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PREPARATION AND CATION COMPLEXING PROPERTIES OF SUBSTITUTED MACROCYCLIC POLYETHER-DIESTER COMPOUNDS CONTAINING THE PYRIDINE SUBCYCLIC UNIT

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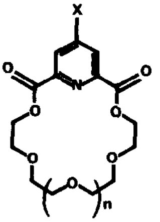
We have previously reported the synthesis and metal cation complexing properties in methanol of compound **1**.[2] This compound formed strong complexes with Na^+, K^+, Ba^{2+}, and Ag^+ with log K values ranging from 4.3 to 4.9.[2] We now report the synthesis of compounds **2**, **3**, **5**, and **6**, the results of a study of the temperature dependent ^1H n.m.r. spectra for the complexes of compounds **1** - **6** with primary alkylammonium cations, and the calorimetric results for the reaction of compound **2** with several uni- and bivalent cations.



1 n = 1, X = H
2 n = 1, X = Cl
3 n = 1, X = OCH_3
4 n = 2, X = H
5 n = 2, X = Cl
6 n = 2, X = OCH_3

The substituted pyridino compounds were prepared from the appropriately substituted 2,6-pyridinedicarbonyl chloride and tetra- or pentaethylene glycol as we have previously reported.[2,3] Compound **2**, for example, was prepared from 4-chloro-2,6-pyridinedicarbonyl chloride and tetraethylene glycol to give white crystals (91%);[4] m.p. 104-105°C. Compounds **3**, **5**, and **6** were similarly prepared: **3** (54%)[4], m.p. 116-117°C; **5** (71%),[4] m.p. 70-71°C; **6** (19%),[4] m.p. 122-123°C. Compound **4** was previously reported.[3]

Formation of complexes of compounds **1** - **6** with primary alkylammonium cations in an equimolar mixture of the two reactants was accompanied by significant chemical shift changes in the ^1H n.m.r. spectra in CD_2Cl_2.[5] The temperature dependencies of the ^1H n.m.r. spectra for the complexes of **1** - **3** with RNH_3ClO_4 (R = phenyl, tert-butyl, and isopropyl) and with RNH_3SCN (R = phenyl) and for the complexes of **4** - **6** with RNH_3ClO_4 (R = phenyl and tert-butyl) have been examined (see Table 1). At low temperatures, the multiplet peak attributable to the ester methylene hydrogens ($COOC\underline{H_2}$) separated into a doublet and a multiplet of equal intensities with a $\Delta\nu$ of 136 - 260 Hz for complexes of **1** - **3** and 43 - 64 Hz for complexes of **4** - **6**. This temperature dependence was not observed in the ^1H n.m.r. spectra for the free ligands. Calculations of the kinetic parameters based on the temperature, T_c at which the two separated peaks coalesced[6-9] in each case are shown in Table 1. The $\Delta G_c^{\neq}$ values calculated from the data obtained in solutions where the molar ratio of crown to salt, C:S, is 1 can be equated to the free energies of activation ($\Delta G^{\neq}_{d+ri}$) for an equilibration of the ammonium ion from one face of the ligand to the other face with both dissociative and ring inversion components. In solutions where the molar ratio C:S = 2:1, the measured $\Delta G_c^{\neq}$ probably involves an equilibration between complexed and uncomplexed ligands and thus can be equated to the free energy of dissociation ($\Delta G^{\neq}_d$).[9] The difference ($\Delta G^{\neq}_{d+ri} - \Delta G^{\neq}_d$) reflects the free energy of ring inversion which for

TABLE 1. Temperature Dependent ^1H n.m.r. Spectral Data and Kinetic Parameters for the Complexation of Primary Alkylammonium Salts with Compounds **1** - **6**.[a]

Molar Ratio (C:S)	RNH_3X		Compound	T_c ±3°C	$\Delta\nu \pm 2$ Hz (T, °C)	k_c sec^{-1}	$\Delta G^{\neq}_c \pm 0.3$ kcal/mol
	R	X					
1:1	$PhCH_2$	ClO_4	1	+10	260 (-50)	577	13.0
			2	0	206 (-50)	518	12.5
			3	+25	246 (-45)	547	13.7
			4	-30	44 (-70)	98	11.6
			5	-25	62 (-70)	137	12.0
			6	-15	48 (-60)	108	12.6
	$PhCH_2$	SCN	1	-40	237 (-55)	528	10.6
			2	-55	260(-100)	577	9.7
			3	-30	255 (-80)	567	11.1
	t-Bu	ClO_4	1	-20	163 (-70)	362	11.8
			2	-30	150 (-70)	332	11.3
			3	-10	136 (-70)	303	12.3
			4	-85	48(-105)	108	9.1
			5	-90	43(-105)	93	8.9
			6	-75	64(-100)	142	9.5
	iPr	ClO_4	1	-10	194 (-70)	430	12.2
			2	-20	194 (-60)	430	11.7
			3	-10	196 (-60)	435	12.2
2:1	$PhCH_2$	ClO_4	1	-5	238 (-50)	528	12.3
			2	-10	251 (-60)	557	12.0
			3	0	233 (-50)	518	12.5

