The Formation of Complexes between Aza Derivatives of Crown Ethers and Primary Alkylammonium Salts. Part 1. Monoaza Derivatives

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The monoaza derivatives of crown ethers form complexes with primary alkylammonium thiocyanates analogous to those formed by the crown ethers. The n.m.r. spectra of the complexes show temperature dependence which can be analysed in terms of various types of guest exchange processes and conformational changes of the host molecules. In particular, rapid conformational changes of the host macrocycle, accompanied by changes in hydrogen bonding to the guest cation, can occur without dissociation of the complex. The complexes of the monoaza 15-crown-5 analogues involve only a single face of the host macrocycle, and the substituent on the host nitrogen atom and the guest molecule are *syn*-related in the complex. The monoaza 18-crown-6 analogues form two diastereomeric complexes, having *syn*- and *anti*-relationships between the guest molecule and the substituent on the nitrogen atom of the host.

THE remarkable ability of macrocyclic polyethers of the crown type, such as 18-crown-6 (1), to form complexes with alkali-metal cations and a wide range of other cations including primary alkylammonium cations, was discovered by Pedersen.[1] This observation has been followed up by several groups,[2] and crown ethers have been designed and synthesised that show high chiral selectivity in complex formation [3] and also in the catalysis of chemical reactions.[4] The design of the polyether molecule, known as the host molecule, has generally been based upon an examination of molecular models, from which factors such as appropriate relationships between binding sites in the host molecule and those in the smaller component of the complex, the guest molecule, and the presence of non-bonded interactions between the guest and host components can be evaluated. Although this approach has been successful detailed structural information depends upon the X-ray analysis [5] of suitable crystalline complexes. Furthermore although the basic structural assumptions used for the design of specific complexing agents have been shown to be correct the detailed structure may differ significantly [6] from proposals based upon molecular models.

The use of aza derivatives of crown ethers,[7] for example (2), permitted an examination of both the structural and dynamic aspects of complex formation using n.m.r. spectroscopy, since it was possible to observe an n.m.r. spectrum at low temperatures which corresponded to the ' frozen ' complex in which a number of site exchange processes were slow on the n.m.r. time scale. Furthermore the X-ray analysis [8] of a crystalline complex (3) of the crown ether analogue (2) with benzylammonium thiocyanate showed that the fifteen-membered ring of (2) provided two sites for the formation of hydrogen bonds to the $\overset{+}{N}H_3$ group of the ammonium cation, the third proton of this group being attached by a hydrogen bond to the thiocyanate counter-ion. The location of the methyl substituents on the nitrogen atoms of the host macrocycle on the same face of the macrocycle as the guest molecule is an important feature of the structure (3). Thus replacement of these methyl groups by

groups containing functionality provides a method for (a) selective binding of guest molecules by using secondary binding interactions and (b) the incorporation of catalytic functions which could potentially have the
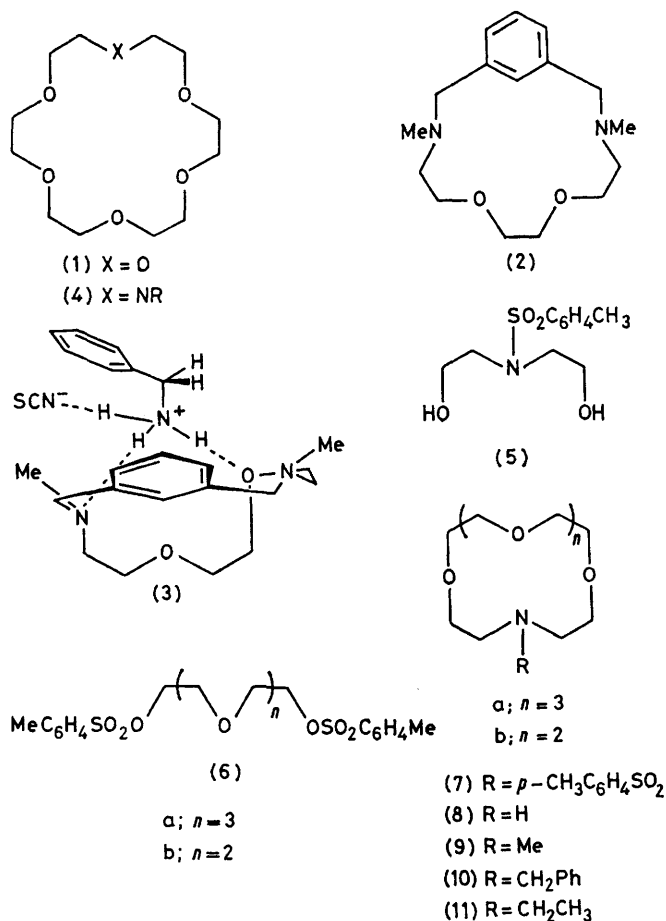
appropriate structural relationship to catalyse reactions of functional groups in the guest molecule.

Before developing these aspects of the chemistry of the diaza systems analogous to (2) it was of interest to examine monoaza derivatives of crown ethers, for example (4), and to examine their ability to take part in complex formation and their suitability as host systems

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for further studies of the type outlined above. The synthesis of the monoaza derivative of 18-crown-6 has been described previously and it can also be synthesised conveniently by the reaction of the dianion from *N*-*p*-tolylsulphonyldiethanolamine (5) with the bistoluene-*p*-sulphonate of tetraethylene glycol (6a). The required product (7a) was obtained in reasonable yield, without the necessity for high-dilution procedures, and it could be converted into the secondary amine (8a) by reduction with lithium aluminium hydride. Methylation of (8a) by the Eschweiler–Clark procedure gave the *N*-methyl derivative (9a) and other derivatives could be obtained either by alkylation [(7a) ⟶ (10a)] or by a sequence of acylation and reduction with lithium aluminium hydride [(7a) ⟶ (11a)]. The corresponding compounds in the monoaza 15-crown-5 series (7b)—(11b) could be prepared by an analogous series of reactions starting with triethylene glycol bistoluene-*p*-sulphonate. Compounds (7)—(11) formed complexes with a variety of primary alkylammonium salts and the more important results are discussed below.

EXPERIMENTAL

N-p-*Tolylsulphonyl*-7-*aza*-1,4,10,13-*tetraoxacyclopentadecane* (7b).—*N*-*p*-Tolylsulphonyldiethanolamine [9] (5) (12.95 g, 0.05 mol) in dry tetrahydrofuran (100 ml) was added dropwise over 1.5 h to a stirred suspension of sodium hydride (3.6 g, 0.15 mol) in dry tetrahydrofuran (350 ml) and the mixture was stirred for a further 2.5 h at room temperature (N_2 atmosphere). Triethylene glycol bistoluene-*p*-sulphonate (6b) (22.9 g, 0.05 mol) in dry tetrahydrofuran (100 ml) was added to the solution of the dianion of (5) and the reaction mixture was stirred at room temperature for 2 days (N_2 atmosphere). Water (500 ml) was added to the mixture, the tetrahydrofuran removed by evaporation, and the product extracted into chloroform (2 × 500 ml). The extract was dried ($MgSO_4$) and evaporated and the residue purified by column chromatography (silica gel) to give the *macrocycle* (7b) as a solid (8.13 g, 44%), m.p. 81—82° (Found: C, 54.4; H, 7.1; N, 3.7. $C_{17}H_{27}NSO_6$ requires C, 54.7; H, 7.3; N, 3.75%); $\delta(CDCl_3)$ δ_A 7.67, δ_B 7.26 (AA'BB' system, J_{AB} 8 Hz, 4 ArH), 3.80—3.20 (m, 2 × NCH_2CH_2O), 3.61 (s, 3 × OCH_2CH_2O), and 2.40 (s, $ArCH_3$).

N-p-*Tolylsulphonyl*-10-*aza*-1,4,7,13,16-*pentaoxacyclo-octadecane* (7a) was synthesised from *N*-*p*-tolylsulphonyl-diethanolamine (12.95 g, 0.05 mol) and tetraethylene glycol bistoluene-*p*-sulphonate (6a) (25.1 g, 0.05 mol) using a method analogous to that used for the macrocycle (7b). The product was obtained after chromatography as an oil (10.3 g, 46%) which crystallised on standing to give a solid, m.p. 51—53° (lit.,[10] 58°).

7-*Aza*-1,4,10,13-*tetraoxacyclopentadecane* (8b).—A stirred solution of the macrocycle (7b) (2.0 g, 5.4 mmol) in dry tetrahydrofuran (50 ml) was treated with lithium aluminium hydride (1.4 g, 37 mmol) and the resulting mixture was heated under reflux with stirring for 48 h. Excess hydride was destroyed by the dropwise addition of ice–water and the precipitated alumina removed by filtration. The residual alumina was extracted with ethyl acetate and the extract and filtrate were combined and evaporated to give the product (8b) as an oil (1.09 g, 92%) which solidified on standing giving a solid, m.p. 27—30°, which was used with-

out further purification for the preparation of derivatives (9)—(11), $\delta(CDCl_3)$ 3.72—3.54 (m, 8 × OCH_2), 2.97 (s, NH), and 2.71 (t, *J* 6 Hz, NCH_2).

7-*Aza*-1,4,10,13,16-*pentaoxacyclo-octadecane* (8a) was prepared in an analogous manner from the *N*-*p*-tolylsulphonyl derivative (7a). The product (8a) was obtained as a pale yellow crystalline solid (83%), m.p. 49—51° (lit.,[10] 48—51°) $\delta(CDCl_3)$ 3.71—3.56 (m, 10 × OCH_2), 2.70 (t, *J* 6 Hz, 2 × NCH_2), and 2.49br (s, NH).

