Synthesis and complexation study of new ExTTF-based hosts for fullerenes

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Synthesis and Complexation Study of New ExTTF-Based Hosts for Fullerenes

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A new series of exTTF hosts has been synthesized for supramolecular binding study of fullerenes C_{60} and C_{70}. Binding constants for C_{60} in chlorobenzene, toluene, toluene/CHCl_{3} and CS_{2} have been calculated for different hosts and a direct structure-affinity relationship has been established. As predicted, receptors with two exTTF moieties (1, 3 and 4) have demonstrated higher binding abilities toward C_{70} than C_{60}. Depending on the linker used to attach the exTTF unit to the core of the host, different binding modes (1:1 and 2:1) have been obtained.

Introduction

Owing to their unique physical and chemical properties such as their broad optical absorption bands and ability to accept up to six electrons reversibly in optimized conditions, fullerenes C_{60} and C_{70} have been the subjects of intense research in the last twenty years. However, their relatively low solubility in common organic solvents and their tendency to form aggregates severely limit their utilization in various types of devices. This serious drawback can be avoided through the covalent modifications of pristine fullerene or through the use of supramolecular chemistry. In the covalent approach, modification of fullerenes allows the preparation of highly soluble derivatives that are easy to manipulate and process. However, most of the methods developed so far lead to the loss of two π-electrons at a [6,6] junction, thus affecting significantly the chemical stability and electronic properties of fullerenes. Hence, a second approach based on supramolecular complexation of pristine fullerenes has been developed in order to keep their electronic nature intact. The basic principle of this strategy is to use hosts that are geometrically and/or electronically compatible with the curved surface of fullerenes in order to bind them strongly enough to create complexes that are stable owing to π-π and electrostatic interactions. In this regard, fullerenes are known to form inclusion complexes with electron-rich macrocycles like calix[n]arenes, cyclotrimeratrylenes, resorcinarenes and porphyrins. In some cases, this strategy can even be used to make fullerenes water-soluble. In addition to macrocycles, tweezer-like molecules based on curved conjugated systems such as coranulene and extended tetraphiafulvalene (exTTF) have been reported.

Tetraphiafulvalene (TTF) and exTTF derivatives are particularly interesting to be used as the recognition units for fullerenes in hosts having a tweezer configuration. In fact, the exTTF unit bears a curved (concave) conjugated face that promotes supramolecular interactions with fullerenes. Moreover, exTTF is an electron-rich unit with low oxidation potential owing to the presence of electron-donating sulfur atoms directly attached to the conjugated system. exTTF showed its utility as recognition unit to bind fullerenes and many reports have been published on the subject. However, to the best of our knowledge, no systematic study on the influence of the linker used in the preparation of exTTF-based hosts on the association constant with fullerenes has been reported. The optimization of this structural parameter could be highly beneficial to increase the binding affinity of exTTF-based hosts towards fullerenes.

Herein, we report the synthesis and characterization of different hosts for fullerenes complexation having two or three exTTF units attached by different linkers to a phenyl core. Our approach was to study the influence of the exTTF linkage, the type of exTTF and the distance between the recognition units on the strength of the supramolecular binding. The long-term objective of this study is to understand the factors affecting the
binding constants between exTTF-based hosts and fullerenes to guide us in the design of highly efficient hosts for fullerenes that could be used not only in solution, but also on electrode surfaces to create organized, bidimensional networks of pristine fullerenes.16

Results and discussion

Synthesis

The six extended-TTF based receptors (1-6) used in the present study are illustrated in Figure 1. Different chemical functions have been used to link the exTTF units to the phenyl core. The design of the linker was based on their rigidity, synthetic versatility and length. Thus, ether, ester and triazole linkers have been tested. In each case, at least one sp3 carbon atom is present within the linker to allow exTTF to wrap properly around fullerenes. The rigid triazole moiety was added to some linkers in order to extend their length without adding additional degree of freedom (host 1 vs. 3). Triazole can be easily prepared in high yield through copper-catalyzed Huisgen cycloaddition reaction,17 or “click chemistry”,18 between an azide-containing unit and a terminal alkyne. Finally, we decided to prepare a host (2) in which an additional phenyl ring was fused on each fulvalene unit. The complexation ability of 2 will be evaluated and compared to the results obtained for host 1 in order to study the effect of extended conjugation on the association constant.

