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TTFV-Based Molecular Tweezers and Macrocycles as Receptors for Fullerenes

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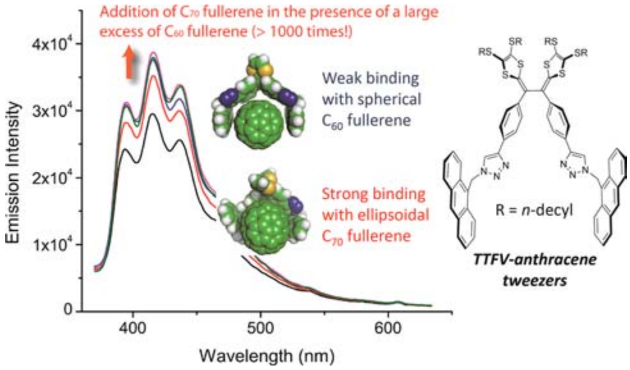
ABSTRACT



Hybrids of tetrathiafulvalene vinylogues (TTFVs) and planar arenes were synthesized via the click reaction to form tweezer-like and macrocyclic structures. These compounds were investigated as receptors for fullerenes (C_{60} and C_{70}) by UV–vis absorption and fluorescence spectroscopy.

With the increasing application of fullerene-containing materials in modern materials science and biological technology, how to detect and separate different types of fullerenes has captured considerable attention.[1] In this context, the use of various synthetic receptors to form guest–host inclusion complexes with fullerenes has been extensively studied.[2] From a practical viewpoint, three important features are desirable for an ideal fullerene receptor as elaborated below. (1) *Selectivity for specific types of fullerenes*. This issue can be tackled by aromatic-rich molecular and macromolecular hosts which are preorganized in such shapes as tweezers, rings, helix, cups, and cages, based upon the notion of concave–convex complementarity.[2,3] (2) *Effective sensory function*. So far, the chemical sensing of fullerenes by rapid and noninvasive methods such as fluorescence spectroscopy has been rarely addressed in the literature.[4] It is worth noting that development of fluorescence turn-on sensors for fullerenes is a challenging task, given that fullerenes usually cause attenuation of emission when bound to various fluorogenic moieties.[4a,5] However,

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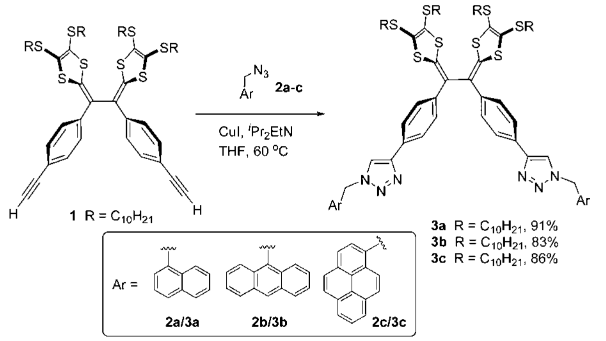
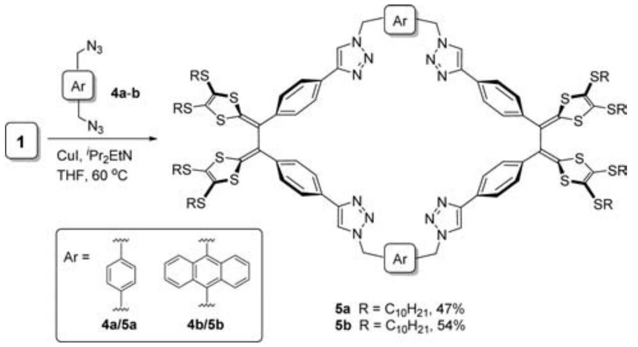
Scheme 1. Synthesis of TTFV-Arene Tweezers **3a**−**c** via Click Reactions



turn-on sensing gives significant advantages compared with turn-off sensing, including good signal-to-noise ratio, high sensitivity, and reduced false signaling. (3) *Controllable reversibility in interactions with fullerenes*. Such a function requires certain switching mechanism(s) to be integrated in the molecular design of fullerene receptors and is beneficial for supramolecular separation of various fullerenes.[6]

