

Neutron diffraction analysis of deuterium transfer in chiral β -thiolactam formation in the crystalline state

Takaaki Hosoya,^a Hidehiro Uekusa,^a Yuji Ohashi,^{a*} Takashi Ohhara,^b Ichiro Tanaka^c and Nobuo Niimura^c

^aDepartment of Chemistry and Materials Science, Tokyo Institute of Technology, O-okayama, Meguro, Tokyo 152-8551, Japan,

^bInstitute of Materials Structure Science, High Energy Accelerator Research Organization, Oho, Tsukuba, Ibaraki 305-0801, Japan, and

^cNeutron Structural Biology, Advanced Science Research Center, Japan Atomic Energy Research Institute, Tokai, Naka, Ibaraki 319-1195, Japan

Correspondence e-mail:
yujihashi@cms.titech.ac.jp

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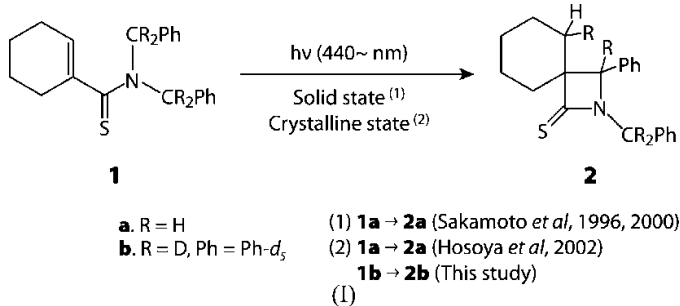
Since *N,N*-dibenzyl-1-cyclohexenecarbothioamide is photoisomerized to the optically active β -thiolactam with the retention of the single-crystal form, the mechanism of chirality induction was identified by X-ray crystal structure analyses during the process of the reaction [Hosoya *et al.* (2002). *Bull. Chem. Soc. Jpn.*, **75**, 2147–2151]. In order to clarify the mechanism of hydrogen transfer in the reaction, the H atoms of the benzyl groups were replaced with deuterium atoms. The crystal structure after photoisomerization was analyzed by neutron diffraction. One of four deuterium atoms of the two benzyl groups is transferred to the C atom of the cyclohexene ring. The absolute configuration of the $-\text{C}^*\text{HD}-$ group (chiral methylene) in the photoproduct β -thiolactam revealed that the deuterium atom occupies the equatorial position. This suggests that the deuterium atom is not transferred from the benzyl group of a neighbouring molecule, but from one of the benzyl groups within the molecule.

1. Introduction

A photoinduced absolute asymmetric synthesis from an achiral *N,N*-dibenzyl-1-cyclohexenecarbothioamide (**1a**) to a chiral β -thiolactam (**2a**) in the solid state has been reported (Sakamoto *et al.*, 1996, 2000), as shown in (I). After many trials, the photoreaction partly proceeded without the destruction of the single-crystalline nature. The structural change from (**1a**) to (**2a**) was directly observed by X-ray crystal structure analysis (Hosoya *et al.*, 2002). It was assumed from the results mentioned above that an H atom is extracted from a benzyl group and transferred to one of the photoexcited alkenyl C atoms of the cyclohexene group at the first stage, and then a new bond between another alkenyl carbon and the benzyl carbon radical produced by the hydrogen abstraction is formed. A four-membered β -thiolactam ring is thus produced. Although the reaction mechanism explaining how the chirality is introduced in the product during four-membered ring formation in a crystal was made clear by X-ray analysis, there remained an unsolved problem as to which hydrogen was transferred, since there are several candidates.

The H-atom or proton transfer is one of the most elemental phenomena and plays a key role in various reactions, for example, absolute asymmetric synthesis *via* intramolecular (Ihmels & Scheffer, 1999; Sakamoto *et al.*, 2000; Sakamoto, 2005) or intermolecular (Tang *et al.*, 1995; Chang *et al.*, 1987) H-atom transfer, photochromism (Hadjoudis & Mavridis, 2004; Naumov *et al.*, 2005), asymmetric hydrogen transfer with catalysis (Zassinovich & Mestroni, 1992; Clapham *et al.*, 2004)

and enzymatic reactions (Soda *et al.*, 2001; Pierre & Thomas, 2005).



If more than two H atoms participate in isomerization reactions, the deuterium labeling technique of the target H atom is a very powerful method to analyze the mechanism of the H- or D-atom transfer by ¹H NMR and IR spectra. However, peak assignments are very difficult to make in the case of a solid-state reaction, in which not only intramolecular H or D atoms, but also intermolecular H or D atoms may be transferred. The single-crystal X-ray analysis of the crystalline-state reaction also cannot determine the hydrogen-transfer mechanism even if the target H atom is replaced with the D atom, because X-ray diffraction usually cannot distinguish the H atom from the D atom. On the other hand, neutron diffraction is able to analyze the position and thermal motion of an H or D atom accurately and to distinguish a D atom from an H atom. When the target H atoms of the reactant molecule are replaced with D atoms as indicators and the reaction proceeds with the retention of the single-crystalline form, the transfer of the target D atom in the crystalline-state reaction can be observed directly. Since the neutron scattering length for the D atom is positive, whereas that of the H atom is negative, the deuterium and hydrogen positions are seen as positive and negative peaks, respectively, in the nucleus density map. Therefore, the D-atom transfer in the crystalline-state reaction can be directly observed by neutron diffraction analysis since the peak heights of the replaced D and H atoms are gradually changed in the process of isomerization.

