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A Molecular Shuttle Driven by Fullerene Radical-Anion Recognition

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Abstract: We describe a electrochemically driven molecular shuttle, in which shuttling takes place by means of fullerene radical-anion recognition that results in a very low operation potential ($E_{1/2} = -0.580$ V vs. decamethylferrocene). This has been achieved by introducing positive charges on the macrocycle, which strengthen the existing π–π interactions between the macrocycle and the electrogenerated fullerene radical anion by means of an electrostatic component. In addition, the synthesis of such a molecular shuttle has been accomplished by developing a new synthetic approach that exploits the controlled translocation of the macrocycle as a selective protecting group.

Keywords: electrochemistry · fullerenes · molecular shuttles · rotaxanes · supramolecular chemistry

Introduction

Bistable rotaxanes or molecular shuttles are a unique platform to perform precise and complex switching operations derived from sub-molecular motion.[1] On this type of molecular interlocked systems, which display the same structural features of an abacus, switching consists of a position change of the ring component (macrocycle) along two different parts of the linear component (thread). A strategy to develop practical applications based on molecular shuttles focuses on the use of electrons to control the position of the macrocycle,[2–13] since electrons can be easily introduced or removed by applying an electric or an electrochemical potential and also allow the interfacing of such molecular systems with existing electronic technologies. In fact, electrochemically switchable molecular shuttles have been shown to be very useful components in nanotechnology and have been applied to prepare artificial molecular muscles,[14] memory devices,[15,16] and nanovalves for drug release,[17] among others. In such electrochemically driven molecular shuttles, easily accessible redox potentials are key to ensure a low-potential operation.[9] Recently, we have reported the use of C_{60} stoppers[18–23] in rotaxanes as units to switch the macrocycle reversibly by exploiting the existing π–π interactions between electrochemically generated fullerene anions and the macrocycle. Indeed, C_{60} can be reduced reversibly with up to 6 electrons and possess easily accessible reduction potentials.[24] However, because π–π interactions are rather weak, the complete translocation of the macrocycle requires the formation of the trianion and thus the application of a large potential ($E_{1/2} = -1.750$ V vs. decamethylferrocene).

Although there is limited data or theory that explains the attracting interactions between π-receptors and anions[25] or radicals[26] with which to develop recognition motifs for electrogenerated fullerene anions, it seemed plausible that a more suitable macrocycle able to bind effectively fullerene radical-anions, will provide not only a low-potential operated molecular shuttle but also an insight into the π–π interactions with radical anions. Herein, we describe a fullerene-stoppered molecular shuttle (rotaxane **3**, Scheme 1) in which shuttling is triggered by applying a very low reduction potential ($E_{1/2} = -0.580$ V vs. decamethylferrocene). This has been achieved by introducing two positive charges on the macrocycle, which strengthen the existing π–π interactions between the macrocycle and the electrogenerated fullerene radical anion by means of an electrostatic component, which results in an excellent recognition motif for fullerene radical anions. Most importantly the synthesis of rotaxane **3** has been accomplished by applying a new synthetic approach that exploits the controlled translocation of the macrocycle as a protecting group. In other words, the reversible transla-

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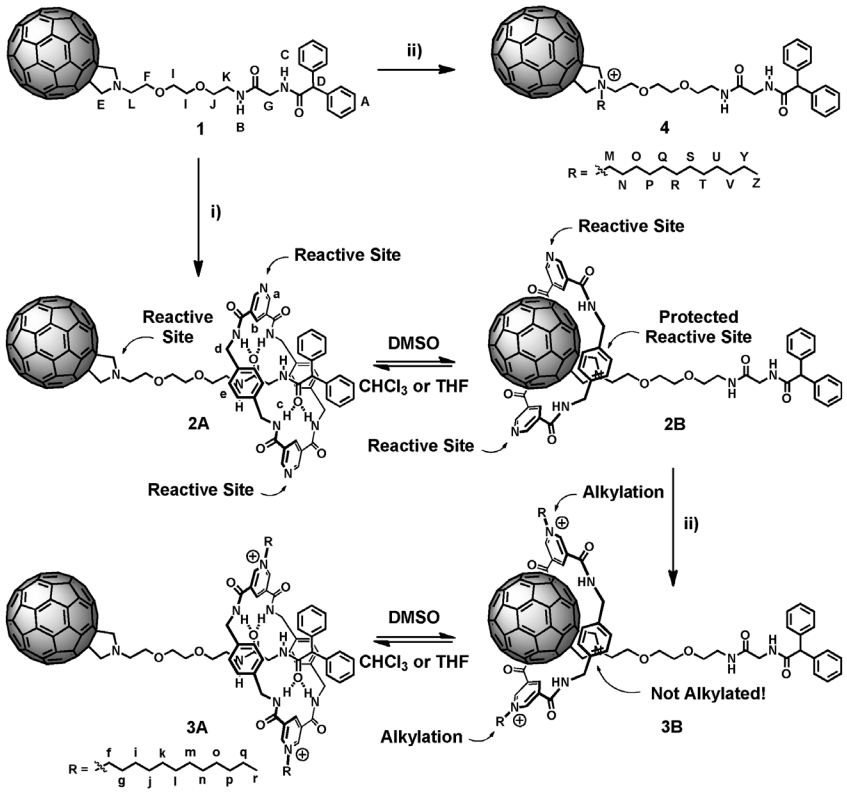


