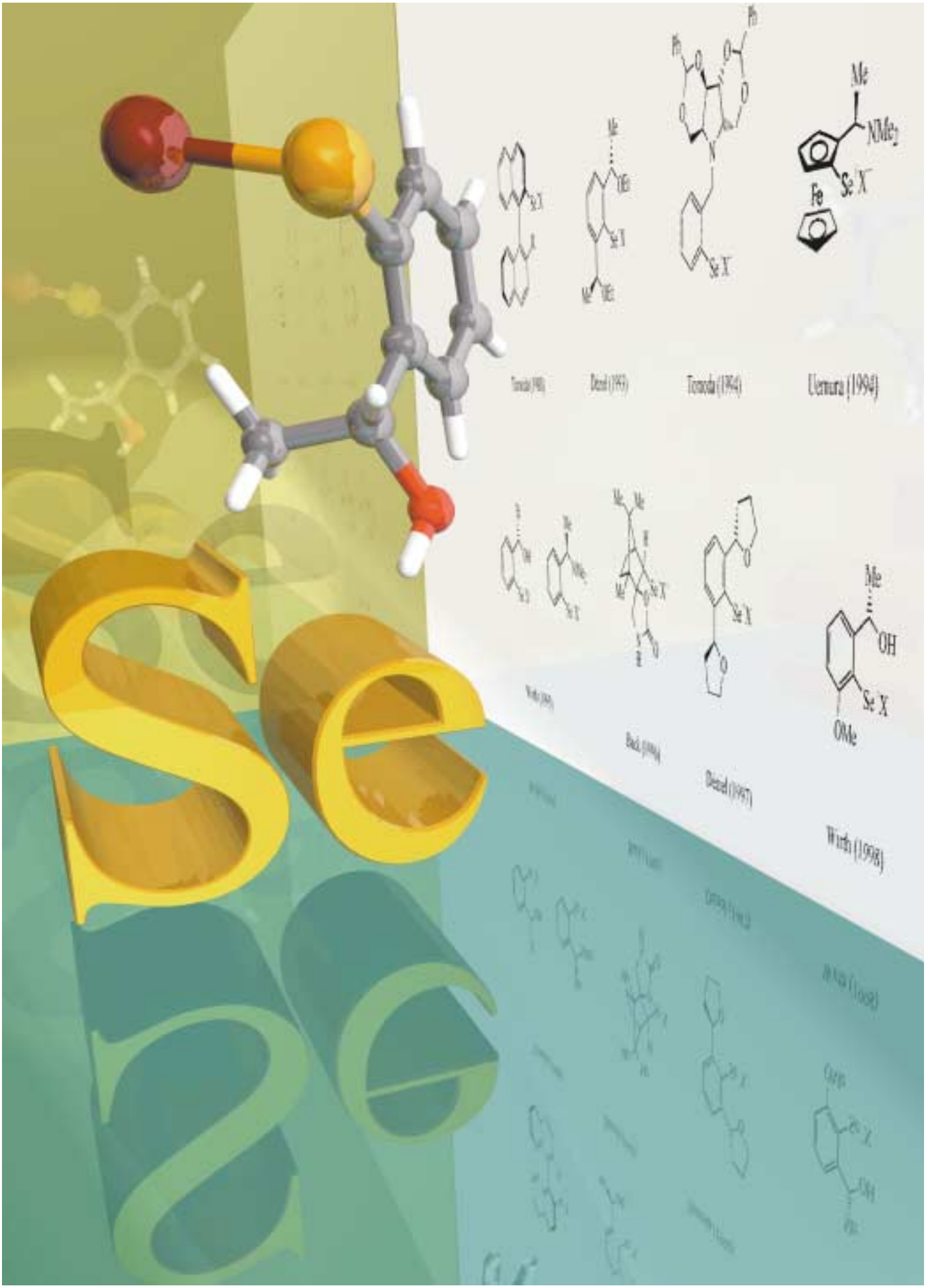

Selenium—a multitalented element: Selenium reagents offer numerous possibilities in organic synthesis—particularly in stereoselective reactions.

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Organoselenium Chemistry in Stereoselective Reactions

Thomas Wirth*

Dedicated to Professor Bernd Giese on the occasion of his 60th birthday

Selenium-based methods have developed rapidly over the past few years and organoselenium chemistry has become a very useful tool in the hands of synthetic chemists. The different reactivity of selenium-containing compounds in contrast to the sulfur analogues has led to versatile and new synthetic methods in organic chemistry. Various functionalities can be selectively introduced into complex molecules under very mild reaction conditions. In this review, the principles of organoselenium chemistry are traced back to their origins and are highlighted with respect to stereoselective synthesis. The unique properties of selenium allow the development of new and highly selective transformations, which can be employed subsequently in new routes for the synthesis of versatile chiral building blocks and for natural product synthesis.

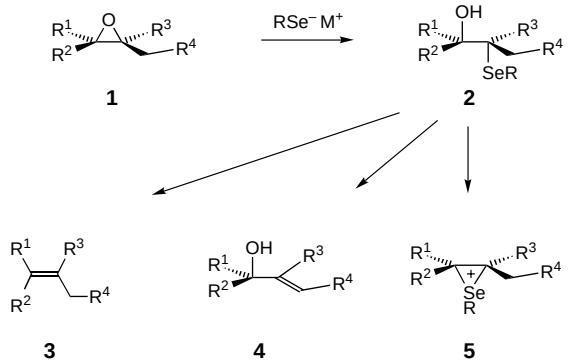
Keywords: organoselenium chemistry · selenium · stereoselective synthesis · synthetic methods

1. Introduction

The discovery of the selenoxide elimination in the early 1970s is believed to have been the major breakthrough for the subsequent developments of organoselenium chemistry.[1] Since that time, a variety of organoselenium reagents has been developed and several are now commercially available. Two recently published books cover the broad range of organoselenium chemistry from practical aspects to synthetic applications,[2] older books or book chapters[3] as well as review articles[4] describe different aspects. There is still a need for efficient stereoselective transformations in organic chemistry, and certain features of selenium-containing compounds make these reagents particularly valuable for those reactions. Within the scope of this review nucleophilic and electrophilic reagents for the introduction of selenium into organic molecules are discussed as well as stereoselective reactions with selenium-containing compounds for the synthesis of valuable building blocks.

