Table III. Microscopic GB, pK_a and log K_{HB} Predicted for Each Group, MeCO and $Me_2NCH{=}N$, in Compound 3

group	GB	pK_a	log K_{HB}[a]
MeCO	213.5	<0[b]	1.67
$Me_2NCH{=}N$	219.5	7.02[c]	1.52

[a] Reference 5. [b] Reference 18. [c] Reference 20.

and $\Delta\nu_{OH}(N^2)$ = 295 cm^{-1}. The resulting GB values are given in Table III. For comparison, the solution Brønsted basicities (as pK_a) and the hydrogen-bonding basicities (as log K_{HB}) for each group are also summarized. These results confirm that the amidine group is the favored site of protonation in both gas phase and solution; however, hydrogen bonding is enhanced by the presence of the acetyl group. As a consequence, in aqueous solution, acetophenones as well as benzonitriles and nitrobenzenes are very weak bases.[9,17,19] The acetyl group forms strong hydrogen bonds with water or other hydrogen-bond-donor solvents, thereby reducing basicity in aqueous solution relative to the intrinsic gas-phase basicity.

Acknowledgment. We thank Professor C. Laurence (Université de Nantes, France) for the values of log K_{HB} for some pyridines. Financial support of the Fonds National Suisse is gratefully acknowledged.

Registry No. 1, 74739-51-8; 1·H^+, 123834-37-7; 2, 119044-58-5; 2·H^+, 123834-38-8; 3, 119044-59-6; 3·H^+, 123834-39-9; 4, 119044-60-9; 4·H^+, 123834-40-2; 5, 56687-95-7; 5·H^+, 123834-41-3; 6, 56638-68-7; 6·H^+, 123834-42-4.

A Study of New Bis(macrocyclic polyamine) Ligands as Inorganic and Organic Anion Receptors

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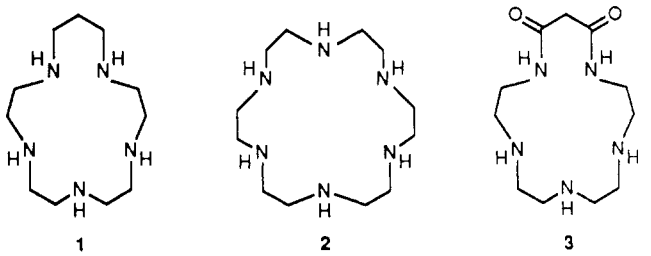
Propylene-bridged bisdioxo[16]aneN$_5$ (**4b**) and diether-bridged (**5a**) and propylene-bridged (**5b**) bis[16]aneN$_5$ ligands [bis(macrocyclic pentaamine)] were synthesized as host molecules for inorganic and organic anion guests. By the polarographic and potentiometric methods, **4b** (di- and tetraprotonated) and **5a** and **5b** (tetra- and hexaprotonated) were found to yield stable 1:1 complexes with citrate^{3-}, AMP^{2-}, ATP^{4-}, HPO_4^{2-}, $[Fe(CN)_6]^{4-}$, and $[Fe(CN)_6]^{3-}$ anions. Comparison of these association constants (K) with those of the parent monomeric polyamines reveals that the attachment of the second polyamine moiety always enhances anion encapsulating abilities, suggesting the formation of sandwich-type complexes. Diprotonated tetraoxo[24]aneN$_8$ **6**, $[\mathbf{6}\cdot(H^+)_2]^{2+}$, forms more stable 1:1 complexes with nucleotide anions than the diprotonated **4b**, $[\mathbf{4b}\cdot(H^+)_2]^{2+}$.

The interaction of organic anion receptors with biologically important anions has received much attention, both for its intrinsic interest and potential applications[1,2] as well as for the role it can play as a model for biological processes.[3,4] In earlier studies it was discovered that the macrocyclic pentaamines ([16]aneN$_5$, **1**) and hexaamines ([18]aneN$_6$, **2**) accommodate three protons within their macrocyclic cavities at neutral pH and that the resulting triprotonated species display selective complexing abilities toward polycarboxylate anions,[5-7] CO_3^{2-},[8] catechols,[9,10] and nucleotide anions (AMP^{2-}, ADP^{3-}, and ATP^{4-}).[11-13] An amide-containing polyamine derivative, dioxo[16]aneN$_5$ (**3**), in its singly and doubly protonated forms, also interacts with these anions to form 1:1 complexes.[11] Recently, studies with more expanded macromonocyclic polyamines (e.g., [21]aneN$_7$, [24]aneN$_8$, [27]aneN$_9$, [30]aneN$_{10}$, etc.) have been reported.[14] Macromonocyclic polyamines studied thus far are limited in their structural variations. Further structural modifications might provide us with more efficient and selective host molecules, as well as with new information on their anion coordination chemistry.

