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COMPLEXES OF PRIMARY ALKYLAMMONIUM SALTS AND SECONDARY DIALKYLAMMONIUM SALTS WITH DIAZAPARACYCLOPHANES

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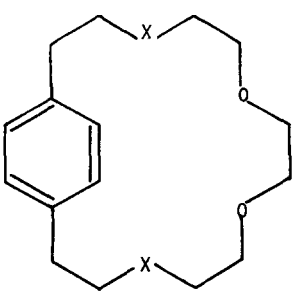
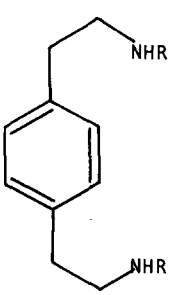
Since the initial report by Pedersen[1] that dibenzo-18-crown-6 complexes with ammonium and primary alkylammonium cations, the design and synthesis of locks[2] which form highly structured molecular complexes with cationic keys[2] has been pursued by a number of groups of researchers.[2-8] With complexes involving crown compounds and primary alkylammonium cations, the primary binding site usually involves hydrogen bonding of at least two of the three acidic hydrogens on the positively charged nitrogen of the cation with suitably disposed heteroatoms in the crown, leaving some, if not all, of the other heteroatoms to participate in stabilising electrostatically the positive charge on nitrogen. The crown heteroatoms which have proved to be efficient in binding primary alkylammonium cations are oxygen and nitrogen both in their sp^2 and sp^3 hybridised states. Examination of Corey-Pauling-Koltun space-filling molecular models of paracyclophanes, *e.g.* (1) or (2), has suggested to us that the π-electron systems associated with their aromatic rings could participate in the binding of primary alkylammonium cations.

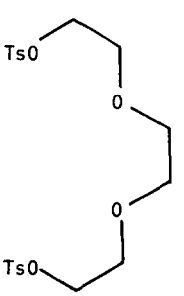
We have tested our hypothesis using the *N,N*-dimethyldiazaparacyclophane (2) as the ligand because *(i)* nitrogen-containing crown compounds are known[6] to form strong complexes with primary alkylammonium cations, *(ii)* it contains suitable probes for investigation of complex formation by dynamic ^{1}H n.m.r. spectroscopy, and *(iii)* it can be synthesised from readily available starting materials, namely *p*-phenylene-β,β'-diethylamine (3)[9] and triethylene glycol bistosylate (4).[10] Reaction of (3) with sodium hydroxide and ethylchloroformate in ether-water gave the bisurethane (5), m.p. 135°C, in 72% yield after recrystallisation from chloroform. Treatment of (5) with 1.1 molar equivalents of (4) in dimethylsulphoxide afforded



(1) X = O
(2) X = NMe
(6) X = NCO_2Et



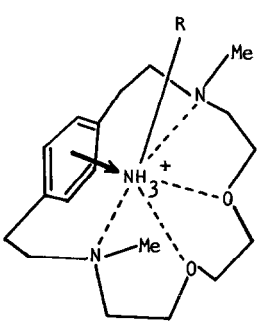
(3) R = H
(5) R = CO_2Et



(4)

the cyclic bisurethane (6) which was obtained pure in 20% yield after vacuum distillation (b.p. 220°C at 0.005 mm Hg). Reduction of (6) with lithium aluminium hydride in ether provided the desired *N,N*-dimethyldiazaparacyclophane (2) in 94% yield after vacuum distillation [b.p. 175°C at 0.005 mm Hg; ^{1}H n.m.r. (CD_2Cl_2): δ 2.24 (6H, s, NCH_3), 2.38 (4H, t, NCH_2CH_2O), 2.50 - 2.80 (8H, AA'BB' system, $ArCH_2CH_2N$), 3.24 (4H, s, OCH_2CH_2O), 3.30 (4H, t, NCH_2CH_2O), and 7.09 (4H, s, C_6H_4)]. We now report that (2) forms complexes in dichloromethane-d_2 with *(i)* primary alkylammonium perchlorates and thiocyanates[11] derived from methylamine (7), ethylamine (8), isopropylamine (9), *tert*-butylamine (10), benzylamine (11), and *(S)*-α-methylbenzylamine *(S)*-(12) and *(ii)* secondary dialkylammonium perchlorates and thiocyanates[11] derived from dimethylamine (13), diisopropylamine (14), dibenzylamine (15), and piperidine (16).

