A latent photoreaction predominates within water-soluble calixarenes: photochemistry of benzoin alkyl ethers†

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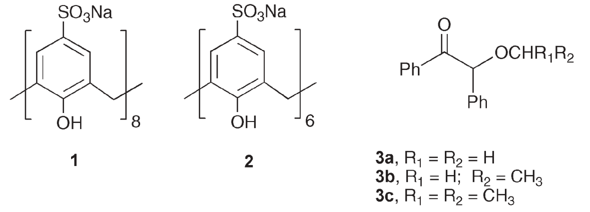
Benzoin alkyl ethers encapsulated in a cisoid conformation within water-soluble *p*-sulfonatocalix[8]arenes preferentially yield the Norrish Type II reaction product deoxybenzoin.

In recent years there has been considerable interest in conducting highly selective photochemical reactions in aqueous media. This requires identification of a host that would make the reactant molecules water-soluble and provide constraint during the course of a reaction. In this context we have been exploring the use of water soluble organic hosts such as cyclodextrins, cavitands, cucurbit[*n*]urils and dendrimers as reaction media.[1] In this Communication we present results of our studies with water-soluble *p*-sulfonatocalix[*n*]arenes ($n = 8$, **1** and $n = 6$, **2**) as reaction media. *p*-Sulfonatocalix[*n*]arenes possess cavities comprising benzene units arranged in a cyclic manner[2] (Scheme 1). The cavity dimensions of the host **2** are 11.7 Å (major diameter) and 5.6 Å (minor diameter) at the upper sulfonato side and 6.0 Å (major diameter) and 4.8 Å (minor diameter) at the lower hydroxyl side.[3] We believe the cavity of host **1**, whose dimensions have not been reported, to be larger than that of host **2**. Owing to their water solubilities and abilities to include organic molecules these calixarenes have been widely used as host molecules in biomimetic and molecular recognition studies.[4] In this presentation we highlight their role in influencing the excited state chemistry of included guest molecules.

In an attempt to examine the efficacy of water-soluble calixarene hosts in controlling product distribution in photochemical reactions, we have investigated the photochemistry of benzoin alkyl ethers (benzoin methyl ether **3a**, benzoin ethyl ether **3b** and benzoin isopropyl ether **3c**) encapsulated within hosts **1** and **2**. The photochemistry of benzoin alkyl ethers has been extensively investigated in organic solvents as well as in various confining environments.[5,6] The results presented below show that the selectivity obtained with *p*-sulfonatocalix[*n*]arenes as hosts is far superior to the ones obtained with any other organized/confined reaction media.[6] To achieve a better understanding of the origin of the selectivity the structure of the host–guest complexes was probed through ^{1}H NMR.

^{1}H NMR studies in D_2O suggested that the benzoin alkyl ethers **3a–c** were included within the cavity of host **1**. Continuous upfield shifts in the NMR signals of the guest protons and absence of two independent signals, one due to the complexed and the other due to the uncomplexed guest molecules, upon addition of the host suggested a fast exchange, on the NMR time scale, between the above two types of guest molecules. Addition of four equivalents of host **1** to one equivalent of **3a–b** showed an upfield shift of the aromatic signals of the guest molecule by 0.3–0.8 ppm, and of the –CH– proton signal by 0.15 ppm. The shift in the alkoxy group ($-OCHR_1R_2$) was less than 0.1 ppm (Fig. 1). The relatively smaller upfield shift of the aliphatic protons suggested that these groups (–CH– and the alkoxy groups) are not included within the cavity of **1**. The upfield shifts in the proton signals of both the phenyl groups suggest them to be within the calixarene cavity. The above ^{1}H NMR shifts are consistent with the model shown in Scheme 2. Probably, as noted above, due to the fast exchange between the uncomplexed and complexed guest molecules no clear conclusions could be drawn from 2D NMR (NOESY) results. To interpret the observed photochemical results it was essential to know the association constants of the benzoin alkyl ethers with the hosts **1** and **2** and these were estimated by ^{1}H NMR titration methods[7,8] to be 386 M^{-1} and 137 M^{-1} for benzoin methyl ether with **1** and **2** respectively. The difference in K values between the two hosts suggests that the host–guest compatibility, not surprisingly, is cavity size dependent.