To this end, we have synthesized new anion receptor molecules, bisdioxo[16]aneN$_5$ (**4b**) and bis[16]aneN$_5$ (**5a** and **5b**), both of which are comprised of two identical



1 2 3

macrocyclic units linked with a polyether or a propylene chain (see Scheme I). The association constants of these

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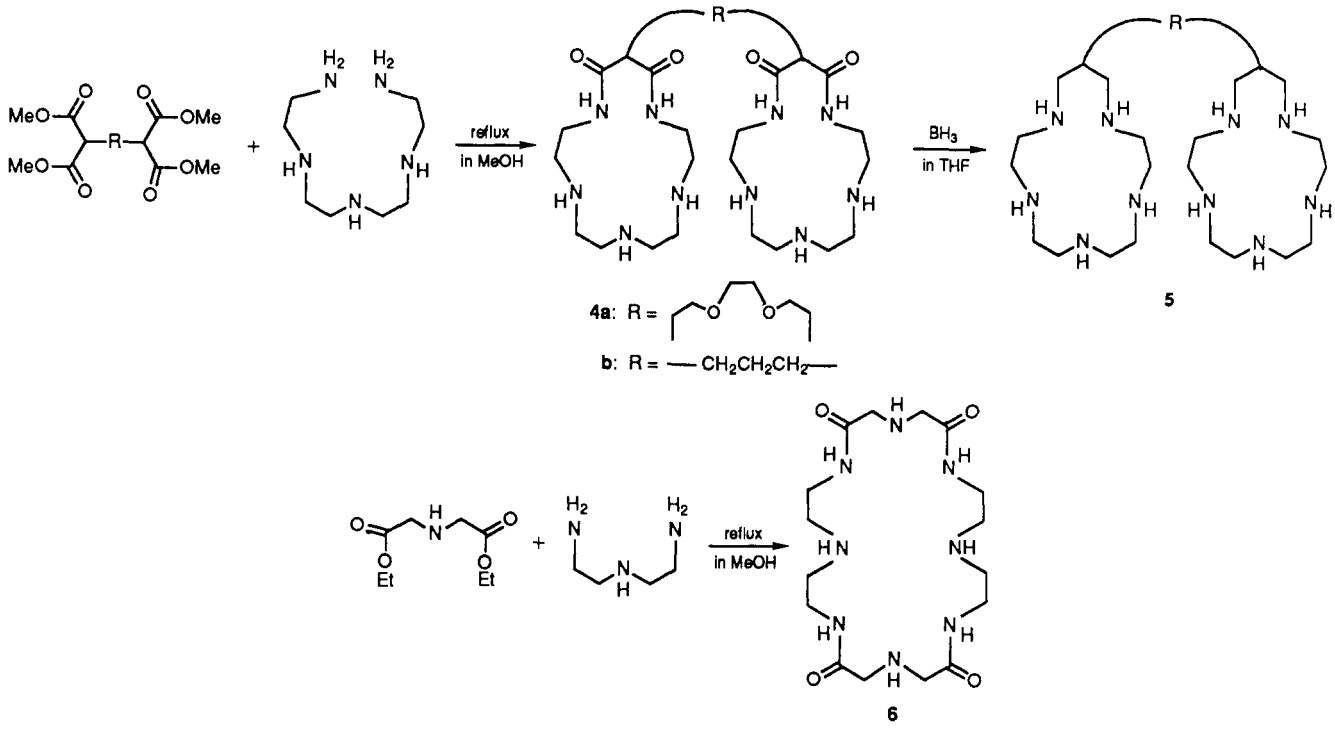
Scheme I



new, ditopic macrocycles, with anions such as citrate^{3-}, HPO_4^{2-}, AMP^{2-}, ATP^{4-}, $[Fe(CN)_6]^{4-}$, and $[Fe(CN)_6]^{3-}$, were determined through pH monitoring and polarographic methods and compared with those for the parent monocyclic macrocycles. Enhanced stability, relative to the parent compounds, is associated with these new **4b**, **5a**, and **5b** hosts. The anion association behavior of still another new host molecule, tetraoxo[24]aneN$_8$ (**6**), was also studied.

