Bis Mono-aza Crown Ethers. The Formation of Intramolecular Complexes with Dications

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Summary The host molecules (**4a**—**d**), containing two crown ether ring systems, form 1 : 1 complexes (**8**) with the bis primary alkylammonium salt (**7**); in the cases of the hosts (**4a**) and (**4b**) guest–host fit is so good that only the intramolecular complex is formed, but for the other host molecules (**4c**) and (**4d**) the complex (**8**) is probably accompanied by the polymeric complex (**9**).

Host crown ethers, *e.g.* (**1a**), and their aza derivatives having a single 15- or 18-membered macrocycle, *e.g.* (**1b**) and (**1c**), have been shown to form complexes (**2**)† with guest primary alkylammonium cations.[1,2] A number of cases have also been described[3,4] in which complex formation has been postulated to involve secondary binding interactions between additional functional groups X and Y

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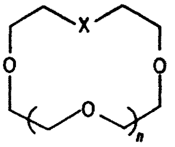
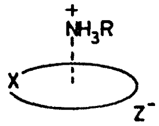
† For simplicity in formulae (**2**), (**3**), (**5**), (**6**), (**8**), and (**9**) the CH$_2$[CH$_2$OCH$_2$]$_4$CH$_2$ systems of the macrocycles are represented by lines.

in the host and guest components as shown diagramatically by the broken line between X and Y in (**3**). These secondary interactions would be expected to both increase guest recognition by the host molecules and to give more highly structured complexes. Binaphthyl systems having two fused crown ether macrocycles have been shown[5] to form complexes with bis primary alkylammonium salts and other polyfunctional guest molecules. It was therefore of interest to examine systems, based upon aza derivatives of crown ethers, in which the host molecule (**4**) has two crown ether macrocycles which could potentially form intramolecular complexes (**5**) with bis primary alkylammonium salts.

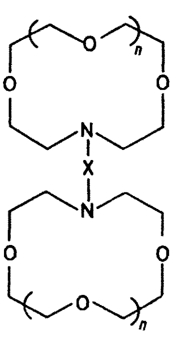


(1)

a; $n = 3$, $X = O$
b; $n = 2$, $X = NR$
c; $n = 3$, $X = NR$

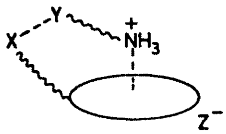


(2)

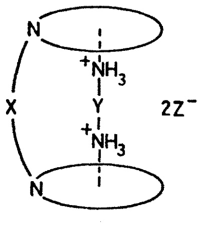


(4)

a; $n = 2$, $X = [CH_2]_4$
b; $n = 2$, $X = [CH_2]_5$
c; $n = 2$, $X = [CH_2]_6$
d; $n = 2$, $X = [CH_2]_7$



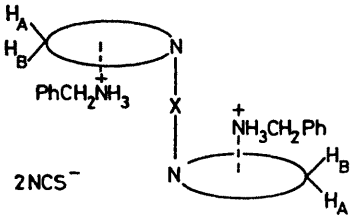
(3)



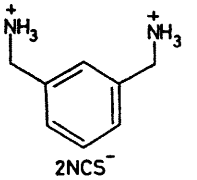
(5)

The host molecules (**4a**—**d**) were readily prepared by the reaction of the mono-aza crown ether (**1b**, R=H) with the appropriate di-acid chloride followed by reduction of the resulting di-amide with lithium aluminium hydride. The hosts (**4a**—**d**) formed *cis,cis*-complexes (**6**) with 2 equiv. benzylammonium thiocyanate in solution. The structure (**6**) follows from the known *cis*-relationship between the guest and the side chain R in the complexes of the monocyclic system (**1b**, R=Me) and the fact that only one type of complex could be detected from the n.m.r. spectrum of a mixture of the two components [2 : 1, guest(G) : host (H) ratio] at low temperatures. Under these conditions guest–host exchange is slow on the n.m.r. time scale, as shown by the non-equivalence of the protons on the two faces of the host macrocycles [see H_A and H_B in (**6**)] and by the recognition of the signals associated with free and complexed host macrocycles in the spectrum of an equimolecular mixture of the two components.

