Complexes of Primary Ammonium Cations with Diazametacyclophanes

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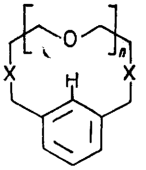
Summary The diazametacyclophanes (**2a**, **b** and **c**) form complexes with primary ammonium thiocyanates; guest–host relationships in these complexes may be studied by examining the temperature dependence of their n.m.r. spectra.

THE pioneering studies of Cram and his co-workers,[1] following the earlier observations of Pedersen,[2] have shown that crown ethers, particularly those of the [18]crown-6 type, can function as host molecules for the formation of complexes with primary ammonium salts. In view of the known greater ability[3] of tertiary amines to form hydrogen bonds as compared with ethers, and the greater variation possible in amine structure and topology,[4] it was of interest to investigate complex formation using host molecules in which one or more of the ring oxygen atoms had been replaced by nitrogen atoms.

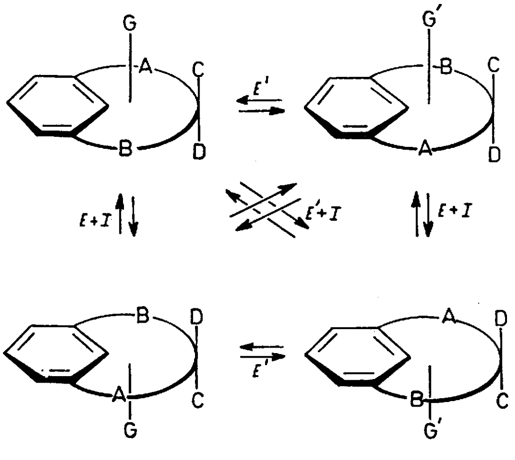


$EtO_2CNHCH_2[CH_2OCH_2]_n CH_2NHCO_2Et$

(3)

(1) $X = NCO_2Et$
(2) $X = NMe$
a; $n = 1$; b; $n = 2$; c; $n = 3$

The metacyclophanes (**1a**, **b**, and **c**) were readily synthesised (*ca.* 40% yield) by the reaction of αα′-dibromo-*m*-xylene with the dianions from the bis-urethanes (**3a**, **b**, and **c**). NaH in Me_2SO was used to generate the dianions but no attempt was made to optimise yields by using conditions of high dilution. Reduction of the cyclophanes (**1a**, **b**, and **c**) with $LiAlH_4$ gave good yields of the amines (**2a**, **b**, and **c**), which were isolated as oils. The n.m.r. spectra of these amines were consistent with the proposed



SCHEME. The labels A and B and C and D refer to the two sides and the two faces of the host molecule respectively. The bonding between guest and host molecule is not precisely indicated, the connecting line only indicates attachment to one or other face of the host. The orientation of the aromatic ring is uncertain; it is drawn in the horizontal plane for this reason although it must be tilted either up or down with respect to this plane in both free and complexed host molecules.

TABLE

Spectral changes, exchange processes, and free energy barriers for primary ammonium thiocyanate complexes of amines (**2a**, **b**, and **c**)

Host	Guest	Temperature/°C	Spectral changes	$\Delta G^{\ddagger a}$/kcal mol^{-1} $\pm 0{\cdot}3$	Process
(**2a**)	—	-41	$ArCH_2N,AB \rightarrow A_2$	$11{\cdot}0^b$	*I*
(**2a**)	(*R*,*S*)-$PhCHMeNH_3^+NCS^-$	-90	$ArCH_2N$,AB unchanged NMe, $2 \times Me_A$, unchanged	$<9{\cdot}4^c$	*E′*
(**2b**)	$PhCH_2NH_3^+NCS^-$	-45	$ArCH_2N, AB \rightarrow A_2$	$10{\cdot}8$	*E*
(**2b**)	(*R*,*S*)-$PhCHMeNH_3^+NCS^-$	-45	$ArCH_2N, AB \rightarrow A_2^d$	$10{\cdot}9$	*E*+*E′*
		-55	$NMe, Me_A + Me_B \rightarrow 2 \times Me_{AB}$	$10{\cdot}6$	*E*+*E′*
(**2b**)	$Me_3CNH_3^+NCS^-$	-80	$NCH_2, AB \rightarrow A_2$	$9{\cdot}4$	*E*
(**2c**)	$PhCH_2NH_3^+NCS^-$	-65	$ArCH_2N, AB \rightarrow A_2$	$9{\cdot}9$	*E*
(**2c**)	(*R*,*S*)-$PhCHMeNH_3^+NCS^-$	-65	$ArCH_2N, AB \rightarrow A_2^d$	$9{\cdot}8$	*E*+*E′*
		-77	$NMe, Me_A + Me_B \rightarrow 2 \times Me_{AB}$	$9{\cdot}7$	*E*+*E′*

