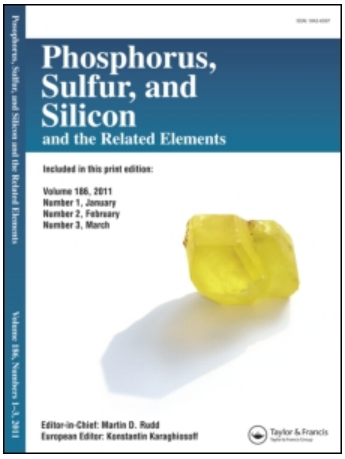

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OPTICALLY PURE CHALCOGENURANES: SYNTHESIS AND STEREOCHEMISTRY OF THEIR REACTIONS

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OPTICALLY PURE CHALCOGENURANES: SYNTHESIS AND STEREOCHEMISTRY OF THEIR REACTIONS

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An overview of our recent studies on the asymmetric syntheses, stereochemical studies, reactions and applications of chiral chalcogenuranes is described. Chiral chalcogenuranes, including halooxachalcogenuranes and spirooxachalcogenuranes, have been synthesized by highly diastereoselective oxidation of the 2-*exo*-hydroxy-10-bornyl chalcogenides. The stereochemistry of chalcogenuranes have been confirmed as with a trigonal bipyramidal (TBP) geometry. Nucleophilic substitution reactions of these compounds provided a good method to prepare the chiral chalcogenonium (IV) compounds with excellent diastereoselectivity. Our results indicated that the reactivity of the axial bonds of chalcogenuranes plays an important role in the control of the stereochemistry of the reactions. The mechanistic and stereochemical research on the nucleophilic substitution reactions have been carried out which indicated that two kinds of pathways, dissociative and associative routes, might exist. The applications of the reactions through the asymmetric [2, 3] sigmatropic rearrangement and enantioselective protonation with optically active selenonium (IV) compounds have been investigated to give good to high selectivities.

1. INTRODUCTION

Although the mechanistic and stereochemical research on the nucleophilic substitution reaction of compounds at a tetracoordinated carbon atom has been widely studied and S_N1 or S_N2 pathway has been accepted as the general concept of organic reactions, the research on that of a pentacoordinated atom is quite limited to some achiral silicon and phosphorus com-

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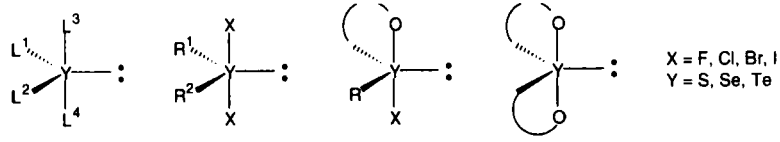
pounds.[1] Chalcogenurane **1** has been known as a kind of pentacoordinated (including the equatorial lone pair electrons) hypervalent compounds with a trigonal bipyramidal (TBP) geometry.[2] The chalcogenuranes, especially acyclic halochalcogenuranes **1a**, cyclic halooxachalcogenuranes **1b** and spirooxachalcogenurane **1c**, are of great interest in view of their structural features and reactivities (Figure 1).[2a] Thus, the stereochemical study on the reaction of chalcogenuranes would lead to the general comprehension of the reaction occurs at the pentacoordinated, and furthermore, the multi-coordinated heteroatom-containing compounds.

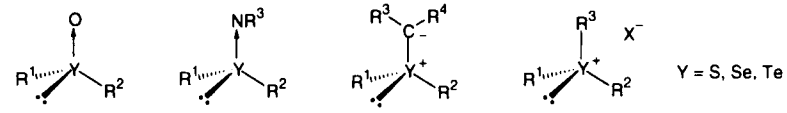


1 **1a** **1b** **1c**

FIGURE 1

On the other hand, many efficient methods for the construction of the chirality at a carbon atom with high diastereomeric or enantiomeric excess have been developed through the nearly several decades struggle.[3] Comparatively, building the chirality at a heteroatom is still difficult. As regarding with tetracoordinated (including the lone pair electrons) chalcogenonium (IV) compounds **2** (Figure 2), there is no general method for the synthesis of their chiral species. Although the properties as well as applications of the optically active sulfur (IV) **2** (Y = S) compounds, such as sulfoxides **2a** (Y = S), sulfilimines **2b** (Y = S), sulfonium ylides **2c** (Y = S) and sulfonium salts **2d** (Y = S), have been investigated well, the isolation or synthesis of the corresponding optically active organoselenonium (IV) **2** (Y = Se) and organotelluronium (IV) compounds **2** (Y = Te) is still very limited even they rationally exist with the similar structure of their sulfur analogues.[4] The most important reason is that the acknowledge of the mechanism and stereochemistry of the reactions to generate these compounds is not understood so well. One way to give deep understanding in this field is to study the intermediate species of the reactions concerning these compounds.

Chalcogenuranes **1** have been proposed as key intermediates or transition states in various reactions involving the chalcogenium compounds[5–9],



Chalcogenoxide Chalcogenonium imide Chalcogenonium ylide Chalcogenonium salt

2a **2b** **2c** **2d**

FIGURE 2

such as Swern oxidation[5] and Pummerer rearrangement[6,7], and recently some groups have proposed that the chalcogenurane species is also the key intermediates in some biomimic reactions of enzymes.[9] Therefore, the synthesis and stereochemical research on the nucleophilic substitution reaction of the chiral chalcogenuranes is apparently important to investigate the stereochemistry of their reactions and to find the novel method for synthesis of chiral chalcogenonium (IV) compounds. We have carried out intensive investigation of the chemistry of chiral chalcogenuranes for the past few years. Much of our work has involved the synthesis, structure determination and stereochemistry of the reactions of halooxachalcogenuranes and spirooxachalcogenuranes by using the 2-*exo*-hydroxy-10-bornyl group as a chiral ligand. This account will systematically discuss the synthesis, property and reactivity of chalcogenuranes and will focus on the mechanistic and stereochemical research of the reaction of these chiral hypervalent chalcogenium compounds.

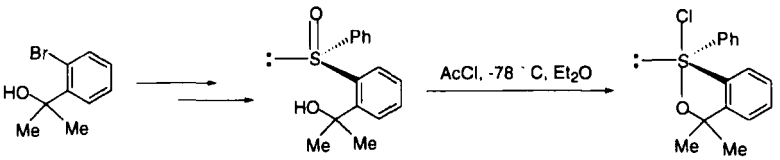
2. SYNTHESIS OF OPTICALLY PURE CHALCOGENURANES

The synthesis of the optically active chalcogenuranes can be achieved by two methods: 1) generation of the chirality at the chalcogenium atom *via* asymmetric synthesis or optically resolution; 2) construction of the chirality at the chalcogenium atom by introduction with a chiral auxiliary. We use the latter method since the former one is still impractical to prepare various chalcogenuranes for the lack of the proper chiral precursors or efficient method. We selected the 2-*exo*-hydroxy-10-bornyl group as a chiral ligand for following reasons: 1) the bulky protective factor of the bornyl group and the five-numbered ring effect may stabilize the chalcogenuranes and give high diastereoselectivity of their formation; 2) both the enantiomers of this ligand can be obtained from commercially available 10-cam-

phorsulfonic acids which are not expensive; 3) compounds with this ligand may readily be isolated as crystals, which make the stereochemical research of them easy and clear by the X-ray analysis; 4) many examples using the camphor derivatives in the asymmetric reactions have been known to give good selectivities.[10]

