for the preparation of these large polyaza-crowns have been reported. The most common synthetic procedure requires the use of N-tosyl groups to both protect and activate the nitrogen atoms in the cyclization step.[2,3,13-16] Ring closure occurs by a condensation reaction of N-tosylated polyamines with the appropriate ditosylate ester or dihalide in DMF and in the presence of base. These reactions allow the production of polyaza macrocycles in moderate yields,[14-16] but removing the N-tosyl groups requires drastic conditions and is not always straightforward.

Another cyclization process uses the template ring closure formation of a cyclic di- or tetraSchiff base. This is a simple process, but it is often difficult to choose the correct template metal ion or to predict certain ring-contraction reactions where the template cation does not coordinate with all of the ring nitrogen atoms.[5,17] In some cases, reduction of the cyclic polySchiff base and removal of the template ion have been difficult.[1,5,18-22]

A nontemplate method for the formation of a macrocyclic polySchiff base has also been studied. This proce-

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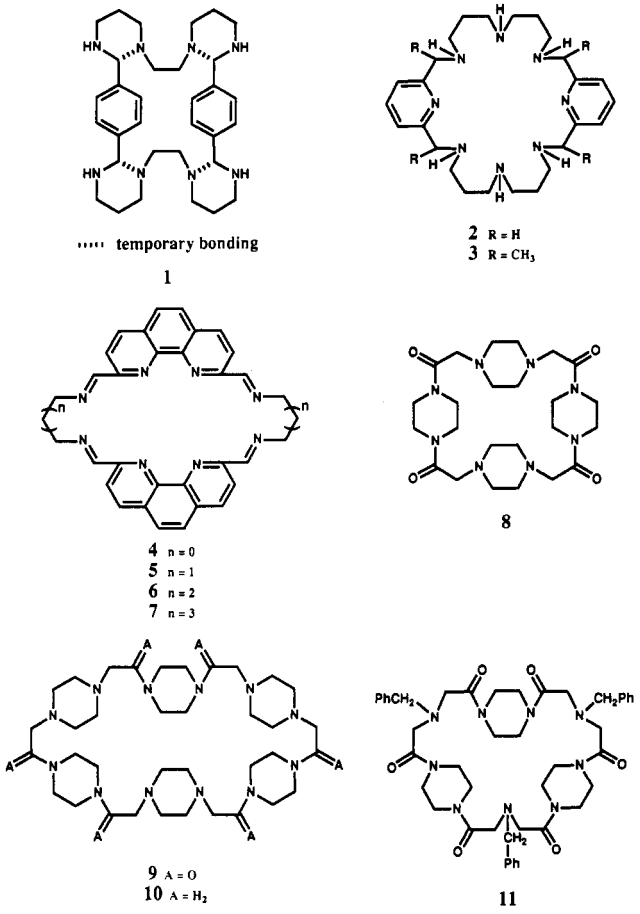
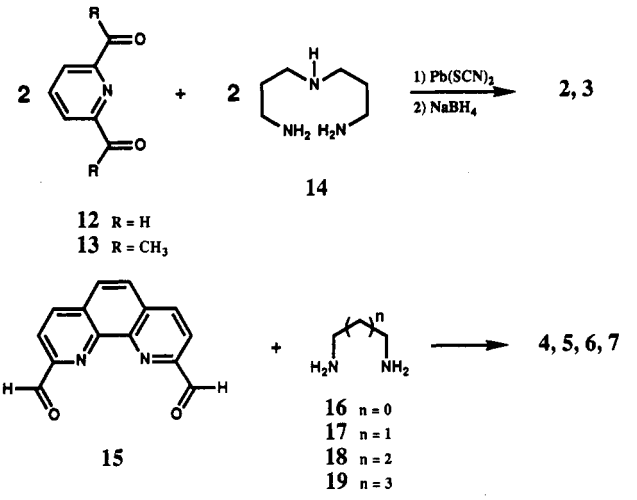


Figure 1. Polyazamacrocycles.

