Optical Activity of Oxo Amide Crystals

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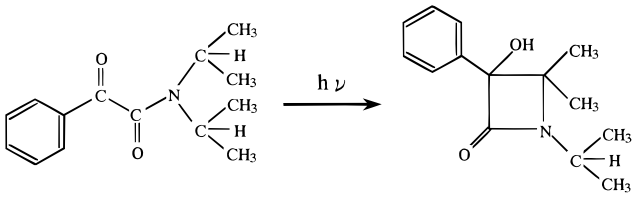
Abstract: It has been known that oxo amide crystals made up of achiral molecules can be photochemically converted into optically active β-lactams by irradiation with a high pressure mercury lamp. Although the oxo amide crystal belongs to an enantiomorphic class D_2, its optical activity could not be detected so far. We successfully measured the components of the gyration tensor of the oxo amide crystal by using the HAUP (high accuracy universal polarimeter) method: $g_{11} = -3.5 \times 10^{-4}$ (−79°/mm), $g_{22} = -1.4 \times 10^{-4}$ (−32°/mm), $g_{33} = -3.0 \times 10^{-4}$ (−68°/mm) at 305 K, where the optical rotatory powers are indicated in parentheses. It has been proved by direct experiments that the optical activity of the reactant and the product in this reaction system remains unchanged over the photocyclization process.

Introduction

Optical activity (OA)[1] of a noncentrosymmetrical molecule takes place when the displacement of some electron in the molecule is restricted to a helical path under the inhomogeneous electromagnetic field. Such a constraint to the helical path is caused by vicinal actions among the neighboring atoms in the molecule. It becomes possible[2] from the same reason that a crystal made up of achiral molecules becomes optically active when the degree of freedom of molecules, *e.g.*, rotation and orientation about chemical bonds, are severely restricted by forming a crystalline lattice. Quartz and diacetyl phenolphthalein[2] are typical examples, their crystalline states being optically active but immediately loosing OA in liquid solutions.

Among optically active crystals composed of achiral molecules some crystals can be used as starting materials for absolute asymmetric synthesis of useful chemicals.[3,4] One of us (F.T)[5] successfully obtained optically active β-lactams 3-hydroxy-1-isopropyl-4,4-dimethyl-3-phenyl-azetidin-2-one (**2**), important antibiotics, by photocyclizations of optically active crystals of achiral oxo amide *N*,*N*-diisopropylphenylglyoxylamide (**1**) (Scheme 1). The space groups of both **1** and **2** crystals were established by X-ray structure analyses[6] as equally enantiomorphic D_2^4, which permits OA of both signs. Although the optical rotatory power of a solution of **2** was measured, *e.g.*, $[\alpha]_D = +123°$ (*c* 0.5 in $CHCl_3$), OA of both crystals could not really be measured so far due to the presence of birefringence. Determinations of the absolute configurations of the structures of the reactant and the product were too difficult to be made, although recently those of *m*-chlorophenyl-*N*,*N*-diisopropylglyoxylamide and the corresponding β-lactams were successfully determined.[7]

Scheme 1



1 **2**

As there were no ways to determine OA of **1** crystal by using the existing methods, we[5] identified crystals of **1**, which gave **2**-crystals with (+) and (−) signs of OA in solutions, as (+)- and (−)-**1** respectively. However this identification is essentially tentative and presupposes that OA remains unchanged between the reactant and the product over the photochemical conversion. To be more general, such indeterminacy of OA of solids has been a long unresolved problem, which prevented accurate elucidation of the solid state asymmetric syntheses. We[8−10] developed the HAUP (high accuracy universal polarimeter) method, which enables us to measure simultaneously OA and birefringence Δn of crystals belonging to any systems. We applied the HAUP method to **1** crystals in order to investigate the above mentioned reaction more accurately.