2.1. Synthesis and Stereochemistry of Optically Pure Halooxachalcogenuranes

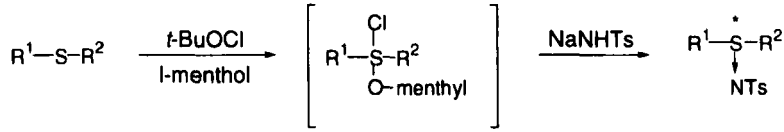
Twenty years ago, Martin *et al.* reported the first synthesis of chiral chlorosulfurane **3** by treatment of optically active sulfoxide with acetyl chloride, however the optical purity and stereochemistry of the chiral chlorosulfurane **3** were not clear (Scheme 1).[11a,b]



3

SCHEME 1

And recently, Oae and Matsugi *et al.* completed the synthesis of optically active sulfonium (IV) compounds through the formation of the chiral chlorosulfurane **4** as an important intermediate (Scheme 2).[11c–e]



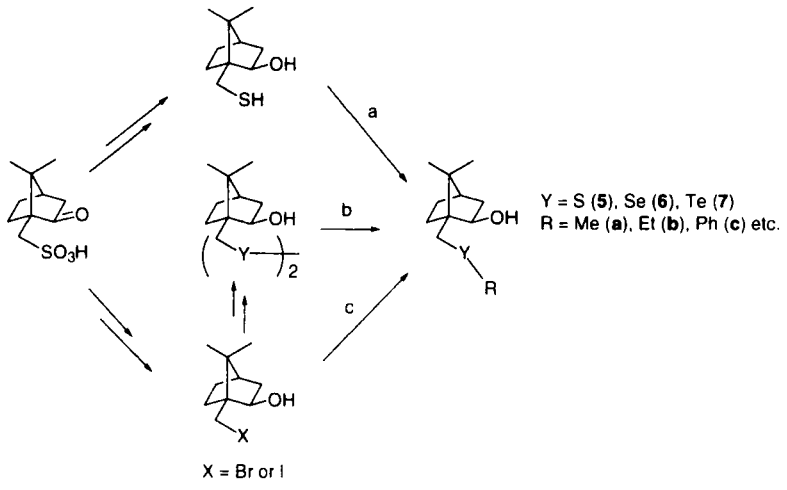
4

SCHEME 2

2.1.1. Synthesis of 2-exo-Hydroxy-10-bornyl Chalcogenides

Our synthesis of the chiral halooxachalcogenurane was starting from the synthesis of 2-*exo*-hydroxy-10-bornyl chalcogenides **5–7**. Sulfides **5**[12]

could be obtained by the reaction of (1*S*)-(-)-10-halo-2-*exo*-borneol with thiols or (-)-10-mercaptoisoborneol with alkyl halides (Scheme 3). The selenides **6**[13] (tellurides **7**[14]) were prepared by the reaction of (1*S*)-10-halo-2-*exo*-borneol with sodium aryl or alkylselenolates (tellurolates), or the reaction of alkyl halides with sodium bornylselenolate cellurolate) which was prepared from di-(2-*exo*-hydroxy-10-bornyl) diselenide (telluride) and sodium borohydride.

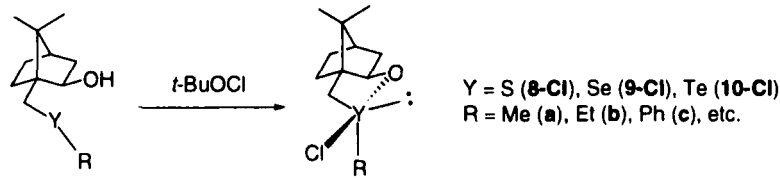


SCHEME 3

2.1.2. Synthesis of Halooxachalcogenuranes

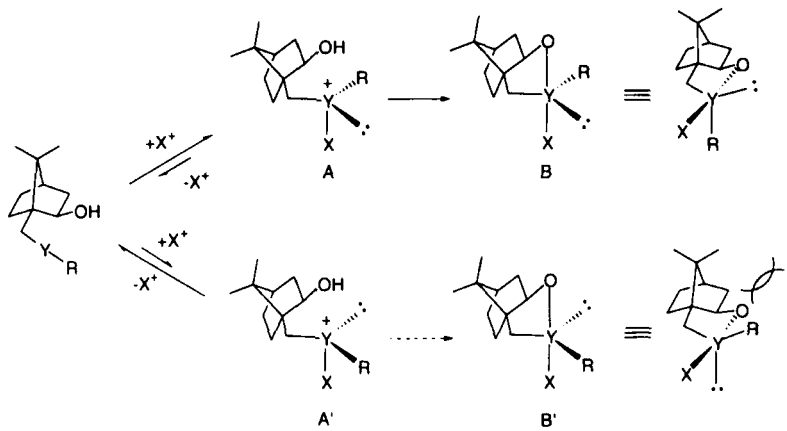
Reaction of chalcogenides **5–7** with *tert*-butyl hypochlorite gave chlorochalcogenuranes **(8–10)-Cl** as single diastereomers in high yield, respectively (Scheme 4). Chloroselenuranes and telluranes were obtained as stable solid or crystals, while chlorosulfuranes **8-Cl** were unstable to moisture. However, we confirmed the structure of chlorosulfuranes **8-Cl** by spectroscopic manner. Chlorochalcogenuranes **(8–10)-Cl** are all optically stable and no any isomerization can be detected at room temperature for a reasonably long time. The stability is considered resulted from the bulky protective factor of the bornyl group and the five-membered ring effect.

We considered the diastereoselectivity of the reaction was induced from the bulkiness of the bornyl group. As shown in Scheme 5, oxidation of the



SCHEME 4

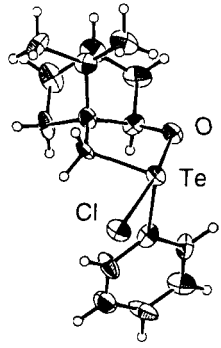
lone pair electrons of the chalcogen atom followed by cyclization should give both distereoisomers **B** and **B'** of the chlorochalcogenuranes, however, since the formation of the **B'** is strongly disfavorable through the destabilization by the steric repulsion between the bornyl moiety and the substituent bound to the chalcogenium atom, the generation of **B** would be predominately favored (Scheme 5).



SCHEME 5

2. 1. 3. Stereochemistry and Spectral Properties of the Chiral Halochalcogenuranes

The structures and stereochemistry of these compounds have been determined by X-ray analyses of chlorophenylselenurane **9c-Cl** and chlorophenyltellurane **10c-Cl**, which indicated that the halochalcogenuranes have the slightly distorted trigonal bipyramidal (TBP) structures (Figure 3).

