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# REACTIONS IN THE SOLID STATE. III.* STRUCTURAL ASPECTS OF PHOTOCHEMICAL REACTIONS IN CRYSTALLINE INCLUSION COMPOUNDS.

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**Abstract.** - Stereoselective photochemical dimerization to products adopting the syn head-to-tail configuration is obtained by irradiation of crystalline inclusion compounds. The structural aspects of these reactions regarding the relations between the arrangement of the host molecules in the crystalline lattice forming the matrix and the packing of the potentially reactive molecules included in the matrix are discussed.

The possibilities of using non-symmetrical host molecules as a probe for stereoselective and enantioselective intramolecular photochemical reactions are also discussed.

* Part II: J. Org. Chem. 1985, 50, 2154.

## Introduction:

In the last four decades much effort has been directed toward studying and understanding the photochemical and photophysical behaviour of potentially reactive centres in the solid state. This long term of research was rewarding in respect to the understanding of the structural aspects involved and the control of photochemical reactions within the crystalline lattice.[1] The limiting conditions for such reactions were set up in terms of distances and relative orientations between the potentially reacting centres.

G.M. Schmidt, in an excellent review[1a], proposed four concurrent and connected phases in the recent history of research on solid-state photochemistry: "(a) the phase of topochemical principle. (b) The phase of the locus of solid-state reactions. (c) The phase of crystal engineering. (d) The phase of systematic solid-state photochemistry".
The first two phases are believed to be fully understood, and the research done so far provides a basis for the knowledge of when and why a photochemical reaction will occur in the crystal lattice. Phase (c) is the key to phase (d). As long as the chemist will not be able to control the packing of the potentially reactive molecules in the crystal lattice, the goal of systematic solid-state photochemistry will not be reached. Although highly stereoselective and enantioselective reactions have been successfully accomplished in crystals of the neat reactive compounds[1], it was not recognized as a general synthetic method. Most of the unique photoproducts obtained by photochemical reactions in the solid state, although sometimes very important, were much more the result of "shooting in the dark" rather than a planned synthesis. To our disappointment phase (c) is still the weakest point in this promising chain of phases.

**The scope of limitations:**

In order that photochemical reactions in the solid-state will be recognized as a general synthetic method it should meet some criteria which will have advantages over the classical photochemical or other synthetic methods in the gasous phase or in solutions: (a) it should be an easy reaction to handle. (b) The reaction should be clean e.g. leading to one main product with no side reaction. (c) The yield should be high. (d) The photoproduct should be uniquely and easily planned. In general, chemical reactions in the solid-state are limited and we will briefly discuss these limitations.

The basic assumption is that any reaction in the solid state occurs with a minimum amount of atomic or molecular movements. The amount of movement is dependent upon the surrounding or the packing in the crystal lattice. From that respect there is a difference between intra- and inter-molecular photochemical reactions. In intra-molecular photochemical reactions involving rigid molecules where the conformation of the reactants are similar in both solutions or in the crystal, the same products are expected, unless the reaction involves large configurational changes which are prevented by external restraints imposed, for example, by rigid surroundings in the crystal lattice. Such external restraints to motion are pronounced when non-rigid molecules should undergo large conformational change prior to the photochemical reaction. In inter-molecular photochemical reactions, such as dimerization, oligomerization and polymerization, the relative orientation between molecules and the distances between the reacting centres are important. The topochemical rules state[1a] that the stereochemistry of the product is determined by the contact geometry (parallel or antiparallel) of nearest-neighbour double bonds, provided that the centre-to-centre distance is of the order of 4 Å. In all types of photochemical reactions in the solid-state the reactivity is highly dependent upon the packing of the reactant molecules in the crystal lattice (these reactions which occur at dislocations cannot be used for planned syntheses).

