Formation of Complexes between Aza Derivatives of Crown Ethers and Primary Alkylammonium Salts. Part 4.† Diaza-18-crown-6 Derivatives

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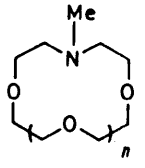
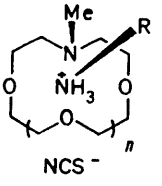
Diaza analogues of 18-crown-6 (7b) and (10b), benzo-18-crown-6 (8b), and dibenzo-18-crown-6 (9b) form strong complexes in methylene chloride with primary alkylammonium thiocyanates. The n.m.r. spectra of these complexes show temperature dependence which can be explained in the terms of different types of guest exchange processes. The complexes of the dibenzo-18-crown-6 analogue (9b) appear to exist in one form only but the spectra of the complexes of the other 18-crown-6 analogues (7b), (8b), and (10b) indicate that two or more different types of complex are in equilibrium. The possible nature of these closely related but different species is discussed.

In Part 1 [1] we discussed the formation of complexes between primary alkylammonium thiocyanates and the monoaza derivatives (1) of crown ethers. This study showed that the monoaza-15-crown-5 derivative (1a)



(1)



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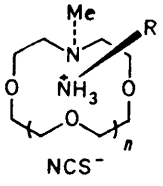
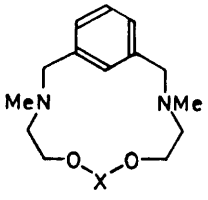


(3)

a; $n = 2$
b; $n = ?$



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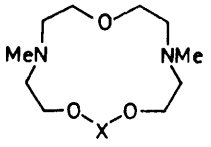

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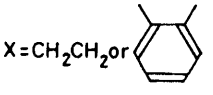

formed complexes in which the primary alkylammonium cation had a *cis*-relationship to the NMe group as shown in (2a) and the diastereoisomeric *trans*-complex (3a) was not detectable. In contrast with this result the monoaza-18-crown-6 derivative (1b) formed an equilibrium mixture of complexes of both types (2b) and (3b) in *ca.* 1 : 1 ratio.

The diaza derivatives of crown ethers (4) and (5), having 15-membered rings, behave [2,3] in a similar way to the monoaza system (1a) and also form only a single type of complex believed to have the all-*cis*-structure, as for example complex (6). It was anticipated, however, that diaza-18-crown-6 systems would form mixtures of diastereoisomeric complexes and a number of such compounds were synthesised to test this expectation.

† Part 3, ref. 2*b*.

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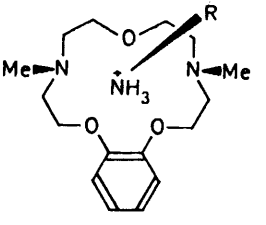
The required diaza-18-crown-6 systems (7)—(10) were synthesised by routes analogous to those used in earlier work [2] for the synthesis of diaza-15-crown-5 analogues. Thus, the 18-crown-6 analogue (7a) was prepared by the reaction of the dianion from the biscarbamate (11) with the bistoluene-*p*-sulphonate (12); reduction of (7a) with lithium aluminium hydride gave the diamine (7b). The monobenzo derivative (8b) was synthesised by a similar route from the biscarbamate (11) and the bistoluene-*p*-sulphonate (13). The synthesis of the dibenzo deriva-



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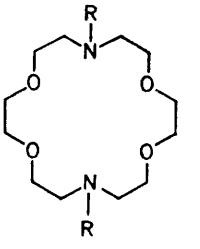

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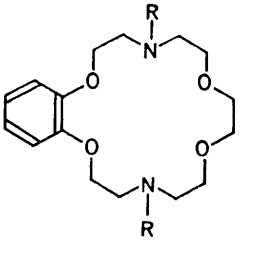

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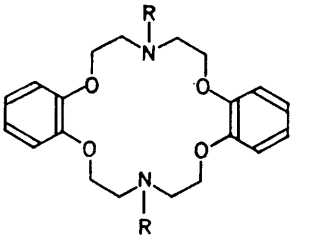

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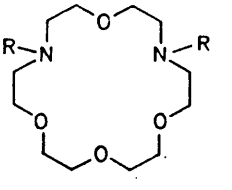


a; R = CO_2Et
b; R = Me
c; R = H
d; R,R = H,Me
e; R = CO_2CH_2Ph

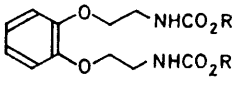
(10)

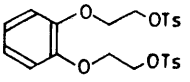
tive (9b) proved a little more difficult since reduction of the biscarbamate (9a) with lithium aluminium hydride gave a mixture of the required *NN'*-dimethyl derivative (9b) together with the monomethyl derivative (9d) and the unmethylated amine (9c).[4] This mixture could be converted into the required diaza-dibenzo-18-crown-6 derivative (9b) by Eschweiler–Clark methylation or, alternatively, the macrocycle (9e) could be obtained from the reaction of the biscarbamate (14b) with the bistoluene-*p*-sulphonate (13); debenzylation of (9e) followed by methylation gave the *NN'*-dimethyl derivative (9b).

$EtO_2CNHCH_2(CH_2OCH_2)_nCH_2NHCO_2Et$ $TsOCH_2(CH_2OCH_2)_2CH_2OTs$

(11) $n = 2$
(15) $n = 3$

(12)





(14)
a, R = Et
b, R = CH_2Ph

(13)

$BrCH_2CH_2OCH_2CH_2Br$

(16)

Ts = *p*—$CH_3C_6H_4SO_2$

The isomer (10b) of the diaza-18-crown-6 derivative (7b) was synthesised from the biscarbamate (15) and the dibromide (16); the biscarbamate (10a), resulting from the cyclisation reaction, gave the required 18-crown-6 derivative (10b) on reduction with lithium aluminium hydride.

The four 18-membered macrocyclic diamines (7b)—(10b) formed complexes with primary alkylammonium thiocyanates that could be examined by n.m.r. line-shape methods.[1,2,5,6] These studies are described in the final section of this paper.

EXPERIMENTAL

General.—see Part 2.[2a]

N.M.R. Spectra.—These were determined using either a Varian HA 100 (100 MHz) or a Perkin-Elmer R34 (220 MHz) spectrometer and *ca.* 0.1M solutions in either deuteriochloroform or deuteriomethylene chloride. Temperatures were controlled within the range −110 to +30° and were calibrated using a methanol sample. Solutions of complexes were prepared by dissolving the appropriate amounts of the two components in *ca.* 0.5 ml of solvent immediately prior to running the spectra. Thiocyanate salts of primary amines were prepared as described in earlier papers of this series.

NN'-*Bisethoxycarbonyl*-1,10-*diaza*-4,7,13,16-*tetraoxacyclo-octadecane* (7a).—*NN'*-Bisethoxycarbonyl-1,8-diamino-3,6-dioxaoctane (11) (5.84 g, 0.02 mol) in dry dimethyl sulphoxide (75 ml) was added dropwise to a stirred suspension of sodium hydride (1.12 g, 0.048 mol) in dry dimethyl sulphoxide (125 ml). After 3 h the dianion of (11) had been formed. Triethylene glycol bistoluene-*p*-sulphonate (12) (10.0 g, 0.024 mol) in dry dimethyl sulphoxide (75 ml) was added to the solution of the dianion and the mixture stirred under N_2 for 3 days. The reaction mixture was acidified (200 ml; 2N-HCl) and the product extracted into chloroform. The organic extract was washed with water, dried ($MgSO_4$), and evaporated and the residual oil purified by chromatography on silica. The *macrocycle* (7a) (2.85 g, 35%) was obtained as a solid, m.p. 75—78° (Found: C, 52.9; H, 7.1; N, 8.1. $C_{18}H_{34}N_2O_8$ requires C, 53.2; H, 6.9; N, 8.4%); $\nu_{max.}$ 1 680 cm^{-1}; δ($CDCl_3$) 4.12 (q, *J* 7 Hz, 2 × OCH_2CH_3), 3.72—3.52 (m, 4 × NCH_2CH_2O + 2 × OCH_2CH_2O), and 1.24 (t, *J* 7 Hz, 2 × OCH_2CH_3).

