O1(G'), 3.8 Å between O1(G) and C1(G'), and 4.6 Å across the gap C4(G')···C4(G). Therefore, the occupancies of G and G' were kept fixed at 0.25, yielding $R = 0.099$, $R_w = 0.097$, and an isotropic U value of 0.077 (3) Å^2 for the guest atoms.

We had assumed for G and G' a cis C_β—C_α—C=O conformation as had been definitely indicated by the difference map in which the oxygen peaks were by far the highest (Figure 14) and by the evidence already provided above in the analysis on DCA–methyl pentyl ketone. Moreover, the acetyl moieties of the ethyl methyl ketone G and G' molecules occupy almost the same locations (relative to steroid host) in the channel as the corresponding $H_3CCOC_2H_4$ moieties of methyl pentyl ketone. Nevertheless, least-squares calculations were carried out to verify the positions of atoms O1 and C1 of ethyl methyl ketone in a procedure akin to that adopted on methyl pentyl ketone. The refinement yielded $R = 0.095$ and $R_w = 0.094$. The refined geometries of the guests, shown in Scheme IX (in angstroms) did not distinguish between the oxygen and methyl groups certainly not in terms of the esd's in the C=O and C—CH_3 bond lengths. Nevertheless, in terms of all the facts presented here, there can be no doubt as to the cis conformation of C_β—C_α—C=O in ethyl methyl ketone.

Structure Determination (at 293 K). The final x, y, and z coordinates of DCA–ethyl methyl ketone at 103 K were used as a starting model for refinement of the room-temperature crystal structure. An R value of 0.097 was obtained. The isotropic thermal parameter of the guest molecules converged to 0.169 (6) Å^2, keeping the occupancies of G and G' each fixed at 0.25.

5.8. DCA–Cyclohexanone (at 293 K). The crystal structure was solved by MULTAN[25] although we had strong reason to believe that the host structure was isomorphous with that of DCA–di-*tert*-butyl diperoxymonocarbonate,[12] as indeed it proved to be. The host structure belongs to the γ motif. The C and O atoms of the guest molecule were unambiguously located, not being subject to disorder by virtue of the 14-Å c axis. The occupancy of the guest molecule was taken to be 0.5, its maximum possible value. Refinement proceeded smoothly to an R value of 0.086; the average U value of the guest C and O atoms was 0.23 Å^2.

5.9. Results of X-ray Crystal Structure Refinements. Details on the final cycle of refinements are given in Table III. The atomic x, y, and z coordinates and U_{eq} of DCA–acetone (at 103 K), APA–acetone, DCA–diethyl ketone, DCA–cyclohexanone, DCA–ethyl methyl ketone (at 103 K), and DCA-methyl pentyl ketone are listed in Tables IV–IX, respectively. Anisotropic temperature factors U_{ij}, bond lengths, and bond angles are listed in supplementary material Tables 4S–9S; the x, y, and z coordinates of DCA–acetone (at 293 K) and DCA–ethyl methyl ketone (at 293 K) are listed in Tables 4S and 8S, respectively.

Acknowledgment. We thank Prof. M. D. Cohen for fruitful discussions. We thank the Israel/U.S. Binational Science Foundation and the Israel Academy of Science and Humanities for financial support.

Registry No. 1, 66014-00-4; **1** (methyl ester), 95484-83-6; **2**, 66014-23-1; **2** (methyl ester), 95484-84-7; **3**, 66971-13-9; **3** (methyl ester), 95615-84-2; **4**, 66014-20-8; **5**, 95484-85-8; **6**, 83035-68-1; **6** (methyl ester), 95484-86-9; **7**, 58678-36-7; **7** (methyl ester), 95484-87-0; **8**, 77522-07-7; **9**, 95484-88-1; **9** (methyl ester), 95484-89-2; **10** (isomer 1), 95586-12-2; **10** (methyl ester) (isomer 1), 95484-90-5; **10** (isomer 2), 95586-13-3; **10** (methyl ester) (isomer 2), 95484-91-6; **11** (isomer 1), 95586-14-4; **11** (isomer 2), 95586-15-5; DCA·$^3/_5$acetone, 83035-57-8; DCA·$^1/_2$(diethyl ketone), 83047-97-6; DCA·$^1/_2$cyclohexanone, 95484-92-7; DCA·$^1/_2$(ethyl methyl ketone), 83035-64-7; DCA·$^1/_3$(methyl pentyl ketone), 95484-93-8; APA·acetone, 66971-12-8.

Supplementary Material Available: Thermal parameters, bond angles, and bond lengths of molecules A and B (26 pages). Ordering information is given on any masthead page.

Reaction Pathways in Crystalline Host–Guest Inclusion Complexes: Rotation by a Net 180° of the Acetyl Group on Photoaddition of Guest–Acetophenone and –*m*-Chloroacetophenone to the Atom C5 of Host Deoxycholic Acid

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Abstract: The crystalline host–guest channel inclusion complexes 5:2 (DCA) deoxycholic acid–acetophenone ($C_6H_5C'OCH_3$) and 3:1 DCA–*m*-chloroacetophenone ($CLC_6H_4C'OCH_3$) each yield on UV irradiation a photoproduct via addition of guest to the steroid tertiary carbon atom C5 with the formation of a new chiral carbon center C'(OH)(CH_3)(C_6H_5)(DCA) of S configuration. The crystal structures of the two host–guest complexes were determined by low-temperature (103 K) X-ray diffraction; a low-temperature (16 K) neutron study was made on DCA–$C_6H_5COCD_3$. The inclusion compounds DCA–$C_6H_5COCH_3$ and DCA–$CLC_6H_4COCH_3$ each contain two crystallographically independent guest molecules G and G' arranged along the channel axes such that both G and G' should form the same diastereomeric product at C5. A comparison of the stereochemistry of each of the two isolated photoproducts and the host–guest arrangements at the reaction sites in each corresponding complex indicates that photoaddition of the guest molecule to C5 takes place with a net rotation of 180° by the guest acetyl group.

1. Introduction

1.1. Statement of the Problem. In the previous paper in this issue,[2] we described the regiospecific solid-state photoaddition of several guest aliphatic ketones to the host deoxycholic acid (referred to as DCA) in the channels of the bile acids. A comparative analysis of the stereochemistries of the reaction products formed,

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(2) Popovitz-Biro, R.; Tang, C. P.; Chang, H. C.; Lahav, M.; Leiserowitz, L. *J. Am. Chem. Soc.*, preceding paper in this issue.

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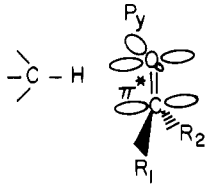
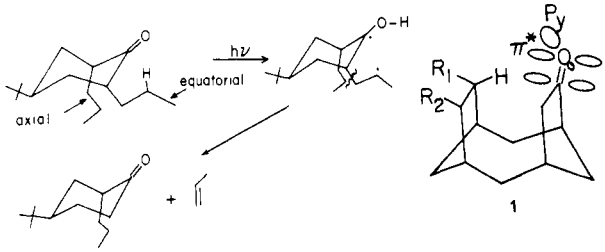
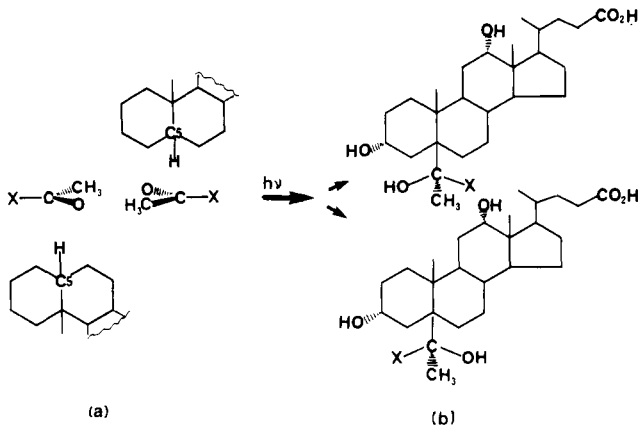
Scheme I



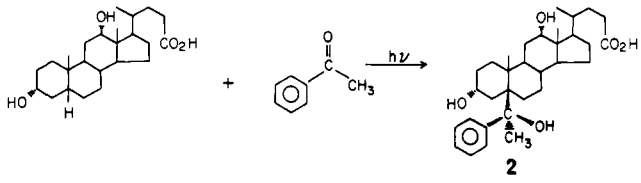
Scheme II



Scheme III



Scheme IV



with the corresponding host–guest arrangements at the sites of reaction prior to photoaddition, demonstrated the topochemical nature of this reaction. In all the complexes where reaction occurred, the plane of the guest carbonyl system >C=O tends to be perpendicular to the C–H bond of the steroid hydrogen to be abstracted. Consequently, in these systems, the P_y orbital of the guest oxygen atom tends to be perpendicular to the C–H bond, and the π^* orbital tends to be parallel to the C–H bond (Scheme I). A number of theoretical and experimental studies have been carried out probing the mechanism of the hydrogen abstraction in terms of the orientation of the to-be-abstracted hydrogen vis-a-vis the carbonyl >C=O system. Zimmerman[3] suggested that the hydrogen abstraction is dominated by the electrophilic attack of the P_y orbital of the $n - \pi^*$ excited carbonyl group. This suggestion was further supported by Salem's symmetry plane assumption,[4] stating that the most favorable orbital interaction is one in which the >C=O and H—X groups are coplanar. On the experimental side, Turro[5] observed that irradiation of 2,6-

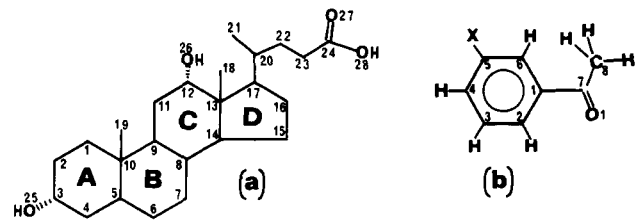


Figure 1. Atom labeling. (a) Deoxycholic acid (DCA). (b) Acetophenone, x = H; *m*-chloroacetophenone x = CL.

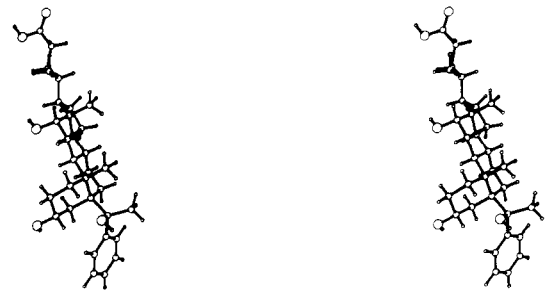


Figure 2. Photoproduct **2** from DCA–acetophenone in its own crystal structure.

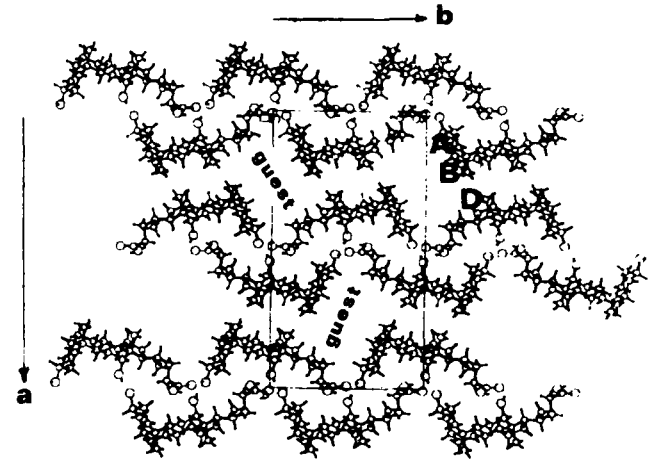


Figure 3. Packing arrangement of DCA molecules in the α motif viewed along the channel *c* axis. The guest molecules are not shown.

di-*n*-propylcyclohexanone yields the less stable axial isomer of 2-*n*-propylcyclohexanone, which he rationalized by an in-plane approach of the equatorial C–H bond toward the P_y orbital of the excited carbonyl (Scheme II). From these results, however, the author could not exclude unambiguously the possibility that hydrogen can be abstracted by the π^* orbital as well. In this respect, Sugiyama et al.[6] noticed that in compound **1**, where the π^* orbital is directly aligned toward hydrogen H, the carbonyl oxygen atom does not abstract that atom upon photoirradiation. Scheffer, Trotter, and co-workers,[7] in their studies on the photochemistry of rigid tetrahydro-1,4-naphthoquinones in solution and in the solid state, confirmed that the abstracted hydrogens are almost coplanar with the carbonyl system >C=O, deviating from it by an angle no more than 8°. Recently similar studies were carried out on low-melting α-cyclohexylacetophenones. In these systems, the hydrogen lies outside the mean plane of the carbonyl group. The C–H bond of the to-be-abstracted hydrogen and the carbonyl group tends to be parallel.[8]

(3) Zimmerman, H. E. *Adv. Photochem.* **1963**, *1*, 183 and references cited therein.
(4) Dauben, W. G.; Salem, L.; Turro, J. N. *Acc. Chem. Res.* **1975**, *8*, 41.
(5) Turro, N. J., Weiss; D. W. *J. Am. Chem. Soc.* **1968**, *90*, 2185. Davies, K.; Dalton, J. C.; Turro, N. J. *Mol. Photochem.* **1971**, *3*, 71.
(6) Sugiyama, N.; Nishio, T.; Yamada, K.; Aoyama, H. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 1879.
(7) Scheffer, J. R. *Acc. Chem. Res.* **1980**, *13*, 283. Trotter, J. *Acta Crystallogr, Sect. B* **1983**, *B39*, 373.
(8) Ariel, S.; Ramamurthy, V.; Scheffer, J. R.; Trotter, J. *J. Am. Chem. Soc.* **1983**, *105*, 6959.

