in 4 mL of TFA and CH_2Cl_2 (1:1) and stirred at room temperature for 45 min. The reaction mixture was worked up as described in the general procedure.

***cyclo*-[Z-D-Ser-Pro-Gly-Sar-Val-Z-D-Ser-Pro-Gly-Sar-Val] (12).** A solution of the above TFA salt and *N*-methylmorpholine (0.012 mL, 0.10 mmol) in 50 mL of dry THF was added over 3.5 h to an ice-cold, stirred solution of EDC (42 mg, 0.22 mmol) and HOBt (47 mg, 0.35 mmol) in 150 mL of dry THF. After completion of the addition, the reaction mixture was stirred for 1 h at 0 °C and for 4.5 days at room temperature. The solvent was removed in vacuo and the residue was taken up in EtOAc (30 mL). The EtOAc layer was washed successively with water (1 × 15 mL), 1 N HCl (2 × 10 mL), 1 N aqueous $NaHCO_3$ (2 × 10 mL), water (1 × 10 mL), and brine (1 × 10 mL). The solution was then dried (Na_2SO_4) and concentrated in vacuo to yield an oily residue, which on trituration with diethyl ether gave the cyclized product **15** as a white solid (60 mg, 55%). This material was found to be identical (TLC, NMR, and mp) with that obtained from the cyclization of decadepsipeptide **11**.

Racemization Studies. General Procedure. Two to three milligrams of each of the cyclic depsipeptides **2** and **15**, and also the linear decadepsipeptides **12** and **18**, were hydrolyzed (3–4 mL of 6 N HCl, 100–110 °C, 12–13 h) in a sealed glass tube. The solvent was removed under a stream of air. To the residue was added 2 mL of a saturated solution of HCl in 2-propanol and the tube was resealed under nitrogen and heated at 100 °C for 2 h. The solvent was evaporated and the residue was treated at room temperature for 0.5 h with 2 mL of 30% trifluoroacetic anhydride in methylene chloride. The solvent was evaporated completely under a stream of air. The residue was redissolved in dry methylene chloride (1 mL) and a 2-μL sample solution was injected into a gas chromatograph (Hewlett-Packard Model 5880A) to analyze the enantiomeric pairs of amino acids on a chiral phase capillary column.[13] Parallel control experiments were conducted by trating each of D-serine, L-valine, and L-proline (2–3 mg each) to the same sequence of reactions, followed by analysis. No racemization of the chiral residues in the above depsipeptides was observed.

Acknowledgment. Appreciation is expressed to the National Institutes of Health (AI 15759) for support of this research and to the Colorado State University Regional NMR Center (funded by National Science Foundation Grant No. CHE-8208821) for 360-MHz NMR data.

Registry No. **2**, 103131-27-7; **3**, 103131-28-8; **4**, 103131-29-9; **5**, 103131-30-2; **6**, 103131-31-3; **7**, 103131-32-4; **8**, 103131-33-5; **9**, 103131-34-6; **10**, 103131-35-7; **11**, 103131-37-9; **12**, 103131-38-0; **12**·2HBr (deprotected), 103131-55-1; **13**, 103131-39-1; **14**, 103131-40-4; **15**, 103131-41-5; **16**, 103131-42-6; **17**, 103131-43-7; **17**·TFA, 103148-55-6; **18**, 103131-44-8; **19**, 103148-54-5; Z-D-Ser-OH, 6081-61-4; BOC-L-Val-OH, 13734-41-3; BOC-Gly-OH, 4530-20-5; BOC-Gly-OTce, 103131-45-9; Gly-OTce·TFA, 103131-46-0; BOC-L-Pro-OSu, 3392-10-7; BOC-Pro-Gly-OTce, 103131-47-1; Z-Yd-Ser(BOC-Val)-OH, 103131-48-2; Pro-Gly-OTce·TFA, 103131-50-6; Z-D-Ser(BOC-Val)-Pro-Gly-OH, 103131-51-7; BOC-Sar-OTce, 103131-52-8; Sar-OTce·TFA, 103131-54-0; Z-D-Ser(H-Val·TFA)-OCpa, 103131-58-4; BOC-Sar-OH, 13734-36-6; Z-D-Ser(H-Sar-Val·TFA)-OCpa, 103131-60-8; Z-D-Ser(H-Gly-Sar-Val·TFA)-OCpa, 103131-62-0; BOC-L-Pro-OH, 15761-39-4; Z-D-Ser(*N*-(isobutoxycarbonyl)-Pro-Glyu-Sar-Val)-OCpa, 103131-63-1; Z-D-Ser[Z-D-Ser(H-Pro-Gly-Sar-Val·TFA)-Pro-Gly-Sar-Val]-OH, 103131-65-3; *p*-chlorophenacyl bromide, 536-38-9; 2,2,2-trichloroethanol, 115-20-8; (*p*-nitrophenyl)-quinoline-2-carboxylate, 103131-56-2; quinaldic acid, 93-10-7.

Modification of Photochemistry by Cyclodextrin Complexation: Competitive Norrish Type I and Type II Reactions of Benzoin Alkyl Ethers

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The photochemical Norrish type I and type II reactions of cyclodextrin-bound benzoin methyl ether, benzoin ethyl ether, and benzoin isopropyl ether have been investigated in aqueous solution and in the solid state. Irradiation in cyclodextrin media leads to a large change in product distribution from that found in benzene and methanol. In aqueous solution type II products compete with type I, and in the solid state type II products constitute more than 90% of the product distribution. This sensitivity was interpreted as a measure of changes in the ground state distribution of reactive and nonreactive (type II) conformers brought about by cyclodextrin inclusion. Cage effects also play a significant role in altering the product distribution. ^1H NMR and X-ray powder photographic studies provide support for complexation.

The control and modification of reactivity through incorporation of molecules into organized assemblies remains an area of considerable interest. A specific subarea that has attracted recent interest concerns reactivity of molecules incorporated into "host–guest" systems.[1] These studies have paved the way to an intriguing number of possibilities by which photoreactivity can be modified. Cyclodextrins, one of the most commonly used "host" systems possess hydrophobic cavities that are able to include in aqueous solution a variety of organic compounds whose character may vary from hydrophobic to ionic.[2] Internal diameters and depths of cyclohexaamylose or α-cyclodextrin (4.2–8.8 and 7.8 Å), cycloheptaamylose or β-cyclodextrin (5.6–10.8 and 7.8 Å), and cyclooctaamylose or γ-cyclodextrin (6.8–12.0 and 7.8 Å) provide cavities for appropriately sized guest molecules. The recognized potential of cyclodextrin–guest interactions as models for enzyme active sites has prompted numerous investigations of these systems.[3] Although the potential of cyclodextrins as "reaction vessels" for thermal reactions has been widely

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(1) *Inclusion Compounds*, Atwood, J. L., Davies, J. E. D., Mac Nicol, D. D., Eds.; Academic: London, 1984; Vol. 1–3.

(2) Bender, M. L.; Komiyama, M. *Cyclodextrin Chemistry*; Springer Verlag: Weinheim, West Germany, 1978. Szejtei, J. *Cyclodextrin and Their Inclusion Complexes*; Akademiai Kiado: Budapest, 1982. Tabushi, I.; Kuroda, Y. *Adv Catal.* **1983**, *32*, 417.

(3) Tabushi, I. *Acc. Chem. Res.* **1982**, *15*, 66. Saenger, W. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 344. Breslow, R. *Science (Washington, D.C.)* **1982**, *218*, 532.

