ORGANIC LETTERS

2007
Vol. 9, No. 18
3575−3578

Making a Difference on Excited-State Chemistry by Controlling Free Space within a Nanocapsule: Photochemistry of 1-(4-Alkylphenyl)-3-phenylpropan-2-ones

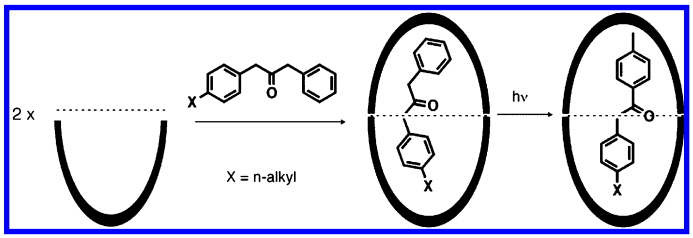
Arun Kumar Sundaresan and V. Ramamurthy*

Department of Chemistry, University of Miami, Coral Gables, Florida 33124

murthy1@miami.edu

Received June 13, 2007

ABSTRACT



The free space within a reaction cavity plays a determining role during the excited-state reaction of 1-(4-alkylphenyl)-3-phenylpropan-2-ones included within a capsule formed by two molecules of a deep cavity cavitand. By controlling the free space within the reaction cavity through remote alkyl substitution on the reactant ketone it is possible to control the yield of the rearrangement product shown above.

Consideration of "free space" is crucial in systems with confined reaction sites such as enzymes and solid-state as this space should accommodate the different structures and dimensions of the reactants and the ensuing products.[1] We report below the important role played by the same feature, namely free space during excited-state reactions of 1-(4-alkylphenyl)-3-phenylpropan-2-ones **1b**−**e** (Scheme 1) within the host octa acid (OA) capsule (Figure 1).[2] Most importantly, we find that within OA capsule in water it is possible to control the free space and consequently the product selectivity through remote substitution of the reactant molecule.

The excited state α-cleavage of dibenzylketone (DBK, **1a**) has become the benchmark to assess the efficacy of a medium as a "cage" following the initial discovery by Turro and co-workers[3] that the product distribution of this reaction could be controlled by organized assemblies such as micelles.[4] The sequence of reactions upon excitation of dibenzylketone is outlined in Scheme 1. In solution as well as in most confined media the primary radical pair (RP-1) resulting from α-cleavage decarbonylates to yield a secondary arylmethyl radical pair (RP-2). The reaction medium that greatly influences the coupling of the RP-2 leading to cage effect generally has little effect on the reactions of the RP-1. We have recently reported the influence of a 10 Å × 20 Å capsule (pseudocylindrical with narrow ends) made up of two molecules of OA on the branching of the primary radical pair, benzyl, and phenylacyl radicals resulting from DBK.[5] Within the capsule, benzyl radical derived from DBK predominantly couples with phenylacyl radical at the para position before decarbonylation of the latter could occur. In

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(2) Gibb, C. L. D.; Gibb, B. C. *J. Am. Chem. Soc.* **2004**, *126*, 11408−11409.

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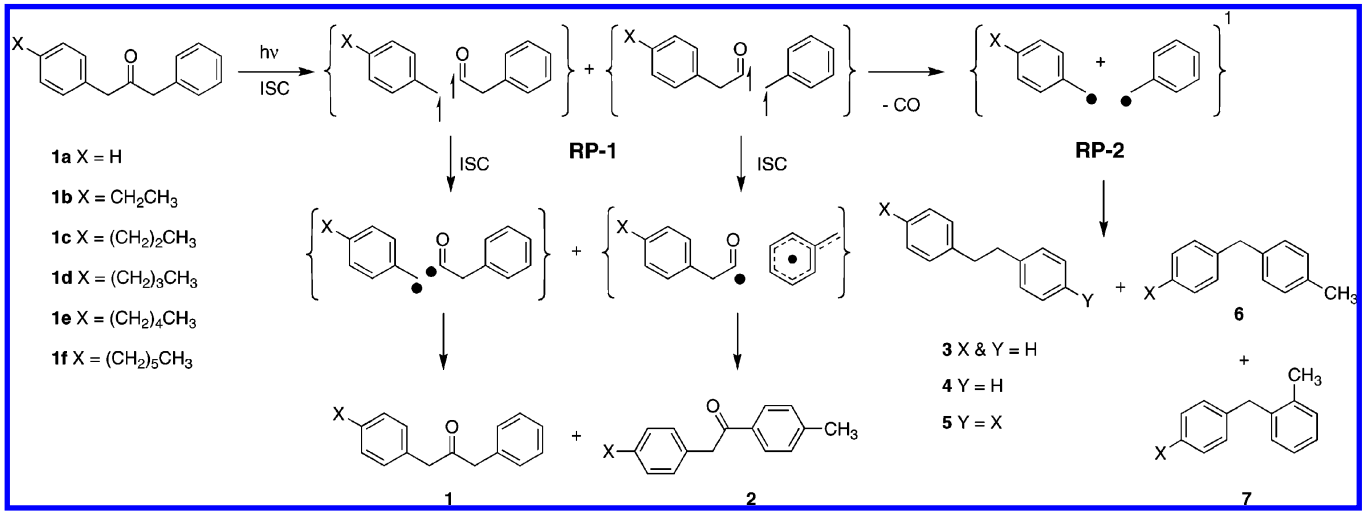
10.1021/ol0713990 CCC: $37.00
Published on Web 08/01/2007

