A FINE-TUNING OF PHOTOREACTIVITY OF LARGE RING 2-PHENYLCYCLOALKANONES ADSORBED IN CYCLODEXTRINS

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Abstract *The photochemistry of solid complexes of large ring 2-phenylcycloalkanones adsorbed in cyclodextrin cavities results in significant yields of enals as disproportionation products, at the expense of the para-rearrangement, depending on both the ring size of the cyclanone and the cavity size of the cyclodextrin. This behavior contrasts with its photoreaction in homogeneous solutions which yields predominantly para-cyclophanes.*

Introduction The quest for chemical catalysis and selectivity through host-guest complexation has received considerable recent attention.[1] For example, inclusion complexes of cyclodextrins have been successfully utilized in catalysis and selectivities in numerous thermal reactions.[2] Cyclodextrins are commonly available in three distinct forms, termed α, β and γ, which possess internal cavity diameters of 4.9 Å, 6.2 Å and 7.9 Å, respectively. Depending on the size, the shape and the hydrophobicity of the guest organic molecules, the hydrophobic cavities of cyclodextrins accommodate guest organic molecules and form inclusion complexes both in aqueous solution and in the solid state.[3] In addition to their extensive potential as inclusion complexes, the promise of cyclodextrins[1,4,5] and other constrained spaces[1,6] as reaction vessels for photochemical transformations has been recently recognized and exploited. For example, photochemical studies of Norrish type I and type II reactions of aryl alkyl ketones and dibenzylketone and its derivatives,[5] have clearly shown that complexation of ketones with cyclodextrins can influence the conformation of both the guest molecules and radical pair and biradical intermediates, thereby modifying photoreactivity. In this report, we illustrate how the constraints imposed by the size of the cyclodextrin cavity, when coupled to the size of the guest ketone, can 'tune' the photochemical behavior of large ring 2-phenylcycloalkanones

Results and Discussion In the present study, large ring 2-phenylcycloalkanones of ring sizes, 10, 12 and 15 were selected to study their photochemical behavior in cyclodextrin media. Addition of 2-phenylcycloalkanones to saturated aqueous solutions of cyclodextrins precipitates in each case an inclusion complex as a white solid.[7] Whereas these isolated complexes of β and γ-cyclodextrins have a very low solubility in water, the α-cyclodextrin complexes are freely soluble in water, and are difficult to precipitate. The solid state NMR spectra of the precipitates exhibited sharp signals for both host carbons and guest carbons; every carbon of the guest and the host could be unambiguously assigned. On the other hand, only broad unassignable signals were observed when 1:1 powder mixtures of the ketones and cyclodextrins were prepared by grounding intimately the pure materials. Additional support for the assignment of a host-guest complex to the precipitated materials was available from T_1 relaxation times and contact-times.[8] By extracting guest ketones from a known amount of the complex, the approximate molar ratios of host and guest could be established (**Table 1**). Photolysis of the redissolved precipitates in aqueous solution led to significant yields of products (apparently due to oxidation reactions) not observed either in organic solvents or in the photolysis of the solid complexes. As a result of the poor selectivity of the photolysis of the complexes in aqueous solution, we report here only the photochemical behavior of the complexes in the solid phase.[9]

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The products obtained upon photolysis of large ring 2-phenylcycloalkanones in methanol (which is typical of the products obtained in other organic solvents) and in the solid state cyclodextrin complexes are summarized in **Table 1**. In methanol as in other organic solvents, upon photoexcitation, large ring 2-phenylcycloalkanones yield paracyclophanes (C_n, **Scheme 1**) as the major photoproducts, with enals (E_n) as minor photoproducts.[10] From the standpoint of organic photochemistry, complexation with cyclodextrins causes the products of large cyclanones to resemble those of smaller cyclanones ($C_n < 9$) which yield enals as the predominant products.[10]

