Synthesis and lithium ion selectivity of 14-crown-4 derivatives having bulky subunits: *cis* and *trans* isomers of 2-phenylcyclohexano-14-crown-4, 2,3-diphenylcyclohexano-14-crown-4 and 2,3-di-(1-adamantyl)-14-crown-4

Yoshito Tobe,*[,a] Yuko Tsuchiya,[a] Hidekazu Iketani,[a] Koichiro Naemura,[a] Kazuya Kobiro,*[,b,d] Mayumi Kaji,[b] Sachiko Tsuzuki[b] and Koji Suzuki[c]

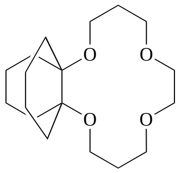
[a] *Department of Chemistry, Faculty of Engineering Science, Osaka University, 1-3 Machikaneyama, Toyonaka, Osaka 560, Japan*
[b] *Niihama National College of Technology, 7-1 Yagumo-cho, Niihama, Ehime 792, Japan*
[c] *Department of Applied Chemistry, Faculty of Science and Technology, Keio University, 3-14-1 Hiyoshi, Kohoku-ku, Yokohama 223, Japan*
[d] *Present address: Inoue Photochirogenesis Project, ERATO, 4-6-3 Kami-shinden, Toyonaka, Osaka 565, Japan*

cis- and _trans_-2-Phenylcyclohexano-14-crown-4, _cis_- and _trans_-2,3-diphenylcyclohexano-14-crown-4, and _cis_- and _trans_-2,3-di-(1-adamantyl)-14-crown-4 have been prepared and their ion selectivities toward alkali metal cations examined by means of the extraction of alkali metal picrates, the measurement of stability constants of the complexes with lithium or sodium perchlorate, and the electrode response potential measurement for the ion-sensitive membranes. The remarkable dependence of the complexation ability to Li^+ on the _cis_/_trans_ stereochemistry of the ionophores is discussed on the basis of their geometries estimated by molecular mechanics calculations and the structures of _cis_- and _trans_-diphenylcyclohexano derivatives determined by X-ray structure analyses. In order to assist the discussion, the X-ray structure analyses of the lithium picrate complex of decalino-14-crown-4 and the 2:1 'sandwich-type' complex of benzo-14-crown-4 with sodium perchlorate have also been undertaken.

Introduction

Much interest has been focused on lithium ionophores with regard to their ion-selective analysis and extraction and their biological applications.[1] For example, lithium ion-selective electrodes have potential applications to medical and clinical use in the therapy of manic-depressive psychosis.[2] The most important issue in the use of lithium ion ionophores in biological system is their selectivity against the interfering sodium ion which is most abundant. A number of Li^+-selective ionophores such as dioxadiamides,[3] a phenanthroline derivative,[4] and crown-4 ethers[5] have been synthesized, many of which exhibited Li^+/Na^+ selectivity up to a value of 10^2. A hybrid system composed of a 14-crown-4 ring and amide groups exhibited Li^+/Na^+ selectivity in the order of 10^3 ($\log K^{\mathrm{pot}}_{\mathrm{Li,j}} = -3.25$).[6] However, still higher selectivity is required for their practical use. In this connection, it is important to elucidate fundamental factors which govern the Li^+/Na^+ selectivity.

We reported previously that decalino-14-crown-4 **1** and its derivatives having a bulky subunit on one of the ethano bridges of the macro ring exhibited excellent Li^+/Na^+ selectivities (in the order of 10^3).[7] The basis of this molecular design is twofold: (1) The decalin unit would preorganize the crown ring to bind Li^+ favourably. We believed, at first intuitively, that the O–C–C–O torsion angle involving the decalin unit must be near 60° or even smaller, which is suitable for binding the smaller Li^+ ion rather than Na^+ owing to the favourable orientation of the lone-pair electrons of the donor oxygen atoms. (2) The bulky subunit would prevent the formation of 2:1 (crown ether: cation) complexes with the larger Na^+ ion because of the steric hindrance between the two ionophores. We also reported that crown ethers such as didecalino-14-crown-4 **2a** having two bulky subunits, one at each side of the ethano bridge, exhibited even better Li^+/Na^+ selectivity in the extraction of alkali metal picrates.[8] Recently, an improved synthesis of a didecalino derivative **2b** and related compounds was reported by Sachleben *et al.*, who confirmed the excellent properties of the didecalino system as a Li^+ extractant.[9] However, we found the ionophores having two bulky subunits were far less selective than those with one bulky subunit as ion carriers for Li^+-selective electrodes.[7c]



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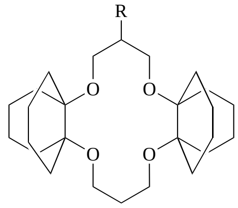
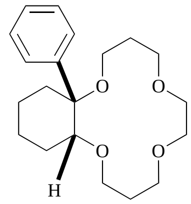


2a R = H
2b R = Me

Recently, we reported that the phenylcyclohexano unit and the adamantyl group incorporated in homochiral 18-crown-6 ethers and related phenolic crown ethers exerted effective steric hindrance as chiral barriers in complexations with chiral amines or amino acids.[10] It occurred to us that these bulky subunits may well serve as alternatives for the decalino group in Li^+-selective ionophores. Moreover, it would also be interesting to investigate the steric effects on the Li^+/Na^+ selectivity for the pairs of *cis*/*trans* diastereomers. In this connection, we prepared *cis* and *trans* isomers of 2-phenylcyclohexano-14-crown-4 (**3** and **4**), 2,3-diphenylcyclohexano-14-crown-4 (**5** and **6**), and 2,3-di-(1-adamantyl)-14-crown-4 (**7** and **8**), and investigated their selectivity and binding ability towards alkali metal cations.[11] The Li^+/Na^+ selectivities were determined by means of the extraction of alkali metal picrates, the measurement of stability constants with lithium and sodium perchlorate, and the electrode response potential measurement for the ion-sensitive membranes. The difference between the complexation abilities of the ionophores **1** and **3**–**8** is discussed on the basis of their geometries estimated by molecular mechanics calculations, and the structures of *cis*- and *trans*-diphenylcyclohexano derivatives **5** and **6** were determined by X-ray crystallographic analyses.



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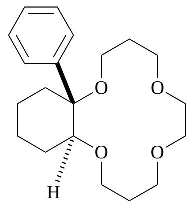

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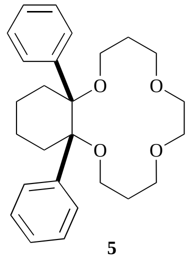

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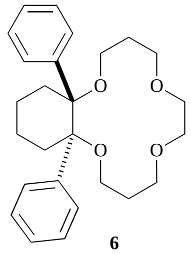

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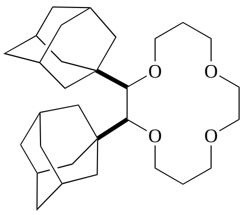

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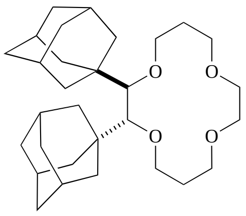

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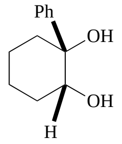
Results and discussion

Syntheses of ionophores 3–8

The crown ethers **3**–**8** were prepared by condensation of the corresponding diols **9**–**14** with ditosyl derivative **15b**[5b] or dimesyl derivative **15c** of 4,7-dioxadecane-1,10-diol **15a**. *cis*- and *trans*-1-Phenylcyclohexane-1,2-diol **9**[12] and **10**[13] and *trans*-1,2-diphenylcyclohexane-1,2-diol **12**[10a] were prepared according to the reported procedures. *cis*-Diol **11** was prepared by the intramolecular pinacol coupling of 1,6-diphenylhexane-1,6-dione[14] using the protocol of Corey *et al.*[15] (Scheme 1). During the course of our work, a stereoselective preparation of *meso*-di-(1-adamantyl)ethanediol **13** by the $NaBH_4$ reduction of 1,2-di-(1-adamantyl)-2-hydroxyethanone **16a**[16] was reported [*meso*-**13**:(±)-**14** = 5:1];[17] the observed high stereoselectivity was attributed to chelation control. In fact, the $NaBH_4$ reduction of non-chelating acetate **16b** was reported to afford a mixture of *erythro*- and *threo*-hydroxyacetates in the ratio 1.5:1.[17] In order to improve the stereoselectivity in the reduction under non-chelation control, we thought that the hydroxy group of acyloin **16a** should be converted to a highly sterically demanding group. Indeed, the $LiAlH_4$ reduction of *tert*-butyldimethylsilyl ether **16c** followed by hydrolysis gave (±)-diol **14** with high stereoselectivity [*meso*-**13**:(±)-**14** = 1:23; Scheme 1].



