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A General Metal-Assisted Synthesis of α-Halo Oxime Ethers from Nitronates and Nitro Compounds

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An approach to the synthesis of α-halo oxime ethers from readily accessible nitronates and nitro compounds via bis(oxy)enamines is reported. A key step of the strategy involves the unprecedented reaction of bis(oxy)enamines with a metal (Co, Zn, Mg, Mn) halide that acts as both a promoter and halide (Br, I, Cl) source. A variety of cyclic and acyclic ethers of α-halo oximes, including previously unavailable trimethylsilyl ethers of α-iodo oximes, have been synthesized in good-to-high yields.

Introduction

α-Halo oximes and their ethers **1** (Figure 1) are widely used as versatile intermediates in organic synthesis as a result of their unique reactivity.[1] Acyclic α-halo oximes[1] and their silyl ethers[2] serve as the major precursors of conjugated nitrosoalkenes, which are an important class of heterodienes in Diels–Alder reactions.[1,2] Nucleophilic substitution of the halogen in oxime ethers **1** provides an easy route to various functionalized oxime derivatives.[3] Furthermore, α-halo oxime ethers **1** are convenient substrates for palladium-catalyzed C–C cross-coupling,[4a] catalytic carbonylation,[4b] and aza-Reformatsky reactions,[4c,4d] as well as for coupling with organic cuprates.[4e]

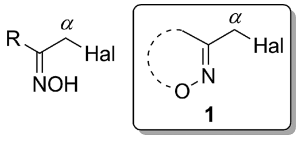

Figure 1. α-Halo oximes and their ethers **1**.

Subsequent reductive transformation of the oxime group provides access to a variety of polyfunctionalized nitrogen-containing products.[5] In this context, six-membered cyclic ethers of α-halo oximes are of special interest because they have proved to be useful intermediates in the stereoselective synthesis of unnatural β- and γ-amino acids,[6a,6b] functionalized pyrrolidines,[3f,6a] pyrroles,[3f] tetrahydrofurans,[6c] dihydrofurans,[6d] γ-lactams,[6e] and oxaazaspirononanones.[6f] Owing to their high synthetic potential, α-halo oxime ethers **1** have found widespread applications in the target-oriented synthesis of natural and bioactive molecules both in academia[1,7,8] and the pharmaceutical industry.[9]

Although synthetic approaches to α-halo oximes are well developed,[1j,2] the synthesis of their *O*-ethers **1**, especially cyclic ones, still represents a nontrivial task that lacks a general solution (e.g., see ref.[8a]). In this work, a general approach to the synthesis of cyclic and acyclic ethers of α-halo oximes **1** from nitronates or aliphatic nitro compounds has been developed.

Results and Discussion

Recently we reported the synthesis of six-membered cyclic ethers of α-halo oximes **1** by the silylation of readily accessible nitronates **2** employing an excess of halotrimethylsilane in the presence of a base [Scheme 1, Equation (1)].[3f,3g] In this process nitronate **2** is transformed into a cyclic bis(oxy)enamine (**3**) upon reaction of the first equivalent of the $(CH_3)_3SiHal$/base mixture [step (1)].[3h,3g] The reaction of bis(oxy)enamine **3** with a second equivalent of halotrimethylsilane affords the corresponding 3-halomethyl-5,6-dihydro-4*H*-1,2-oxazines **1** as a result of a formal S_N' substitution of the silyloxy group [step (2)].[3g] Our extensive studies over the last few years[3f,6] have revealed several substantial drawbacks to this method: 1) The targeted products are usually obtained in low-to-moderate yields (typically 35–60%) and their synthesis is poorly scalable;[3f] 2) the protocol is applicable only to six-membered

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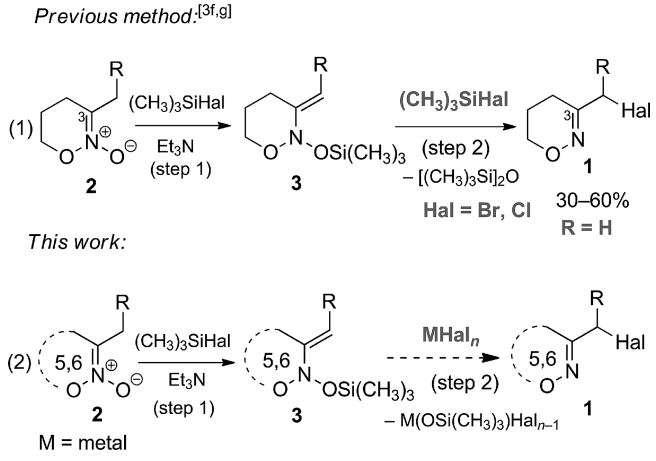
cyclic nitronates, with acyclic nitronates not affording the corresponding α-halo oxime ethers **1** upon silylation;[10] 3) only 3-methyl-substituted cyclic nitronates can efficiently undergo the process, in the case that R ≠ H [Scheme 1, Equation (1)] the desired products are formed in less than 20% yield;[3g] 4) only cyclic ethers of α-chloro and α-bromo oximes can be obtained, the synthesis of the corresponding iodides not being possible because of the highly reactive character of iodotrimethylsilane.[3g]



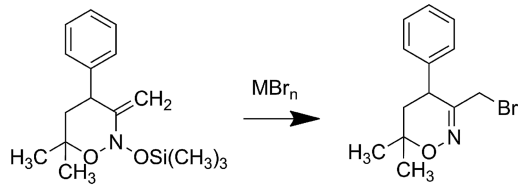
Scheme 1. Known and suggested approaches to the synthesis of α-halo oxime ethers **1** from nitronates **2**.

A more detailed study of process **2**→**1** revealed that limitations 1–3 are associated only with step (2) (Scheme 1). Thus, regardless of the nature of the initial cyclic nitronate **2**, bis(oxy)enamines **3** are produced in nearly quantitative yields in step (1).[3g,3h] Furthermore, step (1) also proceeds smoothly for five-membered and acyclic nitronates **2** leading to the corresponding cyclic and acyclic *N*,*N*-bis(oxy)enamines **3**.[10,11] We speculated that the replacement of halotrimethylsilane by less reactive metal halides in step (2) may allow the selectivity to be improved and the substrate scope of the process **3**→**1** to be expanded [Scheme 1, Equation (2)].

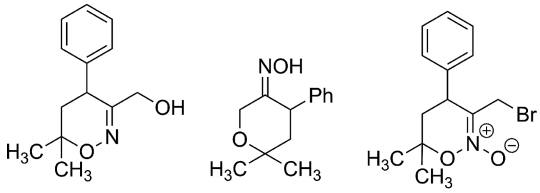
To validate this hypothesis, the interaction of model cyclic *N*,*N*-bis(oxy)enamine **3a** with a series of bromides of main group and transition metals as well as some non-metals was investigated (Table 1).

As expected, highly reactive non-metal bromides (HBr, PBr_3, Me_3SiBr) and $AlBr_3$ (Table 1, entries 1–4) led to the desired 3-bromomethyl-1,2-oxazine **1a** in poor yields accompanied by many byproducts among which cyclic oxime derivatives **4a** and **5a** were identified (for selective synthesis of these products from cyclic nitronates, see ref.[11a–11c]). On the other hand, triethylammonium bromide did not react with bis(oxy)enamine **3a** at all (Table 1, entry 5). Similarly, no conversion of the starting material was observed in the reaction with calcium bromide, and only traces of product **1a** were detected in the reaction of **3a** with LiBr (Table 1, entries 6 and 7). In contrast, magnesium and indium bromides furnished **1a** in relatively good yields (Table 1, entries 8 and 9). In the case of indium bromide, 3-hydroxy-substituted 1,2-oxazine **4a** (21%) was found to be the major by-

Table 1. Reaction of model enamine **3a** with metal and non-metal bromides.



Entry	MBr_n (equiv.)	Conditions (additive, solvent, temperature, time)	Yield of **1a** [%]
1	Me_3SiBr (1.5)	CH_3CN, –30 °C, 0.5 h[a]	65[a]
2	PBr_3 (1.0)	CH_2Cl_2, 20 °C, 2 h	30
3	$AlBr_3$ (1.0)	CH_2Br_2/CH_2Cl_2, 20 °C, 2 h	0[b]
4	HBr (2.0)	THF/CH_2Cl_2, H_2O, 20 °C, 1.5 h	33[c,d]
5	$Et_3NH^+Br^-$ (2.0)	THF/CH_2Cl_2, 20 °C, 2 h	0[e]
6	LiBr (2.0)	THF/CH_2Cl_2, 20 °C, 2 h	traces[c,f]
7	$CaBr_2$ (2.0)[g]	THF/CH_2Cl_2, 20 °C, 2 h	0[c]
8	$MgBr_2$ (2.0)	THF/CH_2Cl_2, 20 °C, 2 h	71
9	$InBr_3$ (1.0)	THF/CH_2Cl_2, 20 °C, 2 h	79[h]
10	$BiBr_3$ (1.0)	THF/CH_2Cl_2, 20 °C, 2 h	32[c]
11	$NiBr_2$ (2.0)	THF/CH_2Cl_2, 20 °C, 2 h	14[i]
12	$ZnBr_2$ (2.0)	THF/CH_2Cl_2, 20 °C, 2 h	74[j]
13	$MnBr_2$ (2.0)	DMF/CH_2Cl_2, 20 °C, 2 h	80[k]
14	$CuBr_2$ (2.0)	CH_3CN/CH_2Cl_2, 20 °C, 2 h	12[l]
15	$CoBr_2$ (2.0)	THF/CH_2Cl_2, 20 °C, 2 h	89[m]
16	$CoBr_2$ (0.5)	THF/CH_2Cl_2, 20 °C, 2 h	77[n]
17	$CoBr_2$ (2.0)	2 equiv. H_2O, THF/CH_2Cl_2, 20 °C, 2 h	89[c]
18	$CoBr_2$ (2.0)	MS 4 Å, THF/CH_2Cl_2, 20 °C, 2 h	88[c]
19	$CoBr_2$ (2.0)	4 equiv. Et_3N, THF/CH_2Cl_2, 20 °C, 2 h	90[c]
20	LiBr (2.0) + $CoBr_2$ (0.1)	THF/CH_2Cl_2, 20 °C, 2 h	26[o]



