Structural Selectivity in the Formation of Inclusion Complexes by Tricyclic Derivatives of Diaza-12-crown-4

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Summary The tricyclic host molecules (**1c**—**e**) form inclusion complexes with suitable guest ammonium salts and with copper(II) chloride; complex formation with the bisammonium salts (**4**) is accompanied by host recognition of the length of the guest molecule.

It was recently reported[1] that the tricyclic hosts (**1a**, **b**) have geometrical requirements for complex formation with primary alkylammonium salts that inevitably lead to the formation of inclusion complexes, *e.g.* (**2**). The tricyclic systems (**1c**—**e**), based upon the diaza-12-crown-4 system

Table. Chemical shifts of guest cations in inclusion complexes with hosts (**1c**—**e**)

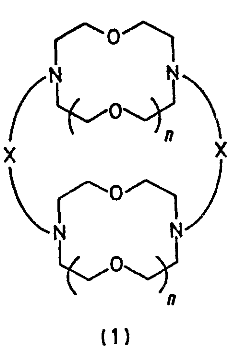
Host	Guest	Ratio[c]		N.m.r. spectrum of guest[a,b]			
(H)	(G)	G:H	Temp/°C	α-CH_2 or Me	β-CH_2	γ-CH_2	δ-CH_2
(**1c**)	(**4**, *n* = 2)	1:1	25	0·89 (3·08)			
			−100	−0·86, 2·44			
(**1c**)	(**4**, *n* = 3)	1:1	−50	1·64 (2·99)	1·82 (1·98)		
(**1d**)	(**4**, *n* = 4)	1:1	25	1·50 (3·03)	0·28 (1·79)		
(**1e**)	(**4**, *n* = 4)	1:1	25[d]	2·76 (3·03)	1·58 (1·79)		
			−90[d]	0·71, 1·05	0·10, −0·42		
(**1e**)	(**4**, *n* = 5)	1:1	−20	0·72 (2·95)	0·00 (1·74)	−0·41 (1·50)	
(**1e**)	(**4**, *n* = 6)	1:1	−20	1·04 (2·95)	−0·55 (1·72)	0·07 (1·46)	
(**1e**)	(**4**, *n* = 7)	1:1	−60	0·52 (2·91)	0·29 (1·67)	0·04 (1·39)	−0·30 (1·39)
(**1c**)	$Me\overset{+}{N}H_3NCS^-$	1:1	−90	1·54,[e] 1·78 (2·54)			
(**1c**)	$Me\overset{+}{N}H_3ClO_4^-$	2:1	−70	0·33, 3·04 (2·54)			
(**1d**)	$Me\overset{+}{N}H_3NCS^-$	2:1	−60	0·96 (2·54)			
(**1e**)	$Me\overset{+}{N}H_3NCS^-$	2:1	−60	0·44 (2·54)			

[a] All spectra were run at 220 MHz using a Perkin-Elmer R34 spectrometer for solutions in CD_2Cl_2 containing a little CD_3OD. Chemical shifts (±0·05) relative to Me_4Si. [b] Methylene groups in guest (**4**) are labelled as $H_3\overset{+}{N}CH_2(\alpha)CH_2(\beta)CH_2(\gamma)$ *etc.* Chemical shifts in parentheses refer to uncomplexed guest salt. [c] The ratio is the maximum for complete complexation of the guest salt. [d] The spectrum at 25 °C indicates little or no complex formation. [e] For a 2 : 1 G : H ratio only a broad signal, δ 1·58, was observed for the complexed guest together with a sharp signal, δ 2·54, for the free guest.

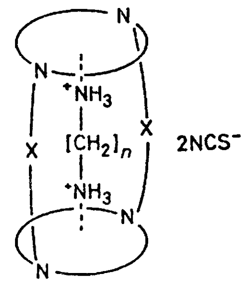
(**3**)[2,3] were synthesised by the reaction of the diamine (**3**, R = H) with the appropriate bisbromomethyl arene.

