August, 1991] © *1991 The Chemical Society of Japan* NOTES *Bull. Chem. Soc. Jpn.*, *64*, *2575—2577 (1991)* 2575

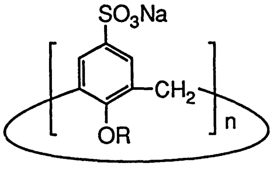
A New Calix[6]arene-Based Uranophile with Phosphonate Groups as Ligands

Takeshi Nagasaki, Takashi Arimura, and Seiji Shinkai*
Department of Organic Synthesis, Faculty of Engineering, Kyushu University, Fukuoka 812

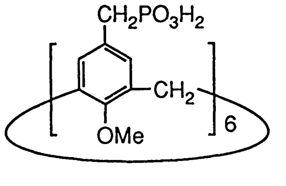
(Received March 1, 1991)

Synopsis. A new calix[6]arene-based uranophile which has six phosphonomethyl groups on the upper rim was synthesized. This compound forms a 1 : 1 complex with uranyl ion (UO_2^{2+}). The stability constant was estimated to be $10^{17.5}$ M^{-1},[#] which is satisfactorily comparable with those for calix[6]arene-based uranophiles bearing OH or COOH groups on the lower rim.

The selective extraction of uranium from sea water has been of much concern for chemists because of its importance in relation to energy problems. In order to design such a ligand that can selectively extract uranyl ion (UO_2^{2+}), one faces a difficult problem, namely, the ligand must strictly discriminate between UO_2^{2+} and other metal ions which are present in great excess in sea water. A possible unique solution for this dlfficult problem is to use a cyclic ligand suitably structured to perform the UO_2^{2+} binding. As UO_2^{2+} complexes adopt either a pseudoplanar pentacoordinate or hexacoordinate structure,[1] a macrocyclic ligand with a nearly coplanar arrangement of either five or six donating groups would serve as a specific ligand for UO_2^{2+} (i.e., as a uranophile). This sort of approaches has been reported by a few research groups.[2–5] We recently found that pentasodium 31,32,33,34,35-pentahydroxycalix[5]arene-5,11,17,23,29-pentasulfonate (**1**$_5$) and hexasodium 37,38,39,40,41,42-hexahydroxycalix[6]arene-5,11,17,23,29,35-hexasulfonate (**1**$_6$) have remarkably high stability constants ($K_{\text{uranyl}}=10^{18.7-19.2}$ M^{-1}) and selectivity factors ($K_{\text{uranyl}}/K_{M^+}=10^{10-17}$) in water.[6,7] In particular, the "super-uranophile" nature of the calix[6]arene derivatives is of great significance from a practical viewpoint because they can be synthesized from commercially-available calix[6]arene-37,38,39,40,41,42-hexol in good yields.[8,9] The remarkably high selectivity is attributed to the rigid skeleton of calix[5]arene and calix[6]arene which can provide the pre-organized penta- and hexacoordination geometry for the binding of UO_2^{2+} but cannot accommodate a square-planar or tetrahedral coordination geometry appropriate for other metal cations.[6,7,10,11] We here synthesized 37,38,39,40,41,42-hexamethoxy-5,11,17,23,29,35-hexakis(phosphonomethyl)calix[6]arene (**2**) and estimated the stability constant for the complex formation with UO_2^{2+}.



1$_n$
R=H or CH_2COOH



2

Results and Discussion

pH Dependence. It is known that both calix[*n*]arenepolyols and their *O*-carboxymethyl derivatives (**1**$_n$: R=CH_2COOH) are poorly soluble in water.[10,12] To determine the stability constant, the moderate solubility in water is required. To satisfy this requirement we previously introduced sulfonate groups into the *p*-positions to the hydroxyl groups on the lower rim. On the other hand, compound **2** showed sufficient solubility in water.