To develop new fullerene receptors with the three features above-mentioned, we identified the diphenyl-substituted tetrathiafulvalene vinylogue (TTFV) as a key building block for the following reasons. First, TTFVs and derivatives are good electron donors with highly reversible redox activities.[7a] Therefore, integration of a TTFV moiety into a fullerene receptor system should further strengthen the binding with fullerenes via π−π stacking and/or charge-transfer interactions. Second, diphenyl-TTFVs exhibit redox-controlled structural switchability. For instance, the structure of a diphenyl-substituted TTFV adopts a pseudo-cisoid, V-shaped conformation in the neutral state and is switched to a transoid conformation upon oxidation.[7] Finally, the regular V-shape of a neutral diphenyl-TTFV upon covalent expansion can lead to tweezer-like and macrocyclic structures, which in turn would create suitable π-cavities for hosting fullerenes. Based on the above rationales, we have designed and synthesized a new class of TTFV-arene hybrids as fullerene receptors. The compounds are divided into two distinctive types—molecular tweezers and macrocycles—in terms of molecular structures and shapes.

Scheme 2. Synthesis of TTFV-Based Macrocycles **5a** and **5b** via Click Reactions



Scheme 1 outlines the synthesis of a series of TTFV-based molecular tweezers **3a**−**c**. Three azido-arenes **2a**−**c**, where the aryl groups are 1-naphthyl, 9-anthryl, and 1-pyrenyl respectively, were chosen to react with acetylenic TTFV **1** via a well established click reaction, i.e., a Cu-catalyzed alkyne−azide coupling reaction (CuAAC).[7b,8] The click reactions were conducted in THF at 60 °C for several hours in the presence of CuI and *i*-Pr_2EtN, affording the desired TTFV tweezers **3a**−**c** in high yields ranging from 83% to 91%. The molecular structures of **3a**−**c** were confirmed by various spectroscopic characterizations, and their tweezer-like molecular shapes were evidenced by the single crystal X-ray structure of an analogous dianthryl-TTFV compound.[7c]

In a similar manner, TTFV **1** was coupled with diazido-arene **4a** or **4b** via the CuAAC reaction, wherein the amounts of TTFV **1** and respective diazido-arene were controlled at a 1:1 ratio. The click reactions led to the formation of [2 + 2] macrocyclic adducts **5a** and **5b** in yields of 47% and 54% respectively (Scheme 2), which are quite efficient for a one-pot cyclization process. The relatively high yields can be attributed to a "templating effect" imposed by the Cu(I) catalyst, for it is known that the triazole group resulting from the click reaction can coordinate to transition metal ions to form stable complexes.[9] It is proposed that such an effect enhances the preorganization of reactive intermediates to favor macrocyclization over other possible side reactions.

The supramolecular interactions of tweezers **3a**−**c** with C_{60} and C_{70} fullerenes were investigated by UV−vis and fluorescence titration experiments conducted in chlorobenzene. Of great interest are the fluorescence responses of these compounds to C_{60} and C_{70} fullerenes. Dinaphthyl-TTFV **3a** and macrocycle **5a** did not show any significant fluorescence changes upon titration of fullerenes, likely due to their arene units (i.e., naphthalene and benzene) being very poor fluorophores. For tweezers **3b**,**c** and macrocycle **5b**, the arene units (anthracene and pyrene) are much better fluorophores. These compounds show moderate to weak fluorescence, as a result of the quenching effect by the central electron-donating TTFV unit via a photoinduced electron transfer (PET) mechanism.[7b] Upon addition of C_{60} fullerene, dianthryl-TTFV **3b** showed only a slight degree of fluorescence enhancement (Figure 1A).

