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Cyclodextrin-mediated regioselective photo-Fries reaction of 1-naphthyl phenyl acylates

Smriti Koodanjeri, Ajit R. Pradhan, Lakshmi S. Kaanumalle and V. Ramamurthy*

Department of Chemistry, Tulane University, New Orleans, LA 70118, USA

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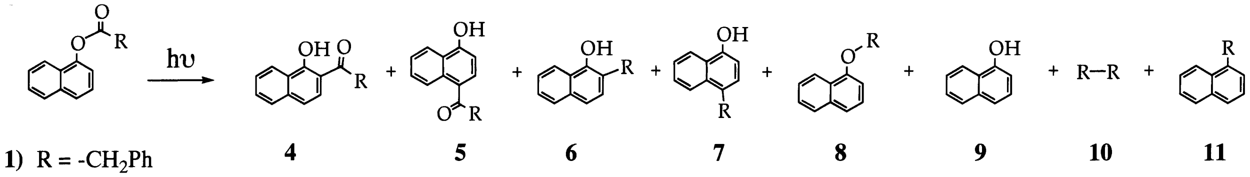
Abstract—1-Naphthyl phenyl acylates upon irradiation in solution yield eight products via β-cleavage process. However, excitation of these molecules as included in γ-cyclodextrin results in a single product (>95%). This medium dependent product selectivity is attributed to conformational and translational restrictions enforced on the reactant as well as intermediates by the cyclodextrin cavity. © 2003 Elsevier Science Ltd. All rights reserved.

With the current emphasis on performing molecular transformations under environmentally friendly conditions, photochemistry of organic molecules in media such as cyclodextrins, detergents, zeolites and crystals has gained special importance.[1] In spite of tremendous progress in understanding the excited state properties of molecules, photochemical reactions are seldom used in industrial synthesis of commercial products. The fact that most photochemical reactions yield a multitude of products has discouraged synthetic chemists to involve photochemical strategies in the construction of complex molecules. During the last two decades, it has been established that a number of organized assemblies, most of which are environmentally friendly, can steer excited state reactions to yield a single product.[2] Reactions of organic crystals are noteworthy in this context.[3] Highly selective photochemical transformations under solvent free conditions in media such as zeolites and cyclodextrins have also been reported.[4] In this letter we provide an example where one can channel a reaction that yields eight products in solution to give a single product (Scheme 1) by using cyclodextrin as the reaction medium.[5]

Solid cyclodextrin–reactant complexes were prepared by addition of ether solution of 1-naphthyl phenyl acetates (**1**, **2** and **3**; Scheme 1) to a saturated aqueous solution of γ-cyclodextrin and stirring overnight.[6] The precipitate formed was filtered and washed several times with diethyl ether to remove uncomplexed guest molecules. The precipitate was then dried under reduced pressure (10^{-2} torr) at 50°C for 12 h. The molar ratio of 1-naphthyl phenyl acetates and the CD was calculated by estimating the amount of guest extracted from a known amount of the complex. In general the ratios of CD to the guests were estimated to be close to 1:1. The complexes were characterized by their UV, X-ray powder diffraction and solid state NMR. The UV absorption spectra of the CD complex and the solution are identical. The X-ray powder dif-



1) R = $-CH_2Ph$
2) R = $-CH(CH_3)Ph$
3) R = $-C(CH_3)_2Ph$

Scheme 1.

Keywords: cyclodextrin; photo-Fries reaction; 1-naphthyl phenyl acylates; product control.

* Corresponding author. Tel.: 504 862 8135; fax: 504 865 5596; e-mail: murthy@tulane.edu

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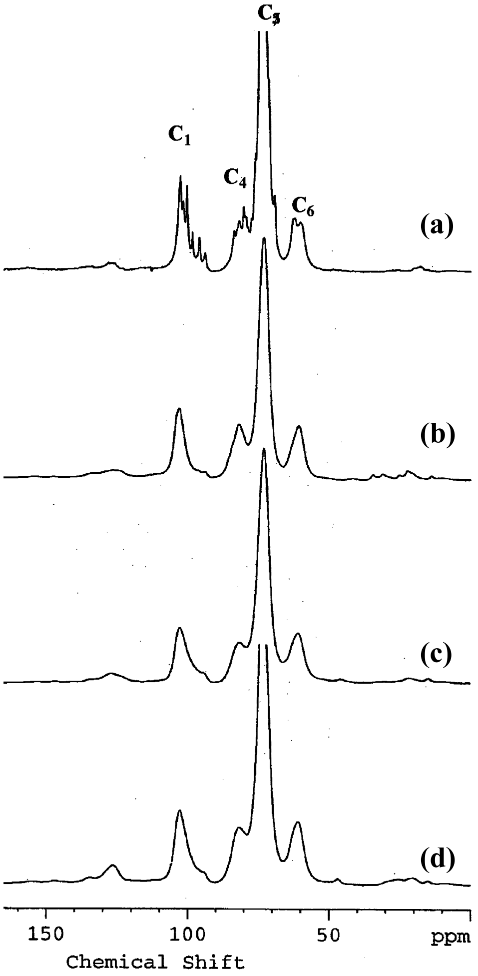


