4,7,13,16-Tetraoxa-1,10-diazabicyclo[8.8.2]icosane; a Highly Selective Sodium Cation Complexer

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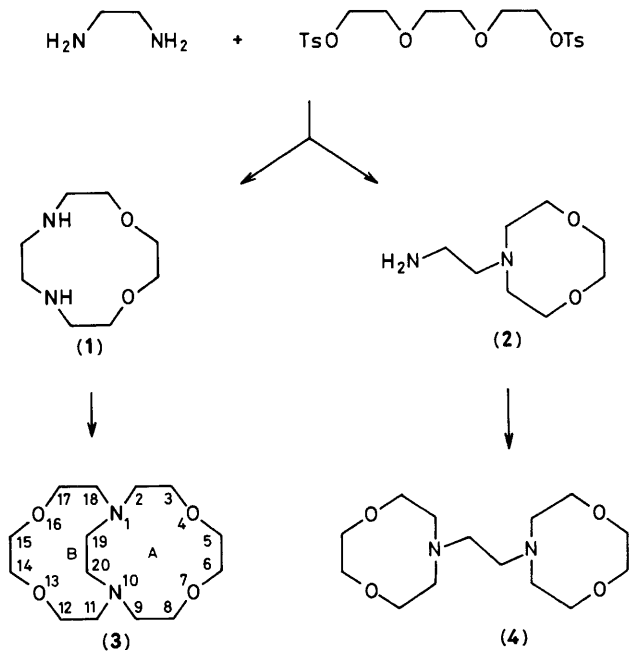
A one-pot reaction provides a novel type of bicyclic ligand with strong affinity for alkali cations and a selectivity due to the invariability of the complexing conformation of the 12-membered ring.

We have already reported on bicyclic amino-ether ligands designed for complexation of cations the size of Na^+, Ca^{2+}, and La^{3+}, which consist of two 12-membered rings joined together by one[1] or by two[2] ethylene bridges. In the former ligand the two rings are not preorganized for complexation, while the latter has a structurally very closed cavity. We now report on a novel bicyclic type of ligand having one 12-membered ring 1,4-condensed on the other. Both rings are thereby brought together for complexation, still leaving the structure open enough to allow easy access for the cation.

In an experiment set up to prepare 1,4-dioxa-7,10-diazacyclododecane (**1**) from ethylenediamine (1 mol) and triethyleneglycol ditoluene-*p*-sulphonate (1 mol) in refluxing acetonitrile with suspended Na_2CO_3, it turned out that the further reaction of the cyclic diamine with a second mole of the ditoluene-*p*-sulphonate was much faster. The bicyclic ligand (**3**) was formed directly and as the almost exclusive non-polymeric product. The isomeric bicyclic ligand (**4**) was formed in only very small amounts, and the monocyclic intermediates (**1**) and (**2**) were not identified in the reaction mixture. Ligand (**3**) was isolated as its crystalline sodium toluene-*p*-sulphonate complex, from which the free ligand could be obtained by pyrolysis *in vacuo* [m.p. 65 °C, ^{13}C n.m.r. (CD_3OD): δ 52.8, 57.6, 71.6, 71.3].

The complexation properties of (**3**) were studied by titration with dry alkali thiocyanates in methanol, monitored by ^{13}C



Ts = tosyl

Table 1. Crystallographic data for ligand (**3**) and three alkali cation complexes.

Complex	(**3**)	(**3**)·LiSCN·½H_2O	(**3**)·NaSCN	(**3**)·KSCN
Space group	*Pbcn*	$P2_1/n$	$P2_1/m$	$P2_1/m$
a/Å	7.841(3)	10.201(3)	8.318(3)	7.799(2)
b/Å	14.072(4)	14.364(3)	11.921(7)	12.131(5)
c/Å	14.210(5)	12.855(4)	10.177(4)	10.301(2)
α/°	—	—	—	—
β/°	—	104.44(3)	111.90(3)	103.28(2)
γ/°	—	—	—	—
Z	4	4	2	2
D_m/g cm^{-3}	1.20	1.30	1.30	1.32
D_c/g cm^{-3}	1.22	1.32	1.31	1.35
Observed reflections	1063	2485	1353	1414
R/%	3.4	6.4	3.6	4.6
R_w/%	3.5	6.9	4.1	6.1
Number of refined parameters	147	218	186	186

Table 2. Torsion angle sets (in degrees) of the four units of each twelve-membered ring of free and complexed ligand (**3**).