Table I. ^{13}C NMR Data on Photoaddition Products 2 and 3

	2	3
C1	32.5	32.3
C2	30.9	30.9
C3	69.2	69.3
C4	38.1	38.0
C5	49.3	49.1
C6	29.1	29.7
C7	28.8	28.8
C8	37.5	37.6
C9	36.3	36.4
C10	41.7	41.7
C11	30.8	30.9
C12	75.2	75.2
C13	46.7	46.7
C14	49.2	49.1
C15	24.7	24.7
C16	28.4	28.5
C17	47.9	47.9
C18	13.0	13.0
C19	20.6	20.4
C20	36.4	36.4
C21	17.6	17.6
C22	31.7	31.6
C23	31.7	31.6
$C(OH)CH_3$	85.3	85.1
$C(OH)CH_3$	30.1	30.1
phenyl C's	128.1	127.3
	129.0	128.0
	129.0	128.0
	129.4	128.0
	153.0	154.3

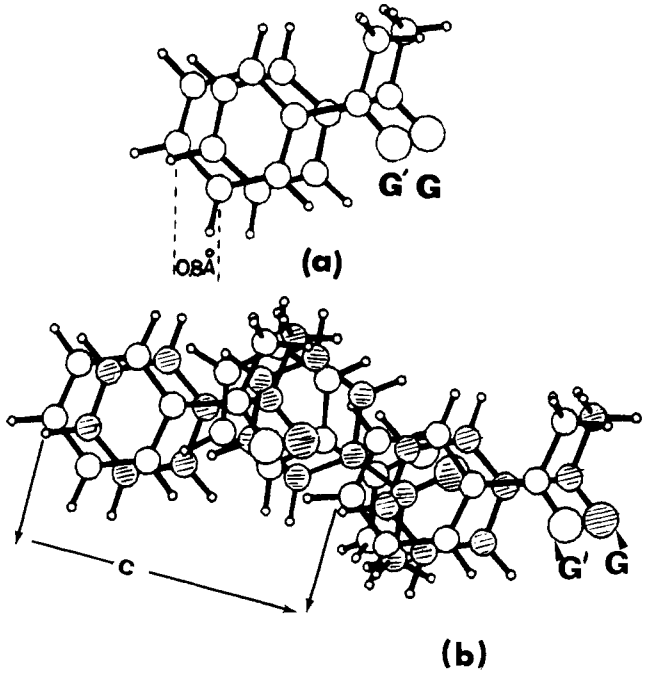


Figure 4. (a) Overlapping pair of guest acetophenone molecules $G(x,y,z)$ and $G'(x,y,z')$ referred to the same molecular site. (b) Molecular overlap of acetophenone guest molecules G (shaded atoms) and G' (unshaded atoms) in the channel. The arrangement may be derived from the molecular pair in (a) by applying 2_1 symmetry to G and G' along the channel.

The deoxycholic acid–ketone complexes are ideal for probing the relative roles of the P_y and π^* orbitals in the abstraction process because the carbonyl plane >C=O of the guest–ketone tends to be perpendicular to the steroid C–H bond of the to-be-abstracted H atom. Prochiral ketones are appropriate guests for this purpose because the prochirality allows a correlation to be made between the absolute configuration of the new chiral center of the photoproduct with the relative orientation of the guest >C=O and host H—C groups prior to reaction. Moreover, we have recently

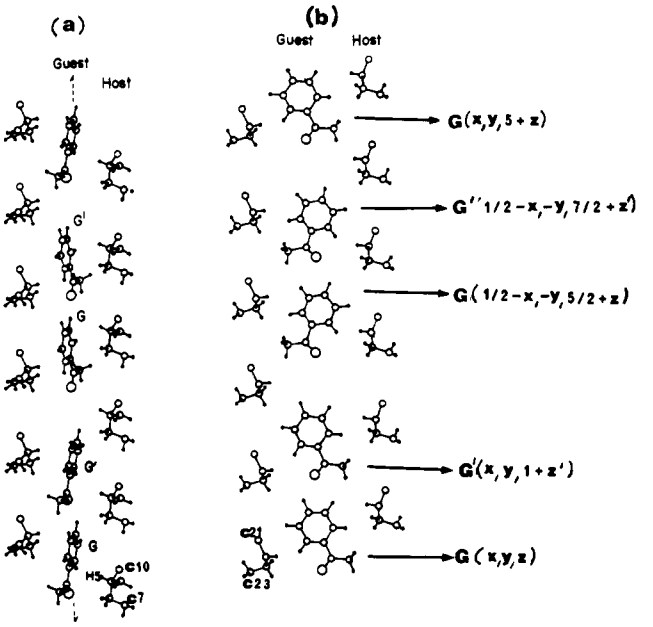


Figure 5. Closest-packed arrangement of acetophenone molecules in a channel derived from the two independent molecules $G(x,y,z)$ and $G'(x,y,z')$ shown in Figure 4. (The coordinates of the channel 2_1 axis are $x = {}^1/_4$, $y = 0$.) (a) View edge-on to plane of guest molecules. The channel walls shown are a part of steroid rings A and B. (b) View perpendicular to plane of guest molecules. The channel walls are a part of the steroid side chain.

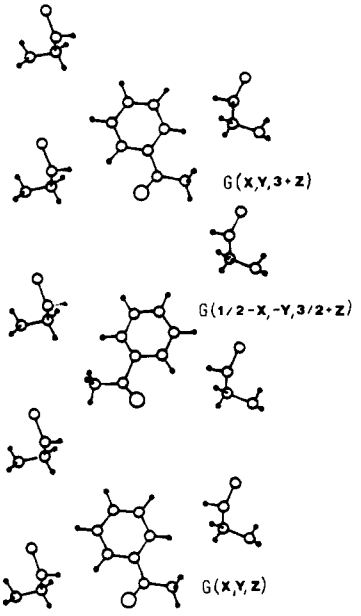


Figure 6. String of nearest neighbor acetophenone G molecules in the channel. The channel 2_1 axis passes through x, $y = {}^1/_4$, 0.

observed that the ketone complexes of the bile acids maintain their crystalline integrity on photoreaction. This fact provided a new tool to elucidate the fine details of the molecular pathway of a reaction by allowing one to determine the crystal structure both before and after reaction.

1.2. Selection of the Models. In the previous paper in this issue,[2] it was demonstrated that the prochiral methyl alkyl ketones (H_3C–CO–C_nH_{2n+1}, n = 2–5) are unsatisfactory for the above purpose because these guests from pseudocentrosymmetric pairs (Scheme IIIa) in the channels of DCA arranged in such a way as to yield the two diastereomeric photoproducts (Scheme IIIb). These host–guest arrangements cannot be exploited to elucidate the comparative role of P_y vs. π^* orbitals in the hydrogen ab-

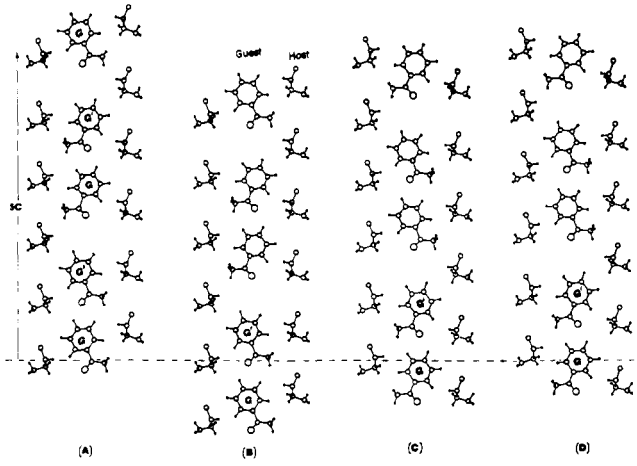


Figure 7. Four disordered guest arrangements in a given channel which differ in their z coordinates. The host–guest contacts are the same for all arrangements.

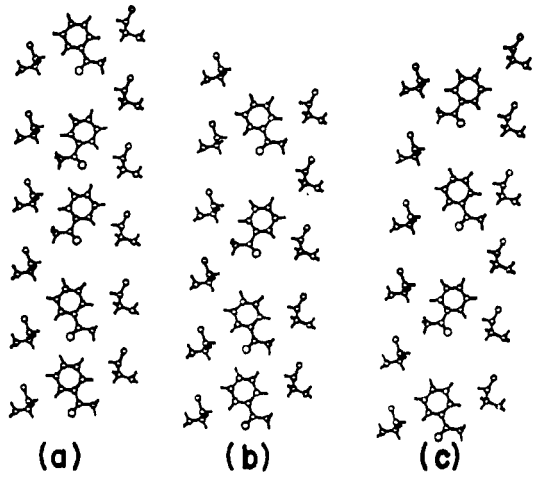


Figure 8. Three guest arrangements for which intermolecular potential energies were calculated: (a) 4:10 guest-host arrangement derived from the X-ray study; (b) 3:8 guest–host arrangement; (c) 1:3 guest–host arrangement.

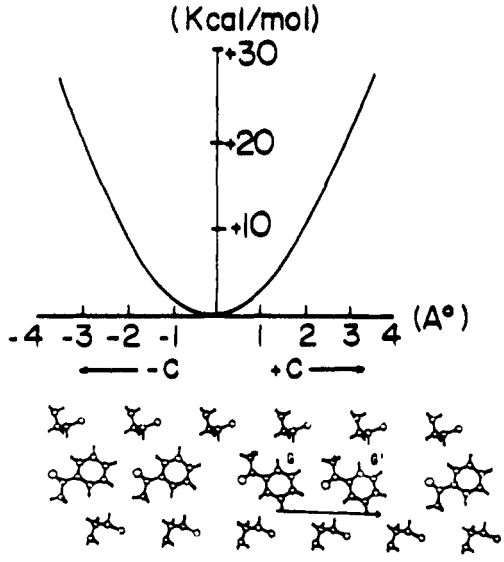


Figure 9. Variation in lattice energy as a result of moving the X-ray-derived chain of acetophenone molecules as a unit along the channel axis.

straction. In an attempt to circumvent such difficulties, we initiated a study with acetophenones as occluded guests, a choice which eventually proved to be auspicious. Here we describe

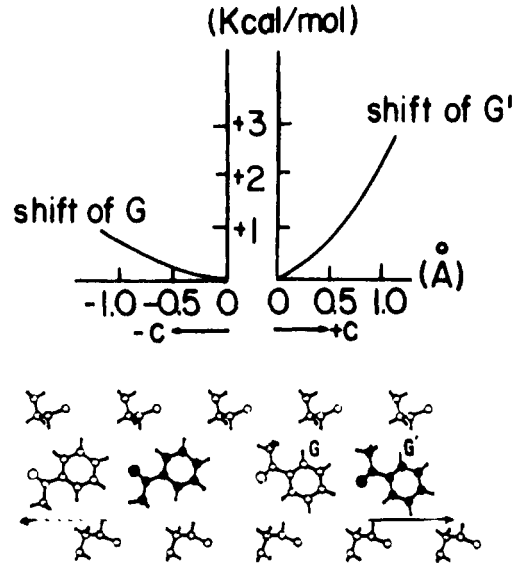


Figure 10. Variation in lattice energy as a result of moving the acetophenone molecules G′ and G separately, along the $+c$ and $-c$ directions respectively.

