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Chirality Inversion in a Crystal Only by Photoirradiation

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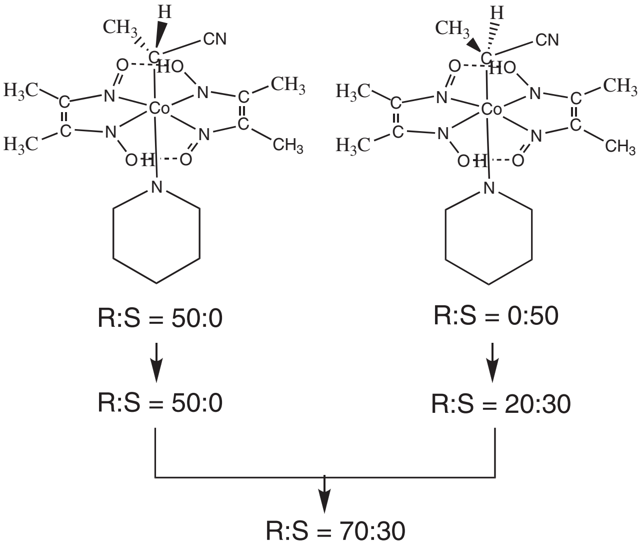
When a crystal of [(*S*)-1-cyclohexylethylamine]bis(dimethylglyoximato)[(*S*)-1-(ethoxycarbonyl)ethyl]cobalt(III) was irradiated with a halogen lamp, the absolute configuration of the (*S*)-1-(ethoxycarbonyl)ethyl group gradually changed from *S* to *R* with retention of the single crystal form. After 24 h exposure, the change became within experimental error and the *S*:*R* ratio of the 1-(ethoxycarbonyl)ethyl group was found to be 18:82 by X-ray crystal structure analysis. The crystals with the (*R*)- and (*racemic*)-1-(ethoxycarbonyl)ethyl groups instead of the (*S*)-enantiomer have isomorphous structures to the crystal with the (*S*)-enantiomer. Both of the crystals were also changed to the same structure as that with the (*S*)-enantiomer on exposure to the halogen lamp. This marvelous ratio of 18:82 was clearly explained with the shape of the reaction cavity for the photoreactive 1-(ethoxycarbonyl)ethyl group in each crystal structure. A pseudo-isomorphous crystal of the complex with the (*S*)-enantiomer was obtained under the same conditions but it contains a water molecule as solvate. The (*S*)-1-(ethoxycarbonyl)ethyl group in the crystal gradually changed to the disordered racemate with retention of the single-crystal form. The different reaction pathway between the pseudo-isomorphous crystals with and without a water molecule was explained with not only the size but also the shape of the reaction cavity for the photoreactive group.

Asymmetric synthesis starting from an achiral reagent and in the absence of any external chiral agent has long been a fascinating challenge to chemists[1] and is also a central problem to the origin of optically active substances on earth.[2] Especially, asymmetric reactions in chiral crystals formed by achiral compounds are defined "absolute asymmetric synthesis," since the asymmetry is introduced from the physical conditions such as chiral crystal environment. The first example was reported in the solid–gas reaction from 4,4′-dimethylchalcone and bromine to its chiral *trans*-dibromide in 6% enantiomeric excess in 1969.[3] Since then, many examples have been reported. Recently excellent review articles on absolute asymmetric synthesis have been published.[4] We observed that a chiral β-lactam was produced from the achiral oxoamide crystal.[5] Furthermore, the chiral alkyl groups bonded to the cobalt atoms were found to be formed from the achiral ones in the chiral crystals of bis(dimethylglyoximato)cobalt(III), cobaloxime, complexes.[6–8] The reason why the chiral groups appeared in the photoreactions was clearly explained using the concept of reaction cavity.[9]



Scheme 1.

Not only the asymmetric reactions in chiral crystals, we observed an unusual generation of optical activity in a racemic crystal of enantiomers.[10] A racemic mixture of (1-cyanoethyl)bis(dimethylglyoximato)(piperidine)cobalt(III), (1-cyanoethyl)(piperidine)cobaloxime, which contains the chiral 1-cyanoethyl group, crystallizes in a chiral space group, $P2_12_12_1$, in which the (*R*)- and (*S*)-enantiomers occupy crystallographically independent positions in the asymmetric cell. Irradiating a single crystal of D configuration with visible light caused the racemization of the (*S*)-enantiomer while the (*R*)-enantiomer remained unaltered as shown in Scheme 1. This indicates that the number of (*R*)-enantiomers increases at the expense of *S* and so the overall composition of the crystal changes from racemic to enriched in the (*R*)-enantiomer. The reason why only (*S*)-enantiomer is racemized was explained by the fact that the reaction cavity for the (*S*)-enantiomer is sufficiently large for racemization whereas that for the (*R*)-enantiomer is too small. At first, we assumed that the ratio of the (*R*)- to (*S*)-enantiomers should be 3 to 1, that is 75:25, at the final stage because all the (*S*)-enantiomers should change the racemic ones and the (*R*)-enantiomers should remain unaltered. However, the ratio of *R*:*S* became 70:30, not 75:25 at the final stage.[11] In order to ascertain the result, five kinds of crystals with different compositions of *R*:*S* ratios, which are isostructural to the racemic crystal, were irradiated with visible light. The *R*:*S*

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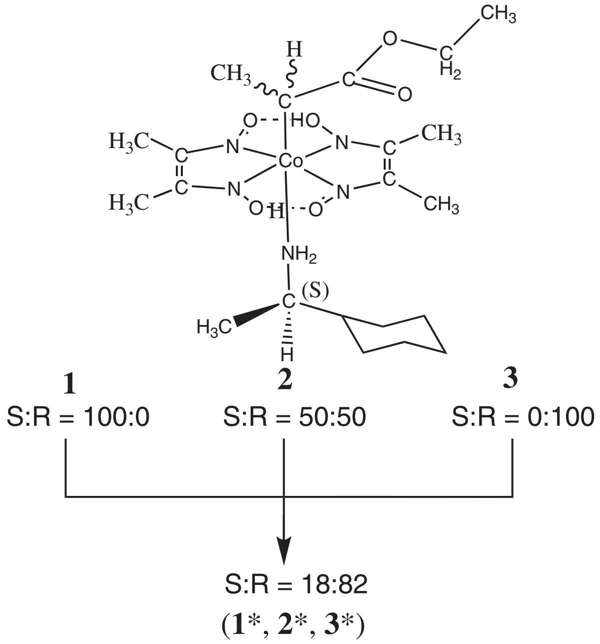


