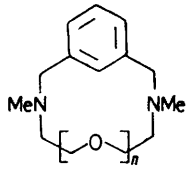
Formation of Complexes between Macrocyclic Diamines and Primary Ammonium Thiocyanates: Recognition of Two Types of Exchange Processes

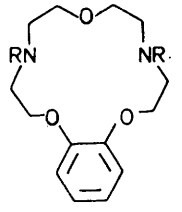
By LESLIE C. HODGKINSON, STEPHEN J. LEIGH, and IAN O. SUTHERLAND*
(*Department of Chemistry, The University, Sheffield* S3 7HF)

Summary The dissociation and recombination of the complexes formed between macrocyclic diamines as host molecules and primary ammonium thiocyanates as guest molecules give rise to two types of exchange processes which may be studied by n.m.r. line shape methods; the relative strengths of guest–host binding may be determined using these kinetic methods for a series of complexes of a single host molecule.

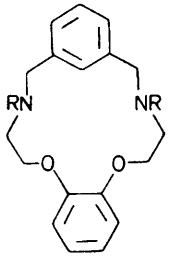
THE diazametacyclophanes (**1**) act as host molecules[1] and form strong complexes in non-polar solvents with benzyl- and phenylethyl-ammonium thiocyanates as guest molecules. These complexes are analogous to those formed by



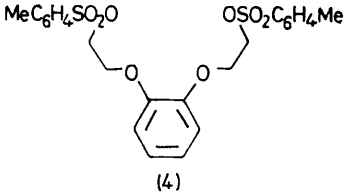
(1)
a, $n = 2$
b, $n = 3$



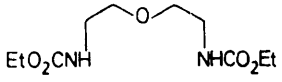
(2)
a, R = CO_2Et
b, R = Me



(3)
a, R = CO_2Et
b, R = Me



(4)



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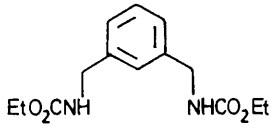

(6)

crown ethers[2] but guest–host binding in the case of (**1**) is sufficiently strong to be studied using the temperature dependence of the n.m.r. spectrum of the complex. We now report a more detailed study of the exchange processes that are detectable in this way.

The macrocyclic diamines (**2**) and (**3**) were synthesised by the reaction of the catechol derivative (**4**) with the anions (sodium hydride–dimethyl sulphoxide) derived from the diamides (**5**) and (**6**). Reduction ($LiAlH_4$) of the ethoxycarbonyl derivatives (**2a**) and (**3a**) gave the *NN'*-dimethyldiamines (**2b**) and (**3b**).

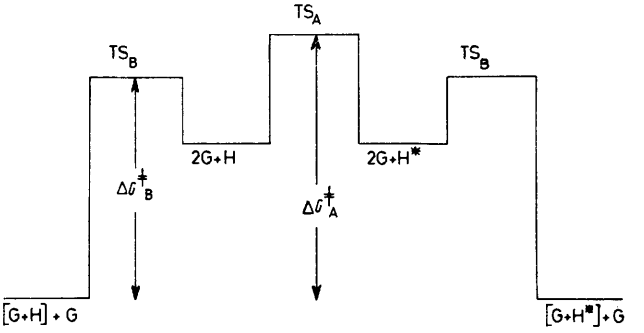

FIGURE. The free energy profile for the dissociation of a guest host complex [G + H] in the presence of excess guest molecules G. H and H* refer to the host molecule in conformations related by inversion.

The diamines, (**2b**) and (**3b**), both form strong complexes with primary alkylammonium thiocyanates and the n.m.r. spectra of these complexes at low temperatures are consistent[1] with slow guest-host exchange. In particular, two types of exchange process, A and B, can be recognised for the complex between the diamine (**2b**) and (*R*)-1-phenylethylammonium thiocyanate. The first type, A, involves exchange of the guest molecule between different faces of the host molecule, resulting in spectroscopic changes of the type that have previously been discussed.[1] The second type of exchange process, B, involves exchange of guest molecules on only a single face of the host molecule. Processes of this second type, B, can be detected by n.m.r. spectroscopy using a solution containing a 2 : 1 molar ratio of guest to host and following the exchange of suitable protons between sites in a complexed guest molecule and an uncomplexed guest molecule. The results of a study of this type are summarised in Table 1. The faster rate of process B as compared with process A (Table 1) is consistent with the free energy profile for the exchange processes shown in the Figure. Exchange processes B, involving only a single face of the host molecule, require only dissociation of the complex and are associated with the transition state TS_B, and the free energy of activation $\Delta G^{\ddagger}_B$. Processes A, involving both faces of the host molecule, require dissociation of the complex together with conformational inversion of the host macrocycle associated with the transition state TS_A, and the free energy of activation, $\Delta G^{\ddagger}_A$. For the example summarised above and in Table 1, and for all other cases examined in this way, this process A is the slower of the two.

