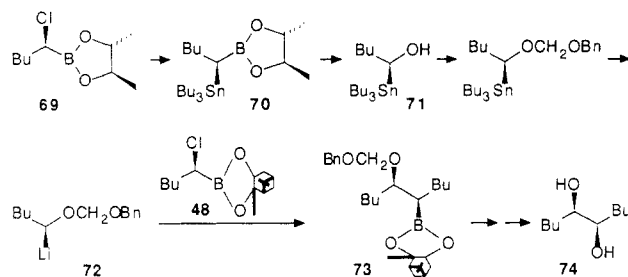vening steps are stereospecific.

The reason the 2,3-butanediol ester **69** was used for the preparation of the tin compound **70** was that the pinanediol ester **48** proved unsuitable, apparently because of steric hindrance. The reaction of **48** with (tributylstannyl)lithium yielded a mixture of products, and attempted deboronation of the impure intermediate to the α-tributylstannyl alcohol **70** failed.

In recent work, we have repeated the foregoing scheme with DIPED esters throughout. The (*S,S*) enantiomer of **73** was obtained without any evidence of meso diastereomer at the ~1% detection threshold.[28]

Concluding Remarks

Our new highly stereoselective method of chiral synthesis is clearly powerful and wide ranging. In terms of the variety of groups permitted on the chiral carbon and the combinations of functionality that can be assembled easily on adjacent chiral carbons, it is the most general directed asymmetric synthesis known.

The cost of generality is that each chiral carbon has to be introduced separately. However, alternative chiral syntheses require approximately the same number of steps. The Masamune–Sharpless sugar synthesis[38] and the chiral aldol condensation[51,52] each introduce two chiral centers in one operation, but that has to be preceded by an operation to produce an olefin of controlled geometry. The total number of steps required in order to produce a finished pair of chiral centers is about the same with our method as with each of the others, and which method is most efficient in a given situation depends on the details of the target structure and available starting materials.

The organolithium and magnesium reagents used in our syntheses are inherently costly, and requiremer.'s for low temperatures add an additional cost. Hor·*·'er, we have generated (dihalomethyl)lithiums frc ʌ �magnesiumDA and dihalomethane with in situ capture by ṭ.ɔrate or boronate esters at temperatures up to –5 °C.[26,53] Borate esters are inexpensive.

We look forward to future applications of this chemistry to syntheses of greater complexity.

(51) (a) Masamune, S.; Kaiho, T.; Garvey, D. S. *J. Am. Chem. Soc.* **1982,** *104,* 5521–5523. (b) Masamune, S.; Lu, L. D.-L.; Jackson, W. P.; Kaiho, T.; Toyoda, T. *J. Am. Chem. Soc.* **1982,** *104,* 5523–5526.
(52) Evans, D. A.; Vogel, E.; Nelson, J. V.; Taber, T. R. *J. Am. Chem. Soc.* **1981,** *103,* 3099–3111.
(53) Matteson, D. S.; Sadhu, K. M. U.S. Patent 4 529 309, June 25, 1985.

Photochemistry and Photophysics within Cyclodextrin Cavities

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Cyclodextrins (CDs) are cyclic oligosaccharides that possess internal cavities capable of complexing hydrophobic organic and organometallic molecules in aqueous solution. The physical chemistry of complexation by CDs has been extensively studied.[1] Three distinct CDs are commonly available, each having a slightly different cavity diameter: α-CD (cyclohexaamylose), with a 6.5-Å cavity; β-CD (cycloheptaamylose), with 7.5-Å cavity;

and γ-CD (cyclooctaamylose), with a 9.0-Å cavity. These molecules are shaped like truncated cones, with a smaller and a larger diameter opening at, respectively, the primary hydroxyl and the secondary hydroxyl faces of the cyclic sugar network. The interior of the cavities is lined with ether oxygens and presents a relatively hydrophobic surface to an incoming guest. The guest is stabilized within the cavity of all the CDs primarily by hydrophobic forces. The variable cavity diameter of the CDs has been used advantageously to sequester guests based on their size: e.g., simple benzene derivatives fit easily within α-CD, while larger aromatics can be accommodated within β-CD (e.g., naphthalene) or γ-CD (pyrene).

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David F. Eaton was born in Peterborough, NH, in 1946. He received his A.B. degree from Wesleyan University, where he did undergraduate research with the late Peter Leermakers. He obtained his Ph.D. in 1972 from the California Institute of Technology, working with George Hammond. Before joining Du Pont in 1973, he spent a postdoctoral year with T. G. Traylor at the University of California at San Diego.

(1) (a) Bender, M. L.; Komiyama, M. *Cyclodextrin Chemistry;* Springer-Verlag: New York, 1978. (b) Saenger, W. *Angew. Chem., Int. Ed. Engl.* **1980,** *19,* 344. (c) Breslow, R. *Science (Washington, D.C.)* **1982,** *218,* 532. (d) Tabushi, I. *Acc. Chem. Res.* **1982,** *15,* 66. (e) Saenger, W. In *Inclusion Compounds;* Attwood, J. L., Davies, J. E., MacNicol, D. D., Eds.; Academic: New York, 1984; Vol. 2, p 231. (f) D'Souza, V. T.; Bender, M. L. *Acc. Chem. Res.* **1987,** *20,* 146.