dure often gave a polymeric material after the cyclization reaction and has been successfully used to form crowns and cryptands in only a few cases. While there is no need to remove a metal ion, the nontemplate process requires the use of rigid starting materials such as 2,6-pyridinedicarbaldehyde, terephthaldicarbaldehyde, 2,5-thiophenedicarbaldehyde, and other such systems.[4,17,23-30] The rigid dialdehydes can react with diamines or polyamines such as *N,N'*-bis(3-aminopropyl)-1,2-diaminoethane or *N,N'*-bis(3-aminopropyl)-1,3-diaminopropane to form the macrocyclic polySchiff base. It needs to be mentioned that an internal secondary amine that is three carbons removed from the terminal primary amine can react in concert with the primary amine and the aldehyde to form a 1,3-diazacyclohexane. Indeed, compound **I** (see Figure 1) was formed when terephthaldicarbaldehyde reacted with *N,N'*-bis(3-aminopropyl)-1,2-diaminoethane.[25] The bonds indicated by the dotted lines were cleaved when **1** was treated with lithium aluminum hydride to give the corresponding di-1,4-benzooctaaza-36-crown-8. The previous reaction is similar to a method used to protect 1,3-diamine units in a polyamine chain.[31-33]

Scheme I. Preparation of Pyridino and Phenanthrolino Macrocycles



We now report the convenient synthesis of nine new peraza macrocyclic ligands with large cavities and containing either pyridine, phenanthroline, or piperazine subcyclic units (2–11, Figure 1). These pyridino-, phenanthrolino-, and piperazino-crowns have been prepared to have polyaza-crowns with rigid groups in the backbone. Polyaza-crowns without rigid members can change conformation, which allows them to complex with cations of many sizes, thereby decreasing their overall cation selectivity. Ligands **2** and **3** were prepared by ring closure by use of a template process and **4–7** by a nontemplate reaction. Ligands **8–11** were prepared by use of our new crablike ring closure reaction of a bis(α-chloro amide) and a diamine.[34,35] The structures of **5** and **8** as determined by an X-ray crystallographic technique and the log K_a values for the protonation of ligand **2** are also reported.

Results and Discussion

Ligands **2** and **3** were prepared by a Pb(II)-template catalyzed cyclization reaction of 2,6-pyridinedicarbaldehyde or 2,6-diacetylpyridine with bis(3-aminopropyl)amine followed by reduction of the tetraSchiff base (see Scheme I). The Schiff bases were reduced, the metal ions removed, and the products purified by column chromatography to give 91 and 66% yields of **2** and **3**, respectively. The synthetic sequence was patterned after that used by Nelson and co-workers[1,5,18,20] to give 2:2 cyclocondensation products. Compound **2** is a new material. Nelson and co-workers[1,5,20] prepared **3**, but they only reported that the reduction of the tetraSchiff base was performed with sodium borohydride and did not describe the purification of **3** or its spectral data.[1,5]

During the preparation of **3**, after the initial cyclization reaction, the solid Pb(II)–tetraSchiff base complex was filtered. The filtrate was evaporated to give a smaller amount (about one-third) of yellow crystals. The initial solid and yellow crystals obtained from the filtrate were each reduced by an excess of sodium borohydride. A TLC analysis of the reduced product showed that each reaction mixture gave the same two major products. Each mixture

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was chromatographed, and the major products were isolated. The ^1H NMR, IR, and MS spectra for the two products were identical except for slight differences in the δ 3.7–3.8 and 7.0–7.6 region of the NMR spectra. These results indicate that these two products are different diastereoisomers of **3**. Others have reported stereoisomeric products in the metal-template Schiff base cyclization reaction.[36-39]

The Ag(I) complex of Schiff base **2** was prepared as previously for the Pb(II) complexes with silver nitrate as the template salt. This product could not be reduced, and the metal ion could not be removed with use of the same procedures as mentioned previously for the Pb(II) complexes.

Macrocyclic ligands **4–7** were prepared by a nontemplate condensation of 1,10-phenanthroline-2,9-dicarbaldehyde with 1,2-diaminoethane, 1,3-diaminopropane, 1,4-diaminobutane, or 1,5-diaminopentane. The yields of these macrocycles were in the 50–70% range and were ~10% higher when the reactions were carried out under dilute conditions. The macrocycles were filtered from the solvent. The melting points of **4–7** were >260 °C with decomposition. The solids contained water of hydration originating from the condensation reaction. These Schiff base macrocycles were not soluble in most solvents, but **5** and **7** were recyrstallized from DMF. Small amounts of macrocycles **4** and **6** were recrystallized for analytical purposes in large amounts of chlorofrom (**4**) or a DMSO–acetonitrile mixture (**6**).

