Journal of Inclusion Phenomena and Molecular Recognition in Chemistry **19:** 41–53, 1994.

The Design of Cone-fixed Calix[4]arene Analogs by Taking *syn*-[2.*n*]Metacyclophanes as a Building Block

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(Received: 3 March 1994; in final form: 16 November 1994)

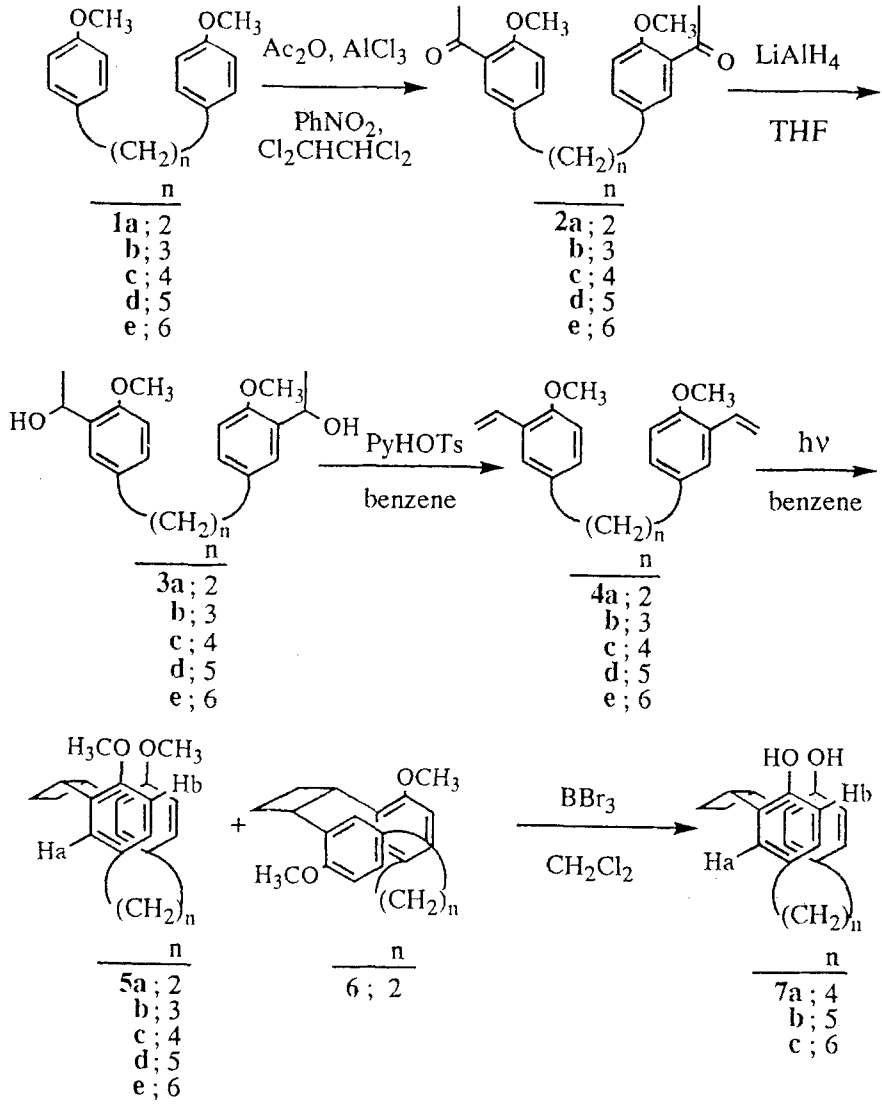
Abstract. Rigidified calix[4]arene analogs were synthesized from *syn*-[2.*n*]metacyclophanes as a building block. Their structure was firmly locked in the cone conformation. An enlarged calix[4]arene analog was obtained after the cyclobutane ring cleavage of the parent analog by Birch reduction. Several ionophores have been derived from the analogs and been found to select the larger ions during the extraction of alkali metals, transition metals, and lanthanoids. The ionophore having oligoethylene glycol units showed an effective catalytic activity for S_N2 reactions such as ester synthesis, Williamson ether synthesis, and Finkelstein reaction in several media.

Key words: Syn-conformer, cyclophane, metal ion, extraction, catalytic activity.

1. Introduction

The chemistry of calix[*n*]arene attracts much attention in many interesting applications such as the binding of organic molecules and inorganic ions [1]. Accordingly, the modifications of calixarene and its derivatives are widely investigated to explore the new aspects in this chemistry. Rigidification is one of the most important modifications which usually results in arranging binding sites favorably for various guests and giving specific selectivities in affinity. Many successful examples in this respect are disclosed in the synthesis for the families of calix[4]arenes by using bisphenol derivatives as a building block [2]. In order to make calixarenes conformationally rigid, alkylidene bridges and/or bulky substituents were also introduced and it resulted in better selectivity and efficiency for binding metal ions [3]. Recently, we reported the photochemical synthesis of *syn*-dimethoxy[2.*n*]metacyclophanes, whose stereochemistry was controlled by the steric effect of the methoxyl group [4]. These cyclophanes with a *syn* conformation were used as a building block for the construction of a more rigid calix[4]arene skeleton [5], because many macrocyclic compounds composed of a metacyclophane skeleton are reported as artificial receptors [6]. In this review, we report the synthetic method using *syn*-dimethoxy[2.*n*]metacyclophane by [2 + 2] photocycloaddition and the first

* This paper is dedicated to the commemorative issue on the 50th anniversary of calixarenes.