Especially if a chiral —C*HD— methylene is produced from the achiral =CH— group, the position of the D atom, *i.e.* the absolute configuration of the chiral methylene, indicates the source of the D atom. There were some previous reports about the determination of the absolute configuration of such a chiral —C*HD— methylene by neutron diffraction (Yuan *et al.*, 1988, 1994). However, there are some serious problems to overcome in the neutron diffraction analysis of the crystalline-state reaction. Owing to the weak intensity of the neutron beam compared with that of X-rays, it was necessary to use a large crystal of more than 1 mm³ in order to collect enough intensity data, although it is not easy to make such large crystals for most organic compounds. Moreover, the light should penetrate into the large crystal, because the photo-reaction should proceed not from the surface of the crystal but inside the crystal. Owing to the difficulties, only a few exam-

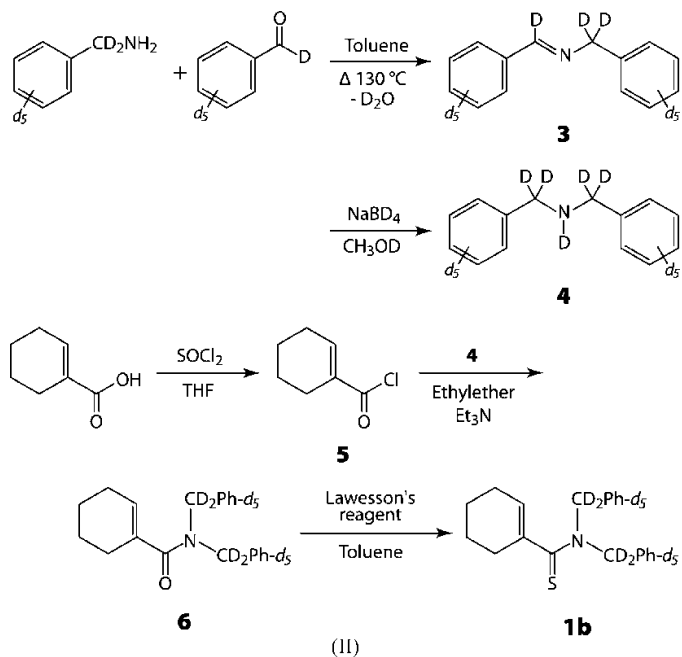
ples of crystalline-state reactions in cobaloxime complexes have been reported by neutron diffraction (Ohgo *et al.*, 1996*a,b*, 1997; Ohhara *et al.*, 2000, 2001, 2002).

We intended to apply neutron diffraction analysis to the crystalline-state photoreaction of the α,β-unsaturated thioamide mentioned above in order to determine the H-atom transfer mechanism. The preliminary result has already been reported (Hosoya *et al.*, 2003).

2. Experimental

2.1. Preparation

N,N-Di(benzyl-*d*₇)-1-cyclohexenecarbothioamide (**1b**) was prepared in a similar way to the procedure reported (Hosoya *et al.*, 2002) for the corresponding α,β-unsaturated amide by the thionation of the carbonyl group with Lawesson's Reagent (Thomsen *et al.*, 1984), as shown in (II).



2.1.1. Dibenzylamide-*d*₁₅. A toluene solution (10 ml) of benzyl-*d*₇-amine (3.179 g, 28.11 mmol), benzaldehyde-*d*₆ (3.159 g, 28.11 mmol) and a few boiling stones were placed in a 200 ml round-bottomed flask equipped with a Dean–Stack fractionating column, a Dimroth condenser and a mantle heater. The mixture was refluxed at *ca* 403 K with an azeotropic distillation of the water produced. When the generation of water stopped, the mixture solution was cooled down to room temperature and the toluene was evaporated. A yellow oil of *N*-benzylidenebenzylamine-*d*₁₃ (**3**) was obtained.

The imine (**3**) was dissolved in methanol-*d* (100 ml) and reduced with sodium borodeuteride (NaBD₄, 1.18 g, 28.11 mmol). After stirring for 2 h, the solvent was evaporated. Dibenzylamine-*d*₁₅ (**4**) was extracted by diethyl ether from the residual colourless liquid and neutralized by DCl (35 wt %, 3.77 g, 37.3 mmol) solution. The resulting white powder was washed with acetone and diethyl ether, yielding

6.95 g (27.84 mmol, 99%). Then (4) was regenerated from the DCl salt by the addition of a D₂O solution of NaOD, and then extracted with diethyl ether.

2.1.2. *N,N*-Di(benzyl-*d*₇)-1-cyclohexenecarbothioamide. 1-Cyclohexene-1-carboxylic acid (2.50 g, 19.8 mmol) was dissolved in 20 ml of THF and placed in a 100 ml flask equipped with a dropping funnel. The solution was cooled with an ice bath. Under stirring, 7.93 ml of thionyl chloride (SOCl₂, 19.8 mmol) was added dropwise over a period of 10 min. A Dimroth condenser was used rather than a dropping funnel and the mixture was refluxed (oil bath temperature *ca* 363 K) for 2 h. After removing thionyl chloride and THF by distillation, a brownish-yellow liquid, 1-cyclohexene-1-carbonyl chloride (5), was obtained.