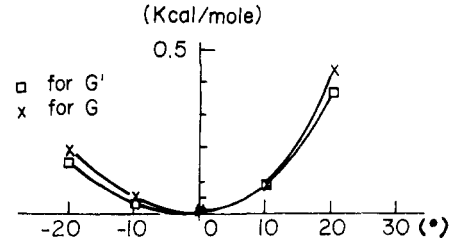


Figure 11. Variation in lattice energy as a result of separately rotating the acetyl groups $COCH_3$ of G and G′.

reactions carried out on complexes of deoxycholic acid (DCA) occluded with acetophenone and with *m*-chloroacetophenone (Figure 1).

2. Crystalline Molecular Complex DCA–Acetophenone

2.1. Solid-State Photochemistry. Crystals of the complex were obtained from a solution of DCA with acetophenone in methanol. Irradiation of these crystals for about 30 days, $\lambda > 300$ nm, yielded a single topochemical addition product **2** with 25% yield, as shown in Scheme IV. The molecular structure of photoproduct **2** (Figure 2) was unambiguously assigned from an X-ray analysis (see section 5.9) and ^{13}C NMR. ^{13}C NMR analysis easily differentiates between the two diastereoisomers, as shown for photoproducts[2] from DCA–ethyl methyl ketone and DCA–methyl propyl ketone. TLC analysis and a ^{13}C NMR analysis of the product (Table I) indicate that only a single diastereoisomer is formed.[9]

2.2. Crystal Structure and the Guest Arrangement in the Channel. The crystal structure of DCA–acetophenone was determined via low-temperature X-ray and neutron diffraction analyses (see sections 5.5 and 5.7). The host DCA molecules are arranged in the α motif[2] (Figure 3), as would be expected for nonbulky guest molecules. Two independent guest molecules, G and G′, were located in the channel. These two molecules nearly coincide in terms of the diffraction analysis; G and G′ differ in position only in the z coordinate along the channel axis by a separation of 0.8 Å as shown in Figure 4. We shall deduce that the guest molecules are arranged along each channel as depicted in Figure 5. They form close-packed pairs GG′ separated by gaps. Within each pair, G and G′ are related along the z direction by

(9) The protons of methyl-19 appear as two singlets due to hindered rotation around the C(5)–$COH(CH_3)$(Ph) bond. When crystals of the product were dissolved at −60 °C, only one conformation was observed; after heating above 30 °C, the second conformer started to appear.

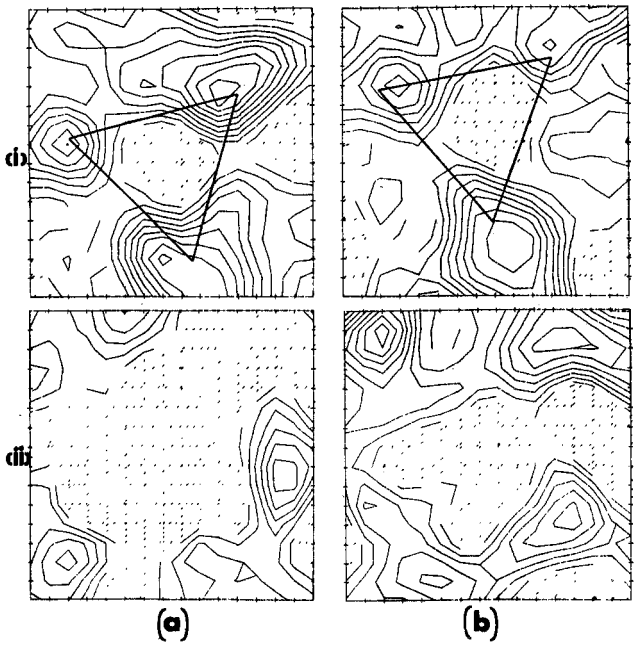


Figure 12. Neutron study of DCA–$C_6H_5COCD_3$. Difference density syntheses using calculated structure factors based on contribution of DCA–C_6H_5COC. The four maps were calculated in planes perpendicular to the C7—C8 (i.e., C—CD_3) and C7—0 (i.e., C=O) bonds of guests G and G′. Each plane passes through a point which lies on extension of bond at a distance 1.1 Å sin(110–90)° from atom C8 or O1. (a) Molecule G. (b) Molecule G′. (i) Maps perpendicular to the C7—C8 bond. The three peaks of each map correspond to a symmetric D_3 methyl group as demonstrated by the good fit to the triangles of sides 1.8 Å which is the intramolecular distance between D atoms of a methyl group. (ii) Maps perpendicular to the C7–O1 bond. Neither map shows evidence of a D_3 group.

Table II. Distances *d* (Å) between the Guest C=O Group and the Host DCA

C=O	DCA	*d*, 103 K	*d*, 293 K
	(a) DCA–Acetophenone		
O(G)	H5	3.1	3.1
	$H6_{eq}$	3.2	3.2
	$H6'_{ax}$	3.4	3.2
C(G)	C5	3.8	3.9
	C6	3.8	3.9
O(G′)	H5	2.9	3.0
	H6	3.7	4.0
	H6′	3.9	3.6
C(G′)	C5	3.8	3.9
	C6	4.1	4.0
	(b) DCA–*m*-Cloroacetophenone		
O(G)	H5	2.4	
	H6[a]	3.5	
	H6′[a]	3.3	
C(G)	C5	4.0	
	C6[a]	3.5	
O(G′)	H5	2.4	
	H6	3.8	
	H6′	3.8	
C(G′)	C5	3.6	
	C6	3.9	

[a] Symmetry operation $^1/_2 - x, -y, ^1/_2 + z$ was applied to the guest atom.

a pseudotranslation of $c + 0.8$ Å. The neighboring pairs are related by a $5c/2$ translation plus a rotation about the 2_1 axis which passes along the center of the channel.

Deduction of the Guest Arrangement from the Diffraction Analysis. The occupancies of G and of G′, i.e., the molar ratio of guest to host, were refined by X-ray structure factor least squares to values of 0.202 (6) and 0.215 (8), respectively. These two individual occupancies were kept fixed at 0.2 in the X-ray least-squares refinement. We shall now make use of the principle of closest molecular packing to demonstrate that the maximum total guest occupancy is 0.4, with individual occupancies of G and G′ equal to each other at 0.2. Furthermore, we shall show that the occupancy of 0.4 arises from a unique packing within the channel; any other feasible arrangement would lead to a lower occupancy.

The observed individual occupancies of G and G′ indicate that, on the average, one in every five crystallographic sites of G, and G′, is occupied. First we examine whether the channels are occupied by separate extended strings of G and of G′ molecules, namely GGGGG and G′G′G′G′G′. Let the coordinates of a G molecule be *x*, *y*, and *z* and that of G′ be *x*, *y*, and *z*′ where $z' = z + 0.8$ Å/c, G and G′ being referred to the same molecular site as shown in Figure 4a. A generated string of closest-packed

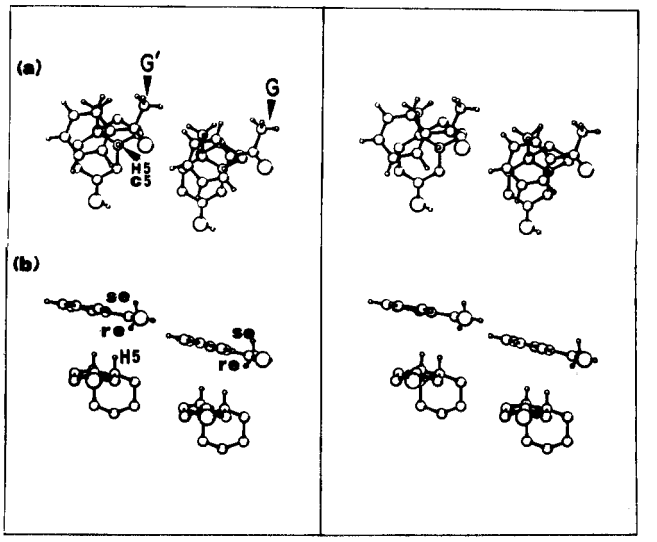


Figure 13. DCA–acetophenone. Host–guest packing at site of reaction. The two guest molecules G and G′ and ring A of the steroid are shown. H atoms omitted on ring A but for H5. (a) View along the steroid H5–C5 bond. (b) View perpendicular to the H5–C5 bond.

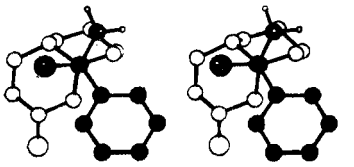
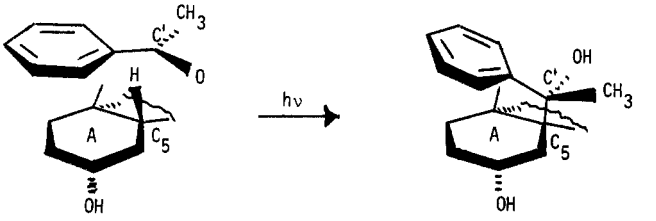
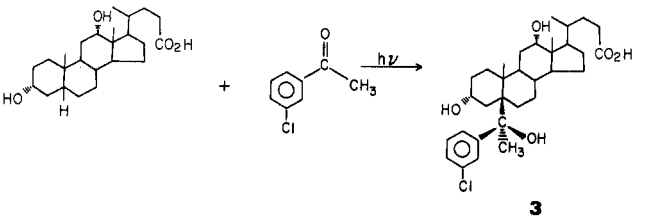


Figure 14. Moiety $C^*OHCH_3C_6H_5$ and rings A and B of photoproduct **2** of DCA–acetophenone in its own crystal structure (see also Figure 2). View along the C*–C5 bond. C and O of rings A and B in open circles.

Scheme V



Scheme VI



3

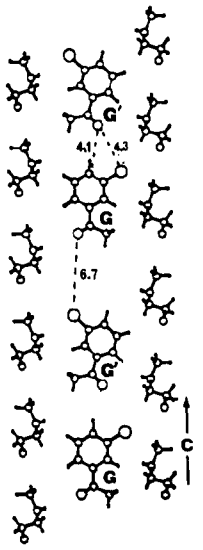


Figure 15. Deduced packing arrangement of chloroacetophenone molecules in the channel viewed perpendicular to the plane of the guest molecule.

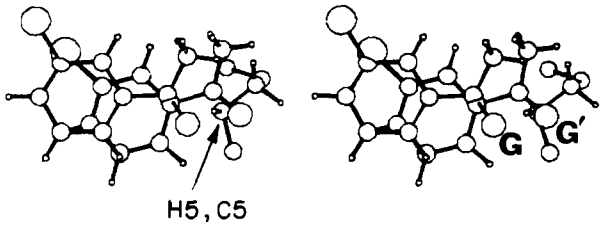


Figure 16. Host–guest packing at site of reaction showing chloroacetophenone molecules G and G′, as referred to the same steroid site, and parts of neighboring rings A and B of steroid. H atoms H5, H6, and H6′ are drawn.

G molecules is shown in Figure 6. The nearest neighbor of $G(x,y,z)$ along the channel would be $G(^1/_2 - x,-y,^3/_2 + z)$ because of the twofold screw symmetry along the channel c axis. In other words, one in three consecutive sites may be occupied in separate strings of G and G′ molecules, resulting in a maximum total occupany of 1:3, which is incompatible with the derived total value of 0.42 (1). Substituting a G′ molecule for G at any molecular site, in the string, i.e., $G'(x,y,z')$ instead of $G(x,y,z)$, would leave the maximum occupancy unchanged at 1:3. It is possible to construct a denser arrangement only if G and G′ form the close-packed pair $G(x,y,z)$ and $G'(x,y,1 + z')$ shown in Figure 5. G and G′, in this pair, are separated by the length of the c axis + 0.8 Å to bring about an acceptable intermolecular H···O contact between C4(G)–H and 0(G′) of 3.1 Å. When translation and 2_1 symmetry are applied (the 2_1 axis passes through the channel center at $x = {}^1/_4$, $y = 0$), the nearest neighbor that follows $G'(x,y,1 + z')$ in the $+z$ direction is $G(^1/_2 - x,-y,^5/_2 + z)$ followed by $G'(^1/_2 - x,-y,^7/_2 + z')$, the latter two also forming the close-packed GG′ pair. The next nearest molecule, $G(x,y,5 + z)$, is removed by a translation distance of $5c$ from the starting guest $G(x,y,z)$. This guest structure has a total guest occupancy of $2/5 = 0.4$, with values of 0.2 for both G and G′. It is the densest possible arrangement given that the crystal structure contains only the two independent guest molecules $G(x,y,z)$ and $G'(x,y,z')$. This arrangement fits the X-ray structure-factor least-squares results excellently. The guest molecules thus form a one-dimensional superstructure in the channel with a translation repeat of $5c$ = 36 Å. Room-temperature oscillation photographs about the c axis of single crystals of DCA–acetophenone did not appear to reveal any explicit evidence of this superstructure in terms of diffuse reciprocal layers corresponding to the $5c$ repeat distance or, what would appear to be more likely, a $5c/2$ repeat distance which represents the separation along z between the close-packed GG′ pairs in the channel. Nor were we clearly able to discern evidence of this superstructure by low-temperature (103 K) X-ray diffraction measurements. We infer therefore that the diffuse layers were too weak to be observed or that there must be an occasional break of the superstructure pattern along the channel axis. Naturally such faults would reduce the total guest occupancy. In a given channel, there are five different arrangements of the one-dimensional guest superstructure, four of which are shown in Figure 7. Thus, there are 25 different arrangements of the one-dimensional guest superstructure in a disordered unit cell, because there are two symmetry-related channels per unit cell (see Figure 3).