Scheme 1.

synthesis and characterization of calix[4]arene analogs firmly locked in the cone conformation.

2. Synthesis of *syn*-[2.*n*]Metacyclophanes

The synthetic route of dimethoxy[2.n]metacyclophanes is shown in Scheme 1. α,ω-Bis(p-methoxyphenyl)alkanes **1** were used as starting materials [7]. Diketones

TABLE I. Conformational Analysis of Cyclophanes **5**, **6** and **7**

Compound	Observed			Corrected	Assignment
	Ha	Hb	$\Delta\delta^a$	$\Delta\delta^{b,c}$	
5a	7.03	6.08	0.95	0.72	*syn*
6	4.38, 5.18	6.83, 6.89	–2.45 – –1.71	–2.68 – –1.94	*anti*
5b	7.05	6.24	0.81	0.58	*syn*
5c	7.04	6.32	0.72	0.49	*syn*
5d	7.04	6.43	0.61	0.38	*syn*
5e	6.98	6.49	0.49	0.26	*syn*
7a	6.95	6.36	0.59	0.33	*syn*
7b	6.95	6.46	0.49	0.23	*syn*
7c	6.91	6.50	0.41	0.15	*syn*

[a] $\Delta\delta = \delta_{Ha} - \delta_{Hb}$.

[b] Corrected by –0.23 ppm for **5** and **6**, since 2,4-dimethylanisole gives the chemical shifts difference between Ha (3–) and Hb (6–) positions.

[c] Corrected by –0.26 ppm for **7**.

2 were obtained in 58–93% yields by treatment with acetic anhydride and $AlCl_3$ in nitrobenzene and 1,1,2,2-tetrachloroethane at room temperature for 12 h [8]. Diols **3** were obtained in quantitative yields by the reduction with $LiAlH_4$ in THF at room temperature for 1 h. Diolefins **4** were obtained in 72–92% yields by dehydration with pyridinium *p*-toluenesulfonate in benzene under reflux for 5 days. [2 + 2] Photocycloaddition of diolefins **4** was carried out by irradiation with a 400 W high-pressure Hg lamp (Pyrex filter) in benzene for 26–92 h under N_2 [9–11]. After evaporation, [2.*n*]metacyclophanes **5b–e** were isolated in 61–87% yields by column chromatography. [2.2]Metacyclophanes **5a** and **6**, however, were found to be an equilibrium mixture, so that they could not be separated with either HPLC or TLC. But the ^1H NMR peaks for each isomer were detected separately.

Structural determination was carried out by NMR spectroscopy in $CDCl_3$, including COSY, NOESY, ^{13}C, and DEPT experiments. The cyclobutane ring of metacyclophanes **5** and **6** was assigned to be of *cis* configuration by the ^1H NMR chemical shifts (δ3.72 – 4.74) of the cyclobutane methine protons [12]. The direction of the cyclobutane ring to the methoxyl group was easily confirmed by NOESY experiments; i.e., the methylene protons of the cyclobutane ring clearly show an NOE interaction with the Ha aromatic protons (see Scheme 1). The methoxyl groups possess NOE interactions with not only the methine protons of the cyclobutane ring but also the Hb aromatic protons. Accordingly, the cyclobutane ring is concluded to face to the opposite direction of the methoxyl groups as shown in Scheme 1. The ^1H NMR chemical shifts of the Ha and Hb aromatic protons are listed in Table I. According to the molecular framework examination, **5** and **6** are apt to take a *syn* conformation [13, 14], because the steric interaction between the

methoxyl group and the cyclobutane methylene protons seems to be severe, if they take an *anti* conformation.

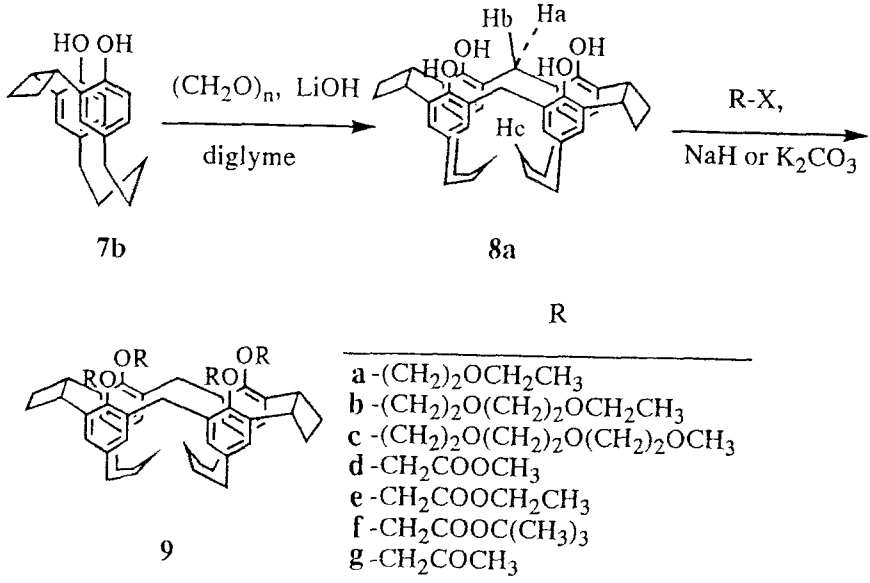
The conformation was experimentally determined by the $\Delta\delta$ value [15] as shown in Table I [16–18]. It was also confirmed by ^{1}H NMR spectra, since the *syn* conformer showed a symmetrical spectral pattern of C_s symmetry, while the *anti* conformer displayed an unsymmetrical one due to C_1 symmetry. The anisotropic shielding effect of the CH_3O group on the chemical shift of Hb was estimated by using 2,4-dimethylanisole as a model, whose proton chemical shifts corresponding to Ha and Hb are δ6.95 and 6.72, respectively. Hence, the chemical shift deviation due to the effect of the CH_3O group is calculated as 0.23 ppm. Dimethoxy[2.*n*]metacyclophanes **5b–e** are concluded to be of *syn* conformation because the corrected $\Delta\delta$ value is positive with small values from 0.26 to 0.58. According to ^{1}H NMR and COSY spectra, [2.2]metacyclophanes **5a** and **6** formed a mixture of *syn*- and *anti*-isomers in the ratio of 4 : 3. *syn*-Dimethoxy[2.2]metacyclophane is highly strained, so that the repulsion between benzene rings is considered to overcome the steric hindrance between the methoxyl groups and the ethano bridge.