The major problem is therefore crystal engineering which is yet beyond our control. One way to bypass this problem is to design crystalline molecular inclusion host-guest compounds where the packing of the host molecules within the crystal lattice will enable the potentially reactive guest molecules to pack in much looser way to undergo photochemical reactions. An imporant advantage of this method is that an additional parameter, namely the choice of various host molecules, is on hand when planning such reactions. Known examples and some new results concerning this relatively new approach are discussed below.

**Discussion:**

Much effort has been directed toward searching for selective chemical transformation in micelles[2], liquid crystals[3], crown ethers[4a], cryptates[4b], cyclodextrins[5], and monolayers[6]. In these attempts the idea is to use organized media in which the reactants will be constrained and therefore the number of possible products will be minimized.
A classical example of this approach is the solid-state photochemistry of guest aliphatic ketones inside the channels of host deoxycholic and apocholic acid[7a,b] where the photochemical reaction occurs between the host and the guest molecules.

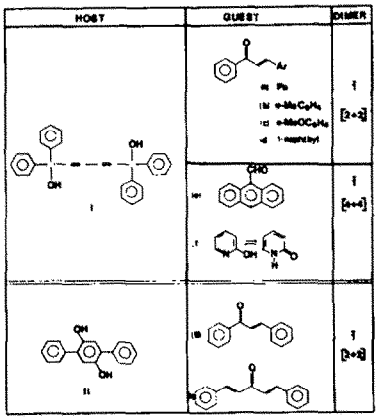
This paper is concerned with a different approach. It is concentrated on the structural aspects of various photochemical reactions of reactant guest molecules introduced within a matrix formed by the host molecules where the host provides "hanging" sites through hydrogen bonding for organization of the guest molecules. Two classes of host compounds have been tested: (I) 1,1,6,6,-tetraphenyl-hexa-2,4-diyne- 1,6-diol and (II) 2,5-diphenylhydroquinone. (See Table 1).

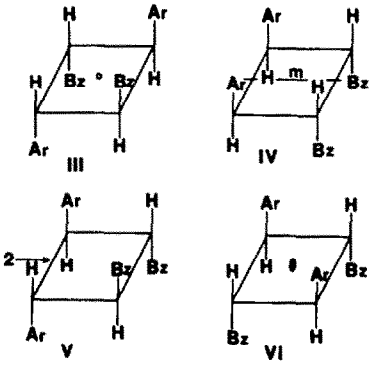
Two types of photochemical reactions will be discussed: (A) intermolecular [2+2] and [4+4] photocyclodimerization and (B) intramolecular photocyclization.

**(A) Intermolecular photochemical reactions.**

Details of the various inclusion compounds prepared[8] with I and II are given in Table 1.

Table 1. Summary of experimental results showing the host, guest and the symmetry of the dimeric product.




Other inclusion compounds of I with derivatives of chalcone such as o-$ClC_6H_4$, 2-Furyl and 2-Thienyl were found to be light-stable for reasons yet unknown. All other compounds (eight in total) yielded the same **syn** head-to-tail dimeric isomer (having a molecular inversion centre). Four typical examples of the inclusion compounds (I:2a; II:2h; I:2f; I:2e) which lead to either [2+2] or [4+4] photocyclodimerization were used for X-ray crystal structure analysis[9] aiming to find the correlation between the packing arrangement and the photochemical reactivity.

In principle one (or more) of four possible isomers may be obtained in both [2+2] or [4+4] photocyclodimerizations (shown schematically for chalcone derivatives III - VI).

Different behaviour can be observed depending upon the experimental conditions. **Trans**-chalcone (a) isomerizes to its **cis** isomer or polymerizes[10] when its solution is irradiated, while irradiation of the crystals of the neat compound gives a complex mixture of stereoisomers in low yields.[11] Dibenzylideneacetone (h) dimerizes to the all-**trans**-substituted cyclobutane[12] (a two fold axis running in the cyclobutane ring, V) when its solution is irradiated, while the crystals of the neat compound are light-stable. However, irradiation of the crystalline inclusion compounds of I:2a and II:2h reveal exclusively the same **syn** head-to-tail isomer (III). On the other hand 2-pyridone[13] (f), (irradiated in solution or in the inclusion compound) and 9-anthraldehyde[14] (e) (irradiated as its neat crystalline compound and as its inclusion compound) gave the **syn** head-to-tail isomer (III).

