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Review

Optically Active Selenoxides: Structural and Synthetic Aspects

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Abstract: Synthetic approaches to the preparation of non-racemic selenoxides and the problem of their optical stability are discussed in this mini review.

Keywords: selenoxides; chirality; stereogenic selenium atom; asymmetric synthesis; optical resolution; racemization

1. Introduction

Sulfoxides are the logical and obvious reference point when one is considering the reactivity and optical activity of selenoxides. This is due to the fact that the reactivity of both groups of heterorganic derivatives of general structures **1** and **2** (Figure 1) is dominated mainly by the presence of a highly polarized heteroatom–oxygen bond, and their optical activity is associated with their tetrahedral geometry, which induces the optical activity of compounds in which two different carbon chains and/or rings are bonded to a stereogenic heteroatom.

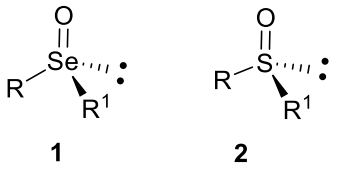
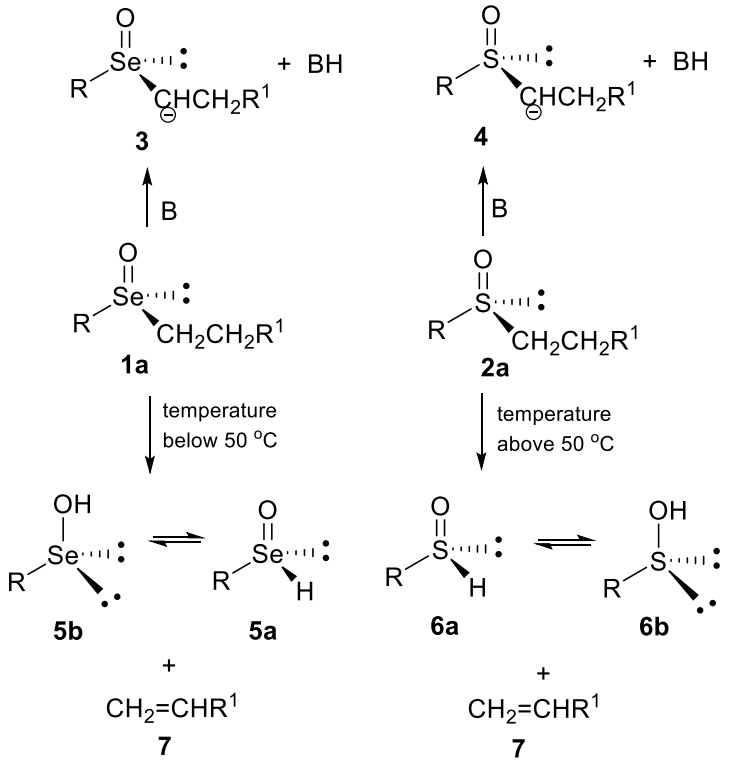


Figure 1. General structure of selenoxides and sulfoxides.

The highly polarized heteroatom-oxygen bond is responsible for the interesting oxidative properties of sulfoxides [1] and selenoxides [2], and their ability to:

a) generate the α-carbanions **3** [3] or **4** [4] for compounds containing the acidic α-methylene hydrogen atoms **1a** or **2a** (Scheme 1);

b) undergo an internal type elimination of the E2 type for compounds containing β-hydrogen atoms, which leads to the formation of the corresponding, generally very unstable, seleninic **5** or sulfenic **6** acids and unsaturated carbon derivatives **7** (Scheme 1) [5,6]. It should be noted here that both acids can exist as chiral tetravalent (**5a** or **6a**) or achiral divalent (**5b** [7–9] or **6b** [10–12]) tautomers.



Scheme 1. Deprotonation and elimination reactions of selenoxides and sulfoxides.

When considering the optical activity of unsymmetrical selenoxides, it should be noted that their pyramidal configuration at selenium was for the first time proved only in 1946 by mixed crystal studies [13,14] and that the first attempts to resolve 4-carboxydiphenyl selenoxide **8** and 4-carboxyphenyl methyl selenoxide **9** (Figure 2) via diastereoisomeric salts with enantiomerically pure amines were unsuccessful [15].

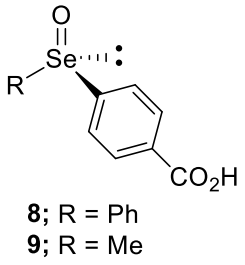
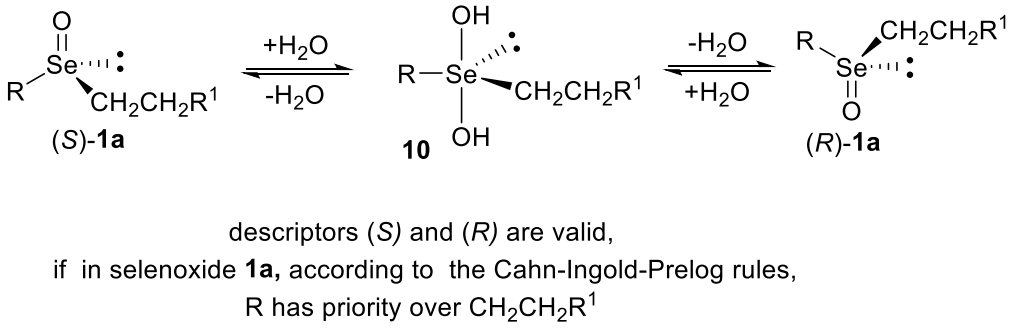


Figure 2. 4-Carboxydiphenyl selenoxide **8** and 4-carboxyphenyl methyl selenoxide **9**.

The failure to observe resolution, which was in sharp contrast with the ease of resolution of the related sulfoxides [16] (due to the addition of water to unsymmetrical selenoxides, which should give rise to symmetrical dihydroxides) was mentioned in this paper. However, it was rejected by the authors because specific rotation of a dry sample of diastereoisomeric salts of the selenoxide **8** with enantiomerically pure α-phenylethylamine was observed by recrystallizing it from dry ethyl acetate was not changed. An open suggestion that the inability to isolate selenoxide enantiomers is due to the rapid formation of hydrates in the presence of water was formulated only in 1952 in a review paper [17]. This reaction is illustrated for the selenoxide **1a** and the formed dihydroxyselenuranes **10** in Scheme 2.



Scheme 2. Rapid hydrate formation by selenoxides in the presence of water.

This proposal was later supported by NMR experiments using benzyl phenyl selenoxide **11** as the model compound according to which the chemical shift between the nonequivalent methylene protons H_A and H_B disappeared in an aqueous solution, which indicates the apparent loss of stereogenity of the selenium atom in this medium due to the formation of the corresponding dihydroxyselenurane [18]. The configurational instability in aqueous media was also observed for selenoxides **12** [19] and **13** (Figure 3) [20]. It is interesting to note that racemic and meso forms of selenoxide **13** were separated.

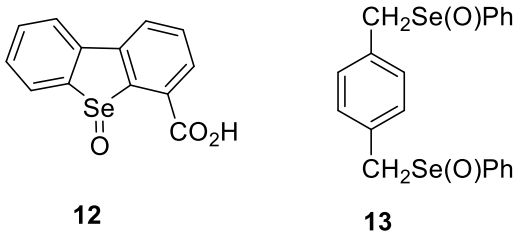


Figure 3. Selenoxides **12** and **13** configurationaly instable in aqueous media.

According to a current terminology, dihydroxyselenuranes such as **10** can be considered as hypervalent molecules [21–23] Due to the presence of two apical hydroxyl groups in the trigonal bipyramid formed as an intermediate, they are achiral [24]. It can be expected, that the isolation of selenoxides in enantiomerically pure, or at least enriched form, could be possible when the formation of hydrated form is slowed down. This can be realized most easily by introduction at least a single, sterically demanding substituent. Successful experiments on the isolation of optically active selenoxides, described after 1970, fully confirmed this assumption. It is the intent of this mini review to present the available information on the preparation and optical stability of selenoxides, in order to stimulate the additional research on this topic. It should be noted here that in the years 1987–1995 short reviews were published in Japanese by Japanese authors conducting research on this topic. [25–27]. There are also two brief accounts in English that describe experiments on the synthesis, stereochemical aspects and the application in asymmetric synthesis of chiral chalcogen oxides carried out in the laboratories of authors, in which optically active selenoxides are also mentioned [28,29]. A few year later, a brief discussion devoted to optically active selenoxides was included into the Chapter 16 of "The Chemistry of Organic Selenium and Tellurium Compounds" from Patai's "Chemistry of Functional Groups" [30].

Below, we are going to discuss the synthesis of optically active selenoxides, which have been obtained in the form of diastereomeric mixtures or in enantiomeric form since 1970 using the following procedures:

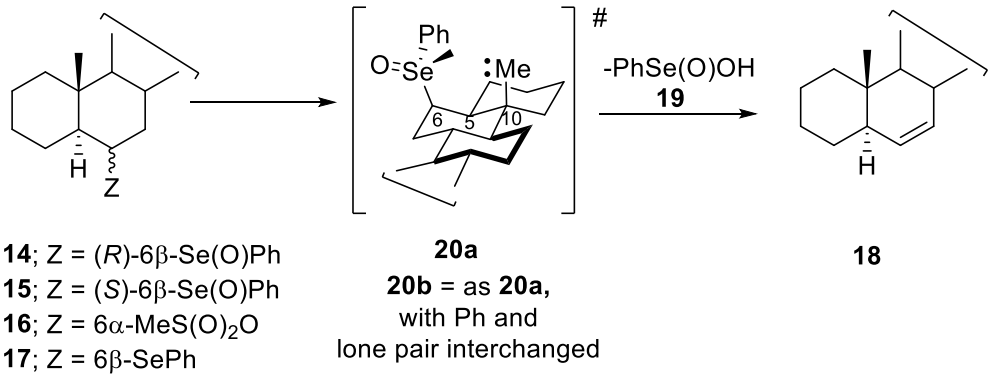
a) reaction of diastereoisomerically pure precursors;
b) asymmetric oxidation of prochiral selenides;
c) chromatographic and nonclassical resolution of racemates by forming complexes with an optically active hydrogen bond donor;

d) kinetic resolution of racemates;
e) reaction of enantiopure, cyclic seleninic esters with organometallic reagents.

2. Synthesis of Optically Active Selenoxides

2.1. Diastereoisomeric Selenoxides

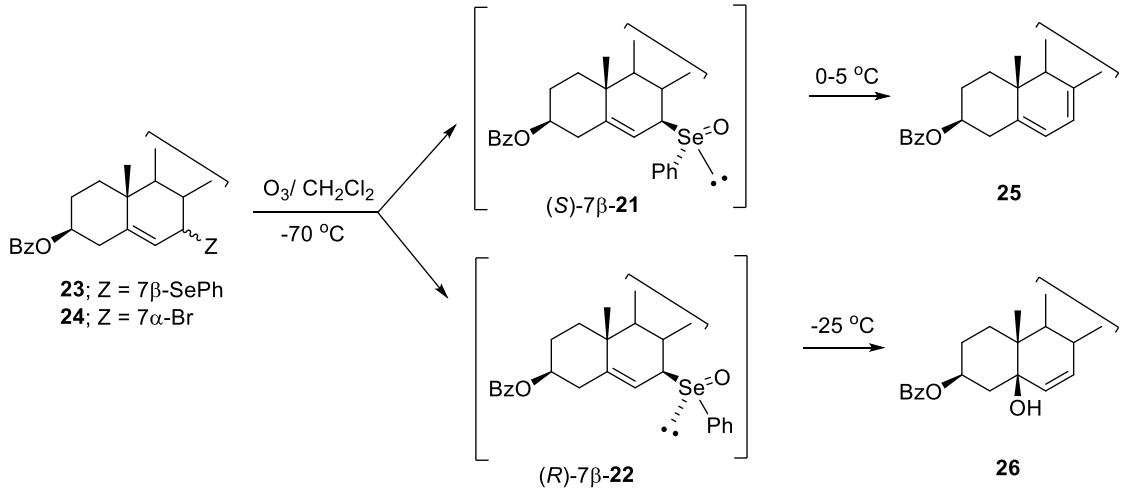
The first selenoxides whose optical activity results from the presence of a stereogenic selenium atom constitute diastereoisomeric, steroidal selenoxides **14** and **15**, which were described in 1970 [31]. Their synthesis was based on the oxidation of 6β-phenylseleno-5α-cholestane **17** which contains a prochiral divalent selenium atom (prepared by the reaction of 6α-methanesulphonyloxy-5α-cholestane **16** with sodium benzeneselenolate) with ozone [32]. It was found that this asymmetric oxidation, carried out in dichloromethane at −78 °C, gave a mixture of the selenoxides (*R*)-6β-**14** and (*S*)-6β-**15** in the ratio 2:1. Separated p by chromatography at −50 °C did not interconvert at temperatures between −78 °C and 25 °C in organic solvent in the presence of water. This indicates that their racemization via reversible hydrate formation (or pyramidal inversion) is not observed under these conditions. However, both diastereoisomerically pure selenoxides **14** and **15** were found to decompose at room temperature, affording only *5-α*-cholest-6-ene **18** and benzeneseleninic acid **19** (Scheme 3). It is interesting to note that the (*S*)-6β-**15** gave the olefin **18** after 4 h at 0 °C, while the other one remains unchanged. These difference i in the decomposition rate was proposed to be related with the cyclic intramolecular mechanism common to syn-eliminations [33]. In line with this mechanism, the transition state **20a** which leads from the (*S*)-6-β-phenylselenoxide **15** to 5a-cholest-6-ene **18** is appreciably less sterically compressed than that of the transition state **20b** responsible for the formation of the unsaturated steroid **18** from the (*R*)-isomer **14** (Scheme 3).