2. Nucleophilic Reagents

Nucleophilic selenium reagents are easily formed from various precursors; for example, by reduction of either elemental selenium or diselenides or by insertion of selenium into organometallic reagents.[5] Selenolates are highly reactive, soft nucleophiles that can be introduced into a variety of organic compounds. Their chemistry began with the nucleophilic ring opening of epoxides **1**, which proceeds in an *anti* stereospecific fashion (Scheme 1).[6] The β-hydroxyselenides **2** can be used for various subsequent transformations. For instance, *trans* elimination from compounds **2** gives alkenes of type **3**.[7] The overall reaction sequence is a deoxygenation of epoxides to alkenes with retention of configuration.[8] The *syn* elimination of the corresponding selenoxides affords allylic alcohols **4** with high selectivities.[6] This reaction sequence has been utilized in various natural product syntheses.[9] Treatment of β-hydroxyselenides **2** with acids results in an



1 **2** **3** **4** **5**

Scheme 1. Ring opening of epoxides with selenolates and subsequent reactions.

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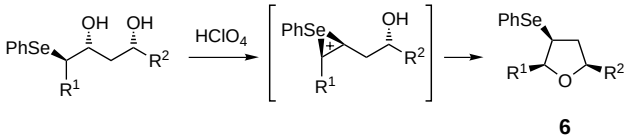
activation of the hydroxy group and in formation of seleniranium[10] ions **5**, which can be opened in an inter- or intramolecular fashion to yield further functionalized compounds.

Seleniranium ions are usually generated by reaction of alkenes with selenium electrophiles (see Section 3). A stereoselective synthesis of substituted cyclic ethers such as tetrahydrofuran derivatives **6** is possible by using such a reaction sequence (Scheme 2).[11]



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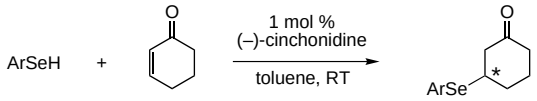
Scheme 2. Synthesis of tetrahydrofuran derivatives via seleniranium intermediates.

The chemistry of nucleophilic selenium reagents with respect to asymmetric synthesis began with the addition of selenols to α,β-unsaturated carbonyl compounds catalyzed by chinchona alkaloids (Scheme 3).[12] Products of type **7** were obtained in up to 43% *ee*.



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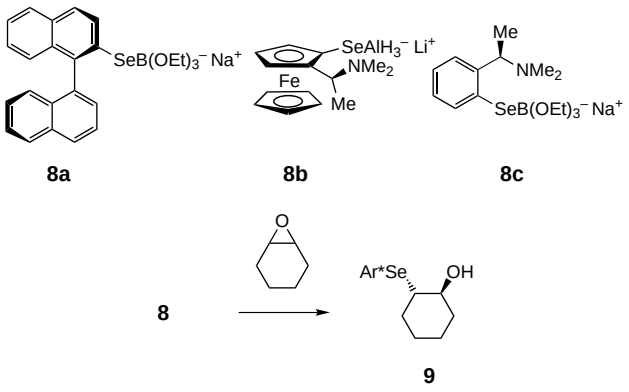
Scheme 3. First asymmetric synthesis with selenium reagents.

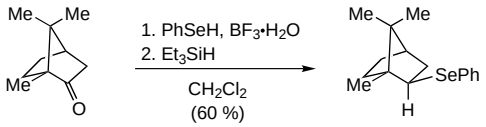
The nucleophilic ring opening of epoxides was the first reaction, in which chiral selenium reagents were used. Binaphthyl selenolates such as **8a** can react with *meso* epoxides yielding products **9** with up to 50% *de*.[13] New developments include the ferrocenyl selenolates **8b** which can open cyclohexenoxide with up to 69% *de* (Scheme 4).[14] Chiral selenolates such as **8c** without an axial chiral element are much less efficient, the product **9** is formed with only 11% *de*.[15] Interestingly, the counterion of the selenolates and the reaction conditions seem to have a dramatic influence on the yields and selectivities of the epoxide-opening reactions. The origin of these effects is not yet fully understood.

Selenolates can also be used for addition reactions to activated carbonyl groups. If chiral ketones like camphor



Scheme 4. Stereoselective ring opening of cyclohexene oxide.

are employed, the Lewis acid catalyzed hemiselenoacetal formation and the subsequent reduction of the selenonium ion yields enantiomerically pure selenides of type **10** (Scheme 5).[16]



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Scheme 5. Selenolate addition to carbonyl groups.