The structure of **5** was determined by an X-ray crystallographic study of the **5**$(DMF)_2$ crystals (discussed in the following text). The ^1H NMR and IR spectra for compounds **4–7** are similar to each other, indicating that all have the same macrocyclic structure as shown in the X-ray crystallographic analysis for **5**. The molecular peaks for **4** and **6** were not found in the MS analyses; however, the fragmentation patterns were similar to that for **5** and **7**. TetraSchiff base **7** is believed to be a mixture of 1:1 and 2:2 cycloadditions of **15** and **19**. The MS spectrum for this compound contained peaks for the M^+ for the 1:1 (302) and 2:2 (604) products. Evidently, a five-carbon space between nitrogen atoms is enough to allow for the small ring that results from 1:1 cycloaddition. The two products could not be separated.

Reduction of tetraSchiff base **5** with sodium borohydride was not successful. Similar macrocyclic tetraSchiff bases, but containing pyridine subcyclic groups, also could not be reduced by the same method.[40] However, metal complexes of those and other unsaturated macrocycles were successfully reduced.[40,41]

Piperazine has been incorporated into small and occasionally large macrocyclic compounds.[42-48] The piperazine-containing macrocycles are rigid, the ring is preorganized, and they have a strong preference to complex metal ions that are small enough to fit in the cavity.[44] For example, ligand $[12]N_4$ containing one piperazine ring has a large macrocycle effect in that it has a 9.6 log unit greater affinity for Ni(II) than does the open-chain analogue. The Ni(II) ion is actually compressed by 0.05 Å by the highly preorganized piperazino$[12]N_4$ ligand.[44]

Scheme II. Preparation of "Belt" Compounds

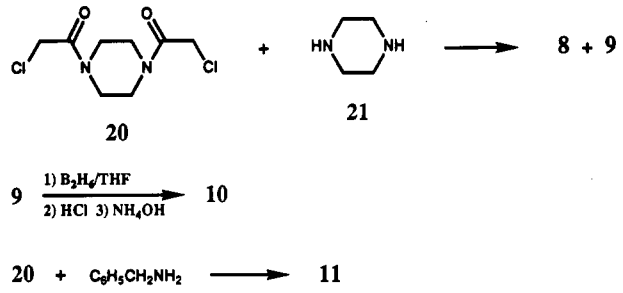

Table I. Interactions (C–H•••O) between Ligand 5 (Figure 2) and the DMF Solvent Molecule

D–H···A	H···A (Å)	D···A (Å)	D–H···A (deg)
C17, H17, OM	2.526	3.574	169.9
C9, HC9, OM	2.368	3.405	158.3
C12, H12, OM	2.462	3.445	147.3
C17, HB2, OM	2.671	3.658	162.8

New piperazine-containing ligands **8–11** have a cavity that will be too large to coordinate with one metal ion. On the other hand, a large macrocycle containing two piperazine units had unusual selectivity for lithium ions.[47] These new "belt" compounds should have interesting complexation properties.

Ligands **8–11** were prepared from *N,N'*-bis(2-chloroacetyl)piperazine (**20**) in a crablike cyclization process (Scheme II). Reactions of bis(α-chloro amides) with various diamines to prepare polyaza-crown compounds have been studied extensively in our laboratory.[34,35,49-51] Ligands **8** and **9** were prepared by reacting **20** and piperazine under dilution techniques in acetonitrile using sodium carbonate as the base. Changing the degree of dilution allowed the production of **8** and **9** in different ratios. In general, the 3:3 cyclization product **9** was favored in more concentrated solutions. Both **8** and **9** are relatively insoluble in organic solvents so that separation is difficult. Ligand **8** dissolves best in chloroform so that the crude solid was triturated with chloroform to remove as much of **8** as possible. The solid was then triturated with acetonitrile to remove as much of **9** as possible. The combined solution was evaporated, and the residue was separated by column chromatography on silica gel. A small amount of **9** was reduced by the usual method with borane to give **10** in a 21% yield. It is interesting that **10** contained one molecule of THF as shown in the NMR spectra.

Ligand **11** was prepared by the reaction of **20** with benzylamine to give the 3:3 cyclization product. A 2:2

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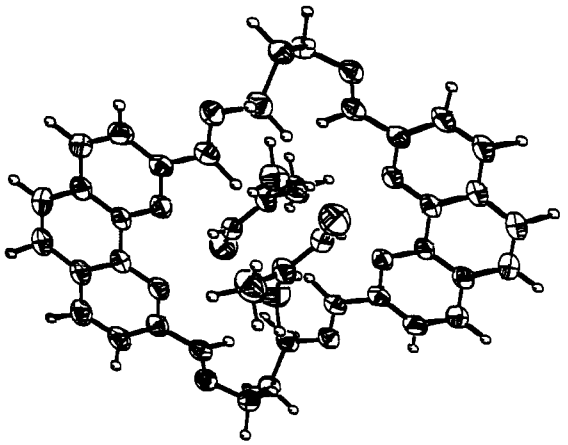

Figure 2. Computer drawing of **5** including two molecules of DMF. The thermal ellipsoids have been drawn at the 50% probability level. Hydrogen atoms have been omitted for clarity.