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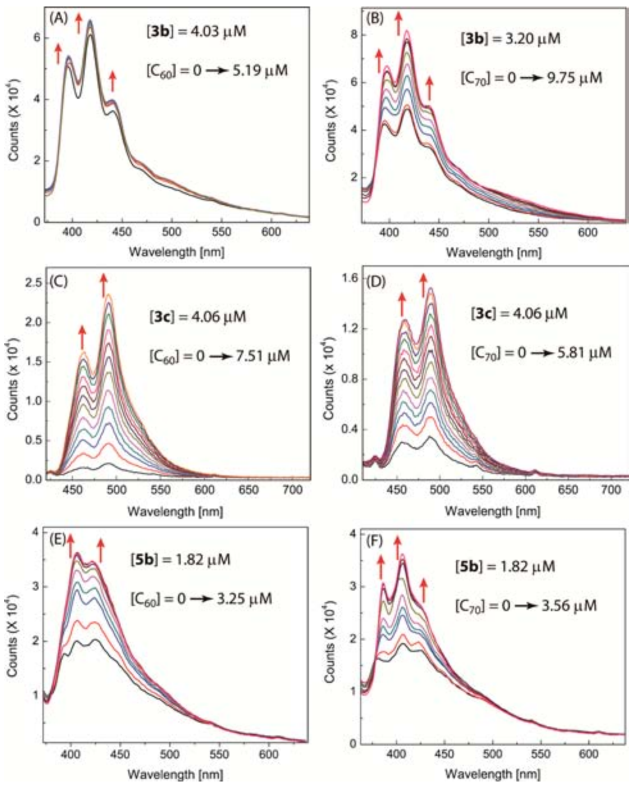

Figure 1. Fluorescence spectral changes of (A) **3b** upon addition of C_{60} (λ_{ex} = 350 nm), (B) **3b** upon addition of C_{70} (λ_{ex} = 350 nm), (C) **3c** upon addition of C_{60} (λ_{ex} = 375 nm), (D) **3c** upon addition of C_{70} (λ_{ex} = 375 nm), (E) **5b** upon addition of C_{60} (λ_{ex} = 350 nm), (F) **5b** upon addition of C_{70} (λ_{ex} = 340 nm).

Table 1. Binding Constants for TTFV Tweezers and Macrocycles with Fullerenes Obtained from Global Spectral Analysis of the Fluorescence Spectral Titration Data

host	guest	complexation ratio (H/G)	log β_{11} (M^{-1})	log β_{12} (M^{-2})
3b	C_{60}	–	–	–
3b	C_{70}	1:1	4.90 ± 0.05	–
3c	C_{60}	1:1	4.87 ± 0.04	–
3c	C_{70}	1:1	4.72 ± 0.03	–
5b	C_{60}	1:2	–	11.10 ± 0.06
5b	C_{70}	1:2	–	10.11 ± 0.11

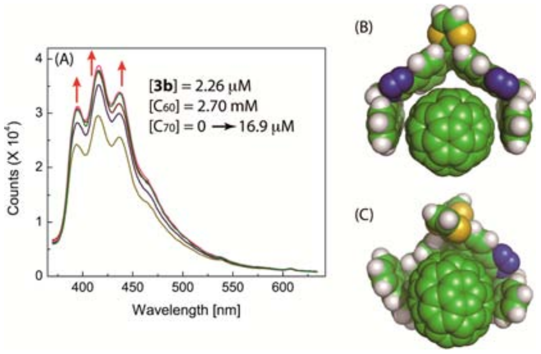

Figure 2. (A) Fluorescence spectral changes of **3b** upon addition of C_{70} in the presence of a large excess of C_{60} (λ_{ex} = 350 nm). CPK models of optimized molecular structures for the complexes of (B) **3b** with C_{60}, and (C) **3b** with C_{70}.

When **3b** was titrated with C_{70}, however, significant fluorescence enhancement was observed (Figure 1B). In contrast, dipyrenyl-TTFV **3c** and macrocycle **5b** showed prominent fluorescence turn-on responses to both C_{60} and C_{70} (Figure 1C to 1F). In particular, **3c** led to a 11.4-fold enhancement at the end point of titration with C_{60} and a 4.4-fold enhancement with C_{70}. The fluorescence turn-on properties are likely originated from the interactions of electron-accepting fullerenes with the electron-donating TTFV moiety in the excited state, which attenuates nonradiative decay pathways including the PET mechanism.