[a] Based upon coalescence data at the stated temperature. [b] Similar values are obtained for this inversion barrier for the benzylammonium and phenylethylammonium thiocyanate complexes. [c] Based upon observed line broadening of *ca.* 9 Hz probably associated with processes other than site exchange; the complex with the *R*-ammonium salt shows signal separation at −60 °C. [d] With a chiral guest molecule two AB systems are observable at low temperatures for these protons.

structures; the n.m.r. spectra of (**2b**) and (**2c**) were essentially unchanged at low temperature (−90 °C) other than by some line-broadening, and the n.m.r. spectrum of the monothiocyanate of the amine (**2b**) showed a similar lack of temperature dependence. The n.m.r. spectrum of the amine (**2a**) was markedly temperature dependent, and below −40 °C it was consistent with slow conformational inversion on the n.m.r. time scale ($\Delta G^{\ddagger}$ 11·0 kcal mol^{-1} based upon the coalescence behaviour of the AB system from the benzylic methylene groups) (*cf.* ref. 5).

The addition of primary ammonium thiocyanates (1 mol. equiv.) to solutions of the amines (**2a**, **b**, and **c**) in either $CDCl_3$ or CD_2Cl_2 caused marked changes in their n.m.r. spectra and in particular in the chemical shifts of the $ArCH_2N$ and NCH_2 methylene groups, the $N\text{-}CH_3$ groups, and the aromatic-H indicated in the formula. These spectral changes we associate with complex formation, and the spectra of the solutions showed temperature dependence which is summarised in the Table. This may be rationalised on the basis of the Scheme, assuming that complex formation involves a single face of the molecule.

In the Scheme the symbols G and G′ refer to chiral guest molecules of opposite chirality and the total Scheme therefore applies to possible equilibria and site exchange processes in molecular complexes with racemic guests [*e.g.* (*R*,*S*)-α-phenylethylammonium thiocyanate]. The symbols *E*, *E′*, and *I* relate to processes as follows: *E* refers to intermolecular or intramolecular face to face guest exchange with no change in guest chirality, *E′* refers to intermolecular guest exchange with a change in guest chirality, and *I* refers to conformational inversion of the host molecule. A number of situations may be envisaged for differing relative rates of the processes *E*, *E′*, and *I*; we shall refer to two cases which may be distinguished on the basis of our n.m.r. data.

Case 1 (Process *I* fast[†] at all temperatures). For fast *E* and *E′*, at high temperatures, the pairs of sites of types C and D and A and B will be averaged and at low temperatures, when *E* and *E′* become slow,[†] neither type of site-averaging occurs. This situation is illustrated for a racemic guest by the (*R*,*S*)-α-phenylethylammonium thiocyanate complexes of (**2b**) and (**2c**), which show non-equivalence of pairs of sites related in both manners at low temperatures. For achiral guest molecules, such as benzylammonium or t-butylammonium thiocyanates, G and G′ are identical, and using (**2b**) and (**2c**) as the host molecules only non-equivalence of sites related as C and D is observable at low temperatures.

Case 2 (Processes *E* and *E′* fast at all temperatures). This case has been studied only for the amine (**2a**), for which conformational inversion becomes slow at low temperatures. For an achiral guest molecule, such as benzylammonium thiocyanate, or a racemic guest, such as (*R*,*S*)-α-phenylethylammonium thiocyanate, sites of types A and B are averaged at all temperatures but sites of types C and D are only averaged when process *I* is fast. For a single enantiomer of a chiral guest the pairs of sites related as A and B are averaged only when process *I* is fast, and at temperatures where *I* is slow sites of the types A and B and C and D are distinguishable. This type of behaviour is shown by the complex of the amine (**2a**) and (*R*)-α-phenylethylammonium thiocyanate, but although in principal sites related as C and D, which do not lie on a C_2 axis, are non-equivalent even when *I* is fast, this is not observable in our experiments.

It is evident from the data summarised in the Table that the free energy barrier associated with the processes *E* and *E′* is a function of both guest and host structure. This is consistent with highly structured complexes as found, for example, for the analogous complexes of ammonium salts with crown ethers.[1]

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[†] 'Fast' and 'slow' in this discussion refers to fast and slow on the n.m.r. time scale.

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