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ELUCIDATION OF REACTION PATHWAYS IN HOST-GUEST COMPLEXES BY CRYSTAL ENGINEERING. PHOTOADDITION OF CARBONYL GROUP OF GUEST ACETOPHENONES AND PROPIOPHENONES TO HOST DEOXYCHOLIC ACID

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ABSTRACT

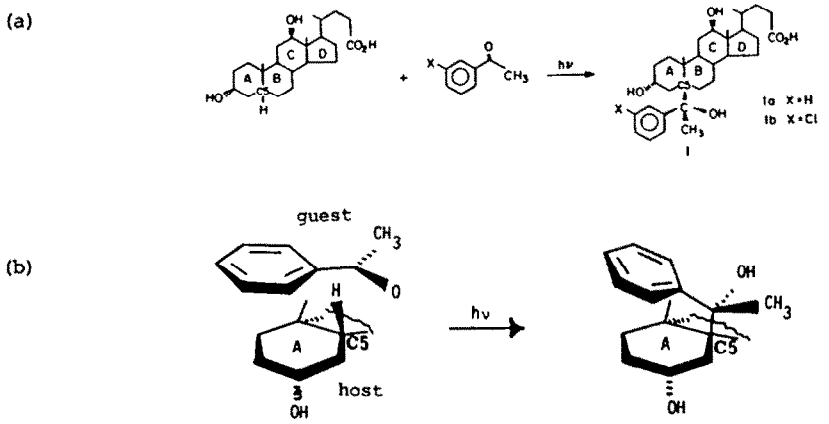
The two inclusion complexes of guest acetophenone and m-chloro-acetophenone with host deoxycholic acid (DCA) each yielded on UV irradiation a single diastereomeric photoaddition product at steroid atom C5, of configuration S at the generated stereogenic centre ($DCAOHCH_3C_6H_4$). Comparison of the host-guest arrangement at the sites of reaction with the S configuration at the new chiral atom C of the photoproducts indicates a net rotation of 180° by the guest acetyl group prior to C-C bond formation since the guest molecules expose their Re faces to the C5-H5 steroid bonds[1]. To elucidate this rotation, photochemical and crystallographic studies were performed on four DCA complexes with engineered guest ketone arrangements. The guests were p-fluoroacetophenone and (p-substituted) propiophenones ($XC_6H_4CO_2C_2H_5$, X=H, F, Cl). The crystal structures of two isolated photoproducts are also reported. The channels of DCA-fluoroacetophenone contain two independent guest molecules G' and G, respectively exposing their Re and Si faces to the steroid C5-H5 bond vectors at the potential sites of reaction. Only one diastereomeric photoproduct was obtained with addition at atom C5, with absolute configuration S at the generated stereogenic centre, akin to that of the DCA-acetophenone complexes. The reaction is interpreted in terms of a 180° rotation of the acetyl group of the G' molecule; the absence of the R diastereomer is explained by a preclusion of photoaddition of guest G to DCA because of guest packing along the channel. The guest arrangements in the two complexes DCA-propiophenone and DCA-p-fluoropropiophenone are almost isomorphous. There are two independent guest molecules G and $\bar{G}$ related by a pseudo centre of inversion. Each of the two guest molecules exposes its Re face to a steroid C5-H5 bond at a site of reaction. Thus photoaddition takes place with and without 180° rotation of the propionyl group since the two complexes each yield the two diastereomeric photoproducts at C5. DCA-p-chloropropiophenone yields only one diastereomeric photoproduct at C5, with absolute configuration R about the new stereogenic centre. The crystal structure analysis suggests three independent guest molecules G, G' and $\bar{G}$; G and G' are related by pseudo two fold screw symmetry along the channel axis; $\bar{G}$ is related to G and G' by pseudo centre of inversion; once again the guests G, G' and $\bar{G}$ appear to expose their Re faces to the C5-H5 bonds at the sites of reaction.

INTRODUCTION

In a preceeding paper[1] we described the crystal structures of the channel inclusion complexes 5:2 deoxycholic acid (labelled DCA)-acetophenone and 3:1 DCA-m-chloroacetophenone which yield the single diastereomeric products 1a and 1b respectively on UV photoirradiation (Scheme 1a).

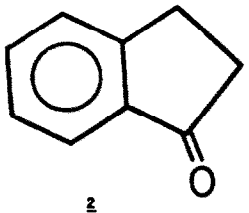
*Footnote
These results in the form of Tables 1s-7s have been deposited with the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW.

At the potential site of reaction in the host-guest arrangement (Scheme 1b), the prochiral configuration about the guest carbonyl C atom is Re. After photoreaction, the absolute configuration about this C atom, i.e. the newly generated chiral atom of product 1, is S (Scheme 1). This result reveals a net rotation of 180° of the acetyl group of the guest prior to bond formation. The question we pose is whether the rotation is orbital steered or whether formation of the missing diastereomer is precluded on steric grounds.



Scheme 1

This question may be approached via the following experimental routes: (i) Design of a host-guest arrangement in which the prochiral guest ketone exposes its Si face to the steroid C5-H5 bond, instead of face Re as in Scheme 1, and which should then yield the diastereomeric product of absolute configuration R at the newly generated chiral C centre if the photoreaction is orbital steered. (ii) Inhibition of the 180° rotation of the ketone moiety by attaching a flexible bulky ketone group to the phenyl ring or by using rigid guest molecules such as indanone 2. Were photoaddition to occur in either case (i) or (ii) we could infer that the 180° rotation in the DCA-acetophenone systems is orbital steered and not due to steric forces which would preclude the formation of the other diastereomer.



2

Choice of Guest Molecules:

We tried to engineer the host-guest arrangement in which the guest ketone exposes its Si face to steroid C5-H5 bond by modifying the already known arrangement of guest acetophenone molecules through atomic substitution. The crystal structure of DCA-acetophenone contains two independent guest acetophenone molecules G and G' forming close-packed pairs G G' within a channel (Fig.1). These two paired molecules are almost parallel to each other and separated by 8Å along the channel c axis of length 7.2Å.

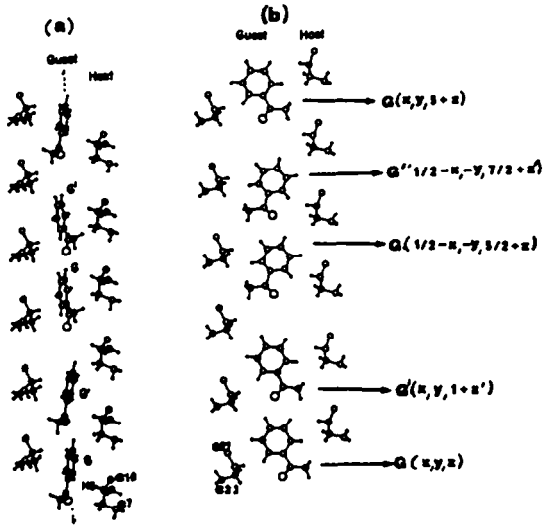


Fig.1: DCA-acetophenone. Packing of guest acetophenone molecules in the channel.
(a) View edge-on to plane of guest molecules; (b) view perpendicular to plane of guest molecules.

The neighbouring close-packed G G' pairs in a channel are related by a 5c/2 translation plus a rotation about the channel 2_1-axis so forming a one-dimensional superstructure with a 5c translation repeat. The host-guest arrangement of DCA-acetophenone at the site of reaction is depicted schematically in Fig.2 showing the guest molecules G' and G(original) separated by 8Å. We considered the possibility of modifying this arrangement by inducing a substituted acetophenone molecule G to occupy a new position, G(new) approximately 9.2Å removed from G' along the -c direction.

In this way the Si face of a substituted acetophenone may be exposed to the steroid C5-H5 bond. We were assisted in this line of reasoning by an energy calculation on DCA-acetophenone (Fig.10 in Ref.1) according to which, molecule G can be more easily displaced in the -c direction than can G' in +c from their respective stable positions. Thus by a suitable p-substitution of the guest phenyl ring, G would be displaced along the -c direction, G' remaining essentially unmoved. We chose p-fluoroacetophenone as an appropriate guest.

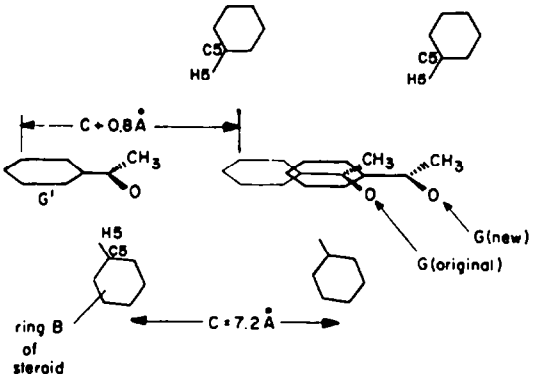


Figure 2

A schematic arrangement of host DCA and G' acetophenone molecules in which G has been shifted along the c axis from its original position by a distance sufficient to expose the Si side of its acetyl group to the steroid C5-H5 bond.

Another approach to generate the "missing" diastereoisomer would be to make use of a keto alkyl group sufficiently bulky to inhibit rotation by 180°, but which would still react with the steroid. Consequently, we chose the propionyl group $COCH_2CH_3$. We considered the ethyl moiety large enough to induce prohibitive steric contacts with the neighbouring molecules during 180° rotation but sufficiently flexible to permit photoaddition.

We studied, accordingly, the crystal photochemistry of DCA with guest molecules, p-fluoroacetophenone, p-H, p-F, and p-Cl-propiophenones (Fig.3).

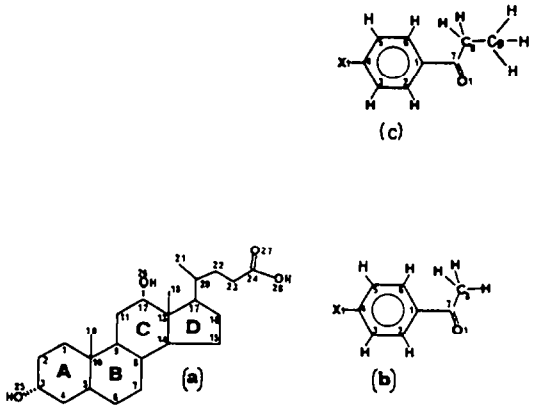


Fig.3: Atom numbering. (a) deoxycholic acid; (b) acetophenones (X=H, F); (c) propiophenones (X=H, F, Cl)

RESULTS

DCA-p-Fluoroacetophenone

Crystal structure and guest arrangement: The crystal structure of DCA-p-fluoroacetophenone was determined by low temperature (103°K) X-ray diffraction (see Experimental). The host DCA molecules are arranged in the α-motif (Fig.3 in ref.1). Two independent guest molecules, G and G', were located in the channel. These two molecules overlap in terms of the diffraction analysis. G and G' are almost parallel to each other with very similar x and y coordinates; they differ only in z along the channel axis by 1.64Å as shown in Fig.4a. Despite the pronounced overlap between G and G' (see Fig.4b) their oxygen and methyl carbon atoms were clearly located and differentiated (see Experimental). The occupancies of G and G', i.e, the guest/host molar ratios, were refined freely by structure-factor least-squares to values of 0.113(4) and 0.258(4), respectively, with a total of 0.371(6).