HAUP Measurement of Optical Activity

1 crystals grown from benzene solution[5] were vitreous prisms, where (010) terrace planes were well developed. They were subjected to HAUP measurements. According to Weissenberg photographs of (−) and (+) specimens, the same lattice constants, say, $a = 12.802$ (12.794) Å, $b = 13.896$ (13.902) Å, and $c = 7.487$ (7.506) Å, were obtained. They were in good

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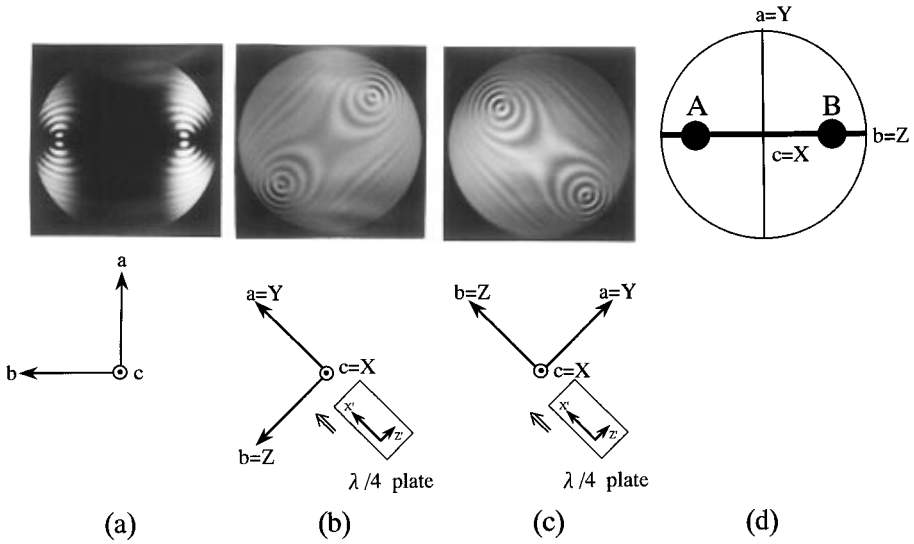

Figure 1. Conoscopic figures observed on (001) plane of **1** crystal: (a) indicates figure at an extinction position, (b) and (c) figures at 90° different diagonal positions, and (d) optical nature of the crystal.

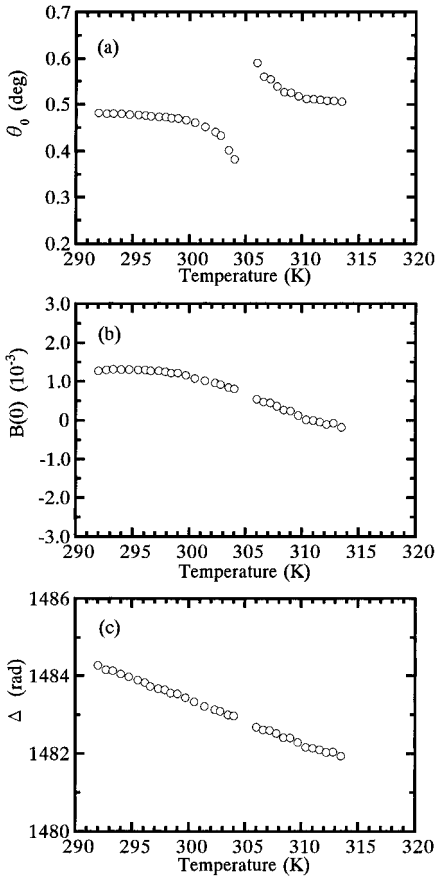

Figure 2. Temperature dependences of θ_0 (a), $B(0)$ (b), and Δ (c) of (100) plane of (−)-**1**.

agreement with a previous report[6] (written in parentheses). Also the extinction rules of the reflections were consistent with the space group of D_2^4.