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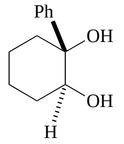

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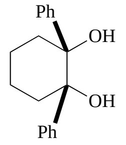

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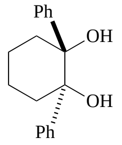

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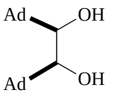

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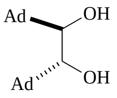
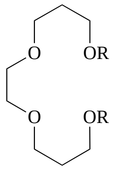
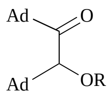


14

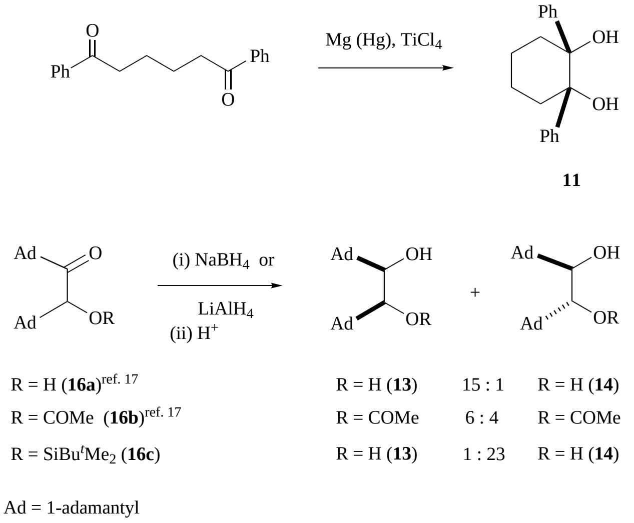
Ad = 1-adamantyl



15a R = H
15b R = Ts
15c R = Ms



16a R = H
16b R = COMe
16c R = $SiBu^tMe_2$



Scheme 1 Stereoselective preparation of *cis*-diol **11** and stereospecific preparation of *meso*-diol **13** and (±)-diol **14**

The condensation of diols **9**–**14** with ditosyl (**15a**) or dimesyl (**15b**) derivatives was carried out under high-dilution conditions in tetrahydrofuran (THF) using NaH as a base and $LiClO_4$ as a template. The isolated yields of the crown ethers **3**–**8** were 50, 35, 4, 3, 2, and 50%, respectively. It should be noted that the yields of crowns *trans*-**4**, *trans*-**6**, and *cis*-**7** were considerably lower than those for the corresponding isomers, *cis*-**3**, *cis*-**5**, and *trans*-**8**. The low yields of the *trans* isomers **4** and **6** are ascribed to the low population of the conformation suitable for cyclization. Namely, since it is not possible to form a 14-membered ring from diaxial alkoxides derived from diols **10** and **12**, the products must be formed from energetically less favourable diequatorial alkoxides in which the phenyl group(s) occupies an axial position. Similarly, the low efficiency in the cyclization of *meso*-diol **13** is due to the *anti* orientation of the hydroxy groups in its most stable conformer, in which the two adamantyl groups occupy *anti* positions. The O–C–C–O torsion angle of the most stable conformer of **13** was estimated to be 168° by MM3* calculations.[18]

Alkali metal ion selectivities of ionophores 3–8

In order to achieve insight into the selectivities of the ionophores **3**–**8** toward alkali metal ions, we first carried out extraction experiments of alkali metal picrates in a water/CH_2Cl_2 system. As shown in Table 1, *cis*-diphenylcyclohexano derivative **5** exhibited the largest extractability for Li^+, which was comparable to that of decalino-14-crown-4 **1**.[7a] Although the extractabilities of *cis*-phenylcyclohexano and *trans*-diadamantyl derivatives **3** and **8** were moderate, they showed high Li^+/Na^+ selectivity values which were as large as those of

Table 1 The extraction of alkali metal picrates in water/CH_2Cl_2 system by ionophores **1** and **3**–**8**

	Extractability[a] (%)					
Ionophore	Li^+	Na^+	K^+	Rb^+	Cs^+	Li^+/Na^+ selectivity
1[b]	81	5	1	1	0	16
3	42.8	7.7	1.4	<1	<1	7.7
4	3.1	<1	<1	<1	<1	*c*
5	74.1	4.8	1.1	1.0	1.1	15
6	1.6	<1	<1	<1	<1	*c*
7	<1	<1	*d*	*d*	*d*	*c*
8	38.9	1.2	<1	<1	<1	32

[a] [ionophore] = 7.00×10^{-4} mol dm^{-3}, [picric acid] = 7.00×10^{-5} mol dm^{-3}, [alkali metal hydroxide] = 1.00×10^{-1} mol dm^{-3} at 25 °C. The extractability (Ex) is defined as follows: Ex = $[M(CE)Pic]_{org}/[MPic]_0$, where M, CE, Pic and $[MPic]_0$ denote alkali metal, crown ether, picrate, and the initial concentration of alkali metal picrate in the aqueous phase, respectively. The initial concentration of alkali metal picrate in the aqueous phase is equal to that of picric acid in the aqueous phase, because a large excess of a metal hydroxide was used. The equation is thus rewritten as follows: Ex = $[M(CE)Pic]_{org}/[HPic]_0$, where $[HPic]_0$ is the initial picric acid concentration in the aqueous phase. [b] Ref. 7*a*. [c] The Li^+/Na^+ selectivity was not determined because of the low extractability of crowns **4** and **6** for Na^+ and of crown **7** for both Li^+ and Na^+. [d] Not determined.

compounds **1** and **5**. On the other hand, *trans* isomers **4** and **6** exhibited only low extractability for Li^+ and nearly negligible extractability for other metal cations. Moreover, *cis*-diadamantyl derivative **7** did not show any extractability even for Li^+ under similar conditions.

Next, the binding constants for phenylcyclohexano derivatives **3**–**6** with lithium and sodium perchlorate were determined by the titration method using ^7Li and ^{23}Na NMR spectra in order to obtain more quantitative information on the ion selectivities (Table 2). The NMR measurements were undertaken in cyclohexanone at 80 °C in order to attain the rapid equilibrium between free and complexed ions on the NMR time-scale.[19] The use of low boiling solvents such as THF, acetone, and acetonitrile led to the broadening or splitting of the signals owing to the slow exchange rate between the two cationic species. The formation of 1 : 1 (ionophere : cation) complexes under these conditions was checked by Job's plot[20] for all complexes for which the stability constants were determined. The binding constants for diadamantyl derivatives **7** and **8** were not measured, however, because of the limited solubility of the ionophores in cyclohexanone. As can be seen from Table 2, *cis* isomers **3** and **5** showed high Li^+/Na^+ selectivity as well as high stability constants for Li^+. On the other hand, the binding constants of *trans* derivatives **4** and **6** to Li^+ were much smaller than those of the corresponding *cis* isomers. The stability constants for the Na^+ complexes of compounds **4** and **6** were too small to be determined with reasonable accuracy.

Finally, the performance of the ionophores **3**–**6** and **8** as ion carriers for ion-selective electrodes was investigated by the measurement of the electrode response potential using poly(vinyl chloride) (PVC)-membrane electrodes containing these ionophores. The selectivity coefficients are summarized in Fig. 1 and Table 3. As shown in Fig. 1, *cis*-diphenyl derivative **5** exhibited excellent selectivity for Li^+ ($\log K^{\text{pot}}_{\text{Li,Na}} = -3.1$), in good agreement with its extractability and binding constants. This selectivity is comparable to that of decalino derivative **1** (−3.3).[7b,c] To our dismay, however, *cis*-phenylcyclohexano and *trans*-diadamantyl derivatives **3** and **8**, which showed moderate selectivity in the metal-extraction and -binding constants, exhibited substantially lower selectivities (−1.9 and −2.0, respectively) than that of compound **5**.

Structures of ionophores 1 and 3–8

In order to understand the difference between the complexation abilities of the ionophores **1** and **3**–**8**, their structures were examined by molecular mechanics calculations using the MM3* force-field.[18] The most stable conformers are shown in Fig. 2 and the steric energies and O–C–C–O torsion angles involving the bulky subunits are listed in Table 4. As shown in Table 4, *cis* isomers **3** and **5** are considerably more stable than the corresponding *trans* isomers **4** and **6**, as is *trans*-**8** compared with *cis*-**7**. Fig. 2 shows that the geometries of the 14-membered ring of crowns **1**, **3**, **4** and **6** look similar while that of *cis*-diphenyl derivative **5** adopts a nearly symmetrical pseudo-chair conformation. Closer scrutiny of the geometries (Table 4), however, reveals that the O–C–C–O torsion angles of *trans* isomers **4** and **6** are considerably larger (approximately 70°) than those of *cis* isomers **1**, **3** and **5** (59–66°).

