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"oxene", but the present study demonstrates that the insertion of an electrophilic species into a C–H bond can exhibit *normal* β-secondary KIEs. For this reason, we conclude that studies of β-secondary KIEs do not permit the discrimination of concerted and stepwise mechanisms for insertion reactions in alkanes. It remains to be determined whether α-secondary KIEs are better in this regard.

Experimental Section

2-Bromo-2-phenylpropane[9] and 2-(dichloromethyl)-2-phenylpropane[7] (2) were prepared by literature procedures. Gas chromatography (GC) was performed on capillary columns (Supelco SPB-1, 30 m × 0.53 mm), as was coupled gas chromatography–mass spectrometry (GC–MS) (Hewlett-Packard HP-1 capillary column, 12.5 × 0.20 mm; Hewlett-Packard 5971A GC-MS system). Mass spectra were recorded repeatedly at close intervals across the entire peaks of emerging compounds of interest (there is substantial fractionation of protic and deuteriated species on the capillary columns), and the isotopic composition of each compound was determined from analysis of the sum of these spectra.

2-Phenyl[2-^2H]propane (3). A mixture of 2-bromo-2-phenylpropane (4.91 g, 24.7 mmol) and $LiAlD_4$ (1.00 g, 23.8 mmol, 98 atom % D) in ether (50 mL) was refluxed for 6 h and left to stir overnight. Water and dilute HCl were added, the organic layer was separated, and the aqueous phase was extracted once with ether. The combined organic phases were washed with water and then dried over anhydrous $MgSO_4$. The ethereal solution was hydrogenated over 10% Pd on C (0.3 g) at 4 atm for 3.5 h. The catalyst was filtered off, the ether was evaporated, and the residual oil was distilled to give compound 3 (1.54 g, 12.7 mmol, 51%). GC analysis indicated the purity of this material to be 98.6%: ^{1}H NMR ($CDCl_3$) δ 7.34 (m, 5 H, aromatic), 2.99 (septet, J_{HH} = 7 Hz, 0.41 H, benzylic), 1.35 and 1.34 [overlapping d (J_{HH} = 7 Hz) and t (J_{HD} = 1 Hz), 6 H, methyls]. The NMR spectral data indicate that 59% of the molecules contained one deuterium atom at the α-carbon. GC–MS analysis indicated the isotopic composition to be as follows: d_0, 41%; d_1, 59%; d_2, <1%. Because this material already contained a satisfactory ratio of deuteriated and unlabeled cumene, it was used directly in isotopic competition experiments.

2-Phenyl[1,1,1,3,3,3-$^2H_6$]propane (4). A mixture of phenylmagnesium bromide in ether (16 mL of a 3.0 M solution) and THF (16 mL) was cooled to 0 °C, and acetone-d_6 (3.5 mL, 52 mmol, 99.5 atom % D) was added dropwise with stirring over 15 min. The mixture was warmed to room temperature, stirred for 2 h, and then poured into water; dilute sulfuric acid was added to dissolve a white precipitate. The organic layer was separated, and the aqueous phase was extracted with ether. The combined organic extracts were dried and concentrated to give crude deuteriated 2-phenyl-2-propanol (6.0 g). This material was dissolved in 2:1 EtOAc/EtOH (225 mL), concentrated HCl (1 mL) and 10% Pd on C (0.4 g) were added, and the mixture was hydrogenated at 4 atm for 20 h. The catalyst was filtered off, hexane and water were added, and the organic layer was separated, dried, and concentrated to give 5.2 g of a yellow liquid. Distillation of this material yielded colorless compound 4 in several fractions, the best of which (1.82 g) was estimated to be >99% pure by GC: ^{1}H NMR ($CDCl_3$) δ 7.33 (m, 5 H, aromatic), 2.95 (s, 1 H, benzylic). The NMR spectral data indicate that the methyl groups were at least 98% deuteriated. GC–MS analysis indicated the isotopic composition to be d_6, >99%. For use in isotopic competition experiments, mixtures of 4 and unlabeled cumene was prepared. The isotopic compositions of these mixtures were determined by GC–MS and NMR analyses, which were in good agreement, but the mass spectral values were used for all calculations of kinetic isotope effects.