The packing arrangements in all four inclusion compounds are similar. The compounds crystallize in a centrosymmetric triclinic unit cell. Both I and II host molecules occupy a crystallographic centre of inversion. Moreover, the guest molecules which are hydrogen bonded to the host's hydroxyl groups are related by a crystallographic centre of inversion. Stereoscopic drawings of the arrangement perpendicular to the plane of the reacting centres as well as drawings including the important geometrical parameters for the four inclusion compounds are shown in Figures 1-8 for I:2a, II:2h, I:2f and I:2e respectively.

In all four cases the distances between the potentially reactive centres ranges between 3.787 to 4.042 Å, which are in the range of the limit proposed[1a] (4.2Å). One of the advantages of using the host molecules I or II is the flexible packing they provide depending upon the size of the guest molecules. This effect is easily seen in Figures 1,3,5 and 7. When the size of the guest molecule is of the order of the size of the host molecule (e.g. chalcone and I or dibenzylidene acetone and II) the host molecules accommodate themselves to form a channel with a parallelogramic cross section, where the guest molecules are enclosed and held by hydrogen bonds in anti-parallel fashion (see Figures 1,3).

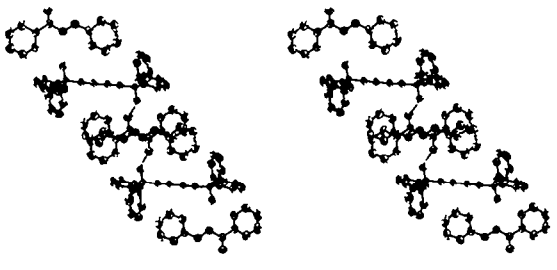


Fig. 1: Stereoscopic drawing of the packing arrangement in I:2a down the plane of the reacting centres (marked by filled ellipsoids).

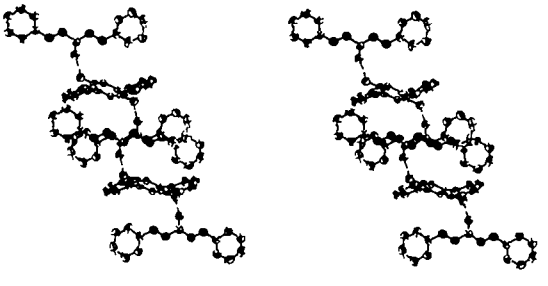


Fig. 3: Stereoscopic drawing of the packing arrangement in II:2h down the plane of the reacting centres (marked by filled ellipsoids).

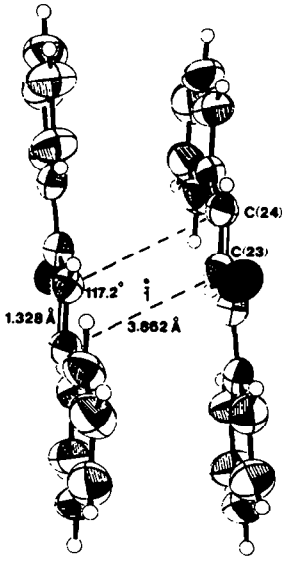



Fig. 2: Relevant geometric parameters involving the reacting centres in I:2a.

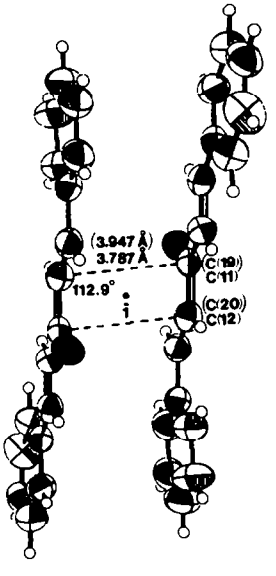



Fig. 4: Relevant geometric parameters involving the reacting centres in II:2h.