We first estimated pK_a values of **2** and sodium methoxybenzylphosphonate (**3**). The titration curve for **2** is illustrated in Fig. 1. The pK_a values for **2** were estimated to be 2.91 and 8.86 and those for **3** to be 2.16 and 7.71. The result indicates that the phosphonate group in **2** show the pK_a values higher by 0.75—1.15 pK units than that in **3**. A Henderson–Hasselbach plot ($\text{pH}=\text{p}K_a-n\cdot\log\,[(1-\alpha)/\alpha]$ where n becomes greater than unity when the dissociation groups interact with each other) for the second acid dissociation of the phosphonate groups in **2** gave $n=1.5$ whereas that for the second acid dissociation of the phosphonate group in **3** gave $n=1.0$. The results establish that the pK_a values for **2** are raised because of the intramolecular interactions among the phosphonate groups.

Addition of **2** to uranyl dinitrate ($UO_2(NO_3)_2$) solution at 25 °C increased the UV and visible absorption band over a wide wavelength range (225—600 nm) owing to the competitive association of **2** with UO_2^{2+} (the spectrum is similar to Fig. 1 in Ref. 7). The spectral change after mixing was relatively slow: it usually took 4 to 5 h to reach the equilibrium spectrum. On the other hand, addition of acyclic **3** (used as a

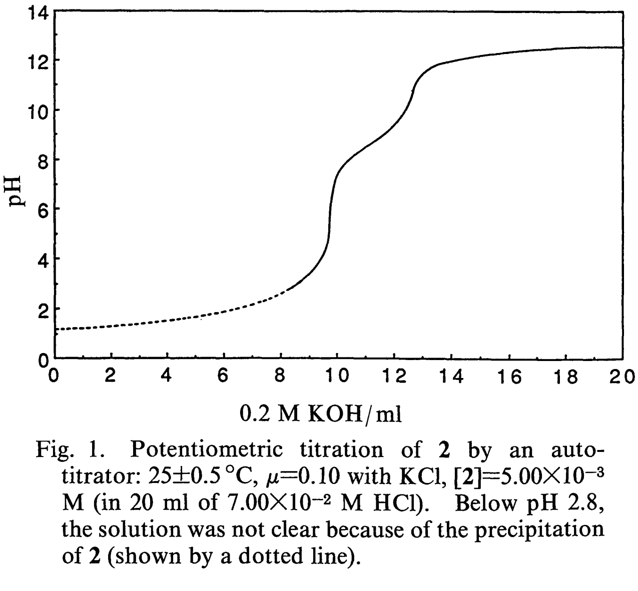


Fig. 1. Potentiometric titration of **2** by an autotitrator: 25±0.5 °C, $\mu=0.10$ with KCl, $[\mathbf{2}]=5.00\times10^{-3}$ M (in 20 ml of 7.00×10^{-2} M HCl). Below pH 2.8, the solution was not clear because of the precipitation of **2** (shown by a dotted line).

[#] 1 M=1 mol dm^{-3}.

reference compound: [3]=6·[2]) to uranyl dinitrate solution did not increase the absorption band. The difference shows that the efficient UO_2^{2+} binding to **2** is based on the ring structure of calix[6]arenehexol.

In Fig. 2, we plotted the absorbance at 449 nm (a shoulder of the spectrum: A_{449}) against pH. It is seen from Fig. 2 that the A_{449} for **2** sharply increases at pH 8—9, forms a plateau at pH 11.4—11.8, and decreases above pH 12. The increase at pH 8—9 is ascribed to the dissociation of the phosphonate groups whereas the decrease above pH 12 is ascribed to the competitive association of UO_2^{2+} with OH^- present in great excess at this pH range. In fact, the precipitation of the hydroxide complex was observed pH 12.5. Judging from the pK_a values determined above, the "active" ligands for the UO_2^{2+}-binding are dianionic phosphonate groups (i .e., $-CH_2P(=O)O_2^{2-}$). Careful examination of Fig. 2 reveals, however, that at around pH 8.86 (average pK_a of **2**) the complex formation scarcely takes place. In other words, the plot of A_{449} versus pH (Fig. 2) shifts to higher pH region than the titration curve (Fig. 1). The discrepancy suggests that the half-dissociated **2** bearing three $-CH_2P(=O)O_2^{2-}$ and three $-CH_2P(=O)O_2H^-$ cannot yet serve as the "active" ligand. We consider that the coordination ability of the $-CH_2P(=O)O_2^{2-}$ groups is suppressed by the intramolecular hydrogen-bonding interaction with the $-CH_2P(=O)O_2H^-$ groups.

