Mechanistic Course of the Asymmetric Methoxyselenenylation Reaction

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Abstract: In alkoxyselenenylation reactions of alkenes intermediate seleniranium ions **1** are formed. In competition experiments it was shown that the formation of these intermediates is reversible. The seleniranium ions of type $\mathbf{20}^+$ formed by addition of chiral selenium electrophiles to alkenes are the decisive intermediates in the asymmetric methoxyselenenylation reaction. Their stabilities are strongly dependent on the strength of the selenium−heteroatom interaction. This was shown experimentally, because an independent method has been used for the synthesis of different diastereomeric seleniranium ions. Furthermore, calculations have been carried out to determine the relative stabilities of the diastereomeric seleniranium ions $\mathbf{20}^+$. The results obtained from the calculations support the experimental findings.

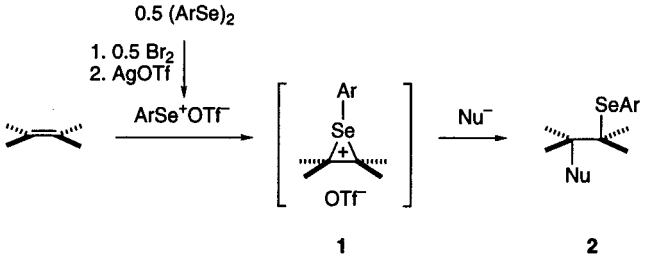
Introduction

The stereoselective functionalization of nonactivated C=C double bonds is still a great challenge in asymmetric synthesis. Beside stoichiometric reactions, only few catalytic variants have been developed up to now.[1] Stoichiometric addition reactions with chiral reagents deserve further investigations. In recent times organoselenium compounds gained an increasing popularity in organic chemistry because of their mild and selective reactions.[2] Electrophilic selenium reagents are often utilized for the functionalization of double bonds.

The addition of selenium electrophiles to alkenes leads to seleniranium ions **1** as heterocyclic three-membered ring intermediates. These seleniranium ions are then attacked by a nucleophile from the anti side leading to addition products **2** (Scheme 1). The selenides **2** are versatile building blocks for subsequent reactions. A homolytic cleavage of the carbon−selenium bond generates radicals and is the entry into radical chemistry. Oxidation of the selenide to the selenoxide and β-hydride elimination can again introduce double bonds into the molecule, which are then functionalized in the allylic position. Furthermore, deprotonation in α-position to the selenium can be used for carbanionic chemistry.

Recently we[3] and other research groups[4−7] developed chiral selenium compounds which are versatile reagents in asymmetric addition reactions to alkenes. A wide variety of different alkenes can be employed. Therefore, asymmetric β-alkoxyselenenylation reactions are possible as well as intramolecular selenolactonizations, selenoetherifications, or aminoselenenylations leading to addition or cyclization products with high stereoselectivities. We already have established the versatility of such addition products as potent building blocks in enantioselective synthesis of various natural products.[8]

Scheme 1



(1) (a) For asymmetric dihydroxylation, see: Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483−2547. (b) For asymmetric epoxidation see: Jacobsen, E. N. In *Comprehensive Organometallic Chemistry II*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Hegedus, L. S., Eds.; Pergamon Press: New York, 1995; Vol. 12, Chapter 11.1.

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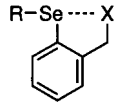
Scheme 2



3

All these selenium compounds of type **3** (Scheme 2) are carrying a heteroatom X (oxygen or nitrogen) in a 1,3-distance to the selenium. An intramolecular interaction between the heteroatom and the selenium has been proven in different ways.

Crystal structures of 2-formylbenzeneselenenyl bromide[9] and 2-nitrobenzeneselenenyl thiocyanate[10] show that the molecules have a planar T-shaped structure. This interaction was also shown to be present in the gaseous phase by electron diffraction of 2-nitrobenzeneselenenyl bromide.[11] In all cases the selenium−oxygen distances are larger than the sums of the covalent radii (1.83 Å) but clearly smaller than the sum of the van der Waals radii (3.40 Å).[12] By temperature dependent ^{1}H NMR analysis combined with ab initio calculations of 2-selenobenzylamine halides, the selenium−nitrogen bond dissociation energy was estimated to be higher than 18.8 kcal/mol.[13] The interaction causes also an upfield shift in ^{77}Se NMR signals.[3,13] Calculations of orbital occupancies by natural bond orbital (NBO) analysis of selenium electrophiles are indicating an interaction between a lone pair of the heteroatom and the σ^*-orbital of the selenium atom.[13] This interaction induces a conformational rigidity into the molecule. In asymmetric β-alkoxyselenenylation this interaction is assumed to play a determinant role in forming the preferred diastereomer in the addition products **2**.