Scheme 2.

ratios of all crystals at the final stage became 70:30 if the crystals have D configuration. This is because the shape of the cavity becomes almost symmetric if the *R*:*S* ratio reaches 70:30 at the final stage. The chloroform solution of the crystals after photoirradiation showed the optical rotation ($[\alpha]_{\mathrm{D}} = 30°$). Similar results were obtained for the cobaloxime complex crystal with pyrrolidine instead of piperidine as an axial base ligand, although the space group is $P1$.[11]

Then we tried to observe a simple inversion of a chiral group in a chiral crystal of the cobaloxime complex. After many trials a bulkier group, 1-(ethoxycarbonyl)ethyl (ece), was selected. When the axial amine was replaced with 1-cyclohexylethylamine (che-amine), interesting phenomena were observed. The chirality of (*S*)-ece group of the [(*S*)-che-amine][(*S*)-ece]cobaloxime, **1**, which is shown in Scheme 2, gradually changed to the opposite *R* configuration with retention of the single crystal form on exposure to the halogen lamp. Since one of four bonds around the chiral carbon atom of the (*S*)-ece group should be cleaved for the chirality inversion, the Co–C bond must be cleaved during the photoirradiation as observed in many photoreactions of cobalt complexes. To confirm such an unusual chirality inversion more minutely, the crystals with the (*racemic*)-ece and (*R*)-ece groups instead of (*S*)-ece group, **2** and **3**, respectively were also examined. It was found that the crystals of **2** and **3** are isostructural to **1**. On exposure to the halogen lamp, both of **2** and **3** were transformed to the same structure as that of **1** with retention of the single crystal form. This paper reports the process of the chirality inversion only by photoirradiation and explains the reason why such a chirality inversion occurs in a crystal using the concept of reaction cavity.

Experimental

Preparation. [(*S*)-che-amine][(*S*)-ece]cobaloxime, **1**, was synthesized from [(*racemic*)-ece](pyridine)cobaloxime, **4**, by exchange of axial ligand, resolution of diastereoisomers and exchange of axial ligand, as shown in Scheme 3. Compound **4** was synthesized in a way similar to that reported previously.[12] The axial base ligand was replaced with water using ion-exchange resins (DOWEX 50W-X8) according to a reported method.[13] The aqua complex of **5** was easily obtained.

Synthesis of [(*S*)-ece][(*S*)-1-phenyl-2-(*p*-tolyl)ethylamine]-cobaloxime (6). Compound **5** (6.00 g, 14.7 mmol) was dissolved in an aqueous methanol solution of 230 mL (methanol and water, 200 and 30 mL, respectively). Then (*S*)-1-phenyl-2-(*p*-tolyl)ethylamine (3.00 mL) was dissolved and stirred for 1 h. Compound **6′** was precipitated. The recrystallization was repeated with aqueous methanol solution until the specific optical rotation $[\alpha]_{\mathrm{D}}^{20}$ became −30° in chloroform solution. The diastereomerically pure compound **6** was obtained. The aqua complex of **7** was easily obtained in the same way as that of **5**.

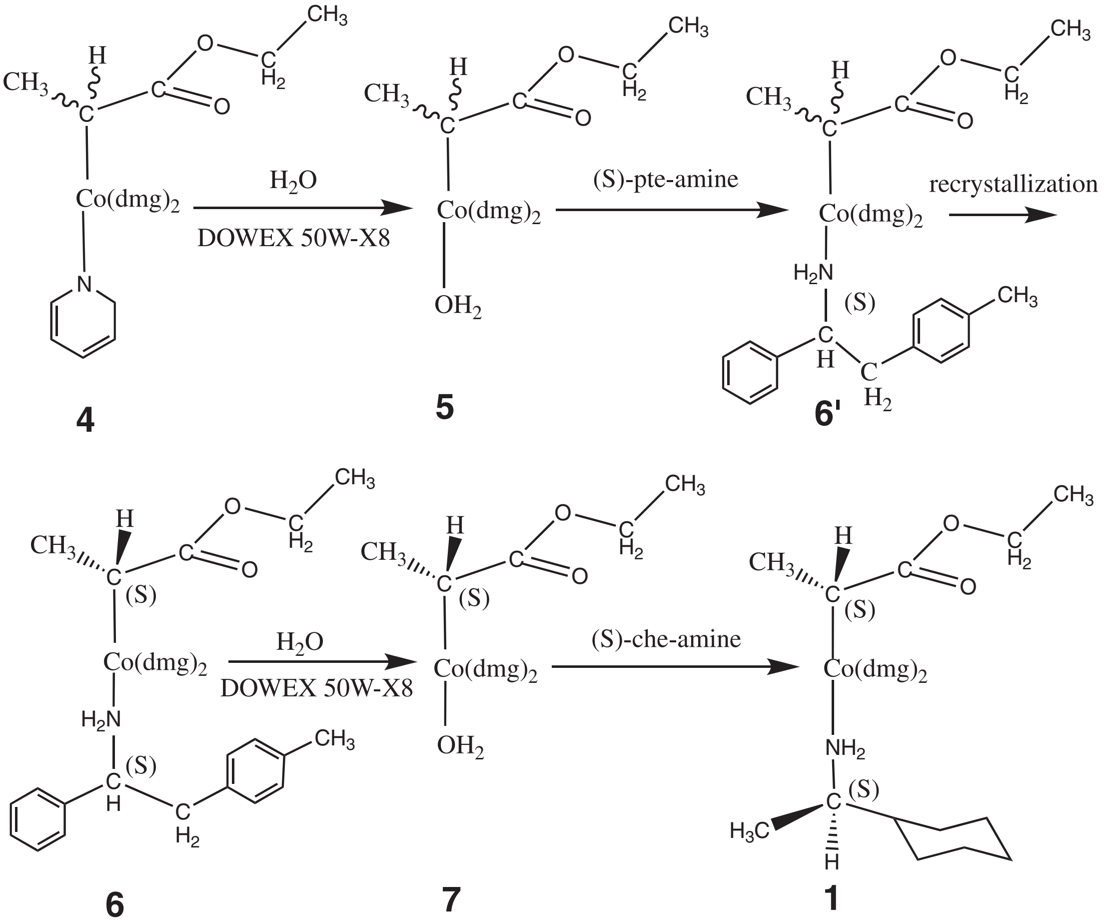
Synthesis of [(*S*)-che-amine]cobaloxime with (*S*)-ece, (*racemic*)-ece, and (*R*)-ece Groups (1, 2, and 3). The aqua complex of **7** (1.00 g, 2.50 mmol) was dissolved in methanol solution (100 mL). The compound of (*S*)-che-amine (0.37 mL) was added and stirred for 1 h. The solvent was removed with distillation under reduced pressure. The compound **1** was obtained with recrystallization from the precipitate in an aqueous methanol solution. At first, we tried to obtain the compound **1** by resolving a pair of diastereoisomers which have 1-che-amine as an axial base ligand instead of **6′**, but it was unsuccessful. The reason will be discussed later.

