Crystalline-State Photoisomerization of α,β-Unsaturated Thioamide Analyzed by X-rays

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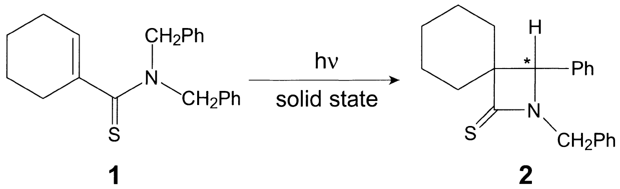
When a crystal of *N*,*N*-dibenzyl-1-cyclohexenecarbothioamide was exposed to UV light at 263 K, the cell dimensions were gradually changed with retention of the single crystal form. Since the crystal gradually decomposed after 330 h, the irradiation was stopped and the structure was analyzed by X-rays. The thioamide molecule was converted by 65.0% to the thiolactam molecule. The thioamide and thiolactam molecules were observed as a disordered structure in the crystal. The disordered structure clearly indicates that the hydrogen atom of one of the benzyl groups is extracted by one of the olefin carbon atoms of the cyclohexenyl group and that the benzyl carbon atom makes a bond with another olefin carbon to form a thiolactam ring. The mechanism of the ring formation and the chirality of the produced thiolactam are well explained from the reaction cavity.

The crystalline-state reaction is very effective in analyzing the reaction mechanism since a molecular structural change occurs in a crystal keeping the single crystal form.[1] In most solid-state reactions, however, the crystal decomposed when more than 10 to 20% reactant molecules were converted to the product. Recently it became possible to analyze the structure of the product molecule by X-rays even if the product is approximately 10% of the reactant in the crystal.[2–5] This indicates that most solid state photoreactions can be observed in a single crystal by X-ray analysis since the crystallinity may be conserved in the early stages of the reaction (nearly 10% conversion). Such reactions cannot be called single-crystal to single-crystal reactions, since the crystal decomposes when all the reactant molecules are converted to the products. The crystalline-state reaction includes such a partial conversion.

The absolute asymmetric synthesis in the solid state has been extensively studied, in which the chiral product is produced from the achiral reactant in a chiral crystal environment.[6–18] Among the cases studied, *N*,*N*-dibenzyl-1-cyclohexenecarbothioamide, **1**, was photoisomerized to optically active β-thiolactam, 1-benzyl-4-phenyl-2-thioxoazetidine-2-thione-3-spirocyclohexane, **2**, as shown in Scheme 1.[19] Since the reactant crystal has a chiral space group, $P2_1$, the powdered sample with the same chirality gave very high optical yield (94% ee) on exposure to UV light. For the related compounds, the similar absolute asymmetric syntheses were observed.[19–21] In order to make clear the mechanism of the asymmetric induction, we intended to compare the crystal structures before and after irradiation. Since the powdered sample after irradiation showed different X-ray diffraction pattern, it was considered that the reaction proceeded with destroying the crystallinity. The powdered sample after irradiation was recrystallized and the structure was analyzed by X-rays. Comparing the molecular structures before and after the photoreaction, researchers have proposed the process of four-membered ring formation.[19–21]



Scheme 1.

Since the reactant and product molecules are similar to each other,[21] it was assumed that the photoisomerization may proceed with keeping the single crystal form if the photoirradiation would be done carefully. Many trials were performed to make the reaction proceed with retention of the single crystal form. Although the conversion was about 65.0%, the crystal did not decompose significantly and the intensity data were obtained. This paper reports the process and mechanism of the photoisomerization on the basis of the structural change in the crystalline-state reaction.

Experimental

Preparation. The compound, **1**, was prepared using Lawesson's reagent[22] from corresponding α,β-unsaturated amide synthesized from corresponding α,β-unsaturated acid chloride and amine.[23] Yellow prismatic crystals were obtained from a diethyl ether solution, mp 346–347 K.

