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Optical Resolution and Racemization Mechanism of a Tellurinic Acid

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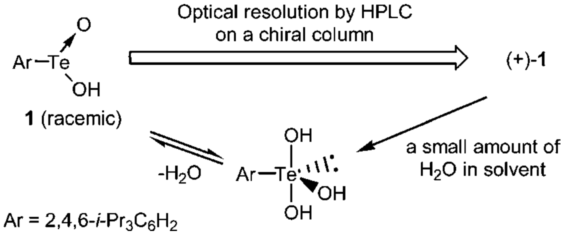
ABSTRACT



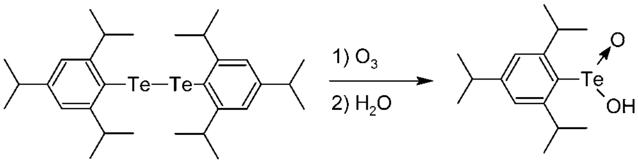
Optically active tellurinic acid was obtained for the first time by chromatographic resolution of racemic 2,4,6-triisopropylbenzenetellurinic acid (1) using a chiral column. Optically active tellurinic acid (+)-1 was stable toward racemization in hexane, although racemization occurred in hexane/2-propanol. The kinetic studies for the racemization, oxygen exchange reaction using $H_2{}^{18}O$, and theoretical studies clarified that the racemization of the optically active tellurinic acid in solution proceeds via a hypervalent tellurane formed by addition of water remaining in solvent.

Recently, we reported the optical resolution of areneseleninic acids by means of liquid chromatography on an optically active column[1,2] and the isolation of optically pure methaneseleninic acid as a stable solid by chiral crystallization.[3] As far as we know, no study has been reported on optically active tellurinic acids, which are analogues of the seleninic acids. Moreover, there are few reports on the preparation of racemic tellurinic acids so far.[4]

We examined the optical resolution of an arenetellurinic acid by means of liquid chromatography on optically active columns and succeeded in obtaining an optically active tellurinic acid for the first time. In this paper, we report the optical resolution and the kinetic studies of the racemization of a tellurinic acid.

2,4,6-Triisopropylbenzenetellurinic acid (**1**) was prepared in 32% yield from the corresponding ditelluride by oxidation with ozone followed by hydrolysis (Scheme 1). Tellurinic acid **1** showed broad signals in both the aromatic and aliphatic regions on the ^1H NMR ($CDCl_3$) spectrum, and broad bands centering on 3400 (OH) and 647 (Te═O) cm^{-1}

Scheme 1. Preparation of 2,4,6-Triisopropylbenzenetellurinic Acid (**1**)



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on the IR (KBr) spectrum. These results may be due to intermolecular interactions among tellurinic acids both in solution and in the solid state.

When tellurinic acid **1** was subjected to chromatography on two types of chiral column (4.6 mm × 250 mm), one packed with amylose carbamate derivative-silica gel and the other with cellulose carbamate derivative-silica gel, using hexane/2-propanol as the eluent, the chromatograms showed only one peak. However, we surmised that the ratio of the enantiomers differs between the former portion and the latter portion of the peak. Then tellurinic acid **1** was subjected to chromatography on a larger column (10 mm × 250 mm) that was packed with cellulose carbamate derivative-silica gel using hexane as the eluent, and the eluates were divided into several fractions. The fraction corresponding to the first half of the peak showed a positive specific rotation $\{[\alpha]^{28}_{435}\ 2.5 \times 10^{3}$ (*c* 0.0012, hexane)$\}$, as well as a positive first Cotton effect and a negative second Cotton effect at 270 and 238 nm (Figure 1), respectively, on the circular dichroism spectrum, whereas the following fractions showed no Cotton effect. In the case of optically active seleninic acids, concentration of the eluates caused complete racemization.[1,2] By contrast, concentration of the hexane solution of (+)-**1** did not reduce the molar ellipticity, indicating that no racemization of the optically active tellurinic acid took place by concentrating the eluate under reduced pressure. To our knowledge, this is the first report of the isolation of an optically active tellurinic acid, although the enantiomeric excess was not determined.

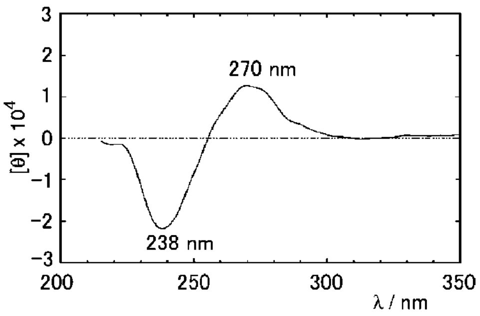

Figure 1. Circular dichroism spectrum of (+)-**1** in hexane.

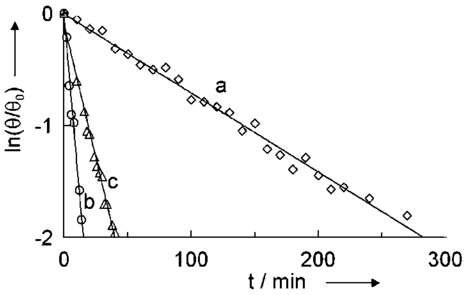

Figure 2. First-order rate plots for the racemization of optically active tellurinic acid (+)-**1** (ca. 0.02 mM): (a) in hexane/2-propanol (99/1); (b) in 2-propanol/H_2O (4/1); (c) in 2-propanol/D_2O (4/1).

