Exceptionally Stable Alkali Metal Complexes of a Torand

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According to ^{1}H NMR competition studies, tri-n-butyl torand (**5**), an open-face ligand, binds sodium and potassium trifluoromethanesulphonate more strongly than encapsulating ligands like [2.2.1]- and [2.2.2]-cryptand.

Pedersen's seminal discovery and study of crown ethers[1] inspired the development of several families of complexing agents for alkali metal ions.[2] As exemplified by structural formulae (**1**)—(**5**), crown ethers (**1**), cryptands (**2**),[2,3] cryptaspherands (**3**),[2,4] and spherands (**4**)[2,5] constitute a host family series of increasing preorganization (rigidity) and increasing encapsulation (solvent exclusion). Binding strength and selectivity also generally increase in the progression from (**1**) to (**4**).[2] Torands[6] [*e.g.* (**5**)][7] are radically different from other neutral hosts for alkali metals in that they are relatively rigid yet *non*-encapsulating. Tri-n-butyl torand (**5**) was recently synthesized and found to sequester calcium.[7] We have now discovered that (**5**) forms exceptionally stable complexes with alkali metal ions.

Torand (**5**) was first isolated as a calcium trifluoromethanesulphonate (triflate) complex from a two-component macrocyclization reaction.[7] Currently, the monotriflate salt [(**5**)·CF_3SO_3H·$2H_2O$]† is obtained in 30% yield from the cyclization precursors.[7] This salt is readily converted to various alkali metal complexes. Triflate salts of (**5**), free (**5**), and its complexes with metal triflates and picrates are all soluble in dichloromethane. When CH_2Cl_2 solutions of (**5**)·CF_3SO_3H·$2H_2O$ were shaken with aqueous solutions of sodium hydroxide or potassium carbonate and the residues from the organic layers were recrystallized, complexes were obtained having the compositions (**5**)·$NaCF_3SO_3$·1.5EtOH·0.5H_2O† and (**5**)·KCF_3SO_3·$3H_2O$.† The free ligand was also liberated from its salt by treatment with tetra-n-butylammonium hydroxide in n-butanol/acetonitrile, yielding (**5**)·Me_3CN·$2H_2O$† as fine beige needles, m.p. >250 °C (decomp.). Solutions of free (**5**) in CH_2Cl_2 were then shaken with aqueous alkali metal picrates to provide (**5**)·Li(picrate)·1.5H_2O,† (**5**)·Na(picrate),† (**5**)·K(picrate),† (**5**)·Rb(picrate),† and (**5**)·Cs(picrate).† Alkali metal complexes of (**5**) could be decomposed by washing their CH_2Cl_2 solutions with aqueous triflic acid, resulting in extraction of the alkali metal triflate into the aqueous phase.

The stabilities of the alkali metal picrate complexes of torand (**5**) were initially examined by distribution between chloroform and water.[8] In these experiments, 1.3 mM solu-

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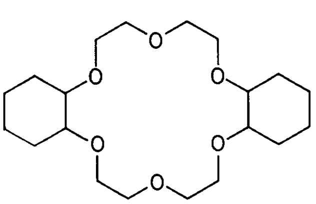
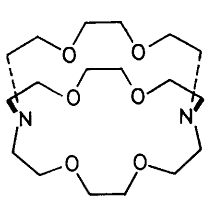
† Stoicheiometry consistent with C, H, and N microanalytical data and spectroscopic properties (^{1}H NMR and IR).



(1)



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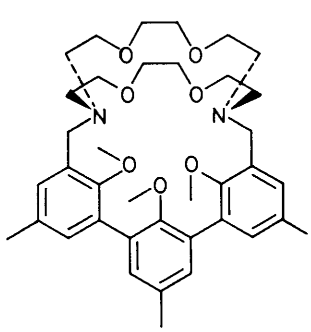

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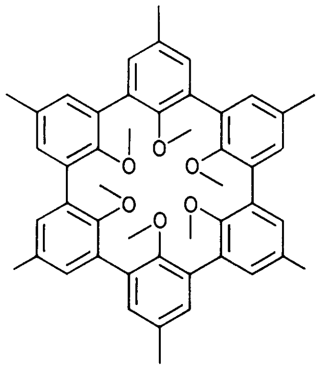

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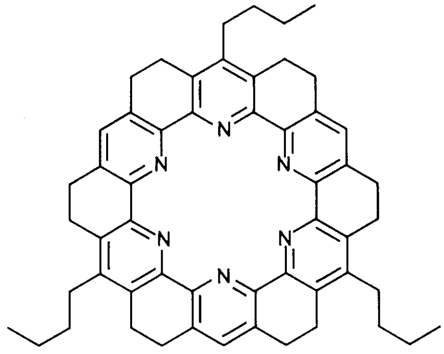

(5)

Table 1. Stabilities (log K_s) of sodium and potassium picrate complexes of hosts (**1**)—(**5**) in D_2O-saturated $CDCl_3$ at 25 °C.

