Host–Guest Chemistry

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Supramolecular Click Chemistry with a Bisammonium-C_{60} Substrate and a Ditopic Crown Ether Host**

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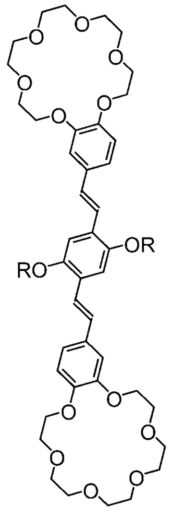
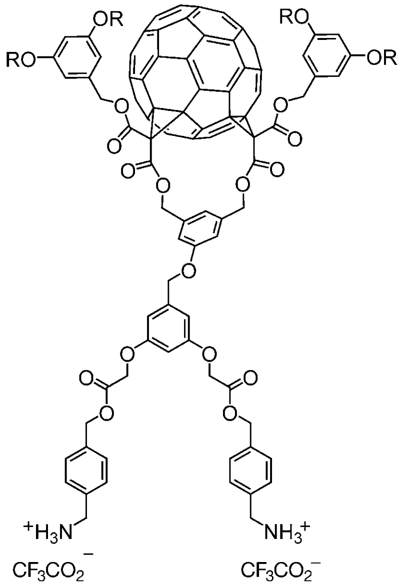
Fullerenes and their derivatives have shown a wide range of chemical and physical properties which make them attractive candidates for a variety of interesting applications in supramolecular chemistry.[1] Indeed, spectacular noncovalent architectures incorporating fullerene moieties have been described over the past few years. Examples include rotaxanes,[2] catenanes,[3] self-assembled coordination compounds,[4] liquid-crystalline inclusion complexes,[5] and photoactive supramolecular devices.[6–10] As part of this research, we have recently reported supramolecular donor-fullerene systems based on the self-assembly of C_{60} derivatives bearing an ammonium unit with crown ethers.[7–9] However, the ammonium–crown ether interaction is itself weak.[7] Consequently, the binding constants are rather low and only a small fraction of the two components are effectively associated in solution. This result prompted us to design systems with additional recognition elements to increase the binding constants.[8,9] For example, evidence of π-stacking interactions between the C_{60} sphere and the porphyrin moiety in a supramolecular array has been obtained from a porphyrin–crown ether conjugate and a fullerene derivative bearing an ammonium unit.[8] In this case, the association constant (K_a) for the complex is increased by two orders of magnitude relative to K_a values for the complexation of the same ammonium cation with other crown ether derivatives. We now report the preparation and the characterization of a very stable supramolecular complex obtained from bis(crown ether) receptor **1**[9] and bisammonium fullerene ligand **2**. As a result of the perfect complementarity of the two components, biscationic substrate **2** can be "clicked"[10] onto the ditopic crown ether derivative **1**, thus leading to a noncovalent macrocyclic 1:1 complex.

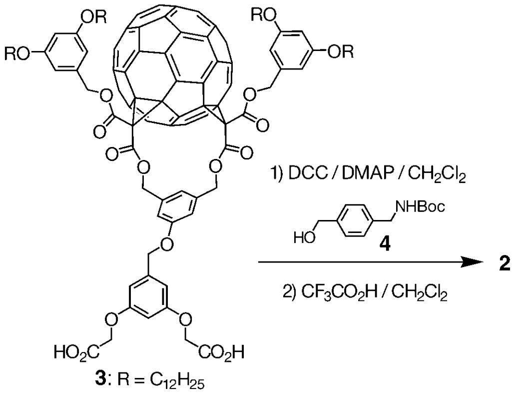


1: R = C_8H_{17}



2: R = $C_{12}H_{25}$

The synthesis of **2** is depicted in Scheme 1. The C_s symmetrical fullerene bisadduct precursor **3** was prepared in nine steps according to a literature procedure.[11] Treatment of diacid **3** with alcohol **4**[7] and *N,N'*-dicyclohexylcarbodiimide (DCC) in the presence of 4-dimethylaminopyridine (DMAP) and 1-hydroxybenzotriazole (HOBt) gave bisamine **5** protected with *tert*-butyloxycarbonyl (Boc) groups in 37% yield.



Scheme 1. Preparation of compound **2**.

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Subsequent treatment with CF_3CO_2H afforded **2** as its trifluoroacetate salt in 84% yield.

The binding behavior of bisammonium **2** with the bis(crown ether) receptor **1** in $CDCl_3$ was first investigated by ^1H NMR spectroscopy at 298 K. Comparison of the ^1H NMR spectra of **1**, **2**, and an equimolar mixture of both components revealed complexation-induced changes in chemical shifts (Figure 1). In particular, a dramatic downfield shift is seen for the signal of H_K of **2** upon addition of **1**. This downfield shift indicates the formation of a macrocyclic 1:1 supramolecular complex where proton H_K is located on top of the conjugated π system of **1**.