Table 2 The stability constants for the lithium and sodium ion complexes of ionophores **3**–**6**[a]

Ionophore	$K(LiClO_4)$ (mol^{-1} dm^3)	$K(NaClO_4)$ (mol^{-1} dm^3)	Li^+/Na^+ selectivity
3	5100	28	180
4	400	*b*	*c*
5	7000	23	300
6	130	*b*	*c*

[a] Determined by ^7Li or ^{23}Na NMR spectrometry in cyclohexanone at 80 °C. [b] Not determined because the association constants were too small to be determined with reasonable accuracy. [c] Not determined.

The single-crystal X-ray analyses were undertaken for *cis*- and *trans*-diphenylcyclohexano derivatives **5** and **6** (Fig. 3) and the structures were compared with those estimated by MM3* calculations. One of the oxygen atoms (O3) in the X-ray structure of *cis*-**5** has a large thermal parameter, presumably due to a disorder of this atom. In contrast to the calculated structure, the 14-membered ring of *cis*-**5** does not adopt a pseudo-chair conformation. On the other hand, the structure of *trans* isomer **6** possesses a crystallographic C_2 axis passing through the midpoints of bonds C(7)–C(7*), C(1)–C(1*) and C(5)–(5*) and the crown ring adopts a pseudo-chair conformation.[20] The observed O–C–C–O torsion angles (55.6° for **5**, 76° for **6**) are qualitatively in agreement with those for the calculated structures.[21] Thus, taking into account the conformational flexibility of the 14-membered ring,[22] it is reasonable to assume that the calculated structures represent at least one of the lowest-energy conformations.

With regard to the conformation of diadamantyl derivatives **7** and **8**, the 14-membered ring of compound *cis*-**7** is substantially deformed into a conformation having a large O–C–C–O torsion angle (92°). The corresponding *trans*-isomer **8**, on the other hand, adopts a nearly eclipsed conformation with a small O–C–C–O dihedral angle (0°).

Relationship between structure and complexation ability and ion selectivity of ionophores 1 and 3–8

In order to understand the remarkable difference between the complexation abilities of the ionophores **1** and **3**–**8**, we first compared the O–C–C–O torsion angles of the subunit portion of the ionophores with those of the metal-ion complexes. Recently, Hay and Rustad devised the MM3′ parameters for aliphatic ether–alkali metal complexes based on *ab initio* molecular orbital and molecular mechanics (MM3) calculations.[23] They reported that the best-fit O–C–C–O torsion angle for the Li^+-dimethoxyethane chelate was smaller (54°) than those for the corresponding Na^+ (58°) and K^+ (62°) chelates. The observed torsion angles for the Li^+ complexes of *syn*-dicyclohexano-14-crown-4 **17**[22] and didecalino derivative **2b**[24a] are consistent with the calculated value (55° and 51°, respectively). However, Sachleben reported that the torsion angles of the Li^+ complexes of nonamethyl-14-crown-4 **18**[24b] and tetrakis(spirocyclopentano) derivative **19**[24a] are larger than the best-fit angle (73° and 74°, respectively). Since the Li^+-extractability of compound **2b** is twice as much as that of compound **18** and 10^3-

Table 3 Ion selectivity factors (log $K^{pot}_{Li,j}$) of the electrodes based on the ionophores **3**–**6** and **8**

	log $K^{pot}_{Li,j}$									
Ionophore	Li^+	Na^+	K^+	Rb^+	Cs^+	NH_4^+	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}
3	0	−1.9	−1.8	−2.7	−3.3	−3.1	−5.1	−4.7	−4.7	−4.7
4	0	−1.8	−1.8	−1.8	−1.6	−1.8	−4.1	−3.7	−3.7	−3.6
5	0	−3.1	−3.6	−3.8	−3.7	−3.7	−5.5	−5.4	−5	−5
6	0	−1.3	−3.4	−3.5	−1.6	−1.9	−4.4	−4.1	−4.2	−4
8	0	−2	−1.9	−1.8	−1.7	−1.9	−3.8	−3.7	−3.6	−3.8

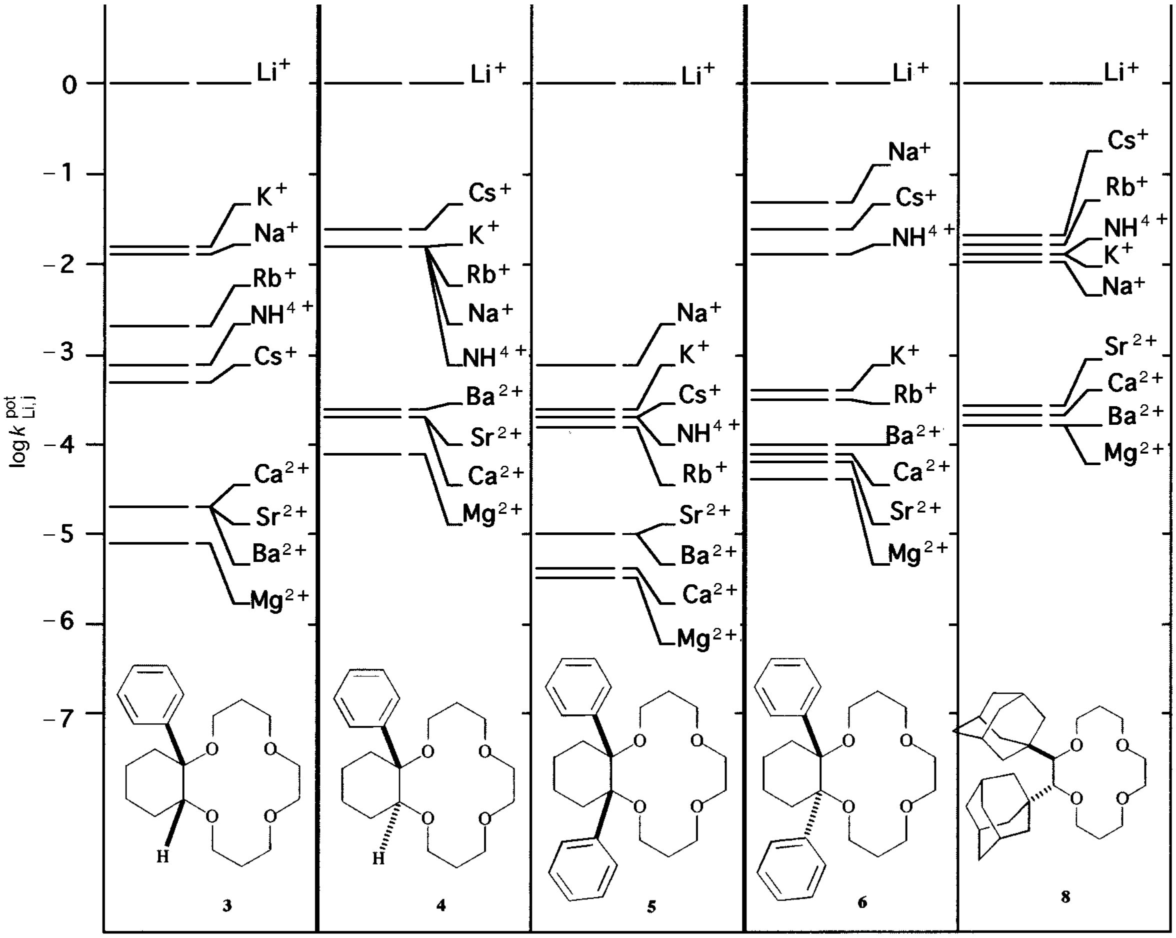


Fig. 1 Selectivity coefficients (log $K^{pot}_{Li,j}$ j = interfering ion) of the electrodes based on ionophores **3**–**6** and **8**. The membrane compositions were 3% (by weight) ionophore, 67.3–67.4% membrane solvent BBPA [bis(1-butylphenyl) adipate], 20 mol% (relative to the ionophore) potassium tetrakis-(*p*-chlorophenyl)borate (KTpClPB) and 28.8–28.9% poly(vinyl chloride) (PVC). The measurements were carried out at 25.0 ± 0.5 °C.

times larger than that of spiro compound **19**,[9] we assume that the small O–C–C–O torsion angle (54°) is one of the important factors for strong binding to Li^+. In order to confirm this assumption, we undertook an X-ray structure analysis of the lithium picrate complex of decalino-14-crown-4 **1**, which exhibited high Li^+-extractability.[7a] As shown in Fig. 4, the structure is similar to that of the LiNCS complex of didecalino-14-crown-4 derivative **2b**.[24a] The crown ring of the complex adopts a pseudo-chair conformation and the Li^+ is located 0.70 Å above the mean-plane of the four oxygen atoms [O(1)–O(2)–O(3)–O(4)]. The O–C–C–O torsion angle of the decalin unit is 51°, supporting the above assumption. It is clearly seen from Table 4 that the ionophores **1** and **5** with relatively small torsion angles (62° and 60°, respectively) exhibited the best complexation ability to Li^+. Consequently, it is deduced that the pre-organization of the O–C–C–O torsion angle to a best-fit angle plays an important role in the complexation ability of ionophores to Li^+.

