In Situ X-ray Observation of Pedal-like Conformational Change and Dimerization of *trans*-Cinnamamide in Cocrystals with Phthalic Acid

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Abstract: In the crystals of phthalic acid *trans*-cinnamamide (1:2), two molecules of cinnamamide are connected with phthalic acid via a hydrogen bond to form a three-component assembly. The C=C double bonds of two cinnamamides take a criss-crossed arrangement with a center-to-center distance of 4.252(3) Å and with a twist angle of 97.1(4)°. After a partial single-crystal-to-single-crystal transformation, X-ray analysis revealed the *β*-type photodimer of cinnamamide in the assembly at 13.2(3)% conversion. This suggests that the pedal-like conformational change occurred for one of the cinnamamide molecules and the C=C bond of the other cinnamamide moved approximately parallel to form a cyclobutane ring.
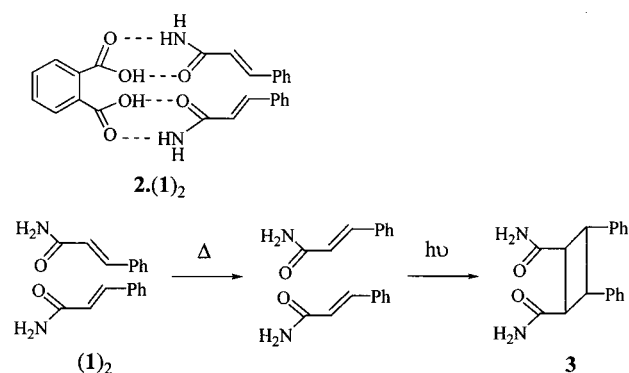
Introduction

The photodimerization of *trans*-cinnamamides in the solid state exclusively produce the *β*-type photodimer.[1] Preparation of the hydrogen-bonded cocrystals is an efficient way to control the molecular orientation.[2] Photolysis of cocrystals of **I** of *trans*-cinnamamide (**1**) with phthalic acid (**2**) (amide:acid = 2:1) has been investigated to obtain the *β*-type photodimer **3**. Photoirradiation of powdered crystals of **I** with a 400-W high-pressure Hg lamp for 20 h at room temperature gave **3** in 37% yield.[3] X-ray structure analysis indicated that two molecules of *trans*-cinnamamide are connected to the phthalic acid to form a three-component assembly by the hydrogen bonds. These two cinnamamide molecules are nearest neighbors in the crystal, but their C=C double bonds are in a criss-crossed arrangement.[3] A pedal-like conformational change was expected before the photodimerization, since dynamic disorder caused by a pedal-like motion has been observed in crystals of *trans*-stilbenes, 1,2-diphenylethanes, azobenzenes, and salicylideneaniline.[4] However, there was also a possibility that the reaction occurs predominantly at the crystal defects. To see what really happens in the crystal, in situ observation of the photoreaction has been carried out by single-crystal X-ray diffraction.

Experimental Section

Preparation of the Crystals. Colorless crystals of **I** were grown by slow evaporation from 2-propanol solution of the mixture of phthalic acid and *trans*-cinnamamide (1:2). They are platelike crystals with a

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Scheme 1

well-developed (010) face especially elongated along the [101] direction and lose their crystallinity with cutting because the layers parallel to the crystal face easily slip relative to each other (see Figure 3).

Photoirradiation to the Single Crystal. Photoirradiation far into the long wavelength absorption tail is effective to protect the single crystals from degradation by the photoreaction.[5] The crystal of **I** became yellow and melted in 1 h without a filter for the incident light from the 250-W ultrahigh-pressure Hg lamp. The UV spectra of the 2-propanol solution of **I** showed a $\pi-\pi^*$ absorption at 271 nm, and almost no absorption longer than 320 nm. When the wavelength of the incident light was selected around 365 nm by using a band path filter, no change was observed in the lattice constants. Light of shorter wavelength was then introduced through a long-pass filter UV34 ($T = 10\%$ at 330 nm) to initiate the photoreaction. The changes in the lattice constants were monitored on an X-ray four-circle diffractometer AFC-7R. The X-ray diffraction ability of the crystal decreased and a peak half-width of X-ray diffraction increased gradually from 0.40° to 0.54°. To ensure the sufficient resolution of the structure analysis, photoirradiation through UV34 was stopped after 6 h, and X-ray intensities were measured. The crystal after photoirradiation is denoted as **I′**.