The compound **2** was obtained in the same way except the aqua complex **5** was used instead of **7**. Compound **3** was obtained in the same way except (*R*)-che-amine instead of its (*S*)-enantiomer.[14] The crystals of the complexes **1**, **2**, and **3**, which are called **I**, **II**, and **III**, were obtained from aqueous methanol solutions.

In the course of recrystallization of **1**, a different type of crystal, **IV**, was obtained. X-ray analysis indicated that the crystal is a pseudo-polymorph containing one water molecule in an asymmetric unit. The separate crystallization was unsuccessful and discrimination of two types of the crystals is not easy without X-ray analysis.

Photoirradiation. A halogen lamp (HOYA-SCHOOL MEGALIGHT 100) was placed at a distance of 5 cm from each crystal. A filter (R-64, TOSHIBA) was inserted between the crystal and the lamp. This means that light with the wavelengths between 640 to 800 nm was exposed to the crystal at room temperature. The unit-cell dimensions were determined at 1 h time intervals. For each crystal the change of the cell dimensions became within the experimental errors after 24 h exposure. Therefore, the crystal data and three-dimensional intensity data of the crystals **I**, **II**, **III**, and **IV** were obtained after 24 h exposure under the same conditions as those before photoirradiation at 223(2) K.

Crystal Structure Analyses before and after 24 h Photoirradiation. A crystal of **I** suitable for X-ray work (0.30 × 0.20 × 0.20 mm^3) was mounted on a Rigaku R-AXIS RAPID diffractometer. The crystal data are shown in Table 1. There is one molecule in an asymmetric unit of a chiral unit-cell with the space group, $P2_12_12_1$. The crystal structure was analyzed with the program SIR97[15] and was refined with the program SHELXL97.[16] All the non-hydrogen atoms were refined with anisotropic temperature factors. All the hydrogen



Scheme 3.

atoms were obtained geometrically and were refined assuming riding motion with isotropic temperature factors. The crystal data and three-dimensional intensity data, which is called **I***, were obtained after 24 h photoirradiation using the same crystal before photoirradiation. The unit-cell volume increased by 4.6(2) $Å^3$ after photoirradiation. The occupancy factors of the atoms of the (*S*)-ece group bonded to the cobalt atom decreased and new peaks, which were assigned to the inverted (*R*)-ece group, appeared around the original (*S*)-ece group as a disordered structure. The newly appearing atoms, C1R, C2R, C3R, C4R, C5R, O1R, and O2R, were refined with anisotropic temperature factors whereas the original atoms of C1S to O2S were refined with isotropic temperature factors. The other atoms except the hydrogen atoms were refined with anisotropic temperature factors whereas the hydrogen atoms were refined in the same way as before photoirradiation. The crystal data after photoirradiation and experimental details are also shown in Table 1.

For the crystal of **II**, the crystal and intensity data were obtained using a crystal of 0.40 × 0.40 × 0.20 mm^3 before and after 24 h photoirradiation. Before photoirradiation, the crystal structure was found to be isostructural to that of **I**. The refinement details were almost the same as those of **I**. After photoirradiation the unit-cell increased by 20.0(6) $Å^3$ and had the same volume as that of **I*** within experimental error. The disordered atoms of the ece group were refined with anisotropic temperature factors before photoirradiation and were done in the same way as that of **I***. The structure after photoirradiation, **II***, is the same as that of **I*** within experimental error. The crystal data and the refinement details before and after photoirradiation (**II** and **II***) are also listed in Table 1.

For the crystal of **III**, the crystal and intensity data were obtained using a crystal of 0.30 × 0.30 × 0.20 mm^3 before and after 24 h photoirradiation. Before photoirradiation, the crystal structure was also isostructural to that of **I**. The refinement details were almost the same as those of **I**. After photoirradiation the unit-cell increased by 14.8(2) $Å^3$ and had the same volume as that of **I*** within experimental error. The disordered atoms of the newly appeared group (C1S, C2S, C3S, C4S, C5S, O1S, and O2S) were refined with isotropic temperature factors after photoirradiation. The structure after photoirradiation, **III*** is the same as that of **I*** within experimental error. The crystal data and the refinement details before and after photoirradiation (**III** and **III***) are also listed in Table 1.

For the crystal of **IV**, the crystal and intensity data were obtained using a crystal of 0.50 × 0.10 × 0.10 mm^3 before and after 24 h photoirradiation. The crystal structure is completely different from that of **I**. The data collection and the refinement details were in a way similar to those of **I**. After photoirradiation the unit-cell increased by 102.5(8) $Å^3$, which is distinct from the expansion observed in the crystals, **I**, **II**, and **III** (4.6–40.0 $Å^3$). The disordered atoms of the newly appeared group (C4R and C5R) were refined with isotropic temperature

Table 1. Crystal Data and Experimental Details before and after 24 h Photoirradiation for **I**, **II**, **III**, and **IV**

