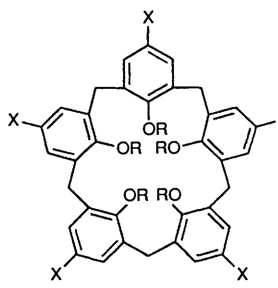
Kinetic Studies of Calixarene-based Cyclic and Non-cyclic 'Super-uranophiles'

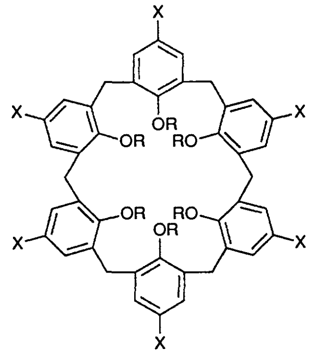
Takeshi Nagasaki, Kazuhiko Kawano, Koji Araki and Seiji Shinkai*
Department of Organic Synthesis, Faculty of Engineering, Kyushu University, Fukuoka 812, Japan

The kinetic parameters for the binding of UO_2^{2+} to calixarene-based 'super-uranophiles', *para*-sulphonatocalix[*n*]arenes (*n* = 5, 6 and 8: $\mathbf{1}_n$) and their non-cyclic analogue, 3,5-bis{[2-hydroxy-3-(2-hydroxy-3-methyl-5-sulphonatophenyl)methyl-5-sulphonatophenyl]methyl}-4-hydroxybenzenesulphonate (**2**) have been evaluated at 25 °C and pH 10.40. The reaction of UO_2^{2+} and **2** is speeded up by a factor of 85 compared to that of UO_2^{2+} and $\mathbf{1}_6$.

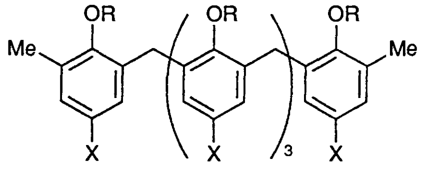
The selective extraction of uranium from sea water has attracted extensive attention from chemists because of its importance in relation to energy problems. In order to design such a ligand that is capable of selective extraction of uranyl ion (UO_2^{2+}), one faces a difficult problem: *i.e.* the ligand must strictly discriminate UO_2^{2+} from other metal ions present in great excess in sea water. It has been established that UO_2^{2+} complexes adopt either a pseudoplanar pentacoordinate or hexacoordinate structure.[1] This suggests that a macrocyclic host molecule having a nearly coplanar arrangement of either five or six ligand groups would serve as a specific ligand for UO_2^{2+} (*i.e.*, as a uranophile).[2] Calixarenes are cyclic oligomers made up of phenol units.[3] We recently found that calix[5]arene-*p*-pentasulphonate ($\mathbf{1}_5$) and calix[6]arene-*p*-hexasulphonate ($\mathbf{1}_6$) have remarkably large, record-breaking stability constants ($K_{\text{uranyl}} = 10^{18.7-19.2}$ dm^3 mol^{-1}) and selectivity factors ($K_{\text{uranyl}}/K_{M^{n+}} = 10^{10-17}$) in water.[4] The results are attributed to the moderately rigid skeleton of calix[5]arene and calix[6]arene which can provide the pre-organized penta- and hexa-coordination geometry for the binding of UO_2^{2+}. A preliminary kinetic study on $\mathbf{1}_6$ indicated that the binding rate is relatively slow, the half-life at room temperature being *ca.* 1 h. This is supposed to be the sole defect of the calixarene-based uranophiles. What is taking so long? Rebek *et al.*[5] found that the reaction rate for the binding of 18-crown-6 to $Hg(CN)_2$ or $Hg(CF_3)_2$ (linear guest cation) is very slow. As UO_2^{2+} is also a linear guest cation ($O{=}U{=}O^{2+}$), the slow binding rate may be a characteristic of a reaction between linear guest cations and cyclic host ligands. If so, this phenomenon would be attributed, as pointed out by Rebek *et al.*,[5] to the slow *exo*- to *endo*-complex (rotaxane-type complex) step which must experience a high-energy conformation in order to permit UO_2^{2+} to penetrate the calixarene ring [as in eqn. (1)]. As an attempt to remove this defect, we have designed a non-cyclic calixarene analogue **2** which does not necessarily experience such a high-energy conformation as an obligatory path and compared its equilibrium and kinetic parameters with those of $\mathbf{1}_n$ (*n* = 5, 6 and 8).