X-ray Crystal Structure Analyses. The structure of **I** was determined previously based on the X-ray intensity data measured on a

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Table 1. Crystal Data and Experimental Details

	I	**I′** [a]
chemical formula	$C_8H_6O_4 \cdot (C_9H_9NO)_2$	
formula weight	460.49	
temperature/K	298(1)	
crystal size/mm	$0.8 \times 0.3 \times 0.2$	
crystal system	triclinic	
space group	$P\bar{1}$	
Z	2	
a/Å	9.562(3)	9.507(2)
b/Å	17.401(4)	17.422(2)
c/Å	7.523(3)	7.591(2)
α/deg	90.82(2)	90.68(2)
β/deg	105.72(2)	105.79(2)
γ/deg	75.51(2)	75.55(1)
V/Å³	1164.7(6)	1169.5(4)
D_x/Mg m^{-3}	1.313	1.308
θ_{max}(Mo Kα)/deg	27.5	26.0
no. of reflcns measd	5674	4904
no. of independent reflcns	5350	4614
no. of parameters refined	403	358
$R(F)$ [$F^2 > 2\sigma (F^2)$]	0.041	0.072
$\Delta\rho_{min}, \Delta\rho_{max}$/e Å^{-3}	−0.29, 0.26	−0.28, 0.26

[a] **I′** is the structure of **I** after photoirradiation.

Rigaku AFC-5S four-circle diffractometer.[3] The structure has been redetermined in the present study to compare directly with that after the photoirradiation by measuring X-ray data on a Rigaku AFC-7R diffractometer. The data were collected on the same crystal throughout the experiment. Crystal data and experimental details are listed in Table 1.

I′: As an initial structure model, all the non-H atoms of the cinnamamide monomers and phthalic acid were refined anisotropically. The hydroxyl H atoms of the cinnamamide monomers were located from difference syntheses and refined isotropically. The other H-atom positional parameters were calculated geometrically, and fixed with $U_{iso}(H) = 1.2U_{eq}$ (parent atom). Then, the site occupation factors of the atoms in the cinnamamide monomers were tentatively set to 0.90, and some cycles of least-squares refinement were made. Non-H atoms of the cinnamamide photodimer (the O5*−O6*, N7*−N8*, C17*− C20*, and C26*−C29* atoms) could be located on difference syntheses and they were refined isotropically with $U_{iso} = U_{eq}$ (corresponding atom in the monomers). The bond distances of the cinnamamide photodimer were restrained to the corresponding values of the α-photodimer.[6] The other C atoms of the phenyl rings (C21*−C25* and C30*−C34*) were introduced as rigid groups. The population of the dimer was refined to 13.2(3)%. The *R* value reduced to 0.072, which is significantly smaller than that (0.106) of the initial nondisordered model before introducing the photoproduct. The programs used in the calculations were SHELXL97 and TEXSAN.[7]

Results and Discussion

Change in Molecular Structure. In the crystals of **I**, phthalic acid and two cinnamamide molecules form a three-component assembly connected by the hydrogen bonds (Figure 1). The C18−C19 and C27−C28 bond axes are criss-crossed with the twist angle of 97.1(4)° and the center-to-center distance 4.252(3) Å. The C18···C27 and C19···C28 distances are 4.858(3) and 3.815(3) Å, respectively.

