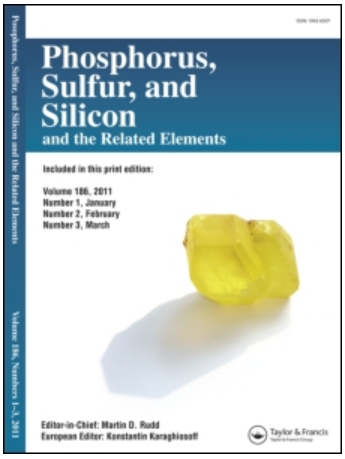

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Synthesis and Stereochemistry of Chiral Selenoxides and Telluroxides

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Synthesis and Stereochemistry of Chiral Selenoxides and Telluroxides

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Optically pure selenoxides stabilized by bulky substituents and/or intramolecular coordination with amino group were isolated by optical resolution of a diastereomeric mixture of selenoxide and chromatographic separation of a racemic mixture of selenoxide using an optically active column. Optically pure telluroxides stabilized by similar techniques were also isolated by chromatographic resolution. The absolute configu-rations were determined by X-ray crystallographic analysis and circular dichroism spectra. Kinetic studies on the racemization of these chiral chalcogen oxides were examined, and a mechanism for the racemization via achiral hydrate was proposed based on the $H_2{}^{18}O$ tracer studies.

Keywords: chiral selenoxide; chiral telluroxide; optical resolution; optically active column; absolute configuration; racemization

INTRODUCTION

A tricoordinate organic sulfur compound, sulfoxide, has a chirality on the central sulfur atom. Many enantiomerically pure sulfoxides were synthesized and isolated as stable crystals, and their structure and reactions have been studied in datail.[1] Moreover, asymmetric reactions utilizing optically active sulfoxide as a chiral source are becoming a very important technique in recent asymmetric organic synthesis since the asymmetric reactions using optically active sulfoxides afford chiral products in high enantiomeric excess.[2] Optically active selenoxide and telluroxide corresponding to the sulfoxide can also be synthesized and isolated since selenium and tellurium are homologous with sulfur, and these compounds will have similar structures. A selenoxide possessing a steroid frame of diastereomeric excess was first synthesized by Jones et al. in 1970,[3] and thereafter several optically active selenoxides having a steroid frame were reported but the compounds were only stable at low temperatures.[4] Selenoxides of enantiomeric excess possessing the chiral center only on the selenium atom were first synthesized by Davis et al., but the optical purities of the obtained selenoxides were only several percent.[5] Moreover, they reported that the selenoxides racemized very rapidly. Thus, it has been considered that optically pure selenoxides are too difficult to isolate as stable crystals, and hence there were hitherto only a few reports on the synthesis and stereochemistry of optically active selenoxides and there was no reports of optically active telluroxides.

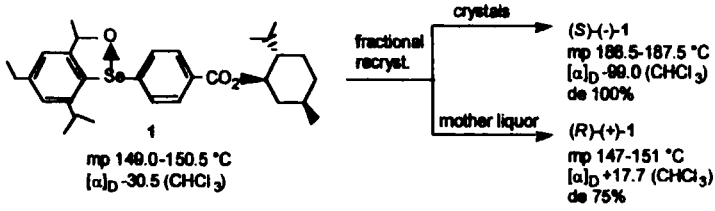
We have succeeded in isolating enantiomerically pure selenoxides and telluroxides as crystals for the first time which were stabilized by bulky substituents (kinetic stabilization).[6] We have also isolated enantiomerically pure selenoxides and telluroxides as crystals by stabilization with intramolecular coordination of amino group on the chalcogen atom (thermodynamic stabilization). This article describes a brief account of the synthesis, stereochemistry, and kinetics and mechanism for the racemization of these chiral chalcogen oxides.

1. OPTICALLY PURE SELENOXIDES

1.1. Synthesis and Stereochemistry of Kinetically Stabilized Optically Pure Selenoxide

It is anticipated that the rate of racemization of optically active selenoxide via a hydrate intermediate by addition of water will be fast since selenium-oxygen bond of selenoxides has high polarity, and therefore, selenoxide will easily react with water. However, optically active selenoxide can be expected to be isolated as stable crystals if the selenoxide has a bulky group and is sterically protected around the selenium atom (kinetic stabilization). A diastereomeric mixture of 4-(-)-menthyloxycarbonylphenyl 2',4',6'-triisopropylphenyl selenoxide (*dia.*-**1**) {mp 149.0-150.5 °C, $[\alpha]_D$ -30.5 ($CHCl_3$)} was synthesized. The diastereomeric mixture *dia.*-**1** was optically resolved by fractional recrystallization from methanol. Diastereoisomerically pure selenoxide

(-)-1 {mp 186.5-187.5 °C, $[\alpha]_D$ -99.0 ($CHCl_3$), de 100%} and diastereoisomerically excess selenoxide (+)-1 {mp 147-151 °C, $[\alpha]_D$ +17.7 ($CHCl_3$), de 75%} were isolated as stable crystals.[7]



The absolute configuration around the selenium atom of optically pure selenoxide (-)-1 was determined to be *S* by X-ray crystallographic analysis (Figure 1), and therefore, that of (+)-1 was determined to be *R* by the specific rotation and CD spectra (Figure 2).

