Syntheses of phosphate diesters having *p-tert*-butylcalix[4]arene and alkyl group as ester moieties, and their selective lithium cation transport abilities through liquid membranes

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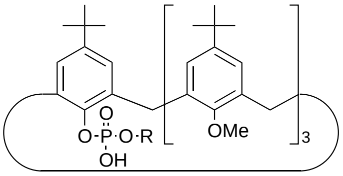
Phospate diesters, 2a, 2b and 2c, having *p-tert*-butylcalix[4]arenes and alkyl groups as ester moieties exist as an equilibrium of cone and partial-cone conformations in solution and selectively transport Li^+; however, the conformations of the calix[4]arene moieties in the Li and Na complexes of 2a as the methyl ester and/or 2b as the ethyl ester in solution are cone only, although that of the K complex exists as a mixture of cone and partial-cone conformers.

Calix[4]anene derivatives show highly selective complexing abilities, toward transition metal,[1–3] Na,[4–7] K[6–8] and Cs[9,10] cations. However, reports of selective complexing ability for the Li^+ are rare.[11] Also, the relationship between the complexing ability for metal cations and the conformation of calix[*n*]arene derivatives has been reported.[12] In previous papers, we reported that photoresponsive azocrown ethers,[13] benzocrown ethers,[13] dibenzocrown ethers[15,16] and crown ethers[17] having alkylphosphoric acid groups as side arms are useful as selective and efficient Li^+ carriers for liquid–liquid extraction and liquid membrane transport. In connection with these findings, we have synthesized phosphate diesters, **2a**, **2b** and **2c** having 25,26,27-trimethoxy-28-hydroxy-*p-tert*-butylcalix[4]arenes and alkyl groups (R = Me, Et, Pr^n) as ester moieties and studied the complexing abilities with alkali metal cations.



2a R = Me
b R = Et
c R = Pr^n

The host molecules **2a**, **2b** and **2c**, were prepared by the treatment of 25,26,27-trimethoxy-28-hydroxy-*p-tert*-butylcalix[4]arene **1**[18] with alkyldichlorophosphate followed by hydrolysis in 37, 22 and 35% yields, respectively.† The ^1H NMR spectra of **2a** showed the signals of the methyl protons of the Bu^t groups as singlets at δ 1.27, 1.30 and 1.33, the signals of the methylene protons as doublets at δ 3.20, 3.25, 4.32 and 4.65, the signals of the methoxy protons of the anisole moieties as singlets at δ 3.81 and 3.88 together with the other proton peaks. These results show the presence of the cone conformers of **2a**. In addition to these peaks, the ^1H NMR spectra arising from the partial-cone of **2a** contained the signals of the methyl protons of the Bu^t groups as singlets at δ 1.06, 1.33 and 1.41, the signals of the methylene groups as a doublet at 3.14 and 4.57 and a singlet at 3.73 (4 H), and the signals of the methoxy protons of the anisole moieties as singlets at 3.14 and 3.67 together with other proton peaks. The ^{31}P NMR spectra‡ of **2a** showed two peaks at δ −5.77 and −6.29. From these data and other NMR measurements (COSY, DEPT, NOSY), **2a** in solution at 25 °C exists as an equilibrium between the cone and partial-cone conformations. As shown in Fig. 1, in order to convert the cone to partial-cone only the *p-tert*-butyl anisole moiety, which is *trans* to the phosphate ester substituted ring, needs to invert. The conformation of **2b** and **2c** were determined by similar methods. The spectral data showed that **2a**, **2b** and **2c** exist as a mixture of cone and partial-cone isomers (5 : 3) in $CD_3CN–CDCl_3$ (7 : 3) at 25 °C (2 : 3 ratio in $CDCl_3$). These results suggest that the equilibrium between the cone and partial-cone isomers in **2a**, **2b** and **2c** is sensitively affected by the solvent polarity; the cone % increases with solvent polarity. These findings are consistent with the result obtained for 25,26,27,28-tetramethoxy-*p-tert*-butylcalix[4]arene by Iwamoto *et al.*[12] In the cone conformation, four dipoles in **2** are forced to orient into the same direction whereas in the partial-cone conformation, one dipole is reversed.

