reduced pressure. To the crude mixture was added sodium amalgam (8 g, 1.5% Na/Hg) with NaOD/D_2O (5 mL, 1 M), and the reaction was stirred for 3 h. The mixture was diluted with water, the mercury decanted off, and the product extracted into pentane. The combined pentane extracts were dried over $MgSO_4$ and filtered and the solvent removed under reduced pressure to yield an oil (142 mg, 73%) shown to be a mixture of 7-*syn*-(deuteriomethyl)-2-*exo*-methoxybicyclo[2.2.1]heptane (**11b**) (43%) and 4-*exo*-deuterio-2-*exo*-methoxybicyclo[3.2.1]octane (**12b**) (48%). Separation was effected by preparative GLC. 4-*exo*-Deuterio-2-*exo*-methoxybicyclo[3.2.1]octane (**12b**): ^{1}H NMR δ_H ($CDCl_3$) 3.30 (s, OMe), 3.18 ($W_{h/2}$ = 6 Hz, H2endo), 2.38 (s, $W_{h/2}$ = 9.6 Hz, H1), 2.14 (s, $W_{h/2}$ = 16.2 Hz, H5), 1.84 (d, $^2J_{8s,8a}$ = 10.9 Hz, H8s), 1.65 (m, H6exo, H7exo, H7endo), 1.55–1.42 (H3exo, H3endo, H6endo), 1.38 (d, $^3J_{4endo,3endo}$ = 9.1 Hz, H4endo), 1.16 (m, $^3J_{8a,5}$ = $^3J_{8a,1}$ = 5.7 Hz, H8a); ^{2}H NMR δ_D ($CHCl_3$) 1.62 (D4exo); ^{13}C NMR δ_C ($CDCl_3$) 80.4 (C2), 55.8 (OMe), 38.0 (C1), 34.2 (C5), 32.3 (C8), 28.5 (t, $J_{^{13}C,^2H}$ = 18.9 Hz, C4), 27.3 (C7), 26.8 (C6); MS, $C_9H_{15}OD$ requires $M^{+\bullet}$ 141.1264, found $M^{+\bullet}$ 141.1264.

7-*syn*-(Deuteriomethyl)-2-*exo*-methoxybicyclo[2.2.1]heptane (**11b**): ^{1}H NMR δ_H ($CDCl_3$) 3.28 (m, $^3J_{2endo,3endo}$ = 7.5 Hz, $^3J_{2endo,3exo}$ = 3.2 Hz, H2endo), 3.26 (s, OMe), 2.10 (br d, $^3J_{1,6exo}$ = 3.1 Hz, H1), 1.95 (t, $^3J_{4,5exo}$ = $^3J_{4,3exo}$ = 3.0 Hz, H4), 1.8–1.65 (H3exo, H3endo), 1.65 (t, $^3J_{7anti,CH_2D}$ = 6.6 Hz, H7anti); 1.55–1.45 (H5exo, H6exo), 1.09–1.05 (H5endo, H6endo, CH_2D); ^{2}H NMR δ_D ($CHCl_3$) 1.07 (CH_2D); ^{13}C NMR δ_C ($CDCl_3$) 85.7 (C2), 56.2 (OMe), 43.8 (L.B., C1), 43.6 (L.B., C7), 40.5 (L.B., C4), 37.1 (C3), 29.0 (C5), 26.6 (C6), 12.7 (t, $J_{^{13}C,^2H}$ = 19.1 Hz, CH_2D) (L.B. indicates the presence of a small ^{13}C–^{2}H coupling).

Reaction of 2 with Methanol-*d*/*p*-Toluenesulfonic Acid. Reaction of *exo*-tricyclo[3.2.1.0^{2,4}]octane (**2**) (150 mg) with methanol-*d* was carried out as previously described to give a pale yellow oil (174 mg, 91%), shown to consist of 7-*syn*-(deuteriomethyl)-2-*exo*-methoxybicyclo[2.2.1]heptane (**11b**) (15%) and 4-*exo*-deuterio-2-*exo*-methoxybicyclo[3.2.1]octane (**12b**) (76%). Separation was effected by preparative GLC. The spectral data for these compounds are identical with those obtained from the sodium amalgam reduction of the products from reaction of *exo*-tricyclo[3.2.1.0^{2,4}]octane (**2**) with mercuric acetate/methanol above. 4-*exo*-Deuterio-2-*exo*-methoxybicyclo[3.2.1]octane (**12b**): MS 3% D_0, 90% D_1, 7% D_2.

Acknowledgment. We acknowledge grants from the Research Committee of the New Zealand Universities Grants Committee.

Registry No. **1**, 22389-16-8; **2**, 13377-46-3; **3a**, 85698-98-2; 4-*endo*-**3b**, 113925-23-8; 4-*exo*-**3b**, 118760-52-4; **3c**, 118716-26-0; **4b**, 113947-64-1; **7**, 118716-27-1; 8, 2565-97-1; **9**, 118722-48-8; **10a**, 118760-53-5; **10b**, 118716-28-2; **11a**, 118716-29-3; **11b**, 118716-30-6; **12a**, 85698-97-1; **12b**, 118722-49-9; *endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene, 3635-94-7; bicyclo[3.2.1]octan-2-*exo*-ol, 1965-38-4; bicyclo-[3.2.1]octan-2-one, 5019-82-9; mercuric acetate, 1600-27-7; methanol-*d*, 1455-13-6.

Selective Carriers of Ammonium Ions. 1. Synthesis and Template Effect of CsCl and X-ray Structure and Ionophoric Properties of Polyether Crowns Containing 1-Methyl-3,5-bis(methylene)-1*H*-pyrazole Units

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Received July 15, 1988

A new series of asymmetric crown ethers of cyclic (**7**, **8**) and acyclic structure (**9**) containing 1-methyl-3,5-bis(methylene)-1*H*-pyrazole units have been synthesized. Crowns **7** and **8** having 18 and 36 ring atoms have been obtained in 24% and 25% yields respectively by 1:1 and 2:2 cyclization of 1-methyl-3,5-bis(chloromethyl)-1*H*-pyrazole and disodium tetraethylene glycolate under the template effect of CsCl. When the Cs^+ cation was not present in the above reaction, the crowns **7** and **8** were formed in lower yields. The X-ray structure of smaller crown **7** showed a flexible irregular cavity which presents an internal overall twist that changes the pseudo-2-fold axis of symmetry in the neighborhood of the pyrazole ring into a pseudo mirror plane for the rest of it. A ^{1}H and ^{13}C NMR study has shown that in the $Eu(fod)_3$–crown **7** complex, the pyrazolic sp^2 nitrogen and the oxygens belonging to the polyether cavity are cooperatively acting as donor sites, the Eu^{3+} being near the pyrazole side least hindered by the methyl group. The transport rates of alkali and ammonium ions are much higher for all polyether ligands **7**–**9** than for ester crowns **3** and **4** evaluated before. The larger crown, **8**, is a selective carrier of NH_4^+ in relation to K^+ and Na^+ ions. However, the smaller crown, **7**, and its acyclic analogue **9** (which shows a "plateau" selectivity toward NH_4^+ and alkali ions) are better carriers of K^+ ions.

Introduction

In view of the important role played by substituted ammonium ions in chemistry and biology, the development of receptor molecules capable of recognizing and transport of such substrates is of special interest.[1,2]

Macrocyclic polyethers bind primary ammonium ions by anchoring the NH_4^+ group into their circular cavity via three $^+$N–H···O hydrogen bonds[3–6] and are able to carry organic ammonium cations, in particular, physiologically active ones.[7] In general, however, these polyethers bind the alkali cations K^+ and Rb^+ appreciably stronger than R–NH_3^+ groups[8] whereas the opposite selectivity would

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(1) Lehn, J. M. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 89.

(2) Izatt, R. M.; Bradshaw, J. S.; Nielsen, S. A.; Lamb, J. D.; Christensen, J. J.; Sen, D. *Chem. Rev.* **1985**, *85*, 271.

(3) Stoddart, J. F. *Chem. Soc. Rev.* **1979**, *7*, 85; *Annu. Rep. Prog. Chem., Sect. B* **1983**, 353.