Parameter	**I**	**I***	**II**	**II***	**III**	**III***	**IV**	**IV***
Formula	$C_{21}H_{40}CoN_5O_6$		$C_{21}H_{40}CoN_5O_6$		$C_{21}H_{40}CoN_5O_6$		$C_{21}H_{42}CoN_5O_7$	
Temperature/K	223(2)		223(2)		223(2)		223(2)	
Crystal system	orthorhombic		orthorhombic		orthorhombic		orthorhombic	
Space group	$P2_12_12_1$		$P2_12_12_1$		$P2_12_12_1$		$P2_12_12_1$	
a/Å	11.5975(1)	11.5625(4)	11.538(1)	11.596(1)	11.5549(5)	11.5805(3)	8.5748(3)	8.823(2)
b/Å	13.5583(1)	13.4572(5)	13.534(2)	13.447(2)	13.3232(5)	13.4670(4)	15.0581(5)	15.355(2)
c/Å	16.3010(5)	16.5027(5)	16.329(3)	16.481(3)	16.5801(7)	16.4615(5)	19.9384(8)	19.759(4)
α/°	90	90	90	90	90	90	90	90
β/°	90	90	90	90	90	90	90	90
γ/°	90	90	90	90	90	90	90	90
Volume/Å^3	2563.21(8)	2567.80(15)	2549.9(6)	2569.9(6)	2552.5(2)	2567.3(1)	2574.5(2)	2676.8(8)
Z	4	4	4	4	4	4	4	4
d_{calcd}/Mg m^{-3}	1.341	1.339	1.348	1.338	1.347	1.339	1.382	1.329
Crystal size/mm^3	0.30 × 0.20 × 0.20		0.40 × 0.40 × 0.20		0.30 × 0.30 × 0.20		0.50 × 0.10 × 0.10	
θ range/°	2.31–27.48	2.63–27.48	2.16–27.46	2.47–27.46	1.96–27.48	2.15–27.48	1.69–27.47	2.65–27.47
Refrections collected/unique	5806/5806	5872/5872	23027/5809	23254/5670	30218/5849	42015/5882	36995/5886	32006/6043
R(int)	0	0	0.0886	0.0692	0.0747	0.059	0.0542	0.0826
Data/retraints/parameters	5806/0/306	5872/0/342	5809/0/378	5670/0/343	5849/0/311	5882/0/342	5886/0/320	6043/1/340
Flack, X	0.06(3)	0.03(2)	0.04(2)	0.005(16)	0.001(18)	0.005(19)	0.002(11)	0.01(2)
GOF	1.169	0.864	1.133	1.049	1.575	1.515	1.041	1.051
$R1$ ($I > 2\sigma(I)$)	0.0557	0.0443	0.0545	0.0461	0.0515	0.0486	0.0318	0.0564
$wR2$ ($I > 2\sigma(I)$)	0.1375	0.0899	0.1286	0.1162	0.1386	0.1331	0.0767	0.1056
$R1$ (all data)	0.066	0.0635	0.0624	0.0492	0.0549	0.0505	0.0348	0.0761
$wR2$ (all data)	0.1422	0.0945	0.1339	0.1189	0.1410	0.1347	0.0786	0.1145
$\Delta\rho_{max}/\Delta\rho_{min}$/e Å^{-3}	0.791/ −0.311	0.400/ −0.309	0.274/ −0.459	0.435/ −0.310	0.271/ −0.297	0.566/ −0.370	0.197/ −0.417	0.417/ −0.746

factors. The distance between C4 and C4R was constrained. The crystal data and the refinement details before and after photoirradiation (**IV** and **IV***) are also listed in Table 1.

The crystallographic data have been deposited with Cambridge Crystallographic Data Centre: Deposition numbers CCDC 828333–828340 for **I**, **I***, **II**, **II***, **III**, **III***, **IV**, and **IV***. Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, U.K.; FAX: +44 1123 336033; e-mail: deposit@ccdc.cam.ac.uk).

Results

Structural Change of I before and after Photoirradiation. The crystal structure viewed along the a axis is shown in Figure 1. There is one molecule in an asymmetric unit. There is a hydrogen bond, N5–H5···O5, between the molecules, as shown in the dotted line. The molecules are linked as a chain along a 2_1-screw axis parallel to the a axis by the hydrogen bond. There is no unusual short contact between the molecules except the hydrogen bond. The molecular structure is shown Figure 2. The absolute configuration of the ece group is S and the conformation of the methyl group is *syn*, the torsion angle of O2–C3–C4–C5 being 34.4(7)°. The cyclohexyl ring of (S)-che-amine takes a chair conformation.

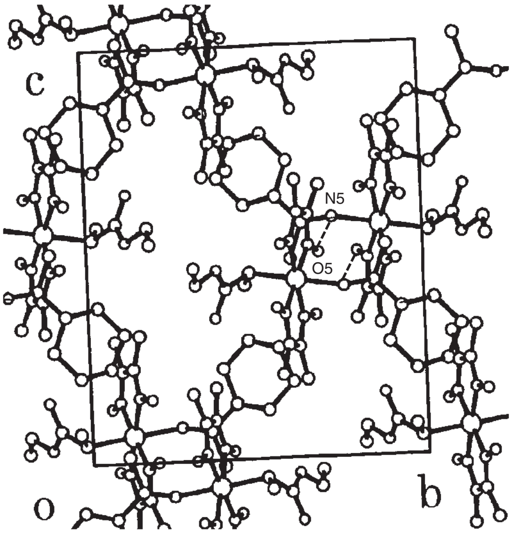


Figure 1. Crystal structure of **I** viewed along the a axis. The dotted lines indicates the N–H···O hydrogen bonds.

When the crystal was exposed to the halogen lamp, the cell dimensions gradually changed with retention of the single crystal form and the change became within experimental error after 24 h exposure. The crystal structure is essentially the same as that of **I**, except several peaks around the (S)-ece group. The molecular structure of **I*** is shown in Figure 3. The newly appeared peaks are assigned to the atoms of the ece group with R configuration. To examine the structural change, the ece groups before and after photoirradiation are projected on the cobaloxime plane in Figure 4. The structure of the newly appeared ece group with R configuration is a mirror image of that with S configuration, if the mirror is placed perpendicular to the cobaloxime plane and parallel to the C–C bonds of cobaloxime, passing through the cobalt atom. This structural

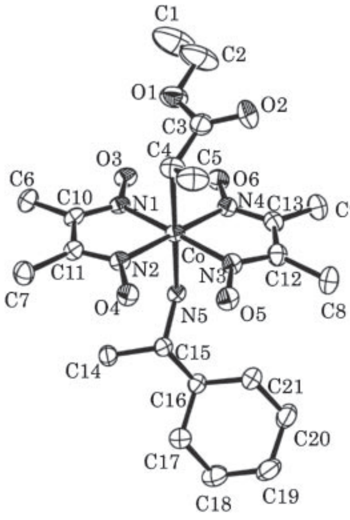


Figure 2. Molecular structure of **I**. The thermal ellipsoids are drawn at 50% probability level. Hydrogen atoms are omitted for clarity.