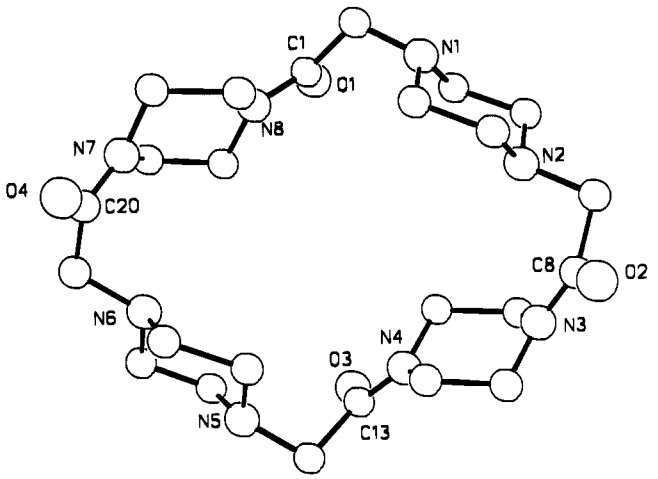

Figure 3. Computer drawing of **8**. Hydrogen atoms and chains of disordered atoms have been omitted for clarity. All atoms have been assigned the same radius.

cyclization product was produced in a 2–3% yield under high dilution conditions. This latter material was observed on a TLC analysis. A small amount was isolated and the molecular weight was determined, but no other analyses were carried out. Ligand **11**, the 3:3 cyclization product, was isolated in a 20% yield. The TLC analysis of the cyclization reaction mixture showed small amounts of other products that probably were the 4:4 and higher order cyclization products.

The structures of macrocycles **5** and **8** have been determined by X-ray crystallography. Tables of atomic parameters for the atoms of **5** and **8**, the bond lengths and angles of **5** and crystal and experimental data for **5** and **8** are included in the supplementary material. Molecule **5** lies about a center of symmetry as shown in the computer drawing (Figure 2). The two DMF solvent molecules are related by the same center of symmetry. Cyclophane-type polyamines containing DMF solvent molecules have not been observed; however, chloroform solvent molecules have been included in those solid compounds.[24,52] The chemically equivalent chemical bonds agree very well (see Table IIIS in the supplementary material). The solvent molecules are located above and below the cavity but do not interact strongly with the ligand. Table I lists possible weak interactions involving hydrogens of the ligand and the ketone oxygens of the solvent.

Table II. Stepwise Protonation Constants for 2 in 0.1 M KCl Aqueous Solution at 25 °C[a]

no. of protons	protonation constant (log *K*)
1	9.97
2	9.32
3	7.93
4	7.35
5	6.97
6	6.38
7	≤2
8	<2

[a] μ = 0.100 M (KCl); T = 25.0 ± 0.01 °C; repeated three times with standard deviations smaller than ±0.02.

A computer drawing of **8** is shown in Figure 3. It is evident that two of the piperazine rings contain amide nitrogens while the other two contain amine nitrogens. The problem of the disorder is discussed in the Experimental Section. The disordered atoms are not shown in the Figure. Because of the problems associated with the disorder there is not good agreement between chemically similar bonds, but the average bond lengths for groups of similar bonds are reasonable. These averages are as follows: C—C, 1.55 Å; C—N, 1.44 Å; and C=O 1.24 Å. As shown in Figure 3, the four piperazine rings are in the chair conformation. This is reasonable because, assuming that conformational energies for piperazine rings are similar to those of cyclohexane, the chair form has lower energy than the boat form. Structural studies of smaller ligands containing piperazine subcyclic groups show that when the molecules form complexes the six-membered rings adopt the boat conformation[43,53] so that both nitrogens can be involved in complexation. Apparently the energy gained by having both nitrogens interact with the metal is sufficient to overcome the energy differences between the chair and the boat form. A possible explanation for the problems encountered in this study is that a small fraction of the six-membered rings exist in the boat form at any one time and this causes disorder in the resulting average structure. A low-temperature study of the compound is planned.

