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Metal-induced regulation of fullerene complexation with double-calix[5]arene†

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The metal-induced regulation of fullerene complexation with double-calix[5]arene is described. The receptor shows strong binding to C_{70} only in the presence of Cu^+.

The allosteric effect is one of the fascinating features in biological systems. In allosteric regulation, binding of an effector to a remote site leads to a conformational change at the active site. This conformational change facilitates or deactivates the binding affinity to its substrate and, hence, it can regulate the activity of the enzyme. It is of interest to imitate this feature in simple artificial organic molecules.[1,2]

There has been intense activity on developing fullerene receptors.[3] We have reported that the calix[5]arene and its derivatives gave effective binding to fullerene.[4] In this paper, a bridged double calix[5]arene having two bipyridine units as a ligation site is described. The receptor has two conformationally coupled binding units: one is a calix[5]arene part for fullerene, the other is a bipyridine part toward a transition metal. When the transition metal binds to the bipyridine in a tetrahedral fashion, the two calix[5]arenes come closer to produce a deep cavity to take up fullerenes. This structural regulation by the transition metal complexation should lead to the regulation of the fullerene binding.

The synthesis of bipyridine unit **3** was carried out through palladium chemistry. Introduction of the trimethyltin group onto bromomethylnicotinate **2** under palladium catalysis, following Stille's coupling with 2,5-dibromopyridine afforded 5′-bromo-5-methoxycarbonyl 2,2′-bipyridine. Treatment of the bipyridine with hexamethylditin with Pd(0) furnished bipyridine derivative **3**. The linker unit bridging the two calix[5]arenes was synthesized. Ditosylate **4**,[5] which is readly available from resorcinol, was treated with sodium azide in DMF at 80 °C to give the corresponding diazide. Hydrogenolysis of the azide groups then gave diamine **5** (Scheme 1). The synthesis of double-calix[5]arene **1** (Fig. 1) started from calix[5]arene **6**[6] according to Scheme 2. Treatment of aluminium trichloride, followed by iodination with $BTMAICl_2$ gave the iodocalix-[5]arene in good yield. Protection of the five hydroxy groups on the lower-rim produced pentaacetyl calix[5]arene **7**. Coupling reaction of **7** with **3** was performed under Still's conditions to give the coupled product. Hydrolysis of the ester group and deprotection of the acetyl groups then afforded carboxylic acid

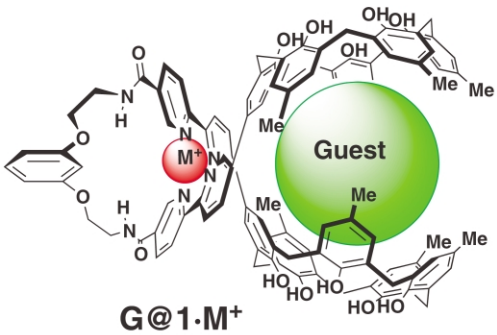
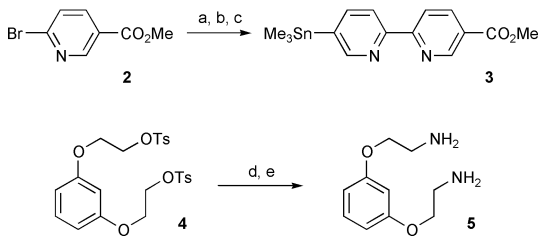
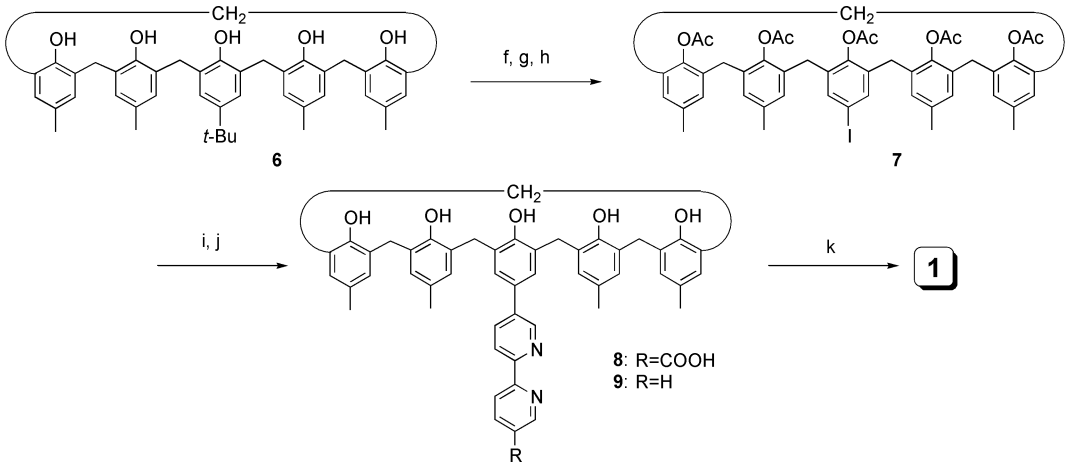


Fig. 1 Structure of **1** with transition metal.