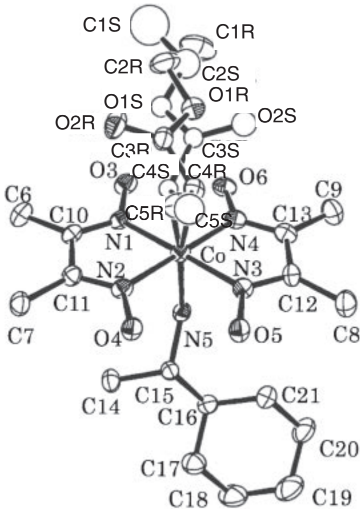


Figure 3. Molecular structure of **I***. The thermal ellipsoids are drawn at 50% probability level. Hydrogen atoms are omitted for clarity.

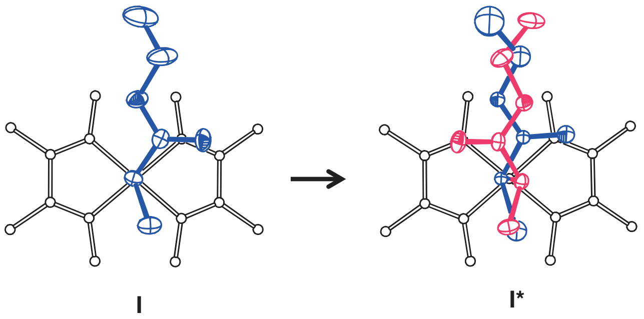


Figure 4. Structural change of the ece group from **I** to **I***.

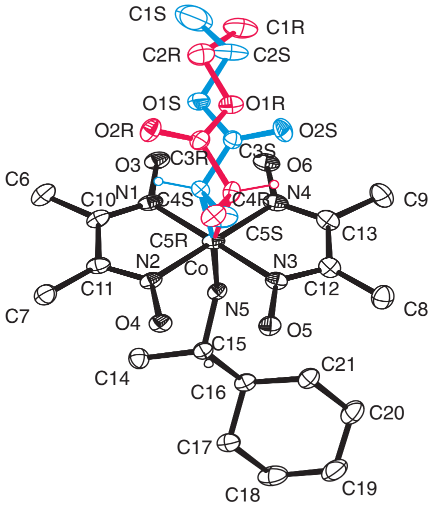


Figure 5. Molecular structure of **II**. The *S*:*R* ratio of the disordered ece group is 50:50. The thermal ellipsoids are drawn at 50% probability level. Hydrogen atoms are omitted for clarity.

change indicates the following reaction process; the Co–C bond was cleaved by photoirradiation, the produced ece radical rotated by 180° around the long axis of the radical and the radical remade a bond to the Co atom. Such a radical rotation mechanism was already examined using neutron diffraction for the cobaloxime crystals with cyanoethyl, cyanopentyl, and cyanobutyl groups as axial alkyl groups.[17]

To our surprise, most of the (*S*)-ece groups in the crystal were changed to the opposite configuration and the ratio of *S*:*R* became 17.4:82.6(5). This means that the chiral group in the molecule was inverted only by photoirradiation. To our knowledge, this is the first observation of chirality inversion of a chiral group in a crystal only by photoirradiation, although a variety of racemization of chiral groups has been reported.[18] When the photoirradiated crystal are solved in an aqueous methanol solution, the optical rotation of the solution would probably show an opposite value to that containing complex before photoirradiation, since the optical rotatory power of the (*S*)-che-amine is very small compared with that of the 1-ece group bonded to the cobalt atom. Regrettably, the crystals after the photoirradiation were too small to measure the optical rotation.

This is essentially the same as that observed in the racemic-to-chiral transformation of the piperidine and pyrrolidine complex crystals with the cyanoethyl group.[11]

Structural Changes before and after Photoirradiation of II and III. In order to make clear the chirality inversion mechanism, especially the reason why the *S*:*R* ratio became such a marvelous one, the cobaloxime complex crystals with the (*racemic*)-ece and (*R*)-ece groups, **II** and **III**, respectively, were prepared.[14]

The crystal structures of **II** and **III** are isomorphous to **I**, except the slight difference of the cell dimensions, as shown in Table 1. The molecular structure of **II** is shown in Figure 5. The (*racemic*)-ece group takes a disordered structure and the structure is nearly the same as that of **I***, except the *S*:*R* ratio is 50:50. The molecular structure of **III** is shown in Figure 6. The absolute configuration of the ece group is *R* and the conformation of the methyl group is *syn*, the torsion angle of O2–C3–C4–C5 being $-32.7(5)^\circ$. It is clear that the structure of the ece group is essentially the same as that with *R*

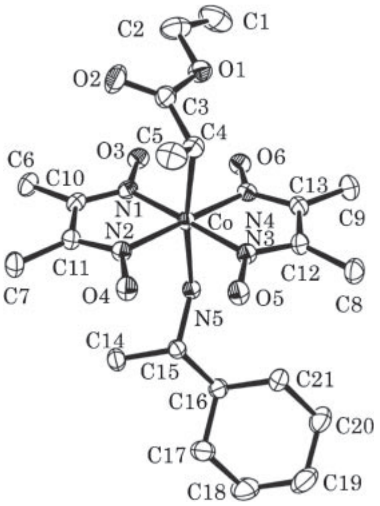
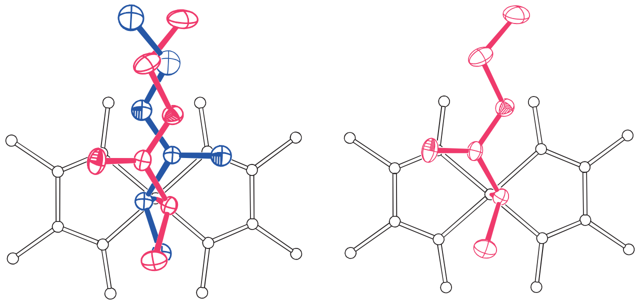


Figure 6. Molecular structure of **III**. The thermal ellipsoids are drawn at 50% probability level. Hydrogen atoms are omitted for clarity.