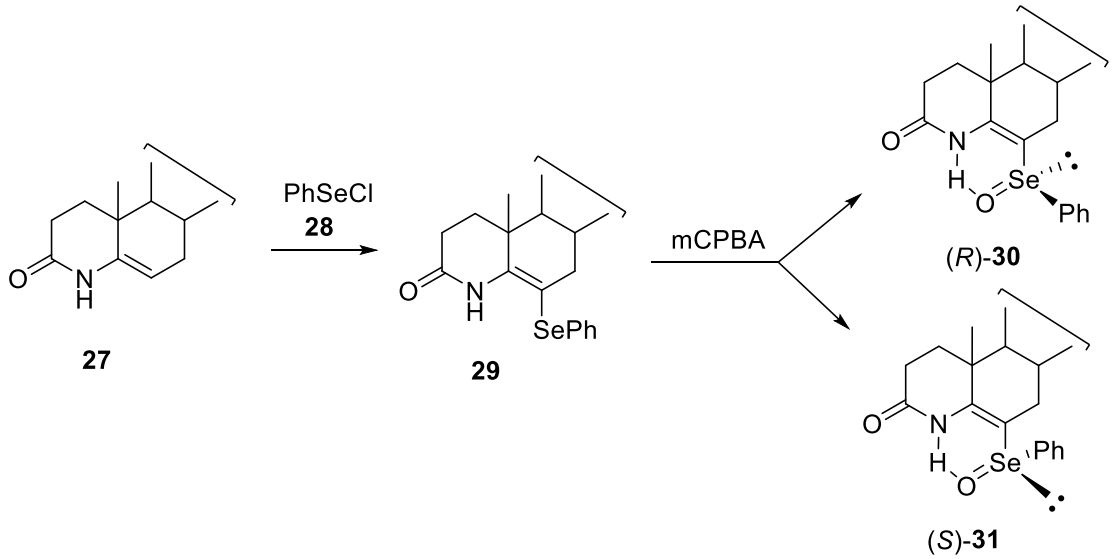
Scheme 3. Formation of unsaturated steroid **18** from selenoxide **14**.

Generation of diastereoisomeric steroidal selenoxides **21** and **22**, which were too labile to be isolated was observed during the oxidation of 7β-phenylselenocholesteryl benzoate **23**, (prepared by the reaction of 7α-bromocholesteryl benzoate **24** with sodium benzeneselenolate), with ozone at −70 °C in a methylene chloride solution. Their configurational stability and the absolute configuration at the newly generated stereogenic center on a selenium atom was suggested, taking into account an observation that the 3-benzoate of coprost-6-en-3b,5-diol **26** and 7-dehydrocholesteryl benzoate **25** were formed in approximately equal yields of 45%. Interestingly, when temperature was slowly raised, the presence of **26** was detected by thin layer chromatography (TLC) at about −25 °C whilst **25** appeared only at about −5 to 0 °C (Scheme 4). If the selenoxides **21** and **22** were configurationally unstable it the interconversion of **22** to **21** should lead predominantly to the product **26**, which was not detected [34]. The sequential treatment of 4-aza-5-pregnene-3,20-dione **27** with benzeneselenenyl chloride **28** and 1 equivalent of m-chloroperbenzoic acid (MCPBA) was found to afford a 2:1 mixture of selenoxide diastereomers (*R*)-**30** and (*S*)-**31** (Scheme 5). This mixture of selenoxide stereoisomers

remained unchanged after one week. Whereas, the pure, major diastereoisomer (*R*)-**30** similarly treated epimerized to the same 2:1 mixture within 3 h.



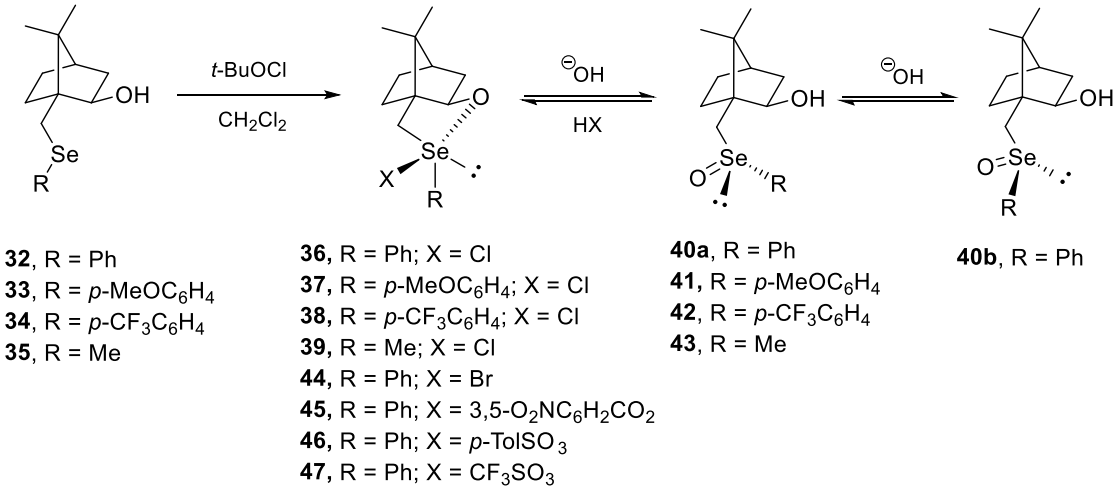
Scheme 4. Formation of 3-benzoate of coprost-6-en-3b,5-diol **26** and 7-dehydrocholesteryl benzoate **25**.



Scheme 5. Diastereoselective oxidation of azasteroidal selenide **29**.

It was suggested that the 2:1 ratio reflects the relative thermodynamic stabilities of the two diastereoisomers [35]. The abnormally low field of the NMR signals of the enamidic hydrogen atoms in the stereoisomers **30** and **31** was related to the presence of strong intramolecular hydrogen bonds between the selenoxide oxygens and these hydrogen atoms. A series of diasteroisomeric hydroxyselenoxides **40**–**43** containing the bornyl moiety was prepared by hydrolysis at 0 °C of diasteroisomeric chloroselenuranes **36**–**39** (X = Cl) which were formed rapidly (10 min at 0 °C) as single stereoisomers (89–100% yield) upon the reaction of bicyclic hydroxyselenides **32**–**35** with *t*-butyl hypochlorite (Scheme 6). It was found that the treatment of selenoxide **40a** with a base afforded an equilibrium mixture of **40a** and **40b** (2:1) whereas the treatment with an acid (HCIO4) of selenoxide **40a** or a mixture of the selenoxides **40a** and **40b** predominantly gave **40a**, and that selenurane **36** was formed both from **40a** and a mixture of **40a** and **40b**. The starting chloroselenurane **36** was recovered as a single diastereomer (100% yield) upon treatment of the selenoxide **40** with HCl, A similar reaction of **40** with HBr gave bromoselenurane **44** (96% yield). The reaction of the hydroxyselenoxide **40** with

strong organic acids (3,5-dinitrobenzoic, *p*-toluenesulfonic or trifluoromethanesulfonic)in the presence of $MgSO_4$ gave the corresponding selenuranes **44**–**47**, respectively (Scheme 6) [36,37].



32, R = Ph
33, R = *p*-$MeOC_6H_4$
34, R = *p*-$CF_3C_6H_4$
35, R = Me

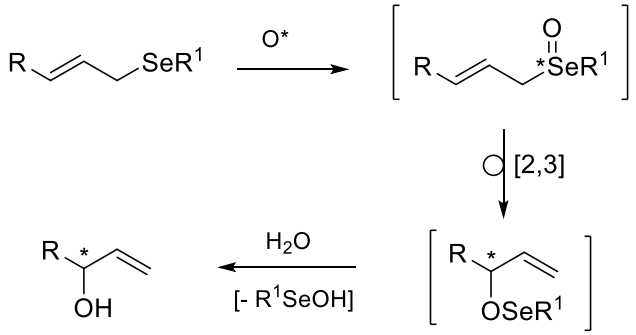
36, R = Ph; X = Cl
37, R = *p*-$MeOC_6H_4$; X = Cl
38, R = *p*-$CF_3C_6H_4$; X = Cl
39, R = Me; X = Cl
44, R = Ph; X = Br
45, R = Ph; X = 3,5-$O_2NC_6H_2CO_2$
46, R = Ph; X = *p*-$TolSO_3$
47, R = Ph; X = CF_3SO_3

40a, R = Ph
41, R = *p*-$MeOC_6H_4$
42, R = *p*-$CF_3C_6H_4$
43, R = Me

40b, R = Ph

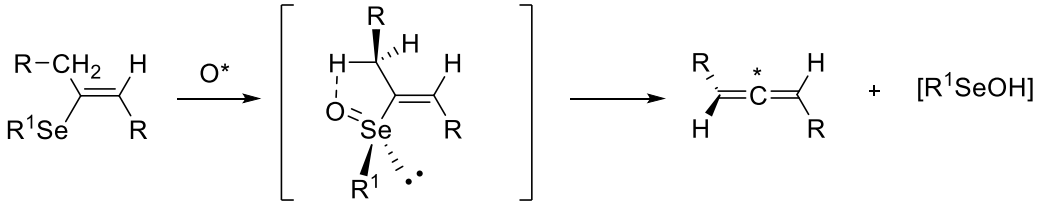
Scheme 6. Hydrolysis of diasteroisomeric selenuranes **36**–**47**.

It is well known that allyl selenoxides undergo very fast [2,3]sigmatropic rearrangement, producing allylic alcohols (Scheme 7), while vinyl selenoxides are able to eliminate selenic acid, which leads to the cumulene system (Scheme 8). The asymmetric version of both methods can be used to synthesize optically active alcohols or allenes, respectively [38–41].



* means a stereogenic center,
O means an oxidant

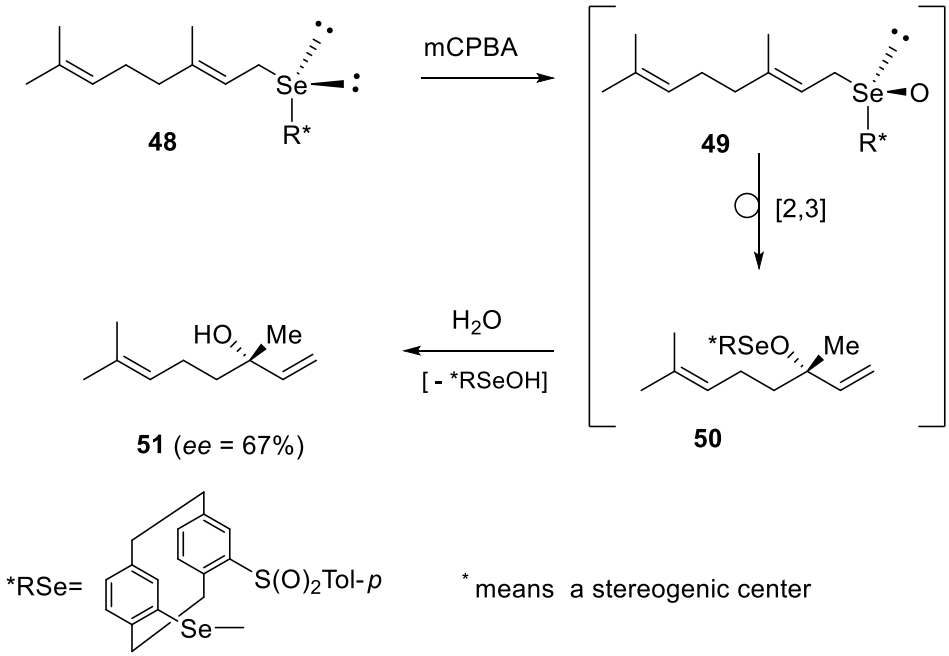
Scheme 7. [2,3]Sigmatropic rearrangement of allyl selenoxides generated in situ.