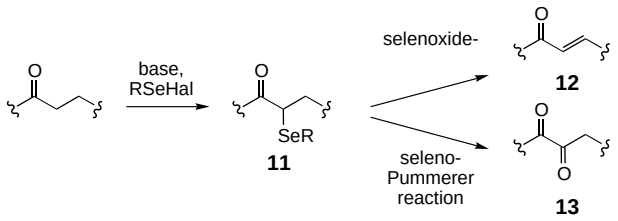
Other versatile reactions with selenium nucleophiles such as substitution reactions with aryl or alkyl halides, Michael reactions, or ester and lactone cleavages are not discussed herein, because these reactions have not been used in stereoselective synthesis. Also polymer-bound selenium nucleophiles have not yet been employed to perform the above-mentioned reactions.[5]

3. Electrophilic Reagents

Very versatile precursors for the preparation of various electrophilic selenium reagents are the corresponding diselenides. They can be transferred easily into selenenyl halides or into selenenyl compounds with non-halide counterions. These electrophilic reagents can react with a variety of carbon or

Thomas Wirth, born in 1964, studied Chemistry in Bonn, Germany, and stayed there to carry out his diploma work with Prof. S. Blechert. He then moved along with his supervisor to the Technical University of Berlin, where he received is Ph.D. in 1992. After a postdoctoral stay with Prof. K. Fuji at Kyoto University, Japan, as a JSPS fellow, he started 1994 his independent research at the Universität of Basel, Switzerland, obtaining his habilitation on stereoselective oxidation reactions in 1999. In the fall of 1999 he was a guest lecturer at the University of Toronto, Canada, and in spring 2000 he was a visiting scientist at the Chuo University in Tokyo, Japan. In September 2000 he was appointed as a Professor of Organic Chemistry at Cardiff University, Wales, UK. He was awarded the Werner-Prize from the New Swiss Chemical Society (NSCG) in October 2000.

heteroatom nucleophiles to produce a wide range of different selenenylated compounds. The α-selenenylation of carbonyl compounds leads to products **11**. Although a stereogenic center is formed in this reaction, no asymmetric versions have been reported up to now—probably, because this reaction usually is followed by a selenoxide elimination and allows the conversion to synthetically important, achiral α,β-unsaturated carbonyl compounds **12**.[4d] From conformationally flexible ketones only *E*-configured enones **12** were obtained. The reaction sequence, shown in Scheme 6, was independently

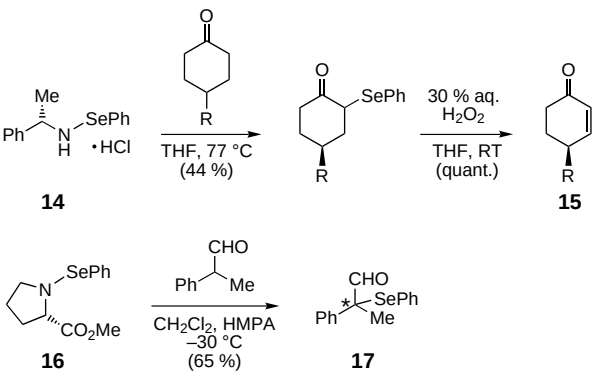


Scheme 6. α-Selenenylation of ketones and subsequent reactions.

reported by several research groups in the early 1970s.[17] The introduction of α,β-unsaturation in carbonyl compounds with organoselenium chemistry is very important and frequently applied in total syntheses.[4d, 18] The α-selenenylation of carbonyl compounds can also be followed by a seleno-Pummerer reaction to give 1,2-bisketones **13**.[19] Silylenol ethers can also be α-selenenylated in high yields[20] and the products of type **11** have been used recently in diastereoselective reductions.[21]

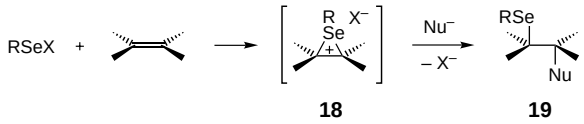
The reactions of selenium electrophiles with heteroatom nucleophiles are synthetically less important, but this reaction has been used for the preparation of the first chiral electrophilic organoselenium compounds. Phenylselenenyl bromide reacts with chiral amines to give selenenamides such as **14**. These reagents have been used in stereoselective α-selenenylations of cyclohexanones. After selenoxide elimination the cyclohexenones **15** were obtained in up to 26% *ee* (Scheme 7).[22] Similar reagents such as **16** seem to be more efficient as shown in the α-selenenylation of 2-phenylpropanal, which leads to **17** in up to 60% *ee*.[23]

Selenium electrophiles are quite powerful and able to react with double bonds to generate, after addition of a nucleophile,



Scheme 7. Stereoselective α-selenenylation of ketones. HMPA = hexamethylphosphoric acid amide.

the corresponding addition products.[24] The two steps of the addition reaction involve the formation of seleniranium intermediates **18**, followed by a nucleophilic attack to yield the addition products **19** (Scheme 8). These reactions exhibit *anti* stereoselectivity with the nucleophile attacking usually at the higher substituted carbon atom (Markownikoff regioselectivity). Some mechanistic investigations have been performed earlier.[25] Reactions with hindered alkenes led to the isolation and structural determination of seleniranium species.[26] The products **19** of these selenenylations are very useful, because a wide range of alkenes as well as nucleophiles can be employed in these transformations and many different subsequent reactions are possible.[27]



Scheme 8. Electrophilic selenenylation of alkenes.

It was recognized early that apart from the *anti* stereoselectivity and the Markownikoff regioselectivity the electrophilic attack could be favored upon one of the two faces of the π system. The facial selectivity is dependent on the alkene, which is usually attacked by the selenium electrophiles from the sterically less hindered side.[28] Even reactions with alkenes having sterically equally accessible faces can be performed stereoselectively. For this purpose chiral electrophilic selenium reagents are of particular interest, which have been developed recently and applied to stereoselective synthesis. A common feature of these reagents is a heteroatom that coordinates to the positively charged selenium atom. Such an intramolecular interaction between the heteroatom and the selenium atom has been proven in different ways. X-ray structural data of suitably substituted compounds,[29] NMR spectral data of such reagents,[30] and ab initio calculations[30a, 31] all indicate the interaction of a lone pair of electrons of the heteroatom with the σ^* orbital of the selenium atom. This induces a conformational rigidity into these molecules as shown in **20** (Figure 1). This interaction can