0022-3263/86/1951-3085$01.50/0

Scheme I

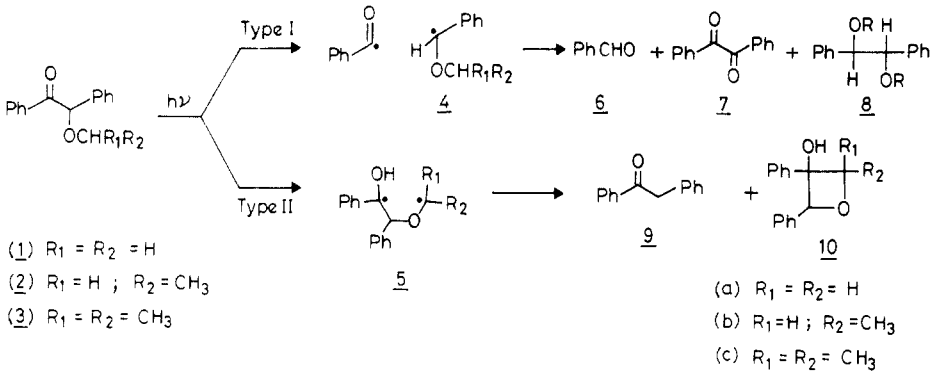


Table I. Variation in the ^{1}H NMR Chemical Shifts of β-Cyclodextrin Protons in the 1:1 Complexes of Benzoin Alkyl Ethers

compound	chemical shifts of β-cyclodextrin protons, δ[a,b]					
	H-1	H-2	H-3	H-4	H-5	H-6
β-cyclodextrin	1359.6	975.7	1059.6	958.4	1030.0	1039.1
β-cyclodextrin complexes						
benzoin methyl ether	1354.4 (−5.2)	978.2 (+2.5)	1038.3 (−21.3)	953.0 (−5.4)	961.5 (−68.5)	1022.5 (−16.6)
benzoin ethyl ether	1357.1 (−2.5)	984.0 (+8.3)	1049.8 (−9.8)	958.3 (−0.1)	994.4 (−35.6)	1034.1 (−5.0)
benzoin isopropyl ether	1359.0 (−0.6)	977.5 (+1.8)	1055.5 (−4.1)	957.8 (−0.6)	1009.8 (−20.2)	1034.5 (−4.6)

[a] Chemical shifts with respect to Me_4Si as reference at 270 MHz. [b] Chemical shift differences ($\delta = \delta_{complex} - \delta_{\beta\text{-CD}}$) are given in parentheses. Negative values denote upfield shift.

acknowledged, their use in photochemical reactions is yet to be fully explored.[4] In this context, we have investigated the photochemical behavior of benzoin alkyl ethers complexed with cyclodextrin.

The photolysis of benzoin alkyl ethers in solution has been extensively studied, and the main details of the reaction have been elucidated.[5] They undergo α–cleavage to form benzoyl–benzyl radical pair, which subsequently undergoes free radical reaction to give, as main products, the pinacol ethers and benzil together with minor amounts of benzaldehyde. γ-Hydrogen abstraction which is the predominant photochemical reaction for α-alkoxy acetophenones[6] ($k_H \simeq 10^9$ s^{-1}) does not compete with the α-cleavage reaction ($k_\alpha \simeq 10^{10}$ s^{-1}) in the case of benzoin alkyl ethers (Scheme I). The absence of the potentially feasible type II hydrogen abstraction in these molecules can be either due to the low occupancy of benzoin alkyl ethers in the necessary cisoid conformation or can be attributed to the inherently high rate and high efficiency of type I process. Cyclodextrin encapsulation, though it may not alter the rate of α-cleavage is expected to increase the probability of recombination of the radical pairs resulting from the type I cleavage.[7] This cage effect would reduce the efficiency of type I product formation. Further, it appeared probable that benzoin alkyl ethers when included in cyclodextrin could adopt the desired conformation for type II reaction. These two features, we anticipated, would allow a reasonable competition between type II and type I reactions. The goal of the present investigation is to probe whether the cyclodextrin encapsulation can impose any conformational control and restricted movement on the guest molecule and thus bring about selective organic transformation. Benzoin methyl ether (**1**), benzoin ethyl ether (**2**), and benzoin isopropyl ether (**3**) have been investigated in this connection, and the results are presented below.

Results

The present study covers two aspects—one concerns the photolysis of benzoin alkyl ethers (**1–3**) bound to cyclodextrin and the other attempts to provide support for the formation of inclusion complexes. Since the complexes of **1–3** with cyclodextrin did not yield suitable single crystals for X-ray crystallographic studies, no such investigation was pursued. Addition of **1–3** to saturated aqueous solutions of β-cyclodextrin precipitated a white solid which dissolves in an excess of water. The X-ray powder pattern of the precipitated white solid differed considerably from those of cyclodextrin and the respective benzoin alkyl ethers. This suggested complexation of **1–3** with β-cyclodextrin. The complex of benzoin methyl ether with β-cyclodextrin was taken as the model for structural analysis of the complex in aqueous solution. The 270-MHz ^{1}H NMR spectra of aqueous solutions of β-cyclodextrin and solutions containing various ratios of the host to the guest were recorded. The cyclodextrin protons were identified in the 270-MHz spectra by their specific coupling pattern.[8] The chemical shifts of β-cyclodextrin protons in the uncomplexed and in the complexed forms were utilized for drawing conclusions regarding the nature of the complex. Figure 1 shows a plot of the chemical shift differences for β-cyclodextrin protons as a function of the ratio of benzoin methyl ether to β-cyclodextrin. In order to obtain information regarding the relative structures of the complexes of the three benzoin alkyl ethers, their ^{1}H NMR spectra

(4) Ohara, M.; Watanabe, K. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 820. Yamada, K.; Kohmoto, S.; Iida, H. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1171. Vekama, K.; Irie, T.; Hirayama, F. *Chem. Lett.* **1978**, 1109. Takeshita, H.; Kumamoto, M.; Kouno, I. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1006. Tamaki, T. *Chem. Lett.* **1984**, 53. Chenevert, R.; Voyer, N. *Tetrahedron Lett.* **1984**, *25*, 5007. Liu, J. H.; Weiss, R. G. *J. Photochem.* **1985**, *30*, 303. Liu, J. H.; Weiss, R. G. *Isr. J. Chem.* **1985**, *25*, 228. Chenevert, R.; Plante, R. *Can. J. Chem.* **1983**, *61*, 1092.

(5) Lewis, F. D.; Lauterbach, R. L.; Heine, H. G.; Hartmann, W.; Rudolph, H. *J. Am. Chem. Soc.* **1975**, *97*, 1519. Adams, S.; Gusten, H.; Schute-Frohlinde, D. *Tetrahedron* **1974**, *30*, 4249. Sander, M. R.; Osborn, C. L. *Tetrahedron Lett.* **1974**, 415. Heine, H. G. *Tetrahedron Lett.* **1972**, 4755. Pappas, S. P.; Chattopadhyay, A. *J. Am. Chem. Soc.* **1973**, *95*, 6484.

(6) Lewis, F. D.; Turro, N. J. *J. Am. Chem. Soc.* **1970**, *92*, 311.

(7) Nageswara Rao, B.; Turro, N. J.; Ramamurthy, V. *J. Org. Chem.* **1986**, *51*, 460. Singh, S.; Usha, G.; Tung, C. H.; Turro, N. J.; Ramamurthy, V. *J. Org. Chem.* **1986**, *51*, 941.

(8) Demarco, P. V.; Thakkar, A. L. *J. Chem. Soc., Chem. Commun.* **1970**, 2.