Scheme 1. Synthesis of **2** and **3**. i) Dinicotinoyl chloride, *p*-xylylene diamine, NEt_3, $CHCl_3$, room temperature, 32%; ii) dodecyl iodide, [D_6]DMSO, 60°C, 48 h, 8–14%.

tion of the macrocycle over a reactive site has been used to inhibit an undesired reaction by means of selective encapsulation.

Results and Discussion

Rotaxane synthesis—shuttling as a protecting group: Rotaxane **3** was synthesised in two steps from thread **1**, as described in Scheme 1. First, rotaxane **2** was synthesised from thread **1**[18] following the methodology introduced by Leigh et al.,[27] in which the diamide residue of thread **1** acts as template in the synthesis of benzylic amide macrocycles. The reaction of thread **1** with dinicotinoyl chloride and *p*-xylylene diamine yielded rotaxane **2** with two pyridyl rings on the macrocycle. Rotaxane **2** displays solvent-switchable behaviour similar to other fullerene rotaxanes.[18–20] In fact, NMR experiments confirmed the existence of rotaxane **2** in two solvent-dependent translational isomers. In solvents with low hydrogen-bond basicity, such as $CDCl_3$, the macrocycle stays preferentially on the diamide station by hydrogen-bond interactions between the macrocycle and the diamide (translational isomer **2A**, Scheme 1). NMR confirms this, since protons C and G in rotaxane **2** appear shielded with respect to thread **1** because of the anisotropic effect of the macrocycle (Figure 1a and b). Conversely, in [D_6]DMSO the hydrogen bonds between the diamide station and the macrocycle are weakened and this allows the macrocycle to switch to the other end of the thread and π-stack to the fullerene (translational isomer **2B**, Scheme 1). This is confirmed by up-field shifts of protons E of the rotaxane **2** with respect to thread **1** (Figure 1d and e).

In principle, the alkylation of the pyridine groups on the macrocycle of rotaxane **2** should provide the desired rotaxane **3**. However, it is known that the fulleropyrrolidine ring can also be alkylated to give fulleropyrrolidinium salts.[29] We foresaw that the encapsulation of the fulleropyrrolidine by the macrocycle (translational isomer **2B**) could act as a protective group inhibiting alkylation of the fulleropyrrolidine, since there are a examples in which encapsulation have been used to protect threaded substrates from chemical degradation.[22,29–32] In addition, since the macrocycle is only mechanically bonded the protection should be perfectly reversible by changing the position of the macrocycle, providing new perspectives for mechanically interlocked molecules in organic synthesis. The reaction of thread **1** with dodecyl iodide[30] in DMSO yields fulleropyrrolidinium salt **4** (Scheme 1). Conversely, when rotaxane **2** was allowed to react with an excess of dodecyl iodide (3, 27 and 45 equivalents) in DMSO, only rotaxane **3** was obtained after chromatographic purification and the formation of the corresponding trialkylation by-product was not detected.

