Stereoselective Electrophilic Cyclisation of *O*-Homoallyl Hydroxylamine Derivatives

Birgit Janza, Armido Studer*

Fachbereich Chemie , Universität Marburg, Hans-Meerwein-Straße, 35032 Marburg, Germany
Fax +49(6421)2825629; E-mail: studer@mailer.uni-marburg.de

Received 18 June 2002

Dedicated to Prof. Dr. Dieter Seebach on the occasion of his 65th birthday.

Abstract: Electrophilic cyclisations of various *O*-homoallyl hydroxylamine derivatives are discussed. Non-protected *O*-homoallyl hydroxylamines undergo oxidative cyclisations to isoxazolines. The new isoxazoline synthesis comprises an initial electrophilic cyclisation to form intermediate isoxazolidines, which are subsequently oxidized to isoxazolines. Cyclisations can be conducted with various electrophiles (*t*-BuOCl, PhSeBr, NBS and NIS). Oxidation can be suppressed if the starting *O*-homoallyl hydroxylamines are *N*-sulfonylated. The electrophilic cyclisation then provides *N*-sulfonylated isoxazolidines with moderate *cis*-selectivity (up to 7:1). Electrophilic cyclisation of *N*-acylated *O*-homoallyl hydroxylamines provides isoxazolines or isoxazolidines depending on the reaction conditions (reagents). The *t*-BuOCl-mediated cyclisation affords isoxazolines via an oxidative cyclisation, whereas the NIS-induced reaction provides the 5-*exo*-cyclisation product with high stereoselectivity (*cis*:*trans* = 13:1).

Key words: stereoselective synthesis, electrophilic additions, isoxazolidines, isoxazolines, oxidative cyclisations

Electrophilic cyclisations of alkenes containing internal nucleophiles are well established for the preparation of heterocycles in synthetic organic chemistry.[1] Various electrophiles have been successfully used to induce these cyclisations and the nucleophilic moiety can also be readily varied. Thus, a large number of different heterocycles can be prepared using this approach. *N*-Heterocycles, which occur in numerous natural products, have been synthesized via electrophilic cyclisations using *N*-centered nucleophiles. Carbamates,[2] ureas,[3] hydrazines,[4] amines,[5] amides[6] and oximes[7] were used as *N*-nucleophiles in these studies. There are also some reports on the cyclisation of *O*-allyl hydroxylamines.[8]

Recently, we initiated a program towards the study of stereoselective 5-*exo*-cyclisation reactions using alkoxyaminyl radicals.[9] During these studies we observed that *O*-homoallyl hydroxylamine derivatives undergo electrophilic cyclisations with good to excellent selectivities.[10] Herein, we disclose our first results on this subject.

Alkoxyamine **1** was readily prepared from the corresponding alcohol using the Mitsunobu reaction with *N*-hydroxyphthalimide/diisopropyl azodicarboxylate/Ph_3P and subsequent hydrazinolysis (85%).[11] All the other alkoxyamines described herein were prepared in an analogous manner. We first studied the electrophilic cyclisation of **1** using *tert*-butyl hypochlorite (1 equiv) in CH_2Cl_2 at room temperature (Scheme 1). Isoxazoline **2** was obtained in 24% yield along with unreacted starting material. The desired isoxazolidine **3** was not identified. Thus, oxidation of isoxazolidine **3** with *t*-BuOCl is faster than the electrophilic cyclisation of alkoxyamine **1**. Isoxazolidine **3** is obviously readily chlorinated to provide *N*-chloroalkoxyamine **4**, which upon HCl-elimination eventually leads to the isolated isoxazoline **2**.[12] With 3 equivalents of *t*-BuOCl the highest yield of the electrophilic 5-*exo*-cyclisation/oxidation product was obtained (69%).

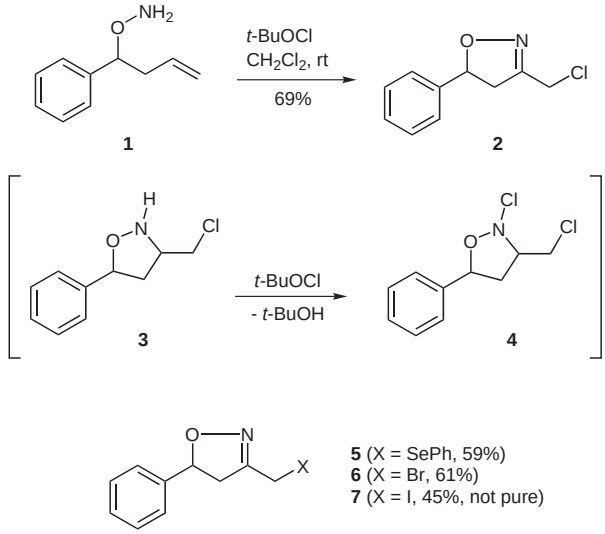
We further tested, whether the electrophilic cyclisation/oxidation can also be performed with other electrophiles. We found that the reaction of alkoxyamine **1** with phenylselenyl bromide (3 equiv) in acetonitrile in the presence of Na_2CO_3[13] at room temperature provides isoxazoline **5** in 59% yield. A slightly better yield was obtained for the oxidative cyclisation of **1** using *N*-bromosuccinimide (NBS, CH_2Cl_2, r.t.→**6**, 61%). The analogous reaction with *N*-iodosuccinimide (NIS) provided iodide **7** (~45%). However, the reaction was not clean anymore, and iodide **7** could not be isolated in analytically pure form.

Thus, the oxidative cylisation can be readily performed with different electrophilic reagents providing isoxazolines bearing interesting functional groups. Phenylselenides and alkyl halides are useful compounds for further synthetic manipulations. Isoxazolines are interesting compounds in organic synthesis, which are generally prepared by nitrile oxide cycloaddition reactions.[14] Our method provides a new approach to this important class of compounds.[15]

In order to suppress the oxidation, we decided to decrease the basicity of the nitrogen atom of the initially formed isoxazolidine. To this end, the alkoxyamine **1** was sulfonylated using benzenesulfonyl chloride and Et_3N in THF to give *N*-alkoxysulfonamide **8** (84%). We first tested its electrophilic cyclisation using *t*-BuOCl. However, the reaction appeared to be very slow. We therefore studied other electrophilic chlorine sources and were pleased to find that upon using NaOCl in $CHCl_3$ in the presence of acetic acid smooth cyclisation occurred (r.t., 24 h).[16] As expected, oxidation was completely suppressed, and the cyclisation product **9** was formed in 61% yield as a 4.4:1 *cis*/

Synthesis 2002, No. 14, Print: 07 10 2002.
Art Id.1437-210X,E;2002,0,14,2117,2123,ftx,en;C03202SS.pdf.