Scheme 1. Reaction Pathway for Photolyis of 1-(4-Alkylphenyl)-3-phenylpropan-2-one **1**



this presentation, we demonstrate that the yield of the rearrangement product resulting from rotation and the coupling of the benzyl radical to phenylacyl radical is determined by available free space in the capsule. This free space and hence product distribution could be controlled by alkyl substitution at the para position of the phenylacyl radical not involved in the rotation. This striking phenomenon is unique to the OA capsule as in an isotropic solution the remote alkyl substituent has no effect on product distribution.[6]

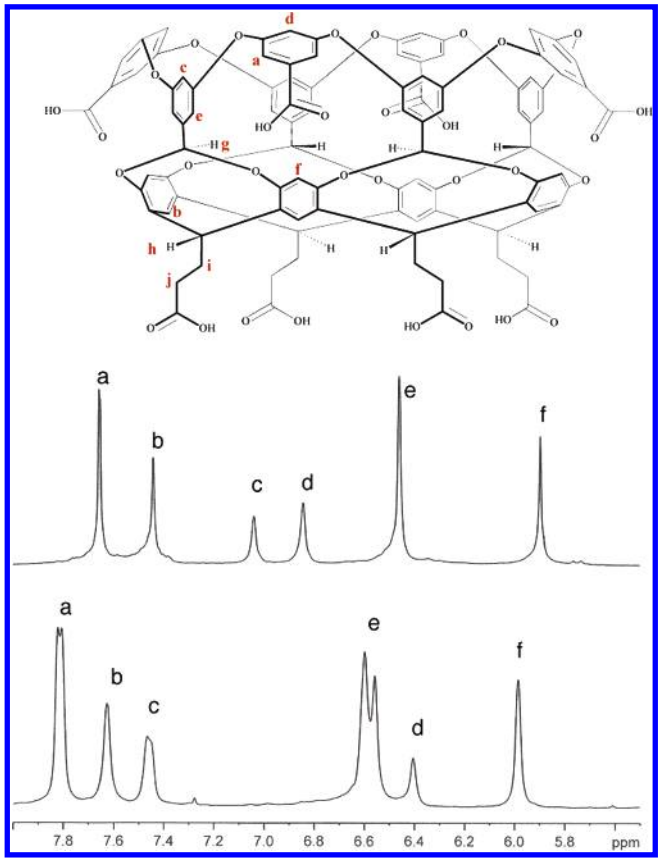


Figure 1. Structure of octa acid (top) and partial ^{1}H NMR (500 MHz, D_2O) spectra showing the aromatic signals of the octa acid, 1 mM in buffered D_2O (middle) and a 2:1 complex of octa acid and **1b** (bottom).

Addition of 1 equiv of 1-(4-alkylphenyl)-3-phenylpropan-2-ones **1b**−**e** to a solution of host OA in buffered D_2O solution (2×10^{-3} M in 2×10^{-2} M sodium tetraborate) and sonication for 30 min led to a capsular assembly by capping of each molecule of ketones **1b**−**e** by two molecules of OA (for details, see the Supporting Information). Formation of 1:2 (guest/host) capsular complex in water was established through ^{1}H NMR titration and Pulsed Field Gradient Spin−echo NMR experiments (for spectra, see the Supporting Information). The two sets of ^{1}H NMR signals due to the two molecules of OA that form the capsule in the presence of **1b**−**e** suggests an asymmetric capsule with the two aryl rings of the ketone located in the two hemispheres of the capsule (Figure 1).