Scheme 1

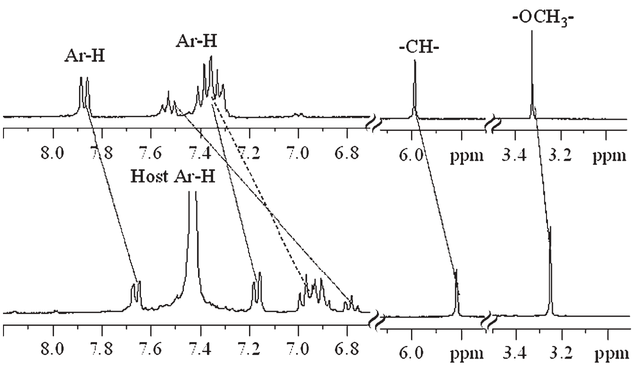


Fig. 1 Partial ^{1}H NMR spectra of **3a** (top) and **3a** in the presence of four equivalents of **1** (bottom).

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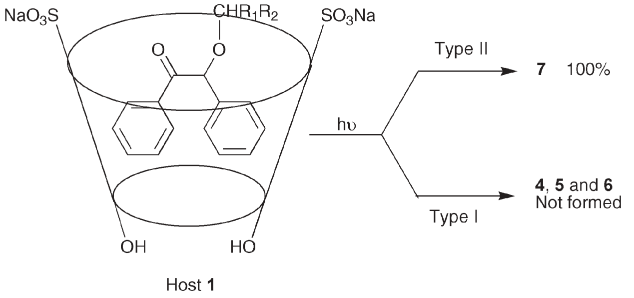
† Electronic Supplementary Information (ESI) available: Experimental protocol, determination of association constants and concentration of the complex. See http://dx.doi.org/10.1039/b507517c



Scheme 2

Table 1 Product distribution (% relative yield) obtained during the photolysis of **3a–c**[a] within **1** and **2**

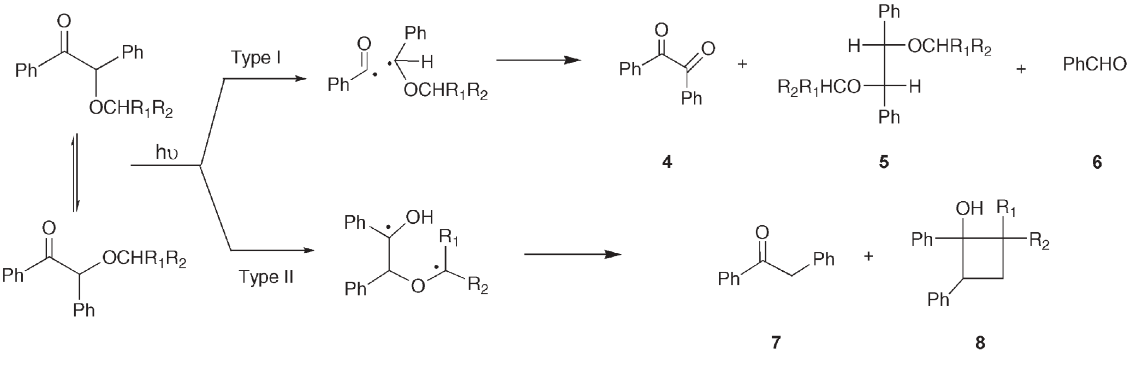
Guest	Host	Guest : host[b]	Pinacol ether	Deoxybenzoin
3a	Water	—	92	8
3a	**1**	1 : 4	9	91
3a	**1**	1 : 8	4	96
3a	**2**	1 : 4	43	57
3a	**2**	1 : 8	30	70
3a	PHBSA[c]	1 : 64	96	4
3b	Water	—	88	12
3b	**1**	1 : 4	18	82
3b	**1**	1 : 8	4	96
3b	**2**	1 : 4	48	52
3b	**2**	1 : 8	32	67
3c	Water	—	93	7
3c	**1**	1 : 4	23	77
3c	**1**	1 : 8	15	85
3c	**2**	1 : 4	43	57
3c	**2**	1 : 8	35	65