* means a stereogenic center,
O means an oxidant

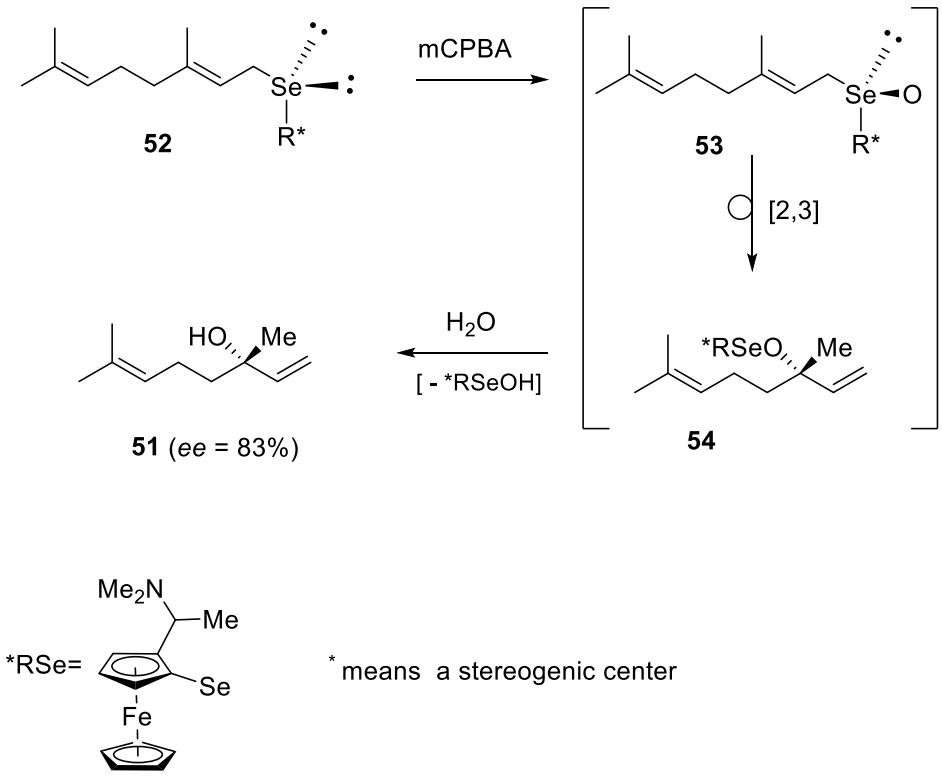
Scheme 8. Oxidative conversion of vinyl selenides into allenes.

The first example of this methodology, which was used in the preparation of optically active allylic alcohol, was reported in 1991 [42] and was based on the in situ generation of the optically active, diastereoisomerically enriched, geranyl [2.2]paracyclophanyl selenideoxide **49** by treatment of the corresponding optically active geranyl selenide **48** with meta-chloroperbenzoic acid (MCPBA). This protocol gave linalool **51** with 67% enantiomeric excess (ee) via selenenic ester **50** which was formed as a result of the [2,3]sigmatropic rearrangement of selenoxide **49** (Scheme 9).



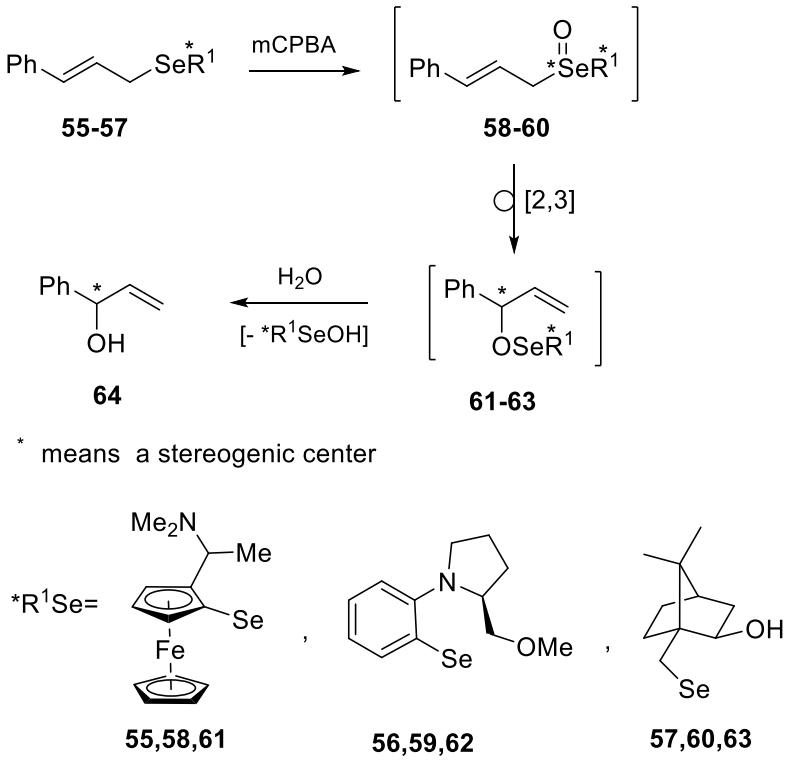
Scheme 9. Oxidative conversion of geranyl [2.2]paracyclophanyl selenide **49** into optically active linalool **51**.

A similar oxidation of geranyl selenide **52** bearing a chiral ferrocenyl group afforded the corresponding diasteromeric selenoxides **53**, which upon the [2,3]sigmatropic rearrangement gave optically active linalool **51** in moderate yields and an improved ee (83%) (Scheme 10) [43].

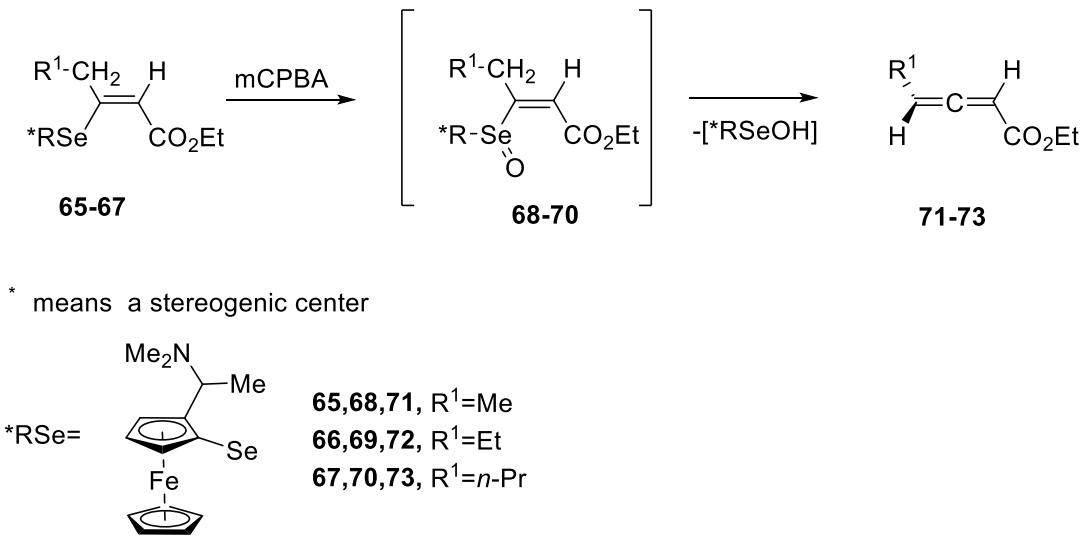


Scheme 10. Oxidative conversion of ferrocenyl selenide **52** into optically active linalool **51**.

This approach was also applied in the synthesis of a series of cinnamyl selenides **55**–**57** bearing other chiral groups. The diasteroisomeric selenoxides **58**–**60** upon [2,3]sigmatropic rearrangement gave, via diastereoisomeric esters **61**–**63**, enantiomerically enriched 1-phenyl-2-propen-1-ol **64** in with ee in the range of 63–89% (Scheme 11) [44]. The chiral, diasteroisomeric selenoxides **68**–**70** generated similarly from the corresponding optically active ferrocenyl vinylic selenides having (Z)-configuration **65**–**67** underwent the in situ seleninic acid elimination to afford axially chiral allenecarboxylic esters **71**–**73** in moderate chemical yields (21–59%) with ee from 16 up to 89% (Scheme 12) [43].



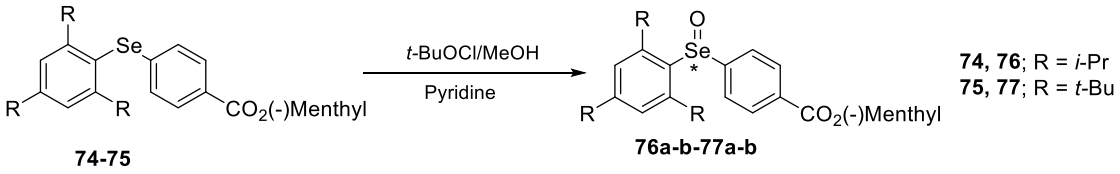
Scheme 11. Oxidative conversion of cinnamyl selenides **55–57** into optically active 1-phenyl-2-propen-1-ol **64**.



Scheme 12. Oxidative conversion of vinyl selenides **65–67** into allenes **71–73.**

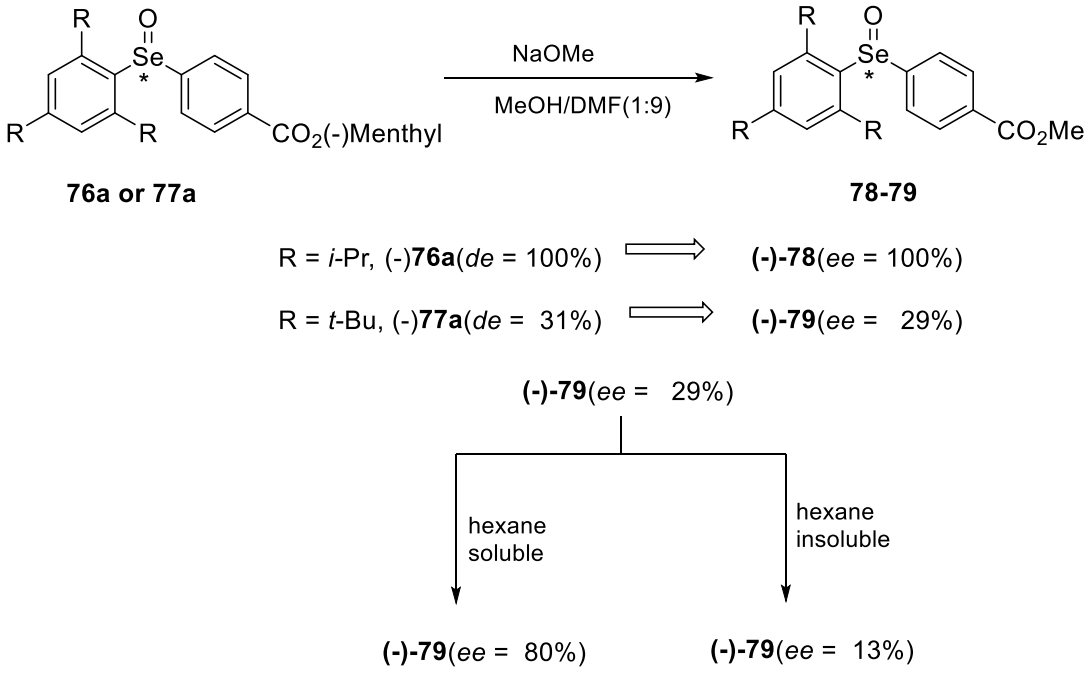
Two optically stable, diastereoisomeric selenoxides **76a–b**-**77a–b** were prepared by oxidation of the 4-[(-)-menthyloxycarbonyl] phenyl aryl selenides **74–75** with t-butyl hypochlorite-pyridine-methanol (Scheme 13). The selenoxide **76a** after five recrystallizations from methanol, was diastereoisomericaly pure (HPLC analysis using an achiral column). Dextrorotatry diastereoisomer **76b** was also obtained from the mother liquid with 75% diastereoisomeric excess. A similar oxidation of the selenide **75** gave, with slight asymmetric induction (de = 7.6%), diastereoisomeric 4-[(-)-menthyloxycarbonyl] phenyl 2,4,6-tri-t-butyphenyl selenoxides **77a–b**. Fractional crystallization of this diastereoisomeric mixture

gave a sample of the levorotatory diastereoisomer **77a** having de = 31.1% (estimated by measurement of the ^{77}Se NMR spectrum) [45].