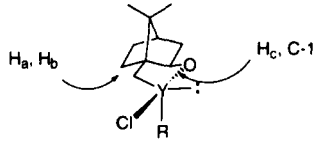


10c-Cl

FIGURE 3 ORTEP drawing of 10c-Cl

Previous investigation on the spectral properties of sulfuranes has indicated that chemical shift of the carbon in the alkoxy ligands of spirosulfuranes is very responsive to the change of the nature of the apical substitutes, thus, some characteristics of the spectra of halochalcogenuranes **(8–10)a, c-Cl** are summarized in Table I.

TABLE I ^{1}H NMR and ^{13}C NMR chemical shifts of chlorosulfuranes, selenuranes and telluranes



entry	*compound*	*Y*	*R*	*Ha*	*Hb*	*Hc*	*C-1*
1	**8a-Cl**	S	Me	4.13	4.52	4.88	101.6
2	**9a-Cl**	Se	Me	3.84	4.23	4.49	96.8
3	**10a-Cl**	Te	Me	3.40	3.59	4.19	93.7
4	**8c-Cl**	S	Ph	4.57	4.69	4.34	100.4
5	**9c-Cl**	Se	Ph	4.15	4.32	3.97	96.3
6	**10c-Cl**	Te	Ph	3.42	3.62	3.81	93.2

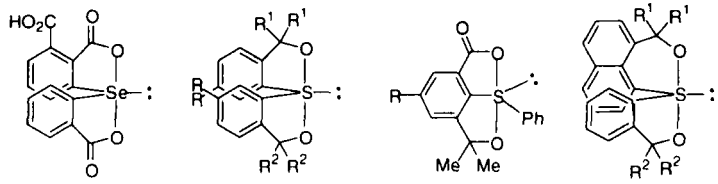
The Ha, Hb and Hc in the ^{1}H NMR as well as the C-1 in the ^{13}C NMR spectra of halochalcogenuranes have large downfield shifts relative to that of the corresponding chalcogenides. Among the chlorochalcogenuranes, the chlorosulfuranes have the largest and the telluranes have the smallest chemical shift values. While with the same structure, the peaks shift to upfield when the center atom changes from S to Se, or Se to Te; and the absorption of aryl chalcogenuranes appeared at lower field as compared with that of the alkyl analogous (Table I).

2. 2. Synthesis and Stereochemistry of Optically Pure Spirochalcogenuranes

Concerning the synthesis and isolation of the spirochalcogenuranes, a chiral selenurane and several spirosulfuranes have been reported previously (Figure 4). Lindgren reported the optical resolution of chiral selenurane **11** with a free acid group through recrystallization of its quinine salt from ethyl acetate-menthanol. However, the optical purity and stereochemistry of **11** were not clear.[15] Kapovits *et al.* have reported the synthesis of both (+)- and (-)-sulfuranes **12a** *via* the reaction of corresponding optical active (+)- and (-)-sulfoxides with acetyl chloride in presence of triethylamine.[16] Isolation of optically pure spirosulfurane **12b** has also been successfully carried out by Allenmark *et al.* by using the chiral HPLC.[17] Recently, Martin and co-workers have reported their synthesis of optically active spirosulfuranes **12c, d** *via* the reaction of sulfoxides with chiral acid.[18] They have also reported the nonclassical resolution of optically active spirosulfuranes **12e, f** with a tridentate ligand by using the 2, 2′-dihydroxy-1, 1′–binaphthol as a chiral host.[18] However, there is only one paper reported recently on the synthesis of optically active spirosulfuranes **12g, h**, starting from the optically active sulfoxides, with definite determination of the structures (Figure 4).[19]

2.2.1. Synthesis of Spirochalcogenuranes

Synthesis of optically pure spirochalcogenuranes **14a-e** and **16a-d** with 2-*exo*-hydroxy-10-bornyl group as a chiral ligand has been achieved by reaction of chiral sulfides **13a-e** and selenides **15a-d** with *t*-BuOCl and Et_3N in high yield and as single diastereomers, respectively (Schemes 6 and 7).[20,21] The reactions were believed to proceed through the diastereo-

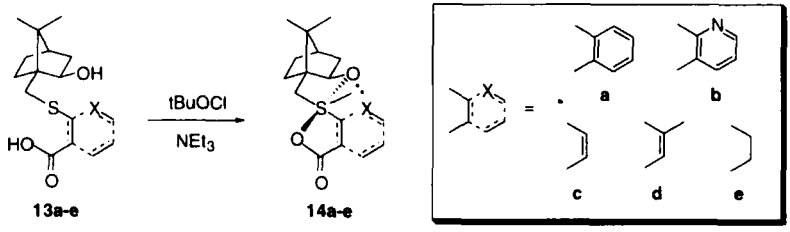


11

12a: R = H, R^1 = H, R^2, R^2 = O
12b: R = H, R^1, R^1 = R^2, R^2 = O
12c: R = H, R^1 = R^2 = Me
12d: R = *t*-Bu, R^1 = R^2 = CF_3
12e, R = *H*
12f, R = *t*-Bu
12g: R^1 = H, R^2, R^2 = O
12h: R^1, R^1 = O, R^2, R^2 = H

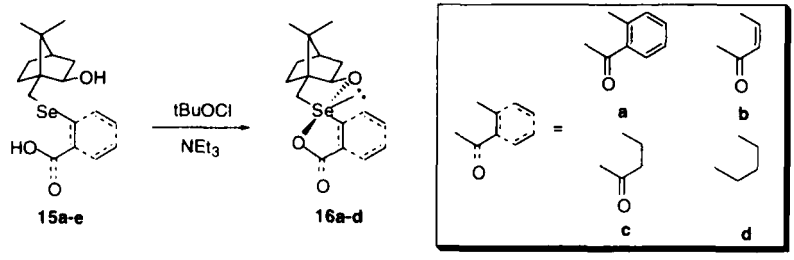
FIGURE 4

selective generation of the intermediates of chlorosulfuranes **8-Cl** and chloroselenurane **9-Cl** followed by the intramolecular cyclization.



13a-e **14a-e**

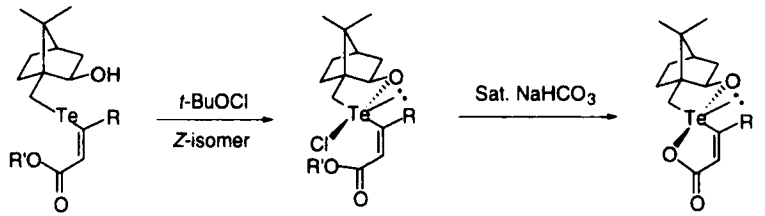
SCHEME 6



15a-e **16a-d**

SCHEME 7

On the other hand, since the unstability of the tellurides, the spirotelluranes **19a, b** were prepared by hydrolysis of the *Z*-chlorotelluranes **18a, b**. The formation of the spirotellurane was considered through the successive hydrolysis of esters followed by the dissociation of the Te-Cl bond and the attack of the carboxylate anion to the resulting telluronium cation (Scheme 8).[21]