The hosts (**1c**—**e**) formed complexes with methylammonium thiocyanate in deuteriomethylene chloride† in the ratios indicated in the Table, which were characterised by their n.m.r. spectra‡ as inclusion complexes. The maximum ratio of guest to host depends, as expected, upon the size of the host cavity and only the larger cavities of (**1d**) and (**1e**) can accommodate two molecules of the guest salt. Unexpectedly, however, it was possible to insert two molecules of guest cation into the small cavity of (**1c**) if methylammonium perchlorate was used in place of thiocyanate; in this 2:1 complex two NMe signals were observed at low temperatures, one (δ 0·33) to high field of uncomplexed methylammonium perchlorate (δ 2·54) and the other (δ 3·04) to low field. One NMe group therefore lies in the shielding zone of the aromatic rings of (**1c**) and the other lies in the deshielding zone,[4] these two different positions of the NMe groups presumably being determined by the small size of the host cavity. Hosts (**1c**—**e**) also formed complexes with copper(II) chloride in ethanol, which were expected to be of the inclusion (cryptate) type by analogy with the known structures of other complexes of polyaza-12-crown-4 systems.[5] On the basis of spectroscopic measurements in the range 600—820 nm, host (**1c**) forms only a 1:1 complex, host (**1d**) forms both 1:1 and 2:1 complexes, and host (**1e**) forms a 2:1 complex; these ratios are in accordance with the sizes of the host cavities and the expected steric requirements of the guest.

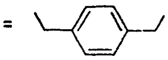
The tricyclic hosts (**1c**—**e**) form complexes in deuteriomethylene chloride with a range of bis primary alkylammonium salts (**4**), the optimum value of *n* in (**4**) for complex formation being determined by the length of the

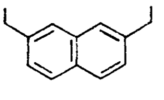


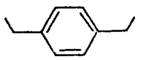
(1)

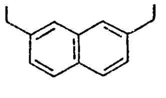


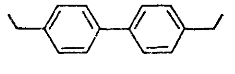
(2)

a; *n* = 2, X = 

b; *n* = 2, X = 

c; *n* = 1, X = 

d; *n* = 1, X = 

e; *n* = 1, X = 

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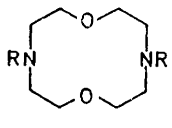
† A little deuteriomethanol was added in all cases to increase the solubility of the complex.

‡ The n.m.r. spectra at low temperatures indicated that in some cases the complex consisted of a number of different stereoisomers; details will be discussed in the full paper.

host cavity. Spectroscopic evidence for the formation of inclusion complexes is recorded in the Table. Host (**1c**) forms a 1 : 1 inclusion complex with the salt (**4**, $n = 2$) and the different chemical shifts (δ 0·86 and 2·44) of the two methylene groups of the guest observable at −100 °C show that they occupy different environments in the complex relative to the two aromatic rings of the host (**1c**).



(3)

a; R = Me

b; R = H

$H_3\overset{+}{N}[CH_2]_n\overset{+}{N}H_3 \quad 2NCS^-$

(4)

The observed differences are not inconsistent with qualitative estimates of shielding based upon space-filling (CPK) models of the complex. The complex between host (**1c**) and the salt (**4**, $n = 3$) is poorly defined and complex formation is only important at low temperatures. The larger cavity of host (**1d**) accommodates the salt (**4**, $n = 4$).

Host (**1e**) has the longest cavity of the three host molecules studied. N.m.r. spectra suggest that complex formation is relatively unimportant for the guests (**4**, $n = 3$ and 8) which are, respectively, too short and too long to fit the host cavity. The four salts (**4**, $n = 4$—7) do form inclusion complexes and competition experiments were carried out using an excess of two competing guests. On the basis of the n.m.r. spectra of these solutions, and the well resolved chemical shifts of the methylene groups of the guest salts, a number of conclusions can be drawn. The guest (**4**, $n = 5$) is complexed in preference to the guest (**4**, $n = 4$), the guests (**4**, $n = 5$) and (**4**, $n = 6$) are complexed almost equally strongly, and the guest (**4**, $n = 6$) is complexed in preference to the guest (**4**, $n = 7$). The host (**1e**) therefore selects the two salts (**4**, $n = 5$ and 6) in preference to any other bisammonium salt (**4**). Competition between the bis ammonium salt (**4**, $n = 6$) and methylammonium thiocyanate for the host (**1e**) was also studied; the results show that both guests are complexed almost equally readily and the advantages of the two binding sites in the guest (**4**, $n = 6$) are probably offset by the loss of rotational freedom in the polymethylene chain that accompanies complex formation.

The results described here show that high selectivity may be observed for the formation of guest–host complexes in which the host has two binding sites that are complementary to two functional groups of the guest.

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[4] For discussions see L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' 2nd edn., Pergamon, Oxford, 1969, p. 94; A. Agarwal, J. A. Barnes, J. L. Fletcher, M. J. McGlinchey, and B. G. Sayer, *Canad. J. Chem.*, 1977, **55**, 2575.

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