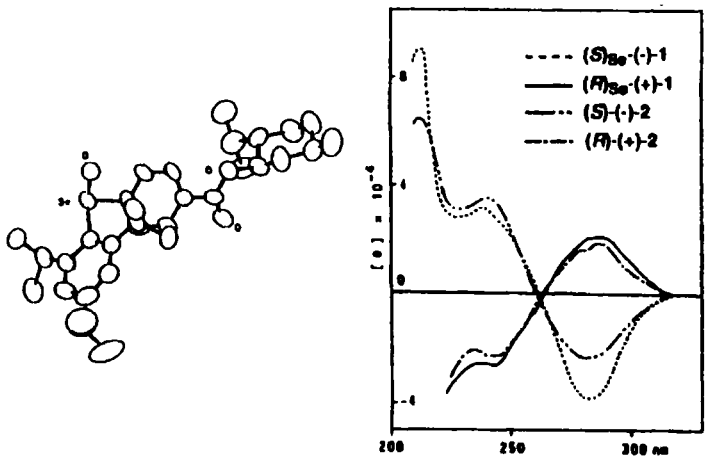
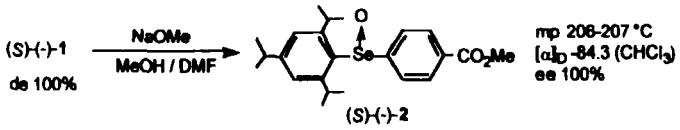


FIGURE 1. X-ray molecular structure of $(S)_{Se}$-(-)-1

FIGURE 2. CD spectra of $(S)_{Se}$-(-)-1, $(R)_{Se}$-(+)-1, (*S*)-(-)-2, and (*R*)-(+)-2

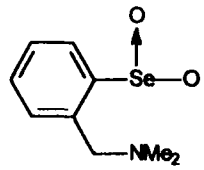
Enantiomerically pure 4-methoxycarbonylphenyl 2',4',6'-triisopropylphenyl selenoxide (*S*)-(-)-(**2**) was isolated by the transesterification of the (-)-menthyl group of diastereoisomerically pure selenoxide (*S*)-(-)-**1** to a methyl group by treating with sodium methoxide in methanol-DMF (1:9). This is the first example for the isolation of enantiomerically pure selenoxide as stable crystals. The optically active selenoxides, (*S*)-(-)-**1**, (*R*)-(+)-**1**, and (*S*)-(-)-(**2**) are stable even under atmospheric moisture at room temperature and can be stored as crystals without racemization.



1.2. Synthesis and Stereochemistry of Thermodynamically Stabilized Optically Pure Selenoxide

Although we have succeeded in isolating the enantiomerically pure diaryl selenoxide (*S*)-(-)-(**2**) for the first time as stable crystals by taking advantage of kinetic stabilization using bulky substituents, isolation of an optically pure alkyl aryl selenoxide is very difficult since it readily undergoes racemization by atmospheric moisture even though the aryl group possesses bulky substituents. Fortunately, there is another method for stabilizing molecular structures, i.e., thermodynamic stabilization by intramolecular coordination of a Lewis base such as an amino group. Racemic mixtures of 2-(*N*,*N*-dimethylaminomethyl)-

phenyl methyl selenoxide (*rac.*-**3a**), 2-(*N*,*N*-dimethylaminomethyl)-phenyl benzyl selenoxide (*rac.*-**3b**), and 2-(*N*,*N*-dimethylaminomethyl)-phenyl phenyl selenoxide (*rac.*-**3c**), which are expected to be stabilized by intramolecular coordination of the amino group to the selenium atom, were designed and synthesized.[8]



3a: R = Me
3b: R = CH_2Ph
3c: R = Ph

The racemic mixture of selenoxides **3a-c** were optically resolved by means of HPLC using an optically active column. When *rac.*-**3a** was subjected to an optically active column packed with amylosecarbamate derivative/ silica gel using HPLC on an analytical scale (hexane/ethanol = 75/25), satisfactory separation into two peaks corresponding to each enantiomer of **3a** was observed on the chromatogram, as shown in Figure 3. Using the same column, *rac.*-**3b** and -**3c** were also excellently resolved into two peaks corresponding to their enantiomers.

