Supramolecular Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713649759

Metal Ionically-controlled Optical Signaling Based on a Chromoionophore-derived Calix[4]crown

Yuji Kubo[a]; Satoru Obara[a]; Sumio Tokita[a]
[a] Department of Applied Chemistry, Faculty of Engineering, Saitama University, Saitama, Japan

Online publication date: 29 October 2010

To cite this Article Kubo, Yuji , Obara, Satoru and Tokita, Sumio(2002) 'Metal Ionically-controlled Optical Signaling Based on a Chromoionophore-derived Calix[4]crown', Supramolecular Chemistry, 14: 2, 171 — 177
To link to this Article: DOI: 10.1080/10610270290026077
URL: http://dx.doi.org/10.1080/10610270290026077

Supramolecular Chemistry, 2002 Vol. 14 (2-3), pp. 171–177

Invited Paper

Metal Ionically-controlled Optical Signaling Based on a Chromoionophore-derived Calix[4]crown

YUJI KUBO*, SATORU OBARA and SUMIO TOKITA

Department of Applied Chemistry, Faculty of Engineering, Saitama University, Shimo-ohkubo, Saitama 338-8570, Japan

(Received 31 August 2001; In final form 11 September 2001)

A chromoionophore-derived calix[4]crown, 1, possessing an effective signal-controllable function by metal ionic inputs has been newly synthesized, whose function is mainly of our interest, by transforming the process of receptor activation to one that may be detected by an optical signal (i.e. color change), the basic feature of antagonist–agonist competition may be reproduced readily and visually detected. The process would be particularly new within the field of optical read-out receptors. Further, from the standpoint of material sciences, the controllable signal function may not only be welcome for molecular information processing, but also contribute to the design of new sensory materials.

Keywords: Chromoionophore; Calixarene; Crown ether; Chemosensor; Molecular information processing

INTRODUCTION

The search for artificial receptors effecting the selective complexation and optical cascade signaling of chemically- and/or biologically-important species continues to attract considerable attention in supramolecular chemistry. Indeed, chromogenic- [1] and fluorogenic- [2] receptors have been explored as a potential use of chemosensor materials [3]. Towards this end, in principle, one has favored to employ the methodology that the desirable sensors should enhance the optical response as the host–guest interaction is strengthened. However, in naturally occurring receptor systems, chemical recognition characteristics involving ligand affinities do not necessarily correlate with the chemical stimulus–response (transduction) [4]. For example, although agonists and antagonists generally bind to closely related sites within a receptor, only agonists are able to promote receptor activation whereas, by definition, antagonist binding does not [5]. Further, the estimation of thermodynamics parameters for ligand-binding interactions often indicates that antagonists more strongly bind a receptor than agonists [5,6]. Thus, in reversible competitive antagonism, the presence of the antagonist serves to decrease, by direct competitive binding probability, a favorable and physiologically effective agonist–receptor interaction. The interesting issue of this paper is to synthesize a new chromogenic receptor possessing a simplified and replicated antagonism; by transforming the process of receptor activation to competitive cation-induced colorimetric signal control, the basic feature of antagonist–agonist competition could be reproduced readily and visually detected. The behavior, from the standpoint of material science, may be welcome for molecular information processing [7] as well as new sensory system. The intriguing aspect is reported here.

RESULTS AND DISCUSSION

To develop a metal ion-driven model agonist–antagonist system which we aim here, the following criterion may, in principle, be required; the

*Corresponding author.

ISSN 1061-0278 print/ISSN 1029-0478 online © 2002 Taylor & Francis Ltd
DOI: 10.1080/10610270290026077

