Acta Cryst. (1998). B**54**, 907–911

Crystal-to-Crystal Diastereoselective Transformation of 2,4,6-Triisopropyl-4′-(*S*)-phenylalaninocarbonylbenzophenone Methyl Ester

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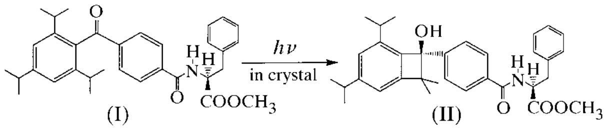
(*Received 29 September 1997; accepted 14 April 1998*)

Abstract

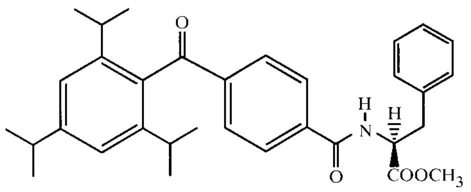
Dissymmetry of the photoproduct was induced by using a chiral substituent, (*S*)-methylphenylalanine, in the title compound {*N*-4-(2,4,6-triisopropylbenzoyl)benzoyl]-(*S*)-phenylalanine methyl ester (I)}. On irradiation with light from a 250 W ultra-high-pressure Hg lamp for 7 h through a long-pass filter, the photoreaction in a crystal was 100% complete without the loss of crystallinity. The crystal structures (I), before, and (II) {*N*-[4-(7-hydroxy-3,5-diisopropyl-8,8-dimethylbicyclo[4.2.0]octa-1,3,5-trien-7-yl)benzoyl]-(*S*)-phenylalanine methyl ester}, after photocyclization, have been determined by X-ray diffraction. For comparison, a crystal structure analysis has also been carried out for the photoproduct (III) of the 3′-COOMe derivative after recrystallization {methyl 3-(7-hydroxy-3,5-diisopropyl-8,8-dimethylbicyclo[4.2.0]-octa-1,3,5-trien-7-yl)benzoate}. The dihedral angle between the central carbonyl plane and the triisopropylphenyl ring deviates from 90° by 10 (1)° in (I), which makes an imbalance in the intramolecular O(carbonyl)$\cdots$H(methine) distances of the isopropyl groups at positions 2 and 6. The crystal structure of (II) indicates that the nearer methine H was predominantly abstracted by the carbonyl O atom in the reaction. The absolute configuration around the asymmetric C atom in the cyclobutenol ring of the product is *S*.

1. Introduction

A crystal-to-crystal photoreaction can potentially obtain information on the process of a topochemical reaction and/or detect metastable intermediate structures by X-ray diffraction (Ohashi *et al.*, 1995). However, in most cases the problem is crystal cracking during the reaction. This problem has been technically overcome by Enkelmann *et al.* (1993) by studying the [2 + 2] photodimerization of α-*trans*-cinnamic acid by tuning the wavelength of light. When radiation in the tail of the absorption band is selected using a long-pass filter, the solid-state photoreactions may proceed homogeneously (Novak *et al.*, 1993).



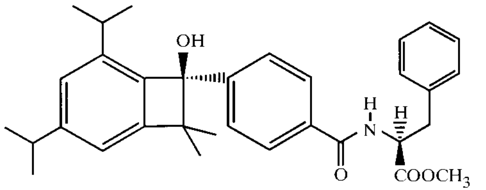
2,4,6-Triisopropylbenzophenones photocyclize efficiently into the corresponding benzocyclobutenols, not only in solution, but also in the solid state (Ito *et al.*, 1988). The crystal structures of 3′- or 4′-substituted derivatives [*R* = H, *m*-OMe, *m*-COCl, *m*-COOMe, *p*-Me, *p*-$C(CH_3)_3$, *p*-OMe, *p*-COOH, *p*-COCl, *p*-COOMe and *p*-COOEt] were reported in the preceding paper along with some relationships between the crystal structures and photoreactivities (Fukushima *et al.*, 1998). Asymmetric synthesis utilizing the crystalline environment is one of the most promising fruits of solid-state reactions. Limited to the triisopropylbenzophenones, the asymmetric photocyclization of *p*-COOH derivatives in crystals of salts formed with several optically active amines has been studied (Koshima *et al.*, 1994; Fu *et al.*, 1997). In the present study an optically active substituent, (*S*)-methylphenylalanine, has been introduced to yield the non-centrosymmetric crystal structure. Asymmetric synthesis using the powder sample proceeded with a diastereomer excess (d.e.) of 87% (Ito *et al.*, 1998). However, the recrystallization of the photoproduct gave only very thin needle crystals. The structure of the major photoproduct could finally be determined by the crystal-to-crystal conversion technique.



