

TOPOCHEMICAL SOLID STATE PHOTODIMERIZATION OF NON-IDEALLY ORIENTED MONOMERS: 7-CHLOROCOUMARIN AND 7-METHOXYCOUMARIN

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Summary

Photodimerizations of 7-chlorocoumarin and 7-methoxycoumarin in the solid state were studied; *syn* head-to-head and *syn* head-to-tail dimers are the respective products of irradiation in the solid state. X-ray crystal structure analyses of 7-chlorocoumarin and 7-methoxycoumarin reveal unusual features. 7-Chlorocoumarin is arranged in a β -type packing, the centre-to-centre distance between the reactive double bonds being 4.454 Å, which lies outside the limit accepted at present of 3.5 - 4.2 Å. In contrast, the reactive double bonds of 7-methoxycoumarin are rotated by about 65° with respect to each other with the centre-to-centre distance between the double bonds being 3.83 Å. In spite of these unfavourable arrangements photodimerization of these two coumarins in the solid state occurs through a topochemical process with large dimer yields.

1. Introduction

The reactions of cinnamic acids are examples of [2 + 2] photodimerization, a reaction which has been studied in a large number of crystalline compounds that belong to a variety of families. On the basis of crystallographic data for a wide range of derivatives of *trans*-cinnamic acids, it has become clear that unless potentially reactive groups are separated by less than about 4.2 Å no photodimerization will occur in the solid state [1]. Further, Schmidt has drawn attention to the fact that the reactive double bonds must be aligned parallel and must be coplanar for dimerization to occur. He pointed out the example of methyl-*m*-bromo *trans*-cinnamate which shows no dimerization even after prolonged irradiation although the double bonds are separated by only 3.93 Å. In this monomeric crystal, however, the ethylenic bonds are non-parallel (the double bonds are related by a glide plane) [2]. Further, the precise value of the critical distance for photodimerization in the solid state has not been unequivocally established; the limit of 4.2 Å is set by the absence of experimental data in the range from 4.2 to

4.7 Å, above which photodimerization does not occur [3]. Recently, a few examples have been reported which are exceptions to the traditionally accepted criteria regarding the alignment of the reactive double bonds [4 - 6]. In these cases the reactive double bonds are rotated with respect to one another by about 60°. We present here our observations on the crystal structures and solid state photochemical behaviour of 7-chlorocoumarin and 7-methoxycoumarin. Surprisingly, these do not follow the conventional topochemical distance and alignment criteria for photodimerization in the solid state.

2. Experimental section

7-Chlorocoumarin (melting point, 129 °C) and 7-methoxycoumarin (melting point, 119 °C) were prepared by methods reported in the literature [7] and were recrystallized from ethanol. Powdered samples of these coumarins were exposed to UV radiation from a medium pressure mercury lamp (450 W). During the irradiation the temperature of the sample did not rise above 40 °C. Photodimerization was monitored by ¹H nuclear magnetic resonance (NMR) and thin layer chromatography (TLC). Irradiation was continued until no further reaction occurred. The product dimer was separated in each case by preparative TLC (silica gel-(benzene-chloroform)) and each was identified by its spectral properties. In the case of 7-methoxycoumarin, the structure of the dimer was confirmed by X-ray crystallography. The spectral properties of the two dimers obtained are listed in Tables 1 and 2.

2.1. X-ray crystal structure analyses of 7-chlorocoumarin, 7-methoxycoumarin and the *syn* head-to-tail dimer of 7-methoxycoumarin

Single crystals of 7-chlorocoumarin and 7-methoxycoumarin were obtained from ethanol and benzene respectively by slow evaporation. Single crystals of the dimer of 7-methoxycoumarin were obtained from chloroform-dimethyl sulphoxide by slow evaporation. The intensity data were

TABLE 1

Syn head-to-tail dimer of 7-methoxycoumarin (melting point, 207 - 209 °C)

IR (Nujol)	1750 cm ⁻¹ (carbonyl)
¹ H NMR (CDCl ₃ -DMSO-d ₆) ^a	δ = 3.71 ppm (6 H; s); δ = 4.15 - 4.19 ppm (2 H; m); δ = 4.23 - 4.27 ppm (2 H; m); δ = 6.20 ppm (2 H; d; J = 2.4 Hz); δ = 6.67 ppm (2 H; dd; J = 2.4 Hz, J = 8.4 Hz); δ = 7.04 ppm (2 H; d; J = 8.4 Hz)
Mass spectrometry (70 eV)	m/e = 352 (M ⁺)

s, singlet; m, multiplet; d, doublet; dd, doublet of doublets.