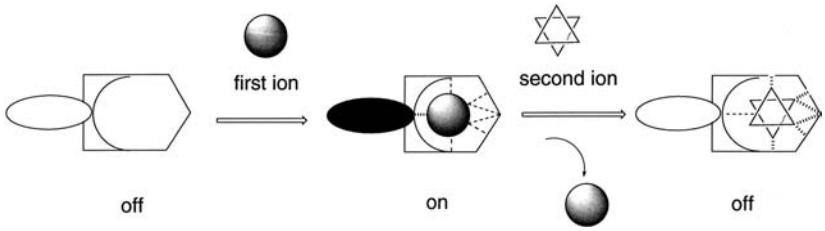
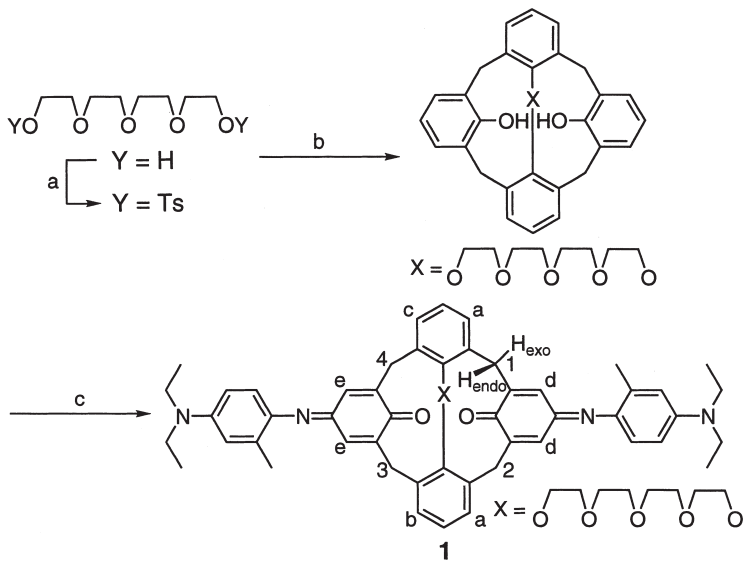


FIGURE 1 A simplified model for competitive antagonism using a chromoionophore.

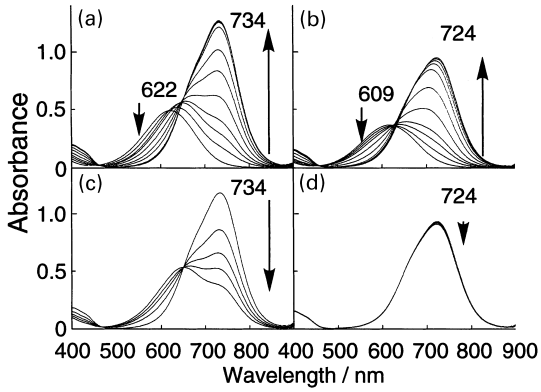
chromoionophore should show a colorimetric effect ("off–on" step) with the first ion, and then, if the second ion can not only bind to the system with greater affinity than the first ion, but also induce almost no colorimetric effect, the second ion would release the first ion efficiently to bring about an active "on–off" signal switch (Fig. 1). Bis(indoaniline)-derived calix[4]crown-5, **1** [8,9] was employed as a suitable candidate, which contains paired indoaniline chromophores† that allow a color change to be induced when a cation becomes encapsulated within the cavity. Here, a critical feature of this system is the use of the crown-strapped cavity. This means that an alkali metal ion can be bound with high affinity as dedicated that calix[4]crown-5 derivatives possess high K^+-selectivity [10,11]. Whereas it is occurred to us that the carbonyl groups of the chromophores, being more polar donor group than ether, strongly favors Ca^{2+} over either Na^+ or K^+ [12]. Indeed, we reported that bis(ethyl acetate)-derived calix[4]-arene-indoaniline conjugate **2** efficiently encapsulated Ca^{2+} with a remarkable bathochromic shift of absorbance in the spectra, making it of potential use as optical sensor for Ca^{2+} detection [13,14]. Taken together, if an alkali metal ion such as K^+, which is bound by the macroring crown-oxygens, would form more favorable complexation with **1** than Ca^{2+}, the Ca^{2+}-induced signal response could be selectively switched off by the cation. Consequently, it is expected that system **1** will define a rather unique chromogenic system capable of effective "off–on–off" signal control as shown in Fig. 1. As detailed below, this does indeed occur.

System **1** was synthesized from calix[4]arene [15] *via* a set of straight-forward steps involving a Williamson synthesis with 3,6,9-trioxaundecane-1,11-diylbistosylate in the presence of a base, and condensation with 2-amino-5-(diethylamino)toluene monohydrochloride under an alkaline condition in the presence of $KMnO_4$ (Scheme 1). Based on our previous work [13,14], system **1** was expected to complex Ca^{2+} with high efficiency within its cavity. Indeed, an EtOH solution of **1** showed a remarkable bathochromic shift ($\Delta\lambda = 112$ nm) and an increase in



SCHEME 1 Synthesis of **1** (a) TsCl, NaOH, THF/H_2O; (b) calix[4]arene, *tert*-BuOK, dry toluene; (c) 2-amino-5-(diethylamino)toluene monohydrochloride, DBU, KMnO4, acetone/MeOH. Ts = *p* − toluene sulfonyl.

†Based on the fact that –N = moiety of the indoaniline chromophore is tilted, a system possessing the plural chromophores has several topological isomers. As we do not discuss the topology in this study, the structure has been depicted as shown in Scheme 1. Also, the depiction of **2** is in a similar manner.