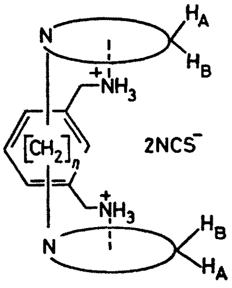
The n.m.r. spectra of 1 : 1 mixtures of the host molecules (**4a**—**d**) and the bis primary alkylammonium salt (**7**) were examined over the temperature range −110 — +25° C. Only a single type of complex was detectable for the host molecules (**4a**) and (**4b**); the bridging methylene groups X in the spectra showed significant shifts to high field as compared with the complexes (**6**) with benzylammonium thiocyanate [Table, and see Figure 1(a) for details of the spectrum of the complex of (**4b**)]. These chemical shifts are consistent with the formation of an intramolecular complex (**8**) in which the aromatic ring of the guest lies over the central methylene groups of the $[CH_2]_n$ bridge. In accordance with the formulation (**8**) the spectra of these complexes show evidence for hindered inversion of the crown ether ring systems [see H_A and H_B in (**8**) and Figure 1(b)] at temperatures below 0 °C.



(6)

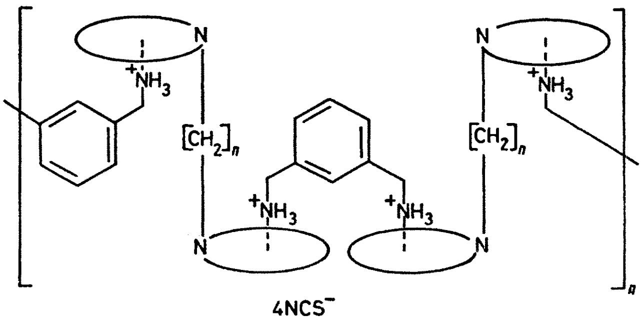


(7)



(8)

At very low temperatures further spectral changes occur [Figure 1(c)] consistent with a hindered conformational change within the complex, possibly involving the interconversion of diastereomeric complexes (*cf*. ref. 2). The n.m.r. spectrum of the host (**4b**) and 0·5 equiv. of the guest (**7**) shows signals associated with free and complexed host below 0 °C (Figure 2) indicating that guest–host exchange is slow on the n.m.r. time scale at these temperatures.



(9)

TABLE. N.m.r. spectra[a] of complexes of bis mono-aza crown ethers (4) with the salt (7) (1 : 1 G : H ratio).

		N.m.r. spectrum of host[b,c]			
Host	X[b]	α-CH_2	β-CH_2	γ-CH_2	δ-CH_2
(4a)	$[CH_2]_4$	1·89 (2·63)	0·90 (1·40)		
(4b)	$[CH_2]_5$	2·10 (2·42)	0·89 (1·43)	0·89 (1·12)	
(4c)	$[CH_2]_6$	2·30 (2·38)	1·05 (1·42)	1·05 (1·18)	
(4d)	$[CH_2]_7$	2·42 (2·43)	1·39 (1·40)	1·20 (1·20)	1·20 (1·20)

[a] Spectra recorded at 220 MHz for 0·1 M solutions in CD_2Cl_2 containing a little CD_3OD at 25 °C. Chemical shifts listed as δ p.p.m. relative to Me_4Si. [b] The bridge X is labelled as NCH_2(α) CH_2(β) CH_2(γ) *etc.* [c] The values in parentheses refer to the corresponding protons in a 2 : 1 complex (G : H ratio) with benzylammonium thiocyanate in CD_2Cl_2 at 25 °C.