Next, we looked at the conformational flexibility of the crown ring because the ionophores **3** and **8**, which are not pre-organized to bind Li^+ (the MM3* O–C–C–O torsion angles: 66° and 0°, respectively; Table 4), possess moderate binding ability to Li^+. The flexibility of the crown rings was estimated from the variable-temperature NMR (VT-NMR) spectra. The VT-NMR spectra of the *cis*-phenylcyclohexano and *cis*-diphenylcyclohexano derivatives **3** and **5** revealed that a chair–chair interconversion of the cyclohexane subunits took place rapidly on the NMR time-scale (conformers **A** and **B**; Scheme 2a). For example, while 18 signals were observed in the ^{13}C NMR spectrum of compound **3** ([$^2H_8$]toluene) at 70 °C owing to the rapid equilibrium between the two conformers, the signals split into two sets of peaks at −80 °C with an approximate intensity ratio of 1 : 3. Similarly, the ^{13}C NMR signals of compound **5** split into two sets of peaks at −80 °C with equal intensities. The barriers for the conformational change were estimated by simulating the exchange rates at various temperature based on a line-shape analysis using DNMR2.[25] The $\Delta G^{\ddagger}$ (25 °C)-value for the rotation was calculated from an Eyring plot to be 53.5 ± 5.0 and 45.6 ± 4.2 kJ mol^{-1}, for compounds **3** and **5**, respectively. Consequently, *cis*

Table 4 The energies and O–C–C–O torsion angles estimated by the molecular mechanics calculations (MM3*) for ionophores **1** and **3**–**8**

Ionophore	Steric energy[a] (kJ mol^{-1})	Torsion angle[b] (deg)
1	245.6	62
3	328.5 (0.0)	66
4	247.1 (8.6)	71 (72)
5	333.2 (0.0)	60 (59)[c]
6	344.4 (11.2)	69 (69)[d]
7	413.2 (21.9)	92 (90)
8	391.3 (0.0)	0 (1)

[a] The steric energies relative to the more stable conformer of the diastereomeric pairs are given in parentheses. [b] The O–C–C–O torsion angle involving the bulky subunits. In the case of compounds **4**–**8**, there are three to five conformers with geometries similar to those of the minimum structures. The average O–C–C–O torsion angles for these conformers, whose steric energies are within 4.2 kJ mol^{-1} of the minima, are given in parentheses (unweighted for their population). [c] The observed (X-ray analysis) angle is 55.6°. [d] The observed (X-ray analysis) angle is 76°.

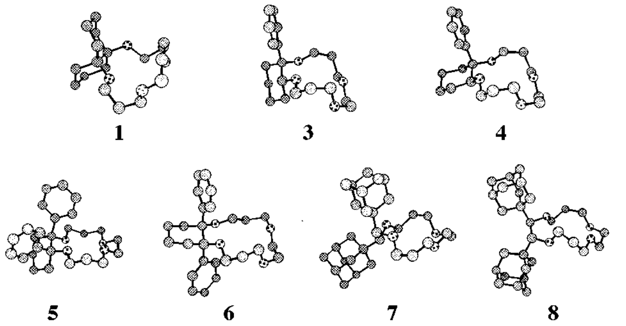


Fig. 2 CHEM3D illustrations for the most stable conformers of ionophores **1** and **3**–**8** derived by the conformation search by MacroModel using the MM3* parameters. Meshed circles are carbon atoms and those with spots are oxygen atoms. Hydrogens are not shown, for clarity.

isomers **3** and **5** can adopt a best-fit conformation without substantial energy cost to bind Li$^+$. On the other hand, such a conformational change was not observed for *trans* isomers **4** and **6**, because it is not possible to form a 14-membered ring for the diaxial oxygen atoms (conformer **D**; Scheme 2b). Moreover, contraction of the O–C–C–O torsion angle would bring about considerable strain in the cyclohexane unit (conformer **C**; Scheme 2b). Therefore, a substantial energy cost would be paid by *trans* isomers **4** and **6** in adopting a best-fit conformation to bind Li$^+$.

cis-Diadamantyl derivative **7** exhibited, in the ^{1}H NMR spectrum (400 MHz, [$^2H_8$]toluene, 30 °C), two singlets due to the methine protons (Ad-C*H*-O) at δ 3.41 and 2.89. The signal did not change even at 80 °C, and so the barrier for conformational change should be higher than 70 kJ mol^{-1} (interconversion between conformers **E** and **G**; Scheme 2c). This is due to the highly strained geometry of the transition state of the rotation, in which the two adamantyl groups are eclipsed (conformation **F**; Scheme 2c). Consequently, it must be highly unfavourable for compound **7** to reduce the inherently large O–C–C–O torsion angle in order to adopt a best-fit conformation for binding a metal cation. On the other hand, the most stable conformer of *trans*-diadamantyl derivative **8** estimated from the MM3* calculations adopts an eclipsed conformation (conformer **H**; Scheme 2d). It is, therefore, not difficult for compound **8** to adopt a *gauche* conformation (conformation **I**; Scheme 2d) which is suitable for cation binding. Indeed, a *gauche* conformation (O–C–C–O torsion angle 64°) was found by the MM3* calculations to be only 13.7 kJ mol^{-1} higher than the most stable conformer **H**. Consequently, we deduced that the steric energy required to adopt a best-fit conformation for Li$^+$ binding is also an important factor in determining the binding ability to Li$^+$.

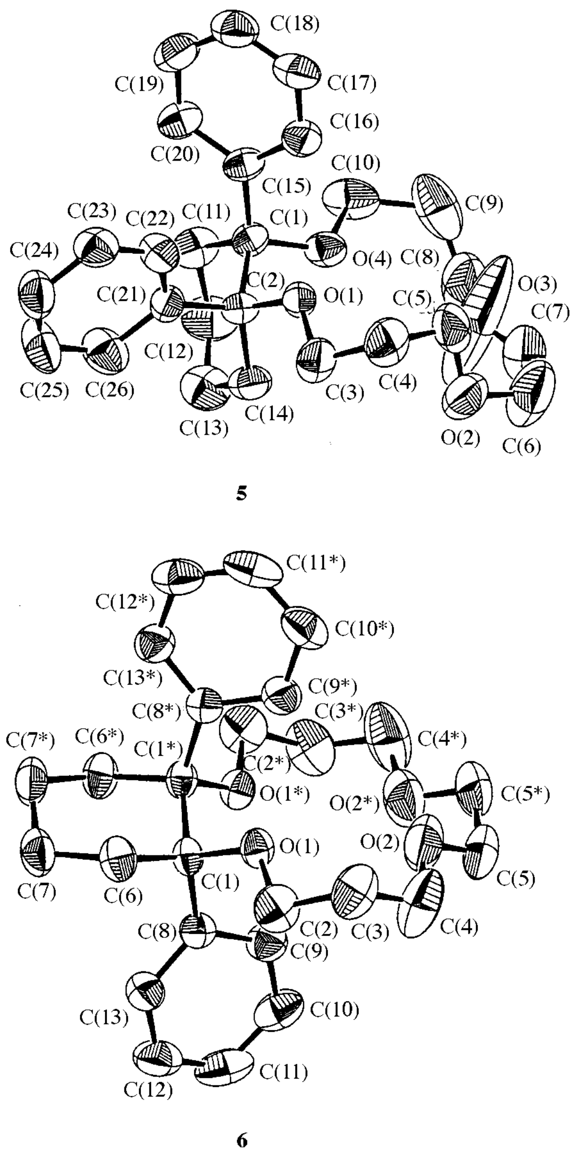


Fig. 3 Molecular structures of *cis*-diphenylcyclohexano-14-crown-4 (**5**: top) and *trans*-diphenylcyclohexano-14-crown-4 (**6**: bottom) determined by X-ray crystallographic analyses. Hydrogens are not shown, for clarity.