ISSN 0039-7881

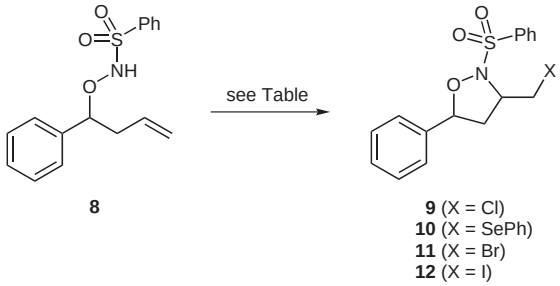


Scheme 1 Electrophilic cyclisation/oxidation of alkoxyamine **1**

trans mixture of isomers (Scheme 2, Table 1, entry 1). The selectivity was determined by ^{1}H NMR spectroscopy. The relative configuration of the major isomer was unambiguously assigned by NOE experiments. We then tested the Se-induced electrophilic cyclisation using PhSeBr (1.5 equiv) in acetonitrile in the presence of Na_2CO_3 at room temperature. The cyclisation product **10** was isolated in 73% yield (*cis*/*trans* = 4.4:1, entry 2). The relative configuration was assigned in analogy to chloride **9**. An even better yield was obtained for the NBS-mediated cyclisation. Bromide **11** was isolated in 79% with a 4.8:1 diastereoisomer ratio (entry 3). In contrast to the oxidative cyclisation described above, the NIS-induced reaction worked well for the sulfonylated alkoxyamine **8**. Iodide **12** was isolated in 70% yield (dr = 5.0:1, NIS, CH_2Cl_2, r.t., 24 h, entry 4). Reactions performed with elemental iodine instead of NIS provided similar results (entries 7 and 8).

We also tested whether the selectivity can be further increased upon decreasing the reaction temperature. At –20 °C, the reaction took 36 hours for completion and the selectivity could be slightly increased (dr = 6.3:1, entry 5). The same cyclisation was also conducted at –68 °C. After 3 days only 60% conversion was obtained, and iodide **12** was formed as a 7.0:1 *cis*/*trans* mixture of isomers (entry 6). Since the cyclisation at –68 °C was not efficient anymore, cyclisations at even lower temperatures were not performed.

We next decided to study the influence of the substituent at the nitrogen atom on the stereoselectivity of the cyclisation. The acylated alkoxyamine **13** was readily prepared from alkoxyamine **1** (AcCl, THF, Et_3N, 0 °C, 92%). To our surprise, reaction with *t*-BuOCl in CH_2Cl_2 at room temperature for 24 hours afforded the oxidative cyclisation product **2** (40%) along with unreacted starting material (60%, as determined by ^{1}H NMR spectroscopy). None of the desired isoxazolidine **14** was identified. We repeated the reaction using 3.5 equivalents of the electrophile under otherwise identical conditions. Isoxazoline **2** was isolated in 55% yield (Scheme 3). Obviously the *N*-



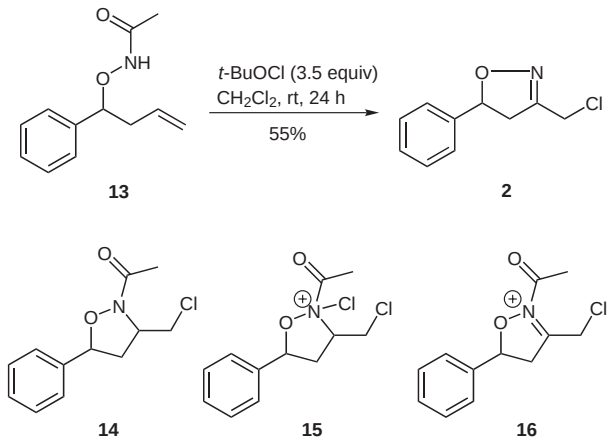
Scheme 2 Stereoselective electrophilic cyclisation of *N*-alkoxysulfonamide **8**

Table 1 Cyclisation of *N*-Alkoxysulfonamide **8** under Different Conditions

Entry	Reagent	Temp.	Product	*cis*:*trans*	Yield (%)
1	NaOCl	r.t.	**9**	4.4:1	61
2	PhSeBr	r.t.	**10**	3.8:1	73
3	NBS	r.t.	**11**	4.8:1	79
4	NIS	r.t.	**12**	5.0:1	70
5	NIS	–20 °C	**12**	6.3:1	-[a]
6	NIS	–68 °C	**12**	7.0:1	-[b]
7[c]	I_2	r.t.	**12**	5.0:1	74
8[d]	I_2	r.t.	**12**	5.1:1	69

[a] 99% conversion after 36 h, product not isolated.
[b] 60% conversion after 3 d, product not isolated.
[c] Reaction conducted in $CHCl_3$ in the presence of aq $NaHCO_3$.
[d] Reaction conducted in MeCN.

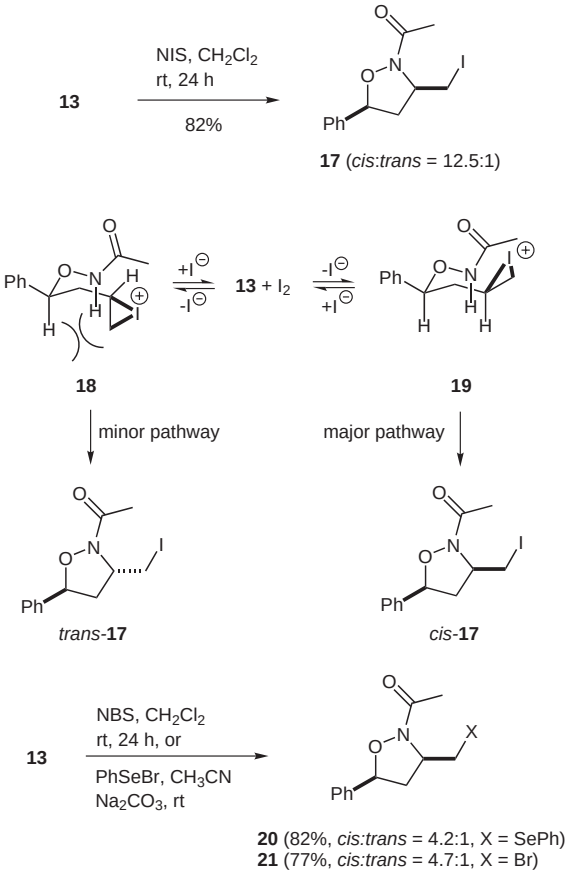
atom of the acylated isoxazolidine **14** is nucleophilic enough to be chlorinated with *t*-BuOCl to form intermediate **15**. HCl-elimination then affords the acyliminium ion **16**, which eventually provides isoxazoline **2**. We believe that the *N*-atom of the acylated isoxazolidine **14** is slightly pyramidalized and has therefore enhanced nucleophilicity.[17]



Scheme 3 Oxidative cyclisation of acylated alkoxyamine **13** with *t*-BuOCl

To suppress the oxidation, we decided to decrease the reactivity of the electrophile. Indeed, with NIS the oxidative cyclisation product **7** was not formed anymore, and iodide **17** was isolated in 65% yield (Scheme 4).[18] We were very pleased to observe that the cyclisation occurred with high selectivity (*cis*:*trans* = 12.5:1). The two isomers were readily separated using flash chromatography [→ *cis*-**17** (76%); → *trans*-**17** (6%)]. The relative configuration of the major isomer was assigned by NOE experiments.

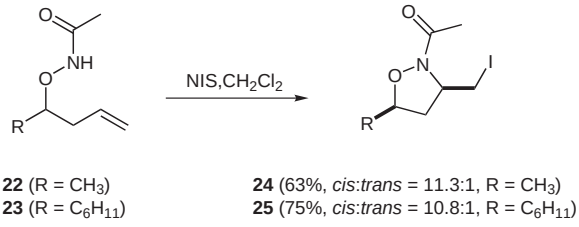
We suggest the following model to explain the stereochemical outcome of the cyclisation: Initial iodonium ion formation is probably not stereoselective. Thus, the diastereoisomeric intermediates **18** and **19** are formed in equal amounts. The cyclisations are supposed to occur through chair type conformations as depicted in Scheme 4. 1,3-Diaxial interaction in the case of diastereoisomer **18** increases the activation energy for the formation of the *trans* isomer. Since the initial iodonium ion formation is reversible, the 'non-productive' isomer **18** can readily be converted back to the starting olefin **13**.



