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Easy One-Pot Synthesis of Energy Transfer Cassettes

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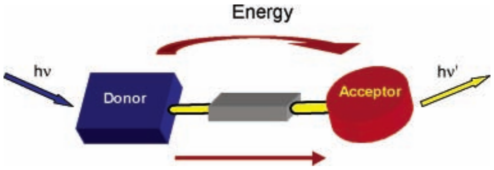
ABSTRACT

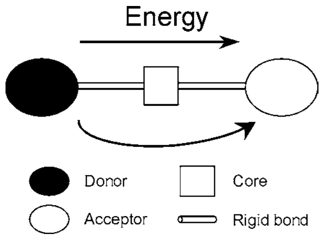


Novel cassettes suitable for energy transfer are presented involving simple and efficient condensation methods. The new rigid cassettes obtained by Schiff base formation are capable of undergoing energy transfer from a donor to an acceptor core both through space and through bonds.

Energy transfer (ET) studies involving energy migration from a donor to an acceptor have been numerous in hope of ultimately mimicking the primary pathways of efficient photosynthesis. Fundamental work has focused on synthesizing materials in hope of understanding the photophysics[1] and photochemistry[2] to decipher the means of efficient light harvesting. Applications of these results have been found in structural relationships as a function of transfer efficiency and direct application in the area of light-harvesting materials and biology as visualizers for both structural identification features and isolation means.

The main pathways investigated for ET can be characterized as occurring in two ways: (i) through-space and (ii) through-bonds, illustrated in Scheme 1.[3] The former is a Förster-type exchange in which the donor's emission from the singlet state overlaps with the absorption of the donor. The net outcome is radiative energy transfer from donor to acceptor with transfer possible over a limited distance governed by the relationship of R^{-6} distance separating the two chromophores.[4] The requirement of spectral overlap for Förster ET places an upper limit on the range of fluorescence wavelengths from multiple dye cassettes irradiated using a single excitation wavelength.

Scheme 1. Schematic Representation of Rigid Energy Transfer Cassette Capable of (a) Through-Space and (b) Through-Bond Energy Transfer



The second type is a nonradiative ET from a donor to an acceptor connected by a conjugated bond. This mode of transfer normally involves dyes that communicate with the other chromophore by means of the conjugated bond. Contrary to the Förster mechanism, the through-bond route does not require mutual overlap of the emission spectrum of the donor and absorption of the acceptor. This allows incorporation of a donor that strongly absorbs at a specific wavelength and an acceptor that emits well outside the

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(1) Webber, S. E. In *New Trends in the Photochemistry of Polymers*; Allen, N. S., Rabek, J. F., Eds.; Elsevier Applied Science Publishers: New York, 1985; p 19.

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normal Förster range with emissions at different wavelengths other than those used for excitation. With fast energy transfer and suppression of nonradiative decay pathways, the through-bond transfer involving conjugated bonds is not as constrained by distance separation, in contrast to the Förster route. This fluorescence resonance energy transfer (FRET) through-bond mechanism is readily used in biotechnology; consequently, much attention has focused on the synthesis for obtaining highly efficient syntheses of imaging dyes for labeling biological systems and subsequent visualization.

The major challenge currently encountered for efficient energy transfer cassettes either for through-space or through-bonds is their syntheses, which are not straightforward.[5] These require challenging and iterative[6] methods for aryl–aryl bond formation using Suzuki[7] or Wittig[8] methodologies. Such approaches require tedious purifications to isolate the desired products and are often compounded with low to moderate yields.[5] The severe limitation is the use of anhydrous solvents and strict oxygen-free reaction environments. Here, we report an easy, one-pot, selective synthetic route leading to ET cassettes involving mild reaction conditions and their characterization. Our approach entails the simple condensation of mutually compatible precursors (aldehyde and amine) leading to a conjugated Schiff base under extremely mild reaction conditions. This self-assembly approach of ET cassettes has the advantage of relative ease with which the new conjugated materials are formed under catalytic conditions without the use of stringent reaction conditions. Moreover, with the Schiff base approach we were able to control the reaction leading to stepwise condensation for asymmetric conjugated ET cassettes comprising a donor and an acceptor separated by an aryl core. The ET cassettes and their analogues synthesized are reported in Figure 1.

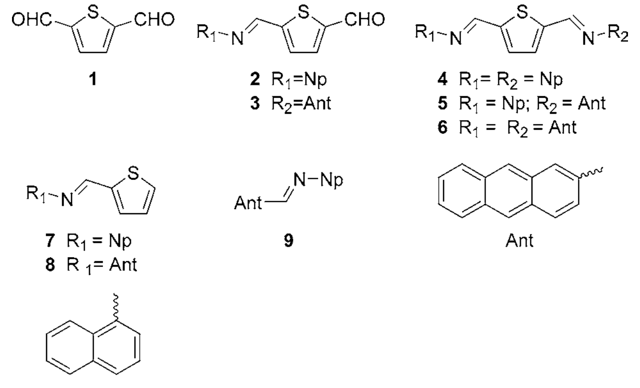

Figure 1. Energy transfer cassettes and their analogues all synthesized by Schiff base formation.

