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Efficient asymmetric selenomethoxylation and selenohydroxylation of alkenes with a new sulfur containing chiral diselenide

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Abstract

The synthesis of a new chiral non-racemic sulfur containing diselenide is described. The electrophilic selenium reagent, produced from this diselenide by treatment with bromine and silver triflate, has been used to effect the selenomethoxylation and the selenohydroxylation of alkenes. These addition reactions occurred with good chemical yield and with high diastereoselectivities. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: asymmetric synthesis; chiral diselenides; selenomethoxylation; selenohydroxylation.

Chiral non-racemic selenium compounds have been recently employed to effect successful asymmetric syntheses. Several research groups have been deeply involved in the preparation of different types of optically active diselenides[1,2] since these are commonly used as starting materials to produce organoselenium reagents. Chiral electrophilic selenium reagents, which can be simply prepared in situ from diselenides, were allowed to react with alkenes in the presence of external or internal nucleophiles and afforded the corresponding addition or cyclization products, respectively, with moderate to high asymmetric induction.[2,3]

A common characteristic of all the various chiral diselenides described in the literature is the close proximity of an oxygen or a nitrogen atom to the selenium atom. This is exemplified in Scheme 1 by the diselenide **1**, which is one of the products prepared and investigated by Wirth.[1] It has been reported on several occasions that selenium can interact with nearby heteroatoms. In some cases, the existence of this intramolecular interaction has been demonstrated by theoretical calculations as well as by crystal structure determinations and by NMR spectroscopy.[4,5] This interaction, which is depicted by structure **2** in Scheme 1, and which is suggested to be due to an orbital interaction between the heteroatom lone pair and the low-lying antibonding orbital of the SeY (n-σ^*_{SeY}) will force the chiral center to come close

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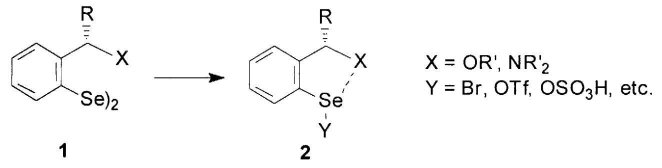
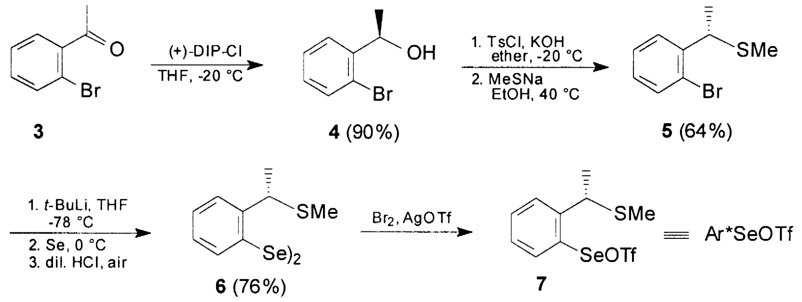
to the reaction center during the addition of the selenenylating agent to the alkene and this will result in asymmetric induction. Moreover, the same interaction should also dictate the structure of the active selenium reagent, thus playing a fundamental role in the formation of the preferred diastereomer of the addition products.



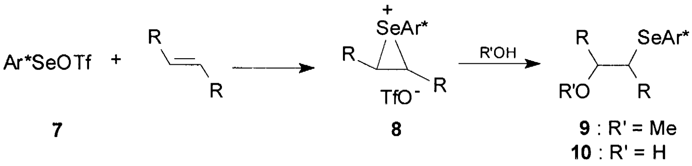
Scheme 1.