Scheme 4 Stereoselective cyclisation of olefin **13**

We also tested Se- and Br-induced cyclisations. The Se-mediated cyclisation using PhSeBr as electrophile occurred with lower selectivity (*cis*:*trans* = 4.2:1, 82%). The NBS-mediated cyclisation of **13** afforded a similar result. Bromide **21** was formed as a 4.7:1 *cis*:*trans*-mixture of diastereoisomers in 77% yield. The diastereoisomers can be readily separated.

We also studied the influence of the substituent R (see Scheme 5) on the diastereoselectivity of the NIS-mediated cyclisation (1,3-stereoinduction). As for the phenyl substituted derivative discussed above, the methyl substituted alkoxyamine **22** and the cyclohexyl substituted congener **23** provided the corresponding cyclisation products in good yields with high selectivity [→ **24** (63%, *dr* = 11.3:1), → **25** (75%, *dr* = 10.8:1)]. The relative configuration of the major isomer was assigned in analogy to iodide **17**. Thus, for all R-substituents tested so far, a similar high 1,3-stereoinduction was obtained.



Scheme 5 NIS-induced stereoselective 5-*exo*-cyclisations

In conclusion, we have presented a new approach for the preparation of isoxazolines starting from *O*-homoallyl hydroxylamine derivatives. The starting alkoxyamines are readily prepared from the corresponding alcohols. The new isoxazoline synthesis comprises an initial electrophilic cyclisation reaction to form intermediate isoxazolidines, which are subsequently oxidized to isoxazolines. The oxidative cyclisation can be conducted with various reagents such as *t*-BuOCl, PhSeBr, NBS and NIS and are easy to perform at ambient temperature. Our method nicely complements the traditional isoxazoline syntheses. Furthermore, we have shown that the oxidation can be suppressed if the starting *O*-homoallyl hydroxylamines are *N*-sulfonylated. The electrophilic cyclisation can again be performed with various electrophiles to afford *N*-sulfonylated isoxazolidines with moderate *cis*-selectivities (up to 7:1).

Electrophilic cyclisations using *N*-acylated *O*-homoallyl hydroxylamines provided very interesting results. The *t*-BuOCl-mediated cyclisation afforded isoxazolines via an oxidative cyclisation. However, with the milder NIS as electrophile, oxidation could be suppressed, and the 5-*exo*-cyclisation product was obtained with high stereocontrol (*cis*:*trans* = 13:1). Lower selectivities were obtained for the PhSeBr and NBS-mediated cyclisations. Thus, upon switching the electrophile, one can chose between an oxidative cyclisation (*t*-BuOCl → isoxazolines) or a conventional highly stereoselective electrophilic cyclisation (NIS → isoxazolidines) starting from the same olefin. Isoxazolidines as well as isoxazolines are very useful compounds in synthetic organic chemistry.

^{1}H NMR, ^{13}C NMR and NOESY spectra were recorded on a Bruker DRX-500, DRX-400, ARX-300 or ARX-200 spectrometer. IR spectra were recorded on a Bruker IFS-200 or a Nicolet MagnaIR 750 spectrometer. Mass spectra were recorded as EI-MS

on a Varian CH7 and as HRMS on a MAT 95S instrument. Elemental analyses were performed on a Heraeus CHN-Rapid analyser. Solvents were purified by standard methods. Air and moisture sensitive compounds were handled under argon using Schlenk techniques.

O-(1-Phenylbut-3-enyl)hydroxylamine (1)

1-Phenylbut-3-ene-1-ol (1.44 g, 9.72 mmol), Ph_3P (2.96 g, 11.25 mmol) and *N*-hydroxyphthalimide (1.83 g, 11.25 mmol) were dissolved in THF (60 mL). The solution was cooled to 10 °C, and diisopropyl azodicarboxylate (2.6 g, 11.25 mmol) was added over 30 min. The mixture was allowed to warm to r.t. and stirred for 4 h. Hydrazine monohydrate (1.05 mL, 22 mmol) was added and the stirring was continued for further 30 min. After addition of H_2O, the mixture was extracted with methyl *tert*-butyl ether (MTBE)–pentane (1:1). The organic layer was separated and dried ($MgSO_4$). Evaporation of the solvent and purification by flash chromatography (FC) [MTBE–pentane, 1:9] afforded **1**; yield: 1.35 g (85%).

IR (film): 3317, 1641, 1583, 1454, 1182, 916, 702 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.39–7.29 (m, 5 H_{arom}), 5.87–5.67 (m, 1 H, CH_2=C*H*), 5.22 (br s, 2 H, NH_2), 5.12–5.00 (m, 2 H, CH=CH_2), 4.56 (dd, *J* = 7.4, 6.0 Hz, 1 H, HCON), 2.68–2.33 (m, 2 H, CH_2).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 141.29 (C), 134.36 (CH), 128.43 (CH), 127.75 (CH), 126.69 (CH), 117.02 (CH_2), 86.57 (CH), 40.51 (CH_2).

MS (EI): *m*/*z* = 163 $[M]^+$, 131, 116, 105, 91, 77, 65, 53.

Anal. Calcd for $C_{10}H_{13}NO$ (163.22): C, 73.59; H, 8.03; N, 8.58. Found: C, 73.28; H, 8.25; N, 8.87.

Isoxazolines 2, 5, 6, and 7; General Procedure (GP 1)

O-(1-Phenylbut-3-enyl)hydroxylamine (**1**) was dissolved in CH_2Cl_2 or MeCN. A solution of the electrophile in CH_2Cl_2 or MeCN was added at r.t. After stirring at r.t. for 24 h, sat. aq $Na_2S_2O_3$ was added. The organic layer was separated, washed with sat. aq $NaHCO_3$ and brine, and dried ($MgSO_4$). After evaporation of the solvent, the crude product was purified by FC.

3-Chloromethyl-5-phenylisoxazoline (2)

According to GP 1, from **1** (0.2 g, 1.2 mmol) and *tert*-butyl hypochlorite (0.38 g, 3.6 mmol) in CH_2Cl_2 (15 mL). FC (MTBE–pentane, 1:9) afforded **2**; yield: 161 mg (69%).

IR (film): 3448, 1740, 1618, 1493, 1456, 1262, 922, 759, 699 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.28–7.23 (m, 5 H_{arom}), 5.59 (dd, *J* = 11.2, 8.5 Hz, 1 H, HCON), 4.27 (s, 2 H, CH_2Cl), 3.45 (dd, *J* = 17.3, 11.3 Hz, 1 H, CH_2), 3.01 (dd, *J* = 17.2, 8.5 Hz, 1 H, CH_2).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 154.54 (C), 140.21 (CH), 128.76 (CH), 128.36 (C), 125.64 (CH), 83.09 (CH), 42.42 (CH_2), 37.74 (CH_2).

MS (EI): *m*/*z* = 195 $[M]^+$, 160, 142, 128, 117, 104, 89, 78, 42.

HRMS: *m*/*z* $[M^+]$ Calcd for $C_{10}H_{10}ClNO$, 195.0451. Found: 195.0459.

3-Phenylselenylmethyl-5-phenylisoxazoline (5)

According to GP 1, from **1** (0.2 g, 1.2 mmol), phenylselenyl bromide (0.87 g, 3.7 mmol) and Na_2CO_3 (300 mg) in MeCN (25 mL). FC (MTBE–pentane, 1:9) afforded **5**; yield: 252 mg (59%).