Due to our previous success with thiophene aryl units,[9] we pursued their incorporation into energy transfer cassettes and their subsequent ET studies. This unit has led to conjugated materials that exhibit high solubility unlike its 1,4-disubstituted aryl analogue. To create the ET cassette, we coupled the thiophene aryl linker (**1**) to both an anthryl unit and a naphthyl unit via simple imine bond formation in high yields by refluxing in chloroform. These chromophores are well-known for their acceptor and donor properties, respectively, and have been well characterized.[10]

The reaction conditions required are mild involving the use of catalytic mineral acid and are easily amenable to include a wide range of other common solvents capable of absorbing water byproducts such as ethanol, toluene, DMF, and 2-propanol. Such a desired property shifts the otherwise reversible reaction in favor of the products, which is further assisted by the thermodynamic stability of conjugated bond formation. Moreover, the condensation reaction is straightforward, exhibiting selective symmetric or asymmetric trimer formation through simple control of the number of equivalents employed and the sequence added under one-pot conditions leading to the preferred “E” conformation.

Good ET cassette properties for labeling biological systems require donor components with strong absorbances at the excitation wavelength and acceptor components with strong emissions. A steric hindrance element is also required to twist the donor or acceptor out of planarity to prevent the system from behaving as a single conjugated dye. However, a large deviation from planarity must not occur, otherwise the through-bond energy transfer from the donor to the acceptor will be suppressed, resulting in nonradiative decay processes and lack of transfer. The Schiff bases synthesized have strong absorbances, yet their spectra do not exhibit any strong color changes. These C═C isoelectronic bonds are further known to be forced out of planarity by the nitrogen’s lone pair,[11] resulting in the desired twist between the two chromophores. Confirmation of this behavior arises from the crystal structure of cassette **2** (Figure 2) that shows the naphthyl donor unit to be twisted out of planarity by 45°. Consequently, the modular cassette unit acts as an independent chromophore and not as a conjugated dye.[12] A similar trend is also

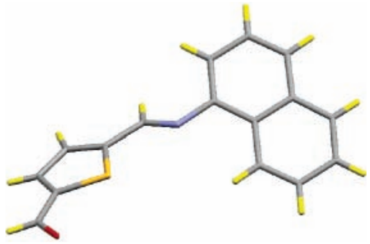

Figure 2. Crystal structure representation of cassette **2**.

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observed with the crystal structure of ET cassette **4**. From the crystal data, the N=C bond distance between the donor unit and the thiophene linker is shorter, relative to its all-carbon analogue (Table 1), consequently inducing a steric hindrance element without the use of additional functional groups by complicated synthesis such as those previously reported.[13] Communication from the donor to the acceptor moiety is still possible with fluorescence emission from the anthryl unit being observed.

Table 1. Crystallographic Structural Data of ET Cassette **2**

bond	cassette **2**	alkyl analogue[a]
plane angle[b]	135°	180°
−C=N−[c]	1.240 Å	1.310 Å[d]
−N−Aryl−	1.412 Å	
−CH−Aryl−	1.459 Å	1.458 Å

[a] Refers to *trans*-1,2-di-2-thenylethylene from Zobel et al.[14] [b] Angle between the aryl linker and chromophore planes. [c] Angle between $C_{26}-N_2-C_{27}-C_{28}$. [d] Relative to the all-carbon analogue in a.

Further evidence of the chromophores acting as independent units from the linker is seen in the ground-state absorption spectra with the anthryl-based cassettes (Figure 3). Here, the characteristic structured anthryl absorption spectrum is observed in the UV region for **3**, **5**, and **8**, confirming the cassette's conjugation with conservation of the independent chromophore features. The absorption in the visible range is dominated by the lowering of the excited electronic $\pi-\pi^*$ levels resulting from stabilization of the conjugation bond.

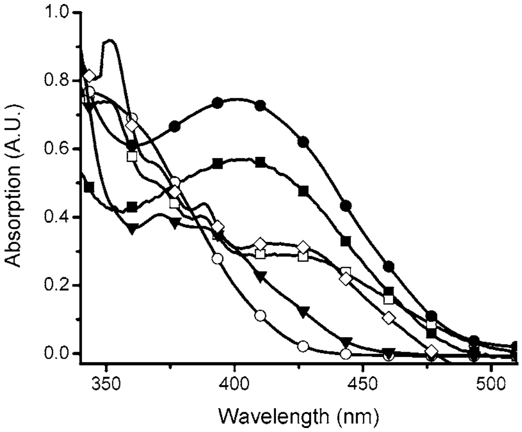

Figure 3. Ground-state absorption of cassettes **4** (■), **5** (●), **6** (□), **7** (○), **8** (▼), and **9** (◇) recorded in acetonitrile at 25 °C.