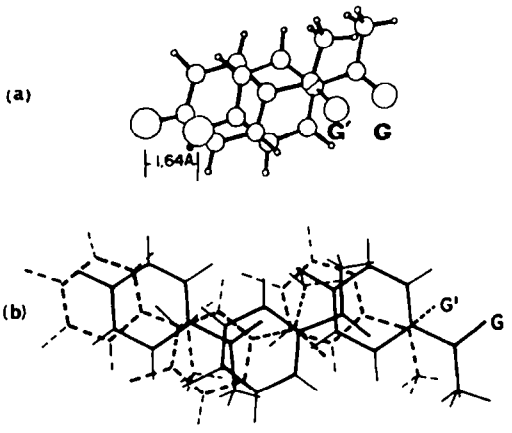


Figure 4

(a) Overlapping pair of guest fluoroacetophenone molecules G(x,y,z) and G'(x,y,z').

(b) Molecular overlap of fluoroacetophenone G and G' molecules in the channel. The arrangement may be derived from that in Fig.4a by applying 2_1 symmetry along the channel to G and G'.

We shall deduce that the guest molecules are arranged along each channel as depicted in Fig.5. These guest molecules form close-packed triplets G' G G' as a basic unit. The neighbouring triplets along the channel axis are related by a translation repeat of 4c. Within the triplet the two G' molecules are related by a translation of 5c/2 plus a rotation about the 2_1-axis which passes along the centre of the channel; G at (x,y,z) and G' at (x,y,1+z') of the triplet are related by a pseudo translation of c+1.64A° along the channel. This guest arrangement embodies occupancies of 0.25 for G' and 0.125 for G corresponding to a G'/G molar ratio of 2/1 and a total occupancy of 3/8=0.375.

Deduction of the guest arrangement: Packing the G and G' molecules in separate strings G G G G G or G'G'G'G'G', would yield a maximum guest occupancy of 1/3 as was demonstrated for acetophenone (see Fig.6 in Ref.1). Such an occupancy is distinctly less than the X-ray derived value of 0.371(6). Further, for such an arrangement of the guests, the individual occupancies would be equal to each other with maximum values of 1/6=0.1667, which is completely incompatible with the observed values. Moreover, one would also be hard put to explain the presence of two independent G' and G molecules with a relative offset along the channel axis of just the right magnitude to yield a reasonable intermolecular contact between such a pair as shall be demonstrated below. Indeed, only by assuming this intermolecular contact between G and G' molecules shall we be able to account for the observed occupancies.

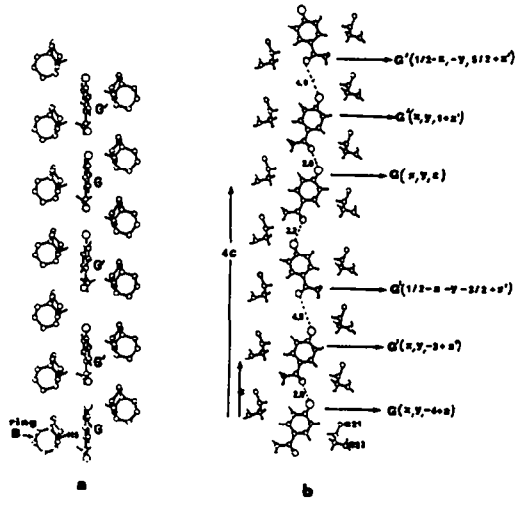


Fig.5: The packing motif of fluoroacetophenone in a channel. Only part of the steroid molecules forming the channel wall are shown. (The channel 2_1 -axis has coordinates x=1/4, y=0). (a) view edge-on to plane of guest molecule; (b) view perpendicular to plane of guest molecule.

We construct the closest-packed channel motif given the refined positions of the guests. Let the coordinates of G be x,y,z and that of G' be x,y,z', where z'=z+1.64Å/c. Here G and G' are referred to the same molecular site (Fig.4a). The molecules closest to G(x,y,z) in the +c and -c directions as shown in Fig.6 are G'(x,y,1+z') and G'(-1/2-x,-y,-3/2+z') respectively, with acceptable intermolecular O...F distances of 2.9 and 3.2A° respectively, to yield the close-packed triplet G'G G'. The next-nearest molecule to G'(x,y,1+z') is G(1/2-x,-y,5/2+z), followed by G'(1/2-x,-y,7/2+z') and then G(x,y,5+z). This arrangement is analogous to the acetophenone motif (Fig.1), with a guest occupancy of 0.4 and a G'/G molar ratio of 1/1. This motif (Fig.6) may yield the observed occupancy of 0.371(6) by assuming random guest vacancies, with equal occupancies of 0.185 for G and G'. But this model is incompatible with the observed G'/G molar ratio of 0.258(4)/0.113(4)=2.26(9).

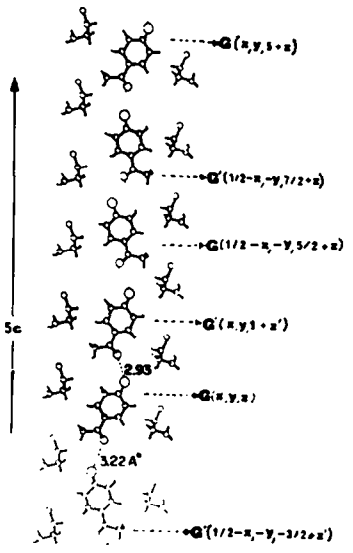


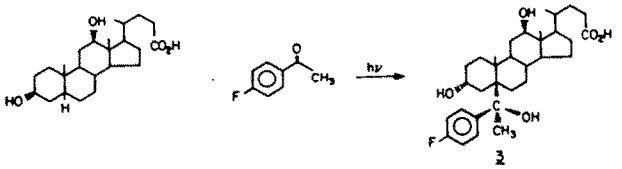
Fig.6 A postulated (incorrect) packing arrangement of fluoroacetophenone molecules G and G' in a channel, akin to that of acetophenone (Fig.1), so yielding equal guest occupancies of 0.2 for G and G' (The channel 2_1 axis passes through x=1/4, y=0).

Taking the close-packed triplet G'(1/2-x,-y,-3/2+z') G(x,y,z) G'(x,y,1+z') as the basic unit and generating a string therefrom by a translation repeat of 4c yields the arrangement shown in Fig.5 which embodies a G'/G molar ratio of 2/1 and a total guest occupancy of 3/8=0.375. The observed total occupancy of 0.371(6) is within one e.s.d. of the model value of 0.375. The observed individual occupancies, 0.258(4) for G' and 0.113(4) for G, are each reasonably close to the corresponding model values of 0.25 and 0.125. In this respect we note that the refined occupancy parameters of G' and G are correlated because of the pronounced molecular overlap between G and G' (see Fig.4b) in the structure-factor least-squares analysis (see Experimental).

Consequently, the motif shown in Fig.5 with a total occupancy of 0.375 and G'/G molar ratio of 2/1 best fits the diffraction analysis, and so in the final stages of refinement (see Experimental) the individual occupancies of G' and G were kept fixed at 0.25 and 0.125 respectively.

We now attempt to rationalize why the guest molecules do not adopt the closest-packed arrangement (Fig.6) with a total occupancy of 0.4 and a G'/G molar ratio of 1/1. According to intermolecular potential energy calculations on DCA-acetophenone[1], the site of guest G' is more stable than that of G by 0.5 Kcal/mol. Moreover, in order to increase the separation between acetophenone G' and G it costs much less energy to move G along -c than to move G' along +c. This calculation is compatible with the observed positions of fluoroacetophenone G' and G relative to the corresponding acetophenone pair; fluoroacetophenone G' occupies almost the same location as acetophenone G', whereas fluoroacetophenone G has moved relative to acetophenone G along -c by approximately 0.6Å. Thus there is hardly any doubt that fluoroacetophenone G'

Scheme 2



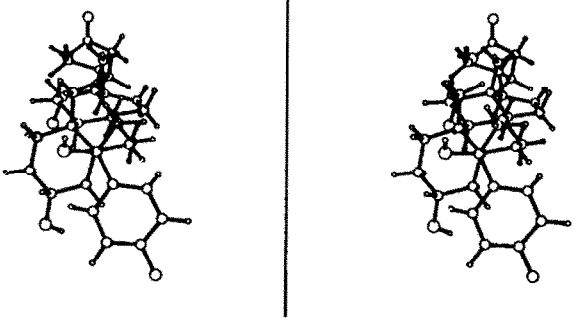


Fig.7: The photoproduct 3 from DCA p-fluoroacetophenone in its own crystal structure.

fluoroacetophenone molecules yielding a G'/G molar ratio of 2/1 appears to be a compromise between densest guest-packing in the channel and favourable host-guest contacts.

Solid-state photochemistry: Irradiation of the crystalline material of DCA-p-fluoroacetophenone for about 30 days, > 300nm, yielded a single topochemical addition product 3 (25% yield) (Scheme 2). The structure of 3 (Fig.7) was assigned from ^{13}C-NMR and an X-ray analysis described in Experimental. According to the chromatographic analysis and ^{13}C-NMR spectra only one diastereomer of the addition product was formed. The absolute configuration is S about the newly generated chiral C centre of photoproduct 3. This photoproduct is analogous to that obtained from DCA-acetophenone[1]. In fact the crystal structures of these two photoproducts are isomorphous.

Structure-reactivity relationship in DCA-p-fluoroacetophenone: The host-guest contacts at the sites of reaction are given in Table 1a. Molecule G' makes contact with the potentially reactive steroid C5-H5 bond (Fig.8), exposing the Re face of its acetyl group to C5-H5, in exactly the same way as does its counterpart G' in DCA-acetophenone (Fig.13 in ref.1). The O(G')...H5 distance is 2.8Å, decidedly less than that from O(G') to H6eq and H6ax of 3.6 and 3.7Å, respectively. Thus these relative distances are completely compatible with photoaddition to C5. The fluoroacetophenone G molecule exposes mainly the Si face of its acetyl group to a steroid C5-H5 bond, with O(G)...H5 and C7(G)...C5 distances of 2.6 and 4.07Å respectively, and exposes partially its Re face to another C5-H5 bond, with O(G)...H5 and C7(G)...C5 distances of 3.7 and 4.05Å,respectively, (Table 1a and Fig.8). In contrast, the G guest molecule in DCA-acetophenone exposed only its Re face to the steroid C5-H5 bond. Therefore, on cursory inspection of the guest packing of DCA-p-fluoroacetophenone, one may expect that photo-irradiation would yield two diastereomeric products, one from G' and the other from G.

Photoirradiation, however, yielded the single diastereomeric product 3 with an S configuration at the new chiral centre, (see Fig.7), the same as that of the DCA-acetophenone addition product.

On the basis of the topochemical results of DCA-acetophenone, only fluoroacetophenone G' should react and G should be inert. But this argument is flimsy for one might claim that in DCA-fluoroacetophenone, G reacts with no net rotation of the acetyl group. Indeed we shall demonstrate below that in the DCA-(substituted)propiophenone series, photoaddition also takes place with no net rotation of the propionyl group.