Formation of 1:1 complexes with the salts of the amines (7) - (16) in dichloromethane-d_2 was accompanied by significant changes[12] in the ^{1}H n.m.r. spectrum of (2). Consequently, we have examined the temperature dependences of the ^{1}H n.m.r. spectra of the 1:1 complexes of (2) with *(i)* (9) - (16).$HClO_4$ and *(ii)* (7)-*(S)*-(12).HSCN and (14) - (16).HSCN. In the case of the complexes between (2) and the primary alkylammonium salts (7).HSCN and (9) - (11).$HClO_4$, the singlet (A_2) observed for the aromatic protons of (2) at +30°C separated into two equal intensity singlets (AB) at low temperatures. This temperature dependence of the signal for the aromatic protons was not evident in the case of the free ligand (2). The kinetic and thermodynamic data summarised in the Table for these 1:1 complexes may be interpreted in terms of exchange of cations between opposite faces of (2). Moreover, the 1:1 complexes must be of a face-to-face type in which rotation of the phenylene ring through the macrocyclic ring is slow on the ^{1}H n.m.r. time scale. The exchange process must also involve complete or partial dissociation of the complexes in order that inversion of the macrocyclic ring, as well as inversion at both nitrogens, can occur. The $\Delta G_c^{\ddagger}$ values in the Table can be equated with the free energies of activation ($\Delta G_{d+rni}^{\ddagger}$) for a face-to-face equilibration with both dissociative and conformational inversion components. The ^{1}H n.m.r. spectroscopic data is consistent with the achiral complexes having C_s symmetry as represented by the general structure (17) where the phenylene ring is portrayed as occupying a plane perpendicular to that of the mean plane of the macrocyclic ring. The signals for the benzylic-methylene, *N*-methylene, and *O*-methylene protons also exhibit temperature dependence, although in nearly all cases this is difficult to interpret because of the overlapping and broad nature of the signals.[13] The protons in the two enantiotopic *N*-methyl groups resonate as one singlet at low temperatures in all the achiral complexes (17). However, the singlet for the *N*-methyl protons separates into two equal intensity singlets at low temperatures in the '2:1 complexes' of (2) with (7).$HClO_4$, (10).$HClO_4$, and (11).$HClO_4$. This reflects the equilibrium proportions of complexed and uncomplexed (2) and arises from exchange of the cations with a single face of (2) in a process



(17) R, Achiral - C_s symmetry

(18) R, Chiral - C_1 symmetry

Table. Temperature dependent ^{1}H n.m.r. spectral data and kinetic and thermodynamic parameters for the complexation of primary alkylammonium salts with (2)[a]

$RNH_3^+X^-$ R	Molar ratio L:K	^{1}H N.m.r. probes[b]	T_c °C ±3	Δν(temp, °C) ± 2Hz	k_c, sec^{-1}	$\Delta G_c^{\ddagger}$ ±0.3kcal mol^{-1}	Process
(7).$HClO_4$[c] Me	2:1	NCH_3	-56	9(-70)	20	11.3	*d*
(7).HSCN[d] Me	1:1	C_6H_4	-30	31(-55)	69	12.1	*d* + *rni*
(9).$HClO_4$[c] $CHMe_2$	1:1	C_6H_4	-50	18(-70)	40	11.3	*d* + *rni*
(10).$HClO_4$[d] CMe_3	1:1	C_6H_4	-65	34(-80)	75	10.2	*d* + *rni*
	2:1	NCH_3	-90	14(-95)	31	9.3	*d*
(11).$HClO_4$[d] CH_2Ph	1:1	C_6H_4	-50	11(-65)	24	11.5	*d* + *rni*
		NCH_2	-25	101(-55)	224	11.7	*d* + *rni*
	2:1	NCH_3	-40	77(-90)	171	10.7	*d*
(11).HSCN[d] CH_2Ph	1:1	C_6H_4	-50	31(-60)	69	11.0	*d* + *rni*
		NCH_2	-30	125(-50)	278	11.4	*d* + *rni*
(12).HSCN[d] CHMePh[e]	1:1	NCH_3	-70	57(-100)	127	10.7	*d* + *rni*