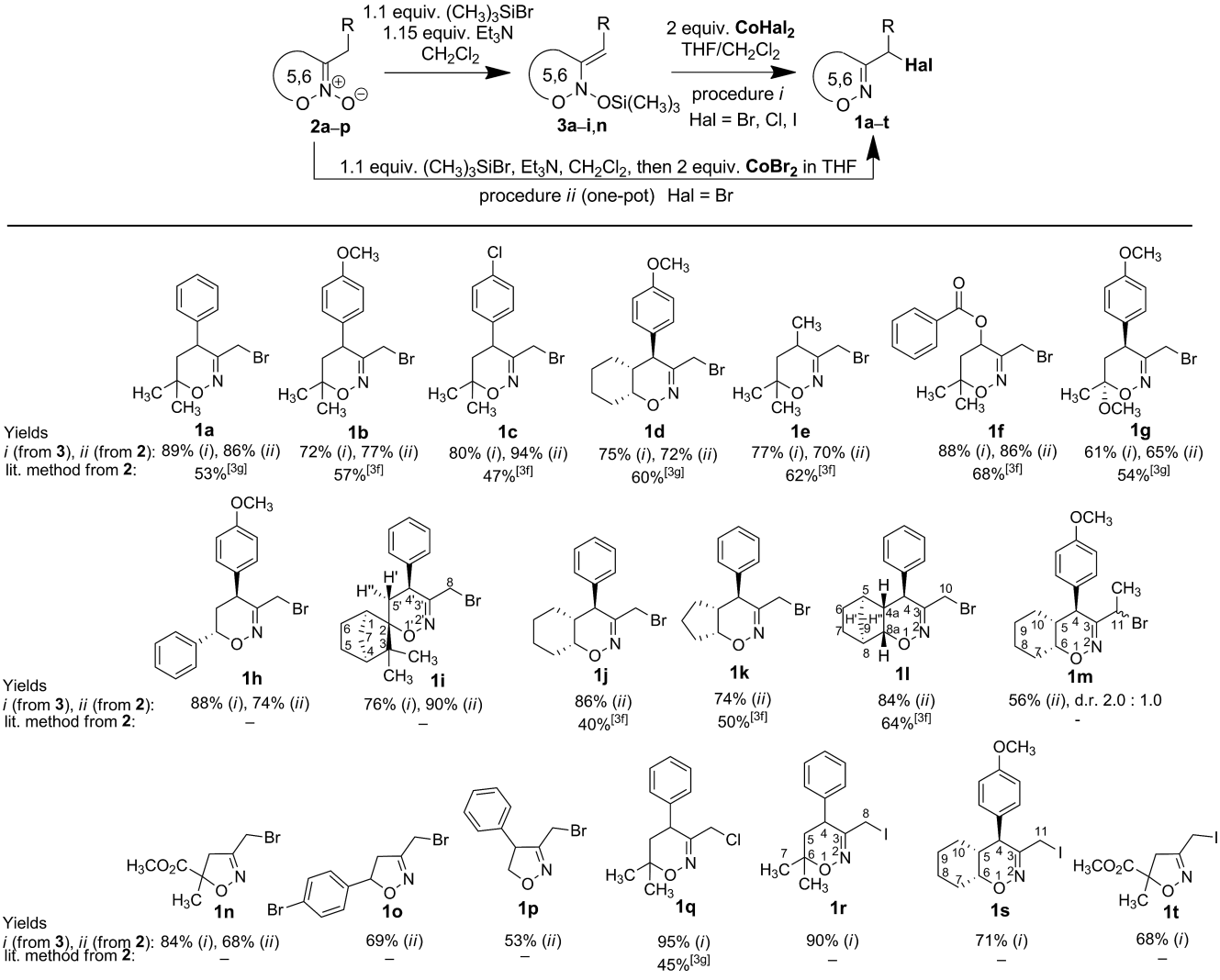
[a] See ref.[3g] [b] Complex mixture of products that contains 27% of **4a** and 13% of **5a**. [c] Yields determined by ^1H NMR spectroscopy by using an internal standard. [d] Yield of **4a**: 23%. [e] Conversion of **3a**: 0%. [f] Conversion of **3a**: 35%. [g] $CaBr_2 \cdot xH_2O$ ($x \leq 1$) was used. [h] Yield of **4a**: 21%. [i] Conversion of **3a**: 24%. [j] Yield of **4a**: 13%. [k] Yield of **4a**: 15%. [l] 3-Bromomethyl-substituted nitronate **6a** was isolated as the major product (27%). [m] Average of three experiments (±6%). [n] Conversion of **3a**: 95%. [o] Conversion of **3a**: 38%.

product after aqueous work-up. The reaction of bismuth bromide with **3a** produced a complex mixture of products that contained only about 30% of the desired bromide **1a** (Table 1, entry 10). Transition-metal bromides, which are softer Lewis acids, furnished product **1a** in high yields, with the exception of nickel(II) and copper(II) bromides. The low yield of **1a** and conversion of enamine **3a** in the reaction with $NiBr_2$ may be associated with its poor solubility in organic solvents (Table 1, entry 11). In the case of $CuBr_2$, the major product was found to be 3-bromomethyl-substituted cyclic nitronate **6a**, probably arising

from an electrophilic bromination of bis(oxy)enamine **3a** (Table 1, entry 14).[11d] The best result was obtained with anhydrous cobalt(II) bromide in THF (Table 1, entry 15).

Further studies revealed that 0.5 equiv. of $CoBr_2$ is enough for the formation of bromide **1a** in 77% yield, which indicates that both bromine atoms are transferred from the cobalt to the carbon atom (Table 1, entry 16; for the structure of the $CoBr_2$ species in THF solution, see ref.[12a]). However, the use of an excess of $CoBr_2$ slightly increased the yield of product **1a** (cf. entries 15 and 16 in Table 1). The reaction of enamine **3a** with $CoBr_2$ was found to be insensitive to water; the process gave almost the same yield under absolute conditions as in the presence of 2 equiv. of water (cf. entries 17 and 18 in Table 1). Furthermore, the addition of a base (triethylamine) did not influence the yield of bromide **1a** substantially (Table 1, entry 19). These results indicate that product **1a** is formed directly in the reaction of enamine **3a** with $CoBr_2$ and not with HBr, which may be generated upon the hydrolysis of the latter. Unfortunately, we were not able to synthesize **1a** in the catalytic variant of the reaction by using 10 mol-% of $CoBr_2$ as catalyst and LiBr as the source of the bromide anion (Table 1, entry 20). It is likely that the cobalt trimethylsiloxide arising from the reaction is sufficiently inert and not transformed back into $CoBr_2$ upon the action of LiBr {for stable complexes of $Co[OSi(CH_3)_3]_2$ with LiBr see ref.[12b]}.

As can be seen from Scheme 2, the $CoBr_2$ procedure (procedure *i*) can be applied to a broad range of bis(oxy)enamines **3a**–**i**,**n** leading to the corresponding products **1a**–**i**,**n** in high yields. In addition to six-membered cyclic bis(oxy)enamines **3a**–**i**, the five-membered analogue **3n** also successfully reacted with $CoBr_2$ (product **1n** in Scheme 2). Importantly, cobalt(II) chloride and iodide also reacted with bis(oxy)enamines **3** to yield the respective cyclic ethers of α-chloro and α-iodo oximes (products **1q**–**1t** in Scheme 2). It is noteworthy that cyclic ethers of α-iodo oximes such as **1r** and **1s** cannot be obtained by silylation of the cyclic nitronates **2**[3g] discussed above [see Scheme 1, Equation (1) and discussion]. In contrast to cobalt(II) chloride, bromide, and iodide, cobalt fluoride proved to be unreactive, evidently because of its poor solubility. At the



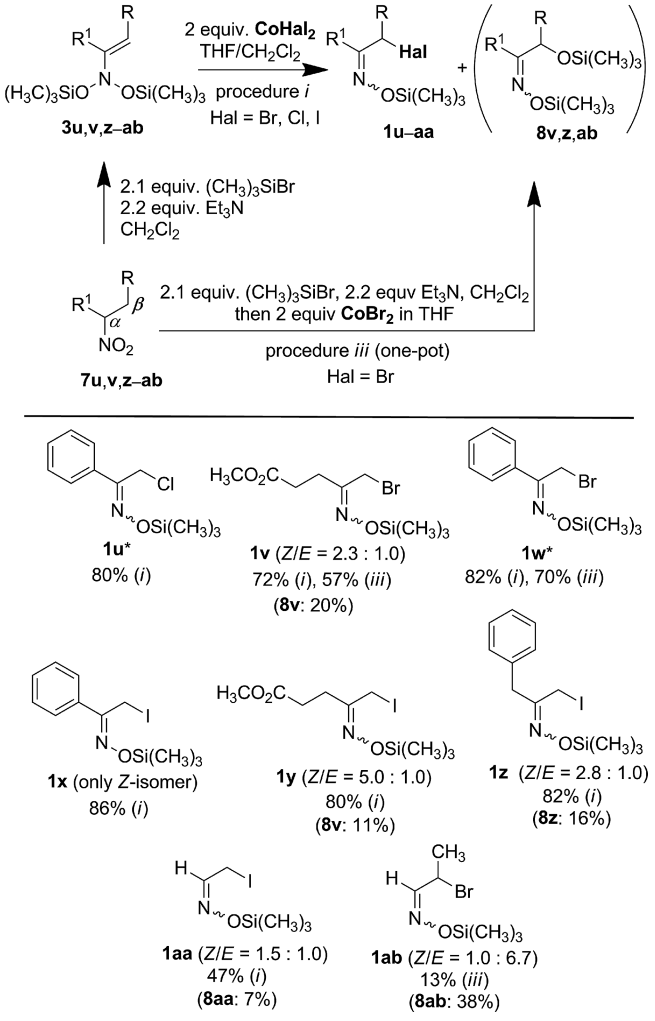
Scheme 2. Synthesis of the cyclic α-halo oxime ethers **1a**–**t** by procedures *i* and *ii*, yields of the isolated products are given.

same time, the reaction of enamine **3a** with the more soluble $CoF_2 \cdot 2H_2O$ resulted in an indecipherable mixture of products.[13]

The cyclic ethers of α-bromo oximes **1a**–**p** can be readily synthesized by a one-pot protocol from the corresponding nitronates **2** without isolation of the intermediate bis(oxy)-enamines **3** (procedure *ii*, Scheme 2). In this procedure the nitronate is silylated with bromotrimethylsilane (1.1 equiv.) in the presence of triethylamine followed by the addition of a solution of $CoBr_2$ in THF. As can be seen from the data given in Scheme 2, the yields of bromides **1** obtained by the one-pot procedure *ii* in most cases are higher or comparable to those obtained by procedure *i*. These results as well as the lability of bis(oxy)enamines **3** make the application of the one-pot procedure *ii* more preferable for the synthesis of bromides **1** than the two-step procedure *i*. However, the cyclic ethers of α-iodo oximes should be synthesized in two steps, that is, by the silylation of nitronates **2** with the $(CH_3)_3$-SiBr/Et_3N mixture followed by aqueous work-up to separate the forming bis(oxy)enamines **3** from triethylammonium bromide in the first step, and the subsequent reaction of **3** with cobalt(II) iodide according to procedure *i* in the second step. Application of the one-pot procedure *ii* in this case would lead to a mixture of α-halo oxime ethers (see below).