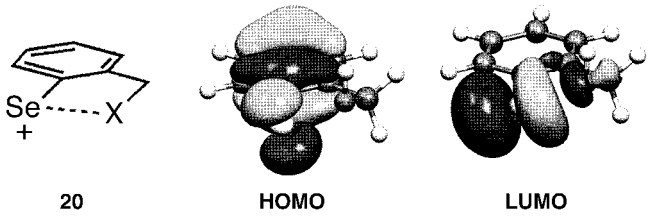
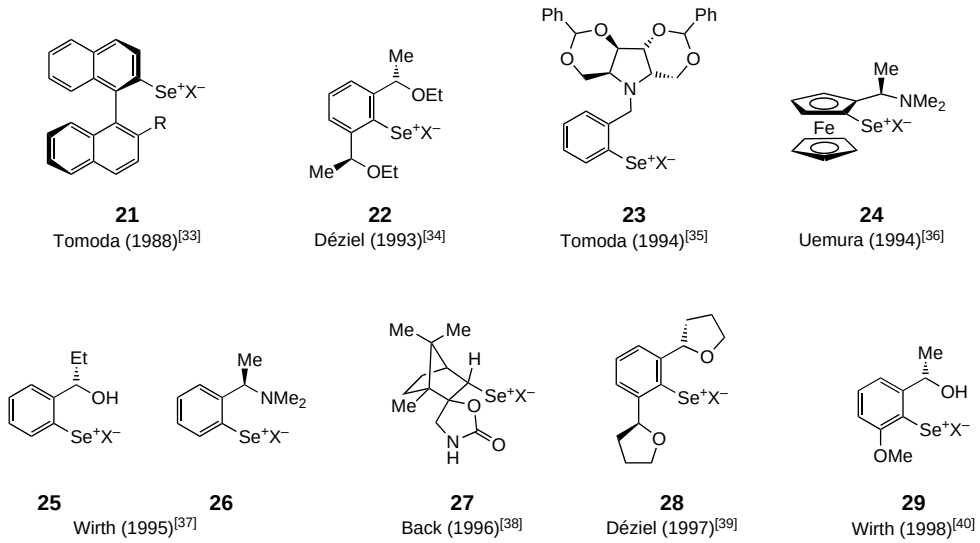


Figure 1. HOMO and LUMO of selenium electrophiles of type **20** (X = OH).

also be seen in the LUMO (X = OH).[32] The LUMOs of the selenium electrophiles are relatively low in energy and their interaction with the HOMOs of the alkenes should play the predominant role in the electrophilic addition reactions.

The introduction of chiral elements into molecules of type **20** leads to chiral selenium electrophiles. They are usually prepared from the corresponding diselenides. Scheme 9 shows



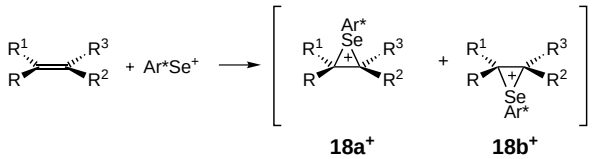
21 Tomoda (1988)[33] **22** Déziel (1993)[34] **23** Tomoda (1994)[35] **24** Uemura (1994)[36]

25 **26** Wirth (1995)[37] **27** Back (1996)[38] **28** Déziel (1997)[39] **29** Wirth (1998)[40]

Scheme 9. Chiral selenium electrophiles.

chiral selenium electrophiles **21**–**29**, which have been employed in stereoselective addition reactions.[33–40]

Different chiral motifs can be found in these reagents. Depending on the complexity, the synthetic route to these reagents sometimes consists of many steps. All the reagents in Scheme 9 have been extensively employed in the stereoselective oxyselenenylation of alkenes. As already pointed out in Scheme 8, these reactions typically proceed via seleniranium ion intermediates of type **18** resulting in an *anti* addition of the moieties ArSe and Nu. The formation of the seleniranium ions is reversible, but at low temperatures the reaction is under kinetic control. The mechanistic course of the oxyselenenylation reaction with the chiral reagents **22** and **25** has been investigated in detail.[31, 41] The presence of a chiral moiety in these reagents results in a differentiation between the two faces of unsymmetrically substituted alkenes. The attack of the alkene double bond from either the *Re*- or the *Si*-side is different from the steric and electronic point of view, and the resulting seleniranium ions **18a**$^+$ and **18b**$^+$ are diastereomers (Scheme 10). On the other hand, symmetrical (*Z*)-alkenes lead to identical seleniranium ions and the stereoselectivity is determined by the nucleophilic attack in the product-forming step.[33a, 38e]



18a$^+$ **18b**$^+$

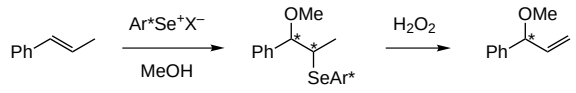
Scheme 10. Formation of diastereoselective seleniranium ions.

The stereoselectivities observed with the reagents **22** and **25** can be rationalized by the relative stability of the transition states for the attack of nucleophiles on the seleniranium intermediates of type **18**. The reaction pathways have been calculated at an ab initio level. It was found that the cationic species involved in the reaction are stabilized by solvent molecules, although the solvent–selenium interaction is relatively weak and reversible.[41] Furthermore, alkenes with aromatic substituents can π-stack with the aryl surface of the reagents, leading to seleniranium ions with higher stabilities than alkenes with alkyl substituents. The independent synthesis of the diastereomeric seleniranium ions allowed a detail study of the different stabilities of these intermediates.[31] Up to now little effort has been made to understand the role of the counterion in asymmetric selenenylation reactions; for instance in the above-mentioned calculations the nature of the counterion was not considered. However, the counterion has an influence on the stereochemical outcome of the reaction. In Table 1 the results of the methoxyselenenylation of (*E*)-1-phenylpropene **30** with various selenium electrophiles are summarized. These reactions lead to addition products **31**; the absolute configuration of the elimination product **32** is also indicated. The addition reactions of various selenium electrophiles to styrene have also been compared and similar results have been obtained.[24]

However, these trends can unfortunately not be generalized. Applying other reaction conditions or using different alkenes can result in different stereoselectivities and sometimes even in a reverse face selection. Less nuclophilic counterions lead to more electrophilic selenium reagents, and the results of various experiments reveal that more electrophilic reagents yield higher stereoselectivities in these addition reactions.[35d, 42]

A variety of different nucleophiles have been investigated in selenenylation reactions. It was found that even functionalized nucleophiles could be used in these reactions, which

Table 1. Stereoselective methoxyselenenylation of (*E*)-1-phenylpropene.