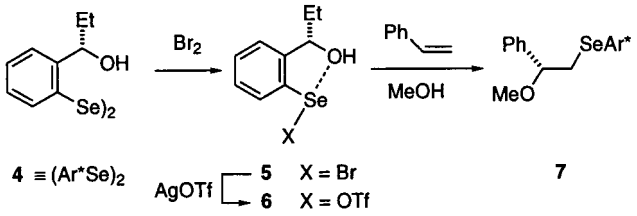
Although the chemistry with chiral selenium compounds has led to very promising results, no efforts for the understanding of the chirality transfer have been reported up to now. Therefore we focused our interest on the mechanism of the chirality transfer and report herein our results based on experimental and on theoretical investigations.

Results

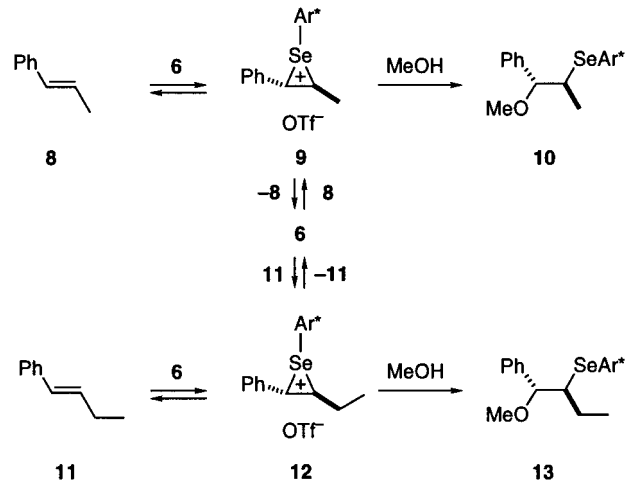
We have investigated the β-methoxyselenenylation reaction of styrene with a series of chiral selenium electrophiles and found that **6** is a very efficient reagent, yielding the addition product **7** in diastereomeric ratios up to 96:4.[3b] The selenium electrophile **6** is obtained from the corresponding diselenide **4** after treatment with bromine and subsequent exchange of the bromide in **5** with silver triflate (Scheme 3).[14]

Employing the chiral selenium electrophile **6** with the (*S*)-configuration, we observed the (*R*)-configuration at the newly generated stereocenter of the main diastereomer **7**,[3a,b] which was proven by independent synthesis.[15] This corresponds to a favored *re* attack of styrene. Because the formation of the

Scheme 3



Scheme 4



seleniranium ion is the determining step of stereochemistry, we conclude that the reaction of the alkene with the chiral selenium electrophile must lead preferentially to one seleniranium ion.

In analyzing the process of chirality transfer, we first investigated the formation of the seleniranium ion. We found its formation from the alkene and the selenium electrophile to be reversible under the reaction conditions. After the formation of the seleniranium ion **9** from the selenium electrophile **6** and (*E*)-1-phenylpropene (**8**) at −100 °C in diethyl ether, a second alkene, (*E*)-1-phenylbutene (**11**), was added.[16] After the reaction was quenched with methanol, both addition products **10** and **13** were isolated. This is due to a decomplexation−complexation mechanism via the selenium cation **6**. Adding the alkenes in a different order leads again to the formation of both addition products. The equilibrium between **9** and **12** did not affect the stereoselectivity of the reaction, and the products **10** and **13** were isolated with 85% de and 80% de, respectively (Scheme 4).

On the basis of these results, we conclude that the diastereomeric seleniranium ions resulting from a *re* attack and from a *si* attack to styrene are formed in not equivalent amounts and must therefore have a different stability.

For the examination of their stability, we decided to synthesize the seleniranium ions resulting from a *re* attack and from a *si* attack to styrene independently by a reaction developed by Toshimitsu et al.[17] By protonation of β-hydroxy selenides and a subsequent intramolecular S_N2 displacement by selenium, the generation of seleniranium ions is possible. Using chiral β-hydroxy selenides in this reaction should allow the independent generation of the desired seleniranium ions.

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(13) Iwaoka, M.; Tomoda, S. *J. Am. Chem. Soc.* **1996**, *118*, 8077−8084.

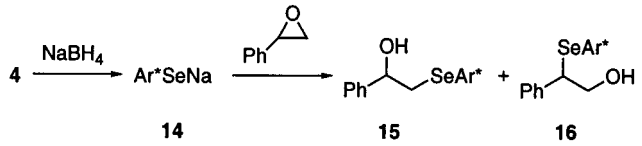
(14) The formation of the two electrophilic species **5** and **6** was observed by ^{77}Se NMR spectroscopy.[3b]

(15) The diastereomeric ratio was determined by NMR or by GC analysis (β-permethylated, 25 m, 90 kPa, 40 °C) of (1-methoxyethyl)benzene after cleavage of the selenium moiety. For the radical cleavage, see: Clive, D. L. J.; Chittattu, G. J.; Farina, V.; Kiel, W. A.; Menchen, S. M.; Russell, C. G.; Singh, A.; Wong, C. K., Curtis, N. J. *J. Am. Chem. Soc.* **1980**, *102*, 4438−4447.