N-*Methyl*-7-*aza*-1,4,10,13-*tetraoxacyclopentadecane* (9b).—The macrocycle (8b) (200 mg, 0.91 mmol) was heated with formic acid (1 ml, 25 mmol) and formaldehyde (1 ml, 37% aqueous solution, 10 mmol) on a steam-bath for 16 h. Hydrochloric acid (20 drops, 11N) was added and the solution was evaporated. The residue was dissolved in aqueous sodium hydroxide (25 ml, 2N) and the solution extracted with chloroform (2 × 20 ml). The extracts were dried ($MgSO_4$) and evaporated giving the *product* (9b) as an oil (191 mg, 92%) which was purified by short path distillation (88—90° at 0.005 Torr) (Found: C, 56.5; H, 9.8; N, 6.0%; *M*, 233.1624. $C_{11}H_{23}NO_4$ requires C, 56.6; H, 9.9; N, 6.0%; *M*, 233.1627), $\delta(CDCl_3)$ 3.74—3.54 (m, 8 × OCH_2), 2.68 (t, *J* 6 Hz, 2 × NCH_2), and 2.32 (s, NCH_3).

N-*Methyl*-7-*aza*-1,4,10,13,16-*pentaoxacyclo-octadecane* (9a) was prepared in an analogous manner from the corresponding secondary amine. The *product* (87%) was obtained as an oil which was purified by short path distillation (157—160° at 0.15 Torr) (Found: C, 56.0; H, 9.7; N, 4.9%; *M*, 277.1886. $C_{13}H_{27}NO_5$ requires C, 56.3; H, 9.7; N, 5.0%; *M*, 277.1889), $\delta(CDCl_3)$ 3.72—3.58 (m, 10 × OCH_2), 2.69 (t, *J* 5 Hz, 2 × NCH_2), and 2.32 (s, NCH_3).

N-*Ethyl*-7-*aza*-1,4,10,13-*tetraoxacyclopentadecane* (11b).—7-Aza-1,4,10,13-tetraoxacyclopentadecane (8b) (219 mg, 1.00 mmol) was acetylated using acetyl chloride (1.00 mmol) in dichloromethane (10 ml). The product (84%) in dry ether (20 ml) was reduced by stirring with lithium aluminium hydride (100 mg) for 2 h at room temperature. Excess hydride was destroyed by dropwise addition of ice–water and the ether solution was combined with ethyl acetate washings of the precipitated alumina. Evaporation gave the N-*ethyl compound* (11b) (95%) as an oil purified by short path distillation (95—100° at 0.01 Torr) (Found: *M*, 247.1780. $C_{12}H_{25}NO_4$ requires *M*, 247.1783); $\delta(CDCl_3)$ 3.72—3.58 (m, 8 × CH_2O), 2.75 (t, *J* 6 Hz, 2 × NCH_2), 2.61 (q, *J* 8 Hz, CH_2CH_3), and 1.04 (t, *J* 8 Hz, CH_2CH_3).

N-*Ethyl*-7-*aza*-1,4,10,13,16-*pentaoxacyclooctadecane* (11a) was prepared by an analogous sequence from 7-aza-1,4,10,-13,16-pentaoxacyclooctadecane (8a) to give the N-*ethyl compound* (11a) (overall yield 78%) as an oil purified by short path distillation (120—125° at 0.01 Torr) (Found: C, 57.8; H, 9.7; N, 4.6%; *M*, 291.2046. $C_{14}H_{29}NO_5$ requires C, 57.7; H, 10.0; N, 4.8%; *M*, 291.2046); $\delta(CDCl_3)$ 3.76—3.59 (m, 10 × OCH_2), 2.76 (t, *J* 6 Hz, 2 × NCH_2), 2.59 (q, *J* 8 Hz, CH_2CH_3), and 1.02 (t, *J* 8 Hz, CH_2CH_3).

N-*Benzyl*-7-*aza*-1,4,10,13-*tetraoxacyclopentadecane* (10b).—The secondary amine (8b) (200 mg, 0.92 mmol) was heated under reflux for 1 h in dry acetonitrile containing benzyl bromide (180 mg, 1.02 mmol) and anhydrous potassium carbonate (350 mg). The resulting mixture was cooled, filtered, and evaporated. The residual oil was purified by chromatography on alumina to give the N-*benzyl derivative* (10b) as an oil (220 mg, 77%). A sample was purified by short path distillation (142—146° at 0.01 Torr) (Found: C, 65.7; H, 8.8; N, 4.4%; *M*, 309.1930. $C_{17}H_{27}NO_4$ requires C, 66.0; H, 8.7; N, 4.5%; *M*, 309.1940); $\delta(CDCl_3)$

7.34—7.20 (m, 5 ArH), 3.76—3.59 (m, $CH_2Ar + 8 \times OCH_2$), and 2.78 (t, J 5.5 Hz, 2 × NCH_2).

N-*Benzyl-7-aza*-1,4,10,13,16-*pentaoxacyclooctadecane* (10a)

3.73—3.53 (m, $CH_2Ar + 10 \times OCH_2$), and 2.78 (t, J 5 Hz, 2 × NCH_2).

N.m.r. Spectra.—These were recorded using a Perkin-

TABLE 1

N.m.r. spectra [a] of complexes of monoaza crown ether analogues (9) and 18-crown-6 with primary alkylammonium salts

Host	Guest	Ratio H:G	$t/°C$ (±2)	NCH$_3$	NCH$_2$	CH$_2$	CH	CH$_3$	$\overset{+}{NH_3}$
					Spectrum of host [b]	Spectrum of guest [c]			
(9a)			25	2.25	2.58 (t, J 5 Hz)				
(9a)	PhCH$_2$$\overset{+}{N}H_3NCS^-$	1:1	25	2.00 (Me12)	2.54 (br t, AB12)	3.97			
			−30	1.93 (br, Me12)	{ 2.27 (br d, J 11 Hz, B12), 2.78 (br t, J 11 Hz, A12)	3.93			
(9a)	(R)-PhCHMe$\overset{+}{N}$H$_3$NCS$^-$	1:1	−80 30	1.78 (Me1), 2.11 (Me2) 2.02 (Me12)	2.25 (m, B1), 2.78 (br m, A1) 2.48 (m, AD12 + BC12)		4.28	1.58	
			−40	1.96 (br, Me12)	{ 2.23 (br m, C12 + D12) 2.60 (br m, B12), 2.80 (br m, A12)		4.32 (br)	1.58	
			−80	1.83 (Me1), 2.04 (Me2)	{ 2.18 (m, D1), 2.43 (m, C1), 2.60 (m, B1), 2.82 (m, A1)		4.30 (br)	1.58 (br)	7.82 (br s, G1) 7.99 (br s, G2)
(9a)	(R)-PhCHMe$\overset{+}{N}$H$_3$NCS$^-$	1:2	30	2.04 (Me12)	2.50 (m, AD12 + BC12)		4.35	1.62	
			−80	1.83 (Me1), 2.04 (Me2)	{ 2.19 (m, D1), 2.44 (m, Cl), 2.61 (m, B1) 2.81 (m, A1)		4.29 (br)	1.57 (br C) 1.62 (br F)	7.82 (br s, G1) 7.98 (br s, G2) ~7.4 (Fs)
(9a)	(R,S)-PhCHMe$\overset{+}{N}$H$_3$NCS$^-$	1:1	20	2.03 (Me12)	2.50 (br t, ABCD12)		4.35	1.62	
			−40	1.97 (br, Me12)	2.26 (br, CD12), 2.72 (br, AB12)				
			−80	{ 1.84 (Me1) 2.04 (Me2)	{ 2.18 (m, D1), 2.44 (m, C1) 2.61 (m, B1) 2.83 (m, A1)				
(9b)	PhCH$_2$$\overset{+}{N}H_3NCS^-$	1:1	26	2.32	2.68 (t, J 6 Hz)				
			10	2.08	2.55 (br t, ABCD)	3.97			
			−60	1.92	{ 2.34 (br d, J ~12 Hz, BD), 2.60 (br d, J ~12 Hz, AC)	3.93			
			−110	1.90 (br)	~2.05 (m, D), ~2.33 (m, C) ~2.69 (m, B), ~2.82 (m, A)				
(9b)	(R)-PhCHMe$\overset{+}{N}$H$_3$NCS$^-$	1:1	30	1.81 (Me12)	{~2.37 (m, BC12) {~2.50 (m, AD12)		4.28	1.58	
			−60	1.48 (Me12)	2.13 (d, J 12 Hz, D12), 2.27 (m, C12 + B12) 2.70 (dd, J ~12, 8 Hz, A12)		4.23 (br)	1.58	
			−110	0.96 (Me1)	1.85 (m, D1), 2.00 (m, C1), 2.26 (m, B1), 2.80 (m, A1)			1.53 (br)	
(9b)	(R,S)-PhCHMe$\overset{+}{N}$H$_3$NCS$^-$	1:1.3	25	1.88 (Me12)	2.50 (t, ABCD12)		4.32 4.27	1.60 1.57	
			−30	~1.60 (br, Me12)	{2.27 (br, BD12), {~2.50 (br, AC12)				
			−70	1.38 (Me12)	{ 2.07 (br d, D12), 2.22 (m, C12 + B12), 2.70 (m, A12)		4.20 (br)	1.55	
			−110	0.97 (Me1)	{ 1.86 (m. D1), 2.00 (m, C1), 2.27 (m, B1), 2.80 (m, A1)			1.54(br)	
(9b)	(R,S)-PhCHMe$\overset{+}{N}$H$_3$NCS$^-$	1:2	25	1.98 (Me12)	2.57 (t, ABCD12)		4.37 4.34	1.63 1.63	
			−30	~1.70 (br, Me12)	{ 2.32 (br, BD12), 2.57 (br, AC12)				
			−70	1.40 (Me 12)	{ 2.07 (m, D12), ~2.25 (m, B12 + C12), 2.70 (m, A12)		4.32 (C) 4.22 (F)	1.56 (C) 1.64 (F)	
(1) (1)	PhCH$_2$$\overset{+}{N}H_3NCS^-$ or ClO$_4^-$	1:1	26 26		3.60 (s) 3.57 (ABCD)	3.91			
			−60		3.57 (m, AC + BD)	3.84 (q, J 7 Hz)			
			−110		3.38 (m, D), 3.51 (m, C), 3.65 (m, A + B)	~3.78			~7.60
(1)	PhCH$_2$$\overset{+}{N}H_3NCS^-$	1:2	26		3.56 (ABCD)	4.00			~7.5 (C) 8.07 (F
(1)	Ph$_2$CH$\overset{+}{N}$H$_3$NCS$^-$	1:1	−85 −20		3.55 (br s, AC + BD) 3.53 (ABCD)		5.40		7.79
			−60		{ 3.43 (m, BD), 3.57 (m, AC), 3.66 (H) [d]		~5.4		7.81
			−110		{ 3.42 (br, BD), 3.57 (br, AC)		~5.35		81 7.81
(1)	Ph$_2$CH$\overset{+}{N}$H$_3$NCS$^-$	2:1	+26 −80		3.53 (ABCD) 3.43 (br, BD), 3.55 br, AC)		5.49 ~5.45 (F) ~5.4(C)		7.81 (C) 8.82 (F)
(1)	(R,S)-PhCHMe$\overset{+}{N}$H$_3$NCS$^-$	1:1	26		3.56		4.29 4.20 (septet)	1.67	
			−60		{ 3.57 (br, A12 + B12 + C12), 3.46 (m, D12)				
			−110		{ 3.60 (br, A1 + B1 + C1 + D1 + A2 + B2 + C2) 3.13 (br, D2)		4.08 (br)	1.69 (br)	7.37
(1)	(R,S)-PhCHMe$\overset{+}{N}$H$_3$NCS$^-$	1:2	26		3.55		4.33	1.67	
			−80		3.40 (br, D12), 3.53 (br, A12 + B12 + C12)		{4.13 (C) {4.25 (F)	1.65	{7.33 (C) {8.13 (F)
			−110		{ 3.12 (br, D2), 3.57 (br, A1 + B1 + C1 + D1 + A2 + B2 + C2)				