IR (film): 3058, 2924, 1578, 1496, 1437, 1335, 899, 739, 699 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.89–7.46 (m, 2 H_{arom}), 7.32–7.15 (m, 8 H_{arom}), 5.51 (dd, *J* = 11.0, 8.3 Hz, 1 H, HCON), 3.85 (d, *J* = 13.0 Hz, 1 H, CH_2SePh), 3.70 (d, *J* = 12.7 Hz, 1 H, CH_2SePh), 3.44 (dd, *J* = 16.4, 11.0 Hz, 1 H, CH_2), 3.04 (dd, *J* = 16.8, 8.1 Hz, 1 H, CH_2).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 155.89 (C), 140.76 (CH), 133.24 (CH), 129.26 (CH), 128.57 (CH), 128.51 (CH), 128.02 (C), 127.75 (C), 125.74 (CH), 82.32 (CH), 43.84 (CH_2), 22.64 (CH_2).

MS (EI): *m*/*z* = 317 $[M]^+$, 211, 160, 142, 129, 117, 115, 91, 77.

Anal. Calcd for $C_{16}H_{15}NOSe$ (316.26): C, 60.76; H, 4.78; N, 4.43. Found: C, 60.70; H, 4.94; N, 4.65.

3-Bromomethyl-5-phenylisoxazoline (6)

According to GP 1, from **1** (0.2 g, 1.2 mmol) and *N*-bromosuccinimide (0.66 g, 3.7 mmol) in CH_2Cl_2 (15 mL). FC (MTBE–pentane, 1:9) afforded **6**; yield: 180 mg (61%).

IR (film): 3442, 2966, 1680, 1609, 1494, 1343, 1224, 918, 759, 624 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.42–7.25 (m, 5 H_{arom}), 5.65 (dd, *J* = 11.1, 8.3 Hz, 1 H, HCON), 4.20 (s, 2 H, CH_2Br), 3.54 (dd, *J* = 17.1, 10.9 Hz, 1 H, CH_2), 3.11 (dd, *J* = 16.8, 8.5 Hz, 1 H, CH_2).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 154.59 (C), 140.17 (CH), 128.75 (CH), 128.37 (C), 125.80 (CH), 83.31 (CH), 42.65 (CH_2) 23.65 (CH_2).

MS (EI): *m*/*z* = 241 $[M]^+$, 211, 160, 148, 129, 104, 91, 78, 43.

HRMS: *m*/*z* $[M^+]$ Calcd for $C_{10}H_{10}{}^{81}BrNO$, 243.0083. Found: 243.0079.

3-Iodomethyl-5-phenylisoxazoline (7)

According to GP 1, from **1** (0.2 g, 1.2 mmol) and *N*-iodosuccinimide (0.83 g, 3.7 mmol) in CH_2Cl_2 (15 mL). FC (MTBE–pentane, 1:9) afforded **7**; yield: 196 mg (containing starting material and other impurities).

^1H NMR (200 MHz, $CDCl_3$): δ = 7.39–7.25 (m, 5 H_{arom}), 5.60 (dd, *J* = 11.0, 8.5 Hz, 1 H, HCON), 4.10 (s, 2 H, CH_2I), 3.58 (dd, *J* = 16.8, 11.0 Hz, 1 H, CH_2), 3.15 (dd, *J* = 17.0, 8.3 Hz, 1 H, CH_2).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 155.59 (C), 140.18 (CH), 128.74 (CH), 128.36 (CH), 127.48 (C), 82.98 (CH), 43.79 (CH_2), 43.16 (CH_2).

N-(1-Phenylbut-3-enyloxy)benzenesulfonamide (8)

O-(1-Phenylbut-3-enyl)hydroxylamine (**1**; 0.4 g, 2.5 mmol) and Et_3N (0.34 mL, 2.5 mmol) were dissolved in THF (10 mL). The solution was cooled to 0 °C, and benzenesulfonyl chloride (0.33 mL, 2.5 mmol) was added. The mixture was allowed to warm to r.t. and stirred for 3 d. After addition of H_2O, the mixture was extracted with Et_2O. The organic layer was separated, washed with H_2O and brine, and dried ($MgSO_4$). Evaporation of the solvent and purification by FC (MTBE–pentane, 1:10) afforded **8**; yield: 640 mg (84%).

IR (KBr): 3207, 1449, 1385, 1347, 1173, 751, 684 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.94–7.89 (m, 2 H_{arom}), 7.65–7.52 (m, 3 H_{arom}), 7.34–7.23 (m, 5 H_{arom}), 6.79 (s, 1 H, NH), 5.86–5.66 (m, 1 H, CH_2=C*H*), 5.12–4.99 (m, 3 H, HCO, CH=CH_2), 2.67–2.38 (m, 2 H, CH_2).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 139.47 (C), 139.66 (C), 133.74 (CH), 133.69 (CH), 128.96 (CH), 128.62 (CH), 128.42 (CH), 128.29 (CH), 127.11 (CH), 117.66 (CH_2), 88.07 (CH), 39.62 (CH_2).

MS (EI): *m*/*z* =: 262 $[M – allyl]^+$, 131, 91, 77, 41.

Anal. Calcd for $C_{16}H_{17}NO_3S$ (303.38): C, 63.34; H, 5.65; N, 4.62. Found: C, 63.00; H, 5.32; N, 4.28.

N-Phenylsulfonylisoxazolidines 9–12 and *N*-Acetylisoxazolidines 17, 20, 21, 24, and 25; General procedure (GP 2)

The alkoxysulfonamide **8** or alkoxyacetamide **13**, **22**, **23** was dissolved in CH_2Cl_2, $CHCl_3$ or MeCN. A solution of the electrophile in CH_2Cl_2 or MeCN was added at r.t. After stirring at r.t. for 24 h, sat. aq $Na_2S_2O_3$ was added. The organic layer was separated,

washed with sat. aq $NaHCO_3$ and brine, and dried ($MgSO_4$). After evaporation of the solvent the crude product was purified by FC.

2-Benzenesulfonyl-3-chloromethyl-5-phenylisoxazolidine (9)
According to GP 2, from **8** (0.2 g, 0.66 mmol), NaOCl (13% in H_2O, 0.4 mL, 0.7 mmol) and glacial AcOH (0.11 mL, 1.9 mmol) in $CHCl_3$ (5 mL). FC (MTBE–pentane, 1:9) afforded **9**; yield: 140 mg (61%) as a mixture of two diastereoisomers [dr (*cis*/*trans*) = 4.4: 1]. The ratio was determined by ^{1}H NMR spectroscopy of the crude product.

IR (KBr): 3066, 1698, 1453, 1330, 1214, 1156, 768, 728, 611 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ (*cis*-isomer) = 7.95–7.93 (m, 2 H_{arom}), 7.65–7.36 (m, 3 H_{arom}), 7.30–7.11 (m, 5 H_{arom}), 5.10 (dd, *J* = 12.8, 9.6 Hz, 1 H, HCON), 4.58 (m, 1 H, HCN), 3.85 (dd, *J* = 10.9, 4.8 Hz, 1 H, $ClCH_2$), 3.59 (dd, *J* = 10.9, 8.5 Hz, 1 H, $ClCH_2$), 2.83–2.78 (m, 1 H, CH_2), 2.28–2.18 (m, 1 H, CH_2); δ (*trans*-isomer) = 7.95–7.93 (m, 2 H_{arom}), 7.65–7.36 (m, 3 H_{arom}), 7.30–7.11 (m, 5 H_{arom}), 4.95 (dd, *J* = 10.6, 2.8 Hz, 1 H, HCON), 4.44–4.41 (m, 1 H, HCN), 3.74 (dd, *J* = 11.3, 5.1 Hz, 1 H, $ClCH_2$), 3.64 (dd, *J* = 6.8, 4.6 Hz, 1 H, $ClCH_2$), 2.66–2.63 (m, 1 H, CH_2), 2.41–2.38 (m, 1 H, CH_2).