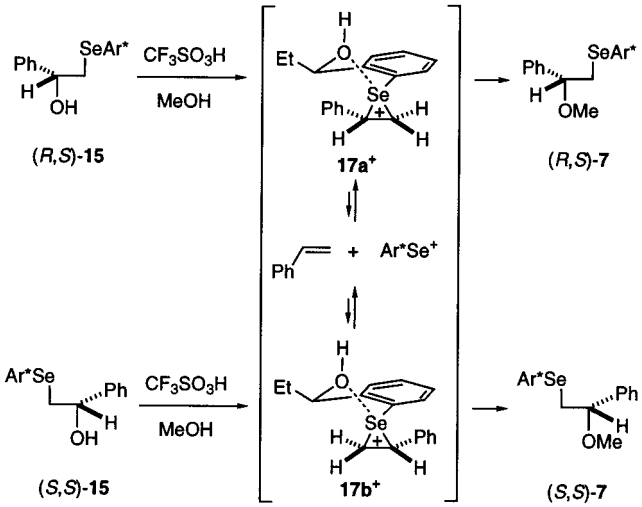
(16) After addition of each alkene, the reaction mixture was stirred at −100 °C for 90 min.

(17) (a) Toshimitsu, A.; Hayashi, G.; Terao, K.; Uemura, S. *J. Chem. Soc., Perkin Trans. 1* **1986**, 343−347. (b) Toshimitsu, A.; Ito, M.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1989**, 530−531. (c) Toshimitsu, A.; Nakano, K.; Mukai, T.; Tamao, K. *J. Am. Chem. Soc.* **1996**, *118*, 2756−2757. (d) Toshimitsu, A.; Terada, M.; Tamao, K. *Chem Lett.* **1997**, 733−734.

Scheme 5



Scheme 6



The chiral β-hydroxy selenides **15** are obtained by reaction of the selenolate **14** with styrene oxide having either the (*R*)-configuration or (*S*)-configuration. After separation from the regioisomers **16**, the precursor molecules (*R*,*S*)-**15** and (*S*,*S*)-**15** for the selective generation of the seleniranium ions are obtained (Scheme 5).

The seleniranium ions are generated by treatment of the β-hydroxy selenides **15** with trifluoromethanesulfonic acid at −25 °C.[18] Subsequent reaction with methanol yields the β-methoxy selenides **7**. They are identical to the methoxyselenenylated products of styrene using the chiral selenium electrophile **6** (see Scheme 3) and are analyzed in the same way.

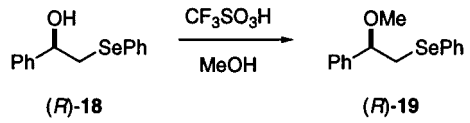
Employing compound (*R*,*S*)-**15** in this reaction, the seleniranium ion **17a**$^+$ is formed selectively (Scheme 6). Seleniranium ion **17a**$^+$ corresponds to the *re* attack of **6** to styrene which was assumed to be the most stable seleniranium ion and therefore formed in excess during the methoxyselenenylation reaction. Indeed, the reaction of **17a**$^+$ with methanol leads to optically pure β-methoxy selenide (*R*,*S*)-**7** without any loss of chiral information at the benzylic position.

The same reaction was then performed using (*S*,*S*)-**15**. The seleniranium ion **17b**$^+$ is generated first and can be regarded as the product of a *si* attack to styrene with selenium electrophile **6**. This seleniranium ion is less stable than **17a**$^+$ which is confirmed by the results. Subsequent reaction with methanol lead to a 3:1 mixture of (*S*,*S*)-**7**:(*R*,*S*)-**7**. The addition product (*S*,*S*)-**7** with (*S*)-configuration at the benzylic position is obtained as the major diastereomer, but a decreased optical purity at the benzylic position is observed.

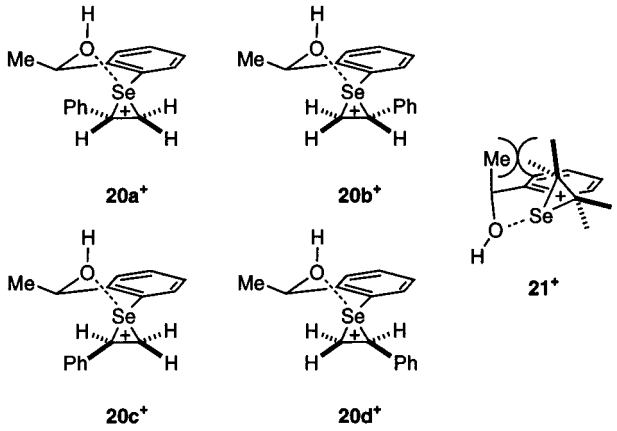
This result is rationalized by partial conversion of the less stable seleniranium ion **17b**$^+$ into the more stable seleniranium ion **17a**$^+$ before reaction with methanol by a decomplexation−complexation mechanism as outlined in Scheme 6. Because this reaction is performed in methanol, the additon reaction is competing and the major product is still the diastereomer (*S*,*S*)-**7**.