[a] The ratio of products obtained for 25–35% conversion of the reactant based on GC analysis. Cyclobutanol was formed in less than 3% upon irradiation of **3a–c** in water. [b] The numbers represent mixing ratios of the host and the guest. Stoichiometry of the complex is determined to be 1 : 1.[7] [c] The monomer sodium salt of *p*-hydroxybenzenesulfonic acid (PHBSA) was used instead of the calixarene host.

In the excited state, benzoin alkyl ethers are capable of undergoing Type I (α-cleavage) and Type II (γ-hydrogen abstraction) reactions (Scheme 3).[5] During solution irradiations, benzoyl–benzyl radical pairs, the product of Type I process, yield benzil **4** and pinacol ether **5** as major products with a minor amount of benzaldehyde **6**. Generally, deoxybenzoin **7** and cyclobutanol **8**, the Type II (γ-hydrogen abstraction) products are formed only in minor amounts (Scheme 3). Consistent with this, upon photolysis of benzoin alkyl ethers **3a–c** in aqueous solution (pH: 7) pinacol ether **5** was obtained as the major product. Although an equal amount of benzil, the coupling product of benzoyl radicals, is expected, it was formed in lower amounts than pinacol ether **5**. The reason for the low yield of benzil **4** (in water) is believed to be due to conversion of benzoyl radical to benzaldehyde and benzoic acid. The water solubility of the secondary products prevented quantitative extraction and analysis. Hence the Type I reaction was monitored by the GC yields of pinacol ether and the Type II reaction by that of deoxybenzoin and cyclobutanol.

To determine the effectiveness of calixarenes in controlling the excited state chemistry of included guest molecules, a comparison was made between the photobehavior of benzoin alkyl ethers **3a–c** in aqueous solution in the presence and absence of calixarenes **1** and **2** (Table 1). In the absence of the host, the faster α-cleavage ($k_\alpha \approx 10^{10}$ s^{-1}) process compared to γ-hydrogen abstraction ($k_\gamma \sim\approx 10^{9}$ s^{-1}), led to **4** and **5** as major products. Irradiation of the complexes (guest : host = 1 : 8) of benzoin alkyl ethers **3a–c** with **1** in aqueous solution resulted in selective formation of the Type-II product **7** (~90%) (Table 1).[7] Due to the moderate association constant, even when the host is present in eight mole excess, 24% of the guest is expected to remain uncomplexed resulting in reaction from complexed and uncomplexed benzoin alkyl ethers.[7,8] By monitoring the product distribution from benzoin methyl ether with respect to the concentration of the host **1** we were able to estimate the percentage of the deoxybenzoin that would be obtained when all the reactant molecules are complexed.[7] Surprisingly, quantitative formation of deoxybenzoin is expected from benzoin methyl ether included within the host **1**. It is important to note that in aqueous solution in the absence of host **1** deoxybenzoin was formed in 8% yield from benzoin methyl ether (Table 1) while the fully complexed reactant is expected to yield the same in 100% yield. Such a total reversal in product distribution has not been observed with benzoin alkyl ethers in any other media.[6]

Preferential formation of the Type II product deoxybenzoin within calixarene **1** most likely results from the inclusion of benzoin alkyl ethers in a conformation that favors γ-hydrogen abstraction, which is also supported by ^{1}H NMR results (Scheme 2). Further, the entrapment of the benzoyl–benzyl radical pair formed from Type I (α-cleavage) process within the calixarene cavity would result only in the regeneration of the reactant. The