The yields of the cyclic ethers of α-bromo and α-chloro oximes **1** are on average about 30% higher than those reported in the literature[3f,3g] obtained by silylation of nitronates **2** with an excess of $(CH_3)_3SiBr$ or $(CH_3)_3SiCl$ (cf. the yields given in Scheme 2). The method developed here is scalable, as demonstrated by the synthesis of bromide **1a** from 20 mmol of nitronate **2a** by the one-pot procedure *ii* while maintaining its efficiency (83% yield). Notably, not only primary, but also secondary halides **1** can be obtained from nitronates **2** with R ≠ H by using procedure *ii* (e.g., see **1m** in Scheme 2[14]).

Another significant advantage of the metal-mediated approach developed is its applicability to acyclic bis(oxy)enamines **3** (procedure *i*, Scheme 3). The reactions of enamines **3u**,**v**,**z**,**aa** with cobalt(II) halides furnished the corresponding silyl ethers of α-halo oximes **1u**–**1aa** in good-to-high yields. The major side-reaction observed in these experiments was the rearrangement of acyclic bis(oxy)enamines **3** to produce trimethylsilyl ethers of α-silyloxy oximes **8** (see Scheme 3).[15] In particular, in the reaction of bis(oxy)enamine **3v** with $CoBr_2$, about 20% of the rearrangement product **8v** was formed; in the case of the internal enamine **3ab** (generated in situ from nitro compound **7ab**), the corresponding α-silyloxy oxime ether **8ab** was the major product (yield 38%), whereas only a negligible amount of the desired trimethylsilyl α-bromo oxime ether **1ab** was detected by ^1H NMR spectroscopy. The reactions of terminal bis(oxy)enamines **3u**,**v**,**z**,**aa** with CoI_2 proceeded more smoothly than those with $CoBr_2$. The corresponding trimethylsilyl α-iodo oxime ethers **1x**–**1aa** were obtained in yields of about 80% and contained almost no impurities (Scheme 3). Note that silyl ethers of α-iodo oximes are virtually unknown.[16] Trimethylsilyl α-bromo oxime ethers are also poorly available; the only route to their synthesis is the radical bromination of trimethylsilyl ethers of oximes.[8] However, this method has a limited substrate scope because many α-bromo oxime silyl ethers are thermally unstable.[8] Furthermore, primary bromides (such as **1v** and **1w**) cannot be synthesized by this route. Therefore the suggested approach significantly expands the range of available α-halo oxime silyl ethers.

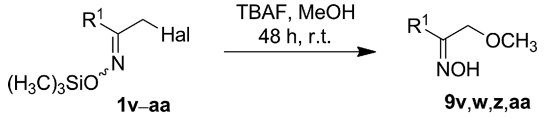


Scheme 3. Synthesis of trimethylsilyl ethers of α-halo oximes **1u**–**ab** by procedures *i* and *iii*: **3u**, **7u** (R^1 = Ph, R = H); **3v**, **7v**, **8v** (R^1 = $CH_2CH_2CO_2CH_3$, R = H); **3z**, **7z**, **8z** (R^1 = CH_2Ph, R = H); **3aa**, **7aa**, **8aa** (R^1 = H, R = H); **3ab**, **7ab**, **8ab** (R^1 = H, R = CH_3). The yields of isolated products **1u**–**aa** were recalculated with respect to the purity of compounds determined by ^1H NMR spectroscopy using an internal standard (see the Exp. Sect.). * Single isomer with unknown configuration.

α-Bromo oxime silyl ethers could be prepared in one-pot from the corresponding nitro compounds, as demonstrated by the synthesis of the products **1v** and **1w** (procedure *iii*, Scheme 3). In procedure *iii*, the corresponding bis(oxy)enamines **3u** and **3v** were generated in situ by the double silylation of nitro compounds **7u** and **7v** with $(CH_3)_3SiBr$/Et_3N. The subsequent addition of a solution of $CoBr_2$ in THF furnished the target α-bromo oxime silyl ethers **1w** and **1v**, respectively. Thus, procedure *iii* enables a single-step

C–H activation of the usually inert β-carbon atom of the aliphatic nitro compounds.

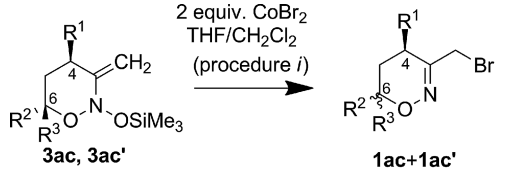
The structures of the new cyclic α-halo oxime ethers **1** were determined by ^{1}H and ^{13}C NMR and IR spectroscopy, high-resolution mass spectrometry, and elemental analysis. α-Iodo oxime ethers are not stable at ambient temperature and decomposed upon exposure to light to produce molecular iodine (λ_{max} = 537 nm in hexane). α-Halo oxime silyl ethers **1v**–**1aa** are also quite labile compounds and easily underwent hydrolysis and polymerization even in $CDCl_3$.[8a,8c] Attempts to isolate these products in an analytically pure state were not successful because they decomposed upon vacuum distillation or column chromatography.[17] At the same time, the crude products **1v**–**1aa** (Scheme 4) demonstrated a high degree of purity (typically 80–90%, according to ^{1}H NMR spectroscopy using an internal standard). The structures of **1v**–**1aa** were unambiguously determined by ^{1}H, ^{13}C, and ^{29}Si NMR, IR spectroscopy, and EI mass spectrometry. Further confirmation of the identity and purity of the products **1v**–**1aa** was their facile methanolysis with TBAF in methanol[8a] to give stable α-methoxy oximes **9** (Scheme 4). The assignment of signals of acyclic oxime derivatives **1** and **9** to *E*/*Z* isomers was guided by the known relationships between the chemical shifts of atoms attached to the oxime group and its configuration.[10c]



9v (R^1 = $CH_2CH_2CO_2CH_3$): 70% (from **1v**), 72% (from **1y**)
9w (R^1 = Ph): 71% (from **1w**), 62% (from **1x**)
9z (R^1 = CH_2Ph): 74% (from **1z**)
9aa (R^1 = H): 69% (from **1aa**)

Scheme 4. Methanolysis of trimethylsilyl ethers of α-halo oximes **1v**–**aa**.

The reactions of metal bromides with 6-alkoxy-substituted six-membered cyclic bis(oxy)enamines **3** warrants special discussion. A significant complication in the case of these substrates is the epimerization and destruction of the acetal center at C-6, which is sensitive to Lewis acids (Scheme 5).



45% (from **3ac**),
ratio **1ac**/**1ac'** = 3.5 : 1.0
71% (from **3ac'**),
ratio **1ac'**/**1ac** = 25 : 1.0

Scheme 5. Reaction of bis(oxy)enamines **3ac** and **3ac′** with $CoBr_2$: **1ac**, **3ac** (R^1 = 4-CH_3O-C_6H_4, R^2 = OEt, R^3 = H); **1ac′**, **3ac′** (R^1 = 4-CH_3O-C_6H_4, R^2 = H, R^3 = OEt).

Thus, the treatment of the diastereomerically pure cyclic bis(oxy)enamine **3ac** bearing an ethoxy group at C-6 with $CoBr_2$ produced the desired bromide in only moderate yield and as a mixture of the major 4,6-*trans* isomer (**1ac**) and minor 4,6-*cis* epimer (**1ac′**) (Scheme 5). Interestingly, under the same reaction conditions, isomeric bis(oxy)enamine **3ac′** possessing an ethoxy group *cis* to the aryl furnished the corresponding bromide **1ac′** in good yield and almost without epimerization (the amount of epimer product **1ac** was less than 4%, Scheme 5). Similarly, in the synthesis of product **1g** containing a ketal carbon atom (C-6), no noticeable epimerization was observed (see Scheme 2).

The degree of epimerization and the yield of product **1ac** obtained from bis(oxy)enamine **3ac** depend on the nature of the metal bromide employed (Table 2). Thus, screening of metal bromides in the reaction with **3ac** (generated in situ from nitronate **2ac**, see top part of Scheme 6) revealed that the smallest amount of epimer **1ac′** and the highest yield of **1ac** were obtained with $MgBr_2$ in THF (Table 2, entry 4, procedure *iv*).

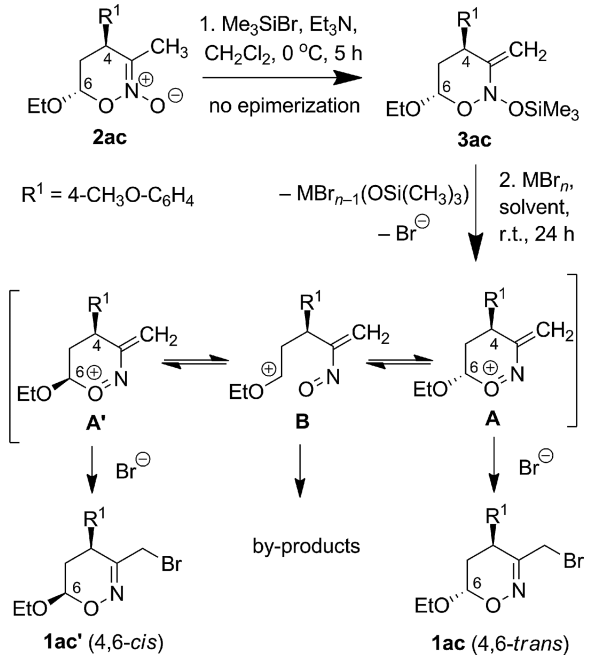
Table 2. Screening of metal bromides in the reaction with bis(oxy)-enamine **3ac** (generated in situ from nitronate **2ac**).

Entry	MBr_n (2 equiv.), solvent	Yield of **1ac** + **1ac′** [%][a]	Ratio of **1ac**/**1ac′**[b]
1	$CoBr_2$, THF/CH_2Cl_2 (procedure *ii*)	51	2.9:1.0
2	$ZnBr_2$, THF/CH_2Cl_2	63	4.4:1.0
3	$MnBr_2$, DMF/CH_2Cl_2	56	5.7:1.0
4	$MgBr_2$, THF/CH_2Cl_2 (procedure *iv*)	70	5.8:1.0
5	$NiBr_2$, DMF/CH_2Cl_2	8	0.9:1.0
6	$InBr_3$, THF/CH_2Cl_2	7	4.0:1.0

[a] Yields of products isolated by column chromatography. [b] Determined by ^{1}H NMR analysis of the crude reaction mixtures.

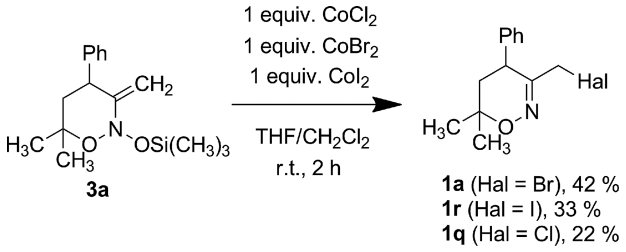
Partial epimerization of the acetal C-6 in **3ac** provides insights into the mechanism of the reaction of bis(oxy)enamines **3** with metal halides (Scheme 6). In fact, neither initial nitronate **2ac** nor the final bromide **1ac** underwent epimerization upon reaction with $CoBr_2$/$Et_3NH^+Br^-$. The starting material was quantitatively recovered in these experiments. This suggests that the reaction of bis(oxy)enamines **3** with metal halides proceeds via the generation of the nitrosonium cation of type **A**, which may undergo 1,2-oxazine ring-opening and epimerization through a reversible ring/chain process **A**⇌**B**⇌**A′** (Scheme 6). The absence of epimerization in the case of isomeric 4,6-*cis*-bis(oxy)enamine **3ac′** (Scheme 5) may be due to a high thermodynamic preference for cation **A′** over cation **A** (Scheme 6). Therefore it is likely that the transformation **3**→**1** proceeds by S_N1' substitution of the trimethylsilyloxy group by the halide anion assisted by the metal ion acting as a Lewis acid.