![Figure 1 Structures of hosts 1-6.](image)

Host 1 was prepared according to the reported literature12d procedure for the sake of comparison with hosts 2-6. The synthesis of host 2 is described in Scheme 1. The 2-dimethoxyphosphinyl-1,3-benzodithiole 9 was prepared from benzo[d][1,3]dithiole-2-thione according to the literature in 40% overall yield.19 The reaction of TBS-protected anthraquinone 8 with 2-dimethoxyphosphinyl-1,3-benzodithiole 91% using the Wittig–Horner-Emmons20 reaction in dry THF in the presence of n-butyllithium at -78 °C yielded the corresponding product 10 in 75% yield. Deprotection of the benzylic alcohol 10 was conducted in a 1M HCl solution in a mixture of 9:1 THF/MeOH for 1 hour,21 yielding the desired product 11 in 98%. Esterification reaction between alcohol 11 and isophthalic acid 12 using water soluble 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide coupling reagent22 yielded the host 2 in 70% yield after purification by column chromatography.

![Scheme 1 Synthesis of host 2.](image)

For the synthesis of hosts 3, 5 and 6, an azido-containing exTTF unit had to be prepared and the strategy used is presented in Scheme 2. The synthesis of 2-azido-anthraquinone 16 was achieved via two different routes. In the first attempt, a diazonium salt intermediate was formed from the 2-amino-anthraquinone 13 and quenched with sodium azide to provide the desired product 14 in 36% yield.23 The reaction of the resulting product 14 with product 1524 through a Wittig–Horner-Emmons reaction in dry THF in the presence of n-butyllithium at -78 °C yielded the corresponding product 16 in 13% yield. The very low yield obtained for this reaction could be explained by the poor solubility and relative instability of compound 14 under Wittig-Horner conditions. Thus, we decided to bypass the use of intermediate 14 by designing a second synthetic route to compound 16 involving the formation of a triazene, which increased significantly the solubility of the compound (Route B, Scheme 2). In this case, triazene can be viewed as an azide “protecting group” since it can be easily transformed into azide in one step at the very end of the synthesis. Starting again from compound 13, the amine group was transformed into a triazene through the formation of a diazonium salt to yield compound 17 in 60% yield.25 Similarly to compound 14, a Wittig–Horner reaction on compound 17 with product 15 yielded compound 18, which was further treated with potassium hydrogenosulfate and sodium azide to yield the desired compound 16 in 71% after purification by precipitation with methanol.
Scheme 2 Synthesis of azide-containing exTTF unit 16.

Having compound 16 in hands, we undertook the preparation of hosts 3, 5 and 6 by click chemistry and the synthetic routes are depicted in Scheme 3. For host 3, the benzylic ether linkers were introduced by reacting 1,3-dihydroxybenzene with propargyl bromide in standard SN2 conditions to yield compound 19 in 56% yield.26 Then, compounds 16 and 19 were coupled using standard copper-catalyzed 1,3-dipolar cycloaddition27 reaction conditions to afford the triazole tweezer-like host 3 in 41% yield. It is important to note that dimethylsulfoxide (DMSO) was chosen because it was the best solvent tested to solubilize compound 16.

Encouraged by this positive result, we decided to expand this chemistry to molecules containing three exTTF units. Reaction of tri-alkyne derivatives 2028 and 2129 with compound 16 using the above-mentioned conditions for the preparation of host 3 did not yield the desired product. Even by changing the solvent to dimethylformamide (DMF) and heating the solution to 70 °C, no reaction was observed. It was reported in the literature that microwave irradiation could enhance the rate of the reaction and, consequently, limit the formation of side products.30 Thus, we tried the same reaction using microwave irradiation and after 1.5 hours at 80 °C, the desired host 5 was obtained in 60% yield. Using the same conditions, compound 16 was reacted with compound 20 and host 6 was obtained in 39% yield.