Isotopic competition experiments were conducted in the following manner. A known mixture of unlabeled and deuteriated cumene (200 μL, 1.44 mmol), DME (100 μL), and sodium trichloroacetate (35 mg, 0.19 mmol) was placed in a screw-capped tube. The tubes were placed in an oil bath at 120 °C for 15 h. After being cooled, the reaction mixtures were diluted with 2.0 mL of pentane and filtered through paper. The resulting solutions were analyzed directly by GC and GC–MS.

For the large-scale experiment 4, a mixture of unlabeled and deuteriated cumene (1.50 mL, 10.8 mmol), DME (0.75 mL), and sodium trichloroacetate (0.40 g, 2.2 mmol) was treated as described above. The reaction mixture was analyzed by GC and GC–MS, and then a portion of this material was fractionated by preparative GC (145 °C; column: 5% OV-17, 8 ft × 0.25 in). For ^{1}H NMR analysis the sample of the isolated product 2 was dissolved in deuteriochloroform and shaken with a few drops of D_2O (to remove the H_2O peak normally observed at δ ~1.6). The spectrum was recorded at 270 MHz by using a 6-s data acquisition of 65 536 points with a 15-s delay between acquisitions to ensure complete proton relaxation. Peak areas were determined by digital integration.

Acknowledgment. This work was supported in part by National Institutes of Health Grant AI24146. We thank Kathy Valentine for assistance with critical NMR measurements.

Registry No. 1, 98-82-8; 2, 4850-86-6; 3, 4019-54-9; 4, 20201-29-0; D_2, 7782-39-0; dichlorocarbene, 1605-72-7; sodium trichloroacetate, 650-51-1; acetone-d_6, 666-52-4; 2-bromo-2-phenylpropane, 3575-19-7; 2-phenyl-2-propanol-*1,1,1,3,3,3-d*$_6$, 72235-68-8.

Supplementary Material Available: ^{1}H NMR and mass spectral data from the primary kinetic isotope effect determination (2 pages). Ordering information is given on any current masthead page.

Stereospecific Photodimerization of Coumarins in Crystalline Inclusion Complexes. Molecular and Crystal Structure of 1:2 Complex of (*S*,*S*)-(−)-1,6-Bis(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol and Coumarin

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Proximity of molecules is a crucial factor in many solid-state photochemical processes.[1,2] The biomolecular photodimerization reactions in the solid state depend on the relative geometry of reactant molecules in the crystal lattice with center-to-center distance of nearest neighbor double bonds of the order of ca. 4 Å. This fact emanates from the incisive studies of Schmidt and Cohen.[2] One of the two approaches to achieve this distance requirement is the so-called "Crystal-Engineering" of structures, which essentially involves the introduction of certain functional groups that display in-plane interstacking interactions (Cl···Cl, C–H···O, etc.) in the crystal lattice.[3,4] The chloro group is by far the most successful in promoting the β-packing mode,[2,5] though recent studies have shown its limitations.[6] Another approach involves the use of constrained media in which the reactants could hopefully be

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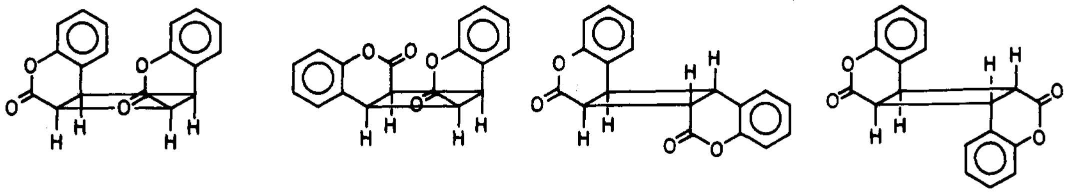
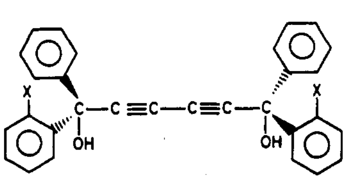
Chart I