II **III**

Figure 7. Conformations of the ece groups projected on the cobaloxime planes in **II** and **III**. The (*R*)-ece group in **II** takes essentially the same conformation as that in **III**.

configuration of the racemic one, as shown in Figure 5. This is clearly shown in Figure 7, in which the structures of the (*R*)-ece groups of **II** and **III** are projected on the cobaloxime plane.

When the crystals of **II** and **III** are exposed to the halogen lamp, the unit cell dimensions gradually changed with retention of the single crystal form and the changes became within experimental errors after 24 h exposure. The unit-cell volumes of **II*** and **III*** became 2569.9(6) and 2567.3(1) Å^3, respectively, which is the same as that of **I***, 2567.8(2) Å^3 within experimental error. The crystal structures of **II*** and **III*** are identical to that of **I***.

The molecular structure of **II*** and **III***, of course, are identical to that of **I*** within experimental errors. The structures of the disordered ece groups of **II*** and **III*** are the same as that of **I***, which is shown in Figure 3. The *S*:*R* ratios of the ece groups in **II*** and **III*** became 18.4:81.6(4) and 17.7:82.3(5), respectively. The average ratio among **I***, **II***, and **III*** is about 18:82. This means that the marvelous *S*:*R* ratio of 18:82 is not accidental but inevitable for the photoreactions of **I**, **II**, and **III**.

Structural Change of IV before and after Photoirradiation. In order to ascertain that the chirality inversion of the ece group by photoirradiation observed in **I** is caused by the crystal environment around the photoreactive group, the photoreaction of the monohydrate crystal **IV** was examined. The crystal structure before photoirradiation, viewed along the *a* axis, is shown in Figure 8. The crystal structure is different from that of **I**, which is shown in Figure 1. The O7 atom of the water molecule makes three hydrogen bonds with O5 and O6 of the neighboring cobaloximes, O7–HO7A···O5 and O7–HO7B···O6, respectively, and N5 of the amine, N5–H51···O7. These bonds connect the molecules along the *a* and *b* axes.

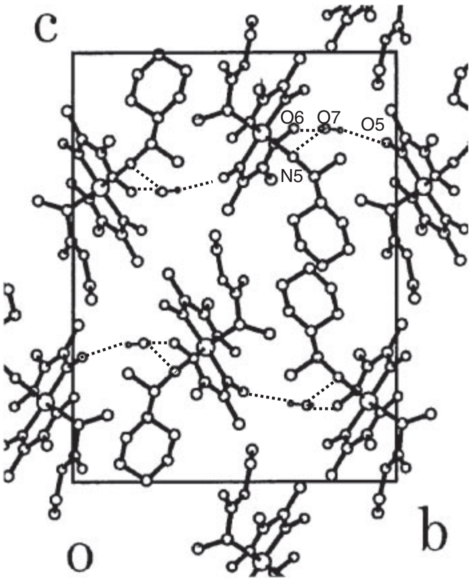


Figure 8. Crystal structure of **IV** viewed along the *a* axis. The dotted lines indicates the N–H···O and O–H···O hydrogen bonds.

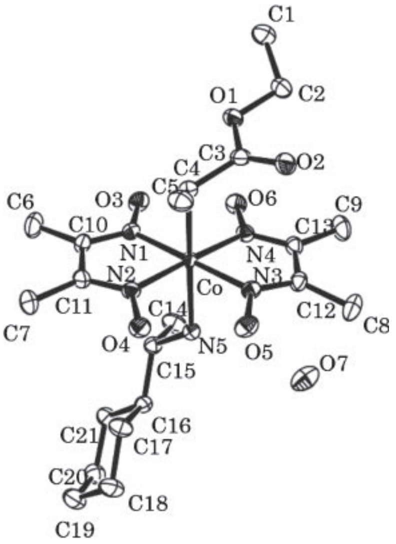


Figure 9. Molecular structure of **IV**. The thermal ellipsoids are drawn at 50% probability level. Hydrogen atoms are omitted for clarity.

The molecular structure is shown in Figure 9. The conformation of the axial ligand, (*S*)-che-amine, takes a chair form similar to that in **I**. However, the rotation angle around the Co–N bond is different from that of **I** as shown in Figure 2, the torsion angles of N2–Co–N5–C15 being 78.2(2)° and

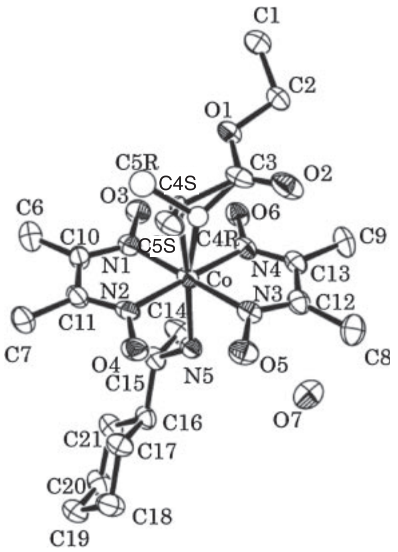


Figure 10. Molecular structure of **IV***. The thermal ellipsoids are drawn at 50% probability level. Hydrogen atoms are omitted for clarity.

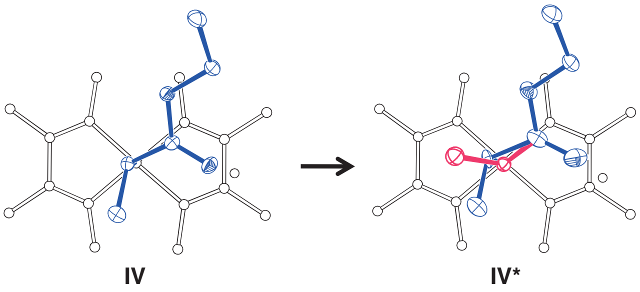


Figure 11. Structural change of the ece group in the photoreaction of **IV**. Only C4 and C5 atoms take the inverted positions. Therefore, the methyl group of C5 is changed from *syn* to *anti* conformation.