Figure 2 shows the structure of **I′** after photoirradiation. The β-truxinamide **3** was observed with 13.2(3)% population, which was estimated by X-ray analysis.[8] The atom labels of the dimer correspond to those of the monomers with an asterisk. The C18*−C19* bond axis in the cyclobutane ring is approximately parallel to the C18=C19 bond, whereas the C27*−C28* is

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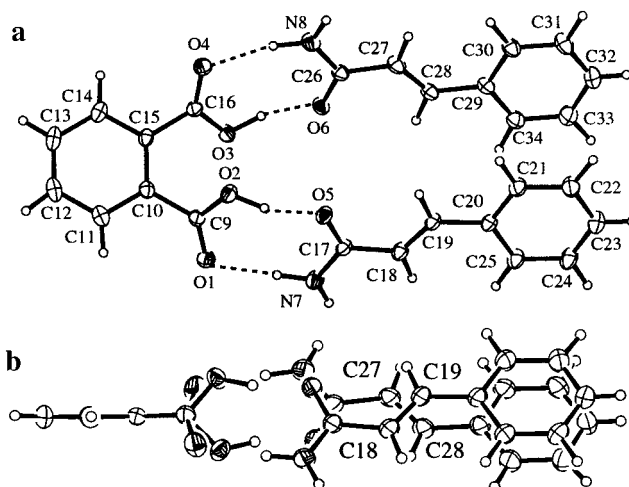
Figure 1. (a) The structure of two *trans*-cinnamide molecules connected by phthalic acid with hydrogen bonds in **I** and (b) its side view. Displacement ellipsoids are plotted at the 30% probability level. Dashed lines represent hydrogen bonds.
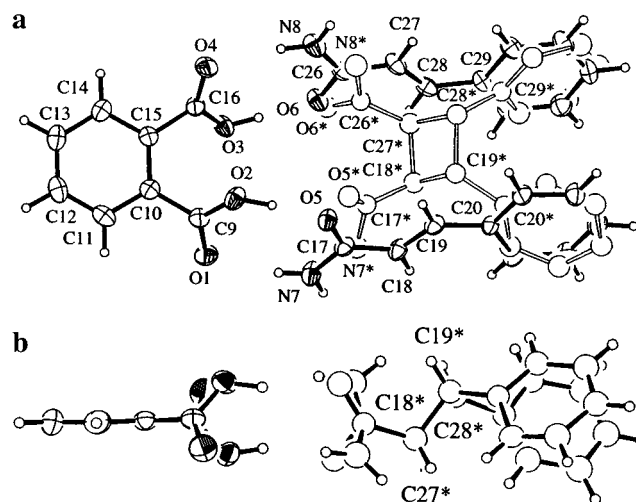

Figure 2. (a) The disordered structure in **I′** (after photoirradiation) which contains cinnamamide photodimer with a site occupancy factor of 13.2(3)% (the atoms with asterisks) and (b) its side view omitting the unreacted cinnamamide monomers.

twisted relative to the original C27=C28 bond. This fact indicates that a pedal-like rotation around the C27=C28 bond occurred before the photodimerization.[9] It is interesting that the distances of the atom movement are similar for two amide molecules: C18 to C18* 1.86(3) Å, C19 to C19* 1.45(2) Å; and C27 to C27* 1.84(3) Å, C28 to C28* 1.37(2) Å. The phenyl rings of the photodimer, which were refined as rigid groups, take similar positions to those in the monomers.

Figure 2b is a side view of the cinnamamide photodimer with the phthalic acid. The H atoms bonded to C27* and C28* are directed roughly antiparallel to the initial C−H orientations shown in Figure 1b. In the pedal-like rotation, one of these olefin

(8) A photolysis of powder crystals of **I** yielded β-truxinamide (37%), *cis*-cinnamamide (5%), and α-truxillamide (3%), which were estimated by NMR and HPLC analyses.[3] The structure of **I′** gives a view at ca. 13% conversion, which is not the maximum yield, but is the limit for single-crystal X-ray analysis. Even if the byproducts were accommodated in the crystal lattice of **I′**, their populations seemed to be below the detection limit for X-ray analysis.