Table II. Product Distribution upon Photolysis of Benzoin Isopropyl Ether[a,b]

	product distribution, %				
	benzaldehyde	pinacol ether	benzil	deoxybenzoin	oxetanol
benzene	37.3	39.5	23.0		
methanol	27.3	61.7	10.8		
β-CD–solution (1:1)	36.9	48.6	7.2	2.8	4.2
β-CD–solution (5:1)	36.1	44.2	9.2	5.1	5.2
γ-CD–solution (1:1)	36.4	44.8	8.6	5.1	4.7
β-CD–solution (5 °C)	42.8	37.6	4.7	1	15.2
β-CD–solution (55 °C)	33.5	55.2	10.3	1.0	
β-CD–solid[c]	7.0			78.0	15.0
β-CD–solid/oxygen[d]				14.0	1
γ-CD–solid[c]	6.0			82.0	12.0

[a] Products were identified by GC (5% SE-30 on Chromosorb P, 5 ft × $^1/_8$ in.). Error: ±5%. Conversion: 20%. [b] All solution irradiations were carried out after passing nitrogen through the solution for 45 min. [c] Degassed and irradiated in sealed tubes; mp of the complex, 230–232 °C; host–guest ratio, 1.51. [d] The type I radicals were quenched by the oxygen and gave benzoic acid and isopropyl benzoate as other products in 43% and 42%, respectively.

Table III. Product Distribution upon Photolysis of Benzoin Ethyl Ether[a,b]

	product distribution, %				
	benzaldehyde	pinacol ether	benzil	deoxybenzoin	oxetanol
benzene	41.7	50.1	8.2		
methanol	31.4	59.5	9.1		
β-CD–solution (1:1)	42.6	46.1	4.3	3.9	3.0
β-CD–solution (5:1)	45.4	39.0	5.6	6.1	3.7
β-CD–solid[c]	11.4			79.0	17.0
β-CD–solid/oxygen[d]				6.2	9.9

[a] Products were analyzed by GC (5% SE-30 on Chromosorb P, 5 ft × $^1/_8$ in.). Error limit: ±5%. Conversion: 20%. [b] All solution irradiations were carried out after purging with nitrogen for 45 min. [c] Degassed and irradiated in sealed tubes; mp of the complex, 224–226 °C; host–guest ratio, 1.52. [d] The type I radicals were quenched by oxygen and gave benzoic acid and ethyl benzoate as other products in 44% and 40%, respectively.

were recorded in presence of excess of cyclodextrin. The results are summarized in Table I.

Photolysis of benzoin alkyl ethers **1–3** in N_2 saturated benzene and methanol resulted in the formation of benzaldehyde, benzil, and an equimolar mixture of diastereomeric pinacol ethers. Under poorly deaerated conditions, minor amounts of benzoic acid and alkyl benzoates were also obtained. Solution results are consistent with the original literature reports.[5] Although de Mayo and coworkers[9] have reported a small amount (5%) of type II products in methanol, under our experimental conditions no type II products were detected. Photolysis in cyclodextrin media provided a significant difference in behavior. Although, benzoin ethers **1–3** did not form complex with α-cyclodextrin, they readily formed complexes with β- and γ-cyclodextrin, and the complexes were soluble in water. Photolyses of aqueous solution of β-cyclodextrin complexes as well as those of solid complexes were conducted. Results are summarized in Tables II–IV. While in benzene and methanol only type I products were formed, in aqueous cyclodextrin solutions type II products were also obtained. Both cyclization (oxetanol) and cleavage (deoxybenzoin) products were obtained from the type II 1,4-biradical (Scheme 1). Most significant results were obtained upon irradiation of the solid cyclodextrin complexes of **1–3**. Under these conditions in all three cases products resulting from type I reaction were absent, and type II products were obtained in near quantitative yield. Similar results were obtained in γ-cyclodextrin. This is remarkable considering that irradiation of crystalline benzoin ethers results in no reaction. Recently, formation of type II products from benzoin ethers on silica gel surfaces has been reported.[9] It is important to note that the yields of type II products in cyclodextrin media are remarkably higher than on silica gel surfaces.

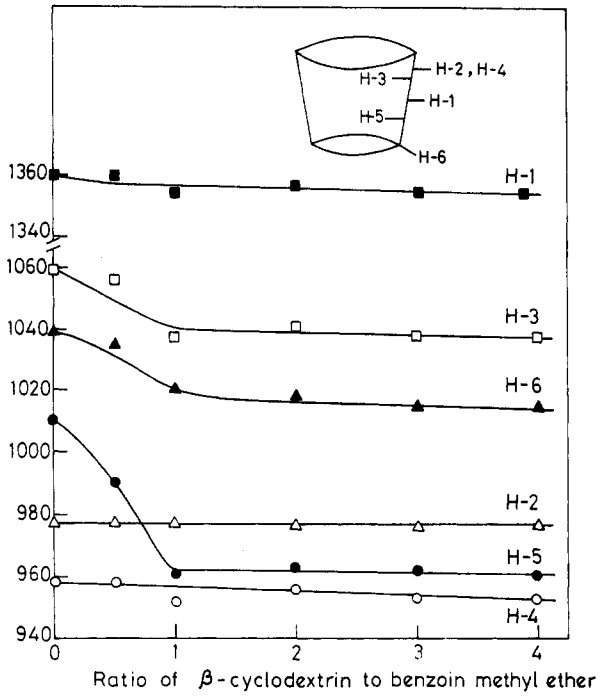


Figure 1. ^{1}H NMR chemical shift differences of β-cyclodextrin protons as a function of benzoin methyl ether–cyclodextrin ratio.

All photoproducts except oxetanol are known compounds and were characterized by comparison with the authentic samples. Spectral data for oxetanols **10** are given in the Experimental Section. IR shows the presence of OH group. ^{1}H NMR spectral data are comparable to those of oxetanols derived from α-alkoxyacetophenones[6] and aryl alkyl ketones.[10] In principle benzoin methyl ether and benzoin isopropyl ether can give two isomers and benzoin

(9) de Mayo, P.; Nakamura, A.; Tsang, P. W. K.; Wong, S. K. *J. Am. Chem. Soc.* **1982**, *104*, 6824.

(10) Lewis, F. D.; Hilliard, T. A. *J. Am. Chem. Soc.* **1972**, *94*, 3852.

Table IV. Product Distribution upon Photolysis of Benzoin Methyl Ether[a,b]

	product distribution, %				
	benzaldehyde	pinacol ethers	benzil	deoxybenzoin	oxetanol
benzene	17.7	58.0	24.1		
methanol	26.4	61.9	10.4	1.3	
β-CD-solution (1:1)	22.8	54.4	7.0	11.6	4.0
β-CD-solution (5:1)	13.7	53.3	13.7	14.8	4.2
β-CD-solid[c]	8.0			69.3	22.7
β-CD-solid/oxygen[d]				15.6	10.5

[a] Products were analyzed by GC (5% SE-30 on Chromosorb P, 5 ft × $^1/_8$ in.). Error limit: ±5%. Conversion: 20%. [b] All solution irradiations were carried, after purging nitrogen for 45 min. [c] Degassed and irradiated in sealed tubes; mp of the complex, 205–207 °C; host–guest ratio, 1.36. [d] The type I radicals were quenched by oxygen and gave benzoic acid and methyl benzoate as other products in 35% and 36%, respectively.

ethyl ether four isomers. However, in all cases only one isomer was obtained. At this stage we are not able to unequivocally assign the geometry of the oxetanol.