Scheme 3

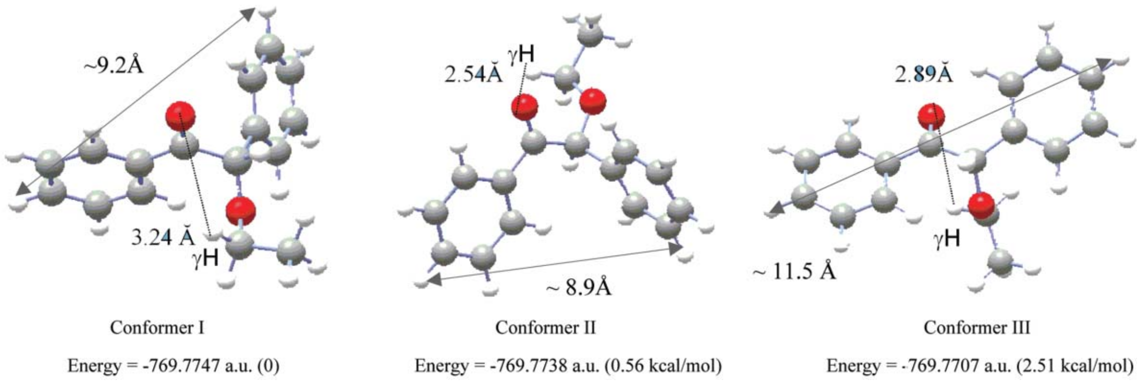


Fig. 2 Geometry optimised conformers of **3b** using RB3LYP/6–31G(*). The relative energy difference between the given conformer and the most stable conformer is shown in parentheses.

above reasonings suggest that the product selectivity within calixarene **1** is due to two factors: conformational control and cage effect. If these were true, we anticipated that a slightly smaller cavity (*e.g.*, calixarene **2**) should allow cage escape and thus lower the relative yield of the Type II product. Photobehavior of **3a–c** within **2** is in agreement with this prediction (Table 1). Once again, estimation of the product distribution at infinite concentration of the host **2** suggested that deoxybenzoin would result in 85% yield from the host complexed benzoin methyl ether.[7] To make sure that the observed results are not an artifact, photolysis of benzoin methyl ether in aqueous solution containing 1 : 64 mole ratio of sodium salt of *p*-hydroxybenzenesulfonic acid (the monomer unit of the host calixarenes) was performed. As shown in Table 1 the sodium salt of *p*-hydroxybenzenesulfonic acid had no influence on the product distribution. This supports the conclusion that the confinement provided by the cavities of **1** and **2** is responsible for the observed selectivity.

Since we believed that the selectivity is the result of conformational control by the host cavity, we attempted to gain an understanding of the conformational energy distribution in the case of benzoin ethyl ether **3b**. *Ab initio* computations of benzoin ethyl ether at RB3LYP level, 6–31G(*) basis set using Gaussian 98 program resulted in three conformers of closer energies (Fig. 2). Vibrational frequencies with no Raman intensities computed for all three structures were found to be positive. The computed molecular dimensions suggest that all three conformers could fit within the cavities of calixarenes **1** and **2**. Computed energies for three conformers indicate that conformers I and II are more stable than conformer III (–C=O and –OEt are *gauche* to each other). In conformer I, the carbonyl group and the –OEt are *anti* to each other and the distance between the carbonyl and γH is 3.24 Å, while in conformer II, the carbonyl and the –OEt are *syn* to each other and the distance between the carbonyl and γH is 2.54 Å. Based on computational data, upon irradiation while both conformer I and II will undergo α-cleavage, conformer II will also undergo γ-hydrogen abstraction. Conformer II is slightly higher in energy (0.5 kcal mol^{-1}) than conformer I. In spite of slightly higher energy ^{1}H NMR and photochemical results suggest that the guest molecule exists preferably as conformer II within the calixarene cavity.

In summary, water-soluble *p*-sulfonatocalix[*n*]arenes are useful hosts to solubilize organic molecules in water and to provide confinement during the course of a photoreaction. These hosts have the ability to force guest molecules into a conformation that brings out latent photoreactions in aqueous media. Their use in 'Green Chemistry' should be further explored.

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