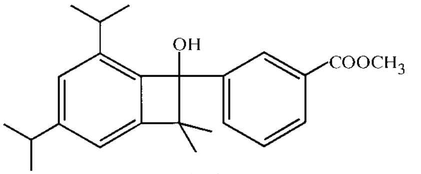
(I)

2. Experimental

The photoreactivity of (I) was examined using a powder sample sandwiched between Pyrex plates and irradiated with a 400 W high-pressure Hg lamp at 273 K in Ar for 2 h. The yield (84%) and d.e. (87%) were estimated based on ^{1}H NMR spectra using a shift reagent. The details for the preparation and photolysis of (I) are reported elsewhere (Ito *et al.*, 1998). Crystals of (I) were grown from a methanol solution. The cyclobutenol derivative (III) was prepared by photocyclization of the 3′-COOMe derivative of 2,4,6-triisopropylbenzophenone and recrystallized from methanol (Ito *et al.*, 1985).



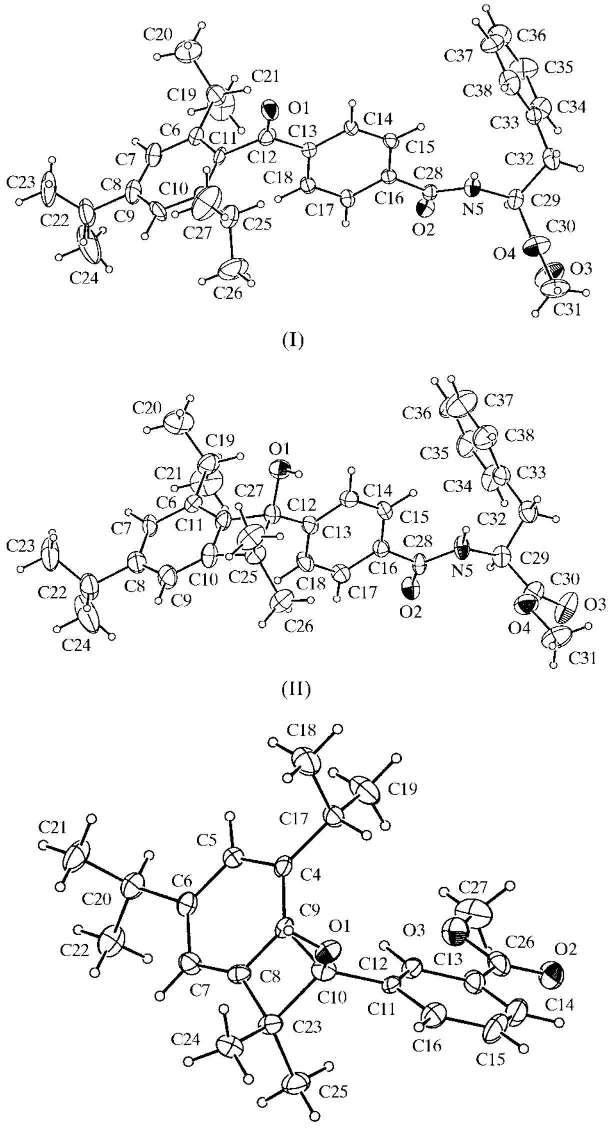
(II)



(III)