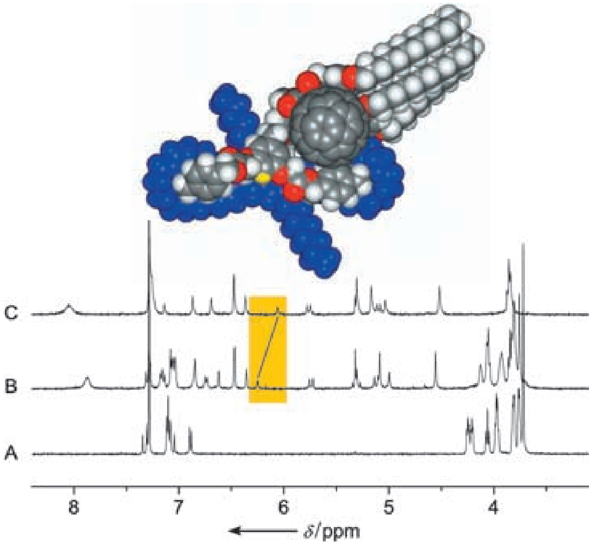

Figure 1. Top: calculated structure of the macrocyclic supramolecular complex [(**1**)·(**2**)] (molecular modeling studies were performed with Spartan). Bottom: ^1H NMR spectrum (400 MHz, 25 °C) of equimolar $CDCl_3$ solutions of **1** (A), **2** (C), and a 1:1 mixture of **1** and **2** (B); the downfield shift of the signal corresponding to proton H_K (shown in yellow) upon addition of **1** shows that this proton must be close to the π-conjugated system of **1** in the supramolecular complex, which is in good agreement with the proposed structure.

Further evidence for the formation of a 1:1 macrocyclic complex was obtained by electrospray mass spectrometry (ESMS).[12] The ES mass spectrum (positive mode; Figure 2) recorded under mild conditions (extracting cone voltage V_c = 200 V) of a 1:1 mixture of **1** and **2** is dominated by a doubly charged ion signal at *m*/*z* 1723.1 which can be assigned to the 1:1 complex after loss of the trifluoroacetate counteranions (calculated *m*/*z* 1723.11). A very minor signal corresponding to the 2:1 complex was also detected at *m*/*z* 2226.7 (calculated *m*/*z* 2226.76). Under harsher conditions (V_c = 400 V) the spectrum was still dominated by the doubly charged ion signal at *m*/*z* 1723.1 and no significant fragmentation of the supramolecular assembly [(**1**)·(**2**)] could be observed. Indeed, the spectra are almost identical regardless of the V_c value. This behavior is in sharp contrast to the ESMS analysis of supramolecular complexes of **2** with simple crown ether derivatives in which important fragmentation occurs at high V_c values (see Supporting Information). These observations show the high stability of the noncovalent array [(**1**)·(**2**)]. It is also worth noting that the major signal obtained in the ES mass spectra of a 10:1 mixture of **1** and **2** corresponds to the [(**1**)·(**2**)] complex. Under these conditions, the intensity of the signal corresponding to the 2:1 complex [$(\mathbf{1})_2$·(**2**)] is lower than 5% of the signal corresponding to the macrocyclic 1:1 complex, thus providing additional evidence for the high stability of [(**1**)·(**2**)].

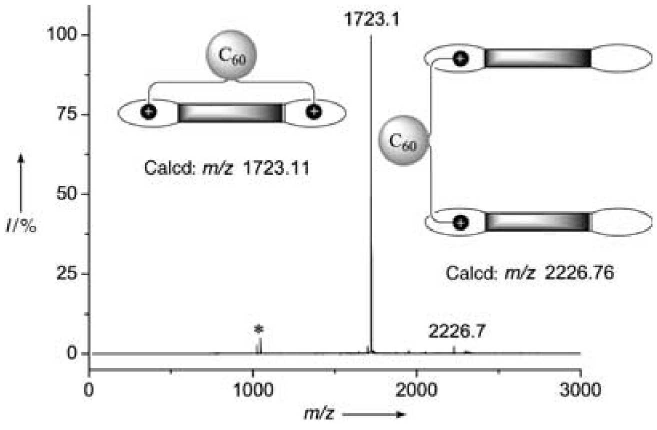

Figure 2. ES mass spectrum (V_c = 200 V) of a 1:1 mixture of **1** and **2** in CH_2Cl_2 ([(**1**)] = [(**2**)] = 5×10^{-6} M); the signal at *m*/*z* 1046.2 (*) is assigned to $[\mathbf{1}+K]^+$ (calculated *m*/*z* 1046.40).