Further evidence for the S_N1' mechanism comes from competition reactions of bis(oxy)enamine **3a** with a mixture of three cobalt halides. Despite the significant difference in the nucleophilicity of the halide anions, all three cyclic α-halo oxime ethers were obtained in comparable amounts (see Scheme 7).[18] The absence of selectivity in the reactions



Scheme 6. Reaction of bis(oxy)enamine **3ac** with $CoBr_2$.

with cobalt halides implies the participation of a highly reactive cationic intermediate and a reaction of S_N1' character.



Scheme 7. Competition reactions of bis(oxy)enamine **3a** with a mixture of cobalt halides.

Conclusions

The reactions of bis(oxy)enamines with metal (e.g., Co, Zn, Mg, Mn) halides results in a transfer of the halide anion to the carbon atom through a novel metal-assisted S_N1'-type substitution process. The reaction is general and proceeds efficiently for both cyclic and acyclic bis(oxy)enamines. Based on the selective reactions of bis(oxy)enamines with cobalt halides, new one- and two-step procedures for the synthesis of cyclic and acyclic α-halo oxime ethers from available nitronates and aliphatic nitro compounds have been developed. These methods involve the formal C–H activation of the usually inert β-carbon atom of nitro compounds. The approach described herein does not suffer from the drawbacks of previous methods and significantly expands the range of α-halo oxime ethers available.

Experimental Section

All reactions were performed in oven-dried (150 °C) glassware. Column chromatography was performed by using Kieselgel 40–60 μm 60A. 1D and 2D NMR spectra were recorded at room temperature in $CDCl_3$ with a Bruker AM 300 spectrometer. The chemical shifts (^1H, ^{13}C) are given in ppm (δ) relative to the solvent signal. Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br. (broad). FTIR spectra were recorded with a Bruker Alpha-T spectrometer. Peaks in IR spectra data are reported in cm^{-1} along with the following relative intensities: s (strong), m (medium), w (weak), br (broad), sh (shoulder). UV/Vis spectra were recorded with a Shimadzu UVmini-1240 spectrometer (data are reported in nm). Elemental analysis (average of two combustions) was performed at the Analytical Laboratory of the N. D. Zelinsky Institute of Organic Chemistry. HRMS was performed with an electrospray ionization (ESI) spectrometer equipped with a time-of-flight (TOF) detector. EI mass spectra were recorded with a Finnigan MAT Incos 50 spectrometer (70 eV). Optical rotation angles were measured with a DIP-360 polarimeter. Concentrations c are given in g/100 mL, $[\alpha]_D$ values are given in units of 10^{-1} deg cm^2 g^{-1}. Analytical TLC was performed on precoated silica gel plates (QF-254). Visualization was accomplished with UV light and a solution of anisaldehyde/H_2SO_4 in ethanol. Tetrahydrofuran was distilled first from $LiAlH_4$, stored under sodium benzophenone ketyl, and distilled by using a vacuum trap-to-trap technique prior to use. CH_2Cl_2, MeCN, Et_3N, and $(CH_3)_3SiBr$ were distilled from CaH_2. Hexane and EtOAc were distilled without drying agents. Commercial-grade pentane was used as received.

All inorganic reagents, nitroethane, and 1-nitropropane were commercial-grade and used as received. The initial cyclic nitronates **2a**,[3h] **2b**,[3f] **2c**,[3f] **2e**,[3f] **2f**,[3g] **2g**,[3h] **2h**,[3g] **2m**,[11a] **2n**,[19] **2o**,[20] **2p**,[20] **2ac**,[3h] and **2ac′**,[3h] and bis(oxy)enamines **3a**,[3h] **3b**,[11c] **3c**,[11a] **3d**,[3h] **3e**,[11b] **3f**,[3g] **3g**,[3h] **3h**,[3g] **3n**,[20] **3u**,[10b] **3v**,[10a] **3z**,[10c] **3aa**,[10a] **3ab**,[10a] **3ac**,[3h] and **3ac′**[3h] were synthesized according to known methods. Nitronates **2d**, and **2j–l** were prepared following the procedure used for the synthesis of **2d**[3h] with small modifications: for compounds **2d**, **2j**, and **2l**, the reaction mixtures were kept at –30 °C for 20 h, for compound **2k**, the reaction mixture was kept at –30 °C for 30 min.

(1*R*,2*S*,4*S*,4′*S*)-3,3,3′-Trimethyl-4′-phenyl-4′,5′-dihydrospiro[bicyclo[2.2.1]heptane-2,6′-[1,2]oxazine] 2′-Oxide (Nitronate 2i): A solution of camphene (4.08 g, 30 mmol) in CH_2Cl_2 (10 mL) followed by $SnCl_4$ (2.34 mL, 20 mmol) were added to a stirred solution of [(1*E*)-2-nitroprop-1-en-1-yl]benzene[21] (3.26 g, 20 mmol) in CH_2Cl_2 (35 mL) at –60 °C under argon. The resulting deep-red solution was stirred at around –60 °C for 0.5 h and then maintained for 48 h at –30 °C with occasional stirring. Then the reaction mixture was poured into a mixture of EtOAc (200 mL) and a saturated solution of K_2CO_3 (200 mL), and the aqueous layer was back-extracted with EtOAc (100 mL). The combined organic layers were then washed with a saturated solution of K_2CO_3 (50 mL), water (50 mL), and brine (50 mL), dried (Na_2SO_4), and the solvents evaporated in vacuo. The resulting white solid was triturated with pentane and dried until a constant weight, yield 4.84 g (81%). White solid, m.p. 143–145 °C (with dec.), recrystallized from hexane. $[\alpha]_D$ = –38.0 (c = 1.0, $CHCl_3$, 27 °C). ^1H NMR ($CDCl_3$, 300.13 MHz, COSY, HSQC, NOESY): δ = 0.90 and 1.14 (2 s, 3 H and 3 H, 2 CH_3), 1.24 (d, J = 10.6 Hz, 1 H, 7-H), 1.29–1.44 and 1.55–1.67 (2 m, 2 H and 2 H, 5-H and 6-H), 1.84 (s, 3 H, 8-H), 1.80–1.89 (m, 2 H, 4-H and 5′-H), 2.30 (m, 2 H, 7-H and 5′-H), 2.47 (d, J = 4.2 Hz, 1 H, 1-H), 3.53 (dd, J = 7.4, 10.7 Hz, 1 H, 4′-H_{ax}), 7.19 (d, J = 7.0 Hz, 2 H, o-C_6H_5), 7.33 (t, J = 7.0 Hz, 1 H, p-C_6H_5), 7.37 (t, J =

7.0 Hz, 2 H, *m*-C_6H_5) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, HSQC): δ = 17.2 (C-8), 22.4 and 23.7 (C-5 and C-6), 22.5 and 23.7 (2 CH_3), 33.4 (C-5′), 34.8 (C-7), 42.5 (C-1), 44.1 (C-4′), 44.9 (C-3), 49.3 (C-4), 92.3 (C-6′), 122.1 (C-3′), 127.6, 127.8, and 129.1 (*o*-, *m*-, *p*-C_6H_5), 140.6 (*i*-C_6H_5) ppm. Characteristic 2D NOESY correlation: 4′-H_{ax}/1-H. $C_{19}H_{25}NO_2$ (299.41): calcd. C 76.22, H 8.42, N 4.68; found C 75.92, H 8.27, N 4.60.

(1*R*,2*S*,4*S*,4′*S*)-3,3-Dimethyl-3′-methylene-4′-phenyl-2′-[(trimethylsilyl)oxy]spiro[bicyclo[2.2.1]heptane-2,6′-[1,2]oxazinane] [Bis(oxy)enamine 3i]: A solution of bromotrimethylsilane (1.00 mL, 7.58 mmol) in CH_2Cl_2 (2.3 mL) was added to a stirred solution of nitronate **2i** (1.485 g, 4.96 mmol) and triethylamine (1.08 mL, 7.76 mmol) in CH_2Cl_2 (11.3 mL) at –78 °C under argon. The mixture was kept at –78 °C for 48 h with occasional shaking, then diluted with hexane, and transferred into a mixture of hexane (50 mL) and 0.25 M $NaHSO_4$ (50 mL). The aqueous layer was back-extracted with hexane (30 mL). The combined organic layers were washed with 0.25 M $NaHSO_4$ (30 mL), water (30 mL), and brine (30 mL), dried (Na_2SO_4), and the solvents evaporated in vacuo to give 1.835 g (90%) of bis(oxy)enamine **3i**. Owing to the labile character of **3i** it was stored as a 0.5 M solution in CH_2Cl_2 at –30 °C. Colorless oil. $[\alpha]_D$ = +52.8 (*c* = 1.0, $CHCl_3$, 27 °C). ^{1}H NMR ($CDCl_3$, 300.13 MHz, COSY, HSQC): δ = 0.27 [s, 9 H, Si(CH_3)$_3$], 0.90 and 1.06 (2 s, 3 H and 3 H, 2 CH_3), 1.20 (d, *J* = 9.8 Hz, 1 H, 7-H), 1.27–1.41 and 1.48–1.59 (2 m, 2 H and 2 H, 5-H and 6-H), 1.78 (s, 1 H, 4-H), 1.97 (dd, *J* = 6.1, 13.1 Hz, 1 H, 5′-H'_{eq}), 2.01 (dd, *J* = 11.5, 13.1 Hz, 1 H, 5′-H'_{ax}), 2.26 (d, *J* = 9.8 Hz, 1 H, 7-H), 3.25 (d, *J* = 3.1 Hz, 1 H, 1-H), 3.61 (dd, *J* = 6.1, 11.5 Hz, 1 H, 4′-H'_{ax}), 3.85 (d, *J* = 1.5 Hz, 1 H, 8-H), 4.98 (d, *J* = 1.4 Hz, 1 H, 8-H), 7.27–7.39 (m, 5 H, *o*-, *m*-, *p*-C_6H_5) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, HSQC): δ = –0.6 [Si(CH_3)$_3$], 22.9 and 24.0 (2 CH_3), 23.3 and 24.1 (C-5 and C-6), 34.9 (C-7), 35.1 (C-5′), 42.7 (C-1), 43.5 (C-4′), 45.0 (C-3), 49.7 (C-4), 88.1 (C-2), 96.5 (C-8), 127.0, 128.5, and 128.9 (*o*-, *m*-, *p*-C_6H_5), 141.2 (*i*-C_6H_5), 158.6 (C-3′) ppm. ^{29}Si NMR ($CDCl_3$, 59.63 MHz, DEPT): δ = 25.9 ppm. HRMS: calcd. for $[C_{22}H_{34}NO_2Si]^+$ 372.2353; found 372.2346; calcd. for $[C_{22}H_{33}NO_2SiNa]^+$ 394.2173; found 394.2163. Purity determined by ^{1}H NMR with internal standard (trichloroethylene): ca. 90%.