A preliminary test of crystal-to-crystal transformation was made on α-*trans*-cinnamic acid ($\lambda_{\max}$ of π–π^* = 273 nm in UV absorption), which is monoclinic with a = 7.750 (5), b = 17.969 (7), c = 5.636 (3) Å, β = 96.80 (5)° at 297 K. The light from a 250 W ultra-high-pressure Hg lamp (Ushio SP3-250D) was led to the crystal on a four-circle diffractometer using a flexible light guide made with quartz (Ushio AF-101BQ). The outlet-to-crystal distance was set to be 20 mm and the light was passed through the long-pass filter UV36 (T = 15% at 350 nm). After photoirradiation for 7 h, the crystal was still clear and complete conversion was estimated from the lattice constants, a = 7.711 (5), b = 18.571 (10), c = 5.669 (2), β = 106.64 (4)°. An increase in b and a widening of β from 96 to 106° during the conversion were reported by Enkelmann *et al.* (1993). The crystal-to-crystal photocyclization of (I) ($\lambda_{\max}$ = 278 nm) was carried out as described above. The irradiation was continued for 15 h through the UV36 filter. The peak half-width of X-ray diffraction increased from 0.15 to 0.6–0.8°, but the indexing of reflections and data collection could be carried out normally. Lattice constants altered accordingly, as seen in Table 1. ^{1}H NMR spectra of the crystal specimen used for X-ray data collection of (II) were measured to confirm that the conversion was 100% with a d.e. of 90–100%. An IR study was also carried out to confirm sufficient irradiation time. The carbonyl stretching peak ($\nu_{\mathrm{C{=}O}}$ = 1665 cm^{-1}) almost disappeared after 1 h of photoirradiation of single crystals with dimensions of 0.5 mm. When a KBr disk of the powder sample of (I) was irradiated, the reaction was completed within 5 min.

The X-ray intensities were measured on a Rigaku AFC-5 four-circle diffractometer with Mo $K\alpha$ radiation (λ = 0.71073 Å) monochromated by a graphite plate. Crystal data, experimental conditions and refinement details are listed in Table 1. The positional and anisotropic displacement parameters of non-H atoms were refined on F by full-matrix least squares. The hydroxy H atom was located by difference synthesis. Other H-atom positions were calculated geometrically and a riding refinement was performed for all the H atoms (C—H,



(I)

(II)

(III)

Fig. 1. The molecular structures of (I)–(III) with displacement ellipsoids at the 20% probability level. H atoms are represented by circles of radii 0.1 Å.