Finally, the steric hindrance of the bulky subunits, which prevents formation of a 2 : 1 complex, leading to a high Li$^+$/Na$^+$ selectivity, should be considered. Regarding the formation of 2 : 1 'sandwich-type' complexes, such host : guest stoichiometry has frequently been observed in complexes with large cations relative to the ring size of the crown ethers. For example, it has been shown that dibenzo-18-crown-6 formed 2 : 1 and 3 : 2 complexes with large cations such as Rb$^+$ and Cs$^+$.[26] On the other hand, we have reported that didecalino-18-crown-6 **2a** gave only 1 : 1 complexes with any cation tested, owing to the steric hindrance of the decalin group.[27] Similarly, we found that only 1 : 1 crystalline complexes were isolated from the reaction of decalino-14-crown-4 **1** with $LiClO_4$ or $NaClO_4$ regardless of the initial molar ratio of **1** and the salts. Moreover, in solution, ionophores **3**–**6** formed 1 : 1 complexes with $LiClO_4$, and the formation of 1 : 1 complexes with $NaClO_4$ was also confirmed for hosts **3** and **5**, as described above. With regard to a planar oblate ionophore, benzo-14-crown-4 **20**,[28] we found that it formed only a 1 : 1 complex with $LiClO_4$ with a stability constant of 1100 mol^{-1} dm^3 in cyclohexanone at 80 °C. On the other hand, compound **20** formed both 1 : 1 and 2 : 1 complexes with $NaClO_4$ as judged from Job's plot. In accord with the stoichiometry in solution, we isolated a 1 : 1 complex of compound **20** with LiNCS and a

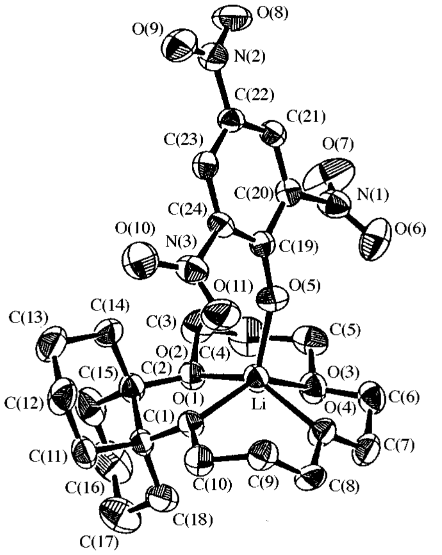
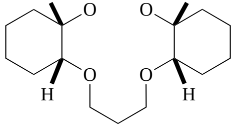


Fig. 4 Molecular structure of lithium picrate complex of decalino-14-crown-4 **1** determined by X-ray crystallographic analysis. Hydrogens are not shown, for clarity.



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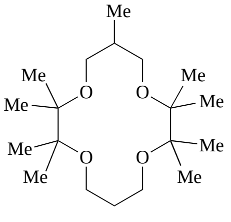

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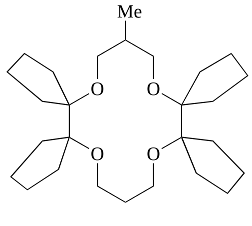

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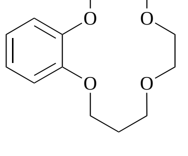
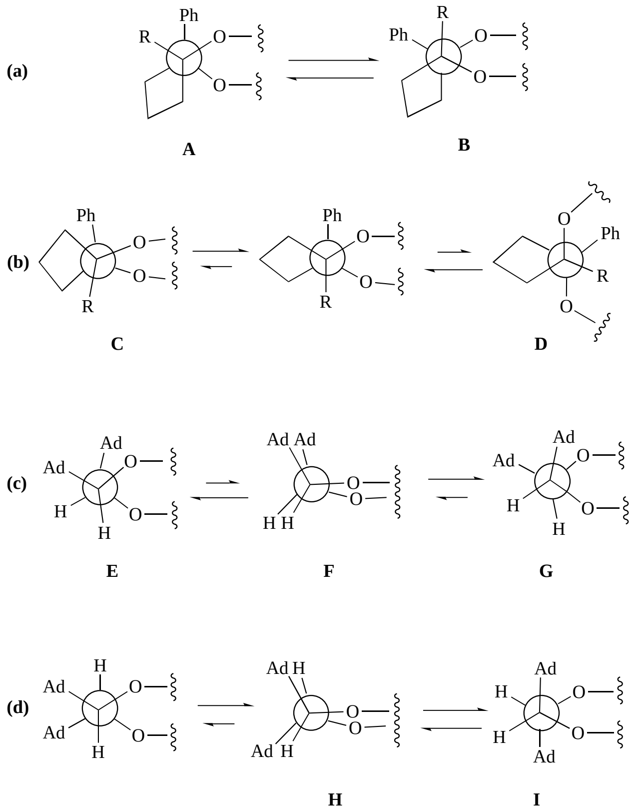


20

2:1 complex with $NaClO_4$.[29] Fig. 5 shows the molecular structure of the 2:1 'sandwich-type' complex determined by an X-ray crystallographic analysis. The sodium atom is located 1.55 Å above the mean plane of the four oxygen atoms [O(1)–O(2)–O(3)–O(4)]. The side view of the molecular structure indicates clearly that there is little steric interaction between the benzene rings of the two ionophores. One can easily imagine that substituting the benzene ring of compound **20** with a bulky group, such as decalino or diphenylcyclohexano, would bring about substantial steric repulsion between the two ionophores.

In conclusion, we have found that *cis*-diphenylcyclohexano derivative **5** exhibited the highest selectivity as well as complexation ability toward Li^+, which were as good as those of the previously reported decalino-14-crown-4 **1**. While *cis*-phenylcyclohexano and *trans*-diadamantyl derivatives **3** and **8** showed moderate complexation ability toward Li^+, *trans*-phenylcyclohexano and *trans*-diphenylcyclohexano derivatives **4** and **6** showed small binding ability and *cis*-diadamantyl derivative **7** did not show any binding ability. The relatively high Li^+-selectivity of *cis*-phenylcyclohexano, *cis*-diphenylcyclohexano, and *trans*-diadamantyl derivatives **3**, **5** and **8** is ascribed to the pre-organization of the O–C–C–O torsion angle, small steric energy required to adopt a best-fit conformation for Li^+ binding, and the steric hindrance of the bulky subunits which prevents the formation of a 2:1 complex.



Scheme 2 Schematic representation of the conformational behaviour of ionophores **3**–**8**. (a) **3** (R = H) and **5** (R = Ph), (b) **4** (R = H) and **6** (R = Ph), (c) **7** and (d) **8**.

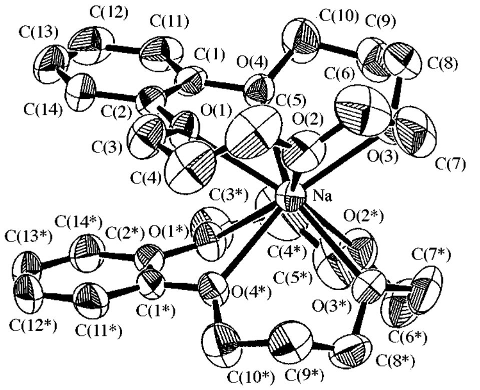


Fig. 5 Molecular structure of sodium perchlorate (1:2) complex of benzo-14-crown-4 **20**, determined by X-ray crystallographic analysis. Hydrogens and perchlorate anion are not shown, for clarity.

Experimental

^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-GX-270 (^1H, 270 MHz; ^{13}C, 67.5 MHz) or an AL-400 spectrometer (^1H, 400 MHz) in $CDCl_3$ at 30 °C. *J*-Values are given in Hz. IR and mass spectra were taken with a Hitachi 260-10 and a JEOL JMS-DX-303-HF spectrometer, respectively. GLC was conducted with a Shimadzu GC-8A gas chromatograph equipped with a 5% SE-52 column. Analytical high-performance liquid chromatography (HPLC) was carried out with a Shimadzu LC-10AS chromatograph equipped with a Inertsil ODS column, and preparative HPLC separations were performed with a JAI LC-908 chromatograph equipped with JAIGEL 1H and 2H with $CHCl_3$ eluent. Light petroleum refers to the fraction with distillation range 40–65 °C.

Materials

cis- and *trans*-1-Phenylcyclohexane-1,2-diol **9**[12] and **10**,[13] *trans*-1,2-diphenylcyclohexane-1,2-diol **12**,[10a] 1,6-diphenylhexane-1,6-dione,[14] di-(1-adamantyl)-2-hydroxyethanone **16a**,[16] 4,7-dioxadecane-1,10-diol **15a**,[5b,c] and its ditosyl derivative **15b**,[5b] were prepared according to the literature procedures.