In order to avoid confusions in detecting the signs of OA of specimens, we made the HAUP measurements on (100), (010), and (001) planes of the same (−)-**1** specimen first. These planes were polished by fine (0.3 μm) Al_2O_3 powders. The lengths d of the intersections of the rectangular parallelpiped specimen were 813, 1256, and 1197 μm along a, b, and c axes, respectively. From the symmetry of this crystal, the gyrations G_1, G_2, and G_3 measured on (100), (010), and (001) planes equal gyration tensor components g_{11}, g_{22}, and g_{33}, respectively.

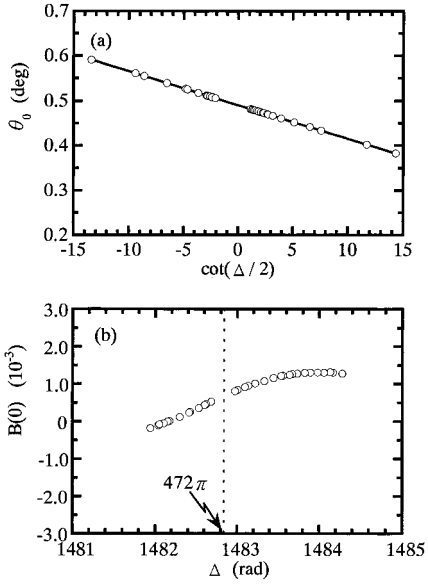

Figure 3. Relation between θ_0 and cot(Δ/2) (a) and between $B(0)$ and Δ (b).

In order to determine the signs of the gyration tensor components, it was necessary to clarify the optical nature of the specimen. Conoscopic figures observed on (001) plane are shown in Figure 1, parts a−c, 1a at an extinction position and 1b and 1c at 90° different diagonal positions, where a λ/4 plate was inserted. From Figure 1a, it was evident that the a axis was the optical Y axis since it was perpendicular to the optical plane, (100) plane. Birefringence increased when the b axis paralleled the Z' axis of the λ/4 plate as shown in Figure 1b, while the reverse was the case in Figure 1c. Therefore the b axis must be the optical Z axis; the optical nature of the **1** crystal is expressed stereographically in Figure 1d.

In order to evaluate the linear dichroism of the specimen, the extended HAUP[11] method was used first in this experiment. However we found that it was less than 1.3×10^{-7} in any directions for the wavelength of 4965 Å (Ar laser). Therefore we could ignore it and used the simple method[8] in the following measurements. Temperature dependences of θ_0, $B(0)$, and Δ of (100) specimen are shown in Figure 2. Here Δ is the optical

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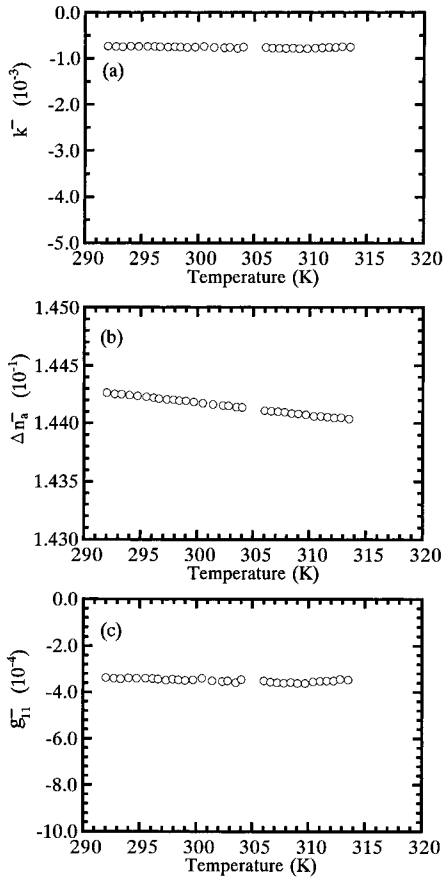

Figure 4. Temperature dependences of k^- (a), Δn_a^- (b), and g_{11}^- (c) of (100) plane of (−)-**1**.