Photoirradiation. When the crystals suitable for X-ray work were irradiated with high-pressure mercury lamp at 173 K for 2 h,

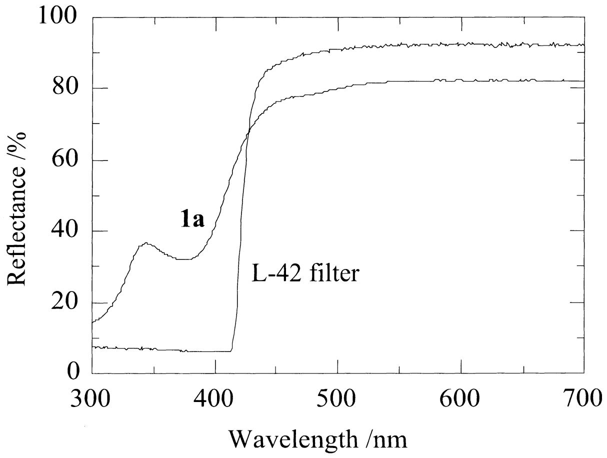


Fig. 1. UV/vis Spectra of **1** and L-42 sharp-cut filter.

Table 1. Result of Crystalline-State Reaction of **1**

Entry	Filter	Temp	Irradiation	Conversion*
		K	h	%
1	L-42	263	19	39.7
2			37	47.5
3			118	57.5
4			330	65.0
5	Y-44	268	254	25.5
6			500	41.4

*Determined by occupancy factors with X-ray diffraction.

they were easily broken apart. This indicated that the reaction occurred from the surface of the crystal and that the reaction rate was too fast. The UV/vis spectra of **1** are shown in Fig. 1. In order to keep the single crystal form, it was suggested to use the light with longer wavelength than the absorption maximum of the compound.[24] After several trials, the best conditions to keep the single crystal form were obtained when the crystal on the cold plate (NISSIN Cool Plate NCP-2215) was irradiated at 263 K using the Xe lamp (USHIO SUPER BRIGHT 152S) with a L-42 filter (HOYA L-42). The structures were analyzed after 19, 37, 118, and 330 h irradiation and the conversion ratio at each stage was estimated from the occupancy factor of the product molecule, which is shown in Table 1. Since the crystallinity became gradually worse, the irradiation condition was fixed in the way shown in entry 4 after this stage.

X-ray Measurement and Refinement. A crystal of 0.3 × 0.1 × 0.1 mm was mounted on a RIGAKU R-AXIS RAPID and the intensity data were collected. Then the same crystal was irradiated in the conditions of entry 4 and then the intensity data were collected in the same way before irradiation. The structures before and after irradiation were analyzed by the direct method using the program *SIR*-97[25] and were refined by the full-matrix least-squares with the program *SHELXL*-97.[26] In the refinement of the structure after irradiation, the bond distances of the reactant molecule were fixed to keep the same ones before irradiation. The positions of the hydrogen atoms were obtained geometrically and not refined. The positional parameters before irradiation are substantially the same as those reported previously.[19] The crystal data and experimental details are given in Table 2. The CIF data are deposited as Document No. 75043 at the Office of the Editor of Bull. Chem. Soc. Jpn. Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition numbers 190702 and 190703.

Results and Discussion

Crystal and Molecular Structure before Irradiation. The crystal structure before irradiation viewed along the b axis is shown in Fig. 2. The molecular structure is shown in Fig. 3; it is the same as that reported previously.[19] The distance between C2 and C8 is 2.863(2) Å. The four-membered ring is formed if a single bond is made between the two atoms after irradiation. The distances between C3 and the hydrogen atoms

