Isolation, Stereochemistry, and Configurational Lability of Optically Active Telluroxides

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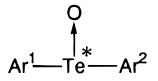
Received March 10, 1997

Ever since an optically active enantiomeric selenoxide was obtained for the first time by Davis and co-workers in 1983,[1,2] there have been several reports on the isolation of optically active selenoxides[3] by various approaches, such as optical resolution of diastereomeric mixtures,[4] chromatographic resolution of enantiomeric mixtures using an optically active column,[5] complexation with a chiral ligand,[6] and asymmetric oxidation of selenides.[7,8] Optically active selenoxides have also been extensively studied as key intermediates in asymmetric synthesis.[3,8a−d,9,10] Optically active telluroxides have also been recently reported as transient key intermediates in asymmetric reactions by Uemura and co-workers.[11] However, optically active telluroxides have not yet been isolated, perhaps because telluroxides undergo racemization *via* a hydrate,[12] formed by the addition of water, much faster than selenoxides.[13] We report here the first isolation of optically active telluroxides by means of optical resolution using an optically active column. Their stereochemistry and configurational labilities are also examined.



1: Ar^1 = mesityl; Ar^2 = 2,4,6-tri-*t*-butylphenyl
2: Ar^1 = phenyl; Ar^2 = 2,4,6-tri-*t*-butylphenyl
3: Ar^1 = mesityl; Ar^2 = 2,4,6-triisopropylphenyl
4: Ar^1 = phenyl; Ar^2 = 2,4,6-triisopropylphenyl

Mesityl 2,4,6-triisopropylphenyl telluroxide (**3**) was subjected to several optically active columns[14] using high-performance liquid chromatography at an analytical scale. Two peaks corresponding to each enantiomer of **3** were observed separately when an optically active column such as AS, AD, OB, or OJ was used, and the best separation was obtained on a column packed with amylose carbamate derivative/silica gel (AS). Using the AS column, 2,4,6-tri-*tert*-butylphenyl mesityl telluroxide (**1**) and 2,4,6-tri-*tert*-butylphenyl phenyl telluroxide (**2**) were also resolved into two peaks corresponding to the enantiomers, as shown in Figure 1, while telluroxide **4**, which has less bulky substituents, showed only one peak. Racemic telluroxide **2** was resolved into its enantioisomers better than **1**. Deterioration of asymmetric recognition for **1** is probably due to steric hindrance around the telluroxide moiety or to the similarity of the bulkiness of the two aryl groups on the tellurium atom of **1**. The chromatogram of telluroxide **3** showed an unusual shape which indicated that racemization was occurring in the column. These results show that a substituent more bulky than a 2,4,6-triisopropylphenyl group is needed to inhibit racemization.

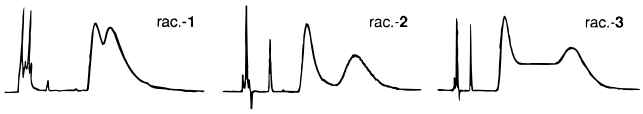


Figure 1. Chromatographic separation of racemic telluroxides **1**, **2**, and **3** on an optically active column (AS) by means of HPLC.

We attempted to resolve the racemic telluroxides **1** and **2** into their optical isomers at a preparative scale using medium-pressure liquid chromatography with the same type of column.[15] In the optical resolution of telluroxide **2**, the first eluted enantiomer had a positive optical rotation {$[\alpha]_D$ 123.0 (*c* 0.16, MeCN)} while the second enantiomer had a negative optical rotation {$[\alpha]_D$ −68.8 (*c* 0.23, MeCN)}. However, the optical purities corresponding to the specific rotations could not be determined because racemization occurred readily.[16] Optically pure telluroxide (+)-**1**[17] was finally obtained (20 mg) from the

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(14) Daicel Chiralpak (4.6 × 250 mm): AS and AD (amylose carbamate derivative/silica gel); OB and OJ (cellulose ester derivative/silica gel); OC, OD, OF, and OG (cellulose carbamate derivative/silica gel).

(15) Daicel Chiralpak AS (10 × 250 mm). The eluents used were hexane/isopropyl alcohol = 98:2 and 95:5 for **1** and **2**, respectively.

(16) Optically pure (+)-**2** was obtained in solution, as confirmed by HPLC analysis. However, after measurement of the specific rotation and circular dichroism spectra, HPLC analysis showed partially racemized (+)-**2**.