In all the diselenides described so far the heteroatom was either oxygen or nitrogen. We now report the synthesis of the first sulfur containing chiral diselenide and the asymmetric addition reactions of the corresponding electrophilic reagent to several kinds of alkenes. The structure of this diselenide **6** (Scheme 2) is very similar to those of the corresponding oxygen or nitrogen containing diselenides **1**. Diselenide **6** was synthesized from the optically active alcohol **4** (Scheme 2) which was obtained by chiral reduction of 2′-bromoacetophenone **3** with (+)-*B*-chlorodiisopinocampheylborane.[6] The alcohol (98% ee) was transformed into the tosylate and then treated with sodium methanethiolate to afford the sulfide **5**. Metal–halogen exchange reaction with *n*-BuLi gave the lithiated intermediate which was treated with selenium metal. Successive oxidative work-up gave the di-2-[(1*S*)-1-(methylthio)ethyl]phenyl diselenide **6**, which was purified by column chromatography. Compound **6** was enantiomerically pure when it was analyzed by proton NMR spectra in $CDCl_3$ in the presence of (*S*)-(+)-1-(9-antryl)-2,2,2-trifluorethanol. Compound **6** was transformed in situ into the selenenyl triflate **7**, by treatment with bromine and AgOTf.



Scheme 2.

The efficiency of the electrophilic reagent **7** in stereoselective syntheses was tested by determining the diastereomeric ratios obtained in the asymmetric selenomethoxylation and selenohydroxylation of alkenes (Scheme 3) which afforded compounds **9** and **10**, respectively, as a mixture of the two possible diastereomers. These reactions occur through the intermediate formation of the seleniranium ions **8** and, in the case of (*E*)-alkenes, it is the facial selectivity during the initial formation of these intermediates that determines the diastereoselectivity of the addition process.[7]

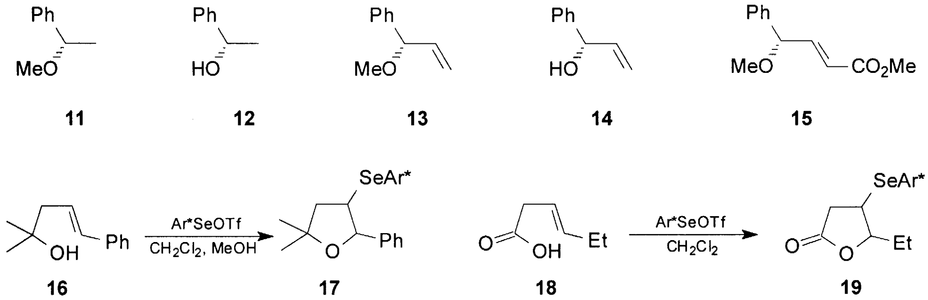


Scheme 3.

In the case of the selenomethoxylation reactions, **7** was prepared by adding bromine and then AgOTf to the solution of **6** in methylene chloride at −78°C. An excess of the alkene dissolved in methanol was then added and the mixture was stirred at the same temperature for the time indicated in Table 1. The reactions of selenohydroxylation were instead carried out by preparing **7**, at −78°C, in THF. An excess of the alkene and 1 ml of water were added and the mixture was left to reach room temperature. The progress of the reactions was monitored by TLC and/or proton NMR spectroscopy. Reaction times are indicated in Table 1. Reaction mixtures were worked-up in the usual way and compounds **9** and **10** were purified by column chromatography. In no case could the two diastereomers be separated. The diastereomeric ratios were determined by proton NMR spectroscopy and, in the case of compound **10**, also by GC–MS. Chemical yields and diastereomeric ratios (d.r.) are reported in Table 1.

The results of these experiments indicate that good diastereoselectivity was obtained in every case with the only exception being that of the selenomethoxylation of cyclohexene. The diastereomeric ratios obtained in the selenomethoxylation of alkenes are considerably better than those obtained starting from the diselenides of type **1** and are more or less similar to those observed with the most efficient diselenides which have been described so far in the literature.[1,2] Of particular relevance are the good results obtained in the asymmetric selenohydroxylation reactions. The only previous example of these reactions was reported by us[8] using the camphorselenenyl sulfate, produced by oxidation of the diselenide, described by Back et al.,[9] with ammonium persulfate. The diastereomeric ratios obtained with the electrophilic reagent **7** and reported in Table 1 are considerably higher than those observed with the camphor derivative. It is noteworthy that in these selenohydroxylation reactions a good facial selectivity is obtained by working at room temperature. In fact, in all the other types of addition of chiral electrophilic selenium reagents to alkenes, efficient asymmetric inductions are obtained only by working at very low temperatures.