Experimental Section

Bridged Bis(macrocyclic pentaamines) 4 and 5. Typically, the synthetic procedure of **4a** and **5a** was as follows. 2,2′-[1,8-(3,6-Dioxaoctanediyl)]bis(dimethyl malonate) (17.0 g, 45 mmol) and 1,11-diamino-3,6,9-triazaundecane (15.3 g, 81 mmol) in dry MeOH (0.7 L) were refluxed for 3 weeks. After evaporation of the solvent, CH_3CN was added to crystallize the residue. Recrystallization from MeOH/CH_3CN yielded 15,15′-[1,8-(3,6-dioxaoctanediyl)]bis(14,16-dioxo-1,4,7,10,13-pentaazacyclohexadecane) (**4a**) (mp 191 °C) as colorless crystals in 4.2% yield (1.34 g). IR (KBr pellet): ν_{CO} 1675 cm^{-1}. ^{1}H NMR ($CDCl_3$/CD_3OD): δ 1.9–2.3 (4 H, m, CCH_2C), 2.5–2.9 (24 H, m, NCH_2C), 3.0–3.8 (10 H, m, $CONCH_2$, COCHCO), 3.4–3.6 (8 H, m, OCH_2C). Reduction of **4a** (0.90 g, 1.4 mmol) with freshly distilled BH_3·THF (77 mmol) in 200 mL of THF yielded 15,15′-[1,8-(3,6-dioxaoctanediyl)]bis(1,4,7,10,13-pentaazacyclohexadecane) (**5a**) as its 10HCl salt purified by recrystallization from H_2O–MeOH–EtOH [1.0 g, 78% yield, mp 163 °C dec]. ^{1}H NMR (free form in $CDCl_3$): δ 1.4–1.7 (4 H, *m*, CCH_2C), 1.7–2.0 (2 H, m, CCHC), 1.8–2.3 (10 H, m, NH), 2.3–3.2 (40 H, *m*, NCH_2-), 3.4–3.7 (8 H, m, OCH_2C). Anal. Calcd (found) for $C_{28}H_{64}N_{10}O_2$·10HCl·3H_2O: C, 33.92 (34.12); H, 8.13 (8.29); N, 14.13 (14.08). The physical data for propylene-bridged bismacrocycles [with 2,2′-(1,3-propanediyl)-bis(diethyl malonate)] are follows: **4b**: ν_{CO} = 1670 cm^{-1} (KBr pellet); ^{1}H NMR (D_2O) δ 1.2–1.5 (2 H, m, CCH_2C), 1.7–2.1 (4 H, m, $=CCH_2C$), 2.5–3.0 (24 H, m, NCH_2C), 3.0–3.8 (10 H, m, $CONCH_2$, COCHCO); yield = 8%, mp 245 °C. **5b**: ^{1}H NMR (free form in $CDCl_3$) δ 1.1–1.4 (6 H, m, $CH_2CH_2CH_2$), 1.5–1.8 (2 H, m, =CHC), 1.95 (10 H, s, NH), 2.4–2.9 (40 H, m, NCH_2); yield 80%, mp 180 °C dec. Anal. Calcd (found) for $C_{25}H_{58}N_{10}$·10HCl·H_2O: C, 34.07 (34.24); H, 8.01 (8.13); N, 15.89 (15.88).

Tetraoxo[24]aneN$_8$ (6). Iminodiacetic acid diethyl ester (15.7 g, 0.08 mol) and 1,5-diamino-3-azapentane (8.2 g, 0.08 mol) in 500 mL of dry ethanol were refluxed for 1 week. Silica gel column chromatography (eluent $CHCl_3$/MeOH = 10:1) of the reaction mixture could successfully separate 2,6,14,18-tetraoxo-1,4,7,10,13,16,19,22-octaazacyclotetracosane (**6**) (tetraoxo[24]-aneN$_8$) from a monomer, dioxo[12]aneN$_4$.[15] Subsequent recrystallization from EtOH afforded **6** (1 g, mp 198 °C) in 6.5% yield. IR (KBr pellet): ν_{CO} = 1658 cm^{-1}. ^{1}H NMR ($CDCl_3$/CD_3OD): δ 2.68 (8 H, t, NCH_2C), 3.18 (8 H, s, NCH_2CO), 3.27 (8 H, *t*, $CONCH_2C$). M^+ = 400. TLC (silica gel, Merck Art. 5567; eluent $CHCl_3$/MeOH/28% aqueous NH_3 = 5:1:0.2) R_f = 0.1 for **6**, R_f = 0.3 for dioxo[12]N_4.[15] Anal. Calcd (Found) for $C_{16}H_{32}N_8O_4$: C, 47.99 (47.95); H, 8.05 (7.72); N, 27.98 (27.67).

All chemicals were of analytical reagent grade and were used without further purification. ^{1}H NMR (100 MHz) spectra were obtained on a JEOL FX-100 spectrometer at 22 °C.