Irradiations in aqueous solutions containing excess of cyclodextrin (5 equiv) did not produce any significant variation in the product distribution. This indicated that the complex formed is essentially a 1:1 adduct and the observed product distribution is mainly due to the complexed material. Interesting observations were made when the irradiation was conducted at both low (5 °C) and high (55 °C) temperatures in aqueous cyclodextrin solution. Although the proportion of type I to type II products did not significantly vary, the ratio of cyclization to cleavage products from type II 1,4-diradicals was temperature dependent.

Stability constants of the complexes were measured following the methods of Benesi and Hilderbrand.[11] It has been reported by several groups of workers that there is a change in the UV absorption spectra of substrates on complexation.[12] UV absorption spectra of the three benzoin alkyl ethers in aqueous solutions with varying amounts of β-cyclodextrin were recorded. Increased amounts of β-cyclodextrin resulted in increase in optical density with a slight change in the absorption maxima. The differences in optical densities (ΔOD) were noted at a wavelength where maximum shifts were observed on addition of β-cyclodextrin. The plots of $a_o b_o/\Delta OD$ vs. $(a_o + b_o)$ were linear for all the three compounds (a_o and b_o are the concentrations of cyclodextrin and ketone, respectively). From the slopes and intercepts of these linear plots the dissociation constants were estimated on the basis of the method of Benesi and Hilderbrand.[11] The values obtained for the three compounds are as follows: benzoin methyl ether, 6.0×10^{-4} M^{-1} L; benzoin ethyl ether, 9.6×10^{-5} M^{-1} L; benzoin isopropyl ether, 6.6×10^{-5} M^{-1} L. The above low values of dissociation constants imply that the cyclodextrin complexes of all the three benzoin ethers are quite stable.

Discussion

Significant results obtained upon photolysis of benzoin alkyl ethers in cyclodextrin medium are the following. The type II process which is absent in benzene and methanol occurs in competition with the type I process in aqueous cyclodextrin solution. Most importantly, the photolysis of solid cyclodextrin complexes results in the type II products in near quantitative yield. ^{1}H NMR studies and X-ray powder photographs support the formation of the complex between the cyclodextrin and benzoin ethers 1–3 in aqueous solution and the solid state, respectively.

(a) Evidences for the Formation of Cyclodextrin–Benzoin Alkyl Ether Complexes. Demarco and Thakkar[8] have shown that ^{1}H NMR can provide evidence for the inclusion of an aromatic substance into cyclodextrins. Their reasoning is based on the expectation that if inclusion occurs the screening environment should be sensed by hydrogens on the inner surface (H_3 and H_5) but not by hydrogens on the outer surface. In Figure 1 the chemical shift differences for β-cyclodextrin protons as a function of the ratio of benzoin methyl ether to β-cyclodextrin are plotted. The concentration of benzoin methyl ether was varied from 0.5 to 4 mol per equiv of β-cyclodextrin and the spectra of the D_2O solutions were recorded. The chemical shift differences do not change appreciably beyond 1:1 ratio, suggesting the formation of a 1:1 complex. Upfield shifts were observed for H_3, H_5, and H_6 protons, while the protons H_1, H_2, and H_4 occupying the outer wall of the cyclodextrin cavity remained virtually unaffected. H_5 is shifted upfield to a greater extent (−70 Hz) when compared to H_3 (−20 Hz) and H_6 (−20 Hz). The above chemical shift behavior for the cyclodextrin protons definitively establishes that one of the phenyl rings of benzoin methyl ether is positioned within the cycloamylose cavity.

Another striking observation in the spectra of benzoin methyl ether in aqueous cyclodextrin solution is the appearance of pairs of equal intensity singlets for the CH and OCH_3 protons of benzoin methyl ether. This can be attributed to the formation of diastereomeric complexes from the racemic mixture of benzoin methyl ether. From NMR integration, within experimental error, we could not observe any preference for inclusion of one of the optical isomers.

Formation of solid inclusion complexes between cyclodextrin and benzoin ethers 1–3 was evident from X-ray powder photographs. The X-ray powder pattern of the precipitated solid differed from those of the guest and the host in all cases.

(b) Speculations on the Structure of the Complexes. Before attempting to understand the possible structure of the cyclodextrin complexes, it is essential to know the stoichiometry of the complexes. It is known that the stoichiometry of the complex depends on the sizes of the guest and the cyclodextrin cavity. While on the basis of the sizes of benzoin alkyl ethers, cyclodextrin complexing two ketones can be ruled out, one cannot eliminate the possibility of 2:1 (cyclodextrin–benzoin ether) complexes with one phenyl group in each cyclodextrin cavity. Our belief that the benzoin ethers form 1:1 complexes is based on NMR results. As seen in Figure 1, the cyclodextrin protons shift reaches a saturation limit with 1 mol equiv of cyclodextrin; further addition results in no change. Furthermore, the molar ratio of the solid complexes (as estimated by GC after extraction of the ketone from the known amount of the complex) suggests that one molecule

(11) Benesi, H. A.; Hilderbrand, J. H. *J. Am. Chem. Soc.* **1949**, *71*, 2703.

(12) Cramer, F.; Saenger, W.; Spatz, H. Ch. *J. Am. Chem. Soc.* **1967**, *89*, 14. Breslow, R.; Campbell, P. *Bioorg. Chem.* **1971**, *1*, 140. Van Etten, R. L.; Sebastian, J. F.; Clowes, G. A.; Bender, M. L. *J. Am. Chem. Soc.* **1967**, *89*, 3242.

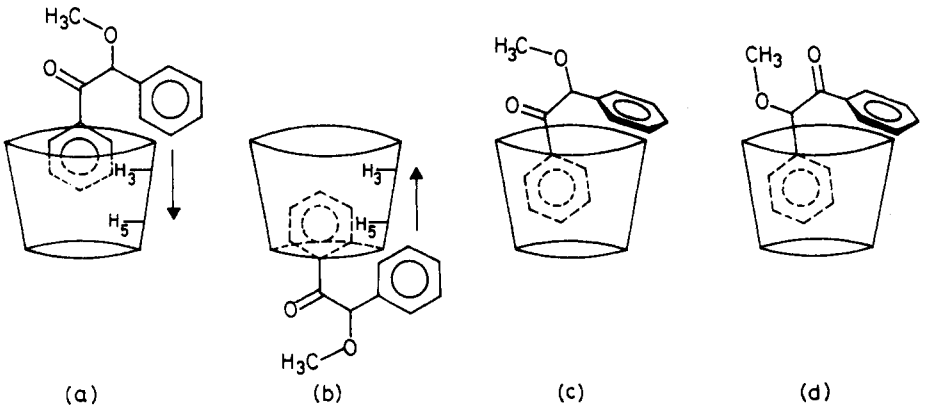


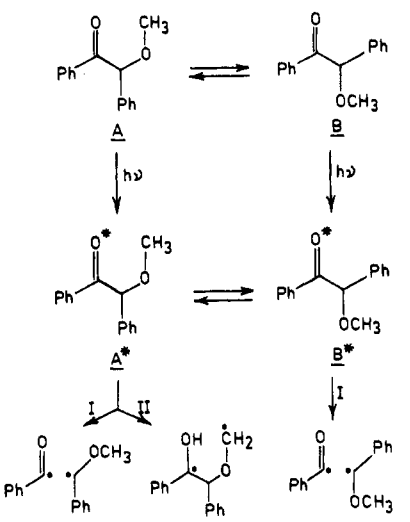
Figure 2. Possible structures of β-cyclodextrin–benzoin methyl ether complex.

of cyclodextrin is complexed with one molecule of ketone. Therefore, we base our further arguements on the assumption that the stoichiometry of the complexes is 1:1. We realize that additional substantiation would be desirable.