[a] All spectra were run in CD_2Cl_2 at the stated temperatures. Chemical shifts are given in p.p.m. relative to Me$_4$Si. [b] The labels Me12, AB12 *etc.*, refer to the labels used in Schemes 1—9 and Figures 1—8. The description br refers to a broad multiplet signal in which fine structure is not resolved or to a broadened singlet, s refers to singlet d to doublet, t to triplet, q to quartet, and m to multiplet. [c] For spectra with an H:G ratio of 1:2 the descriptions F and C refer to free and complexed guest respectively. [d] The label H indicates that this signal arises from an excess of the host species.

was prepared from the secondary amine (8a) and benzyl bromide as an oil (83%), purified by short path distillation (155—158° at 0.01 Torr) (Found: C, 64.3; H, 8.8; N, 3.8%; M, 353.2198. $C_{19}H_{31}NO_5$ requires C, 64.6; H, 8.8; N, 4.0%; M, 353.2202); δ(CDCl$_3$), 7.48—7.15 (m, 5 ArH),

Elmer R34 220 MHz spectrometer for deuteriomethylene chloride or deuteriochloroform solutions of the complexes (*ca.* 0.1M solutions). Temperatures were controlled within the range −110 to +30° and were calibrated using a methanol sample; measurements are probably accurate to

$\pm 2°$. Solutions of complexes were prepared by dissolving appropriate amounts of the two components in *ca.* 0.5 ml of solvent immediately prior to running the spectra. Thiocyanate salts were prepared from the appropriate amine hydrochloride and sodium thiocyanate and were crystallised from ethanol. The chemical shifts of the free host molecules and of their complexes are recorded in Table 1. The temperature dependence of the n.m.r. spectra was studied and a number of site exchange processes detected as described later. The associated energy barriers were obtained by approximations that have been discussed elsewhere.[11] In

changes in the n.m.r. spectrum of the host molecule, and (iii) in all cases temperature dependence of the n.m.r. spectrum of the complex. In some cases the spectral changes were poorly defined due to very broad n.m.r. lines at low temperatures and the discussion that follows is based upon the better resolved spectra, particularly those of the *N*-methyl derivatives (9a and b). For convenience the n.m.r. spectra of the complexes of the fifteen- and eighteen-membered ring systems are discussed separately. In addition a number of complexes

TABLE 2

Temperature dependence of the n.m.r. spectra of complexes of monoaza crown ether analogues (9) and 18-crown-6 with primary alkylammonium salts, and details of associated energy barriers

Host	Guest	Ratio H : G	Signal[a]	Spectral changes[b]	$t/°C$ (± 5)	$\Delta G^{\ddagger}$[c]$/$ kcal mol^{-1} (± 0.5)	Process
(9a)	$PhCH_2\overset{+}{N}H_3NCS^-$	1:1	NCH$_2$	A12 + B12→AB12	−8	12.6	E + I
			NCH$_3$	Mel + Me2→Me12	−50	10.7	E
(9a)	$PhCH_2\overset{+}{N}H_3NCS^-$	1:2	NCH$_2$	A12 + B12→AB12	−6	12.7	E + I
			NCH$_3$	Mel + Me2→Me12	−65	9.9	E
(9a)	$(R)\text{-}PhCHMe\overset{+}{N}H_3NCS^-$	1:1	NCH$_2$	{ A1D2 + D1A2→AD12 / B1C2 + C1B2→BC12	−16	12.2	E + I
			NCH$_3$	Mel + Me2→Me12	−56	10.9	E
			$\overset{+}{N}$H$_3$	G1 + G2→G12	−62	10.4	E
(9a)	$(R)\text{-}PhCHMe\overset{+}{N}H_3NCS^-$	1:2	NCH$_3$	Mel + Me2→Me12	−60	10.5	E
			CH$_3$	F + C→FC	−80	9.8	E1 + E2
			$^+$NH$_2$	F + C→FC	−55	10.5	E1 + E2
(9a)	$(R,S)\text{-}PhCHMe\overset{+}{N}H_3NCS^-$	1:1	NCH$_2$	AC1BD2 + BD1AC2→ABCD12	−14	12.4	E + I, E1 + I, E2 + I
			NCH$_2$	{ A1 + C1[+B2 + D2]→AC1BD2 / B1 + D1[+A2 + C2]→BD1AC2	−55	10.6	E, E1, E2
			NCH$_3$	Mel + Me2→Me12	−54	10.7	E,E2
(9b)	$PhCH_2\overset{+}{N}H_3NCS^-$	1:1	NCH$_2$	AC + BD→ABCD	−24	12.3	E + I
			NCH$_2$	{ B + D→BD / A + C→AC	−105	8.0	C
(9b)	$(R)\text{-}PhCHMe\overset{+}{N}H_3NCS^-$	1:1	NCH$_2$	{ A12 + D12→AD12 / B12 + C12→BC12	−16	12.3	E + I
			NCH$_3$	Mel + Me2→Me12	ca. −92	ca. 8.4	C
(9b)	$(R)\text{-}PhCHMe\overset{+}{N}H_3$ NCS$^-$	1:1.3	NCH$_2$	BD12 + AC12→ABCD12	−20	12.0	E + I, E1 + I
			NCH$_3$	Mel + Me2→Me12	ca. −90	ca. 8.5	C
(9b)	$(R,S)\text{-}PhCHMe\overset{+}{N}H_3$ NCS$^-$	1:2	NCH$_2$	BD12 + AC12→ABCD12	−18	12.1	E + I, E1 + I
			CH$_3$	F + C→FC	−65	10.2	E,E1
			$^+$NH$_3$	F + C→FC	−66	10.2	E,E1
(1)	$PhCH_2\overset{+}{N}H_3NCS^-$ or ClO$_4^-$	1:1	OCH$_2$	{ A + C→AC / B + D→BD	−100	8.4	
(1)	(R)- or $(R,S)\text{-}PhCHMe\overset{+}{N}H_3$ NCS$^-$	1:1	OCH$_2$	{ A1 + A2→A12 / B1 + B2→B12 } { C1 + C2→C12 / D1 + D2→D12	−100	8.0	

[a] NCH$_3$, NCH$_2$, and OCH$_2$ signals refer to the host molecule, other signals are associated with the guest molecule. [b] The labels A12, B12, *etc.* are used as in Table 1, Schemes 1—9, and Figures 1—8. G1 and G2 refer to guest signals in the two diastereoisomeric complexes. F and C refer to the signals of free and complexed guest species respectively. [c] Calculated using the approximations referred to in ref. 11 that are appropriate for a coalescing AB system or two coalescing singlet signals.

view of the rather broad lines obtained from the complexes at low temperatures, the spectra were not of adequate quality to justify a full line-shape analysis. Details of site exchanges and the approximate values of energy barriers are summarised in Table 2.

RESULTS AND DISCUSSION

Complex Formation.—The macrocycles (9)—(11) of both series formed complexes in CDCl$_3$ and CD$_2$Cl$_2$ with primary alkylammonium thiocyanates as evidenced by (i) increased solubility of the guest ammonium salt, (ii)

of the simple crown ether, 18-crown-6 (1), were examined and where these results extend and complement those of a recently reported study [12] they will be discussed in this paper.

Complexes of Monoaza 15-*Crown*-5 *Systems.*—Previous results obtained for a wide range of diaza crown ether analogues [7] have shown that ^{1}H n.m.r. line-shape studies can give quantitative information on the relative strengths of guest–host binding in related complexes and similar methods have been used in a thorough investigation [12] of both the equilibria and the kinetics of

complex formation for a range of crown ethers. The principal objective of the work described in this paper was to obtain structural information for complexes in solution to complement that obtained, or obtainable, by X-ray crystallographic studies of crystalline complexes. Thus the crystal structure of the complex (3), indicates a structure of C_1 symmetry and our earlier n.m.r. observations indicated that even at low temperatures ($-60°$) signals in the n.m.r. spectrum are averaged by a process that, for example, exchanges the two N-methyl groups between the two different environments clearly apparent in (3). The monoaza systems presented a simpler structural problem and accordingly complexes were examined in which the guest molecule was achiral (benzylammonium thiocyanate) or chiral (phenylethyl-ammonium thiocyanate), and in the latter case both the

FIGURE 1 ^{1}H N.m.r. spectrum (220 MHz) of host NCH$_2$ and NCH$_3$ protons of the complex of (9b) with benzylammonium thiocyanate in CD$_2$Cl$_2$ (host : guest ratio 1 : 1). The spectra at $+10$ and $-60°$ are recorded on the 5 p.p.m. scale and at -95 and $-110°$ on the 10 p.p.m. scale

racemic (R,S)-salt and the enantiomerically pure (R)-salt were used.