The spectral titration data were subjected to a global spectral analysis using the *SPECFIT* program to determine the binding stoichiometry and binding constants.[3b,7b,10] Meaningful spectral fitting could not be attained from the UV−vis titration results due to the complex spectral overlap of various colorful species. The fluorescence data, however, allowed good spectral fitting to be achieved to quantitatively elucidate the binding properties. Dianthryl-TTFV **3b** exhibits selective affinity for C_{70} only, whereas dipyrenyl-TTFV **3c** shows a strong affinity for C_{60} and C_{70} with similar binding constants. Obviously, the planar arene "tips" of the TTFV tweezers play an important role in the binding events, and it can be concluded that increasing the degree of π-conjugation of the arene units facilitates the binding with fullerenes as well as enhances the fluorescence turn-on responses.

From the binding studies, dianthryl-TTFV tweezer **3b** appears to show a very high selectivity for C_{70} over C_{60} (Table 1). Such a property suggests potential use in selective sensing and recognition of C_{70}. To test this kind of sensory performance, fluorescence titration of C_{70} to a solution of **3b** in the presence of a large excess of C_{60} (> 1000 mol equiv) was conducted and the results are shown in Figure 2A. To our satisfaction, a significant fluorescence turn-on response to C_{70} was still retained in this titration experiment, demonstrating the remarkable efficacy of tweezer **3b** in discriminating trace C_{70} out of excessive C_{60}.

The high selectivity of **3b** in terms of binding with C_{70} can be rationalized by a molecular mechanics study.[11] As shown in Figure 2B, the optimized structure for the 1:1 complex of **3b** and C_{60} shows $\pi-\pi$ contacts only between C_{60} and the two anthracene units. The spherical shape of C_{60} does not allow the central TTFV moiety to be involved

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(11) Molecular mechanics calculations were done using the *SYBYL* force field implemented in the Spartan'10 software (Wave function, Inc., Irvine, CA). Alkyl chains were replaced with H atoms to save computational expense.

in the π-interactions with C_{60}. The lack of contact between C_{60} and the central TTFV moiety thus accounts for the very weak binding as well as insignificant fluorescence changes in the titration results. The 1:1 complexation of **3b** with C_{70}, on the contrary, shows that apart from the C_{70} and anthracene interactions, one of the dithiole rings of the TTFV also has direct π–π contact with C_{70} (Figure 2C). The ellipsoidal shape of C_{70} makes a very good fit in the π-cavity created by the dianthryl-TTFV framework of tweezers **3b**, rendering it a highly selective receptor for C_{70} over C_{60}. The direct contact between C_{70} and the TTFV unit is believed to hinder the PET and hence lead to fluorescence enhancement.

In contrast to dianthryl-TTFV **3b**, the relatively larger π-surface of the dipyrenyl groups in **3c** gives rise to more intimate π–π contact with C_{60} and C_{70} fullerenes (see Figure 3A and B), resulting in strong binding strength but without particular selectivity. The interactions of macrocycle **5b** with C_{60} or C_{70} follow a 1:2 binding ratio as disclosed by global spectral analysis. Modeling studies suggest that this unique binding feature is attributable to the "bucket"-like molecular shape of macrocycle **5b**, which is preorganized well to allow for two molecules of fullerenes to be loaded inside its extended π-cavity (Figure 3C and 3D).