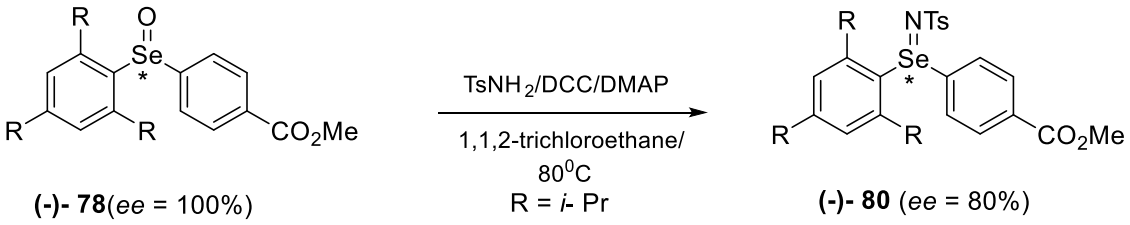


Scheme 13. Asymmetric synthesis of optically active diaryl selenoxides **76**–**77**.

The levorotatory enantiomer of 4-[(-)-methoxycarbonyl] phenyl 2,4,6-tri-iso propyl phenyl selenoxide **78** was obtained by transesterification of diastereoisomerically pure 4-[(-)-menthyloxycarbonyl] phenyl 2,4,6-tri-isopropylphenyl selenoxide **76a** in *N*, *N*-dimethylformamide DMF) at room temperature (Scheme 14). On the other hand, transesterification of the levorotatory diastereoisomer **77a** (de = 31.1%) with sodium methoxide in methanol gave a sample of the selenoxide **79** with 29% ee. s Its washing with hexane left a solid that showed only 13% ee, while a sample of the selenoxide **79** isolated from the hexane solution exhibited a much higher enantiomeric excess (80%) [45]. The dehydration conversion of enantiomerically pure selenoxide (-)-**78** (*p*-toluenesulfonamide ($TsNH_2$) / dicyclohexylcarbodiimide (DCC)/ 4-(dimethylamino)pyridine (DMAP)//80 °C) in 1,1,2-trichloroethane gave optically active 4-(methoxycarbonyl) phenyl(2,4,6-triisopropylphenyl)selenonium (*N*-toluene-4-sulfon)imide (-)- **80** in 29% chemical yield. Its enantiomeric excess was determined to be 80% by ^{1}H-NMR measurement using an optically active shift reagent {Eu(hfc)$_3$} (Scheme 15) [46].



Scheme 14. Transesterification of diastereoisomerically pure selenoxide **76a** with methanol.

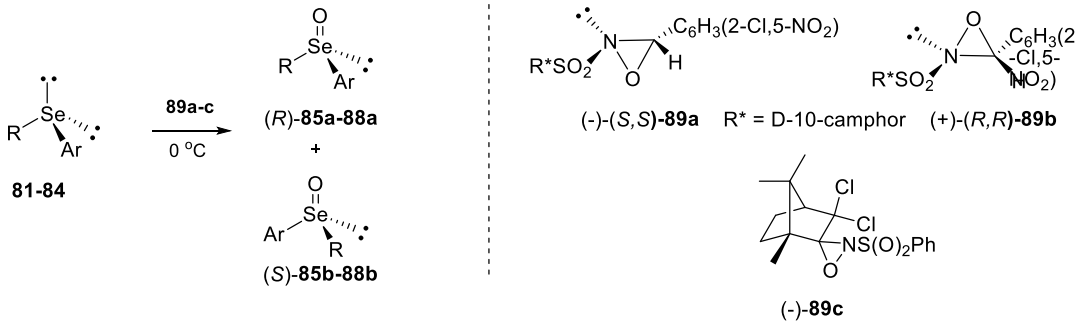


Scheme 15. Conversion of enantiomerically pure selenoxide (-)-**78** into optically active selenoniumimide (-)-**80**.

2.2. Enantiomeric Selenoxides

2.2.1. Asymmetric Oxidation

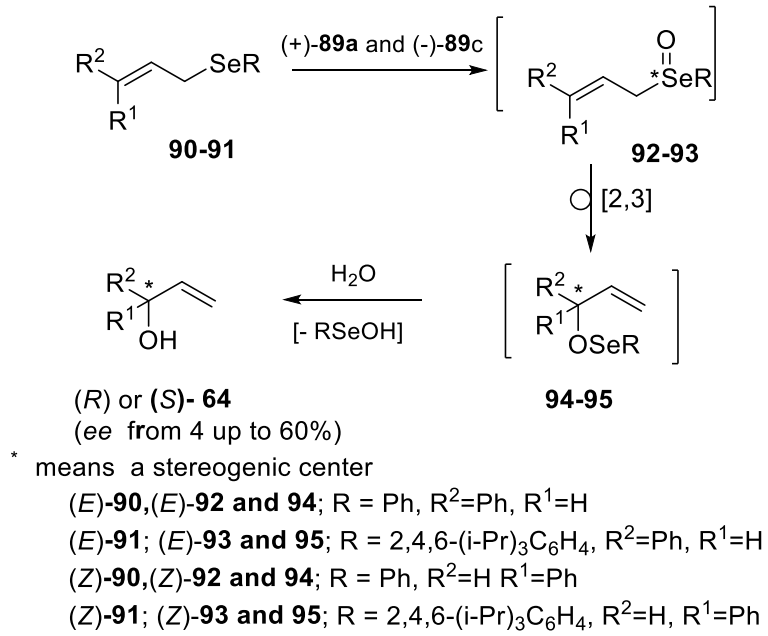
Among the different approaches to the synthesis of enantiomeric selenoxides, asymmetric oxidation of the prochiral, unsymmetrical selenides with optically active oxidizing agents can be considered the method of choice. The first asymmetric oxidations of methyl phenyl selenide **81** by chiral 2-sulfonyloxaziridines **89a** or **89b**, carried out in the Davis laboratory, was found to give the corresponding methyl phenyl selenoxide **85** with ee only around 9% ee under anhydrous conditions [47]. Later, *N*-(phenylsulfonyl) (3,3-dichlorocamphoryloxaziridine) **89c** was found to be more efficient reagent for the enantioselective oxidation of prochiral selenides **81**–**84** Using this reagent, the corresponding alkyl aryl selenoxides **85**–**88** were isolated for the first time with ee hagher than 90%..(Scheme 16) [48,49].



(**81**,R = Me, Ar=Ph)/**89a** **85a+85b** (*ee* = 9-13%)
(**81**,R = Me, Ar=Ph)/**89c** **85a+85b** (*ee* = 95%)
(**82**,R = Me, Ar= 2,4.6-i-Pr-C_6H_2)/**89c** **86a+86b** (*ee* = 95%)
(**83**,R = Et, Ar= 2,4.6-i-Pr-C_6H_2)/**89c** **87a+87b** (*ee* = 91%)
(**84**,R = $CH_2C_6H_4$-OMe-p, Ar= 2,4.6-i-Pr-C_6H_2)/**89c** **88a+88b** (*ee* = 95%)

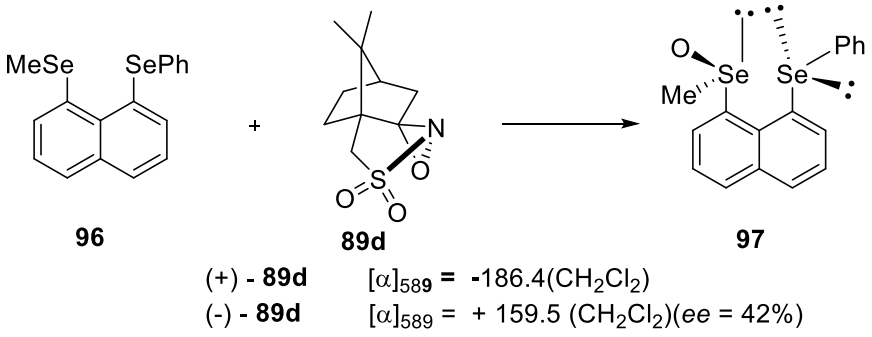
Scheme 16. Asymmetric synthesis of optically active selenoxides **85**–**88**.

The above-mentioned oxaziridines (+)**-89a** and (-)-**89c** were used also for the in situ generation of (E)- and (Z)-aryl cinnamyl selenoxides **92** and **93** by oxidation of the corresponding cinnamyl selenides **90** and **91.** Their instant [2,3]sigmatropic rearrangement to allylic selenenates **94**–**95** afforded 1-phenylallyl alcohol **64** as the final product (Scheme 17) [49].



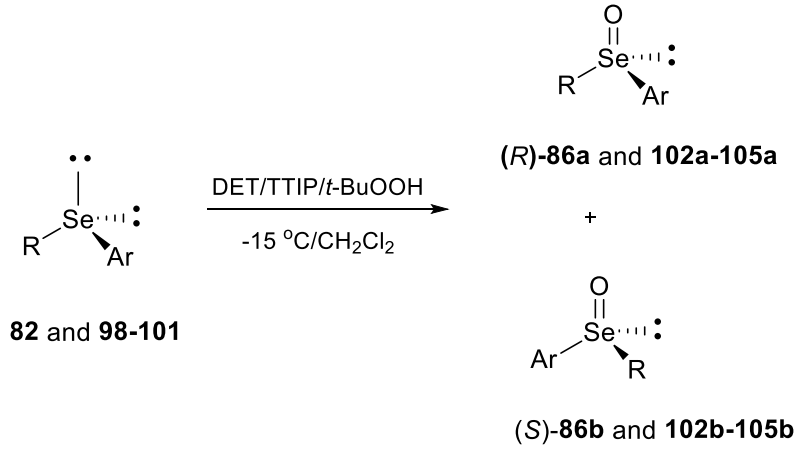
Scheme 17. Oxidative conversion of allylic selenides **90–91** into optically active.allyl alcohols **64**.

Diastereoisomeric (+) and (-)-(camphorylsulfonyl)oxaziridines **89d** [50] were used for the enantioselective oxidation of 1-phenylselenyl-8-methylselenylnaphthalene **96**. It was found that this reaction afforded regioselectively enantiomerically enriched 1-phenylselenyl-8-methylseleninylnaphthalene **97**, which maintains, in a standard laboratory environment, stereochemical integrity at a stereogenic seleninyl selenium atom at room temperature for several days (Scheme 18) [51]. A relatively high optical stability of the selenoxide **97** results from stabilization to racemization by intramolecular coordination between the dicoordinated, divalent selenium atom of the phenylselenenyl group at position 1 and a stereogenic seleninyl selenium atom at position 8 of the naphthalene ring.



Scheme 18. Enantioselective oxidation of 1-phenylselenyl-8-methylseleninylnaphthalene **96**.

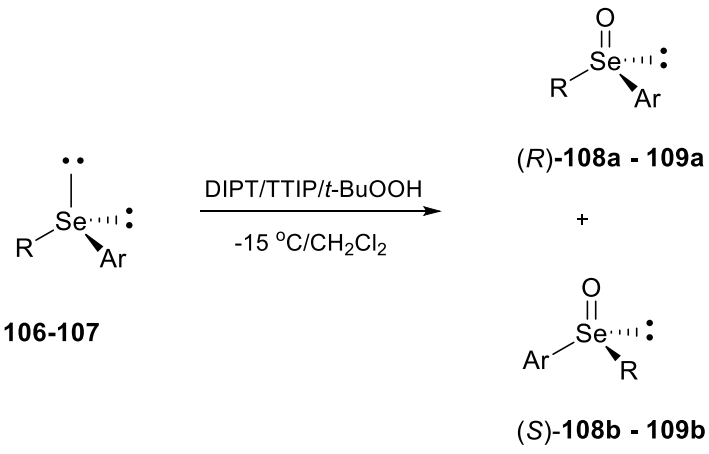
A few enantiomerically enriched alkyl aryl selenoxide **86** and **102–105** were synthesized by the asymmetric oxidation of the corresponding alkyl aryl selenides **82** and **98–101** using a mixture of *t*-butylhydroperoxide with optically active dialkyl tartrates and titanium or aluminium tetraalkoxides such as the Lewis acids (Sharpless reagent) (Scheme 19) [52]. It was found that the most effective combination was that of diethyl tartrate (DET) and titanium tetraisopropoxide (TTIP). It gave the highest ee value (32.7%) for methyl 2,4,6-tri-t-butylphenyl selenoxide **98** when the oxidation was carried out in methylene chloride at −15 °C.