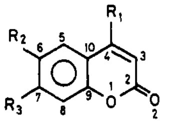
a) Syn head-to-head b) Syn head-to-tail c) Anti head-to-head d) Anti head-to-tail

aligned. In this connection host systems such as the cyclodextrins, cavitands, spherends and calixarenes with varying cavity sizes and different forces of interaction come to mind.[7] Another strategy appears to be the design of inclusion host–guest compounds where the packing of the host molecules is such that the guest molecules could be accommodated within the voids of the crystal lattice.[8]

Toda and co-workers have discovered recently that 1,1,6,6-tetraphenylhexa-2,4-diyne-1,6-diol (Ia) and its chiral chloro derivative 1,6-bis(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol (Ib) include a variety of organic compounds and form crystalline complexes stoichiometrically.[9] It has been observed that the hydroxyl groups of the diols act as anchors for holding two guest molecules in space through hydrogen bonds. Recent reports on the use of these host compounds for enantioselective reactions in the solid state are remarkable in that the guest molecules that are light stable in their crystalline state are observed to photodimerize in the inclusion compounds with the achiral host (Ia).[8,10,11]



Ia. X = H ; Ib. X = Cl



II $R_1 = R_2 = R_3 = H$

III $R_1 = R_2 = H$; $R_3 = CH_3$

IV $R_1 = R_2 = H$; $R_3 = OMe$

V $R_1 = R_2 = CH_3$; $R_3 = H$

VI $R_1 = R_3 = CH_3$; $R_2 = H$

VII $R_1 = Cl$; $R_2 = R_3 = H$

In continuation of our studies on the photodimerization of coumarins in solution as well as in the crystalline state,[12] we have investigated the photodimerization of coumarins by forming solid inclusion complexes with the above diols (Ia and Ib) and the results are discussed in this paper.

Coumarins, in principle, can form four possible dimers: syn head-to-head (a), syn head-to-tail (b), anti head-to-head (c), and anti head-to-tail (d) (Chart I). Although coumarin (II) in the crystalline state was originally considered to be photoinert,[13] careful experiments carried out recently in our laboratory revealed that three isomeric dimers are formed upon irradiation. Molecular packing in the crystals of coumarin dictates that the photoreaction must be defect initiated.[14] Thus, it is ideal to investigate its photochemical behavior when complexed with Ia and Ib. It was observed that the inclusion complex of coumarin (II) with the achiral host (Ia) was photoinert, whereas the complex with the chiral host (Ib) yielded the syn head-to-head dimer with ca. 100% yield upon irradiation.

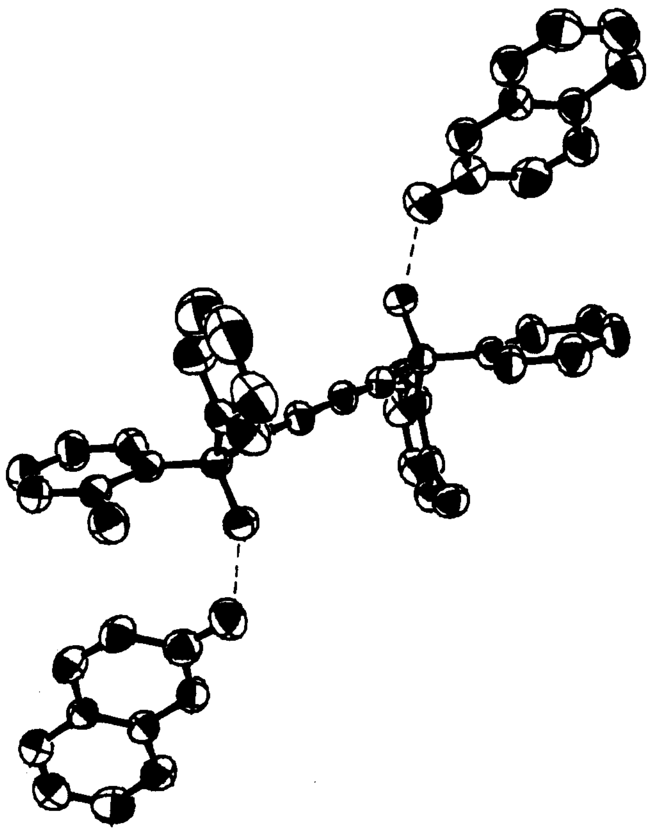


Figure 1.