General Procedure for the Synthesis of α-Halo Oxime Ethers 1a–i,n,q-aa,ac,ac′ from Bis(oxy)enamines 3a–i,n,u,v,z,aa,ac,ac′ (Procedure *i*): A solution of bis(oxy)enamine **3** (1 mmol) in CH_2Cl_2 (2 mL) was added to a stirred solution of cobalt(II) bromide, chloride, or iodide (2 mmol) in THF (4 mL) at room temperature under argon. After 2 h of stirring the resulting blue solution was diluted with EtOAc (10 mL) and poured into a mixture of EtOAc (100 mL) and a saturated solution of K_2CO_3 (100 mL; for cyclic oxime ethers **1a**–**i**,**n**,**q**–**t**,**ac**,**ac′**, 0.25 M $NaHSO_4$ solution can be used instead of K_2CO_3 to dissolve the inorganic precipitate formed upon aqueous work-up). The aqueous layer was back-extracted with EtOAc (50 mL). The combined organic layers were washed with a saturated solution of K_2CO_3 (or 0.25 M $NaHSO_4$; 50 mL), water (50 mL), and brine (50 mL), dried (Na_2SO_4), and the solvents evaporated in vacuo. The products **1a**,**b**,**d**,**e**,**g**–**i**,**n**,**q**–**t**,**ac**,**ac′** were purified by flash chromatography on silica gel, and the products **1c** and **1f** by crystallization. The unstable products **1u**–**aa** were dissolved in pentane and filtered through a short column filled with charcoal (0.5 cm) and Celite (0.5 cm) layers to remove polymer products and traces of inorganic salts. The filtrates were evaporated to give products **1v**–**aa**, which were used for analytical purposes. The yields are given in Schemes 2, 3, and 5. The yields of products **1u**–**1aa** were recalculated with respect to the purity of the compounds determined by ^{1}H NMR spectroscopy with an internal standard.

General Procedure for the Synthesis of Cyclic α-Halo Oxime Ethers 1a–p from Cyclic Nitronates 2a–p,ac (Procedure *ii*): Bromotrimethylsilane (0.145 mL, 1.1 mmol) was added to a stirred solution of cyclic nitronate **2** (1 mmol) in CH_2Cl_2 (2 mL) and triethylamine (0.160 mL, 1.15 mmol) at 0 °C under argon. The mixture was stirred at 0 °C for 5 h. Then a solution of cobalt bromide (0.438 g, 2 mmol) in THF (4 mL) was added. After an additional 24 h at room temperature, the resulting blue solution was diluted with EtOAc (10 mL) and poured into a mixture of EtOAc (100 mL) and a saturated solution of K_2CO_3 (100 mL; a 0.25 M $NaHSO_4$ solution can be used instead of K_2CO_3 to simplify the work-up). The aqueous layer was back-extracted with EtOAc (50 mL). The combined organic layers were washed with a saturated solution of K_2CO_3 (50 mL), water (50 mL), and brine (50 mL), dried (Na_2SO_4), and the solvents evaporated in vacuo. The products **1a**,**b**,**d**,**e**,**g**–**p**,**ac** were isolated by flash chromatography on silica gel, and the products **1c** and **1f** by crystallization. The yields of the products are given in Scheme 2 and Table 2.

General Procedure for the Synthesis of α-Halo Oxime Ethers 1v,w from Nitro Compounds 7u,v (Procedure *iii*): Bromotrimethylsilane (0.275 mL, 2.1 mmol) was added to a stirred solution of nitro compound **7u** or **7v** (1 mmol) in CH_2Cl_2 (2 mL) and triethylamine (0.305 mL, 2.2 mmol) at 0 °C under argon. The mixture was kept at 0 °C with occasional stirring for 96 (**7u**) or 24 h (**7v**). Then a solution of cobalt bromide (0.438 g, 2 mmol) in THF (4 mL) was added. After an additional 24 h at room temperature the resulting blue solution was diluted with EtOAc (10 mL) and poured into a mixture of EtOAc (100 mL) and a 0.25 M $NaHSO_4$ solution (100 mL). The aqueous layer was back-extracted with EtOAc (50 mL). The combined organic layers were washed with $NaHSO_4$ solution (50 mL), water (50 mL), and brine (50 mL), dried (Na_2SO_4), and the solvents evaporated in vacuo. The resulting crude products were dissolved in pentane and filtered through a short column filled with charcoal (0.5 cm) and Celite (0.5 cm) layers to remove polymer products and traces of inorganic salts. The filtrates were evaporated to give unstable products **1w** and **1v**, respectively. The yields are given in Scheme 3.

Procedure for the Synthesis of 3-Bromomethyl-1,2-oxazine 1ac from Nitronate 2ac (Procedure *iv*): Bromotrimethylsilane (0.145 mL, 1.1 mmol) was added to a stirred solution of cyclic nitronate **2ac** (1 mmol) in CH_2Cl_2 (2 mL) and triethylamine (0.160 mL, 1.15 mmol) at 0 °C under argon. The mixture was kept at 0 °C with occasional stirring for 5 h. Then a slurry of magnesium bromide (0.368 g, 2 mmol) in THF (4 mL) was added and the mixture was left to stand at room temperature overnight. Then the mixture was diluted with EtOAc (10 mL) and poured into a mixture of EtOAc (100 mL) and a saturated solution of K_2CO_3 (100 mL). The aqueous layer was back-extracted with EtOAc (50 mL). The combined organic layers were washed with a saturated solution of K_2CO_3 (50 mL), water (50 mL), and brine (50 mL), dried (Na_2SO_4), and the solvents evaporated in vacuo. The residue was subjected to column chromatography on silica gel (eluent EtOAc/hexane = 1:10) to give 0.23 g (70%) of a mixture of **1ac** and **1ac′** as a colorless oil (ratio **1ac**/**1ac′** = 5.8:1).

The ^{1}H NMR spectra and physical properties of the products **1a**–**g**,**j**–**l**,**q**,**ac**,**ac′**,**4a**,**5a**,**6a** are in agreement with data reported previously (see the Supporting Information). The atom labelling of the products **1i**,**l**,**s** as well as **2i**,**3i** is depicted in Scheme 2.

***rel*-(4*S*,6*S*)-3-(Bromomethyl)-4-(4-methoxyphenyl)-6-phenyl-5,6-dihydro-4*H*-1,2-oxazine (1h):** Yield 88% (procedure *i*), 74% (procedure *ii*). Colorless oil that solidified upon standing at 0 °C, m.p. 100–101 °C. R_f = 0.7 (EtOAc/hexane = 1:1). ^{1}H NMR ($CDCl_3$,

300.13 MHz, COSY, HMQC): δ = 2.28 (ddd, J = 13.0, 11.9, 11.5 Hz, 1 H, 5-H_{ax}), 2.52 (dd, J = 13.0, 8.2 Hz, 1 H, 5-H_{eq}), 3.68 (d, J = 9.9 Hz, 1 H, CHBr), 3.82 (s, 3 H, OCH_3), 4.02 (d, J = 9.9 Hz, 1 H, CHBr), 4.13 (dd, J = 8.2, 11.5 Hz, 1 H, 4-H_{ax}), 4.97 (d, J = 11.9 Hz, 1 H, 6-H_{ax}), 6.92 (d, J = 8.3 Hz, 2 H, o-$C_6H_4OCH_3$), 7.22 (d, J = 8.3 Hz, 2 H, m-$C_6H_4OCH_3$), 7.33–7.46 (m, 5 H, o-, m-, p-C_6H_5) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, HMQC): δ = 31.4 (CH_2Br), 34.2 (C-5), 35.7 (C-4), 55.4 (OCH_3), 73.9 (C-6), 114.7 (o-$C_6H_4OCH_3$), 126.6, 128.4, and 128.6 (o-, m-, p-C_6H_5), 129.4 (m-$C_6H_4OCH_3$), 132.6 (p-$C_6H_4OCH_3$), 139.0 (i-C_6H_5), 154.2 (C-O), 159.1 (C=N) ppm. $C_{18}H_{18}BrNO_2$ (360.25): calcd. C 60.01, H 5.04, N 3.89; found C 59.89, H 4.90, N 4.02.

(1*R*,2*S*,4*S*,4′*S*)-3′-(Bromomethyl)-3,3-dimethyl-4′-phenyl-4′,5′-dihydrospiro[bicyclo[2.2.1]heptane-2,6′-[1,2]oxazine] (1i): Yield 76% (procedure *i*), 90% (procedure *ii*). White solid, m.p. 117–121 °C (with dec.), recrystallized from hexane. R_f = 0.8 (EtOAc/hexane = 1:1). $[\alpha]_D$ = –6.6 (c = 1.0, $CHCl_3$, 27 °C). ^{1}H NMR ($CDCl_3$, 300.13 MHz, COSY, HMQC, NOESY): δ = 0.91 (s, 3 H, CH_3), 1.16 (s, 3 H, CH_3), 1.20 (d, J = 10.3 Hz, 1 H, 7-H), 1.28–1.43 (m, 2 H, 6-H), 1.53–1.64 (m, 2 H, 5-H), 1.84 (dd, J = 13.9, 12.6 Hz, 1 H, 5′-H′$_{ax}$), 1.85 (s, 1 H, 4-H), 2.19 (d, J = 10.3 Hz, 1 H, 7-H), 2.33 (dd, J = 13.9, 7.2 Hz, 1 H, 5′-H′′$_{eq}$), 2.46 (d, J = 3.8 Hz, 1 H, 1-H), 3.65 (d, J = 9.8 Hz, 1 H, 8-H), 3.73 (dd, J = 12.6, 7.2 Hz, 1 H, 4′-H_{ax}), 3.98 (d, J = 9.8 Hz, 1 H, 8-H), 7.26 (d, J = 7.4 Hz, 2 H, o-C_6H_5), 7.34 (t, J = 6.7 Hz, 1 H, p-C_6H_5), 7.39 (dd, J = 7.4, 6.7 Hz, 2 H, m-C_6H_5) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, HMQC, DEPT): δ = 22.3 and 24.2 (2 CH_3), 22.4 and 23.8 (C-5 and C-6), 31.3 (C-5′), 31.8 (C-8), 34.6 (C-7), 39.1 (C-4′), 43.2 (C-1), 44.6 (C-3), 49.3 (C-4), 87.8 (C-2), 127.6, 128.2, and 129.2 (o-, m-, p-C_6H_5), 139.3 (i-C_6H_5), 156.0 (C-3′) ppm. Characteristic 2D NOESY correlations: o-C_6H_5/5′-H′$_{ax}$, 5′-H′′$_{eq}$/6-H, 4′-H_{ax}/1-H, 5-H/CH_3. FTIR (KBr): $\tilde{\nu}$ = 2939 (s, sh), 2860 (s), 1593 (s), 1493 (s), 1455 (s), 1423 (s), 1388 (m), 1366 (m), 1207 (s), 1093 (m), 1023 (s), 973 (s), 952 (s), 931 (m), 907 (s), 777 (s), 757 (s), 704 (s), 655 (m), 603 (m), 526 (s) cm^{-1}. HRMS: calcd. for $[C_{19}H_{25}BrNO]^+$ 362.1114 and 364.1094; found 362.1110 and 364.1095. $C_{19}H_{24}BrNO$ (362.31): calcd. C 62.99, H 6.68, N 3.87; found C 63.09, H 6.57, N 4.07.