To ensure that the formation of the trialkylation by-product is truly inhibited and thus that the encapsulation of the macrocycle is acting as a protective group, the same reactions (with 3, 27 and 45 equivalents of dodecyl iodide) were carried out in [D_6]DMSO and the reaction mixtures were directly analysed by NMR spectroscopy at different times and compared with the spectrum of thread **4**. The NMR spectrum of thread **4** shows a distinctive AB system at $\delta =$ 5.5 ppm that corresponds to protons E of the alkylated fulleropyrrolidine (Scheme 1 and Figure S1 in the Supporting Information). Therefore, by monitoring the $\delta = 5.5$ ppm region of the reaction mixtures, it is possible to detect and quantify the alkylation (if any) of the fulleropyrrolidine of rotaxane **2**. As a matter of fact, when the experiments were carried out on rotaxane **2**, no traces of the characteristic AB system of the alkylated fulleropyrrolidine were observed

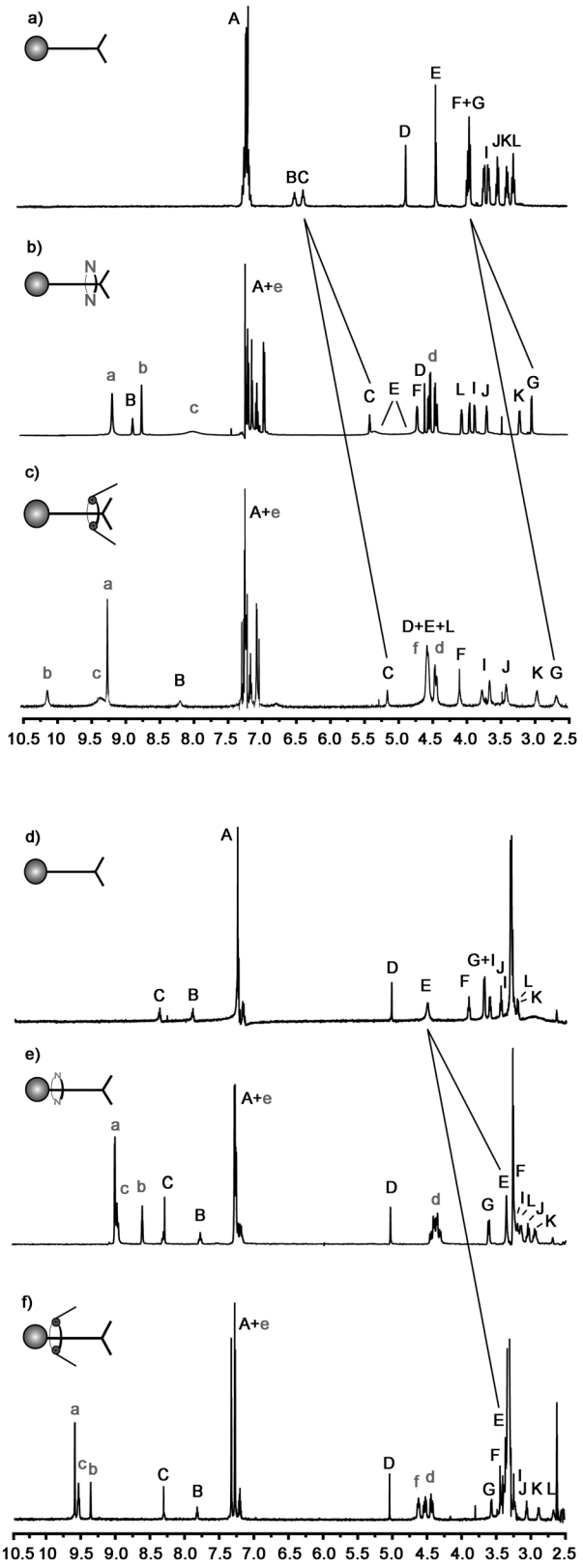


Figure 1. Partial NMR spectra of thread **1**, rotaxane **2** and rotaxane **3** in $CDCl_3$ (a, b, and c, respectively) and DMSO (d, e, and f, respectively). The assignments correspond to the lettering shown in Scheme 1.

(Figure S1 in the Supporting Information), even after prolonged reaction times, confirming that the macrocycle is indeed inhibiting the alkylation reaction of the fulleropyrrolidine.[35] The low yields of the reaction are associated with the diminished stability of rotaxane **2** in polar solvents, which has been previously noted for similar rotaxanes even at room temperature.[19] This is in agreement with the NMR spectra of the crude reaction mixture that displays the formation of multiple new peaks that we were unable to assign (Figure S1 in the Supporting Information), and also with the fact that no traces of rotaxane **2** were recovered after chromatography.