(18) The formation of seleniranium ions via S_N2-displacement does not occur at temperatures below −25 °C.

Scheme 7



Scheme 8



The formation of styrene according to this mechanism could not be demonstrated. Perfoming the reaction starting with (*S*,*S*)-**15** in the presence of (*E*)-1-phenylpropene (**8**) leads, however, to the formation of substantial amounts of **10** beside the products (*R*,*S*)-**7** and (*S*,*S*)-**7** in the reaction mixture. This is an indirect proof of the decomplexation−complexation mechanism mentioned above.

Additionally a reaction with a 1:1 mixture of (*R*,*S*)-**15** and (*S*,*S*)-**15** was performed. The products (*R*,*S*)-**7** and (*S*,*S*)-**7** are formed in a diastereomeric ratio of about 1.7:1, confirming the results obtained by the independent experiments with either (*R*,*S*)-**15** or (*S*,*S*)-**15**.

These experimental observations clearly show the different stabilities of the seleniranium ions involved. They are due to the rigidity of the system caused by the selenium−oxygen interaction. A last proof for this interaction being the reason for the energetic difference between the diastereomeric seleniranium ions **17a**$^+$ and **17b**$^+$ is the reaction of the chiral alcohol (*R*)-**18**[19] *without* a side chain in the ortho position to selenium. Under the same reaction conditions the interconversion of the seleniranium ions is again in competition to their reaction with methanol. No stabilization of the initially formed seleniranium ion is possible, and the product (*R*)-**19**[20] is isolated with 63% ee (Scheme 7).

Calculations

In addition to the experiments ab initio calculations were performed to investigate the structural and electronic properties of the seleniranium ions which occur as intermediates of the methoxyselenenylation reaction described above. The four diastereoisomeric seleniranium ions **20a**$^+$−**20d**$^+$ (Scheme 8) can be formed by the addition of styrene to a chiral selenium electrophile of type **6**. For the calculations, compounds with a methyl group instead of an ethyl group at the asymmetric center were used. With these compounds, similar results are obtained in the methoxyselenenylation reaction.[3b] The distorted trigonal

(19) Spectroscopic data: Krief, A.; Dumont, W.; Clarembeau, M.; Bernard, G.; Badaoui, E. *Tetrahedron* **1989**, *45*, 2005−2022. Preparation: Sakakibara, M.; Katsumata, K.; Watanabe, Y.; Toru, T.; Ueno, Y. *Synthesis* **1992**, 377−379.

(20) Tiecco, M.; Chianelli, D.; Tingoli, M.; Testaferri, L.; Bartoli, D. *Tetrahedron* **1986**, *42*, 4897−4906.