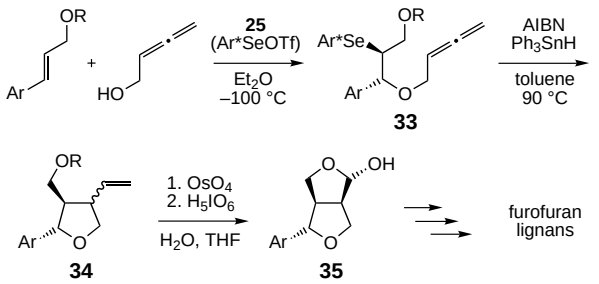


30 **31** **32**

Ar*Se$^+$X$^-$	X$^-$	Conditions solvent	T [°C]	*de* **31** [%]	Yield of **31** [%]	Config. **32**	Ref.
21[a]	Br$^-$	MeOH	25	24	49	[c]	[33d]
21[b]	Br$^-$	MeOH	25	79	87	*R*	[33d,f]
22	TfO$^-$	Et_2O	−78	86	82	*S*	[34a]
23	Br$^-$	CH_2Cl_2	−78	52	85	*R*	[35d]
23	PF_6^-	CH_2Cl_2	−78	95	58	*R*	[35d]
24	TfO$^-$	CH_2Cl_2	−78	96	99	*S*	[36d]
25	TfO$^-$	Et_2O	−100	80	45	*S*	[37c]
28	TfO$^-$	Et_2O	−78	98	81	*S*	[39]
29	TfO$^-$	Et_2O	−100	85	51	*S*	[40]

[a] R = H. [b] R = 1-(2,4-Dinitrophenyl)-pyrrolidin-2-yl-carboxamide. [c] Configuration not determined.

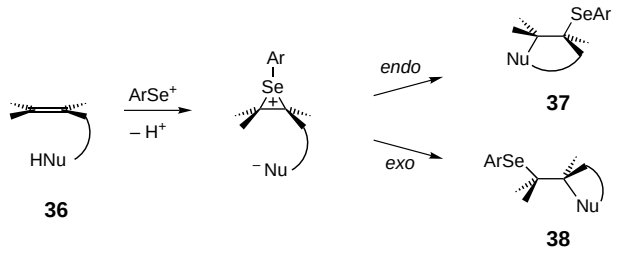
allowed a subsequent radical cyclization. This reaction sequence was applied to the synthesis of furofuran lignans as shown in Scheme 11. Stereoselective selenenylation using selenium electrophile **25** and an allenyl alcohol as nucleophile gave addition products of type **33** in good yields and diastereoselectivities. After the radical cyclization reaction the vinylic side chain of the tetrahydrofuran derivative **34** is oxidized, providing a fast access to furofurans of type **35**, versatile building blocks for the synthesis of various lignans.[43]



Scheme 11. Total synthesis of furofuran lignans by a sequence of selenenylation and subsequent radical cyclization. AIBN = 2,2′-azobisisobutyronitrile; Tf = CF_3SO_2.

Other external nucleophiles such as carbamates or azides (Nu^- in Scheme 8) can be employed in these addition reactions as well. Although these reactions are also *anti* additions and sometimes proceed with high regioselectivity, chiral selenium electrophiles have not been investigated yet.

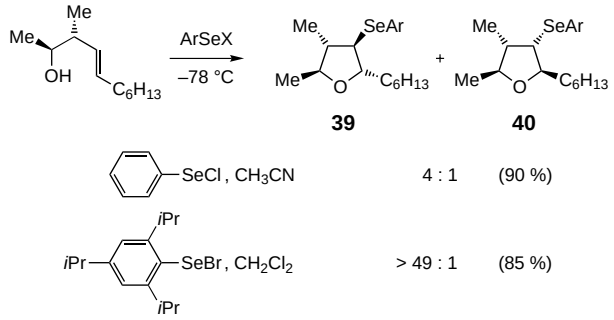
Internal nucleophiles in selenenylations lead to cyclization reactions, which have been employed in various syntheses for a long time.[44] Depending on the chain length and on the substitution pattern of the alkene **36**, the addition reaction can occur by an *endo* or by an *exo* pathway leading to cyclic products of type **37** or **38**, respectively. As shown in Scheme 12, the cyclization reactions are stereospecific *anti* additions like their intermolecular counterparts, and calcu-



Scheme 12. Selenium-mediated cyclization reactions.

