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Notes

Reactions in the Solid State. 4.[†] Enantioselective Photochemical Reactions in Crystalline Inclusion Compounds

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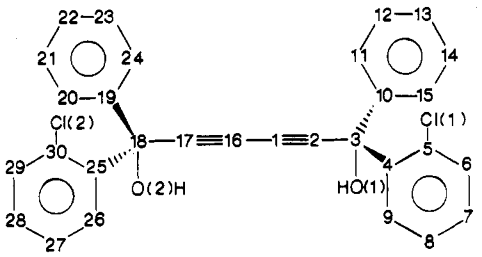
1,1,6,6-Tetraphenylhexa-2,4-diyne-1,6-diol has been found to cocrystallize—that is, act as a host in "inclusion compounds"—with a variety of "guest" molecules possessing carbonyl group(s).[1,2] Presumably the diol host molecule, in which the hydroxyl groups are highly protected by the terminal phenyl groups, is incapable of forming efficient hydrogen bonds with itself (as far as we are aware, crystals of the pure host have not yet been obtained) but can do so with appropriate guest molecules.[1,2]

If the guest molecule is photochemically reactive, a photochemical reaction may occur within the crystal (the crystal is destroyed in this process). Two types of such photochemical reactions have been studied: (1) intermolecular reactions between pairs of guest molecules, such as [2 + 2] and [4 + 4] photocyclodimerization[1-4] and (2) intramolecular reactions.[4,5] Both types of reactions are stereospecific; crystallographic studies of four such inclusion compounds show that the stereospecificity is controlled by the packing of the photoreactive guests with the host.

If, now, the host molecule is optically active, the photochemical reaction that takes place within the crystal may be enantioselective.[4,6] We report here the crystal structures of two such systems where enantioselective photochemical reactions are known to take place. In each case the host molecule is 1,6-bis(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol (**1**); the guest molecules are tropolone ethyl ether (**2**) and *N*,*N*-dimethyl-α-oxobenzeneacetamide (**3**).

Irradiation of tropolone alkyl ethers[7] in solution is known to produce, as an initial product, a racemic mixture of the alkyloxybicyclo[3.2.0]hepta-3,6-diene-2-ones of type **4** (see Scheme I). However, irradiation of the crystalline inclusion compound of **2** with the *S*-(−) isomer of **1** results in the 1*S*,5*R*-(−) isomer of **4** in 100% optical purity, as shown in Scheme I.

Photocyclization of α-oxo amide to form β-lactams has long been studied in connection with a synthetic approach to penicillin derivatives.[8,9] It has been found[10] that the photocyclization product depends both on the substituent on the α-oxo amide and on the solvent. Thus, irradiation of *N*,*N*-dialkyl-α-oxo amides in methanol yields the corresponding oxazolidin-4-ones as main products, while irradiation of *N*,*N*-dibenzyl-α-oxo amides in an aprotic solvent gives predominantly the corresponding β-lactams.



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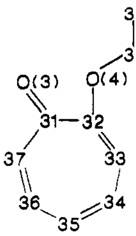

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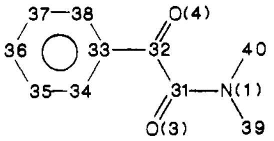

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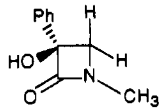
In all cases the β-lactam derivatives are obtained as racemic mixtures, of cis and trans isomers, since the reaction proceeds via a zwitterionic intermediate;[11] no efficient enantioselective control of the photocyclization reaction in solution has yet been reported, although 15% ee of the β-lactam derivative has been obtained by solid-state photolysis of the complex of *N*,*N*-dimethylpyruvamide with desoxycholic acid.[12] Recently, photocyclization of three different α-oxo amide in solid-state inclusion compounds with various host molecules has been reported;[4] in all these experiments only β-lactams (and no oxazolidin-4-one) were formed, and in some cases the reaction was enantiospecific. In one example,[13] the (*S*)-(−)-**5** enantiomer was obtained in 100% purity upon photolysis of the inclusion compound of (*S*)-(−)-**1** with **3**.



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In an attempt to understand the details of the enantioselectivity of these solid-state photolysis reactions, we have carried out crystal structure studies of the inclusion compounds **1**–**2** and **1**–**3**.

[†] Part 3: Kaftory, M. *Tetrahedron* **1987**, *43*, 1511.