A diethyl ether solution (100 ml) of (4) (4.00 g, 19.8 mmol) and equimolar triethylamine (6.8 ml, 19.8 mmol) were placed in a 200 ml round-bottomed flask, and cooled with an ice bath. Under vigorous stirring, 10 ml of a diethyl ether solution of (5) was added dropwise through the dropping funnel over a period of 30 min. A vigorous and exothermic reaction occurred and a white solid was precipitated. After 2 h stirring, the mixture was suction-filtered. The filtrate was washed successively with 2*N* HCl, saturated sodium hydrogen carbonate (NaHCO₃) solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate (Na₂SO₄), and then the solvent was removed with a rotary evaporator. A white powder, *N,N*-di(benzyl-*d*₇)-1-cyclohexenecarbothioamide (6) was obtained and isolated by silica-gel column chromatography (*n*-hexane/ethyl acetate = 8/1).

Lawesson's reagent (3.03 g, 7.5 mol) and (6) (4.79 g, 15.0 mol) were dissolved in 100 ml of toluene and placed in a 200 ml two-necked flask. The mixture was refluxed at *ca* 353 K for 2 h. After cooling and evaporation of the solvent, *N,N*-di(benzyl-*d*₇)-1-cyclohexenecarbothioamide (1*b*) was separated from the solution mixture by silica-gel column chromatography (*n*-hexane/ethyl acetate = 5/1), and recrystallized from the diethyl ether solution. Crystals large enough for

neutron diffraction measurement were obtained. Four α -H atoms of the two benzyl groups in (1*b*) were successfully deuterated by over 98%, which was confirmed by ¹H NMR measurement of the crystals. A small single crystal [0.30 × 0.10 × 0.10 mm³, crystal (I)] and a large one [4.50 × 1.50 × 1.40 mm³, crystal (II)] were prepared for X-ray and neutron diffraction analyses, respectively. Crystal (II) was subsequently photo-irradiated. A small single crystal for X-ray diffraction measurement after irradiation [0.20 × 0.20 × 0.10 mm³, crystal (II')] was cut out from the central part of crystal (II) after carrying out the neutron diffraction measurement of (II).

2.2. Photoirradiation

The photoreaction in a single crystal usually occurs from the surface of the crystal and the crystal easily decomposes into microcrystalline particles. It is very difficult to isomerize a crystal large enough for neutron diffraction without the loss of crystallinity. It is very important for a photoreaction in the crystalline state to be able to select the irradiation wavelengths. Use of wavelengths corresponding to the absorption tail has been recommended (Enkelmann *et al.*, 1993). Fig. 1 shows the UV-vis reflectance spectra of the powdered crystals with the spectrophotometer (JASCO V-560). A peak around a wavelength of 375 nm corresponds to the excitation of a C=C bond of the cyclohexene group. The wavelengths from a xenon lamp (SAN-EI SUPER BLIGHT 152S with USHIO xenon short-arc lamp UXL-151DO) were selected with two filters; a Y-44 sharp-cut filter (TOSHIBA), cutting off the light shorter than 440 nm, and a heat-absorbing water filter. The selected wavelengths are also shown in Fig. 1. Small crystals with a volume of *ca* 0.2 mm³ were irradiated with light for 500 h as mentioned above as a preliminary experiment. Crystal structure analysis after irradiation showed that more than 40% of the molecules were isomerized to β -thiolactam. For crystal (II), both sides were irradiated under the conditions mentioned above for 1500 h at 273 K on a cool plate (NISSIN Cool Plate NCP-2215). Although the crystal after irradiation did not seem to be decomposed, the rocking curve of each reflection was expanded. This indicates that a slight increase in mosaicity may occur due to the photoreaction.

2.3. X-ray diffraction analysis of (1*b*) before and after irradiation

X-ray diffraction data on (I) and (II') were collected at 100 and 173 K using a Rigaku R-AXIS RAPID diffractometer (Mo *K* α radiation) and equipped with a Rigaku nitrogen gas-flow type cryostat. The data were collected by the ω -scan method with a 5.0° oscillation width and 200 s exposure time per frame. The data were integrated, scaled, sorted and averaged by *PROCESS AUTO* (Rigaku Corporation, 1998). The structures were solved by direct methods using *SHELXS97* (Sheldrick, 1997*a*).

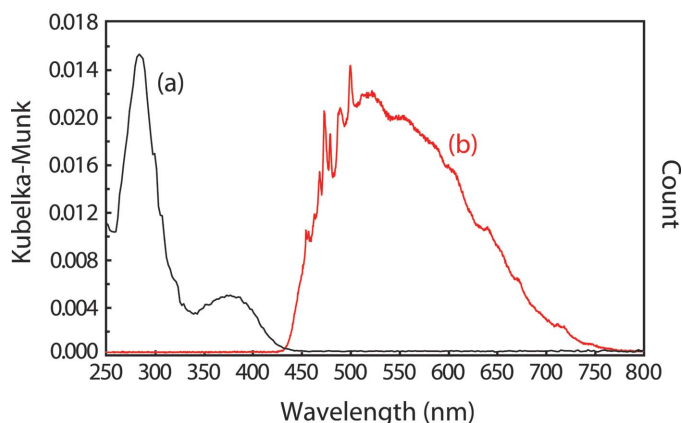


Figure 1
(*a*) UV-vis reflectance spectrum of a crystal of (1*b*) in MgSO₄ (2.0 wt %) at 297 K. The spectrum was converted from reflectance into Kubelka-Munk. (*b*) Light wavelength distribution of xenon lamp through a fiber-optic waveguide, a Y-44 sharp cut filter (HOYA) and a heat absorbing water filter.