82, R = Me, Ar= 2,4.6-*i*-Pr_3-C_6H_2 **86a+86b** (*ee* = 28.2%)
98, R = Me, Ar= 2,4.6-*t*-Bu_3-C_6H_2 **102a+102b** (*ee* = 32.7%)
99, R = *t*-$BuCH_2$, Ar= 2,4.6-*t*-Bu_3-C_6H_2 **103a+103b** (ee = 11.4%)
100,R = $PhCH_2$, Ar= 2,4.6-*t*-Bu_3-C_6H_2 **104a+104b** (*ee* = 6.6%)
101,R = 2-$MeOC_6H_4CH_2$, Ar= 2,4.6-*t*-Bu_3-C_6H_2 **105a+105b** (*ee* = 16.7%)

Scheme 19. Asymmetric oxidation of selenides **82** and **98**–**101**.

Almost simultaneously, asymmetric oxidation of 2-methoxy -2,2-diphenylethyl aryl selenides **106**–**107** to the corresponding selenoxides **108**–**109** showing ee values in the range of 18–40% was reported by Tiecco at al.. They used as a reagent, $Ti(OC_3H_7\text{-}i)_4$, L-(+)- or D-(-)- diisopropyltartrate (DIPT), and t-BuOOH in molar ratio 1:2:1 (Scheme 20) [53].

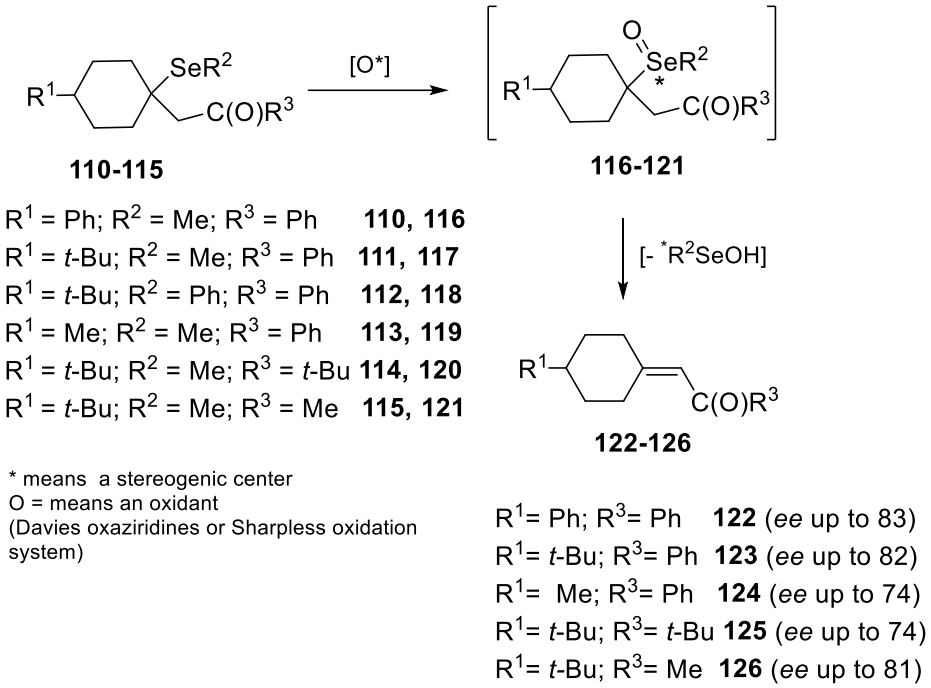


106, R = $Ph_2(OMe)CH_2$, Ar = Ph **(+)**-DIPT **108a+108b** (*ee* = 18.0%; (-)-(*S*)
106, R = $Ph_2(OMe)CH_2$, Ar = Ph **(-)**-DIPT **108a+108b** (*ee* = 20.0%; (+)-(*R*)
107, R = $Ph_2(OMe)CH_2$, Ar = 2-$MeOC_6H_4$ **(+)**-DIPT **109a+109b** (*ee* = 40.0%; (-)-(*S*)
107, R = $Ph_2(OMe)CH_2$, Ar = 2-$MeOC_6H_4$ **(-)**-DIPT **109a+109b** (*ee* = 40.0%; (+)-(*R*)

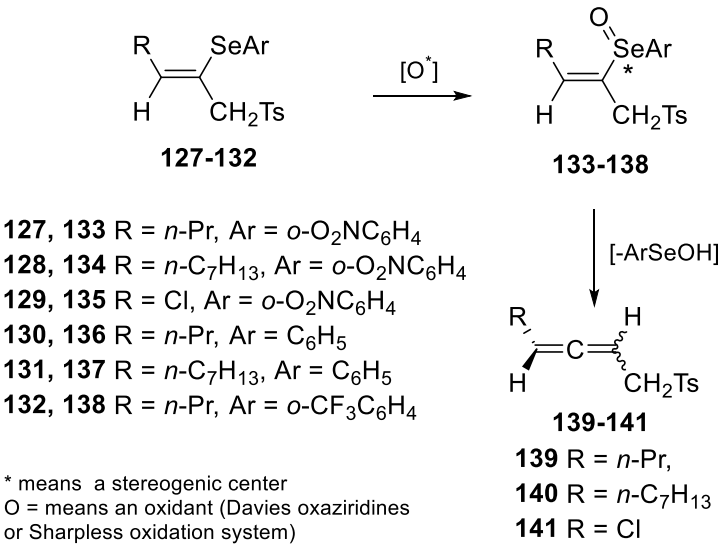
Scheme 20. Asymmetric oxidation of selenides **106**–**107**.

In an efficient synthesis of axially chiral alkyl and aryl cyclohexylidenemethyl ketones **122**–**126**, isolated in excellent chemical yields and with high enantiomeric excess (up to 83% ee), based on seleninic acid elimination optically active, non-isolable cyclohexyl selenideoxides **116**–**121** constitute key, chiral precursors. They were prepared in situ by oxidation of cyclohexyl selenides **110**–**115**, having

the Z configuration, with either Davis camphoryloxaziridines or under Sharpless oxidation conditions (Scheme 21) [54]. The instant decomposition of non-isolable, selenoxides **133–138** (derived from some aryl vinyl selenides **127–132** using Sharpless or Davis oxidants) with elimination of an appropriate seleninic acid resulted in the formation of chiral allenyl sulfones **139–141** with up to 42% enantiomeric excess (ee) (Scheme 22)[55].

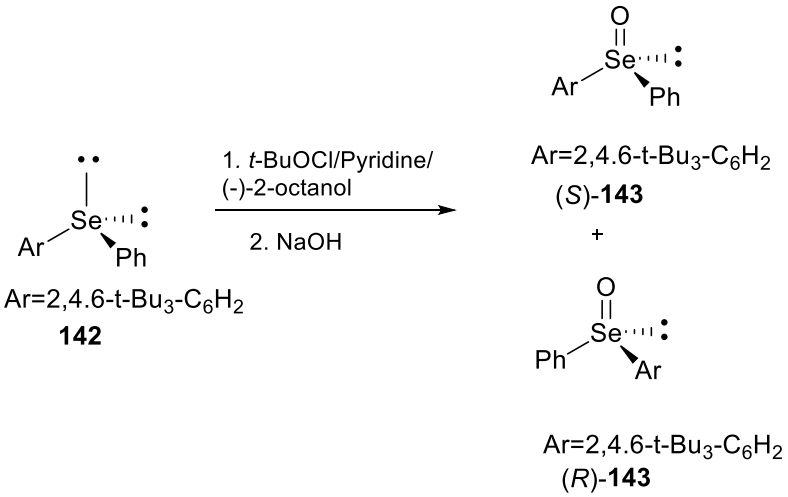


Scheme 21. Oxidative conversion of selenides **110–115** into optically active cyclohexylidenemethyl ketones **122–126**.



Scheme 22. Oxidative conversion of aryl vinyl selenides **127–132** into optically active allenic sulfones **139–141**.

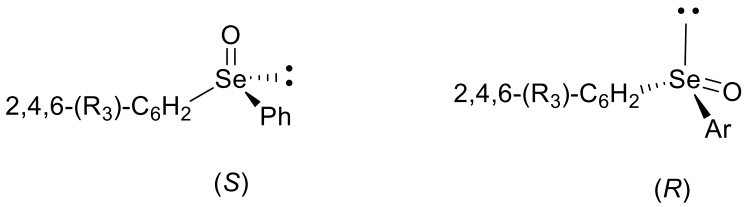
T The treatment of phenyl tri-*t*-butylphenyl selenide **142** with *t*-butyl hypochlorite in the presence of (-)-2-octanol and pyridine followed by basic hydrolysis gave optically active phenyl tri-*t*-butylphenyl selenoxide **143** with a germinal enantiomeric excess (ee = 1%) (Scheme 23) [56].



Scheme 23. Asymmetric oxidation of phenyl tri-*t*-butylphenyl selenide **142**.

2.2.2. Chromatographic and Non-Classical Resolution of Racemates by Forming Complexes with an Optically Active Hydrogen Bond Donor

The first optical resolution by column chromatography using a chiral column was applied for diaryl selenoxides that possess no functional groups. I By this approach the racemic diaryl selenoxides **143**–**149** (Figure 4) were partially resolved on a medium pressure column chromatography system [(R)-iV-(3,5-dinitrobenzoyl) phenylglycine/aminopropylsilica (particle size 40 μ) columne]. Enantiomeric excess for fast eluting enantiomers ranged from 12 to 66%, and for slowly eluting enantiomers from 4 to 41% [47,48].



R = *t*-Bu; Ar = Ph **143**
R = *i*-Pr; Ar = Ph **144**
R = *i*-Pr; Ar = *o*-MeOC$_6$H$_4$ **145**
R = *i*-Pr; Ar = *p*-Tol **146**
R = Et; Ar = Ph **147**
R = Me; Ar = Ph **148**
R = Me; Ar = p-Tol **149**

Figure 4. diaryl selenoxides **143**–**149** that possess no functional groups.

Later on, column chromatography on a chiral column was applied to separate enantiomers selenoxides configurationally stabilized by intramolecular coordination to the stereogenic selenium atom. Thus, racemic 2-((dimethylamino)methyl)phenyl alkyl (or aryl) selenoxides **150**–**152** (Figure 5), containing an amino group able to coordinate with the selenium atom, were resolved into enantiomers by means of HPLC chromatography using an chiral column It is interesting to note that the. vthe stabilization energy (ca. 3 kcal mol^{-1}) for this interaction was determined by variable temperature ^{1}H-NNMR experiments [59].

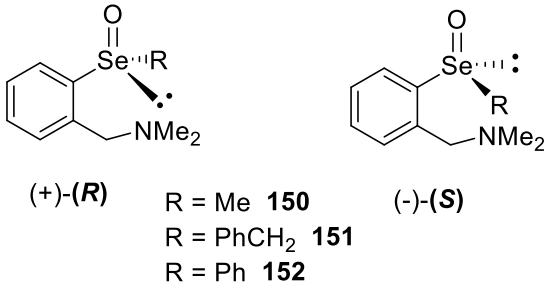


Figure 5. 2-(Dimethylamino)methyl)phenyl alkyl (aryl) selenoxides **150**–**152**.

A similar optical resolution (Figure 6) was applied to racemic 2-(methylchalcogenomethyl)diphenyl selenoxides **153**–**154** and 2-{2_-(*N*, *N*-dimethylamino)ethyl}-phenyl alkyl (or aryl) selenoxides **156**–**158**. However, selenoxide **155** could not be resolved by this procedure [60].