	Unit 1—4(A) and 10—13(B)			Unit 4—7(A) and 13—16(B)			Unit 7—10(A) and 16—1(B)			Unit 10—1(A) and 1—10(B)		
	NC	CC	CO	OC	CC	CO	OC	CC	CN	NC	CC	CN
(**3**) (free ligand)[a]	−151	71	−107	−170	−85	78	−157	76	78	−152	65	81
(**3**)·LiSCN·½H_2O[b]	−162	55	100	−165	53	74	−172	56	90	−160	55	75
(**3**)·NaSCN[b]	−160	58	90	−166	60	73	−166	61	73	−158	64	80
(**3**)·KSCN[b]	−157	63	80	−167	60	76	−162	69	60	−159	70	80

[a] Rings A and B identical by symmetry. [b] Average of very similar values in rings A and B.

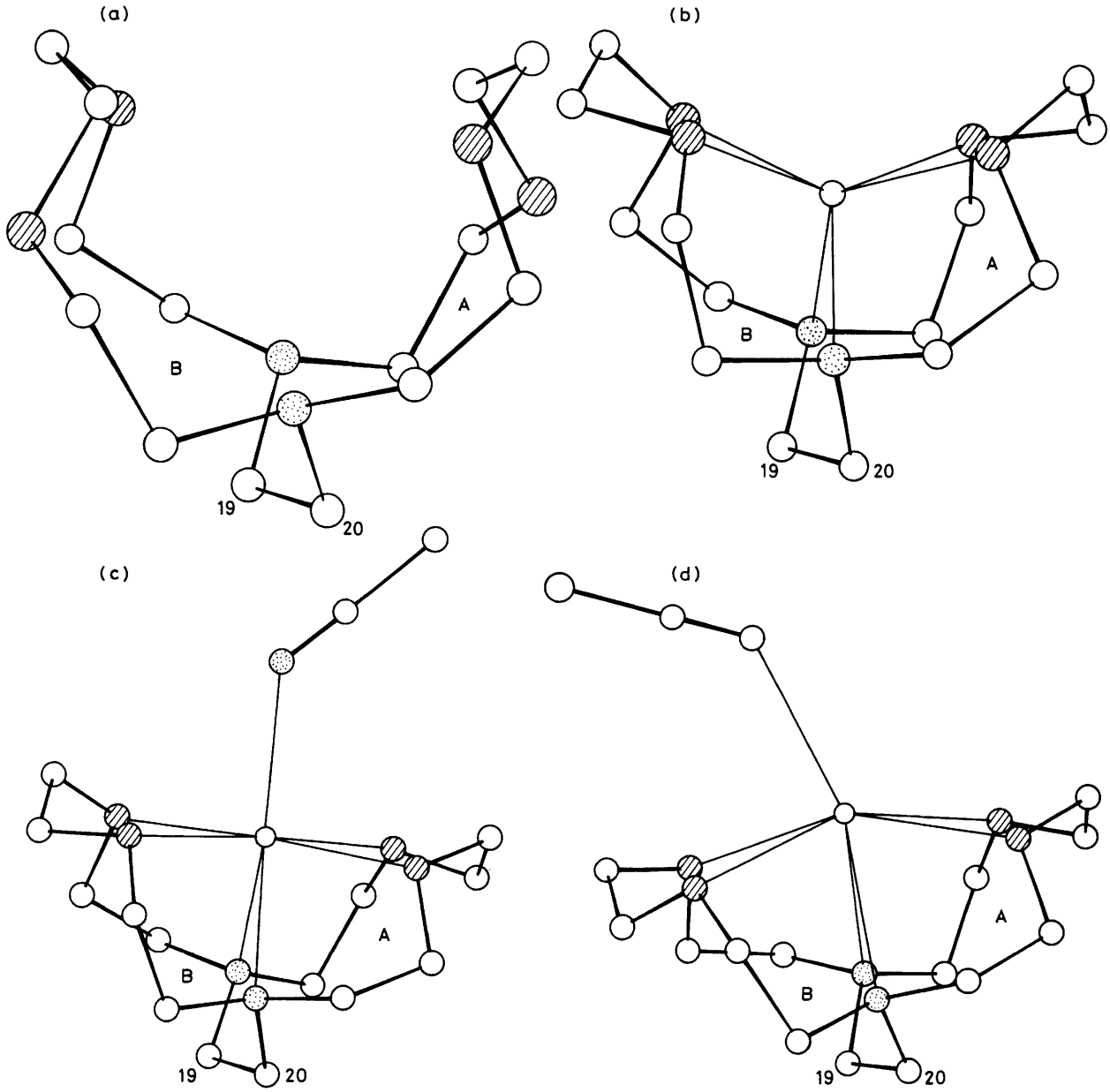


Figure 1. The crystal conformation of ligand (**3**) in (a) the uncomplexed state; and in its complexes with (b) LiSCN, (c) NaSCN, and (d) KSCN. Key numbering A, B, 19, and 20 refers to Table 2 through formula (**3**).