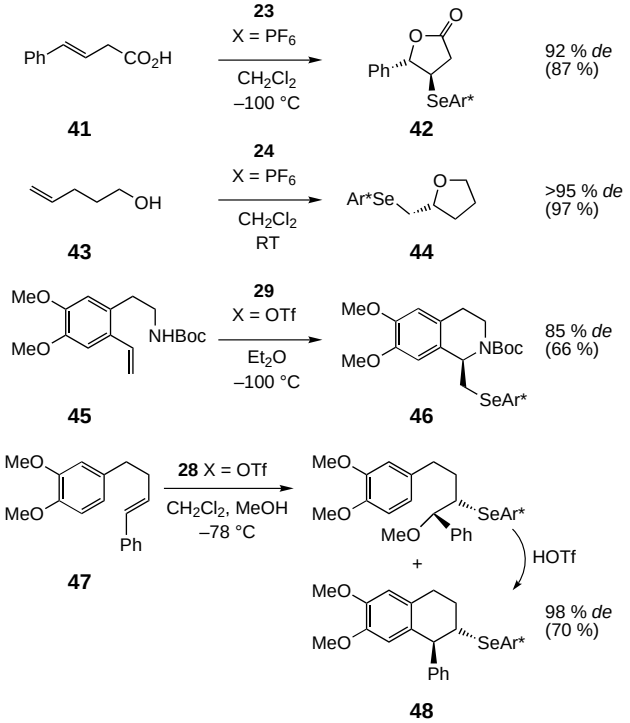
lations on the course of this reaction have been perfomed recently.[45] This reaction type has been used widely for the synthesis of different cyclic compounds and recently it was found that stereoselective ring-closing reactions are possible using chiral electrophilic selenium reagents.

The seleniranium intermediates can be generated from the corresponding β-hydroxyselenides, as shown in Scheme 2, or from suitably substituted alkenes. Depending on the alkene and on the selenium electrophile, cyclizations can be performed with high selectivities. The size of the electrophilic reagent has a large influence on the diastereomeric ratio of the **39** and **40**, which varies from 4:1[46] to >49:1 (Scheme 13).[47]



Scheme 13. Stereoselective cyclizations with achiral selenium electrophiles.

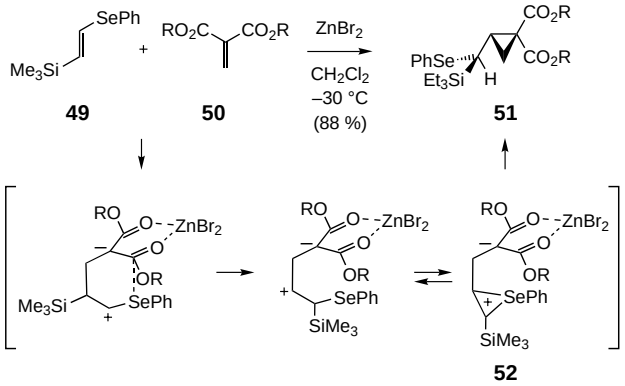
Almost all chiral selenium electrophiles shown in Scheme 9 have been employed in stereoselective cyclization reactions. Oxygen, nitrogen, and carbon nucleophiles have been used to construct different cyclic systems by intramolecular cyclizations. Depending on the alkene and on the nature of the electrophilic reagent, different selectivities have been observed. First applications of stereoselective selenocyclization reactions have also been reported in natural product synthesis. Some selected examples are shown in Scheme 14. The unsaturated carboxylic acid **41** has been used as a substrate for stereoselective selenolactonizations to give **42**, for which the selenium electrophiles **23**[35b] and **28**[39] were found to be quite efficient. Substituted tetrahydrofuran derivatives like **44** can be synthesized from the corresponding unsaturated alcohols



Scheme 14. Stereoselective cyclizations with chiral selenium electrophiles. Boc = *tert*-butoxycarbonyl.

43, in the series of aliphatic alkenes only a few selenium electrophiles like **24** lead to high selectivities.[48] The intramolecular amidoselenenylation was found to be a versatile reaction for the preparation of **46**, a precursor in the synthesis of the tetrahydroisoquinoline alkaloid salsolidine.[49] Also carbocycles can be formed by this methodology as shown in the cyclization of **47**. Methanol as external nucleophile competes, but the subsequent treatment with trifluoromethanesulfonic acid allows the synthesis of **48** in very high selectivities.[50]

The Lewis acid promoted stereoselective [2+1] cycloaddition reaction of 1-seleno-2-silylethene **49** to dicarboxylates **50** (R = *t*Bu) proceeds probably also via seleniranium intermediates **52**. After a selenium-assisted 1,2-silicon migration process a stabilized seleniranium intermediate can be formed which is opened under formation of the cyclopropane derivative **51**.[51] The use of chiral dicarboxylates **50** (R = (−)-menthyl) allows the synthesis of cyclopropanes **51** with up to 86% *de* (Scheme 15).[52]

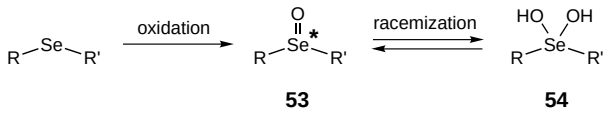


Scheme 15. Synthesis of cyclopropanes from vinylselenides.

4. Rearrangements

Selenoxide eliminations and [2,3] sigmatropic rearrangements of various selenium-containing compounds are useful tools in the hand of synthetic organic chemists.[53] The application of these transformations in stereoselective synthesis was developed only recently. The use of optically active organoselenium compounds with a chiral center at the selenium atom is the prerequisite for the stereoselective synthesis. In contrast to the analogous sulfur-based chemistry, the activation energies for rearrangements with organoselenium compounds are much lower making them ideal for use in stereoselective synthesis. The selenoxide elimination reaction has not only brought organoselenium chemistry into the focus of organic chemists, but because of the extremely mild reaction conditions this rearrangement has also been applied in many syntheses since its discovery.