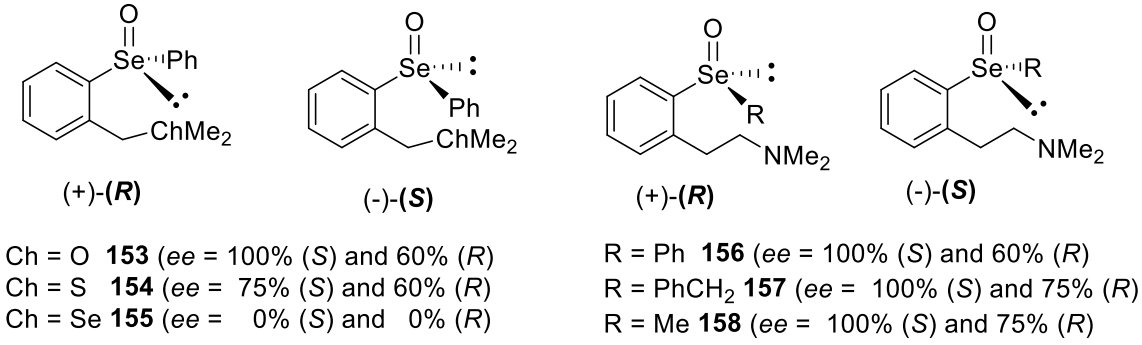


Figure 6. 2-2-(Methylchalcogenomethyl)diphenyl selenoxides **153**–**154** and 2-{2_-(*N*,*N*-dimethylamino) ethyl}-phenyl alkyl (or aryl) selenoxides **156**–**158**.

Three enantiomerically pure 8-(dimethylamino)-1-aryl(alkyl)-naphthyl selenoxides **159**–**161** (Figure 7) were isolated by chromatographic resolution using a chiral column ((Daicel Chiralpak AS; 10 × 250 mm). It is interesting to note that the first eluted enantiomer of selenoxide **159** had a positive specific rotation, whereas the first eluted enantiomer of selenoxides **160**–**161** had a negative specific rotation [61,62].

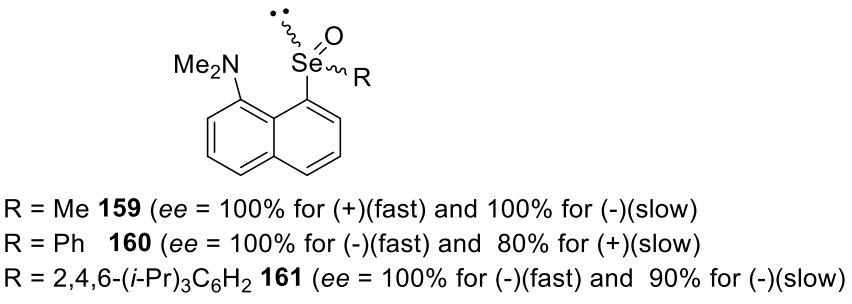


Figure 7. 8-(Dimethylamino)-1-aryl(alkyl)-naphthyl selenoxides **159**–**161**.

In addition to chromatographic resolutions mentioned above, several simple aryl alkyl **85** and **162**–**167** and dialkyl selenoxides **168**–**170** (Figure 8) were resolved into pure enantiomers via complexation with enantiomerically pure 2,2′-dihydroxy-1,1′-binaphthol **171** or 1,6-di(o-chl**o**rophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol **172**. Enantiomeric excess of sulfoxides selenoxides **85** and **162**–**167** in the complex with **171** was found to be almost 100%. Moreover, dynamic kinetic resolution (DKR) of selenoxides via hydrate formation gave in some cases enantiomerically pure selenoxides in yields above 100% [63].

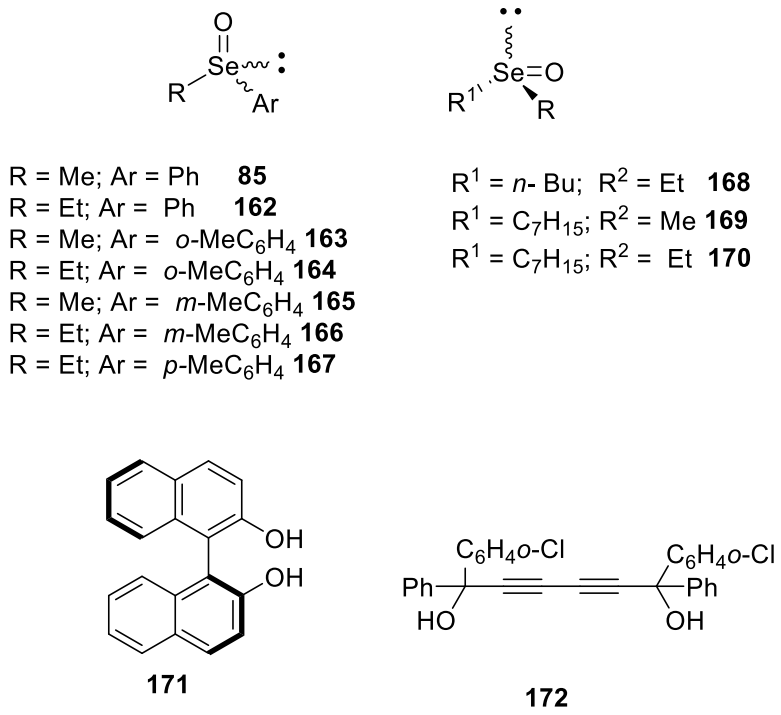
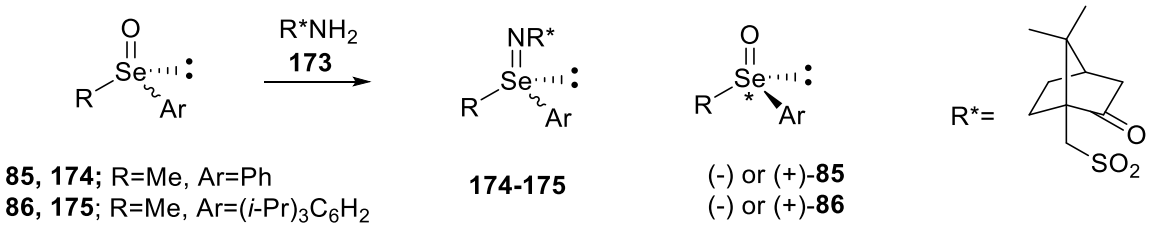


Figure 8. Aryl alkyl **85** and **162**–**167** and dialkyl selenoxides **168**–**170**.

2.2.3. Kinetic Resolution of Racemates

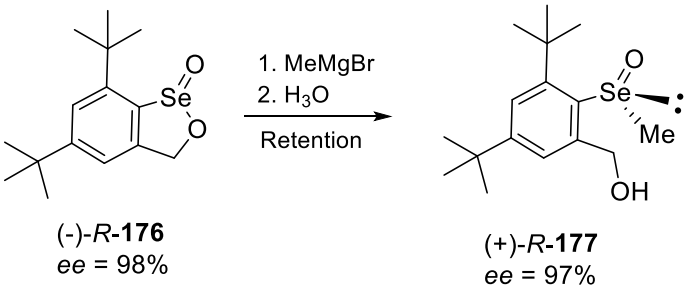
In fact, the first optically active, enantiomerically enriched selenoxides were isolated in a kinetic resolution reaction when racemic methyl phenyl selenoxide **85** or methyl tri-isopropylphenyl selenoxide **86** were subjected to the reaction with a half molar equivalent of (-)- or (+)-camphorsulfonamide **173** (Scheme 24) [64].



Scheme 24. Kinetic resolution reaction of racemic alkyl phenyl selenoxides **85**–**86**.

2.2.4. Reaction of Enantiopure, Cyclic Seleninic Ester with an Organometallic Reagent

There is a single literature report on a conversion of optically active, cyclic seleninate ester into optically active selenoxide. Thus, the reaction of optically active seleninate ester (+)-(*R*)-**176** with ee equal to 98%, (obtained by HPLC chromatography on a chiral column) and methylmagnesium bromide was found to afford with retention of configuration at the stereogenic selenium atom, 2-(hydroxymethyl)-4,6-di-t-butylphenyl methyl selenoxide (-)-(*R*)-**177** (ee = 97%) (Scheme 25) [65].



Scheme 25. Reaction of optically active seleninate ester (+)-(*R*)-**176** with methylmagnesium bromide.

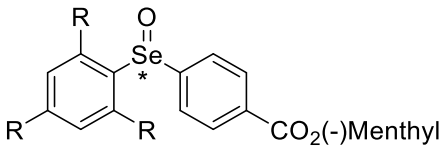
3. Absolute Configurations and Enantiomeric Excesses of Optically Active Selenoxides

The absolute configuration of the levorotatory enantiomer of selenoxide **78** was established to be *S*, taking into accounts the result of X-ray crystallographic analysis of the diastereoisomerically pure, levorotatory selenoxide **76a** and the lack of inversion of configuration around the stereogenic selenium atom during the transesterification from (-)-(S_{se})-**76** to methyl esters (-)-**78** (Scheme 14) [45]. This determination was also supported by the presence of negative Cotton effects at the same wavelength region (284 nm) in the circular dichroism CD spectra of (-)-(**76**) and (-)-(**78**). The (*S*) absolute configurations around the stereogenic selenium atom of the other selenoxides (-)-(**77**) and (-)-(**79**) were deduced from their CD spectra in which also negative Cotton effects in this region (292 nm) were observed. The enantiomeric excesses of the selenoxides mentioned above were determined by HPLC using a chiral column. The extent of the asymmetric induction during the asymmetric oxidation of methyl phenyl selenide **81** to the corresponding selenoxide **85** (Scheme 16) was determined by adding to their solution successive amounts of tris[3-(heptafluoropropylhydroxymethylene d-camphorate]-europlum (III), Eu(hfc)$_3$. The absolute configuration around the stereogenic selenium atom of the selenoxide **85** was determined by the analysis of ^{1}H-NMR spectra recorded for the reaction mixture or for the isolated sample in the presence of (+)-2,2,2-trifluoro-l-(9-anthryl)ethanol. The extent of the asymmetric induction during the enantiselective oxidation of 1-phenylselenyl-8-methylselenylnaphthalene **96** to the corresponding, enantiomerically enriched 1-phenylselenyl-8-methylseleninylnaphthalene **97** (Scheme 18) was determined by analyzing ^{1}H-NMR spectra of the isolated selenoxide **97** measured in the presence of enantiomerically pure BINOL or *t*-butylphenylphosphinothioic acid as a chiral solvating agent (CSA). The extent of the asymmetric induction during the asymmetric oxidation of alkyl aryl selenides **82** and **98**–**101** to the corresponding selenoxides **86** and **102**–**105** with Sharpless reagent (Scheme 19) [52] was determined by ^{1}H-NMR using tris[3-(heptafluoropropylhydroxymethylene d-camphorate]-europlum (III), Eu(hfc)$_3$ as chiral shift reagent (CSR). Their absolute configurations were suggested based upon comparison with circular dichroism spectra of the appropriate alkyl aryl sulfoxides. The *S* absolute configuration of the levorotatory enantiomers of 2-(dimethylamino)methyl)phenyl alkyl (or aryl) selenoxides **150**–**152** was suggested by comparison of their specific rotations, circular dichroism spectra, and behavior on the optically active column with those of the sulfur analogue [44]. The common features that exist between the CD spectra of selenoxides **143**–**149** and optically active p-tolyl mesityl sulfoxide and p-tolyl 2,4,6-triisopropylphenyl sulfoxide were used to assign the absolute configuration of the dextrarotatory selenoxide enantiomers [57,58]. The relationship between the absolute configurations around a stereogenic selenium atom of 2-(methylchalcogenomethyl)diphenyl selenoxides **153**–**154** and 2-{2-(N,N-dimethylamino)ethyl}-phenyl alkyl (or aryl) selenoxides **156**–**158** and the chiroptical properties of the enantiomers of was clarified by comparing with those of sulfur analogues [60]. Earlier, the absolute configurations of the optically active chalcogen oxides **159**–**161** were assigned by comparison of their specific rotations and CD spectra with those of their sulfur analog [61,62]. Similarly, the absolute configuration of dextrorotatory 2-(hydroxymethyl) phenyl methyl selenoxide (+)-**177** was determined to be R by comparison of its specific rotations and CD spectra with those of that (*R*)-2-(hydroxymethyl) phenyl methyl sulfoxide. Enantiomeric excess of selenoxides **85** and **162**–**167** in

their complexes with BINOL **171** was determined from the ^{1}H-NMR spectra [48]. The optical excesses of 2-methoxy-2, 2-diphenylethyl aryl selenoxides **108**–**109** were determined by HPLC using a chiral column [53].