The n.m.r. spectrum of the benzylammonium thio-

* Subsequent discussion shows that this is oversimplified and that in fact the situation is as depicted in Scheme 1 for (12a) ⇌ (12b).

† In this discussion 'fast' and 'slow' will refer to the n.m.r. time scale.

cyanate complex of (9b) in CD$_2$Cl$_2$ showed temperature dependence which is illustrated in Figure 1. The NCH$_2$ protons gave the expected triplet signal at normal probe

SCHEME 1 Guest–host exchange processes and conformational interconversions for complexes of monoaza 15-crown-5 systems with an achiral guest. In Schemes of this type a multiple label AC etc. indicates that a situation is being considered in which exchange of protons between the sites A and C etc. is already rapid on the n.m.r. time scale

temperature which separated into two broad multiplet signals assignable to the A and B protons of a four spin system (NCH$_A$H$_B$CH$_2$O) * as the temperature of the solution was lowered. This change is consistent with slow † exchange of the guest molecule between the two faces of the host at temperatures below $-22°$; the exchange process would require dissociation of the complex, inversion of the conformation of the host macrocycle, and recombination of free guest and free host [cf. Scheme 1, (12a) ⇌ (12b)].‡ Processes of this type have previously been observed for the diaza analogues of crown ethers and they have been designated as E + I. At still lower temperatures ($< -102°$) the two broad multiplet NCH$_2$ signals separated to give two pairs of signals A and B and C and D [see (13)] § as would be expected for a complex having structure (13) in which individual hydrogen atoms of the NCH$_2$ groups are represented by the appropriate labels. The process C that becomes fast above $-102°$ is evidently associated with the interconversion of the two conformations (13a and b) and involves an energy barrier significantly lower (Table 2) than that associated with the process E + I. The value of this energy barrier ($\Delta G^\ddagger$ ca. 8.0
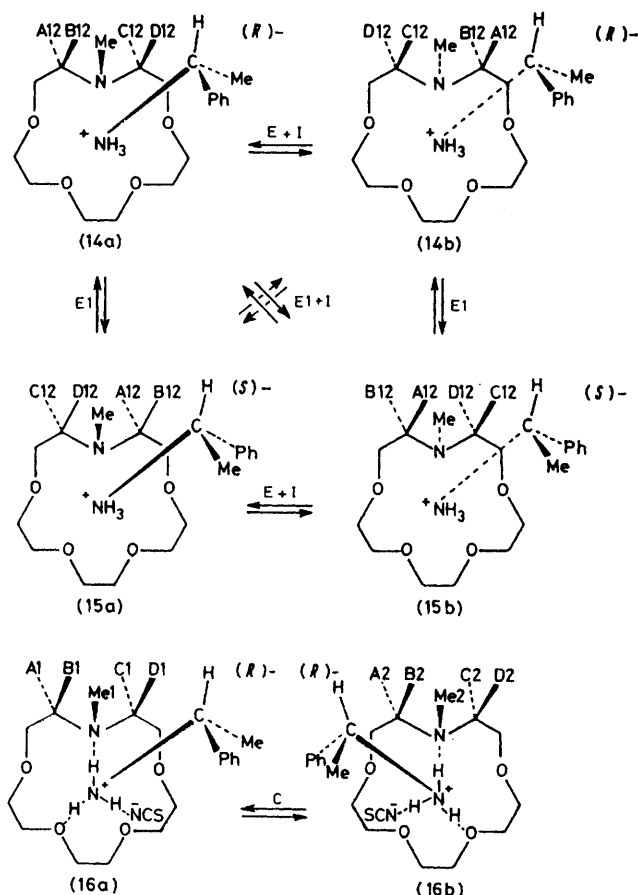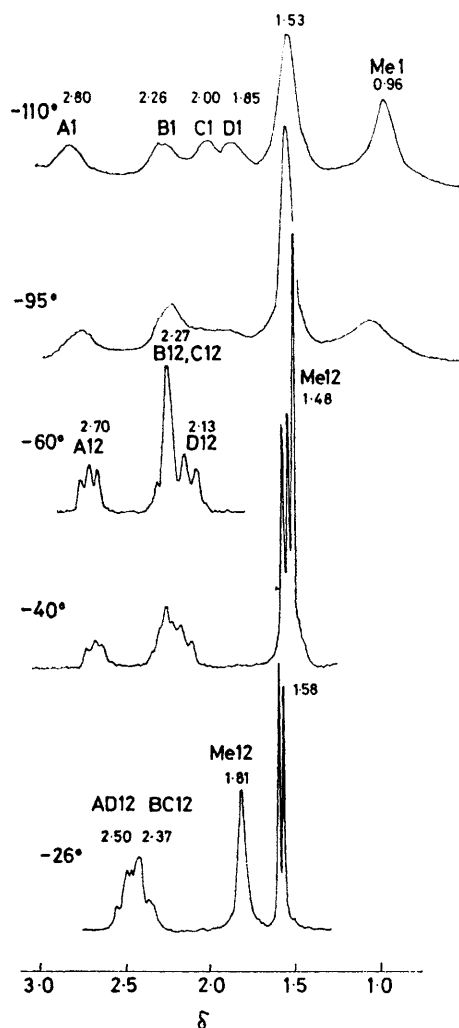
‡ For ease of representation, and by analogy with structure (3), the structure of complexes in Schemes 1, 2, 4, and 5 are drawn with the hydrogen bonds and positive charges located as shown. This is not intended to exclude the possibility that in some cases the proton in an MeN $\cdots$ H—NH$_2$R system may reside on the nitrogen atom of the host macrocycle rather than the guest NH$_2$ group.

§ Labels such as A, B, C, D etc. used in Schemes and Figures are arbitrary, it is not possible to make assignments from the evidence available.

kcal mol^{-1}) for the process (13a) $\rightleftharpoons$ (13b) is compatible with a mechanism involving (a) some breaking of hydrogen bonds and (b) a change in sign of a torsion angle about an OC–CO bond passing through the eclipsed conformation. These conformational changes and guest–host exchange processes are illustrated in Scheme 1, which shows the effects of these processes upon the four protons (NCH$_A$H$_B$ and NCH$_C$H$_D$) associated with the four sites A—D of the 'frozen' structure. The actual site exchanges associated with each type of process are shown more directly in Scheme 3a which permits a rapid appreciation of their effects upon the n.m.r. spectrum.

The above conclusions can be checked by the use of a chiral guest which may be either enantiomerically pure (R)- or racemic (R,S)-phenylethylammonium thiocyanate. The temperature dependence of the n.m.r. spectrum of the complex of (9b) with (R)-phenylethyl-

FIGURE 2 ^{1}H N.m.r. spectrum (220 MHz) of host NCH$_2$ and NCH$_3$ and guest CH$_3$ protons of the complex of (9b) with (R)-phenylethylammonium thiocyanate in CD$_2$Cl$_2$ (host : guest ratio 1 : 1). The spectra are all recorded on the 10 p.p.m. scale

ammonium thiocyanate in CD$_2$Cl$_2$ is shown in Figure 2. The NCH$_2$ protons are observed as a multiplet at normal

probe temperature corresponding to a fast rate on the n.m.r. time scale for the processes C and E + 1 in

SCHEME 2 Guest–host exchange processes and conformationa interconversions for complexes of monoaza 15-crown-5 systems with a chiral guest

Scheme 2. It is noted that in this case the four signals corresponding to the averaged sites A12, B12, C12, and D12 of (14a and b) are only exchanged in the pairs indicated by Scheme 3b as a result of the process E + 1. As the solution is cooled the four multiplet signals associated with the sites A12—D12 separate out in accord with a slow process E + I with process C remaining fast on the n.m.r. time scale. Finally below —95° further complex changes occur, which are not clearly resolved and must be associated with the separation of signals corresponding to the eight different NCH$_2$ sites of the two diastereomeric conformations (16a and b). In particular this process affects the NMe signal (see Figure 2 and Scheme 2), in contrast with the situation for the achiral guest for which the two conformations (13a and b) are related as enantiomers with a corresponding lack of effect on the NMe signal. The two conformations (16a and b) have rather different populations and only signals associated with the major conformer are resolved; it is clear from the temperature range in which the spectral changes occur that the energy barrier associated with the process (16a) $\rightleftharpoons$ (16b) is of the same order as that

associated with the closely related process (13a) ⇌ (13b).

The spectrum (Figure 3) of the complex of (R,S)-phenylethylammonium thiocyanate with the host (9b) is virtually identical with that of the (R)-guest at temperatures below −70° but at higher temperatures differences are apparent. Thus at normal probe temperatures the NCH_2 protons give rise to a triplet signal since site averaging occurs as a result not only of processes E + I and C but also the processes E1 and E1 + I which involve exchange of (R)- and (S)-guests (Schemes 2 and 3b). As the temperature is lowered the processes E + I and E1 + I become slow but process E1, which does not require a

of this type may however not be too significant since it has been shown for simple crown ethers that bimolecular processes may make a contribution to guest exchange. It is therefore simpler to relate the strength of the complex to the magnitude of the energy barrier for the process E + I which does not show a significant dependence upon the concentration of the guest species.