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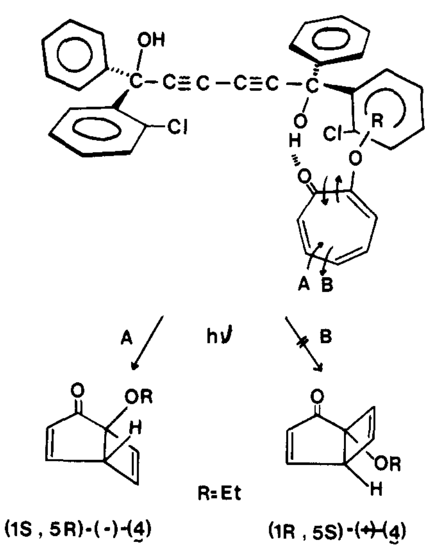
Scheme I



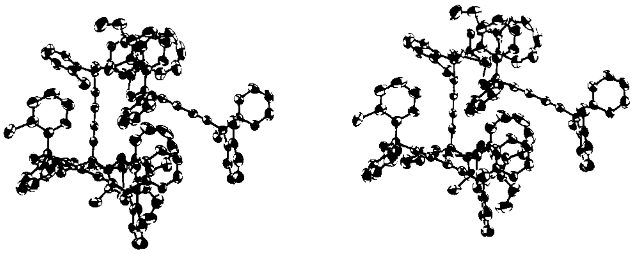


Figure 1. Stereoscopic view of host–guest molecules in 1–2 showing the hydrogen bond network.

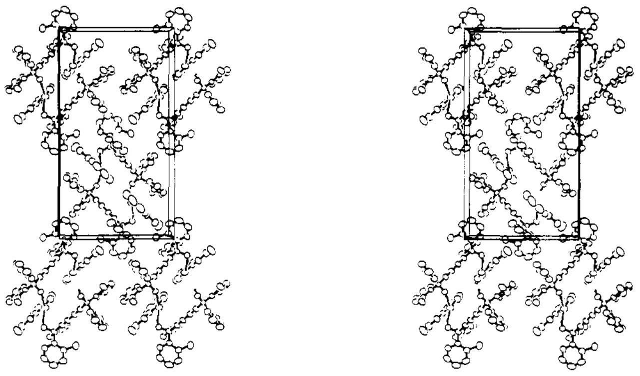


Figure 2. 1–2 stereoscopic view of the packing arrangement in the unit cell.

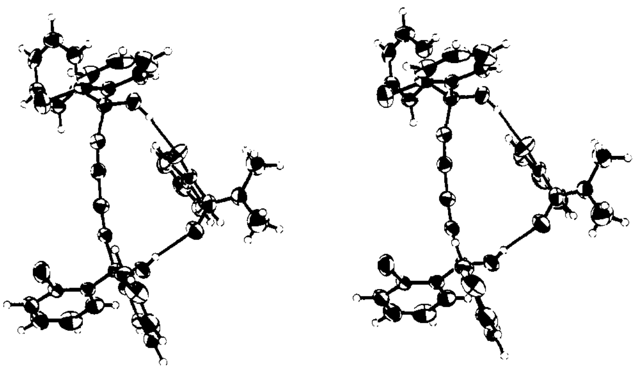


Figure 3. Stereoscopic view of 1–3 host–guest molecules.

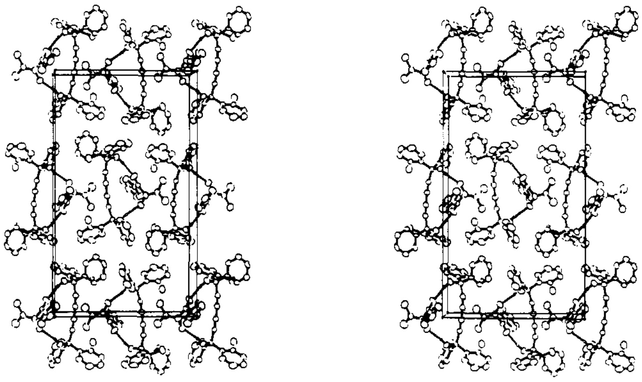


Figure 4. 1–3 stereoscopic view of the packing arrangement in the unit cell.