Finally, controllability over reversible interactions of fullerenes with TTFV-arene hybrids was investigated. The TTFV moiety is known to undergo reversible protonation/deprotonation processes associated with dramatic conformational changes.[7a,12] Such properties have been recently applied by our group to achieve reversible wrapping and release of single-walled carbon nanotubes using a TTFV-phenylacetylene polymer.[12] Herein we expected the same reversible mechanism to control the binding and release of fullerenes. To demonstrate this property, the complexes of macrocycle **5b** and C_{60} were subjected to titration with trifluoroacetic acid (TFA). For clear data analysis, two absorption bands at 334 and 646 nm were monitored by UV–vis spectroscopy. The absorption at 334 nm is due to three colorful species: free C_{60}, free **5b**, and **5b/**C_{60} complexes. Figure 4A shows that, upon titration of **5b** with C_{60}, the absorption at 334 nm follows a bell-shaped trend with a maximum at the point where ~1.5 equiv of C_{60} is added. Figure 4B shows the absorbance changes of **5b**/C_{60} complexes at 334 nm as a function of increasing [TFA]. The plot exhibits an inverted bell-shaped trend with the minimum coinciding with the midpoint of titration. As a comparison, the titration of **5b** with TFA exhibits only a decreasing trend for the absorbance at 334 nm (Figure 4C), while monitoring the absorbance at 646 nm, which is the signature absorption band for the protonated TTFV,[12b] reveals a continuous increase of protonated TTFV cations (Figure 4D). Based on these titration analyses, the spectral trend in Figure 4B can be convincingly assigned to the dissociation of the complexes of $2C_{60}$@**5b** with increasing protonation of the TTFV moieties in macrocycle **5b**.

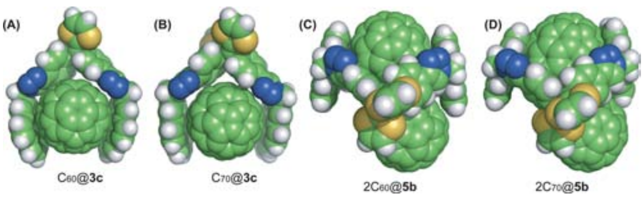

Figure 3. CPK models of optimized molecular structures for the complexes of (A) C_{60}@**3c**, (B) C_{70}@**3c**, (C) $2C_{60}$@**5b**, and (D) $2C_{70}$@**5b**.

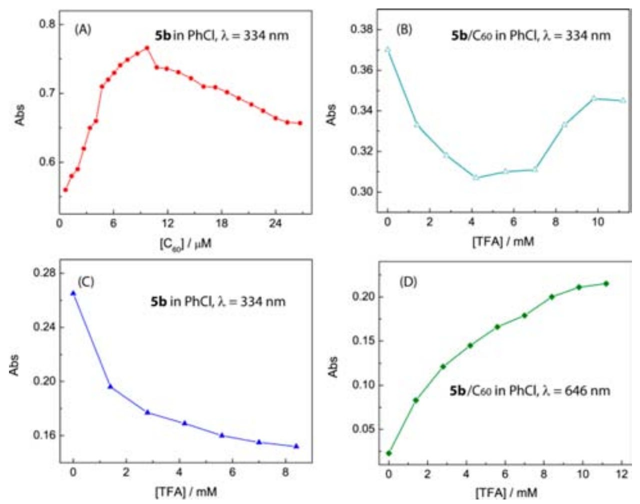

Figure 4. (A) Absorbance of **5b** (7.0 μM) at 334 nm as a function of [C_{60}]. (B) Absorbance of **5b** (6.1 μM) and C_{60} (30.3 μM) at 334 nm as a function of [TFA]. (C) Absorbance of **5b** (4.3 μM) at 334 nm as a function of [TFA]. (D) Absorbance of **5b** (6.1 μM) and C_{60} (30.3 μM) at 646 nm as a function of [TFA]. All titrations were done in chlorobenzene at rt.

In conclusion, we have not only prepared a series of TTFV-arene based molecular tweezers and macrocycles but also studied their supramolecular interactions with C_{60} and C_{70} fullerenes. Our results point to a great potential in achieving selectively sensing and separation of different fullerenes by molecular tailoring of TTFV-arene hybrids.

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Supporting Information Available. Synthetic procedures and spectroscopic characterization for new compounds and relevant analysis of spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.