Scheme 9

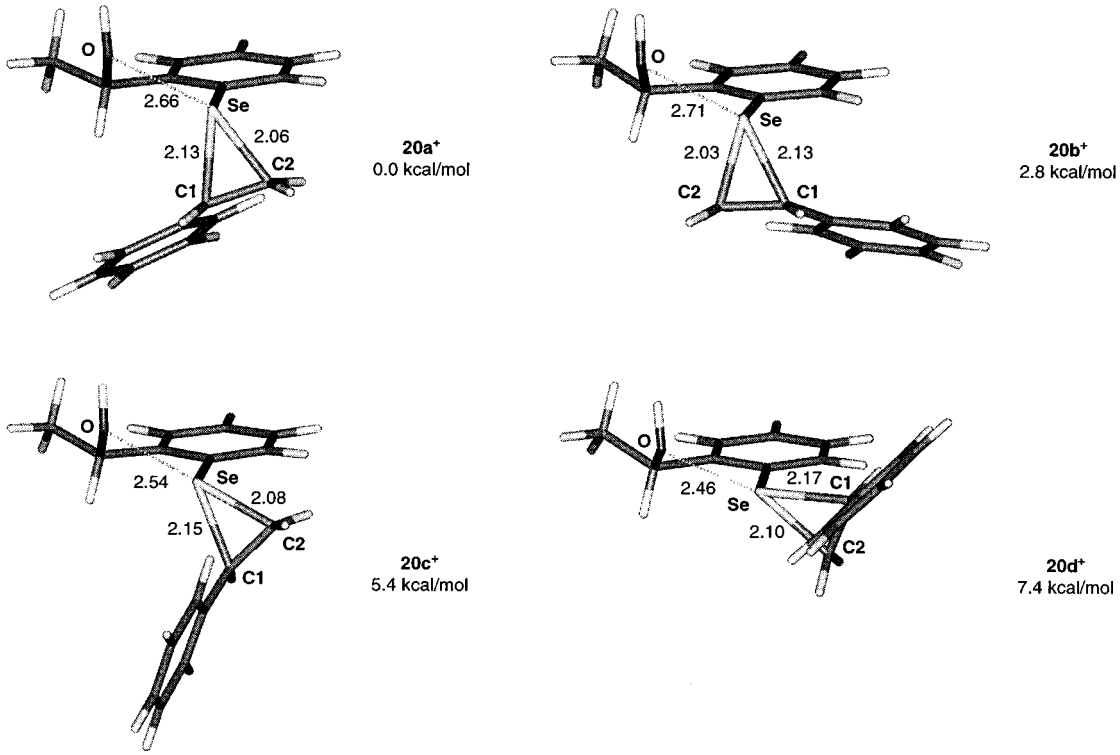


Table 1. Geometry Parameters for the MP2/3-21G*-Optimized Seleniranium Ions **20a**$^+$−**20d**$^+$[a]

	20a$^+$	**20b**$^+$	**20c**$^+$	**20d**$^+$
Se−C1	2.13	2.13	2.15	2.17
Se−C2	2.06	2.03	2.08	2.10
Se−O	2.66	2.71	2.54	2.46
Se−C_{aryl}	1.94	1.93	1.96	1.97
∠O−Se−alkene[b]	130.6	120.0	156.8	175.2
∠C_{aryl}−Se−alkene[b]	96.5	98.8	98.7	98.5
atomic charges				
Se	+0.883	+0.904	+0.839	+0.813
C1	−0.269	−0.306	−0.248	−0.255
C2	−0.550	−0.523	−0.533	−0.505

[a] Distances are in angstroms; angles are in degrees. The atomic charges were determined by NPA using the MP2/6-31G*//MP2/3-21G* density. [b] Se−alkene stands for the bisector of the angle C1−Se−C2.

bipyramidal structure resulting from an selenium−oxygeninteraction can alternatively also be obtained by the conformation shown in **21**$^+$. Due to the strong steric interaction between the methyl group and the alkene, we focused our investigations on the conformations of the diastereoisomers **20a**$^+$−**20d**$^+$.

The optimized geometries of the seleniranium ions **20a**$^+$−**20d**$^+$ are shown in Scheme 9. In all structures the alkene is bonded slightly asymmetrically to the selenium atom reflecting the asymmetry of the highest occupied molecular orbital (HOMO) of styrene which is involved in the selenium−alkene bonding. The bond lengths vary from 2.03 to 2.10 Å for the shorter Se−C2 bond and from 2.13 to 2.17 Å for the Se−C1 bond (Table 1). These bonds are longer than the selenium−aryl bond (Se−C_{aryl}), which varies between 1.93 and 1.97 Å.

There is a remarkable correlation between the Se−O distance and the O−Se−alkene angle (see Table 1). In the structures **20c**$^+$ and **20d**$^+$ the alkene and the oxygen are arranged in an almost T-shaped manner with an O−Se−alkene angle close to 180°. This facilitates the interaction of the oxygen lone pair with the antibonding molecular orbital of the selenium−alkene bonding. Therefore stronger selenium−oxygen interactions and weaker selenium−alkene bondings are found for **20c**$^+$ and **20d**$^+$ than for **20a**$^+$ and **20b**$^+$. That is expressed in the respective bond lengths shown in Scheme 9 and Table 1.

The natural population analysis (NPA) predicts a higher charge of about 0.25 for atom C1 than for atom C2 in all diastereomers (Table 1). This confirms the preference of carbon atom C1 over carbon atom C2 for a nucleophilic attack. This fact was also observed in all our methoxyselenenylation experiments. For the structures **20c**$^+$ and **20d**$^+$, the charge of the selenium is less positive than for **20a**$^+$ and **20b**$^+$. This is in agreement with the stronger selenium−oxygen interaction in the diastereoisomers **20c**$^+$ and **20d**$^+$.

Due to the reversibility of the seleniranium formation from the selenium electrophile and the alkene, the stereoselectivity should be influenced by the relative stabilities of the seleniranium ions **20a**$^+$−**20d**$^+$. The lowest energy is found for the diastereoisomer **20a**$^+$, which corresponds to the *re* attack of the selenium electrophile to styrene leading to the methoxyselenenylated product with the (*R*)-configuration at the new stereocenter. Diastereoisomer **20b**$^+$ is yielding the methoxyselenenylated product with opposite configuration and is found to be more than 2.5 kcal/mol (see Scheme 9) higher in energy. For the diastereoisomers **20c**$^+$ and **20d**$^+$ which cannot gain from π-stacking, energy differences of 5.4 and 7.4 kcal/mol are calculated.