Table 1
Experimental details.

	(I)	(II')	(II)
Crystal data			
Chemical formula	C ₂₁ H ₉ D ₁₄ NS	C ₂₁ H ₉ D ₁₄ NS	C ₂₁ H ₉ D ₁₄ NS
<i>M_r</i>	335.43	335.43	335.43
Cell setting, space group	Monoclinic, <i>P</i> ₂ ₁	Monoclinic, <i>P</i> ₂ ₁	Monoclinic, <i>P</i> ₂ ₁
<i>a</i> , <i>b</i> , <i>c</i> (Å)	8.5992 (7), 10.1263 (7), 10.0412 (7)	8.7075 (5), 10.2068 (6), 10.0908 (9)	8.9117 (11), 10.5512 (17), 10.3463 (13)
β (°)	98.364 (4)	99.909 (3)	102.589 (8)
<i>V</i> (Å ³)	865.07 (11)	883.45 (11)	949.5 (2)
<i>Z</i>	2	2	2
<i>D_x</i> (Mg m ⁻³)	1.234	1.208	1.173
Radiation type	Mo <i>K</i> α	Mo <i>K</i> α	Neutron
Wavelength (Å)	0.71073	0.71073	1.51000
No. of reflections for cell parameters	7397	8684	1880
θ range (°)	2.0–25.3	2.0–27.5	5.8–49.0
μ (mm ⁻¹)	0.19	0.18	0.21
Temperature (K)	173 (2)	173 (2)	293 (2)
Crystal form, colour	Prism, pale yellow	Prism, pale yellow	Prism, pale yellow
Crystal size (mm)	0.30 × 0.10 × 0.10	0.20 × 0.20 × 0.10	4.50 × 1.50 × 1.40
Data collection			
Diffractometer	Rigaku RAXIS-RAPID	Rigaku RAXIS-RAPID	BIX-III
Data collection method	ω scan	ω scan	ω scan
Absorption correction	Multi-scan (based on symmetry-related measurements)	Multi-scan	Gaussian
<i>T_{min}</i>	0.946	0.964	0.591
<i>T_{max}</i>	0.982	0.982	0.784
No. of measured, independent and observed reflections	7397, 2850, 2807	8684, 3665, 3573	1880, 1301, 1300
Criterion for observed reflections	<i>I</i> > 2σ(<i>I</i>)	<i>I</i> > 2σ(<i>I</i>)	<i>I</i> > 2σ(<i>I</i>)
<i>R_{int}</i>	0.031	0.038	0.044
θ_{\max} (°)	25.3	27.5	49.0
Range of <i>h</i> , <i>k</i> , <i>l</i>	–10 ⇒ <i>h</i> ⇒ 10 –12 ⇒ <i>k</i> ⇒ 11 –12 ⇒ <i>l</i> ⇒ 12	–11 ⇒ <i>h</i> ⇒ 11 –12 ⇒ <i>k</i> ⇒ 13 –13 ⇒ <i>l</i> ⇒ 13	–8 ⇒ <i>h</i> ⇒ 8 –10 ⇒ <i>k</i> ⇒ 10 –10 ⇒ <i>l</i> ⇒ 10
Refinement			
Refinement on	<i>F</i> ²	<i>F</i> ²	<i>F</i> ²
<i>R</i> [<i>F</i> ² > 2σ(<i>F</i> ²)], <i>wR</i> (<i>F</i> ²), <i>S</i>	0.027, 0.062, 1.07	0.043, 0.116, 1.06	0.079, 0.197, 1.08
No. of reflections	2850	3665	130
No. of parameters	301	270	297
H-atom treatment	Independent	Constrained	Mixture of independent and constrained refinement
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0352P)^2 + 0.1521P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0758P)^2 + 0.1336P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.1086P)^2 + 0.1004P]$, where $P = (F_o^2 + 2F_c^2)/3$
(Δ/σ) _{max}	< 0.0001	< 0.0001	< 0.0001
Δρ _{max} , Δρ _{min} (e Å ⁻³)	0.16, –0.17	0.39, –0.17	0.04, –0.04
Extinction method	SHELXL	SHELXL	None
Extinction coefficient	0.050 (3)	0.032 (4)	–
Absolute structure	Flack (1983)	Flack (1983)	Determined by (II')
Flack parameter	–0.02 (5)	–0.02 (7)	–

Computer programs used: *PROCESS-AUTO* (Rigaku Corporation, 1998), local program, *HKL* (HKL Research, Inc.; Otwinowski & Minor, 1997), *CrystalStructure3.6* (Rigaku Corporation, 2004), *SIR2004* (Burla *et al.*, 2005), *SHELXS97* (Sheldrick, 1999a), initial structure determined by X-rays, *SHELXL97* (Sheldrick, 1997b), *ORTEP3 for Windows* (Farrugia, 1997).