(9) Taking into account the alteration in the directions of the C18−C17 (amide) and C19−C20 (Ph) bond axes during the photodimerization, the conformational change around the C18=C19 bond has also a component of the pedal-like motion.[5a]
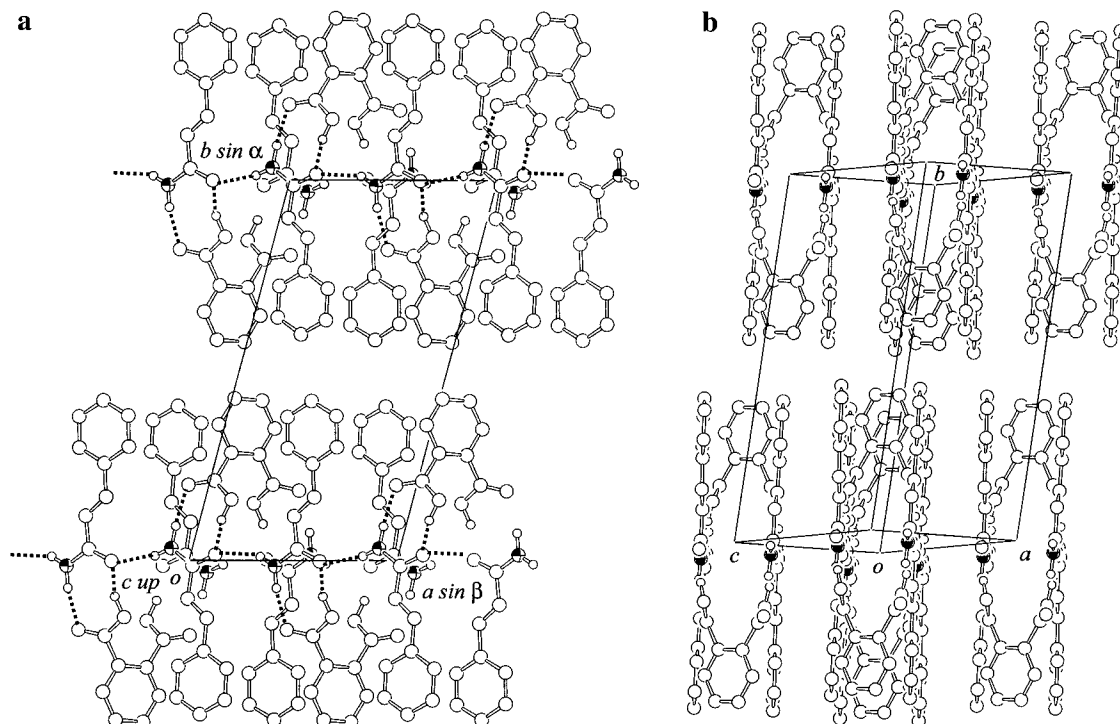
Figure 3. Projections of the crystal structure of **I** (a) along the *c* axis and (b) nearly along the [101] direction. Dashed lines represent hydrogen bonds in the ribbon structure along [101].
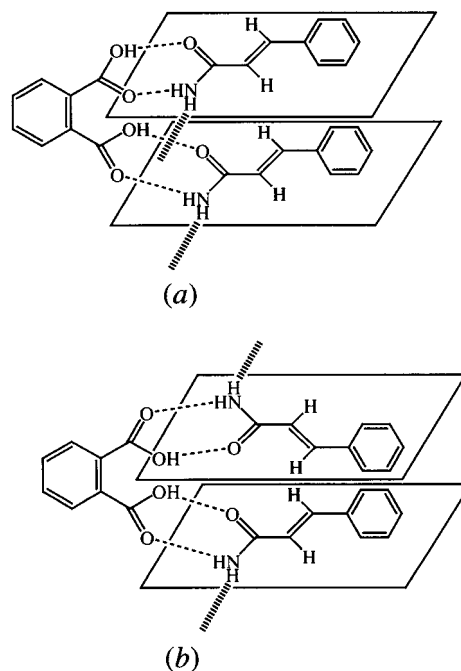
H atom, H27 or H28, will be directed close to the C18 or C19 atom, respectively. The C19···C28 distance of 3.8 Å is too narrow to take such a configuration, but the C18···C27 distance is as long as 4.8 Å in **I**, and the C27−H27···C18 linear configuration may be allowed as the transition state.

