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“Too Small, Too Big, and Just Right” − Optical Sensing of Molecular Conformations in Self-Assembled Capsules

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The interior space of encapsulation complexes such as **1.1** (Figure 1) is a well-defined host environment in which the conformations and reactivity of molecular guests can be regulated.[1] The spatial constraints of **1.1** are quite severe, due its ability to completely surround a guest with an effectively rigid and continuous cell. This host provides a yet untapped opportunity to study the photophysics of encapsulated guests.[2] Here, we use **1.1** to alter the photoluminescence of benzil derivatives by regulating the conformational space available to them. We find a surprising and counterintuitive effect occurs when a surplus, rather than a deficit, of conformational space is made available to the guest. These results illuminate the internal dynamics of the encapsulation complexes and hint at label-free sensing strategies for small organic molecules.

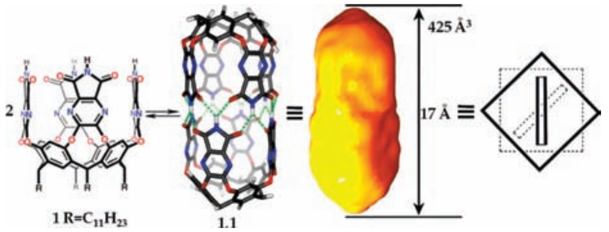

Figure 1. Tetraimide cavitand **1**, the dimeric capsule **1.1**, the shape of the space inside **1.1** calculated with using GRASP software,[3] and a schematic view along the central axis.

The inner dimensions of **1.1** are reasonably complementary to benzil and its derivatives (**2a**−**d**, Figure 2), molecules whose photophysical properties have been well-studied in many contexts[4] including host−guest complexes.[5] The benzils typically exist in *cis*-skewed geometries in their electronic ground states, a conformation largely dictated by electrostatic repulsion between the proximal carbonyl groups. Models and previous work on similarly sized compounds suggested that dimethylbenzil **2a** would be a good guest for **1.1**: The guest occupies 54% of the host’s interior, ideal for reversible encapsulation,[6] and the energy-minimized structure of the complex using semiempirical methods, such as AM1, shows that the phenyl rings of **2a** are oriented diagonally in the square prisms of the capsule’s ends (Figure 1). ^{1}H NMR spectroscopy confirms that **2a** is readily encapsulated in deuterated mesitylene. Upon excitation at 320 nm, the phosphorescence of benzils **2a**−**d** is quenched in solution by molecular oxygen unless the latter is carefully excluded from the sample. But when it is protected within **1.1**, **2a** emits a bright green light at 564 nm, with no need to degas the sample (Figure 3). The emission at 564 nm has been well-characterized as phosphorescence from a *trans*-planar triplet state, the lowest energy conformation on the excited state surface[7] and one that is expected to fit well within the capsule. For example, 4,4′-dimethylstilbene, a guest of the same length and comparable shape as *trans*-planar **2a**, is an excellent guest for **1.1**.[1a] At 311 μM concentrations of both host and guest, the encapsulation of **2a** is quantitative by ^{1}H NMR (see Supporting Information (SI)).

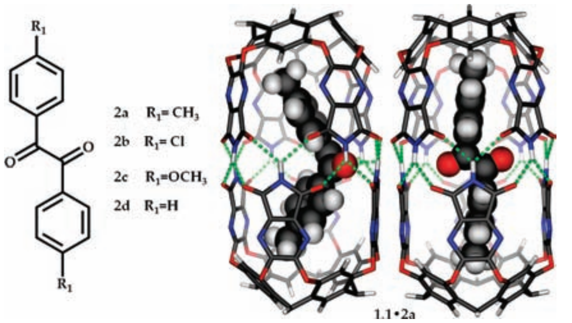

Figure 2. Benzil analogues **2a**−**d** (left). Energy minimized structure (AM1) of 4,4′-dimethoxybenzil **2a** within capsule **1.1** (middle) and encapsulated **2a** in the *trans*-planar conformation(right).

The known physical constraints of **1.1** offered the opportunity to alter the excited state behavior. It is known, from attempts both *in* and *ex silico*, that 4,4′-diethylstilbene is not a guest for **1.1**; its length simply cannot be accommodated while preserving the necessary seam of hydrogen bonding between complementary imides. Reasoning that its *trans*-planar excited state geometry would be likewise inaccessible, we therefore sought to squeeze the more flexible diethylbenzil into the host capsule but were unsuccessful. However, excision of only two hydrogen atoms at each end in the form of dimethoxybenzil **2c** created a sufficiently smaller guest to slip into the host, but only when **2c** is twisted about the central single bond. The chemical shifts of the imide protons of **1.1** confirm a weaker hydrogen bond with **2c** (9.81 ppm) as compared to **2a** (9.99 ppm) (see SI).