The average structure of **8** obtained in this study appears to be an acceptable representation of the molecule. The cavity of the ligand is large (see Figure 3). This is caused by the rigidity of the piperazine rings and the fact that they are all in the chair conformation. If each six-membered ring is considered as contributing four atoms to the size of the ring, the ring system is the same as a 24-crown-8 ligand. In order to utilize all donor atoms in the formation of a complex, the piperazine rings will have to assume the boat conformation. Unfortunately, largely due to the insolubility of **8** in most solvents, it has not been possible to prepare metal-ion complexes with this ligand in order to verify the possible conformational change.

Ligand **2** was designed to bind selectively in the protonated form with several small inorganic and organic anions. To be an anion receptor, the macrocycle must be rigid and highly protonated. The use of the pyridine rings in **2** and **3** greatly decreases the flexibility of the polyammonium framework as compared to other ditopic polyammonium ligands.[54] Another important property that distinguishes **2** and **3** from their linear or nonrigid macrocycle counterparts such as hexaaza-18-crown-6 or hexaaza-24-crown-8 is their ability to be fully protonated at

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neutral pH values. This is shown by the fact that the overall basicity of **2** (Table II) is high enough to allow the formation of a large amount of fully protonated species at neutral pH values. This fulfills the condition required for the complexation of most inorganic anions. Anionic binding by this protonated macrocycle is currently under investigation.

Experimental Section

The proton NMR spectra were obtained in $CDCl_3$ at 200 MHz. Elemental analyses were performed by MHW Laboratories, Phoenix, AZ. Molecular weights were determined by the electron impact method. Starting materials were purchased from Aldrich Chemical Co. or Schweitzerhall Co. (2,6-diacetylpyridine). 2,6-Pyridinedicarbaldehyde (**12**)[23] and 1,10-phenanthroline-2,9-dicarbaldehyde (**15**)[55] were prepared as reported. Bis(2-chloroacetyl)piperazine (mp 129–130 °C) (**20**) was prepared as reported for similar compounds.[34]

Preparation of Macrocycles of 2 and 3 (Scheme I). Powdered $Pb(SCN)_2$ (3.23 g, 0.01 mol) was mixed with 500 mL of CH_3OH for 30 min. Compound **12** (1.58 g, 0.012 mol) or **13** (1.95 g, 0.012 mol) and 1.56 g (0.012 mol) of **14** were added, and the resulting mixture was vigorously stirred at 60 °C for 6–16 h. The solution was filtered and evaporated to 250 mL. In the case of the preparation of **3**, the solid filtered from the reaction mixture was suspended in 250 mL of CH_3OH. $NaBH_4$ (6 g) was added to the solutions, and the mixtures were stirred under reflux for 16 h. The solvents were evaporated, and 40–50 mL of 30% aqueous NaOH was added. These solutions were extracted three times with 150-mL portions of spectrograde CH_2Cl_2. The combined organic layers were evaporated under reduced pressure, and the residue was chromatographed on a short 200/400 mesh silica gel column with CH_3OH/NH_3 (10/1), then (5/1), and finally (3/1) as eluants. The solvent was evaporated, and the residue was dissolved in a toluene/$CHCl_3$ mixture and filtered through a glass fiber filter to give 2.6 g (91%) of **2** as a liquid that solidified to a semisolid and 2.1 g (66%) of **3** as a semisolid. The spectral properties of these materials are as follows. **Compound 2**: ^1H NMR δ 1.65 (m, 8 H), 2.0 (b, 6 H, disappeared in D_2O), 2.6 (m, 16 H), 3.85 (s, 8 H), 7.1 (d, 4 H), 7.55 (t, 2 H); MS (*m/e*) 469 (92), 468 (94), 347 (100), 290 (24), 237 (30), 233 (34), 218 (40); IR (neat) 3283, 2861, 2810, 1590, 1582, 1575, 1453, 1128, 787 cm^{-1}. Anal. Calcd for $C_{26}H_{44}N_8$: C, 66.63; H, 9.46. Found: C, 66.49; H, 9.46. **Compound 3**: ^1H NMR δ 1.3 (d, 12 H), 1.6 (m, 8 H), 2.0 (b, 6 H disappeared in D_2O), 2.4 (m, 16 H), 3.7 (q, 4 H), 7.0 (dd, 4 H), 7.5 (dt, 2 H); MS (m/e) 526 (62), 524 (70), 375 (100), 318 (40), 104 (28). Anal. Calcd for $C_{30}H_{52}N_8$: C, 68.66; H, 9.99. Found: C, 68.60, H, 10.02.