Examination of the aromatic substrate induced chemical shifts in the ^1H NMR spectrum of the cycloamyloses provides a convenient method for determining the direction of substrate penetration into the cavity.[9,13] For example, if H_3 resonance is shifted while H_5 is unaffected, clearly the substrate is entering from the wide C-2, C-3 hydroxyl face of the cavity (Figure 2a). Similarly, if H_5 shifts upfield while H_3 is unaffected, substrate penetration probably is occuring from the narrow, primary hydroxyl face (Figure 2b). Shifting of both resonances is not easily interpreted and could result either from very deep substrate penetration or from nonspecific penetration where the substrate enters the cavity from both faces. Benzoin alkyl ether investigated here come under the third category wherein shifting of both H_3 and H_5 is observed. For the three systems examined (benzoin methyl ether, ethyl ether, and benzoin isopropyl ether) H_5 is shifted upfield to a greater extent when compared to H_3 and H_6 (Table I). Penetration via the narrower end without deeper penetration (so that H_3 is not affected to the same extent as H_5) may not be preferred for benzoin ethers simply because very little of the substrate would fit into the cavity. Therefore, deeper penetration via the wider end of the cavity may be expected. Under these circumstances the lesser shielding of H_6 can be attributed to the rotation of the CH_2OH group and their presence at the periphery resulting in a greater average distance between the aromatic ring and these protons. H_3 would expected to be shielded to the same extent as H_5 if penetration had occurred via the wider end. The decreased shielding experienced by H_3, we believe, is due to the magnetic anisotropic effect of the two aromatic clouds on H_3, i.e., shielding by the aromatic nucleus present vertically inside the torous and deshielding by the other aromatic nucleus acting as a lid partially covering the top surface of the cavity (Figure 2c,d).

From the ^1H NMR spectra of the three complexes it is clear that the magnitudes of the upfield shifts in protons H_3, H_5, and H_6 decrease as the bulk of the alkyl substituent increases from methyl to isopropyl (Table I). This may be attributed to the reduction in the degree of penetration into the cyclodextrin cavity by the guest molecule as the steric effect of the alkyl substituent increases. Thus the results are consistent with the conclusion that the benzoin ethers enter the cavity through the wider end. However, no definitive conclusion could be drawn, as to which phenyl ring of the benzoin ether enters the cyclodextrin cavity (Figure 2c,d). It was anticipated that internuclear nuclear Overhauser effect, if observed, would lead to some predictions as to which ring enters the cavity. However no internuclear nuclear Overhauser effect was observed.

Scheme II

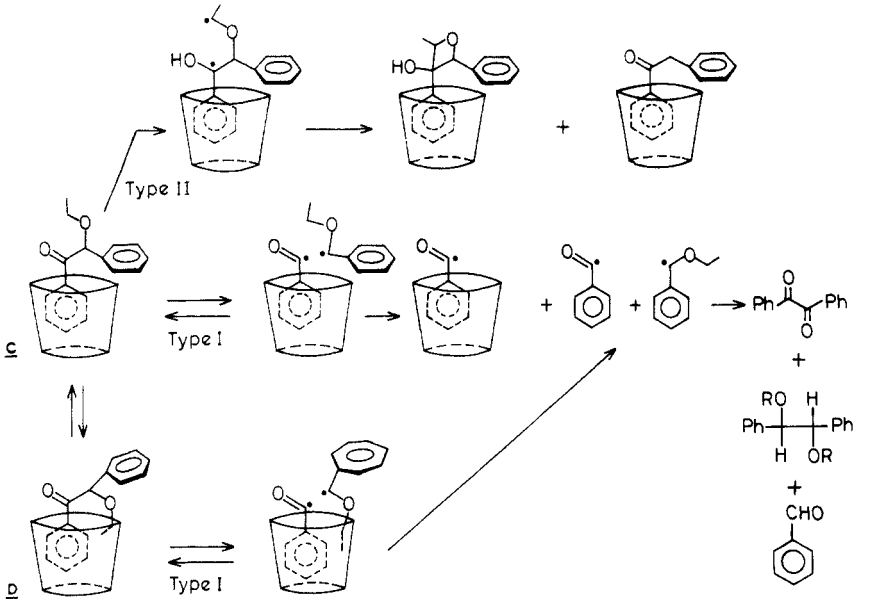


Photochemical Behavior. General. On the basis of the rates of α-cleavage measured for benzoin ethers ($k_\alpha \simeq 10^{10}$ s^{-1})[5] and the hydrogen abstraction rates reported for closely related systems[6] such as α-methoxyacetophenone (3.2×10^9 s^{-1}), α-ethoxyacetophenone (8.4×10^9 s^{-1}), and α-isopropoxyacetophenone (8.2×10^9 s^{-1}) a competition between the type I and type II reactions would be expected for benzoin ethers **1–3**. However, both the literature reports[5] and our own observations (Tables II–IV) indicate that this is not the case in organic solvents and only type I occurs. As illustrated in Scheme II, γ-hydrogen abstraction requiring a six-membered transition state can occur only from the conformer A, whereas cleavage will occur from all possible conformers (A, B, etc.) of benzoin ethers. Two limiting conditions are possible when conformational isomers (such as the above) can react photochemically in solution to yield different products.[14] The

(13) Wood, D. J.; Hruska, F. E.; Saenger, W. *J. Am. Chem. Soc.* **1977**, *99*, 1735. Behr, J. P.; Lehn, J. M. *J. Am. Chem. Soc.* **1976**, *98*, 1743. Mac Nicol, D. D. *Tetrahedron Lett.* **1975**, 3325. Otagiri, M.; Vekama, K.; Ikeda, K. *Chem. Pharm. Bull.* **1975**, *23*, 188. Takamura, K.; Inoue, S.; Kusu, F. *Chem. Lett.* **1983**, 233. Gelb, R. I.; Schwartz, L. M.; Laufer, D. A. *J. Am. Chem. Soc.* **1978**, *100*, 5875. Uekama, K.; Hirayama, F.; Matsno, N.; Kanuma, H. *Chem. Lett.* **1978**, 703.

(14) Lewis, F. D.; Johnson, R. W.; Johnson, D. E. *J. Am. Chem. Soc.* **1974**, *96*, 6090. Lewis, F. D.; Johnson, R. W.; Kory, D. R. *J. Am. Chem. Soc.* **1974**, *96*, 6100.

Scheme III



activation energies for conformational isomerization in the excited state (e.g., A* ⇄ B*, Scheme II) can be either less than (case I) or greater than (case II) the activation energies of the primary photochemical steps. In case I, the ratio of the photoproducts will depend upon the energy difference for the transition states leading to the products. The conformer populations are quite irrelevant as far as the determination of products yield is concerned (Curtin–Hammet principle).[15] In case II, the ratio of the final products will depend upon the excited conformer population (A*, B*, etc.) and hence (since excitation is much faster than molecular motion) also on the ground-state conformer distribution.

Based on the above model and the products isolated it can be concluded that only B* undergoes reaction in the excited surface of benzoin ethers. Thus the absence of appreciable amounts of conformer A* can be attributed to one of the following molecular features: (a) the population of the conformer A in the ground state is negligible, and the barrier for conversion of B* to A* must be large compared to its reaction; (b) alternatively, the barrier for conversion of A* to B* is small compared to its reaction, and thus only B* undergoes photoreaction in spite of the presence of appreciable amounts of A in the ground state. Therefore, in order to bring about the type II reaction of **1–3**, it is necessary to either increase the ground-state distribution of A and/or increase the barrier for interconversion of A* to B*. Results presented here on the photochemistry of benzoin ethers in presence of cyclodextrin suggest that such a phenomenon might be responsible for the quantitative yields in the solid state and significant yields (in solution) of the type II products.