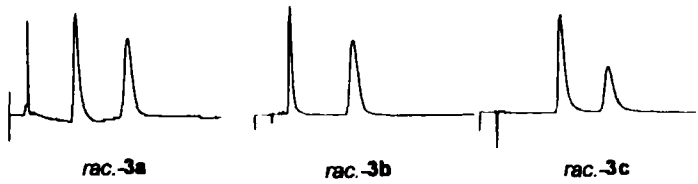


FIGURE 3. Chromatographic resolution of selenoxides **3a-c**

Then, we attempted to resolve racemic selenoxide *rac.*-**3a** into the optical isomers on a preparative scale using a larger column of the same type, and both optically pure enantiomers showing negative specific rotation (-)-**3a** {$[\alpha]_D$ -120.8 (*c* 0.32, $CHCl_3$) and positive one (+)-**3a** {$[\alpha]_D$ +119.8 (*c* 0.23, $CHCl_3$) were obtained from first and second eluate, respectively, by repeated chromatographic resolution. Similarly, optical resolution of racemic selenoxides *rac.*-**3b** and -**3c** yielded their optically active isomers. The results are summarized in Table 1.

TABLE 1. Specific rotation of optically active selenoxides **3a-c**

selenoxide	optical purity[a]	$[\alpha]_D$ ($CHCl_3$)	$[\alpha]_{435}$($CHCl_3$)
(-)-**3a**	100	-120.8 (*c* 0.32)	-313.2(*c* 0.32)
(+)-**3a**	100	119.8 (*c* 0.23)	296.6 (*c* 0.23)
(-)-**3b**	100	-300.4 (*c* 0.50)	-757.4(*c* 0.50)
(+)-**3b**	100	299.2 (*c* 0.50)	791.6 (*c* 0.50)
(-)-**3c**	100	- 48.1 (*c* 0.26)	-117.8(*c* 0.26)
(+)-**3c**	90	37.2 (*c* 0.17)	86.0 (*c* 0.17)

[a]Optical purity was determined by HPLC analysis.

The CD spectra of optically active selenoxides **3a**, **3b**, and **3c** with negative specific rotations showed negative first Cotton effects at 270, 279, and 275 nm in cyclohexane, respectively, while (+)-**3a**, -**3b**, and -**3c**

showed positive first Cotton effects in the corresponding regions, as shown in Figure 4. However, their absolute configuration could not be determined solely by their specific rotations and CD spectra. Optically active sulfoxide having similar substituents, (*S*)-(-)-**4**, was synthesized with inversion of configuration from $(S)_S$-(-)-menthyl-(-)-*p*-toluene-sulfinate (*S*)-(-)-**5** according to Andersen's method.[1a] The CD spectrum of optically active sulfoxide (*S*)-(-)-**4** showed negative Cotton effect at ca. 284 nm, which corresponded well with those of optically active selenoxides with negative specific rotations (-)-**3a-c**.

Furthermore, sulfoxide (*S*)-(-)-**4** was eluted faster than (*R*)-(+)-**4** through the optically active column. Therefore, on the basis of the similarity of the signs of their specific rotations and CD spectra, and their behaviours on the optically active column, the absolute configuration of selenoxides (-)-**3a-c** was assigned to be *S*-form, while that of (+)-**3a-c** was *R*-form.

The optically active selenoxides **3a-c** were stable toward racemization in the solid state and also in a chloroform solution, however, these selenoxides racemized in methanol solution. The rates of racemization were in accordance with the first-order rate equation, and the rate constants for the racemization of (*S*)-(-)-**3a**, **-3b**, and **-3c** in methanol at 27 °C were 2.28×10^{-4}, 4.58×10^{-5}, and 5.58×10^{-6} s^{-1}, respectively. Addition of water to the methanol solution accelerated the racemization. These results indicate that the racemization in methanol is occurring by a trace amount of water remaining in the solvent despite careful purification. When an excess amount of $H_2{}^{18}O$ (97% atom% ^{18}O excess) was added to a methanol solution of (*S*)-(-)-**3c** (ee 87%) and