In studies of solid-state photochemistry,[2] it has been recognized that the topochemical relations among neighboring molecules and atoms dictate the outcome of photochemical excitation. This is less true for photoreactions conducted in other organized media, such as liquid crystals, micelles, silica surfaces, and zeolites, because the degrees of freedom are greater.[3] Similarly, photochemistry within CD cavities involves features quite distinct from those of crystalline solids and, to some extent, from those of other organized media as well. The interior of the cavity constitutes an isolated environment. The restricted shape and size of the cavity geometrically constrain the guest and can stabilize conformations that are less favored in free solution. CDs, in principle, can play a useful role in regulating the traffic of the incoming chemical reagents or reactive intermediates toward certain accessible positions of the entrapped species by encircling and hence protecting the rest of the reactive sites with its molecular network. The hydrophobic nature of the cavity can affect photoprocesses that are sensitive to solvent polarity or dielectric properties. Finally, since included species are usually present only as single molecules within the cavity, photochemistry is restricted to intramolecular events, except in cases of multiple occupation of cavities. These features offer opportunities to the photochemist to use the CD cavity as a vehicle to focus experiments only on certain specific aspects of a mechanistic problem and to use it as a microvessel to carry out selective phototransformations. Cyclodextrins have been used successfully as enzyme models[1c,d,f] but their applications in photochemistry have hardly been explored.

We have been exploring the use of CDs as hosts to examine photochemical and photophysical processes that occur in molecules complexed within them and especially to compare behavior when bound to that which occurs in solutions and in the solid state. Furthermore, we have also used this approach to modify the basic optical properties of molecules. Such a systematic study we hope will help in understanding, predicting, and controlling the chemical and physical properties of organic molecules included in CD.

Modification of Photophysical and Photochemical Processes by Cyclodextrin

Conformational Control. Conformationally flexible molecules containing multiple loci for excitation present a great challenge to the photochemist to unravel the complex interplay between structure and reactivity. CDs can aid the photochemist in this endeavor by allowing the formation of conformationally rigid complexes that effectively isolate a conformer for casual

(2) (a) Ramamurthy, V.; Venkatesan, K. *Chem. Rev.* **1987**, *87*, 433. (b) Schmidt, G. M. *Pure Appl. Chem.* **1971**, *27*, 647. (c) Cohen, M. D.; Green, B. S. *Chem. Br.* **1973**, *9*, 420. (d) Thomas, J. M. *Philos. Trans. Roy. Soc. London* **1974**, *277*, 251. (e) Thomas, J. M.; Morsi, S. E.; Desvergne, J. P. *Adv. Phys. Org. Chem.* **1977**, *15*, 63. (f) Thomas, J. M. *Pure Appl. Chem.* **1979**, *51*, 1065. (g) Addadi, L.; Ariel, S.; Lahav, M.; Leiserowitz, L.; Popovitz-Biro, R.; Tang, C. P. *Chemical Physics of Solids and Their Surfaces*, Specialist Periodical Reports; Royal Society: London, 1979; Vol. 8, p 202. (h) Schmidt, G. M. J., et al. *Solid State Chemistry*; Ginsburg, D., Ed.; Verlag Chemie: New York, 1976. (i) Desiraju, G., Ed. *Organic Solid State Chemistry*; Elsevier: New York, 1987.

(3) (a) For recent examples, see: Tetrahedron Symposium-in-Print No. 29, *Organic Chemistry in Anisotropic Media*; Scheffer, J., Ramamurthy, V., Turro, N. J., Eds.; *Tetrahedron* **1987**, *43*(7), 1197–1745. (b) Kalyanasundaram, K. *Photochemistry in Microheterogeneous Systems*; Academic: New York, 1987.

Scheme I

Scheme II
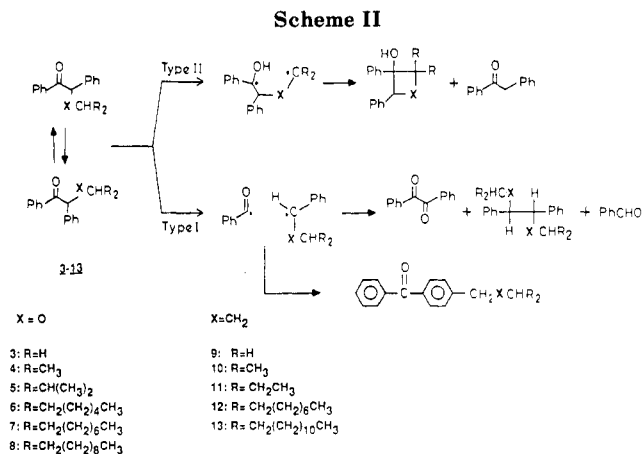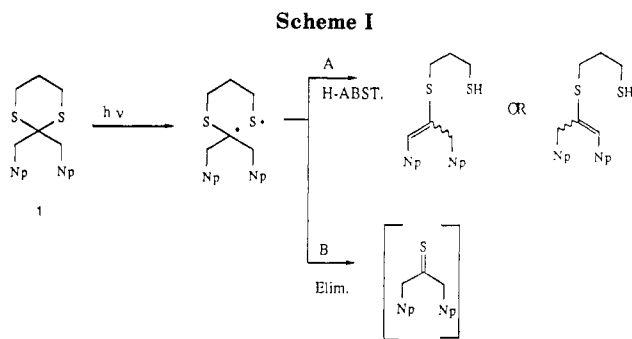
Table I
Photophysical Parameters for
1,1′-Bis(α-methylnaphthyl)dithiane (1) and Related Model Compounds

quantity[a]	1-methyl-naph-thalene	1,3-di(1′-naphthyl)-propane	1-(α-methyl-naphthyl)-dithiane (2)	1,1′-bis(α-methyl-naphthyl)-dithiane (1)
ϕ^f_{Np}	0.2	$(0.022)^b$	0.023	0.022
τ^f_{Np}, ns	76.6	8	5.1	3.75
ϕ^f_{ex}		$(\sim0.02)^b$		0.039
τ^f_{ex}, ns		32		69.8
$k_{M\to ex}$, s^{-1}		1.2×10^8		3×10^8
ϕ^P(77 K)	0.023		0.20	0.27
τ^P, s	2.1		0.6	0.5