Irradiation of Cyclodextrin Complexes in the Solid State. Perusal of Tables II–IV reveals that the photolysis of cyclodextrin complexes of **1–3** in the solid state leads to deoxybenzoin and oxetanols in high yields (≃90%). The importance of the cyclodextrin cavity in bringing about this remarkable change in photobehavior of **1–3** is revealed by the following observations. When microcrystalline compounds **1–3** under identical conditions were irradiated they were recovered unchanged even after 3 days.[16] Further, irradiation of a mechanical mixture of cyclodextrin and benzoin ethers did not yield the type II products. The proposed mechanism based on Scheme II is illustrated in Scheme III. Complexes C and D represent two of the several possible structures of benzoin ether–cyclodextrin complexes. For the sake of brevity and clarity, the others are not included, and the point is conveyed by these two extreme situations. While complex C can give both the type I and type II reactions, complex D can undergo only the type I reaction. Interconversion between C and D both in the ground and excited states would severely be restricted in the solid state.

Formation of oxetanols and deoxybenzoin under conditions wherein the motion of the atoms is restricted suggests that at least a few of the benzoin ether molecules are included by cyclodextrin in a conformation suitable for γ-hydrogen abstraction. At this stage, one cannot exclude the possibility of cyclodextrin encapsulating both the conformers and thus giving a mixture consisting of both C and D. If there is no interconversion between C* and D*, as would be anticipated in the solid complexes, the total yield of the type II products would only reflect the ground-state distribution of C and D. The most remarkable observation was the isolation of the type II products in yields >60% (of the isolated products) with the rest being starting benzoin ethers. The conversion reaches ≃60%, at which stage the competitive absorption by one of the products, deoxybenzoin, acts as an internal filter and slows down the reaction. Therefore, it can be inferred that a majority (and not a few) of the benzoin ether molecules are trapped by cyclodextrin in the conformation suitable for the type II process. Thus the photochemistry of benzoin ethers is an example of the use of cyclodextrin in controlling the conformation of the guest molecule and thus altering the nature of the excited-state chemistry.

Although such a dramatic alteration in the conformation of organic molecules has not been reported earlier, there are several 1,3-diaryl systems that are inferred to possess different conformations in cyclodextrin and in organic solvents.[17] These studies are restricted to aqueous cy-

(15) Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw Hill: New York, 1962; pp 149–153.

(16) Tomioka, H. S.; Izawa, Y. *J. Chem. Soc., Chem. Commun.* **1980**, 445.

clodextrin solutions and no information in the solid state is available. In these examples 2,2-bis(α-naphthylmethyl)-1,3-dithiane, 1,3-dinaphthylpropane and related compounds, dibenzylammonium chloride, bis(α-naphthylmethyl)ammonium chloride, and bis(4-biphenylylmethyl)ammonium chloride interactions between aryl groups in the ground states are normally repulsive, causing them to adopt predominantly trans–trans and trans–gauche conformations. The differences seen in the emission properties of the above compounds in organic solvents and when complexed with cyclodextrins indicate that major conformational changes are imposed in the guest by the host during complexation. It has been proposed that the cyclodextrin induces a conformational transition to the eclipsed state in which interaction between the two aryl rings is feasible. Similarity between these reported systems and benzoin ethers is obvious.

Since both the type I and type II reactions are expected from C*, absence of the type I products in the photolysis mixture was surprising. A clue to this intriguing behavior became available when the complexes were irradiated in an aerated atmosphere. Under these conditions, in addition to the type II products (which were no longer quantitative), benzoic acid and alkyl benzoates were isolated in ≃85% yield (Tables II–IV). These are the oxygen trapped products of the type I benzoyl–benzyl radical pair. Therefore, it is clear that the type I reaction does indeed occur in the absence of oxygen but the radical pair generated by this process undergoes geminate recombination. Thus the near quantitative formation of the type II products under degassed conditions is the result of two features—a conformational effect and a super cage effect, of which the former facilitates the occurrence of the type II and the latter suppresses the formation of the type I products.

It is worthy of note that when the crystals of benzoin ethers were irradiated in an oxygen atmosphere, benzoic acid and alkyl benzoates were isolated, although the crystals were resistant to reaction under degassed conditions.[16] The lack of type II products in the crystals even under conditions wherein the type I radical pairs are totally returned probably reflects the lack of suitable conformers (favorable for type II) in the crystals. Attempts are under way to ascertain this proposition.

Photolysis of Cyclodextrin Complexes in Aqueous Solution. Analysis of the solution results, which are less dramatic than the solid-state behavior, should address the following important questions: (i) Where does the reaction occur, i.e., from the bound substrates or from the unbound free ketones in aqueous medium? (ii) Is there an interconversion between the conformational isomers C and D within the photochemical time scale? (iii) What is the cause for the slight enhancement of the type II reaction in the presence of cyclodextrin.

On the basis of the following observations, we assume that the observed products result from the benzoin ether complexed to cyclodextrin and not from the free uncomplexed **1–3**. The measured stability constants for all the three benzoin ethers are quite high (≃10^4). This points out that the complexes are quite stable. Since the concentrations of the uncomplexed substrate would be ~10^{-2} M in a molar solution of the 1:1 complex, >99% of **1–3** will be in the complexed form in an equimolar mixture of the substrate and β-cyclodextrin. However, we realize that if the photochemically promoted reactions are slow relative to this equilibrium, then it is quite possible for very much less than 1% unbound substrate to account for all the reaction products. In this context, it should be noted that the benzoin ethers were generally insoluble in water and photolysis of aqueous suspensions of **1–3** resulted in no reaction even after 24 h. Further, we assume that the association constants for the biradical intermediate (type II) and the excited ketone are virtually the same as for the ketone in the ground state. Although information on these are highly desirable, they are presently not available.

The influence of cyclodextrin on the type I and type II products in aqueous cyclodextrin solution needs to be analyzed in terms of three factors: micro solvent effect on excited-state reactivity, encapsulation effects of the preferred conformation, and cage effect. Changes in product distribution for **1–3** between benzene, methanol, and aqueous cyclodextrin, although small, is significant. It is important to note that either nil or very little type II products were obtained both in benzene and methanol. This probably suggests that the medium polarity or hydrogen-bonding effect plays only a minor role in altering the course of excited-state reactions of benzoin ethers. In order to ascertain the importance of cyclodextrin in bringing about the type II reaction, one should compare the product distribution in water in the presence and absence of cyclodextrin; however, benzoin ethers were too insoluble in water in the absence of cyclodextrin to conduct comparative runs.

The fact that the type I products are obtained in ≃90% yield in aqueous cyclodextrin solution suggests that the cage effect is small under these conditions. This is further supported by the relative quantum yields measured for **1–3** between aqueous cyclodextrin and benzene. Cyclodextrin reduces the quantum yield of the disappearance of **1–3** only by a factor of ≃0.6 with respect to benzene. The relatively low cage effect in aqueous solution is not unexpected as in an 1:1 complex, a part of the molecule would be free to diffuse into the aqueous medium after α-cleavage. Therefore, the "super cage effect" may not be expected to operate in solution, although this contributes significantly in the solid state.

