# Hydrogen-Bonding Self-Assembly of Multichromophore Structures

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The process of self-assembly involves the noncovalent interaction of two or more molecular subunits to form an aggregate whose novel structure and properties are determined by the nature and positioning of the components. Complex, multicomponent aggregates require intermolecular interactions that are both directional and selective, such as hydrogen bonds. Natural examples of such self-assembly are provided by double-helical[2] and triple-helical[3] DNA or the multichromophore structures of the photosynthetic reaction center[4] or light-harvesting antennae apparatus.[5] In these cases, the structure of the aggregate is determined by the chemical information encoded in the oligonucleotide sequence or in the arrangement of binding groups on the protein surfaces.

Our goal in this work was to develop simple chemical analogues of self-assembly in solution. We sought to link redox or photoactive chromophores to simple hydrogen-bonding subunits.[6] Depending on the complementarity of the binding regions, the subunits would form ordered aggregates with electron or energy communication between the chromophores.[7] The simplest aggregate would be of type **1** in which two different subunits are linked by a single binding region (Scheme I). Incorporation of two H-bonding sites into the central subunit would lead to symmetrically self-assembled triad **2**. This novel noncovalent approach to the construction of photoactive systems is simpler and potentially more general than using covalent linkages between chromophores.[8]

The self-assembling interactions were based on the hexa-hydrogen-bonding complementarity between barbiturate derivatives and two 2,6-diaminopyridine units linked through an isophthalate spacer.[9] More basic 4-alkoxypyridines[10] were used in the recognition design in order to maximize the association constants[11] and so provide significant subunit aggregation, even at low ($<10^{-6}$ M) concentrations. This self-assembling strategy is a general one, and many choices for the chromophore components are possible. In this work we have used simple fluorescent or redox components such as porphyrin, naphthalene, and ferrocene derivatives.[12] The porphyrin subunit **3** was prepared from the corresponding porphyrin mono Cbz monoamine and the activated barbiturate acid.[13] The second component was also readily variable. Reaction of 5-nitroisophthaloyl dichloride with the monoacyldiaminopyridine followed by reduction ($TiCl_3$) gave amine **4**, which was acylated with dansyl chloride, 2-(alkoxycarbonyl)-6-naphthoyl chloride, or ferrocenecarbonyl chloride to give components **5**, **6**, and **7**, respectively.

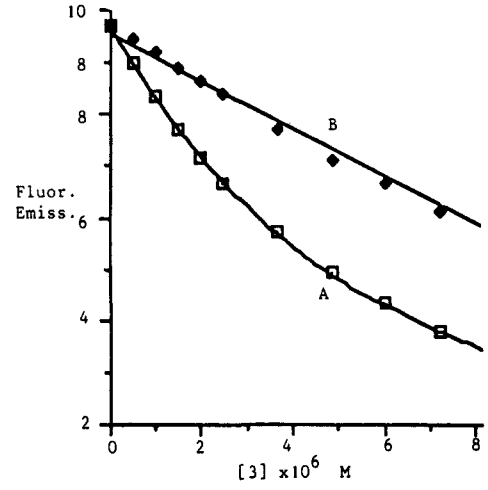



**Figure 1.** Plot of fluorescence emission at 528 nm vs concentration of **3** for (A) [**5**] = $1 \times 10^{-6}$ and (B) [**5**] = $1 \times 10^{-6}$ M and [barbital] = $1.1 \times 10^{-2}$ M. Excitation wavelength = 345 nm.

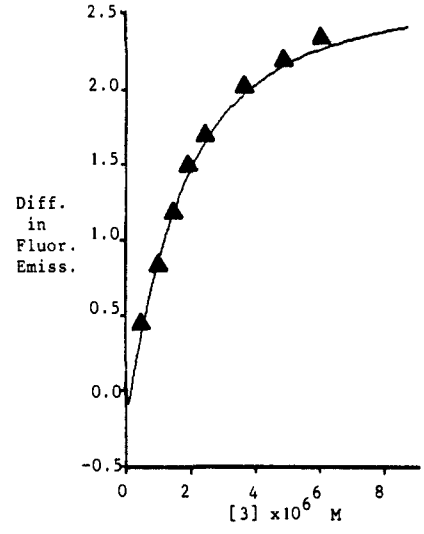
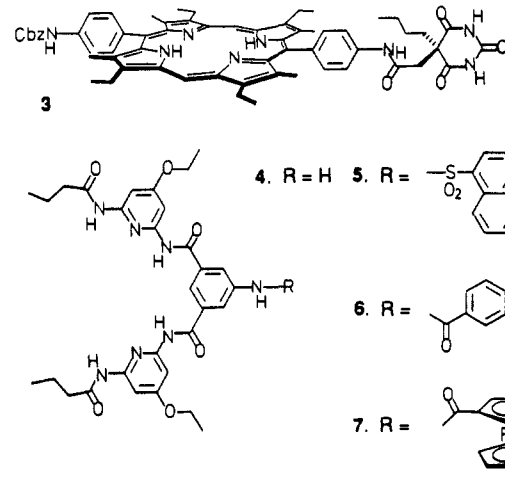