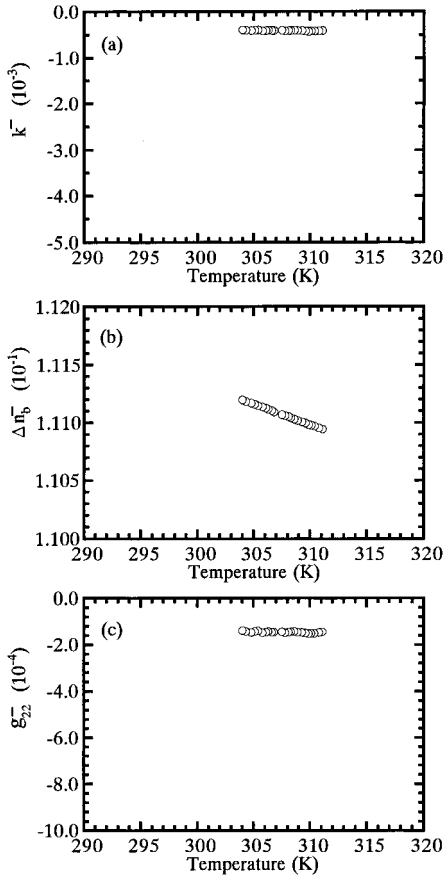

Figure 5. Temperature dependences of k^- (a), Δn_b^- (b), and g_{22}^- (c) of (010) plane of (−)-**1**.

Table 1. Systematic Errors and Thicknesses of Specimens of Oxo Amide

		systematic error			
specimen	thickness(μm)	$p(10^{-4})$	$q(10^{-4})$	$\gamma(10^{-4})$	$\delta Y(10^{-4})$
(−)-(1 0 0)	813	−1.5	4.1	−5.6	3.4
(−)-(0 1 0)	1256	−1.5	−2.1	0.6	4.4
(−)-(0 0 1)	1197	−1.5	2.3	−3.8	−1.0
(+)-(0 0 1)	522	−1.5	32.6	−34.1	8.2

retardation, but θ_0 and $B(0)$, characteristic terms of the HAUP method, should be referred to refs 8 and 9. From these measurements the systematic errors[8,9] γ and δY could be determined. θ_0 and $B(0)$ are written as

$$\theta_0 = -\frac{1}{2}(p+q)\cot\left(\frac{\Delta}{2}\right) - \frac{1}{2}\delta Y \qquad (1)$$

and

$$B(0) = (\gamma - 2k)\sin\Delta + 2\delta Y \cos^2\left(\frac{\Delta}{2}\right) \qquad (2)$$

where $\gamma = p - q$, p and q representing the parasitic ellipticities of the polarizer and analyzer, respectively. k stands for ellipticity. Relations between θ_0 and $\cot(\Delta/2)$ and between $B(0)$ and Δ are indicated in Figure 3, parts a and b. From the derivative of θ_0 vs $\cot(\Delta/2)$ in Figure 3a, $p + q$ was determined to be 2.6×10^{-4}. Subsequently p could be determined to be -1.5×10^{-4} by using a $LiNbO_3$ crystal as the standard crystal,[10] but the description of the detailed procedure is omitted here. Therefore γ was evaluated to be -5.6×10^{-4}. δY was determined from the value of $B(0)$ at $\Delta = 472\pi$ in Figure 3b. As γ and δY were thus determined, the ellipticity k could be evaluated from (2). Δn was calculated from the relation