^aDMSO, dimethyl sulphoxide.

TABLE 2

Syn head-to-head dimer of 7-chlorocoumarin (melting point, 235 - 236 °C)

IR (Nujol)	1765 cm ⁻¹ (carbonyl)
¹ H NMR (CDCl ₃ -DMSO-d ₆)	δ = 4.08 - 4.11 ppm (2 H; m); δ = 4.16 - 4.23 ppm (2 H; m); δ = 6.76 ppm (2 H; d; J = 8.1 Hz); δ = 6.92 ppm (2 H; d; J = 1.9 Hz); δ = 6.98 ppm (2 H; dd; J = 8.1 Hz, J = 1.9 Hz)
Mass spectrometry (chemical ionization; NH ₃)	m/e = 378 (M + NH ₄ ⁺); m/e = 361 (M + 1)

m, multiplet; d, doublet; dd, doublet of doublets.

collected using an Enraf-Nonius CAD-4 diffractometer. The structures of 7-chlorocoumarin and 7-methoxycoumarin were solved by direct methods using the program MULTAN-80 [8], whereas that of the dimer of 7-methoxycoumarin was determined using the program MULTAN-78 [9]. A full matrix least-squares program SHELX 76 [10] was used for refinement. The structural details and measurement conditions are given in Table 3.

3. Results and discussion

Of the coumarins studied so far by us [11, 12] the most unusual is 7-methoxycoumarin. The dimer yield was about 90% within 24 h of irradiation of the crystalline 7-methoxycoumarin as monitored by NMR integration. The structure of the dimer as established by X-ray crystallography corresponded to the *syn* head-to-tail configuration [12]. Most unexpectedly, X-ray crystal analyses of the monomer revealed that the potentially reactive double bonds of the monomer molecules within the asymmetric unit are rotated by 65° with respect to each other, the centre-to-centre distance between the double bonds being 3.83 Å (Fig. 1). A very similar observation has been made in the recently reported structure of 2,5-dibenzylidenecyclopentanone [5]. Since the double bonds are not topochemically pre-oriented for the formation of a single dimer, two dimers, namely the *anti* head-to-head and the *syn* head-to-tail, could result if rotation of the molecules is allowed in the crystal lattice. Formation of the *anti* head-to-head dimer would require a total rotation of 115° whereas the *syn* head-to-tail dimer would require 65°.

To explain the dimer formation, initiation of the reaction at a dislocation site in the crystal was originally proposed [12]. Attempts to verify this hypothesis through electron microscopy studies were beset with difficulties owing to failure in preparing good samples. However, evidence from other considerations, albeit indirect, is not in support of our original proposal. It was observed from the progress of the dimerization with respect to the time of irradiation that there was no perceptible evidence for an induction period,