Results

Stereoscopic drawings[14] of the host–guest linkage and of the packing in the unit cell are shown in Figures 1 and 2 for the 1–2 complex and in Figures 3 and 4 for the 1–3 complex.

There are no surprises in either the bond distances and angles or the conformations of either of the guest molecules. The geometry of the tropolone ethyl ether molecule (2) is similar to that found for chanootin[15] and for *N*-desacetyl-*N*-methylcolchicine.[16] The ring is nearly planar in all three compounds, although two of the torsion angles in 2 are slightly greater, at 6.2° and 8.4°, than any found in the other two compounds. The torsion angle between the two keto groups in 3 is 101°, slightly smaller than the 108° found in crystals of benzil.[17]

The general conformation of the host molecule 1 is roughly the same in both structures, the carbon atoms at the ends of the hexa-2,4-diyne chain being eclipsed with respect to one another and their substituent hydroxyl groups being syn. However, there is a distinct difference with respect to the diyne chain, which is effectively linear in the 1–2 complex but noticeably curved in the 1–3 complex (see Figure 3). The individual bond angles at the four acetylenic carbon atoms are not greatly different, ranging from 174.3° to 179.4° in 1–2 and from 168.8° to 176.3° in 1–3; but the deviations of these atoms from the line joining the two end carbon atoms are less than 0.15 Å for 1–2 but as much as 0.36 and 0.46 Å for 1–3. The curvature of this latter diyne grouping approaches that found in 1,3,7,9-cyclododecatetrayne[18,19] (bond angles, 165.1–168.7°; displacements from 1–6 line, 0.6–10Å), which has severe geometrical constraints. It seems quite clear that the curving seen in the 1–3 compound is an accommodation to the –OH···O hydrogen bonds from the hydroxyl groups of the host to the carbonyl groups of the guest and that the energy needed for bending the diyne chain is regained in the formation of these hydrogen bonds. The O···O distances in the hydrogen bonds, which appear to be the predominating interactions between the host and guest molecules, are 2.805 and 2.843 Å.

Guest–host hydrogen bonds are also a feature of the 1–2 structure (Figure 1); in this case, however, the guest

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molecule has but one carbonyl group which accepts hydrogen bonds from two different host molecules. Stacking interactions between the tropolone ring and the phenyl rings of the host molecules seem to be very important in this structure (see Figure 2).

Enantioselectivity. The guet molecules **2** and **3** undergo different photochemical reactions; **2** undergoes photochemical electrocyclic ring closure (see Scheme I) while **3** undergoes H abstraction followed by ring closure. Tropolone ethyl ether undergoes a disrotatory closure either through path A or through path B (see Scheme I) to form (−)-**4** or (+)-**4**, respectively. It seems that the enantioselectivity is controlled by the ethyl ether substituent. Mean plane calculation through the tropolone moiety shows that atoms O(4), C(38), and C(39) [see atomic notation in **2**] are displaced by 0.11, 0.19, and 0.31 Å, respectively, from this plane. The direction of the displacement is consistent with path A.

The enantioselectivity of **3** is controlled by the conformation about the O=C—C=O single bond. The observed torsion angle is 101° and in the absence of a mirror symmetry related molecule (torsion angle of −101°), a single enantiomer is formed.

Conclusions

Systematic study of related compounds is needed to prove that the enantioselectivity is governed by the conformation of the potochemical reactive species and by the space provided by the molecular packing. It is clear, however that the chiral host molecule holds the guest in a specific conformation (as at the active site of an enzyme) and hence that the chirality of the product is dictated by the chirality of the host.

Experimental Section

The preparation and the photolysis of the inclusion compounds **1–2** are described in ref 1 and 4.

Preparation of a 1:1 Complex of (−)-1 and 3. When a solution of (−)-**1** (1.0 g, 2.1 mmol) and **3** (0.37 g, 2.1 mmol) in ether–petroleum ether (1:1) (10 mL) was kept at room temperature for a day, a 1:1 complex of (−)-**1** and **3** was obtained as colorless prisms (1.02 g, 74.5%; mp 126–127 °C. Found: C, 72.8; H, 4.87; N, 2.21. Calcd for $C_{40}H_{31}NO_4Cl_2$: C, 72.73; H, 4.73; N, 2.12.