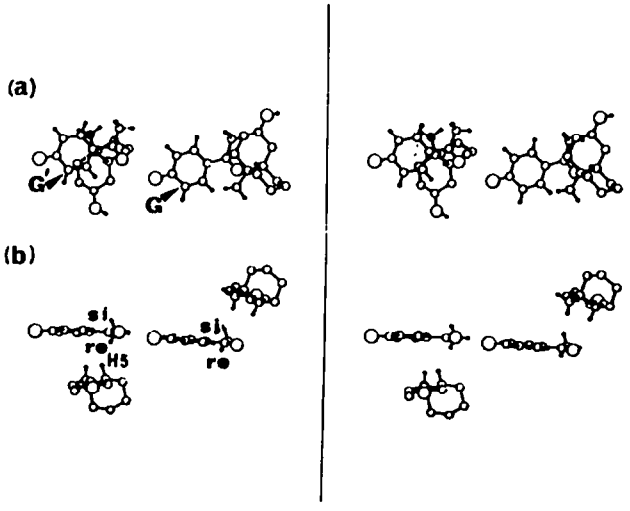


Fig.8: DCA-fluoroacetophenone. Host-guest packing at site of reaction. The two guest molecules G and G' and ring A of the steroid are shown. (a) view along the steroid H5-C5 bond. (b) view perpendicular to the H5-C5 bond.

We may attempt to resolve this ambiguity by considering the possible changes in position of G and G' on photoaddition to C5. G' would barely change its position along the channel axis and so would not incur unfavourable contacts with the neighbouring guest molecules (see Fig.8). On the other hand, G would necessarily be shifted by approximately 2.5Å along the -c direction on photoreaction (see Fig.8), and so would be sterically too close to a neighbouring G' guest. On this basis, only G' should react. This question was fully resolved by determining the crystal structure of the partially reacted complex[2]. DCA-p-fluoroacetophenone did not satisfy the original aim of yielding the "missing" addition product of absolute configuration R about the newly generated chiral C centre. Nevertheless it provided a system where the reactivity appears to be determined not only by the host-guest geometry but also by the nearest-neighbour arrangement of guest molecules.

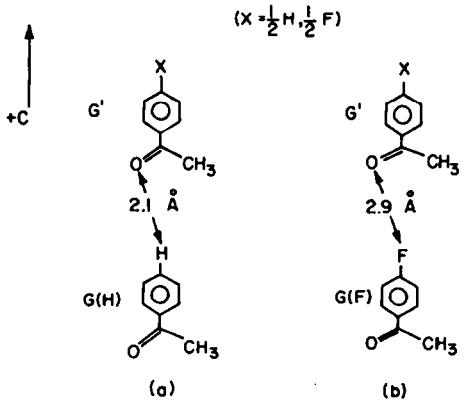
DCA-(Acetophenone, p-Fluoroacetophenone)

The interpretation of the reaction pathway in the complexes of 5:2 DCA-acetophenone and 8:3 DCA-p-fluoroacetophenone is directly dependent on determining which atom of the guest acetyl group is oxygen and which is methyl carbon. This distinction was made on DCA-m-

chloroacetophenone by X-ray diffraction and on DCA-acetophenone by X-ray and neutron diffraction studies and by potential energy calculations, all results matching[1]. For DCA-fluoroacetophenone the differentiation was done by X-ray diffraction. The refined occupancies of the guest molecules in these three crystal structures are in excellent agreement with the deduced arrangements of guest molecules along the channels. We did not, however, observe from room-temperature X-ray diffraction photographs any evidence of the deduced one-dimensional superstructures of the guest molecules, acetophenone and fluoroacetophenone.

The lack of superlattice reflections may be understood in terms of the following arguments. In the crystal structure of DCA-acetophenone there are five different ways of positioning the one-dimensional superstructure along the channel axis with respect to a host molecule on the channel wall (see Fig.1, and Fig.7 in ref.1). These five channel structures are energetically equivalent. Nearest-neighbour channels are separated by 13.6Å and so the interactions between their occluded guests are too weak to fix the relative positions of their superstructures along the channel axes. There are two channels per unit cell and thus 25 different arrangements of the one-dimensional guest superstructure in a disordered unit cell. In DCA-fluoroacetophenone there are four different arrangements of the superstructure (Fig.5) along a channel axis and thus 16 different arrangements in a disordered unit cell. The absence of observed superlattice reflections can be attributed to complete disordering of this nature in the crystal. In order to provide further supporting evidence for the correctness of the deduced guest arrangements we carried out a low-temperature (103°K) X-ray structure analysis on the ternary complex DCA-(acetophenone *p*-fluoroacetophenone). If the guest arrangements of the two binary complexes are correct we may expect the following guest structural features of the ternary complex as drawn in Scheme 3.

Scheme 3



The G' site may be occupied by either acetophenone, labelled G'(H), or fluoroacetophenone, labelled G'(F). If the nearest neighbour of G' along the -c direction is

acetophenone G(H), then the close-packed pair G'G(H), shown in Scheme 3a, should be identical to the G'G(H) pair in DCA-acetophenone (see Fig.1). If G' is followed along -c by G(F) then this G'G(F) pair, as shown in Scheme 3b, should be arranged as in DCA-p-fluoroacetophenone (Fig.5). Consequently the ternary complex should contain three guest sites G', G(H) and G(F) with an occupancy of 0.2 for G', and 0.1 for G(F) and for G(H). Moreover the relative positions of G', G(H) and G(F) along the channel axis, should match those in the crystal structures of the two binary complexes.

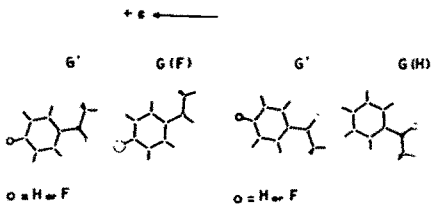


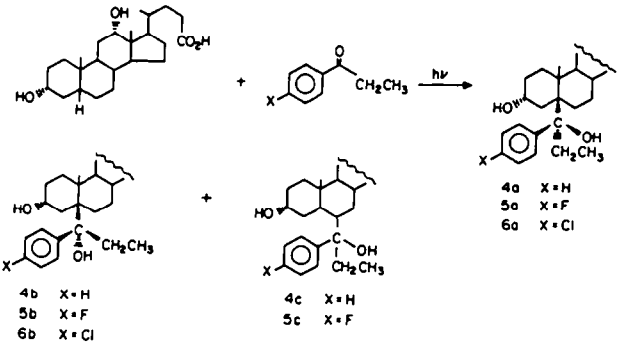
Figure 9
DCA-(acetophenone, p-fluoroacetophenone).
Packing arrangement, within a channel showing close packed pairs G'G(F) and G'G(H) related by pseudo 2_1 symmetry. A molecule G' which may be either G'(H) or G'(F) may be followed along the -c direction by either G(H) or G(F).

The structure-factor least-squares analysis of this ternary complex, (see Experimental), yielded three sites G', G(H) and G(F), akin to those found in the two binary complexes. The refined occupancies for G', G(H) and G(F) were 0.20, 0.14 and 0.07 respectively; the molar ratio of 0.14/0.07 for G(H)/G(F) is accounted for in the Experimental section. The guest packing arrangement is shown in Fig.9. The least-squares analysis once again demonstrated the same orientation of the acetyl group for G' as was found in the two binary complexes. All in all, there can be no doubt that the atomic positions and molecular arrangements of the guests in the two binary complexes are correct.

DCA-(Substituted) Propiophenones

Solid state photochemistry: UV-irradiation of DCA-propiophenone under argon gave two diastereomeric photoproducts 4a and 4b, at site C5, and product 4c at site C6 (Scheme 4, X=H). Irradiation of DCA-p-fluoropropiophenone under argon yielded the analogous diastereomers 5a, 5b, and 5c (Scheme 4); 5a being the major product. DCA-p-chloropropiophenone yielded upon irradiation the photoproduct 6b, with traces of the diastereomer 6a. We were however, not able to obtain crystals of products 4c and 5c sufficiently large and suitable for an X-ray molecular structure determination. The absolute configuration of 5b was assigned by an X-ray analysis of 7 (see Experimental and Fig.17) which was derived by acidic dehydration of 5b in glacial acetic acid. The absolute configuration about the new chiral C centre linked to C5 for each of the products 4a, 4b, 5a, 5b, 6a and 6b was assigned by comparative ^{13}C-NMR analysis

with the photoproducts of DCA-acetophenone, and DCA-p-fluoroacetophenone (see Experimental) and by comparative CD measurements. The absolute configuration about this new chiral C centre proved to be S for products 4a, 5a and 6a, as in the photoproducts 1 and 3 from DCA - (substituted) acetophenones, and R for 4b, 5b and 6b.



Scheme 4

Guest packing in DCA-propiophenone and DCA-p-fluoropropiophenone: The low temperature (103°K) crystal structures of these two complexes were refined to R(F) values of 0.057 and 0.081 respectively (see Experimental). These two crystal structures proved to be essentially isomorphous.

The positions of the guest atoms were located by several procedures. We deduced that the channels contain two crystallographically independent molecules G and $\bar{G}$. The occupancies of the two propiophenone guest molecules G(H) and $\bar{G}$(H) are 0.247(2) and 0.119(2) respectively; the corresponding values of p-fluoropropiophenone G(F) and $\bar{G}$(F) are 0.247(2) and 0.080(2). Their total occupancy values of 0.366(3) and 0.327(3) respectively indicate that in the two crystal structures all possible guest sites are occupied. This deduction is based on packing considerations; only every third consecutive site along a channel can be occupied by a guest molecule G or $\bar{G}$. Thus, the maximum guest occupancy is 1/3. This value fits the observed occupancy of 0.327(3) for fluoropropiophenone excellently, but less so for propiophenone with a value of 0.362(3). We had constrained the total occupancy of molecules G(H) and $\bar{G}$(H) to a value of 1/3 in the structure-factor least-square analysis (see Experimental). The agreement index R(F), remained unchanged at 0.057; the guest occupancies of G(H) and $\bar{G}$(H) converged to 0.223(2) and 0.110(2) respectively. This model is equally as good as the unconstrained one in terms of structure-factor least-squares, and has the advantage of a total guest occupancy equal to 1/3.

The molecular orientations, positions and relative occupancy values of G and $\bar{G}$ in both complexes indicate that the guest molecules may pack in the two different chain arrangements as shown in Figs.10a,b and 11a,b. In one arrangement (Figs.10a and 11a) the guest molecules G and

$\bar{G}$ occupy consecutive sites generating a chain G $\bar{G}$ G $\bar{G}$ G etc., the G and $\bar{G}$ molecules being related by a pseudo centre of inversion. Since the occupancy of G is greater than that of $\bar{G}$, the remaining (Figs.10b and 11b) G molecules form a chain G G G G etc., in which the nearest-neighbour molecules are related by twofold screw symmetry as shown in Figs.10b and 11b. The interatomic distances between nearest-neighbour molecules in all these chains are acceptable (see Figs.10 and 11).

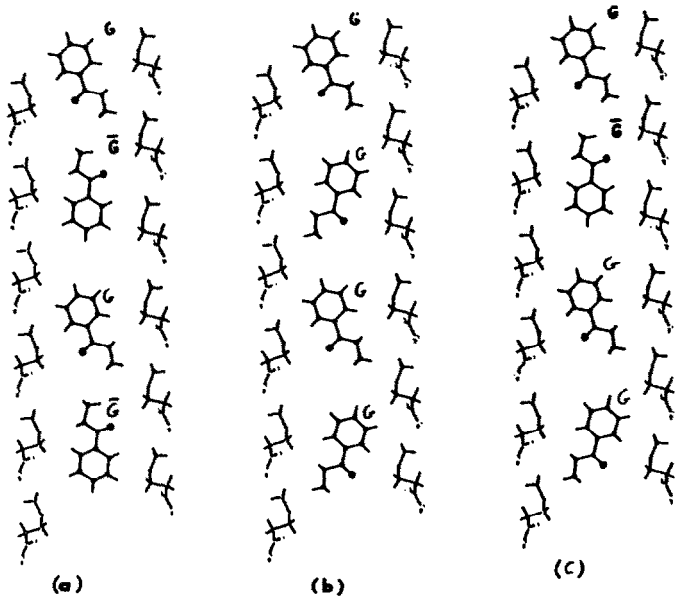


Figure 10: DCA-propiophenone.