NN'-*Dimethyl*-1,10-*diaza*-4,7,13,16-*tetraoxacyclo-octadecane* (7b).—The biscarbamate (7a) (406 mg, 1.00 mmol) in ether (25 ml) was treated with lithium aluminium hydride (400 mg, 10.5 mmol) and the mixture stirred at room temperature for 3 h. Excess of hydride was destroyed by the addition of ice–water and the resulting alumina removed by filtration. The organic filtrate was combined with ether washings of the alumina and evaporated giving the *macrocyclic diamine* (7b) as an oil (280 mg, 97%) which could be purified by distillation at 127—132° and 0.01 Torr (Found: *M*, 290,2196. $C_{14}H_{30}N_2O_4$ requires *M*, 290.2208); δ($CDCl_3$) 3.51 (s, 2 × OCH_2CH_2O), 3.51 (t, *J* 6 Hz, 4 × OCH_2CH_2N), 2.58 (t, *J* 6 Hz, 4 × OCH_2CH_2N), and 2.23 (s, 2 × NCH_3).

Catechol Bis-(2-phthalimidoethyl Ether).—The bistoluene-*p*-sulphonate (13) (50.6 g) reacted with potassium phthalimide (30.0 g) in dimethylformamide at 100° for 5 h giving the *product* as a solid (27.4 g, 60%), m.p. 173—175° (Found: C, 68.5; H, 4.6; N, 5.9. $C_{26}H_{20}N_2O_6$ requires C, 68.4; H, 4.4; N, 6.1%); δ($CDCl_3$) 7.98—7.58 (2 × AA'BB' system, 8 ArH), 6.86 (s, 4 ArH), and 4.39—3.88 (2 × A_2B_2 system, 2 × OCH_2CH_2N).

Catechol Bis-(2-aminoethyl Ether).—Two methods were used.

(a) Catechol bis-(2-phthalimidoethyl ether) (11.4 g, 0.025 mol) was heated with hydrazine hydrate (3 ml, 0.06 mol) in ethanol (100 ml) for 1 h. The mixture was acidified to pH 1 (6N-HCl) and heated under reflux for a further 30 min. The mixture was cooled, diluted with water, washed with chloroform, and made basic by the addition of aqueous sodium hydroxide (10N). The product was extracted into chloroform (100 ml) and the extract dried and evaporated, giving the diamine as an oil (4.1 g, 84%).

(b) Catechol bis-(2-hydroxyethyl ether) bistoluene-*p*-sulphonate (13) (5.06 g, 0.01 mol) was stirred with sodium azide (2.6 g, 0.04 mol) in dry dimethyl sulphoxide (25 ml) for 24 h. The reaction mixture was diluted with water (50 ml) and the product extracted into ether (2 × 25 ml). The extracts were dried and evaporated giving catechol bis-(2-azidoethyl ether) (2.4 g, 100%) as a solid, m.p. 86—88°; $\nu_{max.}$ 2 100 and 2 060 cm^{-1}; δ($CDCl_3$) 7.00 (s, 4 ArH), 4.21 (t, *J* 5.5 Hz, 2 × OCH_2), and 3.62 (t, *J* 5.5 Hz, 2 × CH_2N_3). The bisazide (2.4 g) was reduced with lithium aluminium hydride (0.04 g, 0.01 mol) in ether (20 ml) at room temperature for 24 h. Excess of hydride was destroyed by the dropwise addition of water and the organic layer combined with ether washings of the precipitated inorganic salts. The extracts were dried and evaporated giving the diamine as an oil (1.3 g, 67%) which was used without further purification for the preparation of the carbamates (14a and b).

Catechol Bis-(N-*ethoxycarbonyl*-2-*aminoethyl Ether*) (14a).—Catechol bis-(2-aminoethyl ether) (2.5 g, 0.013 mol) was stirred with water (10 ml) and ether (10 ml) at 0°. Ethyl

chloroformate (3 ml, 0.03 mol) in ether (5 ml) was added dropwise followed by the addition of aqueous sodium hydroxide (1.0 g in 10 ml H_2O). The mixture was allowed to warm to room temperature and stirred for 1 h and the ether layer was removed and combined with ethereal extracts (2 × 10 ml) of the aqueous layer. The combined ether solutions were dried and evaporated giving the *product* (14a) which crystallised from chloroform–petroleum (b.p. 40—60°) as a solid, m.p. 60—61° (2.1 g, 50%) (Found: *M*, 340.1634. $C_{16}H_{24}N_2O_6$ requires *M*, 340.1634); $\nu_{max.}$ 3 310 and 1 710 cm^{-1}; δ($CDCl_3$) 6.97 (s, 4 ArH), 5.64br (s, 2 × NH), 4.16 (q, *J* 7 Hz, 2 × OCH_2CH_3), 4.10 (t, *J* 5 Hz, 2 × OCH_2), 3.56 (q, *J* 6 Hz, 2 × CH_2NH), and 1.23 (t, *J* 7 Hz, 2 × OCH_2CH_3).

Catechol Bis-(N-*benzyloxycarbonyl*-2-*aminoethyl Ether*) (14b).—This compound was prepared, using a method similar to that for the ethoxycarbonyl derivative (14a), from the diamine (2.5 g, 0.013 mol) and benzyl chloroformate (5 ml, 0.03 mol). The *product* (14b) crystallised from chloroform–ether as a solid, m.p. 103—104° (3.6 g, 62%) (Found: C, 67.1; H, 6.3; N, 6.2. $C_{26}H_{28}N_2O_6$ requires C, 67.2; H, 6.1; N, 6.0%); $\nu_{max.}$ 3 440 and 1 720 cm^{-1}; δ($CDCl_3$) 7.30 (s, 10 ArH), 5.57br (s, 2 × NH), 6.91 (s, 4 ArH), 5.10 (s, 2 × $PhCH_2$), 4.01 (t, *J* 5 Hz, 2 × OCH_2), and 3.49 (q, *J* 5 Hz, 2 × CH_2NH).

NN′-*Bisethoxycarbonyl*-7,16-*diaza*-1,4,10,13-*tetraoxa*-2,3-*benzocyclo-octadec*-2-*ene* (8a).—This compound was prepared, using a method similar to that used for the macrocycle (7a), from *NN′*-bisethoxycarbonyl-1,8-diamino-3,6-dioxaoctane (11) (2.90 g, 0.01 mol), the catechol derivative (13) (5.06 g, 0.01 mol), and sodium hydride (0.96 g), in dry dimethyl sulphoxide (50 ml). The *product* (8a) was purified by column chromatography (silica gel) giving an oily solid (2.1 g, 50%), b.p. *ca.* 290° at 0.2 Torr (Found: *M*, 454.2310. $C_{22}H_{34}N_2O_8$ requires *M*, 454.2315); $\nu_{max.}$ 1 690 cm^{-1}; δ($CDCl_3$) 6.90 (s, 4 ArH), 4.50—3.40 (m, 5 × OCH_2CH_2N + 2 × OCH_2CH_3), and 1.24 (t, *J* 7 Hz, 2 × OCH_2CH_3).