4. Configurational Stability of Optically Active Selenoxides

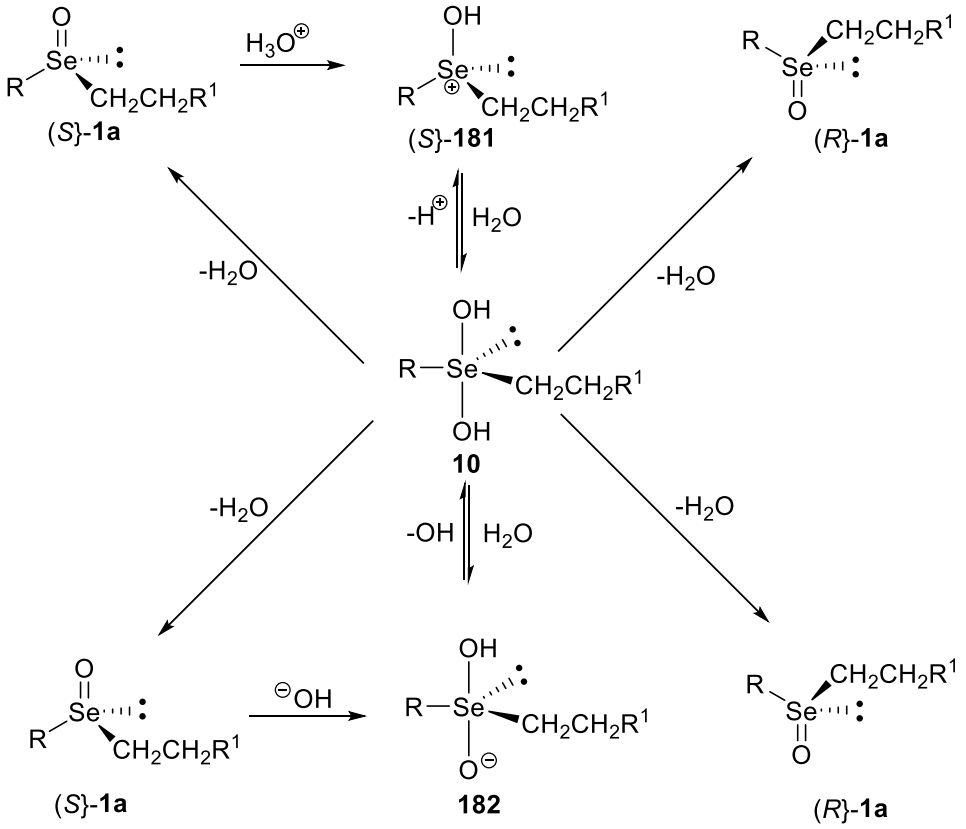
Bearing in mind the very close structural similarity between sulfoxides and selenoxides it can be expected, simply by analogy, that the same racemization mechanisms will operate for different selenoxides. Three basic mechanism of thermally induced racemization of sulfoxides, including a pyramidal inversion, are very well understood, mainly due to the classical studies of the Mislow's group [66–68]. At the same time, extensive studies, mainly from the Oae group, explained in detail various chemically induced racemization of the reach family of sulfoxides [68,69]. In contrast to sulfoxides, mechanistic studies on thermally and chemically induced racemization of selenoxides are rather limited. There is only a single paper devoted to thermal racemization of selenoxides by a pyramidal inversion mechanism. In this publication, the free energies of activation (AG*) for the epimerization of a few diastereoisomeric, optically active diaryl selenoxides have been reported. They were calculated on the basis of the coalescence temperature of signals of two nonequivalent ^{77}Se nuclei observed in the ^{77} Se- NMR spectra of a series of diasteroisomeric 4-[(-)-menthyloxycarbonyl] phenyl 2,4,6-tri-alkylphenyl selenoxides **76**, **77** and **178**–**180** (Figure 9). These values, ranging from 61 to 85.8 kJ mol^{-1}, clearly indicate that the rate of epimerization of the selenoxides is strongly dependent on the bulkiness of the ortho substituents [70]. It should be noted here that the activation barriers for alkyl aryl and diaryl sulfoxides are considerably higher (150–180 kJ/ mol) [66–68].



178; R = H
179; R = Me
180; R = Et

Figure 9. 4-[(-)-Menthyloxycarbonyl] phenyl 2,4,6-tri-alkylphenyl selenoxides **178**–**180**.

The facile formation of achiral hydrates, mentioned for the first time in the paper which reported the first unsuccessful attempts to resolve 4-carboxydiphenyl selenoxide **8** and 4-carboxyphenyl methyl selenoxide **9** via diastereoisomeric salts with brucine, L-menthylamine, and enantiomerically pure α-phenylethylamine [18], can be considered as an oldest example of the chemically induced racemization of selenoxides. Later, racemization of selenoxides **143**–**144**, **147**–**148** and **150**–**152** was studied in detail by CD measurements [57,58] In a chloroform solution, the CD spectra of selenoxides **150**–**152** were unchanged even after five days. However, racemization was observed in methanol and addition of water to the methanol solution accelerated this racemization. These results indicate that the racemization in methanol was caused by a trace amount of water. The half-lives of racemization for selenoxide (*S*)-(-)-**152** corresponded well with those for selenoxide (*R*)-(+)-**148**. Moreover, racemization of (*S*)-(-)-**150-152**, was accelerated by the addition of *p*-toluenesulfonic acid or sodium hydroxide, especially in the case of (*S*)-(-)-**150**, whereas the racemization of selenoxide (*R*)-(+)-**148** was not accelerated by the addition of sodium hydroxide. This results can be explained if one assumes operation of the mechanism shown for selenoxide **1a** on Scheme 26. According to this mechanism the formation of hydroxyselenonium salt **181** is the rate determining step (RDS) in acidic media, whereas racemization in basic media is caused by the addition of hydroxide ion to a selenium atom in **1a** followed by protonation of the oxygen atom in **182** to give an achiral hydrate **10**.



Scheme 26. The mechanism of racemization of selenoxides by the formation of hydrates in the presence of water.

The half-lives of racemization for selenoxides **162**–**166** complexed with BINOL **171**, determined by polarymetric measurements at 19 °C, was found to be in the range of minutes (from 6.5 to 19.5) in methanol, while for the complex of the selenoxide 164 dissolved in chloroform was equal to 3.7 h [63].

5. Conclusions

In the present review, synthetic approaches to the preparation of non-racemic selenoxides and the problem of their optical stability are described. The purpose of this mini review is to provide available information on both topics in order to stimulate additional research in this field. The rationale for this research topic is the structural similarity between selenoxides and sulfoxides, which play a very important role as new synthetic reagents, biologically active compounds and new functional materials [71]. Therefore, it is reasonable to expect that optically active selenoxides should be just as useful as sulfoxides when they have sufficiently high optical stability. The literature data discussed in this review show how this goal can be achieved, and this is the main reason for publishing it in its current form. It is reasonable to expect that further research will allow the preparation of model compounds containing sterically demanding substituents, which in turn enable the preparation of optically active selenoxides with optical stability comparable to sulfoxides. Experimental works currently carried in our laboratories, focused on methodological and stereochemical aspects of flow processes [72] and mechanochemical procedures, allow us to have legitimate hope for reaching this goal.

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References

1. Twidell, T.T. Oxidation of Alcohols by Activated Dimethyl Sulofoxide and Related Reactions. *Synthesis* **1990**, *10*, 857–870. [CrossRef]
2. Młochowski, J.; Lisiak, R.; Wójtowicz-Młochowska, H. Organoselenium and Organotellurium Oxidation and Reduction. In *PATAI'S Chemistry of Functional Groups*; Wiley: Hoboken, NJ, USA, 2011; pp. 1083–1160.
3. Ponthieux, S.; Paulmier, C. Selenium-Stabilized Carboanions. *Organselenium Chem.* **2000**, *208*, 113–142.
4. Mikolajczyk, M.; Drabowicz, J.; Kielbasinski, P. *Chiral Sulfur Reagents: Applications in Asymmetric and Stereoselective Synthesis*; CRC Press: Boca Raton, FL, USA, 1998.
5. Nishibayashi, Y. Uemura Selenoxide Elimination and [2,3]Sigmatropic Rearrangement. *Organselenium Chem.* **2000**, *208*, 201–234.
6. Nomoto, A.; Ogawa, A. ChemInform Abstract: Preparative Uses of Organoselenium and Organotellurium Compounds. In *The Chemistry of Organic Selenium and Tellurium Compounds*; Rappoport, Z., Ed.; John Wiley and Sons: Hoboken, NJ, USA, 2012; pp. 623–688.
7. Ishii, A.; Matsubayashi, T.; Takahashi, T.; Nakayama, J. Preparation of a selenenic acid and isolation of selenoseleninates. *J. Org. Chem.* **1999**, *64*, 1084–1085. [CrossRef]
8. Reich, H.J.; Jasperse, C.P. Organoselenium chemistry. Preparation and reactions of 2,4,6-tri-tert-butylbenzeneselenenic acid. *J. Org. Chem.* **1988**, *53*, 2389–2390. [CrossRef]
9. Goto, K.; Nagahama, M.; Mizushima, T.; Shimada, K.; Kawashima, T.; Okazaki, R. The first direct oxidative conversion of a selenol to a stable selenenic acid: Experimental demonstration of three processes included in the catalytic cycle of glutathione peroxidase. *Org. Lett.* **2001**, *3*, 3569–3572. [CrossRef]
10. Penn, R.E.; Block, E.; Revelle, L.K. Methanesulfenic Acid. *J. Am. Chem. Soc.* **1978**, *100*, 3622–3624. [CrossRef]
11. Goto, K.; Holler, M.; Okazaki, R. Synthesis, Structure, and Reactions of a Sulfenic Acid Bearing a Novel Bowl-Type Substituent: The First Synthesis of a Stable Sulfenic Acid by Direct Oxidation of a Thiol. *J. Am. Chem. Soc.* **1997**, *119*, 1460–1461. [CrossRef]
12. Ishii, A.; Komiya, K.; Nakayama, J. Synthesis of a Stable Sulfenic Acid by Oxidation of a Sterically Hindered Thiol (Thiophenetriptycene-8-thiol)1 and Its Characterization. *J. Am.Chem. Soc.* **1996**, *118*, 12836–12837. [CrossRef]
13. Rheinboldt, H.; Giesbrecht, E. The Configuration of Organic Selenoxides: Mixed Crystals of Selenoxides with Sulfoxides. *J. Am. Chem. Soc.* **1946**, *68*, 2671–2673. [CrossRef]
14. Rheinboldt, H.; Giesbrecht, E. Mixed Crystals of Sulfoxides, Sulfones, Selenoxides and Selenones. *J. Am. Chem. Soc.* **1947**, *69*, 644–646. [CrossRef]
15. Gaythwaite, W.R.; Kenyon, J.; Phillips, H. CCXCVII.—The quadrivalency of selenium. Part I. 4-Carboxydiphenyl and p-carboxyphenyl methyl selenoxides. *J. Chem. Soc.* **1928**, 2280–2287. [CrossRef]
16. Harrison, A.; Kenyon, J.; Phillips, J. Phillips. *J. Chem. Soc.* **1926**, 2079–2786. [CrossRef]
17. Campbell, T.W.; Walker, H.G.; Coppinger, G.M. Some Aspects of the Organic Chemistry of Selenium. *Chem. Rev.* **1952**, *50*, 279–349. [CrossRef]
18. Ōki, M.; Iwamura, H. The configuration of the selenoxides. *Tetrahedron Lett.* **1966**, *7*, 2917–2920. [CrossRef]
19. Burlant, W.J.; Gould, E.S. Metalation of Dibenzoselenophene. *J. Am. Chem. Soc.* **1954**, *76*, 5775–5776. [CrossRef]
20. Cinquini, M.; Colonna, S.; Landini, D. Diastereomeric diselenoxides. *Bol. Sci. Fac. Chim. Ind. Bol.* **1969**, *27*, 207–209.
21. Musher, J.I. The Chemistry of Hypervalent Molecules. *Angew. Chem. Int. Ed.* **1969**, *8*, 54–68. [CrossRef]
22. Akiba, K. *Chemistry of Hypervalent Compounds*; Akiba, K., Ed.; Wiley-VCH: New York, NY, USA, 1999.