TABLE 3
Crystallographic data and details of measurements

	7-Chlorocoumarin	7-Methoxycoumarin	Syn head-to-tail dimer of 7-methoxycoumarin
Temperature (K)	293	293	293
Crystal dimensions (mm × mm × mm)	0.6 × 0.4 × 0.1	0.5 × 0.4 × 0.2	0.4 × 0.3 × 0.3
Cell dimensions			
<i>a</i> (Å)	4.454(1)	6.834(3)	14.767(3)
<i>b</i> (Å)	30.488(7)	10.672(4)	12.068(5)
<i>c</i> (Å)	5.684(2)	12.600(7)	18.798(2)
α (deg)	90	108.19(3)	90
β (deg)	91.21(2)	95.23(4)	90
γ (deg)	90	95.22(3)	90
<i>V</i> (Å ³)	771.6	848.7	3350.0
<i>Z</i>	4	4	8
Space group	<i>P</i> 2 ₁ / <i>n</i>	<i>P</i> $\bar{1}$	<i>Pbcn</i>
Molecular weight	180.60	176.00	352.00
<i>D</i> _{cal}	1.554	1.377	1.280
<i>D</i> _{meas} (aqueous KI; flotation)	1.56	1.36	1.28
Radiation used	Cu K α ($\lambda = 1.5418$ Å)	Mo K α ($\lambda = 0.7107$ Å)	Mo K α ($\lambda = 0.7107$ Å)
μ (mm ⁻¹)	3.81	0.14	0.13
θ_{\max} (deg)	60	23	23
<i>N</i> (<i>m</i>) ^a	1476	2397	3354
<i>N</i> (<i>S</i>) ^b	874	1395	2338
<i>R</i> ^c	0.086	0.056	0.050

^a*N*(*m*) is the number of independent reflections measured.

^b*N*(*S*) is the number of reflections with a measured intensity significantly above that of the background at the 3 σ level.

^cThe minimized function $\sum \omega(|F_0| - |F_c|)^2$ was used and the program SHELX-76 was used for refinement.

whereas an induction period was noticed in cases where the photoreaction originated from defects (Fig. 2). The absence of any induction period clearly indicated that the photoreactivity must not be defect initiated. Therefore, to estimate the inherent orientational flexibility of the molecules in the crystal lattice, lattice energy calculations were carried out using a computer program WMIN developed by Busing [13]. Much to our surprise the energy calculations reveal the presence of orientational flexibility for both molecules present in the asymmetric unit in the ground state. Indeed a total rotation of about 24° (in the direction to generate the *syn* head-to-tail dimer) in the ground state is possible without much increase in the lattice energy [14].

In most crystals, electronic excitation increases the attractive forces so that the excited molecule is bound more tightly to its nearest neighbour

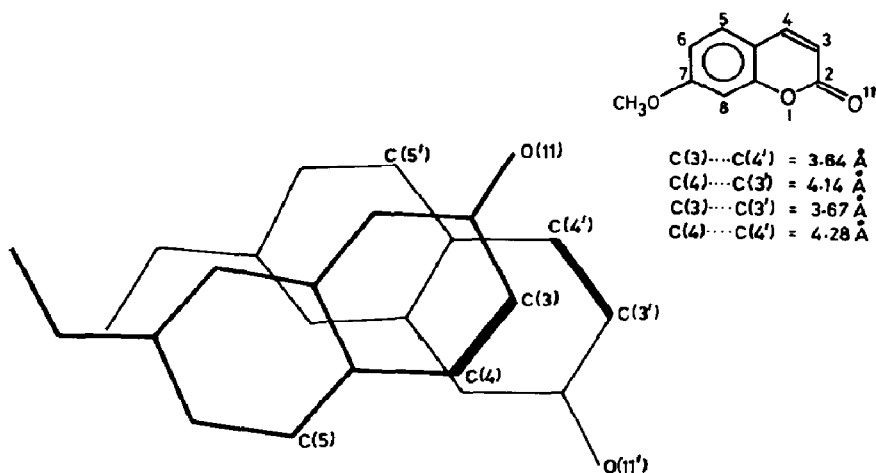


Fig. 1. Perspective view of the asymmetric unit (crystal coordinates) of 7-methoxycoumarin (centre-to-centre distance between double bonds, 3.83 Å).