Guest Arrangement by Potential Energy Calculations and Neutron Diffraction. To furnish complementary evidence for the correctness of the guest arrangement derived from the X-ray and neutron diffraction analyses, we examined possible guest arrangement in terms of atom–atom potential energy calculations.[10-13] A similar approach has been recently applied to the inclusion compounds of DCA with phenanthrene and *p*-(dimethylamino)azobenzene to help establish the locations of the guest molecules.[14]

We first consider lattice energies of channel motifs as a function of guest occupancy. The highest possible guest–host molar ratio is 4:9 for an arrangement in which the neighboring guest molecules would be separated along the channel by 8 Å, which is the distance between G and G′ molecules of the close-packed pair (Figure 5) derived from the X-ray diffraction study. The repeat translation distance along the channel would be $9c \simeq 64$ Å = 8 × 8 Å. Such an arrangement may be precluded because it would need to incorporate four independent guest molecules, as against the two (G, G′) derived from the diffraction analysis; moreover, such a motif would incur poor guest–host contacts as shall become evident below. Thus, the motif of the highest guest occupancy examined via lattice energies was that derived from the X-ray study, with an occupancy of 4:10 (Figure 8a). A plausible arrangement with the next most dense packing is found in DCA–*p*-fluoroacetophenone described in the following paper in this series.[15] The motif is shown in Figure 8b, containing a guest occupancy of 3:8 with a G′/G molar ratio of 2:1. We may construct an analogous motif with a G′/G molar ratio of 1:2. A crystal structure containing a random arrangement of these two strings would have a total guest occupancy of 3:8 and a G/G′ molar ratio of 1:1, values close to what was found in the present X-ray study. A third plausible arrangement is the string of G′, or G, molecules (Figure 8c) with a guest occupancy of 1:3. The relative lattice energies of these three crystal structures a, b, and c are 0, +0.4, and +1.1 kcal/mol,[16] respectively. Thus, the most stable structure is the X-ray-derived complex.[17]

Next, the lattice energy was calculated on moving the X-ray derived chain of molecules in the channel in steps of 1 Å. At each

(10) A computer program written by A. T. Hagler and R. Sharon (CMIN2, Department of Chemical Physics, Weizmann Institute, Rehovot, Israel) was used for calculation of lattice energies by atom–atom potentials. Lattice energy minimization was done for several interactions with respect to the nine parameters defining the Cartesian components of the unit cell vectors as well as the six translational and rotational parameters for each, but one, of the molecules in the unit cell. A cutoff distance of 11 Å was used for all minimizations. A 9–6–1 potential was used with energy parameters for the O, C, and H atoms (given in Table 1S, supplementary material) taken primarily from force field studies of amides and carboxylic acids[11] but for the oxygen of the acetyl group and the arom. C–H groups. For the O atom of the acetyl group, we assumed that the net negative charge is 0.38 e instead of 0.46 e found for the corresponding carbonyl O atom. Here we were assisted by quantum chemical calculations on formaldehyde and formic acid.[12] The partial charges of C and H of the phenyl group were taken at −0.08 e and +0.08 e, respectively.[13]

(11) Lifson, S.; Hagler, A. T.; Dauber, P. *J. Am. Chem. Soc.* **1979**, *101*, 5131 and references therein.

(12) Eisenstein, M. Ph.D. Thesis, The Feinberg Graduate School, Weizmann Institute, Rehobot, Israel, 1981.

(13) Williams, D. E. *Acta. Crystallogr., Sect. A* **1974**, *A30*, 71.

(14) De Sanctis, S. C., *Acta Crystallogr., Sect. B* **1983**, *B39*, 366.

(15) Chang, H. C.; Weissenger, Y.; Frolow, F.; Popovitz-Biro, R.; Lahav, M.; Leiserowitz, L., unpublished results.

(16) One mole = one mole of DCA + the molar fraction of guest, which equals 0.4, 0.375, and 0.333 for arrangements a, b, and c, respectively.

Table III. Cell Constants and Experimental Data on X-ray and Neutron Intensities of (a),(b) DCA–Acetophenone ($C_6H_5COCD_3$), (c),(d) DCA–Acetophenone ($C_6H_5COCH_3$), (e) DCA–*m*-Chloroacetophenone, (f) 5β-(*S*)(1-Phenylethanol)deoxycholic Acid (Photoproduct **2**)

	a	b	c	d	e	f
cryst temp, K	16	83	103	293	103	293
formula[a]	$C_{24}H_{40}O_4$ $^2/_5(C_8H_5D_3O)$	$C_{24}H_{40}O_4$ $^2/_5(C_8H_5D_3O)$	$C_{24}H_{40}O_4$ $^2/_5(C_8H_8O)$	$C_{24}H_{40}O_4$ $^2/_5(C_8H_8O)$	$C_{24}H_{40}O_4$ $^1/_3(C_8H_7OCl)$	$C_{32}H_{48}O_5$
a, $\sigma(a)$, Å[b]	25.199 (6)	25.285 (8)	25.243 (7)	25.589 (6)	25.283 (8)	12.107 (2)
b	13.602 (3)	13.611 (4)	13.606 (2)	13.709 (3)	13.639 (4)	15.115 (5)
c	7.192 (2)	7.192 (3)	7.198 (2)	7.247 (2)	7.198 (4)	7.522 (2)
β, deg						94.08 (3)
Z	4	4	4	4	4	2
V, Å^3	2465	2475	2475	2542	2470	1373
space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_1$
D_x, g/cm^3			1.17	1.14	1.17	1.24
mp, °C			177–178	177–178	170–172	216
diffractometer	Brookhaven neutron diffractometer		CAD-4	Siemens	CAD-4	Siemens
crystal size of specimen, (mm × 10^3)	5 × 5 × 22		2 × 3 × 6	2 × 2 × 4	2 × 3 × 5	1 × 1 × 4
radiation[c]	N(=1.1611 Å)		X(Mo Kα)	X(Cu Kα)	X(Mo Kα)	X(Cu Kα)
μ, cm^{-1}	2.95		0.9	6.3	1.0	6.6
θ(maximum)	52		36	70	33	70
ω/θ scan ratio	1/1		3/2	1/1	6/5	1/1
max scan time, s			60	50	80	50
no. of reflects[d]	2564		15196	5425	5930	5415
	1313		6488	2770	5812	2712
R_m[e]	0.033		0.038	0.03	0.025	0.04

[a] The guest–host molar ratios of compounds c and e, equal to 2:5 and 1:3, respectively, were determined by X-ray structure-factor least-squares refinement. [b] λ(Mo Kα$_1$) = 0.70926 Å, λ(Cu Kα$_1$) = 1.54041 Å. [c] N = Neutron radiation; X = X-rays. [d] Two values given for each compound are total and independent number of reflections measured. [e] $R_m = \sum|F^2 - \bar{F}^2|/\sum F^2$ where F is an observed structure factor and $\bar{F}$ the weighted mean of the corresponding symmetry-related set of observed structure factors.

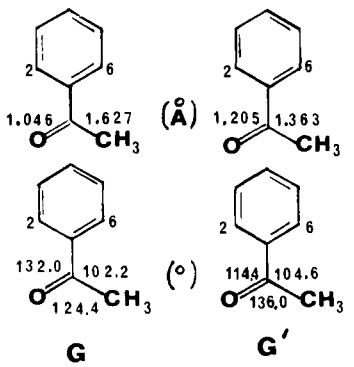


Figure 17. Bond lengths and bond angles of the acetyl groups of acetophenone G and G′ after constrained–restrained refinement.

Scheme VII

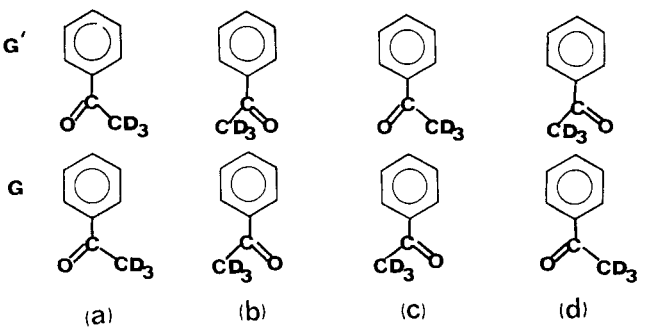


Table IV. X-ray Structure-Factor Refinement of (a) DCA–Acetophenone at 103 K, (b) DCA–Acetophenone at 293 K, (c) DCA–*m*-Chloroacetophenone at 103 K, and (d) Photoproduct **2** at 293 K from DCA–Acetophenone

	a	b	c	d
no. of refined parameters	429	428	407[a]	334
criterion for F_{obsd} exclusion	$F < 3\sigma(F)$	$F < 3\sigma(F)$	$F < 3\sigma(F)$	$F < 2\sigma(F)$
no. of reflect used in refinement	4260	2511	2536	2686
weighing scheme	$1/(\sigma^2(F) + 0.002F^2)$	1	$1/(\sigma^2(F) + 0.002F^2)$	1
R	0.059	0.058	0.075	0.041
R_w	0.051	0.058	0.076	0.041

[a] H atoms belonging to a CH_2 or a CH_3 group of steroid (DCA) constrained for most groups to have same isotropic temperature factor.

step, the energy was minimized for two or three cycles. The energy minimum (Figure 9) corresponds to the observed arrangement, and the sharp rise in the curve on both sides of the minimum clearly demonstrates the role played by the host–guest interactions in determining guest packing.[18] The energy was also calculated on a movement of G′ and G separately from their X-ray-derived positions. These energy curves (Figure 10) show not only a rise in energy on guest displacement but that guest G can be more easily displaced along the $-c$ direction than guest G′ can be displaced along the $+c$ direction.

In order to support the results of the X-ray analysis that the acetyl and phenyl moieties of the guest molecules are coplanar, the crystal energy was calculated on rotation of the acetyl groups of G and of G′ separately about the exocyclic C(phenyl)–C(carbonyl) bonds. These calculations (Figure 11) show that planar guest molecules yield the lowest lattice energy.

The oxygen and methyl carbon atoms of G and G′ occupy regions of atomic overlap in the X-ray structure analyses (see Figure 4). Thus, several strategies were adopted by using X-ray structure-factor least squares (see section 5.5) to unambiguously locate these two atoms and to distinguish between them. However, this X-ray study could not definitely establish that there is no minor amount of orientational disorder of the methyl C and O atoms of the guest acetyl group. The neutron study, at a temperature of 16 K on DCA–$C_6H_5COCD_3$ (see section 5.7), confirmed the positions of the oxygen and methyl carbon atoms of

(17) It is relevant that the calculated lattice energy difference between observed and hypothetical crystal structures may be as low as 0.5 kcal/mol. See: Berkovitch-Yellin, Z.; Leiserowitz, L. *J. Am. Chem. Soc.* **1982**, *104*, 4052 and references therein.

(18) One may also infer from this curve that the closest-packed arrangement of guest molecules with a 4:9 guest–host molar ratio would be less stable than the X-ray derived arrangement.