17a, R = H, R' = Me
17b, R = *n*-Pr, R' = Et

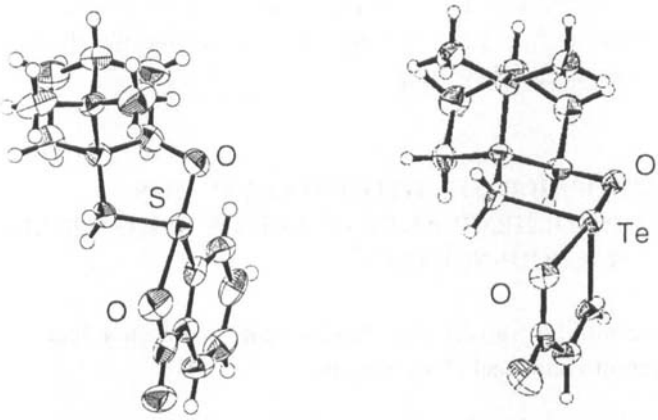
18a, R = H, R' = Me
18b, R = *n*-Pr, R' = Et

19a, R = H
19b, R = *n*-Pr

SCHEME 8

2. 2. 2. Stereochemistry and Spectral Properties of the Chiral Spirochalcogenuranes

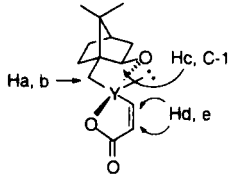
Previous investigation on the crystallographic structures of some achiral spirosulfuranes has indicated that the sum of the O-S-O distances in diacyloxyspirosulfuranes are longer than those in dialkoxy analogues but shorter than in the mixed alkoxyacyloxy derivatives, and the length of S-O(acyloxy) is usually longer than that of the S-O(alkoxy) in the alkoxyacyloxyspirosulfurane.[22] The X-ray analyses of **14a** and **14b** gave the similar results, which shown a "alkoxy-sulfurium-carboxylate zwitterion characteristic" as that of the racemic spirosulfuranes.[22] Similarly, the X-ray analysis of spirotellurane **19a** provided, firstly, the structural information on the chiral spirotellurane, which indicated that spirotellurane **19a** has a slightly distorted trigonal bipyramidal (TBP) geometry around the central tellurium atom with the angle of the O-Te-O moiety of 177.1°, the length of Te-O(acyloxy) is longer than that of the Te-O(alkoxy) in this alkoxyacyloxyspirotellurane which reflects the polarized nature of the hypervalent O-Te-O bond resulting from the difference in the electronegativities of the apical ligands (Figure 5).



14a **19a**

FIGURE 5 ORTEP drawings of **14a** and **19a**

TABLE II ^{1}H NMR and ^{13}C NMR chemical shifts of spirochalcogenuranes **14c**, **16b** and **19a**



14c, Y = S
16b, Y = Se
19a, Y = Te

entry	*compound*	*Y*	*Ha, Hb*	*Hc*	*Hd, He*	*C-1*
1	**14c**	S	3.19, 4.40	4.33	6.80, 6.84	95.7
2	**16b**	Se	3.06, 4.18	4.26	7.02, 7.24	94.9
3	**19a**	Te	2.60, 3.55	4.06	7.43, 7.45	93.7

Regarding the spectral properties of spirochalcogenuranes **14, 16** and **19**, the chemical shifts of the protons Ha, Hb, Hc and carbon C-1 in the NMR spectra of spirochalcogenuranes are considerably downfield shift as compared with that of their chalcogenides, respectively. We have compared the spectroscopic characteristics of these compounds having the same structure but with a different chalcogenium atom at the center of the spiro ring

(Table II). The chemical shifts of the protons (Ha, Hb and Hc) and carbon (C-1) are shifted upfield, respectively, when the chalcogenium change from S to Se, or from Se to Te, while at the same time, the alkene protons (Hd, He) are shifted downfield

3. NUCLEOPHILIC SUBSTITUTION REACTION AND STEREOCHEMICAL RESEARCH OF THE OPTICALLY PURE CHALCOGENURANES

3. 1. Nucleophilic Substitution Reaction and Stereochemical Research of Halooxachalcogenuranes

Usually, there are two kinds of nucleophilic substitution reactions occurred at a chalcogenium atom in chalcogenuranes : 1) reaction of a pentacoordinated chalcogenurane to give another pentacoordinated product with the similar TPB structure; 2) reaction of a pentacoordinated chalcogenurane to give a tetracoordinated chalcogenonium (IV) products with tetrahedron structure around the chalcogenium atom. There is no problem to discuss the stereochemistry of the former reaction using terms of *inversion* and *retention* similar with that of the nucleophilic substitution reactions of the tetrahedron carbon compounds, since there are only two possibilities for the reaction : if the product is with the same stereochemistry as the reactant, it is a configuration *retention* reaction; while the reaction give the product with the opposite stereochemistry at the central chalcogenium atom can be expressed as a configuration *inversion* reaction. However, for the latter reaction, there is still no clear concept to definite the stereochemical process. Thus, to express the stereochemistry of the reaction of chiral halooxachalcogenuranes well, we have proposed the term *retention* as "the reaction of the halooxachalcogenurane **C** resulted in the formation of the chalcogenonium (IV) compound with stereochemistry of **D**". The formation of **E** is naturally considered as the *inversion* of configuration at the chalcogenium atom (Figure 6).[23]

3.1.1. Nucleophilic Substitution Reaction and Stereochemical Research of Chlorosulfuranes

Martin *et al.* have studied the mechanism of the basic hydrolysis of chlorosulfuranes, and proposed an associative mechanism involving a hexacoor-

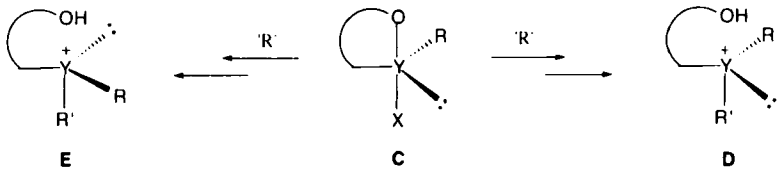
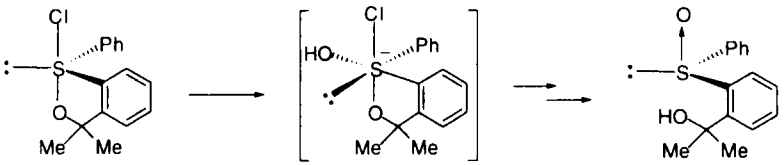


FIGURE 6

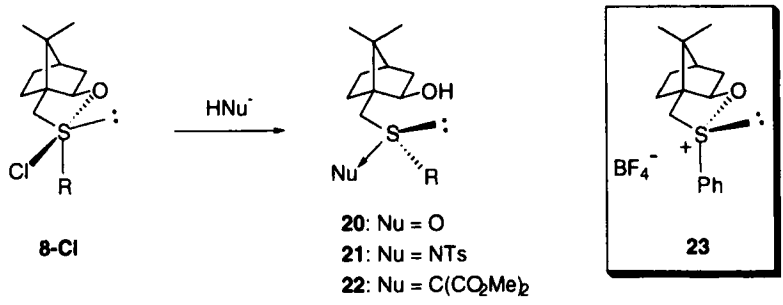
dinated sulfur species **F** with a negative charge on sulfur (Scheme 9).[11a, b] Their conclusion is based on the stereochemical results and kinetic studies.