(4) Cram, D. J.; Cram, J. M. *Acc. Chem. Res.* **1978**, *11*, 8.

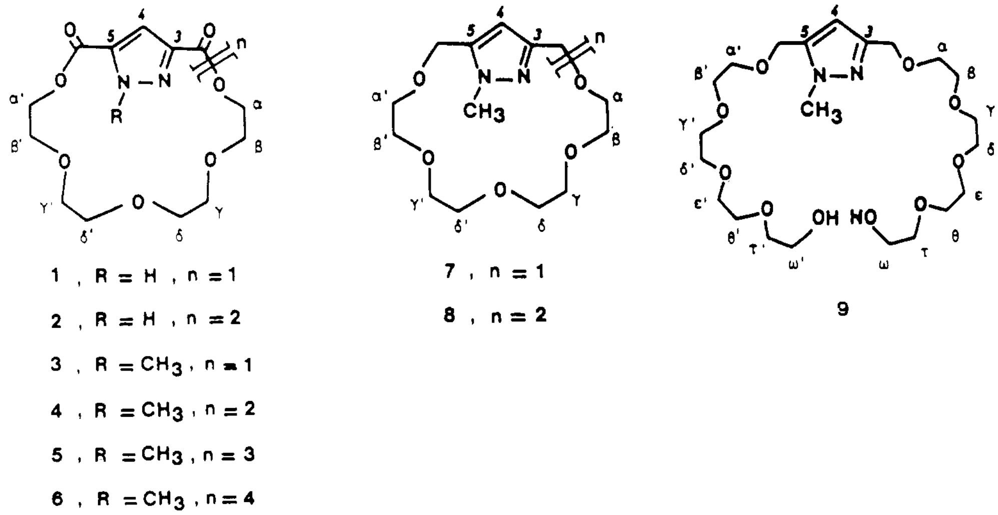
(5) Hayward, R. C. *Chem. Soc. Rev.* **1983**, *12*, 285.

(6) Sutherland, I. O. *Chem. Soc. Rev.* **1986**, *15*, 63.

(7) Bacon, E.; Jung, L.; Lehn, J. M. *J. Chem. Res., Synop.* **1980**, 136; *J. Chem. Res., Miniprint* **1980**, 1964.

(8) Izatt, R. M.; Terry, R. E.; Haymore, B. L.; Hansen, L. D.; Dalley, N. K.; Avondet, A. G.; Christensen, J. J. *J. Am. Chem. Soc.* **1976**, *98*, 7620.

0022-3263/89/1954-1391$01.50/0



1 , R = H , n = 1

2 , R = H , n = 2

3 , R = CH_3 , n = 1

4 , R = CH_3 , n = 2

5 , R = CH_3 , n = 3

6 , R = CH_3 , n = 4

7 , n = 1

8 , n = 2

9

Figure 1.

be desirable for the design of receptor molecules aimed at the complexation and transport of biogenic amines and drugs of great biological importance such as norephedrine or dopamine.[9]

The ammonium ion cannot be discriminated very effectively from K^+ by size. However, there is a marked difference in the charge distribution being spherical in the latter and tetrahedral in the former case. If the lock–key concept is applied, a trigonal symmetrical arrangement of NH binding sites is deduced as the main receptor characteristic for primary ammonium ions. Since $^+NH \cdots N$ hydrogen bonding is stronger than $^+NH \cdots O$, selective binding of $R{-}NH_3^+$ may be achieved making use of the oxaazamacrocycles.[6,10] Thus, simple diaza-crown ethers have shown high transport abilities for primary and secondary ammonium cations while they offered low transport rates for K^+ and other metal ions.[11] Also, the pyrido crown ethers and their analogues have received much attention as specific ligands for primary ammonium cations in relation to K^+ ion.[12-14] They have successfully been evaluated as carriers of NH_4^+ and applied to the highly selective transport of biogenetic amines and drugs.[15-17] These findings strongly suggested the introduction of sp^2 nitrogens belonging to azoles as donor atoms into the macrocyclic cavity of 18C6. It has recently been reported that polyether crowns containing a triazole subunit form complexes with benzylammonium cation, but not with potassium or lithium.[18] Consequently they behave as worse carriers of Na^+ and K^+ ions.[19] Since 1-alkyl-1*H*-pyrazole has one sp^2 nitrogen donor site, Tarrago and co-workers have studied the ionophoric properties of 18C6 coronands containing 1,3-disubstituted pyrazole units. The above authors reported that replacement of two oxygen atoms by two sp^2 pyrazolic nitrogens decreases the complexing ability of the 18-crown cavities toward most of the cations except $t\text{-}BuNH_3^+$.[20] However, other more rigid analogues containing four pyrazolic sp^2 nitrogen atoms were shown to be better carriers of Ca^{2+} and Na^+ than NH_4^+ ions.[21]

Recently, we have been interested in the synthesis and complexing behavior of 3,5-pyrazolo polyether crowns having different sizes, donor sites, symmetry, and steric hindrance. On this subject, we have previously reported the synthesis and complexing behavior of di- and tetraester crowns having 18 and 36 members, **1**–**4**, containing one or two pyrazole units 1-H or 1-methyl substituted.[22] Furthermore, two larger polyether hexa- and octaester crowns, **5** and **6**, having 57 and 76 members, respectively, were also obtained[23] (Figure 1). Since large ring systems such as DB30C6 form complexes with metal cations and primary alkylammonium salts,[9,24] macrocycles of both 18 and 36 members **1**–**4** have been evaluated as carriers of alkali and ammonium ions.[25,26] Using a transport system composed of a neutral aqueous salt solution, a chloroform membrane, and a receiving water phase, the larger crowns **2** and **4** were shown to be better carriers of alkali and ammonium ions than their smaller analogues **1** and **3**, respectively. The symmetry is responsible for the higher efficiency of both *N*-H-substituted carriers **1** and **2** in relation to their asymmetric analogues **3** and **4**, respectively. In fact, crown **2**, having 36 members, is an efficient and selective carrier of K^+ in relation to Na^+ and NH_4^+ ions. However, both crowns **3** and **4** are more selective for ammonium than alkali ions. According to their asymmetric behavior toward lanthanide shift reagents,[22,25] the above selectivity could be dependent on the steric hindrance induced by the *N*-Me substituent (next to the pyrazolic sp^2 nitrogen) around the complexation site.[8] Since molecular flexibility highly contributes to the efficiency of a carrier, we have now

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[9] Lindenbaum, S.; Rytting, J. H.; Sternson, L. A. In *Progress in Macrocyclic Chemistry*; Izatt, R. M., Christensen, J. J., Eds.; John Wiley & Sons: New York, 1979; Vol. 1, p 219.

[10] Lehn, J. M.; Vierling, P. *Tetrahedron Lett.* **1980**, *21*, 1323.

[11] Tsukube, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2685.

[12] Lamb, J. D.; Izatt, R. M.; Garrick, D. G.; Bradshaw, J. S.; Christensen, J. J. *J. Membr. Sci.* **1981**, *9*, 83.

[13] Newcomb, M.; Timbo, J. M.; Walba, D. M.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 6392.

[14] Bradshaw, J. S.; Maas, G. E.; Lamb, J. D.; Izatt, R. M.; Christensen, J. J. *J. Am. Chem. Soc.* **1980**, *102*, 467.

[15] Tsukube, H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3882.

[16] Tsukube, H. *Tetrahedron Lett.* **1982**, *23*, 2109.

[17] Maruyama, K.; Tsukube, H.; Araki, T. *J. Chem. Soc., Chem. Commun.* **1980**, 1222.

[18] Bradshaw, J. S.; Nielsen, R. A.; Tse, P.; Arena, G.; Wilson, B. E.; Dalley, N. K.; Lamb, J. D.; Christensen, J. J.; Izatt, R. M. *J. Heterocycl. Chem.* **1986**, *23*, 361.

[19] Alonso, J. M.; Martín, M. R.; de Mendoza, J.; Torres, T.; Elguero, J. *Heterocycles* **1987**, *26*, 989.

[20] Lupo, B.; Gal, M.; Tarrago, G. *Bull. Soc. Chim. Fr.* **1984** (2), 464.