Table 1. *Experimental details*

	(I)	(II)	(III)
Crystal data			
Chemical formula	$C_{33}H_{39}NO_4$	$C_{33}H_{39}NO_4$	$C_{24}H_{30}O_3$
Chemical formula weight	513.68	513.68	366.5
Cell setting	Orthorhombic	Orthorhombic	Orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_1nb$
a (Å)	10.798 (3)	11.525 (9)	11.691 (2)
b (Å)	30.042 (3)	28.238 (11)	17.510 (3)
c (Å)	9.407 (3)	9.317 (8)	10.683 (2)
V (Å^3)	3051.6 (13)	3032 (4)	2186.9 (7)
Z	4	4	4
D_x (Mg m^{-3})	1.118	1.125	1.113
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
Wavelength (Å)	0.71073	0.71073	0.71073
No. of reflections for cell parameters	25	23	25
θ range (°)	10–15	8.2–13.4	10–15
μ (mm^{-1})	0.073	0.073	0.072
Crystal form	Prism	Prism	Prism
Crystal size (mm)	0.6 × 0.4 × 0.4	0.7 × 0.4 × 0.3	0.5 × 0.5 × 0.5
Crystal colour	Colourless	Colourless	Colourless
Data collection			
Diffractometer	Rigaku AFC-5	Rigaku AFC-5	Rigaku AFC-5
Data collection method	ω scans	ω scans	θ–2θ scans
Absorption correction	None	None	None
No. of measured reflections	3056	2946	1087
No. of independent reflections	3056	2946	1087
No. of observed reflections	1526	1410	822
Criterion for observed reflections	$\lvert F_o\rvert > 3\sigma(\lvert F_o\rvert)$	$\lvert F_o\rvert > 3\sigma(\lvert F_o\rvert)$	$\lvert F_o\rvert > 3\sigma(\lvert F_o\rvert)$
$\theta_{\max}$ (°)	25	25	20
Range of h, k, l	$0 \rightarrow h \rightarrow 13$ $0 \rightarrow k \rightarrow 36$ $0 \rightarrow l \rightarrow 11$	$0 \rightarrow h \rightarrow 12$ $0 \rightarrow k \rightarrow 33$ $0 \rightarrow l \rightarrow 11$	$0 \rightarrow h \rightarrow 11$ $0 \rightarrow k \rightarrow 16$ $0 \rightarrow l \rightarrow 10$
No. of standard reflections	3	3	3
Frequency of standard reflections	Every 100 reflections	Every 100 reflections	Every 100 reflections
Intensity decay (%)	2.6	None	None
Refinement			
Refinement on	F	F	F
R	0.080	0.077	0.049
wR	0.070	0.066	0.047
S	1.34	1.31	1.16
No. of reflections used in refinement	1526	1410	822
No. of parameters used	343	343	243
H-atom treatment	H atoms riding	H atoms riding	H atoms riding
Weighting scheme	$w = 1/[\sigma^2(F) + 0.0009F^2]$	$w = 1/[\sigma^2(F) + 0.0009F^2]$	$w = 1/[\sigma^2(F) + 0.0009F^2]$
$(\Delta/\sigma)_{\max}$	0.02	0.01	0.01
$\Delta\rho_{\max}$ (e Å^{-3})	0.23	0.21	0.14
$\Delta\rho_{\min}$ (e Å^{-3})	−0.22	−0.22	−0.13
Extinction method	None	None	None
Source of atomic scattering factors	*International Tables for X-ray Crystallography* (1974, Vol. IV)	*International Tables for X-ray Crystallography* (1974, Vol. IV)	*International Tables for X-ray Crystallography* (1974, Vol. IV)
Computer programs			
Data collection	*MSC/AFC* (Molecular Structure Corporation, 1988)	*MSC/AFC* (Molecular Structure Corporation, 1988)	*MSC/AFC* (Molecular Structure Corporation, 1988)
Cell refinement	*MSC/AFC* (Molecular Structure Corporation, 1988)	*MSC/AFC* (Molecular Structure Corporation, 1988)	*MSC/AFC* (Molecular Structure Corporation, 1988)
Data reduction	Local programs	Local programs	Local programs
Structure solution	*CRYSTAN-GM* (Edwards *et al.*, 1995)	*CRYSTAN-GM* (Edwards *et al.*, 1995)	*CRYSTAN-GM* (Edwards *et al.*, 1995)
Structure refinement	*CRYSTAN-GM* (Edwards *et al.*, 1995)	*CRYSTAN-GM* (Edwards *et al.*, 1995)	*CRYSTAN-GM* (Edwards *et al.*, 1995)
Preparation of material for publication	*CRYSTAN-GM* (Edwards *et al.*, 1995)	*CRYSTAN-GM* (Edwards *et al.*, 1995)	*CRYSTAN-GM* (Edwards *et al.*, 1995)

Table 2. *Comparison of selected geometric parameters (Å, °)*

	(I)	(II)		(III)
C10—C11	1.416 (14)	1.381 (16)	C8—C9	1.375 (13)
C11—C12	1.520 (14)	1.522 (16)	C9—C10	1.518 (12)
C12···C25	2.89 (1)	1.637 (16)	C10—C23	1.623 (13)
C12···C19	2.97 (2)	3.40 (2)	C10···C17	3.44 (1)
C25—C10	1.483 (16)	1.518 (16)	C23—C8	1.507 (13)
C12—O1	1.226 (13)	1.428 (13)	C10—O1	1.437 (9)
C12—C13	1.475 (13)	1.539 (15)	C10—C11	1.508 (12)
C10—C11—C12	117.8 (9)	96.4 (9)	C8—C9—C10	94.2 (8)
C11—C12···C25	60.8 (8)	83.7 (8)	C9—C10—C23	85.4 (7)
C12···C25—C10	60.6 (9)	86.7 (9)	C10—C23—C8	85.3 (7)
C25—C10—C11	120.8 (9)	93.2 (10)	C23—C8—C9	95.2 (8)
C11—C12—O1	120.6 (9)	113.8 (9)	C9—C10—O1	117.2 (7)
C13—C12—O1	120.6 (9)	109.7 (8)	C11—C10—O1	105.9 (8)
C11—C12—C13	118.8 (8)	111.9 (9)	C9—C10—C11	117.0 (8)
C10—C11—C12—C13	99.4 (12)	117.9 (11)	C8—C9—C10—C11	116.4 (10)
C11—C12—C13—C14	171.8 (13)	139.2 (14)	C9—C10—C11—C12	−9.8 (9)
C15—C16—C28—N5	29.4 (9)	19.6 (10)		
C16—C28—N5—C29	−177.6 (11)	−175.4 (14)		
C28—N5—C29—C30	−105.3 (11)	−102.2 (13)		
N5—C29—C30—O4	−49.8 (10)	−13.7 (10)		
N5—C29—C32—C33	−62.2 (9)	−60.6 (10)		
C29—C32—C33—C34	−87.5 (12)	−75.7 (14)		