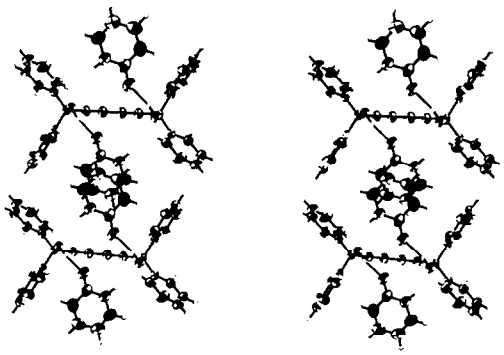


Fig. 5: Stereoscopic drawing of the packing arrangement in I:2f down the plane of the reacting centres (marked by filled ellipsoids).

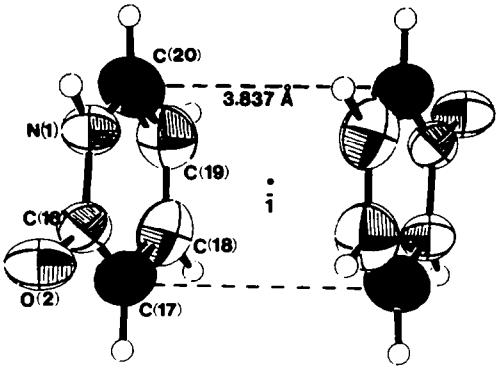



Fig. 6: Relevant geometric parameters involving the reacting centres in I:2f

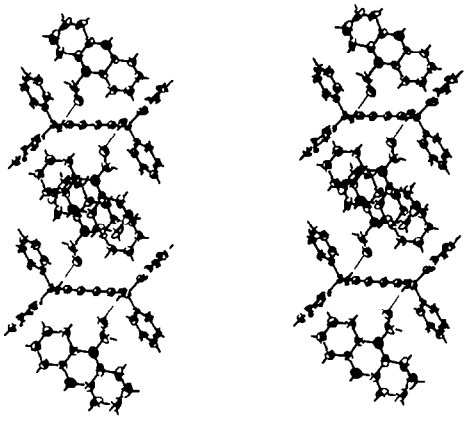


Fig. 7: Stereoscopic drawing of the packing arrangement in I:2e down the plane of the reacting centres (marked by filled ellipsoids).

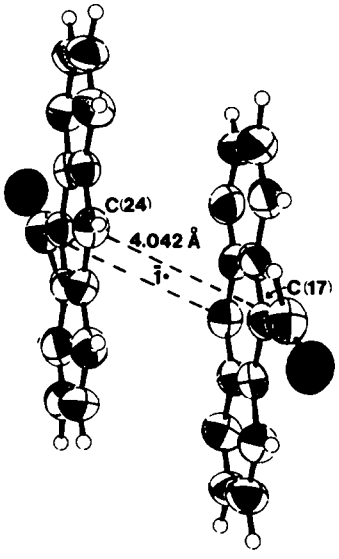



Fig. 8: Relevant geometric parameters involving the reacting centres in I:2e.

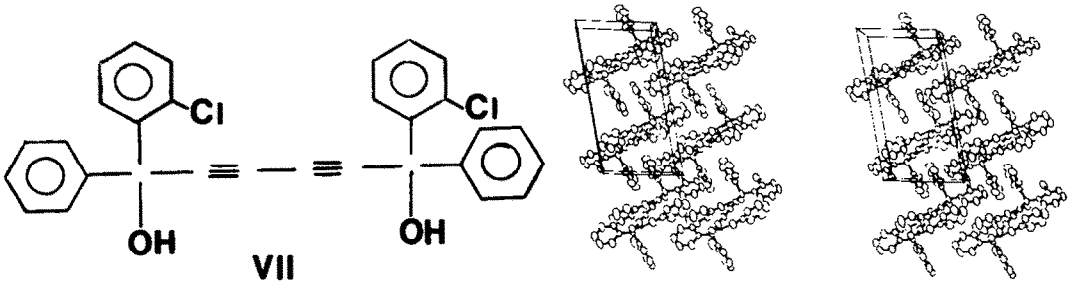
When the size of the guest molecule is smaller than the host (e.g. 2-pyridone and 9-anthraldehyde with I) the latter forms a channel with a hexagonal cross section enclosing the guest molecules in an anti-parallel fashion (see Figures 5,7).