[21] Lupo, B.; Tarrago, G. *Bull. Soc. Chim. Fr.* **1984** (2), 473.

[22] Elguero, J.; Navarro, P.; Rodríguez-Franco, M. I. *Chem. Lett.* **1984**, 425.

[23] Navarro, P.; Rodríguez-Franco, M. I.; Samat, A. *Synth. Commun.* **1987**, *17*, 105.

[24] Timko, J. M.; Moore, S. S.; Walba, D. M.; Hiberty, P. C.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 4207.

[25] Elguero, J.; Navarro, P.; Rodríguez-Franco, M. I.; Cano, J. H.; Foces-Foces, C.; Samat, A. *J. Chem. Res., Synop.* **1985**, 312; *J. Chem. Res., Miniprint* **1985**, 3401.

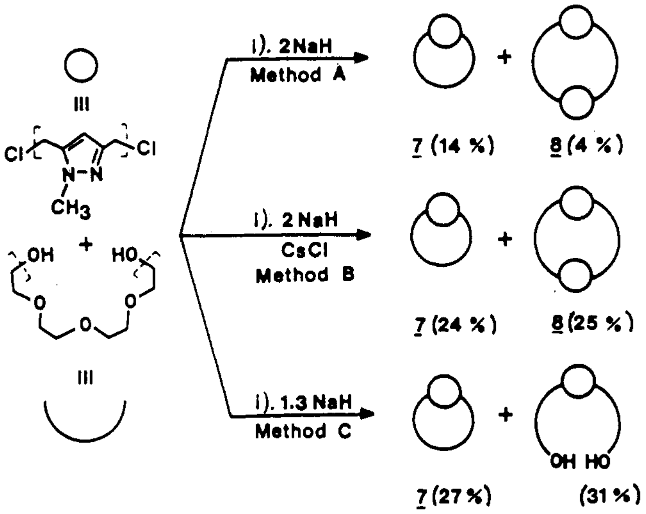
[26] Navarro, P.; Rodríguez-Franco, M. I. *J. Chem. Soc., Chem. Commun.* **1988**, 1365.

Table I. ^1H NMR Spectral Data (300 MHz, $CDCl_3$, δ) of Ligands 7–9 (Figure 1)

	pyrazole ring		polyether chain		
ligand	4-H	1-CH_3	H_2C–Pz(3)	H_2C–Pz(5)	$O(CH_2)_2O$
7	6.53 (s, 1 H)	3.78 (s, 3 H)	4.60 (s, 2 H)	4.55 (s, 2 H)	3.65 (m, 16 H)
8	6.24 (s, 2 H)	3.83 (s, 6 H)	4.52 (s, 4 H)	4.49 (s, 4 H)	3.63 (m, 32 H)
9[a]	6.23 (s, 1 H)	3.83 (s, 3 H)	4.52 (s, 2 H)	4.48 (s, 2 H)	3.60 (m, 32 H)

[a] At δ 3.03 (m, 2 HO), disappear by treatment with D_2O.

Scheme I[a]



[a] (i) High dilution, N_2, dimethoxyethane (DME), 2 h at 60 °C and 20 h at 25 °C.

Table II. ^{13}C NMR Spectral Data (75 MHz, $CDCl_3$, δ) of Ligands 7–9 (Figure 1)

	7	8	9
C(3)	149.3	148.1	147.9
C(4)	106.7	106.5	106.6
C(5)	140.1	139.6	139.5
C–N	36.2	36.5	36.5
C–Pz(3)	66.7	66.8	66.7
C–Pz(5)	63.1	63.3	63.2
C-α	69.2	69.5	69.3
C-α′	68.2	69.2	69.2
C-β,β′	70.7	70.6	70.2
C-γ,γ′	70.7	70.6	70.5
C-δ,δ′	70.6	70.6	70.5
C-ϵ,ϵ′θ,θ′	–	–	70.5
C-τ,τ′	–	–	72.7
C-ω,ω′	–	–	61.4

obtained a new series of *N*-methyl-substituted polyether crowns of non-ester structure in order to evaluate their ionophoric properties toward both spherical and tetrahedral cations. In this work we report the synthesis of crowns **7** and **8**, the template effect of CsCl on it, and the crystal structure by X-ray diffraction of smaller and more hindered compound **7**. In order to evaluate the macrocyclic effect of the above crowns in their ionophoric behavior, we have also synthesized podand **9** having two hydroxy terminal groups which are able to form a pseudocavity in complexing processes. Considering that the Eu^{3+} can be taken as a model of cations having spherical symmetry, a ^1H and ^{13}C NMR study on the complexing behavior of smaller crown **7** toward $Eu(fod)_3$ has been carried out. Furthermore, both cyclic (**7** and **8**) and acyclic (**9**) ligands have been evaluated as carriers of alkali and ammonium ions through a liquid membrane of chloroform, and these new data have been compared with the data previously reported for di- and tetraester analogues **3** and **4** of more rigid structure.

Synthesis and Template Effect of CsCl

The new ligands **7–9** have been synthesized from 1-methyl-3,5-bis(chloromethyl)-1*H*-pyrazole and tetraethylene glycol (TEG) as starting materials with dimethoxyethane (DME) as solvent and NaH as base in high-dilution conditions as is indicated in Scheme I.

1-Methyl-3,5-bis(chloromethyl)-1*H*-pyrazole was previously obtained from diethyl 1-methyl-1*H*-pyrazole-3,5-dicarboxylate by following a method recently described by us.[27] Since the problem encountered in the synthesis of macrocycles is the ring closure of alicyclic precursors, we have studied the cation catalysis ("template effect") of CsCl. We previously noted in the synthesis of ester crowns **3–6** that Cs^+ cation promoted 3:3 and 4:4 cyclizations from which crowns **5** and **6** were obtained in low yields (6% and 4%), respectively. However, no effect on the 1:1 and 2:2 cyclizations was observed in order to enhance the yields in which crowns **1** and **2** were obtained in the absence of CsCl.[23]

Now, in the synthesis of polyether crowns **7** and **8**, we have found the following results: When high-dilution conditions were used in the absence of CsCl (method A), reaction of 1-methyl-3,5-bis(chloromethyl)-1*H*-pyrazole with disodium tetraethylene glycolate afforded crowns **7** and **8** as the result of 1:1 and 2:2 cyclizations in 14% and 4% yields, respectively. However, when an equimolar amount of CsCl was added to the above reaction (method B), the Cs^+ cation favored the above 1:1 and 2:2 cyclizations, enhancing the yields of crowns **7** and **8** (24% and 25%, respectively). In order to obtain the acyclic ligand **9**, a third experiment was carried out, without CsCl, using high-dilution conditions (method C). Reaction of 1-methyl-3,5-bis(chloromethyl)-1*H*-pyrazole with a DME solution of NaH and TEG in molar ratio 1.3:1 afforded the dihydroxy derivative **9** in 31% yield together with the smaller crown **7** in 27% yield. Purification of the above ligands was effected by extraction in neutral solution, followed by flash chromatography on silica gel. The smaller crown **7** was isolated as a solid, which after crystallization from *n*-hexane melted at 56–57 °C. The other cyclic and acyclic ligands **8** and **9** were isolated as pure syrups (**8**, R_f 0.40; **9**, R_f 0.35 in chloroform/acetone, v/v 1:3). All pyrazolo crowns **7** and **8** as well as the podand **9** showed 300-MHz ^1H NMR and 75-MHz ^{13}C NMR spectra in agreement with their structures (Tables I and II, respectively).

In these spectra, the CH_2 groups adjacent to the pyrazolic ring can be distinguished from the other $O–CH_2$ groups. Furthermore, in each compound the CH_2 protons closest to the C-3 pyrazolic aromatic ring are slightly deshielded in relation to the CH_2 ones next to the C-5 pyrazolic carbon. The ^1H NMR of acyclic ligand **9** also shows a broad signal corresponding to its two hydroxy groups which disappears by treatment with D_2O.

In the mass spectra of the pyrazolo crown ethers **7** and **8**, which were registered by electronic impact (EI) and

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[27] Iturrino, L.; Navarro, P.; Rodríguez-Franco, M. I.; Contreras, M.; Escario, J. A.; Martínez, A.; Pardo, M. R. *Eur. J. Med. Chem.* 1987, *22*, 445.