The synthetic route to dihydroxy[2.*n*]metacyclophanes **7** is shown in Scheme 1. Anisole derivatives **5** and **6** were treated with excess of boron tribromide in dry CH_2Cl_2 at r.t. for 12 h [19]. Phenol derivatives **7b** and **c** were obtained in 95 and 93% yields, respectively. On the other hand, **5c** did not give any desired products under the same conditions. Since the reaction gave a complex product mixture, we chose milder conditions. Thus, **5c** was carefully treated with an equimolar amount of BBr_3 at 0°C for 2 h and then gave **7a** in 78% yield. Unfortunately, **5a**, **5b**, and **6** did not give any phenol products.

The configuration of the cyclobutane ring for dihydroxy[2.*n*]metacyclophanes **7** was assigned to be *cis* by the chemical shift of its methine protons (δ4.31 – 4.46). The conformation of **7a–c** was determined by the corrected $\Delta\delta$ value as shown in Table I. The $\Delta\delta$ values are small and range from 0.15 to 0.33. Accordingly, we concluded that **7a–c** take a *syn* conformation. So the structure of **7a–c** is the same as the corresponding dimethoxy[2.*n*]metacyclophanes **5** even after the cleavage of methoxyl groups.

3. Synthesis of Cone-fixed Calix[4]arene Analogs

We examined the synthesis of a three-bridged calix[4]arene by using *syn*-dihydroxy-[2.5]metacyclophane **7b** as a building block (see Scheme 2). This is because we thought that it is not only an easy preparation but we could also take advantage of the *syn* conformation. Thus, cyclophane **7b** (2.0 g, 6.5 mmol) was treated with LiOH (0.31 g, 13 mmol) and paraformaldehyde (2.0 g, 65 mmol) in 20 mL of diglyme at 140–150°C for 12 h under N_2 to afford desired product **8a** [5]. Interestingly, a remarkable template effect was observed on this condensation reaction; i.e., lithium hydroxide gave **8a** in excellent 89% yield. When other larger metal

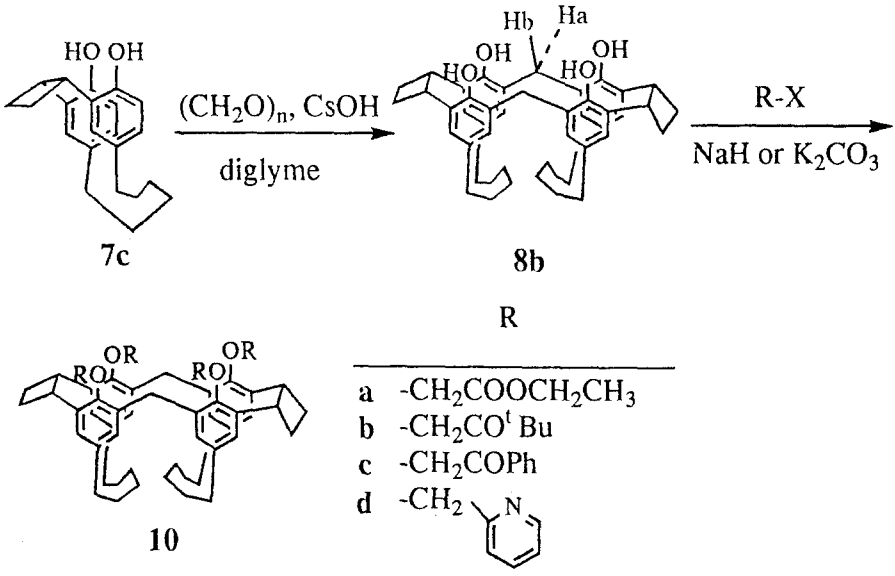


Scheme 2.

ions were used, the yield was gradually decreased in the order of Na^+ (42%), K^+ (15%), and Rb^+ (5%). Then finally cesium hydroxide did not give **8a** at all under the same reaction conditions.