Polarographic Studies. The appratuses used for the polarographic measurements are the same as those applied to the study of the Hg(II)-macromonocyclic polyamine complexation.[16,17] The special features of the dropping mercury electrode (DME) have been described elsewhere.[16,17] All the polarographic measurements used 5.0 × 10^{-2} M Tris–$HClO_4$ or 3.0 × 10^{-2} M borate buffer solutions containing 2.0 × 10^{-4} M polyamine and an ample excess of anion with an ionic strength (I) of 0.20 M $NaClO_4$. Those buffers had practically no effect on the half-wave potentials of anodic waves.

Electrophoresis. Electrophoresis was performed on an ADVANTEC SE-33 and a Atto VC Stabilizer ST-1081. Separax (6 × 22 cm^2, Jookoo Co. LTD) was used as the supporting medium for each run. Experimental procedures employed in the electrophoresis were the same as those applied to the previous macrocyclic polyamine–polycarboxylate system.[5] $[Fe(CN)_6]^{4-}$ spots were detected by staining the finished strips with Cu^{2+}_{aq} solution.

pH Studies. pH titrations were performed by using a Mettler automatic titrator DL-40RC at 25.00 ± 0.05 °C and I = 0.20 M

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($NaClO_4$) in Ar. The mixed-protonation constants, K_n, were determined with 0.200 M aqueous $(Et)_4NOH$ and 50 mL of 10^{-3} M ligand solutions acidified with 0.200 M $HClO_4$. The $-\log K_n$ (pK_n) values determined are 10.11, 9.82, 9.38, 8.66, 6.52, 5.67, 3.93, <2, <2, <2 for **5a**, 9.38, 9.37, 8.58, 6.90, <2, <2 for **4b**, 10.12, 9.87, 9.20, 8.60, 7.08, 5.81, <3, <2,<2, for **5b**, and 8.32, 7.43, 5.67, 4.73 for **7**. For pH measurement, solutions containing 10^{-3} M ligand (in fully protonated form) and a large excess of anion were used. The values of $-\log [H^+]$ used for the calculation were estimated from pH readings at I = 0.20 M: $-\log [H^+]$ = pH − 0.13.

Results and Calculations

Two bis[16]aneN$_5$ ligands **5a** and **5b** gave well-defined reversible anodic Hg dissolution waves on DME at pH > 7.5. On the other hand, at pH < 7.5 the anodic waves completely merge into the Hg reduction wave. Thus, complex formation of **5a** and **5b** with anions (except for $[Fe(CN)_6]^{4-}$ and $[Fe(CN)_6]^{3-}$) has been studied at pH > 7.5 by the same polarographic method reported earlier.[16,17] However, when anions were $[Fe(CN)_6]^{4-}$ and $[Fe(CN)_6]^{3-}$, a large one-electron redox wave (for $Fe^{3+} \rightleftarrows Fe^{2+}$) occurring +0.24 V vs SCE disturbed the anodic Hg dissolution waves. Hence, the pH-metric method[16] was employed for the bismacrocycles (**4b**, **5a**, and **5b**) with these anion and with ATP^{3-} (at low pH region).

Complexation Measurement by Polarographic Method. For diether-bridged bis[16]aneN$_5$ (**5a**, L), the polarographic behavior is similar to that for **1**,[5] indicating the reaction mechanism at DME to be expressed as eq 1.

$$Hg + H_iL^{i+} \rightleftarrows [HgH_jL]^{(2+j)+} + (i-j)H^+ + 2e^- \quad (1)$$

The plots of $\log (i/(i_d - i))$ against dc potential gave invariably straight lines with reciprocal slopes of ca. 30 mV/decade. The half-wave potentials $E_{1/2}$ of the host ligands upon addition of a large excess of guest anions (A^{n-}) shifted as in the case of **1**. Hence, the analysis was carried out as in the previous manner.[16,17]

For propylene-bridged bis[16]aneN$_5$ (**5b**, L), the limiting currents of the anodic waves were also proportional to the bulk concentration of [L] and also to the square-root of the Hg pressure at DME. However, these currents were exactly twice as high as for **5a** at the same concentration. The plots of $\log [i/(i_d - i)]$ against dc potential gave invariably straight lines with reciprocal slopes of ca. 15 mV/decade. The half-wave potentials shifted to more negative values by increasing the solution pH, which obeys eq 2. These facts agree with the electrode reaction of **5b** to be given by eq 3.