Preparation of ionophores

***cis*-1,2-Diphenylcyclohexane-1,2-diol 11.** To an ice–salt-cooled suspension of magnesium amalgam prepared from magnesium powder (730 mg, 30.0 mg-atom) and mercury(II) chloride (236 mg, 0.87 mmol) in THF (11 cm^3) was added titanium(IV) chloride (2.33 g, 12.3 mmol) followed by the addition of a solution of 1,6-diphenylhexane-1,6-dione (1.0 g, 3.8 mmol) in 25 cm^3 of THF. The mixture was stirred at room temp. for 28 h; then saturated aq. K_2CO_3 was added. The mixture was filtered through a pad of Celite and the filtrate was extracted with diethyl ether. The organic layer was washed with saturated aq. NaCl and dried over $MgSO_4$. Removal of the solvent followed by chromatography on silica gel (hexane–EtOAc, 9:1) gave *title diol* **11** (240 mg, 24%) as an oil which solidified on storage, mp 80–82 °C; ν_{max}(KBr)/cm^{-1} 3350, 1055, 750 and 700; δ_H 7.0–7.1 (10 H, m), 2.94 (2 H, br s), 2.2–2.3 (2 H, m) and 1.9–2.0 (6 H, m); δ_C 144.1 (s), 127.1 (d), 126.8 (d), 126.6 (d), 77.2 (s), 35.8 (t) and 21.9 (t); *m/z* (EI) 268 (M$^+$, 8%) and 105 (100) [Found (EI): M$^+$, 268.1463. $C_{18}H_{20}O_2$ requires *M*, 268.1444].

4,7-Dioxadecane-1,10-diyl bismethanesulfonate 15c. To a solution of diol **15a** (10.0 g, 56.1 mmol) and triethylamine (55 cm^3) in CH_2Cl_2 (200 cm^3) was added a solution of methanesulfonyl chloride (37.2 g, 325 mmol) in the same solvent (150 cm^3) at −20 °C. The mixture was stirred overnight at room temp.; then water was added. The organic layer was separated and washed successively with 10% aq. HCl, saturated aq. $NaHCO_3$, and saturated aq. NaCl and dried over $MgSO_4$. After removal of the solvent *in vacuo*, the residue was chromatographed on silica gel (hexane–EtOAc, 1:1) to afford bissulfonate **15c** (18.4 g, 98%) as a pale yellow oil, ν_{max}(neat)/cm^{-1} 1350, 1170, 1110, 980 and 940; δ_H 4.35 (4 H, t, *J* 6.4), 3.59 (8 H, s + t, *J* 5.9), 3.01 (6 H, s) and 2.02 (4 H, quintet, *J* 6.2).

***cis*-2-Phenylcyclohexano-14-crown-4 3.** To a gently refluxed suspension of 60% NaH (4.20 g, 105 mmol) and $LiClO_4$ (5.60 g, 52.8 mmol) in THF (1000 cm^3) was added dropwise a solution of diol **9** (5.00 g, 26.0 mmol) and dimesyl compound **15c** (9.60 g, 28.6 mmol) in the same solvent (1000 cm^3) under nitrogen during 10.5 h. The mixture was heated for 22 h while another batch of 60% NaH (1.00 g, 25 mmol) was added. After being cooled, the mixture was treated with ice–water and most of the THF was evaporated off. The residue was extracted with diethyl ether and the extract was washed with saturated aq. NaCl and then dried ($MgSO_4$). The solvent was removed and the residue was chromatographed on silica gel (hexane–EtOAc, 92:8) to afford the *title crown* **3** (2.45 g, 28%) as a solid. The reaction of diol **9** with ditosyl analogue **15b** gave the crown **3** in 50% yield under similar conditions, mp 88–90 °C (from hexane); ν_{max}(KBr)/cm^{-1} 1120, 760 and 710; δ_H 7.42–7.46 (2 H, m), 7.30–7.36 (2 H, m), 7.23 (1 H, tt, *J* 1.5 and 7.2), 3.94 (1 H, dd, *J* 2.5 and 8.1), 3.84–3.89 (1 H, m), 3.55–3.78 (10 H, m), 3.21 (1 H, dt, *J* 15.2 and 5.2) and 1.2–2.1 (12 H, m); δ_C 142.7 (s), 127.7 (d), 127.5 (d), 126.6 (d), 79.8 (s), 79.7 (br d), 70.7 (br t), 70.5 (t), 67.4 (t), 66.8 (t), 63.8 (t), 59.0 (br t), 36.3 (br t), 30.6 (t), 3.05 (t), 26.3 (t), 22.8 (br t) and 22.1 (t); *m/z* (EI) 334 (M$^+$, 34%) and 158 (100) (Found: C, 71.75; H, 9.1. $C_{20}H_{30}O_4$ requires C, 71.8; H, 9.0%).

***trans*-2-Phenylcyclohexano-14-crown-4 4.** The reaction of diol **10** (5.20 g, 27.0 mmol) with dimesyl compound **15c** (9.60 g, 28.7 mmol) was carried out as described above using 60% NaH (4.20 g, 105 mmol) and $LiClO_4$ (5.60 g, 52.8 mmol) in 2000 cm^3 of THF for 20 h. The reaction mixture was worked up as above and the product was purified by preparative HPLC to give the *title crown* **4** (338 mg, 3.8%) as an oil, ν_{max}(neat)/cm^{-1} 1120, 765 and 705; δ_H 7.75 (2 H, d, *J* 7.2), 7.21–7.34 (3 H, m), 3.38–4.06 (11 H, m), 3.13 (1 H, ddd, *J* 4.2, 5.9 and 9.9), 2.48 (1 H, dd, *J* 9.7 and 13.2) and 1.3–1.9 (12 H, m); δ_C 139.4 (s), 130.2 (d), 127.3 (d), 127.0 (d), 86.7 (d), 81.4 (s), 71.2 (t), 70.0 (t), 67.6 (t), 67.1 (t), 66.4 (t), 59.4 (t), 37.4 (t), 30.9 (t), 30.6 (t), 29.7 (t), 25.4 (t) and 23.9 (t); *m/z* (EI) 334 (M$^+$, 25%), 158 (72) and 91 (100) [Found (EI): M$^+$, 334.2144. $C_{20}H_{30}O_4$ requires *M*, 334.2126]. For elemental analysis, the *$LiClO_4$ complex of compound* **4** was prepared as described below for those of crowns **1** and **20**, mp 208–210 °C (Found: C, 54.3; H, 6.8. $C_{20}H_{30}ClLiO_8$ requires C, 54.5; H, 6.9%).

***cis*-2,3-Diphenylcyclohexano-14-crown-4 5.** The reaction of diol **11** (7.40 g, 27.6 mmol) with ditosyl compound **15b** (13.8 g, 28.6 mmol) was carried out as described above using 60% NaH (4.00 g, 100 mmol) and $LiClO_4$ (5.60 g, 52.8 mmol) in 2000 cm^3 of THF for 14 days. During the reaction, another batch of 60% NaH (9.6 g, 240 mmol) and diester **15a** (15.8 g, 32.5 mmol) was added. The reaction mixture was worked up as above to give the *title crown* **5** (3.98 g, 35%) as a solid, mp 63–65 °C; ν_{max}(KBr)/cm^{-1} 1120 and 700; δ_H 7.2–7.5 (10 H, m), 3.99 (2 H, dt, *J* 3.5 and 8.7), 3.7–3.9 (6 H, m), 3.44 (2 H, dt, *J* 3.2 and 8.4), 3.00 (2 H, ddd, *J* 4.2, 5.9 and 9.6) and 1.6–2.0 (12 H, m); δ_C 141.9 (s), 129.7 (d), 126.4 (d), 126.3 (d), 81.9 (s), 70.8 (t), 68.8 (t), 58.1 (t), 30.0 (t), 29.7 (t) and 22.2 (t); *m/z* (EI) 410 (M$^+$, 2%) and 158 (100) (Found: C, 76.1; H, 8.4. $C_{26}H_{34}O_4$ requires C, 76.05; H, 8.35%).

***trans*-2,3-Diphenylcyclohexano-14-crown-4 6.** The reaction of diol **12** (7.00 g, 26.0 mmol) with ditosyl derivative **15b** (13.8 g, 28.6 mmol) was carried out as described above using 60% NaH (4.00 g, 100 mmol) and $LiClO_4$ (5.60 g, 52.8 mmol) in 2000 cm^3 of THF for 14 days. During the reaction, another batch of 60% NaH (7.2 g, 180 mmol) and **15b** (12.6 g, 25.9 mmol) was added. The reaction mixture was worked up as above and subsequent preparative HPLC purification gave the *title crown* **6** (328 mg, 3.0%) as a solid, mp 151–152 °C; ν_{max}(KBr)/cm^{-1} 1140, 1120, 1100 and 710; δ_H 7.93 (4 H, d, *J* 7.4), 7.35 (4 H, t, *J* 7.4), 7.26 (2 H, t, *J* 7.2), 3.52–3.76 (8 H, m), 3.35 (2 H, ddd, *J* 4.2, 7.9 and 9.6), 3.26 (2 H, ddd, *J* 4.8, 7.3 and 9.0), 2.28–2.34 (2 H, m), 1.9–2.1 (4 H, m) and 1.4–1.7 (6 H, m); δ_C 141.6 (s), 130.8 (d), 127.1 (d), 126.1 (d), 85.6 (s), 70.0 (t), 67.6 (t), 60.8 (t), 35.0 (t), 29.8 (t) and 23.3 (t); *m/z* (CI) 411 (M$^+$ + 1, 54%) and 161 (100) (Found: C, 76.3; H, 8.4%).