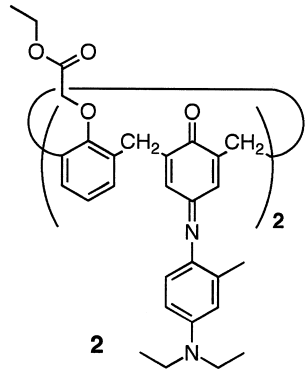


FIGURE 2 (a) UV/Vis absorption spectra of **1** upon addition of Ca^{2+} (0, 1, 2, 3, 5, 7.5, 10, 15, 20, 30, 50 μM, bottom to top). (b) A competition between Ca^{2+} and K^+; the figure shows the absorption change of **1** by adding K^+ (0, 10, 20, 30, 50 μM, top to bottom) in the presence of 50 μM of Ca^{2+}. (c) UV/Vis absorption spectra of **2** upon addition Ca^{2+} (0, 1, 2, 3, 5, 7.5, 10, 15, 20, 30, 50 μM, bottom to top). (d) Absorption change of **2** by adding K^+ (0, 10, 20, 30, 50 μM, top to bottom) in the presence of 50 μM of Ca^{2+}. These data have been collected in EtOH at 298 K where concentrations of receptors **1** and **2** are 10 μM.

absorption intensity upon addition of Ca^{2+}, resulting in an immediate color change from blue to green. At a [Ca^{2+}] to [**1**] ratio of 5:1, a new absorption band at 734 nm was observed ("off–on" switch), while the absorption band of **1** disappeared completely (Fig. 2(a)). Independent Job plot analysis [16] was consistent with the formation of a 1:1 stoichiometric complex. This then allows an association constant (K_a) of $1.8 \times 10^6\ M^{-1}$ to be calculated using a nonlinear least-squares curve fitting procedure. The Ca^{2+}-induced bathochromic shift is mainly attributed to efficient ion–dipole interactions between the encapsulated Ca^{2+} and the quinonecarbonyl groups of the indoaniline chromophores. In contrast, upon interaction with K^+ under similar conditions, very little interaction between this cation and the chromophores was obtained. However, of particular interest is that a competitive titration, involving addition of K^+ to a solution of **1** and 5 equivalant of Ca^{2+}, exhibited reversed spectral changes ("on–off" switch) as shown in Fig. 2(b); in other words, addition of K^+ inhibited almost completely the normal Ca^{2+}-induced color change.‡ This latter phenomenon was readily detected visually. The above findings are clearly consistent with the encapsulated Ca^{2+} being released from **1** in a reversible and competitive fashion as K^+ was added. Alternatively, system **2** as a control in this study, the magnitude of the signal response being coupled with that of the guest-affinity, was not subject to the inhibition for similar Ca^{2+}-induced color change (Fig. 2(c) and (d)).

Semi-quantitative assessment of the competitive complexation process came from Fast atom bombardment (FAB) mass spectrometric analyses (Fig. 3). The formation of a 1:1 complex between **1** and Ca^{2+} was confirmed by monitoring the peaks of m/z 970 ($[M + Ca]^+$) and 1027 ($[M - H + Ca + SCN]^+$) using *m*-nitrobenzyl alcohol matrix. When adding K^+ to the stage of **1**·Ca^{2+} complex, the peak due to the Ca^{2+} complex was almost completely suppressed, whereas a new peak signal at 968 ($[M - H + K]^+$) could be detected. These results

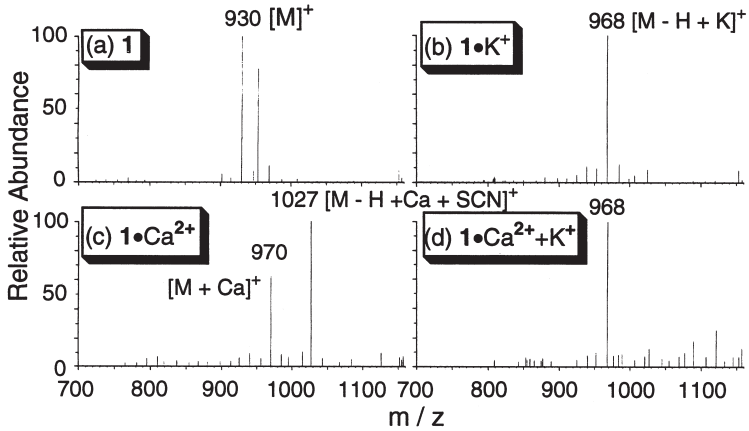


FIGURE 3 FAB mass spectra of **1** (a), **1**·K^+ (b), **1**·Ca^{2+} (c) and **1**·Ca^{2+} + K^+ (d), respectively, (counter ion: SCN^-, NBA matrix).