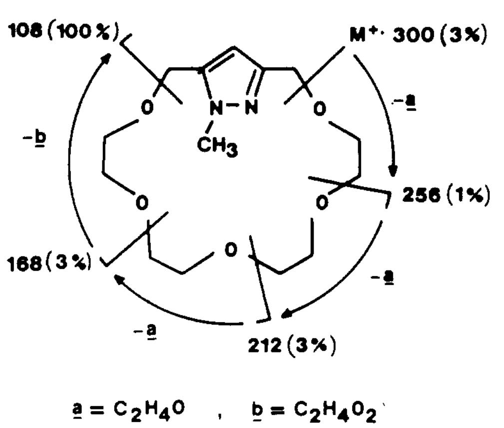

Figure 2. Fragmentation pattern observed in the MS of crown 7 registered by electronic impact (EI).

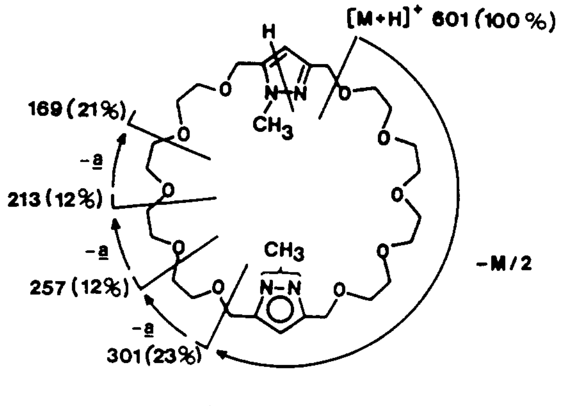

Figure 3. Fragmentation pattern observed in the MS of crown 8 registered by chemical ionization with methane (CI-CH_4).

chemical ionization with methane (CI-CH_4), respectively, the molecular ion peak was observed. All mass spectra show a pattern in which C_2H_4O fragments are lost successively as indicated in Figures 2 and 3.

The base peak in 7 is at *m/z* 108. However, in 8 both the molecular ion MH^+ and the base peak are under the same signal at *m/z* 601. All the above ligands 7–9 gave satisfactory elemental analyses (C, H, N).

Crystalline Structure of Crown 7

In a previous paper, we reported the crystalline structure of smaller and more hindered diester crown 3. The pyrazolic nitrogens are turned outside its ellipsoidal cavity (area = 11.844 Å^2, which is only adequate to interact with Li^+ and Na^+ ions).[25] The uncomplexed cavity of diester crown 3, considering just the cycle formed by C(18), O(15), O(12), O(9), O(6), and O(3), adopts the nonplanar form of a distorted boat flattened at C(18), also distorted toward an envelope at O(9) (see Figure 4a).

Now, we have determined the crystalline structure of more flexible polyether analogue 7 and compared it with the one of 3. The most important aspect of the structure depicted in Figure 4b is immediately apparent: the ranges of the bond lengths in the macrocycle, 1.482 (4)–1.496 (4) Å for the C–C bonds and 1.408 (4)–1.433 (3) Å for the C–O, are within normal values.[25,28] In relation to the structure of 3, there is an increase in the angular values at C(21)–N(19)–C(1), N(19)–C(1)–C(2), C(2)–C(1)–C(18), and C(18)–C(17)–C(16) (see Table III).

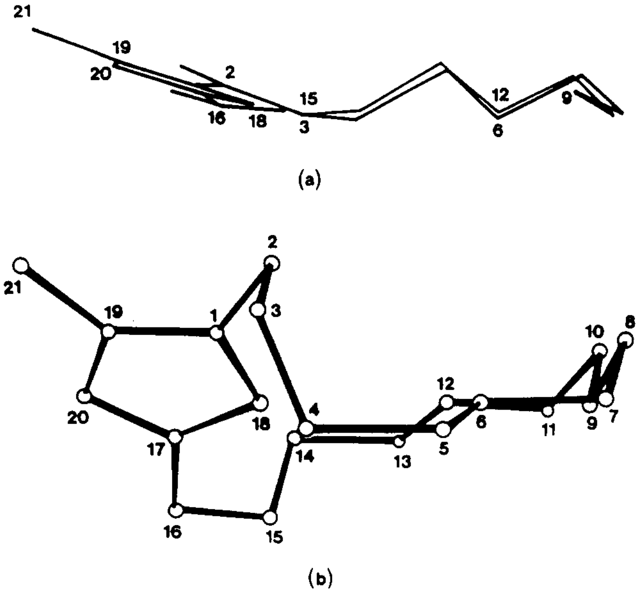

Figure 4. An ORTEP[40] view of the overall conformations of crowns 3 (a) and 7 (b), showing atom numbering.

Table III. Geometry of Crown 7

	Bond Distances, Å		
N(20)–N(19)	1.362 (3)	C(13)–O(12)	1.419 (4)
N(19)–C(1)	1.352 (3)	O(12)–C(11)	1.408 (4)
N(19)–C(21)	1.446 (3)	C(11)–C(10)	1.495 (5)
C(1)–C(18)	1.374 (3)	C(10)–O(9)	1.413 (3)
C(18)–C(17)	1.402 (3)	O(9)–C(8)	1.418 (3)
C(1)–C(2)	1.495 (3)	C(7)–O(6)	1.423 (4)
C(17)–C(16)	1.504 (3)	O(6)–C(5)	1.409 (3)
C(8)–C(7)	1.482 (4)	C(5)–C(4)	1.496 (4)
C(16)–O(15)	1.411 (3)	C(4)–O(3)	1.428 (3)
O(15)–C(14)	1.420 (5)	O(3)–C(2)	1.433 (3)
C(14)–C(13)	1.488 (5)	N(20)–C(17)	1.330 (3)
	Bond Angles, deg		
N(19)–N(20)–C(17)	104.6 (2)	C(16)–O(15)–C(4)	113.4 (2)
N(20)–N(19)–C(21)	119.4 (2)	O(15)–C(14)–C(13)	108.9 (3)
N(20)–N(18)–C(1)	111.8 (2)	C(14)–C(13)–O(12)	108.8 (2)
C(1)–N(19)–C(21)	128.7 (2)	C(13)–O(12)–C(11)	112.8 (2)
N(19)–C(1)–C(2)	122.6 (2)	O(12)–C(11)–C(10)	108.8 (2)
N(19)–C(1)–C(18)	107.0 (2)	C(11)–C(10)–O(9)	110.3 (2)
C(18)–C(1)–C(2)	130.4 (2)	C(10)–O(9)–C(8)	112.7 (2)
C(1)–C(18)–C(17)	104.9 (2)	O(9)–C(8)–C(7)	110.4 (3)
N(20)–C(17)–C(18)	111.7 (2)	C(8)–C(7)–C(6)	108.4 (2)
C(18)–C(17)–C(16)	128.1 (2)	C(7)–O(6)–C(5)	113.8 (2)
N(20)–C(17)–C(16)	120.1 (2)	O(6)–C(5)–C(4)	109.5 (2)
C(17)–C(16)–C(15)	111.6 (2)	C(5)–C(4)–O(3)	114.3 (2)
C(4)–O(3)–C(2)	115.2 (2)	C(1)–C(2)–O(3)	113.2 (2)

The overall conformation of the macrocycle presents a twist of almost 90° with respect to the previously reported analogue with ester groups, in the moiety involving the pyrazole group. So, there are present variations from the anti/gauche sequence of the torsion angles in the macrocycle.

This variation may be described by comparing the sequences of the torsion angles in 7 and in its ester analogue 3, both structures being centric. We define interval values as s, [0° ± 30°]; $g^\pm$, [±60° ± 30°]; $e^\pm$, [±120° ± 30°]; a, [180° ± 30°]. If we start at the C(1)–C(18) torsion, then at C(1)–C(2), and so on, we have

$$a, s, a, e^-, g^-, a, a, g^+, a^+; a^-, g^-, a, a, g^+, e^+, a, s, a$$

for 3, and we have

$$a, e^+, g^-, g^-, g^+, a, a, g^+, a; a, g^-, a, a, g^+, a, g^+, s, a$$

for 7, where the ";" sign separates the pseudosymmetric parts. It can be seen that it is near the pyrazole group that

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(28) Browne, C. M.; Ferguson, G.; McKerbey, M. A.; Mulholland, D. L.; O'Connor, T.; Parvez, M. *J. Am. Chem. Soc.* 1985, *107*, 2703–2712.