***meso*-1,2-Di-(1-adamantyl)ethane-1,2-diol 13.** To a solution of acyloin **16a** (5.00 g, 15.2 mmol) in 650 cm^3 of ethanol was added portionwise $NaBH_4$ (1.73 g, 45.7 mmol). The mixture was stirred at room temp. for 44 h; another portion of the hydride (1.73 g) was added during this period. Then the mixture was diluted with water and extracted with $CHCl_3$. The extract was washed with saturated aq. NaCl and dried over $MgSO_4$. The solvent was removed *in vacuo* to leave a solid (4.90 g, 98%). The ratio of *meso*-**13**:(±)-**14** was determined by the ^{1}H NMR spectrum to be 1:19. In order to remove the trace (±)-isomer, the product (5.49 g, 16.6 mmol) obtained as described above was dissolved in 960 cm^3 of $CHCl_3$ and the solution was treated with lead tetraacetate (736 mg, 1.66 mmol) at room temp. for 1 h. The mixture was filtered and the solvent was removed by evaporation *in vacuo*. Chromatography on silica gel ($CHCl_3$) gave meso-**13** (3.83 g, 70% recovery) as a single diastereomer (by ^{1}H NMR spectroscopy), mp 260–262 °C (from EtOH); ν_{max}(KBr)/cm^{-1} 3420 and 1000; δ_H 3.15 (2 H, br s), 2.00 (6 H, br m) and 1.4–1.8 (26 H, m); δ_C 79.8 (d), 38.3 (t), 37.7 (t), 37.4 (s) and 28.6 (d); *m/z* (EI) 330 (M$^+$, 100%) and 165 (54) (Found: C, 79.8; H, 10.3. $C_{22}H_{34}O$ requires C, 79.95; H, 10.35%).

1,2-Di-(1-adamantyl)-2-(*tert*-butyldimethylsiloxy)ethanone 16c. To an ice-cooled suspension of oil-free potassium hydride (140 mg, 3.3 mmol) and 18-crown-6 (8 mg, 0.03 mmol) in 4 cm^3 of THF was added dropwise a solution of acyloin **16a** (1.00 g, 3.05 mmol) in 20 cm^3 of THF under nitrogen. The ice-bath was removed and a solution of *tert*-butyl(chloro)dimethylsilane (0.50 g, 3.3 mmol) in 20 cm^3 of THF was added. The mixture was stirred at room temp. for 1.5 h; then water was added to quench the reaction. The mixture was extracted with diethyl ether and the extract was dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was chromatographed on silica gel (hexane–benzene, 2 : 1) to give *siloxy product* **16c** (792 g, 60%) as a solid, mp 179–180 °C (from benzene–MeOH); ν_{max}(KBr)/cm^{-1} 1710, 1260, 1250, 1090, 1085, 1010, 865, 845 and 780; δ_H 4.16 (1 H, s), 1.46–2.04 (30 H, m), 0.88 (9 H, s), 0.08 (3 H, s) and 0.01 (3 H, s); *m*/*z* (FAB) 443 (M^+ + 1, 17%) and 279 (100) (Found: C, 75.65; H, 10.4. $C_{28}H_{46}O_2Si$ requires C, 75.95; H, 10.45%).

(±)-1,2-Di-(1-adamantyl)ethane-1,2-diol 14. To an ice-cooled suspension of $LiAlH_4$ (1.42 g, 37.3 mmol) in 22 cm^3 of THF was added dropwise a solution of the above ketone **16c** (1.42 g, 37.3 mmol) in 180 cm^3 of THF under nitrogen. The ice-bath was removed and the mixture was stirred at room temp. for 3 h; then water was added to quench the reaction followed by addition of aq. 1 M NaOH. The mixture was extracted with diethyl ether and the extract was dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was washed with hexane to leave *title diol* **14** as a solid (3.57 g, 87%), mp 283–285 °C (from benzene, sealed tube); ν_{max}(KBr)/cm^{-1} 3400 and 1085; δ_H 3.20 (2 H, br s), 2.17 (2 H, br s), 1.99 (6 H, br m) and 1.5–1.8 (24 H, m); δ_C 74.0 (d), 38.1 (t), 37.2 (t), 36.8 (s) and 28.3 (d); *m*/*z* (EI) 330 (M^+, 100%) (Found: C, 80.2; H, 10.45. $C_{22}H_{34}O$ requires C, 79.95; H, 10.35%). The ratio of *meso*-**13** : (±)-**14** in the crude product was determined by the ^1H NMR spectrum to be 23 : 1.

***cis*-2,3-Di-(1-adamantyl)-14-crown-4 7.** The reaction of diol **13** (2.80 g, 8.48 mmol) was carried out as described above using **15b** (a total of 57.1 g, 118 mmol), 60% NaH (11.0 g, 275 mmol), and $LiClO_4$ (1.61 g, 15.2 mmol) in 440 cm^3 of THF. The *product* **7** (137 mg, 2%) was isolated by chromatography on silica gel (EtOAc–hexane, 1 : 9) as a solid, mp 162–163 °C (from EtOAc); ν_{max}(KBr)/cm^{-1} 1130, 1110, 1070 and 1030; δ_H 3.9–4.0 (2 H, m), 3.6–3.8 (4 H, m), 3.5–3.6 (4 H, m), 3.41 (1 H, dt, *J* 4.2 and 4.0), 3.31 (1 H, s), 3.01 (1 H, dt, *J* 4.2 and 4.0), 2.85 (1 H, s) and 1.6–2.0 (34 H, m); δ_C 92.7 (d), 86.2 (d), 70.6 (t), 70.5 (t), 70.0 (t), 67.6 (t), 66.9 (t), 64.9 (t), 40.6 (t), 39.9 (t), 38.4 (s), 37.5 (t), 37.0 (t), 36.9 (s), 30.6 (t), 29.4 (t), 28.9 (d) and 28.7 (d); *m*/*z* (EI) 472 (M^+, 6%), 173 (93) and 135 (100) (Found: C, 75.9; H, 10.4. $C_{30}H_{48}O_4$ requires C, 76.25; H, 10.25%).

***trans*-2,3-Di-(1-adamantyl)-14-crown-4 8.** The reaction of diol **14** (2.50 g, 7.58 mmol) was carried out as described above using ditosyl compound **15b** (a total of 14.1 g, 28.9 mmol), 60% NaH (1.76 g, 43.6 mmol), and $LiClO_4$ (1.61 g, 15.2 mmol) in 1000 cm^3 of THF for 7 days. The *product* **8** (1.80 g, 50%) was isolated by chromatography on silica gel (EtOAc–hexane, 1 : 9) as a solid, mp 218–219 °C (from EtOAc); ν_{max}(KBr)/cm^{-1} 1050, 1020 and 1005; δ_H 4.03 (2 H, ddd, *J* 2.9, 8.8 and 11.3), 3.87 (2 H, ddd, *J* 2.9, 8.8 and 11.2), 3.7–3.8 (2 H, m), 3.5–3.6 (4 H, m), 3.10 (2 H, ddd, *J* 4.0, 4.0 and 8.0), 2.82 (2 H, s), 1.95 (6 H, br m) and 1.5–1.8 (28 H, m); δ_C 84.1 (d), 71.2 (t), 68.6 (t), 68.3 (t), 39.1 (t), 37.3 (t), 37.2 (s), 31.4 (t) and 28.6 (d); *m*/*z* (EI) 472 (M^+, 6%) and 173 (100) (Found: C, 76.0; H, 10.25%).

Benzo-14-crown-4 20. A mixture of NaOH (4.19 g, 105 mmol), $LiClO_4$ (12.1 g, 114 mmol), and 80 cm^3 of dimethyl sulfoxide (DMSO) was stirred at 60 °C for 30 min. To the mixture was added a solution of *o*-dihydroxybenzene (10.1 g, 91.7 mmol) in 50 cm^3 of DMSO and the mixture was stirred for 1 h at 60 °C, then a solution of 1,10-dichloro-4,7-dioxadecane[5c] (19.6 g, 91.2 mmol) in 10 cm^3 of DMSO was added during 3 h. The mixture was stirred for 20 h at 110 °C. After being cooled, the mixture was diluted with water and extracted by CH_2Cl_2. The organic phase was washed with brine and dried over $MgSO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel (light petroleum–diethyl ether, 98 : 2) to give the *title crown* **20** (9.11 g, 40%) as an oil. An analytical sample was obtained by preparative HPLC, ν_{max}(neat)/cm^{-1} 1260, 1120, 1050 and 750; δ_H 6.94 (4 H, m), 4.15 (4 H, t, *J* 5.2), 3.79 (4 H, t, *J* 5.2), 3.68 (4 H, s) and 2.00 (4 H, m); δ_C 149.8 (2 C, s), 122.1 (2 C, d), 117.2 (2 C, d), 70.7 (2 C, t), 67.3 (4 C, t) and 29.9 (2 C, t).