Thus the n.m.r. spectra of the complexes of the monoaza 15-crown-5 system (9b) lead to the following conclusions. (i) The structure of the complex must lack symmetry as indicated in formulae (13) and (16), and the two-site attachment of the guest NH_3 group shown in these formulae with a third hydrogen bond to the thio-
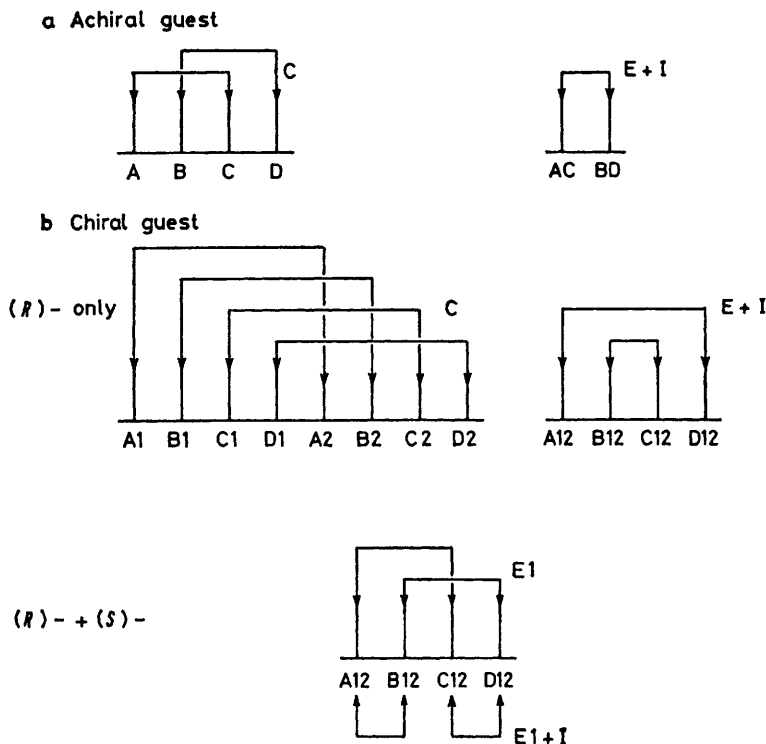
SCHEME 3 Site exchanges associated with the NCH_2 protons of monoaza 15-crown-5 complexes. The site averaging associated with the fast process C has been incorporated into the schemes associated with the slower processes E + I, E1, and E1 + I

substantial conformational change of the host molecule, remains fast on the n.m.r. time scale and only two signals are observed corresponding to the averaged sites AC12 and BD12. When the temperature is lowered further the process E1 also becomes slow and the four signals A12—D12 are separately resolved. At this point the spectrum becomes identical with that of the complex of the (R)-guest. Processes related to E1, involving just exchange of guest molecules, are also observable in the spectra of complexes prepared using two equivalents of the guest species, as shown in our earlier work using diaza analogues of crown ethers. Thus in the presence of excess (R)- or (R,S)-phenylethylammonium thiocyanate the n.m.r. spectrum of the complex shows two poorly resolved signals for the guest ArCH proton below −65° and two signals for the guest CH_3 protons. The magnitudes of the associated energy barriers for the exchange processes

cyanate counter ion is consistent with this lack of symmetry and also provides a satisfying link with the crystal structure of the complex (3). (ii) Conformational changes and reorganisation of the hydrogen bonding interconvert the pairs of complexes (13a and b) and (16a and b). The energy barriers associated with these processes are significantly lower than those associated with dissociation of the complex since the energy barrier for dissociation must be at least as large as that for the process E1. It is probable that fast structural reorganisation of this type is a general phenomenon in crown ether complexes with ammonium salts, although in many cases it will not be an identifiable process. (iii) The single NMe signal observable at all temperatures for the complex of (9b) with benzylammonium thiocyanate is consistent with a single orientation of the NMe group with respect to the mean plane of the macro-

cycle. The crystal structure (3), the examination of molecular models, and the high field shift associated with
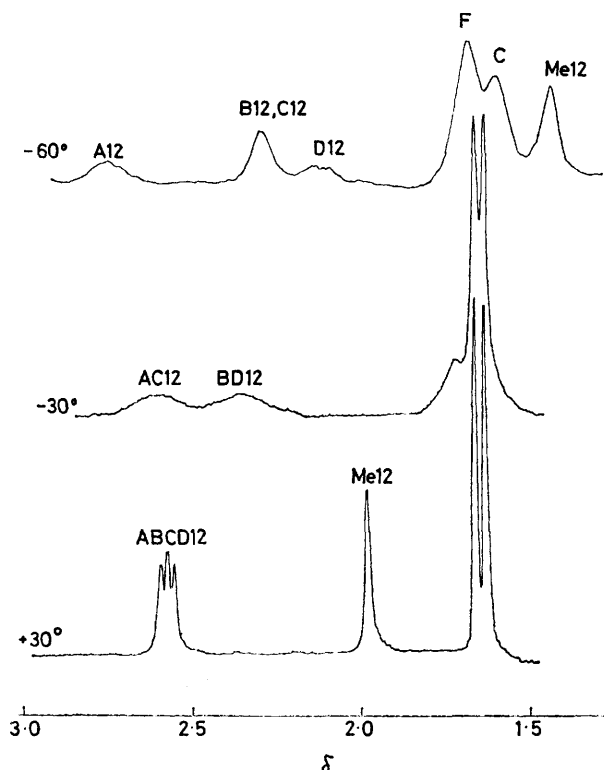

FIGURE 3 ¹H N.m.r. spectrum (220 MHz) of host NCH_2 and NCH_3 and guest CH_3 protons of the complex of (9b) with (R,S)-phenylethylammonium thiocyanate in CD_2Cl_2 (host : guest ratio 1 : 2). The signals labelled F and C in the spectrum recorded at 60° refer to the CMe groups of free and complexed guest molecules respectively. The spectra are recorded on the 5 p.p.m. scale

this methyl group when the guest molecule contains a phenyl substituent are all consistent with a preferred *syn*-relationship between the NMe group and the guest molecule as indicated in formulae (12)—(16). This situation contrasts with that found for monoaza 18-crown-6 systems.

Complexes of Monoaza 18-*Crown*-6 *Systems.*—The temperature dependence of the n.m.r. spectrum of the benzylammonium thiocyanate complex of the 18-crown-6 derivative (9a) is shown in Figure 4. The NCH_2 protons separate into two multiplet signals below —5° consistent with slow face to face exchange of the guest cation by the process E + I shown in Scheme 4. These multiplets are resolved as a triplet and a doublet at —30° consistent with a synclinal relationship between the two heteroatoms of the OCH_2CH_2N unit. At lower temperatures additional temperature dependence associated with the host NMe signal, indicates that the complex consists of an equilibrium mixture of two diastereoisomeric species giving rise to two NMe signals with an intensity ratio of 2.2 : 1 (Figure 4, —80° spectrum). The signals of the NCH_2 groups also change slightly but separate signals associated with the two species are not resolved. This

spectral behaviour can be rationalised in terms of the two types of complex (17) and (18), shown in Scheme 4 and the site exchanges summarised in Scheme 6a. The interconversion of the species (17) and (18) involves a dissociation–recombination process and no major conformational change of the host macrocycle, it can therefore take place more rapidly than the process E + I which interconverts pairs of complexes related as (17a and b) or (18a and b). Thus the signals observed at 0 and —30° represent averaged signals as indicated by the site labels in Scheme 4 and Figure 4. The further possibility that species related as (17a) and (18b) are interconverted by a process I that involves inversion of the conformation of the host macrocycle without dissociation of the complex cannot be ruled out at this stage.

The spectral behaviour of the (R)-phenylethyl-ammonium thiocyanate complex of (9a) is illustrated in Figure 5. At +26° the NCH_2 signals are observable as a multiplet, similar to that observed for the NCH_2 protons of the analogous complex of (9b); this is consistent with rapid interconversion of the complexes (19) and (21) by the processes illustrated in Scheme 5 and the site exchanges outlined in Scheme 6b. The NCH_2 multiplet broadens and separates into four signals assignable to the averaged sites A12—D12 (Figure 5 and Scheme 5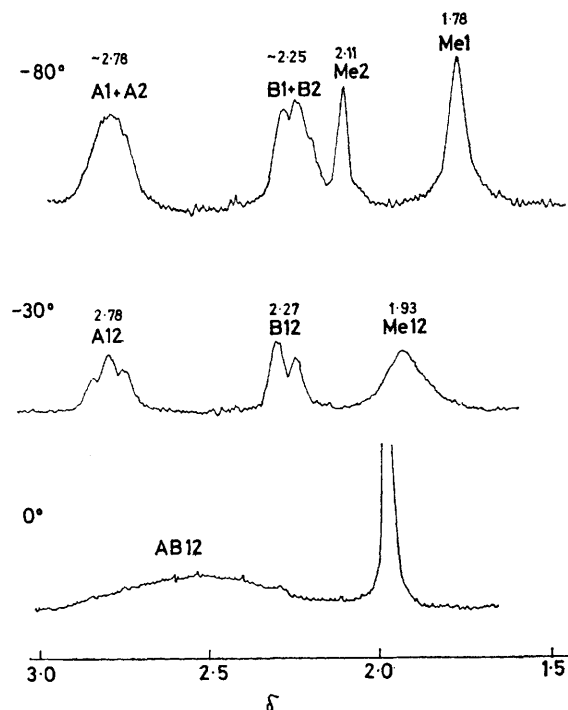) at —40°. At lower temperature the NCH_2 signals show further temperature dependence and at —80° four reasonably well resolved multiplets are

FIGURE 4 ¹H N.m.r. spectrum (220 MHz) of host NCH_2 and NCH_3 protons of the complex of (9a) with benzylammonium thiocyanate (host : guest ratio 1 : 1). The spectra are all recorded on the 5 p.p.m. scale

observable corresponding to the four sites A1—D1 of the major diastereoisomer. The NMe signals separates into two signals, intensity ratio 1.7 : 1, below −54° indicating the presence of two diastereoisomers. In addition the $\overset{+}{N}H_3$ signal of the guest cation separates into two signals with a similar ratio of intensities (G1 and G2, Figure 5) corresponding to the two diastereoisomeric complexes. The host signals behave in a similar way in the presence of excess guest (1 mole host : 2 moles guest) but the guest $\overset{+}{N}H_3$ signal and CH₃ signal show temperature dependence associated with slow interconversion of the two types of complex (see broken lines in Figure 5) and slow interconversion of complexed and free guest cations in the same temperature range. This is con-

limited spectral evidence available. For the (R)-guest only the left hand side of Scheme 5 and the upper part of Scheme 6b are relevant. In the absence of accurate line shape analysis it is reasonable to conclude that the interconversion of the diastereoisomeric complexes occurs at a similar rate to the exchange of guest molecules and that dissociation of the complex is the rate-determining step in both cases.