Table IV. Conformational Characteristics of Crown 7

Torsion Angles, deg					
C(1)–C(18)–C(17)–C(16)	−177.6 (2)	C(13)–O(12)–C(11)–C(10)	173.7 (2)	O(3)–C(2)–C(1)–C(18)	−102.1 (3)
C(18)–C(17)–C(16)–O(15)	−19.3 (3)	C(7)–O(6)–C(5)–C(4)	178.2 (2)	C(4)–O(3)–C(2)–C(1)	61.4 (2)
C(17)–C(16)–O(15)–C(14)	−77.5 (3)	C(8)–C(7)–O(6)–C(5)	−163.4 (2)	C(5)–C(4)–O(3)–C(2)	75.8 (3)
C(16)–O(15)–C(14)–C(13)	161.1 (2)	O(12)–C(11)–C(10)–O(9)	68.0 (3)	O(6)–C(5)–C(4)–O(3)	−72.2 (3)
O(15)–C(14)–C(13)–O(12)	−76.6 (3)	C(11)–C(10)–O(9)–C(8)	−168.6 (2)	O(9)–C(8)–C(7)–O(6)	−68.3 (3)
C(14)–C(13)–O(12)–C(11)	174.7 (2)	C(2)–C(1)–C(18)–C(17)	179.0 (2)	C(10)–O(9)–C(8)–C(7)	174.5 (2)
Pseudotorsion Angles, deg					
C(18), O(15), O(12), O(9)	52.3 (1)	O(9), O(6), O(3), C(18)	36.0 (1)		
O(15), O(12), O(9), O(6)	−40.5 (1)	O(12), O(9), O(6), O(3)	−31.5 (2)		
O(6), O(3), C(18), O(15)	65.5 (3)	O(3), C(18), O(15), O(12)	−108.0 (3)		

Table V. Selected Intramolecular Distance[a] into the Hole of Crown 7

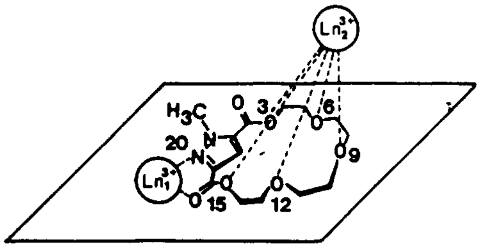
N(20)···O(15)	3.628 (2)	C(18)···O(9)	4.235 (2)
O(15)···O(12)	2.925 (3)	C(18)···O(15)	2.926 (2)
O(12)···O(9)	2.857 (3)	C(18)···O(3)	3.479 (2)
O(9)···O(6)	2.854 (2)	O(9)···O(15)	5.013 (3)
O(6)···O(3)	2.987 (2)	O(9)···C(2)	4.858 (2)
O(3)···N(20)	4.353 (2)	O(6)···O(12)	4.685 (2)

[a] In angstroms.

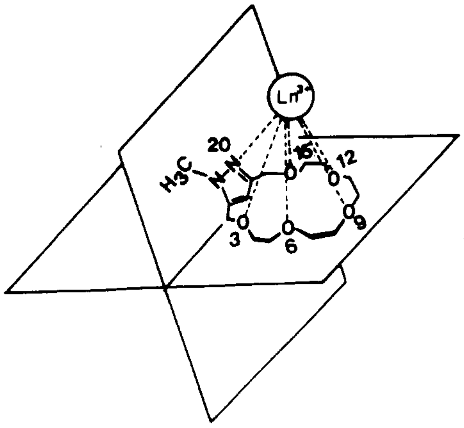
the pseudo mirror plane disappears (see Table IV and Figure 4b). This situation leaves for the oxygen atoms plus the apex C(18) atom a six-membered set, a form quite distorted from that of the flattened boat[25] and nearer to that of a distorted skew, with O(9), O(6), O(12), and C(18) near a plane and then O(3) up and O(15) below it. These last two atoms are at +1.311 (3) and −0.342 (2) Å from the pyrazole ring, which is forming an angle of 40.0° with the above-mentioned plane. The irregular hole formed inside the macrocycle can then be characterized by the distances shown in Table V. The perimeter of the above hole in 7 (25.918 Å) is slightly larger than in crown 3 (25.550 Å). Taking into account that flexibility in 7 is much higher than in 3, it can be thought that in a cation complexation process the pyrazolic nitrogens can be favorably oriented in order to exert a cooperative effect with the oxygens belonging to the polyether chain as active donor sites.

^1H and ^{13}C NMR Behavior of Ligand 7 in the Presence of $Eu(fod)_3$

It is known that trivalent lanthanide cations form stable complexes with crown ethers having an adequate ring size (five or six oxygen atoms).[29] On the other hand, both ester groups[30] and pyrazole[31] strongly interact with lanthanide shift reagents (LSR). We have previously reported the ^1H and ^{13}C NMR behavior of crowns 1–4 with LSR.[22,25,26] From the above studies, it was established that in the complex formed by $Eu(fod)_3$ and crown 3 there are two separate ligating positions: a first one where the lanthanide cation is bound to the sp^2 nitrogen N(20) and the neighbor carbonylic oxygen O═C(16), and a second complexation site in rapid equilibrium with the first one where the lanthanide is preferentially interacting with the O(9) and in a lesser amount with the O(6) and O(12) oxygens belonging to the polyethylene chain. The carbonylic oxygen O═C(2), which is more hindered and does not have the cooperative effect of the "pyridynic" nitrogen atom N(20), seems to play a minor role in the complexation of crown 3 (Figure 5a). According the above results, it was claimed that the intramolecular crown cavity of 3 may be responsible for its transport properties without the cooperative effect of the sp^2 nitrogen belonging to the pyrazolic ring.[25]



(a)



(b)

Figure 5. Schematic interaction of trivalent lanthanide cations with crowns 3 (a) and 7 (b) suggested by the LIS produced in their ^1H and ^{13}C NMR spectra.

In order to ascertain better information on potential sites of metal-ion complexation of crown 7 of enhanced flexibility in relation to 3, the lanthanide-induced shifts (LIS) produced in the ^1H and ^{13}C NMR spectra of 7 have also been studied by using $CDCl_3$ as a solvent. The ^1H and ^{13}C chemical shifts of the free ligand 7 were measured (Tables I and II) and the shifts induced by $Eu(fod)_3$ determined by using concentrations $[Eu(fod)_3/ligand]$ between 0.03 and 0.20 as indicated in the Experimental Section. These data were extrapolated for a limiting concentration of $[Ln(fod)_3/ligand] = 1$. Positive and negative signs are used for downfield and upfield induced shifts, respectively. The results are shown in Table VI and compared with those previously reported for crown 3.[25] In 7, the upfield shifts for pyrazole carbons C(18) and C(1), the other carbons being shifted downfield, are in agreement with the "wrong-way" shifts found for carbons in position β relative to the complexation sites due to contact terms.[32]

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(29) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*; Wiley: New York, 1980; p 981.

(30) Hinckley, C. C.; Boyd, W. A.; Smith, G. V.; Behbahany, F. *Nuclear Magnetic Resonance Shift Reagents*; Sievers, R. E., Ed.; Academic Press: New York, 1973.

(31) Claramunt, R. M.; Elguero, J.; Jacquier, R. *Org. Magn. Reson.* **1971**, *3*, 595.

(32) Elguero, J.; Marzin, C.; Roberts, J. D. *J. Org. Chem.* **1974**, *39*, 357.