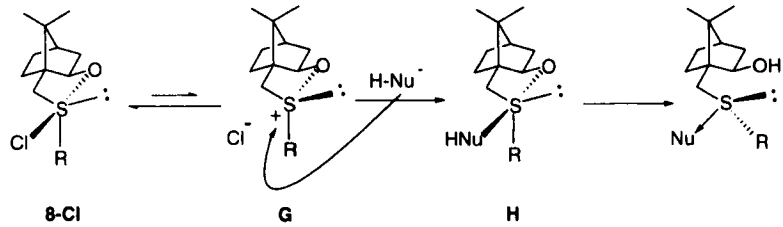
SCHEME 9

Hydrolysis of chlorosulfuranes **8** under a basic condition gave sulfoxides **20** as single diastereomers in moderate to good yield. When NaNHTs was used as a nucleophile, optically pure *N*-*p*-tosylsulfilimines **21** were obtained as single diastereomers in high yield. The absolute configuration of the sulfur atom in **20c** and **21c** was determined by X-ray analyses (Figure 7). Reaction of the alkoxychlorosulfuranes **8** with $NaCH(CO_2Me)_2$ gave sulfonium ylides **22** as mixtures of diastereomers at sulfur atom in almost quantitative yield (Scheme 10).[12]

From the absolute configuration of the products, the nucleophilic substitution reaction of **8** is likely to proceed through a dissociative pathway as shown in Scheme 11. Dissociation of S-Cl bond followed by stereoselective association of the resulting alkoxysulfonium ion **G** with nucleophiles would provide **H**. Concomitant cleavage of S-O bond of **H** would afford the products. Pyramidal inversion at sulfur atom of ylides[4] give a thermodynamically controlled mixture of the products (Scheme 11).



SCHEME 10

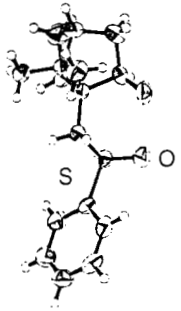


SCHEME 11

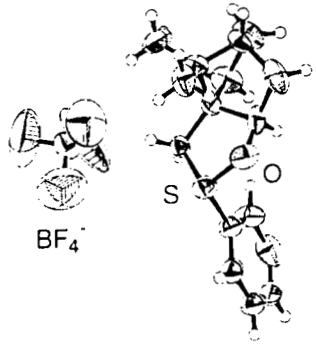
To confirm the mechanism, we have carried out the isolation and hydrolysis of a key alkoxysulfonium intermediate. Alkoxysulfonium salt **23** was obtained in 96% yield and as a single diastereomer by treatment of chlorosulfurane **8c** with silver tetraflouroborate.[24] The salt **23** was characterized by spectroscopic means and X-ray analysis (Figure 7). Hydrolysis of salt **23** was performed under the same condition as that of chlorosulfuranes to give sulfoxide **20c** in quantitative yield as the sole product. Therefore, the reaction could be considered to proceed *via* the same stereochemical process as that of the chlorosulfurane, and the hydrolysis of chlorosulfurane would proceed through the intermediate of sulfonium cation like **23**. The result strongly supports the dissociative mechanism of the hydrolysis of chlorosulfurane (Scheme 11).

3.1.2. Nucleophilic Substitution Reaction and Stereochemical Research of Halooxaselenuranes

Optically pure selenoxides **24** could been obtained as sole products by the addition of aqueous $NaHCO_3$ to a CH_2Cl_2 solution of chloroselenuranes



20c



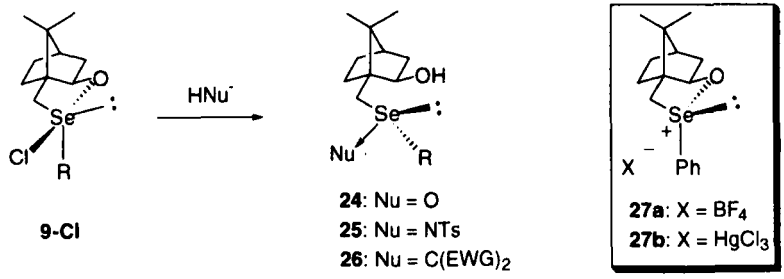
23

FIGURE 7 ORTEP drawings of **20c** and **23**

9-Cl at 0 °C instantaneously (Scheme 12).[13] The absolute configuration of the selenium atom in **24c** was determined by X-ray analysis, which indicated that the hydrolysis of chloroselenuranes **9-Cl** proceeded, similar as that of chlorosulfuranes, with retention of the configuration at the selenium atom. As compared with sulfoxides, selenoxides are known to be less optically stable and tendency to isomerize or epimerize at the selenium atom through pyramidal inversion or formation of the pentacoordinated intermediates.[4] Selenoxides **24** are stable at room temperature in the solid state, and the configurational stability of them seems to reflect the stabilization by an intramolecular hydrogen bond between the seleninyl oxygen and the secondary hydroxy group.[13]

Reaction of chloroselenuranes with NaNHTs was expected to afford the optically active *N*-*p*-tosylselenonium imides **25**, however, **25** could not be obtained as single products since they are always mixed with selenoxides **24**. Selenonium imides are known to be unstable to moisture and readily to hydrolyze to give the corresponding selenoxides.[25]

In contrast with *N*-*p*-tosylselenonium imides, the selenonium ylides have higher chemical and optically stability. Nucleophilic substitution reaction of chloroselenurane **9c-Cl** with active methylene compounds proceeded in highly stereoselective manner with retention of the configuration to give chiral selenonium ylides **26** (Scheme 12). The absolute



SCHEME 12

configuration of the selenium atom in **26** was determined by X-ray analysis. Chiral selenonium ylides could also be prepared by reaction of corres ponding optically pure selenoxides with active methylene compounds.[26]

Nucleophilic substitution reaction of chloroselenuranes were also considered to proceed through the formation of the selenonium cation as the key intermediate. Trying to isolate the selenonium cation by exchange of the contain anion similar as that of the sulfonium cation, however, gave the products as selenurane-Lewis Acid complexes. The X-ray analyses of the **27a** and **27b** indicated that the anions still interact with the selenonium cation as shown in Figure 8.[27]