As shown in Figure 2, ^{1}H signals of the alkyl chain of the guest are the most upfield shifted. When bound in the cavity of OA, the arrangement of **1b** is such that the methyl group experiencing the most dramatic magnetic shielding ($\Delta\delta$ = −2.7 ppm) conforms to its location deep within one of the tapering ends of the cavity. Elongation of the substituent chain (ethyl to butyl) alters the chemical shift of terminal methyl slightly ($\Delta\delta$ = −3.1 to −3.4 ppm; Figure 2). As can be deduced from the NMR (Figure 2) the methyl group in these cases is most likely anchored at the inner core of the cavitand and other methylene units are accordingly arranged. Consistent with this suggestion in the NOESY spectra of **1b**, **1c**, and **1d** a correlation between the methyl and methylene groups of the guest and H_e, H_f and H_g of the host was observed. Difficulties in locating the ^{1}H signals of the

(6) (a) Johnston, L. J.; de Mayo, P.; Wong, S. K. *J. Am. Chem. Soc.* **1982**, *104*, 307−309. (b) Kraeutler, B.; Turro, N. J. *Chem. Phys. Lett.* **1980**, *70*, 266−269.

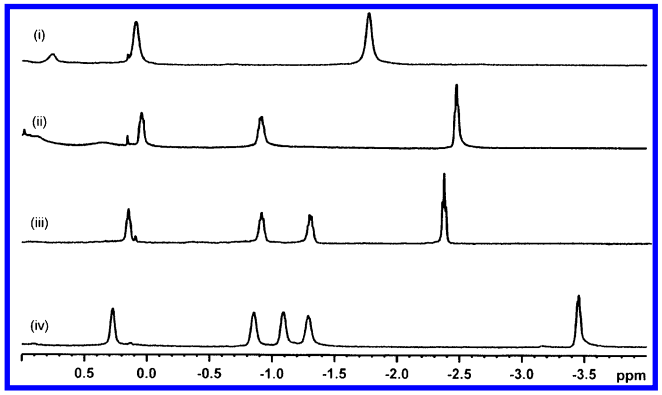


Figure 2. Alkyl region of ^{1}H NMR (500 MHz, D_2O) spectra of 2:1 complexes of octa acid with (i) **1b**, (ii) **1c**, (iii) **1d**, and (iv) **1e**.

unsubstituted benzyl ring leaves us unable to verify if its position is dependent on the remote alkyl chain. The observed additional 1 ppm chemical shift for the methyl signal ($\Delta\delta = -4.4$ ppm) with a pentyl chain as the substituent suggests either a greater interaction between this ketone and the phenyl groups of the cavitand or its insertion between the phenyl rings of the cavitand and ring of the guest ketone. Interestingly, in this case the NOESY spectra suggested that the methyl group interacts only with H_g and not even with H_f suggesting that the chain might be folded in this case. The ^{1}H NMR data suggest that 1-(4-butylphenyl)-3-phenylpropan-2-one is the longest molecule that could fit in a linear fashion with probable tail bending within the capsule. Consistent with this hypothesis, with longer (19.05 Å) 1-(4-hexylphenyl)-3-phenylpropan-2-one even after sonication for over 2 h at 50 °C no inclusion within OA capsule occurred.

As expected, photolysis of **1b**−**e** in hexane (30 min under nitrogen saturated conditions) resulted exclusively in the three diarylethanes AA (**3**), AB (**4**), and BB (**5**), in the statistical ratio of 1:2:1 without any influence of the alkyl chain on the products or their distribution.[3] Following irradiation (30 min) under identical conditions of **1b**−**e** inclusions in OA capsule (1:2 complex) in borate buffer, products were extracted with chloroform, analyzed by GC, GC−MS, and ^{1}H NMR and identified by comparison with authentic samples (Table 1 and for details, see the Supporting Information). The noteworthy influences of OA capsule on product distribution include: (a) The exclusive formation of diarylethane AB as product with the absence of both AA and BB. Such a high cage effect hitherto unobserved in solution with any host to our knowledge, is not unusual in crystals and in zeolites where diffusion of radicals is restricted.[7] (b) Rearrangement products **2b**−**e** absent from hexane or borate buffer reactions were formed in varying yields within OA capsule and (c) most importantly, their yield was dependent on the length of alkyl chain at the para position (Table 1).

Formation of only AB (**4**) (and rearranged AB **6** and **7**) is suggestive of incarceration within the capsule of both RP-2

Table 1. Product Distribution upon Photolysis of Compounds **1a**−**e** Encapsulated in Octa Acid[a]

	photoproducts				
substrate	**2**	**3**	**4**	**5**	**6** + **7**
1a	49	38			13
1b	41		36		23
1c	45		32		23
1d	15		51		34
1e	0		80		20

[a] Yields are average of at least three different runs and are estimated by GC analysis. Average conversion of each reaction was maintained between 25−35%. Photochemistry of **1a** was reported earlier.[5] The mass balance in all reactions was in the range of 80−100%.

as well as RP-1 during their entire lifetime. Absence of AA and BB is consistent with the postulate that the capsule does not come apart during the lifetime of RP-2. Although the exceptionally high (100%) cage effect (AB/(AB + BB + AA)) in the capsule is interesting, we focus our attention on the para-rearrangement product.