Scheme 1

n = 10-15 E_n (trans and cis-Enals) C_n (para-cyclophane)
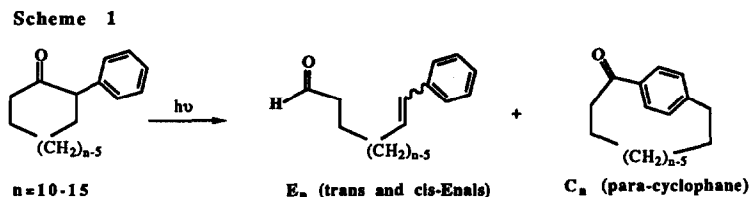
Table 1 Photochemistry of 2-phenylcycloalkanones: Influence of cyclodextrin complexation on product distribution[a,7,9]

| Medium	n=10		n=12		n=15	
	E/C	H:G	E/C	H:G	E/C	H:G
Methanol	0.12	--	0.11	--	0.07	--
α-CD complex	3.4	2.3	5.6	2.6	9.0	2.2
β-CD complex	1.3	1.7	3.6	1.7	9.0	2.1
γ-CD complex	0.5	1.2	2.0	1.3	4.0	1.3

a: E and C represents Enal (trans and cis mixture) and para-cyclophane respectively; E/C ratios were obtained from GC analysis (25m, SE-30 column, 5%) and contribute 95%-100% of the photolysis products; Conversions were limited to < 20%; Error limit in E/C ratios is ~5%; Error limit in the calculation of H:G ratios is ± 10%.

From **Table 1** the salient result is that cyclodextrin complexation has a dramatic effect on the photolysis product distribution compared to homogeneous solvents.The ratio of E_n to C_n, (E/C), obtained with 2-phenylcycloalkanones of ring sizes, 10, 12 and 15, may be taken as a measure of product tuning caused by complexation to cyclodextrins (α, β and γ). In all cases, complexation substantially increased the yields of E_n at the expense of C_n, the latter products being predominantly formed in isotropic solvents. The dependence of E/C ratio on the cavity size of the cyclodextrin and on the ring size of the ketone reveals that , for a given ketone, *enal yield increases as the cavity size decreases; i.e., cyclophane formation is favored by increasing cavity size.* For a given cyclodextrin the *enal yield increases with the ring size of the ketone; i.e., cyclophane formation is disfavored by increasing ring size.* Furthermore, among the two enal cis-trans isomers formed by photolysis of the complexes, at low conversion, the trans isomer is always the major isomer in all of the systems studied. At higher conversions, some trans/cis isomerization due to secondary photolysis is noticed.

We seek to explain why the observed photochemical behavior of large ring cyclanones in cyclodextrin complexes depends on both the cavity dimensions of the cyclodextrins employed and the ring size of the guest cyclanone and why the product distribution is substantially different in solution photochemistry. From earlier mechanistic studies,[11] it has been established that Norrish type I α-cleavage occurs in 2-phenylcycloalkanones from the molecular triplet state to give triplet acyl-benzyl biradicals which undergo intersystem crossing to give observed photoproducts. In isotropic solvents, the acyl-benzyl type biradical resulting from α-cleavage *prefers overwhelmingly* to undergo para-coupling to give paracyclophane, rather than intramolecular hydrogen transfer (disproportionation)
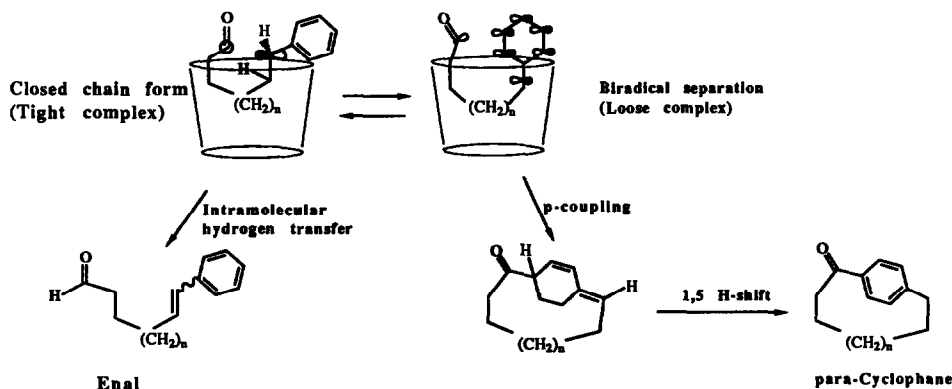
which leads to enals. The para-coupling pathway requires considerable conformational change; the radical termini must be separated by conformationally "opening up" the initially generated "closed chain" biradical conformation. On the other hand, disproportionation leads to enals with little need for conformational change from the "closed chain" shape of the biradical produced by α-cleavage of the starting cyclanone. Previous results on the behavior of radical pairs adsorbed in zeolite molecular sieves has demonstrated that the "tightness" or "looseness" of the constrained space in which the guest is adsorbed can be critical in determining product structures.[6] The basic idea of the interpretation is that in a constrained space the reactions of a primary geminate radical pair is determined by competitive pathways of rotation and diffusional motions of the pair. These motions are postulated to be controlled by the constraining space of the internal surface.