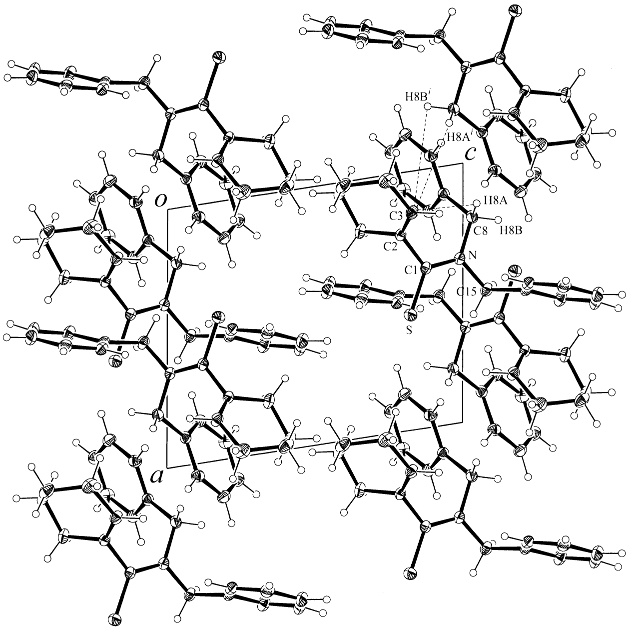


Fig. 2. Crystal packing of an initial **1**: view along the *b* axis. Three dashed lines show the distances between C3 atom and H8A, H8A^i, or H8B are 2.74, 4.70, or 4.18 Å, respectively.

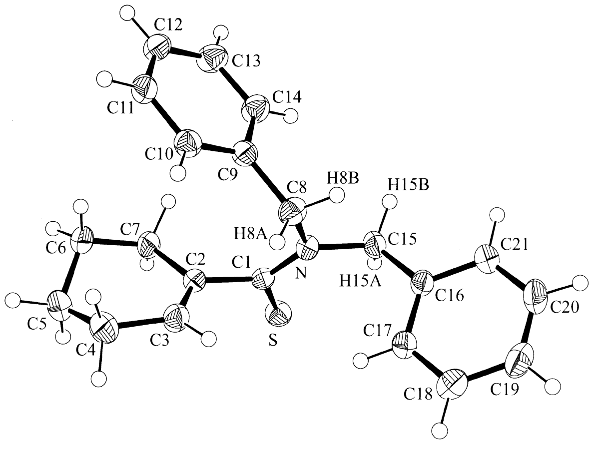


Fig. 3. Molecular structures of the thioamide **1** analyzed by X-ray diffraction. The thermal ellipsoids are drawn at the 50% probability level. The same structure as those reported previously.[2]

of the neighboring molecules are shown in Fig. 2, since the C3 atom extracts a hydrogen atom from the neighboring CH group and becomes a methylene carbon when the four-membered ring is formed. The shorter ones, C3···H8A^i and C3···H8B^i (i indicates the equivalent position of (−x, −0.5 + y, 2−z)), are 4.18(2) and 4.70(2) Å, respectively. The distances between C3 and the hydrogen atoms within a molecule, C3···H8A and C3···H8B, are 2.74(2) and 4.09(2) Å, respectively.

Molecular Structure after Irradiation. When the crystal was irradiated, the *a*, *b*, and *c* axes and the angle *β* gradually expanded and the unit-cell volume increased, as shown in Table 2. The crystal structure after 118 h irradiation is approximately the same as that before irradiation except for the new peaks which appeared around the original molecule. The new peaks were assigned to be the atoms of *β*-thiolactam produced by photoirradiation. The disordered structure composed of the original thioamide and the produced *β*-thiolactam molecules is shown in Fig. 4. It must be emphasized that the atoms of the peripheral part of both molecules occupy nearly the same positions and that the atoms of the central part move to a great extent. The C8 atom moved by 1.416(7) Å to make the four-membered ring. Such favorable conditions seem to make it possible to keep the single crystal form at the early stage of the photoreaction.

Molecular Motion in a Crystal. When the four-membered ring is formed, it is clear that a single bond is formed between C2 and C8. The two atoms should come as close as 1.64(1) Å in the photoreaction. Although C8 moved by 1.416(7) Å, C2 shifted only by 0.311(7) Å, as shown in the disordered structure. In order to make clear the reason why only C8 shifted to make the thiolactam ring, the reaction cavities for the cyclohexene ring and the benzyl group were calculated, as

