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Isolation, absolute configuration, and chiral crystallization of optically active seleninic acid ☆

Yusuke Nakashima,[a] Toshio Shimizu,[a] Kazunori Hirabayashi,[a] Nobumasa Kamigata,[a,*] Masanori Yasui,[b] Masaki Nakazato[b] and Fujiko Iwasaki[b]

[a]*Department of Chemistry, Graduate School of Science, Tokyo Metropolitan University, Minami-ohsawa, Hachioji, Tokyo 192-0397, Japan*
[b]*Department of Applied Physics and Chemistry, The University of Electro-Communications, Chofu, Tokyo 182-8585, Japan*

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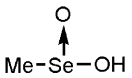
Abstract—An optically pure seleninic acid was isolated as stable crystals for the first time by chiral crystallization. The relationship between the absolute configurations and the circular dichroism spectra of the enantiomers could be determined by X-ray crystallographic analysis.

Chalcogenic acids are tricoordinated chalcogen compounds having pyramidal structures around the chalcogen atoms.[1,2] Therefore, chiral centers exist on the chalcogen atoms of the chalcogenic acids. However, to our knowledge there are no reports of the optical resolution of chalcogenic acids. One reason for the lack of any reports is that optically active chalcogenic acids racemize rapidly. Another reason is the instability of arenesulfinic acids, which are known to undergo disproportionation.[3]

Recently, we succeeded in the optical resolution of areneseleninic acids by means of liquid chromatography on a chiral column, and found that the racemization of areneseleninic acids is suppressed to some extent by bulky substituents at the *ortho* position of the benzene ring.[4,5] However, chiral areneseleninic acids racemize in solution (particularly at high concentrations) and the concentration of the eluate leads to complete racemization. Therefore, optically active seleninic acids are difficult to isolate as stable solids.

Chiral crystallization is a well known method for isolating of optically active compounds that readily racemize in solution.[6] If seleninic acids crystallized in a chiral space group, isolation of the enantiomers of the seleninic acids as stable crystals would be realized. We examined the recrystallization of some seleninic acids and found that methaneseleninic acid crystallized in a chiral space group from methanol/toluene. We describe herein the isolation of an optically pure seleninic acid as stable crystals by chiral crystallization. The absolute configurations of the enantiomers of methaneseleninic acid was assigned on the basis of X-ray crystallographic analysis.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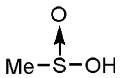
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Methaneseleninic acid (**1**), prepared by oxidizing of dimethyl diselenide with hydrogen peroxide,[7] was recrystallized. Circular dichroism spectra were measured in the solid state (KBr disk made from a single crystal) in order to check whether a crystal is chiral or not, because methaneseleninic acid is considered to racemize rapidly in solution. Each crystal of **1** obtained by recrystallization from methanol/toluene[8] showed a positive or negative Cotton effect at around 250 nm (Fig. 1), whereas crystals of **1** obtained by recrystallization from methanol did not show any Cotton effect.

Keywords: Seleninic acid; Optically active compounds; Absolute configuration; Chiral crystallization.

☆ Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2004.01.107

* Corresponding author. Tel.: +81-426-77-2556; fax: +81-426-77-2525; e-mail: kamigata-nobumasa@c.metro-u.ac.jp

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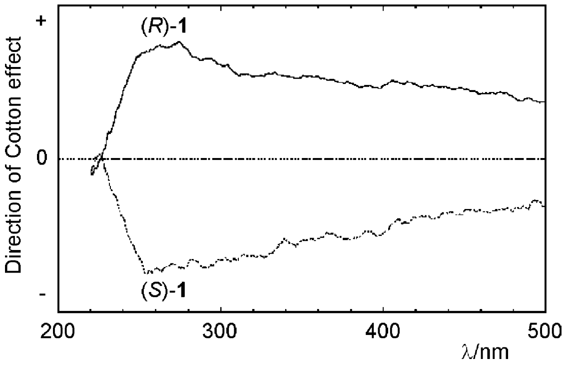

Figure 1. Circular dichroism spectra of enantiomers of methaneseleninic acid (**1**) in the solid states (KBr disk).

