# Photo-Fries reaction in water made selective with a capsule†

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**The water soluble capsule formed by a deep cavity cavitand with eight carboxylic acid groups controls product distribution during photo-Fries rearrangement of naphthyl esters in water by restricting the mobility of primary singlet radical pair.**

The multitude of products from photoreactions in general, preclude their use in routine and commercial synthesis of organic compounds. With the aim of devising strategies to control product distributions in photochemical reactions, particularly those that function in aqueous media, we have been exploring the use of water soluble confined assemblies. In the current study we have used the host deep-cavity cavitand **1**, a molecule with eight carboxylic acid groups located at the periphery that engender water-solubility under basic conditions. Previously, **1** has been shown to form a capsule in the presence of hydrophobic guest molecules (Fig. 1).[1]

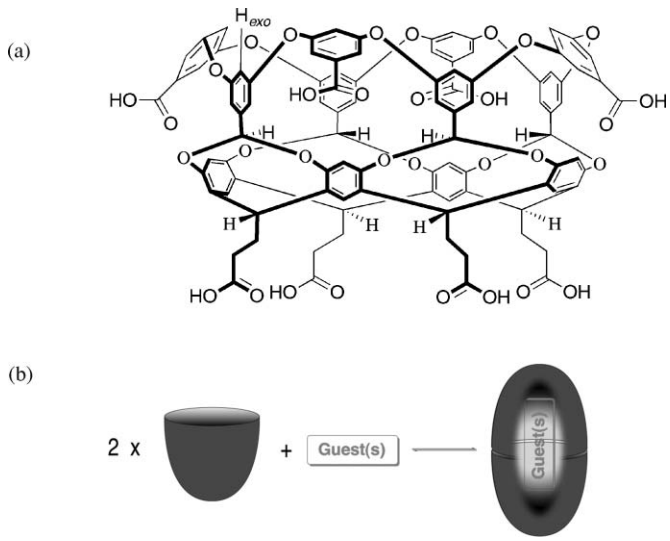


**Fig. 1** a) Deep-cavity cavitand **1**. b) Schematic of the templated dimerization of **1**.

More recently we have established that on the microsecond time-scale $\mathbf{1}_2$ can restrict the translational—but not rotational—freedom of the triplet radical pair derived from dibenzylketones.[2] To explore the efficacy of the capsule in restricting (templating) sub-microsecond time-scale processes, we report here on photo-Fries rearrangement reactions,[3–5] excited state processes that occur *via* singlet radical pairs. Specifically, we focus on naphthyl esters **2a–c**, molecules that in solution form a bewildering array of products in hydrocarbon solvents (Scheme 1).

As summarized in Table 1, upon excitation in hexane, β-cleavage (with respect to the naphthyl ring) of **2a** yields *ortho* and *para* rearranged naphthol ketones **3a** and **4a** as well as a small amount of naphthol (**5**) (Table 1). Esters **2b** and **2c** form virtually every compound depicted in Scheme 1 in hexane. Reactions were conducted in aqueous basic (pH ~ 8.9) conditions to serve as a control in the host **1**. Under these conditions naphthyl esters **2a–c** are thermally hydrolyzed to naphthol and the corresponding acids within a few hours at room temperature (**2c** being least prone to hydrolysis). Although irradiation in basic aqueous solution gave less photoproducts, a side reaction namely thermal hydrolysis complicated the photoprocess. Although in hexane hydrolysis was not a problem, multiple product formation made the photo-Fries reaction of **2a–c** less useful. As described below cavitand **1** was able to prevent thermal hydrolysis in basic aqueous solution and encourage formation of a single photoproduct. Thus the results described below are novel both with respect to hexane as well as aqueous solution.

However, in the presence of two equivalents of **1**, no hydrolysis of these esters **2a–c** occurred suggesting encapsulation and protection from the basic aqueous solution. Confirmation of encapsulation within $\mathbf{1}_2$ came from $^1$H NMR analysis of **2c** and its **2c**@$\mathbf{1}_2$ complex (Fig. 2). Integration identified the stoichiometry as 2 : 1, while peak shifts of the guest and signal splitting of the host confirmed encapsulation. Thus, characteristic of encapsulation is the 0.5 ppm difference between the methyl signals of the free and bound guest (Fig. 2a and 2c); a phenomenon induced by the magnetic shielding by the aromatic walls of $\mathbf{1}_2$. Furthermore, the signals of the free host **1** (Fig. 2b) are split in the complex (Fig. 2c) because the $C_s$ symmetric guest spins rapidly (on the 500 MHz timescale) around the $C_4$ axis of the cavity, but tumbles slowly around the pseudo $C_2$ rotation axis of the capsule. In other words at any given moment, one hemisphere of the cavitand binds the guest's naphthalene ring while the other binds the phenyl ring, hence presenting magnetically unique areas (inset).