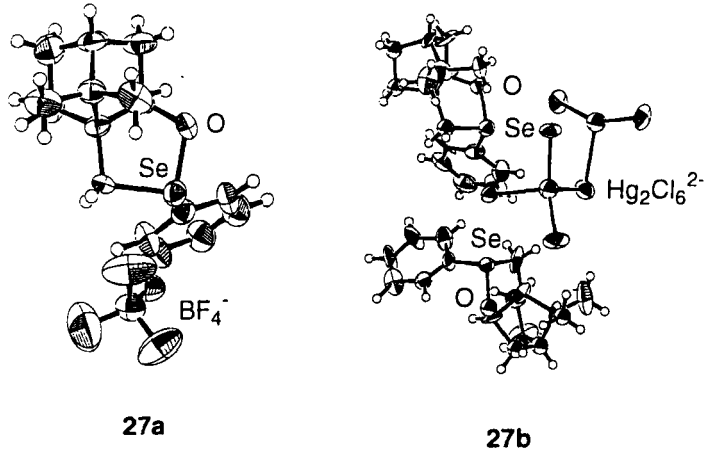
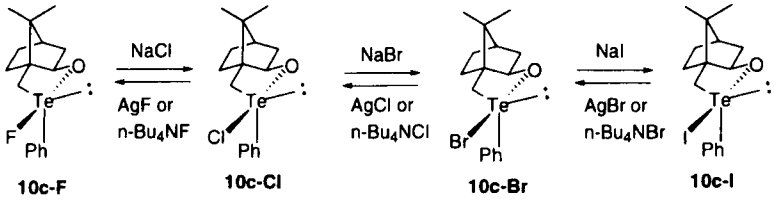


FIGURE 8 ORTEP drawings of **27a** and **27b**

3.1.3. Nucleophilic Substitution Reaction and Stereochemical Research of Halooxatelluranes

3.1.3.1. Halogen Exchange Reaction of Halooxatelluranes

Halogen exchange reaction of halooxatelluranes **10** was observed when treatment of **10** with NaX, AgX, or tetrabutylammonium halide (TBAX) (X = halogen) as shown in Scheme 13. Fluoro, bromo, and iodotelluranes could be prepared by the reactions. The X-ray analyses of products indicated that the displacement reaction of halotelluranes proceeded with retention of configuration. An S_Ni pathway was considered to account for the stereochemistry of this halogen exchange reaction.[28] Similar reactions of halosulfurane and haloselenuranes have also been observed.[13,24]



SCHEME 13

3.1.3.2. Synthesis of Chiral Telluronium Salts *via* Nucleophilic Substitution Reaction of Halooxatelluranes

To obtain the optically active tetracoordinated telluronium(IV) compounds, nucleophilic substitution reactions of halotelluranes with HO^-, $TsHN^-$ and $(EWG)_2CH^-$ have been carried out, which however, gave the mixture of decomposed products.[29]

Then the reaction of halotelluranes with lithium or Grignard reagent was performed to seek the method for synthesis of the optically active telluronium (IV) compounds such as telluronium salts. Application of chalcogenonium salts in organic synthesis has attracted much attention during nearly several decades.[30] There are many examples of the application of chiral sulfonium salts in the asymmetric synthesis of optically active epoxides, however, few enantiomerically pure telluronium salts has been reported (Figure 9).[31]

The synthesis of optically pure telluronium salts **29** has been developed in high yield and with high selectivity *via* reaction of chiral alkoxytellu-

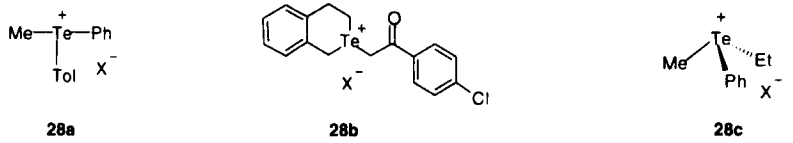
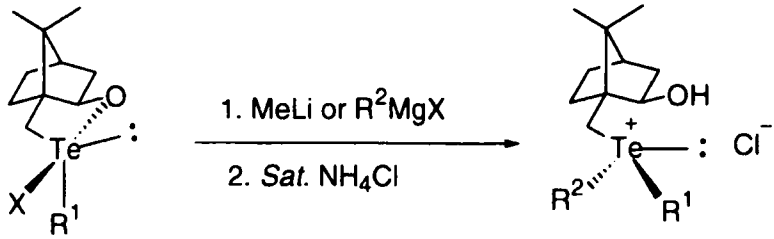


FIGURE 9

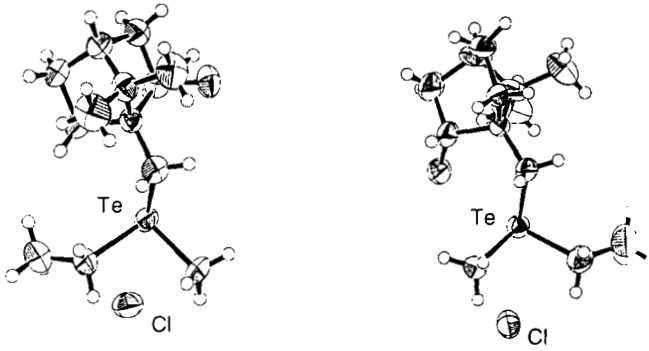
ranes **10** with organolithium or Grignard reagents. The method has been used for the asymmetric synthesis of chiral benzyl and allyl telluronium salts (Scheme 14). Structures of these salts have been confirmed by X-ray analyses of **29a** (R^1=Me, R^2=Et) and **29b** (R^1=Et, R^2=Me) which indicated that the salts have their tetrahedron structures around the tellurium atom (Figure 10). The telluronium salts are optically stable and did not isomerize after standing the salts at room temperature for several weeks.[14b,23]



10 **29**

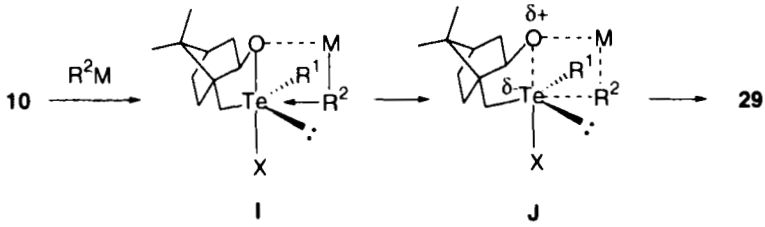
SCHEME 14

The stereochemistry of the salts indicated that the reaction proceeded through a different pathway as the nucleophilic substitution reactions of the chlorosulfuranes and selenuranes mentioned above. The reaction may proceed through the pathway shown in Scheme 15: initial coordination of lithium or Grignard reagents with the oxygen atom of bornyl group induced the attack of carbanion from the direction shown in Scheme 15. The coordinated metal induced the cleavage of the Te-O bond followed by the dissociation of Te-X bond to afford telluronium salts with the observed configuration at the tellurium atom in high diastereoselectivity.