Scheme 3 Synthesis of hosts 3, 5 and 6.
Finally, we decided to develop a tripodal host of 1,3,5-triphenylbenzene bearings three exTTF units attached to the meta positions (host 7, Scheme 4) to have clear comparisons between tripodal and bipodal hosts and to maximize interactions between fullerenes and the concave surface of the exTTF. Also, we hypothesized that this structure can adopt a conical conformation ideal for fullerenes complexation. Toward this goal, we started the synthesis by coupling the extended-TTF 22 with 3-bromophenol using diethylazodicarboxylate and trimethylphosphine and the desired product was isolated in 44% yield. Subsequently, boronic ester was prepared by cross-coupling reaction between exTTF 23 with bispinacolato diboron using PdCl2(PPh3)2 as catalyst. The resulting product 24 was isolated as a yellow solid in 38% yield. Surprisingly, all the attempts to obtain host 7 from a Suzuki-Miyaura cross-coupling between compound 25 and 1,3,5-tribromobenzene failed. Rather, compound 4 was obtained. The structure of compound 4 was confirmed after careful analysis by 1H and 13C NMR spectroscopy and high-resolution mass spectrometry. This product was isolated by flash column chromatography in 26% yield. Because of its tweezer-like configuration, we decided to study its ability to bind fullerenes (vide infra).

**Complexation Study**

The complexation studies between hosts 1-6 and C60 and C70 were conducted by UV–visible spectroscopy by monitoring the spectral changes at the 430 nm band upon addition of a fullerene solution. Chlorobenzene, toluene, CH2Cl2/toluene and carbon disulfide (CS2) were used as the solvents. In a standard experiment, aliquots of a solution of fullerene (4.16 x 10^-5 M) were added to a solution of host (1.1 or 2.2 x 10^-3 M). The difference in the absorbance band (ΔAbs) of the host at 430 nm band was plotted against total concentration of fullerenes and fitted to the Hill equation (Eq. 1) using Microcal Origin 7 software. In these conditions, only hosts 1, 3 and 4 showed appreciable affinity for fullerenes. Thus, hosts 2, 5 and 6 will not be discussed further in the following section.

\[ \Delta\text{Abs} = (\Delta\text{Abs}_{\text{max}} [\text{Cs}]^a K_a)/\left(1 + K_a [\text{Cs}]^a\right) \]  

(1)

Where \( K_a \) is the association constant and \( n \) the Hill coefficient and [Cs] the concentration of host.

**Example of UV-visible titration experiment of host 3 (2.2 x 10^-5 M) in chlorobenzene with C60 is shown in Figure 2. As expected, addition of C60 produce a decrease of the intensity of the band peaking at 430 nm, associated with the π transition of the exTTF unit. This decrease is accompanied by the appearance of a new transition (λ_max 475 nm) band, which is attributed to the interaction between C60 and host 3. The presence of an isobestic point at 454 nm and a Job plot analysis (SI, Page S11) suggest a 1:1 stoichiometry. Interestingly, a sigmoidal binding curve was observed, which is generally associated to a cooperative event. The variation in absorption at 445 nm was fitted to the Hill equation (R² = 0.997), giving a \( K_a \) value of 395 M^-1 with a Hill coefficient of \( n = 1.0 \). For the reported host 1, we obtained similar absorption spectra upon addition of C60 with an isobestic point at 454 nm, suggesting a 1:1 complex as reported in the literature. In our case, a \( K_a \) value of 450 M^-1 was obtained for host 1 in chlorobenzene, meaning that the incorporation of a triazole unit within the linker in host 3 has not a positive effect on the host-C60 interaction. Expectedly, the hosts 1 and 3 bind to C70 preferentially over C60 due to its egg shape, providing flatter π-surface. However, a sufficient titration experiment could not be performed for host 1 and thus a clear

![Image](https://example.com/image.png)
determination of the binding constant with C$_{70}$ was difficult to obtain (Figure S9). Luckily, host 3 showed a better selectivity for C$_{70}$ ($K_a$ of host 3/C$_{70}$ = 8.3). This difference in selectivity can be attributed to the presence of two triazole units that increase the distance between the two TTF units and therefore a better interaction between C$_{70}$ and host 3 was observed ($K_a$ = 3290 M$^{-1}$, Figure 3). Thus, the conformation and adaptability towards C$_{60}$ and C$_{70}$ are likely to be the most significant factors affecting the $K_a$ values. Attempts to co-crystallize hosts 1 and 3 with fullerences have not been successful.