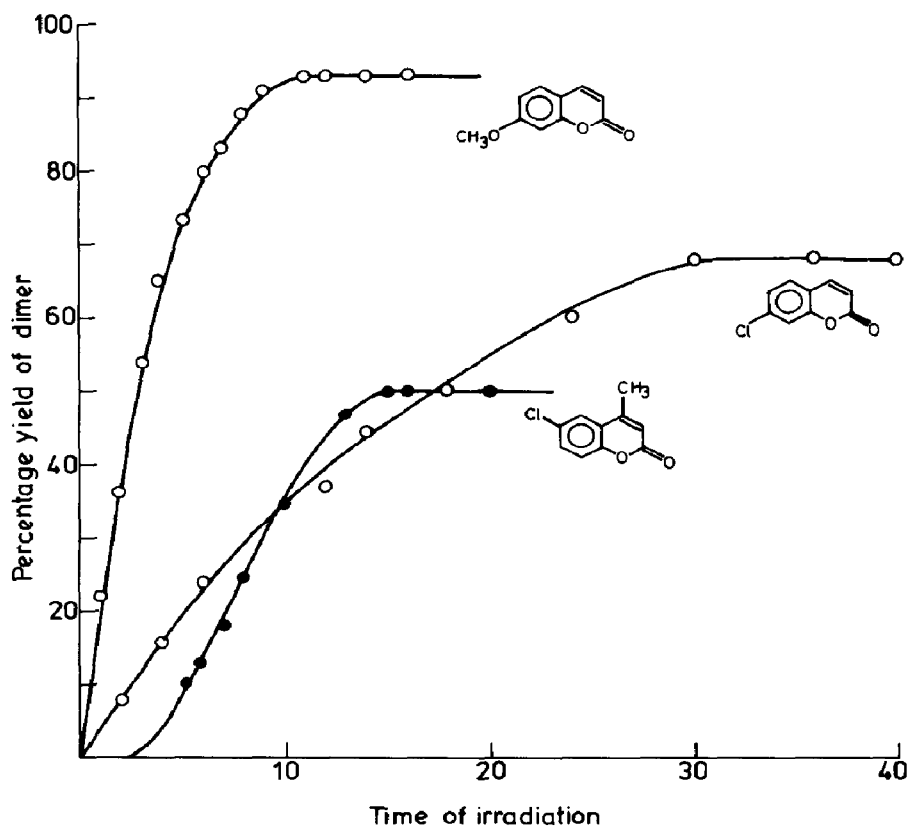


Fig. 2. Duration of irradiation vs. yield of dimer (the irradiation time is given in hours for 7-methoxycoumarin and 7-chlorocoumarin and in days for 4-methyl-6-chlorocoumarin).

[15]. With the increase in the attractive forces between the reactive molecules on excitation it may be expected that the motion of the molecule to achieve a maximum overlap will become facile. We propose that additional rotation (in addition to that available in the ground state) to generate the *syn* head-to-tail dimer is achieved as a result of the interaction between the excited and the ground state molecules. The radiation energy absorbed by the reactive molecules would be large enough to allow the molecules to undergo rotation. However, it seems to be essential to postulate an inherent flexibility within the crystal lattice for these molecules to undergo rotation as this would allow us to understand the large yield of the dimer. Indeed, as indicated above, such orientational flexibility in the ground state of 7-methoxycoumarin is revealed by lattice energy calculations. The present example is yet another case of topochemical dimerization between non-parallel neighbouring double bonds. The positive aspect of the occurrence of photoreactive structures, in spite of the fact that the double bonds are non-parallel, is that there is no absolute necessity to achieve the stringent condition of exact parallelism and coplanarity of the reactive double bonds in crystal engineering operations.