NN′-*Dimethyl*-7,16-*diaza*-1,4,10,13-*tetraoxa*-2,3-*benzocyclo-octadec*-2-*ene* (8b).—This compound was prepared by reduction of the biscarbamate (8a) (389 mg, 0.86 mmol) using lithium aluminium hydride (100 mg, 2.6 mmol) in dry ether (10 ml). The *product* (8b) was obtained as an oil (191 mg, 96%), b.p. *ca.* 220° at 0.5 Torr (Found: *M*, 338.2205. $C_{18}H_{30}N_2O_4$ requires *M*, 338.2205); $\lambda_{max.}$ 235.5 (ε 5 900) and 277.5 nm (2 800); δ($CDCl_3$) 6.83 (s, 4 ArH), 4.03 (t, *J* 6 Hz, 2 × $ArOCH_2$), 3.52 (s, OCH_2CH_2O), 3.57 (t, *J* 6 Hz, 2 × OCH_2), 2.87 (t, *J* 6 Hz, 2 × NCH_2), 2.70 (t, *J* 6 Hz, 2 × NCH_2), and 2.29 (s, 2 × NMe).

NN′-*Bisbenzyloxycarbonyl*-7,16-*diaza*-1,4,10,13-*tetraoxa*-2,3:11,12-*dibenzocyclo-octadeca*-2,11-*diene* (9e).—This compound was prepared, using a method similar to that used for the diaza-18-crown-6-derivative (7a), from the catechol derivatives (13) (4.80 g, 8.7 mmol) and (14b) (4.40 g, 8.7 mmol) and sodium hydride (0.9 g) in dry dimethyl sulphoxide (160 ml). The crude product crystallised from chloroform–ether giving the *dibenzocyclo-octadecadiene derivative* (9e) as a solid (2.6 g, 50%), m.p. 221—224° (Found: *M*, 626.2609. $C_{36}H_{38}N_2O_8$ requires *M*, 626.2628); $\nu_{max.}$ 1 680 cm^{-1}; δ($CDCl_3$) 7.32 (s, 10 ArH), 6.81 (s, 8 ArH), 5.13 (s, 2 × $PhCH_2O$), and 4.30—3.75 (m, 4 × NCH_2CH_2O).

7,16-*Diaza*-1,4,10,13-*tetraoxa*-2,3:11,12-*dibenzocyclo-octadeca*-2,11-*diene* (9c).—A solution of the biscarbamate (9e) (313 mg, 0.5 mmol) in acetic acid (2 ml) was heated with hydrogen bromide in acetic acid (2 ml; 45%) on a steam-bath for 3 min. The mixture was diluted with water (20 ml), washed with chloroform (10 ml), and made basic by the addition of aqueous sodium hydroxide (10N). The product was extracted into chloroform (2 × 20 ml) and the extracts dried and evaporated giving the *diamine* (9c) as a solid, m.p. 168—173° (161 mg, 90%) which was used without further purification (Found: *M*, 358. $C_{20}H_{26}N_2O_4$ requires *M*, 358); $\nu_{max.}$ 3 315 cm^{-1}; δ($CDCl_3$) 6.89 (s, 8 ArH), 4.10 (t, *J* 4 Hz, 4 × $ArOCH_2$), 3.13 (t, *J* 4 Hz, 4 × CH_2N), and 2.15br (s, 2 × NH).

NN′-*Dimethyl*-7,16-*diaza*-1,4,10,13-*tetraoxa*-2,3:11,12-*dibenzocyclo-octadeca*-2,11-*diene* (9b).—The diamine (9c) (161 mg, 0.45 mmol) was heated on a steam-bath for 16 h with formic acid (0.2 ml, 5 mmol) and formaldehyde (0.2 ml, 37% aqueous solution, 2 mmol). The mixture was evaporated after the addition of hydrochloric acid (4 drops, 11N) and the residue extracted into chloroform (2 × 5 ml) from aqueous sodium hydroxide (5 ml, 2N). The extracts were dried and evaporated giving the NN′-*dimethyldiamine* as a solid which was recrystallised from chloroform–ether to give a sample, m.p. 158—160° (87 mg, 50%) (Found: *M*, 386.2201. $C_{22}H_{30}N_2O_4$ requires *M*, 386.2206); $\lambda_{max.}$ 237.5 (ε 12 500) and 279 nm (7 700); δ($CDCl_3$) 6.85 (s, 8 ArH), 4.07 (t, *J* 6 Hz, 4 × $ArOCH_2$), 3.08 (t, *J* 6 Hz, 4 × CH_2N), and 2.38 (s, 2 × NMe).

NN′-*Bisethoxycarbonyl*-1,13-*diaza*-4,7,10,16-*tetraoxacyclo-octadecane* (10a).—This compound was prepared, using a similar method to that used for the biscarbamate (7a), from 1,11-diamino-*NN′*-bisethoxycarbonyl-3,6,9-trioxaundecane (15) (10.0 g, 0.0298 mol), bis-(2-bromoethyl) ether (16) (6.9 g, 0.0298 mol), and sodium hydride (1.5 g, 0.063 mol) in dimethyl sulphoxide (100 ml). The product was purified by chromatography giving the *biscarbamate* (3.1 g, 25%) as an oil which could be purified by short path distillation at 140° and 0.03 Torr (Found: *M*, 406.2307. $C_{18}H_{34}N_2O_8$ requires *M*, 406.2315); $\nu_{max.}$ 1 695 cm^{-1}; δ($CDCl_3$) 4.11 (q, *J* 7 Hz, 2 × OCH_2CH_3), 3.7—3.2 (m, 4 × OCH_2CH_2N + 2 × OCH_2CH_2O), and 1.23 (t, *J* 7 Hz, 2 × OCH_2CH_3).

NN′-*Dimethyl*-1,13-*diaza*-4,7,10,16-*tetraoxacyclo-octadecane* (10b).—A solution of the biscarbamate (10a) (539 mg, 1.33 mmol) in ether (15 ml) and lithium aluminium hydride (400 mg, 10.6 mmol) gave the required macrocyclic diamine (10b) (306 mg, 80%) as an oil, b.p. 160° at 0.03 Torr (Found: *M*, 290.2198. $C_{14}H_{30}N_2O_4$ requires *M*, 290.2205); δ(CD_2Cl_2) 3.7—3.4 (m, 8 × OCH_2), 2.56 (t, *J* 6 Hz, 4 × NCH_2), and 2.23 (s, 2 × NCH_3).

RESULTS AND DISCUSSION

The n.m.r. spectrum of the complex of the diaza-18-crown-6 derivative (7b) with benzylammonium thiocyanate (Table 1) showed upfield shifts of the NCH_2 and NMe signals in CD_2Cl_2 at 25° relative to the spectrum of the host macrocycle alone. This change in the n.m.r. spectrum of the host macrocycle, together with the increased solubility of the guest ammonium salt,[7] indicated that a complex had been formed. At −40° the NCH_2 signals had separated into two sets of signals, assignable to the protons on the upper and lower face of the host macrocycle, consistent with a slow rate on the n.m.r. time scale for the process E + I (ref. 1 and Scheme 1). The NMe signal consisted of two broad singlets at −40° which sharpened and were finally resolved as four singlets (Table 1, Me1—4) as the temperature was lowered to −80°. This result requires the presence of

TABLE 1

N.m.r. spectra [a] of complexes of the diaza-18-crown-6 derivatives (7b) with primary alkylammonium thiocyanates