(a) Pseudo-centrosymmetrically related dimers of G(H) and $\bar{G}$(H) molecules arranged along a channel. Distances between atoms of G and $\bar{G}$ are 4.1Å between methyl C atoms and 3.9 Å between the para H atoms.

(b) String of G (H) molecules related by twofold screw symmetry. The intermolecular distance between C(methyl) and C(4) is 4.9 Å.

(c) String of molecules in which the repeat unit is G$\bar{G}$G. From top to bottom along -c is G(x,y,z) $\bar{G}$(x,y, z), followed then by G(1/2-x,-y,-9/2+z) $\bar{G}$(1/2-x,-y,-9/2+z), G(1/2-x,-y,-15/2+z), etc.

The relative occupancies of these two different chains G $\bar{G}$ G $\bar{G}$ G $\bar{G}$ and G G G G G for the propiophenone and p-fluoro-propiophenone molecules are 0.93 [=0.119/(0.247-0.119)] and 0.97 [=0.110/(0.223- 0.110)] respectively. We have assumed here that every $\bar{G}$ molecule makes contact with a G molecule; otherwise it is difficult to account for the presence of two molecules G and $\bar{G}$ arranged just so as to form nicely-packed pairs. In fact, similar dimer

arrangements were deduced in the DCA-methylalkyl ketone complexes[3]. Naturally, it is possible to pack the propiophenone or p-fluoropropiophenone molecules in a chain which is a composite of the two chain motifs G $\bar{G}$ G $\bar{G}$ and G G G G. Such a possibility is highly likely in DCA-propiophenone where the guest occupancy ratio G(H)/$\bar{G}$(H) = 2.0(1). The proposed packing arrangement of guest propiophenone molecules given an occupancy ratio of G(H)/$\bar{G}$(H) = 2/1, is depicted in Fig.10c; the chain comprises triplets G(x,y,z), $\bar{G}$(x,y,z) and G(x,y,-3 +z) related by a twofold screw symmetry with a translation repeat of 9c/2.

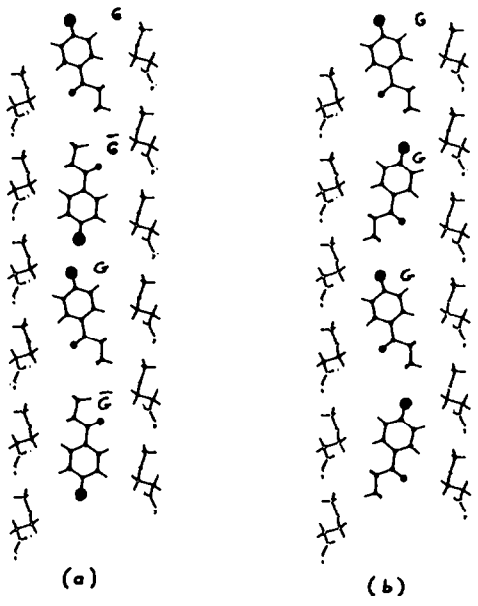


Figure 11: DCA-p-fluoropropiophenone.
(a) Pseudo-centrosymmetrically related dimers of G(F) and $\bar{G}$(F) molecules arranged along a channel. Distances between atoms of G and $\bar{G}$ are 4.0 Å between methyl C atoms and 3.0 Å between F atoms.

(b) String of G(F) molecules related by twofold screw symmetry. The intermolecular distance between C(methyl) and F is 3.4 Å.

Structure-Reactivity Relationship in DCA-propiophenone and DCA-p-fluoropropiophenone: UV irradiation of crystalline DCA-propiophenone and DCA-fluoropropiophenone yielded the two diastereomeric photoaddition products 4a, 4b, 5a, and 5b at atom C5 (see scheme 4). The host-guest geometries at the sites of reaction are depicted in Figs.12 and 13. Host-guest distances are listed in Tables 1b and 1c. Each G and $\bar{G}$ molecule exposes its Re face to a potentially reactive C5-H5 centre. Therefore formation of the products 4a and 5a necessitates rotation by a net 180° of the propionyl group prior to photoaddition, as was found in the DCA-(substituted) acetophenone series[1]. On the other hand, the products 4b and 5b are formed without rotation of the propionyl group.

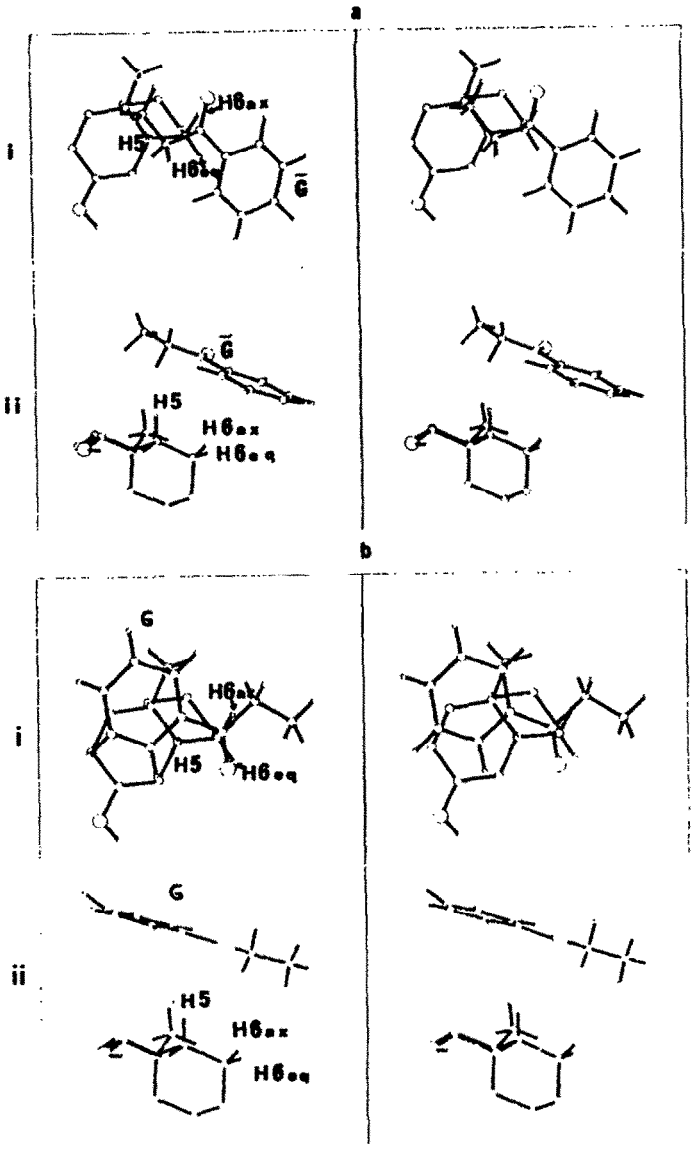


Figure 12: DCA-propiophenone.
Host-guest packing at sites of reaction for (a) guest molecule $\bar{G}$(H); (b) guest molecules G(H). (i) view along the steroid H5-C5 bond; (ii) view perpendicular to the H5-C5 bond.

These two results may be explained in terms of the guest packing. The propionyl groups in the arrangements shown in Figs.10a and 11a cannot easily undergo a rotation of 180° because that could eventually lead to unfavourable short contacts between neighbouring guest methyl groups. Therefore were reaction involving molecules G or $\bar{G}$ to take place at such a site the propionyl group would have to bind to the steroid without rotation. In contrast, the propionyl group in the arrangements shown in Figs.10b and 11b could perhaps undergo a rotation of 180° without inducing prohibitively short contacts with the nearest-neighbour guest molecules.

Thus we may envisage photoaddition to take place with or without a net rotation of 180° of the propionyl group depending upon the local environment of the guest molecules.

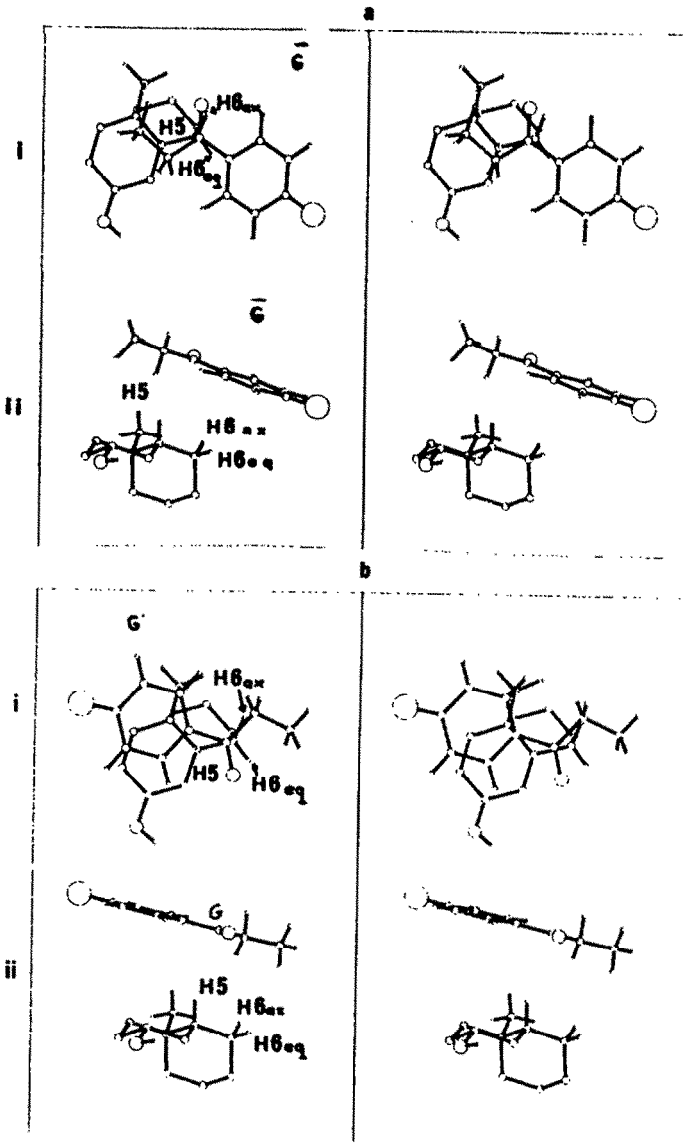


Figure 13: DCA-p-fluoropropiophenone.
Host-guest packing at sites of reaction for (a) a guest molecule G(F); (b) guest molecules G(F). (i) View along the steroid H5–C5 bond; (ii) view perpendicular to H5–C5 bond.