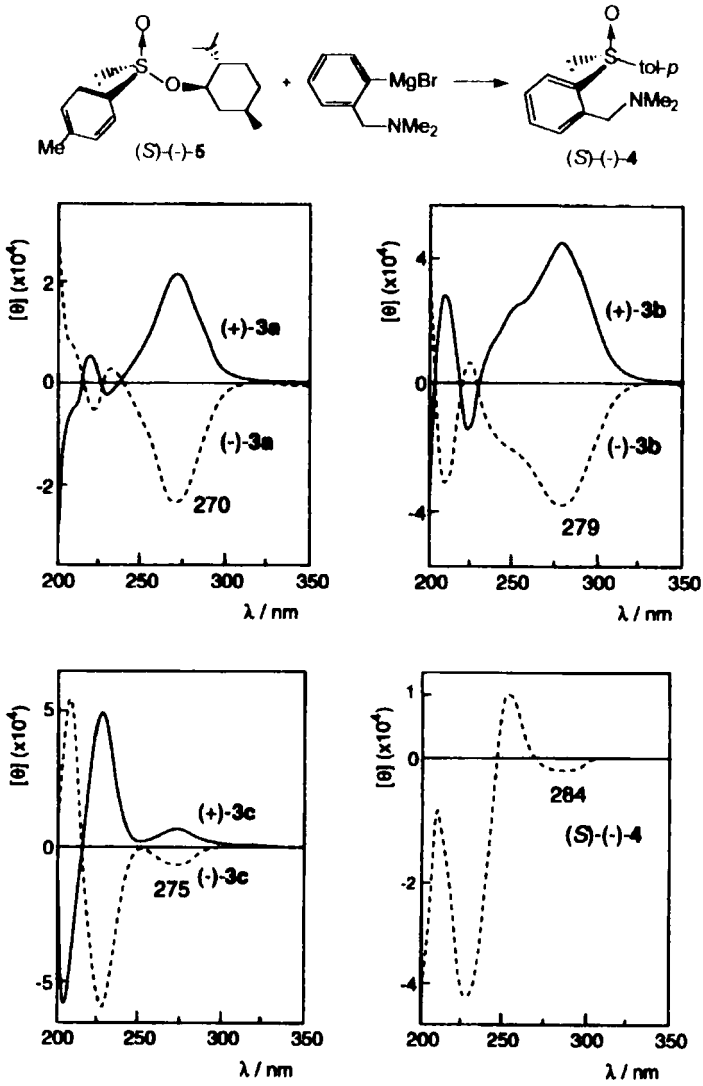
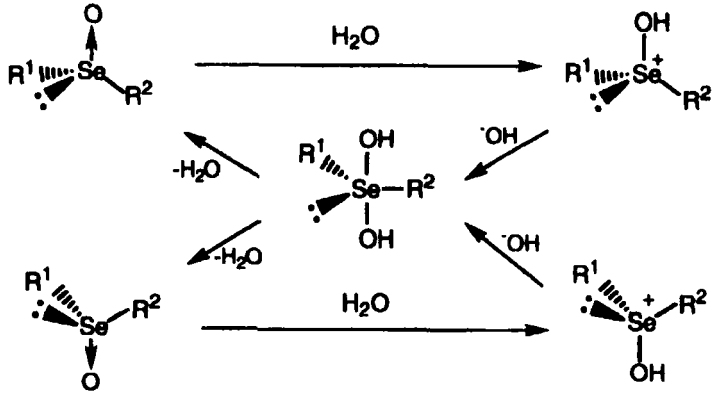


FIGURE 4. CD spectra of optically active selenoxides **3a-c** and sulfoxide (*S*)-(-)-**4** in cyclohexane

stirred at room temperature, a good linear correlation was observed between increment of ^{18}O enrichment and decrement of enantiomeric excess. A mechanism involving formation of an achiral tetracoordinated hydrate was proposed, as shown in Scheme 1.



SCHEME 1

Although optically active selenoxides **3a-c** racemized in methanol, the introduction of *N,N*-dimethylaminomethyl moiety at ortho-position on their phenyl group is very effective to suppress the racemization. For example, optically active selenoxide (*S*)-(-)-**3a** is much more stable (the half-life for the racemization in methanol at 27 °C was 50 min) compared with optically active methyl phenyl selenoxide of which racemization completed within 1 min.[5] The stabilizing effect of the intramolecular coordinatoin of an amino group to the selenium atom was examined by variable-temperature ^1H NMR measurement. Although methyl protons of the amino group of *rac.*-**3a** were observed as a singlet

signal in acetone-d_6 at room temperature which overlapped with that of acetone, two singlet signals corresponding to the two methyl groups were observed at 188 K, due to coordination of the nitrogen atom to the selenium atom, and ν_{ab} was 359 Hz. The two signals coalesced at 212 K to give a broad singlet, as shown in Figure 5. Similar results were also observed in CD_2Cl_2, and the coalescence temperature was 220 K; the ν_{ab} was 255 Hz at 193 K. On the basis of these observations, the exchange energy of the two methyl groups of *rac.*-**3a** was estimated to be 9.45 in acetone-d_6 and 9.97 kcal mol^{-1} in CD_2Cl_2. These values include the coordination energy of the amino group to the selenium atom and the rotation energy of the CH_2-N bond or inversion energy on the nitrogen atom. The rotation barrier of the CH_2-N bond (6.7 kcal mol^{-1}) of *N*-cyclohexyl-*N*-methyl benzylamine has been calculated by HF/3-21G to be larger than the inversion energy (3.8 kcal mol^{-1}) on the nitrogen atom.[9] Therefore, the difference between the observed value, obtained from the ^{1}H NMR measurement, and the rotation energy of the CH_2-N bond should represent the coordination energy of the amino group to the selenium atom. Thus, the coordination energies for selenoxide **3a** were estimated to be 2.8 and 3.3 kcal mol^{-1} in acetone-d_6 and CD_2Cl_2, respectively.

The observed coordination energies are not so large than we have initially expected. Thus, the (*N*,*N*-dimethylamino)methyl group is considered to be effective for stabilizing the selenoxide toward racemization not only by the intramolecular coordination (thermodynamic stabilization) but also steric effect of bulkiness of the substituent (kinetic stabilization).