There are strong indications that the ability of the host molecule to preserve its inversion centre in the crystal lattice control the overall packing arrangement. Thus the guest molecules are related by an inversion centre in the crystal lattice.

Although the host molecules I and II have several rotational degrees of freedom (around single bonds), the molecules occupy a crystallographic centre of inversion in the lattice. It seems that this specific structure is stabilized by packing forces. We therefore may expect that the same mutual orientations between the reacting centres found in the examples studied will also be observed with other reactant molecules leading to the same isomeric products.

We therefore assume that destruction of the chemically inversion centre in these host molecules might lead to a different packing arrangement, and perhaps to isomers of different symmetries. An attempt to study this assumption was made by using an optically active

halo-derivative of I (see VII), which was used for optical resolution of 3-methylcycloalkanones and 5-methyl-γ-butyrolactones by complexation,[15] as the host, and 2-pyridone (f) as the guest. Unfortunately the inclusion compound was found to be light-stable, but its crystal structure was elucidated in order to find the effects on the packing. Comparison of the crystal structure of I:2f and VII:2f shows that the substitution by chlorine atoms resulted a conformational change of the 1:2 host: guest unit (for comparison see stereoscopic drawings given as Figures 5 and 9).



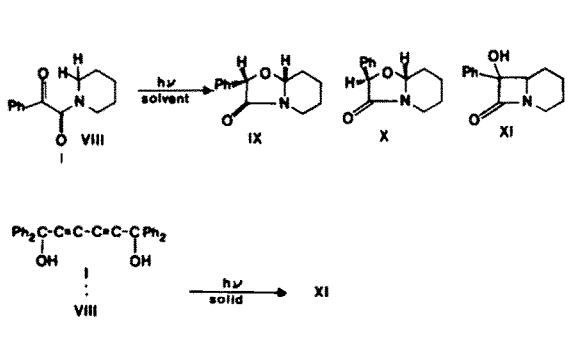

VII

Fig. 9: Stereoscopic drawing of the packing arrangement in VII:2f.

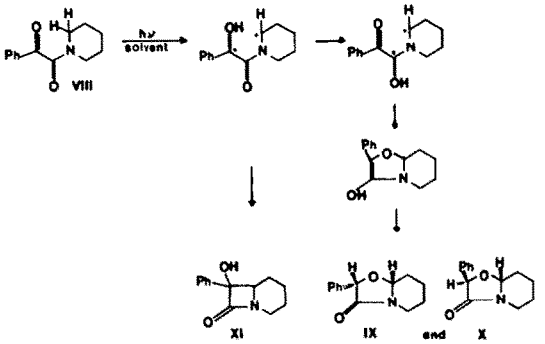
There are some differences between the rotation angles of the various phenyl rings relative to the mean plane of the diyne-diol fragment, probably dictated by the Cl substituent, but the main difference is seen in the angle between the mean plane of the 2-pyridone moiety and the diyne-diol fragment; this angle is 81.0° in I:2f an 31.6, 32.9° in VII:2f. This variation in the arrangement causes the two reactant molecules to be too far from each other and therefore to be light-stable.

(B) **Intramolecular photochemical reactions.**

An interesting example of intramolecular photochemical reaction was found when a crystal of the inclusion compound of (I) and the ketoamide (i) also marked as (VIII) (see Scheme 1) was irradiated. The reaction yields the β-lactam derivative (XI) while irradiation of a solution or the solid of the ketoamide[16] yields three products as shown in Scheme 1.