***rel*-(4*S*,4a*R*,5*R*,8*S*,8a*R*)-3-(Bromomethyl)-4-phenyl-4a,5,6,7,8,8a-hexahydro-4*H*-5,8-methano-1,2-benzoxazine (1l):** Yield 84% (procedure *ii*), m.p. 114–117 °C (with dec.), recrystallized from hexane. R_f = 0.8 (EtOAc/hexane = 1:1). ^{1}H NMR ($CDCl_3$, 300.13 MHz, COSY, HSQC, NOESY): δ = 1.07–1.18 (m, 2 H, 6-H_{endo} and 7-H_{endo}), 1.22 (d, J = 10.5 Hz, 1 H, 9-H′), 1.47 (m, 1 H, 6-H_{exo}), 1.62 (m, 1 H, 7-H_{exo}), 2.04 (d, J = 4.0 Hz, 1 H, 5-H), 2.12 (d, J = 10.5 Hz, 1 H, 9-H′′), 2.20 (dd, J = 10.1, 6.8 Hz, 1 H, 4a-H_{ax}), 2.57 (d, J = 4.9 Hz, 1 H, 8-H), 3.30 (d, J = 10.1 Hz, 1 H, 4-H_{ax}), 3.80 (d, J = 6.8 Hz, 1 H, 8a-H_{eq}), 3.87 (d, J = 10.2 Hz, 1 H, 10-H), 3.91 (d, J = 10.2 Hz, 1 H, 10-H), 7.28–7.43 (m, 5 H, o-, m-, p-C_6H_5) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, HSQC): δ = 24.6 (C-7), 28.5 (C-10), 29.0 (C-6), 33.4 (C-9), 40.3 (C-5), 42.1 (C-4), 42.3 (C-8), 53.4 (C-4a), 83.1 (C-8a), 127.6, 128.7, and 129.7 (o-, m-, p-C_6H_5), 137.2 (i-C_6H_5), 171.0 (C-3) ppm. Characteristic 2D NOESY correlations: 4a-H_{ax}/8a-H_{eq}, 4-H_{ax}/o-C_6H_5, 8a-H_{eq}/8-H, 4-H_{ax}/5-H, 8a-H_{eq}/7-H_{endo}, 4a-H_{ax}/6-H_{endo}, 4-H_{ax}/9-H′′, 4a-H_{ax}/o-C_6H_5. $C_{16}H_{18}BrNO$ (320.23): calcd. C 60.01, H 5.67, N 4.37; found C 60.21, H 5.73, N 4.38.

***rel*-(4*S*,4a*R*,8a*R*)-3-(1-Bromoethyl)-4-(4-methoxyphenyl)-4a,5,6,7,8,8a-hexahydro-4*H*-1,2-benzoxazine (1m):** Obtained by procedure *ii* from nitronate **2m** as a mixture of two isomers in a ratio of 2.0:1.0 (yield 56%) accompanied by products **10m**[11a] (5%) and **11m**[11a] (4%). After column chromatography a fraction containing both isomers in a ratio of 6.0:1.0 was obtained, which was used for analytical purposes. White solid, m.p. 73–81 °C. R_f = 0.7 (EtOAc/hexane = 1:1). Major isomer: ^{1}H NMR ($CDCl_3$, 300.13 MHz, COSY, HMQC): δ = 1.27–1.49 (m, 4 H, 7-H, 8-H, 9-H, 10-H), 1.58–1.79 (m, 4 H, 5-H, 8-H, 9-H, 10-H), 1.93 (d, J = 6.8 Hz, 3 H, CH_3), 2.06–2.10 (m, 1 H, 7-H), 3.57 (s, 1 H, 4-H_{eq}), 3.81 (s, 3 H, H_3CO), 4.01 (m, 1 H, 6-H), 4.46 (q, J = 6.8 Hz, 1 H, 11-H), 6.89 (d, J = 8.6 Hz, 2 H, o-$C_6H_4OCH_3$), 7.03 (d, J = 8.6 Hz, 2 H, m-$C_6H_4OCH_3$) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, HMQC, DEPT): δ = 20.0, 24.8, and 27.2 (C-8, C-9, C-10), 21.6 (CH_3), 29.2 (C-7), 38.5 (C-5), 43.6 (C-4), 47.3 (C-11), 55.3 (OCH_3), 69.3 (C-6), 114.4 (o-$C_6H_4OCH_3$), 129.2 (m-$C_6H_4OCH_3$), 133.2 (p-$C_6H_4OCH_3$), 155.1 (C-O), 158.9 (C-3) ppm. Minor isomer: ^{1}H NMR ($CDCl_3$, 300.13 MHz, COSY, HMQC): δ = 1.27–1.49 (m, 4 H, 7-H, 8-H, 9-H, 10-H), 1.44 (d, J = 7.1 Hz, 3 H, CH_3), 1.58–1.79 (m, 4 H, 5-H, 8-H, 9-H, 10-H), 2.06–2.10 (m, 1 H, 7-H), 3.63 (s, 1 H, 4-H_{eq}), 3.81 (s, 3 H, H_3CO), 4.12 (m, 1 H, 6-H), 4.46 (q, J = 7.1 Hz, 1 H, 11-H), 6.89 (d, J = 8.6 Hz, 2 H, o-$C_6H_4OCH_3$), 7.05 (d, J = 8.6 Hz, 2 H, m-$C_6H_4OCH_3$) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, HMQC, DEPT): δ = 19.3, 25.1, 29.4, and 29.7 (C-7, C-8, C-9, C-10), 21.6 (CH_3), 38.1 (C-5), 41.3 (C-4), 51.1 (C-11), 55.3 (OCH_3), 68.9 (C-6), 114.1 (o-$C_6H_4OCH_3$), 129.2 (m-$C_6H_4OCH_3$), 133.9 (p-$C_6H_4OCH_3$), 155.1 (C-O), 158.9 (C-3) ppm. $C_{17}H_{22}BrNO_2$: C, 57.96; H, 6.29; N, 3.98; found C, 58.35; H, 6.49; N, 3.93.

Methyl 3-(Bromomethyl)-5-methyl-4,5-dihydroisoxazole-5-carboxylate (1n): Yield 84% (procedure *i*), 68% (procedure *ii*). Colorless oil. R_f = 0.7 (EtOAc/hexane = 1:1). ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ = 1.66 (s, 3 H, CH_3), 3.03 (d, J = 17.3 Hz, 1 H, CH), 3.60 (d, J = 17.3 Hz, 1 H, CH), 3.81 (s, 3 H, OCH_3), 4.11 (d, J = 11 Hz, 1 H, CHBr), 4.18 (d, J = 11 Hz, 1 H, CHBr) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT): δ = 23.1 (CH_2), 23.4 (CH_3), 44.5 (CH_2Br), 53.0 (OCH_3), 87.0 (C-O), 155.0 (C=N), 171.9 (C=O) ppm. FTIR (neat): $\tilde{\nu}$ = 3031 (w), 2986 (m), 2956 (m), 2847 (w), 1741 (s), 1615 (m), 1435 (s, sh), 1378 (m), 1350 (m), 1304 (s), 1206 (s), 1175 (s), 1135 (m), 1104 (m), 986 (m), 918 (s), 850 (m), 767 (m), 672 (m), 625 (m) cm^{-1}. HRMS: calcd. for $[C_7H_{11}BrNO_3]^+$ 235.9917 and 237.9900; found 235.9920 and 237.9902. $C_7H_{10}BrNO_3$ (236.06): calcd. C 35.62, H 4.27, N 5.93; found C 35.81, H 4.24, N 6.00.

3-(Bromomethyl)-5-(4-bromophenyl)-4,5-dihydroisoxazole (1o): Yield 69% (procedure *ii*). White solid, m.p. 48–50 °C (pentane/Et_2O = 5:1). R_f = 0.65 (EtOAc/hexane = 1:1). ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ = 3.10 (dd, J = 17.1, 8.2 Hz, 1 H, HC), 3.56 (dd, J = 17.1, 11.1 Hz, 1 H, HC), 4.21 (s, 2 H, CH_2Br), 5.63 (dd, J = 11.1, 8.2 Hz, 1 H, HC), 7.22 (d, J = 8.3 Hz, 2 H, C_6H_4Br), 7.52 (d, J = 8.3 Hz, 2 H, C_6H_4Br) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT): δ = 23.4 and 42.7 (CH_2 and CH_2Br), 82.6 (CH), 122.4 (p-C_6H_4Br), 127.5 and 132.0 (o-C_6H_4Br and m-C_6H_4Br), 139.3 (C-Br), 154.6 (C=N) ppm. $C_{10}H_9Br_2NO$ (319.00): calcd. C 37.65, H 2.84, N 4.39; found C 37.70, H 2.77, N 4.24.

3-(Bromomethyl)-4-phenyl-4,5-dihydroisoxazole (1p): Yield 53% (procedure *ii*). Colorless oil. R_f = 0.8 (EtOAc/hexane = 1:1). ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ = 3.68 (d, J = 10.9 Hz, 1 H, CHBr), 4.26 (d, J = 10.9 Hz, 1 H, CHBr), 4.43 (dd, J = 8.0, 7.1 Hz, 1 H, CH-C_6H_5), 4.64 (d, J = 11.0, 7.1 Hz, 1 H, CHO), 4.78 (d, J = 11.0, 8.0 Hz, 1 H, CHO), 7.21–7.45 (m, 5 H, o-, m-, p-C_6H_5) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT): δ = 22.3 (CH_2Br), 53.6 (CH), 77.8 (CH_2O), 127.6, 128.2, and 129.4 (o-, m-, p-C_6H_5), 137.5 (i-C_6H_5), 157.6 (C=N) ppm. $C_{10}H_{10}BrNO$ (240.10): calcd. C 50.02, H 4.20, N 5.83; found C 49.96, H 4.24, N 5.94.