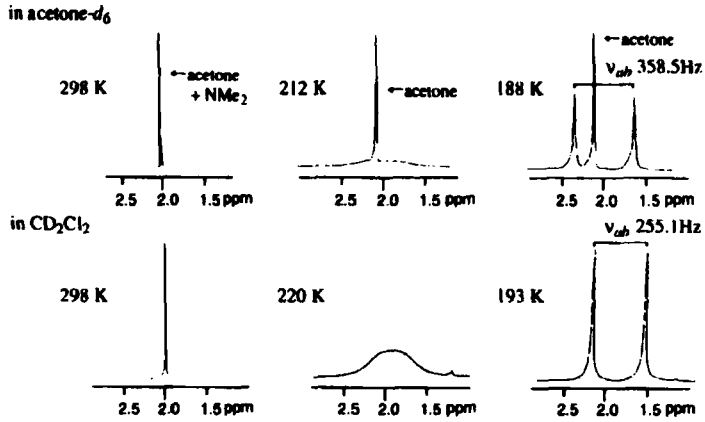


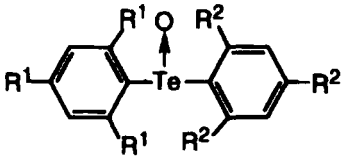
FIGURE 5. ^1H NMR signals for the amino group of variable-temperature NMR spectra for racemic selenoxide *rac*-**3a** in acetone-d_6 and CD_2Cl_2

2. OPTICALLY PURE TELLUROXIDES

2-1. Synthesis and Stereochemistry of Kinetically Stabilized Optically Pure Telluroxide

We have succeeded in isolating optically pure diaryl selenoxides as stable crystals by introduction of bulky substituents on the selenium atom (kinetic stabilization) and alkyl aryl selenoxides by intramolecular coordination of amino group on the selenium atom (thermodynamic stabilization). This success challenged us to attempt to isolate optically pure telluroxides, since the formation of optically active telluroxides has

only been reported as transient key intermediates in asymmetric reactions.[10] First of all, we prepared diaryl telluroxides **6a-e** possessing bulky substituents and tried to isolate each enantiomer in optically pure form by means of optical resolution using an optically active column.[11]



6a: R^1 = Me, R^2 =CMe_3
6b: R^1 = H, R^2 =CMe_3
6c: R^1 = Me, R^2 =$CHMe_2$
6d: R^1 = H, R^2 =$CHMe_2$
6e: R^1 = H, R^2 =$CH(SiMe_3)_2$

When racemic mesityl 2,4,6-triisopropylphenyl telluroxide (**6c**) was subjected to an optically active column with a chiral stationary phase (Daicel Chiralpak AS) using HPLC at an analytical scale, two peaks corresponding to each enantiomer of **6c** were observed. 2,4,6-Tri-*tert*-butylphenyl mesityl telluroxide (**6a**) and 2,4,6-tri-*tert*-butylphenyl phenyl telluroxide (**6b**) were also resolved into two peaks corresponding to the enantiomers, as shown in Figure 6. Racemic telluroxide **6b** was resolved into its enantioisomers better than **6a**. Deterioration of asymmetric recognition for **6a** is probably due to steric hindrance around the telluroxide moiety or the similarity of the bulkiness of the two aryl groups on the tellurium atom of **6a**. The chromatogram of telluroxide **6c** showed an unusual shape maybe because racemization was occurring in the column. Furthermore, 2,4,6-triisopropylphenyl phenyl telluroxide (**6d**) showed only one peak which indicated that racemization is occurring very rapidly in the column since telluroxide **6d** possessing less bulky substituents. These results show that a substituent

more bulky than a 2,4,6-triisopropylphenyl group is needed to inhibit racemization. However, the optical resolution of 2,4,6-tris[bis(trimethylsilyl)methyl]-phenyl phenyl telluroxide (**6e**) possessing very bulky 2,4,6-tris[bis(tri-methylsilyl)methyl]phenyl (Tbt) group could not be achieved perhaps the very bulky Tbt group inhibited recognition of the asymmetry of the telluroxide moiety on the chiral stationary phase.

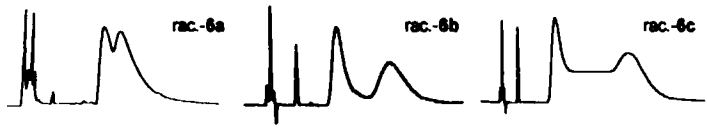


FIGURE 6. Chromatographic separation of racemic telluroxides **6a-c** on an optically active column by means of HPLC