No Cotton effect was observed in methanol solution even within 5 s after the dissolution of a chiral crystal of **1** at room temperature. These results indicate that one single crystal may be constituted by only one enantiomer and the enantiomer of **1** racemizes very rapidly in solution.

The crystal structure of **1**, which showed a negative Cotton effect, was determined by X-ray crystallographic analysis. The crystal is orthorhombic and belongs to the chiral space group $P2_12_12_1$, and the two oxygen atoms of the OH and Se=O groups can be discriminated on the basis of the bond distances between the selenium atom and the oxygen atoms, as shown in Figure 2.[9] The hydrogen atom of the OH group was found on the D-map. It was found that the single crystal is composed of one enantiomer and the absolute configuration on the selenium atom was determined to be *S*-form. The packing structure revealed intermolecular hydrogen bonds existing between the hydrogen atom of OH and the oxygen atom of Se=O, and the molecules are connected lengthwise via the hydrogen bonds. The atomic distance between the oxygen of Se=O and the oxygen of OH of the neighboring molecule is 2.548(3) Å, which is slightly shorter than that of acetic acid (2.63 Å),[10] and is almost the same as that of benzeneseleninic acid (2.52 Å).[11] This is the first example of the isolation of optically active seleninic acid as a stable solid and the determination of its absolute configuration.

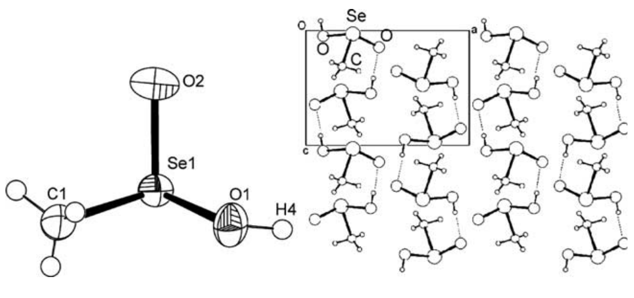

Figure 2. Crystal structure and crystal packing of optically pure methaneseleninic acid (*S*)-**1**. Selected bond lengths (Å) and bond angles (°): Se1–O1 1.753(2), Se1–O2 1.669(2), Se1–C1 1.914(4), O1–Se1–O2 103.50(12), O1–Se1–C1 93.59(15), O2–Se1–C1 100.79(15).

The isolation of optically active seleninic acid **1** in bulk was accomplished by chiral crystallization. A chiral single crystal was pulverized and seeded in a supersaturated methanol/toluene solution of **1**. Ten crystals were selected at random from the crystals obtained, and their circular dichroism spectra were measured independently in the solid state (KBr disk). In one case that used (*S*)-**1** as seed crystal, 99% of **1** was recovered as crystals, and all 10 crystals showed negative Cotton effects (*S*-form), which may mean that the absolute configuration of all the crystals obtained in the pot is *S*. However, in another case of using (*S*)-**1**, 97% of **1** was recovered, and seven crystals showed negative Cotton effects whereas three crystals showed positive Cotton effects. The results indicate that the reproducibility of this method is low (in 4 of 13 cases, all 10 crystals from one pot showed the same sign of the Cotton effect as seed crystals). Therefore, the preparation of a large single crystal was attempted to obtain a lump of enantiomerically pure **1**. In a supersaturated methanol solution of **1** (1 g), a chiral single crystal of **1** was tied with a string. A crystal grown in the methanol solution was hung again in the supersaturated solution that was prepared by dissolving other precipitates in the mother liquor by heating, and it developed into a large chiral single crystal of an enantiomer of **1**. The optical purity of the crystals was confirmed by measuring of the circular dichroism spectra (KBr disk) of some broken pieces of crystal originating from a single crystal. In one case, 753 mg of a single crystal with the *R*-form was obtained in 75% recovery yield. In another case, 701 mg of a crystal with the *S*-form was obtained in 69% recovery yield.