Table 2. Optical Rotatory Powers of Crystals

crystal	λ (Å)	T (K)	ρ (deg mm^{-1})
$AgGaS_2$	4850		950[a]
$Ca_2Sr(C_2H_5COO)_6$	5890	293	4.2[b]
α-$LiIO_3$	6328		−86.7[c]
$[N(CH_3)_4]_2ZnCl_4$	6328	292	0.02[d]
α-SiO_2	6328	293	25.1[e]
TeO_2	6328		87[f]
$BaMnF_4$	6328	133	5.7[g]
$(NH_2CH_2CO_2H)_3H_2SO_4$	6328	305	1.9[h]
poly-L-lactic acid	5145	298	−9200[i]
L-glutamic acid (ρ_3)	6328	293	5.4[j]
oxo amide (ρ_1)	4965	305	−79
oxo amide (ρ_2)	4965	305	−32
oxo amide (ρ_3)	4965	305	−68

[a] Taken from ref 14. [b] Taken from ref 15. [c] Taken from ref 16. [d] Taken from ref 17. [e] Taken from ref 10. [f] Taken from ref 18. [g] Taken from ref 19. [h] Taken from ref 20. [i] Taken from ref 21. [j] Taken from ref 22.

$$\Delta = \frac{2\pi}{\lambda}\Delta n d \qquad (3)$$

where λ expresses the wavelength of the incident light. G can be obtained from the relation

$$k = \frac{G}{2\Delta n \bar{n}} \qquad (4)$$

where $\bar{n}$ represents the mean refractive index. It was determined to be 1.61 by using Chaulnes' method.[12] Temperature depend-

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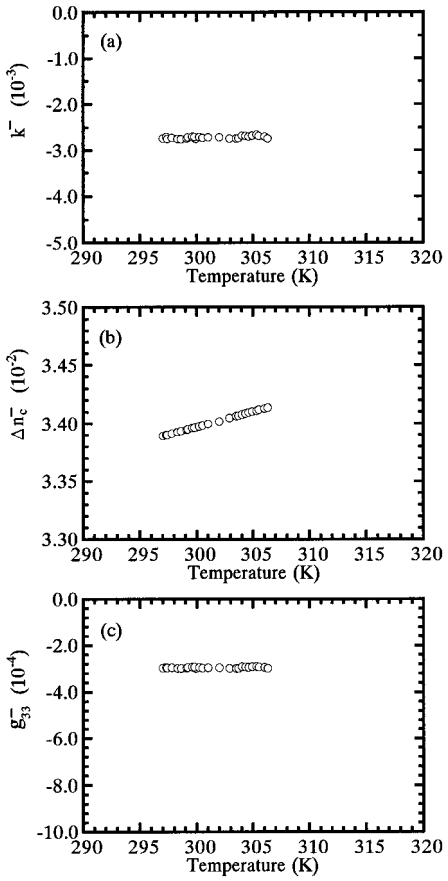

Figure 6. Temperature dependences of k^- (a), Δn_c^- (b), and g_{33}^- (c) of (001) plane of (−)-**1**.

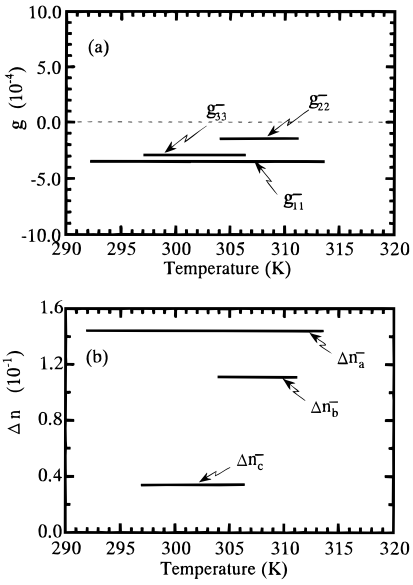

Figure 7. Temperature dependences of all the components of the gyration tensor (a) and birefringences (b) of (−)-**1**.

ences of k^-, Δn_a^-, and G_1^- ($= g_{11}^-$) were clarified as shown in Figure 4, parts a−c, where a superscript − designates (−)-crystal. g_{11}^- is about -3.5×10^{-4}, and independent of temperature. Δn_a^-, which is approximately the same magnitude as calcite, manifests the negative temperature coefficient.