Then, racemic telluroxides **6a-c** were attempted to resolve into their optical isomers at a preparative scale using medium-presssure liquid chromatography with the same type of column. In the optical resolution of telluroxide **6b**, the first eluted enantiomer had a positive specific rotation {$[\alpha]_D$ +123.0 (*c* 0.16, CH_3CN)} while the second enantiomer had a negative specific rotation {$[\alpha]_D$ -68.8 (*c* 0.23, CH_3CN)}. However, the optical purities could not be determined because racemization occurred readily. Optically pure telluroxide (+)-**6a** {ee 100%, mp 96.3-97.4 °C, $[\alpha]_D$ +22.5 (*c* 0.36, CH_3CN), $[\alpha]_D$ +25.3 (*c* 0.22, $CHCl_3$)} was finally isolated from the first eluate by repeated resolution, and its optical purity was confirmed by ^1H NMR measurement in the presence of dimethyl L-(+)-tartrate as an optically

active shift reagent. At the same time, optically active telluroxide (-)-**6a** was obtained in 93% ee {mp 113.7-114.6 °C, $[\alpha]_D$ -21.3 (*c* 0.38, CH_3CN), $[\alpha]_D$ -23.6 (*c* 0.11, $CHCl_3$)} from the second eluate. This is the first example for the isolation of optically pure telluroxide as stable crystals.

The absolute configuration of optically pure telluroxide (+)-**6a** could not be determined by X-ray crystallographic analysis since the compound did not give a good single crystal. Then, the absolute configuration was estimated by CD spectra. The CD spectra of optically active telluroxides (+)-**6a** and (+)-**6b** showed positive first Cotton effects at 313 and 305 nm, respectively, and (-)-**6a** and (-)-**6b** showed negative firast Cotton effects in the corresponding regions (Figure 7). These first Cotton effects show good correspondence with those of the optically active selenium analogue, 2,4,6-tri-*tert*-butylphenyl phenyl selenoxide {(*R*)-(+)-**7** and (*S*)-(-)-**7**}.[6a] Therefore, the absolute configuration of telluroxides (+)-**6a** and (+)-**6b** is assigned to be *R*-form and that of (-)-**6a** and (-)-**6b** is *S*-form.

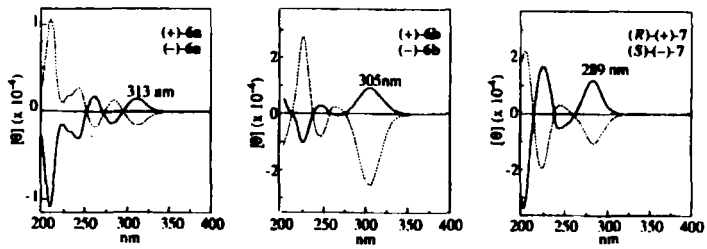


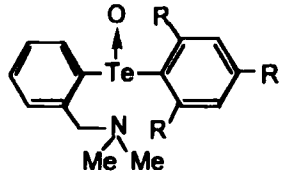
FIGURE 7. CD spectra of optically active telluroxides **6a**, **6b** and selenoxides (*R*)-(+)-**7** and (*S*)-(-)-**7** in acetonitrile

The stabilities of these optically active telluroxides toward racemization were examined. In the solid state, (*R*)-(+)-**6a** did not racemize after 2 weeks, while (*R*)-(+)-**6b** gradually racemized and the racemization completed within 3 days. On the other hand, these telluroxides racemized in chloroform or methanol solutions in spite of the solvent was carefully purified. The rate of racemization for optically active telluroxides (*R*)-(+)-**6a** and **-6b** showed a good linear relationship with first-order rate plots, and the rate constants of (*R*)-(+)-**6a** and **-6b** at 26 °C in chloroform were 2.75×10^{-6} and 7.41×10^{-4} s^{-1}, respectively, and that of (*R*)-(+)-**6a** in methanol was 6.05×10^{-5} s^{-1} while racemization of (*R*)-(+)-**6b** completed within 1 min. These results show that telluroxides racemize more easily than selenoxides, since the first-order rate constant for the racemization of (*R*)-(+)-mesityl phenyl selenoxide was 6.00×10^{-6} s^{-1} in methanol at 26 °C and which did not racemize in chloroform.

2-2. Synthesis and Stereochemistry of Thermodynamically Stabilized Optically Pure Telluroxide

We have succeeded in isolating optically pure telluroxide kinetically stabilized by bulky substituents, however, they were not stable enough toward racemization especially in solutions. Then, we have also tried to isolate optically pure telluroxides stabilized by intramolecular coordination of an amino group on the tellurium atom. Racemic mixtures of 2-(*N*,*N*-dimethylaminomethyl)phenyl mesityl

telluroxide (*rac.*-**8a**), 2-(*N*,*N*-dimethylaminomethyl)phenyl 2',4',6'-triisopropylphenyl telluroxide (*rac.*-**8b**), and 2-(*N*,*N*-dimethylamino methyl)phenyl 2',4',6'-tri-*tert*-butylphenyl telluroxide (*rac.*-**8c**), which are expected to be stabilized by the intramolecular coordination of amino group to the tellurium atom, were designed and synthesized.[12]