The sulfur analogue of **1**, methanesulfinic acid (**2**), has been reported to form crystals that belong to a chiral space group.[12] However, neither determination of the absolute configuration nor measurement of the chiroptical property was successful.[13] Measurement of the circular dichroism spectrum of a single crystal of **2** obtained by recrystallization from ether/hexane was also attempted in the solid state (KBr disk). However, **2** was decomposed during the preparation of the KBr disk, perhaps because **2** has a low melting point (40–42 °C) and is unstable in air.[12] Finally, measurement of the circular dichroism spectrum of **2** was achieved in the solid state (neat; powder). A sample was prepared

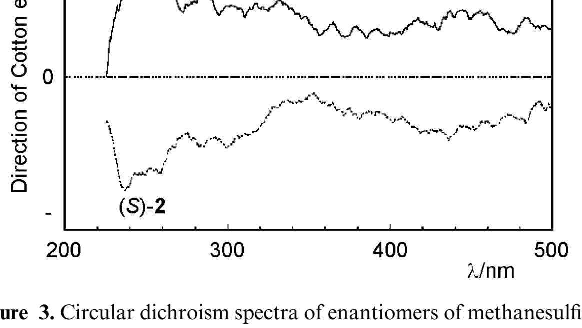

Figure 3. Circular dichroism spectra of enantiomers of methanesulfinic acid (**2**) in the solid states (neat; powder).

according to the following procedure at −196 °C; a single crystal of **2** was pinched between two quartz glasses and pulverized. Then, the circular dichroism spectrum was measured. The circular dichroism spectrum of one sample showed a negative Cotton effect at around 240 nm, as shown in Figure 3, and the shape of the spectrum was similar to that of (*S*)-**1**. On the other hand, one crystal showed a positive Cotton effect in the same region. On the basis of the similarity in circular dichroism spectra between **2** and **1**, the absolute configuration of the crystal of methanesulfinic acid (**2**) that showed a negative Cotton effect was determined to be the *S*-form and that of the crystal with a positive Cotton effect is *R*.

References and notes

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8. The methanol/toluene (1:1) solution (3 mL) of **1** (0.5 g) was allowed to stand for a day at room temperature, and the crystals participated were filtrated.
9. Crystal data of **1** with negative Cotton effect: CH_4O_2Se, $M_r = 127.00$; orthorhombic, space group $P2_12_12_1$, $a = 7.7090(6)$, $b = 8.1174(6)$, $c = 5.4658(6)$ Å, $V = 342.03(5)$ Å^3, $Z = 4$, $T = 293$ K, $D_c = 2.466\ \mathrm{g\,cm^{-3}}$, $\mu = 10.746\ \mathrm{mm^{-1}}$ (Mo Kα 0.71073 Å). A prismatic crystal with dimensions of $0.35 \times 0.25 \times 0.22\ \mathrm{mm^3}$ was used for the data collection. A total of 1782 reflections were measured of which 790 reflections ($R_{int} = 0.024$) including Bijvoet pairs were independent and 775 reflections with $I > 2\sigma(I)$. Lorentz and polarization corrections were made. Absorption correction was applied using a Ψ scan method with $T_{min} = 0.614$, $T_{max} = 0.993$. All H-atoms were located on the D-map and refined with isotropic thermal parameters. Final refinement with 54 parameters against 790 reflections gave $R = 0.0238$, $wR = 0.0530$, and $\Delta\rho_{min} = -0.53$, $\Delta\rho_{max} = 0.42\ \mathrm{e}$ Å^{-3}. Absolute structure parameter was −0.02(3). Crystallographic data (excluding structure factors) for the structures in this paper, have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 227462.
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