N—H and O—H distances of 0.96 Å). Selected geometric parameters are listed in Table 2.†

3. Discussion

3.1. *Molecular structure*

Selected bond lengths, bond angles and torsion angles of (I)–(III) are compared in Table 2. The C12—C25 bond of (II) formed in the photochemical reaction is 1.637 (16) Å, which corresponds well to the C10—C23 distance of 1.623 (13) Å in (III). The other geometrical parameters of the cyclobutenol ring in (II) agree with those of (III) within experimental error. As seen in Fig. 1, the methine H atoms of the isopropyl groups at positions 2 and 6 of (I) are directed towards the carbonyl group and the H atom bonded to C25 was abstracted by O1 on photocyclization. In (I), the dihedral angle between the triisopropylphenyl ring and the carbonyl plane is 80 (1)°, and the O1···C19 and O1···C25 distances are 3.63 (1) and 3.30 (1) Å, respectively. These facts indicate that the carbonyl O atom predominantly abstracted the nearer methine H atom, as expected. The reaction cavity of (I) looks symmetrical for the two isopropyl groups *ortho* to the carbonyl, as shown in Fig. 4(*b*) of the preceding paper (Fukushima *et al.*, 1998).

The torsion angles of the (*S*)-methylphenylalanine moiety in (II) are similar to those in (I), except for N5—C29—C30—O4, indicating a rotation of the terminal COOMe group by 36 (1)° in the crystal transformation.

Table 3. *Movement (Å) of atoms relative to the centre of gravity of the molecule after the photochemical reaction*

Δ*X*, Δ*Y* and Δ*Z* are the components of displacement (Å) along the *a*, *b* and *c* axes, respectively.

	Distance	Δ*X*	Δ*Y*	Δ*Z*
O1	0.26	−0.16	−0.03	0.20
C6	0.30	0.17	−0.23	0.11
C7	0.37	0.27	−0.24	0.10
C8	0.34	0.26	−0.21	0.07
C9	0.22	0.20	−0.10	0.02
C10	0.23	0.18	−0.08	−0.11
C11	0.14	0.07	−0.11	−0.01
C12	0.61	−0.32	0.40	0.34
C13	0.48	−0.29	0.33	0.20
C14	0.47	−0.33	0.33	0.08
C15	0.42	−0.28	0.32	−0.01
C16	0.37	−0.22	0.30	0.00
C17	0.33	−0.15	0.29	0.04
C18	0.38	−0.18	0.31	0.13
C25	0.69	0.20	−0.64	−0.17
C26	1.04	−0.03	−1.04	0.03
C27	0.83	−0.05	−0.83	0.06

The hydroxy group in (III) forms an intermolecular hydrogen bond, O1—H1···O2($\frac{1}{2}+x, \frac{1}{2}-y, \frac{1}{2}+z$) with an O1···O2 distance of 2.804 (9) Å. On the other hand, there is no hydrogen bond involving the O1 atom in (II) and the proton migrating from C25 is accommodated in a space surrounded by H atoms. Crystals with such molecular packing would not be grown from solution.

3.2. *Crystal-to-crystal reaction*

The changes in lattice constants from (I) to (II) were +0.73 (1), −1.80 (1) and −0.09 (1) Å for *a*, *b* and *c*, respectively, and the cell volume decreased by 19 (4) Å^3.