† Electronic supplementary information (ESI) available: spectroscopic and titration data. See http://www.rsc.org/suppdata/cc/b1/b108121g/



Scheme 1 a) $Me_3SnSnMe_3$, $(Ph_3P)_2PdCl_2$–dioxane; b) 2,5-dibromopyridine, $(Ph_3P)_4Pd$–DMF 22% 2 steps; c) $Me_3SnSnMe_3$, $(Ph_3P)_2PdCl_2$–dioxane 69%; d) NaN_3–DMF 70%; e) H_2, Pd/C–MeOH 86%.



Scheme 2 f) $AlCl_3$, phenol–toluene 71%; g) $BTMAICl_2$, $CaCO_3$–MeOH–CH_2Cl_2 74%; h) Ac_2O, pyridine–CH_2Cl_2 90%; i) $(Ph_3P)_4Pd$, **3**, Bu_4NCl–DMF 43%; j) NaOH–MeOH–THF–H_2O 86%; k) WSCI·HCl, TEA, HOBt–CH_2Cl_2 43%.

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8. Connecting the two units of **8** with **5** was carried out in the usual way with EDCI and HOBt to give **1**.

The formation of the metal complex with Cu^+ was achieved by a simple mixing of **1** with one equivalent of **[Cu⁺(MeCN)₄]PF₆⁻** in dichloromethane. The resulting complex **[1·Cu⁺]PF₆⁻** is a brown solid. Complex **[1·Cu⁺]PF₆⁻** showed an absorption band at 370 nm in $CHCl_2CHCl_2$ while that of **1** appeared at 331nm. This characteristic red-shift indicates the formation of the Cu(I) tetrahedral complex with the two bipyridines. Further evidence was obtained by MALDI-TOF mass spectrometry. The mass measurement of the complex gave a peak attributable to the loss of counterion, $[M\text{-}PF_6^-]^+$ {avg. m/z = 1794 for **[1·Cu⁺]**}.

To study the binding properties of **1** and **[1·Cu⁺]PF₆⁻** for C_{60} or C_{70} (Fig. 2), titration experiments were carried out by UV-vis spectrometry in $CHCl_2CHCl_2$. The stoichiometry of receptor **1** to C_{60} and C_{70} was established by Job's plot. The binding constants of the receptor with and without Cu^+ for C_{60} or C_{70} were determined by the Benesi-Hildebrand method (Table 1). Metal-induced regulations were observed. Receptor **1** showed 1 : 2 binding to C_{60} while Cu^+ drove the complexation in a 1 : 1 fashion. In contrast, C_{70} bound to **1**, resulting in a 1 : 1 complex in the presence and absence of Cu^+. Allosteric regulation was seen in C_{70} binding, which was enhanced by Cu^+ complexation. These characteristic changes of the binding ability through the metal complexation are rationalized by the internal flexibility.

The linker moiety of **1** is highly flexible. The entropic cost on the internal flexibility is too high to form the 1 : 1 complex with C_{60}, and leads the low binding ability toward C_{70}. The metal complexation to the bipyridine units fixes the flexible chain to overcome the high entropic cost. Hence, the fixation brings about the regulation of the guest binding; the change of the binding mode and the enhancement of the binding ability.

Complex **[1·Cu⁺]PF₆⁻** preferentially binds (4-fold excess) C_{60} to C_{70}. The selectivity of the guest binding can be explained by the difference of the guest volumes: C_{60}; 510 Å^3, C_{70}; 600 Å^3. While the cavity volume[8] of the receptor (591 Å^3, estimated by MacroModel[9] using AMBER* force field) fits well to that of C_{60}, the volume of the larger guest exceeds that of the host cavity. Of course the cavity can be expanded to some extent to accommodate the larger guest, the resulting deformation of the receptor causing extra strain because of the rigid nature of the metal complexed receptor.[10]

Table 1 Binding constants (M^{-1}) of **1** and **[1·Cu⁺]PF₆⁻** for C_{60} and C_{70} at rt in $CHCl_2CHCl_2$. a) Binding constant of calix[5]arene **9**[4a,7]

	1	$[1\cdot Cu^+]PF_6^-$
C_{60}	98 ± 2[a]	3800 ± 300
C_{70}	250 ± 20	950 ± 50

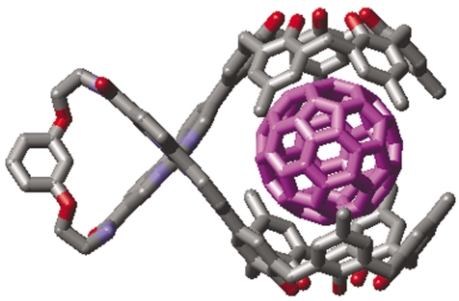

Fig. 2 The calculated structure of the complex **1**·Cu^+ with C_{60} (purple).

We have demonstrated above the regulation of fullerene complexation with receptor **1** through the structural constraints induced by copper(I) complexation.

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