[a] All spectra were recorded in CD_2Cl_2 at 220 MHz on a Perkin Elmer R34 spectrometer with Me_4Si as 'lock' and internal standard. Abbreviations used are: L:K, molar ratio of lock to key; T_c, coalescence temperature; Δν, frequency separation for the appropriate ^{1}H n.m.r. probe with the temperature at which it was measured in parenthesis; k_c, exchange rate constant at T_c calculated from the expression, $k_c = \pi\Delta\nu/2^{\frac{1}{2}}$ (I.O. Sutherland, *Ann. Reports N.M.R. Spectroscopy*, 4, 71 (1971)); $\Delta G_c^{\ddagger}$, free energy of activation at T_c calculated from the Eyring equation; *d*, dissociation of the complex; *rni*, ring and nitrogen inversion of (2).

[b] In all cases, exchange of protons between two equally populated sites, A and B, with little or no mutual coupling is observed. If the sites that represent two time-averaged signals are designated AB, the spectral changes can all be described as AB → A_2.

[c] Kindly supplied by Miss J.C. Metcalfe.

[d] Kindly supplied by Mr. D.A. Laidler.

[e] The *(S)*-enantiomer.

involving dissociation of the complex. Thus, the exchange process measured by the temperature dependence of the ^{1}H n.m.r. spectra of the '2:1 complexes' gives $\Delta G_c^{\ddagger}$ values (see Table) which we can equate with free energies of activation ($\Delta G_d^{\ddagger}$) for dissociation of the complexes. The temperature dependent ^{1}H n.m.r. spectra of (2) - *(S)*-(12).$HClO_4$ and (2)-*(S)*-(12).HSCN are consistent with chiral asymmetric complexes represented by the general structure (18). Although the line-shape behaviour of the aromatic protons is complex[14], the diastereotopic *N*-methyl groups of, for example, (2)-*(S)*-(12).HSCN become anisochronous at low temperatures and hence their protons provide (see Table) a suitable probe from which quantitative information can be obtained.

In both (17) and (18), there appears to be a stabilising interaction between the

π-electron system of the phenylene ring and the primary alkylammonium cation[15] which accounts for the hindered rotation of the phenylene rings in the complex. Interestingly when one of the ammonium hydrogens is replaced by an alkyl group to give a secondary dialkylammonium cation, as in complexes (2) - (13).HX to (2) - (16).HX (X = ClO_4 or SCN), this interaction seems to be impaired at least to the extent that rotation of the phenylene ring is once again fast on the ^1H n.m.r. time scale.

References and Footnotes

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11. The salts derived from the primary alkylamines (7) - *(S)*-(12) and the secondary dialkylamines (13) - (16) all gave satisfactory elemental analyses.
12. For example, complex formation with the thiocyanate salts at +30°C resulted in the following downfield shifts (p.p.m.) of the signals for the aromatic protons in (2) : (7).HSCN, 0.11; (8).HSCN, 0.16; (9).HSCN, 0.15; (10).HSCN, 0.11; (11).HSCN, 0.18; *(S)*-(12).HSCN, 0.14; (14).HSCN, 0.08; (15).HSCN, 0.11; (16).HSCN, 0.01. Note that the shifts are smaller in the complexes involving the secondary dialkylammonium thiocyanates.
13. Only in the case of the 1:1 complexes formed between benzylamine perchlorate (11).$HClO_4$ and (2), and benzylamine thiocyanate (11).HSCN and (2), does the signal for the *N*-methylene protons separate clearly into two signals of equal intensity. The Table shows that the two sets of values for the free energies of activation obtained using *N*-methylene and aromatic protons as different ^1H n.m.r. probes, are in good agreement.
14. In principle, an ABCD system could be observed for the aromatic protons in the asymmetric complexes at low temperatures.
15. Recently, there has been a report (V.K. Frensch and F. Vögtle, *Tetrahedron Lett.*, 2573 (1977)) describing the possibility of π-complexing of sodium ions by a paracyclophane containing ester and ether functions. See also, L.R. Sousa and J.M. Larson, *Abstracts 174th Amer. Chem. Soc. Meeting*, Chicago, August/September, 1977, ORGN 63.