**Figure 2.** Plot of difference in fluorescence emission between A and B of Figure 1 vs concentration of **3**.

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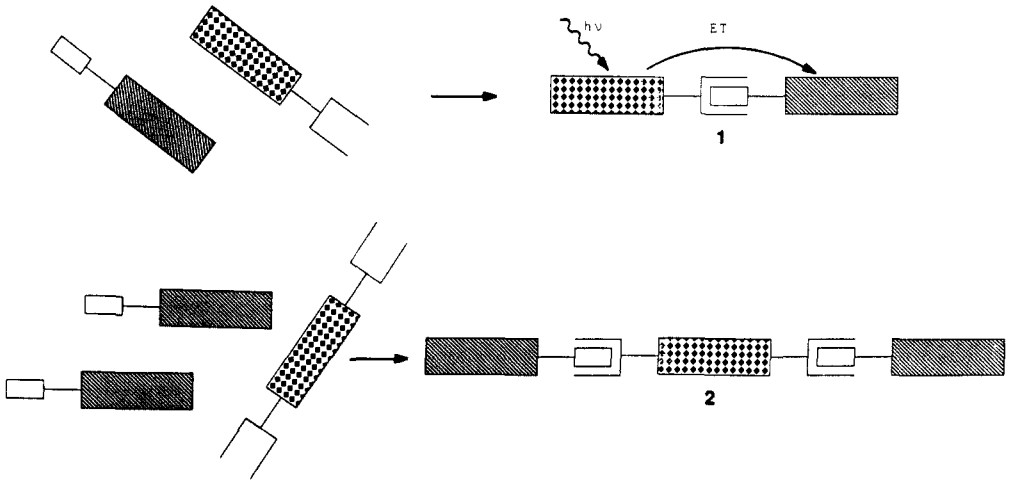
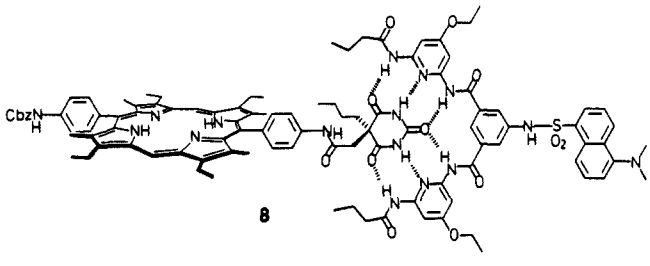
**Scheme I**




Titration of **3** into a $CDCl_3$ solution of **5** (at $\sim 10^{-3}$ M) gave large downfield shifts in the $^1H$ NMR spectrum of the hydrogen-bonding NH resonances and a sharp saturation point at 1:1 stoichiometry, consistent[9] with the formation of a very strong complex of type **8**. The distance between the self-assembled




chromophore centers in **8** is estimated to be ~23 Å.[14] The extent of communication between them was assessed by using fluorescence spectroscopy. Titration of porphyrin **3** ($10^{-6}$ M in $CH_2Cl_2$) into a $CH_2Cl_2$ solution of dansyl receptor **5** (at $10^{-6}$ M) leads to a quenching of the dansyl fluorescence emission at 528 nm.[15] A plot of emission intensity against [**3**] (Figure 1A) shows a nonlinear decrease in the fluorescence as a function of porphyrin–barbiturate concentration. Evidence that this energy transfer quenching is due to complex **8** comes from competition experiments. In the presence of an excess of barbital ($1.1 \times 10^{-2}$ M), a smaller decrease in the fluorescence emission was observed (Figure 1B). Virtually identical behavior is seen on titrating **3** into dansyl ethyl ester, where no significant hydrogen bonding is possible. Thus, in the absence of strong hydrogen bonding there is a weaker and nonspecific concentration quenching[16] between the two components. Subtraction of the (**3** + barbital)/**5** quenching data (Figure 1B) from that of **3**/**5** (Figure 1A) gives a curve (Figure 2) that corresponds to the binding interaction between **3** and **5**. From this was calculated an association constant ($K_a$) of $1.0 \times 10^6$ $M^{-1}$.[17] Time resolved fluorescence measurements (picosecond excitation)[18] using single photon counting detection support this analysis. Dansyl receptor **5** shows a single-exponential decay with $\tau = 16.3$ ns (Figure 3A). On addition of **3** (1.2 equiv), this changes to a two-component decay ($\tau_1 = 0.4$ ns; $\tau_2 = 16.4$ ns) corresponding to emission from the bound (**8**) and unbound forms of **5** that must be present at low concentration (Figure 3B). The tertiary mixture of **5**, **3** (1.2 equiv), and barbital (1000 equiv), where the formation