2.4. Neutron diffraction measurement of (1b) after irradiation

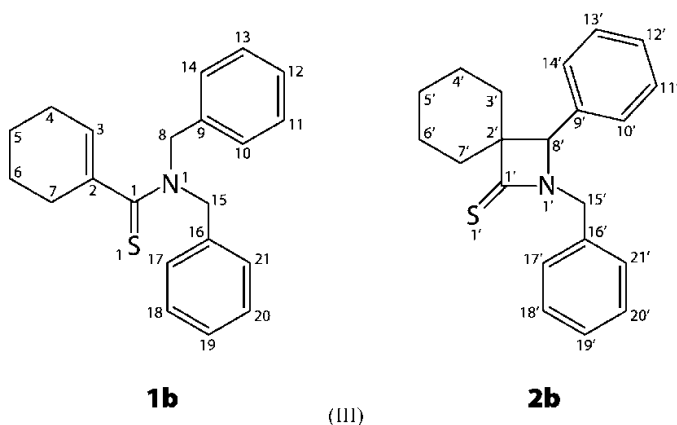
After photoirradiation crystal (II) was fixed on an aluminium plate pin and mounted on a BIX-III diffractometer (Tanaka *et al.*, 2002), equipped with a neutron imaging plate, NIP (Haga *et al.*, 1999), set up at the JRR-3 reactor room of the Japan Atomic Energy Research Institute (JAERI). The diffraction data at 293 K using perfect silicon-crystal-monochromated neutron radiation ($\lambda = 1.51000$ Å) were collected using the ω scan method with a 1.0° oscillation width and 25 min exposure time per frame. Since BIX-III is a single-axis

diffractometer and NIP is short in a longitudinal direction, the data sets were divided by a series of aluminium pin angle values (*ca* 180, 135 and 90°) rather than changing the χ circle position, and the total oscillation ranges were 180, 90 and 90°, respectively. The peaks of the resulting NIP frames were integrated using the *Denzo* program with a resolution range of 45.0–1.0 Å, and then scaled with the *Scalepack* program (Otwinowski & Minor, 1997). A numerical absorption correction by Gaussian integration was carried out using the face indices determined by a SMART CCD diffractometer using the *ABSG* program (Coppens, 1970) included in

PLATON (Spek, 2003). A total of 1301 independent reflections were observed.

3. Results and discussion

Structure refinements were carried out with full-matrix least-squares using *SHELXL97* (Sheldrick, 1997b). Atomic labels used for the structure analyses are shown in Scheme (III). A summary of the experimental conditions and refinement results for crystals (I), (II') and (II) is presented in Table 1.¹ Diagrams of molecular and crystal structures were produced using *ORTEP-3 for Windows* (Farrugia, 1997) and some of these were rendered using *POV-Ray 3.6* (The POV-Ray Team, 2004), and the three-dimensional Fourier map was calculated using the *XFit* program of *XtalView* (McRee, 1992) and rendered by *Raster3D* (Bacon & Anderson, 1988; Merritt & Murphy, 1994).



3.1. Structure before irradiation

The structure of crystal (I) was solved by direct methods using *SHELXS97* and then it was refined with anisotropic atomic displacement parameters (ADPs) for all the non-H atoms. The H and D atoms were located in the difference electron-density maps and all of their parameters including the positional and isotropic atomic displacement parameters were refined freely.

The crystal structure is nearly the same as that of the non-deuterated crystal of (1a) reported previously (Hosoya *et al.*, 2002). Fig. 2 shows the molecular structure of (I) determined by X-rays. The D atoms around C3 were D8A, D8B, D8Aⁱ and D8Bⁱ, and the C3...D distances were 2.68 (2), 4.09 (2), 4.72 (2) and 4.12 (2) Å, respectively [symmetry code (i) $2 - x, -\frac{1}{2} + y, -z$]. The D8A atom among the four D atoms mentioned above occupies an exceptionally close position to C3 and the distance 2.68 (2) Å is much shorter than the sum of the van der Waals radii of the C and D atom, 3.07 Å.

¹ Supplementary data for this paper are available from the IUCr electronic archives (Reference: OG5014). Services for accessing these data are described at the back of the journal.

3.2. Structure after irradiation

3.2.1. X-ray diffraction analysis. The structure of crystal (II') was refined with the non-hydrogen atomic coordinates of (I) as the rigid-model starting parameters. Some extra peaks appeared on the difference electron-density map and the peaks were assigned to a photoproduct β -thiolactam molecule (2b). However, there were no significant peaks corresponding to the two C atoms of the cyclohexyl ring of (2b), C2' and C7'. Therefore, we assumed that these atoms did not move. Since the other atoms of the cyclohexyl group were close to their initial positions, six C—C bond lengths of the group were restrained for the 1.535 (8) Å listed in *International Tables for Crystallography*, Vol. C. Two site-occupancy factors (SOFs) of atoms which belong to (1b) and (2b) were refined and summed up to exactly 1.0, except those of C2 and C7, which were fixed at 1.0. The positional parameters of the H or D atoms were calculated with the riding model and the isotropic ADPs were constrained by 1.2 times those of the bonded atoms for the H or D atoms of the phenyl and methylene groups. The final SOF of (2b) was 0.1481 (8). Although the appearance of the crystal did not alter after photo-irradiation, the final *R* values of the photo-irradiated crystals were somewhat high, probably due to the partial decomposition of the crystal. Fig. 3 shows the molecular structure of (1b) and (2b) observed in crystal (II'). The crystal structure is nearly the same as that of the non-deuterated crystal, (1a) and (2a), reported previously (Hosoya *et al.*, 2002).

