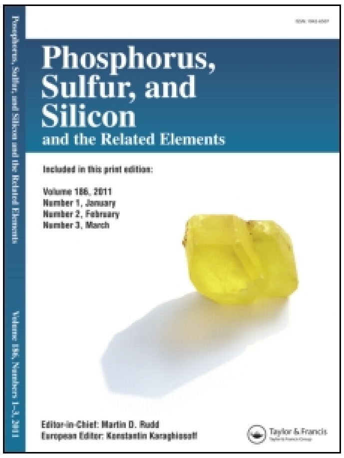

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ASYMMETRIC SYNTHESIS WITH CHIRAL DISELENIDES

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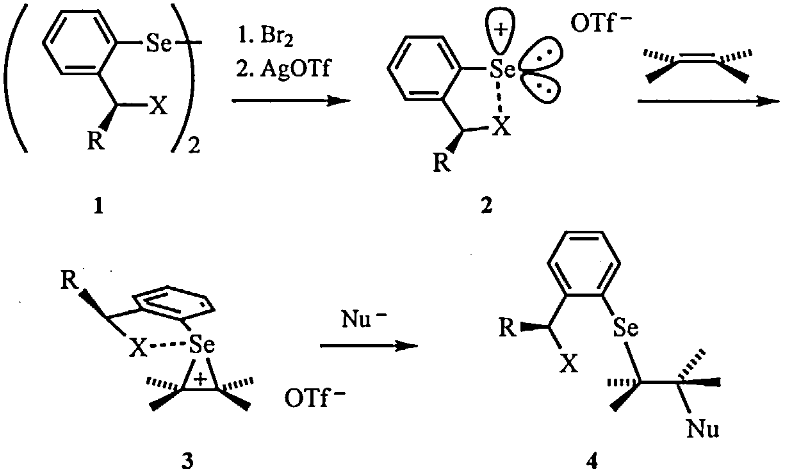
Optically active diselenides are versatile precursors for chiral selenium electrophiles. The mechanism of the methoxyselenenylation of alkenes is discussed as well as the development of a catalytic selenenylation - elimination sequence.

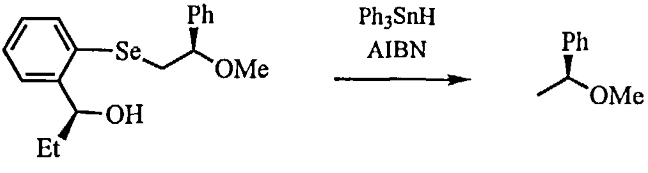
Keywords: asymmetric synthesis, chiral diselenides, total synthesis

The oxidative functionalization of not activated C = C-double bonds in a stereoselective way is still a topic of great interest in asymmetric synthesis. Organoselenium chemistry has provided useful methods for various transformations, but selenium based methodologies have not been used in asymmetric synthesis until recently.

We focused on the use of chiral selenium electrophiles **2** which can easily be generated from the corresponding diselenides of type **1**. We prepared a variety of chiral selenium electrophiles and investigated the influence of the chiral moiety on the stereoselectivity of addition reactions to alkenes.[1] Most of the chiral selenium reagents investigated by us and by others[2] do have a heteroatom which is connected to a chiral carbon atom, in an 1,3-distance to the selenium atom. This heteroatom X can either be nitrogen or oxygen. We could show that the interaction between the heteroatom X and the selenium atom as depicted in **2** is responsible for the stereoselectivity observed in the addition reaction to alkenes. This is predominantely a non-bonding n–σ*-type orbital interaction as it has been proven for other pseudo-high-valent species in solution as well as in solid state.[3]



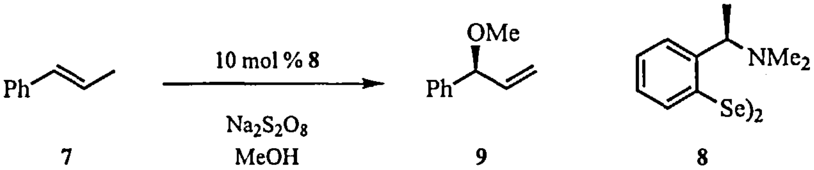
The determining step of the stereochemistry is the formation of the seleniranium ion **3**, because the subsequent attack of the nucleophile always occurs from the *anti*-side. Recent investigations have shown, that the formation of the seleniranium ion **3** from an alkene and the selenium electrophile **2** can be reversible. For the optimization studies which were carried out we used styrene as a monosubstituted alkene in the addition reactions. This means that in principle four different stereoisomeric seleniraniom ions **3** can be formed. Because of the different position of the phenyl moiety they should be different in energy. We observed a high selectivity resulting form a *re*-attack of styrene with a selenium electrophile **2** possessing (*S*)-configuration at the chiral center. Using methanol as nucleophile the addition product **5** was formed with a diastereomeric excess of 92 %. The diastereomeric excess was determined by NMR spectroscopy and by the analysis of the cleavage product **6**. But these experimental data cannot be explained only by steric interactions. Calculations are now being performed to address electronic aspects of these intermediates as well.



5 **6**

We have already established the versatility of this reaction in using the addition products of type **4** as building blocks in various natural product syntheses.[4]

Being also interested in catalytic applications of this methodology, a sequence of methoxyselenenylation and subsequent *β*-hydride elimination was developed. The electrophilic selenium species are generated by reaction with sodium peroxodisulfate.[5] After methoxyselenenylation of (*E*)-1-phenyl-2-propene **7** this oxidant allows the oxidation of the selenide to the instable selenoxide which, after elimination, yields the chiral allylic ether **9**. Diselenide **8** bearing a nitrogen atom in the chiral side chain were found to be superior to the oxygen based diselenides leading to an enantiomeric excess of up to 40 % in the product **9**. Optimization studies of this reaction are in progress.



Acknowledgements

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