Preparation of Macrocycles 4-7 (Scheme I). Compound **15** (2.36 g, 0.01 mol) was dissolved in 240 mL of hot CH_3OH and then cooled to room temperature. This solution was slowly dropped into 0.01 mol of **16**, **17**, **18**, or **19** dissolved in 150 mL of CH_3OH during 15–20 min. The resulting mixture was stirred for 16 h. The solid products were filtered and washed with a small portion of CH_3OH. The yields and physical and spectral properties of **4–7** are as follows.

Macrocycle 4: 56%; mp > 260 °C (crystallized from $CHCl_3$); ^1H NMR δ 2.0 (s, 6 H, disappeared in D_2O), 4.2 (m, 8 H), 7.8 (m, 4 H), 8.3 (m, 8 H), 8.9 (m, 4 H); IR (KBr) 3410, 3037, 2918, 1645, 1616, 1547, 1497, 1423, 1369, 1101, 864, 792, 742, 698, 635, 584 cm^{-1}.; MS (*m/e*) 464 (3), 272 (25), 262 (40), 248 (65), 220 (40), 208 (60), 206 (70), 194 (100). Anal. (before recrystallization) Calcd for $C_{32}H_{24}N_8 \cdot 3H_2O$: C, 66.89; H, 5.25. Found: C, 66.86; H, 4.88.

Macrocycle 5: 60%; mp > 260 °C (crystallized from DMF); ^1H NMR δ 2.4 (m, 4 H), 2.8 (s, 6 H, DMF), 2.95 (s, 6 H, DMF), 3.8 (m, 8 H), 7.85 (s, 2 H), 8.0 (s, 2 H, DMF), 8.4 (m, 8 H), 9.0 (ds, 4 H); IR (KBr) 3416, 3038, 2918, 2835, 1645, 1584, 1549, 1496, 1422, 1361, 1089, 860, 742, 697, 634, 582 cm^{-1}; MS (*m/e*) 549 (100), 274 (95), 259 (90), 223 (40), 208 (36). Anal. (before recrystallization) Calcd for $C_{34}H_{28}N_8 \cdot H_2O$: C, 72.07, H, 5.69. Found: C, 71.93, H, 5.35.

Macrocycle 6: 52%; mp > 260 °C (crystallized from $DMSO/CH_3CN$); ^1H NMR δ 1.6 (s, 8 H, disappeared in D_2O), 1.95 (m, 8 H), 3.9 (m, 8 H), 7.85 (s, 4 H), 8.35 (m, 8 H), 8.95 (s, 4 H); IR (KBr) 3407, 3030, 2920, 2830, 1643, 1620, 1584, 1547, 1496, 1422, 1361, 1094, 860, 783, 744, 697, 634, 579 cm^{-1}; (*m/e*) 492 (6), 273 (38), 208 (100), 194 (40). Anal. (before crystallization) Calcd for $C_{36}H_{32}N_8 \cdot 2H_2O$: C, 70.57; H, 5.91. Found: C, 70.55; H, 5.69.

Macrocycle 7: 71%; mp >260 °C (crystallized from DMF); ^1H NMR δ 1.2 (m, 4 H), 1.8–2.0 (s, 14 H, six disappeared in D_2O), 3.8 (t, 8 H), 7.55 (s, 4 H), 8.1 (ds, 4 H), 8.35 (ds, 4 H), 8.85 (s, 4 H); IR (KBr) 3404, 3039, 2930, 2848, 1645, 1617, 1584, 1497, 1442, 1362, 1212, 1192, 1168, 1137, 1100, 1046, 1021, 965, 930, 861, 795, 743, 636 cm^{-1}; MS (*m/e*) 604 (6), 385 (28), 317 (22), 302 (24), 273 (26), 269 (60), 209 (78), 194 (100), 180 (36). Anal. (before recrystallization) Calcd for $C_{38}H_{36}N_8 \cdot 3H_2O$: C, 69.28; H, 6.42. Found: C, 69.38; H, 6.55.