Scheme 2 Possible orientations of cyclodextrin-2-phenylcycloalkanone inclusion complexes

A (1:1)   B (1:1)   C (1:2)   D (1:2)
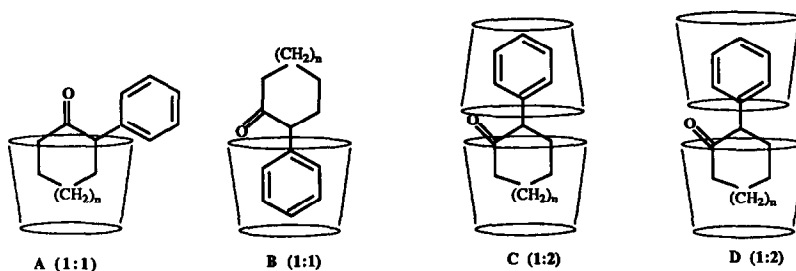
We now discuss our results on the photolysis of large ring cyclanones in cyclodextrin complexes in terms of a similar model. In the absence of an X-ray analysis, we are compelled to employ an intuitive approach to rationalize the observed effects. Because 2-phenyl cycloalkanones have two distinct hydrophobic sites (the chain of CH_2 groups and the phenyl substituent), two types of inclusion complexes are probable i.e., one involving two hosts and one guest and one involving one host and one guest (**Scheme 2**). The experimental stoichiometric ratios (H:G, **Table 1**), which vary from 1.2 to 2.6 are consistent with the occurrence of both types of complexes (1:1 and 2:1, H:G). The relative contributions of these complexes for a given ketone may vary with the size of the cyclodextrin cavity. For example, in complexes with γ-cyclodextrin, the observed molar ratios (H:G = 1.0 -1.3) suggest a 1:1 A type complex in which the cavity diameter is large enough to accommodate the cyclic part of the ketone within the cavity, while the aromatic ring can be expected to lean on the wider torus of the cavity.[11] On the other hand, the higher H:G ratios of 1.7-2.6 obtained with α and β - complexes support a contribution from 2:1 complexes in which two cyclodextrin-

Scheme 3 Mechanism of the product formation in inclusion complexes of cyclodextrins

Closed chain form (Tight complex)   Biradical separation (Loose complex)

Intramolecular hydrogen transfer

p-coupling

1,5 H-shift

Enal   para-Cyclophane

cavities are associated with one ketone or, possibly, mixtures of 1:1 and 2:1 complexes. As an extension of the ideas employed to explain the manner in which the internal surface of zeolites constrains the behavior of radical pairs and influences product distribution we consider a model which involves "loose vs. tight" complexes of the cyclanones and cyclodextrins.