Table 2. Crystal Data and Experimental Details

	1 initial	**1** irradiated
[Crystal data]		
Formula	$C_{21}H_{23}NS$	$C_{21}H_{23}NS$
Formula weight	321.46	321.46
Temperature/K	173(2)	173(2)
Radiation type	Mo $K\alpha$	Mo $K\alpha$
Wavelength/Å	0.71069	0.71069
Crystal system, space group	Monoclinic, $P2_1$	Monoclinic, $P2_1$
a/Å	8.6541(7)	8.8742(5)
b/Å	10.156(1)	10.3984(7)
c/Å	10.1012(9)	10.1689(7)
β/°	98.756(3)	103.437(2)
V/Å^3	877.48(15)	912.67(10)
Z	2	2
Calculated density/Mg m^{-3}	1.217	1.17
Diffractometer	Rigaku R-AXIS RAPID	Rigaku R-AXIS RAPID
μ/mm^{-1}	0.177	0.177
F(000)	344	344
Crystal size/mm	0.30 × 0.10 × 0.10	0.30 × 0.10 × 0.10
Crystal form, color	Prism, yellow	Prism, yellow
[Data collection]		
θ range/°	2.04–27.41	2.06–27.43
Limiting indices	$-11 \leqq h \leqq 11$	$0 \leqq h \leqq 11$
	$-13 \leqq k \leqq 13$	$0 \leqq k \leqq 13$
	$-13 \leqq l \leqq 13$	$-13 \leqq l \leqq 12$
Reflections collected/unique	3960/3960	2190/2190
θ_{max}/°	27.41	27.43
Completeness to θ/%	99.9	99.4
Absorption correction	None	None
T_{max}, T_{min}	0.8304, 0.6082	0.8429, 0.6189
[Refinement]		
Refinement on	F^2	F^2
Data/restraints/parameters	3960/1/300	2190/1/363
Goodness-of-fit on F^2	1.013	1.054
$R_1(F^2 > 2\,s(F^2))$, wR_2	0.0355, 0.0866	0.0585, 0.1450
R_1(all data), wR_2	0.0373, 0.0878	0.0658, 0.1513
$\Delta\rho_{max}$/e Å^{-3}	0.23	0.22
$\Delta\rho_{min}$/e Å^{-3}	−0.32	−0.19
Absolute structure parameter	−0.04(5)	0.02(10)

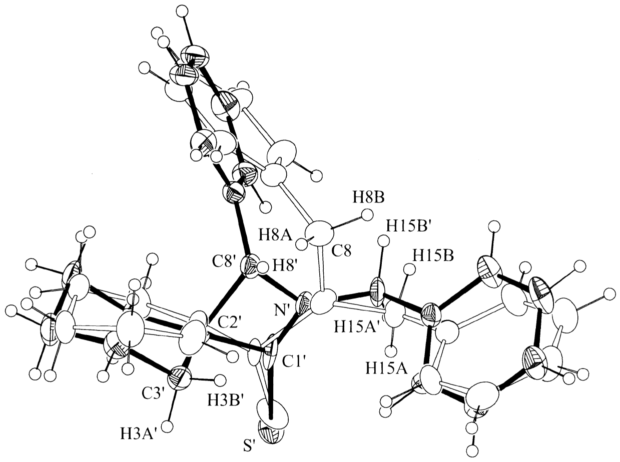


Fig. 4. Disordered molecular structure of **1** and **2** after 118 h irradiation: open line is **1** and solid line is **2**. The conversion is 57.5% (Entry 3). The thermal ellipsoids are drawn at the 20% probability level.