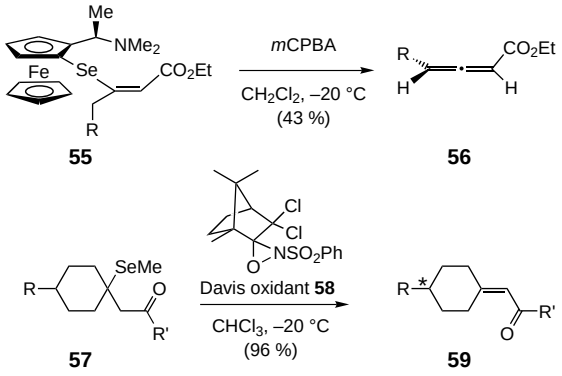
Chiral selenoxides **53** can be obtained either by enantioselective oxidation[54] of the corresponding selenides (R ≠ R′) or by diastereoselective oxidation[55] of selenides bearing a chiral moiety (R or R′: chiral) (Scheme 16). It had been shown that the formation of an achiral hydrate **54** accounts for the fast



Scheme 16. Synthesis and racemization of selenoxides via achiral hydrates.

racemization of selenoxides in the presence of acid and water.[56] Bulky substituents can prevent racemization[57] but in the presence of a β-hydrogen atom the subsequent selenoxide elimination leads to more stable products.

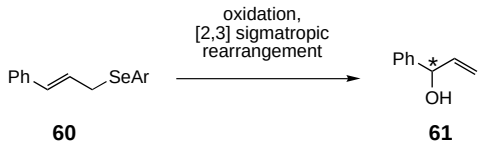
The asymmetric version of the selenoxide elimination after diastereoselective oxidation was first applied to the synthesis of chiral allenes (Scheme 17). Ferrocenyl-substituted vinyl selenides of type **55** are employed in the oxidation–elimination sequence to yield the chiral allenes **56** in up to 89% *ee*.[58] Enantioselective oxidation of selenide **57** is possible with the Davis oxidant **58**, and the cyclohexylidene ketone **59** is obtained in up to 83% *ee*.[59]



Scheme 17. Stereoselective selenoxide eliminations. mCPBA = *meta*-chloroperoxybenzoic acid.

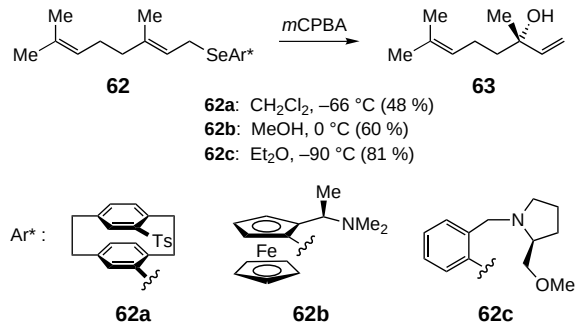
The [2,3] sigmatropic rearrangements via allylic selenoxides involve an oxygen transfer from selenium to carbon and after hydrolysis of the allylic selenenates the allylic alcohols are obtained. It was proven that these rearrangements proceed predominantly via an *endo* transition state.[55] The rearrangement of the allylic selenoxides proceeds much faster than that of the corresponding sulfoxides, and detailed kinetic and thermodynamic studies have been carried out.[60] The stereoselective version of these rearrangements can again be performed either by enantioselective oxidation of achiral allylic selenides or by diastereoselective oxidation of allylic selenides bearing a chiral substituent. Several stereoselective syntheses of allylic alcohols have been reported recently. For instance, oxidation of aryl cinnamyl selenides **60** with the Davis oxidant **58** and subsequent rearrangement gave the allylic alcohol **61** with only modest stereoselectivity (up to 60% *ee*).[54] By the use of the Sharpless oxidant {Ti(O*i*Pr)$_4$, (+)-diisopropyltatrate/*tert*-butyl hydroperoxide}, however, the allylic alcohol **61** can be obtained in up to 92% *ee* (Scheme 18).[61]

Several examples are also known for the diastereoselective oxidation of chiral allylic selenides. One of the test reactions for several chiral compounds is the synthesis of (*S*)-linalool **63**



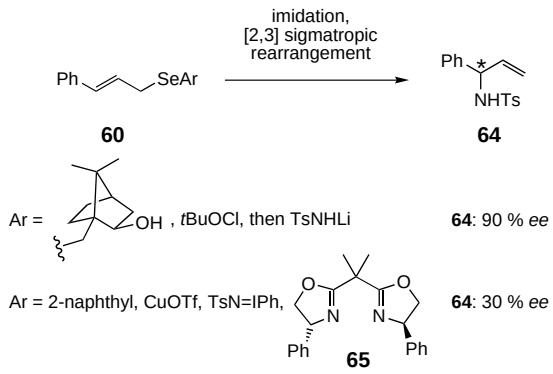
Scheme 18. Stereoselective [2,3] sigmatropic rearrangement of allylic selenides.

from precursors of type **62**. Depending on the chiral moiety, good stereoselectivities can be obtained (**62a**: 67% *ee*, **62b**: 83% *ee*, **62c**: 61% *ee*) as shown in Scheme 19.[55, 58b, 62]



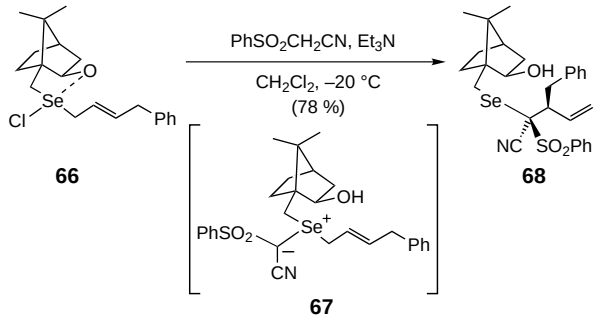
Scheme 19. Synthesis of linalool **63** by [2,3] sigmatropic rearrangements. Ts = *para*-toluenesulfonyl.