Guest	Ratio G : H	Temp. (°C)	Spectrum of host (δ) [b] NMe	NCH_2 [c]	OCH_2 [c]	OCH_2CH_2O	Spectrum of guest (δ) [d] CH	CH_2	CH_3	$\overset{+}{N}H_3$
		25	2.24	2.58	3.52	3.54				
$PhCH_2\overset{+}{N}H_3NCS^-$	1 : 1	25	2.03 (Me1234)	2.46 (AB)	3.59	3.68		3.94		
		−40	1.93 (Me34)	2.26br (B)	3.57	3.70		3.92		8.07br (C23)
			2.07 (Me12)	2.63br (A)						8.23br (C1)
		−80	1.85 (Me4)							8.00 (C3)
			1.88 (Me3)							8.12 (C2)
			2.05 (Me2)							8.31 (C1)
			2.08 (Me1)							
$PhCH_2\overset{+}{N}H_3NCS^-$	2 : 1	25	2.07 (Me1234)	2.49 (AB)	3.59	3.67		3.99		6.81br
		−40	1.99br (Me1234)	2.24br (B)	~3.6br	3.69		3.98		7.1vbr
				2.61br (A)						
		−80	1.87 (Me3)	2.18d, J 12 Hz				3.92		7.8vbr (F + C3)
			1.96 (Me24)	2.30br (d, $J \sim 12$ Hz)						8.10br (C2)
			2.07 (Me1)	2.62 (t, $J \sim 12$ Hz)						8.31br (C1)
				2.73br						
		−105	1.88 (Me3 + Me4)							
			2.08 (Me1 + Me2)							
(*R*)-$PhCHMe\overset{+}{N}H_3NCS^-$	1 : 1	25	2.08 (Me124)	2.42 (AB)	3.57	3.66	4.27	1.56		
		−40	2.01 (Me124)	2.10br (B)			4.26br	1.53		
				2.52br (A)						
		−80	1.91 (Me4)	2.12 (d, $J \sim 12$ Hz)			4.25br	1.52 (C1)		7.87 (C2)
			2.04 (Me1 + Me2)	2.58 (t, $J \sim 12$ Hz)				1.57br (C2)		8.13 (C1)
(*R*)-$PhCHMe\overset{+}{N}H_3NCS^-$	2 : 1	25	2.10 (Me124)	2.46 (AB)	3.57	3.66	4.33	1.61		6.61
		−40	2.02 (Me124)	2.11br (B)				1.59br		8.05
				2.53br (A)						
		−80	1.90 (Me4)	2.10 (d, $J \sim 12$ Hz)				1.49 (C1)		7.78 (C2)
			2.02 (Me1 + Me2)	2.56 (t, $J \sim 12$ Hz)				1.61 (F + C2)		8.12 (C1)

[a] All spectra recorded at 220 MHz for CD_2Cl_2 solutions. The abbreviations d, t, *etc.*, have the usual meanings, br = broad, vbr = very broad signal. [b] Assignments are in accord with Scheme 1, some may be arbitrary. Descriptions Me1 etc. are also in accord with Scheme 1. The descriptions A and B used for the NCH_2 signals are in accord with Table 4. [c] Observed as t, J 6 Hz at 25°. At low temperatures the NCH_2 signals are either complex or as described, the OCH_2 signals are complex. [d] CH, d, $J \sim 7$ Hz unless stated to be broad. C1, C2, *etc.*, refer to the various diastereoisomeric complexes in accord with Figure 1, F refers to the free guest cation.

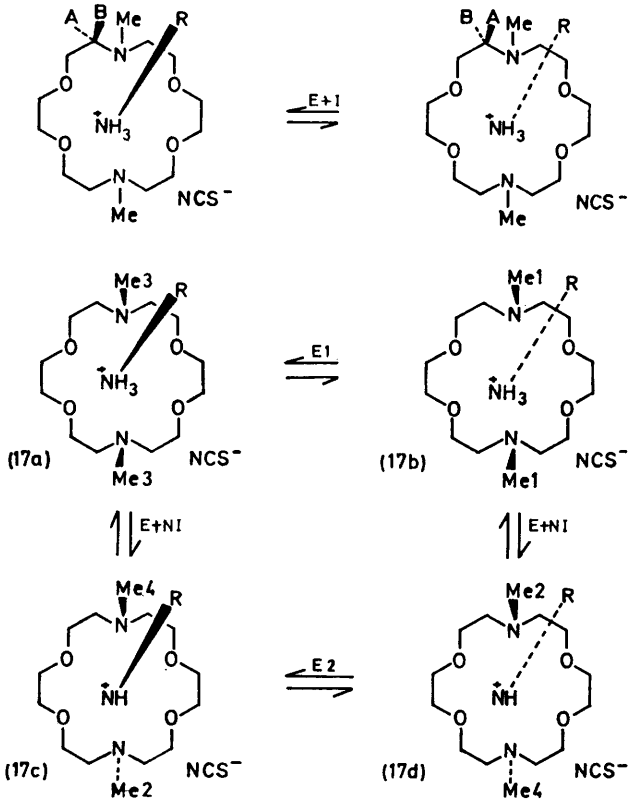
more than one type of complex in the solution. This conclusion was confirmed by examination of the guest $\overset{+}{N}H_3$ signal which was observed as two broad signals at −40° and finally as three signals (Table 1, C1—3) in *ca.* 1 : 1 : 1 ratio at −80° [Figure 1(a)]. In the presence of 1 mol. equiv. excess of benzylammonium thiocyanate these spectral changes were modified. Thus at −80° two of the NMe signals (Me2 and Me4) were observed as a single averaged signal (Table 1, Me24) which broadened and finally separated into two signals as the temperature was lowered to −105°. At −80° one of the guest $\overset{+}{N}H_3$ signals (C3) appeared to be averaged with the $\overset{+}{N}H_3$ signal (F) of the free ammonium salt [Figure 1(a)].

The simplest interpretation of these results is in the terms of the three diastereoisomeric complexes (17a, b, and c ≡ d) shown in Scheme 1.* These complexes (17) account in a satisfying manner for the four NMe signals (Me1—4) and the three $\overset{+}{N}H_3$ signals (C1—3), although the relationship between the complexes cannot be established with complete certainty on the basis of the n.m.r. data. It is interesting to note that the n.m.r. spectrum of the complex of the monoaza-18-crown-6 derivative (1b) with benzylammonium thiocyanate provided analogous evidence for the presence of two diastereoisomeric complexes (2b and 3b, R = CH_2Ph) as expected for a monoaza system.

The exchange process E2 [Scheme 1, (17c) ⇌ (17d)], which averages the n.m.r. signals from Me2 and Me4, is evidently more rapid at −80° in the presence of an excess of guest salt, than the process E1 [(17a) ⇌ (17b)]. This may be a consequence of the minimal conformational changes of the host macrocycle required for the process E2 as compared with E1 which, on the basis of molecular models, appears to involve rotation about some of the bonds of the macrocycle. In the presence of an excess of guest salt it is therefore possible that the process E2 includes a bimolecular component which accounts for

* The hydrogen bonding in (17) is not defined and although for convenience a positive charge and three protons are shown as located on the nitrogen of the guest molecule this is not intended to have structural significance. The available evidence also does not permit the assignment of the four NMe and three $\overset{+}{N}H_3$ signals to the four different NMe and three different $\overset{+}{N}H_3$ environments shown in Scheme 1. Therefore, the site labels used in Scheme 1 are to some extent arbitrary but they are not inconsistent with the spectral data.

the observed increase in rate compared with the situation for a 1 : 1 guest–host ratio. The interconversions (17a) ⇌ (17c) and (17b) ⇌ (17c) require configurational inversion at one of the nitrogen atoms in addition



SCHEME 1

to rotation about some of the bonds of the macrocycle. From a qualitative examination of the n.m.r. line shape changes these processes appear to be comparable in rate with the process E1. The description E + NI is used to stress the requirement for nitrogen inversion. The assignment of the three $\dot{N}H_3$ signals [Table 1 and Figure 1(a), C1—3] to the three species (17) is not possible but this does not affect our interpretation. It is also not possible to define the structures (17) to a greater extent than that shown in Scheme 1.