3.2.2. Neutron diffraction analysis. The structures of crystal (II) were refined with *SHELXL97* using the non-H-atom coordinates of (II') as an initial model. H and D atoms were determined from the difference-Fourier map. The positional parameters of the H and D atoms were refined with restraints of the C—H/D bond distances, except those of the methylene H atoms of the cyclohexenyl [in (1b)] and cyclohexyl [in (2b)] groups, which were calculated using the riding model. The restraints and constraints of the bond distances were carried out using the values of Table 9.5.1.1 in *International Tables for*

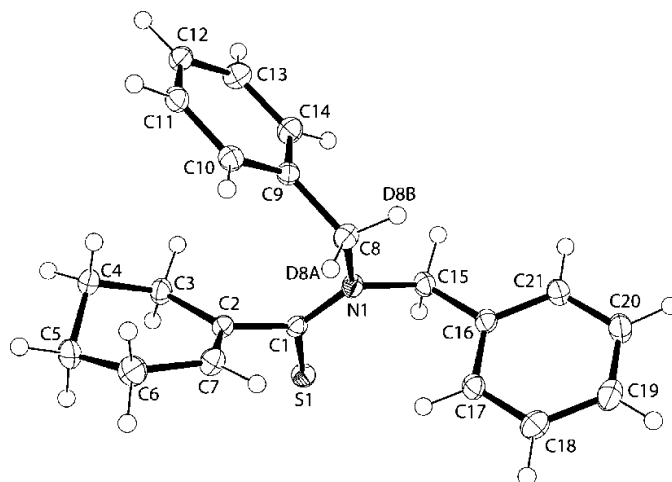


Figure 2
Molecular structure (1b) in crystal (I) (before irradiation, X-rays). Displacement ellipsoids are drawn at the 50% probability level.

Crystallography, Vol. C [C_{Ph}—D: 1.083 (11) Å, C_{methylene}—H₂/D₂: 1.092 (13) Å, C3—H3: 1.077 (12) Å, each standard error was used for the restraints]. The ADPs of all the H atoms and all the atoms of the product β -thiolactam (**2b**) were refined isotropically and those of the other atoms were treated anisotropically. As in the structure refinement of (II'), two site occupancy factors (SOFs) of atoms which belong to (**1b**) and (**2b**) were refined and summed up to exactly 1.0.

Fig. 4 shows a difference-Fourier density map ($F_o - F_c$) for (II) around the C3' atom from neutron diffraction data. The map was calculated with contours at the 3σ level after the refinement of all the atoms, except the H or D atoms bonded

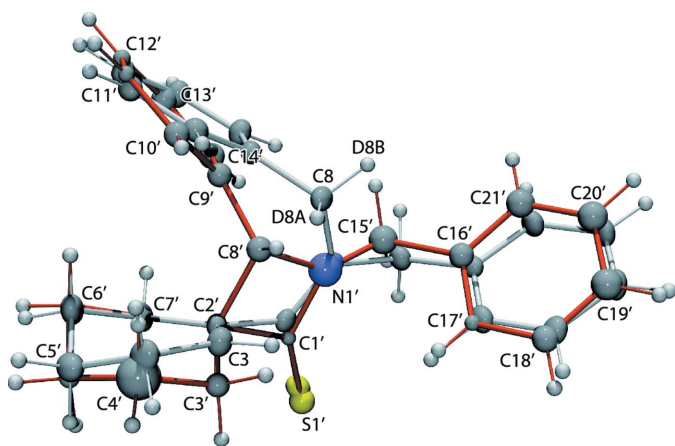


Figure 3

Molecular structure of (1b) and (2b) in crystal (II') (after irradiation, X-rays). Displacement ellipsoids are drawn at the 30% probability level. The reactant (1b) (white bond) and the product (2b) (red bond) are disordered, and the site occupancy factor of (2b) was 0.1481 (8).

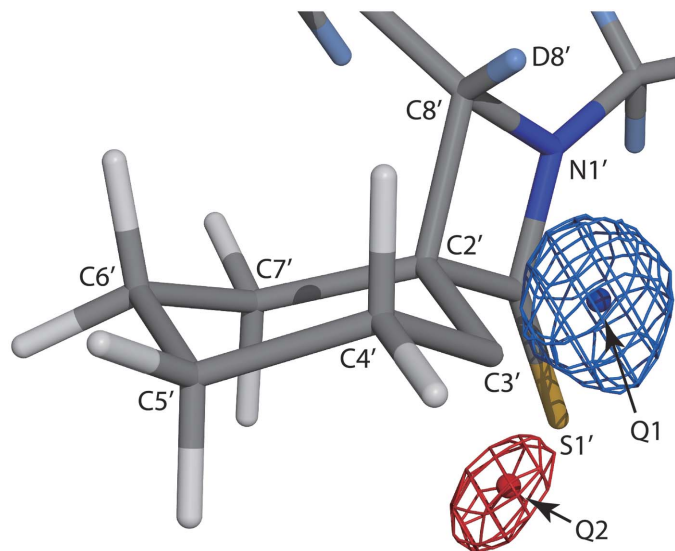


Figure 4

Difference-Fourier map ($F_o - F_c$) around the C3' atom from neutron diffraction data. The map was calculated with contours at the 3σ level. Positive and negative densities are shown as blue and red meshes, respectively, in which peak tops, Q1 (blue) and Q2 (red), are shown at the distances of 1.07 (4) and 1.06 (3) Å from C3', respectively. The peak heights of Q1 and Q2 were at the 5 and 4 σ levels, respectively.