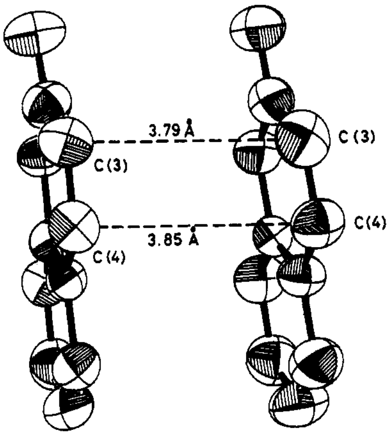


Figure 2.

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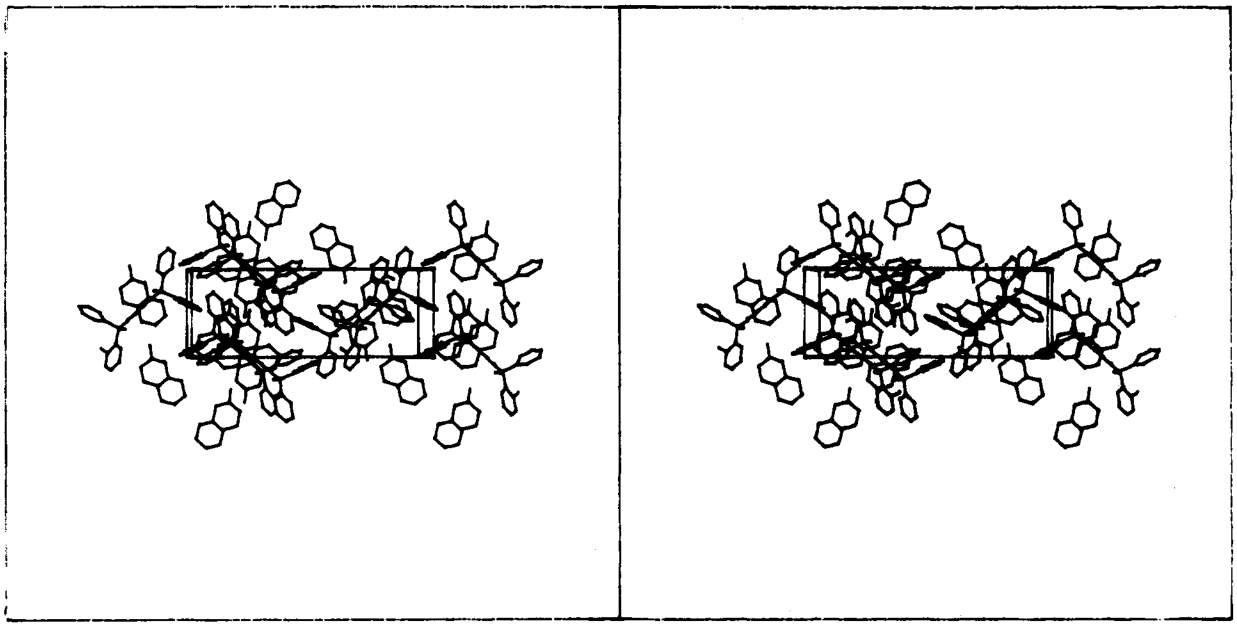

Figure 3.

Single-crystal X-ray structure analysis was done in order to unravel the correlation between the packing arrangement and photochemical reactivity.

The complex crystallized in the chiral space group $P2_12_12_1$. The host molecule takes the trans conformation with respect to the hydroxyl groups at the terminal sp^3 carbons. It is observed that both the hydroxyl groups form O–H···O hydrogen bonds with the carbonyl oxygens of the two coumarins. One of the two coumarins in the asymmetric unit cell upon translation along the *a* axis comes close to the other independent molecule such that the reactive double bonds are at an average distance of 3.8 Å. The juxtaposition of the two coumarins is consistent with the observed syn head-to-head product. Figure 1 shows the ORTEP diagram of the 1:2 complex of Ib and coumarin (II) and the involvement of guest molecules in hydrogen bonding with the hydroxyl groups of the host. Figure 2 depicts the mutual orientation of the coumarins. The stereopacking diagram of the complex molecules is shown in Figure 3.