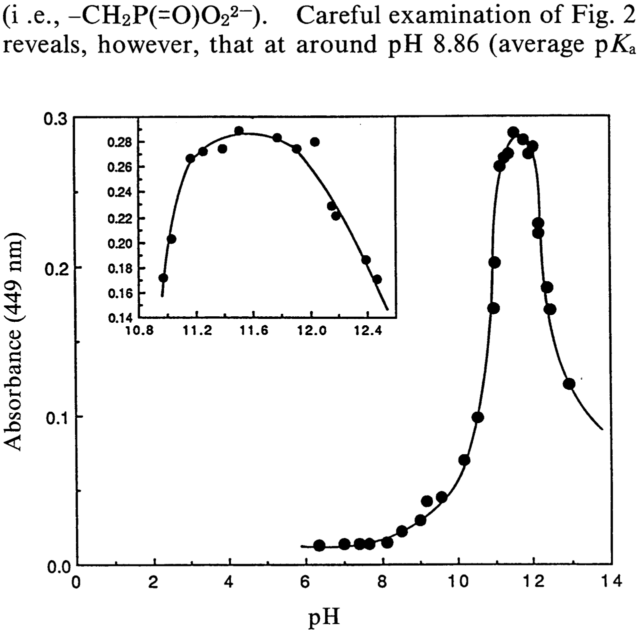


Fig. 2. pH dependence for the formation of the $UO_2\cdot$**2** complex: $[UO_2(NO_3)_2]$=[**2**]=0.33 mM, μ=0.1 with KCl, 25 °C.

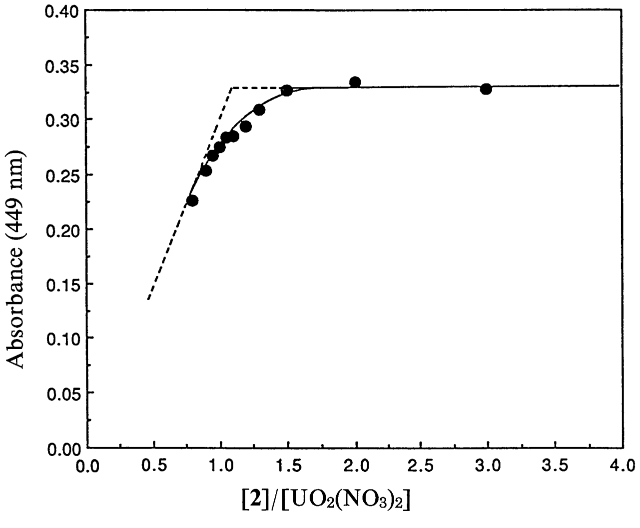


Fig. 3. Molar ratio plot for $UO_2\cdot$**2** complex: $[UO_2(NO_3)_2]$=0.29 mM (constant), pH 11.5 with KOH, μ=0.1 with KCl, 25 °C.

Stoichiometry and Stability Constants. As a prelude to estimate the stability constant, we determined the stoichiometry of the $UO_2\cdot$**2** complex. In Fig. 3, the A_{449} was plotted against [**2**]/[UO_2^{2+}]. A break-point appeared at [**2**]/[UO_2^{2+}]=1.0, supporting the formation of a 1 : complex. From the A_{449} value at the plateau one can estimate the ε_{449} to be 1170 $M^{-1}cm^{-1}$ for the $UO_2\cdot$**2** complex, which is comparable with those (about 1400 $M^{-1}cm^{-1}$) for the $UO_2\cdot$**1** complexes.[7]