Formation of para-rearrangement product, especially whose yield depends on the length of the alkyl chain, to our knowledge is previously less known.[6] We believe an analysis of this process would provide an insight on understanding reactions even at enzyme active sites whose "reaction pockets" are similar in size to the reactant and product molecules. Within the capsule, as illustrated in Scheme 2, formation of the rearrangement product **2** from RP-1 is dictated by the ability of the benzyl radical to rotate while the nearby arylacyl radical remains stationary. Questions remaining to be addressed include: (a) What drives the reorientation of the benzyl radical within the capsule? (b) What is the dependency of benzyl radical reorientation on the *p*-alkyl substitution on the arylacyl radical? (c) What is the correlation between the yield of **2** and the length of the alkyl chain of the arylacyl radical that is not involved in the rotation.

Rotation of the benzyl radical before decarbonylation of the partner arylacyl radical is a key step in the formation of the para-rearrangement product within the OA capsule (Scheme 2). The benzyl radical, an independent species, can on generation find the best position within the capsule irrespective of the second species, arylacyl radical. We believe that space filling (van der Waals) interaction and the binding preference of the benzyl radical where the methyl group occupies the narrow portion of the cavity are the primary sources for the reorientation of the reactive benzyl radical. The observed reorientation product can easily be visualized as illustrated in Scheme 2 that involves α-cleavage from the triplet state (i), inter system crossing before or after reorientation (ii) or (iii), coupling and 1,5 hydrogen shift. The control exerted by the partner radical's alkyl group

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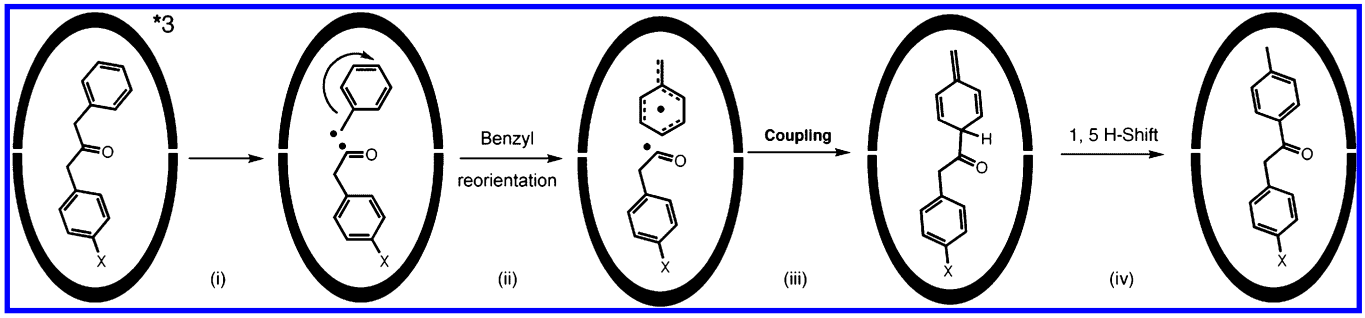
Scheme 2. Reaction Pathway Involved in the Formation of Photoproduct **2**



seemingly determining the capsule's free space on the reorientation of the benzyl radical situated on the opposite end of the capsule is an interesting finding. For example, the yield of products **2b** and **2c** with ethyl and propyl substituted 1-(4-alkylphenyl)-3-phenylpropan-2-ones, respectively, at 41% and 45% decreased to 15% with butyl (**2d**) and to 0% in pentyl (**2e**) substituents. The available free space for the benzyl radical seems to be determined at the reaction's initiation by the location and dimension of the reactant molecule. It is very likely that the free space determined by the alkyl group present at the para position of the reactant ketone that allows the benzyl radical to rotate is severely reduced with pentyl substituted ketone **1e** to allow formation of any rearrangement product. Estimated lengths of ketones **1b**-**1e** (for data, see the Supporting Information) and ketone **1e** with a length of ~17.7 Å expected to fit very tightly within the capsule leaving no room for rotation of the benzyl radical support this idea.

The above study highlights importance of "free space" in reactions in crystals and enzymes to solution phase.[1,9] Thisfactor could be decisive in cases where the dimensions of the reaction cavity are close to that of the reactant.

Control of product formation through a remote group illustrated here within a confined nano space is likely to be general phenomenon in supramolecular assemblies where in addition to electronic and steric factors, free space, and weak interactions control the reaction outcome.

Acknowledgment. We thank the National Science Foundation (CHE-0213042 and CHE-0531802) for financial support and B. Gibb for useful discussions.

Supporting Information Available: Preparation of reactant ketones and key products, experimental details, NMR spectral data host−guest complexes, and computed molecular dimensions of the reactant ketones. This material is available free of charge via the Internet at http://pubs.acs.org.

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