to the C3' atom. In neutron diffraction, a Fourier transform of the diffraction intensities gives the densities of the neutron scattering lengths, which for H and D atoms are -3.739 (1) and 6.671 (4) fm, respectively. Therefore, the H atom is observed as a negative peak, whereas the D atom is a positive peak. A blue positive peak, $Q1$ [$Q1-C3'$: 1.07 (4) Å], and a red negative peak, $Q2$ [$Q2-C3'$: 1.06 (3) Å], were located at the equatorial and the axial positions of the photoproduct cyclohexyl ring, respectively. It is reasonable to assign $Q1$ and $Q2$ to D3' and H3', respectively. In order to examine the H/D occupancies, we performed the refinements for three models of the configuration of the chiral methylene, which are the D-axial, D-equatorial and disordered models.

D-axial model: This is an ordered model in which D3' occupies an axial position of the cyclohexyl group. Peaks Q1 and Q2 were relabelled as H3' and D3', respectively. The positional parameters of all the atoms were fixed and only the ADPs were refined. The result was not satisfactory. U_{iso} of H3' and D3' were 2.0000 (ceiling value in *SHELXL*) and 1.5064, respectively, and the refinement did not converge at all. The R_1 value for this model was 0.0841.

D-equatorial model: This is also an ordered model in which D3' occupies an equatorial position. The refinement condition was the same as the D-axial model. The result was satisfactory. U_{iso} of H3' and D3' were 0.065 (9) and 0.05 (1), respectively, and the refinement converged. The R_1 value for this model was 0.0792.

Disordered model: This is a static disordered model of the two models noted above, *i.e.* D3'(H3')—C3'—H3'(D3'). In this model, the SOFs of H3' and D3' were refined with the restraint that the sum of the SOFs for the D-equatorial and D-axial models was equal to the SOF of the atoms of (2b). The ADPs of H3' and D3' in the D-axial model were fixed to those of D3' and H3' in the D-equatorial model, respectively. The result was that the SOF for the D-equatorial model was 0.228 (1), whereas the D-axial model was 0.001 (1). This indicates that only the D-equatorial model exists predominantly in the

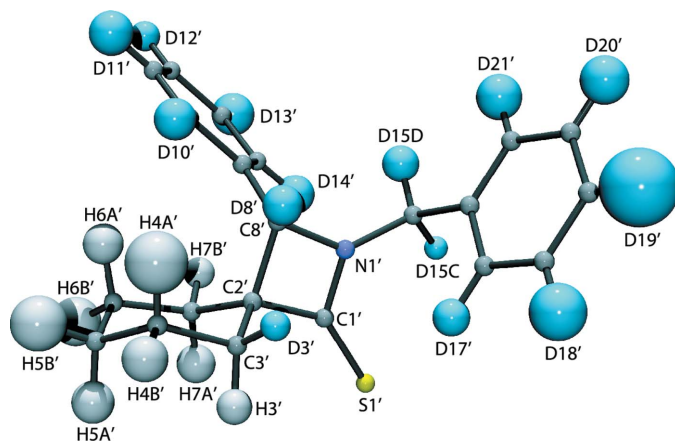
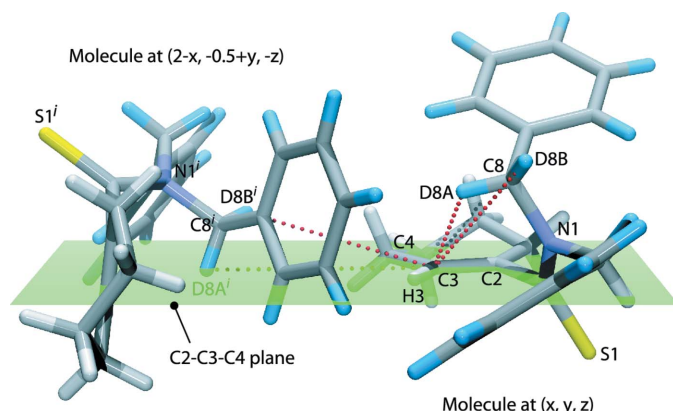


Figure 5

Molecular structure of (2b) in crystal (II) (after irradiation, neutron diffraction). Reactant (1b) was removed for clarity. The isotropic displacement ellipsoids of the H (white) and D (sky blue) atoms are shown, while those of the non-H atoms are shown as small spheres. The site-occupancy factor of (2b) was 0.2365 (9).

**Figure 6**

Two adjacent molecules in crystal (I) are shown. One is an original molecule and another is a molecule related by the symmetry operation $2-x, -\frac{1}{2}+y, -z$. Four D atoms around the C3 atom of the original molecule, D8A, D8B, D8A' and D8B' are shown in half transparent spheres [symmetry code: (i) $2-x, -\frac{1}{2}+y, -z$]. The green half-transparent plane shows a plane defined by the C2, C3 and C4 atoms. The distances from C3 were 2.68 (2), 4.09 (2), 4.72 (2) and 4.12 (2) Å, respectively.

