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Stereoselective Oxidation Reactions

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Abstract. The development of chiral electrophilic reagents for stereoselective oxidative functionalizations is described together with their application in synthesis.

Thomas Wirth, born 1964 in Leverkusen (Germany), studied chemistry at the University of Bonn and stayed there to carry out his diploma work under the guidance of *S. Blechert*. He then moved along with his supervisor to the Technical University of Berlin, where he received his Ph.D. in 1992. For postdoctoral studies, he joined the group of *K. Fuji* at Kyoto University in Japan as a JSPS fellow. In 1994, he started his independent research at the University of Basel where he obtained his habilitation in 1999. Further details of research interests are to be found at http://www.chemie. unibas.ch/OC/Wirth/wirth.html.

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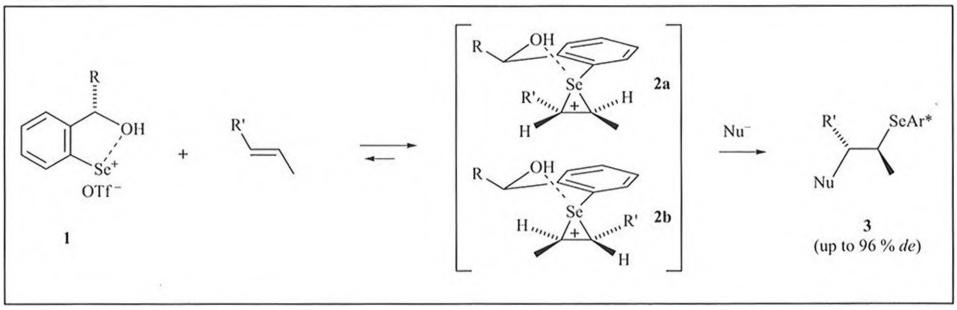
In many areas of synthetic organic chemistry, reactions are needed which produce, in good yields, stereochemically uniform compounds. In this respect, many remarkable efforts have led to a variety of efficient and elegant stereochemical transformations of prochiral substrates. However, there are certain classes of compounds which cannot be efficiently used in these reactions. For example, only a few useful methods are known for the stereoselective functionalization of unactivated or only weakly activated C–H bonds or C=C bonds. In our research projects, we are investigating and developing stoichiometric and catalytic reactions of such compounds leading to products with new stereogenic centers.

Various methods have been developed for the electrophilic attack on unactivated C=C bonds. We are investigating chiral electrophilic reagents for stereoselective addition reactions to double bonds. With both *chiral selenium electrophiles* and *chiral hypervalent iodine compounds*, highly efficient stereoselective reactions are possible.

Chiral Selenium Electrophiles

Chiral selenium electrophiles [1] of type **1** can be easily generated from the corresponding diselenides. Addition to double bonds generates products **3** which are versatile precursors for subsequent

Scheme 1



reactions because of their selenium moiety (*Scheme 1*). We designed and synthesized chiral diselenides by short synthetic sequences. The formation of the intermediate and energetically different diastereoisomeric seleniranium ions **2a** and **2b** is reversible as shown by detailed mechanistic investigations. Calculations of these intermediates and ^{77}Se-NMR spectroscopy support the experimental results.

Lactones or ethers such as **4**, with tetrasubstituted carbon atoms, can be synthesized with high selectivities. The potential of these cyclizations for the generation of new stereogenic centers was demonstrated by the synthesis of the alkaloid salsolidin **5** (*Scheme 2*).

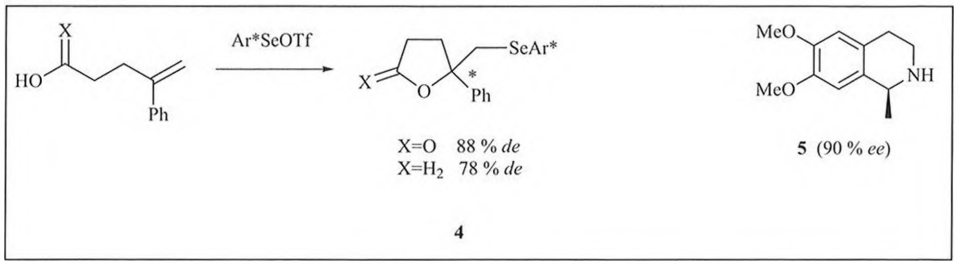
The formation of radicals by homolytic cleaveage of Se–C-bonds can be used for subsequent cyclizations. In a short sequence, we synthesized the furofuran moiety of lignans such as **6** and used this strategy for the enantioselective total synthesis of the natural products samin and membrin (*Scheme 3*).