23. Drabowicz, J.; Halaba, G. ChemInform Abstract: Stereochemical Aspect of the Chemistry of Hypervalent Chalcogen Compounds. *Cheminform* **2010**, *33*, 1–32. [CrossRef]
24. Drabowicz, J.; Kiełbasiński, P.; Zając, A.; Pokora-Sobczak, P. Hypervalent Selenium Derivatives. In *Organoselenium Chemistry between Synthesis and Biochemistry*; Santi, C., Ed.; Bentham Science Publishers: Sharjah, United Arab Emirates, 2014; pp. 120–145.
25. Komatsu, N.; Uemura, S. Recent Advances in Asymmetric Synthesis Using Organochalcogen Compounds. *J. Synth. Org. Chem.* **1995**, *53*, 268–274. [CrossRef]
26. Kamigata, N.; Shimizu, T. Synthesis and Stereochemistry of Optically Active Selenoxides. *J. Synth. Org. Chem.* **1990**, *48*, 229–239. [CrossRef]
27. Kobayashi, M.; Shimizu, T. Synthesis of the Optically Active Diaryl Selenoxides. *Cheminform* **1987**, *7*, 1437–1441.
28. Kamigata, N. Synthesis and Stereochemistry of Chiral Selenoxides and Telluroxides. *Phosphorus Sulfur Silicon Relat. Elem.* **2001**, *171*, 207–229. [CrossRef]
29. Uemura, S. Application of Asymmetric Oxidation and Imidation of Organic Selenides to Organic Transformations. *Phosphorus Sulfur Silicon Relat. Elem.* **2001**, *171*, 13–30. [CrossRef]
30. Drabowicz, J.; Kiełbasiński, P.; Zajac, A. Hypervalent Derivatives of Selenium and Tellurium. In *PATAI'S Chemistry of Functional Groups*; Wiley: Hoboken, NJ, USA, 2011; pp. 891–948.
31. Jones, D.N.; Mundy, D.; Whitehouse, R.D. Steroidal selenoxides diastereoisomeric at selenium; syn-elimination, absolute configuration, and optical rotatory dispersion characteristics. *J. Chem. Soc. D* **1970**, *2*, 86–87. [CrossRef]
32. Ayrey, G.; Barnard, D.; Woodbridge, D.T. 401. The oxidation of organoselenium compounds by ozone. *J. Chem. Soc.* **1962**, 2089–2099. [CrossRef]
33. Cram, D.J. *Steric Effects in Organic Chemistry*; Newman, M., Ed.; Wiley: New York, NY, USA, 1956.
34. Salmond, W.; Barta, M.; Cain, A.; Sobala, M. Alternative modes of decomposition of allylic selenoxides diastereoisomeric at selenium. Preparation of Δ5,7- and 5β-hydroxy-Δ6-steroiods. *Tetrahedron Lett.* **1977**, *18*, 1683–1686. [CrossRef]
35. Back, T.G.; Ibrahim, N.; McPhee, D.J. Studies of enamidic. DELTA.5-4-azasteroidal selenoxides: Preparation, Pummerer reactions, configurational stability, and conversion to carbinol amides. *J. Org. Chem.* **1982**, *47*, 3283–3289. [CrossRef]
36. Kurose, N.; Takahashi, T.; Koizumi, T. First synthesis of optically pure selenuranes and stereoselective alkaline hydrolysis. Their application to asymmetric [2,3]sigmatropic rearrangement of allylic selenoxides. *Tetrahedron* **1997**, *53*, 12115–12129. [CrossRef]
37. Takahashi, T.; Kurose, N.; Kawanami, S.; Arai, Y.; Koizumi, T.; Shiro, M. Optically Pure Haloselenuranes. First Synthesis and Nucleophilic Substitutions. *J. Org. Chem.* **1994**, *59*, 3262–3264. [CrossRef]
38. Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Baldwin, J.E., Ed.; Pergamon Press: Oxford, UK, 1986.
39. Kamigata, N.; Shimizu, T. *Reviews on Heteroatom Chemistry*; Oae, S., Ed.; MYU: Tokyo, Japan, 1991.
40. Tomoda, S.; Usuki, Y.; Fujita, K.; Iwaoka, M. *Reviews on Heteroatom Chemistry*; Oae, S., Ed.; MYU: Tokyo, Japan, 1991.
41. Reich, H.J. *Organoselenium Chemistry*; Liotta, D., Ed.; John Wiley & Sons: New York, NY, USA, 1987.
42. Reich, H.J.; Yelm, K.E. Asymmetric induction in the oxidation of [2.2]paracyclophane-substituted selenides. Application of chirality transfer in the selenoxide [2,3]sigmatropic rearrangement. *J. Org. Chem.* **1991**, *56*, 5672–5679. [CrossRef]
43. Kawakami, R.; Singh, J.D.; Fukuzawa, S.-I.; Uemura, S. Synthesis of [R,S;R,S]- and [S,R;S,R]-Bis[2 -[1-(dimethylamino)ethyl]ferrocenyl] Diselenides and Their Application to Asymmetric Selenoxide Elimination and [2,3]Sigmatropic Rearrangement. *J. Org. Chem.* **1995**, *60*, 4114–4120.
44. Fujita, K.-I.; Kanakubo, M.; Ushijima, H.; Oishi, A.; Ikeda, Y.; Taguchi, Y. Asymmetric [2,3]Sigmatropic Rearrangement of Optically Active Allylic Selenides. *Synlett* **1998**, *1998*, 987–988. [CrossRef]
45. Shimizu, T.; Kikuchi, K.; Ishikawa, Y.; Ikemoto, I.; Kobayashi, M.; Kamigata, N. Synthesis and absolute configuration of optically active selenoxides. X-Ray molecular structure of (–) se -4-menthyloxycarbonylphenyl 2,4,6-tri-isopropylphenyl selenoxide. *J. Chem. Soc. Perkin Trans.* **1989**, *1*, 597–602. [CrossRef]

46. Shimizu, T.; Seki, N.; Taka, H.; Kamigata, N. Stereoselective Transformation of Optically Active Selenoxide into Optically Active Selenonium Imide. *J. Org. Chem.* **1996**, *61*, 6013–6014. [CrossRef]
47. Davis, F.A.; Stringer, O.D.; McCauley, J.P. Asymmetric oxidation of achiral selenides to optically active selenoxides. *Tetrahedron* **1985**, *41*, 4747–4757. [CrossRef]
48. Davis, F.A.; ThimmaReddy, R.; Weismiller, M.C. (-)-.alpha.,.alpha.-Dichlorocamphorsulfonyloxaziridine: A superior reagent for the asymmetric oxidation of sulfides to sulfoxides. *J. Am. Chem. Soc.* **1989**, *111*, 5964–5965. [CrossRef]
49. Davis, F.A.; Reddy, R.T. Asymmetric oxidation of simple selenides to selenoxides in high enantiopurity. Stereochemical aspects of the allyl selenoxide/allyl selenenate rearrangement. *J. Org. Chem.* **1992**, *57*, 2599–2606. [CrossRef]
50. Davis, F.A.; Towson, J.C.; Weismiller, M.C.; Lal, S.; Carroll, P.J. Chemistry of oxaziridines. 11. (Camphorylsulfonyl)oxaziridine: Synthesis and properties. *J. Am. Chem. Soc.* **1988**, *110*, 8477–8482. [CrossRef]
51. Drabowicz, J.; Nakanishi, W.; Haiashi, S. Unpublished preliminary results, manuscript in preparation. 2020.
52. Shimizu, T.; Kobayashi, M.; Kamigata, N. Asymmetric oxidation of alkyl aryl selenides under Sharpless oxidation conditions. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2099–2101. [CrossRef]
53. Tiecco, M.; Tingoli, M.; Testaferri, L.; Bartoli, D. Asymmetric oxidation of prochiral selenides to optically active selenoxides. *Tetrahedron Lett.* **1987**, *28*, 3849–3852. [CrossRef]
54. Komatsu, N.; Matsunaga, S.; Sugita, T.; Uemura, S. Asymmetric selenoxide elimination leading to chiral alkyl and aryl cyclohexylidenemethyl ketones. *J. Am. Chem. Soc.* **1993**, *115*, 5847–5848. [CrossRef]
55. Komatsu, N.; Murakami, T.; Kawakami, R.; Sugita, T.; Uemura, S. Asymmetric selenoxide elimination leading to chiral allenic sulfones. *J. Org. Chem.* **1993**, *58*, 3697–3702. [CrossRef]
56. Kobayashi, M.; Ohkubo, H.; Shimizu, T. Synthesis of selenoxides by oxidation of selenides with t-butyl hypochlorite, and its application for synthesis of optically active selenoxide. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 503–506. [CrossRef]
57. Shimizu, T.; Kobayashi, M. Optically active selenoxides: Chromatographic separation and absolute configuration. *J. Org. Chem.* **1987**, *52*, 3399–3403. [CrossRef]
58. Shimizu, T.; Kobayashi, M. Optical resolution of asymmetric selenoxides by high-performance liquid chromatography using optically active column. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2654–2656. [CrossRef]
59. Shimizu, T.; Enomoto, M.; Taka, H.; Kamigata, N. Optical Resolution and Configurational Stability of Selenoxides Stabilized by Intramolecular Coordination. *J. Org. Chem.* **1999**, *64*, 8242–8247. [CrossRef]
60. Soma, T.; Shimizu, T.; Hirabayashi, K.; Kamigata, N. Stabilizing effect of intramolecular lewis base toward racemization of optically active selenoxides. *Heteroat. Chem.* **2007**, *18*, 301–311. [CrossRef]
61. Taka, H.; Matsumoto, A.; Shimizu, T.; Kamigata, N. Thermodynamically stabilized chiral chalcogen oxides: Optical resolution and stereochemistry. *Heteroat. Chem.* **2001**, *12*, 227–237. [CrossRef]
62. Taka, H.; Matsumoto, A.; Shimizu, T.; Kamigata, N. Optical Resolution of Thermodynamically Stabilized Selenoxides by 8-(Dimethylamino)-1-naphthyl Group. *Chem. Lett.* **2000**, *29*, 726–727. [CrossRef]
63. Toda, F.; Mori, K. Optical resolution of selenoxides by complexation with optically active 2,2?-dihydroxy-1,1?-binaphthol or 1,6-di(o-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol. *J. Chem. Soc., Chem. Commun.* **1986**, 1357–1359. [CrossRef]
64. Davis, F.A.; Billmers, J.M.; Stringer, O.D. First synthesis of simple optically active selenoxides. *Tetrahedron Lett.* **1983**, *24*, 3191–3194. [CrossRef]
65. Nakashima, Y.; Shimizu, T.; Hirabayashi, K.; Iwasaki, F.; Yamasaki, M.; Kamigata, N. Optically Active Seleninate Esters: Isolation, Absolute Configuration, Racemization Mechanism, and Transformation into Chiral Selenoxide. *J. Org. Chem.* **2005**, *70*, 5020–5027. [CrossRef] [PubMed]
66. Rayner, D.R.; Gordon, A.J.; Mislow, K. Thermal racemization of diaryl, alkyl aryl, and dialkyl sulfoxides by pyramidal inversion. *J. Am. Chem. Soc.* **1968**, *90*, 4854–4860. [CrossRef]
67. Andersen, K.K. *Sulphones and Sulphoxides (1988)*; Patai, S., Rappoport, Z., Stirling, C., Eds.; John Wiley & Sons: Chichester, UK, 1988.
68. Mikołajczyk, M.; Drabowicz, J.; Mikoajczyk, M. Chiral Organosulfur Compounds. In *Topics in Stereochemistry*; Wiley: Hoboken, NJ, USA, 2007; Volume 13, pp. 333–468.
69. Oae, S.; Yokoyama, M.; Kise, M. Oxygen Exchange and Racemization Reactions of Sulfoxides in Acetic and Chloroacetic Acid. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 1221–1224. [CrossRef]

70. Shimizu, T.; Yoshida, M.; Kobayashi, M. An estimation of the configurational stability of diaryl selenoxides by means of 77Se NMR spectroscopy. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 1555–1557. [CrossRef]
71. Han, J.; Soloshonok, V.A.; Klika, K.D.; Drabowicz, J.; Wzorek, A. SDE-Phoric functional groups. Chiral Sulfoxides: Asymmetric preparation and problems with the accurate determination of the stereochemical outcome. *Chem. Soc. Rev.* **2018**, *47*, 1307–1350. [CrossRef]
72. Jasiak, A.; Mielniczak, G.; Owsianik, K.; Koprowski, M.; Krasowska, D.; Drabowicz, J. Solvent-Free Michaelis−Arbuzov Rearrangement under Flow Conditions. *J. Org. Chem.* **2019**, *84*, 2619–2625. [CrossRef]