Preparation of Macrocycles 8 and 9 (Scheme II). Compound **20** (1.2 g, 0.005 mol) in 120 mL of CH_3CN and **21** (0.43 g, 0.005 mol) in 120 mL of CH_3CN were slowly and simultaneously added to 120 mL of refluxing and stirring CH_3CN by use of syringe pumps. The resulting mixture was stirred under reflux for 24 h. The mixture was cooled and filtered. The solid was triturated twice with 200-mL portions of spectrograde $CHCl_3$ and once with 200 mL of warm CH_3CN. The $CHCl_3$ solutions and the CH_3CN solution and filtrate were mixed and evaporated. The residue was dissolved in a small amount of $CHCl_3$ and mixed with a few grams of alumina. The mixture was evaporated, and the alumina containing the reaction mixture was added to the top of an alumina column. The products were eluted with CH_3CN/C_2H_5OH (10/1) to give 0.3 g (24%) of **8** as a solid that crystallized from the eluant in 1 day and was recrystallized from DMF, mp > 280 °C, and 0.15 g (12%) of **9**, mp > 300 °C. The spectral properties of these products are as follows. **Macrocycle 8**: ^1H NMR δ 2.5 (m, 16 H), 3.0–4.0 (m, 24 H); MS (*m/e*) 504 (100), 476 (6), 308 (8), 294 (12), 225 (8), 223 (8), 113 (6), 97 (6). Anal. Calcd for $C_{24}H_{40}N_8O_4$: C, 57.12; H, 7.99. Found: C, 57.26; H, 8.00. **Macrocycle 9**: ^1H NMR δ 2.4–2.75 (b s, 24 H), 3.2 (d, 24 H), 3.5–3.7 (b s, 12 H); MS (*m/e*) 756 (100), 728 (6), 548 (6), 86 (4). Anal. Calcd for $C_{36}H_{60}N_{12}O_6 \cdot NaCl$: C, 53.03; H, 7.42. Found: C, 53.15; H, 7.48.

Preparation of Macrocycle 10 (Scheme II). Compound **9** (40 mg, 0.053 mmol) was refluxed in 50 mL of borane–THF for 24 h. The mixture was cooled, water was added to decompose the excess borane, and the resulting mixture was evaporated. The residue was mixed with 30 mL of 18% aqueous HCl and stirred 18 h at room temperature and at 90 °C for 15 min. The mixture was cooled and evaporated under reduced pressure, and aqueous NH_3 was added to attain a pH of 12.5. This solution was extracted three times with 30-mL portions of CH_2Cl_2. NaCl was added to the aqueous layer before the third extraction. The combined CH_2Cl_2 layers were dried over $MgSO_4$. The mixture was filtered and evaporated, giving 10 mg (20%) of **10** as a complex with one molecule of THF; ^1H NMR δ 1.6 (t, 4 H, THF), 2.4 (s, d, 72 H), 3.6 (t, 4 H, THF); ^{13}C NMR δ 29.05 (THF), 52.50, 54.49, 61.84 (THF); IR (KBr) 2926, 1454, 1347, 1334, 1311, 1269, 1261, 1161, 1003, 1014, 975, 942, 933, 800, 698, 555 cm^{-1}; MS (*m/e*) 673 (18), 449 (36), 448 (100), 335 (10), 243 (14), 211 (12). Anal. Calcd for $C_{40}H_{80}N_{12}$: C, 64.41, H, 10.81. Found: C, 57.60; H, 9.74. The sample is contaminated with inorganic material. The calculated ratio of C to H is 5.96 while that found is 5.91, indicating that the observed analysis is satisfactory for **10**, which is contaminated by an inorganic material.

Preparation of Macrocycle 11 (Scheme II). Compound **20** (2.39 g, 0.01 mol) in 60 mL of CH_3CN and 1.07 (0.01 mol) of benzylamine in 60 mL of CH_3CN were slowly and simultaneously added to a stirred, refluxing mixture of 15 g of Na_2CO_3 and 200 mL of CH_3CN over a 48-h period by use of syringe pumps. The resulting mixture was filtered. The solid was mixed with 100 mL of $CHCl_3$ and filtered. The combined CH_3CN and $CHCl_3$ filtrates were evaporated under reduced pressure. The residue was chromatographed on a silica gel column with $C_2H_5OH/CHCl_3$ (3/1) as the eluant to give 0.55 g (20%) of **11** as a solid: mp 120–125 °C; ^1H NMR δ 3.2–3.7 (m, 42 H), 7.3 (s, 15 H); MS (*m/e*) 728 (6), 401 (32), 288 (100), 274 (64), 246 (96), 232 (30), 92 (66), 91 (86). Anal. Calcd for $C_{45}H_{57}N_9O_6$: C, 65.91, H, 7.00. Found: C, 65.84, H, 6.98.