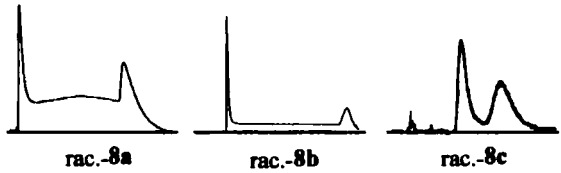


8a: R = Me
8b: R = *i*-Pr
8c: R = *t*-Bu

Chromatographic resolution of telluroxides **8a-c** was examined using several chiral stationary phases at an analytical scale. Racemic telluroxide **8a** was resolved into two peaks corresponding to the enantiomers when a column with cellulosecarbamate derivatives/silica gel (Daicel Chiralcel OD, eluent: hexane/isopropyl alcohol = 60/40) was employed. Similarly, telluroxides **8b** (eluent: hexane/isopropyl alcohol = 70/30) and **8c** (eluent: hexane/isopropyl alcohol = 95/5) could also be resolved into their enantiomers, as shown in Figure 8. The chromatograms of telluroxide **8a** and **8b** showed an unusual shape and indicated that racemization had occurred in the column, while racemization of telluroxide **8c** was not observed. However, when chromatographic resolution was carried out by cooling down the column at -3 °C, telluroxides **8a** and **8b** could be optically resolved very nicely into two peaks corresponding to the enantiomers without racemization in the column. These results show that bulky substituents are also important together with an amino group to inhibit the racemization of telluroxides in the column.

The optical resolution of racemic telluroxides **8a-c** was carried out by HPLC using the same type of optically active column at a praparative scale. Optically pure telluroxides (+)-**8b** {ee 100%, mp 189-191 °C, $[\alpha]_D$ +39.5 (*c* 0.15, $CHCl_3$)} and (+)-**8c** {ee 100%, mp 140-141 °C, $[\alpha]_D$ +166.2 (*c* 0.32, $CHCl_3$)} were isolated from the first eluate, and optically active telluroxides (-)-**8b** {ee 38%, mp 178-182 °C, $[\alpha]_D$ -11.9 (*c* 0.13, $CHCl_3$)} and (-)-**8c** {ee 40%, mp 136-139 °C, $[\alpha]_D$ -66.1 (*c* 0.12, $CHCl_3$)} were obtained from the second eluate, however, optically active telluroxide **8a** could not be isolated because racemization occurred during concentration of the solution.

a) at room temperature



b) at -3 °C

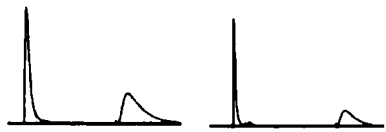


FIGURE 8. Chromatographic separation of racemic telluroxides **8a-c** on an optically active column by means of HPLC

The CD spectra of optically active telluroxides (+)-**8b** and (+)-**8c** showed positive first Cotton effects at 308 and 317 nm, respectively,

and those of (-)-**8b** and (-)-**8c** showed negative Cotton effects in the same region, as shown in Figure 9. The absolute configuration of optically active telluroxides (-)-**8b** and (-)-**8c** was determined by comparing the first Cotton effects of their CD spectra with those of (*S*)-(-)-2-(*N*,*N*-dimethylaminomethyl)phenyl 4'-tolyl sulfoxide {(*S*)-(-)-**4**}.

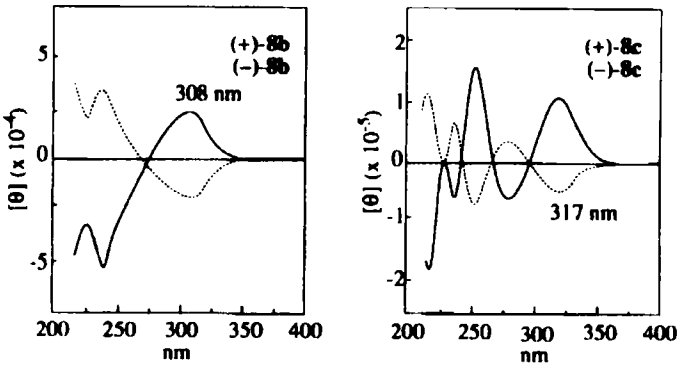
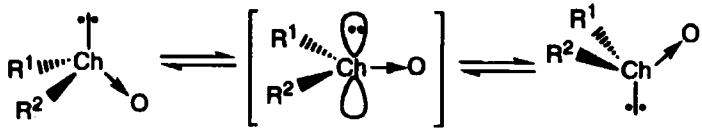


FIGURE 9. CD spectra of optically active telluroxides **8b** and **8c** in cyclohexane

The optically active telluroxide **8c** was stable toward racemization in solid state when it was stored in a desiccator, however, telluroxide **8b** gradually racemized under the same conditions. On the other hand, both telluroxides **8b** and **8c** racemized in a chloroform or methanol solution which were carefully purified. The rates of racemization for (*R*)-(+)-**8b** and (*R*)-(+)-**8c** showed good linear relationship with first-order rate plots, and the rate constants in chloroform at 26 °C were 1.36×10^{-4} and 1.45×10^{-7} s^{-1}, respectively. The racemization of telluroxides proceeded