The structure of **8a** was mainly elucidated by ^1H NMR spectroscopy in $CDCl_3$, including COSY, NOESY, and ^{13}C NMR. Typical findings are summarized as follows: (1) the methylene bridge shows on AB type coupling (Ha at δ3.28 with J=14 Hz and Hb at δ3.97 with J=14 Hz), which is the same as those ascribed to the calixarene cone-form. Moreover, this same coupling constant is maintained even in pyridine-d_5 (Ha at δ3.39 with J=14 Hz and Hb at δ4.32 with J=14 Hz). (2) The Hc proton resonance (δ–0.22) shifts to a higher field by ca. 0.4 ppm from that of the starting material **7b**, due to the additional shielding effect coming from another cyclophane system. (3) The hydroxy protons of **7b**, whose OH–OH distance is estimated as 4.4 Å from a CPK model, resonate at δ5.04, just the typical chemical shift value for simple monomeric phenols, suggesting the lack of a hydrogen bond in the molecule. On the contrary, the hydroxy protons of **8a** resonate at a much lower field, δ7.78. This large down-field shift clearly suggests the presence of intramolecular hydrogen bonding between two adjacent hydroxy groups, attached to each of two metacyclophane units, whose OH–OH distance is estimated to be 2.4 Å from a CPK model.

As mentioned above, we successfully developed a new methodology to obtain cone-fixed calixarene analog **8a**. This method can be applied to make another analog **8b** by using *syn*-dihydroxy[2.6]metacyclophane **7c** as shown in Scheme 3 [20]. In fact, the cesium hydroxide catalyzed reaction gave **8b** in an excellent 78%

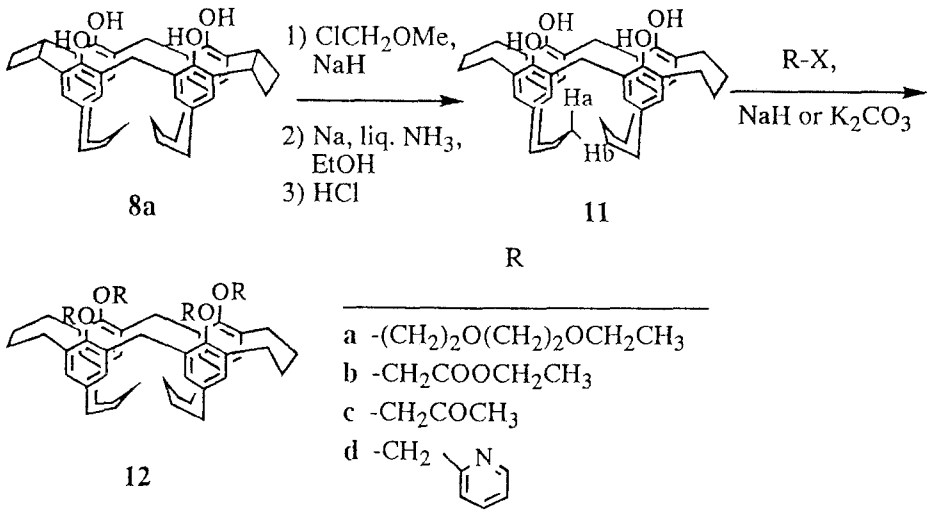


Scheme 3.

yield. When other smaller metal ions were used, the yield was gradually decreased in the order of K^+ (21%) and Li^+ (19%). This template effect is opposite to that using **7b**.

The typical NMR spectroscopic features are summarized as follows: (1) the aromatic protons of **8b** are located at nearly the same position of δ6.71 and 6.85 as those of **8a**. (2) The cyclobutane methine protons of **8b** resonate at δ4.32, shifting to higher field than that of **8a** at δ4.56. (3) Its AB type coupling of the methylene bridge, which demonstrates the cone-form structure, appears in a higher field region from δ3.17 (Ha) and 3.84 (Hb), due to the movement of the methylene protons to the more shielding region, than that of **8a** (Ha at δ3.28 and Hb at δ3.97). (4) The hydroxy protons of **8b** resonate at δ6.71 a moderately higher field than that of **8a** at δ7.78, because the neighboring OH–OH distance for **8b** is estimated about 0.4 Å longer than that for **8a** by the molecular framework examination and also the distance of the opposite hydrogen bond sites of **8b** is approximately estimated ca. 5.0 Å. These results suggest that its hydrogen bonding of two neighboring hydroxy groups is weaker than that of **8a**.

Calix[4]arene analog **8a** can be easily modified by Birch reduction under the reported conditions shown in Scheme 4 [21]. We examined the direct reduction of **8a**, but the desired product **11** was not produced and only the starting material was recovered. This result suggests that phenoxide ion generated in the media prevented the desired radical anion from forming, due to the electronic repulsion between solvated electrons and phenoxides. Accordingly, the phenolic OH group was protected by etherification before Birch reduction. The methoxymethylation



Scheme 4.