‡The Ca^{2+}-induced absorption intensity at 734 nm ("on" state) was scarcely influenced by adding 100 μM of H^+.

TABLE I Absorption spectra and association constants of **1** for metal ions at 298 K in EtOH

	Li^+	Na^+	K^+	Ca^{2+}	Cs^+
$\Delta\lambda$ (nm)*	33	21	12	112	9
$K_a \times 10^4$ (M^{-1})†	ND‡	43	720	180¶	5.6

* $\Delta\lambda = \lambda_{max}$(complex) − λ_{max} (**1**); λ_{max} (**1**) = 622 nm; † Competitive spectrophotometry [17] was employed except for K_a of Ca^{2+}; ‡ No spectral change was obtained even in the presence of 10 mM (1000 equiv.) of Li^+; ¶ Nonlinear least-squares curve fitting procedure was employed.

are consistent with those obtained from the UV/Vis titrations and thus strongly support the notion that reversible competitive complexation takes place between Ca^{2+} and K^+ in the case of receptor **1**. As a next stage, our interest is whether or not, the effective signal control obtained in **1** can be induced by only K^+. Thus, we tested alkali metal ions other than K^+, the results of which as well as the case of K^+ were summarized in Table 1. The signal responses of **1** rely on the corresponding spectral change ($\Delta\lambda = {}_\lambda$ (complex)-${}_\lambda$(**1**)). A large bathochromic shift of 112 nm was obtained upon complexation with Ca^{2+} (*vide supra*). In contrast, addition of alkali metal ions caused only minor changes ranging from 9 to 33 nm. On the other hand, the association constants (K_a) for the complexation of the alkali metal ions to **1** were calculated using a mathematical method that may be applied to competition experiments [17] and **1** was found to have peak affinity with K^+, which was found to be $7.2 \times 10^6\ M^{-1}$; the selectivity of K^+ over Ca^{2+} was 4.0. It is interesting to note that the order of the K_a values ($K^+ > Ca^{2+}$) is contrary to that of the $\Delta\lambda$ values ($Ca^{2+} > K^+$), and then K^+ can inhibit the Ca^{2+}-induced optical signal ("on–off" switch) with high selectivity over other alkali metal ions.

Some NMR studies were carried out in an effort to understand the substrate–receptor interactions. Figure 4 shows ^{1}H NMR spectra, ranging from 3.0 to 4.5 ppm, of receptor **1**, Ca^{2+}-complex, and K^+-complex in CD_3OD at room temperature. Because **1** is somewhat insoluble in methanol in NMR-detectable concentration, the NMR spectrum was obtained at 5.4 mM to exhibit a relatively broadened spectral pattern due to the fact that conformational internal conversion is slow to some degree at room temperature. Upon complexation with Ca^{2+}, however, the solubility in methanol was increased and the obtained NMR spectra (11 mM) changed from the broad signal to split pattern with significant downfield shifts of NCH_2 and the crowned methylenes. One could detect the $ArCH_2Ar$ protons of the calixarene unit as one pair of doublets, assigned to be H_{exo}($\delta = 3.40$ ppm, $J = 12.8$ Hz, 4H) and H_{endo} ($\delta = 4.15$ ppm, $J = 12.6$ Hz, 4H), respectively. Such findings indicate that the Ca^{2+}-complex has been frozen out in a

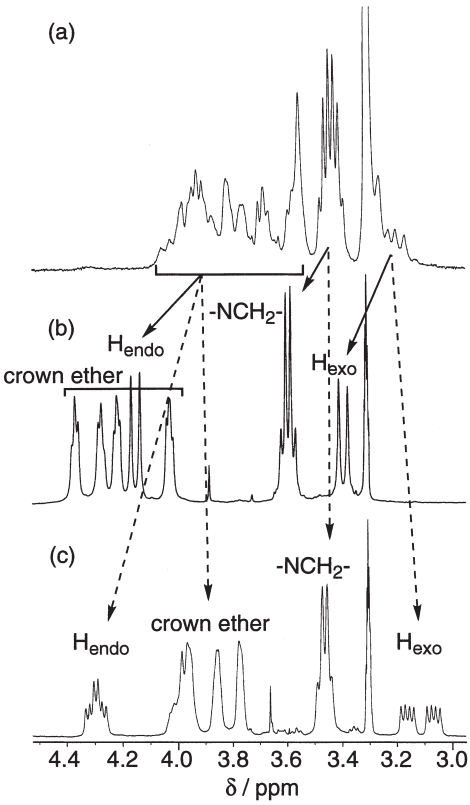


FIGURE 4 ^{1}H NMR spectra (400 MHz, CD_3OD, room temperature) of **1** (a), **1**·Ca^{2+} complex (b) and **1**·K^+ complex (c), respectively.