[a] ϕ^f, ϕ^P: quantum yield for fluorescence and phosphorescence, respectively. τ^f, τ^P: lifetime for fluorescence and phosphorescence, respectively. $k_{M\to ex}$: first-order rate constant for formation of eximer. [b] Estimated from lifetimes and l_{ex}/l_M data.[5]

study. Several examples are presented in this section illustrating this most valuable feature of CDs. In this discussion and those that follow, we have benefited from use of CPK space-filling models and some computer modeling, which is not discussed in detail.

A rich example is found in the photochemistry of 1,1′-bis(α-methylnaphthyl)-1,3-dithiane (1).[4] The molecule is one of the family of 1,3-dinaphthylpropanes[5] that are well-known for their ability to form excimers through conformational motions that bring the two naphthyl groups into face-to-face orientation. In addition, 1 possesses a relatively electron-rich region in the dithiane portion of the molecule[6] that can act as a potential site for photoredox interactions for excited

(4) Arad-Yellin, R.; Eaton, D. F. *J. Am. Chem. Soc.* **1982**, *104*, 6147.

(5) DeSchyrver, F. C.; Collart, P.; Goedeweeck, R.; Swinnen, M.; Vander Auweraer, M. *Acc. Chem. Res.* **1987**, *20*, 159.

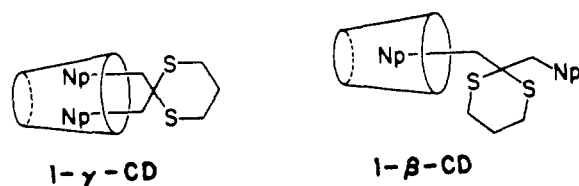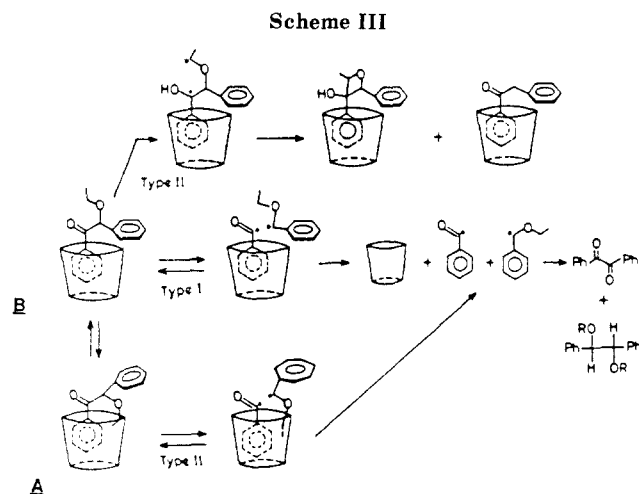(6) The ionization potential of 1,3-dithiane is 8.33 eV: Bock, H.; Wagner, G. *Angew. Chem., Int. Ed. Engl.* **1972**, *84*, 119.

Figure 1. Complexes formed between 1 and β- and γ-CD.

Scheme III

naphthalene chromophores acting as electron acceptors. We anticipated that the photochemistry and photophysics of 1 would reflect the availability of the various conformations, e.g., sickle- and U-conformations, that could be attained. The observed photochemistry of 1 in hydrocarbon solution (300-nm excitation) is depicted in Scheme I. Spectroscopic evidence for interaction between the naphthyl chromophore and the dithiane unit is found in the photophysics of 1[7] and model systems designed to probe the multichromophore nature of 1. Table I lists photophysical parameters observed for 1, 1-methylnaphthalene, and 1-(α-methylnaphthyl)dithiane (2), a molecule containing only one naphthyl chromophore. Compound 1 exhibits emission both from naphthyl-localized chromophores (near 320 nm) and from excimers (near 400 nm). The photophysical data imply, however, that the naphthyl-localized emission (which is the original locus of excitation in 1) is diminished not only by quenching, which leads to excimers, but also by interactions with the sulfur atoms, which can lead to charge-transfer photochemistry.

The effect of introducing cyclodextrin complexation into the photochemistry of 1 is dramatic and depends on the cyclodextrin used. Complexes are formed between 1 and both β- and γ-CD (Figure 1). The complex between 1 and γ-CD is photoinert under conditions in which 1 itself would be converted to its characteristic products. The emission of the complex 1–γ-CD does not show naphthyl-localized emission, but only emits in the region 400–480 nm associated with the excimer emission of 1. In addition, this long-wavelength emission is inefficiently quenched by air or oxygen: its lifetime is long (50–70 ns in deaerated water with only a small decrease to 46–58 ns on introduction of air). These facts led us to conclude[7] that the complex incorporated both naphthyl groups of 1 inside the γ-CD cavity in a face-to-face orientation.[8] In support of this,

an induced circular dichroism was observed in 1–γ-CD in absorption.[9]