was performed with **8a** (31 mM), chloromethyl methyl ether (10 equiv), and NaH (2 equiv) in dry THF/DMF (9/1) at 40–45°C for 12 h under N_2. Birch reduction was done with the ether (4.3 mM), Na (150 equiv), and EtOH (4 equiv) in liq. NH_3/dry THF (1/1) at –60°C for 4 h under N_2. The deprotection was carried out with the crude product (1 mM) in THF/aq. HCl (1/1) at 50°C for 12 h. Analog **11** was obtained in overall 86% yield. The structural determination is summarized as follows: (1) the cyclobutane ring methine protons (δ4.56) of **8a** have disappeared. (2) The AB type coupling of methanobridges is shifted from δ3.28 and δ3.97 for **8a** to δ3.33 and δ4.16 for **11**, due to the release of strain. (3) The inner methine protons (Ha) of **11** resonate at a normal chemical shift of δ0.59 in contrast with that of **8a** at δ–0.22. This result suggests that the distance between benzene nuclei is increased to decrease the shielding effect to these protons. Furthermore, Ha and Hb lie in the unequal environments so that they resonate at different positions, δ0.59 and δ0.84. (4) The hydroxy proton chemical shift of **11** (δ6.14) reveals that it has weaker hydrogen bonding than that of cyclophane **8a** (δ7.78), and therefore the benzene rings of **11** have been pushed apart by reduction of the cyclobutane ring.

Thus, we have successfully obtained rigidified calix[4]arene analogs **8a**, **8b**, and **11**, which kept the cone conformation. Moreover, these analogs are proved to maintain the cone structure from r.t. to 150°C in DMSO-d_6 or from r.t. to 100°C in pyridine-d_5 by VT NMR experiments. Analogs **8b** and **11** are rather limited in their inner movements, although they are more flexible than **8a**.

TABLE II. Extraction (%) of alkali metal, transition metal, and lanthanoid picrates in CH_2Cl_2[a]

Compd	Li^+	Na^+	K^+	Rb^+	Cs^+	NH_4^+	Cr^{3+}	Mn^{2+}	Ag^+	Hg^{2+}	La^{3+}	Sm^{3+}	Yb^{3+}
9a	2.6	1.8	14.0	15.5	18.9	2.4	< 1	9.3	6.9	6.0	–	–	–
9b	1.7	3.0	15.1	23.2	38.4	2.7	5.0	< 1	< 1	12.6	–	–	–
9c	1.9	8.4	25.3	27.5	13.8	2.3	5.0	1.4	8.1	12.1	–	–	–
9d	11.1	10.6	35.0	28.5	27.0	9.9	7.8	7.9	6.7	14.9	–	–	–
9e	15.9	32.8	90.2	95.7	88.3	33.0	16.5	6.3	12.5	26.7	22.1	11.1	8.8
9f	12.1	44.8	50.7	38.8	46.1	36.3	42.5	69.2	60.2	49.6	48.3	33.6	15.4
9g	7.9	13.1	36.3	39.1	38.0	9.9	7.5	7.9	10.2	14.1	–	–	–
10a	7.0	19.5	40.4	42.3	35.5	8.6	11.2	3.0	18.9	15.9	4.8	4.9	2.8
10b	49.1	55.6	57.9	63.6	48.0	44.6	69.1	74.5	96.3	89.3	59.9	44.8	13.8
10c	14.1	17.4	24.1	27.8	21.6	20.1	53.3	34.3	66.6	39.1	49.5	38.4	19.6
10d	4.2	6.1	60.6	46.2	10.9	6.3	96.8	84.6	97.9	97.1	98.0	88.5	47.6
12a	< 1	4.9	5.1	6.2	6.8	< 1	4.2	< 1	< 1	1.7	–	–	–
12b	< 1	4.7	5.4	6.3	6.7	< 1	11.8	2.7	2.9	17.6	–	–	–
12c	< 1	< 1	< 1	< 1	< 1	< 1	8.2	< 1	< 1	12.3	–	–	–
12d	< 1	< 1	< 1	< 1	< 1	< 1	77.6	26.6	98.4	97.6	44.9	39.1	18.6

[a] Extraction conditions: 2.5×10^{-4} M of receptor in CH_2Cl_2; 2.5×10^{-4} M of picric acid in 0.1 M of MOH for alkali metals or 2.5×10^{-5} M of picric acid in 1×10^{-3} M of metal nitrate for transition metals and lanthanoids at 22°C. Receptor solution (5.0 mL) was shaken (10 min) with picrate solution (5.0 mL) and % extraction was measured by the absorbance of picrate in CH_2Cl_2. Experimental error was ±2%.

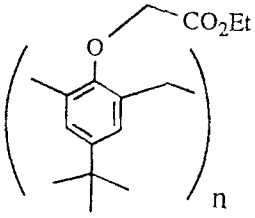
4. Ionophoric Behaviour of Rigidified Calix[4]arene Analogs

Functionalized calixarene analogs **9**, **10**, and **12** were obtained in 63–97% yields from their parents **8a**, **8b**, and **11**, respectively, with R–X and NaH or K_2CO_3 [5]. The cone-fixed conformation of calixarene analogs should affect their ion binding properties. In fact, the methylene protons of **9e** altered their chemical shifts upon titration with metal thiocyanate in $CDCl_3$: i.e., a 1 : 1 mixture of **9e** and KSCN showed broad peaks at δ3.14 and δ3.76 [22]. Hence, it is concluded that the K^+ ion was strongly bound on **9e**. In fact, the binding constant for K^+ ion has the largest value among the alkali metal ions and ammonium ion. The order is K^+ (log Ka=4.56) > Rb^+ (4.31) > Cs^+ (4.12) > NH_4^+ (4.01) > Na^+ (3.84) > Li^+ (3.34). This result suggests that larger alkali metals ions (K^+, Rb^+, and Cs^+) interact more strongly with **9e** than smaller ones (Li^+ and Na^+).