The spectrum of the complex of the host (7b) with (*R*)-phenylethylammonium thiocyanate shows only two host NMe signals at low temperatures (Table 1, Me1 + Me2, and Me4) and two guest $\dot{N}H_3$ signals [Figure 1(b)]. It appears therefore that in this case only two of the three diastereoisomeric structures (17) shown in Scheme 1 are present in solution. This is presumably a consequence of the additional non-bonded interactions between guest and host components for a guest phenylethylammonium cation as compared with a benzylammonium cation. It is therefore reasonable to conclude that in this case the two complexes have the structures (17b) and (17c ≡ 17d), the low field position of the major NMe signal (Table 1, Me1 + Me2, δ 2.04) is in accord with this interpretation. The addition of an excess of the guest salt makes little difference to the spectrum but at low temperatures it is possible to observe signals due to the free (F) and complexed (C1, C2) guest species (Table 1).

Provided that the hydrogen bonding in the complexes (17a and b) is fluxional with respect to the ring heteroatoms and that conformational changes of the host macrocycle not involving nitrogen inversion are rapid on the n.m.r. time scale only a single NMe signal is expected for both the chiral (R = CHMePh) and achiral (R = CH_2Ph) guest cations. The situation for the highly symmetrical host molecule (7b) differs in this respect from that of host molecules of lower symmetry that have been discussed in previous papers of this series. The expectation for a single NMe signal for each complex (17a and b) is in accord with the observed spectra (Table 1).

The n.m.r. spectra of the complexes of the mono-benzo

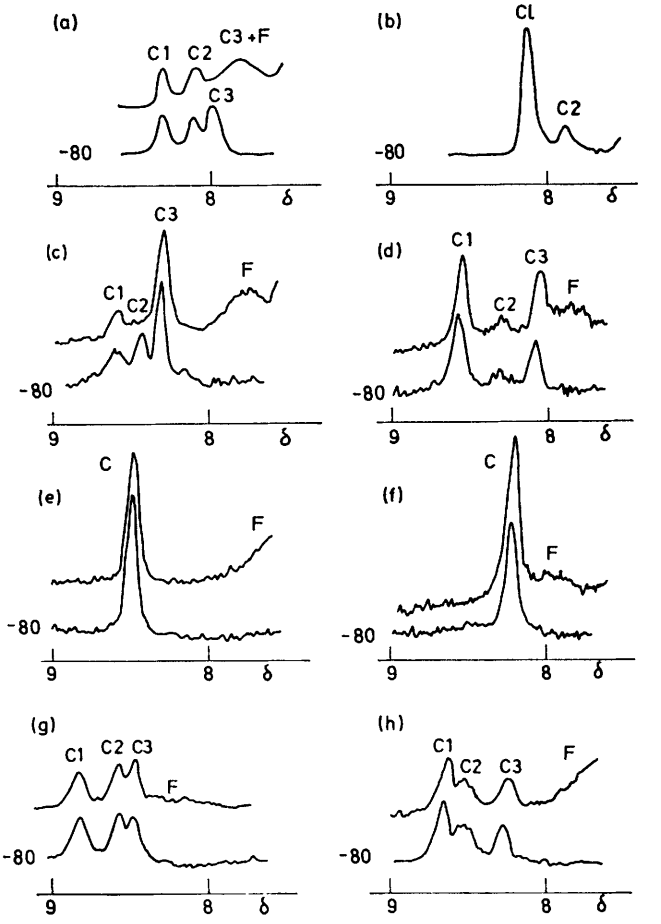


FIGURE 1 ^{1}H N.m.r. spectra (220 MHz) of guest $\dot{N}H_3$ protons in complexes of diaza analogues of 18-crown-6: (a) $PhCH_2\dot{N}H_3NCS^-$ + (7b); (b) (*R*)-$PhCHMe\dot{N}H_3NCS^-$ + (7b); (c) $PhCH_2\dot{N}H_3NCS^-$ + (8b); (d) (*R*)-$PhCHMe\dot{N}H_3NCS^-$ + (8b); (e) $PhCH_2\dot{N}H_3NCS^-$ + (9b); (f) (*R*)-$PhCHMe\dot{N}H_3NCS^-$ + (9b); (g) $PhCH_2\dot{N}H_3NCS^-$ + (10b); (h) (*R*)-$PhCHMe\dot{N}H_3NCS^-$ + (10b). In each case the lower spectrum is for a 1 : 1 G : H ratio and the upper spectrum for a 2 : 1 G : H ratio

derivative (8b) of the diaza-18-crown-6 system are not so clearly defined (Table 2). The three $\overset{+}{N}H_3$ signals of the guest cations (C1—3), observable at low temperatures for both the benzylammonium and phenylethylammonium thiocyanate complexes [Figure 1(c) and (d)] indicate that in both cases three types of complex are present in solution. The relative populations of the three complexes are rather different from those observed for the host (7b) but the reasons for this difference are not obvious. In principle the NMe signals should be sensitive to the presence of a chiral centre in the guest cation but the NMe region is not sufficiently well resolved for additional signals to be identifiable. It seems reasonable to conclude that the three complexes are related in structure in a similar manner to the complexes (17a—c).

The n.m.r. spectra of the complexes of the dibenzo-derivatives (9b) are relatively simple (Table 2) and at low temperatures the guest $\overset{+}{N}H_3$ signals [Table 2 and Figure 1(e) and (f)] indicate the presence of only a single type of complex. Furthermore the NMe signal is observed as a singlet at low temperatures, where the processes analogous to E1, E2, and E + NI (Scheme 1) would be expected to be slow on the n.m.r. time scale. It is therefore necessary to conclude that the complexes of (9b) have structures analogous to (17a or b) and in view of the low field position of the NMe signals (Table 2) we conclude that in this case only the complexes (18) analogous to (17b) are detectable in solution.

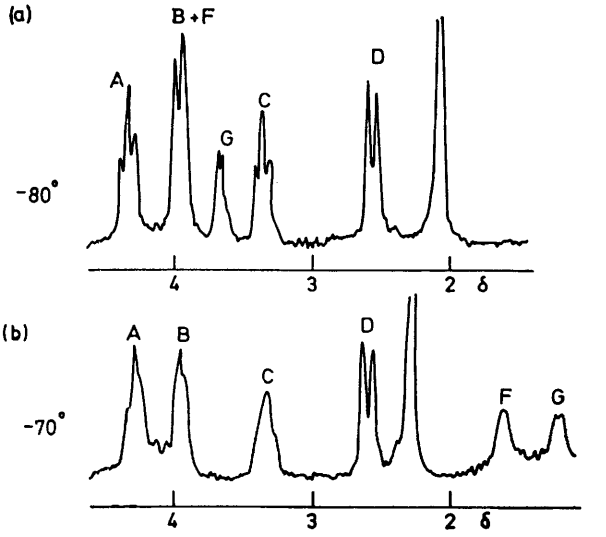


FIGURE 2 ^{1}H N.m.r. spectra (220 MHz) of the host OCH_2CH_2N protons in complexes of the macrocycle (9b): (a) $PhCH_2\overset{+}{N}H_3NCS^-$ + (9b), 2 : 1 ratio; (b) (*R*)-$PhCHMe\overset{+}{N}H_3NCS^-$ + (9b), 2 : 1 ratio

TABLE 2

N.m.r. spectra [a] of complexes of the diaza-18-crown-6 derivatives (8b) and (9b) with primary alkylammonium thiocyanates