The change of the circular dichroism spectrum of (+)-**1** in various solvents was monitored at room temperature to investigate the stability toward racemization of (+)-**1**. No change was observed in the ellipticity at 270 nm on the circular dichroism spectrum of (+)-**1** in hexane even after 3 days, indicating (+)-**1** is stable toward racemization under the given conditions. However, the ellipticity decreased with time in hexane/2-propanol (99/1) and showed a good linear relationship in the first-order rate plots (Figure 2a). Racemization of (+)-**1** was also observed in 2-propanol/H_2O (Figure 2b). The first-order rate constants for the racemization of (+)-**1** in hexane/2-propanol (99/1) and in 2-propanol/H_2O (4/1) are 1.18×10^{-4} and 2.16×10^{-3} s^{-1}, and the half-lives are 98.2 and 5.34 min, respectively. The rate constant in 2-propanol/H_2O is much larger than that in hexane/2-propanol, indicating that a small amount of water in the distilled 2-propanol may have caused the racemization of the optically active tellurinic acid. Two mechanisms of the racemization in which water participates are proposed. One involves the formation of an achiral tellurane by the addition of water to tellurinic acid, and the other involves the formation of an achiral tellurinate anion by deprotonation of tellurinic acid by water. When racemic tellurinic acid **1** was dissolved in 2-propanol/$H_2{}^{18}O$ (4/1, 95 atom %^{18}O) and allowed to stand for 2 h, the ratio of 2,4,6-*i*-$\mathrm{Pr_3C_6H_2Te^{16}O_2H}$:2,4,6-*i*-$\mathrm{Pr_3C_6H_2Te^{16}O^{18}OH}$:2,4,6-*i*-$\mathrm{Pr_3C_6H_2Te^{18}O_2H}$ was 5:3:5 based on the peak intensities on the MS spectrum, meaning that the oxygen atoms of the tellurinic acid were exchanged via an achiral tellurane formed by the addition of water. The rate constant for the racemization was also measured in 2-propanol/D_2O (4/1) (Figure 2c). The rate constant (7.87×10^{-4} s^{-1}) is approximately one-third of that in 2-propanol/H_2O, indicating that there is a primary kinetic isotope effect of the racemization and the rate-controlling step is the protonation to tellurinic acid. Vertex inversion and edge inversion are also first-order mechanisms for the racemization of tricoordinated optically active chalcogen compounds.[5] However, the barriers for vertex inversion and edge inversion of benzenetellurinic acid were estimated to be 82 and 26 kcal mol^{-1}, respectively, by MO calculations (MP2[6]/LANL2DZ[7]) using the Gaussian 98 program,[8] which are too

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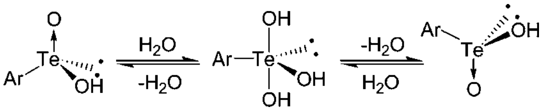
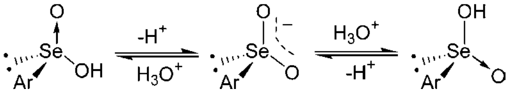
Scheme 2. Mechanism of Racemization of Optically Active Tellurinic Acid in Solution



high for racemization to occur at room temperature. As a result, the racemization of optically active tellurinic acid **1** was concluded to proceed via a hypervalent achiral tellurane formed by the addition of water to the tellurinic acid (Scheme 2). By contrast, the racemization of optically active seleninic acid proceeds via a selenate anion with the extrusion of a proton[2] (Scheme 3). The difference in the mechanism of racemization between optically active seleninic acid and tellurinic acid seems to be that tellurinic acid forms a hypervalent tellurane structure more easily than seleninic acid does. The absolute configuration of (+)-**1** is under investigation.

Scheme 3. Mechanism of Racemization of Optically Active Seleninic Acid in Solution



Supporting Information Available: Experimental procedures; IR, ^{1}H NMR, UV, and MS spectra for **1**; and chiroptical properties of (+)-**1**; and computational data for the theoretical studies. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) **Optical Resolution of 1.** Racemic sample of **1** (30 mg) in hexane (0.5 mL) was charged to a chiral column packed with cellulose carbamate derivative-silica gel (Daicel Chiralcel OD; 10 mm × 250 mm) and eluted with hexane at a flow rate of 1.0 mL min^{-1}. About 1 mg of tellurinic acid was collected from the first half of the peak. The chemical structure was confirmed by ^{1}H NMR spectrum after concentration.

(10) **Kinetic Study for Racemization of (+)-1.** Kinetic studies for racemization of (+)-**1** were examined in solutions (ca. 2×10^{-5} M) at 25 ± 1 °C. The rates of racemization were calculated on the basis of the circular dichroism spectra and were plotted to the first-order rate equation.