Rotaxane **3** displays the same solvent behaviour as rotaxane **2**, which is consistent with the ability of the macrocycle to inhibit the alkylation of the fulleropyrrolidine by dodecyl iodide. In $[D_6]$DMSO, the macrocycle sits on top of the fulleropyrrolidine (translational isomer **3B**, Scheme 1), as confirmed by the upfield shifts of protons E of rotaxane **3** with respect to thread **1** (Figure 1d and f). Conversely, in solvents, such as $CDCl_3$ or $[D_8]$THF, the macrocycle binds diamide by hydrogen bonding (translational isomer **3A**, Scheme 1), as confirmed by the upfield shifts observed for proton signals C and G of rotaxane **3** with respect to thread **1** (Figure 1a and c).

Shuttling by fullerene radical-anion recognition: The ability of rotaxanes **2** and **3** to switch electrochemically has been studied by cyclic voltammetry. The voltammograms showed three reduction waves centred on the fullerene (I, II and III, Figure 2 left), which correspond to the fullerene radical anion, dianion and trianion, respectively. Half-wave potential shifts ($\Delta E_{1/2}$) to less negative potentials are observed in all the redox waves of rotaxane **2** when compared with those of thread **1** (Figure 2 left), which was used a reference. Such anodic shifts provide evidence that π–π stacking interactions between the macrocycle and the fullerene stopper are taking place, which are a direct indication of electrochemically induced shuttling, as previously described.[8,10,18]

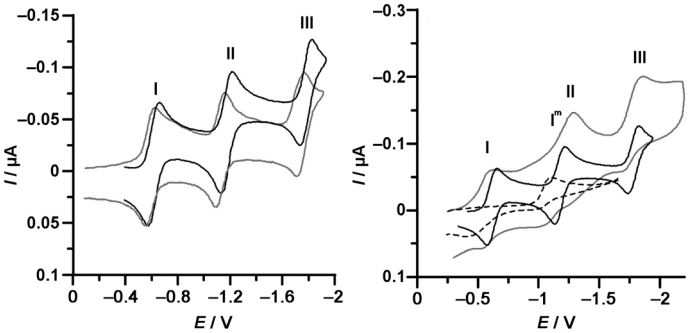
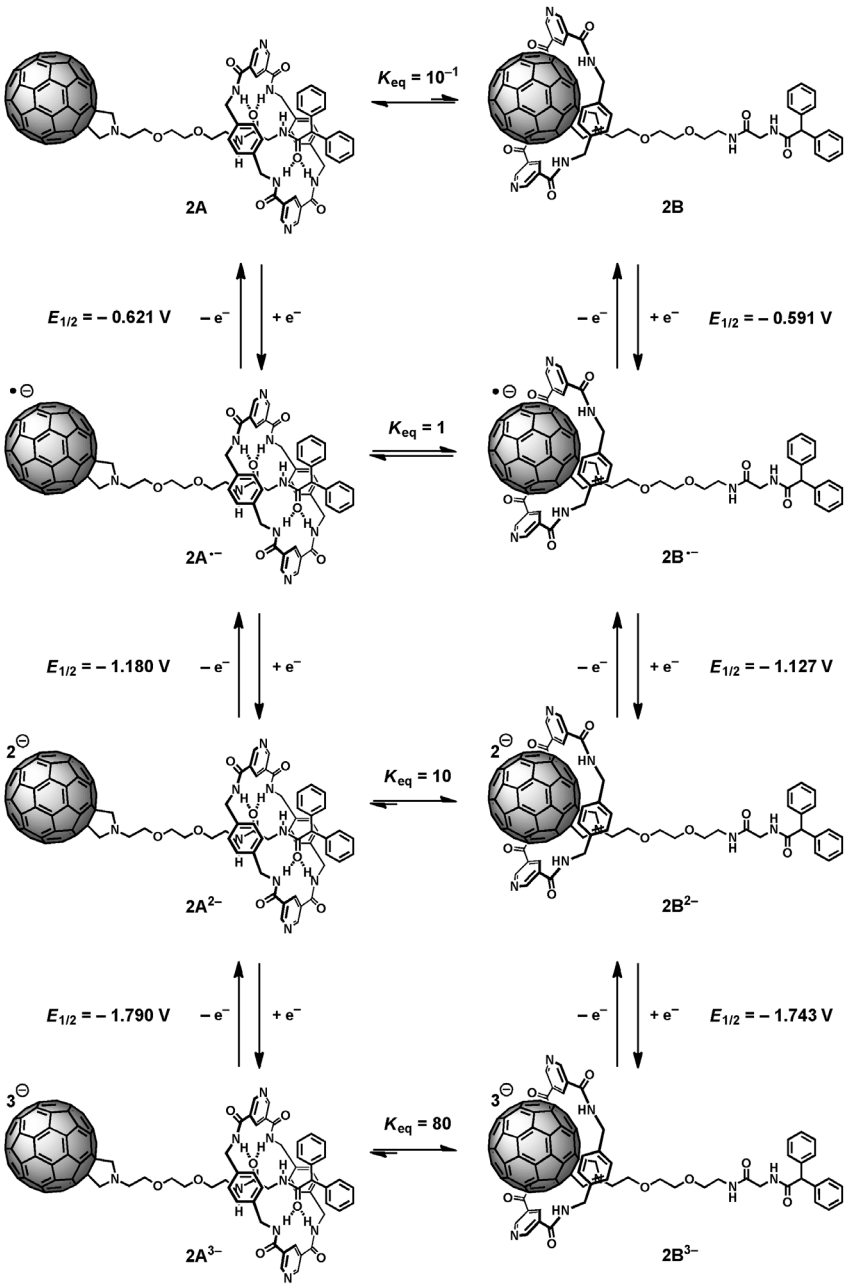