As efforts to obtain suitable single crystals of the complex of coumarin (II) and achiral diol Ia were unsuccessful, X-ray structure analysis could not be carried out to rationalize its photoinertness. It is obvious, however, from infrared stretching frequencies of hydroxyl groups (3350–3450 cm^{-1}) that the carbonyl groups of coumarins are involved in hydrogen bonding. While the complex between achiral diol Ia and coumarin (II) is photoinert, it may be observed that the chiral host is very efficient in inducing β-packing of guest molecules resulting in mirror symmetric photodimer.

The study was extended to the investigation of photobehavior of a few more substituted coumarins when complexed with Ia and Ib. The results are recorded in Table I. It is noteworthy that with the chiral diol Ib as the host, syn head-to-head dimers were compared when 7-methylcoumarin (III) and 7-methoxycoumarin (IV) were used as the guests. However, no dimerization resulted with 4,6-dimethyl (V), 4,7-dimethyl (VI), and 4-chloro (VII) coumarins. Single-crystal analysis of the complexes of any of these guest molecules with the host Ib would throw light on the nature of the molecular packing in the crystals of the photoinert complexes. Unfortunately attempts to obtain crystals of suitable quality for detailed crystallographic studies have not been successful. With the exception of 7-methoxycoumarin (IV), none of the other coumarins photodimerized when complexed with the achiral host Ia, although complex formation is evidenced from IR spectra. The complex of 7-methoxycoumarin (IV) with Ia yielded syn head-to-tail dimer as observed in its pure crystalline state.[15]

Table I. Summary of Experimental Results

guest	host	host:guest	durtn of irradtn (h)	nature of dimer	yield, %
II	Ia	1:2		no dimer	
II	Ib	1:2	9	syn head–head	100
III	Ia	1:2	30	no dimer	
III	Ib	1:2	30	syn head-head	90
IV	Ia	1:2	14	syn head-tail	70
IV	Ib	1:2	14	syn head-head	66
V	Ia	1:2	100	no dimer	
V	Ib	1:2	100	no dimer	
VI	Ia	1:2	100	no dimer	
VI	Ib	1:2	100	no dimer	
VII	Ia	1:2	100	no dimer	
VII	Ib	1:2	100	no dimer	

One of the reasons for the successful execution of dimerization with the host Ib could be attributed to its molecular conformational flexibility as observed in the complexes formed with different guests.[16] Such a situation would be expected to result in different packing arrangements. This is an important consideration in using these diols as efficient hosts for it is mainly the voids in the molecular assembly in the crystal lattice that permit incorporation of guest molecules and reaction between them. Achiral diol Ia possesses a molecular center of inversion. This often coincides with the crystallographic center of symmetry, restricting, thereby, the variations in packing modes.

Conclusions

The results reported so far in the literature[11,17] show that complexation with diol Ia essentially results in α–packing of the guest molecules, giving rise to dimer with a center

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of symmetry. Even with the limited cases discussed here, it turns out that the dimer formed in all the photoreactive complexes with the chiral host (Ib) is mirror symmetric. Further, the results demonstrate that the chiral diol is a much better system than the achiral one in achieving photodimerization of reactive guest molecules with good yield. The large dimer yield is suggestive of the fact that the voids are big enough to permit reorientation of guest molecules upon excitation so as to achieve better overlap of π-orbitals of the reacting centers. The photodimerization reaction reported here appears to be the first case where the chiral diol has been successfully used.

Experimental Section

Preparation of Inclusion Complexes. The complexes of coumarins with Ia and Ib were formed by dissolving 2:1 equiv of guest and host, respectively, in chloroform or methanol and evaporating the solvent at room temperature over a period of 2 days. The complexes were characterized by melting points and broadening of the OH stretching frequency in the IR spectra owing to hydrogen bonding with the carbonyl group of the guest coumarins.