(17) Physical and spectral data for (+)-**1** (ee 100%): mp 96.3−97.4 °C; $[\alpha]_D$ +22.5 (*c* 0.36, MeCN), $[\alpha]_D$ +25.3 (*c* 0.22, $CHCl_3$), $[\alpha]_{435}$ +54.7 (*c* 0.36, MeCN), $[\alpha]_{435}$ +129.6 (*c* 0.22, $CHCl_3$); CD (MeCN) 313 ($[\theta]$ +1.7 × 10^4), 286 ($[\theta]$ −1.5 × 10^4), 264 ($[\theta]$ +1.9 × 10^4), 246 ($[\theta]$ −3.1 × 10^4), 236 (sh, $[\theta]$ −2.1 × 10^4), 212 ($[\theta]$ −1.2 × 10^5) nm; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.31 (s, 9H), 1.33 (s, 18H), 2.04 (br s, 6H), 2.21 (s, 3H), 6.74 (br s, 2H), 7.29 (s, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 21.0, 31.2, 31.6, 33.1, 34.5, 39.6, 124.6, 130.3, 133.1, 138.4, 140.9, 142.3, 151.2, 157.5; IR (KBr) ν_{max} 3000−2800, 1590, 1460, 1390, 1245, 1120, 845, 745 cm^{-1}; UV (MeCN) λ_{max} 211 (ϵ 4.8 × 10^4), 243 (ϵ 2.8 × 10^4) nm; FABMS *m/z* 511 (M^+ + 1, ^{130}Te), 509 (M^+ + 1, ^{128}Te), 494, 492, 389, 261, 245, 203, 119. Anal. Calcd for $C_{27}H_{40}OTe$: C, 63.81; H, 7.93. Found: C, 63.83; H, 8.41.

S0002-7863(97)00760-9 CCC: $14.00

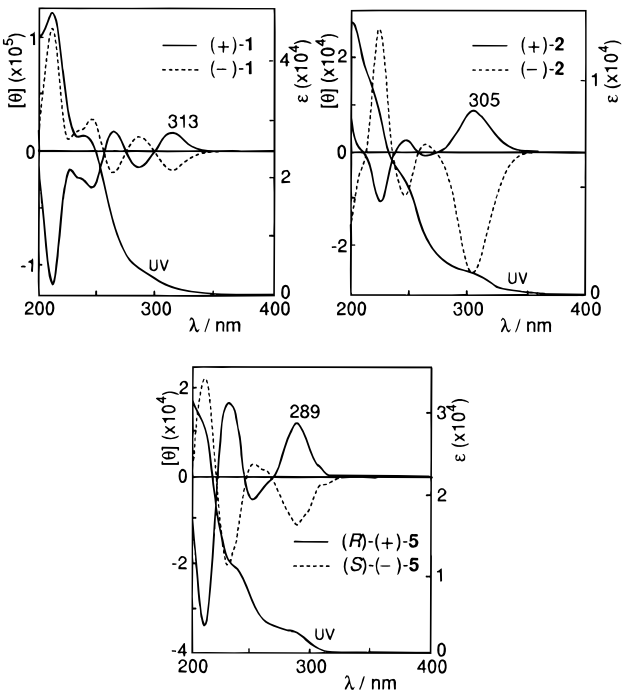

Figure 2. CD and UV spectra of optically active telluroxides (+)-**1**, (−)-**1**, (+)-**2**, and (−)-**2** and selenoxides (*R*)-(+)-**5** and (*S*)-(−)-**5** in acetonitrile.[19]

faster eluent by repeated resolution (two times), and its optical purity was confirmed by ^{1}H-NMR measurement in the presence of dimethyl L-(+)-tartrate as an optically active shift reagent. At the same time, optically active telluroxide (−)-**1**[18] was obtained in 93% optical purity from the later eluent.

Optically active telluroxides (+)-**1** and (+)-**2** show positive first Cotton effects at 313 and 305 nm (benzenoid transition), respectively, and (−)-**1** and (−)-**2** show negative first Cotton effects in the corresponding regions (Figure 2). These first Cotton effects show good correspondence with those of the optically active selenium analogue, 2,4,6-tri-*tert*-butylphenyl phenyl selenoxides ((*R*)-(+)-**5** and (*S*)-(−)-**5**).[5b,19] Therefore, the absolute configuration of telluroxides (+)-**1** and (+)-**2** is assigned to be *R* and that of (−)-**1** and (−)-**2** is *S*.

The stabilities of these telluroxides toward racemization were examined. In the solid state, (+)-**2** (ee 83%) racemized completely after 3 days, while the optical purity of (+)-**1** did not decrease even after 2 weeks (ee 95% to 94%). In methanol that had been freshly distilled from Mg, racemization of telluroxide (+)-**1** (ee 89%) was complete in about 1 day ($k = 6.05 \times 10^{-5}$ s^{-1}; $t_{1/2} = 3.18$ h) as shown in Figure 3, whereas the specific rotation of (−)-**2** was completely lost within 5 min.