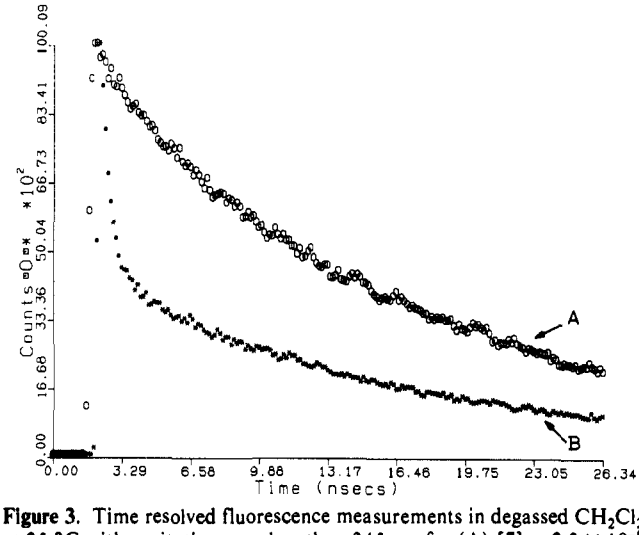
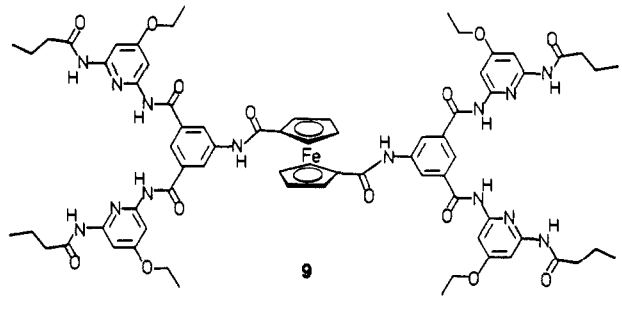



**Figure 3.** Time resolved fluorescence measurements in degassed $CH_2Cl_2$ at 25 °C with excitation wavelength = 345 nm for (A) [**5**] = $2.3 \times 10^{-5}$ M and (B) same as A plus [**3**] = $2.7 \times 10^{-5}$ M.

of **8** is inhibited, shows a single-exponential decay ($\tau = 14.2$ ns). Similar results were seen between **3** and **6** although, as expected, quenching was much reduced with ferrocene **7**.

We are currently extending this concept of preprogrammed, self-assembling structures to the construction of more complex energy- and electron-transfer systems. For example, ferrocene double receptor **9** was prepared from the reaction of ferrocene-1,1′-dicarbonyl dichloride[19] and amine **4**. $^1H$ NMR titration studies between **9** and barbiturate derivatives, including **3**, suggest the formation of a 2:1 complex, which would correspond to a self-assembled tris-chromophore aggregate of type **2**.

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## Long-Range Electronic Interactions in Peptides: The Remote Heavy Atom Effect