$$\frac{E_{1/2}}{\log [1 + K_1(a_{H^+}) + \ldots + K_1K_2\ldots K_{10}(a_{H^+})^{10}]} = 15 \text{ mV} \quad (2)$$

$$2Hg + H_iL^{i+} \rightleftarrows [Hg_2L]^{4+} + iH^+ + 4e^- \quad (3)$$

From these premises the theoretical equation (4), which relates 1:1 H_mL^{m+}–A^{n-} complex formation with $E_{1/2}$, is readily derived, as for carbonate–[6] and catechol–macrocyclic polyamine complexes.[9,10] All the experimental results for **5b**–A^{n-} interactions fit eq 4.

$$[\text{antilog } (E_{1/2}/0.0148) - 1]\cdot M\cdot N = K\cdot[A^{n-}](a_{H^+})^m/K_{10}\ldots K_{11-m} \quad (4)$$

where

$$M = 1 + K_1(a_{H^+}) + K_1\cdot K_2(a_{H^+})^2 + \ldots + K_1\ldots K_{10}(a_{H^+})^{10} \quad (5)$$

$$N = 1 + K_1'(a_{H^+}) + K_1'\cdot K_2'(a_{H^+})^2 + \ldots + K_1'\ldots K_a'(a_{H^+})^a \quad (6)$$

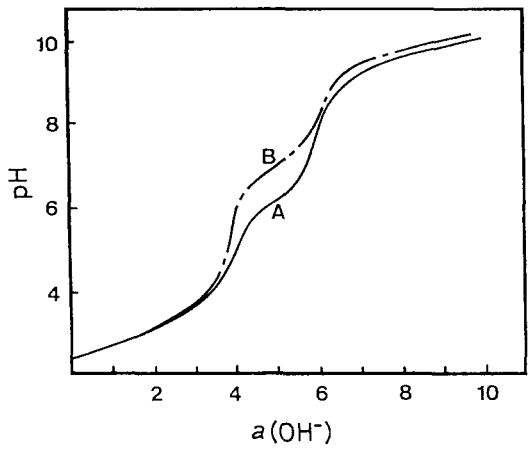


Figure 1. Titration curves of 0.700 mM **5a**·10HCl solutions at 25 °C (A) in the absence of $[Fe(CN)_6]^{3-}$ and (B) in the presence of 23.4 mM $[Fe(CN)_6]^{3-}$.

Table I. Association Constants K^a for 5a, 5b, and 1 at I = 0.20 M and 25 °C

	log K^a				
	5a		**5b**		**1**
anion	H_4L^{4+}	H_6L^{6+}	H_4L^{4+}	H_6L^{6+}	H_3L^{3+}
$[Fe(CN)_6]^{4-}$ [b]	4.76	6.24	4.35	6.51	3.51[c]
$[Fe(CN)_6]^{3-}$ [b]	3.38	4.73	–	–	2.79[c]
$citrate^{3-}$ [b]	3.57	4.63	3.62 (3.70[d])	4.70	2.40[d,e]
AMP^{2-}	3.93[d]	–	–	–	3.11[d,f]
ATP^{4-} [b]	5.08	7.09	5.22 (5.14[d])	7.27	3.62[d,f]
HPO_4^{2-}	2.90[d]	3.8[b]	–	–	2.04[d,f]

[a] Confidence limits are within ±5%. – means no determination. [b] By pH method. [c] Determined in this study. [d] By polarographic method. [e] Reference 5. [f] Reference 10.

$K_1\ldots K_{10}$ and $K_1'\ldots K_a'$ are protonation constants of bismacrocycle **5b** and of guest anions, respectively.

The results of **5a** and **5b** with $citrate^{3-}$, AMP^{2-}, ATP^{4-}, and HPO_4^{2-} are summarized in Table I, together with those reported for **1**.

Complexation Measurements by Potentiometry. Some cases of anion complexations were investigated by pH titrations. A typical titration curve for **5b** in the presence of a large excess of $Fe(CN)_6^{3-}$ is shown in Figure 1. All the titration results with **4b**, **5**, and **6** with $Fe(CN)_6^{n-}$ (A^{n-}) fit eq 7, where x denotes 10, 6, and 4, respectively.

$$K = (P\cdot R - Q\cdot C_L)/(x-m)(C_L - P)C_A\cdot K_1\cdot K_2\ldots K_m\cdot(a_{H^+})^m \quad (7)$$

where

$$H_{i-1}L^{(i-1)+} + H^+ \rightleftarrows H_iL^{i+};\ K_i = [H_iL^{i+}]/[H_{i-1}L^{(i-1)+}](a_{H^+}) \quad (8)$$

$$P = aC_L + [H^+] - [OH^-] = Q[L] + (x-m)[H_mL^{m+}\text{–}A^{n-}] \quad (9)$$

$$Q = 10 + 9K_1(a_{H^+}) + \ldots + K_1\cdot K_2\ldots K_{x-1}(a_{H^+})^{x-1} \quad (10)$$

$$C_L = R[L] + [H_mL^{m+}\text{–}A^{n-}] \quad (11)$$

$$C_A = [A^{n-}] + [H_mL^{m+}\text{–}A^{n-}] \quad (12)$$

$$R = 1 + K_1(a_{H^+}) + \ldots + K_1\cdot K_2\ldots K_x(a_{H^+})^x \quad (13)$$

The similar pH determination of the other anion complexations with **1**, **2**, and **3** was described in detail.[5,8–10,18]