−30.9(3)° for **IV** and **I**, respectively. The rotation angle around the Co–C bond of the (*S*)-ece group is similar to that of **I** shown in Figure 3. The torsion angles of N2–Co–C4–C5 being 40.7(2) and 69.3(4)° for **IV** and **I**, respectively. The conformation of the methyl group, C5, is *syn* as observed in **I**.

When the crystal was exposed to the halogen lamp, the cell dimensions gradually changed with retention of the single crystal form. After 24 h exposure, the unit cell volume greatly increased by 102.3(8) Å^3. Although the crystal structure is essentially the same as that before photoirradiation, the molecular structure became disordered, as shown in Figure 10. Only C4 and C5 atoms are partly changed and therefore the absolute configuration of the ece group is partly changed from *S* to *R*, as shown in Figure 11. The ratio of the occupancy factors of (*S*)- and (*R*)-ece groups was 56:44, which would be close to 50:50 after prolonged photoirradiation.

For the crystal of **IV**, the photoreaction of the ece group is only racemization of the chiral group, which is usually observed in the alkyl-cobaloxime complex crystals.[18] This result clearly indicates that the chirality inversion observed in **I** is caused by the specific environment around the ece group in the crystal structure.

Discussion

Why Does the Marvelous *S*:*R* Ratio Appear? In a serial study of crystalline-state reactions of cobaloxime complexes, it has been observed that the reaction rate and reaction pathway are controlled by the reaction cavity for the reactive group.[19] The reaction cavity is defined as the concave space limited by the envelope surface of the spheres, whose centers are positions of inter- and intramolecular atoms in the neighborhood of the reactive group.[9] Any point in the cavity is then considered to be accessed by the centers of atoms of the reactive group. The atoms of the reactive group should occupy the void space in the reaction cavity after the reaction. Therefore, the larger is the reaction cavity, the faster the reaction rate.

The reaction cavities for the ece group in **I**, **II**, and **III** viewed along the normal to the cobaloxime plane are drawn in Figure 12. Each cavity is divided into two parts by the plane which is perpendicular to the cobaloxime plane and parallel to a C–C bond of the cobaloxime (C10–C11), passing through the cobalt atom. The volume ratio of the left to right sides in each cavity becomes 38:61, 46:54, or 47:53 for **I**, **II**, or **III**, respectively. It must be emphasized that the volume ratio of **II**, is not 50:50 but is 46:54. This is probably due to the asymmetric environment around the *racemic*-ece group in the chiral $P2_12_12_1$ cell.

After the photoirradiation the ece groups of the three crystals, **I***, **II***, and **III***, became essentially the same disordered structure with the *S*:*R* ratio of 18:82. The reaction cavity of **I*** is shown in Figure 13. The ratio of the left to right sides in the cavity is 51:49, which is almost the same as 50:50. The corresponding ratios of the reaction cavities of **II*** and **III*** are 51:49 and 51:49, respectively, and is also the same as **I***.

It is clear that the asymmetric reaction cavities of **I**, **II**, and **III** became nearly the mirror symmetric one in the photoreaction. The ece group may have an equal chance to become *S* or *R* configuration in the symmetric reaction cavity. The marvelous *S*:*R* ratio is caused by the change from asymmetric reaction cavity to symmetric, that is, a change in the shape of the reaction cavity.

In the preparation of **1** and **3** as shown in Scheme 3, the resolution of a pair of diastereoisomers, **2**, by repeating the recrystallization was attempted. Since all the trials were in vain, another amine, (*S*)-1-phenyl-2-(*p*-tolyl)ethylamine, was used instead of (*S*)-1-(cyclohexyl)ethylamine. It was made clear why the optical resolution of **2** was unsuccessful as follows; when the mixture of the diastereoisomers reached an *S*:*R* ratio of 18:82 in the recrystallization, the diastereomeric pair reached a most stable mixture and therefore further resolution may be impossible. In the crystallization, the molecules would assemble with each other and the most stable structure should be formed. In the photoreaction, on the other hand, the Co–C bond would be easily cleaved and the produced alkyl radicals would take the most stable structure in the framework composed of the cobaloximes and axial base ligands. The dynamic property of the collective molecules in the solution may be observed in the structural change of the crystalline state photoreaction.

Why Do I and IV Take a Different Reaction Pathway? The reaction cavity for the ece group of **IV** is shown in Figure 14. The shape of the cavity is curved, compared with that

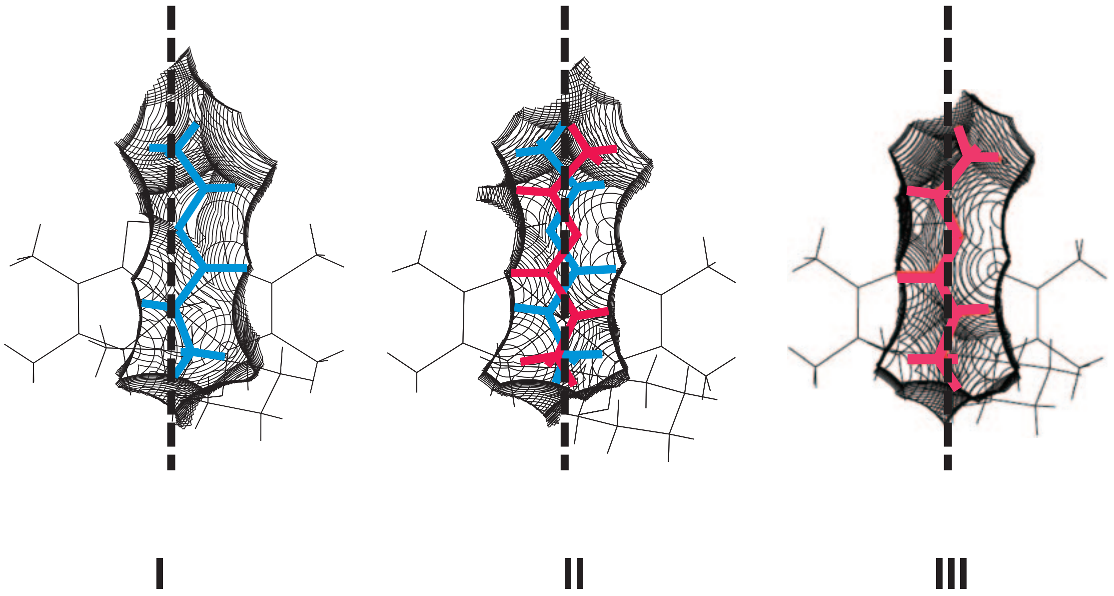


Figure 12. Reaction cavities for the ece groups in **I**, **II**, and **III**. The dotted line in each figure indicates the mirror plane dividing the cavity into two parts. The blue and red colored ece groups have *S* and *R* configurations, respectively.