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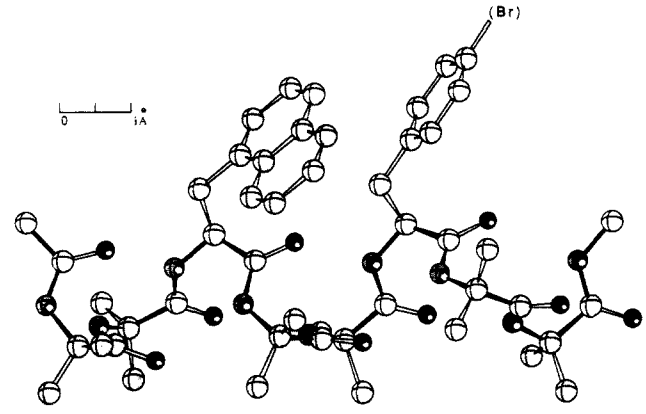
**Introduction.** A proper understanding of electronic interactions between nonconjugated molecular components depends heavily upon the ability to design and build molecular structures that are rigid and whose intercomponent geometry is well defined. The intramolecular heavy atom effect,[1] a variant of the extensively studied intermolecular heavy atom effect ($S_1 \rightarrow T_1$),[2] enables a direct study of the dependence of remote electronic interactions upon molecular structure, but has only been studied at a separation of three $\sigma$ bonds or less. Polypeptides, a basic architectural unit in nature, have been exploited in the past to study singlet excitation transfer,[3] electron transfer,[4] and excitonic interactions.[5] We chose to focus on rigid helical oligopeptides which fold to bring two electronic partners positioned one turn apart into close proximity even though the through-bond separation may remain large. This offers the opportunity to explore mechanisms of electronic interactions such as the question[6] of covalent (through-bond) vs noncovalent (through-space) mechanisms. A further motivation is that the long-range spin-exchange interactions responsible for the remote heavy atom effect may be intimately connected to and shed light upon mechanisms of long-range electronic tunneling.[7] We report here bromine-induced enhanced intersystem crossing in the naphthalene chromophore at 13 $\sigma$ bond separation in $\alpha$-aminoisobutyric acid (Aib) rich oligopeptides containing $\beta$-(1′-naphthyl)-L-alanine (Nap) and *p*-bromo-L-phenylalanine (Bph).

**The Ground State.** In the present study, two octapeptides and two dipeptides were synthesized.[8] The dipeptides, H-Nap-Bph-OMe (bromo dimer, Br-Dim) and H-Nap-Phe-OMe (control dimer, C-Dim), contained no Aib residues and thus had no conformational bias. The control and the bromo octamers (C-Oct and Br-Oct, respectively) contained six host Aib residues to induce a strong helical bias[9] and two guest aromatic residues (see Figure 1). The guest aromatic residues in both octamers were installed




Ac-Aib-Aib-Nap-Aib-Aib-Phe-Aib-Aib-NHMe

**Figure 1.** The Aib-rich control octamer (C-Oct) displayed in a $3_{10}$ helical conformation ($i \leftarrow i + 3$ hydrogen-bonding pattern). This structure is consistent with $^1$H NMR data and exploratory energy minimization results[17] and is similar to that determined by Toniolo and co-workers for the *p*-BrBz-$(Aib)_8$-O-*t*-Bu octamer.[12] The pitch of the $3_{10}$ helix is close to 6 Å (5.85 Å in the X-ray structure of Toniolo's octamer). The Br represents the location of the bromine in Br-Oct, in which Bph replaces Phe. The dark atoms are carbonyl oxygens.

**Table I.** Steady-State and Time-Resolved Fluorescence Data[a,b]

| | relative fluorescence quantum yields[c] | |
|---|---|---|
| solvent | Br-Oct/C-Oct | Br-Dim/C-Dim[d] |
| $CH_3OH$ | 0.36 | 0.79 |
| $CH_3CN$ | 0.32 | 0.82 |
| $CH_3CN$/THF (1:1) | 0.34 | |
| THF | 0.28 | |
| THF/isooctane (1:1) | 0.28 | |

| | lifetime: $\tau_F$, ns | |
|---|---|---|
| solvent | Br-Oct[e,f] | C-Oct |
| $CH_3OH$ | 28.4 ± 0.6 | 60.6 ± 0.6 |
| $CH_3CN$ | 26.6 ± 0.6 | 54.4 ± 2.7 |

[a] All samples were degassed by freeze-pump-thaw. $\lambda_{ex}$ = 290 nm. [b] The concentrations (~10 $\mu$M) were far below that required to initiate self-aggregation (0.6 mM) in similar octapeptides.[10a] The fluorescence quenching in the octamer was also measured to be concentration independent from 5 $\mu$M to 20 $\mu$M. [c] The relative fluorescence yields reported are all ±0.01. [d] The solvents for the dimers contained 0.1% TFA to ensure the exclusive presence of the protonated amine. [e] Br-Oct in both solvents exhibited biexponential decay; the longer (and the major, >75%) component is given in the table.[21] The biexponential decay may be due to the presence of two conformers, which may differ in the side-chain torsional angles or have different backbone conformations. [f] In acetonitrile, the remote heavy atom effect enhances the intersystem-crossing rate constant by an additional $(26.6\ ns)^{-1} - (54.4\ ns)^{-1} = 2.0 \times 10^7\ s^{-1}$.

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