Table II. Association Constants K^a for 4b, 6, and 3 at I = 0.20 M and 25 °C by pH Method

	log K^a				
	4b		6	3[b]	
anion	H_2L^{2+}	H_4L^{4+}	H_2L^{2+}	HL^+	H_2L^{2+}
$[Fe(CN)_6]^{4-}$	2.61	3.9	–	1.75	2.5
$citrate^{3-}$	1.6	2.68	2.50	<0.5	1.3
AMP^{2-}	3.15	4.57	3.84	2.18	3.35
ATP^{4-}	3.67	5.61	4.66	2.68	3.64
HPO_4^{2-}	1.1	2.07	2.05	<0.5	<0.5

[a] Confidence limits are within ±5%. – means no determination. [b] Determined in this study.

All the K values determined pH-metrically are placed in Tables I and II, together with those for the reactions of the relevant monomers.

Discussion

In aqueous solutions of physiological pH, [16]aneN$_5$ (**1**) in its triprotonated form H_3L^{3+} assumes 1:1 complexes with $citrate^{3-}$, AMP^{2-}, ATP^{4-}, HPO_4^{2-}, $[Fe(CN)_6]^{3-}$, and $[Fe(CN)_6]^{4-}$ anions. On the basis of their protonation constants, **5a** and **5b** are presumed to accommodate two protons at pH ~7.5 and three protons at pH ~4.5 into each macrocyclic cavity. The protonated species, H_4L^{4+} and H_6L^{6+}, respectively, form stable 1:1 complexes with inorganic and organic anions (see Scheme II). Thus, quantitatively established anion associations are qualitatively supported by a paper electrophoretic study. In the absence of bis[16]aneN$_5$ (**5a**), a spot of $[Fe(CN)_6]^{4-}$ on a paper moved, as expected, toward the positive electrode in pH 7 Tris buffer solution. On the other hand, in the presence of 1.4 equiv of **5a**, the $[Fe(CN)_6]^{4-}$ spot moved slightly toward the negative electrode under the same conditions (see Figure 2). Similar abnormal electrophoretic behaviors were observed in succinate–[18]aneN$_5$[8] and bicarbonate–[18]aneN$_6$ interactions.[8]

Monocyclic dioxo[16]aneN$_5$ (**3**) (singly (HL^+) and doubly protonated (H_2L^{2+})) interacts with $[Fe(CN)_6]^{4-}$, AMP^{2-}, and ATP^{4-} anions, but only negligibly with inorganic phosphate anion, HPO_4^{2-}. With $citrate^{3-}$ anion, only the H_2L^{2+} species associates.

The findings in the 1:1 association constants K (Tables I and II) are interpreted in terms of electrostatic attractions and hydrogen bonding between the protonated macrocyclic nitrogens and oxyanions. The fact that AMP^{2-} binds $10–10^2$ times more strongly than HPO_4^{2-} implies the involvement of binding forces between adenine base and the macrocycle. All of the association constants K for the complexes of the present bismacrocycles are uniformly greater than those of the corresponding parent monomacrocycles. Although each macrocyclic part of bis[16]aneN$_5$ **5** can accommodate only two protons at pH ~ 7.5 (while monomacrocycle **1** attaches three protons[5]), their complexing abilities are an order of magnitude greater than those of the triprotonated parent monomacrocycle **7**. The complexes of H_6L^{6+} **8** are 2–3 orders of magnitude more stable than those of H_3L^{3+}.

The greater complex stabilities exhibited in the present bismacrocycles may be understood by invoking a ditopic type of interaction between the two macrocycles. As indicated by the lowered protonation constants of **4b**, **5a**, and **5b** with respect to those of the parent monomacrocycles,[5] an increase in the number of protons attached to the bismacrocycles would increase electrostatic repulsions between the two protonated moieties in the same molecules. Anion complexation would serve to reduce these electrostatic repulsions. This effect would be best achieved by invoking a sandwich complex structure, where the donor anion is located between the two protonated macrocycles **8**.[19] Between **5a** and **5b**, no appreciable difference in the magnitude of association constants was found.