Table VI. Comparative ^1H and ^{13}C LIS of Crowns 3 and 7 (Figure 4)

	^1H LIS[a]		^{13}C LIS[a]	
	3[b] (X = O)	7 (X = H_2)	3[b] (X = O)	7 (X = H_2)
(17)C=N(20)	-	-	27.00	16.85
(16)C=X(15)	-	7.22	36.60	21.06
(14)H_2C-O(15)	4.21	7.41	4.80	18.38
(13)H_2C-O(12)	2.74	6.81	4.50	18.35
(11)H_2C-O(12)	4.79	6.81	9.30	16.30
(10)H_2C-O(9)	5.05	5.68	10.00	15.28
(8)H_2C-O(9)	5.05	5.68	10.00	14.67
(7)H_2C-O(6)	4.79	4.10	9.30	12.02
(5)H_2C-O(6)	1.96	2.42	3.80	7.38
(4)H_2C-O(3)	1.57	2.42	4.30	5.69
(2)C=X(3)	-	1.81	1.30	1.28
(1)C-N(19)	-	-	2.77	-1.62
18)C=C(1)	7.26	3.73	1.44	-2.76
(21)Me-N(19)	3.37	1.01	4.21	1.79

[a] In parts per million. [b] These data have been taken from ref 25.

In the complex of 7 with Eu(fod)$_3$, the higher LIS observed in both ^1H and ^{13}C NMR spectra correspond to the methylene groups $H_2C(16)$, $H_2C(14)$, $H_2C(13)$, and $H_2C(11)$. However, the lower ones correspond to the methylenes $H_2C(2)$, $H_2C(4)$, and $H_2C(5)$. In ^{13}C NMR, the deshielding difference between both pyrazole carbons C(17) and C(1) is 18.47 ppm, and the one corresponding to the bridge methylenes $H_2C(16)$ and $H_2C(2)$ is 19.72 ppm. Furthermore, from the values of the methylene effects given in Table VI, it is possible to differentiate all the methylene carbons belonging to the polyethylene chain. Starting at $H_2C(14)$, then at $H_2C(13)$, and so on, we have that in both ^1H and ^{13}C spectra the LIS are decreasing as follows: $H_2C(14) > H_2C(13) > H_2C(11) > H_2C(10) > H_2C(8) > H_2C(7) > H_2C(5) > H_2C(4)$.

This situation is in agreement with a complex in which a single lanthanide cation is preferentially binding with the pyrazolic sp^2 nitrogen together with the ether oxygens O(15) and O(12) and in a lesser extension with the more distant oxygens O(9), O(6), and O(3) as it is suggested in Figure 5b. The above behavior is very different from that observed for the diester crown (3) where both carbonyl groups are hindering the cooperative interaction of the sp^2 nitrogen and the oxygens of ether type with the lanthanide cation.

Transport Properties of Cyclic and Acyclic Ligands 7–9

We have measured the transport rates of alkali and ammonium picrates through a chloroform liquid membrane which contains one of the carriers and which separates two aqueous phases. The guest cation salts are complexed with the carrier from the first aqueous phase and transported to the second one by using a classical experimental apparatus previously reported (see Experimental Section). The transport process occurs by carrier-mediated facilitated diffusion along the concentration gradient of the guest salts. The results are gathered in Table VII and compared with those previously described for their ester analogues 3 and 4. Both polyether crowns 7 and 8 as well as the acyclic ligand 9 are much better carriers of alkali and ammonium ions than 3 and 4. Crown 8 of 36 members is a more efficient carrier than the smaller analogue 7 of 18 members. In Figure 6, the Na$^+$, K$^+$, and NH$_4^+$ transport rates of crowns 3, 4, and 7–9 are graphically compared. In fact, crown 8 is a selective carrier of NH$_4^+$ in relation to Na$^+$ (NH$_4^+$/Na$^+$ = 7.7) and K$^+$ (NH$_4^+$/K$^+$ = 2.2) ions. However, both crown 7 and podand 9 are more selective for K$^+$ in relation to NH$_4^+$ (7, K$^+$/NH$_4^+$ = 1.2; 9, K$^+$/NH$_4^+$ = 1.2) and Na$^+$ ions (7, K$^+$/Na$^+$ = 4.1; 9, K$^+$/Na$^+$ = 1.3), in a similar way as occurs with DB18C6 (K$^+$/NH$_4^+$ = 1.5 and K$^+$/Na$^+$ = 8.8).

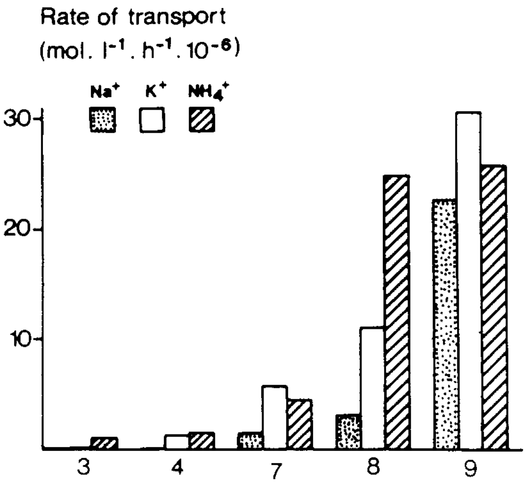

Figure 6. Graphical comparison of the Na$^+$, K$^+$, and NH$_4^+$ transport rates of 3,5-pyrazolo ester and polyether crowns of 18 members (3 and 7) and 36 members (4 and 8) having different flexibility in relation to the acyclic diol 10.

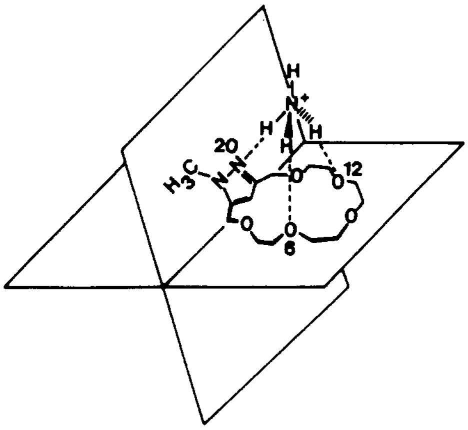

Figure 7. Schematic interaction of NH$_4^+$ ions with crown 7 suggested by the CPK model.

Taking into account the above results concerning the crystalline structure of crown 7 and its complexing behavior with lanthanide cations, the CPK model of 7 proves

Table VII. Transport Rates (×10^{-6} mol h^{-1}) of Alkali and Ammonium Ions across a CHCl$_3$ Phase Containing 7 × 10^{-4} M of Ligand

compd	Li$^+$	Na$^+$	K$^+$	Rb$^+$	Cs$^+$	NH$_4^+$
3[b]	0.55	0.03	0.01	a	a	1.07
4[b]	0.03	0.06	1.37	0.66	0.05	1.52
7	4.90	1.37	5.65	2.33	0.89	4.79
8	7.37	3.20	11.00	6.16	4.75	24.80
9	17.86	22.58	30.65	21.06	6.74	25.84

[a] Measured transport rate equivalent to that of a blank experiment with no ligand in the organic phase (rate lower than 0.01 × 10^{-6} mol h^{-1}). [b] Experimental data taken from ref 25 and 26.

that this flexible $\langle 18NO_5 \rangle$ crown could interact with NH_4^+ ions, forming a complex in which the pyrazolic sp^2 nitrogen and two alternate oxygens can be acting as donor sites forming hydrogen bonding with the guest ammonium hydrogen atoms in a trigonal arrangement, as is indicated in Figure 7. Since the multiple binding sites of the large rings might permit them to act as host for two guest ammonium cations,[33] it is possible that the higher ammonium transport rate of crown 8 in relation to 7 could be due to the formation of a 2:1 complex in which the two pyrazolic sp^2 nitrogens and four oxygens belonging to the polyether cavity of 8 were simultaneously binding with two ammonium ions.

Furthermore, according to our initial hypothesis, the high recognition of crown 8 toward NH_4^+ in relation to alkali ions can be due both to its molecular flexibility and to the presence of the *N*-methyl groups which can be acting as steric barriers in the complexation of alkali ions.

Acyclic ligand 9, which has shown the higher transport rates for both alkali and ammonium ions, is not able to discriminate tetrahedral or spherical ions due to its acyclic structure.

Conclusions

The cation catalysis of CsCl favors the synthesis of polyether crowns of 18 and 36 members containing 1-methyl-3,5-bis(methylene)-1*H*-pyrazole units.