Imine bonds are known to readily undergo reduction with mild reducing agents[15] and reductive amination.[16] However, our repeated attempts did not afford the reduced amine with known mild methods or with drastic reaction conditions such as hydrosilation[17] or nickel[18] or zinc reduction.[19] This suggests that the imine bond is robust and thermodynamically extremely stable due to the increased degree of conjugation. The conjugation is confirmed from the absorption and fluorescence spectroscopic data, which both exhibit a slight bathochromic shift relative to the unaltered donor and acceptor chromophores (Figure 4).

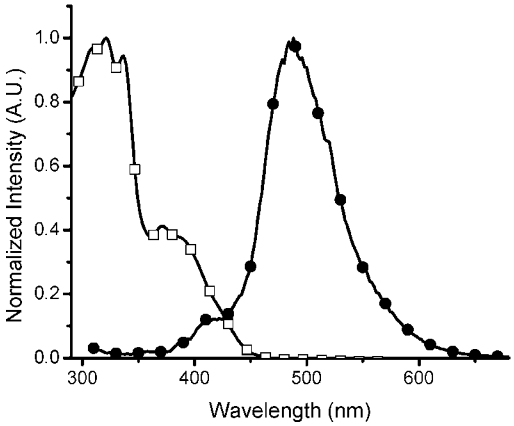

Figure 4. Absorption (□) and fluorescence (●) spectra of energy transfer cassette **8** obtained in deareated acetonitrile at 25 °C.

Compounds **2**, **3**, and **7**−**9** were synthesized as model compounds to examine the influence of the imine conjugated bond upon the spectroscopic properties in addition to the thiophene linker. The compounds contain only the imine linker and either a donor or acceptor with the net outcome being a slight bathochromic emission of the naphthyl and anthryl units. In addition, the anthryl moiety exhibits a loss

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of structured emission resulting from a decrease in the excited-state structure (Figure 4).[20] From the characteristic absorption spectra, the imine bond induces a conjugation, but the donor and acceptor units remain as independent units. The combined absorption and emission spectra (Figure 4) further provide information relating to the energy differences in excited and ground states of the ET cassettes. The intercept gives the relative energy differences of the HOMO−LUMO ground and excited states of the $S_1(0,0) - S_0(0,0)$[21] transition found was 67 kcal/mol for **8** compared to ca. 66 kcal/mol for its all-carbon analogue and 76 kcal/mol for unsubstituted anthracene.[22]

The reference compounds analyzed allow the determination of the ET capability of the ideal cassette **5** comprising both a donor and an acceptor unit. Excitation of this compound in the region of 385−400 nm leads exclusively to emission at 484 nm arising from the emission of the anthryl core. At these excitation wavelengths, corresponding to the lowest energy absorption bands, the energy absorption is exclusively from the naphthyl moiety and not from the anthryl unit arising from energy transfer between the two. Direct excitation of the naphthyl unit at higher absorption wavelengths also leads to ET to the anthryl core with its emission arising from energy transfer. The fluorescence efficiencies results are summarized in Table 2.

In summary, we have demonstrated the easy synthesis of conjugated motifs suitable for energy transfer cassettes. The cassettes involving an energy donor and acceptor were shown to undergo energy transfer with moderate yields. This is in part due to the short imine bond that twists the units out of planarity responsible for preserving the independent properties of the two chromophores. The novel condensation approach applied to ET cassettes opens new opportunities for the easy synthesis of new fluorescent molecular cassettes and biological probes in a one-pot fashion. Further studies are currently underway for the synthesis of analogues and probes with the evaluation of their photophysical properties to be reported.

Table 2. Photophysical Properties of Energy Transfer Cassettes

cassette	λ_{abs} (nm)	λ_{fl} (nm)	Φ_{fl}[a]
2	219, 311, 390	414	0.57
3	255, 324, 388	484	0.24
4	230, 324, 406	410	0.27
5	251, 321, 382	414,[b] 483[c]	0.36
6	227, 256, 325	483	0.35
7	230, 301, 344	414	0.22
8	212, 326, 404	483	0.45
9	257, 324, 425	440,[b] 486[c]	−

[a] Based on the fluorescence quantum yield of anthracene. [b] Emission from naphthalene units. [c] Emission from anthracene units.

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Supporting Information Available: Synthetic procedures, characterization of energy transfer cassettes, and crystallographic details. This material is available free of charge via the Internet at http://pubs.acs.org.

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