Table V. (DCA) Deoxycholic Acid–Acetophenone (at 103 K): (a) x, y, and z Coordinates ($\times 10^4$) and U_{eq}[a] ($\times 10^3$ Å^2) of the C and O Atoms of Deoxycholic Acid (Average $\sigma(U_{eq}) = 0.001$ Å^2), (b) x, y, and z Coordinates ($\times 10^4$) and Isotropic U (Å$^2 \times 10^3$) of H Atoms of Deoxycholic Acid, (c) x, y, and z Coordinates[b] ($\times 10^4$) and U^c (Isotropic) (Å^2,$\times 10^3$) of the Guest Acetophenone Molecules and G′

(a) x, y, z, and U_{eq} of C and O Atoms of Deoxycholic Acid

atom	x	y	z	U_{eq}	atom	x	y	z	U_{eq}
C(1)	1260 (1)	2124 (2)	3537 (3)	22	C(15)	1616 (1)	5597 (1)	−2477 (3)	21
C(2)	702 (1)	1826 (2)	2977 (3)	22	C(16)	1357 (1)	6620 (2)	−2305 (3)	22
C(3)	725 (1)	1116 (2)	1358 (3)	21	C(17)	1063 (1)	6641 (1)	−407 (3)	17
C(4)	1021 (1)	1561 (2)	−271 (3)	19	C(18)	1864 (1)	6114 (2)	1479 (3)	19
C(5)	1584 (1)	1893 (1)	274 (3)	19	C(19)	2148 (1)	2741 (2)	2702 (4)	26
C(6)	1874 (1)	2337 (2)	−1400 (3)	22	C(20)	1062 (1)	7678 (1)	431 (3)	19
C(7)	1660 (1)	3344 (2)	−1942 (3)	20	C(21)	780 (1)	7742 (2)	2312 (3)	26
C(8)	1646 (1)	4060 (1)	−311 (3)	16	C(22)	836 (1)	8441 (2)	−939 (3)	22
C(9)	1338 (1)	3602 (1)	1333 (3)	16	C(23)	257 (1)	8294 (2)	−1493 (4)	28
C(10)	1580 (1)	2609 (1)	1958 (3)	18	C(24)	83 (1)	9088 (2)	−2807 (3)	23
C(11)	1258 (1)	4348 (1)	2901 (3)	17	O(25)	190 (1)	874 (1)	860 (3)	27
C(12)	999 (1)	5312 (1)	2268 (3)	16	O(26)	469 (1)	5106 (1)	1652 (2)	20
C(13)	1325 (1)	5786 (1)	703 (3)	16	O(27)	91 (1)	9956 (1)	−2444 (3)	39
C(14)	1379 (1)	5019 (1)	−868 (3)	17	O(28)	−84 (1)	8758 (1)	−4420 (2)	24

atom	x	y	z	U	atom	x	y	z	U
	(b) x, y, z, and U of H Atoms of Deoxycholic Acid					(c) x, y, z, and U of Guest Molecules			
H(1)	1246 (9)	2546 (17)	4714 (35)	20 (6)					
H(1′)	1417 (9)	1515 (17)	3925 (33)	18 (6)		Acetophenone Molecule G			
H(2)	483 (10)	2391 (17)	2621 (34)	24 (6)	C(7)	2747	174	−158	33 (1)
H(2′)	501 (10)	1511 (19)	3984 (38)	31 (7)	C(1)	2539	13	1761	33 (1)
H(3)	928 (9)	470 (17)	1710 (34)	21 (6)	C(2)	2074	−522	1976	48 (1)
H(4)	1051 (9)	1066 (17)	−1150 (36)	20 (6)	C(3)	1869	−686	3734	48 (1)
H(4′)	815 (8)	2100 (15)	−783 (29)	4 (5)	C(4)	2125	−321	5285	33 (1)
H(5)	1776 (10)	1280 (20)	691 (40)	36 (7)	C(5)	2588	211	5084	48 (1)
H(6)	1823 (9)	1906 (16)	−2438 (34)	15 (5)	C(6)	2796	379	3321	48 (1)
H(6′)	2267 (11)	2431 (18)	−1088 (36)	30 (7)	H(1)	1896	−777	852	48 (1)
H(7)	1869 (10)	3637 (19)	−2986 (39)	30 (7)	H(2)	1530	−1077	3839	48 (1)
H(7′)	1292 (10)	3309 (17)	−2436 (36)	24 (6)	H(3)	1987	−427	6598	48 (1)
H(8)	2013 (10)	4188 (18)	170 (37)	28 (7)	H(4)	2770	472	6213	48 (1)
H(9)	969 (9)	3456 (16)	800 (32)	15 (5)	H(5)	3136	772	3208	48 (1)
H(11)	1034 (9)	4108 (16)	3816 (34)	15 (5)	C(8)	3269	682	−400	58 (3)
H(11′)	1602 (10)	4506 (16)	3430 (34)	20 (6)	H(6)	3270	1341	148	58 (3)
H(12)	971 (9)	5721 (16)	3272 (33)	16 (6)	H(7)	3354	751	−1743	58 (3)
H(14)	1023 (9)	4879 (15)	−1258 (31)	12 (5)	H(8)	3560	272	203	58 (3)
H(15)	2029 (10)	5635 (18)	−2372 (36)	28 (6)	O(1)	2502	−134	−1491	78 (3)
H(15′)	1537 (9)	5240 (16)	−3655 (34)	16 (5)					
H(16)	1623 (10)	7103 (19)	−2251 (37)	27 (6)		Acetophenone Molecule G′			
H(16′)	1082 (11)	6708 (19)	−3387 (40)	34 (7)	C(7)	2683	10	852	33 (1)
H(17)	687 (8)	6448 (14)	−578 (28)	6 (5)	C(1)	2491	−52	2812	33 (1)
H(18)	2067 (9)	6480 (18)	674 (36)	23 (6)	C(2)	2028	−574	3170	48 (1)
H(18′)	2083 (9)	5543 (17)	1883 (33)	22 (6)	C(3)	1838	−647	4970	48 (1)
H(18″)	1816 (9)	6494 (18)	2567 (37)	25 (6)	C(4)	2106	−204	6421	33 (1)
H(19)	2398 (11)	3074 (19)	1788 (38)	39 (8)	C(5)	2566	315	6077	48 (1)
H(19′)	2307 (10)	2101 (19)	2998 (36)	32 (7)	C(6)	2759	392	4271	48 (1)
H(19″)	2173 (9)	3141 (17)	3891 (37)	25 (6)	H(1)	1842	−885	2116	48 (1)
H(20)	1445 (8)	7830 (15)	577 (30)	12 (5)	H(2)	1501	−1031	5180	48 (1)
H(21)	973 (10)	7455 (18)	3265 (38)	32 (7)	H(3)	1979	−242	7760	48 (1)
H(21′)	428 (11)	7408 (19)	2348 (39)	40 (8)	H(4)	2757	633	7134	48 (1)
H(21″)	715 (10)	8402 (20)	2696 (36)	30 (7)	H(5)	3098	778	4053	48 (1)
H(22)	1046 (10)	8435 (18)	−2044 (39)	31 (7)	C(8)	3203	503	467	58 (3)
H(22′)	892 (9)	9107 (17)	−414 (34)	23 (6)	H(6)	3206	1187	891	58 (3)
H(23)	40 (12)	8357 (21)	−456 (44)	45 (8)	H(7)	3276	504	−890	58 (3)
H(23′)	203 (11)	7675 (21)	−2032 (40)	40 (8)	H(8)	3498	126	1113	58 (3)
H(25)	209 (10)	610 (20)	−192 (42)	36 (7)	O(1)	2427	−365	−393	78 (3)
H(26)	252 (10)	5311 (18)	2416 (38)	26 (7)					
H(28)	−175 (13)	9249 (24)	−5066 (49)	63 (10)					

[a] $U_{eq} = {}^1/_3 \sum\sum U_{ij} a_i^* a_j^* a_i a_j$. [b] G and G′ each refined as a rigid body. Thus, all atoms of each molecule have same $\sigma(x)$, $\sigma(y)$, $\sigma(z)$ for G = 3, 6, and 9 ($\times 10^4$), respectively, for G′ = 3, 6, 10 ($\times 10^4$). [c] Atoms within each group [C(7), C(1), C(4)], [C(2)...H(5)], [C(8)...H(8)], and O(1) refined with same U.

G and G′ (see Figure 12) as determined by the X-ray analysis. Moreover, Figure 12 displays no evidence of orientational disorder of the acetyl groups of G and of G′. These results are supported by potential energy calculations. Interchanging oxygen and CH_3 of guest G′ induces relatively unfavorable contacts between the methyl H atoms of G′ and the para H atom of G (see Figure 5); the rise in energy of guest G′ is 1.7 kcal/mol of the guest. Interchanging oxygen and CH_3 of G induces a rise in energy of 1 kcal/mol of the guest. We may conclude that these atom–atom potential energy calculations are completely consistent with the guest structure derived from the X-ray and neutron analyses.

2.3. Structure–Reactivity Relationship in DCA–Acetophenone. The UV irradiation of the crystals was conducted at room temperature, but the crystal structure determined was at 103 K. In order to confirm that the structures at the two temperatures are almost the same, X-ray diffraction data were collected at room temperature, and this structure was refined to an R value of 0.06, (see section 5.6). The guest–host distances at the site of reaction at the two temperatures match to within 0.2 Å (Table IIa) and thus we may safely refer to the low-temperature structure in considering structure–reactivity relationships at room temperature.

The orientation of the G and G′ acetophenone molecules in

Table VI. Deoxycholic Acid–*m*-Chloroacetophenone (at 103 K): (a) *x*, *y*, and *z* Coordinates ($\times 10^4$) and U_{eq} (Å^2, $\times 10^3$) the C and O Atoms of Host Deoxycholic Acid (Average $\sigma(U_{eq})$ = 0.002 Å^2), (b) *x*, *y*, and *z* Coordinates ($\times 10^4$) and Isotropic *U* (Å^2, $\times 10^3$) *U* (Å^2 × 10^3) of Deoxycholic Acid, (c) *x*, *y*, and *z* Coordinates[a] ($\times 10^4$) of the Guest *m*-Chloroacetophenone Molecules G and G′ (All Atoms Were Refined with an Overall *U*(Isotropic) = 0.059 (2) Å^2)

(a) *x*, *y*, *z*, and U_{eq} of C and O Atoms of Deoxycholic Acid

atom	*x*	*y*	*z*	U_{eq}	atom	*x*	*y*	*z*	U_{eq}
C(1)	1257 (2)	2095 (4)	3585 (8)	23	C(15)	1621 (2)	5584 (4)	−2402 (8)	24
C(2)	710 (2)	1793 (4)	3014 (8)	24	C(16)	1355 (2)	6596 (4)	−2227 (8)	24
C(3)	742 (2)	1084 (4)	1378 (8)	22	C(17)	1056 (2)	6616 (3)	−339 (7)	16
C(4)	1038 (2)	1537 (3)	−228 (7)	17	C(18)	1853 (2)	6087 (3)	1592 (8)	19
C(5)	1600 (2)	1870 (4)	339 (8)	22	C(19)	2146 (2)	2733 (4)	2802 (9)	27
C(6)	1890 (2)	2329 (4)	−1358 (9)	23	C(20)	1050 (2)	7641 (3)	516 (7)	20
C(7)	1673 (2)	3338 (4)	−1884 (7)	21	C(21)	765 (2)	7702 (4)	2384 (8)	26
C(8)	1655 (2)	4043 (3)	−233 (7)	17	C(22)	830 (2)	8414 (4)	−852 (8)	22
C(9)	1342 (2)	3581 (3)	1393 (7)	15	C(23)	254 (2)	8253 (4)	−1449 (9)	29
C(10)	1582 (2)	2589 (3)	2035 (7)	17	C(24)	86 (2)	9051 (4)	−2797 (8)	26
C(11)	1250 (2)	4314 (3)	2996 (7)	17	O(25)	208 (2)	844 (3)	841 (6)	27
C(12)	990 (2)	5279 (3)	2339 (7)	16	O(26)	461 (1)	5065 (2)	1673 (5)	20
C(13)	1320 (2)	5760 (3)	784 (7)	16	O(27)	108 (2)	9920 (3)	−2466 (7)	45
C(14)	1385 (2)	5002 (3)	−798 (7)	16	O(28)	−100 (1)	8724 (2)	−4383 (5)	25