^{13}C NMR (50 MHz, $CDCl_3$): δ (*cis*-isomer) = 135.89 (C), 134.14 (CH), 129.24 (CH), 129.16 (CH), 128.98 (CH), 128.67 (CH), 126.87 (CH), 83.66 (CH), 60.93 (CH), 46.54 (CH_2), 41.35 (CH_2).

MS (EI): *m*/*z* =142 $[PhSO_2]^+$, 107, 79, 44.

Anal. Calcd for $C_{16}H_{16}ClNO_3S$ (337.82): C, 56.89; H, 4.77; N, 4.15. Found: C, 56.72; H, 5.01; N, 3.97.

2-Benzenesulfonyl-5-phenyl -3-phenylselenylmethylisoxazolidine (10)
According to GP 2, from **8** (0.1 g, 0.33 mmol), phenylselenyl bromide (0.12 g, 0.5 mmol) and Na_2CO_3 (100 mg) in MeCN (25 mL). FC (MTBE–pentane, 1:9) afforded **10**: 110 mg (73%) as a mixture of two diastereoisomers [dr (*cis*/*trans*) = 3.8: 1]. The ratio was determined by ^{1}H NMR spectroscopy of the crude product.

IR (film): 3026, 1671, 1448, 1361, 1171, 741, 691, 599 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ (*cis*-isomer) = 7.89–7.77 (m, 2 H_{arom}), 7.63–7.44 (m, 5 H_{arom}), 7.33–7.21 (m, 8 H_{arom}), 4.95 (dd, *J* = 10.5, 5.8 Hz, 1 H, HCON), 4.52–4.40 (m, 1 H, HCN), 3.56 (dd, *J* = 12.5, 4.5 Hz, 1 H, $SeCH_2$), 3.12 (dd, *J* = 12.6, 9.2 Hz, 1 H, $SeCH_2$), 2.90–2.77 (m, 1 H, CH_2), 2.24–2.09 (m, 1 H, CH_2); δ (*trans*-isomer) = 7.81–7.79 (m, 2 H_{arom}), 7.63–7.44 (m, 5 H_{arom}), 7.33–7.21 (m, 8 H_{arom}), 5.16 (dd, *J* = 15.5, 5.7 Hz, 1 H, HCON), 4.40–4.30 (m, 1 H, HCN), 3.46 (dd, *J* = 12.8, 4.8 Hz, 1 H, $SeCH_2$), 3.16–3.02 (m, 1 H, $SeCH_2$), 2.60–2.45 (m, 1 H, CH_2), 2.16–2.13 (m, 1 H, CH_2).

^{13}C NMR (50 MHz, $CDCl_3$): δ (*cis*-isomer) = 136.11 (C), 135.46 (CH), 133.90 (CH), 133.03 (CH), 132.73 (C), 129.53 (C), 129.28 (CH), 129.18 (CH), 129.02 (CH), 128.91 (CH), 128.81 (CH), 128.56 (CH), 127.28 (CH), 127.06 (CH), 126.81 (CH), 83.42 (CH), 61.00 (CH), 43.15 (CH_2), 32.51 (CH_2).

MS (EI): *m*/*z* = 317 $[M - SO_2Ph]^+$, 117, 106, 91, 73, 57, 43.

Anal Calcd for $C_{22}H_{21}NO_3SSe$ (458.43): C, 57.64; H, 4.62; N, 3.06. Found: C, 58.00; H, 4.91; N, 2.89.

2-Benzenesulfonyl-3-bromomethyl-5-phenylisoxazolidine (11)
According to GP 2, from **8** (0.1 g, 0.33 mmol) and *N*-bromosuccinimide (0.066 g, 0.33 mmol) in CH_2Cl_2 (15 mL). FC (MTBE–pentane, 1:9) afforded **11**; yield: 99 mg (79%) as a mixture of two diastereoisomers [dr (*cis*/*trans*) = 4.8: 1]. The ratio was determined by ^{1}H NMR spectroscopy of the crude product.

IR (KBr): 3442, 1495, 1292, 1155, 886, 766, 617 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ (*cis*-isomer) = 8.04–7.92 (m, 2 H_{arom}), 7.67–7.51 (m, 3 H_{arom}), 7.35–7.25 (m, 5 H_{arom}), 5.12 (dd, *J* = 10.5, 5.7 Hz, 1 H, HCON), 4.74–4.59 (m, 1 H, HCN), 3.79 (dd, *J* = 10.1, 4.7 Hz, 1 H, $BrCH_2$), 3.52 (dd, *J* = 9.5, 9.5 Hz, 1 H, $BrCH_2$), 2.97–2.84 (m, 1 H, CH_2), 2.33–2.18 (m, 1 H, CH_2); δ (*trans*-isomer) = 8.04–7.52 (m, 2 H_{arom}), 7.67–7.59 (m, 3 H_{arom}), 7.35–7.25 (m, 5 H_{arom}), 5.20 (dd, *J* = 11.5, 5.8 Hz, 1 H, HCON), 4.59–4.43 (m, 1 H, HCN), 3.70 (dd, *J* = 10.1, 4.8 Hz, 1 H, $BrCH_2$), 3.52–3.02 (m, 1 H, $BrCH_2$), 2.68–2.58 (m, 1 H, CH_2), 2.20–2.08 (m, 1 H, CH_2).

^{13}C NMR (50 MHz, $CDCl_3$): δ (both isomers) = 135.73 (C), 135.53 (CH), 134.14 (CH), 129.19 (CH), 129.15 (CH), 128.98 (CH), 128.64 (CH), 128.54 (CH), 127.12 (C), 126.85 (CH), 83.74 (CH), 82.36 (CH), 62.23 (CH), 60.85 (CH), 42.43 (CH_2), 39.64 (CH_2), 34.74 (CH_2), 33.00 (CH_2).

MS (EI): *m*/*z* = 383 $[M]^+$, 288, 257, 242, 211, 141, 131, 104, 91, 77, 40.

Anal. Calcd for $C_{16}H_{16}BrNO_3S$ (382.27): C, 50.27; H, 4.22; N, 3.66. found: C, 49.86; H, 3.95; N, 3.36.

2-Benzenesulfonyl-3-iodomethyl-5-phenylisoxazolidine (12)
According to GP 2, from **8** (0.1 g, 0.33 mmol) and *N*-iodosuccinimide (0.083 g, 0.33 mmol) in CH_2Cl_2 (15 mL). FC (MTBE–pentane, 9:1) afforded **12**: 99 mg (70%) as a mixture of two diastereoisomers [dr (*cis*/*trans*) = 5.0: 1]. The ratio was determined by ^{1}H NMR spectroscopy of the crude product.