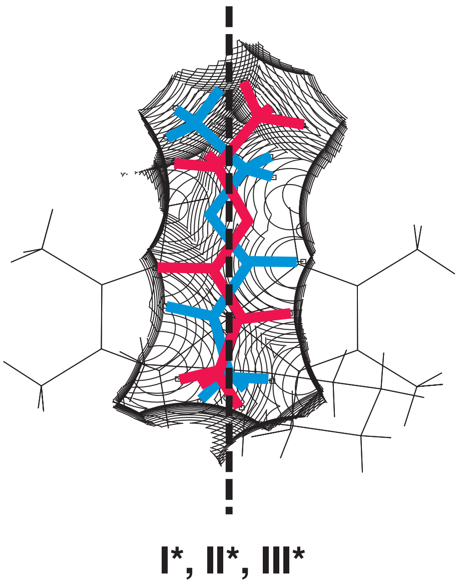


Figure 13. Reaction cavity for the ece group after photoirradiation, **I***, **II***, and **III***. The dotted line indicates the mirror plane dividing the cavity into two parts. The blue and red colored ece groups have *S* and *R* configurations, respectively.

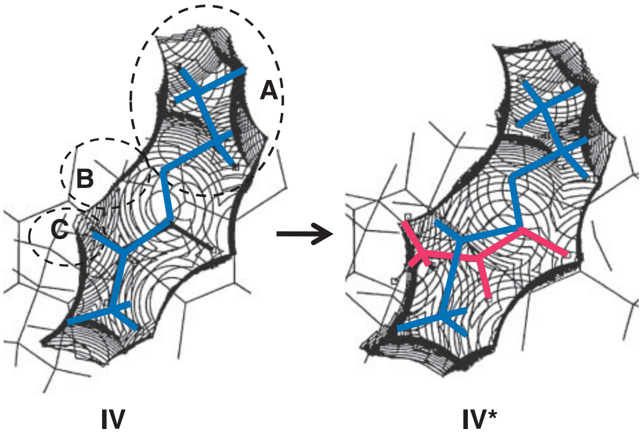


Figure 14. Reaction cavities before and after the photoreaction, **IV** and **IV***. The dashed circles indicate the three regions. A and B may be used for the inversion of C1, C2, and O2 if the same inversion of the ece group as those of **I**, **II**, and **III** would occur. But only C is used for the inversion of C5, because A and B are too narrow.

of **I**. The size of the cavity is 23.5 Å^3 which is much smaller than those of **I**, **II**, and **III**, which are 43.0, 41.2, and 40.4 Å^3, respectively. After the photoreaction, the cavity volume of **IV*** is 27.4 Å^3, which is still smaller than those of **I**, **II**, and **III**. This indicates that the small size of the cavity of **IV** is a reason why **IV** cannot take the same reaction pathway as **I**.

The structure of **IV*** is different from **I***. As shown in Figure 11, only the methyl group of the ece group is inverted to the opposite configuration in **IV***, whereas a whole group is inverted to the opposite configuration in **I***. As shown in Figure 14, the reaction cavity around the peripheral C1 and C2 atoms of the ece group, indicated as A, is very narrow. Moreover, there is no space at the position occupied by the inverted O2 atom, B, which is indicated by the dashed circle. As shown in Figure 14, the inverted ece group with *R* configuration is barely accommodated in the cavity. The larger expansion of the unit-cell volume of **IV** after photoirradiation than those of **I**, **II**, and **III** is necessary to accommodate the inverted methyl group at the space C. It is easier to make the space C than to expand a whole cavity to make the space A and B. This is another reason why **IV** takes a different pathway from the other crystals. This means that not only the small size of the cavity but also the narrow shape of the cavity prevents the crystal of **IV** to take the same pathway as those of **I**, **II**, and **III**.

Conclusion

In summary, it was observed that an unusual reaction of chirality inversion occurred only by photoirradiation in the isomorphous crystals, **I**, **II**, and **III**. The mechanism of the inversion process was analyzed with X-ray crystal structure analyses before and after the photoirradiation since the reactions proceeded with retention of the single-crystal form. The reasons why the chiral ece group bonded to the cobalt atom is inverted to the opposite configuration and why the inversion converges to the marvelous S:R ratio of 18:82 were clearly explained with the concept of the reaction cavity for the photoreactive ece group. Moreover, the pseudo-polymorphous crystal, **IV**, also revealed the crystalline-state photoreaction. However, the change is not a chirality inversion but a racemization. The different reactivity is clearly explained by the difference in the size and shape of the reaction cavity for the ece group in **IV**, compared with the corresponding cavities in **I**, **II**, and **III**. At the active sites of protein molecules, the different residues of the amino acids or the existence of water molecules may have a great influence on the enzymatic reactions. A similar effect to the present one may control the enzymatic reactions.

In general, the reactions in solid state and in the condensed matter, are more complicated than those in gas- and solution state. This is because the motions of molecules and the substituents are strongly limited due to the steric repulsion from the surrounding molecules. This indicates that the steric repulsion should be considered quantitatively when the precise reaction mechanisms in the solid and in condensed matter are taken into account. The reaction cavity for the reactive group is simple but very convenient to explain not only the crystalline-state reactions but also solid-state ones. In most papers reporting solid-state reactions, it has been claimed that the mechanism may be explained topochemically.[20] However, the topochemical concept is not rigidly defined. For example, the 1-ece group in the crystal of **I** is inverted to the opposite configuration whereas the same group in **IV** is racemized. The reaction pathways are completely different between the two crystals. The topochemical principle is unable to explain the different pathways. The reaction cavity is an indispensable tool to explain the mechanism of solid-state reactions. We expect the reaction cavity instead of topochemical considerations should be applied if the crystal structure before the reaction is obtainable.

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