atom	*x*	*y*	*z*	*U*	atom	*x*	*y*	*z*	*U*
	(b) *x*, *y*, *z*, and *U* of H Atoms of Deoxycholic Acid				(c) *x*, *y*, *z*, and *U* of the Guest Molecules G and G′				
H(1)	1216 (22)	2619 (43)	4611 (87)	23 (11)					
H(1′)	1373 (23)	1471 (43)	3944 (87)	23 (11)		*m*-Chloroacetophenone Molecule G			
H(2)	504 (20)	2445 (37)	2557 (74)	22 (10)	Cl(1)	2990	656	8033	
H(2′)	530 (21)	1530 (39)	4080 (81)	22 (10)	C(1)	2375	−146	3143	
H(3)	924 (20)	428 (41)	1573 (80)	25	C(2)	1898	−577	3676	
H(4)	1009 (23)	966 (27)	−1053 (61)	30 (10)	C(3)	1761	−623	5560	
H(4′)	811 (21)	2115 (40)	−721 (83)	30 (10)	C(4)	2099	−230	6940	
H(5)	1792 (18)	1267 (22)	655 (78)	30	C(5)	2572	187	6341	
H(6)	1749 (20)	1932 (33)	−2386 (50)	26 (10)	C(6)	2716	244	4485	
H(6′)	2244 (23)	2364 (38)	−1278 (77)	26 (10)	C(7)	2542	−80	1147	
H(7)	1875 (20)	3609 (36)	−2877 (79)	18 (9)	C(8)	3061	394	687	
H(7′)	1322 (22)	3265 (37)	−2423 (77)	18 (9)	O(1)	2265	−403	−95	
H(8)	2039 (19)	4219 (34)	317 (70)	6 (12)	H(1)	1664	−850	2614	
H(9)	980 (20)	3399 (36)	860 (75)	15	H(2)	1407	−940	5973	
H(11)	1563 (11)	4475 (34)	3745 (58)	11 (8)	H(3)	2001	−263	8347	
H(11′)	997 (19)	3966 (33)	3891 (71)	11 (8)	H(4)	3067	558	4075	
H(12)	967 (19)	5701 (28)	3443 (41)	12 (12)	H(5)	3088	1068	1156	
H(14)	1026 (8)	4763 (40)	−1053 (86)	27 (16)	H(6)	3117	426	−694	
H(15)	2015 (22)	5551 (39)	−2099 (80)	24 (10)	H(7)	3363	−11	1235	
H(15′)	1626 (21)	5180 (38)	−3696 (80)	24 (10)					
H(16)	1617 (19)	7046 (35)	−2196 (73)	10 (8)		*m*-Chloroacetophenone Molecule G′			
H(16′)	1089 (19)	6697 (35)	−3140 (75)	10 (8)	Cl(1)	3402	966	9435	
H(17)	667 (21)	6414 (37)	−421 (77)	22	C(1)	2478	−22	5339	
H(18)	2088 (15)	6437 (30)	734 (53)	10 (7)	C(2)	2067	−469	6321	
H(18′)	2082 (18)	5511 (33)	2029 (67)	10 (7)	C(3)	2071	−469	8268	
H(18″)	1763 (18)	6471 (28)	2706 (37)	10 (7)	C(4)	2487	−12	9261	
H(19)	2377 (24)	3150 (44)	2030 (87)	35 (10)	C(5)	2889	419	8220	
H(19′)	2340 (23)	2202 (44)	2612 (86)	35 (10)	C(6)	2893	431	6292	
H(19″)	2140 (23)	3195 (43)	3868 (87)	35 (10)	C(7)	2494	−4	3254	
H(20)	1412 (10)	7727 (47)	981 (92)	44 (19)	C(8)	2949	491	2300	
H(21)	944 (18)	7319 (32)	3354 (50)	22 (8)	O(1)	2145	−382	2333	
H(21′)	409 (21)	7333 (37)	2402 (76)	22 (8)	H(1)	1772	−788	5530	
H(21″)	727 (21)	8323 (41)	2882 (76)	22 (8)	H(2)	1768	−797	9014	
H(22)	1059 (21)	8270 (37)	−1945 (81)	20 (10)	H(3)	2494	−10	10712	
H(22′)	838 (19)	9052 (38)	−345 (75)	20 (10)	H(4)	3194	756	5553	
H(23)	−23 (22)	8244 (38)	−277 (87)	26 (11)	H(5)	2991	1180	2670	
H(23′)	210 (21)	7540 (39)	−1889 (85)	26 (11)	H(6)	2902	485	913	
H(25)	250 (23)	499 (37)	−319 (44)	38 (17)	H(7)	3291	124	2591	
H(26)	192 (14)	5318 (37)	2493 (64)	25					
H(28)	−272 (19)	9254 (25)	−5025 (72)	18 (15)					

[a] *G* and *G*′ each refined as rigid body. Thus, all atoms of each molecule have same $\sigma(x)$, $\sigma(y)$, $\sigma(z)$ = 5, 9, and 15 ($\times 10^4$), respectively for G and 4, 8, 16 ($\times 10^4$) for G′.

proximity to the (abstracted) H5 atom of the steroid is shown in Figure 13. The O(G′)···H5 distance is 2.9 Å, less by almost 1 Å than either O(G′)···H6$_{eq}$ or O(G′)···H6$_{ax}$. The carbonyl C7(G′)···C5 and C7(G′)···C6 distances are 3.8 and 4.1 Å, respectively (Table IIa). These distances are completely compatible with the reaction involving addition of G′ to C5 of the steroid. The O(G)···H5 distance of 3.1 Å is 0.1–0.3 Å less than that of O(G)···H6 and O(G)···H6′; the C7(G)···C5 and C7(G)···C6 disstances are equal at 3.8 Å. Thus, purely in terms of distances, one might have expected addition of G to C5 and also to C6. Consequently other factors may play a role, such as differences in ease of abstraction of H5 and H6 and that it appears sterically easier to add a large group at C5 than at C6, C5 being more centrally located on the steroid wall. A comparison of the host–guest arrangement in Figure 13 with the absolute configuration S about the newly generated chiral center C(OHCH$_3$C$_6$H$_5$) of the product, as found in its own crystal structure (Figures 14 and 2), shows that the ketone adds from its Si face, which is the more distant from the steroid in the starting structure, rather than from its Re face. This stereochemical relationship, exemplified in Scheme V, implies the need for unusual motion of the guest acetyl group on reaction. Indeed it indicates that on photoexcitation, the acetyl group of

Table VII. Photoproduct 5β-(*S*)(1-Phenylethanol)deoxycholic Acid (**2**): *x*, *y*, and *z* Coordinates (×10⁴) and U_{eq}/U_{iso} (×10³, Å²) (The Averages $\sigma(x)$, $\sigma(y)$, $\sigma(z)$, and $\sigma(U)$ Values for the H Atoms Are 0.0045, 0.0040, 0.0065, and 0.015 Å², respectively)

	x	*y*	*z*	U_{eq}		*x*	*y*	*z*	U_{iso}
C(1)	4474 (3)	2400 (3)	5079 (6)	39	H(1)	4946	1920	5317	33
C(2)	4904 (3)	2890 (3)	3478 (7)	46	H(1′)	4631	2842	6215	43
C(3)	4204 (4)	3691 (3)	3029 (6)	43	H(2)	4975	2343	1713	57
C(4)	2983 (3)	3418 (3)	2703 (5)	35	H(2′)	5652	2975	3621	50
C(5)	2478 (3)	2944 (2)	4280 (4)	26	H(3)	4231	4094	4274	38
C(6)	1304 (3)	2629 (3)	3595 (6)	38	H(4)	2977	3054	1775	36
C(7)	1269 (3)	1921 (3)	2161 (6)	38	H(4′)	2507	3971	2368	26
C(8)	1923 (3)	1113 (3)	2795 (5)	31	H(6)	858	3198	3098	49
C(9)	3134 (3)	1377 (3)	3337 (5)	31	H(6′)	792	2288	4096	66
C(10)	3245 (3)	2112 (3)	4852 (5)	31	H(7)	1522	2190	942	35
C(11)	3837 (3)	545 (3)	3819 (5)	35	H(7′)	644	1819	2004	37
C(12)	3766 (3)	−187 (3)	2411 (5)	33	H(8)	1437	807	3780	45
C(13)	2546 (3)	−457 (2)	1947 (5)	28	H(9)	3388	1681	2172	32
C(14)	1918 (3)	397 (3)	1359 (5)	31	H(11)	3537	207	4881	29
C(15)	787 (3)	60 (3)	602 (6)	42	H(11′)	4657	666	3974	38
C(16)	1064 (4)	−816 (3)	−315 (8)	46	H(12)	4313	−746	2742	41
C(17)	2290 (3)	−1053 (3)	275 (5)	31	H(14)	2243	631	152	36
C(18)	2073 (3)	−882 (3)	3594 (5)	40	H(15)	432	446	−256	31
C(19)	2972 (4)	1709 (3)	6652 (5)	45	H(15′)	387	−92	1653	34
C(20)	2448 (2)	−2063 (2)	478 (4)	32	H(16)	1020	−828	−1605	45
C(21)	3611 (3)	−2298 (3)	1268 (6)	44	H(16′)	487	−1255	−77	40
C(22)	2177 (3)	−2538 (2)	−1308 (5)	35	H(17)	2849	−914	−608	26
C(23)	1995 (3)	−3540 (3)	−1116 (5)	39	H(18)	1443	−1135	3322	107
C(24)	2994 (3)	−4131 (3)	−891 (5)	38	H(18′)	1979	−507	4649	58
O(25)	4582 (3)	4082 (3)	1456 (6)	65	H(18″)	2550	−1325	3873	59
O(26)	4292 (2)	126 (2)	901 (4)	44	H(19)	2183	1437	6773	67
O(27)	2922 (3)	−4882 (2)	−279 (5)	61	H(19′)	3228	2226	7677	89
O(28)	3904 (2)	−3844 (2)	−1493 (4)	50	H(19″)	3498	1302	6832	67
C(29)	2297 (3)	3662 (2)	5844 (4)	35	H(20)	1824	−2295	1318	35
C(30)	1469 (4)	3390 (3)	7210 (6)	48	H(21)	3689	−2914	1304	59
C(31)	1894 (3)	4571 (3)	5056 (4)	37	H(21′)	3778	−2108	2467	73
C(32)	2638 (4)	5267 (3)	4914 (6)	46	H(21″)	4164	−2045	650	72
C(33)	2277 (5)	6098 (3)	4313 (7)	62	H(22)	2747	−2408	−2109	47
C(34)	1187 (5)	6257 (4)	3875 (7)	64	H(22′)	1438	−2341	−1757	48
C(35)	426 (4)	5570 (4)	3991 (6)	55	H(23)	1646	−3777	−2348	71
C(36)	785 (3)	4737 (3)	4597 (5)	44	H(23′)	1630	−3639	−41	50
O(37)	3345 (3)	3798 (2)	6801 (4)	47	H(25)	4012	4073	766	8
					H(26)	4383	−224	327	44
					H(28)	4405	−4471	−1573	190
					H(30)	657	3288	6667	56
					H(30′)	1495	3848	8100	51
					H(30″)	1895	2837	7683	98
					H(32)	3407	5174	5294	44
					H(33)	2733	6598	4203	112
					H(34)	852	6900	3368	151
					H(35)	−312	5740	3733	63
					H(36)	244	4319	4692	69
					H(37)	3155	3872	7664	197

acetophenone undergoes a net rotation of 180°.

3. Crystalline Molecular Complex of DCA–*m*-Chloroacetophenone

3.1. Choice of Guest. In order to further substantiate the bizarre photochemical result from DCA–acetophenone, we conducted a chemical-crystallographic study on DCA–*m*-chloroacetophenone.

3.2. Solid-State Photochemistry. Crystals of the complex were obtained from a solution of DCA and *m*-chloroacetophenone in methanol. Irradiation of this crystalline material, $\lambda > 300$ nm, for about 30 days led to the formation of one (15%) diastereomeric product **3** of addition to position C5 (Scheme VI). The structure assignment of the product was done by ^{13}C NMR analysis with analogy to product **2** (Table I).