The simplest conclusions consistent with the spectral behaviour summarised above and illustrated in Figures 4—6 are as follows. (i) The complex is bound by three point attachment of the guest $\overset{+}{N}H_3$ to the host macrocycle since there is no evidence for a low energy process analogous to that observed for the monoaza 15-crown-5
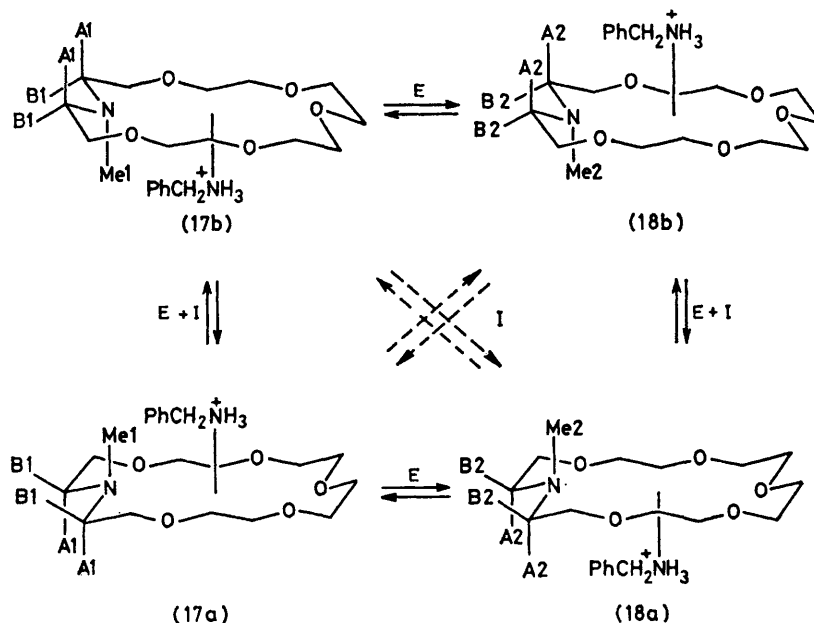
SCHEME 4 Guest–host exchange processes for complexes of monoaza 18-crown-6 with an achiral guest

sistent with an interconversion process E involving dissociation and recombination rather than inversion of the host macrocycle (process 1, Scheme 4). The use of an (R,S)-guest resulted in an analogous series of spectra, with the same relationships to those of the complex of the (R)-guest as shown by the complexes of the 15-crown-5 analogue (9b). The relevant spectral changes are illustrated in Figure 6 and we note the total averaging of all eight NCH₂ sites at +20°, the separation of two NCH₂ signals at −40° corresponding to a slow rate for processes involving face-to-face guest exchange and inversion of the host macrocycle, and finally at −80° the signals for both the NCH₂ and NMe host protons are virtually identical with those for the complex of the (R)-guest. These spectral changes for the complex of the (R,S)-guest may be rationalised in terms of the exchange processes shown in Scheme 5 and the corresponding site exchanges summarised in Scheme 6b. These Schemes are complex and it is not possible to comment in detail upon the rates of individual processes from the

complexes, and this opinion is analogous with opinions regarding ammonium salt complexes with 18-crown-6 systems. (ii) The two diastereoisomeric complexes are related as shown in Schemes 4 and 5, the major complex gives a high field methyl signal and it is assumed that this is the complex in which the guest phenyl substituent is above the same face of the macrocycle as the host NMe substituent. The actual binding sites cannot be defined and on the basis of the examination of models attachment of the hydrogen bonds to either set of three alternate heteroatoms in the host macrocycle seems equally likely. Furthermore there is the possibility that both types of hydrogen bonding schemes operate and that the two complexes related in this way are in an equilibrium which is rapid on the n.m.r. time scale at the lowest available temperature (−110°). (iii) The monoaza 18-crown-6 complexes do not have a unique structure, unlike the complexes of the monoaza-15-crown-5 system. They are therefore less suitable as a basis for the construction of a well defined complex with a fixed

relationship between the side chain on the nitrogen atom and the guest molecule.

The complexes formed between the N-ethyl macrocycle (11a) and alkylammonium thiocyanates give n.m.r. spectra which show temperature dependence, but the changes are not as well defined as those of the N-methyl

meric complexes related as (17) and (18) and the associated energy barrier is similar in magnitude to that found for the analogous complex of the N-methyl derivative (9a).

The complexes of the N-benzyl macrocycle (10a) also have temperature dependent n.m.r. spectra. The spectral changes are not well resolved but can be associ-
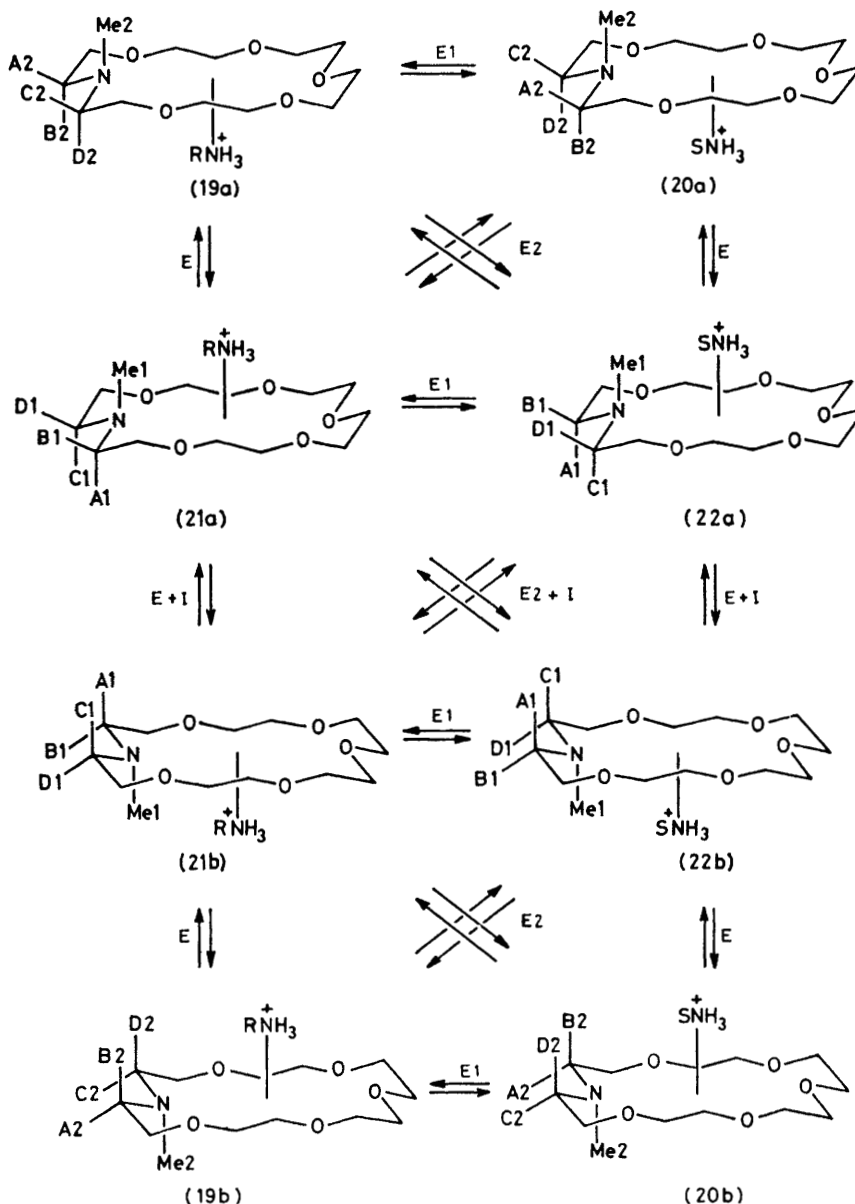
SCHEME 5 Guest–host exchange processes for complexes of monoaza 18-crown-6 with a chiral guest

derivative. Thus the complex of (11a) with (R)-phenylethylammonium thiocyanate shows complex unresolved changes in the NCH$_2$ and OCH$_2$ regions of its n.m.r. spectrum in the temperature range -50 to $-70°$ but the only clearly resolved change is associated with the signal from the guest $\overset{+}{N}H_3$ protons. This signal broadens and separates into two signals, intensity ratio ca. 3 : 1, below $-55°$, this change we associate with slow exchange of the guest species between two diastereoiso-

ated with the presence of two diastereoisomeric complexes, related as (17) and (18), together with a slow process E + I at low temperatures. The derived energy barriers are similar to those for complexes of the N-methyl derivative (9a) and diastereoisomer ratios are also rather similar. Thus the general comments on the spectral behaviour of the complexes of the N-methyl derivative (9a) and the conclusions (i)—(iii) also apply to the N-ethyl (11a) and N-benzyl (10a) derivatives.