All photoreactions were conducted in the presence of four equivalents of host **1** per guest molecule to ensure the absence of any free ester in solution. Results of the photolyses presented in Table 1 reveal that in contrast to the multiple products produced in hexane, all three encapsulated guests gave the corresponding *ortho* rearranged naphthol (**3a**, **b** or **c**) as the exclusive product. To rule out the possibility of selective destruction of the *para* products **4** during the irradiation, the progress of the photolysis of **2a**@$\mathbf{1}_2$ was monitored with $^1$H NMR. In this experiment, only one significant guest was observed at each sampling time, and

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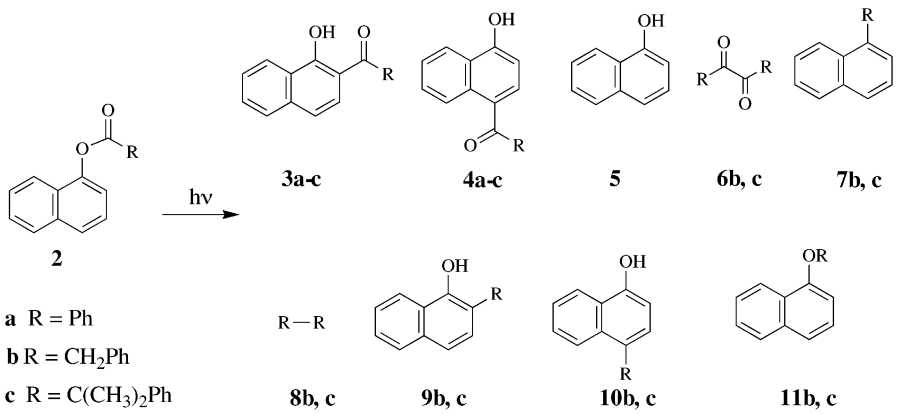
**Table 1** Relative % product distribution for the photolysis of esters **2a–c** encapsulated within $\mathbf{1}_2$

| Medium | **3a–c** | **4a–c** | **5** | **6b, c** | **7b, c** | **8b, c** | **9b, c** | **10b, c** | **11b, c** |
|---|---|---|---|---|---|---|---|---|---|
| **2a**·hexane[a] | 61 | 30 | 9 | | | | | | |
| **2a**@$\mathbf{1}_2$ | 99 | — | — | — | — | — | — | — | — |
| **2a**·buffer[b] | 40 | | 60 | | | | | | |
| **2b**·hexane | 59 | 6 | 9 | 2 | 5 | 2 | 7 | 11 | 1 |
| **2b**@$\mathbf{1}_2$ | 99 | — | — | — | — | — | — | — | — |
| **2b**·buffer[b] | 30 | — | 70 | — | — | — | — | — | — |
| **2c**·hexane | 28 | 15 | 13 | 15 | 6 | 15 | 9 | 14 | — |
| **2c**@$\mathbf{1}_2$ | 99 | — | — | — | — | — | — | — | — |
| **2c**·buffer[b] | 85 | — | 15 | — | — | — | — | — | — |

[a] For substrate **2a**, only photoproducts **3a–5** are expected to form upon irradiation in hexane. [b] Product **5** is from a dark reaction and products **3a–c** are from photoreactions of **2a–c**.