IR (KBr): 3445, 1454, 128, 1160, 883, 766 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ (*cis*-isomer) = 8.03–7.99 (m, 2 H_{arom}), 7.71–7.53 (m, 3 H_{arom}), 7.32–7.26 (m, 5 H_{arom}), 5.13 (dd, *J* = 10.5, 5.5 Hz, 1 H, HCON), 4.65–4.56 (m, 1 H, HCN), 3.61 (dd, *J* = 9.8, 4.3 Hz, 1 H, ICH_2), 3.37 (dd, *J* = 9.5, 9.5 Hz, 1 H, ICH_2), 3.00–2.87 (m, 1 H, CH_2), 2.56–2.10 (m, 1 H, CH_2); δ (*trans*-isomer) = 8.04–7.52 (m, 2 H_{arom}), 7.67–7.59 (m, 3 H_{arom}), 7.35–7.25 (m, 5 H_{arom}), 5.21 (dd, *J* = 11.2, 5.7 Hz, 1 H, HCON), 4.55–4.42 (m, 1 H, HCN), 3.55–3.50 (m, 1 H, ICH_2), 3.35 (dd, *J* = 10.0, 10.0 Hz, 1 H, ICH_2), 2.67–2.58 (m, 1 H, CH_2), 2.26–2.06 (m, 1 H, CH_2).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 135.74, 135.58, 134.12 (CH), 129.21 (CH), 129.15 (CH), 128.99 (C), 128.65 (CH), 126.87 (CH), 83.91 (CH), 61.21 (CH), 44.14 (CH_2), 8.62 (CH_2).

MS (EI): *m*/*z* = 429 $[M]^+$, 288, 257, 131, 104, 91, 77, 40.

Anal. Calcd for $C_{16}H_{16}INO_3S$ (429.27): C, 44.77; H, 3.76; N, 3.26. Found: C, 44.38; H, 4.07; N, 3.13.

***N*-Acetylalkoxyamines 13, 22, and 23; General Procedure (GP 3)**
The alkoxyamine and Et_3N were dissolved in THF and cooled to 0 °C. AcCl was added and stirring was continued for 30 min at 0 °C. After addition of H_2O, the mixture was extracted with Et_2O. The organic layer was separated, washed with H_2O and brine, and dried ($MgSO_4$). After evaporation of the solvent the crude product was purified by recrystallization or FC.

***N*-(1-Phenylbut-3-enyloxy)acetamide (13)**
According to GP 3, from **1** (1.47 g, 9 mmol), Et_3N (1.23 mL, 9 mmol) and AcCl (0.59 mL, 9 mmol) in THF (15 mL). Recrystallization (MTBE–pentane, 1:1) afforded **13**; yield: 1.56 g (92%).

IR (KBr): 3447, 3143, 2945, 1660, 1528, 1358, 1071, 999, 925, 760, 702 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ (mixture of rotamers) = 8.30 (br s, 1 H, NH, rotamer A), 7.79 (br s, 1 H, NH, rotamer B), 7.27–7.26 (m, 5 H_{arom}, rotamer A + B), 5.74–5.66 (m, 1 H, CH_2=C*H*, rotamer A + B), 5.05–4.58 (m, 3 H, HCO, CH=CH_2, rotamer A + B), 2.69–2.66

(m, 1 H, CH_2, rotamer A), 2.50–2.39 (m, 1 H, CH_2, rotamer B), 1.95 (br s, 1 H, CH_3, rotamer B), 1.68 (br s, 1 H, CH_3, rotamer A).

^{13}C NMR (50 MHz, $CDCl_3$): δ (mixture of rotamers) = 167.60 (C, rotamer A + B), 139.33 (C, rotamer A + B), 133.17 (CH, rotamer A + B), 128.34 (CH, rotamer A + B), 118.15 (CH_2, rotamer B), 117.54 (CH_2, rotamer A), 88.52 (CH, rotamer B), 86.47 (CH, rotamer A), 39.44 (CH_3, rotamer A + B), 19.59 (CH_2, rotamer A + B).

MS (EI): *m*/*z* = 205 $[M]^+$, 164, 131, 116, 105, 91, 77, 43.

HRMS: *m*/*z* $[M^+]$ Calcd for $C_{12}H_{15}NO_2$, 205.1102. Found: 205.1093.

2-Acetyl-3-iodomethyl-5-phenylisoxazolidine (17)
According to GP 2, from **13** (0.2 g, 1.0 mmol) and *N*-iodosuccinimide (0.25 g, 1.1 mmol) in CH_2Cl_2 (15 mL). FC (MTBE–pentane, 1:1) afforded *cis*-**17**; yield: 250 mg (76%) and *trans*-**17**; yield: 20 mg (6%) [dr (*cis*/*trans*) = 12.5: 1].

IR (film): 3038, 1745, 1668, 1385, 1336, 1032, 761, 699 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ (*cis*-isomer) = 7.45–7.39 (m, 5 H_{arom}), 4.92 (dd, *J* = 8.6, 5.8 Hz, 1 H, HCON), 4.71–4.57 (m, 1 H, HCN), 3.56 (dd, *J* = 9.8, 3.7 Hz, 1 H, ICH_2), 3.35 (dd, *J* = 9.5, 8.6 Hz, 1 H, ICH_2), 3.02–2.89 (m, 1 H, CH_2), 2.29–2.14 (m, 1 H, CH_2), 2.18 (s, 3 H, CH_3); δ (*trans*-isomer) = 7.44–7.27 (m, 5 H_{arom}), 5.35 (dd, *J* = 6.6, 5.5 Hz, 1 H, HCON), 4.76–4.63 (m, 1 H, HCN), 3.58 (dd, *J* = 9.8, 3.7 Hz, 1 H, ICH_2), 3.34 (dd, *J* = 9.2, 9.2 Hz, 1 H, ICH_2), 2.84–2.70 (m, 1 H, CH_2), 2.66–2.54 (m, 1 H, CH_2), 1.88 (s, 3 H, CH_3).

^{13}C NMR (50 MHz, $CDCl_3$): δ (*cis*-isomer) = 171.69 (C), 135.70 (C), 129.10 (CH), 128.78 (CH), 126.72 (CH), 83.97 (CH), 57.88 (CH), 43.92 (CH_2), 20.48 (CH_3), 9.03 (CH_2).

MS (EI): *m*/*z* = 331 $[M]^+$, 289, 257, 231, 162, 148, 130, 104, 91, 43.

HRMS: *m*/*z* $[M^+]$ Calcd for $C_{12}H_{14}INO_2$, 331.0069. Found: 331.0075.

2-Acetyl-5-phenyl -3-phenylselenylmethylisoxazolidine (20)
According to GP 2, from **13** (0.2 g, 1.0 mmol), phenylselenyl bromide (0.36. g, 1.0 mmol) and Na_2CO_3 (300 mg) in MeCN (15 mL). FC (MTBE–pentane, 1:1) afforded *cis*-**20**; yield: 240 mg (66%) and *trans*-**20**; yield: 57 mg (16%) [dr (*cis*/*trans*) = 4.2: 1].

IR (film): 2935, 1666, 1386, 1034, 739, 698 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ (*cis*-isomer) = 7.59–7.55 (m, 2 H_{arom}), 7.40–7.39 (m, 5 H_{arom}), 7.28–7.25 (m, 3 H_{arom}), 4.86 (dd, *J* = 15.8, 9.0 Hz, 1 H, HCON), 4.76–4.70 (m, 1 H, HCN), 3.49 (dd, *J* = 18.8, 6.4 Hz, 1 H, PhSeCH_2), 3.10 (dd, *J* = 18.6, 12.8 Hz, 1 H, PhSeCH_2), 2.96–2.86 (m, 1 H, CH_2), 2.32–2.17 (m, 1 H, CH_2), 2.10 (s, 3 H, CH_3); δ (*trans*-isomer) = 7.60–7.58 (m, 2 H_{arom}), 7.46–7.7 (m, 8 H_{arom}), 5.33–5.29 (m, 1 H, HCON), 4.88–4.70 (m, 1 H, HCN), 3.53–3.49 (m, 1 H, PhSeCH_2), 3.12–3.02 (m, 1 H, PhSeCH_2), 2.70–2.57 (m, 2 H, CH_2), 1.85 (s, 3 H, CH_3).