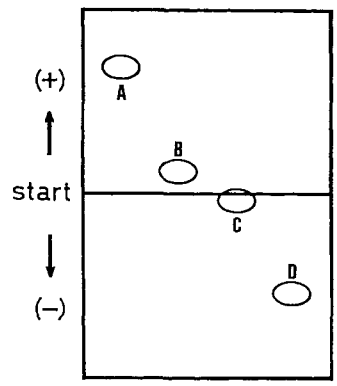
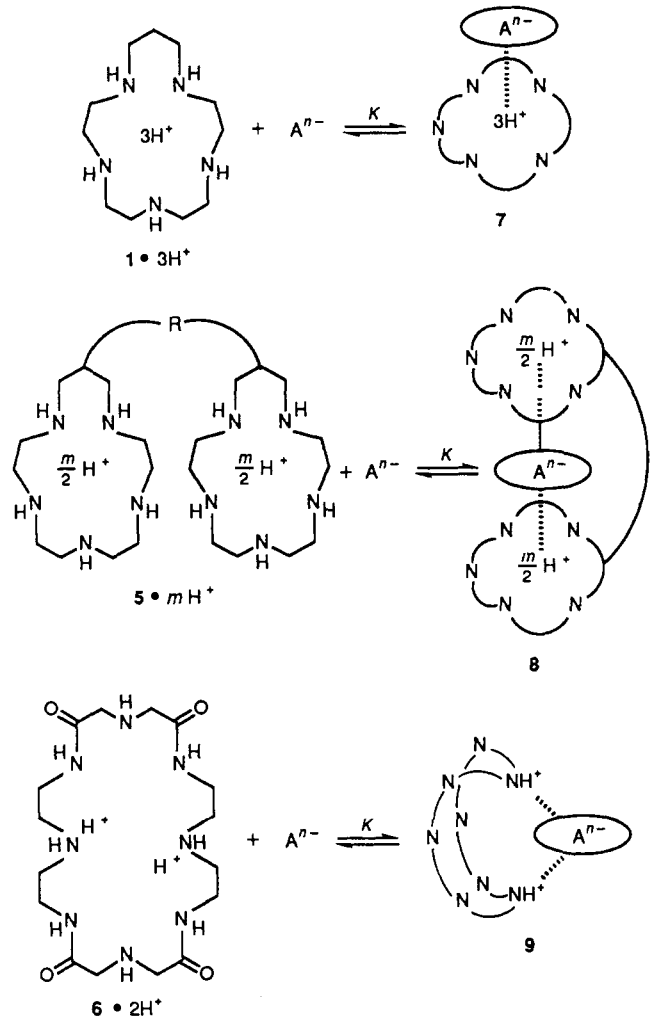


Figure 2. Electrophoretic movement of anion complexes at pH = 7.0 (0.10 M Tris buffer) and 90–110 V (15 min) on acetate cellulose sheet: A, $[Fe(CN)_6]^{4-}$ only; B, $[Fe(CN)_6]^{4-}$ + 2 equiv of **2**·3H$^+$; C, $[Fe(CN)_6]^{4-}$ + 1.4 equiv of **5a**·4H$^+$; D, [18]aneN$_6$·3H$^+$ only.

Scheme II



(18) Kimura, E.; Koike, T.; Kodama, M. *Chem. Pharm. Bull.* **1984**, *32*, 3569.

(19) We have been unsuccessful in isolating these anion complexes. So far only a [30]aneN$_{10}$·8H$^+$–($[Co(CN)_6]^{3+}$)$_2$Cl$_2$ complex structure was determined by X-ray crystal analysis in ref 14.

The association of tetraoxo[24]aneN$_8$ (**6**) with carboxylates and nucleotides was also investigated (see Table II). At neutral pH, **6** takes on two protons and then goes on to form 1:1 complexes **9** with the above anions. The association constants for these complexes are greater than each of those for the doubly protonated, propylene-bridged bisdioxo[16]aneN$_5$ (**4b**), indicating that **6** is a more suitable receptor than **3b**, especially for the nucleotide anions. In fact, Dreiding models suggest that the flexible nucleotide can easily be positioned so as to interact efficiently with diprotonated **6**, through its phosphate and adenine sites.

The bis(macromonocyclic polyamine) and the tetraamide-containing macrocyclic polyamine ligands presented in this study may serve as a new class of efficient receptor molecules. Variations in ring size, donor atom number, and substituent may provide a number of novel, versatile derivatives that could simultaneously expand our knowledge of biological anion transport.

Acknowledgment. We are grateful for financial support from the Ministry of Education, Science and Culture, Japan (Grant-in-Aid for Scientific Research on Priority Area of "Macromolecular Complexes", No. 63612511).