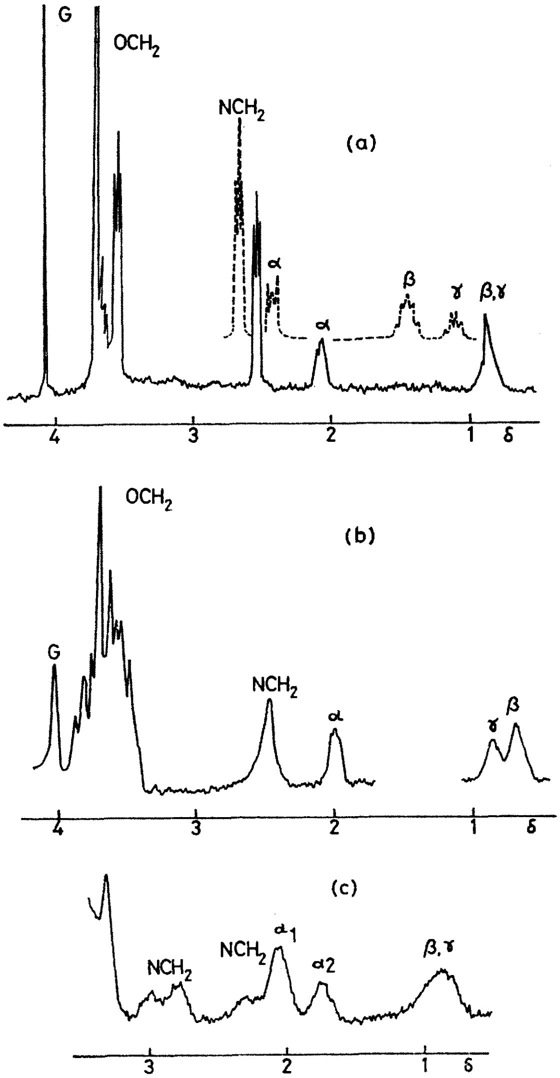


FIGURE 1. N.m.r. spectrum of complex formed between host (**4b**) and guest (**7**) (1 : 1 ratio) at (a) 25, (b) −50, and (c) −105 °C. The spectrum indicated by a broken line in (a) is for the complex of host (**4b**) with 2 equiv. benzylammonium thiocyanate.

The complexes formed by the hosts (**4c**) and (**4d**) show less marked high field shifts for the bridging groups (Table) and at low temperatures additional signals are observable suggesting that two types of complex are present in the solutions. We suggest that these are the intramolecular complex (**8**) and the polymeric complex (**9**) and note that the proportion of (**9**) is higher for (**4d**) than for (**4c**). The n.m.r. spectra of these complexes do not show evidence for hindered conformational changes at low temperatures (⩽ − 100 °C).

The results described here show that flexible host systems, such as (**4**), containing two binding sites use both sites to form intramolecular 1 : 1 complexes with suitable polyfunctional guest molecules provided that guest–host fit is reasonably good. This results, as expected, in a more highly structured complex [*cf.* (**8**)] with presumably twice the binding energy of a complex formed by only a single binding site. This additional binding energy has little effect upon the kinetics of guest–host exchange processes, presumably because they involve consecutive dissociation and recombination at each site. The formation of the complexes (**8**) provides a basis for the design of host molecules forming inclusion complexes with bis primary alkylammonium salts and this aspect is developed in the next communication.

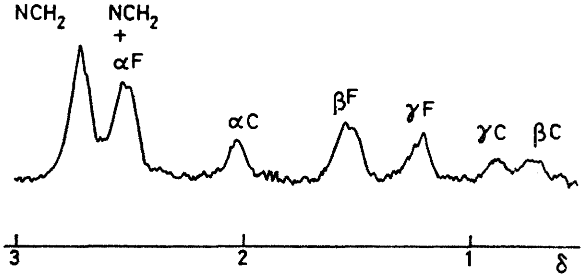


FIGURE 2. N.m.r. spectrum of host (**4b**) and guest (**7**) (0·5 equiv.) at −20 °C. The symbols F and C refer to the free and complexed host species.

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