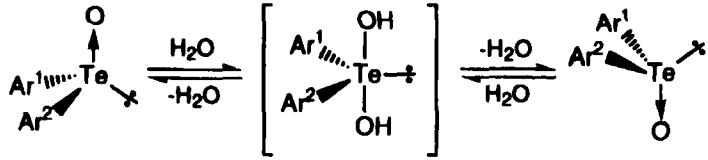
more rapidly in methanol solution at the same temperature, and the first order rate constant of telluroxide (*R*)-(+)-**8c** was 2.00 x 10^{-4} s^{-1}, and telluroxide (*R*)-(+)-**8b** completely racemized within 1 min. These results show that the bulky substituent is also important to prevent the racemization as well as the intramolecular coordination of dimethylamino group on the tellurium atom. When water was added to the methanol solution ($MeOH/H_2O$ = 4/1) of (*R*)-(+)-**8c**, the rate of racemization was accelerated (k_1 = 1.18 x 10^{-3} s^{-1}). These results indicate that the racemization of telluroxides occurs due to a trace amount of water which remains in the solvent in spite of careful purification.

The possibility of a mechanism for the racemization of chalcogen oxides via pyramidal inversion is theoretically examined. The pyramidal inversion energies for dimethyl sulfoxide, selenoxide, and telluroxide were estimated to be 49.1, 53.2, and 63.9 kcal mol^{-1}, respectively, by *ab initio* MO calculations. Therefore, it was found that the mechanism via pyramidal inversion is not realistic inversion for the racemization of selenoxides and telluroxides, at least at room temperature.



Ch = S, Se, Te

Thus, a mechanism for the racemization of telluroxides via an achiral hydrate formed by the addition of water to telluronium atom is proposed.



To confirm this mechanism involving an achiral tetracoordinated hydrate, the oxgen exchange reaction of telluroxide was investigated using $H_2{}^{18}O$. To a methanol solution of (*R*)-(+)-**8c** (ee 47%) was added $H_2{}^{18}O$ (97 atom% ^{18}O excess; 30 equiv), and the mixture was stirred at room temperature. The mass spectrum showed 25, 47, and 60% ^{18}O-enriched telluroxide at ee values of 30, 20, and 8%, respectively as shown in Figure 10.

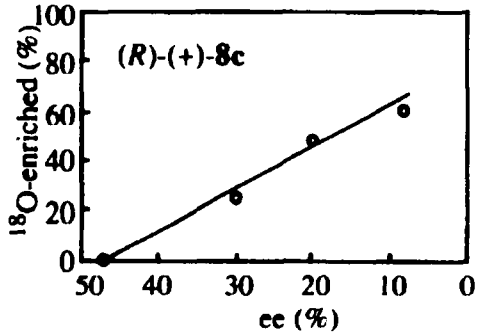


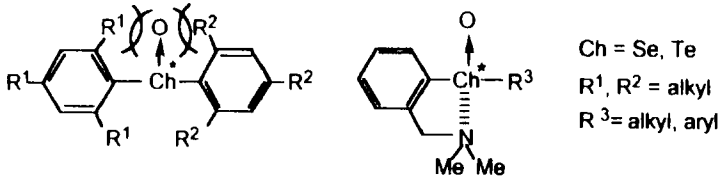
FIGURE 10. Correlation between enantiomeric purity and ^{18}O-labeled (*R*)-(+)-**8c** in methanol in the presence of $H_2{}^{18}O$

The optically active telluroxides (*R*)-(+)-**8b** and -**8c**, which has (*N,N*-dimethylamino)methyl substituent at the ortho-position of phenyl group, are more stable toward racemization than kinetically stabilized

telluroxide (*R*)-(+)-**6b**. These results show that the optically active telluroxide is thermodynamically stabilized by coordination of an intramolecular amino group to the tellurium atom. The coordination energies of telluroxides **8b** and **8c** were determined to be 5.5 and 4.9 kcal mol^{-1}, respectively, by variable temperature ^1H NMR measurements. These energy values are not so large as we have initially expected. Therefore, (*N*,*N*-dimethylamino)methyl group is considered to be preventing the racemization of optically active telluroxides not only by intramolecular coordination of the amino group (thermodynamic stabilization) to the tellurium atom but also steric protection by the bulkiness of the substituent in itself (kinetic stabilization).

CONCLUSION

We succeeded in isolating kinetically and thermodynamically stabilized optically pure selenoxides and telluroxides for the first time by fractional recrystallization of diastereomers and HPLC using optically active columns of racemic mixtures. The absolute configurations were determined by X-ray crystallographic analysis and the signs of their specific rotations and CD spectra with those of sulfur analogues. Optically active telluroxides underwent racemization faster than selenoxides in solid state and in solution. A mechanism for the racemization of chalcogen oxides via achiral hypervalent hydrate is proposed.



kinetically stabilized chalcogen oxide

thermodynamically stabilized chalcogen oxide

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