The crystalline structure of a smaller and more hindered crown 7 corresponds to a flexible macrocycle which presents an overall twist that changes the pseudo-2-fold axis in the neighborhood of the pyrazole ring into a pseudo mirror plane for the rest of it. The above crown 7 forms an asymmetric complex with $Eu(fod)_3$ in which the sp^2 nitrogen atom belonging to the pyrazole ring is cooperatively acting as donor site with the oxygens of its macrocyclic cavity, the lanthanide cation being nearer the pyrazole side least hindered by the methyl group.

The polyether crowns 7 and 8 are, in general, more effective carriers than their di- and tetraester analogues 3 and 4 of more rigid structure.

The dimeric $\langle 36N_2O_{10} \rangle$ crown 8 is a more efficient and selective carrier of ammonium than of alkali ions, which results in an interesting selectivity, $NH_4^+/Na^+ = 7.7$ and $NH_4^+/K^+ = 2.2$. However, both monomeric $\langle 18NO_5 \rangle$ crown 7 and acyclic diol 9 are more selective carriers of potassium than ammonium (7 and 9 $K^+/NH_4^+ = 1.2$) and sodium (7, $K^+/Na^+ = 4.1$; 9, $K^+/Na^+ = 1.3$) ions. The above-mentioned diol, 9, according to its acyclic structure, is showing a "plateau" selectivity toward alkali and ammonium ions.

The interesting selectivity shown by the larger $\langle 36N_2O_{10} \rangle$ crown 8 toward NH_4^+ could be mainly attributed to the cooperative participation of two pyrazolic sp^2 nitrogens and four alternate oxygens belonging to the polyether chains which can simultaneously bind two ammonium cations. Besides, the large flexible cavity of 8 contains two *N*-methyl groups (next to both pyrazole sp^2 nitrogens) which could be spatially hindering the cooperative interaction of the nearer oxygens of ether type with alkali cations. Consequently the *N*-methyl groups are seen to act as steric barriers for cations of spherical symmetry.

Work is now in progress in order to evaluate both crowns 7 and 8 as carriers of alkylammonium ions as well as to obtain and determine the structure of 1:1 and 2:1 ammonium complexes of crowns 7 and 8, respectively.

Experimental Section

Melting points were determined with a Köfler apparatus and are uncorrected. Elemental analyses were carried out by the Organic Chemistry Department of Centro Nacional de Química Orgânica (CSIC), Madrid, Spain. The IR spectra were recorded with a Perkin-Elmer 257 spectrometer and the ^1H NMR and ^{13}C NMR ones with a Varian XL-300 spectrometer using Me_4Si as an internal standard. The mass spectra (MS) were recorded by electronic impact (EI) at 70 eV in a VG-12-250 spectrometer or by chemical ionization with methane (CI, CH_4) in a Hewlett-Packard 5985/GD.

Analytical TLC was performed on aluminum sheets coated with a 0.2-mm layer of silica gel 60 F_{254} (Merck). Chromatographic separations were performed either on columns, using the flash chromatography technique[34] on silica gel (Merck), 200–400 mesh, or by preparative layer chromatography on 20 × 20 cm glass plates coated with a 2-mm layer of silica gel PF_{254} (Merck). Compounds were detected with UV light (254 nm) and/or iodine chamber.

Materials. Dimethoxyethane (DME) was freshly distilled from $LiAlH_4$ prior to its use. 1-Methyl-3,5-bis(chloromethyl)-1*H*-pyrazole (mp 35–36 °C) was obtained in several reaction steps from diethyl 1*H*-pyrazole-3,5-dicarboxylate (mp 54–55 °C) by following a procedure previously reported by us.[27] NaH (80% oil) and tetraethylene glycolate (TEG) were reagent grade and used without further purification.

General Procedure for the Synthesis of Pyrazole Ligands 7–9. Method A. To a refluxing stirred mixture of NaH (22 mmol, oil free) and dry DME (40 mL) under nitrogen was added a solution of TEG (11 mmol) in DME (40 mL), and the mixture was kept at 60 °C until the disodium tetraethylene glycolate was formed (0.5 h). Then, the mixture was diluted with DME (350 mL) with the stirrer operating at 2000 rpm. After the temperature was again stabilized at 60 °C, a solution of 1-methyl-3,5-bis(chloromethyl)-1*H*-pyrazole (10 mmol) in dry DME (350 mL) was added over a period of 3–4 h. After the addition was complete, the reaction mixture was kept for 2 h at 60 °C, then cooled to room temperature, and stirred for 24 h. The resulting reaction mixture was treated with a 15% aqueous solution of ammonium chloride until pH = 7. After the aqueous layer was decanted and extracted with $CHCl_3$ (3 × 100 mL), the chloroformic extracts were mixed with the DME layer previously separated and the organic solvents evaporated to dryness in vacuo to give a syrup. Its analytical (TLC) control showed a mixture, which was purified by flash chromatography on a silica gel column, using first chloroform as eluent and, after mixtures of chloroform, acetone of increasing polarity.

Method B. Following the procedure mentioned above, an equimolar amount of CsCl (11 mmol) was added after the disodium tetraethylene glycolate was formed.

Method C. Following the procedure indicated in method A, a smaller amount of NaH (14.06 mmol) was added in order to prepare the monosodium tetraethylene glycolate instead of the disodium tetraethylene glycolate.

19-Methyl-3,6,9,12,15-pentaoxa-19,20-diazabicyclo[15.2.1]icosa-1(20),17-diene (7). Following either method A, B, or C, after flash chromatography was developed, the fractions of R_f = 0.60 (chloroform/acetone, v/v 1:3) were evaporated to dryness in vacuo, and the residual syrup was crystallized from *n*-hexane to afford crown 7 as a crystalline solid: mp 56–57 °C; yields 14% (method A), 24% (method B), 27% (method C); IR (KBr) 1160, 1140, 1110, 1090 (COC) cm^{-1}; MS (EI), *m/z* 301 (MH^+, 1), 300 (M^+, 3), 257 (3), 256 (1), 213 (10), 212 (3), 169 (3), 168 (3), 139 (30), 137 (14), 125 (17), 124 (30), 123 (62), 122 (16), 121 (18), 109 (53), 108 (100). Anal. Calcd for $C_{14}H_{24}N_2O_5$: C, 55.98; H, 8.05; N, 9.33. Found: C, 56.20; H, 8.30; N, 9.27.

37(38),39(40)-Dimethyl-3,6,9,12,15,21,24,27,30,33-decaoxa-37,38,39,40-tetraazatricyclo[33.2.1.$2^{17,19}$]tetraconta-1(38),19-(40),17,35-tetraene (8). Following either method A or method B, crown 8 was isolated as a pure syrup from the fractions of R_f = 0.40 (chloroform/acetone, v/v 1:3): yields 4% (method A) and 25% (method B); IR (neat) 1170–1070 (br, COC) cm^{-1}; MS ($CI\text{-}CH_4$), *m/z* 602 ($MH^+ + 1$, 32), 601 (MH^+, 100), 599 ($M^+ - 1$, 20), 557 (8), 405 (31), 315 (31), 301 (23), 257 (12), 213 (12), 195

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(33) Johnson, M. R.; Jones, N. F.; Sutherland, I. O. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1637.