Analogous measurements were performed on (010) and (001) planes. Systematic errors γ and δY of these cases are indicated in Table 1 together with thicknesses. Temperature dependences of k, Δn, and g of (010) and (001) planes are depicted in Figures 5 and 6. Both g_{22}^- and g_{33}^- are also negative and independent of

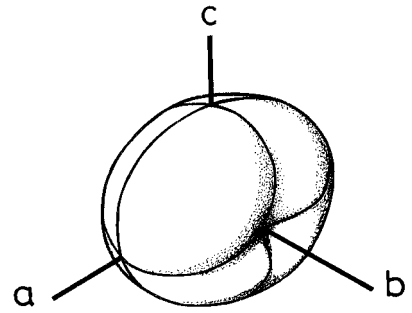

Figure 8. Gyration surface of (−)-**1**.

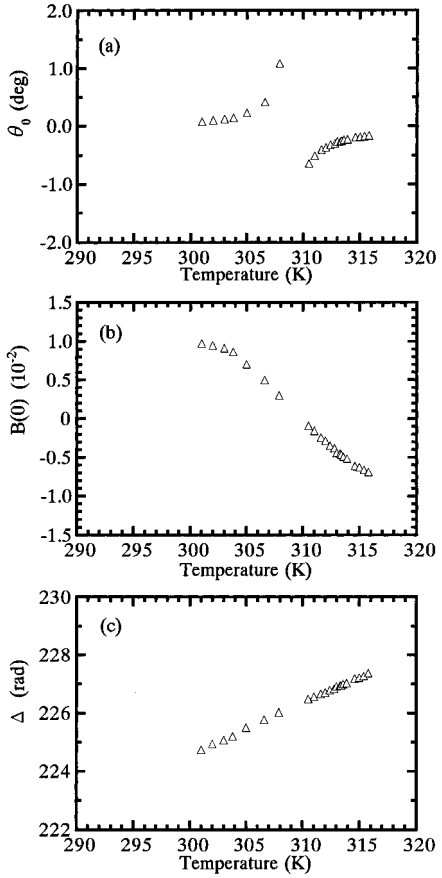

Figure 9. Temperature dependences of θ_0 (a), $B(0)$ (b), and Δ (c) of (001) plane of (+)-**1**.

temperature. It is noticeable that Δn_c^- is one order of magnitude lower than the others and increases with increasing temperatures. Temperature dependences of all the components of the gyration tensor and birefringence are summarized in Figure 7, parts a and b. It was found that the components of the gyration tensors of (−)-**1** crystal are negative and remain almost constant in the present temperature range. The gyration surface[13] of this crystal is a white ovoid as shown in Figure 8. It is seen from the figure that there are no directions where positive gyrations can occur in the crystal.

As for OA of (+)-**1** crystal, a (001) plate specimen were prepared with an area of 2000 × 3500 μm^2 and a thickness of

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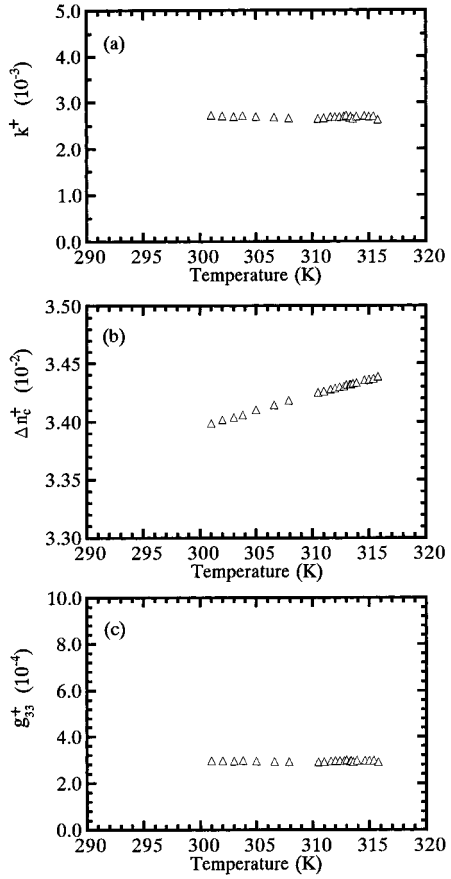

Figure 10. Temperature dependences of k^+ (a), Δn_c^+ (b), and g_{33}^+ (c) of (001) plane of (+)-**1**.