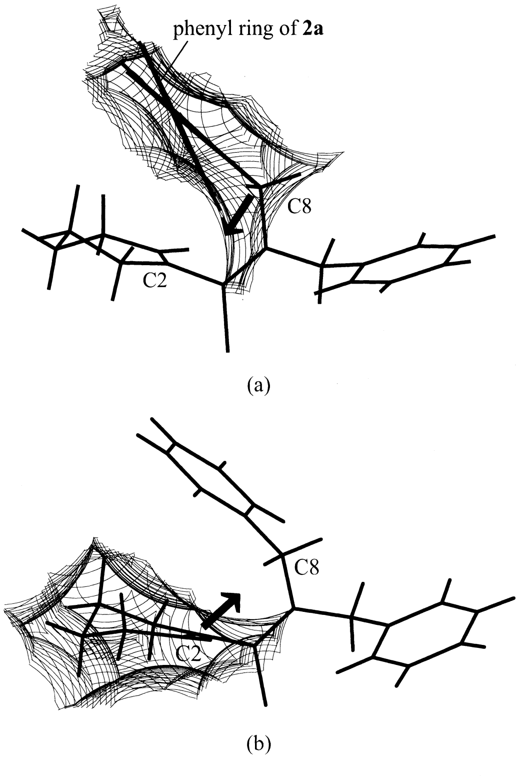


Fig. 5. (a) Reaction cavity for the benzyl group of **1** before irradiation. The arrow indicates the movement of C8 atom if only the atom moves in cyclization of the 4-membered ring. The terminal point is in the reaction cavity of initial benzyl group. Because the cavity has large space enough for planar phenyl ring to move. The phenyl ring of **2** is also shown in this figure. (b) Reaction cavity for the cyclohexene group of **1** before irradiation. The arrow indicates the movement of C2 atom if the atom moves in cyclization of the 4-membered ring. The terminal point is completely out the reaction cavity of initial benzyl group. Because the cavity was not large enough for large cyclohexene group to move.

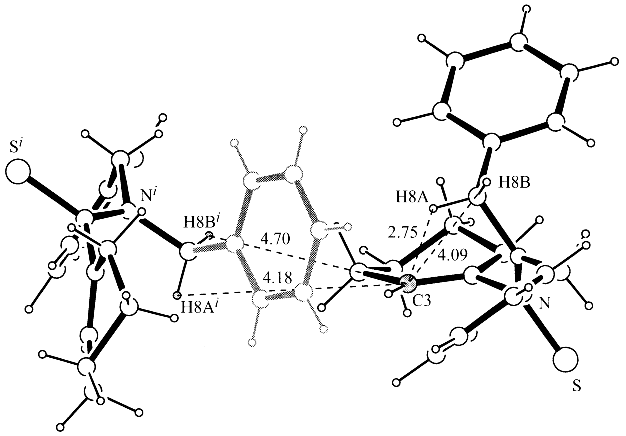


Fig. 6. The intra- and intermolecular distance between C3 and H8A or H8B. A central benzene ring is upward.

shown in Fig. 5, using the program *CAVITY*.[27] Although a wide space is observed around C8, there remains a considerably narrow space around C2. If the C8 atom moves along the arrow to make a bond by 1,416(7) Å, C8 remains in the cavity. However, C2 may go outside the cavity if it moves along the arrow to make a bond. This is a reason why only C8 shows the large movement.

Hydrogen Extraction Mechanism. The final question still remains. Which hydrogen is extracted by C3 when the crystal was exposed to UV light? Since the C–C bond is made between C2 and C8, H8A or H8B within a molecule or in the neighboring molecules should be extracted by C2. Those H8A and H8B atoms around C3 are shown in Fig. 6. The intramolecular H8A atom is probably extracted by C3, since the interatomic distance is the shortest. This indicates that the extracted H and original H3 atoms should occupy the positions above and below the cyclohexane ring. Recently a new compound with deuterium atoms was prepared, which has deuterium atoms at the positions of H8A and H8B. Large crystals suitable for neutron analysis were obtained. If the crystal structures before and after photoirradiation were analyzed by neutron diffraction method, the deuterium atom extracted from C8 and bonded to C3 within a molecule should occupy the position above the cyclohexane ring, the equatorial position H3B′ in Fig. 4. If the deuterium atom at the $\mathrm{H8A}^i$ position may be extracted by C3, it should occupy the position below the cyclohexane ring, the axial position H3A′ in Fig. 4. The structure after irradiation will give a definitive answer to the question which hydrogen atoms, intramolecular or intermolecular, are transferred in the process of the four-membered ring formation. The neutron data collection at Japan Atomic Energy Research Institute (JAERI) is in progress.

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