Figure 2. Cyclic voltammograms of rotaxane **2** (gray solid line, left) and **3** (gray solid line, right), shown with thread **1** (black solid line, left and right) and iodo *N*-dodecyl-3,5-dicarboxypyridinium bisbenzylamide **S2** (black dashed line, right, see also the Supporting Information for synthesis and characterisation). 0.5 mM in a 0.07 M NBu_4PF_6, THF. Working electrode Pt disk 125; scan rate = 1 V s^{-1}; T = 25 °C. Potential vs. decamethylferrocene.



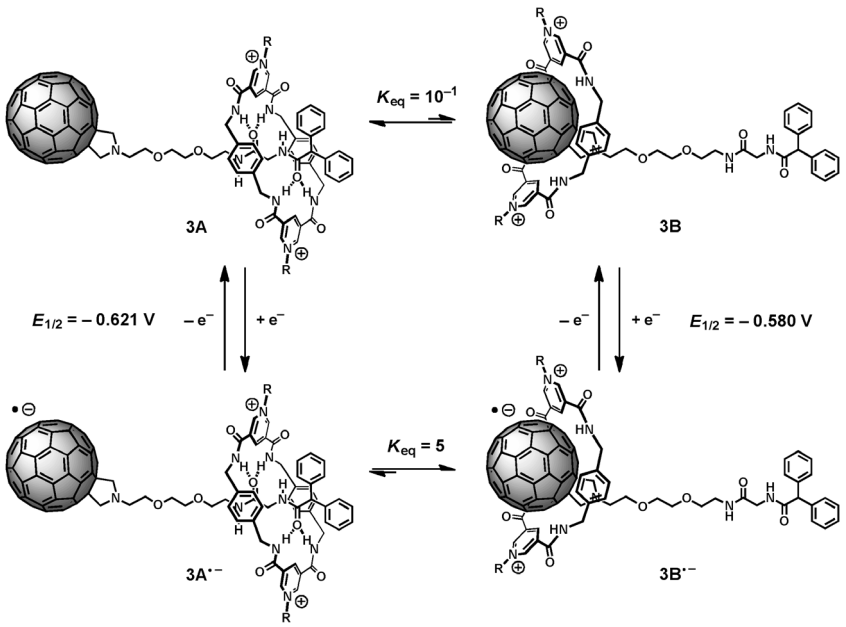
Scheme 2. Square scheme mechanism describing the behaviour of rotaxane **2**.

Simulation of the voltammograms using the square scheme mechanism[36] set out in Scheme 2 allows for the reproduction of the voltammograms and the estimation of the K_{eq} between translational isomers **2A** and **2B** for each redox state. As supported by both NMR spectroscopy and simulations, translational isomer **2A** dominates in the neutral state ($K_{eq} = 10^{-1}$).[37]

Consecutive increase of the negative charge shifts the equilibrium towards **2B**. Upon the first reduction, the interaction between the fullerene radical anion and the macrocycle is sufficiently strong to compete with the hydrogen-bonding station (Scheme 2), with equimolar concentrations of **2A** and **2B** in the equilibrium ($K_{eq} = 1$). After the second and third reductions, the interactions between the negatively charged fullerene and the macrocycle become more apparent, which favour the formation of **2B** over **2A** both for the dianion ($K_{eq} = 10$) and the trianion ($K_{eq} = 80$), respectively.