"flattened" cone conformation [8] with a pseudo C_2 axis of symmetry. This is something inferred from the ^{1}H NMR spectral data wherein the magnitude of the chemical shift between the high- and low-field $ArCH_2Ar$ signals in the Ca^{2+}-complex is smaller than in the case of the K^+-complex (*vide infra*). The Ca^{2+}-complextion process involves an arrangement for the cavity in order to accommodate the Ca^{2+} appropriately (*nest-in*) and efficient ion–dipole interactions between the Ca^{2+} and the donor groups involving the quinone carbonyls of the chromophores.

Meanwhile, complexation with K^+ afforded a different binding motif compared to the Ca^{2+}·**1** complex; the shifts due to the NCH_2 and the crowned methylenes slightly altered and the $ArCH_2$-Ar protons showed a certain split pattern as four pairs of doublets in 1:1:1:1 integral intensity proportions. The chemical shifts for H_{exo} are δ 3.06, 3.08, 3.15, and 3.17 ppm, whereas those for H_{endo} are δ 4.28, 4.29, 4.30, and 4.32 ppm. From these data, although the bound cation forced the calixarene annulus into a "cone", the complex motif was an unsymmetrical. This finding is quite unique because it is known that K^+-complex with a "cone"-type calix[4]crown-5 derivative has usually exhibited one pair of doublet for the bridging methylene resonances [10]. In an attempt to understand the

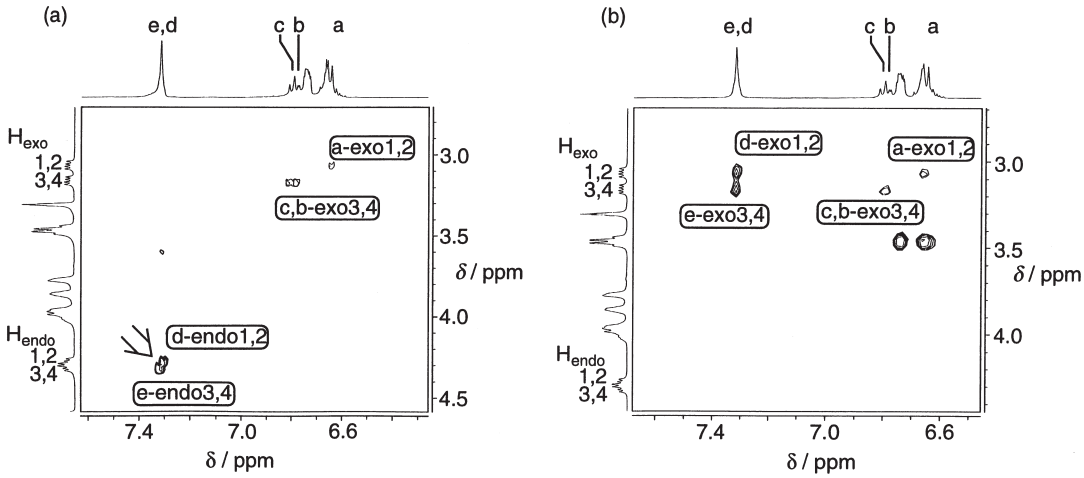


FIGURE 5 COSY (a) and NOESY (b) spectra (400 MHz, CD_3OD, room temperature). Letters 1–4 refer to the bridging methylene of the calix[4]arene unit. Letters (a–c) and (d and e) refer to those of the *m*-PhH and quinoid-H, respectively.