Picrate	(**1**)[a]	(**2**)[b]	(**3**)[b]	(**4**)[c]	(**5**)[d]
Na	6.4	10.6	9.9	14.1	14.7
K	8.3	13.2	13.9	<4.4	14.3

[a] Ref. 8. [b] Ref. 4 [c] Ref. 9. [d] Determined by ^1H NMR competition experiments with (**2**) or [2.2.1]cryptand (estimated error ± 0.4). Calculated values were independent of total ligand concentration between 2×10^{-4} and 3×10^{-3} M.

tions of (**5**) in chloroform were shaken with buffered aqueous solutions of alkali metal picrates (0.1—0.6 mM). All the alkali metal picrates examined (Li, Na, K, and Cs) were completely extracted into the chloroform layer, showing that the log K_s values of these complexes all exceed 11. Crown ethers typically form weaker complexes and incompletely extract alkali metal picrates in such experiments.[1,8]

The stability constants of (**5**)·Na(picrate) and (**5**)·K(picrate) could be estimated by competition with potent complexing agents, such as [2.2.1]- and [2.2.2.]-cryptand (**2**). These experiments were conducted in D_2O-saturated $CDCl_3$, as described by Cram and Ho for measuring stabilities of cryptaspherand complexes.[4] Thus, with various ratios of (**5**)·K(picrate) plus [2.2.2]cryptand (**2**) or of (**5**) plus (**2**)·K(picrate) the equilibrium position was measured by integration of complexed and uncomplexed cryptand ^1H NMR signals. In the case of (**5**)·Na(picrate), [2.2.2]cryptand could not effectively compete for sodium, whereas the ^1H NMR signals of free and sodium-complexed [2.2.1]cryptand could not be resolved completely at 300 MHz. In this case the chemical shift of rapidly exchanging picrate was used to calculate the ratios of (**5**)·Na(picrate) (δ 8.32) and [2.2.1]cryptand·(Na)-(picrate) (δ 8.83).‡

The calculated log K_s values for (**5**)·Na(picrate) and (**5**)·K(picrate) are compared in Table 1 with corresponding values for (**1**)—(**4**). Remarkably, (**5**) generally forms stronger complexes with sodium and potassium picrate even than cryptand (**2**), cryptaspherand (**3**), and spherand (**4**). An experiment involving direct competition of (**5**) with (**3**)·KSCN confirmed that the stabilities of the potassium complexes of these hosts are approximately equal. A smaller homologue of (**3**) forms a stronger complex with Na(picrate) (log K_s 15.4),[4] whereas (**4**)·Li(picrate) is the most stable alkali metal complex formed by the series of ligands considered here (log $K_s > 17$).[9] Despite the exceptional rigidity of the central 18-membered ring in host (**5**), no significant selectivity is observed between potassium and sodium. A trend towards lower selectivity was previously observed in a more flexible, planar nitrogen analogue of 18-crown-6.[10]

Host (**5**) is also remarkable in that the ^1H NMR signals of (**5**) (δ 7.50) and (**5**)·K(picrate) (δ 7.44) exchange rapidly at 300 MHz (δ 7.45 for a 1 : 2 mixture at $\approx 10^{-3}$ M in $CDCl_3$). Line broadening occurs at lower concentration (10^{-4} M), whereas the ^1H NMR signals of (**5**) and (**5**)·Na(picrate) are in slow exchange even at 10^{-3} M. These observations are consistent

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‡ A small concentration dependence of the (**5**)·Na(picrate) chemical shift was taken into account in K_s calculation. This method could not be used for (**5**)·K(picrate) for which the picrate ^1H NMR shift was sensitive to the presence of free (**5**). Protonation of the cryptand was shown to be unimportant by addition of DBN, which did not change the calculated K_s value. Aqueous pK_a values for [2.2.1]cryptand and 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) are 11.8 and 13.5, respectively.

with the transient formation of a 2:1 potassium complex [(**5**)$_2$·K(picrate)] that facilitates exchange but does not significantly alter the equilibrium concentrations of (**5**) and (**5**)·K(picrate). They are inconsistent with a rate-limiting unimolecular dissociation process for (**5**)·K(picrate), which would limit the exchange rate to less than 10^{-7} s^{-1}, assuming that the complexation rate cannot exceed a diffusion-controlled limit of *ca.* 10^{10} s^{-1}.

Torand (**5**) displays a unique combination of properties. Alkali metals bind tightly and rapidly to its exceptionally rigid, open cavity, proving that encapsulation is not required for strong binding. Coplanar preorganization of six pyridine dipoles[10] produces an electron rich cavity that binds Na^+ and K^+ equally well, despite the usual preference of 18-membered macrocyclic ligands for potassium. It remains to be seen whether strong binding and poor selectivity are general consequences of rigid nonencapsulating host structures. Torand (**5**) is also extraordinary in that binding generally occurs within the time of mixing, whereas encapsulating hosts such as (**2**)—(**4**) require periods ranging from minutes to days to reach equilibrium. These good kinetic properties suggest that torands might be useful for rapidly sequestering dissolved metals, which can be recovered by treating the torand complex with dilute acid.

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