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[a] All spectra were recorded in CD_2Cl_2 at 220 MHz on a Perkin-Elmer R34 spectrometer; ^1H n.m.r. probe was $COOC\underline{H}_2$ in each case. T_c = coalescence temperature; $\Delta\nu$ = frequency separation for the ^1H n.m.r. probe; k_c = exchange rate constant at T_c ($k_c = \pi\Delta\nu/2^{1/2}$)[12]; $\Delta G^{\neq}_c$ = free energy of activation at T_c calculated from the Eyring Equation.

the complexes of **1** - **3** is similar to that reported for other systems of restricted rotation[9] but is much less than that reported for the less sterically hindered crown compounds.[8] For compounds **4** - **6**, experiments involving C:S = 2:1 produced ^1H n.m.r. spectra too complex to be analyzed.

For the eighteen-membered rings (**1** - **3**), $\Delta G^{\neq}_c$ for reaction with the four different salts (Table 1) gave the order OCH_3 > H > Cl. This order parallels the basicity of 4-substituted pyridines where OCH_3 > H > Cl.[10] A similar effect for the complexation of benzene diazonium salts by compounds **4** - **6** was observed by Bartsch and co-workers.[11]

In addition to the macrocycles mentioned above, the smaller fifteen-membered ring compounds (n = 0) and the larger twenty-four membered ring compounds (n = 3) analogous to compounds **1** - **6** were synthesized. No ^1H n.m.r. evidence was found for complexation of primary alkylammonium cations by the fifteen-membered ring compounds. The twenty-four-membered ring compounds showed evidence of complexation, but the ^1H n.m.r. spectra for these complexes showed no temperature dependence. The dialkylammonium salts showed no evidence of complexation under the conditions of this investigation with any of the macrocycles studied.

A calorimetric study was made to determine the thermodynamic log K, ΔH, and TΔS for reaction of compound **2** with several inorganic cations in methanol. Table 2 compares these results to corresponding data for compound **1** reported earlier.[2] Two features of the data are significant. First,

TABLE 2. Log K ΔH, and TΔS for Reaction of Inorganic Cations with Compound **2** and Compound **1** (in parentheses) in Methanol at 25°C.

Cation	Log K	ΔH (kcal/mol)	TΔS (kcal/mol)
Na^+	4.14 ± 0.07 (4.29)	-6.03 ± 0.18 (-6.19)	-0.38 (-0.34)
K^+	4.73 ± 0.08 (4.66)	-7.97 ± 0.23 (-9.3)	-1.52 (-2.95)
Rb^+	3.56 ± 0.09 (4.24)	-9.23 ± 0.27 (-9.07)	-4.37 (-3.29)
Cs^+	a (a)	a (a)	
Ag^+	3.76 ± 0.02 (4.88)	-8.04 ± 0.08 (-7.83)	-2.91 (-1.17)
NH_4^+	2.86 ± 0.03 (2.93)	-6.78 ± 0.16 (-7.75)	-2.88 (-3.75)
Li^+,Mg^{2+},Ca^{2+}	b	b	
Sr^{2+}	c	c	
Ba^{2+}	c (4.34)	c (-6.03)	(0.11)

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[a] Reaction of stoichiometry other than 1:1 not resolved.

[b] No measurable heat, indicating ΔH ≈ 0 and/or log K very small.

[c] Ligand decomposition occurs.

addition of the chlorine atom to compound **1** to give compound **2** does not significantly alter the stabilities of alkali metal and NH_4^+ complexes of the ligand although selectivity for K^+ is improved. The Ag^+ complex is significantly destabilized, probably due to the decreased basicity of the pyridyl nitrogen atom resulting from the presence of the 4-chloro group. Thus, the nitrogen atom plays a much more significant role in the binding of Ag^+ by the macrocycle than in the binding of the alkali metal cations. The second significant feature of these data is that compound **2**, unlike compound **1**, decomposes slowly in the presence of Sr^{2+} and Ba^{2+}. Calorimetric measurement of an unusually large amount of heat upon addition of compound **2** to solutions of Sr^{2+} or Ba^{2+} led to initial suspicions of an unusual reaction type. These suspicions were confirmed when the ^1H n.m.r. spectrum of Sr^{2+} or Ba^{2+} mixtures with compound **2** in CD_3OD showed a slow (over two days) decomposition of the ligand, probably via transesterification of both ester linkages. An analogous experiment in the presence of K^+ showed no ligand deterioration. Unfortunately compound **3** is not sufficiently soluble in methanol to allow measurement of data for this compound such as found in Table 2.

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References and Footnotes

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4. Satisfactory molecular weights and elemental analyses were obtained on all newly reported compounds. Melting points are uncorrected. The structures of all compounds are consistent with those derived from i.r. and n.m.r. spectra.

5. For example, the singlet at 3.79 ± 0.01 for the eight OCH_2 hydrogens for compounds **1** - **3** divided into two multiplets of four hydrogens each for the complexes of these compounds.

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