**Scheme 1**

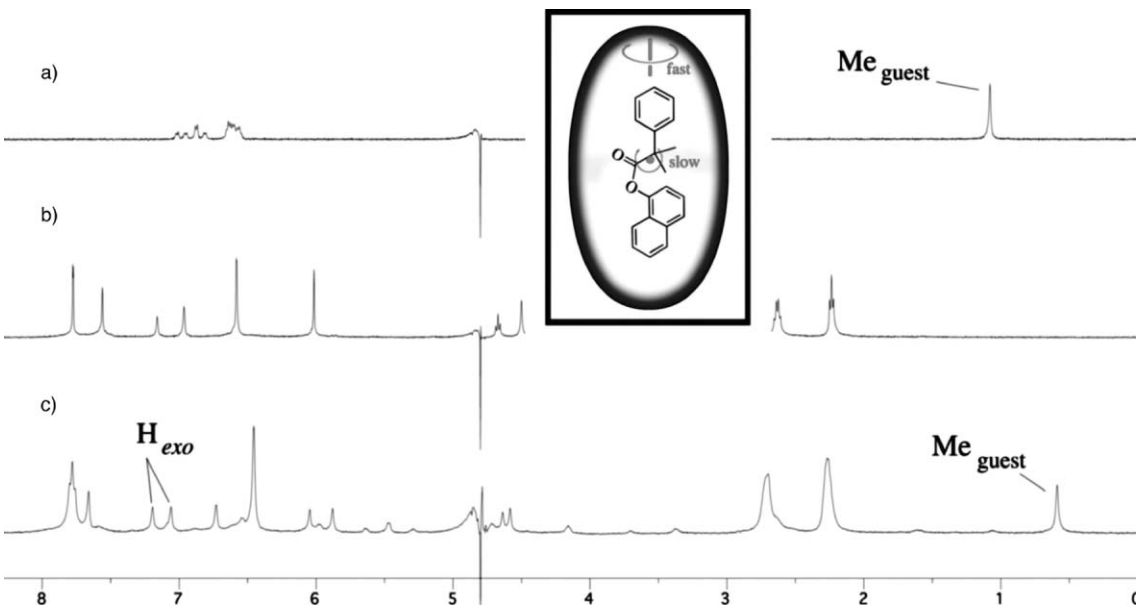
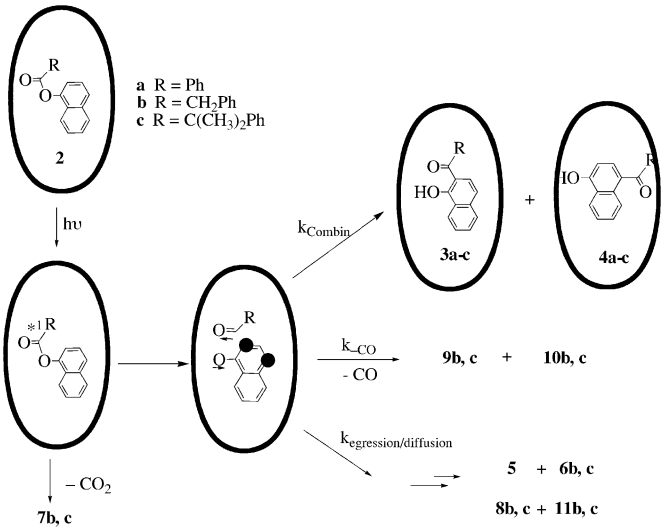



**Fig. 2** $^1$H NMR spectra of: a) Naphthyl ester **2c** in $D_2O$ (compound added as a concentrated DMSO solution; residual DMSO peak at *ca.* 2.5 ppm). b) Free host **1** in buffered (sodium tetraborate) aqueous solution. c) 2 : 1 complex of the host **1** and guest **2c** ($H_{exo}$ proton is indicated in Fig. 1a).

comparison to a sample of **3a**@$\mathbf{1}_2$ formed from the independently synthesized ketone confirmed that the irradiated and encapsulated product was **3a** (Fig. S1†). The selectivity of this encapsulation photochemistry can be understood with the aid of Scheme 2. Photo-Fries reaction has been established to occur *via* the singlet excited state through a β-cleavage process.[3–5] Selective formation of **3a–c**, combined with the absence of **4a–c**, suggest meagre rotational or translational freedom of the singlet radical pair within the capsule. Furthermore, the absence of the corresponding decarboxylation products **9** and **10** suggests a much faster radical




**Scheme 2**

recombination than decarbonylation of the acyl radical; a process occurring in solution with a rate constant of $\sim 10^8$ $s^{-1}$.[6–9] The primary radical pair recombination must therefore occur within the nanosecond time scale. As expected, no products from the combination of identical radicals, *e.g.* **6** or **8**, were observed.

The degree of selectivity observed with $\mathbf{1}_2$ is comparable only to that in zeolites where cation–π interaction plays a key role.[10–12] In water, the relatively rigid structure of the host **1** and the tenacity of the hydrophobic effect holding the reaction capsule together enforce restrictions similar to those in zeolites. Further studies exploring the potential of host **1** as a nano-scale reaction chamber are currently under way.

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