$\mathbf{1}_5$

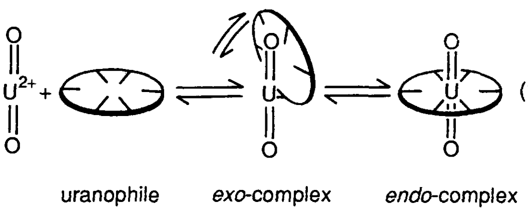


$\mathbf{1}_6$



2

R = H; X = SO_3Na



Preparations of $\mathbf{1}_n$ have been described previously.[4,6] Compound **2** was prepared by sulphonation of 2,6-bis{[2-hydroxy-3-(2-hydroxy-3-methylphenyl)methylphenyl]methyl}phenol.† The product was identified as **2** by IR, ^{1}H NMR spectroscopy and elemental analysis.‡

The measurements were carried out at pH 10.40 (adjusted with carbonate buffer) and 25 °C. The stoichiometry for the uranyl complexes was studied by a continuous variation method. The stability constants ($K_{\text{uranyl}} = [UO_2^{2+}\cdot\text{uranophile}]/[UO_2^{2+}][\text{uranophile}]$) were evaluated by a displacement method (described in ref. 4). The reaction of uranophiles and $UO_2(CO_3)_3^{4-}$ in carbonate buffer solution was followed by monitoring the appearance of a new absorption band at 449 nm. Under the pseudo-first-order conditions ([uranophile] $\ll$ [$UO_2(CO_3)_3^{4-}$]) the reaction obeyed first-order kinetics for up to three half-lives. Although the equilibrium reaction for eqn.

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† This compound was prepared by de-*tert*-butylation of 2,6-bis-{[2-hydroxy-3-(2-hydroxy-3-methyl-5-*tert*-butylphenyl)methyl-5-*tert*-butylphenyl]methyl}-4-*tert*-butylphenol. The methods used for de-*tert*-butylation and sulphonation are similar to those used for the syntheses of $\mathbf{1}_n$.[4]

‡ M.p. > 300 °C, yield 49%; IR (Nujol) ν_{SO}/cm^{-1} 1050, 1170; ^{1}H NMR (D_2O, internal standard DSS) δ 2.27 (6 H, s, CH_3), 4.05 and 4.07 (4 H and 4 H, s and s, $ArCH_2Ar$), 7.40, 7.42, 7.45, 7.48 and 7.51 (2 H each, all s, ArH) (Found: C, 36.5; H, 3.7%. Calc. for $C_{36}H_{29}O_{20}S_5Na\cdot 7H_2O$: C, 36.55; H, 3.66%).

Table 1 Stoichiometry, kinetic parameters and stability constants for the complexes of UO_2^{2+} and calixarene derivatives

Calixarene	Stoichiometry[a] UO_2^{2+} : uranophile	k_{obs}[b]$/10^{-3}$ s^{-1}	k_f/dm^3 mol^{-1} s^{-1}	$k_r/10^{-3}$ s^{-1}	log K_{uranyl}
$\mathbf{1}_5$	1:1	1.15	1.05	0.138	18.9[c]
$\mathbf{1}_6$	1:1	0.111	0.0762	0.0504	19.2[c]
$\mathbf{1}_8$	1:2	2.74[d]	—[e]	—[e]	18.7 (= log K_1)[f] 18.1 (= log K_2)[f]
2	1:1	9.38	2.13	7.13[g]	17.7

[a] Determined by a continuous variation method at $[UO_2(CO_3)_3^{4-}] + [\text{calixarene}] = 1.34 \times 10^{-3}$ mol dm^{-3}. [b] Pseudo first-order rate constant at $[UO_2(CO_3)_3^{4-}] = 4.90 \times 10^{-3}$ mol dm^{-3} in 0.030 mol dm^{-3} carbonate buffer. [c] Cited from ref. 4. [d] Since the reaction obeyed first-order kinetics, it is unlikely that k_{f1} (the pseudo first-order rate constant for the formation of the $UO_2^{2+}\cdot\mathbf{1}_8$ complex) > k_{f2} [the pseudo first-order rate constant for formation of the $(UO_2^{2+})_2\cdot\mathbf{1}_8$ complex]. Thus, the possible kinetic situation is either $k_{f1} \approx k_{f2}$ or $k_{f1} < k_{f2}$. [e] The kinetic equation for the two-step UO_2^{2+}-binding, $UO_2(CO_3)_3^{4-} + \mathbf{1}_8 \rightleftharpoons UO_2^{2+}\cdot\mathbf{1}_8 + 3CO_3^{2-}$ and $UO_2(CO_3)_3^{4-} + UO_2^{2+}\cdot\mathbf{1}_8 \rightleftharpoons (UO_2^{2+})_2\cdot\mathbf{1}_8 + 3CO_3^{2-}$, is too complicated to determine k_f and k_r. [f] $K_1 = [UO_2^{2+}\cdot\mathbf{1}_8]/[UO_2^{2+}][\mathbf{1}_8]$ and $K_2 = [(UO_2^{2+})_2\cdot\mathbf{1}_8]/[UO_2^{2+}][UO_2^{2+}\cdot\mathbf{1}_8]$. These values were estimated by a computer simulation (non-linear least-squares method) of a plot of OD_{449} *vs.* $[\mathbf{1}_8]$ at $[UO_2(CO_3)_3^{4-}] = 1.11 \times 10^{-4}$ mol dm^{-3} (constant), where ε_1 (= 1320 dm^3 mol^{-1} cm^{-1} for $UO_2^{2+}\cdot\mathbf{1}_8$) and ε_2 [= 2290 dm^3 mol^{-1} cm^{-1} for $(UO_2^{2+})_2\cdot\mathbf{1}_8$], which were needed for the simulation, were determined from the absorbances at $[UO_2^{2+}] \ll [\mathbf{1}_8]$ and $[UO_2^{2+}] \gg [\mathbf{1}_8]$, respectively. [g] $k_r[CO_3^{2-}]$ (at $[CO_3^{2-}] = 0.030$ mol dm^{-3}) $= 7.13 \times 10^{-3}$ s^{-1}. Thus, k_r [in eqn. (5)] = 0.238 dm^3 mol^{-1} s^{-1}.