n.m.r. spectroscopy. Slow exchange between free and complexed ligand was observed in the case of K^+ below −28 °C, for Li^+ below 32 °C, and for Na^+ up to at least *ca.* 80 °C, from which decomplexation barriers $\Delta G^{\ddagger}$ of 11, 14, and >16 kcal/mol† respectively were calculated. The sequence of complex stabilities, as determined by pH-metric titration[3] of the free ligand (**3**) and of the complexes separately, using HCl in methanol–water (9:1), was however different, complexation energies $-\Delta G°$ of 4.7, 5.2, and 8.3 kcal/mol† being obtained for Li^+, K^+, and Na^+ respectively. This means that the expectation[4] that the rates of complex formation should be similar and diffusion-controlled (*ca.* 10^{10} mol^{-1} dm^3 s^{-1}) is not fulfilled. This stability sequence was confirmed for methanol solutions by direct observation of ^{13}C n.m.r. lines of individual complexes in equilibrium mixtures. In water the corresponding values were <1, <1, and 4.3 kcal/mol,† again demonstrating the strong Na^+ selectivity.

In order to verify that the Na^+ complex has indeed the expected ligand conformation with both rings in the quadrangular [3333] conformation of the same chirality,[1,2] and also to learn how the rings are modified in the other complexes as well as in the free ligand, the crystal structures were determined by *X*-ray diffraction (Table 1).‡ The essential part of these structures is shown in Figure 1.

† 1 kcal = 4.18 kJ.

‡ The details of the *X*-ray analyses will be published in *Acta Chem. Scand.* The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

It is seen that not only in the Na^+ complex, but also in the Li^+ and K^+ complexes, both rings of (**3**) have chosen the familiar [3333] conformation;[5—7] only the numerical values of the torsion angles vary (Table 2). 'Corner atoms' are at C(3), C(6), C(9), and C(19) for ring A, and at C(12), C(15), C(18), and C(20) for ring B. Particularly large changes of torsion angle are found in each pair of *gauche* bonds at corners 3,9,12, and 18, and in the bridge CC bond. To adapt to the smaller Li cation, the values become reduced from those for the Na complex in the CC bonds involved, but increased in the CO and CN bonds. To adapt to the larger K cation the opposite is observed (Table 2). Handling of mechanical models suggests that it is just these changes that are the most efficient in narrowing and opening the cleft between the rings.

A co-ordination number of seven is found for Na^+ and K^+, the anion being the seventh ligand, whereas Li^+ is hexaco-ordinated without any contact to the anion. Thus, only Na^+ has attained its optimal co-ordination number,[7] and the ligand clearly has the least conformational strain. The optimal co-ordination number in this type of complexes is only five for Li^+.[7] The K^+ ion readily takes co-ordination numbers up to ten, and so in this case it is co-ordinatively unsaturated.

The uncomplexed ligand (**3**) has both rings in the biangular [39] conformation. This can be obtained[6] from the [3333] conformation simply by rotating O(4) through ring A, whereby one hydrogen from C(5) will make contact with the lone pair electrons on N(1) and O(16), and similarly by rotating O(13) through ring B, whereby one hydrogen from C(14) will make contact with N(10) and O(7). In this way, electron pair repulsion is reduced, and the cleft between the two rings is closed up.

On the basis of this easy opening and closing, and the general topology of ligand (**3**), we propose the generic name 'di-ptychand' (di-ptychos = hinged double tablet). The conformational flexibility, including nitrogen inversion, is demonstrated by the fact that geminal site exchange of hydrogens is fast on the n.m.r. scale down to −40 °C for the free, but not for the complexed ligand. This shows that the cation selectivity must be due to a conformational preference rather than to the size of a closed structural cavity as for the cryptands.[3] More lipophilic ligands have been synthesized by replacing ethane-1,2-diamine with propane-1,2-diamine or 3-phenylpropane-1,2-diamine. Geminal exchange then becomes strongly impeded, but the complexation properties remain unchanged. Also di-ptychands with larger rings have been made, but less easily.

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