522 μm. Temperature dependences of θ_0, $B(0)$, and Δ are shown in Figure 9, parts a−c. The systematic errors were determined as $\gamma = -3.41 \times 10^{-3}$ and $\delta Y = 8.2 \times 10^{-4}$. Temperature dependences of k^+, Δn_c^+, and G_3^+ ($= g_{33}^+$) are represented in Figure 10, parts a−c. Temperature dependences of $\Delta n_c^{\pm}$, and $g_{33}^{\pm}$ of both specimens are compared in Figure 11, parts a and b. Δn_c^- and Δn_c^+ of both crystals constitute the same straight line. This fact shows the coincidence of Δn of both crystals and indicates the validity of the present experiments. g_{33}^- and g_{33}^+ are juxtaposed at the same levels but with opposite signs.

We omitted to measure OA on (100) and (010) planes of (+)-**1** crystal, since there was no question that tensor components g_{11}^+ and g_{22}^+ would have the same magnitudes of opposite signs as the corresponding components of (−)-**1**. Temperature dependences of the optical rotatory powers ρ_1^-, ρ_2^-, and ρ_3^- of (−)-**1** are depicted in Figure 12. Also they are compared with other crystals in Table 2. It is seen that the optical rotatory powers of **1** are larger than that of quartz, ρ_1^- and ρ_3^- being approximately three times larger.

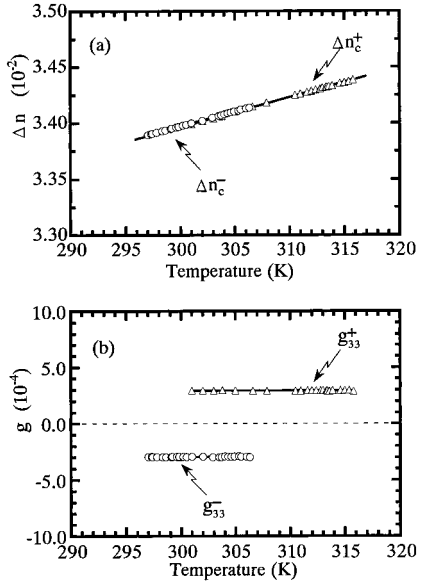

Figure 11. Comparisons of temperature dependences of Δn_c^- and Δn_c^+ (a) and g_{33}^- and g_{33}^+ (b).

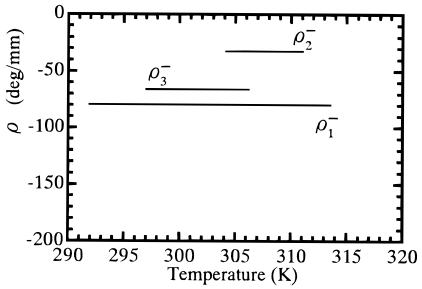

Figure 12. Temperature dependences of optical rotatory powers ρ_1^-, ρ_2^-, and ρ_3^- of (−)-**1**.

Summing up the present paper, we have proved quantitatively that oxo amide crystals which give (−)- and (+)-β-lactams really manifest negative and positive OA. Thus the serious problem in solid state asymmetric syntheses, say, indeterminacy of OA of solids, has been solved by using the HAUP method.

Acknowledgment. This paper is dedicated to Professor Nelson J. Leonard on the occasion of his 80th birthday.

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