Our proposed mechanism for product formation in cyclodextrin complexes is shown schematically (Scheme 3) using the orientation A (Scheme 2). In homogeneous solvents the environment is exceedingly "loose"; as a result the open chain conformations are readily formed and the cyclophane products dominate in all cases. In the case of loose cyclodextrin complexes, the geminate acyl-benzyl biradical generated in closed chain form will have some tendency to 'open-up' its chain by several rotations about C-C bonds, and this results in the separation of radical termini, which is required for the formation of cyclophanes. On the other hand, as the tightness of the complex increases, the biradical will be more and more constrained from forming the open-chain conformation. Thus, the formation of cyclophane becomes inhibited and the enal formation becomes enhanced as the complex gets "tighter". This simple model explains the observed increase of the E/C ratio with ring size of the ketone in a given cyclodextrin since tightness within a given constrained space (α, β, or γ) is expected to increase with increasing ring size. On the other hand, for a given size ketone (10, 12 or 15 membered), the observed increase of E/C ratio with decrease of cavity size can be attributed to the increase of tightness of the complex for a fixed ketone size with the increasing constraints imposed by a decrease of cavity size. Thus the approach presented here qualitatively explains nine pieces of data with one parameter: the relative tightness of the constrained space.

Conclusion The results presented here clearly illustrate that cyclodextrin cavities can impose restrictions on the separation of the radical termini connected by flexible methylene chains. Such restrictions result in selectivity in product distribution and are a simple function of the tightness of the constrained space available to the biradical intermediate.

References
1. Ramamurthy, V. Tetrahedron **1986**, 42, 5753.
2. a) Griffiths, D.W.; Bender, M.L. *Adv. Catalysis.*, **1973**, 23, 209. b) Bender, M.L.; Komiyama, M. *"Cyclodextrin Chemistry"*, Springer, Berlin, **1978**. c) Tabushi, I.; Kuroda, Y. *Adv. Catalysis.*, **1983**, 32, 417.
3. a) Inclusion Compounds; Atwood, J.L., Davies, J.E.D., Mac Nicol, D.D., Eds.; Academic; London, **1984**; Vol. 1-3. b) Hagen, M. Clathrate Inclusion Compounds; Reinhold; New York, 1962.
4. a) Tabushi, I. *Acc. Chem. Res.*, **1982**, 15, 66.b) D'Souza, V.T.; Bender, M.L. *ibid*, **1987**, 20, 146.
5. a) Ramamurthy, V.; Eaton, D.F. *Acc. Chem. Res.*, **1988**, 21, 200; b) Sharat, S.; Usha, G; Tung, C.H.; Turro, N.J.; Ramamurthy,V. *J. Org. Chem.*, **1986**, 51, 941. c) Rao, B.N.; Turro, N.J.; Ramamurthy, V. *J. Org. Chem.*, **1986**, 51, 460.
6. Turro, N. J.; Zhang, Z. *Tetrahedron Letters*, **1987**, 28, 5637.
7. Typical procedure for preparation of the solid inclusion complex: To a saturated solution of cyclodextrin (typical concentrations used are: 0.03M, β-cyclodextrin; 0.5M, α-cyclodextrin, 0.2M, γ-cyclodextrin), 2-phenylcycloalkanones (0.5-0.3 mol equivalents with respect to the cyclodextrin concentration) were added and stirred magnetically at room temperature for 24 h. During that time, cyclodextrin complexes were precipitated as a white solid. The precipitate was washed with cold water (α-complexes were not washed because of their high solubility even in cold water) to remove the uncomplexed cyclodextrin, and dried at 50° C for 10 h.
8. Garces Fred; Pushkara Rao V.; Turro, N.J., unpublished results.
9. Irradiations of the solid cyclodextrin complexes were conducted in pyrex vessels with a Hanovia 450-W medium-pressure-mercury lamp. During the photolysis, samples were tumbled continuously to ensure uniform photolysis. After the photolysis, the complex was dissolved in warm water (45-50° C) and extracted with ether; the data were analyzed by gas-chromatography.
10. a)Lei, X.; Doubleday, C.; Zimmt, M.B.; Turro, N.J. *J. Am. Chem. Soc.*, **1986**, 108, 2444. b) Lei, X.; Doubleday, C.; Zimmt, M.B.; Turro, N.J. *Tetrahedron Lett.*, **1986**, 27, 4675.
11. For similar structures of cyclodextrin inclusion complexes: see a) Reddy, G.; Ramamurthy, V. *J. Org. Chem.*, **1987**, 52, 3952 and 5521. b) Kobayashi, N *J. Chem. Soc., Chem. Comun.*, **1989**, 1126.