Guest packing and structure-reactivity relationship in DCA p-chloropropiophenone: The results of the structure-factor least-squares analysis (see Experimental), in terms of guest packing, are less positive than those of the other two propiophenone complexes. This is because we have invoked as many as three independent guest molecules to produce a feasible guest

packing along a channel. The three guest molecules G(Cl), G(Cl) and G'(Cl), each have occupancy equal to 0.1, yielding a total of 0.3. The deduced guest packing arrangement (see Experimental) along a channel (Fig.14) is comprised of close packed triplets G $\bar{G}$ G' related by a translation repeat of 5c, consistent with a total occupancy of 3/10. The nearest-neighbour G and G' molecules are related by pseudo twofold screw symmetry involving a translation repeat of 3c/2 + approximately 0.6Å. The molecule $\bar{G}$ is related to G and to G' by pseudo centres of inversion.

The host-guest arrangements at the sites of reaction are depicted in Fig.15 and the corresponding distances listed in Table 1d. Each guest molecule exposes its Re face to the potentially reactive C5-H5 centre. Therefore formation of the only one diastereomeric product 6b at C5, indicates that reaction occurs without rotation of the reacting propionyl group. This lack of rotation may be explained in terms of the tightly packed arrangement of guest molecules within the channels.

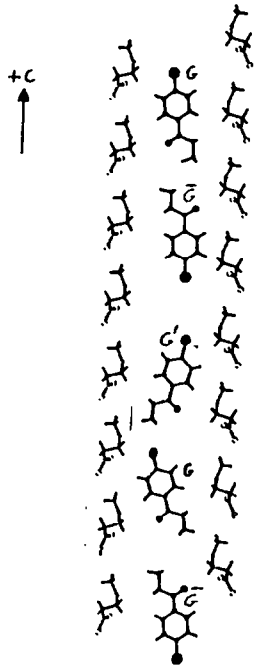


Figure 14: DCA-p-chloropropiophenone.
Packing arrangement of guest molecules along a chain. The repeat unit, from top to bottom, is G(x,y,z), $\bar{G}$(x,y,z), G'(1/2-x,y,-7/2+z). This triplet G$\bar{G}$G' is followed by G(x,y,-5+z), $\bar{G}$(x,y,-5+z), etc.

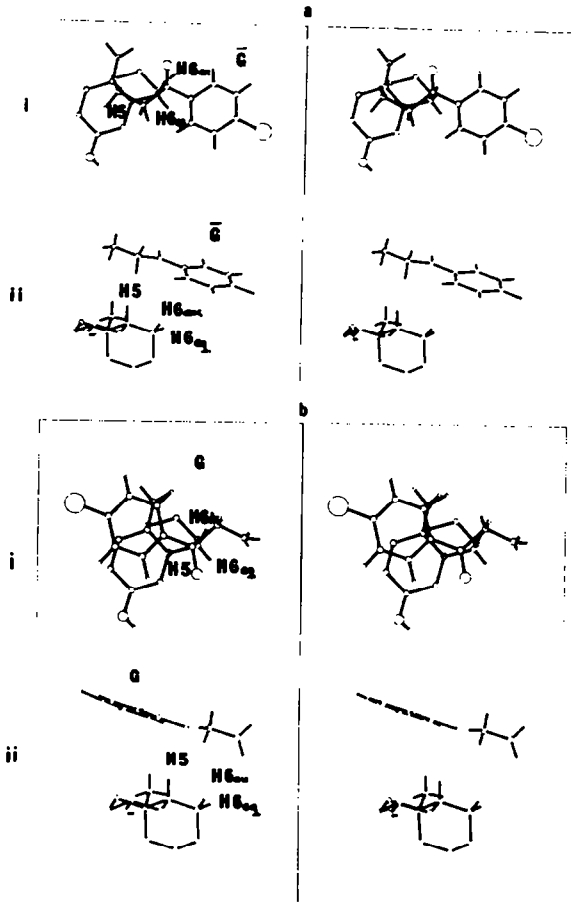


Figure 15: DCA-p-chloropropiophenone.
Host guest packing at sites of reaction for (a) guest molecule G(Cl), (b) for guest molecule G'(Cl). (i) view along steroid H5-C5 bond; (ii) view perpendicular to H5-C5 bond.

CONCLUSION

The crystallographic and photochemical results on the complexes presented here indicate that photoaddition of the ketone may occur with or without a net rotation of 180° of the ketone group. This rotation appears to be orbital controlled for it takes place in those systems where, in terms of steric contacts, reaction may as easily occur without rotation of the ketone. In those systems where contacts between the guest molecules appear to strongly inhibit rotation, photoaddition of the ketone group still takes place but without rotation.

EXPERIMENTAL

We refer to previous papers[1,3] in this series, for general remarks on chemical procedures, X-ray intensity measurements and crystal structure refinement. All DCA complexes were prepared by co-crystallization with the guest from methanol by slow evaporation of the solvent. In typical experiments, 1-2 g . of complex were irradiated at room temperature through pyrex dishes, λ>300nm, for about 30 days. The products were separated by chromatography on silica gel 1:100 (eluted with CH_3Cl/CH_3 OH/AcOH in a ratio of 94.5:5.0:0.5), and by preparative t.l.c. with the same eluent in a ratio of 90.5:9.0:0.5 using U.V. detection and phosphomolybdic acid as a colouring spray.

X-ray intensity measurements on crystals: The X-ray intensity data from the crystals of the five deoxycholic acid complexes cooled to ca. 103°K were measured on a CAD-4 diffractometer using Mo$K\alpha$ radiation with a graphite monochromator. The X-ray data from the two photoproducts 3 and 7 at room temperature were measured on the CAD-4 diffractometer using Cu$K\alpha$ radiation.

Cell dimensions of each crystal (Table 2) were determined by least-squares using 25 reflections. The X-ray intensities of the DCA complexes (for details see Table 3) 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 agreement between two sets of X-ray data totalling 9814 reflections from DCA-fluoroacetophenone; one set was measured with a crystal, of dimension 0.3x0.4x0.6mm, mounted on its long edge; the other set on its shortest edge. The agreement factor Rm (defined in Table 3) between the common 4907 equivalent reflections = 0.049. Absorption corrections were not applied to the intensity data from the crystals; they would have been negligible for the specimen crystals of the DCA complexes.

General remarks on X-ray structure determination and refinement: It was obvious from the intensity diffraction data of all the DCA complexes that their host steroid structures are isomorphous and belong to the known α-motif[1,3]. Thus in each case initial refinement involving only the host molecule was straightforward. The crystal structure of the photoproduct 3 from DCA p-fluoroacetophenone and of 7 derived from the photoproduct 5b of DCA p-fluoropropiophenone were solved using MULTAN[4]. The temperature factors of the C and O atoms of the steroid molecules in all structures were refined anisotropically and their H atoms isotropically. The scattering factors for H, C and O were taken from ref.5.

All least-square refinements were carried out with SHELX[6]. The function refined was $w(F_o-F_c)^2$ where the weight $w = 1/\sigma^2(F_o)$ was obtained from counting statistics and the match between symmetry-related reflections. Overall results on refinement of the crystal structures are given in Table 3.

5β (S) (1-p-fluorophenyl ethanol) deoxycholic acid from DCA-p-fluoroacetophenone (Photoproduct 3): The complex was prepared by crystallizing DCA with excess of p-fluoroacetophenone from absolute alcohol solution. Irradiation and separation as described above.

Photoproduct 3: r.f. 0.65 (silica gel, eluted with $CH_2Cl_2/C_2H_5OH/AcOH$ in a ratio of 94.5:5.0:0.5, m.p. 215-220°C. ^{1}H nmr 0.71 (3H, s, 18-H), 0.98 (3H, d, 21H), 1.24 (3H, s, 19H), 1.72 (3H, s, (CH-C(OH)A) ^{13}C nmr. (CD_3CO_2D) 32.4 (C1), 30.9 (C2), 69.4 (C3), 38.0 (C4), 49.2 (C5), 29.7 (C6), 28.5 (C7), 37.5 (C8), 36.4 (C9), 41.7 (C10), 30.6 (C11), 75.2 (C12), 46.7 (C13), 49.1 (C14), 24.7 (C15), 28.4 (C16), 47.8 (C17), 13.0 (C18), 20.5 (C19), 36.4 (C20), 17.6 (C21), 31.6 (C22), 31.6 (C23), 85.0, [C(OH)Me], 28.8 [C(OH)Me] 114.6, 114.9, 129.5 (phenyl o,m,p).

X-ray structure determination of photoproduct 3: Although the cell constants and X-ray diffraction intensities of the photoproduct 3 from DCA-p-fluoroacetophenone are very similar to those of the solved photoproduct from DCA-acetophenone[1], the C,O and F atoms of 3 were revealed independently by MULTAN[4]. H atoms belonging to groups >C-H and CH_2 were then attached to the carbon atoms of the molecular skeleton. Least-squares refinement and subsequent electron density maps yielded the positions of all the methyl and hydroxyl H atoms The R(F) factor converged to 0.062 (Table 3). The crystal structures of 3 and of the analogous photoproduct from DCA-acetophenone[1] are completely isomorphous.

Refinement of the low-temperature (103°K) structure of DCA-p-fluoroacetophenone: The guest molecules were located as follows. As outlined in the Introduction, we expected fluoroacetophenone would pack in a manner similar to acetophenone[1] (Fig.1), but with an increased separation of approximately 1.3Å between the close-packed molecules G and G'. This expected increase in separation of 1.3Å was deduced as follows: The C-H...O distance between close packed G and G' acetophenone molecules is 3.1Å (see Fig.1). The corresponding C-F...O distance should be approximately 4.4Å. Thus we initiated the least-square refinement of DCA-fluoroacetophenone with the refined positional and thermal parameters of DCA-acetophenone (the p-H atom of acetophenone was not inserted). The occupancies of G and G' were assumed to be 0.2 as in DCA-acetophenone and initially kept fixed.

After several cycles an electron-density difference synthesis displayed two peaks far stronger than any other. These two peaks corresponded very nicely to the fluorine substituents - which had not been inserted into the refinement - in terms of F-C(4) bond length and F-C-C bond angle. At this stage R was 0.090. The fluorine substituents were attached to G and G' with a C-F bond length taken equal to 1.33 Å based on an average weighted value taken from several reported crystal structures. The guest molecules were refined positionally as rigid bodies. The occupancies of G and G' were refined freely, and both molecules were assigned a single isotropic temperature factor. The resulting refinement in which R(F)=0.066 and R_w(F)=0.068, proved to be surprising. The G' and G guest molecules yielded occupancy factors of 0.258(4) and 0.113(4) respectively and a temperature factor=0.06Å^2. Consequently, the occupancies of G and G' were not equal to 0.2 as for acetophenone, nor were they equal to each other. The

total guest-host ratio of 0.371(6) is almost equal to 0.375 which corresponds to a guest-host ratio of 3/8. According to an analysis of the possible packing arrangements of G and G' (see RESULTS on DCA-p-fluoroacetophenone), we fixed the occupancy of guest G' at 0.25 and guest G at 0.125 in the least-squares refinement which yielded an overall thermal parameter of 0.07Å^2 for both guests, and final values of R(F)=0.065 and R_w(F)=0.068.

In order to ascertain that the oxygen and methyl carbon atoms of guest G and G' were correctly placed, we carried out a refinement as was done on DCA-acetophenone[1]. The p-fluorophenyl groups were constrained as rigid bodies and the atoms of the acetyl group (i.e. C7, O1, C8) were refined freely but restraints were imposed on the bond length of C1-C7 of 1.494Å and on the (1...3) nonbonded distance between O1 and methyl C8 of 2.381Å. The resulting bond lengths and angles of the acetyl groups of G and G' (Fig.16) indicate that the oxygen and methyl carbon atoms, as originally inserted in the rigid body refinement, are in their correct sites. An R(F) value = 0.064 was obtained.