Excitation of **1.1•2c** now results in a very different luminescence. Rather than a sharp green emission at 564 nm, a broad blue emission (480 nm) is observed. Previous work has established this emission as fluorescence from a less stable, *cis*-skewed excited state geometry; it has been observed for benzil **2d** in the absence of *trans*-planar emission, but only in a frozen matrix at 77 K.[8]

The completion of the benzil series yielded the most unanticipated result. Unsubstituted benzil **2d** with a packing coefficient of 46% has by far more room within **1.1** than do **2a**−**c**, and the ready encapsulation of stilbene shows that the extended, *trans*-planar geometry of **2d** in its excited state will fit comfortably within the

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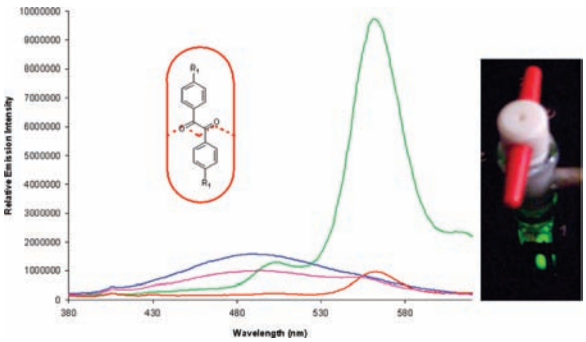

Figure 3. Room-temperature fluorescence spectra at $\lambda_{\mathrm{exc}} = 318$ nm for 10 μM air saturated mesitylene solutions of **1.1•2a** (green), **1.1•2b** (red), **1.1•2c** (pink), **1.1•2d** (blue). Observed green luminescence of **1.1•2a** (right).

capsule walls. We expected, therefore, that exciting **2d** would lead to rapid formation of the *trans*-planar geometry and subsequent green emission at ~560 nm, similar to **2a**−**b**. When encapsulated **2d** (**1.1•2d**/**2d** = 0.80:0.20) is excited, however, we observe not the characteristic emission of the favored (in both solution and typically the solid state) *trans*-planar geometry but a broad peak centered at 480 nm that is unmistakably attributable to that from an excited state *cis*-skewed conformation. No discernible trace of the *trans*-planar emission is observed, even though it dominates the luminescence of encapsulated **2a** and **2b** and is clearly accessible to the encapsulated **2d**.

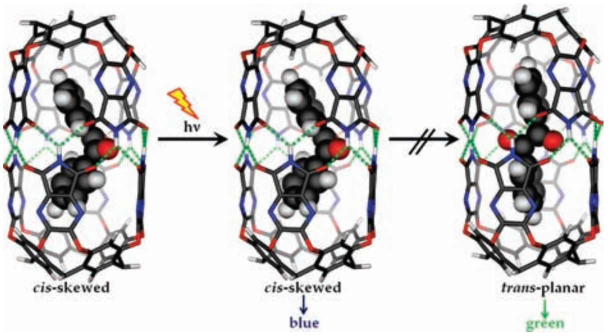

Figure 4. Energy-minimized (AM1) ground state geometry of **2d** within **1.1** is *cis*-skewed (left). Upon excitation, **2d** can fluoresce (middle) but cannot isomerize to the *trans*-planar geometry (right) prior to phosphorescence, as is the case for **1.1•2a** and **1.1•2b**.

What causes this behavior? The complexity of the structures precludes a study in the excited state with high level calculations. We used the previously reported dihedral angels of *cis*-skewed and *trans*-planar excited states as restraints for guests and minimized the complex with semiempirical methods such as AM1. Unexpectedly, these studies reveal that the *cis*-skewed benzil is a better fit than *trans*-planar benzil: in the *cis*, both phenyl rings are nestled diagonally in the square-prism shape of the capsule without steric clashes with the walls; in the *trans*, only one of the phenyl rings can remain diagonal, and the second phenyl is forced into steric clashes with the walls (Figure 4). In addition, the *cis*-conformation places both carbonyl groups closer to the polar seam of hydrogen bonds than the *trans*-planar conformation. The better guests, **2a**−**b**, in their extended *trans*-planar geometries enjoy secondary attractions such as CH−π interactions from the methyl groups of **2a** or halogen−π interactions from **2b** with the aromatic panels in the capsule's tapered ends. These forces, and their near optimal packing coefficients (54% for **2a** and 53% for **2b**), may compensate for the unfavorable steric clash of one phenyl ring and the aromatic walls of the capsule. In contrast, **2c**−**d** are either too big or too small (58% and 46%, respectively). Once excited, **2c** cannot achieve the *trans*-planar state, as it is simply too long to fit; **2d** lacks the compensating attractions and is trapped in the skewed geometry, where it luminesces.[9]

In conclusion, the interplay of restricted geometry and excited state relaxations creates rich photophysics for benzil derivatives confined within capsule **1.1**. Capsules such as **1.1**, with or without glycoluril spacers,[10] have the capacity to surround pairs of guests, in which case the steric environment of one depends directly on the size of the other.[11] One can envision situations in which the photoemission of one chromophore might change in response to the displacement of a coguest by another that is slightly larger or smaller. This could provide for label-free, ratiometric detection of relatively inert small organics.

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Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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