The comparative complexing abilities of **2a**, **2b**, **2c** and **1** toward alkali metal cations (Li^+, Na^+ and K^+) were evaluated using solvent extraction and competitive liquid membrane transport experiments[13–17] and results are summarized in Table 1. The extraction abilities of **1** toward Li^+, Na^+ and K^+ are very low (9.3–11.7%) compared with those of **2a**, **2b** and **2c** and the selectivities for Li^+/Na^+, Li^+/K^+ and Na^+/K^+ are nearly of the same order (0.79–1.15). However, **2a**, **2b** and **2c** showed much higher cation extraction abilities (57–67%) toward alkali metal cations compared with those of **1**, although **2** did not show remarkable selectivities toward alkali metal cations. These results suggest that the alkylphosphoric acid moiety of **2** plays an important role in the complexation of **2** with alkali metal cations under our experimental conditions. Therefore, the selective extraction of **2** toward alkali metal cations could not observed. Next, in order to investigate the selectivity of the complexing abilities toward alkali metal cations in more detail, competitive liquid membrane transport experiments were carried out. In this experiment, practically no ion transport occurred in the absence of **2a**, **2b** or **2c**. The host molecule **1** also exhibited no transport abilities toward the alkali metal cations under these conditions, owing to its hydrophilic character. In contrast, drastic enhancement in the transport abilities was observed by introduction of an alkylphosphoric acid moiety into **1**. These results suggest that the transport ability order of **2a**, **2b** and **2c** toward alkali metal cations was $Li^+ > Na^+ > K^+$, although the alkali cations transport tendency of **2a**, **2b** and **2c** are very similar. Li^+ selectivity (4.55) over K^+ by **2b** was superior to those of **2a** and **2c**. However, **2a** showed higher selectivity of Li^+ over Na^+ compared with those of **2b** and **2c**.

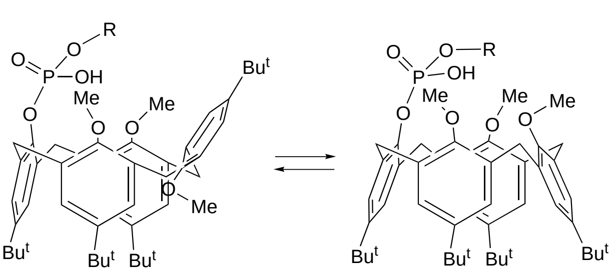


Fig. 1 Equilibrium of **2** between cone and partial-cone conformers

Table 1 Competitive extraction and competitive facilitated transport with **1, 2a, 2b** and **2c**

	Extractability[a] (%)			Selectivity			Transported amount[b]/ 10^{-3} mol			Selectivity		
Compound	Li^+	Na^+	K^+	Li^+/Na^+	Li^+/K^+	Na^+/K^+	Li^+	Na^+	K^+	Li^+/Na^+	Li^+/K^+	Na^+/K^+
1	11	9	12	0.91	0.79	0.0	0.0	0.0	0.0	—	—	—
2a	60	57	65	1.05	0.93	0.89	4.33	2.90	1.80	1.49	2.41	1.61
2b	63	66	67	0.95	0.93	0.97	5.89	4.36	1.30	1.35	4.55	3.35
2c	55	57	62	0.97	0.89	0.92	3.41	2.62	1.41	1.30	2.42	1.30

[a] The extraction abilities of the host molecule with alkali metal cation was examined by the extraction method described previously.[13–17] [b] Conditions: [membrane phase] = 1.0×10^{-3} M of the host molecule in CH_2Cl_2 (6.0 cm^3). [Source phase] = aqueous solution (3 cm^3) containing 1.0 M MOH (M = Li, Na, K); [receiving phase] = 1.0 M HCl (3 cm^3).

Furthermore, **2b** showed the highest selectivity for Na^+/K^+ (3.35) among the investigated host molecules. Therefore, the effects of the length of alkyl groups on transport abilities were negligibly small, however, the length of the alkyl groups affected the selectivity for Li^+/Na^+, Li^+/K^+ and K^+/Na^+.