intriguing complex structure and to cope with NMR analysis, we performed COSY and NOESY experiments. The correlation between the methylenes and Ph (or quinoid)-protons of the calixarene is important for the assignment. First, we noted that the resonances arising from the *m*-PhH splitted three signals at ca. 6.64 (H_a being overlapped with other aromatic protons), 6.78 (H_b), and 6.80 ppm (H_c), which showed appropriate cross-peaks (H_a-$H_{exo1,2}$ and $H_{b,c}$-$H_{exo3,4}$) in the COSY and NOESY spectra (Fig. 5). Furthermore, although the quinoid-H (d and e) exhibited a somewhat broad signal (7.31 ppm), the two-dimensional spectra allowed two types of cross-peaks between the quinoid-H and the bridging methylene resonances (H_d–$H_{endo1,2}$ and H_e–$H_{endo3,4}$ in the COSY; H_d–$H_{exo1,2}$ and H_e–$H_{exo3,4}$ in the NOESY). Most notably, the chemical shifts of H_d and H_e are slightly different from each other, as inferred from the shape of the cross-peak which was indicated by the arrow in the COSY spectrum. These results also supported an argument that the encapsulation with K^+ did not employ pseudo-C_2 axis of symmetry. In this context, variable temperature ^1H NMR experiment with K^+-complex ranging from 301 to 330 K displayed that the singlet of quinoid-H (7.31 ppm) turned to well-distinguishable two singlets (7.28 and 7.32 ppm). As a control, when we performed similar experiment using Ca^{2+}-complex, the corresponding quinoid-H signal remained singlet (7.55 ppm) at 330 K.

Taken together, the intricate NMR spectra suggest an unsymmetrical complexation with K^+. Although we have not yet obtained an X-ray structure of the complex to clarify such a result, Beer *et al.* have reported that, on the basis of the X-ray analysis of the related calix[4]diquinone-5 [18], K^+ deviated 0.43 Å out of the crown plane, pointing out that the K^+ is clearly too large for the crown. These results allow us to consider different complexation modes between both the K^+- and Ca^{2+}-complex. In the former case, the guest cations might be efficiently interacted with convergent crown-oxygens, whereas the latter is more attractively bound by more polar carbonyl groups of indoanilines to induce the drastic color change. As a result, these different modes in the cavity might lead to the fact that the guest-affinity towards **1** is not coupled with the optical signaling of **1**. Hence, the Ca^{2+}-induced color change was inhibited by K^+ with more efficient than other alkali metal ions. This intriguing phenomenon might be attributable that, in the K^+-complex, electrostatic interactions between the K^+ and quinonecarbonyl groups are not significant to prompt color change.

In conclusion, the results described in this paper lead us to suggest a new approach to the generation of optical read-out receptors. In particular, the use of crown-strapped cavity in the indoaniline-calixarene conjugated system leads to distinct attractive binding forces that permit either "carbonyl"- or "crown oxygen"-driving complexation serves to emerge a unique kind of cation-induced signaling that can reproduce the basic features of classic pharmacological receptors. On a different level, systems such as the one described herein might be useful in nanoscale technology. For example, in the case of a photoionic system [19], an effector such as Ca^{2+} could cause the system to "switch on" in terms of a color-based signal. Alternatively, the presence of K^+ could serve to inhibit this latter output and can thus be regarded as a kind of rudimentary "off switch" [7]. Although this system should overcome some difficulty involving switching repeatability and speed, we feel that such possibilities warrant future exploration. Furthermore, the obtained insights in this study would afford some useful information

from the standpoint of designing a molecular sensor in analytical chemistry.

EXPERIMENTAL SECTION

General Methods

NMR spectra were taken on a Bruker AM 400 or ARX 400 (400 MHz) spectrometers. Chemical shifts (δ) are reported downfield from the internal standard Me_4Si. For routine ^1H NMR spectroscopy, a Bruker AC 200 (200 MHz) or a Bruker AC 300P (300 MHz) instruments were used. Absorption spectra were measured using a Shimadzu UV-2100 spectrophotometer. FAB mass spectra were performed by a JEOL JMS-DX 303 double focusing spectrometer. *m*-Nitrobenzyl alcohol was used as a matrix. Elemental analyses were obtained using an EISON EA1108.

Materials

Absolute ethanol (EtOH) for spectroscopic study was an analytical grade purchased from Kanto Chemical Co., Inc.. Toluene was distilled from sodium. The other reagent-grade reactants and solvents were used as received from chemical suppliers. Calix[4]-arene was prepared according to the literature procedure [15].

3,6,9-trioxaundecane-1,11-diylbistosylate

To an aqueous tetrahydrofuran (THF) solution (100 ml) of 3,6,9-trioxaundecane-1,11-diol **2** (15.0 g; 77.3 mmol) and NaOH (11.8 g; 295 mmol) at an ice condition was added dropwise a THF solution (85 ml) of tosyl chloride (32.7 g; 172 mmol) for 3 h. Then the resulting mixture was stirred for 150 min under an ice condition, 1% HCl aqueous solution was added to the solution, and then the mixture was extracted with benzene (300 ml × 2). The combined benzene extract was washed with water (300 ml × 2) followed by 1.1% $NaHCO_3$ aqueous solution (300 ml) and water (300 ml) again and then dried with $CaCl_2$. The solvent was evaporated to give the product: 37.9 g (98% yield).