Conclusions

The asymmetric methoxyselenenylation reaction has been investigated in detail. It was shown that the formation of the seleniranium ion intermediates is reversible. For the first time the diastereomeric seleniranium ions, which are the intermediates in the addition of chiral selenium electrophiles to alkenes, have been prepared independently. Therefore it was possible to detail by experiment the different stabilities of the seleniranium ions involved in the asymmetric methoxyselenenylation. Further-

more, the structures of four different seleniranium ions have been calculated. The results of these calculations are supporting the stereochemical outcome of the asymmetric methoxyselenenylation reactions.

Computational Methods

To include electron correlation contributions, especially π-stacking effects, all calculations were performed on the MP2 level of theory. For the geometry optimizations, the basis set 3-21G* was used which was shown to be a "minimal" basis set for pseudo-high-valent selenium species.[13] On the basis of these geometries, MP2 single point calculations with the basis set 6-31G* were performed to determine the relative energies of the four diastereoisomers.

Additionally, the atomic charges were predicted by NPA using the MP2/6-31G*//MP2/3-21G* density. All calculations were carried out with the program Gaussian 94[21] on DEC Alpha.

Experimental Section

General. All reactions were carried out under argon with anhydrous solvents. ^{1}H NMR spectra (300 MHz) and ^{13}C NMR spectra (75 MHz) were recorded with a Varian Gemini 300 spectrometer, chemical shifts are reported in ppm relative to tetramethylsilane as internal standard, and coupling constants are reported in hertz. Multiplicities in the ^{13}C NMR spectra were determined by the APT pulse sequence. IR spectra were measured with a Perkin-Elmer 781 spectrophotometer. MS spectra were recorded with a Finnigan MAT 312 apparatus. Optical rotations were measured with a Perkin-Elmer 141 polarimeter.

General Procedure for the Transformation of β-Hydroxy Selenides to β-Methoxy Selenides. Trifluoromethanesulfonic acid (0.088 mL, 1 mmol) was dissolved in MeOH (5 mL). After the mixture was cooled to − 25 °C, a solution of the β-hydroxy selenide (0.1 mmol) in MeOH (1 mL) was added slowly and stirring was continued for 12 h. After addition of saturated aqueous $NaHCO_3$ solution (3 mL), the MeOH was evaporated and the solution extracted with *tert*-butyl methyl ether (3 × 5 mL). After the solvent was dried ($MgSO_4$) and evaporated, the residue was purified by preparative TLC (pentane/*tert*-butyl methyl ether, 5:1), yielding the β-methoxy selenides as colorless oils.

(*S*)-1-{2-[(*R*)-(2-Methoxy-2-phenylethyl)seleno]phenyl}-propanol (*R,S*)-7. See refs 3a,b.

(*S*)-1-{2-[(*S*)-(2-Methoxy-2-phenylethyl)seleno]phenyl}-propanol (*S,S*)-7. Colorless oil. ^{1}H NMR ($CDCl_3$): δ 0.97 (t, J = 7.4 Hz, 3H), 1.60 (s, br, 1H), 1.78 (quint, J = 7.1 Hz, 2H), 3.08 (dd, J = 4.7 Hz, J = 12.3 Hz, 1H), 3.20 (s, 3H), 3.31 (dd, J = 8.6 Hz, J = 12.3 Hz, 1H), 4.33 (dd, J = 4.9 Hz, J = 8.4 Hz, 1H), 5.07 (t, 6.5 Hz, 1H), 7.09−7.52 (m, 9H). ^{13}C NMR ($CDCl_3$): δ 10.36 (q), 31.94 (t), 35.93 (t), 56.91 (q), 74.34 (d), 82.97 (d), 126.12 (d), 126.64 (d, 2C), 127.51 (d), 127.92 (d), 128.12 (d), 128.54 (d, 2C), 129.7 (s), 133.53 (d, 2C), 140.8 (s), 146.0 (s).

The methoxyselenenylations of the alkenes **8** and **11** yielding the products **10** and **13**, repectively, were carried out as decribed in ref 3b.