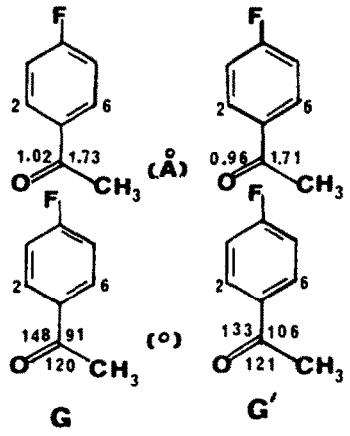


Figure 16
Bond lengths and bond angles of the acetyl groups of fluoroacetophenone G and G' after constrained refinement in which the guest molecules were each refined as two rigid groups, FC_7H_4 and O...C(methyl).

Refinement of the low-temperature (103°K) structure of the Ternary complex DCA-(acetophenone, p-fluoroacetophenone): In accordance with arguments presented on this crystal structure in Results, the determination of the guest molecular arrangement was initiated by inserting the guest molecules G'(H), and G(H) of the binary complex DCA-acetophenone and the guest molecules G'(F) and G(F) of DCA-p-fluoroacetophenone into their corresponding positions in the ternary complex. Thus the starting structure contained three guest sites, two occupied by the completely overlapping molecules G'(H) and G'(F), and the other two by G(H) and G(F) separately. Each of these three molecules was refined as a rigid body with a separate occupancy factor and the same overall thermal parameter. The final cycle of refinement yielded R(F)=0.059 R_w(F)=0.060. The guest occupancies converged to 0.205(4) for the overlapping G'(H) and G'(F) molecules, 0.135(3) for G(H) and 0.075(3) for G(F), with an isotropic U value of 0.057(1) Å^2.

We tested a second model in which the guest structure was composed of close-packed pairs G'(F)G(H), akin to the guest arrangement in DCA-acetophenone which contains the pairs G'(H)G(H). Refinement of this model yielded R(F)=0.067, R_w(F)=0.069, and occupancies of 0.199(5) for G'(F) and 0.197(5) for G(H) and a guest U value of 0.065(2)Å^2. The third model tested comprised sites G'(H) and G(F) as in DCA-p-fluoroacetophenone. Least-squares refinement yielded R(F)=0.066 and R_w(F) 0.071, with occupancies of 0.285(5) for G'(H), 0.124(4) for G(F) and an overall U value of 0.079(2)Å^2. The Hamilton test[7] definitely precludes these two model in comparison with the first.

The refined temperature factors, positions and occupancies of G', G(H) and G(F) of the first model are completely compatible with the deduced guest arrangements in DCA-acetophenone and DCA p-fluoroacetophenone. The total guest occupancy is 0.415(6). The occupancy value 0.205(4) of G' is almost equal to the total occupancy of G=0.135+0.075 = 0.210(4), each being close to 0.2. These results indicate a molar ratio of G'/G equal to 1/1 and a total occupancy of 0.4. The refined occupancies of G(H) and G(F) indicate a higher tendency for site G(H) to be occupied than G(F), in accordance with atom-atom potential energy calculations[1] according to which the potential energy of the site occupied by G(H) is lower than that of G(F).

We ascertained the orientation of the acetyl group of the G' molecule using an approach similar to that adopted for DCA-acetophenone[3] and DCA-p-fluoroacetophenone. The G' molecule was refined as two rigid moieties C_7H_4F and C(8)...O(1) with a fixed interatomic distance between C(8) and O(1). The resulting bond distances C(7)-C(8) of 1.51 Å and C(7)-O(1) of 1.15 Å was in keeping with the positions of the oxygen and methyl carbon atoms of the acetyl group of G' as originally inserted into the structure-factor least-squares analysis. This orientation of the acetyl group of G' is the same as was found in DCA-acetophenone[3] and DCA-fluoroacetophenone.

Crystal Photochemistry of DCA-(Substituted) Propiophenones

DCA-propiophenone: The complex was prepared by crystallization of DCA with excess of propiophenone, from absolute ethanol solution. UV irradiation for thirty days was done under conditions analogous to those described at the beginning of section 4. The separation of the photoproducts was done by chromatography on silica gel eluted with $CH_2Cl_2/C_2H_5OH/AcOH$ in the ratio of 91:7:2.

Photoproduct 4a: rf: 0.48; uv: λ max (EtOH) 240, ϵ (847). ^{13}C nmr (CD_3COOD): 32.5(C1), 29.9 (C2), 69.1 (C3), 38.1 (C4), 50.0 (C5), 28.8 (C6), 28.4 (C7), 37.7 (C8), 36.3 (C9), 41.8 (C10), 29.6 (C11), 75.1 (C12), 46.6 (C13), 49.1 (C14), 24.7 (C15), 28.3 (C16), 47.7 (C17), 13.0 (C18), 20.8 (C19), 36.4 (C20), 17.5 (C21), 31.5 (C22), 31.5 (C23), 181.2 (C24), 127.2 (Ar,p), 127.7 (Ar,m), 128.1, 128.9 (Ar,o), 147.9 [C(Ar)-C(OH)Et], 87.8 [Ar-C(OH)Et], 31.5 [Ar-C(OH)CH_2CH_3], 8.4 [Ar-C(OH)CH_2CH_3], C.D. $\Delta\epsilon_{259, 267} = -0.05$ ($c=5.7\times10^{-3}$M.).

Photoproduct 4b: rf: 0.40; uv: λ max (EtOH) 238 ϵ (417). ^{13}C nmr (CD_3COOD): 32.5 (C1), 28.6 (C2), 69.6 (C3), 33.9 (C4), 51.1 (C5), 30.5 (C6), 28.6 (C7), 38.1 (C8), 36.0 (C9), 41.5 (C10), 29.9 (C11), 75.1 (C12), 46.7 (C13), 49.1 (C14), 24.6 (C15), 28.4 (C16), 47.8 (C17), 12.9 (C18), 20.8 (C19), 36.3 (C20), 17.5 (C21), 31.5 (C22), 31.6 (C23), 181.1 (C24), 130.1 (Ar,P), 128.7, 127.0 (Ar,m), 126.9 (Ar,o), 146.7 [C(Ar)-C(OH)Et], 86.6 [C(Ar)-C(OH)Et], 28.4 [C(Ar)-C(OH)CH_2CH_3], 8.8 [C(Ar)-C(OH)CH_2CH_3]. C.D $\Delta\epsilon_{263, 270} = +0.05$ ($C=6.3\ 10^{-3}$M.).

Photoproduct 4c: rf: 0.24; uv: λ max (EtOH) 245 nm ϵ (395). ^{13}C nmr (CD_3COOD): 36.3 (C1), 29.8 (C2), 72.9 (C3), 44.8 (C4), 45.1 (C5), 31.6 (C6), 27.0 (C7), 37.6 (C8), 34.8 (C9), 36.3 (C10), 29.6 (C11), 74.8 (C12), 47.5 (C13), 49.0 (C14), 24.4 (C15), 28.3 (C16), 47.8 (C17), 13.0 (C18), 24.0 (C19), 36.3 (C20), 17.5 (C21), 32.3 (C22), 32.4 (C23), 181.2 (C24), 128.9 (Ar,P), 127.2(Ar,m), 126.7(Ar,o), 147.9 [C(Ar)-C(OH)Et], 81.7 [C(Ar)-C(OH)Et], 31.6 [C(Ar)-C(OH)CH_2CH_3], 8.5 [C(Ar)-C(OH)CH_2CH_3].

DCA-p-fluoropropiophenone: A 3:1 molecular complex of DCA-p-fluoropropiophenone was precipitated from absolute ethanol solution (mp 164°C). Photoirradiation and product separation were done under analogous conditions to those used for p-fluoroacetophenone and propiophenone. Three products were isolated.

Photoproduct 5a: rf: 0.48 uv: λmax (EtOH) 263, ϵ (715). ^{13}C nmr (CD_3COOD): 32.4 (C1), 29.9 (C2), 68.9 (C3), 38.1 (C4), 50.0 (C5), 28.7 (C6), 28.3 (C7), 37.7 (C8), 36.2 (C9), 41.7 (C10), 29.6 (C11), 75.0 (C12), 46.5 (C13), 49.0 (C14), 24.6 (C15), 28.2 (C16), 47.7 (C17), 12.6 (C18), 20.3 (C19), 36.4 (C20), 17.4 (C21), 31.4 (C22), 31.5 (C23), 181 (C24), 161.2-164.5 C(Ar,P), 129.1-129.8 (Ar,m), 114.6-115.3 (Ar,O), 143.7 [C(Ar)-C(OH)Et], 87.6 [C(Ar) C(OH)Et], 31.6 [C(Ar)C(OH)CH_2 CH_3], 8.4 [C(Ar)C(OH)CH_2CH_3]. C.D. $\Delta\epsilon_{262, 269} = -0.11$ ($C=5.5\ 10^{-3}$M).

Photoproduct 5b: rf: 0.40 uv: λ max(EtOH) 260, ϵ (1073). ^{13}C nmr (CD_3COOD): 32.4 (C1), 28.6 (C2), 69.5 (C3), 34.0 (C4), 51.2 (C5), 30.7 (C6), 28.7 (C7), 38.2 (C8), 36.1 (C9), 41.5 (C10), 29.7 (C11), 75.2 (C12), 46.7 (C13), 49.2 (C14), 24.7 (C15), 28.4 (C16),47.9 (C17), 12.9 (C18), 20.8 (C19), 36.3 (C20), 17.6 (C21), 31.6 (C22), 31.7 (C23), 181.1 (C24), 160.7-164.3(Ar,p), 114.2-115.4(Ar,m),132.2-132.4(Ar,o),142.6[C(Ar)-C(OH)Et], 86.4[C(Ar)C(OH)Et] 28.4 [C(Ar)C(OH) CH_2CH_3], 8.8 [C(ArC(OH)CH_2CH_3] C.D. $\Delta\epsilon_{265, 273} = +0.17$ ($C=5.5\ 10^{-3}$M).

5 β(IR,4"-fluorophenylpropyl) 3α(1'oxy) 12α hydrocholoanic acid (Compound 7):
25 mg of photoproduct 5b left in an nmr test tube with glacial acetic acid, for two weeks was transformed almost quantitatively into compound 7. t.l.c. displays a single product. rf: 0.88. The structure of the compound was assigned by X-ray analysis.

X-ray structure determination of compound 7: The crystal structure of 7 was determined by MULTAN[4]. All the C and O atoms were clearly revealed on an E map. The H atoms belonging to -C-H and CH_2 groups were then attached to this molecule. Least-squares refinement and subsequent electron density difference maps displays yielded the positions of all the methyl and hydroxyl H atoms (Fig.17). The R(F) factor converged to 0.063 (see Table 2).