Based on these observations, we determined the extractability of alkali metal, transition metal, and lanthanoid ions from the aqueous phase to the organic phase [3, 23]. The results for metal picrates are summarized in Table II. The effects of the restricted ring conformation clearly appears in the ion selectivity; i.e., **9** extracted large ions like K^+, Rb^+, and Cs^+ more efficiently than small ones like Li^+ and Na^+. This ion selectivity of **9** resembles that of calix[6]arene derivative **14** rather than calix[4]arene one **13**, because the cavity of cylindrical **9** is as large as that of flexible calix[6]arene **14**. It is interesting to note that the cavity size of **9** is larger than that of calix[4]arene cone conformer **13**, although **9** and **13** have similar structural elements. These results indicate that the cavity size governing ion selectivity is determined by the aromatic ring frameworks rather than the kinds of binding sites. Introduction of bulky *tert*-butyl group **9f** instead of methyl or ethyl

groups remarkably increases the extractability of the small Na^+ ion, probably due to the formation of a large hydrophobic cavity stabilizing the picrate anion [3]. The ion selectivity, however, apparently decreases except for the case of Li^+ ion.

Ionophore **9** apparently exhibited high selectivities and extractabilities for Hg^{2+} and Ag^+ ions in this transition metal extraction, because the rigidified ionophore **9** prefers the large metal ions. Lanthanoids have similar physical properties except the ion radius and the largest ion La^{3+} has nearly the same ion radius as K^+ ion. Ionophores **9e** and **9f** selectively separated La^{3+} ion from all other lanthanoids. In general, the extraction gradually decreased with decreasing ionic size.



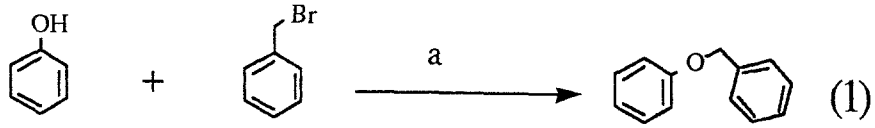
13 n=4
14 n=6

All of **10** are excellent ionophores of alkali, transition metals, and lanthanoids (see Table II). The ion selectivity of **10** is recognized for K^+ and Rb^+ ions among alkali metals, Ag^+ among transition metals, and La^{3+} among lanthanoids. Interestingly, **10d** having picolyl ligands is an excellent ionophore in respect to both selectivity and extractability for alkali metals, transition metals, and lanthanoids. These results show that **10** prefers large ions to small ions. The ion selectivity of **10** is also more marked than that of **9**, because the rotation of binding sites of **10** is more free than that of **9**, due to the formation of the large cavity. The stoichiometry for extraction is determined by the distribution ratio as a function of ionophore concentration ([M]=2.5×10^{-4} to 2.5×10^{-5}). The slopes of log D vs. log [M] plots was unity. This result clearly suggests that the metal ions formed 1 : 1 complexes with ionophore **10**.

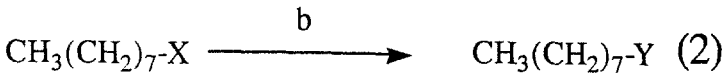
Ionophore **12** showed moderate extraction for alkali metals as depicted in Table II. The ion selectivity of **12** is recognized for Cs^+ ion. This selectivity for the large Cs^+ ion shows that the binding sites of **12** exist largely apart from each other. It has moderate extractability for transition metals with high selectivity. In particular, **12d** having picolyl ligands is an excellent ionophore in respect to both selectivity and extractability for Ag^+ and Hg^{2+}. And also the largest La^{3+} ion in lanthanoids was most efficiently extracted to the organic phase. The extractability of **12d** gradually decreased from large La^{3+} to small Yb^{3+} ion.

5. The Catalytic Activity of Calix[4]arene Analog

The results of ion extraction experiments suggest a possibility that **9** might display a catalytic activity for a nucleophilic substitution reaction with inorganic reagents in organic media. Accordingly, we investigated the catalytic activity of **9c** on



(1)

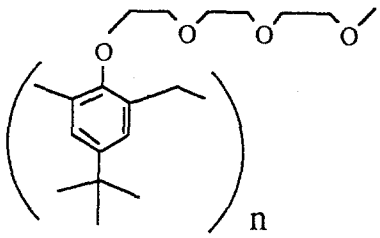


(2)

a) MOH / Cat. / CCl_4 or CD_2Cl_2

b) MY / Cat. / CD_3COCD_3 or CD_3CN

some S_N2 reactions, which were ester synthesis, Williamson ether synthesis, and the Finkelstein reaction, and compared the results with those of calix[n]arene derivatives (n=4 and 6 for **15** and **16**) [24]. A 2-[2-(2-methoxyethoxy)ethoxy]ethyl unit was chosen as a binding site, because it is a stable substituent under neutral and basic conditions [25]. The reaction was followed by ^1H NMR and the rate was estimated as a pseudo-first-order rate constant k (s^{-1}) for the increase of product.