In principle, the [2,3] sigmatropic rearrangements via allylic selenoxides mentioned above can also be performed with selenimides as nitrogen-analogous intermediates.[63] Chiral allylic amines are therefore accessible by this route. Chloramine T (TsNClNa) or *N*-(*p*-tolylsulfonyl)imino(phenyl)iodinane (TsN=IPh) can be used as imidation reagents of either chiral allylic selenides[63a,b] or, with the help of chiral ligands such as the bis(oxazoline) **65**, also for the imidation of achiral allylic selenides.[63c] The rapid selenimide–selenoxide equilibrium must be suppressed by using water-free reaction conditions. Although the stereoselectivities are still low, these reactions open a promising route to chiral allylic amines such as **64** (Scheme 20).



Scheme 20. Stereoselective [2,3] sigmatropic rearrangements leading to chiral allylic amides **64**.

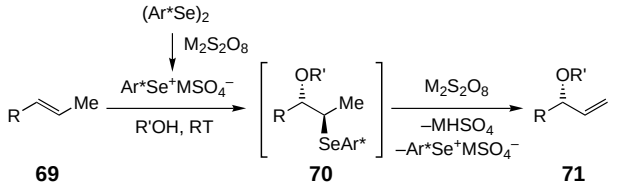
Although selenonium ylides have been known for a long time, it was shown recently that chiral selenonium ylides can be prepared. They can also be quite versatile precursors for [2,3] sigmatropic rearrangements. The reaction of the allylic chloroselenuranes **66** with (phenylsulfonyl)acetonitrile generates the corresponding selenonium ylides **67**, and after the [2,3] sigmatropic rearrangement homoallylselenides **68** are obtained with high stereoselectivities (up to 88% *de*) (Scheme 21).[64]



Scheme 21. Stereoselective [2,3] sigmatropic rearrangement via selenonium ylides.

5. Catalytic Reactions

Selenium-containing reagents can be used as catalysts or as ligands in various stereoselective reactions. For instance, it is possible to perform selenenylation–deselenenylation sequences with only catalytic amounts of selenium species. This reaction sequence provides double bond transpositioned allylic ethers or allylic alcohols from the corresponding alkenes (Scheme 22). This sequence can be performed electrochemically,[65] but stereoselective versions using chiral

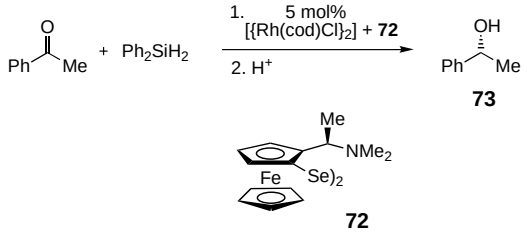


Scheme 22. Selenenylation–elimination sequence with catalytic amounts of diselenides.

diselenides rely on the formation of the selenenyl sulfates from diselenides with peroxodisulfates[66] as electrophilic reagents for the initial addition reaction to the alkene **69**. The resulting selenide **70** is then oxidized by an excess peroxodisulfate and the subsequent elimination reaction yields allylic compounds of type **71**. Different chiral diselenides have been employed in this reaction and after careful optimization of the reaction conditions enantioselectivities up to 75% (R = Ph, R′ = Me in **71**) have been obtained.[67] However, the turnover numbers are still small and further work is needed to improve the catalytic oxyselenenylation–elimination sequence.

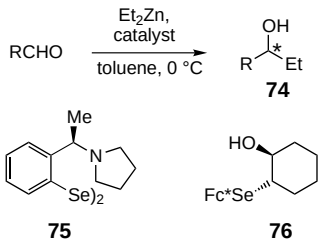
Chiral ferrocenyl diselenides like **72** have been found to serve as efficient ligands for transition metal catalyzed stereoselective reactions such as asymmetric hydrosilylations or transfer hydrogenations of various ketones. Diselenide **72** was found to be the most efficient ligand for the rhodium(I)-

catalyzed hydrosilylation of acetophenone leading to the product **73** with 85% *ee* (Scheme 23).[68] Other ferrocenyl diselenides with variations in the chiral side chain as well as the analogous disulfide and ditelluride afforded the product with much lower enantioselectivity. The same ferrocenyl diselenide **72** has been investigated in rhodium(I)- as well as in iridium(I)- and in ruthenium(II)-catalyzed stereoselective transfer-hydrogenations of ketones. However, the stereselectivities obtained are low in most of the examples reported (up to 48% *ee*).[69]



Scheme 23. Enantioselective hydrosilylation using chiral diselenide ligands. cod = cycloocta-1,5-diene.

Nitrogen-containing diselenides like **75** are very efficient procatalysts for the addition of diethylzinc to aldehydes. The secondary alcohols **74** are obtained in up to 98% yield and with up to 98% *ee* (Scheme 24). It has been shown that the selenium–selenium bond of the diselenides is cleaved rapidly and that catalytically active zinc selenolates are formed. A positive nonlinear relationship (asymmetric amplification) between the optical purities of the catalyst and the product was observed.[70] Other selenium-containing catalysts such as **76** (Fc* = ferrocenyl moiety **62b**) leading to enantioselectivities up to 94% in the products **74** have been investigated as well in this addition reaction.[71]



Scheme 24. Catalytic addition of diethylzinc to aldehydes.

Palladium-catalyzed allylic substitutions can be performed with catalysts containing a selenium atom, but the selectivites obtained are lower than with the chiral phosphorus-containing ligands usually employed in these reactions.[72]

6. Summary and Outlook

Recent advances using selenium compounds in stereoselective reactions are described in this review. Various aspects using chiral selenium reagents in stoichiometric and in catalytic reactions are summarized. Although high stereoselectivities can be obtained for several reaction types such as electrophilic additions to alkenes, low or only modest stereoselectivities are found in other reactions and further work is needed in these areas. Improved and new selenium-containing reagents will surely be developed in the future to gain further benefit from the usually very mild conditions in these reactions. This will lead to enhanced stereoselectivities in known reactions, to new selenium-based transformations and methods, and to new applications of this chemistry.

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