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X-ray Structural Determination of 5 and 8. Single crystals were obtained by slowly cooling the DMF solution of 5 from 120 to 70 °C in the oven and evaporating a DMF solution of 8. The crystal of 5 was sealed in a capillary under nitrogen. Suitable crystals of 5 and 8 were selected, and crystal data and single crystal data were obtained by use of a Nicolet R3 automated diffractometer that utilized graphite-monochromated Mo Kα radiation (λ = 710 69 Å). The lattice parameters and orientation matrix were obtained with a least-squares procedure utilizing several carefully centered reflections. Single-crystal data were obtained with use of a θ–2θ variable scan rate technique. Crystal data and experimental conditions are listed in Table IVS of the supplementary material. The space group for the 5 was $P\bar{1}$, which was obtained from the lattice parameters, single crystal data statistics, and by the successful solution and refinement of the crystal structure. The space group for 8, $Pna2_1$, was determined by examination of systematic extraction and single-crystal statistics.

Both structures were solved by use of direct methods. The refinement for 5 proceeded in normal fashion. The ligand was located about a center of symmetry. ^{1}H NMR data established that these were two DMF solvent molecules for each ligand, and this was substantiated by the structural study. Positions for all hydrogen atoms were obtained from the difference map. The hydrogen atoms were added to the refinement and allowed to ride on the heavy atoms to which they were bonded. Only the thermal parameters of the hydrogen atoms were refined. All heavy atoms were refined anisotropically. The resulting R values were R = 0.048, and R_W = 0.060. Weights were based on counting statistics.

The trial model for 8 was obtained by use of direct methods. The entire molecule was evident in the resulting E map, and the conformation was reasonable. However, it was not possible to refine the structure below 0.18. Several peaks in the difference map that were larger than 1 eÅ^{-3} indicated that the problem in refinement was due to disorder. The difference map contained groupings of peaks with geometry consistent with atomic geometry in organic structures containing carbons, nitrogens, and oxygens that were located near the molecule. These fragments were added to the atom list with occupancy factors of 0.3, but only their isotropic thermal parameters were refined. The R value dropped to 0.14. The two fragments consisting of 9 and 5 atoms were in the neighborhood of the amine six-membered rings, and while neither contained six-membered rings it was possible to visualize at least four atoms of such rings in each fragment. The structure of 8 at this point was consistent with an acceptable conformation, and so refinement was terminated. Scattering factors for both studies were obtained for Vol. 4 of the *International Tables of X-Ray Crystallography*.[56] All computer programs used in this study are contained in the program package SHELXTL.[57]

Determination of the Protonation Constants for 2. The protonation of 2 in aqueous solution was studied by potentiomeric titration of the solution containing the ligand in a 0.1 M KCl solution at 25.0 °C. The titrant was a standard KOH solution. The computer program SUPERQUAD was used to process the potentiomeric data and calculate the protonation constants. The ionic strength was adjusted to 0.10 mol/dm^3 by addition of the appropriate amount of KCl. The emf of these solutions was measured by using a Corning semimicro glass electrode coupled with an Orion 701A digital potentiometer. The pK_a values are given in Table II.

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Supplementary Material Available: Tables of atomic parameters for the atoms of 5 and 8, the bond lengths and angles of 5, and crystal and experimental data for 5 and 8 (7 pages). Ordering information is given on any current masthead page.

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1,2,3-Triazoles from (*Z*)-β-(Formyloxy)vinyl Azides and Triethyl Phosphite

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(*Z*)-Sodium enolates of two α-azido ketones are O-formylated with Me_3CCO_2CHO in high yield to give isolable (*Z*)-β-(formyloxy)vinyl azides, which are converted to 1,2,3-triazoles under the influence of triethyl phosphite. A mechanism is proposed for triazole formation involving 1,5-electrocyclization of a vinyl phosphazide intermediate.

1,5-Electrocyclizations are a class of concerted reactions that are of paramount importance in the preparation of five-membered heterocyclic ring systems.[1] The generality of this reaction type has resulted in the exceptions to the rule being more interesting than the confirmations. Vinyl azides[2] represent one such exception. In general, thermolysis of vinyl azides results in the formation of 2*H*-azirines and N_2 without the intermediacy of 1,2,3-triazoles.[3] The inability of these systems to undergo 1,5-cyclization prior to loss of N_2 is due in part to the energy required to bend the linear azido group into a suitable geometry for such a cyclization. Conversion of vinyl azides to 1,2,3-triazoles[4] occurs only in special cases. α-Azido enamines cyclize to 2*H*-1,2,3-triazoles.[5] This unusual behavior has been attributed to the nucleophilic character of the enamine carbon and the lower rotation barrier of the carbon–carbon double bond.[5a] β-Metalated (Na) vinyl azides also cyclize readily, again likely due to enhanced nucleo-

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