Figure 1. Solid state CP-MAS NMR spectra of (a) γ-cyclodextrin; (b) γ-CD complex with **1**; (c) γ-CD complex with **2**; and (d) γ-CD complex with **3**.

fraction pattern of the precipitated white solid complex differed from that of pure CD suggesting the precipitate to be a true complex and not a mechanical mixture of CD and the guest. The room temperature ^{13}C NMR spectrum of γ-CD is presented in Figure 1. The most important feature of the spectrum is the existence of several resonances for each carbon of γ-CD. Such an observation is mainly correlated with different torsion angles about the C-1 and C-4 linkages between two D-glucopyranose units and different torsion angles describing orientation and hydroxyl group. Figure 1 also presents ^{13}C CP MAS NMR spectra of γ-CD complexes of esters **1**, **2** and **3**. It is clear that γ-CD carbon resonances of the complexes are less resolved compared to the free γ-CD. It is generally accepted that loss in resolution of the cyclodextrin carbon signals is an indication of the inclusion of guests within its cavity.[7]

Photolysis of substrates **1**, **2** and **3** in hexane resulted in a mixture of products (Scheme 1, Table 1).[8] Photolysis of solid complexes of γ-CD and 1-naphthyl phenyl acetates **1**–**3** resulted mainly in the *ortho* rearranged product **4** (Table 1). The best visual representation of the influence of γ-CD on product distribution during the photo-Fries reaction can be seen in Figure 2 where the GC traces of the product distributions upon photolysis of 1-naphthyl 2-methyl 2-phenylpropanoate in hexane solution and within γ-CD are provided. The peaks in the GC trace were identified with the help of authentic samples prepared by solution irradiation and characterizing them by spectral data. Spectral data for the products are available in the literature.[8] Product distributions obtained upon photolysis of esters **1**–**3** in hexane could be understood based on the mechanism provided in Scheme 2.[8] Homolytic cleavage of the esters occurs from their excited singlet state to yield singlet geminate radical pair **A** (naphthoxy and phenyl acetyl radical pair). It is followed by in-cage recombination (giving rearranged products **4** and **5** via dihydro-1-naphthalenone derivatives as intermediates) or cage escape. Decarbonylation of phenylacyl radical within the cage results in the radical pair **B** (naphthoxy and benzyl radical pair). Reactions of these two radicals either within or outside the cage result in products **6**–**9**, whereas coupling between two benzyl radicals outside the cage leads to product **10**. Cage escape of the naphthoxy and phenyl acetyl radical pair **A** would also yield the above products.

The selectivity noted within γ-CD is dramatic, going from eight products in hexane solution to a single product, 2-phenylacyl 1-naphthol (**4**). Lack of formation of products **6**–**10** imply that the primary radical pair **A** do not proceed to the radical pair **B**. This suggests that the recombination of the naphthoxy and phenylacyl radicals within a cyclodextrin cavity must be rapid compared to the cage diffusion and decarbonyla-

Table 1. Product distribution upon photolysis of substrates **1**–**3** in hexane and γ-cyclodextrin

Compound	Medium	Product yields[a]							
		4	**5**	**6**	**7**	**8**	**9**	**10**	**11**
1	Hexane	59	6	7	11	1	9	2	5
1	γ-Cyclodextrin	94	4	–	–	–	2	–	–
2	Hexane	59	9	9	17	1	2	2	1
2	γ-Cyclodextrin	97	3	–	–	–	–	–	–
3	Hexane	28	15	9	14	–	13	15	6
3	γ-Cyclodextrin	98	–	1	1	–	–	–	–

[a] Irradiations were conducted to about 30% conversion. The conversion was achieved in 15 min. All yields presented are an average of at least five independent runs. Error limits on yields ±5%.