The situation is different for the 1–β-CD complex, since the size of the β-CD cavity is too small to accommodate both naphthalene units. A 1:1 complex between 1 and β-CD was isolated. The emission of 1–β-CD in aqueous solution is similar to the naphthalene chromophore localized emission of 1 in hexane. No excimer-like emission is observed. The emission lifetime of 1–β-CD is biexponential, with equal amplitudes observed for each of the two lifetimes. One of the lifetimes is long (55 ns, degassed) and it remains long (46 ns) in air, while the other is short and is strongly quenched by introduction of air (4.4 ns, degassed; 2.6 ns in air). This complex is best represented as one in which one naphthalene chromophore is inside and one outside the β-CD cavity. This picture is especially attractive because it differentiates the two formerly degenerate chromophores of 1. The chromophore that is inside the CD cavity is protected from external quenching by oxygen. The lifetime is similar to that of 1-methylnaphthalene inside β-CD: 39 ns, degassed; 34 ns in air. This protection, however, also prevents the cavity-bound naphthalene from interacting with the electron-rich sulfur portion of the molecule. The unprotected naphthalene is capable of such interaction, which explains its short lifetime. Consistent with this, we find that 1–β-CD is photoactive. The interesting and important question of whether energy transfer occurs between the differentiated chromophores remains open.

The above example illustrates how CD complexation can drastically alter the photophysical behavior of a complex multichromophoric molecule. We anticipate that this technique could be used to advantage to study energy transfer between the similar yet environmentally different chromophores of a single molecule. Yet another consequence of conformational control by CD could be on the chemical reactions undergone by the included molecules. Such examples are presented below.

A remarkable effect was observed on the photochemistry of benzoin alkyl ethers upon complexation to β-cyclodextrin.[10] Benzoin alkyl ethers are known[11] to undergo Norrish Type I reaction as the major photoprocess in isotropic organic solvents. The competing Type II reaction, though feasible in these substrates, is not observed to any significant extent (Scheme II). Benzoin ethers 3–5 readily formed stable ($K_d \sim 10^{-4}$ M) and water-soluble complexes with CD. Although no definite information on the structure of the complex could be obtained, proton NMR studies in aqueous solution revealed that one of the phenyl rings is positioned in the cavity of the CD. Chemical analysis indicated the complex in each case to be 1:1.

The solid complexes of 3–5 upon irradiation yielded only the Type II products in near-quantitative yields. This is in sharp contrast to their behavior as crystalline

(7) Arad-Yellin, R.; Eaton, D. F. *J. Phys. Chem.* **1983**, *87*, 5051.

(8) A similar complex was reported by Turro and co-workers: Turro, N. J.; Okubo, T.; Weed, G. C. *Photochem. Photobiol.* **1982**, *86*, 4422.

(9) CD spectra were obtained by Dr. A. Zask in the laboratory of Professor Nakanishi at Columbia University. D.F.E. thanks them for these experiments.

(10) (a) Dasaratha Reddy, G.; Usha, G.; Ramanathan, K. V.; Ramamurthy, V. *J. Org. Chem.* **1986**, *51*, 3085. (b) Dasaratha Reddy, G.; Ramamurthy, V. *J. Org. Chem.* **1987**, *52*, 3952.

(11) Lewis, F. D.; Lauterbach, R. L.; Heine, H. G.; Hartman, W.; Rudolph, H. *J. Am. Chem. Soc.* **1975**, *97*, 1519.

solids and in benzene. Crystals of **3–5** were photostable, consistent with their X-ray crystal structure.[12a] An inspection of Scheme III reveals that out of the two possible representative conformations A and B available for these substrates, only B is capable of undergoing the Type II process. The preferable complexation of this conformation in the CD cavity would account for the substantial difference. The observation of the Type II process from conformation B, trapped inside the CD cavity, is possible only when the competing Type I reaction is suppressed by the cage effect of the cavity. This is indeed the case as shown by the results of the photolysis of solid complexes in an aerated atmosphere. Under this condition oxygen-trapped products of the initially formed Type I radicals were isolated.

The photolysis of the aqueous solutions of the above complexes in the presence of a large excess of CD afforded a mixture of the Type I and the Type II products.[11] The fact that the Type I products are obtained in more than 90% yield suggests that the cage effect is small in aqueous solution. This is also supported by the relative quantum yields measured between benzene and aqueous solution (1:0.6). The low cage effect in water is not totally unexpected since in a 1:1 complex, a part of the molecule would be free to diffuse away after fragmentation (Scheme III). Thus, while in the aqueous phase, the included molecule enjoys a certain amount of freedom, but this is prevented in the solid complex due to tight packing. Therefore, selectivity is seen in the two media because of the different degrees of freedom that exist in them.

Some chemical evidence supports the above conformational control hypothesis in the absence of firm X-ray structural evidence.[12b] On the basis of the behavior of the short-chain alkyl benzoin ethers, we anticipated that long-chain alkyl ethers would exhibit different behavior. It was speculated that a longer alkyl chain would prefer to reside inside the cavity and therefore conformation A would be preferred instead of B preferred by short chains (Scheme III).[10b] In such a case even in the presence of cage control there is no possibility of observing the Type II process. Results obtained with **6–8** (Scheme II) support this role of conformational control by the CD cavity. Photolysis of the complexes of **6–8** both in aqueous solution and in the solid state gave mostly the Type I products (benzil, benzaldehyde, and pinacol ethers) and differences between benzene and aqueous solutions were small, indicating that these molecules when present in the cavity are unable to attain a conformation required for γ-H abstraction.