Host	Guest	Ratio G : H	Temp. (°C)	Spectrum of host (δ) NMe	NCH_2 [b,e]	NCH_2 [b]	$ArOCH_2$ [b,e]	OCH_2 [b,c]	Spectrum of guest (δ) [d] CH	CH_2	CH_3	$\overset{+}{N}H_3$
(8b)			25	2.29	2.70	2.87	4.02	3.57 3.53 (s)				
(8b)	$PhCH_2\overset{+}{N}H_3NCS^-$	1 : 1	25	2.10	2.59br	2.71br	4.12 (AB)	3.65 (s) 3.75 (s)		3.96		5.8
			−50	2.06	2.4—3.1br (m)		4.02br (B) 4.32br (A)			3.91		8.27br
			−80	2.02 2.12	2.25—3.05br (m)		4.0br (m) 4.30br (t, *J* 11 Hz)			3.87br		8.32 (C3) 8.42 (C2) 8.61 (C1)
(8b)	$PhCH_2\overset{+}{N}H_3NCS^-$	2 : 1	25	2.10	2.60	2.70	4.11 (AB)	3.65 3.74 (s)		4.01		6.59
			−70	2.02	2.1—3.1br (m)		~4.0br (m, B)			3.94br		7.7br (F)
				2.11			4.30br (t, *J* 11 Hz, A)					8.30 (C3) 8.61 (C1)
(8b)	(*R*)-$PhCHMe\overset{+}{N}H_3NCS^-$	1 : 1	25	2.12	~2.6 (m)	~2.6 (m)	4.08	3.66 3.74 (s)	4.24		1.52	5.9br
			−50	2.12	2.2—2.9br (m)		4.09br (AB)		4.27br		1.54	~8.3br
			−100	2.11 2.21	2.9—2.9 (m)		~4.0br (B) ~4.3br (A)				1.42br 1.61br	8.10 (C3) 8.35br (C2) 8.60 (C1)
(9b)	(*R*)-$PhCH\overset{+}{N}H_3NCS^-$	2 : 1	25	2.20	2.91br (CD)		4.12(AB)		4.20		1.49	7.30
			−40	2.23	2.60br (D 3.30br (C)		3.97br (B) 4.20br (A)		4.2br		1.46br	
			−80	2.31	2.61 (d, *J* 14 Hz, D) 3.38br (C)		3.96br (B) 4.29br (A)				1.20 (C) 1.63br (F)	~7.9vbr (F) 8.22 (C)

[a] All spectra run at 220 MHz for CD_2Cl_2 solutions. [b] Observed as t, $J \sim 6$ Hz at 25°. At low temperatures signals are either complex or as described. [c] The OCH_2CH_2O system of (8b) gives a singlet at 25°. [d] CH, q, *J* 7 Hz; CH_3, d, *J* 7 Hz unless otherwise described. The descriptions C, C1, C2, and C3 refer to the complexed guest species and F to the free guest and are used in accord with Figures 1 and 2. [e] The assignments A—D for the complexes of (9b) are in accord with Scheme 2 and Figure 2.

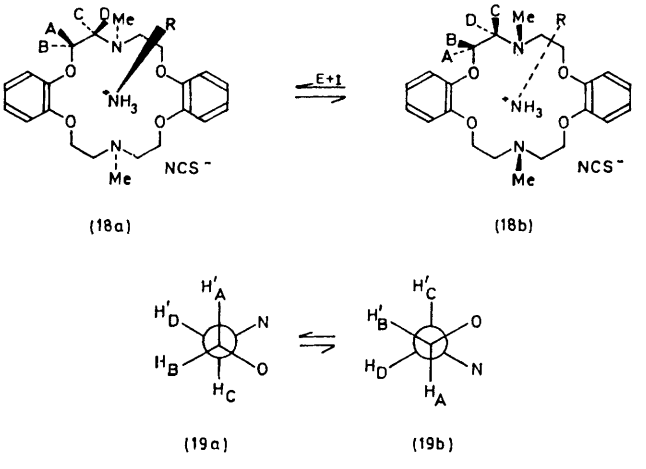
TABLE 3

N.m.r. spectra[a] of complexes of the diaza-18-crown-6 derivative (10b) with primary alkylammonium thiocyanates

Guest	Ratio G : H	Temp. (°C)	Spectrum of host (δ) NMe[b]	NCH_2[c]	NCH_2[c]	Spectrum of guest[d] CH	CH_2	CH_3	$\overset{+}{N}H_3$
		25	2.31	2.68	2.68				
$PhCH_2\overset{+}{N}H_3NCS^-$	1 : 1	25	2.06 (Me1234)	2.58br (AB)	2.58br (AB)		3.96		
		−40	1.39br (Me4)	~2.25br (B)			3.94br		8.59 (C23)
			1.98br (Me3)	~2.84br (A)					8.71 (C1)
			2.13 (Me1 + Me2)						
		−80	1.20 (Me4)	2.1—2.4 (m)			3.90		8.49 (C3)
			1.90 (Me3)	2.7—3.3 (m)					8.59 (C2)
			2.12 (Me2)						
			2.14 (Me1)						8.81 (C1)
$PhCH_2\overset{+}{N}H_3NCS^-$	2 : 1	25	2.01 (Me1234)	2.54br (AB)	2.54br (AB)		3.98		
		−45	1.33br (Me4)	~2.25br (m,B)			3.94br		8.5vbr
			1.95br (Me3)	~2.9br (m,A)					
			2.11br (Me1 + Me2)						
		−80	1.20 (Me4)	2.0—2.4 (m)			3.90 (C)		8.45 (C3)
			1.90 (Me3)	2.7—3.3 (m)			3.98 (F)		8.59 (C2)
			2.11 (Me2)						8.84 (C1)
			2.14 (Me1)						
(*R*)-$PhCHMe\overset{+}{N}H_3NCS^-$	1 : 1	25	2.07 (Me1234)	2.45 (m) ~2.6 (m)	2.55 (m)	4.32		1.61	6.2vbr
		−30	2.0vbr (Me1234)	2.0—3.1vbr		4.29br		1.56	8.4vbr
		−70	1.26 (Me4)	1.8—3.2 (m)		4.1—4.4 (m)		1.49 (C)	8.28 (C3)
			1.63 (Me3)					1.58 (C)	8.52 (C2)
			2.12 (Me2)						8.63 (C1)
			2.30 (Me1)						
(*R*)-$PhCHMe\overset{+}{N}H_3NCS^-$	2 : 1	25	2.06 (Me1234)	2.45 (m) ~2.6 (m)	2.55 (m)	4.37		1.63	6.94
		−30	2.0vbr (Me1234)	2.0—3.1vbr		4.32br		1.61	7.2vbr
		−70	1.24 (Me4)	1.8—3.2 (m)		4.30br		1.47 (C)	8.25 (C3)
			1.63 (Me3)					1.59br (C)	8.53 (C2)
			2.10 (Me2)					1.62br (F)	8.64 (C1)
			2.30 (Me1)						

[a] All spectra recorded at 220 MHz for CD_2Cl_2 solutions. [b] Assignments Me1, *etc.*, are in accord with Figure 3, but individual signals cannot be assigned in Scheme 3. [c] Triplets, $J \sim 5$ Hz or broadened signals at 25°. At low temperatures the signals are very complex. [d] CH_3, d, $J \sim 7$ Hz and CH, q, $J \sim 7$ Hz or broad unresolved signals at low temperatures. C, C1, C2, C3 refer to signals of complexed species in accord with the Figures. F refers to the uncomplexed guest.