Scheme 1




Scheme 2

The inclusion compound is exceptional in the sense that only one of the available hydrogen bonding sites is used for bonding with the guest molecule. Although the crystal structure of the inclusion compound shows that the ketoamide is disordered, (having two available conformations) the conformation of the major conformer is almost identical (there are no significant differences) to the conformation of that molecule as found from the crystal structure of the neat ketoamide (see comparison in Figure 10).

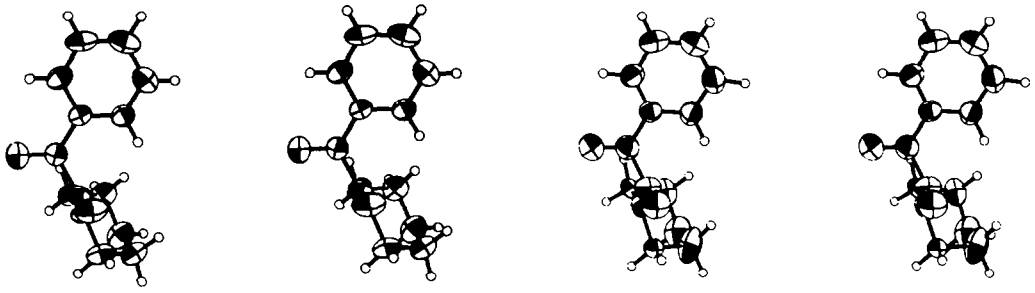



Fig. 10: Molecular structure of the ketoamide (i) (a) in the crystal of the neat compound (b) in the inclusion compound (the molecule with the major occupation).

The differences in the behaviour of the reactant molecule under irradiation may be explained by the mechanism of the reaction,[17] which is given in Scheme 2. The β-lactam derivative (XI) is obtained via a γ-hydrogen abstraction by the excited carbonyl oxygen atom thus forming a biradical followed by a cyclization. This course of reaction is determined by the conformation of the molecule, and is possible both in the crystals of the neat reactant and in the inclusion compound. The mechanism of the reaction which yields the two isomers of the oxazolidine-4-one derivative suggest that it proceeds from the initial stage, discussed above, by a 1,4-hydrogen shift to the second available carbonyl oxygen atom. While this step is possible in the free reactant molecule, it is not possible in the inclusion compound because this carbonyl oxygen is occupied in a hydrogen bond with the host (see Figure 11). While this inclusion compound crystallizes in a non-chiral space group ($P\bar{1}$), both enantiomeric products are available. Following the same idea discussed above, it seems reasonable to believe that enantioselective photochemical reaction will occur if we use an optically active host compound.

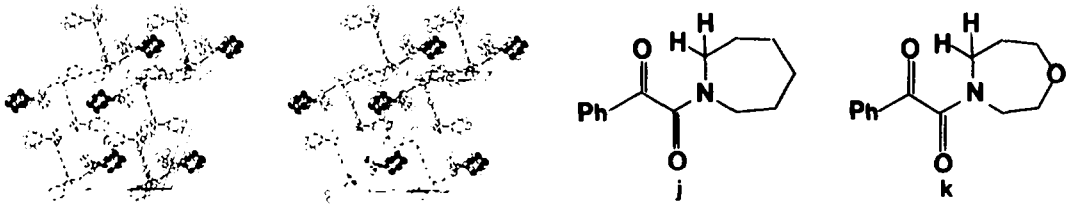



Figure 11: Stereoscopic drawing of the unit cell of I:i.

Two inclusion compounds were prepared VII:2J and VII:k. Preliminary results[18] show that irradiation of the crystalline inclusion compound of (+)-VII:2J gives optically active β-lactam derivative {$[\alpha]_D$-10°} in 67% yield, and irradiation of (+)-VII:k gives optically active β-lactam in a good yield.