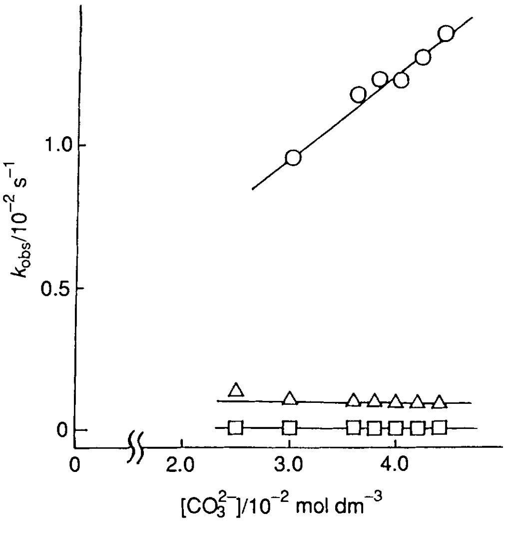

Fig. 1 Plots of k_{obs} *vs.* $[CO_3^{2-}]$: 25 °C, pH 10.40 with 0.030 mol dm^{-3} carbonate, $\mu = 0.15$, [$\mathbf{1}_n$ or **2**] $= 9.30 \times 10^{-5}$ mol dm^{-3} $[UO_2(CO_3)_3^{4-}] = 8.75 \times 10^{-4}$ mol dm^{-3}

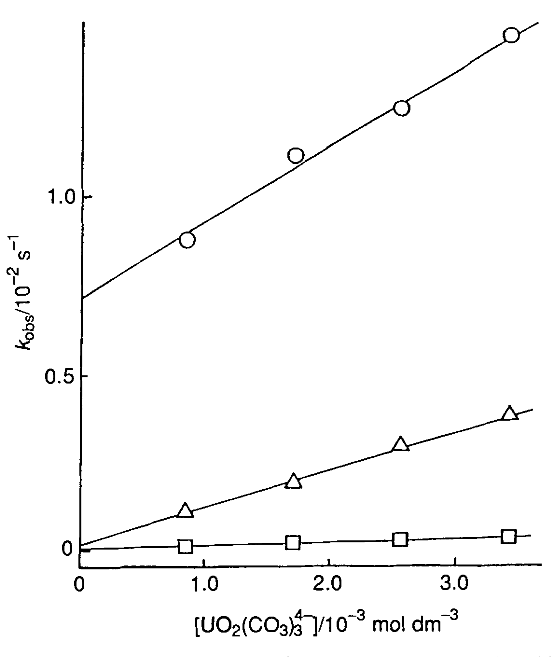

Fig. 2 Plots of k_{obs} *vs.* $[UO_2(CO_3)_3^{4-}]$: 25 °C, pH 10.40 with 0.030 mol dm^{-3} carbonate, $\mu = 0.15$, [$\mathbf{1}_n$ or **2**] $= 4.00 \times 10^{-4}$ mol dm^{-3}