Another example of conformational control is provided by alkyl deoxybenzoins **9–13** (Scheme II).[13] The Type II pathway, which is generally the major reaction in benzene, was further enhanced in aqueous CD solution, and the behavior of **9–13** resembled that of benzoin alkyl ethers, a closely analogous system. Predictable behavior observed with several alkyl deoxybenzoins on the basis of the understanding of the benzoin alkyl ethers provides encouragement for the use of CDs as media for chemical reaction.

(12) (a) Kanagapushpam, D.; Venkatesan, K.; Ramamurthy, V. *Acta Crystallogr.* 1988, *C44*, 894. (b) Kanagapushpam, D.; Venkatesan, K.; Ramamurthy, V., unpublished results.

(13) Dasaratha Reddy, G.; Ramamurthy, V. *J. Org. Chem.* 1987, *52*, 5521.

Scheme IV

14: R= CH₃
15: R= CH₂CH₃
16: R= CH₂(CH₂)₂CH₃

Scheme V
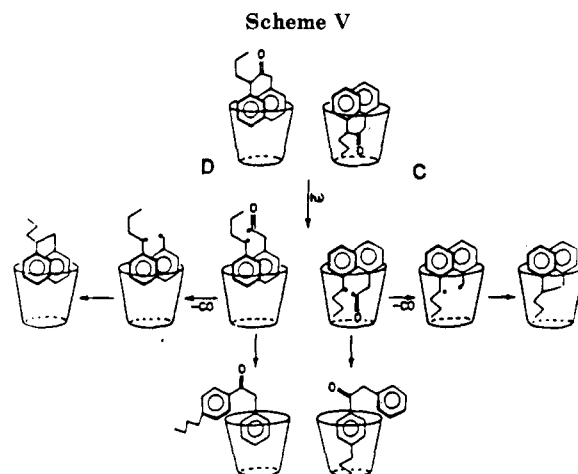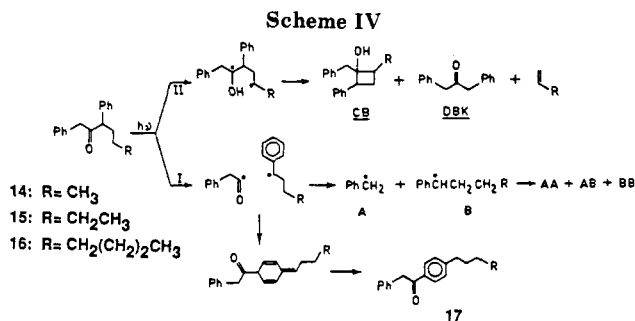
A comparison between the α-alkyl deoxybenzoins and the α-alkyl dibenzyl ketones[14] highlights the differences in the conformational preferences between 1,2-diphenyl and 1,3-diphenyl systems by the cavity of CD. α-Alkyl dibenzyl ketones (**14–16**; Scheme IV) gave products resulting from the Norrish Type I and Type II reaction in benzene and methanol. Irradiation of aqueous solutions of their CD complexes yielded only the Type I derived products. Unexpectedly, a rearrangement product—the α-phenyl acetophenone derivative **17**—dominated the product mixture. Further, only the cage product, AB, was obtained among the three possible diarylethanes. Photolysis of the solid complex gave only AB. The absence of Type II products both in aqueous solution and in the solid state suggests that CD imposes a conformation on α-alkyl dibenzyl ketones that is not suitable for γ-hydrogen abstraction.

The photochemical behavior in the cavity can be understood on the basis of conformations C or D (Scheme V). Chemical analysis indicated the complex to be 1:1. According to Scheme V the primary radical pair generated after cleavage would be compelled to undergo recombination either with or without rearrangement. Further, decarbonylation would result in the benzyl radical fragments trapped inside the cavity leading to the observed AB. The absence of quenching by cupric chloride suggests that both the primary and the secondary radical pair do not escape into the aqueous phase, but instead spend their entire lifetime inside the cavity of CD.

It is important to note that the preferred conformations for 1,2-diphenyl and 1,3-diphenyl systems in the cavity of CD are not the same. It is likely that due to structural restrictions, the two phenyl rings of 1,2-di-

(14) Nageshwer Rao, B.; Syamala, M. S.; Turro, N. J.; Ramamurthy, V. *J. Org. Chem.* 1987, *52*, 5517.

phenyl systems (benzoin ethers and deoxybenzoins) cannot achieve a near-parallel arrangement such that both the phenyl rings can enter the cavity. On the other hand, 1,3-diphenyl systems can achieve the required arrangement and thus easily enter into the cavity of CD. Where space is available (γ- vs β-CD) preference for U-conformations in 1,3-dinaphthyl system 1 was also observed. We speculate that one reason for preference of such a crowded conformation by CD is the need to expose less molecular area to the aqueous exterior when these complexes are present in water.

Microenvironmental Effect. The microenvironment inside and outside the CD cavity is not expected to be the same. Such a variation can have interesting consequences on the photobehavior of included molecules as illustrated with two examples below.