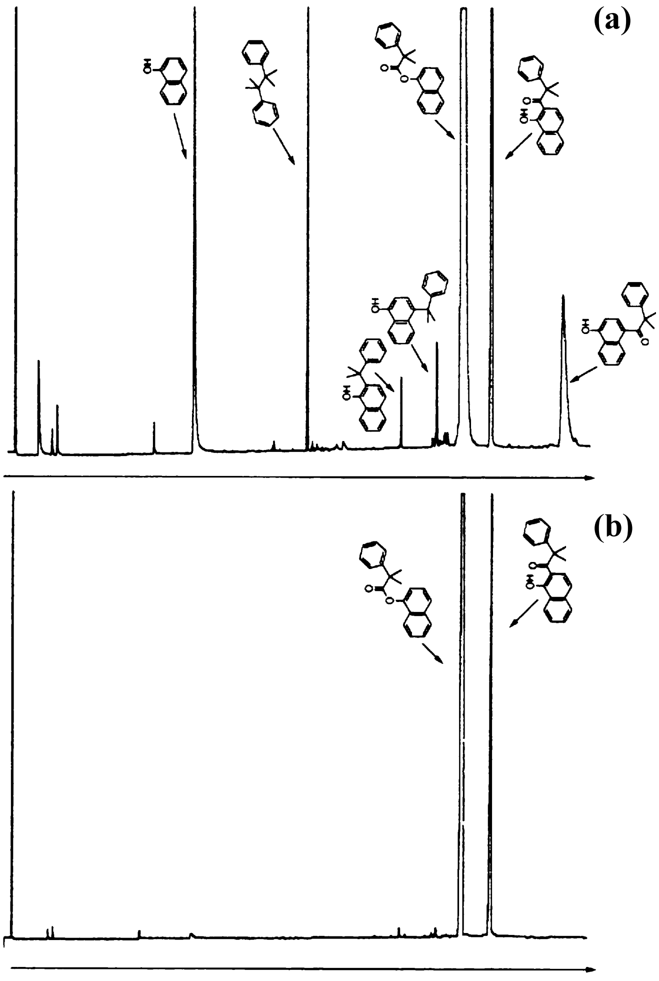
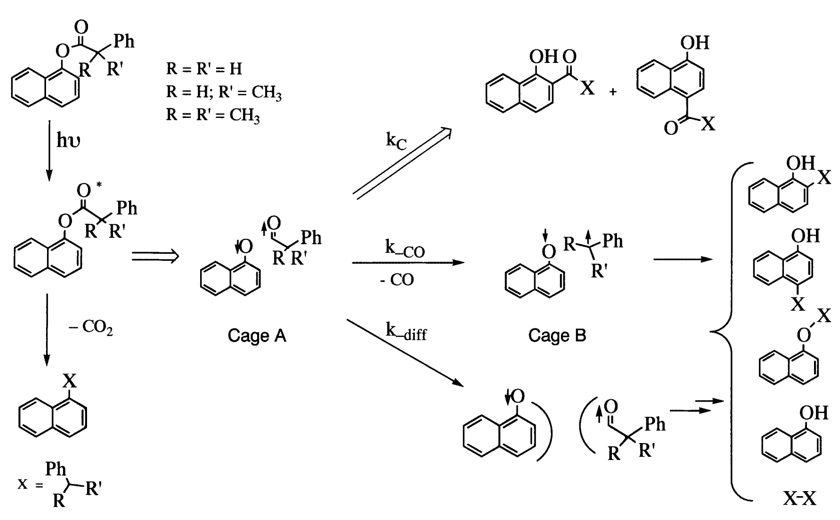


Figure 2. GC traces of the products upon irradiation of ester **3** (a) in hexane solution and (b) in β-cyclodextrin.

tion of the phenylacyl radical. The rates of decarbonylation of phenylacyl and 1-methyl 2-phenylacyl and 1,1′-dimethyl 2-phenylacyl radicals have been estimated to be 4.8×10^{6} s^{-1}, 4.0×10^{7} s^{-1} and 1.5×10^{8} s^{-1}, respectively.[9] It is important to note that even in **3** where the intermediate 1,1′-dimethyl 2-phenylacyl radical decarbonylates ~30 times faster than phenylacyl radical, no decarbonylation products were obtained within γ-CD. Therefore, the radical coupling to yield the *ortho* photo-Fries product **4** must be faster than the decarbonylation rate in 1,1′-dimethyl 2-phenylacyl radical (1.5×10^{8} s^{-1}). This necessitates us to address two questions: (a) Why *ortho* coupling (i.e. rearrangement to 2-position) is preferred over *para* coupling (i.e. rearrangement to 4-position)?; (b) Why the rate of radical coupling is faster than the rate of decarbonylation?