To quantify the interactions between **1** and **2**, complexation was investigated in CH_2Cl_2 by UV/Vis binding studies, in which changes in the spectrum upon addition of increasing amounts of **2** to a solution of **1** in CH_2Cl_2 were monitored (see Supporting Information). The processing[13] of these data allowed the characterization of a single supramolecular complex [(**1**)·(**2**)] in solution ($\log K_1 = 6.3\pm0.4$), which is in excellent agreement with the ESMS and NMR spectroscopic data. Nevertheless, the rather weak complexation-induced changes in the adsorption spectrum prompted further investigation into the binding of **1** and **2** by luminescence experiments. As previously observed for related systems,[7–9] the strong emission of the π-conjugated system of **1** (λ_{em}^{max} = 450 nm, $\phi_{fluo} = 0.65\pm0.06$) is quenched upon binding of **2** through an efficient intramolecular process within the [(**1**)·(**2**)] complex, thus allowing the facile determination of the binding constant by luminescence titrations (Figure 3). Collisions and reabsorption events (see Supporting Information) could be neglected under our experimental conditions. Therefore, the decrease in the luminescence intensity observed in the presence of **2** (Figure 3) is attributed solely to intramolecular photochemical processes. By using a modified Stern–Volmer relationship[14] ($F_0/F = (1 + K_{SV}[(\mathbf{2})])\times\exp(K_1[(\mathbf{2})])$) and assuming $K_{SV}[(\mathbf{2})] \ll 1$, the stability constant of [(**1**)·(**2**)] was obtained ($\log K_1 = 6.40\pm0.01$).[15] This value is in excellent agreement with the result obtained from the absorption binding studies.

Comparison of our results with thermodynamic data available in the literature show that coordination is more than three orders of magnitude stronger in the current system than in related systems (crown ethers and ammonium derivatives).[7] This result is mainly attributed to the two-center

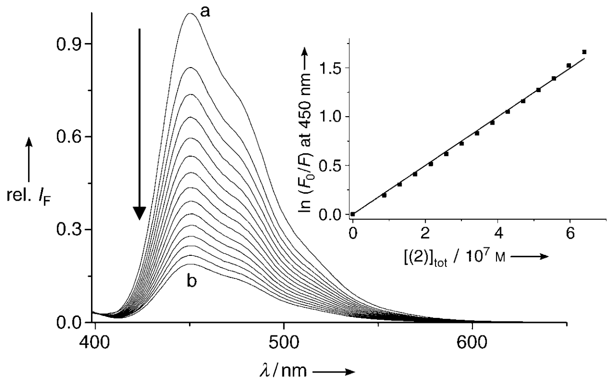

Figure 3. Luminescence titration of **1** with **2**. Solvent: CH_2Cl_2; $T = 25.0 \pm 0.2\,°C$; $\lambda_{exc} = 398$ nm; emission and excitation slit widths 15 nm; 1% attenuator; a) $[(\mathbf{1})]_{tot} = 9.77 \times 10^{-7}$ M; b) $[(\mathbf{2})]_{tot}/[(\mathbf{1})]_{tot} = 0.7$. Inset: variation of $\ln(F_0/F)$ at 450 nm versus the concentration of **2**. The solid line is the result of the linear least-square fit of the experimental data according to $\ln(F_0/F) = K_1[(\mathbf{2})]$.

host–guest topography. In a similar manner to the "click chemistry" concept introduced by Sharpless and co-workers,[10] the "supramolecular click chemistry" principle described herein is a powerful and selective process for the preparation of stable macrocyclic noncovalent arrays. This approach is modular and it appears that it can be easily applied to a wide range of functional groups for the preparation of new supramolecular architectures with tunable structural and electronic properties.

Experimental Section

ESMS: High-resolution ESI mass spectra in the positive mode were acquired on a time of flight mass spectrometer (microTof, Bruker Daltonics, Bremen, Germany). The instrument was calibrated using a solution of cesium iodide (1 mg mL^{-1}) in water/isopropanol (50/50 (v/v)). CsI clusters of the types $[(CsI)_nCs]^+$ or $[(CsI)_nCs_2]^{2+}$ generate ions with m/z values up to about 16000. The ESI-source was heated to 100 °C. Sample solutions were introduced into the mass spectrometer source with a syringe pump (Cole Parmer, Vernon Hills, Illinois, USA) with a flow rate of 5 µL min^{-1}. Scanning was performed over an m/z range of 100–12000, and then the data were averaged for 1 min and smoothed using the Gaussian algorithm. To ensure that the species detected by ESI-MS reflect the species present in solution, the instrument parameters, for example, the sample cone voltage V_c, have been varied.

UV/Vis and luminescence binding studies: the experimental conditions have been described in detail in Ref. [9].

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Keywords: binding studies · crown compounds · fullerenes · host–guest systems · supramolecular chemistry

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