Formation of crystalline complexes of crown ethers 1 and 20 with lithium perchlorate, lithium thiocyanate, and sodium perchlorate

The crystalline complexes were prepared by mixing equimolar or two molar amounts of crown ether **1** or **20** (one or two mol equiv. used) with lithium or sodium perchlorate in acetone or methanol. Slow evaporation off of the solvent at room temp. or vapour diffusion with diethyl ether afforded crystals of the complexes in good yields (64–99%). Since attempts to prepare crystalline products of compound **20** with $LiClO_4$ were unsuccessful, LiNCS was used instead to give a 1 : 1 complex in 72–75% yield. The stoichiometry of the product was determined by elemental analyses. *Complex* **1**·$LiClO_4$; mp 214–215 °C (Found: C, 51.55; H, 7.85. $C_{18}H_{32}ClLiO_8$ requires C, 51.6; H, 7.7%). *Complex* **1**·$NaClO_4$; mp 198–200 °C (Found: C, 49.5; H, 7.55. $C_{18}H_{32}ClNaO_8$ requires C, 49.7; H, 7.4%). *Complex* **20**·LiNCS; mp 203–205 °C (Found: C, 56.6; H, 6.3; N, 4.25. $C_{15}H_{20}LiNO_4S$ requires C, 56.8; H, 6.35; N, 4.4%). *Complex* (**20**)$_2$·$NaClO_4$; mp 184–185 °C (Found: C, 53.75; H, 6.45; Cl, 5.45. $C_{28}H_{40}ClNaO_{12}$ requires C, 53.65; H, 6.45; Cl, 5.65%).

Electrode preparation and emf measurements

Ion-sensitive membranes of the PVC matrix type were prepared according to the previous procedures.[30] The polymeric membrane composition was 3 wt% ionophore, 67.3–67.4 wt% membrane solvent BBPA, 28.8–29.9 wt% PVC, and 20 mol% (relative to the ionophore) potassium tetrakis-(*p*-chlorophenyl)-borate (KTpClPB, Dojindo Laboratories, Kumamoto, Japan). The membrane thickness was ~100 µm. A 6-mm diameter circle was cut from a prepared membrane and placed on the tip of a PVC ion-selective electrode body assembly (Liquid Electrode Membrane Kit, DKK Co., Ltd., Tokyo, Japan). The prepared electrodes were immersed in 0.1 mol dm^{-3} aq. LiCl for over 24 h for preconditioning before use. The external reference electrode was a double-junction-type Ag–AgCl electrode (HS-305DS, Toa Electronics, Ltd., Tokyo, Japan). The electrode response potential (emf) measurements were performed according to the reported procedure at 25 ± 0.5 °C using the electrochemical cell system,[30] Ag;AgCl, 3 mol dm^{-3} KCl | 0.3 mol dm^{-3} NH_4NO_3 | test solution | membrane | 0.1 mol dm^{-3} LiCl, AgCl;Ag.

All test solutions were made from chloride salts without any pH-adjusting buffer reagent. The selectivity coefficient $K_{i,j}^{pot}$ where i is the primary ion (Li^+) and j is the interfering ion, were calculated from the response potentials in an alkali metal or alkaline earth metal chloride solution using the separate-solution method (SSM; [j] = 0.1 mol dm^{-3}) according to the recommendations of IUPAC[31] and JIS.[32]

X-Ray crystallographic structure analyses of crown ethers 5 and 6, lithium picrate complex of crown 1, and sodium perchlorate complex of crown 20

The lithium picrate complex of crown **1** was prepared as follows: A solution of crown ether **1** (30 mg, 0.096 mmol) in 1 cm^3 of CH_2Cl_2 was shaken with a solution of picric acid (300 mg, 1.31 mmol) and $LiOH·H_2O$ (500 mg, 11.9 mmol) in 0.5 cm^3 of water. The organic phase was separated and the solvent was evaporated off to leave a solid, which was dissolved in a mixture of acetone and benzene. The solution was stored in an atmosphere of light petroleum (vapour-diffusion method) to give yellow single crystals; mp 193–195 °C. The sodium perchlorate complex of complex **20** was prepared as described above. X-Ray diffraction data were collected at 23 °C on a Rigaku AFC-7R or AFC-5R (for lithium picrate complex of crown **1**) diffractometer with Mo-Kα radiation (λ = 0.710 69 Å). The structures were solved and refined by using the program package TEXSAN.[33,†]

Crystal data for compound 5. $C_{26}H_{34}O_4$, M = 410.55, monoclinic, space group $P2_1$, $a = 7.999(1)$, $b = 17.241(1)$, $c = 8.724(1)$ Å, $\beta = 108.48(1)°$, $V = 1141.1(2)$ Å^3, $Z = 2$, $D_c = 1.195$ g cm^{-3}, crystal dimensions 0.40 × 0.40 × 0.33 mm. A total of 2914 reflections were collected using the ω–2θ scan technique to a maximum 2θ-value of 55.0°. The structure was solved by direct methods (SHELXS86)[34] and refined by a full-matrix least-squares method with 270 variables and 2142 observed reflections [$I > 3\sigma(I)$]. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final R- and R_w-values were 0.084 and 0.095, respectively. The maximum peak and the minimum peak in the final difference map were 0.74 and −1.01 e$^-$ Å^{-3}.

Crystal data for compound 6. $C_{26}H_{34}O_4$, M = 410.55, monoclinic, space group $C2/c$, $a = 17.263(4)$, $b = 11.720(2)$, $c = 11.716(2)$ Å, $\beta = 109.18(1)°$, $V = 2238.8(6)$ Å^3, $Z = 4$, $D_c = 1.218$ g cm^{-3}, crystal dimensions 0.26 × 0.26 × 0.50 mm. A total of 2794 reflections were collected using the ω–2θ scan technique to a maximum 2θ-value of 55.0°. The structure was solved by direct methods (MULTAN88)[35] and refined by a full-matrix least-squares method with 136 variables and 1421 observed reflections [$I > 3\sigma(I)$]. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final R- and R_w-values were 0.062 and 0.039, respectively. The maximum peak and the minimum peak in the final difference map were 0.55 and −0.32 e$^-$ Å^{-3}.

Crystal data for lithium picrate complex of crown 1. $C_{24}H_{34}LiN_3O_{11}$, M = 547.49, monoclinic, space group $P2_1/c$, $a = 11.429(2)$, $b = 14.270(2)$, $c = 16.453(2)$ Å, $\beta = 101.57(1)°$, $V = 2628.6(7)$ Å^3, $Z = 4$, $D_c = 1.383$ g cm^{-3}, crystal dimensions 0.35 × 0.28 × 0.35 mm. A total of 6589 reflections were collected using the ω–2θ scan technique to a maximum of 2θ-value of 55.0°. The structure was solved by direct methods (SHELXS86)[34] and refined by a full-matrix least-squares method with 352 variables and 3109 observed reflections [$I > 3\sigma(I)$]. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final R- and R_w-values were 0.056 and 0.037, respectively. The maximum peak and the minimum peak in the final difference map were 0.39 and −0.38 e$^-$ Å^{-3}.

Crystal data for sodium perchlorate complex (1 : 2) of crown 20. $C_{28}H_{40}ClNaO_{12}$, M = 627.06, monoclinic, space group $C2/c$, $a = 19.306(4)$, $b = 15.798(4)$, $c = 11.581(7)$ Å, $\beta = 120.95(3)°$, $V = 3029(2)$ Å^3, $Z = 4$, $D_c = 1.375$ g cm^{-3}, crystal dimensions 0.20 × 0.20 × 0.30 mm. A total of 3706 reflections were collected using the ω–2θ scan technique to a maximum 2θ-value of 55.0°. The structure was solved by direct methods (SAPI91)[36] and refined by a full-matrix least-squares method with 210 variables and 2138 observed reflections [$I > 3\sigma(I)$]. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. Owing to the crystallographic C_2 symmetry, the oxygen atoms O(5), O(6), O(7) and O(8) of the perchlorate anion were refined as a disordered structure around the Cl atom with equivalent populations. The final R- and R_w-values were 0.053 and 0.039, respectively. The maximum peak and the minimum peak in the final difference map were 0.22 and −0.26 e$^-$ Å^{-3}.

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† Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, available *via* the RSC Web pages (http://chemistry.rsc.org/rsc/p1pifa.htm). Any request to the CCDC for this material should quote the full literature citation and the reference number 207/170.

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