In order to investigate the conformations of the host moiety in the complexes of **2** with alkali metal cations, the following experiments were carried out. A solution of **2** (3.0×10^{-6} mol) in CD_2Cl_2 (0.45 cm^3) was shaken 100 times with a D_2O solution (0.45 cm^3) containing an alkali metal deuteroxide (1.5×10^{-5} mol) at 25 °C and then the ^1H and ^{31}P NMR spectra of the organic layer were measured. As shown in Fig. 2, the methoxy and methyl protons peaks of the methylphosphoric acid moieties in the Li and Na complexes of **2a** due to the cone conformer shifted down- and up-field by *ca*. 0.25–0.33 and 0.24–0.31 ppm, respectively, while all of the proton peaks due to the partial-cone conformer disappeared. Also, the ^{31}P NMR spectra of Li^+ and Na^+ complexes of **2a** showed only one peak at δ −5.87 and −6.22, respectively, despite the fact that for **2a** itself two peaks were observed. In contrast, the ^1H NMR spectra of the complex of **2a** with K^+ showed the presence of both cone and partial-cone conformers, although the methoxy protons of the anisole moiety due to the cone and partial-cone conformers were shifted down- and up-field by *ca*. 0.03 and 0.01 ppm, respectively; the ^{31}P NMR spectra also showed two peaks at δ −6.13 and −6.40. These results suggest that the host moieties in the complexes of **2a** and/or **2b** with Li^+ and Na^+ adopt only the cone conformation, although the host moiety of the K^+ complex exists as a mixture (1 : 2) of the cone and partial-cone conformers together with a very small amount of other conformers.

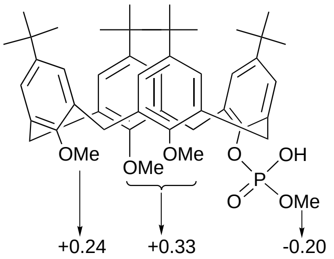


Fig. 2 ^1H NMR chemical shift changes between **2a** and the Li^+ complex of **2a**. Positive and negative values mean down- and up-field shifts, respectively.

Furthermore, titration experiments in $CD_3CN–CDCl_3$ (7 : 3) were carried out by adding 0.25–3.0 equiv. of alkali metal thiocyanate to **2**. Remarkable chemical shift changes appeared in the ^1H and ^{31}P NMR spectra. The downfield shift of the methoxy protons in the cone conformer increases almost linearly with increase in Li^+ and/or Na^+ salt until addition of 1 equiv. relative to **2a**; further addition of alkali metal salt results in only a slight downfield shift change, which suggests the formation of a 1 : 1 complex of **2a** with Li^+ or Na^+. Also, all of the proton peaks in the ^1H NMR spectra due to the partial-cone conformer of **2a** disappeared, and the ^{31}P NMR spectra showed only one peak of the cone conformer when 1 equiv. of the thiocyanate was added. However, when KSCN was added to **2a** and/or **2b**, no chemical shift changes in the ^1H and ^{31}P NMR spectra were observed. This suggests that the host molecules **2a** and **2b** did not complex KSCN, although **2a** and **2b** complex with KOD.

In summary, we have shown that the phosphate diesters, **2a** and **2b**, containing calix[4]arene and alkyl groups as ester moieties selectively complexed Li^+ among the investigated alkali metal cations and the most moieties in the complexes of **2a** and/or **2b** with Li^+ and Na^+ cations adopt only a cone conformation, although the host moiety of the K^+ complex exists as a mixture (1 : 2) of cone and partial-cone conformations.

Footnotes and References

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† Assignment of the ^1H NMR spectra and conformations of **2a**, **2b** and **2c** were carried out using $^1H–^1H$ COSY, $^{13}C–^1H$ COSY, DEPT and NOESY spectroscopy. Satisfactory elemental analyses were obtained for all new compounds.

‡ The chemical shifts of ^{31}P measured from external 85% H_3PO_4.

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