3-(Iodomethyl)-6,6-dimethyl-4-phenyl-5,6-dihydro-4*H*-1,2-oxazine (1r): Yield 90% (procedure *i*). White solid, m.p. 100–103 °C (hex-

ane/Et_2O = 5:1). R_f = 0.8 (EtOAc/hexane = 1:1). ^1H NMR ($CDCl_3$, 300.13 MHz): δ = 1.35 and 1.38 (2 s, 3 H and 3 H, 2 CH_3), 2.00 (dd, J = 13.6, 11.9 Hz, 1 H, 5-H_{ax}), 2.12 (dd, J = 13.6, 8.0 Hz, 1 H, 5-H_{eq}), 3.50 (d, J = 9.3 Hz, 1 H, 8-H), 3.98 (dd, J = 11.9, 8.0 Hz, 1 H, 4-H_{ax}), 4.06 (d, J = 9.3 Hz, 1 H, 8-H), 7.24–7.41 (m, 5 H, *o*-, *m*-, *p*-C_6H_5) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT): δ = 3.9 (C-8), 24.0 and 28.4 (2 *C*H_3), 37.7 (C-4), 40.6 (C-5), 75.6 (C-6), 127.7, 128.3, and 129.4 (*o*-, *m*-, *p*-C_6H_5), 139.4 (*i*-C_6H_5), 156.3 (C-3) ppm. FTIR (thin film): $\tilde{\nu}$ = 3027 (m), 2974 (s), 2922 (s), 1602 (s), 1578 (s, sh), 1493 (s), 1454 (s), 1415 (s), 1384 (s), 1370 (s), 1317 (m), 1272 (s, sh), 1259 (m), 1159 (s), 1123 (s, sh), 1075 (s), 1030 (m), 1015 (m), 965 (s), 933 (s), 885 (s), 866 (s), 821 (m), 783 (s), 758 (s, sh), 745 (s), 703 (s), 651 (m), 581 (m), 545 (s, sh) cm^{-1}. UV/Vis (CH_2Cl_2): λ_{max} = 228, 285 nm. $C_{13}H_{16}INO$ (329.18): calcd. C 47.43, H 4.90, N 4.26; found C 47.43, H 4.77, N 4.21.

***rel*-(4*S*,4a*R*,8a*R*)-3-(Iodomethyl)-4-(4-methoxyphenyl)-4a,5,6,7,8,8a-hexahydro-4*H*-1,2-benzoxazine (1s):** Yield 71% (procedure *i*). White solid, m.p. 86–90 °C (pentane). R_f = 0.5 (EtOAc/hexane = 1:3). ^1H NMR ($CDCl_3$, 300.13 MHz, COSY, HSQC): δ = 1.27–1.49 (m, 4 H, 7-H, 8-H, 9-H, 10-H), 1.57–1.80 (m, 4 H, 5-H, 8-H, 9-H, 10-H), 2.04–2.11 (m, 1 H, 7-H), 3.64 (d, J = 1.5 Hz, 1 H, 4-H_{eq}), 3.70 (d, J = 9.6 Hz, 1 H, 11-H), 3.81 (s, 3 H, H_3CO), 4.01 (m, 1 H, 6-H), 4.16 (d, J = 9.6 Hz, 1 H, 11-H), 6.89 (d, J = 8.7 Hz, 2 H, *o*-$C_6H_4OCH_3$), 7.07 (d, J = 8.7 Hz, 2 H, *m*-$C_6H_4OCH_3$) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT): δ = 5.1 (C-11), 20.1 and 24.8 (C-9 and C-10), 27.1 (C-8), 29.0 (C-7), 38.3 (C-5), 42.8 (C-4), 55.3 (O*C*H_3), 69.4 (C-6), 114.4 (*o*-$C_6H_4OCH_3$), 129.1 (*m*-$C_6H_4OCH_3$), 132.9 (*p*-$C_6H_4OCH_3$), 153.4 (C-O), 158.9 (C-3) ppm. HRMS: calcd. for $[C_{16}H_{21}INO_2]^+$ 386.0611; found 386.0607; calcd. for $[C_{16}H_{20}INO_2Na]^+$ 408.0431; found 408.0424. $C_{16}H_{20}INO_2$ (385.24): calcd. C 49.88, H 5.23, N 3.64; found C 49.98, H 5.00, N 3.59.

Methyl 3-(Iodomethyl)-5-methyl-4,5-dihydroisoxazole-5-carboxylate (1t): Yield 68% (procedure *i*). Yellowish oil unstable at room temp. R_f = 0.4 (EtOAc/hexane = 1:3). ^1H NMR ($CDCl_3$, 300.13 MHz): δ = 1.65 (s, 3 H, CH_3), 3.07 (d, J = 17.2 Hz, 1 H, C*H*), 3.62 (d, J = 17.2 Hz, 1 H, C*H*), 3.8 (s, 3 H, OCH_3), 4.02 (d, J = 10.3 Hz, 1 H, C*H*I), 4.10 (d, J = 10.3 Hz, 1 H, C*H*I) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT): δ = –6.6 (*C*H_2I), 23.4 (*C*H_3), 45.0 (*C*H_2), 53.0 (O*C*H_3), 87.0 (C-O), 156.1 (*C*=N), 171.8 (*C*=O) ppm. HRMS: calcd. for $[C_7H_{11}INO_3]^+$ 283.9778; found 283.9784; calcd. for $[C_7H_{10}INO_3Na]^+$ 305.9598; found 305.9603.

2-Chloro-1-phenylethanone *O*-(Trimethylsilyl)oxime (1u):[22] Yield 80% (procedure *i*). Colorless oil. Single isomer with unknown configuration. ^1H NMR ($CDCl_3$, 300.13 MHz): δ = 0.32 [s, 9 H, Si(CH_3)$_3$], 4.64 (s, 2 H, CH_2), 7.35–7.46 and 7.72–7.80 (2 m, 3 H and 2 H, *o*-, *m*-, *p*-C_6H_5) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT): δ = –0.7 [Si(*C*H_3)$_3$], 32.3 (*C*H_2), 126.3, 128.5, and 129.6 (*o*-, *m*-, *p*-C_6H_5), 133.7 (*i*-C_6H_5), 157.0 (*C*=N) ppm. ^{29}Si NMR ($CDCl_3$, 59.63 MHz, INEPT): δ = 27.6 ppm. MS (EI): *m*/*z* (%) = 243 and 241 (8 and 24) $[M]^{+\cdot}$, 228 and 226 (12 and 34) $[M - CH_3]^{+\cdot}$, 192 (13) $[M - CH_2Cl]^{+\cdot}$, 103 (44) $[M - CH_2Cl - OSi(CH_3)_3]^{+\cdot}$, 77 (66) $[Ph]^{+\cdot}$, 73 (100) $[(CH_3)_3Si]^{+\cdot}$. Purity determined by ^1H NMR spectroscopy with internal standard (trichloroethylene): ca. 95%.

Methyl 5-Bromo-4-{[(trimethylsilyl)oxy]imino}pentanoate (1v): Yield 72% (procedure *i*), 57% (procedure *iii*). Colorless oil. Mixture of isomers (ratio *Z*/*E* = 2.3:1). ^1H NMR ($CDCl_3$, 300.13 MHz, *Z* isomer): δ = 0.17 [s, 9 H, Si(CH_3)$_3$], 2.60 (t, J = 6.5 Hz, 2 H, CH_2-CH_2), 2.72 (t, J = 6.5 Hz, 2 H, CH_2-CH_2), 3.65 (s, 3 H, CO_2CH_3), 4.01 (s, 2 H, CH_2Br) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, *Z* isomer): δ = –1.0 [Si(*C*H_3)$_3$], 21.0, 27.7, and 29.9 (*C*H_2-*C*H_2 and *C*H_2Br), 51.5 (O*C*H_3), 157.1 (*C*=N), 173.0 (*C*=O) ppm. ^{29}Si NMR ($CDCl_3$, 59.63 MHz, INEPT, *Z* isomer): δ = 26.3 ppm. ^1H NMR ($CDCl_3$, 300.13 MHz, *E* isomer): δ = 0.16 [s, 9 H, Si(CH_3)$_3$], 2.55 (t, J = 7.0 Hz, 2 H, CH_2-CH_2), 2.66 (t, J = 7.0 Hz, 2 H, CH_2-CH_2), 3.66 (s, 3 H, CO_2CH_3), 4.15 (s, 2 H, CH_2Br) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, *E* isomer): δ = –0.8 [Si(*C*H_3)$_3$], 22.7, 30.1, and 33.5 (*C*H_2-*C*H_2 and *C*H_2Br), 51.7 (O*C*H_3), 157.1 (*C*=N), 173.0 (*C*=O) ppm. ^{29}Si NMR ($CDCl_3$, 59.63 MHz, INEPT, *E* isomer): δ = 24.7 ppm. FTIR (neat): $\tilde{\nu}$ = 3435 (br, m), 2956 (s), 2851 (w), 1741 (s), 1620 (w), 1553 (m), 1438 (s), 1363 (m), 1317 (m), 1253 (s), 1201 (s), 1172 (s), 1111 (m), 974 (w), 923 (w, sh), 878 (s), 847 (s), 754 (m), 695 (w), 628 (w) cm^{-1}. MS (EI): *m*/*z* (%) = 297 and 295 (5) $[M]^{+\cdot}$, 282 and 280 (5) $[M - CH_3]^{+\cdot}$, 264 and 266 (2) $[M - OCH_3]^{+\cdot}$, 202 (10) $[M - CH_2Br]^{+\cdot}$, 113 (25) $[M - CH_2Br - OSi(CH_3)_3]^{+\cdot}$, 73 (100) $[(CH_3)_3Si]^{+\cdot}$. Purity determined by ^1H NMR spectroscopy with internal standard (trichloroethylene): ca. 75% (contains ca. 20% of **8v**,[15] *E*/*Z* = 6.0:1.0).

2-Bromo-1-phenylethanone *O*-(Trimethylsilyl)oxime (1w): Yield 82% (procedure *i*), 70% (procedure *iii*). Colorless oil. Single isomer with unknown configuration. ^1H NMR ($CDCl_3$, 300.13 MHz): δ = 0.32 [s, 9 H, Si(CH_3)$_3$], 4.45 (s, 2 H, CH_2), 7.40–7.44 and 7.74–7.77 (2 m, 3 H and 2 H, *o*-, *m*-, *p*-C_6H_5) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT): δ = –0.6 [Si(*C*H_3)$_3$], 17.9 (*C*H_2), 126.2, 128.6, and 129.7 (*o*-, *m*-, *p*-C_6H_5), 133.8 (*i*-C_6H_5), 157.2 (*C*=N) ppm. ^{29}Si NMR ($CDCl_3$, 59.63 MHz, INEPT): δ = 27.6 ppm. FTIR: $\tilde{\nu}$ = 3390 (br, m), 3218 (m), 3066 (m, sh), 2946 (m), 1682 (s, sh), 1596 (m), 1567 (s), 1449 (s), 1393 (m), 1349 (s, sh), 1280 (s), 1195 (m), 1014 (w), 1001 (w), 991 (w), 711 (m), 688 (s), 623 (w), 610 (w) cm^{-1}. MS (EI): *m*/*z* (%) = 287 and 285 (18) $[M]^{+\cdot}$, 272 and 270 (22) $[M - CH_3]^{+\cdot}$, 207 and 205 (3) $[M - Ph]^{+\cdot}$, 192 (5) $[M - CH_2Br]^{+\cdot}$, 103 (38) $[M - CH_2Br - OSi(CH_3)_3]^{+\cdot}$, 77 (72) $[Ph]^{+\cdot}$, 73 (100) $[(CH_3)_3Si]^{+\cdot}$. Purity determined by ^1H NMR spectroscopy with internal standard (trichloroethylene): ca. 90%.