29a **29b**

FIGURE 10 ORTEP drawings of **29a** (R^1=Me, R^2=Et) and **29b** (R^1=Et, R^2=Me)



I **J**

SCHEME 15

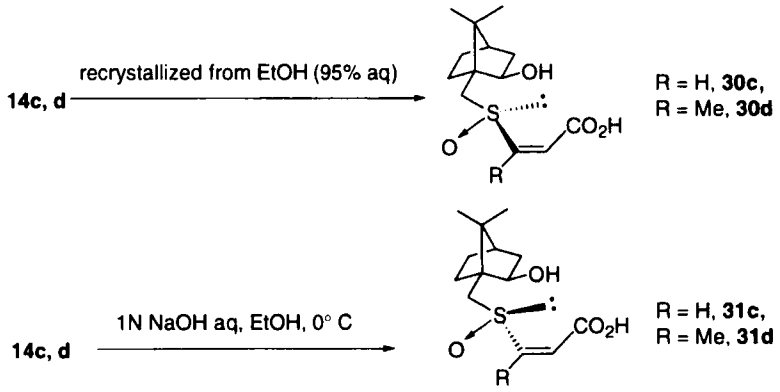
3.2. Nucleophilic Substitution Reaction and Stereochemical Research of Spirosulfuranes

3.2.1. Hydrolysis and Stereochemical Research of Spirosulfuranes

Previous study on the hydrolysis of racemic spirosulfuranes showed that these compounds are readily hydrolyzed to their parent sulfoxides and the stability decreased with increasing electron density at the sulfur atom and enlarging the size of the spirorings from five to six membered.[32]

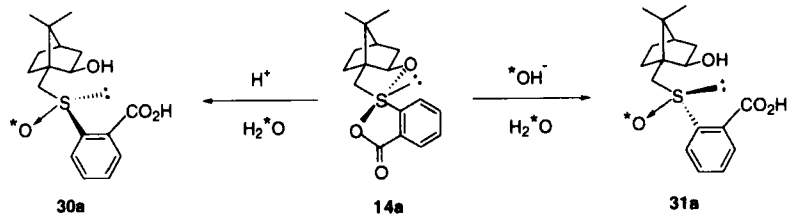
We have carried out the hydrolysis of pirosulfurane **14** under various conditions to study the mechanism and stereochemistry of the reactions.

Recrystallization of **14c, d** from wet solvent (EtOH, 95% aq) gave the products of the hydrolysis, sulfoxides **30c, d**, as single diastereomers in high yields. While the hydrolysis of **14c, d** under basic condition afforded the sulfoxides **31c, d** also in high yield and with excellent diastereoselectivity, but with different stereochemistry at the sulfur atom as compared with that of **30c, d**. The stereochemistry of the products has been determined by X-ray analysis.



SCHEME 16

Interestingly, hydrolysis of spirosulfuranes **14a** under an acidic condition gave sulfoxide **30a** as a single diastereomer in high yield. On the contrary, a basic hydrolysis of **14a** yielded optically pure sulfoxide **31a** in high yield, also as a single diastereomer but with an opposite absolute configuration at the sulfur atom (Scheme 17). The stereochemistry of sulfoxide **30a** and **31a** has been clearly determined by the X-ray analysis as shown in Figure 11.[20]



SCHEME 17

Study of the optically stability of sulfoxides **30a** and **31a** under various conditions has ruled out the possibility of isomerization of the products during hydrolysis. The mass and ^{17}O NMR spectral study of the products indicated that under both of the acidic and basic conditions, the oxygen atoms from H_2O were definitely bound to the sulfur atoms of the products (Scheme 17).

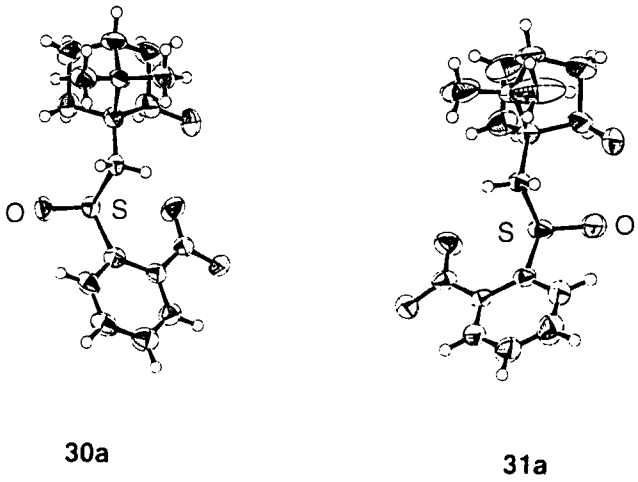
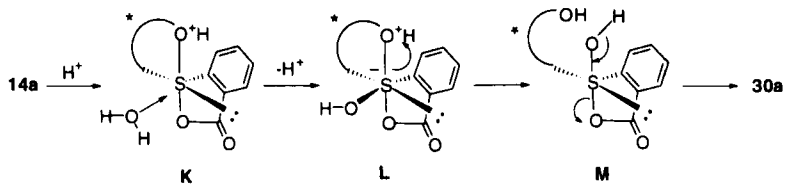


FIGURE 11 ORTEP drawings of **30a** and **31a**

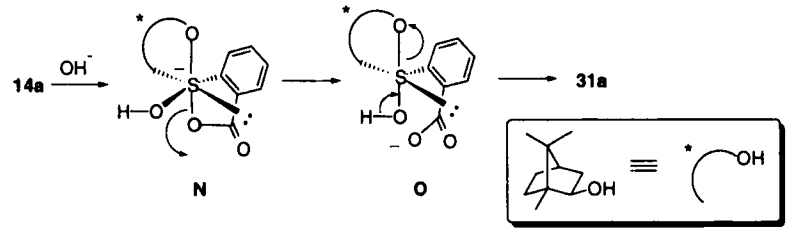
3.2.2. Possible Mechanisms of Hydrolysis of Spirosulfurane: Association versus Dissociation

Two kinds of mechanisms, namely associative (analogous to S_N2-type reactions) and dissociative (analogous to S_N1-type reactions) mechanisms, have been suggested to account for the stereochemical outcome of the reactions. We have proposed an associative mechanism involving the formation of hexacoordinated sulfur species **L** and **N** as shown in Schemes 18 and 19: The different stereochemistry of the products were believed to be induced from the different reactivity of the two axial S-O bonds of the hexacoordinated sulfur species **L** and **N**.[20a]

However, the dissociative mechanism might be an alternative pathway account for the stereochemical results. The stereochemical outcome can be explained readily using the dissociative mechanism by considering the

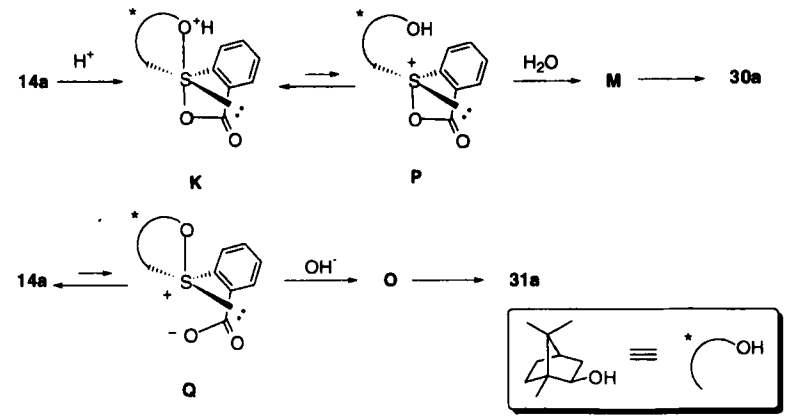


SCHEME 18



SCHEME 19

diastereoselective formation of the sulfonium cations **P** and **Q** as the key intermediates in hydrolysis of the spirosulfurane **14a** under different conditions (Scheme 20). Considering the numerous possible stereoisomers of the hexacoordinated sulfur species in the associative pathway, it might be difficult to responsible for the high diastereoselectivity of the reactions.[20b]



SCHEME 20

4. APPLICATIONS OF CHALCOGENURANES IN ASYMMETRIC REACTIONS

Application of the chiral chalcogenuranes in asymmetric reactions has been carried out by using the optically active allylic selenonium (IV) compounds which were *in situ* generated from the nucleophilic substitution reactions of haloallylic selenuranes. The utilization of the optically stable selenoxides in the asymmetric protonation have also be studied.