(34) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

Table VIII. Final Atomic Coordinates and Thermal Parameters (×10^4) as in $U_{eq} = {}^1/_3\sum[U_{ij}d_i{}^*a_j{}^*a_ia_j \cos(a_i,a_j)]$

atom	X/A	Y/B	Z/C	U_{eq}
C(1)	−0.060 17 (23)	0.077 85 (9)	0.023 56 (23)	355 (6)
C(2)	−0.064 09 (27)	0.085 53 (10)	−0.152 23 (25)	427 (8)
O(3)	−0.178 22 (19)	0.129 93 (8)	−0.242 11 (18)	520 (6)
C(4)	−0.156 46 (31)	0.192 50 (12)	−0.179 12 (32)	537 (9)
C(5)	−0.029 31 (34)	0.227 75 (12)	−0.217 73 (34)	582 (10)
O(6)	0.116 03 (21)	0.203 87 (8)	−0.121 50 (22)	596 (7)
C(7)	0.244 90 (36)	0.233 27 (14)	−0.153 02 (38)	631 (11)
C(8)	0.383 54 (37)	0.192 93 (14)	−0.084 91 (34)	629 (11)
O(9)	0.429 08 (22)	0.192 23 (9)	0.090 34 (22)	616 (7)
C(10)	0.552 05 (31)	0.149 90 (14)	0.161 30 (37)	617 (11)
C(11)	0.573 61 (29)	0.141 35 (15)	0.341 44 (37)	620 (10)
O(12)	0.443 58 (19)	0.109 48 (10)	0.358 84 (20)	617 (7)
C(13)	0.461 06 (34)	0.093 30 (18)	0.525 46 (34)	700 (11)
C(14)	0.312 98 (31)	0.065 41 (14)	0.533 24 (33)	607 (10)
O(15)	0.203 58 (20)	0.114 28 (8)	0.521 68 (18)	517 (6)
C(16)	0.048 40 (29)	0.093 01 (12)	0.475 60 (27)	485 (8)
C(17)	−0.014 27 (24)	0.079 63 (9)	0.293 15 (24)	377 (7)
C(18)	0.041 43 (24)	0.101 55 (9)	0.167 06 (24)	370 (7)
N(19)	−0.167 90 (19)	0.044 17 (8)	0.066 78 (20)	387 (6)
N(20)	−0.140 99 (21)	0.044 58 (9)	0.233 39 (21)	428 (6)
C(21)	−0.298 43 (30)	0.009 17 (15)	−0.038 25 (36)	572 (9)

(99), 179 (25), 177 (22), 169 (21), 167 (28), 165 (20), 153 (34), 151 (51). Anal. Calcd for $C_{28}H_{48}N_4O_{10}\cdot0.5H_2O$: C, 55.16; H, 8.10; N, 9.19. Found: C, 55.39; H, 8.33; N, 9.24.

1-Methyl-3,5-bis(13′-hydroxy-2′,5′,8′,11′-tetraoxatridec-1′-yl)-1*H*-pyrazole (9). Following method C, after the reaction mixture was chromatographed and the fractions of $R_f = 0.35$ (chloroform/acetone, v/v 1:3) were collected and evaporated to dryness in vacuo, the acyclic ligand **9** was isolated as a pure syrup: yield 31%; IR (neat) 3650–3050 (OH), 1180–1160 (COC) cm^{-1}; EM (CI-CH$_4$), *m/z* 496 (MH$^+$ + 1, 8), 495 (MH$^+$, 29), 195 (100). Anal. Calcd for $C_{22}H_{42}N_2O_{10}\cdot1.5H_2O$: C, 50.67; H, 8.63; N, 5.37. Found: C, 50.31; H, 8.22; N, 5.53.

X-ray Diffraction of 7. Crystal data: $C_{14}H_{24}N_2O_5$; monoclinic, $P2_1/c$; $M_r = 300.35$, $a = 9.0593$ (1) Å, $b = 21.3184$ (7) Å, $c = 8.5125$ (1) Å, $\beta = 108.306$ (1)°, $V = 1560.82$ (6) Å^3; $D_{calcd} = 1.278$ g cm^{-3}, $Z = 4$.

Data collection: transparent, colorless, prismatic sample of 0.50 × 0.25 × 0.10 mm dimensions. The spectrum was collected on a Philips PW 1100 diffractometer, with Cu Kα radiation, graphite monochromated, with $w/2\theta$ scans and 1.5° in width. No instabilities were observed during collection. Cell parameters were obtained from a least-squares fit of the 2θ angles of 82 reflections with θ up to 45°. Among the 2644 measured independent data, 2041 were considered observed within a $3\sigma(I)$ criterion.

Solution and Refinement. Direct methods were used for the solution,[35] and refinement was done by one block full matrix least-squares methods.[36] All hydrogen atoms were located by difference synthesis, and then a weighting scheme to flatten the dependences of $\langle w\Delta^2F\rangle$ was introduced. Final R and R_w factors were 0.042 and 0.046, respectively, and the final residual difference synthesis showed no peaks above 0.19 e Å^{-3}. The atomic scattering factors were taken from the *International Tables*.[37] Final atomic parameters are given in Table VIII. Lists of thermal and hydrogen parameters and observed and calculated structure factors have been deposited as supplementary material.

^{1}H and ^{13}C NMR Study of Ligand 7. The ^{1}H and ^{13}C NMR experiments in the presence of LSR were carried out as follows: samples of the ligand **7** with increasing amounts of Eu(fod)$_3$ were prepared from separate 0.1 M deuteriochloroform solutions of compound **7** and 0.13 M of Eu(fod)$_3$. These solutions were mixed and diluted in order to reach concentrations of [Eu(fod)$_3$/ligand] ranging from 0.05 to 0.20. The ^{1}H and ^{13}C NMR spectra of the mixtures were recorded at room temperature, and the corresponding induced shifts in relation to the values measured for the free ligand **7** were calculated. In Table VI, the results obtained by extrapolating the experimental values to [Eu(fod)$_3$/ligand] = 1 are given for ^{1}H and ^{13}C NMR.

Transport Rate Measurements. The transport experiments were performed at room temperature in a similar apparatus as described before.[38,39] A cylindrical glass (4.9 cm, i.d.) holds a glass tube (2.0 cm, i.d.), which separates two aqueous phases. The first aqueous phase (10 mL) contains 5 × 10^{-5} mol L^{-1} of LiOH, 10^{-1} mol L^{-1} of alkali or ammonium nitrate, and 2 × 10^{-3} mol L^{-1} of alkali or ammonium picrate. The second aqueous phase contains 10 mL of deionized water. The membrane phase (40 mL of chloroform, Merck), in which carrier is dissolved (7 × 10^{-4} mol L^{-1}), lies below two aqueous phases and bridges them. This membrane phase is stirred slowly and constantly by magnetic stirrer. A similar experiment was carried out in the absence of carrier. The picrate concentration in the second aqueous phase, monitored spectroscopically, was confirmed to increase linearly with running time (<12 h), and the initial transport rates were calculated. The values indicated in Table VII were estimated from the differences in the transport rates of carrier-containing systems and blank systems (no carrier present). Dibenzo-18-crown-6 was taken as reference ligand, and it showed the following transport rates (×10^{-6} mol h^{-1}: Li$^+$, 5.73; Na$^+$, 22.54; K$^+$, 198.2; Rb, 183.1; Cs$^+$, 83.27; NH$_4^+$, 129).

Acknowledgment. We thank the CICYT for financial support, Grant No. PA 86/0431 and PB/0291.

Registry No. **7**, 118713-61-4; **8**, 118658-90-5; **9**, 118682-72-7; TEG, 112-60-7; Eu(fod)$_3$, 17631-68-4; Li$^+$, 17341-24-1; Na$^+$, 17341-25-2; K$^+$, 24203-36-9; Rb$^+$, 22537-38-8; Cs$^+$, 18459-37-5; NH$_4^+$, 14798-03-9; 1-methyl-3,5-bis(chloromethyl)-1*H*-pyrazole, 115414-08-9.

Supplementary Material Available: Tables of thermal parameters for the non-hydrogen atoms and of hydrogen parameters of **7** (2 pages); table of observed and calculated structure factors for **7** (18 pages). Ordering information is given on any current masthead page.

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[35] Main, P.; Fiske, S. J.; Hull, S. E.; Lessinger, L.; Germain, G.; Declercq, J. P.; Woolfson, M. M. *Multan 80 System*; University of York, England: 1980.

[36] Stewart, J. M.; Machin, P. A.; Dickinson, C. W.; Ammon, H. L.; Heck, H.; Flack, H. "The X-Ray System"; Technical Report No. TR-446, 1976; Computer Science Center, University of Maryland.

[37] *International Tables for X-Ray Crystallography*; Kynoch Press: Birmingham, England, 1974; Vol. IV.

[38] Samat, A.; El Malouli-Bibout, M.; Chanon, M.; Elguero, J. *Nouv. J. Chim.* **1982**, *6*, 483.

[39] Samat, A.; El Malouli-Bibout, M.; Elguero, J. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1717.

[40] Johnson, C. K. "ORTEP"; Technical Report No. ORNL-3794, 1965; Oak Ridge National Laboratory, Oak Ridge, TN.