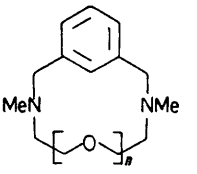
Formation of Complexes Between Macrocyclic Diamines and Primary Ammonium Thiocyanates: Dependence of Binding upon Host Structure

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

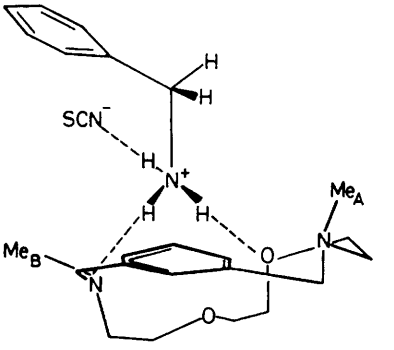
Summary The series of macrocyclic diamines (**3b**) and (**4b**) form complexes with primary alkylammonium thiocyanates with free energies of binding that depend upon ring size; the diamines (**7**) and (**8**) with functional groups in the side chains are readily synthesized and form strong complexes with polyfunctional ammonium thiocyanates.

WE have reported in a previous communication[1] that the metacyclophane derivatives (**1**) form strong complexes in non-polar solvents with benzyl- and 1-phenylethyl-ammonium thiocyanates. An *X*-ray analysis[2] of the crystal structure of the complex of (**1a**) with benzylammonium thiocyanate shows that complex formation involves hydrogen bonding between guest and host molecules as shown (**2**). This structure (**2**) shows two chemically important features: (i) the $-\overset{+}{N}H_3$ group is attached by only two hydrogen bonds to the host molecule and the third hydrogen bond is associated with the thiocyanate counter-ion; (ii) the methyl substituents of the host molecule lie above the face which is involved in complex formation. The first feature indicates that strong binding is restricted to primary alkylammonium thiocyanates and the second feature shows that substituents on the nitrogen atoms that contain functional groups would be correctly located to bind to, or react with, suitable functional groups in the guest molecule. This second aspect of complex formation is under investigation.

The structure of the complex (**2**) in non-polar solvents is believed to be similar to the structure in the crystalline state on the basis of the changes in the ^1H chemical shifts of the NMe groups of the host (**1a**) on complex formation. In all cases where one or more of the groups R^1, R^2, and R^3 of the guest cation $R^1R^2R^3\overset{+}{C}NH_3$ is a phenyl group the NMe groups are shifted to high field (*ca.* 0·3 p.p.m.) in the complex whereas in other cases the NMe groups show small shifts to low fields. This effect becomes increasingly marked at low temperatures and is consistent with one or



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



(2)

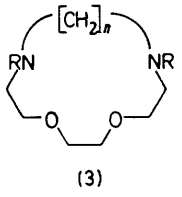
TABLE

Free energy barriers[a] for guest–host exchange using hosts (**3b**), (**4b**), (**8c**), and (**8d**)

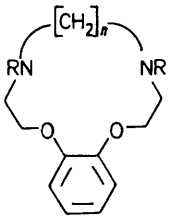
Guest	Host	Spectral changes[b]	T_c/°C(±5)	$\Delta G^{\ddagger b}$ /kcal mol^{-1} (±0·5)
$PhCH_2\overset{+}{N}H_3NCS^-$	(**4b**, $n=4$)	NCH_2, AB → A_2	−90[c]	8·8[c]
$PhCH_2\overset{+}{N}H_3NCS^-$	(**4b**, $n=5$)	NCH_2, AB → A_2	−35	11·4
$PhCH_2\overset{+}{N}H_3NCS^-$	(**4b**, $n=6$)	NCH_2, AB → A_2	−60	10·4
$PhCH_2\overset{+}{N}H_3NCS^-$	(**4b**, $n=7$)	NCH_2, AB → A_2	−60	10·1
$PhCH_2\overset{+}{N}H_3NCS^-$	(**4b**, $n=8$)	NCH_2, AB → A_2	−70	9·5
$PhCH_2\overset{+}{N}H_3NCS^-$	(**3b**, $n=3$)		< −80[d]	<9[d]
$PhCH_2\overset{+}{N}H_3NCS^-$	(**3b**, $n=4$)	NCH_2, AB → A_2	−55	10·4
$PhCH_2\overset{+}{N}H_3NCS^-$	(**3b**, $n=5$)	OCH_2, AB → A_2	−55	10·7
$PhCH_2\overset{+}{N}H_3NCS^-$	(**3b**, $n=6$)	NCH_2, AB → A_2	−65	10·0
$PhCH_2\overset{+}{N}H_3NCS^-$	(**3b**, $n=7$)	NCH_2, AB → A_2	−80[c]	9·4[c]
$PhCH_2\overset{+}{N}H_3NCS^-$	(**3b**, $n=8$)		< −80[d]	<< 9[d]
$PhCH_2\overset{+}{N}H_3NCS^-$	$(PhCH_2NMe.CH_2CH_2OCH_2)_2$		< −90[d]	<< 9[d]
$PhCH_2\overset{+}{N}H_3NCS^-$	(**8c**)	$ArCH_2N$,AB → A_2	−15	12·1
$PhCH_2\overset{+}{N}H_3NCS^-$	(**8d**)	$ArCH_2N$,AB → A_2	−5	12·8
(*R*)-$PhCH\overset{+}{N}H_3CO_2MeNCS^-$	(**8c**)	$ArCH_2N$,AB → A_2	−40	11·0
(*R*)-$PhCH\overset{+}{N}H_3CO_2MeNCS^-$	(**8d**)	$CONMe_2$,Me_A + Me_B → Me_{AB}	−20	12·9
$HOCH_2CH_2\overset{+}{N}H_3NCS^-$	(**8c**)	$ArCH_2N$,AB → A_2	−40	11·0
$HOCH_2CH_2\overset{+}{N}H_3NCS^-$	(**8d**)	$ArCH_2N$,AB → A_2	−15	12·2