(*S*)-1-{2-[(1*R*,2*S*)-(2-Methoxy-1-methyl-2-phenylethyl)seleno]-phenyl}propanol (10). Colorless oil. $[\alpha]^{25}_D$ = −25.8 (c = 0.30, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 0.97 (t, J = 7.1 Hz, 3H), 1.31 (d, J = 7.1 Hz, 3H), 1.78 (quint, J = 7.5 Hz, 2H), 2.52 (d, J = 3.6 Hz, 1H), 3.29 (s, 3H), 3.48 (qd, J = 7.1 Hz, J = 7.1 Hz, 1H), 4.42 (d, J = 4.4 Hz, 1H), 5.08 (m, 1H), 7.12−7.56 (m, 7H), 7.47 (d, J = 7.7 Hz, 1H), 7.55 (d, J = 7.7 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 10.4 (q), 16.3 (q), 31.5 (t), 46.4 (d), 57.4 (q), 74.4 (d), 86.1 (d), 126.5 (d), 126.9 (d, 2C), 127.6 (d), 127.7 (d), 127.9 (d), 128.2 (d, 2C), 128.7 (s), 135.2 (d), 139.3 (s), 147.0 (s). MS (EI): *m*/*z* 364 (10) [M$^+$], 199 (25), 149 (20), 121 (100), 105 (6), 91 (20), 77 (20). HMRS: calcd for $C_{19}H_{24}O_2Se$ [M$^+$] 364.0942, found 364.0953.

(*S*)-1-{2-[(1*R*,2*S*)-(2-Methoxy-1-ethyl-2-phenylethyl)seleno]phenyl}-propanol (13). Colorless oil. $[\alpha]^{25}_D$ = −39.9 (c = 1.96, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 0.95 (t, J = 7.5 Hz, 3H), 0.96 (t, J = 7.3 Hz, 3H), 1.71 (quint, J = 7.4 Hz, 2H), 1.74 (quint, J = 7.4 Hz, 2H), 2.47 (s, br, 1H), 3.26 (s, 3H), 3.37 (td, J = 7.3 Hz, J = 5.0 Hz, 1H), 4.43 (d, J = 5.0 Hz, 1H), 5.05 (t, J = 6.4 Hz, 1H), 7.10−7.36 (m, 7H), 7.43 (dd, J = 7.8 Hz, J = 1.5 Hz, 1H), 7.50 (dd, J = 7.7 Hz, J = 1.3 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 10.4 (q), 12.5 (q), 23.4 (t), 30.8 (t), 55.8 (q), 57.4 (d), 74.7 (d), 85.5 (d), 126.4 (d), 127.1 (d, 2C), 127.6 (d, 2C), 127.7 (d), 128.1 (d, 2C), 129.5 (s), 135.1 (d), 139.5 (s), 146.7 (s). MS (EI): *m*/*z* 378 (15) [M$^+$], 199 (48), 163 (15), 121 (100), 105 (5), 91 (24), 77 (12). HMRS: calcd for $C_{20}H_{26}O_2Se$ [M$^+$] 378.1098, found 378.1120.

Reaction of Styrene Oxide with Ar*SeNa 14. Diselenide (*S,S*)-**4** (431 mg, 1 mmol) was dissolved in ethanol (8 mL), $NaBH_4$ (99 mg, 2.6 mmol) was added, and the mixture was stirred for 30 min until the yellow color disappeared. (*R*)-Styrene oxide (255 mg, 2.1 mmol) was added dropwise, and stirring was continued for 5 h. After the addition of aqueous 1 M NaOH (2 mL), ethanol was evaporated. The solution was extracted with *tert*-butyl methyl ether (3 × 10 mL), the combined organic phases were dried ($MgSO_4$), and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (pentane/*tert*-butyl methyl ether, 2:1). Yield: 378 mg of (*S,R*)-**15** (56%) and 270 mg of (*S,S*)-**16** (40%).

(*S*)-1-{2-[(*R*)-(2-Hydroxy-2-phenylethyl)seleno]phenyl}-propanol ((*S,R*)-15). Colorless oil. $[\alpha]^{25}_D$ = −47.3 (c = 0.99, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 0.95 (t, J = 7.4 Hz, 3H), 1.77 (quint, J = 6.9 Hz, 2H), 2.60 (s, br, 1H), 3.05 (s, br, 1H), 3.13 (dd, J = 9.0 Hz, J = 12.6 Hz, 1H), 3.26 (dd, J = 3.9 Hz, J = 12.6 Hz, 1H), 4.78 (dd, J = 8.6 Hz, J = 3.4 Hz, 1H), 5.07 (t, J = 6.2 Hz, 1H), 7.17 (td, J = 7.5 Hz, J = 1.6 Hz, 1H), 7.19−7.32 (m, 6H), 7.43 (dd, J = 7.7 Hz, J = 1.5 Hz, 1H), 7.54 (dd, J = 7.7 Hz, J = 1.4 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 10.4 (q), 31.1 (t), 38.7 (t), 72.8 (d), 74.8 (d), 125.7 (d, 2C), 126.6 (d), 127.91 (d), 127.94 (d), 128.1 (d), 128.5 (d, 2C), 128.8 (s), 134.2 (d), 142.7 (s), 146.1 (s). MS(EI): *m*/*z* 336 (15) [M$^+$], 230 (66), 214 (36), 201 (53), 183 (100), 107 (74), 91 (52), 77 (70). IR (NaCl, $CHCl_3$): υ 3598, 3377, 3064, 3005, 2968, 2935, 1455, 1398, 1136, 1051, 1016, 972. HMRS: calcd for $C_{17}H_{20}O_2Se$ [M$^+$] 336.0629, found 336.0635.