(2) is formally expressed by eqn. (3), the third-order dependence on the carbonate concentration is actually inconceivable. We thus determined k_{obs} as a function of $[CO_3^{2-}]$. As shown in Fig. 1 {$[UO_2(CO_3)_3^{4-}]$ is maintained constant}, k_{obs} for **2** showed a first-order dependence whereas that for $\mathbf{1}_5$ and $\mathbf{1}_6$ showed a zero-order dependence. This implies that in the $UO_2^{2+}\cdot\mathbf{2}$ complex the non-cyclic chain surrounding the UO_2^{2+} ion is displaced bimolecularly by the nucleophilic attack of CO_3^{2-} whereas in the rotaxane-type $UO_2^{2+}\cdot\mathbf{1}_5$ and $UO_2^{2+}\cdot\mathbf{1}_6$ complexes the UO_2^{2+} ion is protected by the calixarene ring from nucleophilic attack by CO_3^{2-}. The complexes feature unimolecular demetallation followed by association with CO_3^{2-}. Thus, the equilibrium reaction for $\mathbf{1}_5$ and $\mathbf{1}_6$ is expressed by eqn. (4) and that for **2** by eqn. (5).

Plots of k_{obs} *vs.* $[UO_2(CO_3)_3^{4-}]$ are illustrated in Fig. 2. From the slope and the intercept one can determine k_f and k_r, respectively. The results are summarized in Table 1.

$$UO_2(CO_3)_3^{4-} + \text{uranophile} \underset{k_r}{\overset{k_f}{\rightleftharpoons}} UO_2^{2+}\cdot\text{uranophile} + 3CO_3^{2-} \quad (2)$$

$$k_{obs} = k_f[UO_2(CO_3)_3^{4-}] + k_r[CO_3^{2-}]^3 \quad (3)$$

$$k_{obs} = k_f[UO_2(CO_3)_3^{4-}] + k_r \quad (4)$$

$$k_{obs} = k_f[UO_2(CO_3)_3^{4-}] + k_r[CO_3^{2-}] \quad (5)$$

The stoichiometry in Table 1 establishes that $\mathbf{1}_5$, $\mathbf{1}_6$ and **2** form a 1:1 UO_2^{2+}/calixarene complex, whereas $\mathbf{1}_8$, having a large calix[8]arene ring, forms a 2:1 UO_2^{2+}/calixarene complex. The stability constants for $UO_2^{2+}\cdot\mathbf{1}_8$ (K_1 and K_2, respectively) are comparable with those for $\mathbf{1}_5$ and $\mathbf{1}_6$. It is known that the calix[8]arene ring is more flexible than the smaller calixarene rings.[3] Although the phenolic oxygens are not suitably arranged for coordination to UO_2^{2+}, the flexibility would allow an induced-fit type complexation with UO_2^{2+}. In contrast, K_{uranyl} for non-cyclic **2** is somewhat smaller than those values for cyclic $\mathbf{1}_n$.

As expected, the rate constants for non-cyclic **2** are greater than those for cyclic $\mathbf{1}_n$. Examination of kinetic parameters reveals that the rapid equilibration in **2** is not only due to the fast forward complexation rate but also due to the more enhanced reverse decomplexation rate: for example, k_f and $k_r[CO_3^{2-}]$ (at $[CO_3^{2-}] = 0.030$ mol dm^{-3}) for **2** are greater by 28-fold and 141-fold, than k_f and k_r for $\mathbf{1}_6$, respectively. This means that carbonate ligands in $UO_2(CO_3)_3^{4-}$ are easily replaced by noncyclic **2**, but **2** in the $UO_2^{2+}\cdot$**2** complex is more easily replaced by carbonate ligands. The results establish that the reaction of **2** and UO_2^{2+} has a transition state much lower than those for $\mathbf{1}_n$ and UO_2^{2+}. The difference is explained because non-cyclic **2** does not need to experience an energetically unfavourable *exo*- to *endo*-complex step as an obligatory path.

Surprisingly, compound $\mathbf{1}_5$ gave kinetic parameters much greater than those for $\mathbf{1}_6$. Why are the kinetic parameters for $\mathbf{1}_5$ so peculiar? Previously, we found that in the binding of $\mathbf{1}_5$ to UO_2^{2+} four OH groups are dissociated at pH 6 and one OH group remains undissociated: at pH 9 the last OH group is dissociated to form the fully-saturated pentacoordinate complex. In contrast, six OH groups in $\mathbf{1}_6$ are all dissociated at pH 6. This suggests that the calix[5]arene ring *a priori* is distorted and in the binding to UO_2^{2+} the initial and the final state are both destabilized. This view explains well the relatively fast equilibration in $\mathbf{1}_5$.

In conclusion, the present study demonstrated that non-cyclic **2** and calixarene $\mathbf{1}_5$ act as better uranophiles for experiments including dynamic processes (*e.g.*, solvent extraction, membrane transport, *etc.*). Thus, they may be more useful for extracting UO_2^{2+} from sea water.

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