^{13}C NMR (50 MHz, $CDCl_3$): δ (*cis*-isomer) = 132.44 (CH), 129.19 (CH), 128.99 (CH), 128.75 (CH), 127.06 (CH), 126.73 (CH), 83.77 (CH), 57.27 (CH), 42.89 (CH_2), 31.71 (CH_3), 20.44 (CH_2).

MS (EI): *m*/*z* = 361 $[M]^+$, 286, 204, 164, 148, 129, 104, 91, 56, 43.

HRMS: *m*/*z* $[M^+]$ Calcd for $C_{18}H_{19}SeNO_2$, 361.0581. Found: 361.0581.

2-Acetyl-3-bromomethyl-5-phenylisoxazolidine (21)
According to GP 2, from **13** (0.2 g, 1.0 mmol) and *N*-bromosuccinimide (0.180 g, 1.0 mmol) in CH_2Cl_2 (15 mL). FC (MTBE–pentane, 1:1) afforded *cis*-**21**; yield: 180 mg (64%) and *trans*-**21**; yield: 38 mg (13%) [dr (*cis*/*trans*) = 4.7: 1].

IR (film): 3445, 1666, 1375, 912, 734 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ (*cis*-isomer) = 7.45–7.40 (m, 5 H_{arom}), 4.91 (dd, *J* = 10.6, 6.0 Hz, 1 H, HCON), 4.84–4.72 (m, 1 H, HCN), 3.74 (dd, *J* = 10.0, 4.0 Hz, 1 H, $BrCH_2$), 3.51 (dd, *J* = 9.9, 8.0 Hz, 1 H, $BrCH_2$), 2.99–2.86 (m, 1 H, CH_2), 2.41–2.25 (m, 1 H, CH_2), 2.19 (s, 3 H, CH_3); δ (*trans*-isomer) = 7.37–7.27 (m, 5 H_{arom}), 5.35 (dd, *J* = 5.6, 5.6 Hz, 1 H, HCON), 4.81–4.80 (m, 1 H, HCN), 3.74 (dd, *J* = 9.9, 3.4 Hz, 1 H, $BrCH_2$), 3.53 (dd, *J* = 9.0, 9.0 Hz, 1 H, $BrCH_2$), 2.74–2.71 (m, 2 H, CH_2), 1.89 (s, 3 H, CH_3).

^{13}C NMR (50 MHz, $CDCl_3$): δ (*cis*-isomer) = 172.07 (C), 135.73 (C), 129.09 (CH), 128.77 (CH), 126.69 (CH), 83.81 (CH), 57.60 (CH), 42.05 (CH_2), 34.48 (CH_3), 20.41 (CH_2); δ (*trans*-isomer) = 137.15 (C), 129.02 (CH), 128.87 (CH), 126.82 (CH), 81.67 (CH), 57.08 (CH), 38.85 (CH_2), 33.63 (CH_3), 20.63 (CH_2).

MS (EI): *m*/*z* = 283 $[M]^+$, 243, 209, 186, 148, 129, 104, 91, 43.

HRMS: *m*/*z* $[M^+]$ Calcd for $C_{12}H_{14}BrNO_2$, 283.0208. Found: 283.0203.

***N*-(1-Methylbut-3-enyloxy)acetamide (22)**
According to GP 3, from *O*-(1-methylbut-3-enyl)hydroxylamine (150 mg, 1.49 mmol), Et_3N (0.21 mL, 1.49 mmol) and AcCl (0.12 mL, 1.49 mmol) in THF (10 mL). FC (MTBE–pentane, 8:2) afforded **22**; yield: 130 mg (52%).

IR (film): 3197, 1669, 1523, 1373, 1084, 993 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ (mixture of rotamers) = 9.53 (br s, 1 H, NH, rotamer A), 8.99 (br s, 1 H, NH, rotamer B), 5.87–5.73 (m, 1 H, CH_2=C*H*, rotamer A + B), 5.13–5.08 (m, 2 H, CH=CH_2, rotamer A + B), 4.03–4.02 (m, 1 H, HCO, rotamer A), 3.91 (br s, 1 H, HCO, rotamer B), 2.48–2.44 (m, 1 H, CH_2, rotamer A + B), 2.28–2.23 (m, 1 H, CH_2, rotamer A + B), 2.06 (s, 1 H, H_3CCO, rotamer B), 1.93 (s, 1 H, H_3CCO, rotamer A), 1.24 (br s, 1 H, CH_3, rotamer A + B).

^{13}C NMR (75 MHz, $CDCl_3$): δ (mixture of rotamers) = 168.37 (C, rotamer A + B), 133.91 (CH, rotamer A), 133.39 (CH, rotamer B), 117.96 (CH_2, rotamer B), 117.33 (CH_2, rotamer A), 81.83 (CH, rotamer B), 80.76 (CH, rotamer A), 38.94 (CH_3, rotamer A + B), 19.75 (CH_2, rotamer A), 19.47 (CH_2, rotamer B), 17.89 (CH_3, rotamer A + B).

MS (EI): *m*/*z* = 143 $[M^+]$, 102, 84, 68, 58, 41.

***N*-(1-Cyclohexylbut-3-enyloxy)acetamide (23)**
According to GP 3, from *O*-(1-cyclohexylbut-3-enyl)hydroxylamine (100 mg, 0.6 mmol), Et_3N (0.083 mL, 0.6 mmol) and AcCl (0.043 mL, 0.6 mmol) in THF (5 mL). FC (MTBE–pentane, 1:2) afforded **23**; yield: 120 mg (95%).

IR (film): 2927, 1749, 1673, 1449, 1373, 888 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.93 (br s, 1 H, NH), 6.05–5.76 (m, 1 H, CH_2=C*H*), 5.17–5.08 (m, 2 H, CH=CH_2), 3.66–3.60 (m, 1 H, HCO), 2.43–2.32 (m, 2 H, CH_2), 2.10–1.06 (m, 14 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 135.22 (CH), 117.61 (CH_2), 89.85 (CH), 39.61 (CH_3), 34.04 (CH_2), 28.52 (CH_2), 28.47, 26.44 (CH_2), 26.21 (CH_2), 19.96.

MS (EI): *m*/*z* = 211 $[M^+]$, 170, 152, 137, 95, 81, 55.

2-Acetyl-3-iodomethyl-5-methylisoxazolidine (24)
According to GP 2, from **22** (114 g, 0.8 mmol) and *N*-iodosuccinimide (198 g, 0.88 mmol) in CH_2Cl_2 (15 mL). FC (MTBE–pentane, 7:3) afforded *cis*-**24**; yield: 125 mg (58%) and *trans*-**24**; yield: 11 mg (5%) [dr (*cis*/*trans*) = 11.3: 1].

IR (film): 2977, 1662, 1395, 1223, 1104, 1037 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ (*cis*-isomer) = 4.54–4.48 (m, 1 H, HCN), 4.09–4.01 (m, 1 H, HCON), 3.50–3.47 (m, 1 H, ICH_2), 3.23–3.17 (m, 1 H, ICH_2), 2.77–2.65 (m, 1 H, CH_2), 2.12 (s, 3 H,

H_3CCO), 1.80–1.67 (m, 1 H, CH_2), 1.39 (d, J = 5.9, 3 H, CH_3); δ (*trans*-isomer) = 4.83–4.67 (m, 1 H, HCN) 4.19–4.09 (m, 1 H, HCON), 3.41–3.15 (m, 2 H, ICH_2), 2.01 (s, 3 H, H_3CCO), 1.99–1.76 (m, 2 H, CH_2), 1.18 (d, J = 6.2, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ (*cis*-isomer) = 78.67 (CH), 57.77 (CH), 43.26 (CH_2), 20.33 (CH_3), 17.26 (CH_3), 8.95 (CH_2).