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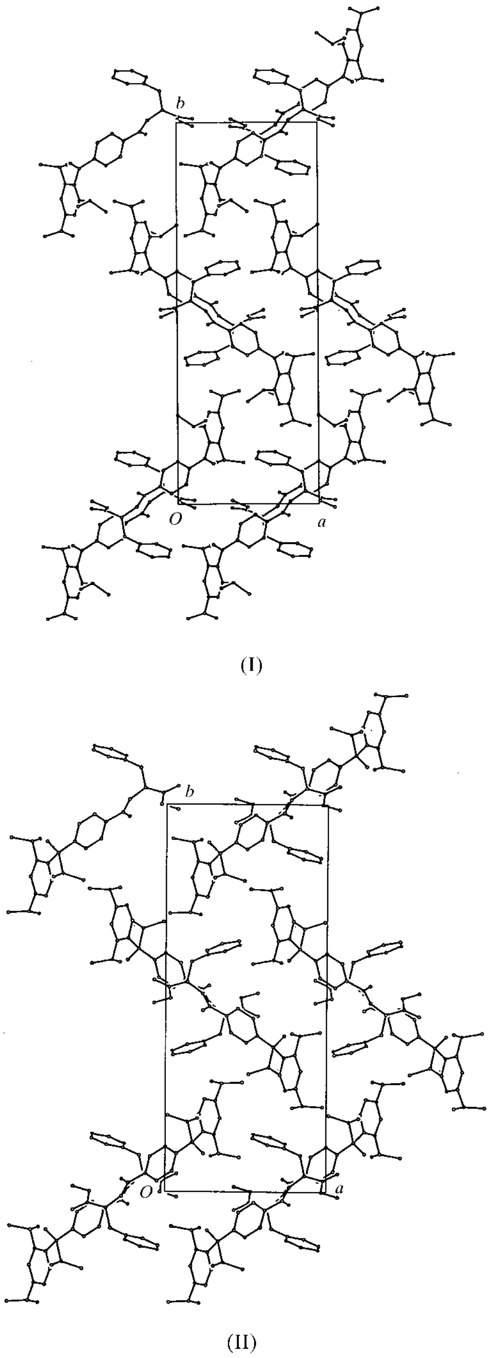
† Supplementary data for this paper are available from the IUCr electronic archives (Reference: OA0013). Services for accessing these data are described at the back of the journal.

As seen in Fig. 2, the triisopropylphenyl ring is almost perpendicular to the *c* axis and the C—C bond created by photoreaction is approximately directed along the *b* axis. This situation corresponds well to the anisotropic alterations in the lattice constants.

Which atoms moved most during the crystal-to-crystal reaction? A direct comparison of the atomic coordinates between (I) and (II) will not provide the answer to this question since the lattice constants are different. Therefore, the atomic coordinates (*x*, *y*, *z*) of (I) and (II) were transferred into the Cartesian coordinates (*X*, *Y*, *Z*) and the centres of gravity of the molecules were made to coincide with each other. The orientations of the molecules in crystals of (I) and (II) almost correspond without any adjustment. The relative displacement of each atom after the photochemical reaction and its components along the crystal axes were calculated and are listed in Table 3. It is apparent that the C12 and C25 (and C26 and C27) atoms moved too close to each other to form a C—C bond. The motions of the C6–C11 and C13–C18 atoms of the phenyl rings are almost translational with respect to the crystal axes. The displacement of the carbonyl O1 atom is relatively small, only 0.26 Å, in contrast to that of the carbonyl C12 atom, 0.61 Å.



(I)

(II)

Fig. 2. Projection of the crystal structure along **c** for (*a*) (I) and (*b*) (II).

4. Conclusions

The crystal-to-crystal transformation of the title compound was successful on irradiation by light at the tail of the longer wavelength side of the absorption. This experimental technique can be adopted for many other photochemical reactions in the solid state, not only to determine the structure of products *in situ* but also to realize the reaction process in crystals.

This work was supported by the Grant-in-Aid on Priority Areas No. 08221230 from the Japanese Ministry of Education, Science, Sports and Culture.

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