3.3. Guest Packing and Structure Reactivity. The crystal structure of DCA–*m*-chloroacetophenone was determined by low-temperature (103 K) X-ray diffraction (see section 5.8). The host structure is almost identical with that of DCA–acetophenone. Two independent guest molecules G and G′ were located in the channel from the structure-factor least-squares refinement. Their occupancies were refined freely to values of 0.167 (3) and 0.168 (3), respectively, yielding a sum of 0.335 (6). These two occupancies are very close to the value of 1:6. There are only two distinct ways of arranging the guest molecules given their refined positions and occupancies according to which one in six of each of the different G and G′ crystallographic sites is occupied. In the one possible motif, the guest molecules are arranged in separate strings GGGG and G′G′G′G′. In each such string, the nearest-neighbor guest molecules are related by one and a half translations along *c* plus a rotation about the 2_1 axis, as in Figure 6 for acetophenone. In other words, if the coordinates of G be *x*, *y*, and *z*, then its nearest neighbor along the channel will be at $^1/_2 - x, -y, ^3/_2 + z$. Such an arrangement has a maximum total guest occupancy of 1:3, which is completely compatible with the refined individual occupancies. In such an arrangement, the nearest neighbor guest atoms would be separated by approximately 5 Å. In the alternative way of arranging the guest molecules, G(x,y,z) and G′($^1/_2 - x, -y, ^3/_2 + z$) follow each other alternately, as shown in Figure 15. In this arrangement the maximum total occupancy is 1:3 and the individual occupancies of G and G′ = 1:6, which is also compatible with experiment. One would tentatively assume that the latter arrangement is the one adopted, otherwise why the necessity for two independent guest molecules G and G′ with equal occupancies and which are arranged to form close-packed pairs. The contact within a closed-packed pair is 4.3 Å between C1(G) and O(G′). Between pairs there is a gap

of 6.7 Å. It is impossible to reduce this large gap to an acceptable value by relating G and G′ by pseudotranslation as in DCA–acetophenone. In such a hypothetical arrangement, G′($^1/_2 - x,-y,^3/_2 + z$) would be followed in the +c direction by G($^1/_2 - x,-y,^5/_2 + z$), instead of by G($x,y,3 + z$); however, the former two molecules would be separated by an prohibitively short Cl(G′)···C(G) contact of 2.3 Å.

According to Figure 16, the C5–H5 bond of the steroid is situated on the Re side of the guest acetyl groups of G and G′, and thus the photochemical addition should follow a similar stereochemical pathway as in DCA–acetophenone. The host–guest distances at the sites of reaction are listed in Table IIb. According to this table and Figure 16, molecule G′ is best positioned to react with atom C5 of the steroid. [O(G′)···H5 2.4 Å, C7(G′)···C5 3.6 Å]. The short O(G)···H5 distance of 2.4 Å as opposed to O(G)···$H6_{eq}$, $H6_{ax}$ distances of 3.3 and 3.5 Å is compatible with the observation that reaction occurs only at C5. However, the relatively long C7(G)···C5 distance of 4.0 Å may preclude photoaddition of G to C5, for we cannot say at this stage whether G reacts as well as G′.

4. Conclusion

This unusual molecular reaction pathway found in DCA–acetophenone and DCA–*m*-chloroacetophenone made it imperative to design a crystalline complex of DCA-substituted acetophenone whose host–guest packing would yield the (missing) diastereomeric photoaddition product, with absolute configuration R at the newly generated chiral carbon. In order to obtain this product, it was necessary to modify the observed guest packing in the channel such that a substituted acetophenone molecule would expose face Si to the steroid C5–H5 bond. This piece of crystal engineering is described in a forthcoming paper.[15]

5. Experimental Section

5.1. General Remarks and Chemical Procedures. Melting points were measured on a Gallenkamp apparatus in capillaries and are uncorrected. ^{1}H NMR spectra were recorded on a Varian A60, HFX-10-Bruker 90-MHZ, and a Bruker WH-270 spectrophotometers by using tetramethylsilane as internal standard. ^{13}C NMR spectra were recorder on a Bruker WH-270 spectrophotometer by using deuterated acetic acid or deuterated methanol as solvents and as an internal lock and tetramethylsilane as internal standard. Mass spectra of the methyl esters of the products were recorded on a Mat 731 high-resolution mass spectrometer. TLC separations were performed on silica gel on aluminum foil, DC-Karten SI (supplied by Riedel de Haen AG, Seelze-Hannover). Column chromatography was performed on Kieselgel 60 (0.063–0.2) supplied by Merck. Irradiation was by Westinghouse sunlamps through Pyrex Petri dishes. Commercial DCA (deoxycholic acid) was purified from fatty acids and cholic acid on a silica gel column eluted by 0.5% acetic acid in ethyl acetate.

All complexes were prepared by cocrystallization of DCA with the guest from methanol by slow evaporation of the solvent. In a typical experiment, 1–2 g of complex was irradiated at room temperature through Pyrex dishes, $\lambda > 300$ nm, for about 30 days. The crystals were generally in the form of powder. Single crystals preserved their integrity during irradiation. The products were separated by chromatography on silica gel 1:100 (eluted with $CH_2Cl_2/CH_3OH/AcOH$ in a ratio of 94.5:5.0:0.5) and by preparative TLC with the same eluent in a ratio of 90.5:9.0:0.5 by using UV detection and phosphomolybdic acid as coloring spray.

5.2. Photoproducts from UV Irradiation of DCA Complexes. Photoproduct 2 from DCA–Acetophenone: TLC $r_f = 0.65$; mp 216–218 °C (methanol/acetic acid); mass spectrum (methyl ester), m/e 404 (M − $C_8H_{10}O$), 273 (M − $C_8H_{10}O$ − H_2O − side chain), 255 (M − C_8H_{10} − $2H_2O$ − side chain), 121 (C_8H_9O); ^{1}H NMR[9] (CD_3OD) δ 0.71 (3 H, s, 18-H), 1.0 (3 H, d, $J = 5$ Hz, 21-H) 1.23 ($^3/_2$ H, s, 19-H), 1.28 ($^3/_2$ H, s, 19-H), 1.73 (3 H, s, $CH_3C(OH)$), 7.18 (5 H, m, $CH_3C(OH)C_6H_5$); UV λ_{max} 258, 290 (ϵ 320, 130); IR 3500, 3440 (OH), 2950 (C—H), 1680 (C=O), 1600 (Ph - H) 770, 720 cm^{-1}. Anal. Calcd for $C_{32}H_{48}O_5$: C, 74.96%, H, 9.44%. Found: C, 74.83%; H, 9.6%.

Photoproduct 3 from DCA–*m*-Chloroacetophenone: TLC $r_f = 0.65$; ^{1}H NMR (CD_3OD) δ 0.72 (3 H, s, 18-H), 0.99 (3 H, d, 21-H), 1.23 ($^3/_2$ H, s, 19-H), 1.28 ($^3/_2$ H, s, 19-H), 1.7 (3 H, s, $CH_3C(OH)C_6H_4Cl$), 7.2 (4 H, m, $CH_3C(OH)C_6H_4Cl$); UV λ_{max} 253 (ϵ 300); IR 3400 (O—H), 2950 (C—H), 1700 (C=O), 1580 (Ph - H) cm^{-1}. Anal. Calcd for $C_{32}H_{47}O_5Cl$: C, 70.24%; H, 8.66%. Found: C, 70.14%; H, 8.61%.

5.3. X-ray Intensity Measurements. DCA Complexes. The X-ray intensities of DCA–acetophenone at room temperature (293 K) were measured on a Siemens three-circle automatic diffractometer. The X-ray data of the DCA–acetophenone and DCA-*m*-chloroacetophenone cooled to ca. 103 K were measured on a CAD-4 diffractometer by using Mo Kα radiation filtered with a graphite monochromator. Cell dimensions (Table III) were determined by least squares using 25 reflections. The X-ray intensities were measured with crystals sufficiently small not to be affected by the inhomogeniety of the X-ray beam due to the graphite monochromator. This was verified by the excellent match between two X-ray data sets on DCA-*p*-fluoroacetophenone described elsewhere;[15] for one of these, the crystal was mounted along its needle direction while for the other the needle was mounted on its side. Details on the X-ray intensity measurements are given in Table III. Absorption corrections were not applied, being negligible.

Photoproduct 2. Needlelike crystals of 5β-(*S*)(1-phenyl-ethanol)-deoxycholic acid (**2**) were obtained by slow evaporation from an ethanol–acetic acid solution. The X-ray diffraction data were measured on a Siemens three-circle diffractometer by using Cu Kα radiation. The cell dimensions (Table III) were determined by least squares from 30 reflections. Absorption corrections[19] were applied to the intensity diffraction data, the crystal exhibited faces {100}, {001}, {101}, and {110} with dimensions given in Table IIIa. The transmission factor applied to the X-ray intensities varied from 1.06 to 1.19.

5.4. General Remarks on X-ray Structure Determination and Refinement. It was obvious from the intensity diffraction data of the two DCA complexes that their host steroid structures are isomorphous, belonging to the known motif.[2] Thus, initial refinement of the host molecule was straightforward. The crystal structure of photoproduct **2** was determined by the use of MULTAN.[20] The least-square refinements were carried out with SHELX.[21] The temperature factors of the C and O atoms of host DCA and of photoproduct **2** were refined anisotropically and their H atoms isotropically. The scattering factors for H, C, and O were taken from ref 22. The function refined was $\sum w(F_o - F_c)^2$ where $w = 1/\sigma^2(F_{obsd})$; $\sigma(F_{obsd})$ was obtained from counting statistics and the match between symmetry-related reflections. Refinement was carried out in two blocks, full matrix not being feasible. The reliability factors given are $R = \sum|F_o - F_c|/\sum F_o$; $R_w = \sum w^{1/2}|F_o - F_c|/\sum w^{1/2}F_o$, $r = \sum w|F_o - F_c|^2/\sum wF_o^2$.

5.5. Refinement of the Low-Temperature (103 K) X-ray Structure of DCA–Acetophenone. The DCA host structure was refined first with isotropic and then anisotropic thermal parameters by using 4260 reflections, for which $F_{obsd} > 3\sigma(F_{obsd})$, yielding $R = 0.13$ (defined above). An electron density diffference map yielded several peaks within the channel, with heights ranging from 1.0 to 1.9 e/Å^3. It was not directly evident from the peak heights and their distribution whether the channel contained more than one guest molecule per asymmetric unit. The peak distribution was coplanar to within 0.2 Å. We proceeded by easily fitting only one guest molecule of acetophenone to the peaks. This molecular model was taken from an accurate low-temperature X-ray diffraction study of crystalline acetophenone.[23] This molecule as guest was refined positionally as a rigid body with a fixed isotropic value of 0.04 Å^2 and an initial occupancy factor of 0.4. The temperature factor of 0.04 Å^2 was assumed reasonable since the average temperature factor of the host atoms was 0.025 Å^2. We had assumed the occupancy of 0.4 for the guest because it was clear at that stage that the molar guest–host ratio could not be higher than 1/2 according to the most hypothetical dense packing of the guest within the channel. On refinement to $R = 0.098$, the occupancy factor of the guest reduced to 0.29, and a difference map yielded seven additional peaks whose heights ranged between 0.8 and 1.1 e/Å^3. These peaks described an acetophenone molecule almost parallel to the original but separated therefrom along the channel axis by approximately 0.8 Å. Therefore, two independent acetophenone molecules, G and G′ as depicted in Figure 4a, were inserted in the channel and refined positionally as rigid bodies.

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Further refinement yielded occupancy factors of 0.215 (8) for G′ and 0.202 (6) for G and a guest thermal parameter of 0.055 Å^2 and an R value of 0.059. Utilizing the result that the crystal structure contains only the two independent guest molecules G and G′, we have demonstrated by packing considerations that the total guest occupancy is maximally 0.4 with individual occupancies of G and G′ maximally 0.2 (see section 2.2). Thus, for further refinement, the occupancies of G and G′ were set equal to 0.2. We replaced the constraint of one isotropic thermal parameter for G and G′ by that in which four different atom groups each had a different isotropic thermal parameter. Refinement yielded the reliability factors R = 0.059, R_w = 0.051, and r = 0.0555. There is pronounced overlap of the G and G′ molecules, due to the small separation of 0.8 Å along the c axis, as well as the overlap induced by the twofold screw axis along the channel (Figure 4b). This overlap necessitated a water-tight strategy for unambiguous location of, and differentiation between, atoms oxygen O1 and methyl carbon C8 of each of the guests G and G′. These atoms had been originally located from difference maps by peak heights and peak–peak distances. We adopted the following least-squares procedures to make certain that they are in their deduced sites. Atoms O1 and C8 were removed from both guest molecules G and G′ and the structure was refined with guest tolyl C_7H_5 groups as rigid bodies with their thermal parameters fixed at their original refined values. R was refined to 0.073. A difference map yielded three, rather than four, peaks with heights of 1.37, 1.30, and 1.20 e/Å^3, corresponding to two resolved oxygen peaks and one unresolved carbon peak. We rationalize this result as follows: in the refined crystal structure, the distance between the methyl carbon atoms C8 of molecules G and G′ of 0.65 Å is appreciably shorter than the corresponding distance of 0.82 Å between the oxygen atoms (Figure 4). Insertion of three guest atoms (i.e., two oxygens and one methyl carbon) yielded the remaining methyl C atom by a difference synthesis. However, it was still necessary to prove that we have correctly differentiated between the oxygen and methyl groups. Thus, we refined a structure in which each guest molecule G and G′ had been rotated by 180° about its long molecular axis C7···C1. Namely, we effectively interchanged the oxygen and methyl positions in G and G′. The refinement, which yielded R = 0.0625, R_w = 0.0554, and r = 0.0621 (defined in section 5.4), indicated that *both* acetyl groups should be in their original positions for the following reasons: (a) The temperature factor U of the guest G atoms increased from 0.078 (3) to 0.102 (3) Å^2 and that of the methyl C atoms decreased from 0.058 (3) to 0.047 (3) Å^2. (b) A difference map showed peaks of height 0.6 e/Å^3 near the two oxygen positions of the original unrotated structure. (c) Applying the Hamilton test,[24] the **R** ratio r_2/r_1 (r_1 and r_2 correspond to the original and rotated guest structures, respectively) equals 0.0621/0.0555 = 1.09. We test this **R** ratio of 1.09 against $\mathbf{R}_{16,4260-184,0.005}$ = 1.004, where 16 = 2× (six positional + two thermal parameters for each guest molecule), 4260 = the number of reflections used, 184 = the number of parameters refined, 0.005 = the significance level.