(*S*)-1-{2-[(*S*)-(2-Hydroxy-1-phenylethyl)seleno]phenyl}-propanol ((*S,S*)-16). Colorless oil. $[\alpha]^{25}_D$ = +150.8 (c = 1.42, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 0.86 (t, J = 7.4 Hz, 3H), 1.54−1.75 (m, 2H), 2.20 (s, br, 1H), 2.62 (s, br, 1H), 3.90−4.05 (m, 1H), 4.32 (t, J = 7.1 Hz, 1H), 4.89 (t, J = 6.6 Hz, 1H), 7.10−7.32 (m, 7H), 7.40 (dd, J = 7.8 Hz, J = 1.6 Hz, 1H), 7.57 (dd, J = 7.7 Hz, J = 1.2 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 10.3 (q), 31.1 (t), 51.7 (d), 65.0 (t), 74.6 (d), 126.6 (d), 127.5 (d), 127.7 (s), 127.8 (d), 127.9 (d, 2C), 128.5 (d, 2C), 128.8 (d), 136.7 (d), 139.6 (s), 147.6 (s). MS (EI): *m*/*z* 336 (15) [M$^+$], 214 (36), 198 (77), 183 (43), 121 (100), 103 (79), 91 (56), 77 (49). IR (NaCl, $CHCl_3$): υ = 3596, 3377, 3064, 3006, 2970, 2935, 1454, 1380, 1136, 1051, 1016, 970. HMRS: calcd for $C_{17}H_{20}O_2Se$ [M$^+$] 336.0629, found 336.0619.

Similar reaction of (*S,S*)-**4** (430 mg, 1 mmol) with (*S*)-styrene oxide led to (*S,S*)-**15** (260 mg, 39%) and (*S,R*)-**16** (330 mg, 49%).

(*S*)-1-({[(*S*)-(2-Hydroxy-2-phenyl)ethyl]seleno}phenyl)propanol ((*S,S*)-15). Colorless oil. $[\alpha]^{25}_D$ = −11.8 (c = 1.06, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 0.97 (t, J = 7.4 Hz, 3H), 1.79 (quint, J = 6.9 Hz, 2H), 2.45 (s, br, 1H), 2.97 (s, br, 1H), 3.14 (dd, J = 9.2 Hz, J = 12.7 Hz, 1H), 3.26 (dd, J = 3.8 Hz, J = 12.7 Hz, 1H), 4.69 (dd, J = 9.2 Hz, J = 3.4 Hz, 1H), 5.12 (t, J = 6.3 Hz, 1H), 7.15−7.32 (m, 7H), 7.49 (dd, J = 7.7 Hz, J = 1.6 Hz, 1H), 7.57 (dd, J = 7.7 Hz, J = 1.3 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 10.3 (q), 30.9 (t), 38.5 (t), 72.1 (d), 74.3 (d), 125.8 (d, 2C), 126.4 (d), 127.90 (d), 127.95 (d), 128.1 (d), 128.5 (d, 2C), 128.8 (s), 133.9 (d), 142.6 (s), 146.4 (s).

(*S*)-1-({[*R*-(2-Hydroxy-1-phenyl)ethyl]seleno}phenyl)propanol ((*S,R*)-16). Colorless oil. $[\alpha]^{25}_D$ = −64.6 (c = 2.28, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 0.88 (t, J = 7.4 Hz, 3H), 1.50−1.72 (m, 2H), 1.95 (s, br, 1H), 2.40 (s, br, 1H), 3.95 (d, J = 6.9 Hz, 1H), 4.35 (t, J = 7.0 Hz,

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1H), 4.92 (t, $J = 6.5$ Hz, 1H), 7.10−7.32 (m, 6H), 7.36 (td, $J = 7.4$ Hz, $J = 1.2$ Hz, 1H), 7.47 (dd, $J = 7.8$ Hz, $J = 1.6$ Hz, 1H), 7.60 (dd, $J = 7.7$ Hz, $J = 1.4$ Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 10.3 (q), 31.2 (t), 51.4 (d), 64.5 (t), 74.4 (d), 126.5 (d), 127.6 (d), 127.8 (s), 127.9 (d), 127.95 (d, 2C), 128.7 (d, 2C), 129.1 (d), 136.9 (d), 139.2 (s), 148.1 (s).

***(R)*-1-Phenyl-1-methoxy-(2-phenylseleno)ethane (19).** $[\alpha]^{25}_D = -19.4$ ($c = 0.455$, $CHCl_3$). For further spectroscopic data, see ref 20.

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