Titrations of host 3 in toluene showed similar behaviour. The $\lambda_{\text{max}}$ at 445 nm decreases as a new band at $\lambda_{\text{max}}$ = 480 nm increases, forming a clear isobestic point at 456 nm. Analysis of Job’s plot (maximum at ca. 0.6) suggests that both 1:1 and 2:1 binding modes exist, although the exact ratio for each of them has not been measured accurately. As for titration in chlorobenzene, the binding curve is sigmoidal, indicating that a cooperative binding might take place. When fitted to the Hill equation, a Hill coefficient of $n = 2.3$ and an apparent binding constant of 1278 M$^{-1}$ were measured. The Hill coefficient is considered a direct indication of the number of available binding sites on the host. A Hill coefficient above 2 ($n > 2$) suggest that the expected tweezer-like conformation of host 3 does not occur. Rather, the complexation between host 3 and C$_{60}$ in toluene could originate from the formation of a sandwich complex between two molecules of host 3 and two fullerences, as previously observed for similar hosts.$^{27}$

Mixtures of solvents such as CH$_2$Cl$_2$/toluene provide an interesting option for the study of the association constant because the solubility of C$_{60}$ decreases in a nonlinear fashion as the percentage of CH$_2$Cl$_2$ increases. Thus, a solution of host 3 in a mixture of CH$_2$Cl$_2$/toluene 1:2 was prepared. Surprisingly, in this case, the binding constant was of the same order of magnitude (1300 M$^{-1}$) as the binding constant in pure toluene. This result suggests that desolvation of the fullerene is not a dominant factor to the energetic of fullerene binding in solution in case of host 3 as it is the case for other hosts reported. In C$_{60}$, the titration of host 3 with C$_{60}$ produced a decrease in the $\lambda_{\text{max}}$ at 437 nm and a new band at $\lambda_{\text{max}}$ = 495 nm appeared, creating a clear isosbestic point at 465 nm, which points to the formation of a 1:1 complex in this solvents system too. The binding curve does not show any sign of cooperativity in this case. For host 3, the binding constant ($K_a$ = 2567 M$^{-1}$) was the same order of magnitude as the binding constant of host 1 (2300 M$^{-1}$).

The thermodynamic parameters for host 3 in chlorobenzene with C$_{60}$ were calculated using the Van’t Hoff equation (Fig S15 and table S1, ESI). The result reveals that the entropy of the complexation is positive ($\Delta S = 1.89$ cal.mol$^{-1}$.K$^{-1}$) and the enthalpy is negative ($\Delta H = -2.95$ kcal.mol$^{-1}$), suggesting relatively weak binding constants between C$_{60}$ and host 3.

Titrations of host 4 with C$_{70}$ (0-20 equivalents) displayed a significant decrease in the $\lambda_{\text{max}}$ at 437 nm along with a pronounced red shift (see SI, Page S29). The binding constant measured for host 4 with C$_{70}$ in chlorobenzene is the higher measured in this study ($K_a$ = 4375 M$^{-1}$). Analyses of the Job’s plot showed the formation of a 1:1 complex in all the solvents. The higher $K_a$ value obtained for host 4 with C$_{70}$ can be attributed to the increased distance between the two ex-TTF units, leaving more space for the C$_{70}$ to enter the recognition pocket compared to hosts 1 and 3, which possess a single phenyl group between the ex-TFF units.

In the light of these results, one can argue that the nature of the linker between the exTTF and the core of the molecule play a non-negligible but limited role. On the other hand, the better $K_a$ values obtained for host 4, especially for C$_{70}$, suggests that the distance between the exTTF unit might be a more critical factor to obtain high affinity between tweezer-like hosts and fullerences. Preparation and study of hosts in which the distance between the exTTF units varies are currently underway.
Conclusions

In the present study, we have demonstrated that hosts 3 and 4 are good hosts for both fullerenes C_{60} and C_{70}. The binding abilities of the host toward fullerenes C_{60} and C_{70} are mainly derived from charge transfer between the electron-rich exTTF and electron-withdrawing fullerene, as well as van der Waals interactions coming from the complementary shape between the concave exTTF and convex fullerene. The solvent effect for the fullerene complexation was clearly observed. Interestingly, two binding modes were observed depending on the nature of solvent. Hosts have shown more affinity toward the less symmetrical C_{70}. Addition of a third exTTF unit did not improve the interaction, probably due to the steric hindrance. Extension of this work to a variety of hosts of different shape and length and different guests will be the focus of future works.

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Notes and references

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