The same experiments performed on rotaxane **3** revealed a different behaviour. Besides the reduction waves of the fullerene (I, II and III), an additional reduction wave was observed (I^m), which falls at a similar potential as the fullerene dianion (Figure 2 right). This reduction process (I^m) was undoubtedly assigned to the reduction of macrocycle by comparison with iodo *N*-dodecyl-3,5-dicarboxypyridinium bisbenzylamide (compound **S2**, see the Supporting Information), which was synthesised and used as a reference. The reduction wave of the radical anion of rotaxane **3** is shifted to even less negative potentials ($\Delta E_{1/2} = -41$ mV) than for rotaxane **2** ($\Delta E_{1/2} = -30$ mV) when compared with thread **1**. This is not only a direct indication of electrochemically induced shuttling, but also, most importantly, an illustration of more efficient shuttling at the radical-anion state.

Simulations were carried out only on the first reduction wave due to the simultaneous reduction of the macrocycle and the fullerene upon the formation of the dianion. As expected, simulations of the first reduction wave of rotaxane **3** using the square scheme mechanism set out in Scheme 3, revealed that **3A** dominates in the neutral state ($K_{eq} = 10^{-1}$),[37] but upon reduction of the fullerene stopper to the radical anion ($E_{1/2} = -0.580$ V vs. decamethylferrocene), the equilibrium is completely shifted and dominated by **3B** ($K_{eq} = 5$). This illustrates the large affinity between the fullerene radical anion and the macrocycle, which is able to overcome four hydrogen bonds to switch.



Scheme 3. Square scheme mechanism describing the behaviour of rotaxane **3**.

Conclusion

Overall we have developed a new type of fullerene-driven molecular shuttle, in which shuttling is achieved by an efficient strategy based on fullerene radical-anion recognition that results in a very low operation potential ($E_{1/2}$ = −0.580 V vs. decamethylferrocene). Molecular shuttles operated under such mild conditions represent a promising step forward towards applications in many fields of nanotechnology. Also, the fact that only one electron is required to operate the shuttle paves the way for developing light-driven systems that uses ability of fullerenes to accept electrons from electron donors upon irradiation, which is currently being explored in our laboratory. In addition, we have described the first synthetic approach that exploits the reversible translation of the macrocycle over a reactive site to inhibit an undesired reaction by means of selective encapsulation. The use of the macrocycle as a protective group reported here provides new perspectives for mechanically interlocked molecules in organic synthesis.

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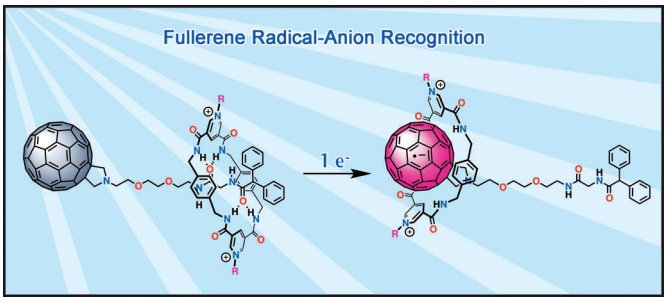

Molecular shuttles: An electrochemically driven molecular shuttle, in which shuttling takes place by means of fullerene radical-anion recognition that results in a very low operation potential ($E_{1/2} = -0.580$ V vs. decamethylferrocene) is described (see scheme). This has been achieved by introducing positive charges on the macrocycle, which strengthen the existing π–π interactions between the macrocycle and the electrogenerated fullerene radical anion by means of an electrostatic component.

Molecular Recognition

A fullerene-driven molecular shuttle…
…in which shuttling is achieved by implementing a strategy based on fullerene radical-anion recognition is reported. The introduction of positive charges on the macrocycle strengthened the existing π–π interactions between the macrocycle and the electrogenerated fullerene radical anion by means of an electrostatic component. For more details, see the Full Paper by A. Mateo-Alonso et al. on page ■ ■ ff.