^1H NMR (300 MHz, $CDCl_3$, TMS): δ 2.45 (6H, s), 3.56 (8H, s), 3.68 (4H, t, $J = 5.0$ Hz), 4.15 (4H, t, $J = 4.8$ Hz), 7.34 (4H, d, $J = 8.1$ Hz), 7.79 (4H, d, $J = 8.5$ Hz).

25,27-Dihedroxycalix[4]crown-5

To an anhydrous toluene solution (200 ml) of calix[4]arene (3.0 g; 7.07 mmol) in the presence of potassium *tert*-butoxide (2.0 g; 17.4 mmol) under reflux, an anhydrous toluene solution (150 ml) of 3,6,9-trioxaundecane-1,11-diylbistosylate (4.3 g; 8.55 mmol) was added dropwise for 140 min. The mixture was then stirred for 4 days under reflux and potassium *tert*-butoxide (3.6 g; 29.4 mmol) was added in two portions at 24 h intervals. The mixture was then washed with 1N HCl aqueous solution, dried with $MgSO_4$, and filtered off. The solvent was then evaporated to give 1.24 g of 25,27-dihedroxy-calix[4]crown-5 (46% yield), and 1.05 g of calix[4]-arene unreacted in this case.

^1H NMR (200 MHz, $CDCl_3$, TMS): δ 3.36 (4H, ABq, $J = 13.2$ Hz), 3.85 (4H, t, $J = 4.9$ Hz), 4.00 (4H, t, $J = 4.9$ Hz), 4.10 (8H, s), 4.43 (4H, ABq, $J = 13.2$ Hz), 6.67 (2H, t, $J = 7.3$ Hz), 6.70 (2H, t, $J = 7.8$ Hz), 6.86 (4H, d, $J = 7.3$ Hz), 7.07 (4H, d, $J = 7.8$ Hz), 7.73 (2H, s).

5,17-Bis(4′-diethylamino-2′-methylphenylimino) calix[4]crown-5-26,28-dione (1)

An acetone–methanol solution (5:1 v/v; 18 ml) involving 25,27-dihedroxycalix[4]crown-5 (101 mg; 0.173 mmol) and 2-amino-5-(diethylamino)toluene monohydrochloride (149 mg; 0.694 mmol) was taken to a basic condition by the addition of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (1 ml). Then $KMnO_4$ (74 mg; 0.468 mmol) was added dropwise to the solution for 18 min and stirred for 1 h at room temperature. After the evaporation of the solvent, the residue was dissolved in $CHCl_3$ (30 ml). The resulting solution was washed with water (20 ml) and 0.05% HCl aqueous solution (20 ml × 7), and was evaporated. The desired products **1** was then purified by MPLC on silica gel (Wakogel C-300) using 0–5% (v/v) CH_3OH in $CHCl_3$ as the eluants and recrystallized from acetone–water system: 70 mg (43% yield).

^1H NMR (400 MHz, [D_6]DMSO, 373 K): δ 1.16 (12H, t, $J = 7.0$ Hz), 2.26 (6H, s), 3.19–3.31 (4H, m), 3.40 (8H, q, $J = 6.9$ Hz), 3.51–3.99 (20H, m), 6.57–6.84 (m, 12H), 7.08 (2H, s), 7.15 (2H, s); ^{13}C NMR (100.7 MHz, $CDCl_3$, 297 K) δ 12.8, 19.0, 32.1, 32.7, 44.5, 69.8, 70.8, 71.0, 71.3, 71.4, 71.5, 73.6, 73.7, 73.8, 108.9, 113.7, 122.7, 123.3, 123.3, 125.1, 129.1, 129.3, 131.1, 131.1, 131.4, 131.4, 135.9, 137.8, 138.3, 141.7, 141.8, 142.7, 147.3, 147.3, 154.4, 155.4, 155.5, 155.6, 185.7; MS (FAB) *m/z* 930 $[M]^+$; Anal. Calcd. for $C_{58}H_{66}N_4O_7 \cdot 0.5H_2O$: C, 74.10; H, 7.18; N, 5.96. Found: C, 73.92; H, 7.22; N, 6.28; UV/Vis (EtOH): λ_{max} (ϵ) 622 (47,000 $cm^{-1}M^{-1}$).

FAB Mass Spectra

Positive-ion FAB mass spectra were recorded on a JEOL JMS-DX 303, where Xe was used as the atom beam accelerated 3 keV, with a mass range of *m/z* 700–1,160. Calibration was performed using

ULTRAMARK 1621 ranging from 700 to 1,250. Spectra were obtained with a magnet scan rate of 10.5 s per scan.