15 n=4
16 n=6

Firstly, we examined the esterification with metal acetate, benzyl bromide, and catalyst **9c**, **15**, or **16**. The reaction proceeded in the presence of these catalysts, but not in the absence of them. Therefore, their catalytic activity is apparent. The rate constants remained in the same range for all runs. Moreover, the reaction was slow (k=10^{-6} – 10^{-7} s^{-1}) because of the low nucleophilicity of acetate ion. Since the substitution by acetate did not give much information on their catalytic activity, we chose the Williamson ether synthesis with phenol, benzyl bromide, metal hydroxide, and catalyst (see Equation 1), because phenolate has high nucleophilicity and hydrophobicity [24]. In fact, the difference of their catalytic activities clearly appeared in this case as shown in Table III. Catalysts made the reaction markedly faster than that without them. In carbon tetrachloride as a nonpolar solvent, the catalytic activity of **9c** increased remarkably when larger ions were used and the maximum rate constant was recorded in the RbOH system. This behavior of **9c** resembles that of calix[6]arene derivative **16** because both **9c** and **16** have the same affinity for large ions. The other experiments were performed in

TABLE III. Rate constant of the reaction between phenoxide and benzyl bromide[a]

base (MOH)	solvent	k (10^{-7} s^{-1})			
		none	**9c**	**15**	**16**
NaOH	CCl_4	4.2	62	50	67
KOH	CCl_4	6.1	79	56	70
RbOH	CCl_4	5.6	160	60	180
NaOH	CD_2Cl_2	8.4	120	90	140
NaOH	sat CD_2Cl_2[b]	17	590	120	390
KOH	CD_2Cl_2	15	520	480	600
RbOH	CD_2Cl_2	18	760	420	990
CsOH	CD_2Cl_2	28	320	220	710

[a] Phenol: benzyl bromide: base: catalyst=1: 1: 3.5: 0.029 (molar ratio); phenol, 0.43 mol/l; temp., 32 ± 1°C. Experimental error was ±10%.

[b] Saturated with D_2O.

dichloromethane as a low polar solvent. The rate constant in this solvent increased by around 2–8 times as compared to that in CCl_4, probably due to the increment of the solubility of ion-catalyst complex and the activity of the nucleophile. The increasing order of rate constant, when **9c** was used, can be explained by its selectivity for binding the alkali metal ion and solubilizing the metal hydroxide; K^+ and Rb^+ are suitable for complexation with **9c**, but the Cs^+ ion is too large to fit the binding site of **9c** effectively [5]. By the addition of a little water to make a two-phase system, the rate became larger, but the order of enhancement by the catalysts did not change. This experimental result shows that the present catalysts can be used as phase transfer catalysts. The order of catalytic activity for this ether synthesis is **15** < **9c** ≤ **16**.

We also examined the Finkelstein reaction of octyl halide involving a conversion from bromide to iodide or from iodide to bromide (see Equation 2) [26]. The results are summarized in Table IV. The Finkelstein reaction proceeded without any catalysts, because halide salts are soluble in various solvents. But, when catalyst was combined in this system, the rate was enhanced clearly by 1.5–2 times (see Table IV). In the case involving a conversion of octyl bromide to iodide, **9c** showed the maximum rate for KI and RbI in acetone or acetonitrile, indicating that its complexation with the alkali metal ion is an important factor to accelerate this reaction. Note that **9c** has the largest rate constant among the catalysts for all metal iodides examined in this reaction.

In the other case involving a conversion of octyl iodide to bromide, **9c** also showed the maximum rate for K^+, Rb^+ and C_s salts, although the reaction of iodide to bromide is difficult. Furthermore, **9c** is again the best catalyst for all

TABLE IV. Rate constant of Finkelstein reaction[a]

substrate	reagent (MY)	solvent[b]	temp.[c] (°C)	k (10^{-7} s^{-1}) none	**9c**	**15**	**16**
n-$C_8H_{17}Br$	KI	A	50	27	42	28	31
	RbI	A	50	22	41	24	24
	CsI	A	50	14	24	18	20
	KI	B	50	–	39	20	28
	RbI	B	50	–	36	17	25
	CsI	B	50	–	31	14	20
n-$C_8H_{17}I$	KBr	B	75	9.2	15	12	13
	RbBr	B	75	–	14	10	11
	CsBr	B	75	–	12	8.0	9.7

[a] Substrate: reagent: catalyst=1: 5: 0.05 (molar ratio); substrate, 0.24 mol/l. Experimental error was ±10%.

[b] A: CD_3COCD_3, B: CD_3CN.

[c] ±2°C.

metal bromides. These results suggest that the cylindrical structure of **9c** gives a favorable environment for this Finkelstein reaction.

6. Conclusion

We successfully synthesized calix[4]arene analogs **8a** and **8b** firmly locked in the cone conformation in excellent yield. An enlarged calix[4]arene analog **11** was also obtained from **8a** by Birch reduction. All ionophores **9**, **10**, and **12** derived from these analogs have been found to select the larger ions in the extraction of alkali metals, transition metals, and lanthanoids. Ionophore **9c** having oligoethylene glycol units showed an effective catalytic activity for some S_N2 reactions in several media.

Acknowledgement

This work was supported in part by grants from the Ministry of Education, Science, and Culture, Japan.