Pioneering work by Weller[15] established that simple aromatic alcohols become strong acids on photoexcitation. β-Naphthol is a prototype of such materials. Dual emission is observed for solutions of β-naphthol in aqueous media of appropriate pH. One emission is associated with the alcohol itself, and the other with the deprotonated alcoholate anion formed in an adiabatic manner. We have examined the influence of added β-CD on the photophysics of β-naphthol.[16,17]

At pH 7.1, β-CD binds β-naphthol with a dissociation constant of 9×10^{-3} M and does not bind β-naphthoate anion as determined by the fluorescence measurements on addition of the CD. Our examination of the time-correlated emission of the β-CD–β-naphthol complex indicates that the photophysics of the complex is entirely different from the emission of naphthol in water. No multiple exponential, rise-and-fall kinetics, anticipated for the formation of β-naphthoate in an adiabatic reaction from excited naphthol, is observed. Only a single-exponential decay from an emission centered at 340 nm is observed. The lifetime is 7.2 ns, longer than that (4.8 ns) expected for β-naphthol in water and shorter than that (9.1 ns) of β-naphthoate emitting at 420 nm in water.[17c] We concluded that the excited β-naphthol included in β-CD does not deprotonate (or if it does deprotonate, the rate is so much slower than the normal aqueous rate as to be unobservable within the lifetime of the alcohol).

The lifetime we observe for the complex is somewhat larger than the value for β-naphthol in nonaqueous, but protic solvents such as methanol (5.9 ns),[18] but smaller than that in ethanol (8.9 ns) or the aprotic solvent cyclohexane (13.3 ns).[19] Deprotonation of β-naphthol does not occur in methanol or ethanol on excitation. The lifetime we observe is also identical with the value

for the radiative lifetime, $(k_f + k_{nr})^{-1}$, in the absence of proton transfer, determined for β-naphthol by Laws and Brand.[17c] We therefore conclude that in the β-CD–β-naphthol complex there is complete suppression of the prototropy and that the lifetime observed reflects the inherent radiative and nonradiative decay of the molecule included in the cavity. It follows that the cavity environment is very similar to that of an alcohol solvent,[20] as probed by β-naphthol. We also conclude that the basicity of the cavity is too low to accept a proton from excited β-naphthol.

Another example relates to polyene photochemistry. On the excited-state surface there is a competition between geometric isomerization and 1,5-H migration in many ionone derivatives.[21] β-Ionone, β-ionylidene aldehyde, and other derivatives readily formed complexes with β-cyclodextrin.[22] While in β-ionone (18), and in β-ionylidene aldehyde (19) there was a remarkable preference for H migration as the cyclodextrin complex in aqueous solution, β-ionylidene nitrile (20) and β-ionylidene ethyl ester (21) exhibited no difference in their behavior between organic solvents and cyclodextrin complex. Points of interest in this context are that the isomerization and the hydrogen migration originate from different excited states, and out of these four compounds only 18 and 19 are known to exhibit solvent-dependent photobehavior.[23] A close examination of the absorption spectra of the cyclodextrin complexes of β-ionone and β-ionylidene aldehyde reveals that there is a switch in the excited-state ordering (nπ* and ππ*), probably due to the polarity experienced by the molecule inside the cavity. Such an effect was not noticed in the other two cases because of the large energy difference between these states in those systems. So, as for β-naphthol, in the β-ionyl series the cavity influences the photobehavior of the included molecule through its microenvironmental effect.

Site Selectivity (Molecular Traffic Control). Of the many different ways in which CD could influence a chemical reaction, one would be by sterically blocking certain potential sites of the substrate from intermo-

Scheme VI

(15) (a) Weller, A. *Z. Phys. Chem.* 1958, 17, 224. (b) Weller, A. In *Progress in Reaction Kinetics*; Porter, G., Ed.; Pergamon: New York, 1961; Vol. 1, p 187.
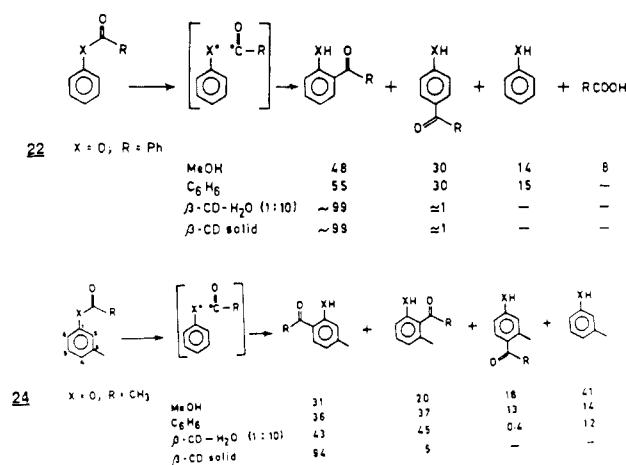
(16) Eaton, D. F. *Tetrahedron* 1987, 43, 1551. Similar studies on steady-state emission of β-CD/β-NpOH were reported by Yorozu and co-workers: Yorozu, T.; Hoshino, M.; Imamura, M.; Shizuka, H. *J. Phys. Chem.* 1982, 86, 4422.

(17) The use of β-naphthol to examine local solute environment has been discussed extensively by others: (a) Huppert, D.; Klodny, E. *Chem. Phys. Lett.* 1981, 63, 401. (b) Harris, C. M.; Selinger, B. K. *J. Phys. Chem.* 1980, 84, 891. (c) Laws, W. R.; Brand, L. *J. Phys. Chem.* 1979, 83, 795. (d) Kishi, T.; Tanaka, J.; Kouyama, T. *Chem. Phys. Lett.* 1976, 41, 497. (e) Amire, S. A.; Burrows, H. D. *J. Chem. Soc., Faraday Trans. 1* 1982, 78, 2033. (f) Lemmetyinen, H.; Demayashkevich, A. B.; Kuzmin, M. G. *Chem. Phys. Lett.* 1980, 73, 98.