The n.m.r. spectrum of the OCH_2CH_2N groups of the host molecule is particularly well defined as an ABCD system for the benzylammonium thiocyanate complex (18; R = CH_2Ph) [Figure 2(a)] and the doublet triplet pattern is consistent with the torsional relationships shown in (19a and b).[8] The protons of the ABCD system would exchange environments in the manner indicated (Scheme 2) as a result of the process E + I, (18a) ⇌ (18b). The assignments in Scheme 2 are based upon



(18a) (18b)

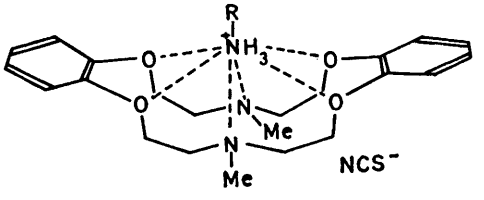
(19a) (19b)

SCHEME 2

what appears to be the most favourable conformation of the macrocycle on the basis of an examination of molecular models. This conformation is in accord with the torsional situation shown in (19a and b) corresponding to the site labels in (18a and b), respectively, where the individual protons of each methylene group are identified as H and H′. The OCH_2CH_2N groups of a complex (18) involving a chiral guest ammonium cation might be expected to give two ABCD systems at low temperature but the spectrum of the (*R*)-phenylethylammonium thiocyanate complex (18; R = CHMePh) [Figure 2(b)] shows a rather poorly resolved ABCD system very similar to that of the benzylammonium thiocyanate complex (18; R = CH_2Ph). Evidently the chemical shift differences between the two ABCD systems are too small to be resolved. The difference in the chemical shift of the NMe signal (Figure 2, Table 2) for the two complexes (18; R = CH_2Ph and R = CHMePh) shows, however, that the host molecule is in a different environment in the two cases.

The signals of the guest cations in the complexes (18) are also revealing (Table 2). Thus the $CH_2\overset{+}{N}$ signal of the guest benzylammonium cation [Figure 2(a), signal G] in the complex shows a significant shift to high field (*ca.* 0.3 p.p.m.) as compared with the uncomplexed species [Figure 2(a), signal F]. The shift to high field of the

CMe group of the phenylethylammonium cation [Figure 2(b), signal G] in the complex as compared with the uncomplexed species [Figure 2(b), signal F] is equally striking (*ca.* 0.3 p.p.m.). These upfield shifts, which are not observed for the analogous complexes of the hosts (7b) and (8b), show that the benzene rings of the host macrocycle (9b) probably tilt in the complex with respect to the average plane of the macrocycle is shown diagrammatically in (20). The methylene protons of the guest $CH_2\overset{+}{N}H_3$ group in the complex of (9b) with benzylammonium thiocyanate are observable as a quartet at low temperatures. Generally this coupling is not resolved in the spectra of complexes of azacrown ether analogues,[2] although it is clearly visible in the spectrum of the corresponding complex of 18-crown-6. This result suggests very strongly that the hydrogen bonding in the complexes of (9b) involves covalent attachment of the three $\overset{+}{N}H_3$ protons to the guest nitrogen atom as shown in (18) and (20).[9] The full details of the structures of these complexes will however not be available until the crystal structures of one or more of the complexes have

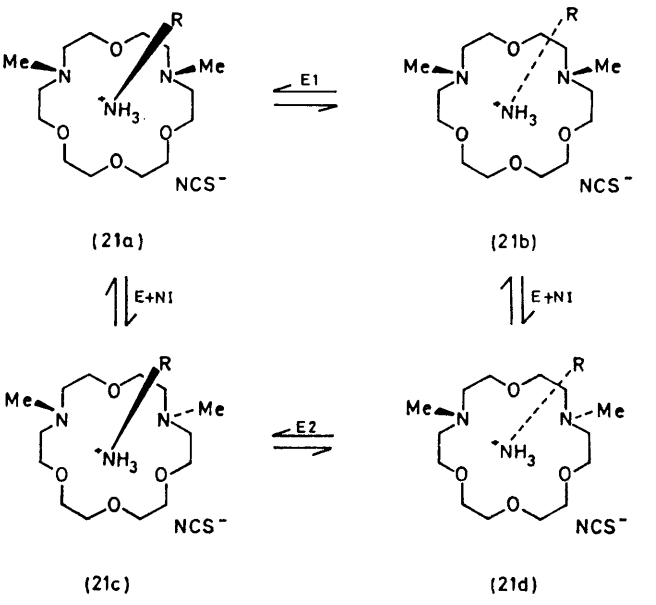


(20)*

* The broken lines in (20) indicate either coulombic interactions or hydrogen bonds.

been determined and even the limited detail indicated in (20) must be regarded as speculative.

The host macrocycle (10b) has a different relationship between the two nitrogen atoms as compared with (7b)—(9b). The n.m.r. spectra of its complexes (Table 3) indicate a number of similarities with the complexes of (7b), although there are also some differences. Thus the guest $\overset{+}{N}H_3$ signals of the complexes of (10b) with both benzylammonium thiocyanate and (*R*)-phenylethylammonium thiocyanate indicate the presence of three diastereoisomeric complexes [Figure 1(g) and (h); C1—3]. It is reasonable to assume, by analogy with the results for the other diaza-18-crown-6 analogues that these three complexes are related as shown in (21a—c) (Scheme 3). In accord with this assignment the spectrum of the benzylammonium thiocyanate complex (21; R = CH_2Ph) shows four NMe signals [Table 3 and Figure 3(a); Me1—4] at low temperatures. Although in principle the n.m.r. spectrum of the (*R*)-phenylethylammonium thiocyanate complex (21; R = CHMePh) could show eight NMe signals, at least four [Table 3 and Figure 3(b); Me1—4] are detectable at −70°. The significant upfield shift of Me4 in the spectra of both complexes (Figure 3) is similar to the upfield shifts observable for the complexes of mono- and di-aza-15-crown-5 analogues and evidently



SCHEME 3

indicates that this NMe group lies in the shielding zone of the phenyl substituent of the guest cation. In spite of this additional evidence it is not possible to assign the NMe signals of either complex to the diastereoisomeric species (21a—c). The spectral regions associated with the NCH_2 and OCH_2 groups are too complex for interpretation (see Figure 3 for the NCH_2 signals).

The temperature dependence of the n.m.r. spectra of the complexes of the host macrocycles (7b)—(10b) may be used to determine the energy barriers[6] for various

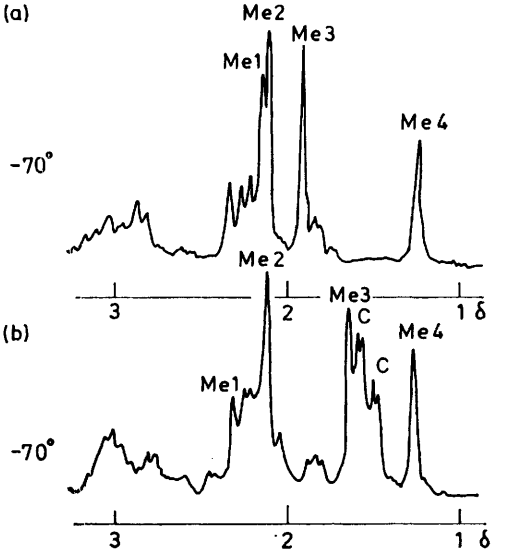


FIGURE 3 ^{1}H N.m.r. spectra (220 MHz) of the host NMe protons in complexes of the macrocycle (10b): (a) $PhCH_2\overset{+}{N}H_3NCS^-$ + (10b), 1 : 1 ratio; (b) (*R*)-$PhCHMe\overset{+}{N}H_3NCS^-$ + (10b), 1 : 1 ratio. The two CHMe doublets (labelled C) observable in spectrum (b) are due to diastereoisomeric complexes but it is not possible to assign them to the complexes C1—3 [see Figure 1(h)]

TABLE 4

Temperature dependence of the n.m.r. spectra of complexes of diaza-18-crown-6 analogues (7b)—(10b) with primary alkylammonium thiocyanates and associated free energy barriers [a]