An interesting observation was made in the case of 7-chlorocoumarin. Irradiation of crystalline 7-chlorocoumarin yielded a single dimer in about 70% yield within 30 h. Dimerization proceeded without an induction period as shown in Fig. 2. The structure of the dimer was deduced from its spectral characteristics listed in Table 2. Unfortunately, confirmation of the structure by X-ray crystallography could not be carried out since it was not possible to obtain suitable single crystals. Chemical ionization mass spectrometry confirmed the formation of the dimer. Four different *cis*-fused dimers may theoretically be formed: *syn* head-to-head, *anti* head-to-head, *syn* head-to-tail and *anti* head-to-tail. ^1H NMR spectra have been utilized previously to draw conclusions regarding the stereochemistry of coumarin dimers [16, 17]. In general, the cyclobutyl protons of the *syn* dimers resonate around $\delta = 4.0 - 4.2$ ppm, whereas those of the *anti* isomers resonate below $\delta = 3.90$ ppm. This shielding is caused by the diamagnetic anisotropic effect of a carbonyl or a phenyl nucleus in the *anti* configuration. In the dimer isolated from 7-chlorocoumarin, the cyclobutyl protons resonate at $\delta = 4.17$ ppm and $\delta = 4.24$ ppm and this suggested a *syn* configuration. The chemical shift of the H(8) proton of coumarin dimers provides sufficient information regarding the head-to-head or head-to-tail configuration. In head-to-tail dimers the H(8) proton is shifted considerably to high field ($\delta = 6.20$ ppm). This strong shielding effect of H(8) is caused by the diamagnetic anisotropy of the phenyl nucleus situated in front of this proton in the *syn* head-to-tail configuration. Absence of any aromatic signal below $\delta = 6.7$ ppm in the dimer isolated suggested that it has the *syn* head-to-head configuration.

The packing arrangement shown in Fig. 3 reveals that the two potentially reactive 7-chlorocoumarin molecules are separated by 4.45 Å, this being the repeat along the *a* axis. Further, the centrosymmetrically related double bonds are closer, the centre-to-centre distance between them being

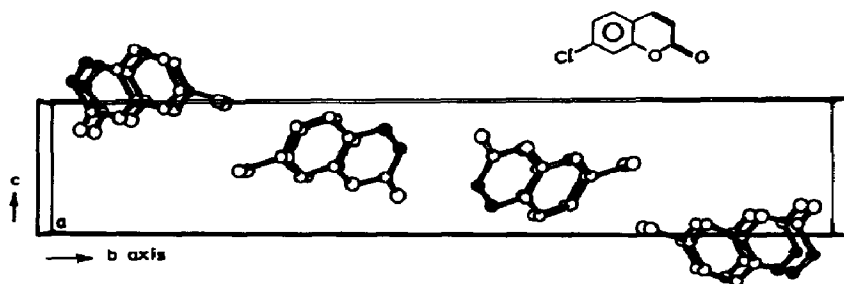


Fig. 3. Molecular packing diagram (β type) for 7-chlorocoumarin along the a axis (monoclinic $P2_1/n$; $a = 4.454 \text{ \AA}$; $b = 30.488 \text{ \AA}$; $c = 5.684 \text{ \AA}$; $\beta = 91.21^\circ$; $Z = 4$).

4.12 \AA . Translationally related coumarins are expected to give the *syn* head-to-head dimer and centrosymmetrically related coumarins are expected to give the *anti* head-to-tail dimer on UV excitation. However, the only dimer obtained on excitation corresponds to the *syn* head-to-head dimer, thus suggesting that the reaction is along the direction of the a axis. It is noteworthy that the distance of 4.45 \AA lies outside the limit of 3.5 - 4.2 \AA so far accepted for the β type. The absence of reaction between centrosymmetrically related monomers in spite of the closer distance (4.12 \AA) could be attributed to the poor overlap between the π orbitals of the reactive double bonds. This becomes evident when the lateral displacement and the angle between the least-square planes through the relevant atoms are compared in these two pairs of molecules. The angle between the least-square plane through the centrosymmetrically related atoms of the reactive bonds C(3), C(4), C(3'') and C(4'') and that passing through C(2), C(3), C(4) and C(10) is 107.0° , whereas the angle between the planes formed by the translationally related atoms C(3), C(4), C(3') and C(4') and C(2), C(3), C(4) and C(10) is 85.3° . Further, the lateral displacement of the centrosymmetrically related double bond is 0.9 \AA , whereas the same for the translationally related atoms is as small as 0.3 \AA . These values indicate that the π orbitals of the translationally related atoms overlap relatively better than do those of the centrosymmetrically related atoms. Thus 7-chlorocoumarin is an example wherein photodimerization occurs between the double bonds separated by more than 4.2 \AA . The examples presented above indicate that a closer examination and modification of the topochemical criteria for photodimerization are necessary.

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