References

1. C.D. Gutsche: *Acc. Chem. Res.* **16**, 161 (1983); S. Shinkai: *J. Incl. Phenom.* **7**, 193 (1989).
2. D.W. Chasar: *J. Org. Chem.* **50**, 545 (1985); V. Böhmer, H. Goldmann, and W. Vogt: *J. Chem. Soc., Chem. Commun.* **1985**, 667.
3. F. Arnaud-Neu,, E.M. Collins, M. Deasy, G. Ferguson, S.J. Harris, B. Kaitner, A.J. Lough, M.A. McKervey, E. Marques, B.L. Ruhl, M.J. Schwing-Weill, and E.M. Seward: *J. Am. Chem. Soc.* **111**, 8681 (1989); V. Böhmer, W. Vogt, and H. Goldmann: *J. Org. Chem.* **55**, 2569 (1990); E. Ghidini, F. Ugozzoli, R. Ungaro, S. Harkema, A.A. El-Fadl, and D.N. Reinhoudt: *J. Am. Chem. Soc.* **112**, 6979 (1990).

4. Y. Okada, K. Sugiyama, Y. Wada, and J. Nishimura: *Tetrahedron Lett.* **31**, 107 (1990); Y. Okada, K. Sugiyama, M. Kurahayashi, and J. Nishimura: *ibid.* **32**, 2367 (1991); Y. Okada, S. Mabuchi, M. Kurahayashi, and J. Nishimura: *Chem. Lett.* **1991**, 1345.
5. Y. Okada, F. Ishii, Y. Kasai, and J. Nishimura: *Chem. Lett.* **1992**, 755; Y. Okada, F. Ishii, Y. Kasai, and J. Nishimura: *Tetrahedron Lett.* **34**, 1971 (1993); Y. Okada, Y. Kasai, F. Ishii, and J. Nishimura: *J. Chem. Soc., Chem. Commun.* **1993**, 976.
6. D.J. Cram: *Science* **219**, 1177 (1983); *Synthesis of Macrocycles*, ed. by R.M. Izatt and J.J. Christensen, Wiley, New York, 1987; C.D. Gutsche: *Calixarenes*, Royal Society of Chemistry, London, 1989; K. Koga and K. Odashima: *J. Incl. Phenom.* **7**, 53 (1989).
7. J. Nishimura, N. Yamada, Y. Horiuchi, E. Ueda, A. Ohbayashi, and A. Oku: *Bull. Chem. Soc. Jpn.* **59**, 2035 (1986).
8. *Organic Reactions Vol. V*, ed. by R. Adams, Wiley, New York, 1949, Chap. 5.
9. J. Nishimura, H. Doi, E. Ueda, A. Ohbayashi, and A. Oku: *J. Am. Chem. Soc.* **109**, 5293 (1987).
10. M. Yamamoto, T. Asanuma, and Y. Nishijima: *J. Chem. Soc., Chem. Commun.* **1975**, 53; T. Asanuma, M. Yamamoto, and Y. Nishijima: *ibid.* **1975**, 56.
11. H. Nozaki, I. Otani, R. Noyori, and M. Kawanisi: *Tetrahedron* **24**, 2183 (1968).
12. J. Nishimura, A. Ohbayashi, H. Doi, K. Nishimura, and A. Oku: *Chem. Ber.* **121**, 2019 (1988).
13. T. Kamada and O. Yamamoto: *Bull. Chem. Soc. Jpn.* **52**, 1159 (1979).
14. T. Kamada and O. Yamamoto: *Bull. Chem. Soc. Jpn.* **53**, 994 (1980).
15. D. Krois and H. Lehner: *Tetrahedron* **38**, 3319 (1982).
16. R.H. Mitchell, T.K. Vinod, and G.W. Bushnell: *J. Am. Chem. Soc.* **107**, 3340 (1985); R.H. Mitchell, G.J. Bodwell, T.K. Vinod, and K.S. Weerawarna: *Tetrahedron Lett.* **29**, 3287 (1988).
17. Y.-H. Lai and S.-M. Lee: *J. Org. Chem.* **53**, 4472 (1988).
18. H. Meier, E. Praß, and K. Noller: *Chem. Ber.* **121**, 1637 (1988).
19. T.W. Greene: *Protective Groups in Organic Synthesis*, Wiley, New York, 1981, p. 91.
20. Y. Okada, Y. Kasai, and J. Nishimura: *Synlett.* in press.
21. A. Greenberg and J.F. Liebman: *Strained Organic Molecules*, Academic Press, New York (1978), p. 58; J. Nishimura, A. Ohbayashi, E. Ueda, and A. Oku: *Chem. Ber.* **121**, 2025 (1988); B.P. Mundy and M.G. Ellerd: *Named Reactions and Reagents in Organic Synthesis*, Wiley, New York, 1988, p. 31.
22. A. Arduini, A. Pochini, S. Reverberi, and R. Ungaro: *Tetrahedron* **42**, 2089 (1986).
23. S.-K. Chang and I. Cho: *Chem. Lett.* **1984**, 477; M.A. McKervey, E.M. Seward, G. Ferguson, B. Ruhl, and S.J. Harris: *J. Chem. Soc., Chem. Commun.* **1985**, 388; T. Nagasaki and S. Shinkai: *Bull. Chem. Soc. Jpn.* **65**, 471 (1992).
24. H. Taniguchi and E. Nomura: *Chem. Lett.* **1988**, 1773.
25. Y. Okada, Y. Sugitani, Y. Kasai, and J. Nishimura: *Bull. Chem. Soc. Jpn.* **67**, 586 (1994).
26. D. Landini and F. Montanari: *J. Chem. Soc., Chem. Commun.* **1974**, 879; M. Cinquini and F. Montanari: *ibid.* **1975**, 393.