Host	Guest	Ratio G : H	Signal	Spectral changes [b,c]	T_c/°C ± 2	$\Delta G^{\ddagger}$/ kcal mol^{-1}	Process [c]
(7b)	$PhCH_2\overset{+}{N}H_3NCS^-$	1 : 1	NCH_2	A + B→AB	−32	12	E + I
			NMe	Me34 + Me12→Me1234	−36	12	E,1 E2
			$\overset{+}{N}H_3$	C1 + C23→C123	−36	12	E + NI
			$\overset{+}{N}H_3$	C2 + C3→C23	−66	10	
(7b)	$PhCH_2\overset{+}{N}H_3NCS^-$	2 : 1	NCH_2	A + B→AB	−31	12	E + I
			NMe	Me1 + Me234→Me1234	−52	11	E1, E + NI
			NMe	Me24 + Me3→Me234	−64	10	
			NMe	Me2 + Me4→Me24	−92	9	E2 [d]
			$\overset{+}{N}H_3$	C1 + FC23→FC123	−52	10	E1, E + NI
			$\overset{+}{N}H_3$	(F + C3) + C2→FC23	−64	10	
(7b)	(*R*)-$PhCHMe\overset{+}{N}H_3NCS^-$	1 : 1	NCH_2	A + B→AB	−24	12	E + I
			NMe	(Me1 + Me2) + Me4→Me124	−53	11	E1, E2,
			$\overset{+}{N}H_3$	C1 + C2→C12	−58	10	E + NI
(7b)	(*R*)-$PhCHMe\overset{+}{N}H_3NCS^-$	2 : 1	NCH_2	A + B→AB	−24	12	E + I
			NMe	(Me1 + Me2) + Me4→Me124	−58	11	E1, E2,
			$\overset{+}{N}H_3$	C1 + C2→C12	−58	10	E + NI
(8b)	$PhCH_2\overset{+}{N}H_3NCS^-$	1 : 1	NCH_2	A + B→AB	−25	12	E + I
			NCH_2	A + B→AB	−40	11	
			CH_2OAr	A + B→AB	−40	11	
			NMe	Me1 + Me2→Me12	−62	11	E1, E2,
			$\overset{+}{N}H_3$	C1 + C2 + C3→C123	−64	10	E + NI
(8b)	$PhCH_2\overset{+}{N}H_3NCS^-$	2 : 1	NCH_2	A + B→AB	−45	11	E + I
			CH_2OAr	A + B→AB	−53	11	
			NMe	Me1 + Me2→Me12	−66	10	E1, E2,
			$\overset{+}{N}H_3$	C1 + C3 + F→C13F	−58	10	E + NI
(8b)	(*R*)-$PhCHMe\overset{+}{N}H_3NCS^-$	1 : 1	NCH_2	A + B→AB	−45	11	E + I
			$\overset{+}{N}H_3$	C1 + C2 + C3→C123	−55	10	E1, E2,
			CMe	C1 + C2→C12	−68	10	E + NI
(8b)	(*R*)-$PhCHMe\overset{+}{N}H_3NCS^-$	2 : 1	NCH_2	A + B→AB	−46	11	E + I
			NMe	Me1 + Me2→Me12	−80	10	E1, E2,
			CMe	C1 + C2 + F→C12F	−73	10	E + NI
			$\overset{+}{N}H_3$	C1 + C2 + C3→C123	−60	10	
(9b)	$PhCH_2\overset{+}{N}H_3NCS^-$	1 : 1	NCH_2	C + D→CD	−13	12.2 ± 0.3	E + I
			CH_2O	A + B→AB	−25	12.0 ± 0.3	E + I
(9b)	$PhCH_2\overset{+}{N}H_3NCS^-$	2 : 1	NCH_2	C + D→CD	−8	12.4 ± 0.3	E + I
			CH_2O	A + B→AB	−19	12.3 ± 0.3	E + I
			$\overset{+}{N}CH_2Ph$	F + C→FC	−52	10.7 ± 0.3	E
(9b)	(*R*)-$PhCHMe\overset{+}{N}H_3NCS^-$	1 : 1	NCH_2	C + D→CD	−25	11.6 ± 0.3	E + I
			OCH_2	A + B→AB	−30	11.7 ± 0.3	E + I
(9b)	(*R*)-$PhCHMe\overset{+}{N}H_3NCS^-$	2 : 1	NCH_2	C + D→CD	−25	11.7 ± 0.3	E + I
			OCH_2	A + B→AB	−30	11.9 ± 0.3	E + I
			CMe	F + C→FC	−60	10.1 ± 0.3	E
(10b)	$PhCH_2\overset{+}{N}H_3NCS^-$	1 : 1	NCH_2	A + B→AB	−20	12	E + I
			NMe	(Me1 + Me2) + Me3 + Me4→ Me1234	−32	11	E1, E2
			$\overset{+}{N}H_3$	C1 + C23→C123	−35	12	E + NI
			$\overset{+}{N}H_3$	C2 + C3→C23	−48	11	
(10b)	$PhCH_2\overset{+}{N}H_3NCS^-$	2 : 1	NCH_2	A + B→AB	−15	12	E + I
			NMe	(Me1 + Me2) + Me3 + Me4→ Me1234	−25	12	E1, E2
			$\overset{+}{N}H_3$	C1 + C2 + C3→C123	−45	11	E + NI
			$\overset{+}{N}CH_2Ph$	F + C→FC	−55	11	
(10b)	(*R*)-$PhCHMe\overset{+}{N}H_3NCS^-$	1 : 1	NCH_2	A + B→AB	−20	12	E + I
			NMe	Me1 + Me2 + Me3 + Me4→ Me1234	−34	11	E1, E2
			$\overset{+}{N}H_3$	C12 + C3→C123	−35	12	E + NI
			$\overset{+}{N}H_3$	C1 + C2→C12	−40	12	
			CMe	C1 + C2→C12	−58	11	
(10b)	(*R*)-$PhCHMe\overset{+}{N}H_3NCS^-$	2 : 1	NCH_2	A + B→AB	−18	12	E + I
			NMe	Me1 + Me2 + Me3 + Me4→ Me1234	−40	11	E1, E2,
			$\overset{+}{N}H_3$	C1 + C2 + C3 + F→C123F	−45	11	E + NI

[a] Energy barriers are based upon rates at the coalescence temperature T_c using the approximations given in ref. 6. For the multi-site exchanges these approximations lead to systematic errors and in these cases values of $\Delta G^{\ddagger}$ are given to the nearest kcal mol^{-1}. [b] For complexes of the hosts (7b), (8b), and (10b) spectral changes in the NCH_2 and OCH_2 regions are very complex. The value of $\Delta G^{\ddagger}$ is based upon the separation of the original triplet signal into two very broad signals as the temperature is lowered. [c] The processes leading to signal coalescence are described in Schemes 1—3. It is generally not possible to comment upon the different energy barriers for the various types of exchange process (other than E + I). [d] The assignment of the lowest energy barrier to the process E2 is in accord with the assignments but other possibilities are not excluded. [e] The labels used for the sites are in accord with Schemes 1—3, Tables 1—3, and Figures 1—3.

types of guest–host exchange processes as described in earlier Parts. The results of these calculations are shown in Table 4. The relationship between these energy barriers and the free energy of association (ΔG_c) has been discussed in a previous Part.[2a] Evidently all four 18-membered host macrocycles discussed in this paper form complexes having rather similar binding energies. Complexes of the diaza-18-crown-6 analogues are less useful for other studies that we plan than the corresponding 15-crown-5 analogues. This is a consequence of the unpredictable stereochemistry of complexes of the former type as compared with the predictable all-*cis*-stereochemistry of the latter. Furthermore it seems probable that for the host (9b), the only macrocycle giving a single type of complex, the relationship between the NMe groups and the guest molecule is *trans* [see (18) and (20)] and not suitable for the introduction of binding or catalytic interactions[10] between the substituents on nitrogen and the group R of the guest ammonium cation.

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