Photoproduct 5c: rf: 0.24; uv: λ max (EtOH)/235mm ϵ (520). ^{13}C nmr (CD_3COOD): 36.3 (C1), 29.8 (C2), 72,9 (C3), 44.9 (C4), 45.3 (C5), 31.6 (C6), 27.1 (C7), 37.6 (C8), 34.9 (C9), 36.3 (C10),

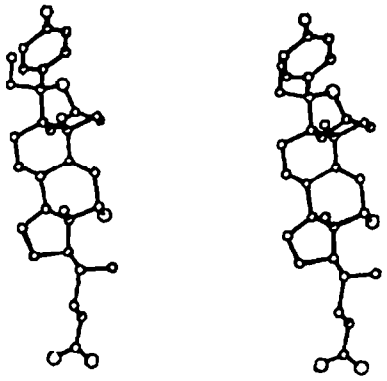


Figure 17
Molecular structure of compound 7, which is a derivative of photoproduct 5b derived from solid state photoreaction between DCA and p-fluoropropiophenone.

DCA-p-chloro-propiophenone: A 3:1 complex was prepared by crystallization of DCA with excess of p-chloropropiophenone from a solution of absolute ethanol, (mp 171°C.). UV irradiation for 30 days and separation of the products by flash chromatography on silica gel with eluent $CH_2Cl_2/C_2H_5OH/AcOH$ in the ratio of 91:7:2 yields one major product 6b and traces of the other diastereomer 6a.

Photoproduct 6b: rf: 0.40 uv: λ max (EtOH) 251mm, ϵ 533. ^{13}C nmr (CD_3COOD) : 32.4 (C1), 28.6 (C2), 69.5 (C3), 33.8 (C4), 51.4 (C5) 30.7 (C6), 28.7 (C7), 38.2 (C8), 36.1 (C9), 41.5 (C10), 29.7 (C11), 75.1 (C12), 46.8 (C13), 49.2 (C14), 24.6 (C15), 28.4 (C16), 47.9 (C17), 12.9 (C18), 20.8 (C19), 36.3 (C20), 17.6 (C21), 31.6 (C22), 31.6 (C23), 180.8 (C24), 132.9(Ar,p), 127.8-128.1(Ar,m), 131.6(Ar,o), 145.7 [C(Ar)-C(OH) Et], 86.5 [C(Ar)C(OH) Et], 28.4 [C(Ar)C(OH) $\underline{CH_2}CH_3$], 8.7 [C(Ar)C(OH)$CH_2.\underline{CH_3}$]. C.D. $\Delta\epsilon_{266,\ 272}$ = +0.3 (c=5.5 10^{-3}M).

Low-temperature (103°K) structures of DCA (p-substituted) propiophenones: The guest arrangements in the three crystal structures of DCA with (p-substituted) propiophenones were analysed in the order given below.

DCA-p-fluoropropiophenone: We first tried to determine the guest arrangement of DCA-propiophenone. The host DCA structure was refined to yield R(F)=0.11. The resulting electron density difference synthesis yielded five strong and distinct peaks within the channel (Fig.18). These peaks are coplanar to within 0.2Å and their heights range from 2.0 to 2.4 e/Å^3. The electron-density distribution exhibits pseudo $2_1/m$ symmetry. This symmetry implies a pseudo centrosymmetric arrangement of the guest molecules, where the pseudo centre of symmetry lies on the crystallographic twofold screw axis. This pseudo symmetry may occur in several ways as depicted in Scheme 5. The channel may contain two independent guest molecules, say G and $\bar{G}$ related by a pseudo centre of symmetry (Scheme 5a). As shown there are two possible ways of generating these pseudo centrosymmetric dimers, namely the molecular pairs $G\alpha$, $\bar{G}\alpha$ and $G\beta$, $\bar{G}\beta$.

A second possibility is provided by a guest molecule of only one orientation with respect to a channel c axis, namely either G or $\bar{G}$, where a molecular pseudo centre of symmetry is induced by conformational disorder of the propionyl groups (either Scheme 5b or 5c) to form disordered pairs ($G\alpha + G\beta$ or $\bar{G}\alpha + \bar{G}\beta$).

This molecular pseudo centre of symmetry, i.e. the centre of the C(phenyl)-C(carbonyl) bond, must tend to coincide with the channel 2_1 axis to produce an electron density distribution of pseudo $2_1/m$ symmetry. Such a constraint is possible since the centre of the C(phenyl)-C(carbonyl) bond of guest G' in DCA-acetophenone (Fig.1) almost coincides with the pseudo centre of symmetry in Fig.18. Moreover, the centre of the acetophenone ring of G' also coincides with the centre of the five peaks forming a ring in Fig.18. Although these considerations indicated starting models for propiophenone guest, the ambiguities in deciding between the different models in Scheme 5 were too numerous.

In order to surmount these ambiguities we decided to use p-fluoropropiopheneone with the expectation that its arrangement in the crystal would be isomorphous to that of propiophenone.

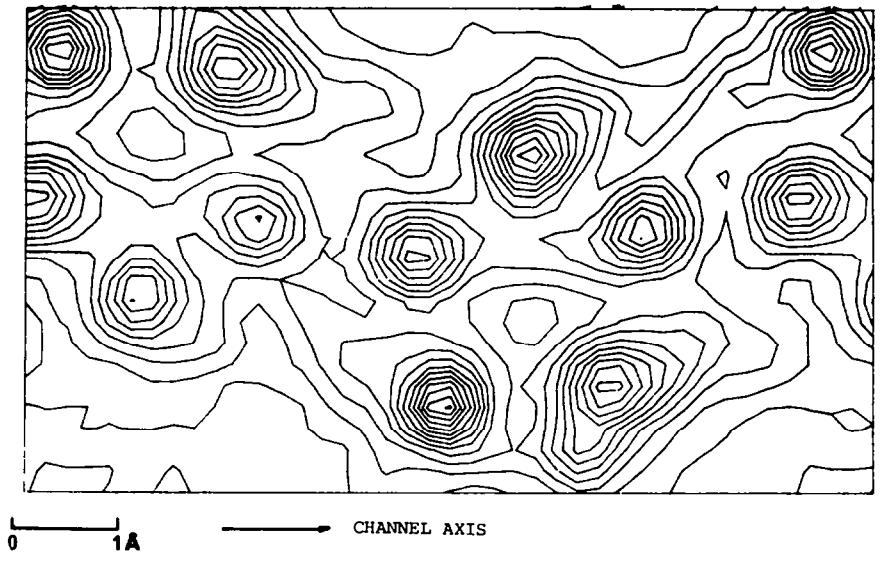
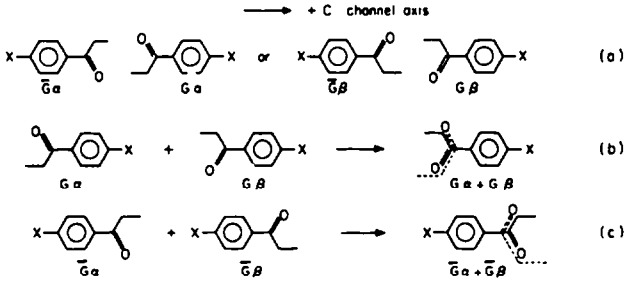


Figure 18: DCA-propiophenone.
Electron-density difference section along the channel, in the best plane of the five and strongest peaks. Contour interval 0.34 e/Å^3.



Scheme 5

This was supported by the observation that the two crystal structures yielded analogous photoproducts (Scheme 4). Thus, X-ray diffraction data were measured from a crystal of DCA-p-fluoropropiophenone at low temperature (103°K). The least-squares refinement of the host structure yielded an R(F) factor =0.11 and an electron difference density map (Fig.19) very similar to that from DCA-propiophenone (Fig.18). The primary difference between these two maps is that one of the peaks in Fig.19 is a distinct doublet.

We concluded that the guest arrangement in the above two crystal structures were sufficiently isomorphous to enable location of the fluorine atom via a $\Delta\rho(xyz)$ synthesis, using as Fourier coefficients the observed structure factors of the two complexes and phases based only on the two host structures. The map contained one outstanding peak which corresponded to a peak of the doublet in Fig.19 and is obviously that of the fluorine atom. A guest molecule was easily fitted to the difference map (Fig.19) using the fluorine atomic position as an anchor point. The molecule, which we label Gα, had a location similar to that of G' in DCA-fluoroacetophenone. We assumed the $COCH_2$ moiety of the propionyl group to adopt the same conformation as that of guest G' in DCA-fluoroacetophenone.

Insertion of this guest Gα with an isotropic temperature factor into least-squares yielded reliability indices R(F) and R_w(F) and a guest occupancy and temperature factor as listed in Table 4a(i). The resulting electron density difference map of this model (i) displayed several strong peaks some as high as 0.9e/Å^3 None of these peaks were located in that position which would have corresponded to a propionyl methyl carbon atom of the alternative conformation corresponding to Gβ. Nevertheless we tested model (ii) by inserting Gβ, instead of Gα for

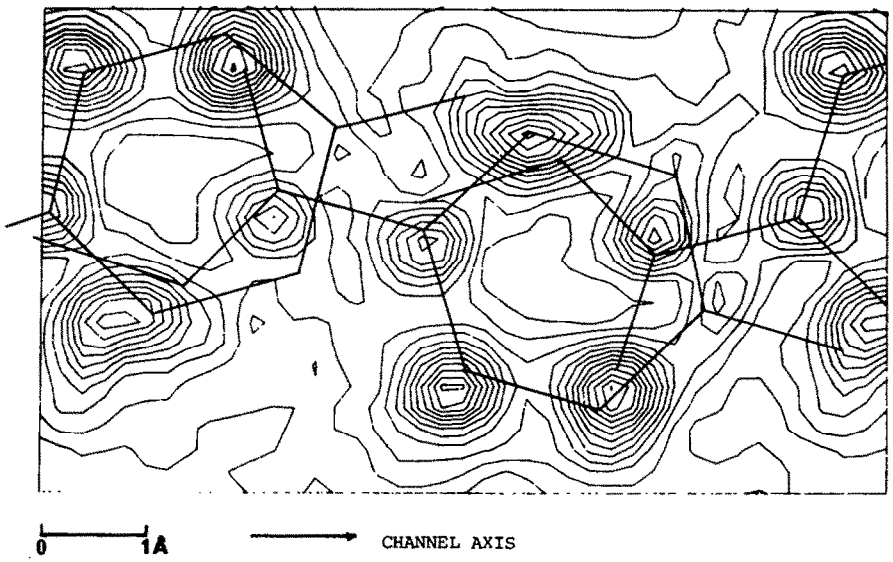


Figure 19: DCA-p-fluoropropiophenone.
Electron-density difference section along the channel in the plane of the five independent and strongest independent peaks. Outline is given of symmetry related positions of dominant molecule Gα . Contour interval 0.34 e/Å^3.

refinement with results given in Table 4a(ii). The strongest peak of 1.9 e/Å^3 in the resulting map was located at the position of the methyl carbon of molecule Gα. We then inserted both Gα and Gβ as in Scheme 5b. They were each given initial occupancies of 0.17. The pertinent results of the refinement of model (iii) are given in Table 4a(iii). The resulting map yielded several peaks in the channel some as high as 0.8e/Å^3 which indicated that the model could not be wholly correct. In this model the refined locations and orientations of Gα and Gβ were distinctly different, in fact their respective fluorine atoms were separated by approximately 0.7Å. This result seemed unlikely since one might have expected that Gα and Gβ would almost coincide but for their methyl groups. At this stage we were certain of the dominant presence of a G molecule, and that Gα was more dominant than Gβ but that the model was still lacking. On re-examination of the electron-density difference map derived from refinement of model (i) in which only Gα was inserted, we found that a molecule $\bar{G}$α, as in Scheme 5a, fitted much better to the peaks than Gβ. Thus we inserted Gα and $\bar{G}$α, as in Scheme 5a. This model (iv) yielded results shown in Table 4a(iv). In order to ascertain the conformation of the propionyl group of $\bar{G}$ we inserted the alternative model (v) containing the other possible conformation of $\bar{G}$, namely $\bar{G}$β. The results of refinement are given in Table 4a(v).