Complexes of 18-*Crown*-6.—Studies of the n.m.r. spectra of complexes of crown ethers such as (1) at low temperatures had not been reported when this work was initiated but recently methods have been reported[12] whereby details of both the dynamics and the associated equilibrium for the formation of complexes with alkylammonium salts may be studied in considerable detail.
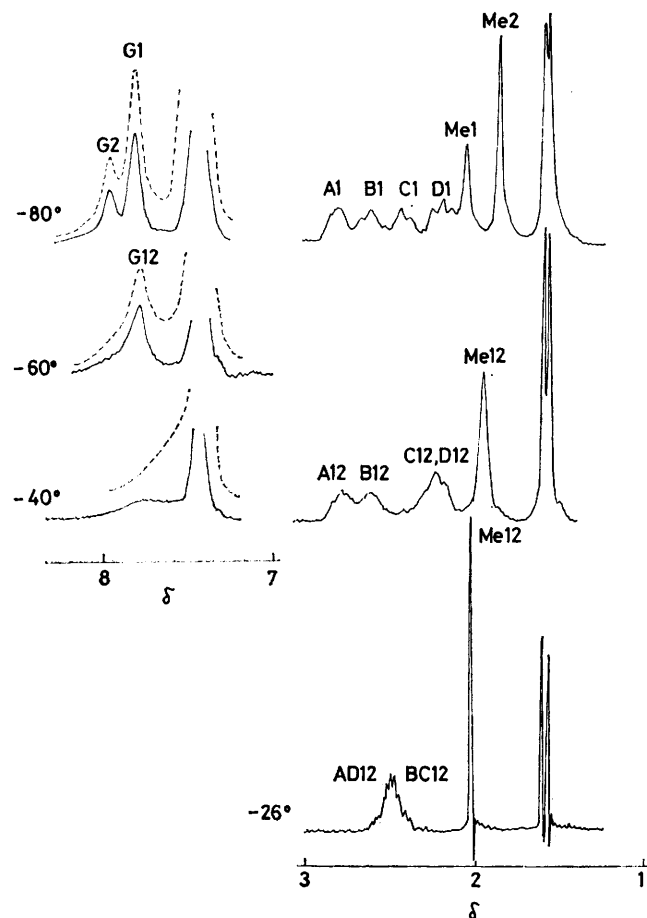

FIGURE 5   [1]H N.m.r. spectrum (220 MHz) of host NCH$_2$ and NCH$_3$ and guest CH$_3$ and NH$_3$ protons of the complex of (9a) with (R)-phenylethylammonium thiocyanate (host:guest ratio 1 : 1). The signals labelled G12, G1, and G2 in the spectrum refer to the NH$_3$ signals of the two diastereoisomeric complexes. The spectra are all recorded on the 10 p.p.m. scale. The spectra shown with broken lines refer to a sample with a host:guest ratio of 1 : 2

The results described in this section are complementary to these studies in that they define the dynamic behaviour of the macrocycle in an 18-crown-6 complex.

The n.m.r. spectrum of the benzylammonium thiocyanate complex of 18-crown-6 is shown in Figures 7a and 7b. Although details of coupling constants cannot be obtained from the rather poorly resolved spectra at low temperatures it is clear that at least two distinct processes must be responsible for the observed spectral changes. Thus the host protons give rise to a singlet at 26° which at −60° is replaced by a symmetrical multiplet corresponding to an AA'BB' system (Figure 7a) and at

−110° the spectrum is asymmetrical and consistent with an ABCD system (Figure 7b). The first of these changes

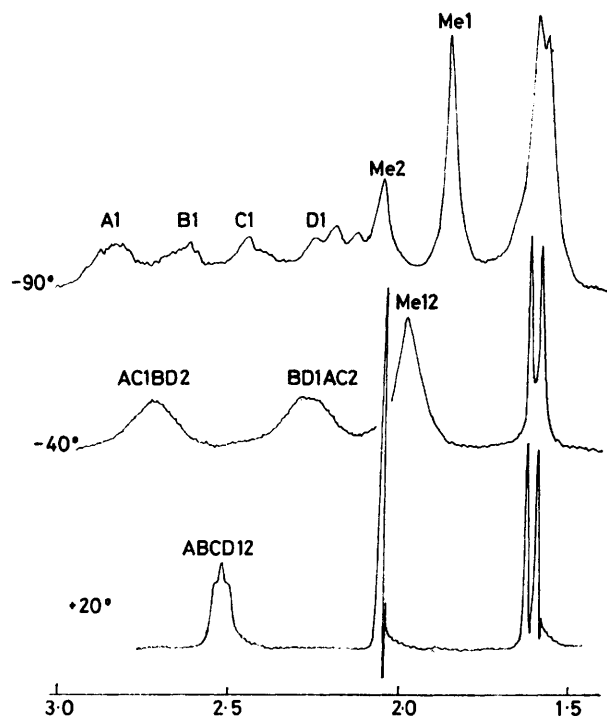FIGURE 6   [1]H N.m.r. spectrum (220 MHz) of host NCH$_2$ and NCH$_3$ and guest CH$_3$ protons of the complex of (9a) with (R,S)-phenylethylammonium thiocyanate (host:guest ratio 1 : 1). The spectra are all recorded on the 5 p.p.m. scale

is in accord with expectation if the change to an AA'BB' system is due to slow face to face exchange of the guest ammonium salt (see process E, Schemes 7 and 9a), as
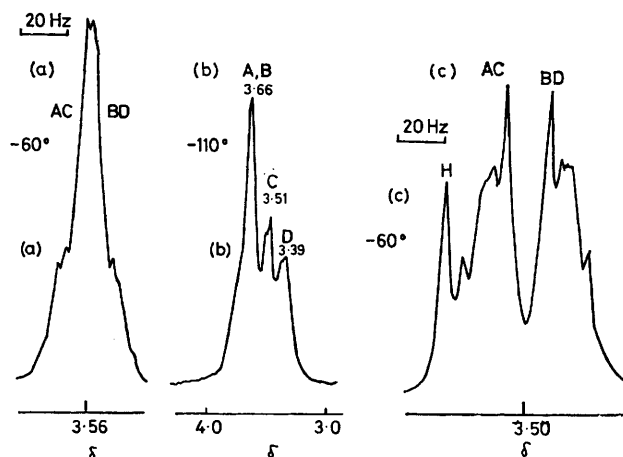

FIGURE 7   [1]H N.m.r. spectrum of the host protons of the complex of 18-crown-6 (1) with (a) and (b) benzylammonium thiocyanate and (c) diphenylmethylammonium thiocyanate (host:guest ratio ca. 1 : 1). Spectra (a) and (b) are recorded on the 500 Hz and 10 p.p.m. scales respectively. Spectrum (c) is recorded on the 500 Hz scale and the signal marked H refers to a slight excess of the host species

would be expected by analogy with the reported n.m.r. behaviour of the t-butylammonium complex. The

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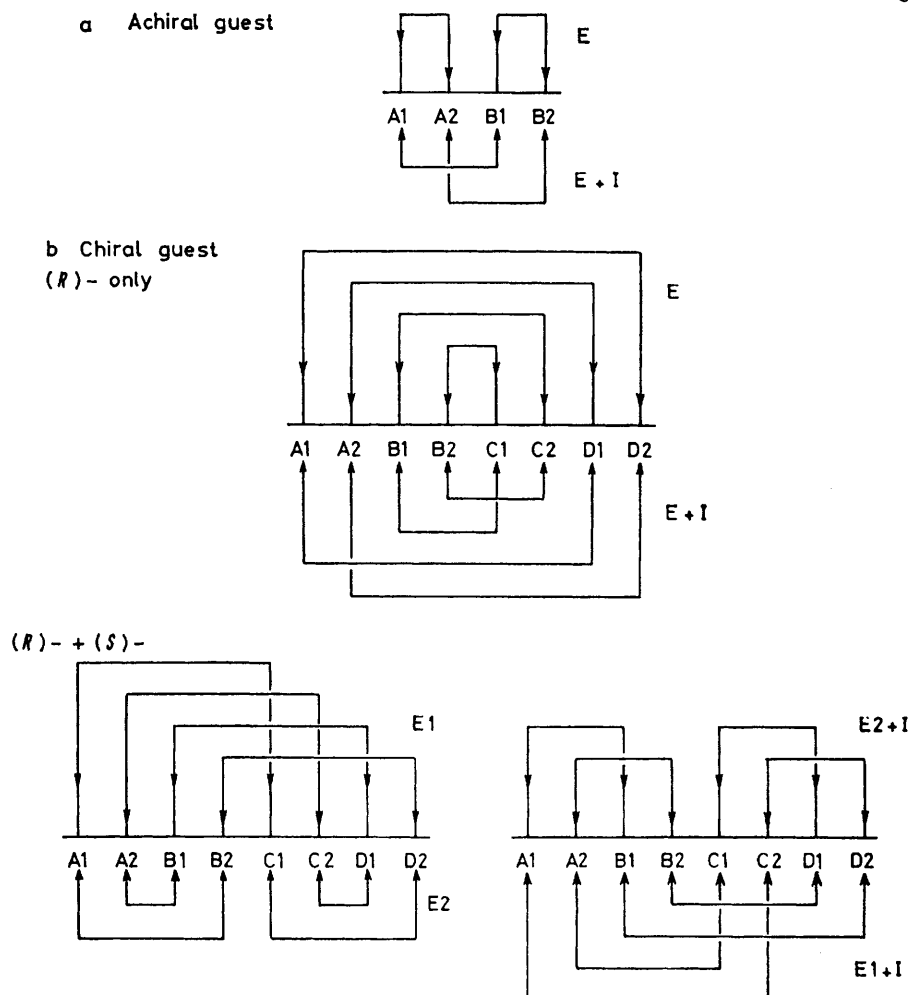
SCHEME 6   Site exchanges associated with the NCH_2 protons of monoaza 18-crown-6 complexes
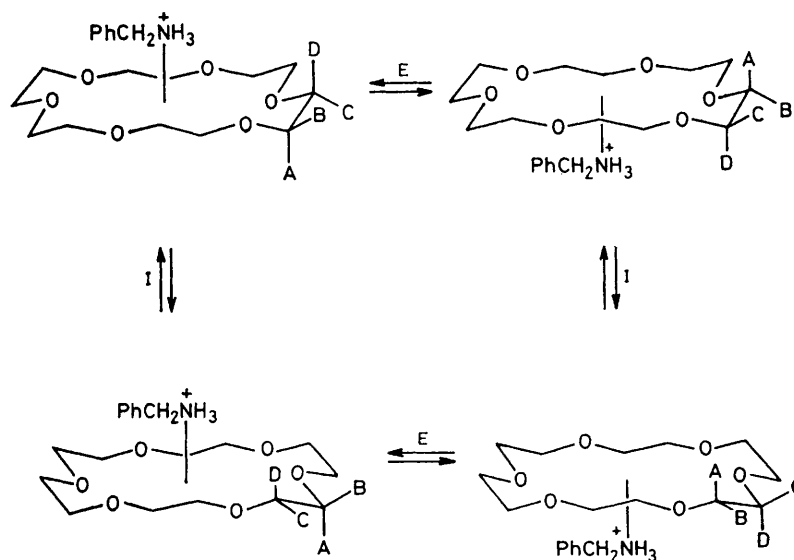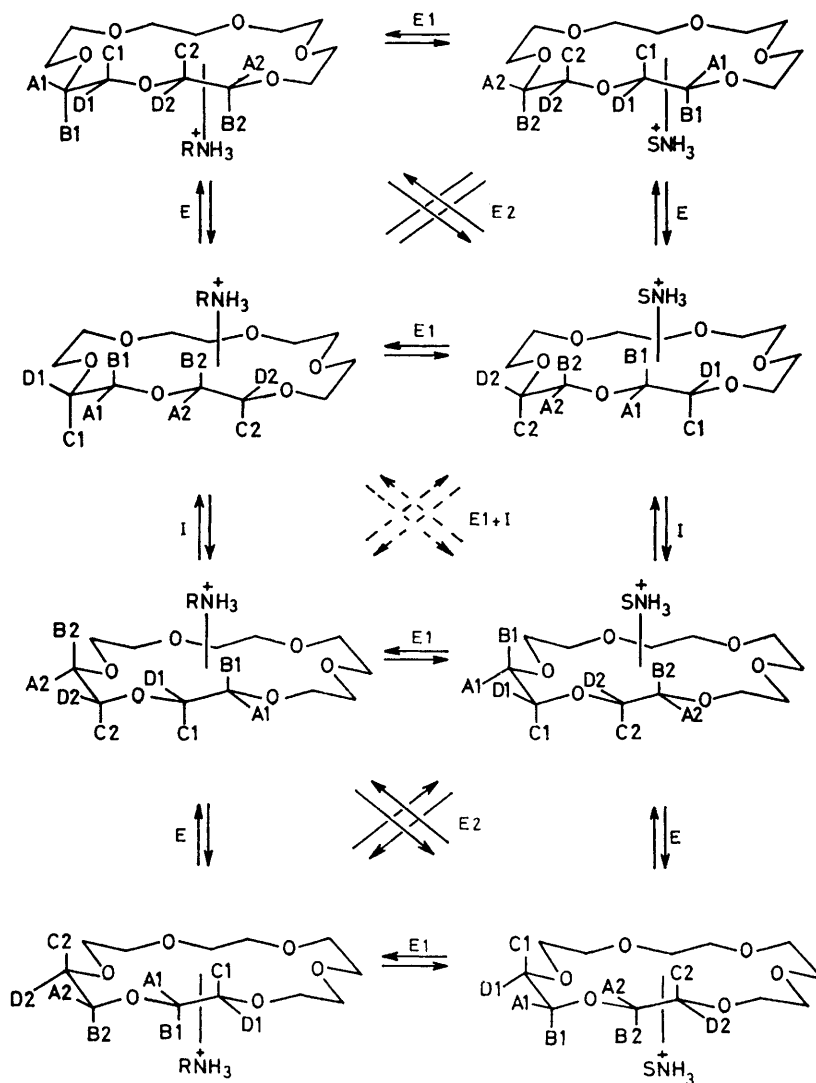