MS (EI): *m*/*z* = 269 [M^+], 227, 162, 128, 86, 43.

2-Acetyl-3-iodomethyl-5-cyclohexylisoxazolidine (25)

According to GP 2, from **23** (0.1 g, 0.47 mmol) and *N*-iodosuccinimide (0.118 g, 0.52 mmol) in CH_2Cl_2 (15 mL). FC (MTBE–pentane, 1:1) afforded *cis*-**25**; yield: 108 mg (68%) and *trans*-**25**; yield: 10 mg (6%) [dr (*cis*/*trans*) = 10.8: 1].

IR (film): 3194, 2927, 1665, 1450, 1083, 991 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ (*cis*-isomer) = 4.52–4.50 (m, 1 H, HCN), 3.63–3.62 (m, 1 H, HCON), 3.48–3.46 (m, 1 H, ICH_2), 3.21–3.15 (m, 1 H, ICH_2), 2.62–2.54 (m, 1 H, CH_2), 2.10 (s, 3 H, CH_3), 1.99–1.95 (m, 1 H, CH_2), 1.84–1.03 (m, 11 H); δ (*trans*-isomer) = 4.52–4.39 (m, 1 H, HCN), 4.00–3.95 (m, 1 H, HCON), 3.55–3.52 (m, 1 H, ICH_2), 3.253.19 (m, 1 H, ICH_2), 2.38–2.20 (m, 2 H), 2.11 (s, 3 H, CH_3), 1.961.92 (m, 1 H, CH_2), 1.75–0.96 (m, 10 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ (*cis*-isomer) = 87.08 (CH), 57.44 (CH), 40.39 (CH_3), 39.56 (CH_2), 29.82 (CH_2), 28.68 (CH_2), 26.11 (CH_2), 25.65 (CH_2), 25.36 (CH_2), 20.21 (CH), 9.17 (CH_2); δ (*trans*-isomer) = 84.44 (CH), 56.70 (CH), 40.61 (CH_3), 37.21 (CH_2), 29.92 (CH_2), 28.57 (CH_2), 26.10 (CH_2), 25.67 (CH_2), 25.43 (CH_2), 20.79 (CH), 7.81 (CH_2).

MS (EI) *m*/*z* = 337 [$M]^+$, 295, 252, 186, 154, 110, 67, 43.

Acknowledgement

We thank the Fonds der Chemischen Industrie for supporting our research.

References

(1) (a) Cardillo, G.; Orena, M. *Tetrahedron* **1990**, *46*, 3321. (b) Frederickson, M.; Grigg, R. *Org. Prep. Proced. Int.* **1997**, *29*, 33. (c) Robin, S.; Rousseau, G. *Tetrahedron* **1998**, *54*, 13681. (d) Wirth, T. *Angew. Chem., Int. Ed.* **2000**, *39*, 3740. (e) Tiecco, M. *Top. Curr. Chem.* **2000**, *208*, 7.

(2) (a) Cooper, M. A.; Ward, D. A. *Tetrahedron Lett.* **1992**, *33*, 5999. (b) Cooper, M. A.; Ward, A. D. *Tetrahedron Lett.* **1994**, *35*, 5065.

(3) (a) Balko, T. W.; Brinkmeyer, R. S.; Terando, N. H. *Tetrahedron Lett.* **1989**, *30*, 2045. (b) Betancor, C.; León, E. I.; Prange, T.; Salazar, J. A.; Suárez, E. *J. Chem. Soc., Chem. Commun.* **1989**, 450.

(4) (a) Tiecco, M.; Testaferri, L.; Marini, F.; Bagnoli, L.; Santi, C.; Temperini, A. *Tetrahedron* **1997**, *53*, 4441. (b) Ternon, M.; Outurquin, F.; Paulmier, C. *Tetrahedron* **2001**, *57*, 10259.

(5) (a) Wilson, S. R.; Sawicki, R. A. *J. Org. Chem.* **1979**, *44*, 287. (b) Tokuda, M.; Yamada, Y.; Suginome, H. *Chem. Lett.* **1988**, 1289. (c) Raner, K. D.; Ward, A. D. *Aust. J. Chem.* **1991**, *44*, 1749. (d) Ferraz, H. M. C.; de Oliveira, E. O.; Payret-Arrua, M. E.; Brandt, C. A. *J. Org. Chem.* **1995**, *60*, 7357.

(6) Robin, S.; Rousseau, G. *Tetrahedron* **1998**, *54*, 13681.

(7) (a) Grigg, R.; Hadjisoteriou, M.; Kennewell, P.; Markandu, J.; Thornton-Pett, M. *J. Chem. Soc., Chem. Commun.* **1993**, 1340. (b) Tiecco, M.; Testaferri, L.; Tingoli, M.; Bagnoli, L. *J. Chem. Soc., Chem. Commun.* **1995**, 235. (c) Tiecco, M.; Testaferri, L.; Tingoli, M.; Bagnoli, L.; Santi, C. *Tetrahedron* **1995**, *51*, 1277. (d) Tiecco, M.; Testaferri, L.; Marini, F.; Sternativo, S.; Santi, C.; Bagnoli, L.; Temperini, A. *Tetrahedron: Asymmetry* **2001**, *12*, 3053.

(8) (a) Tiecco, M.; Testaferri, L.; Tingoli, M.; Santi, C. *Tetrahedron Lett.* **1995**, *36*, 163. (b) Tiecco, M.; Testaferri, L.; Tingoli, M.; Marini, F. *J. Chem. Soc., Chem. Commun.* **1995**, 237.

(9) Janza, B. unpublished results.

(10) To the best of our knowledge, there is only one report describing the electrophilic cyclisation of homoallyloxyamines, see Ref.[8b]

(11) (a) Mitsunobu, O.; Wada, M.; Sano, T. *J. Am. Chem. Soc.* **1972**, *94*, 679. (b) Grochowski, E.; Jurczak, J. *Synthesis* **1976**, 682. (c) Ishikawa, T.; Kawakami, M.; Fukui, M.; Yamashita, A.; Urano, J.; Saito, S. *J. Am. Chem. Soc.* **2001**, *123*, 7734.

(12) Similar electrophilic cyclisation/oxidation reactions have been observed in Se-induced 5-*endo*-type cyclisations of hydrazines, see Ref.[4b]

(13) Ternon, M.; Outurquin, F.; Paulmier, C. *Tetrahedron* **2001**, *57*, 10259.

(14) Caramella, P.; Grünager, P. *1,3-Dipolar Cycloaddition Chemistry*, Vol. 1; Wiley-Interscience: New York, **1984**, 291.

(15) Nitrile oxides can formally be regarded as aldol products, see: Curran, D. P. *Adv. Cycloadd.* **1988**, *1*, 129.

(16) Fuller, A. E.; Hickinbottom, W. J. *J. Chem. Soc.* **1965**, 3228.

(17) Glover, S. A. *Tetrahedron* **1998**, *54*, 7229.

(18) All the cyclisations were performed using racemic olefins. In the schemes only one enantiomer is shown.