UO_2^{2+} is known to form a stable carbonate complex, $[UO_2(CO_3)_3]^{4-}$ and the stability constant ($K_{\text{carbonate}}$= $[UO_2(CO_3)_3^{4-}]/[UO_2^{2+}][CO_3^{2-}]^3$) is estimated to be $10^{12.5}$ M^{-3} at 25 °C and pH 10.4.[13] When **2** is added to the uranyl tricarbonate solution, the competitive displacement of carbonates by **2** takes place and reaches an equilibrium after a few hours. This process is expressed by Eq. 1. One can thus estimate the displacement equilibrium constant (K_e) from the spectral change. Finally, the stability constant for UO_2^{2+} (K_{uranyl}= $[UO_2\cdot\mathbf{2}]/[UO_2^{2+}][\mathbf{2}]$ can be determined by Eq. 2.[14]

$$[UO_2(CO_3)]^{4-} + \mathbf{2} \overset{K_e}{\rightleftarrows} UO_2\cdot\mathbf{2} + 3CO_3^{2-} \qquad (1)$$

$$K_{\text{uranyl}} = K_e \cdot K_{\text{carbonate}} \qquad (2)$$

At pH 10.4 (where 91.4% of the phosphonomethyl groups exist as $-CH_2P(=O)O_2^{2+}$. This pH is not the optimum condition for the formation of the $UO_2\cdot$**2** complex: see Fig. 2) the K_{uranyl} was estimated to be $10^{16.3}$ M^{-1}. This value is smaller by about three orders of magnitude than those for $\mathbf{1}_5$ and $\mathbf{1}_6$[7] (Table 1). Assuming that the $K_{\text{carbonate}}$ is scarcely affected at pH 10.3—11.6, we can calculate the K_{uranyl} at pH 11.5 (where 98.3% of the phosphonomethyl groups exist as $-CH_2P(=O)O_2^{2-}$. This pH is the optimum condition for the formation of the $UO_2\cdot$**2** complex) to be $10^{17.5}$ M^{-1}. This value is smaller only by 1.2—1.7 pK units than those for the $UO_2\cdot$**1** complexes.[7]

In conclusion, the present study demonstrated that the phosphate group serves as an excellent ligand for the complexation with UO_2^{2+}. We are currently devoting our research efforts toword the synthesis of calix[6]arene-based uranophiles bearing phosphonate groups

Table 1. Stability Constants (K_{uranyl}) for Calixarene-Based Uranophiles[a]

Calixarene	pH	log K_{uranyl}
$\mathbf{1}_5$ (R=H)	10.4	18.9±0.6[b]
$\mathbf{1}_6$ (R=H)	10.4	19.2±0.1[b]
$\mathbf{1}_6$ (R=CH_2COOH)	10.4	18.7±0.1[b]
2	10.4	16.3±0.3
2	11.5	17.5±0.2

a) 25 °C, μ=0.1 with KCl, 0.01 M carbonate buffer.
b) Cited from Ref. 7.

on the lower rim.

Experimental

Materials. The synthesis of **2** was independently reported (as communications) by Almi et al.[15] and by us.[16]

37,38,39,40,41,42-Hexamethoxy-5,11,17,23,29,35-hexakis-(*O,O*-diethylphosphonomethyl)calix[6]arene (4). 37,38,39,40,41,42-Hexamethoxy-5,11,17,23,29,35-hexakis(chloromethyl)-calix[6]arene (910 mg; 0.90 mmol) was refluxed in triethyl phosphite (27 g; 160 mmol) for 14 h. After cooling, unreacted triethyl phosphite was distilled under reduced pressure. The residue was dissolved in chloroform and subjected to column chromatography (stationary phase, silica gel; mobile phase, chloroform–methanol (10 : 1 v/v)). The concentration of the eluent gave **4** in 96% yield; mp 149—151 °C; IR (neat) $\nu_{P=O}$ 1245 cm^{-1}, ν_{P-O-C} 960 and 1055 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.21 (6H, t, C-CH_3), 2.75 (2H, d(J_{PH}=21 Hz), ArCH_2P), 3.43 (3H, s, OCH_3), 3.89 (2H, s, ArCH_2Ar), 3.94 (4H, dq(J_{PH}=7.3 Hz, J_{HH}=7.3 Hz), POCH_2C), 6.79 (2H, s, ArH). Found: C, 55.90; H, 7.60%. Calcd for $(C_{13}H_{19}O_4P)_6 \cdot 3H_2O$: C, 55.91; H, 7.22%.