SCHEME 7   Guest–host exchange processes and conformational changes for complexes of 18-crown-6 with an achiral guest

separation of the spectrum into an AA'BB' system is rather clearer for the diphenylmethylammonium salt, and the spectrum of this complex at —60° is shown in Figure 7c.   The averaging of signals at —60° is associ-

ated with an apparent six-fold symmetry at this temperature * and it can only be related to a rapid process whereby all six oxygens in the complex become equivalent; this requires (i) ring inversion and (ii) rapid transfer of the hydrogen bonding between $\overset{+}{N}H_3$ and each of the two sets of three alternate oxygen atoms. At $-110°$ this process is evidently slow on the n.m.r. time scale

ation that the addition of excess benzylammonium thiocyanate to the complex leads to the observation of separate signals for the $\overset{+}{N}H_3$ group of the complexed and free salt at significantly higher temperatures than those at which the spectrum of the host molecule separates out into an ABCD system. The energy barrier associated with the guest exchange process E depends upon the

SCHEME 8   Guest–host exchange processes and conformational changes for complexes of 18-crown-6 with a chiral guest

and the spectrum that is observed is consistent with that of a ' frozen ' complex having only apparent three-fold symmetry. Thus the temperature dependence of the spectrum of the complex is an accord with the behaviour shown in Scheme 7 which leads to the site exchanges outlined in Scheme 9. The process I in Scheme 7 must occur without dissociation of the complex because it gives rise to spectral changes in a significantly lower temperature range than those associated with the exchange process E. This deduction is supported by the observ-

* This description assumes rapid rotation about the $\overset{+}{N}$–C bond of the guest molecule.

concentration of the free guest in solution in accord with the published observation [12] that a bimolecular process can operate for guest exchange in complexes of 18-crown-6.

The n.m.r. spectra of the complexes of 18-crown-6 with either (R)- or (R,S)-phenylethylammonium thiocyanate both show similar temperature dependence (Figure 8), except that in the former case the prochiral methylene groups of the OCH_2CH_2O system of the macrocycle give rise to a barely resolved AA'BB' system at 26° and in the latter they give a singlet. This result is consistent with the site exchanges based upon Scheme 8

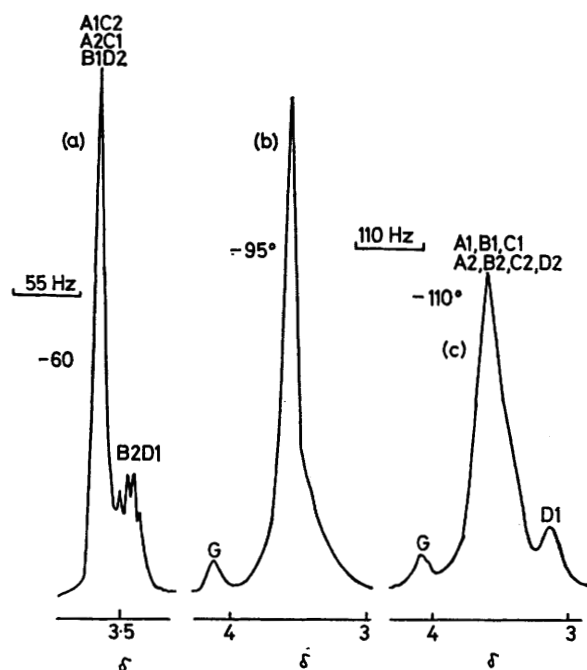which are indicated in Scheme 9, for an (R)-guest it is clear that averaging can only lead to two sites, AD1BC2

FIGURE 8   ¹H N.m.r. spectrum of the host protons and the guest CH proton of the complex of 18-crown-6 (1) with (R,S)-phenyl-ethylammonium thiocyanate (host:guest ratio 1:1). Spectrum (a) is recorded on the 5 p.p.m. scale and spectra (b) and (c) on the 10 p.p.m. scale and G refers to the guest CH signal

and AD2BC1, whereas for an (R,S)-guest the additional exchange processes E1 and E2 lead to averaging over all eight sites.   At −60° the processes E, E1, and E2 all

become slow and in both cases only the site averaging process I occurs with a fast rate leading to the observation of an ABCD system in which the averaged sites A1C2, A2C1, B1D2, and B2D1 have very similar chemical shifts (Figure 8a).   Finally at −110° seven of the sites give rise to a broad singlet signal and only the eighth site is separately resolved (Figure 8c).   The assignment of site labels in Scheme 8 is necessarily arbitrary, as in all similar Schemes in this paper, but this does not affect the validity of our arguments concerning the nature of the exchange processes and conformational changes.   If excess of the guest ammonium salt is added to the complexes it is again possible to observe separate signals for the complexed and free guest at temperatures where the process I(Scheme 8) is still fast on the n.m.r. time scale.

The following conclusions regarding the complexes of 18-crown-6 can be derived from this study.   (i) Guest–host exchange can be studied using n.m.r. line shape methods but precautions are required [12] if the exchange processes are to depend entirely upon a unimolecular dissociation recombination process.   (ii) The macro-cyclic ring system in an 18-crown-6-system is mobile and ring inversion, accompanied presumably by some reorganisation of hydrogen bonds, involves only a low energy barrier.   The spectrum of 18-crown-6 does not show temperature dependence down to −110° suggesting that the ring inversion barrier is low, and the spectrum of the complex with diphenylmethylammonium thiocyanate does not show temperature dependence associated with process I becoming slow on the n.m.r. time scale, even at −110°.   The ring inversion process, if stepwise, would involve at least one eclipsed O–C–C–O system and it does not appear that the additional loss of
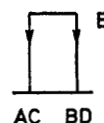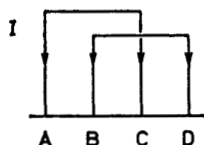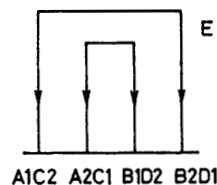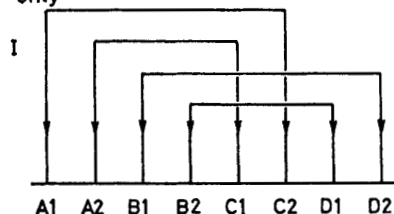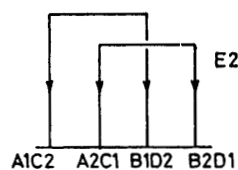

SCHEME 9   Site exchange processes associated with the host protons of 18-crown-6 complexes.   The site averaging associated with the fast process I has been incorporated into the Scheme associated with the slower processes E, E1, and E2

binding energy can be very large in view of the observed low energy barriers ($\Delta G^{\ddagger} \ll 8.5$ kcal mol^{-1}).

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