(18) Lee, J.; Griffin, R. D.; Robinson, G. W. *J. Chem. Phys.* 1985, 82, 4920.

(19) Berlman, I. *Handbook of Fluorescence Spectra of Aromatic Molecules*; Academic: New York, 1971.
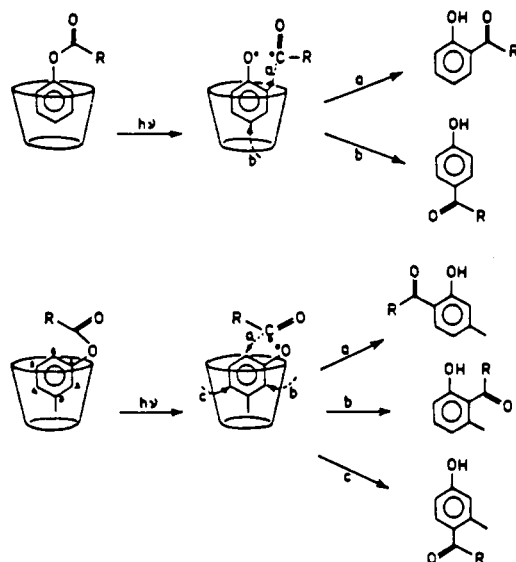
(20) Similar conclusions have been reached by others: (a) Cox, G. S.; Hauptmann, P. J.; Turro, N. J. *Photochem. Photobiol.* 1984, 39, 597. (b) Heredia, A.; Requena, G.; Sanchez, F. G. *J. Chem. Soc., Chem. Commun.* 1985, 1814.

(21) Liu, R. S. H.; Asato, A. E. *Tetrahedron* 1984, 40, 1931.

(22) Arjunan, P.; Ramamurthy, V. *J. Photochem.* 1986, 33, 123.

(23) Ramamurthy, V.; Denny, M.; Liu, R. S. H. *Tetrahedron Lett.* 1981, 22, 2463.

Scheme VII

Scheme VIII

lecular attack by their very mode of complexation.[24] Unimolecular rearrangements that involve an initial cleavage followed by reorganization of the fragments will give rise to one particular isomer specifically when conducted in CD. We have succeeded in exploiting this unique feature of CD complexation in the photo-Fries, photo-Claisen, and related rearrangements.

The well-known photo-Fries rearrangement[25] of phenyl esters and anilides in organic solvents yields a mixture of the *o*- and *p*-phenolic or anilinic ketones via a radical pathway. Selective attack of the initially formed acyl radical at the ortho position of the aromatic ring, with a complete prohibition of the para attack, could be achieved by irradiating ester **22** (and the anilide analogue, **23**, X = NH, R = Ph) as the solid β-cyclodextrin complex or in aqueous solutions containing an excess of β-cyclodextrin (Scheme VI).[26] Even more intriguing were results with complexes of the corresponding *m*-methyl esters and anilides. Ester **24** (and the anilide **25**, X = NH, R = Me), which form a mixture of two ortho- and para-rearranged product when photolyzed in organic solvents revealed not only a complete prohibition of the para rearrangement but also a remarkable preference for one among the two ortho-isomers (Scheme VI) upon encapsulation by β-cyclodextrin (either in the solid state or in aqueous solution). This demonstrates how the acyl radical traffic can be directed toward the only exposed ortho position of the aromatic ring, in a suitably designed complex (Scheme VII).

A tight fit between the host and the guest molecules would be expected to be necessary to bring about maximum selectivity in photoreactions. Results obtained in the photo-Claisen rearrangement[27] of *m*-alkoxyphenyl allyl ethers highlight the importance of this criterion. Of the two possible ortho isomers and the para isomer that are formed during photolysis of *p*-(*n*-propyloxy)phenyl allyl ether (**26**) in organic solvents,

only one ortho isomer was obtained with a remarkable selectivity upon irradiation of the α-cyclodextrin complexes of these substrates. At the same time, the β-cyclodextrin complexes of the same substrates did not yield any significant selectivity. While α-cyclodextrin, with a smaller cavity was able to bring about selectivity, the larger cavity of β-cyclodextrin failed to hold the molecule tightly. The tight fit necessary for achieving selectivity in β-cyclodextrin can be provided simply by increasing the space-filling capacity of the substrate, e.g., by adding a long alkyl chain.[27] Such a strategy has been used by us successfully during the rearrangement of several benzyl phenyl ethers and *m*-alkoxyphenyl esters.[28]

Restriction of Rotational Motion. The CD sleeve that surrounds the guest molecule may not remain physically inert during a photoreaction as seen in the examples below. When a certain mode of decay of an intermediate demands a large degree of perturbation via a rotational motion, the inflexible wall of CD can, in principle, sterically hinder that reaction from taking place. Such an effect was observed in the excited-state chemistry of stilbenes.[29] Stilbenes, upon excitation, undergo facile geometric isomerization in organic solvents to reach a photostationary state rich in the cis isomer (∼85%).[30] Interestingly, isomerization of *trans*-stilbene is restricted by the CD cavity in aqueous solution. However, under the same conditions isomerization of the cis isomer proceeded uninhibited. The cavity restricts the rotational process, so the photostationary state is rich in trans isomer (70%) instead of cis isomer. This behavior was in contrast to that of alkyl cinnamates, where the photostationary state reached in CD was the same as in organic solvents. The restriction of the geometrical isomerization in the case of stilbenes can be attributed to the effect of the CD wall on the 90° twisted intermediate, sterically preventing it from undergoing further rotation to the cis isomer. The cinnamates, with substituents of smaller dimensions, do not experience any retardation to isomerization in CD. A similar effect has recently been reported during the photoisomerization of azobenzene.[31]