Preference for the *ortho* rearrangement during photo-Fries reaction within cyclodextrins has been previously firmly established.[10] Both phenyl acetate and naphthyl acetate preferentially rearrange to the *ortho* isomers upon photolysis as solid cyclodextrin complexes. This is attributed to the ability of cyclodextrin sleeve to protect the *para* positions from being exposed to the attacking acetyl radical. Upon complexation of phenyl acetate and naphthyl acetate, the cyclodextrin encircles the molecule in such a way that only the *ortho* positions are exposed for attack. We believe that a similar phenomenon is involved in the case of 1-naphthyl phenyl acetates **1**, **2** and **3**.

The acyl radical generated by the photo-Fries cleavage has three choices: recombine with the naphthoxy radical at the oxygen center to regenerate the starting material, recombine with the naphthoxy radical at the *ortho* carbon center to form 2-phenylacyl 1-naphthol **4** or decarbonylate to give the radical pair **B** (Scheme 2). The former two are occurring more efficiently than decarbonylation. This we attribute to the manner in which 1-naphthyl phenyl acetate molecules are pre-arranged within γ-CD cavity. Two conformations (folded and open) for 1-naphthyl phenyl acetate molecules computed at B3LYP/6-31G(d) level are shown in Figure 3.[11] Of these open conformation represents a minimum. It has been established that the cavity of γ-CD is large enough to accommodate two naphthalene, two anthracene, and two pyrene molecules.[12]



Scheme 2.

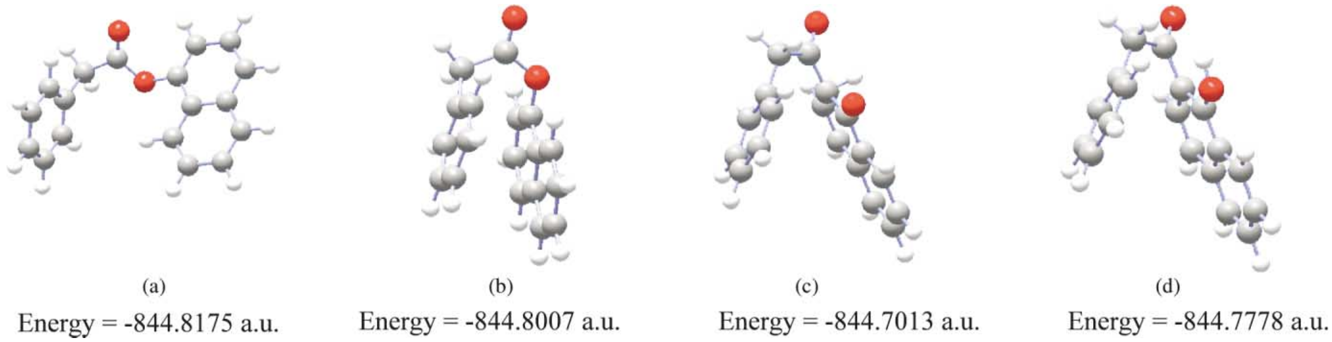


Figure 3. (a) Geometry optimized structures of 1-naphtyl phenyl acetate at RB3LYP/6-31G(d) level. RB3LYP/6-31G(d) level single point energy calculated structures for 1-naphthyl phenyl acetate (b), the primary product 1,2-dihydro-1-naphthalenone (c) and the final product 2-phenylacyl 1-naphthol (d). The folded structures b, c, and d do not represent minima in the gas phase. We believe that within cyclodextrin cavities these may be the preferred structures.

Based on literature precedence, we believe that 1-naphthyl phenyl acetate molecules would prefer the folded conformation shown in Figure 3 within γ-CD. Photolysis of such molecules would generate naphthoxy and phenacyl radical pair in the singlet state adjacent to each other and bond formation at the 2-position could occur with minimal atomic motion and without a spin barrier. As shown in Figure 3, the reactant 1-naphthyl phenyl acetate, the primary product 1,2-dihydro-1-naphthalenone derivative and the final product **4** are structurally similar and all could be easily accommodated within the cyclodextrin cavity as the transformation from the reactant to the product occurs. Thus, the reactant to *ortho* product would be 'topochemically' favored within the restricted cavities of γ-cyclodextrin. We believe that absence of spin barrier and the pre-organization favor the bond formation between the phenylacyl and naphthoxy radical pairs over the decarbonylation process. The examples provided here highlight the remarkable selectivity, readily available and environmentally friendly, cyclodextrins can enforce on a photoreaction that yields as many as eight products.

Acknowledgements

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