Photolysis and Characterization of Dimers. The powdered samples were irradiated by Rayonet lamps ($\lambda > 320$ nm) at room temperature with occasional shaking. The appearance of multiplets for the cyclobutyl protons of the dimers in the ^{1}H NMR spectrum of the irradiated mixture was followed at different intervals of time. The dimers of coumarin (II) and 7-methoxycoumarin (IV) were isolated by extracting the irradiated mixture with ethanol in which the host and guest dissolve but not the dimer. The dimer of 7-methylcoumarin was isolated by PTLC by elution with 10% ethyl acetate in hexane. The dimers were characterized by comparing the multiplicity pattern of cyclobutyl protons in the ^{1}H NMR spectrum with those already reported in the literature[12] and by mass spectral analysis. Percentage of conversions were deduced from the integrations of olefinic and cyclobutyl protons in the NMR spectrum of the irradiated complex.

X-ray Crystallographic Data. 1,1-Bis(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol–Coumarin (1:2) [$C_{30}H_{20}O_2Cl_2$-$2C_9H_6O_2$]. Single crystals amenable for X-ray crystallography were grown by slow evaporation of the solution of 2:1 equiv of II and Ib in a 1:1 mixture of CH_2Cl_2 and CCl_4. The crystals were orthorhombic, space group $P2_12_12_1$, a = 8.451 (1), b = 19.746 (2), and c = 22.775 (2) Å. The calculated density is 1.355 g cm^{-3} for Z = 4. The data were collected on an Enraf nonius CAD-4 diffractometer with Cu Kα (1.5418 Å) radiation using a $\omega/2\theta$ scan mode up to $\theta \leq 65°$. A total of 2737 reflections were significant $[|F_o| \geq 3\sigma(|F_o|)]$. The direct methods program MULTAN87[18] was used for structure solution. The refinement of positional and anisotropic thermal parameters of non-hydrogens and positional and thermal parameters of hydrogens by full matrix least-squares procedures using SHELX76[19] converged to a final R value of 0.058. The final difference Fourier map was featureless with ρ_{max} = 0.28 and ρ_{min} = -0.25 e/Å^3.

Acknowledgment. We wish to record our grateful thanks to Prof. Fumio Toda for very generous supply of the host systems used in the present investigations and for many helpful suggestions. Financial assistance by the Council of Scientific and Industrial Research, India, is acknowledged.

Registry No. Ia, 20583-04-4; Ia·2II, 136538-04-0; Ia·2III, 136538-06-2; Ia·2IV, 136538-08-4; Ia·2V, 136538-10-8; Ia·2VI, 136538-12-0; Ia·2VII, 136538-14-2; Ib, 86436-20-6; Ib·2II, 136538-05-1; Ib·2III, 136538-07-3; Ib·2IV, 136538-09-5; Ib·2V, 136538-11-9; Ib·2VI, 136538-13-1; Ib·2VII, 136538-15-3; II, 91-64-5; II (dimer a), 5248-11-3; III, 2445-83-2; III (dimer a), 93097-92-8; IV, 531-59-9; IV (dimer a), 37818-63-6; IV (dimer b), 37786-10-0; V, 14002-89-2; VI, 14002-90-5; VII, 17831-88-8.

Supplementary Material Available: Full details of the X-ray analyses of host and guest molecules (21 pages). Ordering information is given on any current masthead page.

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Additions and Corrections

Vol. 56, 1991

F. M. Menger. The Negative Rate Constants of Breslow and Huang.

Page 6251. The following passage was inserted by the author during galley proofs and did not appear in the version of the manuscript that was approved for publication by the Editor:

"Dr. Albert Haim of Stony Brook simultaneously and independently uncovered a variety of other problems with the Breslow manuscripts (e.g., the reported rate constants and equations do not fit the theoretical plots). His analysis will be published elsewhere. Neither of us was permitted to publish our work in the journal where the errors originated."

The Editors would not have permitted the manuscript to be published with this passage, had it been in the version of the manuscript that was accepted.