Scheme III can be utilized to comprehend the mechanism of photoreactions of complexes in aqueous solution. Complex C* required for the formation of type II products may have been generated in the excited state either through direct excitation of C or via the excitation of D followed by a rotational process in the excited surface (D* → C*). The former would require a significant population of C in the ground state and the latter a low barrier for rotational process (compared to organic solvent) in the excited state. Although interconversion between D and C is inhibited in the solid state, one cannot rule out its occurrence in solution. In the absence of kinetic data on the reaction and rotational motion we cannot firmly favor any one of these processes. However, an approach to understand the solution results would be to postulate that the solution photochemistry is a derivative of the solid-state behavior. To summarize, both in solution and solid state, the majority of the complexes would have the structure C and C* and undergo both the type I and type II reactions in these two media. Due to the absence of a significant cage effect in solution both the primary processes lead to products, while in solid state due to the cage effect the type I radical pair undergoes total cage recombination and therefore only the type II process leads to products.

A final point of discussion concerns the cyclization/cleavage (oxetanol/deoxybenzoin) ratios of the type II

(17) Emert, J.; Kodal, D.; Catena, R. *J. Chem. Soc., Chem. Commun.* **1981**, 758. Turro, N. J.; Okubo, T.; Weed, G. C. *Photochem. Photobiol.* **1982**, *35*, 325. Arad-Yellin, R.; Eaton, D. F. *J. Phys. Chem.* **1983**, *87*, 5051.

1,4-diradical. A comparison of the behavior of the three benzoin ethers reveals that there exists a trend in the cleavage/cyclization ratio. While benzoin methyl ether favors cleavage, benzoin isopropyl ether prefers cyclization. This behavior is similar to the ones reported for aryl alkyl ketones wherein a definite trend toward increased cyclization with increasing size of γ-alkyl groups has been observed.[18] The results observed with benzoin ethers can be explained on the same basis; namely, the difference in size of the substituent controls the motion required for the formation of type II products. It is not clear whether the cavity imposes any additional restriction on the rotation of the end groups of the 1,4-diradical.

Another interesting observation of practical use was made when the irradiations were conducted at low temperatures. Photolysis of 1–3 in aqueous cyclodextrin at 5 °C resulted in the enhancement of the cyclization yield. Indeed a dramatic variation in the cyclization/cleavage ratio was noticed with respect to temperature (Table II). While at 55 °C in the case of benzoin isopropyl ether only cleavage product was observed, at 5 °C cyclization product constituted the major portion. Similar observations were made with benzoin methyl and ethyl ethers. At this stage it is not clear whether this is a specific cavity effect or is an inherent molecular effect. It is probably important to mention that we did not see similar temperature effects on either valerophenone or α-methoxyacetophenone complexed with cyclodextrin. Therefore, further experimentation is required and is underway to fully understand this phenomenon.

To date there have been four studies which report the influence of solid-state or inclusion complexes on the Norrish type I and type II photobehavior of ketones. Two of these deal with benzoin ethers themselves. As pointed out earlier, benzoin ethers in the crystalline state are reported[16] to undergo no reaction in the absence of oxygen. In an aerated atmosphere the type I radical trapping products were isolated and no type II products were obtained under any other conditions. On silica gel surface, benzoin ethers undergo both the type I and type II reactions.[9] The maximum yield of the type II products were $\simeq$10% of the products isolated. The photolysis of α,α-dimethylvalerophenone adsorbed on a number of commonly available zeolites is reported to give a dramatic changes in type I/type II products ratio.[19] The type I/type II ratio for α,α-dimethylvalerophenone jumped from 0.3 in benzene to >50 in silicalite. Last, a large number of aryl alkyl ketones have been investigated by using Dianin's compound as the host.[20] In these systems the type I/type II ratio increases slightly in proceeding from liquid media to the environment of the solid Dianin's complex. It is needless to emphasize that cyclodextrin encapsulation, especially in the solid state, reported in the present investigation has offered the most dramatic alteration in the photobehavior of aryl alkyl ketones with respect to Norrish type I and type II reactions of aryl alkyl ketones.

Conformational preference of the nature described here has earlier been utilized, elegantly, in thermal reactions.[21] The present study represents the first example of the effective utilization of cyclodextrin to control the type I and type II reactivity. Generally, cyclodextrins are used as hosts mostly in aqueous solutions; the results presented here demonstrate the unusual potential of cyclodextrin as a host in the solid state. An examination of other reactions in an effort to understand the nature of the complexation and to examine the potential synthetic utility is under way.

Experimental Section

Materials. Cyclodextrins (α, β, and γ) were purchased from Aldrich and were used as received. The benzoin alkyl ethers were prepared by reported procedures[22] and were purified by repeated recrystallizations from hexane. The melting points are as follows: 1, 49–51 °C; 2, 62–65 °C; 3, 74–75 °C. Doubly distilled water was used for all the experiments, and solvents were distilled twice prior to use.

Preparation of Cyclodextrin Complexes. To a saturated solution of cyclodextrin in distilled water, equimolar amounts of benzoin alkyl ethers were added and stirred for 24 h. The white precipitate that formed was filtered, washed with diethyl ether, and dried at 50 °C for 10 h. The aqueous solution of the complex was prepared by the addition of a minimum amount of distilled water to the microcrystalline white complex and by warming the solution to 40 °C to obtain a transparent solution.

Photolysis of Cyclodextrin Complexes. The aqueous solutions prepared as above were irradiated for 30 min with a Rayonet reactor fitted with RPR-3000 lamps in Pyrex tubes after being purged with nitrogen for about 45 min. After the irradiation, the products were extracted from aqueous solution with chloroform. Preparative-scale irradiations were carried out to identify the products and small-scale irradiations for mechanistic studies. Products were separated by column chromatography (silica gel, hexane/benzene) and identified by their spectral properties (IR, NMR, and mass spectra) and by comparison with the authentic samples. IR and NMR spectral data for the three oxetanols are provided below. All the other products are already known in the literature.

10a: IR (neat) 3600–3250, 1600, 1140–1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.95 (2 H, dd), 5.90 (1 H, s), 7.20–7.80 (10 H, m).

10b: IR (neat) 3600–3200, 1600, 1130–1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (3 H, d), 5.20 (1 H, q), 5.95 (1 H, s), 7.20–7.80 (10 H, m).

10c: IR (neat) 3650–3100, 1600, 1380–1370, 1140–1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (3 H, s), 1.57 (3 H, s), 6.30 (1 H, s), 7.20–7.80 (10 H, m).

Products obtained from small-scale irradiations were analyzed by gas chromatography (5% SE-30 on Chromosorb P, 5 ft × $^1/_8$ in.). The peaks were identified by coinjection of the authentic samples.

Irradiations of solid samples were carried out with a Hanovia 450-W medium-pressure mercury lamp. Microcrystalline cyclodextrin complexes in Pyrex tubes were degassed by using a vacuum line (10^{-4} mm), sealed, and irradiated (48 h). To obtain a uniform exposure the sample tubes were rotated periodically. Products were extracted by using a chloroform–water mixture. One set of photolyses were carried out under an aerated atmosphere.

Crystalline benzoin alkyl ethers 1–3 were also irradiated under analogous conditions. One set under degassed and sealed conditions and the other under an aerated atmosphere were photolyzed.

Irradiations of all the three benzoin alkyl ethers were also conducted in benzene and methanol. The procedure for irradiations and analyses were similar to the one mentioned above for aqueous cyclodextrin solution.