Typical FAB mass solutions were prepared by mixing the following solutions: (1) a 50 μl portion of a 12 mM EtOH solution of **1**; (2) a 50 μl portion of a 60 mM EtOH solution of KSCN; (3) a 50 μl portion of a 60 mM EtOH solution of $Ca(SCN)_2$. The solution was mixed and evaporated. After the resulting residue was dissolved in 2 μl of EtOH again, 20 μl of *m*-nitrobenzyl alcohol matrix was added to the solution and then was deposited on a FAB probe tip.

Acknowledgements

We wish to acknowledge Mr M. Kubo of Chemical Analysis Center Saitama University for measuring the FAB mass spectra. This work was supported by PRESTO (Precursory Research for Embryonic Science and Technology) of Japan Science and Technology Corporation (JST).

References

[1] Hayashita, T. and Takagi, M. (1996) In: Lehn, J.-M., Atwood, J.L., Davies, J.E.D., MacNicol, D.D., Vögtle, F. and Gokel, G.W., eds, *Comprehensive Supramolecular Chemistry* (Pergamon Press, New York) Vol. 1, p 635.

[2] de Silva, A.P., Gunaratne, H.Q.N., Gunnlaugsson, T., Huxley, A.J.M., McCoy, C.P., Rademacher, J.T. and Rice, T.E. (1997), *Chem. Rev.* **97**, 1515.

[3] Desvergne, J.-P. and Czarnik, A.W. (1997) *Chemosensors Ion and Molecular Recognition NATO Symposium Series*, (Kluwer, Dordrecht).

[4] Leff, P., (1998) In: *Receptor-Based Drug Design* (Marcel Dekker, New York).

[5] Ruiz-Gómez, A., García-Calvo, M., Vázquez, J., Marvizon, J.C.G., Valdivieso, F. and Mayor, Jr, F. (1989), *J. Neurochem.* **52**, 1775.

[6] Weiland, G.A., Minneman, K.P. and Molinoff, P.B. (1979), *Nature* **281**, 114.

[7] Kubo, Y., Obara, S. and Tokita, S. (1999) "Preliminary approach as a new material", *Chem. Commun.*, 2399.

[8] Gutsche, C.D. (1989) "A review of calixarene chemistry", In: Stoddart, J.F., ed, *Calixarene, Monographs in Supramolecular Chemistry* (The Royal Society of Chemistry, Cambridge).

[9] Gutsche, C.D. (1998) "A review of calixarene chemistry" In: Stoddart, J.F., ed, *Calixarenes Revisited, Monographs in Supramolecular Chemistry* (The Royal Society of Chemistry, Cambridge).

[10] Ghidini, E., Ugozzoli, F., Ungaro, R., Harkema, S., El-Fadl, A.A. and Reinhoudt, D.N. (1990), *J. Am. Chem. Soc.* **112**, 6979.

[11] Casnati, A., Pochini, A., Ungaro, R., Bocchi, C., Ugozzoli, F., Egberink, R.J.M., Struijk, H., Lugtenberg, R., de Jong, F. and Reinhoubt, D. (1996), *Chem. Eur. J.* **2**, 436.

[12] Gatto, V.J. and Gokel, G.W. (1984), *J. Am. Chem. Soc.* **106**, 8240.

[13] Kubo, Y., Hamaguchi, S., Niimi, A., Yoshida, K. and Tokita, S. (1993), *J. Chem. Soc., Chem. Commun.*, 305.

[14] Kubo, Y., Tokita, S., Kojima, Y., Osano, Y.T. and Matsuzaki, T. (1996), *J. Org. Chem.* **61**, 3758.

[15] Gutsche, C.D. and Lin, L.-G. (1986), *Tetrahedron* **42**, 1633.

[16] Job, P. (1928), *Ann. Chim. Ser.* **9**, 113.

[17] Conners, K.A. (1987) *Binding Constants, The Measurement of Molecular Complex Stability* (Wiley, New York).

[18] Beer, P.D., Gale, P.A., Chen, Z., Drew, M.G.B., Heath, J.A., Ogden, M.I. and Powell, H.R. (1997), *Inorg. Chem.* **36**, 5880.

[19] de Silva, A.P., Gunaratne, H.Q.N., Gunnlaugsson, T., Huxley, A.J.M. and McCoy, C.P. (1997) "An excellent account", In: Gokel, G.W., ed, *Advances in Supramolecular Chemistry* (JAI Press, Greenwich) **Vol. 4**, p 1.