Addition reactions with subsequent β-elimination can be performed as one-pot procedures, and the chiral selenium compound can be liberated again in the elimination step. Therefore, reactions with substoichiometric amounts of selenium compounds are possible and yield the chiral allylic ether **8** in up to 75% *ee*. Chiral diselenides **7** containing nitrogen as a coordinating heteroatom were also found to be interesting procatalysts. The addition of organozinc reagents to aldehydes can be catalyzed and leads efficiently to alcohols **9** in up to 98% *ee* (*Scheme 4*).

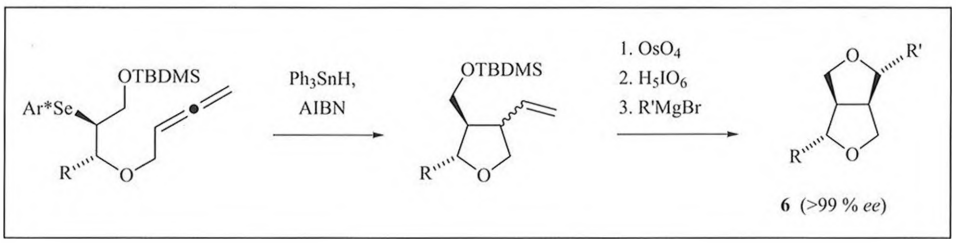
Hypervalent Iodine Compounds

Although well-established, hypervalent iodine compounds have recently become prominent reagents because they are highly efficient oxidizing agents which are compatible with highly functionalized substrates. Apart from their well-known reactions, these compounds can also be used as electrophilic reagents for other oxidative functionalizations. For stereoselective reactions, we developed chiral compounds **10** and reported the first stereoselective reactions using chiral hypervalent iodine compounds [2]. X-ray structures as well as *ab initio* calculations have led to optimized reagents. Stereoselective α-tosylations of ketones and ditosylations of alkenes can be performed with these reagents.

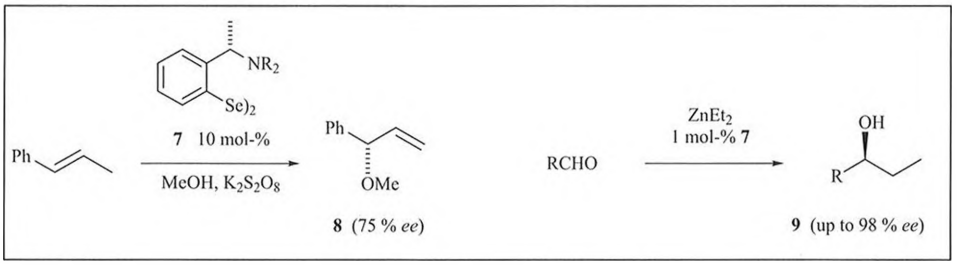
Scheme 2

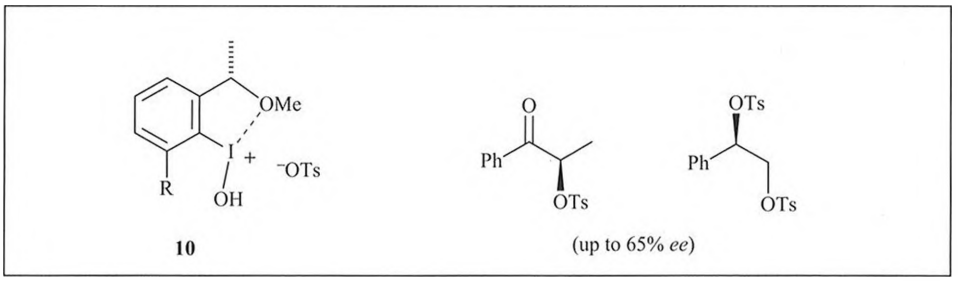


Scheme 3



Scheme 4





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