The newly formed C−C bond axes are nearly along the *a* axis, which corresponds to contraction of the cell constant *a* by 0.055(3) Å. The conversion of 13.2 (3)% in the single crystal of **I** was relatively low but significantly observed. For α-type dimerization of *trans*-4-methylcinnamamide and *trans*-4-chlorocinnamamide, the single-crystal photoirradiation was achieved at 86.2(4) and 48.4(6)% conversion, respectively. Even in a weakly photoactive crystal of *trans*-cinnamamide, a 4.5(2)% α-truxillamide population could be detected by X-ray diffraction.[10]

Criss-Crossed C=C Bonds. In the crystals of cinnamic acid and cinnamamide derivatives, the nearest neighbor C=C bonds are usually parallel (related by translation) or antiparallel (related by center of symmetry). The criss-crossed arrangement (related by glide symmetry) was first reported for methyl *m*-bromocinnamate.[11] The twist angle θ_1 of the C=C bonds was 38.2° with the center-to-center distance 3.93 Å.

Why are the two cinnamamide molecules connected by phthalic acid in **I** related by the noncrystallographic 2-fold axis? Basically, there are two possible arrangements of the cinnamamide molecules: (a) parallel arrangement of the C=C bonds and (b) criss-crossed ones as illustrated in Chart 1. The C=C double bond is always trans to the amino group. One of the H atoms of the amino group will be involved in the inter-supramolecular hydrogen bond. In fact, cinnamamide molecules related by noncrystallographic glide symmetry are linked by the N−H···O hydrogen bond to form a one-dimensional ribbon structure along the [101] direction (Figure 3). Phthalic acid

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Chart 1

molecules bridge the two ribbons at both sides to make a flattened pipe. On the other hand, the parallel arrangement (*a*) could form also a double ribbon structure of the cinnamamide molecules related by translation or glide symmetry. However, the two phenyl groups of the cinnamamide molecules in the assembly (*a*) are too far to make a π − π interaction.

The criss-crossed arrangement of the C=C bonds of *trans*-cinnamamide was also observed in the hydrogen bond assembly in crystals of 4,5-dichlorophthalic acid−*trans*-cinnamamide (1:2) and 3,4,5,6-tetrachlorophthalic acid−*trans*-cinnamamide (1:2).[12] In the cocrystals with benzene−tetracarboxylic acid, two cinnamamide molecules are related by a crystallographic 2-fold axis.[12]

Dynamic Topochemical Principles. Topochemical principles are the basic concepts in organic solid-state reactions. It is known that the separation distance, mutual orientation, and space symmetry of reactive functional groups are crucial. However, there are several cases where the dynamical aspects of the excited molecules should be taken into account.[13] If such reactions are single-crystal-to-single-crystal in nature, the dynamic change of the molecular conformation can be observed in situ by X-ray analysis.[14] There is also a theoretical approach to investigate the dynamic process of the reaction in crystals. The reactivities of photodimerization, where the reactant olefin molecules are not parallel, have been studied and rationalized by the lattice-energy calculations.[15]

There are some classic examples of photoreactions which occur at dislocations and other defects.[13a] Disorder causes alternative reaction pathways.[16] However, the reactions accompanied by disorder should not be classified into the reaction at defect sites, since the reaction occurs in a crystal lattice and is controlled by the bulk topochemistry, where the reaction mechanism can be predicted from the crystal structure of the reactant.

Conclusion

Two *trans*-cinnamamide molecules are oriented in a head-to-head fashion by hydrogen bonds with phthalic acid. They show a criss-crossed arrangement of the C=C bonds, which is the result of the inter-supramolecular hydrogen bonds in the crystal. The pedal-like conformational change before the [2+2] photodimerization was speculated based on the yield of β-truxinamide from the photolysis of powder crystals. In situ X-ray observation of the reaction has revealed the dynamic conformational change of the *trans*-cinnamamide molecules in the crystal lattice.

Supporting Information Available: X-ray structural information on **I** and **I′** (PDF) and an X-ray crystallographic file (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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