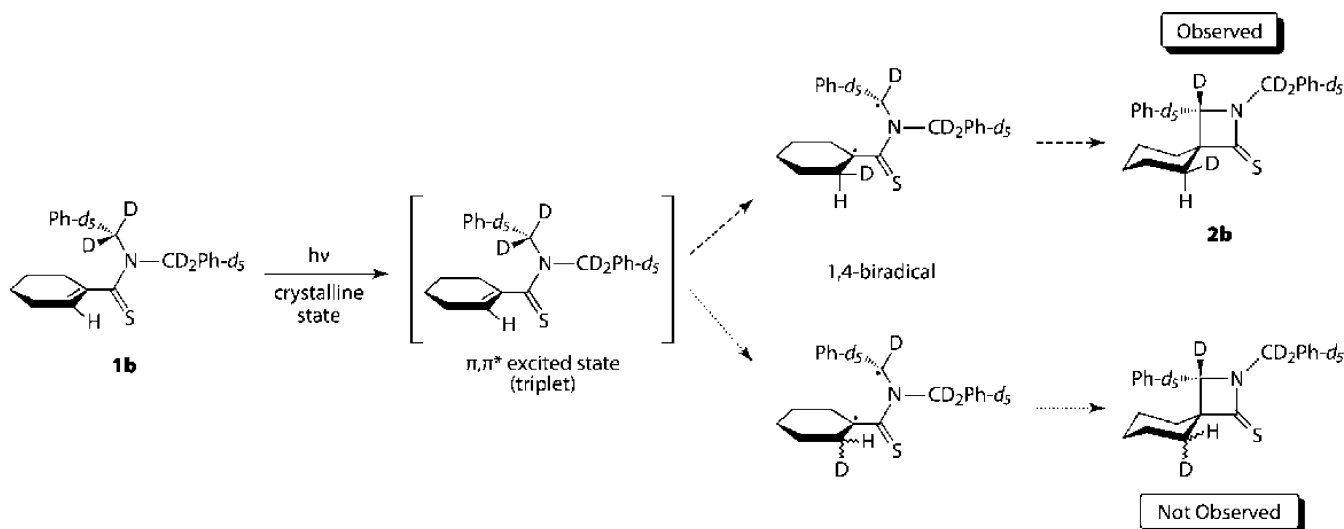
disordered model. Therefore, the disordered model was rejected.

Finally, the structure for the D-equatorial model was refined; the results are shown in Fig. 5. The SOF of the photoproduct β -thiolactam was 0.2365 (9), which is larger than the value obtained for (II') by X-rays, 0.1481 (8). Since the small crystal (II') was cut out from the central part of (II), the difference between the occupancy factors may suggest that the β -thiolactam molecules are preferentially formed at the surface of the large single crystal. The absolute structure of (II) was determined from the X-ray diffraction analysis of (II').

3.3. Deuterium transfer mechanism

This photoreaction is assumed to be initiated from the γ -hydrogen abstraction by the C3 atom of the photoexcited alkene. In the crystal structure of (II) the site-occupancy factor of D3', 0.25 (1), is close to those of the other atoms of β -thiolactam, 0.24 (1). This indicates that one of the four D atoms around the C3' atom is extracted and transferred to the D3' position. Although the hydrogen transfer in the Norrish Type II reaction is considered to occur *via* an intramolecular path, transfer from a neighboring molecule may be possible in the crystalline state. In the initial crystal (I), the D atoms around C3 are D8A, D8B, D8A' and D8B', the C3...D distances being 2.68 (2), 4.09 (2), 4.72 (2) and 4.12 (2) Å, respectively [symmetry code: (i) $2-x, -\frac{1}{2}+y, -z$]. As shown in Fig. 6, the D8A and D8B atoms are on the opposite side of the plane composed of C2, C3 and C4 from the S1 atom. The D8A' and D8B' atoms, on the other hand, are located on the same side of the plane. Fig. 7 shows two possible reaction processes: intra- and intermolecular deuterium transfer. If D8A or D8B may be transferred to the C3 atom within a molecule, it should occupy the equatorial position to the cyclohexyl ring and H3 of the original molecule may be shifted down and placed at the axial position. On the other hand, if D8A' or D8B' is transferred from the neighbouring molecule, it may occupy the equatorial and axial positions at random.

The equatorial D atom observed by neutron diffraction analysis clearly indicates that the photoisomerization proceeded *via* intramolecular deuterium transfer, D8A or D8B. Since the distance between D8A and C3, 2.68 (2) Å, is significantly shorter than that between D8B and C3, 4.09 (2) Å, which is too far for transfer to the C3, it is possible that the D8A atom is transferred to C3 during the reaction *via* the intramolecular path.

**Figure 7**

Reaction mechanism of the chiral thiolactam formation. Dashed and dotted arrows represent the intra- and intermolecular paths, respectively.

4. Summary

Although the previous X-ray and other experimental studies made clear the structural change and the absolute asymmetric induction in the process of optically active β -thiolactam formation from *N,N*-dibenzyl-1-cyclohexenecarbothioamide, the hydrogen-transfer path associated with the isomerization remained uncertain. In order to clarify the hydrogen-transfer process, the H atoms of the benzyl groups were replaced with D atoms. The structure after photoisomerization was analyzed by neutron diffraction, using a large crystal. An absolute configuration of the photoproduct chiral methylene, $-C^*HD-$, was directly determined owing to more than 20% photo-conversion with the retention of the single-crystal form. This indicates that the D atom was transferred *via* the intramolecular path. The role of the neutron diffraction will be more and more important to analyze the hydrogen-transfer mechanism in the crystalline state.

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