[a] Data for CD_2Cl_2 solutions (*ca.* 0·2M) using 1 : 1 ratios of guest and host components. $\Delta G^{\ddagger}$ refers to face to face guest exchange (process A, ref. 5). [b] NCH_2 or OCH_2 approximated as an AB system and exchange rate at the coalescence temperature T_c based upon the usual approximation. [c] Very broad lines at low temperature result in $T_c \pm 10$ °C and $\Delta G^{\ddagger} \pm 1$ kcal mol^{-1}. [d] Line-broadening only at low temperatures.

more† of the NMe groups being located in the shielding zone[3] of the phenyl group of the guest cation, as observed in the crystal structure of the complex (**2**).



(3)

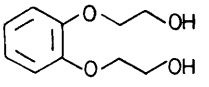


(4)

In (3) and (4): a, R = CO_2Et; b, R = Me

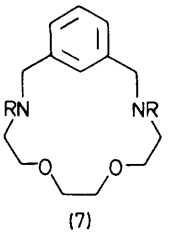
$EtO_2CNH[CH_2]_nNHCO_2Et$

(5)



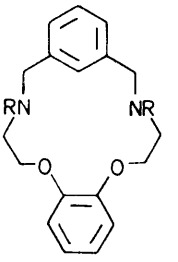
(6)

The recognition that complex formation involves only two hydrogen bonding sites in the macrocycle suggests that the structural requirements for complex formation by the analogues of (**1a**) would be less rigorous[4] than those reported for crown ether complexes. The series of compounds (**3**) and (**4**) were synthesised by the reaction of the dianions of the readily available diamine derivatives (**5**) with either the bistoluene-*p*-sulphonyl derivative of triethylene glycol or of the catechol derivative (**6**). The amines (**3b**) and (**4b**) were prepared by reduction of the urethanes (**3a**) and (**4a**) (with $LiAlH_4$), and the binding strengths of the complexes of (**3b**) and (**4b**) with benzylammonium thiocyanate were compared on a kinetic basis[1,5] using n.m.r. line-shape methods (Table). It is evident that the strength of binding depends upon ring size and is at a maximum for fifteen- and sixteen-membered rings. The complexes of the amines (**3b**, $n = 5$) and (**4b**, $n = 5$) appear to resemble closely those of the diamine (**1a**) on the basis of a preliminary examination using n.m.r. spectroscopy, but the complexes of the other compounds in these series may not have analogous structures.



(7)

a, R = CO_2CH_2Ph
b, R = H
c, R = CH_2CH_2OH
d, R = CH_2CONMe_2
e, R = 



(8)

a, R = CO_2CH_2Ph
b, R = H
c, R = CH_2CH_2OH
d, R = CH_2CONMe_2

The amines (**7b**) and (**8b**) are readily prepared by debenzylation of the macrocycles (**7a**) and (**8a**), and these compounds may be used for the synthesis of host molecules containing functional groups in the side chains. Thus reactions with ethylene oxide, 2-chloro-*NN*-dimethylacetamide, and 2-chloromethylpyridine yield the derivatives (**7c–e**) and (**8c** and **d**). These compounds also act as host molecules for guest alkylammonium cations and the side chain substitution can lead to significantly stronger binding (see Table). In particular the introduction of basic and nucleophilic functions into the side chains is of particular interest for the synthesis of host compounds having catalytic properties.

(*Received, 28th May* 1976; *Com.* 613.)

† The methyl groups Me_A and Me_B are in different environments in (**2**) but these environments are evidently rapidly averaged on the n.m.r. time scale, even at low temperatures (down to −90 °C), by appropriate changes in the sites for hydrogen bonding since only a single NMe signal is observable for the complex (**2**), but for a chiral guest cation two NMe signals are observable (refs. 1 and 5).

[1] S. J. Leigh and I. O. Sutherland, *J.C.S. Chem. Comm.*, 1975, 414.
[2] N. A. Bailey and S. Chidlow, personal communication.
[3] C. E. Johnson and F. A. Bovey, *J. Chem. Phys.*, 1958, **29**, 1012; L. M. Jackman and S. Sternhell, 'Application of NMR in Organic Chemistry,' 2nd edn., Pergamon, Oxford, 1969, p. 94.
[4] J. M. Timko, R. C. Helgeson, M. Newcomb, G. W. Gokel, and D. J. Cram, *J. Amer. Chem. Soc.*, 1974, **96**, 7097.
[5] See preceding communication.