The 1,4-biradical that forms as an intermediate in the Norrish Type II reaction has two modes of further reaction, fragmentation and cyclization.[32] The triplet
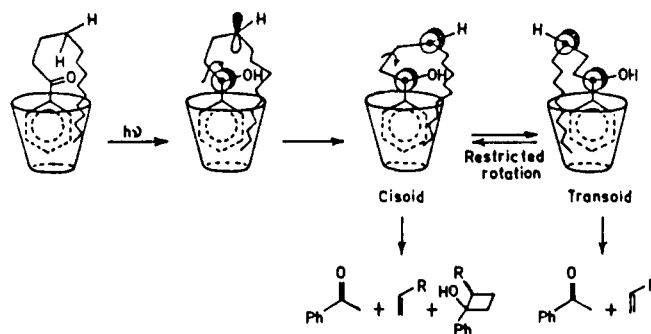
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biradical, which is formed in the cisoid geometry, readily equilibrates with the transoid form, which is more favored in hydroxylic solvents. Intersystem crossing generates the singlet biradical that "remembers" the conformation of the corresponding triplet, and hence the ensuing products reflect the conformational preferences of the triplet biradical. The transoid form can undergo only fragmentation, while the cisoid form can also cyclize to give a cyclobutanol. The equilibrium between the cisoid and the transoid geometries, which lies in favor of the transoid geometry in organic solvents, can be shifted in favor of the cisoid form in CD by the introduction of a long alkyl chain. This anchors the molecule in the cisoid form (Scheme VIII) and brings about increased cyclization at the expense of fragmentation. This was observed in the case of a number of arylalkyl ketones.[33] On the basis of the above arguments, an increase in the alkyl chain length should bring about an increased yield of the cyclized product by arresting the cisoid to transoid conversion progressively as chain length increases. This was also observed.

Molecular Alignment. As part of an evolving interest in materials for nonlinear optical applications, we have employed CDs to organize included species in the solid state. We believe that solid-state composite materials such as those we describe here and others we have prepared in related work[34] represent an alternative to Langmuir–Blodgett films or single-crystal methods to organize molecules.

Organic materials have been observed to possess highly attractive second-order molecular hyperpolarizabilities.[35,36] This molecular attribute is a direct consequence of the highly delocalized nature of electron distributions in classes of organic molecules possessing strong, low-lying charge-transfer excited states. However, simply designing a molecule with strong charge-transfer character is not sufficient to ensure that the bulk solid material will exhibit one important nonlinear optical property, second harmonic generation. This application allows incident coherent radiation from a laser to be converted, with efficiencies that can approach 80% in practice, to light of half the wavelength (twice the frequency) of the input wave. A physical requirement for frequency-doubling solids, which results from the tensor mathematics that govern the process, is that the doubling material must be noncentrosymmetric. Unfortunately, the vast majority of organic molecular, crystalline solids (nearly 85%) are centrosymmetric and are incapable of acting as second harmonic generation (SHG) materials.[37] We desired a methodology that would allow us to systematically study organic and organometallic materials for nonlin-

ear optics. We saw such an opportunity in solid inclusion complexes, including cyclodextrin complexes.

Cyclodextrins are chiral materials and are therefore acentric, and, equally important, the environment experienced by an included guest is also acentric. We reasoned that any CD complex should be capable of SHG, so that systematic study should be feasible. This proved to be the case.[38]

For a series of β-CD complexes of aromatic donor-acceptor molecules, we observed SHG for incident 1.06-μm light from a Nd-YAG laser. Efficiencies, relative to a common organic standard, urea, were as follows: p-nitroaniline, 2–4 × urea (the range of values depended on the preparation); p-(dimethylamino)-cinnamaldehyde, 0.37×; p-(dimethylamino)benzonitrile, 0.015×.[38] β-CD itself exhibits an SHG signal only 0.001 times that of urea. The major point of the results is not that the numbers are especially large, but that they are nonzero. The technique of complexation is able to induce acentricity in the samples to the point at which it is macroscopically observable. Uncomplexed materials are incapable of SHG. Within the series, trends can be noted that suggest that complexes of molecules with more CT character exhibit higher SHG, but this result can be misleading, since the SHG signal samples bulk solid properties and not molecular properties. That is, one must know the solid-state structure of each complex in order to compare with confidence the SHG values within a series. We have not determined X-ray crystal structures for any of the complexes above. However, we have done so for other inclusion complexes that involve hosts such as tris(o-thymotide) or thiourea.[34,39] The structures examined to data have all been polar solids in which dipolar alignment of the hyperpolarizable guest has been effected. We view this inclusion methodology as an intriguing new way to organize chromophores (or in this case, nonlinear "optiphores") in three-dimensional space in specific orientations.

Summary and Projections for the Future

This Account has illustrated ways in which complexation of organic molecules by cyclodextrins can alter their fundamental optical properties. Conformational equilibria can be influenced, leading to new products not found in isotropic media. Complexation can directly influence radiationless processes, by affecting the molecular environment. Finally, in the solid state, molecular alignment can be effected, to yield interesting nonlinear optical properties. We are confident that other effects will be discovered in the future. Stereoselection, bimolecular events, and effects of substituents on the CD itself are only just now being investigated. New hosts, synthetic and natural, will provide new media for photochemists and spectroscopists to exploit.

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