37,38,39,40,41,42-Hexamethoxy-5,11,17,23,29,35-hexakis-(phosphonomethyl)calix[6]arene (2). Compound **4** (810 mg; 0.50 mmol) was refluxed in dioxane (10 ml)-concd HCl (10 ml) mixed solvent for 12 h. After cooling, the solution was evaporated to dryness under reduced pressure and the residue was recrystallized from ethanol–ether: Colorless powder, mp >300 °C, yield 82%; IR (nujol) ν_{OH} 3600 cm^{-1}, $\nu_{P=O}$ 1240 cm^{-1}, ν_{P-O-C} 1005 cm^{-1}; ^{1}H NMR (CD_3OD) δ=2.85 (2H, m, ArCH_2P), 3.01 (3H, s, OCH_3), 3.93 (2H, s, ArCH_2Ar), 6.91 (2H, s, ArH). Found: C, 48.23; H, 5.33%. Calcd for $(C_9H_{11}O_4P)_6 \cdot 3H_2O$: C, 48.44; H, 5.22%.

Determination of the Stability Constants. The stability constants for UO_2^{2+} were evaluated by a displacement method[17] at 25 °C. The details of the method were described previously.[7]

Potentiometric Titration. Potentiometric titration of **2** and **3** ([**2**]=5.00×10^{-3} M and [**3**]=2.00×10^{-2} M in 20 ml of 7.00×10^{-2} M HCl) was carried out at 25±0.5 °C by using an auto-titrator (Kyoto Electronics, Model APB-117). The details of the measurement conditions are described in a caption to Fig. 1.

References

1) R. Graziani and E. Forselline, *J. Chem. Soc., Dalton Trans.*, **1972**, 2059, references cited therein.

2) A. H. Alberts and D. J. Cram, *J. Am. Chem. Soc.*, **99**, 3880 (1977).

3) I. Tabushi, Y. Kobuke, K. Ando, M. Kishimoto, and E. Ohara, *J. Am. Chem. Soc.*, **102**, 5948 (1980).

4) I. Tabushi, Y. Kobuke, and A. Yoshizawa, *J. Am. Chem. Soc.*, **106**, 2481 (1984).

5) Y. Kobuke, I. Tabushi, K. Oh, and T. Aoki, *J. Org. Chem.*, **53**, 5933 (1988).

6) S. Shinkai, H. Koreishi, K. Ueda, and O. Manabe, *J. Chem. Soc., Chem. Commun.*, **1986**, 233.

7) S. Shinkai, H. Koreishi, K. Ueda, T. Arimura, and O. Manabe, *J. Am. Chem. Soc.*, **109**, 6371 (1987).

8) C. D. Gutsche, *Acc. Chem. Res.*, **16**, 161 (1983).

9) C. D. Gutsche, "Calixarenes," Royal Society of Chemistry, Cambridge (1989).

10) S. Shinkai, Y. Shirahama, H. Satoh, O. Manabe, T. Arimura, K. Fujimoto, and T. Matsuda, *J. Chem. Soc., Perkin Trans. 2*, **1989**, 1167.

11) For a comprehensive review for UO_2^{2+} complexes see I. Tabushi and Y. Kobuke, *Nippon Kaisui Gakkaisi*, **36**, 205 (1982).

12) A. Arduini, A. Pochini, S. Riverberi, and R. Ungaro, *J. Chem. Soc., Chem. Commun.*, **1984**, 981.

13) Ref. 4 and related papers cited therein.

14) At pH 11.5 the K_{uranyl} value was constant ($\log K_{\mathrm{uranyl}}$= 17.5±0.2) over the carbonate concentration range 0.004—0.02 M. This indicates that the displacement proceeds according to Eq. 1.

15) M. Almi, A. Arduini, A. Casnati, A. Pochini, and R. Ungaro, *Tetrahedron Lett.*, **45**, 2177 (1989).

16) T. Arimura, T. Nagasaki, S. Shinkai, and T. Matsuda, *J. Org. Chem.*, **54**, 3766 (1989).

17) K. Ueno, "Chelate Kagaku," Nankodo, Tokyo (1971), Chap. 4.