Measurement of Dissociation Constants. A stock solution (9.7×10^{-4} M) of β-cyclodextrin was prepared by dissolving 100 mg in 100 mL of water. Solutions (10 mL) containing varying amounts of β-cyclodextrin stock solution and a constant amount of benzoin alkyl ether (2.3×10^{-3} M in methanol) were prepared in 10-mL standard flasks and stirred well. The amount of methanol (0.1 mL) was constant in all the flasks. UV spectra of these solutions were recorded with a Shimadzu UV-180 spec-

(18) Wagner, P. J.; Kelso, P. A.; Kemppainen, A. E.; McGrath, J. M.; Schott, H. N.; Zepp, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 7506.
(19) Turro, N. J.; Wan, P. *Tetrahedron Lett.* **1984**, *25*, 3655.
(20) Goswami, P. C.; de Mayo, P.; Ramnath, N.; Bernard, G.; Omkaram, N.; Scheffer, J. R.; Wong, J. F. *Can. J. Chem.*, in press.
(21) Vander Jagt, D. L.; Killiam, F. L.; Bender, M. L. *J. Am. Chem. Soc.* **1970**, *92*, 1016. Straub, T. S.; Bender, M. L. *J. Am. Chem. Soc.* **1972**, *94*, 8881. Griffiths, D. W.; Bender, M. L. *J. Am. Chem. Soc.* **1973**, *95*, 1679.
(22) Fischer, E. *Chem. Ber.* **1893**, *26*, 2412.

trophotometer, and optical densities were monitored at 250 nm. A plot of $a_0b_0/\Delta OD$ vs. $a_0 + b_0$ was linear with the slope and intercept being equal to $1/\Delta\epsilon$ and $k_d/\Delta\epsilon$, respectively. The value of K_d was obtained from these linear plots.

Identification of Cyclodextrin Complexes. Powder Diffraction of Solid Complexes. X-ray powder photographs of β-cyclodextrin, benzoin alkyl ethers, and complexes of cyclodextrin with benzoin alkyl ethers were recorded with a Phillips powder diffractometer employing monochromated Cu Kα radiation. Powder patterns of the complexes were different from those of cyclodextrin and benzoin alkyl ethers and therefore it was concluded that microcrystalline complexes have been formed between β-cyclodextrin and benzoin alkyl ether.

NMR Studies. Sample Preparation. Solutions of the 1:1 complexes were prepared by dissolving 2–3 mg of the complex in about 1 mL of D_2O. Solutions containing different proportions of guest to host were prepared by stirring 0.5, 1, 2, 3, and 4 mg of the benzoin methyl ether with a solution of 5 mg of β-cyclodextrin in 1 mL of D_2O for about an hour.

The NMR spectra of all the β-cyclodextrin complexes and β-cyclodextrin and benzoin methyl ether in D_2O and $CDCl_3$ were recorded with a Bruker WH 270 spectrometer equipment with ASPECT 2000 computing system. The difference NOE measurements were made by collecting two sets of free induction decays sequentially in different parts of the computer memory (8K each) corresponding to low power on-resonance saturation of a peak and off-resonance irradiation, respectively. The free induction decays were recorded by alternating between on-resonance and off-resonance irradiation after each scan, and typically 200 scans were employed. A delay of 3 s between scans and an irradiation period of 3 s were used before acquisition (1.5 s) was started. Identical exponential multiplication was done on both the free induction decays. The difference of their Fourier transforms was then compared with the Fourier transform of the off-resonance irradiated free induction decay to estimate the NOE. No special sample preparation was used for the NOE experiment.

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Registry No. **10a**, 92549-02-5; **10b**, 102979-46-4; **10c**, 102979-47-5; β-CD/**3** 1:1 adduct, 102979-42-0; γ-CD/**3** 1:1 adduct, 102979-43-1; β-CD/**2** 1:1 adduct, 102979-44-2; β-CD/**1** 1:1 adduct, 102979-45-3.

Supplementary Material Available: H^1 NMR spectra of β-cyclodextrin and β-cyclodextrin–benzoin methyl ether complex, X-ray powder photographs for (a) β-cyclodextrin, (b) benzoin isopropyl ether, and (c) inclusion complex of β-cyclodextrin with benzoin isopropyl ether, progress of the reaction with respect to time in the case of cyclodextrin–benzoin methyl ether complex, and Benesi–Hilderbrand plots to estimate K_d for all three benzoin ethers are given in Figures 1–4, respectively (5 pages). Ordering information is given in any current masthead page.

Facile Synthesis of 2′-Deoxy-3′-keto- and 2′-Deoxypseudouridine Derivatives and Analogues. Palladium(II)-Mediated Coupling Reactions of Furanoid Glycals

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C-Nucleosides, of either α or β configuration, are formed selectively in a palladium-mediated coupling reaction between furanoid glycals and (1,3-dimethyl-2,4-dioxo-1,3-dihydropyrimidin-5-yl)mercuric acetate. Control of anomeric configuration is accomplished by suitable choice of substituents for glycal 3-*O*- and 5-*O*-hydroxy groups; attack of organopalladium reagent and glycosidic bond formation occurs on the least sterically hindered face of the glycal ring. Removal of substituents from the coupled products yielded 2′-deoxy-3′-keto C-nucleosides, which upon metal hydride reduction produced the corresponding 2′-deoxy C-nucleosides.

In a previous report,[2] we described palladium-mediated coupling of furanoid glycals[3] with (1,3-dimethyl-2,4-dioxo-1,3-dihydropyrimidin-5-yl)mercuric acetate (**1**)[4] which formed regio- and stereospecifically a glycosidic carbon–carbon bond linking C-5 of the pyrimidine moiety and C-1 of a glycal. This study of C-nucleoside[5] synthesis by palladium-mediated coupling of furanoid glycals has now been extended by (a) investigation of the directive effect on organopalladium coupling of various substituents on the glycal oxygens, (b) evaluation of methods for complete or selective removal of C-nucleoside 3′-O and 5′-O directive groups, and (c) preparation of 2′-deoxypseudouridine derivatives by the reduction of corresponding 3′-keto compounds arising as primary products of the coupling reaction or following removal of directive groups of product 3′-enols.

Directive Effect of Oxygen Substituents on Organopalladium Coupling. The stereochemistry of adduct formation in the organopalladium coupling reaction of furanoid glycals leading to C-nucleosides is exquisitely sensitive to steric factors affecting access to the glycal double bond.[2,6,7] The organopalladium reagent (formed by transmetalation of **1**[6,8]) attacks the most accessible face

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(2) Hacksell, U.; Daves, G. D., Jr. *J. Org. Chem.* **1983**, *48*, 2870.
(3) (a) Cheng, J. C. Y.; Hacksell, U.; Daves, G. D., Jr. *J. Org. Chem.* **1985**, *50*, 2778. (b) Ireland, R. E.; Thaisrivongs, S.; Vanier, N.; Wilcox, C. S. *J. Org. Chem.* **1980**, *45*, 48.
(4) Arai, I.; Daves, G. D., Jr. *J. Org. Chem.* **1978**, *43*, 4110.
(5) Hacksell, U.; Daves, G. D., Jr. *Prog. Med. Chem.* **1985**, *22*, 1.
(6) Arai, I.; Lee, T. D.; Hanna, R.; Daves, G. D., Jr. *Organometallics* **1982**, *1*, 742.
(7) Substitution on the double bond does not affect the regiochemistry of the reaction but does depress yields: Lee, T. D.; Daves, G. D., Jr. *J. Org. Chem.* **1983**, *48*, 399.
(8) Kalinoski, H. T.; Hacksell, U.; Barofsky, D. F.; Barofsky, E.; Daves, G. D., Jr. *J. Am. Chem. Soc.* **1985**, *107*, 6476.

0022-3263/86/1951-3093$01.50/0