TABLE 1

Free energy barriers for guest–host exchange using host (**2b**)

Guest	Guest : host ratio	Spectral changes	T_c /°C (±5)	$\Delta G^{\ddagger a}$ /kcal mol^{-1} (±0·3)	Process
$PhCH_2\overset{+}{N}H_3NCS^-$	1 : 1	Host : CH_2N, AB → A_2 [b]	0	13·1	A
(*R*,*S*)-$PhCHMe\overset{+}{N}H_3NCS^-$	1 : 1	Host : N*Me*, $Me_A + Me_B \rightarrow 2 \times Me_{AB}$	−15	12·1	A + B[c]
(*R*,*S*)-$PhCHMe\overset{+}{N}H_3NCS^-$	2 : 1	Host : N*Me*, $Me_A + Me_B \rightarrow 2 \times Me_{AB}$	−21	11·8	0·5B[d]
		Guest : $\overset{+}{N}CHMe$, $Me_A + Me_B \rightarrow 2 \times Me_{AB}$	−47	11·4	B
(*R*)-$PhCHMe\overset{+}{N}H_3NCS^-$	2 : 1	Host : N*Me*, $Me_A + Me_B \rightarrow 2 \times Me_{AB}$	−5	12·6	A
		Guest : $\overset{+}{N}CHMe$, $Me_A + Me_B \rightarrow 2 \times Me_{AB}$	−47	11·4	B

[a] Based upon the exchange rate at the coalescence temperature, calculated using the usual formula (ref. 3). In all cases the solvent is CD_2Cl_2. [b] Approximated as an AB system and based upon both NCH_2 groups. [c] Probably a combination of A and B owing to imperfect stoicheiometry. [d] Exchange B is detectable using the N*Me* signals of the host for excess of an (*R*,*S*)-guest molecule but it is slowed down by a statistical factor of 2 since only exchanges of (*R*)- for (*S*)-guest molecules (or vice-versa) are detectable in this way (see ref. 1).

TABLE 2

Free energy barriers ($\Delta G_A^{\ddagger}$)[a,b] for guest-host exchange using hosts (**1a**) and (**3b**) and $R\overset{+}{N}H_3NCS^-$.

R	Host (**1a**) T_c/°C(±5)	Host (**1a**) $\Delta G_A^{\ddagger}$/kcal mol^{-1} (±0·3)	Host (**3b**) T_c/°C (±5)	Host (**3b**) $\Delta G_A^{\ddagger}$/kcal mol^{-1} (±0·3)
H	−90	8·7		
Me	−61	10·1	−68	9·7
Et	−50	10·7	−62	10·0
$CHMe_2$	−62	10·1	−57	10·2
CMe_3	−80	9·3	−82	9·1
CH_2CH_2Me	−60	10·2		
CH_2CHMe_2	−70	9·7		
CH_2CMe_3	< −100	—[c]		
CH_2Ph	−45	10·8	−40	11·1

[a] For solutions in CD_2Cl_2 (*ca.* 0·2M) containing equimolecular proportions of guest and host. Activation parameters are based upon coalescence of the AB system from the $ArCH_2N$ of the macrocycle. [b] Errors in $\Delta G_A^{\ddagger}$ allow for uncertainty in T_c, $\nu_A - \nu_B$ and J_{AB}. The rate at the coalescence temperature T_c was calculated using the usual formula for an AB system (ref. 3). [c] Line-broadening only at low temperatures, probably $\Delta G^{\ddagger}$ is < 9 kcal mol^{-1}.

The relative values of $\Delta G_A^{\ddagger}$ (see Figure) are directly related to the relative free energies of binding for a series of guest molecules and a single host molecule. This point is illustrated in Table 2 for a series of guest molecules and the host molecules (**1a**) and (**3b**); the relative values of $\Delta G_A^{\ddagger}$, and thus the free energies of binding, are consistent with the expected effects of the non-bonded interactions between the guest and host components in complexes with structures analogous to that of the crystalline benzylammonium thiocyanate complex of (**1a**).[4]

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