We compare models (iv) with the others using the Hamilton test, the results of which are listed in Table 4a. Model (iv) containing molecules Gα and $\bar{G}$α is clearly preferred over the other four at a significance level >99.5%. The refined isotropic temperature factor $\underline{u}$ of the guest molecules (=0.045Å^2 in Table 4a) is reasonable and compares well with acetophenone[1] or p-fluoroacetophenone in their complexes. The total guest occupancy of 0.327(3) is very close to the maximum value of 1/3 as derived in RESULTS on guest packing.

DCA-propiophenone: We used an analogous procedure to determine the packing arrangement of guest propiophenone molecules. Namely, the five p-fluoropropiophenone model structures, just described, were refined using the F(obs) of DCA-propiophenone. Naturally, the fluorine substituent was replaced by a hydrogen atom. The results of these structure-factor least-squares refinements are given in Table 4b, the models of which follow the same order as those in Table 4a for DCA-p-fluoropropiophenone. According to a Hamilton test, model (iv), containing propiophenone Gα and $\bar{G}$α molecules, is the preferred structure at a significance level >99.5%. The total guest occupancy of model (iv) is 0.362(3). According to packing considerations of the guest molecule presented in RESULTS, the total guest occupancy cannot be greater than 1/3. We therefore continued refinement of this model (iv), but constrained the total guest occupancy to a value of 1/3. The results of this model, labelled (iv'), are given in Table 4b. There is no difference between the $R(F)$ and $R_w(F)$ values of models (iv') and (iv). Moreover, their isotropic guest temperature factors, 0.058 and 0.051Å respectively (see Table 4b), are almost the same. Therefore we may safely assume that the total guest occupancy is 1/3.

DCA-p-Chloropropiophenone: Refinement of the host DCA molecule yielded an electron density difference map which displayed a pattern of five peaks in the channel as shown in Fig. 20. These peaks are coplanar to within 0.25Å. This peak distribution, exhibits pseudo symmetry $2_1/m$, as in the other two propiophenone complexes (Figs.18 and 19). The strongest peak lies on the pseudo mirror plane, which must correspond to a chlorine atom. The pseudo centre of symmetry suggests the motif comprises two independent guest molecules G and $\bar{G}$ related by a pseudo centre of symmetry on the 2_1-axis. Naturally the molar ratio of G to $\bar{G}$ need not be 1/1.

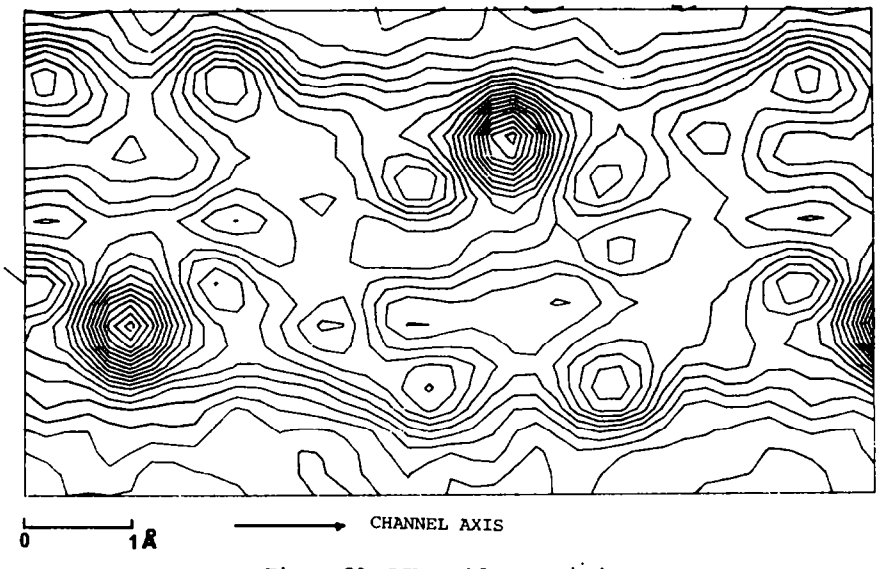


Figure 20: DCA-p-chloropropiophenone.
Electron-density difference section along the channel in the best plane of the strongest peaks. Contour interval 0.21 $e/Å^3$.

We followed a procedure to determine the p-chloropropiophenone guest structure analogous to that of the other two propiophenone complexes, but the guest molecules were refined with six overall anisotropic thermal parameters. The results are listed in Tables 5a and 5b.

It is obvious from the values of the reliability indices $R(F)$, $R_w(F)$ and $R_w(F)^2$ listed in Table 5a that molecule G is more dominant than $\bar{G}$, and that G_α and $\bar{G}_\alpha$ are more dominant than the corresponding G_β and $\bar{G}_\beta$ molecules. Of the seven models (i)-(vii), model (vi), containing G_α and $\bar{G}_\alpha$ as in the other two propiophenone complexes, is preferred in terms of the reliability indices and the Hamilton test values. But the "thermal motion" of guests G_α and $\bar{G}_\alpha$ of model (vi) is too high according to the anisotropic temperature factors U_{ij} of the guest atoms (Table 5b); in fact the U_{ij} values of all seven models (i)-(vii) are too high.

Packing considerations exclude the first five models (i)-(v) since a string of G, or $\bar{G}$, molecules that occupy every third consecutive site along a channel via twofold screw symmetry (as depicted in Fig.10b or 11b) would be precluded by intermolecular contacts; the C(methyl)...Cl distance would be too short at 2.9Å. Moreover, the guest occupancy for such models would be 1/3 which does not match the observed values (Table 5a). An alternative arrangement in which every fourth consecutive site is occupied by translation of 2c is unreasonable for it is too loose with a maximum occupancy of 0.25. This leaves us with models (vi) and (vii). We first focus on model (vi), preferred in terms of the Hamilton test.

A packing arrangement containing molecular dimers G_α and $\bar{G}_\alpha$ of model (vi) as in Fig.10a or 11a, is forbidden because the distance between the Cl atoms of G and $\bar{G}$ is too short at 2.6Å, even though the distance between the methyl C atoms of neighbouring G and $\bar{G}$ molecules is reasonable at 4.0Å. The ratio of the occupancies of $G_\alpha/\bar{G}_\alpha$ for model (vi), =0.21$/0.09$, is 2.2(1) which is sufficiently close to the integer 2 that we may assume a third arrangement of guest molecules similar to that depicted in Fig.10c for propiophenone, namely, a string of triplets G(x,y,z) $\bar{G}$(x,y,z) G(x,y,-3+z) as shown in Fig.21a. But this arrangement still embodies the deficiencies of too short Cl...Cl and Cl...C(methyl) distances and a total occupancy of 1/3 compared to the least-squares value of 0.300(4) as listed in Table 5. We may correct some drawbacks of this arrangement by assuming the motif shown in Fig.21b which incorporates the repeat triplet G(x,y,z) $\bar{G}$(x,y,z) G(1/2-x,y,-7/2+z). This arrangement has the advantage of an occupancy of 0.3 which fits the least-squares value of 0.300 and, also does not incorporate the short Cl...Cl distance between $\bar{G}$(x,y,z) and G(x,y,-3+z). But there still remains the 2.9Å separation between the Cl and C(methyl) atoms of neighbouring G molecules. This short contact may be avoided by taking advantage of the 6Å separation between the Cl atoms of molecules $\bar{G}$ (x,y,z) and G (1/2-x, -y, -7/2 +z) in the motif of Fig.21b. If the latter molecule is brought closer to the former by about 0.6Å, its methyl C atoms will make a reasonable contact of 2.9 + 0.6Å with the Cl atom of G(x,y, -5 +z). Naturally these two G molecules of the triplet would no longer be related by crystallographic symmetry. We label the molecule originally at G(1/2 -x, -y, -7/2 +z) as G'(x,y,z). This modified arrangement of model (vi) also accounts for the high thermal motion along the c axis of the guests of model (vi) (U_{33} = 0.199$Å^2$, Table 5b). The individual occupancies of G, G' and $\bar{G}$ would each equal 0.1. The packing arrangement of such a model is shown in Fig.14. This model was not compared with the original model (vi) via structure-factor least-squares refinement, the measured X-ray diffraction data hardly warrant it. At this stage we may reject the remaining model (vii) for the following reasons although its guest molecules G and $\bar{G}$ can easily fit into the arrangement shown in Fig.14. Most important the ratio of occupancies of $G_\alpha/\bar{G}_\beta$ for this model = 0.240/0.046 = 5.2 does not fit the required value of 2 and so it is not possible to generate a feasible packing arrangement. Also the Hamilton test (Table 5a) disfavours this model as against (vi).

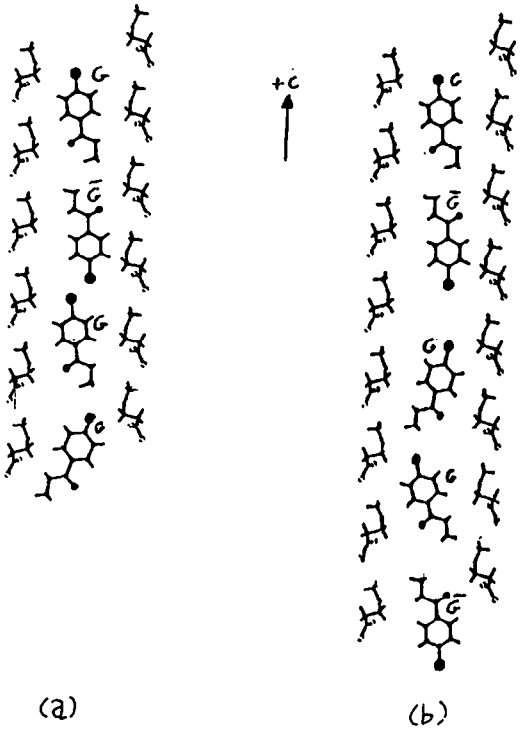


Figure 21
DCA-p-chloropropiophenone.
(a) A packing arrangement of guest molecules in the channel. The intermolecular Cl...Cl distance is 2.6Å and the Cl...C(methyl distance is 2.9Å.
(b) Modification of arrangement (a) in which a spacer of c/2Å (by virture of two-fold screw symmetry) is inserted between molecules $\bar{G}$ and G so that the short Cl...Cl distance is avoided.

Results of refinement: Details on refinement of the crystal structures of the complexes of DCA-p-fluoroacetophenone, DCA-(acetophenone, p-fluoroacetophenone), DCA-propiophenone, DCA-p-fluoropropiophenone, DCA-p-chloropropiophenone, the photoproduct 3 and compound 7 are given in Table 3. Atomic coordinates and equivalent thermal parameters of the crystal structures of DCA-p-fluoroacetophenone, DCA-propiophenone, DCA-p-fluoropropiophenone, DCA-p-chloropropiophenone are listed in Tables 6-9. The atomic coordinates of DCA-(acetophenone, p-fluoroacetophenone), photoproduct 3 and compound 7 are listed in supplementary material, together with the anisotropic temperature factors, bond lengths and bond angles of the other crystal structures (Tables 1s-7s).

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