Photoreaction of a 1:1 Complex of (−)-1 and 3 in the Solid State. The powdered 1:1 complex (0.85 g) of (−)-**1** and **3** was irradiated by a 400-W high-pressure Hg lamp at room temperature, for 27 h with occasional grinding with a pestle and mortar. The reaction mixture was chromatographed on silica gel with benzene–ethyl acetate as solvent to give (−)-**1** (1.0 g, 100%) and 100% ee (−)-**5** (optical purity was determined by HPLC on Chiralcel OC (Daicel Chemical Ind.), $[\alpha]_D$ −99.7° (*c* 0.34, $CHCl_3$) as colorless plates, mp 123–124 °C. Found: C, 67.66; H, 6.28; N, 7.76. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.91.

Other details of analysis of the photolysis products of similar systems are described in ref 4.

Crystal Data. 6-Bis(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol–tropolone ethyl ether [$C_{30}H_{20}O_2Cl_2$–$C_9H_{10}O_2$; **1–2**], orthorhombic, space group $P2_12_12_1$, a = 26.446 (12) Å, b = 14.328 (7) Å, c = 8.679 (4) Å. The calculated density is 1.279 g/cm^3 for Z = 4. At the end of the refinement of 2185 reflexions [$F_o > 1.5\sigma(F_o)$] the agreement factors are R = 0.065 and R_w = 0.054 ($w = 2.4311/[\sigma(F_o)^2 + 0.003F_o^2]$).

1,6-Bis(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol–*N*,*N*-dimethyl-α-oxobenzeneacetamide [$C_{30}H_{20}O_2Cl_2$–$C_{10}H_{11}NO_2$; **1–3**], orthorhombic, space group $P2_12_12_1$, a = 26.656 (12) Å, b = 15.458 (8) Å, c = 8.129 (4) Å. The calculated density is 1.310 g/cm^3 for Z = 4. At the end of the refinement of 2222 reflexions [$F_o > 1.5\sigma(F_o)$] the agreement factors are R = 0.065 and R_w = 0.054 ($w = 0.9865/[\sigma(F_o)^2 + 0.0F_o^2]$). Intensity data were collected on a PW 1100 four-circle diffractometer using ω–2θ scans and graphite-monochromated Mo Kα radiation (λ = 0.7107 Å). Both structures were solved by MULTAN 80[20] and refined by SHELX[21] in two separate blocks consisting of the host molecule in one and the guest and hydrogen atoms in the other. The correct enantiomorph was introduced according to the preparation procedure.[6,4] (For supplementary material see paragraph at the end of the paper).

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Registry No. (*S*)-(−)-**1**·**2**, 107932-02-5; (*S*)-(−)-**1**·**3**, 115118-99-5; (*S*)-(−)-**5**, 115119-00-1.

Supplementary Material Available: Tables of atomic coordinates, isotropic and anisotropic atomic displacement parameters, and bond lengths and angles (14 pages); tables of structure factors (26 pages). Ordering information is given on any current masthead page.

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Alkylation of (1*S*,2*R*,5*R*,6*S*,7*R*)- and (1*R*,2*R*,5*R*,6*S*,7*S*)-5-Methyl-4-oxatricyclo[5.2.1.0^{2,6}]-8-decen-3-one. Application to the Synthesis of (*R*)-3-Alkyl-5-methyl-2(5*H*)-furanones

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The retro-Diels–Alder reaction has been extensively applied for the synthesis of natural products in the last 10 years.[1] In one of the most frequent synthetic strategies, this reaction is used to protect a double bond, generated again after elimination of the diene. We have recently reported the Diels–Alder cycloaddition of (*R*)-angelica lactone, **1**,[2] with cyclopentadiene to afford enantiomerically pure endo and exo adducts, **2** and **3**, respectively.[3] In the present work, we describe the alkylation of both diastereoisomeric adducts and subsequent pyrolysis to provide an easy entry to optically active (*R*)-3-alkyl-5-methyl-2-(5*H*)-furanones **12–15** in good yields. Many of such compounds have a natural origin and interesting properties, e.g., butenolide **12** is a component of mushroom flavor,[4] **13** has fungicidal activity,[5] and **14** is a metabolite from *Streptomyces griseus*.[6] A related route has been published,[7] based on the alkylation of adducts from maleic anhydride and cyclopentadiene, to yield racemic butenolides. On the other hand, the method reported herein provides a general pathway leading to a variety of dialkyl

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