Registry No. **4a**, 113423-16-8; **4b**, 123963-00-8; **5a**, 113450-03-6; **5b**, 123963-01-9; **6**, 123963-02-0; AMP, 61-19-8; ATP, 56-65-5; HPO_4^{2-}, 14066-19-4; $[Fe(CN)_6]^{4-}$, 13408-63-4; $[Fe(CN)_6]^{3-}$, 13408-62-3; citrate^{3-}, 126-44-3; 2,2′-[1,8-(3,6-dioxaoctanediyl)]-bis(dimethyl malonate), 104883-36-5; 1,1-diamino-3,6,9-triazaundecane, 112-57-2; 2,2′-(1,3-propanediyl)bis(diethyl malonate), 82031-49-0; iminodiacetic acid diethyl ester, 6290-05-7; 1,5-diamino-3-azapentane, 111-40-0.

Nitration of Phenylboron Dichloride with Nitronium Tetrafluoroborate. Attempted Nitration of Iodobenzene Dichloride and Phenylphosphorus Dichloride[1a]

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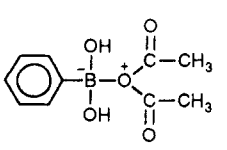
Electrophilic nitration of phenylboron dichloride with nitronium tetrafluoroborate and *N*-nitro-2,4,6-collidinium tetrafluoroborate was investigated in nitromethane solution. The reactions give 10–18% ortho, 67–69% meta, and 15–21% para isomer. NMR studies of the systems also show the formation of PhBFCl and $PhBF_2$ by fluoride exchange as well as their intermediate complexes with the BF_4^- anion. The high meta content is attributed to the nitration of uncomplexed phenylboron dihalides with the $-BX_2$ group exhibiting an –I effect which directs the nitration significantly to the meta position. High para isomer content was obtained when the phenylboron dihalides were mostly complexed by the BF_4^- anion, thereby reducing the –I effect of $-BX_2$ group. The nitration of iodobenzene dichloride gave essentially only nitroiodobenzenes due to the dissociation of $PhICl_2$ and the much faster nitration of PhI as compared to $PhICl_2$. Attempted nitration of $PhPCl_2$ with $NO_2^+BF_4^-$ in CH_3NO_2 led only to oxidation. The oxidation could not be prevented even when trimethyl phosphate was used as solvent or the milder nitrating agent $MeONO_2/BF_3$.

Introduction

Aromatic nitration reactions have been studied extensively with regard to their mechanism, directive effects of various substituents, and synthetic applications.[2] There is substantial interest in electrophilic nitration of organometallic compounds, and this area is comparatively less studied. We have been interested in the Friedel–Crafts chemistry of $PhBCl_2$ and $PhPCl_2$ and their electrophilic substitution as well as in determining the directive effects in these reactions. Combined with continued interest in aromatic nitration, we report here results of the nitration of $PhBCl_2$ and attempted nitration of $PhPCl_2$ with $NO_2^+BF_4^-$ and *N*-nitro-2,4,6-collidinium tetrafluoroborate. A related study of nitration of $PhICl_2$ was also carried out.

Nitration of Phenylboron Dichloride

Among nitrations of boron-substituted aromatics, only that of benzeneboronic acid has been studied. Ainley and Challenger[3] reported that nitration of $PhB(OH)_2$ with mixed acid at –20 °C gave 70% meta substitution, but with nitric acid in acetic anhydride 60% of the ortho isomer was formed. Harvey and Norman[4] reinvestigated these reactions and in agreement with the previous workers found predominant meta substitution in mixed acid (22% ortho, 73% meta, and 5% para) and predominant ortho substitution in HNO_3/acetic anhydride (63% ortho, 23% meta, and 14% para). Predominant meta substitution was attributed to the –K effect of $-B(OH)_2$, and predominant ortho substitution to an anionc complex formation with acetic anhydride, activating ortho:para positions due to the +I effect of boron anion.[4] Nitration in protic acids is



usually accompanied by some nitrodeboronation, and nitrobenzene is often detected in the product mixture. Analogous to $-B(OH)_2$, the presence of a $-BCl_2$ moiety is expected to direct the substitution to the meta position.

(1) (a) Aromatic Substitution. 57. For part 56, see: Olah, G. A.; Bach, T.; Prakash, G. K. S. *J. Am. Chem. Soc.*, submitted. (b) Visiting scientist from Société Nationale des Poudres et Explosifs LeBouchet, France.
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(4) Harvey, D. R.; Norman, R. O. C. *J. Chem. Soc.* **1962**, 3823.

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