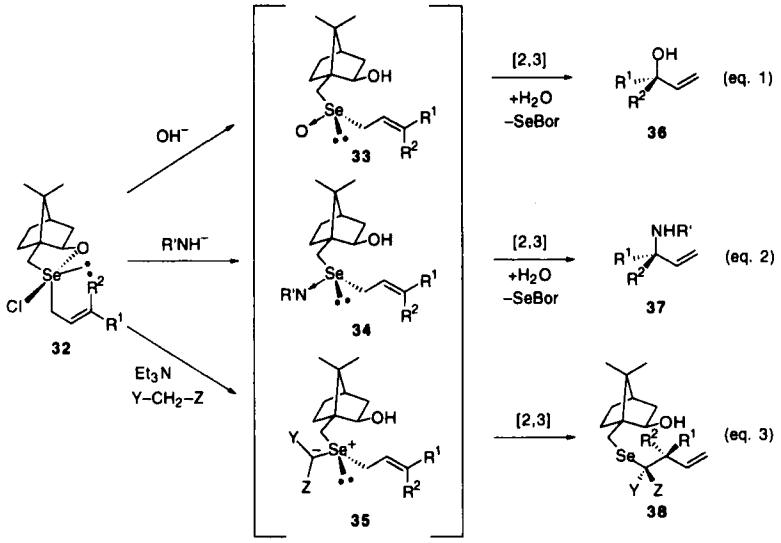
4.1. [2, 3] Sigmatropic Rearrangement of Optically Active Allylic Selenonium Compounds

[2, 3] Sigmatropic rearrangement of optically active allylic selenonium compounds have been reported by several groups[33]. The key steps of their [2, 3] sigmatropic rearrangement are enantio- or diastereoselective formation of optically active allylic selenonium (IV) compounds and the transfer of the chirality from the selenium atom to C-3 of the resulting allylic products. Reaction of the allylic selenides with *t*-BuOCl gave the chloroselenuranes **32**, in high yield and with high diastereoselectivity, which by treatment with aqueous $NaHCO_3$ afforded the corresponding allylic alcohols **36** in modest to high ee through the [2, 3] sigmatropic rearrangement of optically active selenoxides **33** (Scheme 21, eq. 1).[13]

We have also studied the asymmetric [2, 3] sigmatropic rearrangement of the chiral allylic selenimides. Nucleophilic substitution reaction of allylic chloroselenuranes **32** with lithium *N*-protected amides afforded chiral allylic selenimides **34**, which after [2, 3] sigmatropic rearrangement gave chiral allylic amides **37** up to 93% ee (Scheme 21, eq. 2).[34]

The asymmetric [2, 3] sigmatropic rearrangement of the chiral allylic selenonium ylides have also been carried out to give the homoallylic selenides **38** in high yield and with high diastereoselectivity, which provides an excellent method for carbon-carbon bond formation with efficient chiral induction at C-3 stereocenter (Scheme 21, eq. 3).[35]

The high asymmetric induction and the stereochemical course of the asymmetric [2, 3] sigmatropic rearrangement of the chiral selenonium compounds **33, 34** and **35** can be reasonably explained by assuming the five-membered ring transition states *endo*-TS **R** as shown in Figure 12. [13,34,35]



SCHEME 21

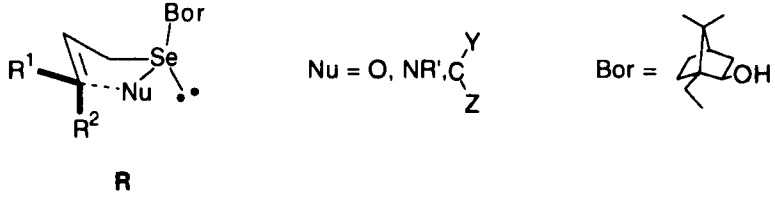
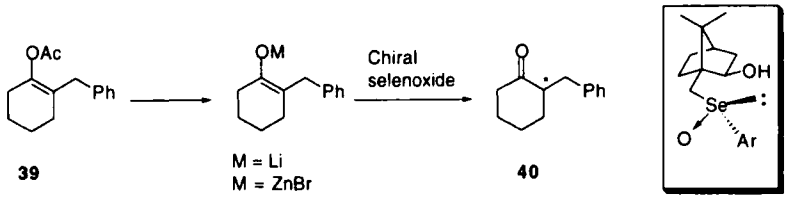


FIGURE 12

4. 2. Enantioselective Protonation of Enolates with Optically Active Selenoxides

The enantioselective protonation of enolates has attracted much attention in the asymmetric synthesis. Enantioface-differentiating protonation of achiral metal enolates of α-alkylcarbonyl compounds **39** has been developed using chiral selenoxide as a chiral proton source. Reaction of zinc bromide enolates of 2-benzylcyclohexanone with chiral selenoxides gave

optically active 2-benzylcyclohexanone **40** with high enantioselecitvity (Scheme 22). Intramolecular hydrogen bonding of the selenoxide as well as chelation effects between the chiral proton source (CPS) and metal enolate would contribute to this asymmetric induction.[36]



SCHEME 22

5. CONCLUSIONS

In conclusion, we have accomplished the synthesis of a series of optically pure halochalcogenuranes and spirochalcogenuranes, using the 2-*exo*-hydroxy-10-bornyl group as a chiral ligand, in high yield and with excellent diastereoselectivity. The defined structures have been determined by X-ray analyses. The systematic investigation of the property of these compounds have been performed. Nucleophilic substitution reaction of the chiral chalcogenuranes provides a good method for the diastereoselective synthesis of the optically pure chalcogenonium (IV) compounds. The stereochemistry of the reactions is dramatically affected by the reaction conditions and the reactivity of apical bonds of the chalcogenuranes. Both of the dissociative and associative pathways of the reactions have be observed. These results are helpful for the understanding of the stereochemistry of nuclophilic reactions concerning multicoordinated heteroatom compounds. The role of the apical ligands on the stereochemistry of nucleophilic substitution reactions of the chalcogenuranes is expected to be utilized in the design of novel methods for the synthesis of optically active chalcogenonium (IV) compounds with a given stereochemistry on the central chalcogenium atom.

Acknowledgements

The results described from our research group have been achieved by our capable and enthusiastic co-workers, whose names are included in the bibliography. The work was supported by Grants-in-Aid for Scientific Research from the Ministry of Education, Sciences, Sports and Culture, Japan.

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