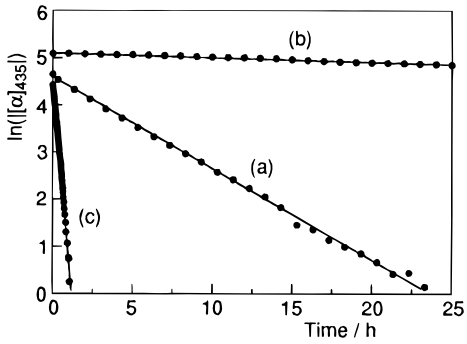

Figure 3. Racemization of optically active telluroxides. (a) (+)-**1** in methanol; (b) (−)-**1** in toluene; (c) (−)-**2** in toluene.

A similar difference in the rate of racemization was observed in toluene that had been freshly distilled from CaH_2 (i.e., the rate constants for racemization of (−)-**1** and (−)-**2** were $k = 3.08 \times 10^{-6}$ s^{-1} ($t_{1/2} = 62.5$ h) and $k = 9.71 \times 10^{-4}$ s^{-1} ($t_{1/2} = 0.20$ h), respectively). These results show that the combination of mesityl and 2,4,6-tri-*tert*-butylphenyl groups as the substituents in a telluroxide is quite useful for inhibiting racemization. We previously reported that optically active selenoxide **5**, which has the same substituents as **2**, did not racemize in methanol even after 5 days.[13] Hence, optically active telluroxides are less stable toward racemization than optically active selenoxides.

There are at least three possible mechanisms for the racemization of telluroxides. One mechanism involves pyramidal inversion, and another involves a four-membered cyclic intermediate formed by dimerization of the telluroxide. The third mechanism involves the formation of an achiral hydrate upon the addition of water. The pyramidal inversion energies for dimethyl chalcogen oxides were estimated from *ab initio* MO calculations.[20] The pyramidal inversion energies for dimethyl sulfoxide, selenoxide, and telluroxide were calculated to be 49.1, 53.2, and 63.9 kcal mol^{-1}, respectively. Therefore, the pyramidal inversion mechanism is not realistic for the racemization of telluroxides, at least at room temperature. The racemization of telluroxides in solution obeyed good first-order kinetics. This observation excludes the second mechanism *via* a dimeric structure. Therefore, racemization may be catalyzed by a trace amount of water which remains in the solvent despite careful purification. Finally, the mechanism which involves the formation of an achiral tetracoordinate hydrate was confirmed by observation of the oxygen exchange reaction of telluroxide. When one drop of $H_2{}^{18}O$ (97 atom %) was added to a methanol solution of (+)-**1** (ee 89%) and stirred at room temperature, the mass spectrum (FAB) showed 41 and 72% ^{18}O-enriched telluroxide[21] at ee values of 34 and 12%, respectively.

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(18) Physical and spectral data for (−)-**1** (ee 93%): mp 113.7−114.6 °C; $[\alpha]_D$ −21.3 (*c* 0.38, MeCN), $[\alpha]_{435}$ −54.4 (*c* 0.38, MeCN); CD (MeCN) 313 ($[\theta]$ -1.6×10^4), 286 ($[\theta]$ $+1.4 \times 10^4$), 264 ($[\theta]$ -1.8×10^4), 246 ($[\theta]$ $+2.9 \times 10^4$), 236 (sh, $[\theta]$ $+1.9 \times 10^4$), 212 ($[\theta]$ $+1.1 \times 10^5$) nm. Other spectra such as ^{1}H- and ^{13}C-NMR, UV, IR, and MS were quite similar with those of (+)-**1**.

(19) Optical purities of (+)-**1**, (−)-**1**, (+)-**2**, (−)-**2**, (*R*)-(+)-**5**, and (*S*)-(−)-**5** for measurement of the CD spectra were 100%, 93%, unknown, unknown, 34%, and 18% ee, respectively.

(20) All geometries at global minima and saddle points for the pyramidal inversion mode were optimized using the second-order Møller−Presset perturbation (MP2) method. The double-zeta plus polarization basis set was used for hydrogen, carbon, oxygen, and sulfur atoms. The (5s4p2d/12s8p5d) and (10s8p4d/16s11p6d) basis sets were used for selenium and tellurium atoms, respectively.

(21) FABMS *m/z* 513 ($M^+ + 1$, $^{130}Te^{18}O$), 511 ($M^+ + 1$, $^{128}Te^{18}O$ and $^{130}Te^{16}O$), 509 ($M^+ + 1$, $^{128}Te^{16}O$).