We can emphatically reject at a significance level > 99.5% the model structure in which the oxygen and CH_3 groups of *both* independent guest molecules are effectively interchanged.

In the third and most conclusive of the tests based on the X-ray data, the guest molecules were refined with their phenyl rings as rigid bodies and with constraints imposed on their acetyl groups; the bond length of C7–C1 was maintained at 1.49 Å and the 1···3 distance O1···C8 at 2.38 Å. On refinement, R = 0.0577 and R_w = 0.0493 were obtained. The refined bond lengths and angles of the acetyl groups of G and G′ (Figure 17) demonstrate that the acetyl oxygen and methyl carbon atoms, as inserted in the original rigid body refinement, are in their correct sites. These refinement results could not, however, rule out a minor amount (up to, say, 15%) of conformationally disordered acetyl groups. This ambiguity was removed by a neutron diffraction study described below.

5.6. Refinement of Room-Temperature X-ray Structure of DCA–Acetophenone. The final x, y, and z coordinates of host and guest were used as input for a refinement of the room temperature structure. The R value converged to 0.059. The average temperature factor U for the host C and O atoms is 0.063 Å^2. For the guest atoms, U = 0.09 Å^2, which is reasonable considering that at a crystal temperature of 103 K, the average temperature factor of the guest atoms, is also 0.03 Å^2 higher than that of the host atoms.

5.7. Neutron Diffraction Study of DCA–Acetophenone ($C_6H_5COCD_3$). The diffraction data were measured at 16 K with an automated four-circle diffractometer at the Brookhaven High-Flux Beam Reactor. The lattice dimensions were determined at 83 and 16 K (see Table III). The number of reflections that were measurable with significant intensities was severely limited by the size of the crystal (0.56 mm^3), which was less than $^1/_{10}$ of that needed in the present study. A full quadrant of data ($\pm hkl$) was collected in the range $0.023 < \sin\theta/\lambda < 0.40$, giving 1622 observations. An additional 942 ($\pm hkl$) reflections, calculated to be the most intense after preliminary refinement against the low-angle data, were measured in the range $0.40 < \sin\theta/\lambda < 0.68$.

The X-ray-derived crystal structure was refined with individual isotropic temperature factors for all the steroid atoms. The C and O atoms of the guest molecules were refined with the same temperature factor; the H and D atoms of G and G′ were assigned a fixed isotropic U of 0.06 Å^2. The guest acetyl $COCD_3$ was allowed the two possible orientations so that four guest model structures (Scheme VII) were tested.

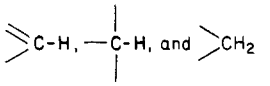
The resulting R and r values for models a–d were (0.1017, 0.1208), (0.1079, 0.1280), (0.1043, 0.1235), and (0.1037, 0.1223), respectively, where a corresponds to the X-ray derived structure. We apply the Hamilton test[24] to compare model a with b, c, and d. r_b/r_a (0.1280/0.1208) = 1.0596, r_c/r_a (0.1235/0.1208) = 1.0224, and r_d/r_a (0.1223/0.1208) = 1.0124. We test these ratios against $\mathbf{R}_{13,1317-283,0.005}$ = 1.015 and $\mathbf{R}_{13,1317-283,0.025}$ = 1.012, where 13 = 2x (six positional and one thermal parameter for each guest), 1317 = number of reflections used, 283 = number of refined parameters, and 0.005, 0.025 = confidence levels.

We may reject models b and c at the 99.5% level and model d at approximately the 97.5% level. Thus, the Hamilton test on the four models a–d is consistent with the X-ray results.

Definitive proof of the correctness of model a was provided by Fourier difference maps. All six deuterium atoms were removed from the structure factor calculations of model a, and difference maps were calculated in the four planes perpendicular to the C7–O7 and C7–C8 bonds of G and G′ where the D_3 groups could be expected to be found. The maps (Figure 12a) show peak distributions corresponding to symmetric D_3 groups in the planes perpendicular to the C7–C8 bonds; the maps perpendicular to the C=O bonds (Figure 12b) do not exhibit (symmetric) D_3 methyl groups. Thus, not only do these maps confirm the X-ray-derived guest structure but also that the oxygen and CD_3 groups do not appear to exhibit any conformational disorder.

5.8. Refinement of Low-Temperature (103 K) Structure of DCA–*m*-Chloroacetophenone. The host structure was initially refined with the final coordinates of DCA–acetophenone, yielding an R value of 0.14. A difference map displayed the two strongest peaks of height 2.2 e/Å^3 located within the channel. They were interpreted as two independent C1 atoms each belonging to a guest molecule. These two peaks are far removed from the central axis of the channel and therefore could hardly be interpreted in terms of superposition of the lighter C and O atoms arising from the molecular overlap inherent in these channel structures. When these two C1 positions were utilized as anchor points in the refinement, the orientations of the two guest molecules G and G′ were determined by fitting *m*-chloroacetophenone molecules to the remaining difference map peaks of average height 0.9 e/Å^3. The G and G′ molecules were refined as rigid bodies, where the molecular model of *m*-chloroacetophenone was taken from the crystal structure of bis(*m*-chlorobenzyl)methane.[25] R converged to 0.076 and R_w to 0.078. Refinement of each of the occupancy factors of G and G′ yielded values of 0.167 (3) and 0.168 (3). An analysis of the possible packing arrangements of the guest molecules G and G′ in the channel (see section 3.3) indicates that the maximum guest occupancy is 1:3 which compares excellently with the observed value of 0.167 + 0.168 = 0.335 (4). Thus, we fixed the occupancy factors of the guests G and G′ to 0.16667 each in the final stages of refinement and obtained final values of R = 0.075 and R_w = 0.076.

5.9. The Crystal Structure of 5β-(*S*)-(1-Phenylethanol)deoxycholic Acid. The C and O atoms of photoproduct **2** were revealed by MULTAN.[20] H atoms belonging to groups



were attached to the C atoms. The subsequent $\Delta\rho(x,y,z)$ maps yielded the positions of all the methyl and hydroxyl H atoms. The R factor converged to 0.04.

6. Results of Refinement

Details on refinement of the crystal structures of deoxycholic acid (DCA) with acetophenone and *m*-chloroacetophenone and of photoproduct 5β-(*S*)-(1-phenylethanol)deoxycholic acid **2** are given in Table IV. The atomic x, y, and z coordinates and

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equivalent thermal parameters of the low-temperature inclusion compounds and of photoproduct **2** are listed in Tables V-VII, respectively. Their bond lengths and angles are listed in supplementary material in Tables 5S, 6S, and 7S, respectively. The x, y, and z coordinates of the room-temperature structure of DCA-acetophenone are listed in Table 5S (d).

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Registry No. 2, 95586-16-6; **2** (methyl ester), 95485-48-6; **3**, 95586-17-7; 5DCA·2$C_6H_5COCH_3$, 83035-58-9; 3DCA·m-$C_6H_5COCH_3$, 83047-96-5; 5DCA·2$C_6H_5COCl_3$, 95485-49-7.

Supplementary Material Available: Thermal parameters, bond angles, and bond lengths (13 pages). Ordering of information given on any current masthead page.

Communications to the Editor

Biomimetic Models for Cysteine Proteases. 2. Nucleophilic Thiolate-Containing Zwitterions Produced from Imidazole-Thiol Pairs. A Model for the Acylation Step in Papain-Mediated Hydrolyses

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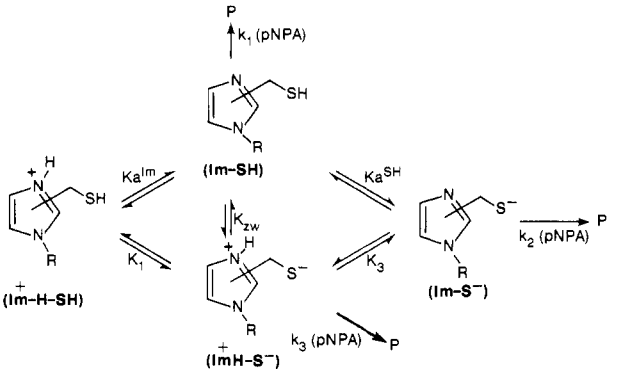
The most widely studied example of the cysteine proteases, papain, cleaves both amide and ester substrates with the formation of the intermediate Cys thiol ester.[1] The pH-rate profile for the hydrolysis of a typical ester substrate (α-*N*-benzoyl-L-arginine ethyl ester) is bell shaped and was interpreted to indicate the involvement of two groups having apparent pK_a's of ~4.3 and 8.2-8.5.[2]

The most recent evidence from spectral and potentiometric titrations and solvent isotope effects[3] indicates that Cys-25 has an unusually low pK_a of 3-4 while that of His 159 is 8.5. These and earlier kinetic studies[4] suggest that Cys-25 and His-159 exist primarily as a zwitterionic imidazolium thiolate ion pair which is catalytically viable at physicological pH.

Although small molecules incorporating both imidazole and thiol units have been studied as nucleophilic catalysts in promoting the hydrolysis of *p*-nitrophenyl acetate (*p*-NPA),[5,6] the kinetic involvement of zwitterions has never been unambiguously demonstrated. Also, there has never been demonstrated a significant cooperative effect in the catalysis of hydrolytic processes by thiol-imidazole intramolecular systems as is thought to occur in the cysteine proteases. Herein we report that **2a** and **3a**[7] (but not

Scheme I



Scheme II

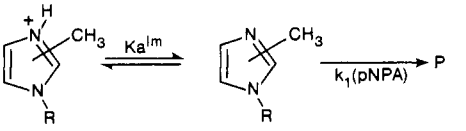


Table I. pK_a Values (Macroscopic and Microscopic) for **1-3**

	macroscopic pK_a[a,b]		microscopic pK_a[c]				
	pK_{a1}	pK_{a2}	pK_1	pK_a^{Im}	pK_3	pK_a^{SH}	K_{Zw}[d]
1a	6.54 (6.68)	9.54 (9.52)	7.72	6.57	8.36	9.51	0.07
2a	6.37 (6.41)	9.26 (9.01)	6.50	6.96	9.13	8.67	2.88
3a	6.31 (6.44)	8.88 (8.83)	6.47	6.83	8.75	8.39	2.29
1b	7.56[e]						
2b	7.94[e]						
3b	7.64[e]						

[a] Values without parentheses are averages of triplicate potentiometric titrations; ±0.05 unit. [b] Bracketed values were obtained as kinetic pK_a values obtained from computer fit to eq 1a.[11] [c] Values as defined in Scheme I and calculated by methods given in ref 12 using titrimetric macroscopic pK_a's and assuming pK_a^{Im} is that of the corresponding *S*-benzyl derivative.[13] [d] K_{Zw} = [Im$^+$H-S$^-$]/[Im-SH] = K_1/K_a^{Im}. [e] Literature values for **1b**, **2b**, and **3b** are 7.51, 8.00, and 7.85, respectively.[14]

(7) Thiols **1a**, **2a**, and **3a** were synthesized from their corresponding alcohols according to the general procedure of Schneider[8] and exhibited spectral and analytical data consistent with their structures (details to be published).

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