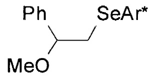
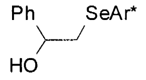
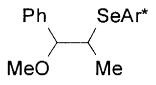
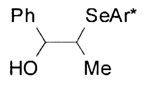
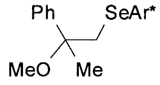
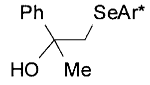
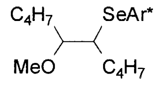
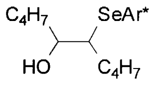
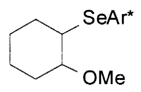
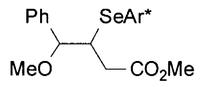
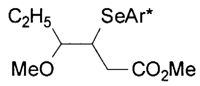
The absolute configurations of the major isomers were established in some cases and were effected by deselenenylation and comparison of the enantiomers thus obtained with commercial products or with compounds described in the literature (Scheme 4). Reductive deselenenylation of **9a** and **10a** with triphenyltin hydride and AIBN in refluxing benzene afforded the (−)-(*S*)-**11**[10] (90%) and the (−)-(*S*)-**12**[8] (78%), respectively. Oxidative elimination of **9b** and **10b** with hydrogen peroxide in methanol afforded (+)-(*S*)-**13**[11] (85%) and (−)-(*S*)-**14**[12] (75%), respectively. Finally, the reaction of **9f** with ammonium persulfate in methanol[8] gave (−)-(*S*)-**15**[13] (68%). In every case the enantiomeric excess of the deselenenylation product was in good agreement with the diastereomeric ratios reported in Table 1.



Scheme 4.

Selenocyclization reactions can also be promoted by the sulfur containing electrophilic reagent **7**. Thus, as indicated in Scheme 4, compound **16** gave the selenoetherification product **17** in 88% yield and with a diastereomeric ratio of 93:7 and compound **18** gave the selenolactonization product **19** in 75% yield and with a diastereomeric ratio of 89:11. In both cases **7** was prepared at −78°C and the reaction mixture was then left to reach room temperature and stirred for 6 h.

Table 1
Reactions of alkenes with the diselenide **6** in CH_2Cl_2 and MEOH at −78°C (selenomethoxylation) and in THF and H_2O at room temperature (selenohydroxylation)

	Starting Alkenes	Selenomethoxylation Products, 9[a]	Time h	d. r.[b] (yield)[c]	Selenohydroxylation Products, 10[a]	Time h	d. r.[b] (yield)[c]
a	Styrene	 **9a**[d]	9	96:4 (80%)	 **10a**	6	95:5 (75%)
b	β-Methylstyrene	 **9b**	6	96:4 (78%)	 **10b**	6	96:4 (72%)
c	α-Methylstyrene	 **9c**[e]	6	90:10 (80%)	 **10c**	4	90:10 (80%)
d	(*E*)-5-Decene	 **9d**	9	90:10 (76%)	 **10d**	6	88:12 (79%)
e	Cyclohexene	 **9e**	7	82:18 (75%)			
f	Methyl styrylacetate	 **9f**	17	90:10 (87%)			
g	Methyl 3-hexenoate	 **9g**	24	90:10 (73%)			

a) The two diastereomers could not be separated. In no case the presence of regioisomers could be detected.
b) The diastereomeric ratios were determined from the proton NMR spectra of the reaction mixtures after purification by column chromatography.
c) Based on the amounts of the diselenide **6** employed.
d) The reaction carried out at -20°C and at 20 °C gave d.r. 90:10 (90% yield) and 80:20 (80% yield), respectively.
e) The reaction carried out at -20°C gave d.r. 87:13 (77% yield).

The results reported in this paper greatly support the suggestion that the intramolecular non-bonded interaction between selenium and a close heteroatom is a very important factor which is responsible for the efficiency of the various chiral electrophilic selenium reagents in asymmetric syntheses. The present data also suggest that the interaction of selenium with sulfur is probably more important than those with oxygen or with nitrogen. Moreover, as already shown by Wirth et al. in the case of oxygen containing diselenides,[14] a more efficient transfer of chirality can probably be obtained by introducing an appropriate substituent in the 3 position of the diselenide **6**.

Acknowledgements

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