Unfortunately we have only preliminary crystallographic data which show that both inclusion compounds crystallize in a chiral triclinic space group P1. This indicates that only one chiral conformation is adopted by the reactant guest molecule which leads to enantioselective photochemical product.

**Conclusions:**

The modified approach to stereoselective solid state photochemical reaction discussed above is at the initial stages. However the advantages of having the ability to design various host compounds which will have various potential arrangements that will control the packing of reactive guest molecules is obvious. The use of enantiomeric host molecules has the advantage of including guest molecules of one handedness, thus enabling enantioselective synthesis by intramoleculear photochemical reactions. This method provides a new tool for syntheses.

**Acknowledgement:**

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**Experimental Section:**

**Preparation of the compounds and photochemistry.**

Procedures for the preparation of the various inclusion compounds are given in Reference 8a,b. In general, diethyl ether solutions of I and 2 mol. equiv. of the various guest molecules were allowed to stand for 3 h at room temperature. The various inclusion compounds were formed as colourless prisms in almost quantitative yield. Irradiation of powdered compounds by a high-pressure mercury lamp at room temperature for 1 to 6 h gave the photoaddition products in good yields (bove 70%).

**Crystallographic details.**

The crystallographic details for the inclusion compounds I:2a and II:2h are given in reference 9. The crystallographic details for I:2f, VII:2f, I:VIII, and VIII are given below.

(I:2f) $C_{30}H_{22}O_2$:2x$C_5H_5NO$, triclinic, space group $P\bar{1}$, a=13.453(7), b=8.084(4), c=7.790(4) Å, $\alpha$=99.03(3), $\beta$=75.63(3), $\gamma$=94.93(3)°. The calculated density is 1.240 g/cm$^3$ for Z=1. R=0.053, Rw=0.0669 for 2171 observed reflections [$F_o>1.5\sigma(F_o)$].

(I:2e) $C_{30}H_{22}O_2$:2x$C_{15}H_{10}O$, triclinic space group $P\bar{1}$, a=12.315(6), b=12.45°(6), c=8.136(4) Å, $\alpha$=102.46(3), $\beta$=94.90(3), $\gamma$=114.14(3)°. The calculated density is 1.271 g/cm$^3$ for z=1. R=0.071, Rw=0.076 for 2275 observed reflections [($F_o>1.5\sigma(F_o)$].

(VI:2f) $C_{30}H_{20}O_2Cl_2$:2x$C_5H_5NO$, monoclinic space group $P2_1$, a=17.101(9), b=11.942(6), c=8.736(4) Å, $\beta$=101.50(2)°. The calculated density is 1.280 g/cm$^3$ for z=2. R=0.765, Rw=0.060 for 2126 observed reflections [$F_o>1.5\sigma(F_o)$].

(I:i) $C_{30}H_{22}O_2$:$C_{13}H_{15}NO_2$, triclinic space group $P\bar{1}$, a=18.193(9), b=11.990(6), c=8.351(4) Å, α=93.72(3), β=97.23(3), γ=71.63(3)°. The calculated density is 1.224 g/cm$^3$ for Z=2. R=0.062, $R_w$=0.065 for 2430 observed reflections [$F_o$.1.5σ($F_o$)].

(i) $C_{13}H^{15}NO_2$, monoclinic space group $P2_1/c$. a=9.584(5), b=11.402(6), c=10.988(5) Å, β=103.08(2)°. The calculated density is 1.234 g/cm$^3$ for Z=4; R=0.080, Rw=0.077 for 1914 observed reflections [$F_o$>0].

Intensity data were collected on a computer controlled Philips PW1100 diffractometer using the ω-2θ scanning technique with graphite-monochromated MoKα radiation (λ=0.7106 Å). The structures were solved either by Multan 80[19], or by SHELX[20], and refined by SHELX[20] using anisotropic atomic displacement parameters for non-hydrogen atoms, isotropic for H.

Tables of structure factors, atomic coordinates, bond distances and angles are deposited.

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