2-Iodo-1-phenylethanone *O*-(Trimethylsilyl)oxime (1x): Yield 86% (procedure *i*). Colorless oil. Single isomer with *Z* configuration. ^1H NMR ($CDCl_3$, 300.13 MHz): δ = 0.34 [s, 9 H, Si(CH_3)$_3$], 4.31 (s, 2 H, CH_2), 7.38–7.46 and 7.72–7.77 (2 m, 3 H and 2 H, *o*-, *m*-, *p*-C_6H_5) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT): δ = –11.3 (*C*H_2), –0.6 [Si(*C*H_3)$_3$], 126.2, 128.6, and 129.7 (*o*-, *m*-, *p*-C_6H_5), 133.8 (*i*-C_6H_5), 158.3 (*C*=N) ppm. ^{29}Si NMR ($CDCl_3$, 59.63 MHz, INEPT): δ = 27.3 ppm. FTIR (neat): $\tilde{\nu}$ = 3060 (w), 2960 (s), 2926 (w), 2902 (w), 1495 (w), 1444 (m), 1418 (m), 1324 (m), 1251 (s), 1159 (m), 1049 (m), 1028 (w), 947 (s), 892 (s), 851 (s), 767 (m), 754 (sh), 692 (m), 632 (w), 586 (w), 510 (w) cm^{-1}. MS (EI): *m*/*z* (%) = 333 (3) $[M]^{+\cdot}$, 318 (2) $[M - CH_3]^{+\cdot}$, 206 (27) $[M - I]^{+\cdot}$, 127 (2) $[I]^{+\cdot}$, 103 (33) $[M - CH_2I - OSi(CH_3)_3]^{+\cdot}$, 77 (64) $[Ph]^{+\cdot}$, 73 (100) $[(CH_3)_3Si]^{+\cdot}$. Purity determined by ^1H NMR spectroscopy with internal standard (trichloroethylene): ca. 80%.

Methyl 5-Iodo-4-{[(trimethylsilyl)oxy]imino}pentanoate (1y): Yield 80% (procedure *i*). Yellowish oil unstable at room temp. Mixture of isomers (ratio *Z*/*E* = 5:1). ^1H NMR ($CDCl_3$, 300.13 MHz, *Z* isomer): δ = 0.19 [s, 9 H, Si(CH_3)$_3$], 2.63 (t, J = 6.3 Hz, 2 H, CH_2), 2.75 (t, J = 6.3 Hz, 2 H, CH_2), 3.67 (s, 3 H, OCH_3), 3.87 (s, 2 H, CH_2I) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, *Z* isomer): δ = –8.3 (*C*H_2I), –0.8 [Si(*C*H_3)$_3$], 27.8 and 30.0 (2 *C*H_2), 51.7 (O*C*H_3), 158.3 (*C*=N), 173.1 (*C*=O) ppm. ^{29}Si NMR ($CDCl_3$, 59.63 MHz, INEPT, *Z* isomer): δ = 26.1 ppm. ^1H NMR ($CDCl_3$, 300.13 MHz, *E* isomer): δ = 0.18 [s, 9 H, Si(CH_3)$_3$], 2.60 (m, 2 H, CH_2), 2.67 (m, 2 H, CH_2), 3.68 (s, 3 H, OCH_3), 4.00 (s, 2 H, CH_2I) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, *E* isomer): δ = –0.7 [Si(*C*H_3)$_3$], 4.9 (*C*H_2I), 30.1 and 30.5 (2 *C*H_2), 51.8 (O*C*H_3), 160.3 (*C*=N), 173.1 (*C*=O) ppm. ^{29}Si NMR ($CDCl_3$, 59.63 MHz, INEPT, *E* isomer): δ = 26.2 ppm. FTIR (neat): $\tilde{\nu}$ = 2957 (s), 2906 (m), 2850 (w),

1741 (s, C=O), 1438 (s), 1420 (m), 1363 (m), 1320 (m), 1252 (s), 1223 (m), 1197 (m), 1170 (s), 1093 (m), 1028 (w), 987 (w), 987 (m), 960 (m), 924 (s), 848 (s, sh), 754 (m), 698 (w), 628 (w), 543 (w), 485 (w), 437 (w) cm^{-1}. MS (EI): *m*/*z* (%) = 343 (1) $[M]^{+\cdot}$, 328 (1) [M – $CH_3]^{+\cdot}$, 312 (2) [M – $OCH_3]^{+\cdot}$, 216 (11) [M – I]$^{+\cdot}$, 202 (2) [M – $CH_2I]^{+\cdot}$, 127 (5) $[I]^{+\cdot}$, 113 (10) [M – CH_2I – $OSi(CH_3)_3]^{+\cdot}$, 73 (75) $[(CH_3)_3Si]^{+\cdot}$. Purity determined by ^{1}H NMR spectroscopy with internal standard (trichloroethylene): ca. 85% (contains ca. 10% of **8v**,[15] *E*/*Z* = 4.0:1.0).

1-Iodo-3-phenylacetone *O*-(Trimethylsilyl)oxime (1z): Yield 82% (procedure *i*). Colorless oil. Mixture of isomers (ratio *Z*/*E* = 2.8:1). ^{1}H NMR ($CDCl_3$, 300.13 MHz, *Z* isomer): δ = 0.27 [s, 9 H, $Si(CH_3)_3$], 3.72 and 3.77 (2 s, 2 H and 2 H, 2 CH_2), 7.20–7.35 (m, 5 H, *o*-, *m*-, *p*-C_6H_5) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, *Z* isomer): δ = –9.2 (CH_2I), –0.7 [$Si(CH_3)_3$], 38.5 ($CH_2C_6H_5$), 127.0, 128.7, and 129.0 (*o*-, *m*-, *p*-C_6H_5), 136.7 (*i*-C_6H_5), 159.7 (*C*=N) ppm. ^{29}Si NMR ($CDCl_3$, 59.63 MHz, INEPT, *Z* isomer): δ = 25.9 ppm. ^{1}H NMR ($CDCl_3$, 300.13 MHz, *E* isomer): δ = 0.25 [s, 9 H, $Si(CH_3)_3$], 3.85 and 3.97 (2 s, 2 H and 2 H, 2 CH_2), 7.20–7.35 (m, 5 H, *o*-, *m*-, *p*-C_6H_5) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, *E* isomer): δ = –0.7 [$Si(CH_3)_3$], 3.89 (CH_2I), 32.0 ($CH_2C_6H_5$), 126.7, 128.7, and 129.1 (*o*-, *m*-, *p*-C_6H_5), 136.7 (*i*-C_6H_5), 162.0 (*C*=N) ppm. ^{29}Si NMR ($CDCl_3$, 59.63 MHz, INEPT, *E* isomer): δ = 25.9 ppm. FTIR (neat): $\tilde{\nu}$ = 3063 (w), 3029 (w), 2959 (m), 2926 (w, sh), 2857 (w), 1602 (w), 1553 (w), 1531 (w), 1495 (m), 1454 (m), 1418 (m), 1252 (s), 1152 (m, sh), 1089 (m, sh), 1030 (s), 965 (s), 925 (m), 885 (s), 848 (s), 740 (s, sh), 700 (s), 628 (w), 576 (w), 540 (w), 462 (w) cm^{-1}. MS (EI): *m*/*z* (%) = 347 (3) $[M]^{+\cdot}$, 332 (5) [M – $CH_3]^{+\cdot}$, 220 (70) [M – I]$^{+\cdot}$, 127 (3) $[I]^{+\cdot}$, 117 (20) [M – CH_2I – $OSi(CH_3)_3]^{+\cdot}$, 91 (100) $[PhCH_2]^{+\cdot}$, 73 (70) $[(CH_3)_3Si]^{+\cdot}$. Purity determined by ^{1}H NMR spectroscopy with internal standard (trichloroethylene): ca. 85% [contains ca. 15% of (*E*)-**8z**[15]].

Iodoacetaldehyde *O*-(Trimethylsilyl)oxime (1aa): Compound **1aa** was obtained by procedure *i* from **7aa** with some modifications: Diethyl ether was used for work-up, all evaporations were conducted at 400 Torr, yield 47% (procedure *i*). Volatile colorless oil unstable at room temp. and upon exposure to light. Mixture of isomers (ratio *Z*/*E* = 1.5:1). ^{1}H NMR ($CDCl_3$, 300.13 MHz, *Z* isomer): δ = 0.25 [s, 9 H, $Si(CH_3)_3$], 3.92 (d, *J* = 6.6 Hz, 2 H, CH_2I), 7.17 (t, *J* = 6.6 Hz, 1 H, C*H*) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, *Z* isomer): δ = –10.9 (CH_2I), –0.9 [$Si(CH_3)_3$], 150.4 (*C*=N) ppm. ^{29}Si NMR ($CDCl_3$, 59.63 MHz, INEPT, *Z* isomer): δ = 27.1 ppm. ^{1}H NMR ($CDCl_3$, 300.13 MHz, *E* isomer): δ = 0.22 [s, 9 H, $Si(CH_3)_3$], 3.89 (d, *J* = 7.0 Hz, 2 H, CH_2I), 7.61 (t, *J* = 6.6 Hz, 1 H, C*H*) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, *E* isomer): δ = –1.9 (CH_2I), –0.9 [$Si(CH_3)_3$], 151.7 (*C*=N) ppm. ^{29}Si NMR ($CDCl_3$, 59.63 MHz, INEPT, *E* isomer): δ = 26.9 ppm. FTIR (neat): $\tilde{\nu}$ = 2961 (s), 2926 (m), 2856 (m), 1734 (w), 1611 (w), 1416 (m), 1254 (s), 1151 (m), 1096 (s, sh), 1021 (s), 930 (s), 875 (s), 848 (s), 805 (s), 752 (s), 695 (w), 558 (w) cm^{-1}. MS (EI): *m*/*z* (%) = 257 (8) $[M]^{+\cdot}$, 242 (37) [M – $CH_3]^{+\cdot}$, 130 (46) [M – I]$^{+\cdot}$, 127 (7) $[I]^{+\cdot}$, 73 (100) $[(CH_3)_3Si]^{+\cdot}$. Purity determined by ^{1}H NMR spectroscopy with internal standard (trichloroethylene): ca. 75% [contains ca. 10% of (*E*)-**8aa**[15]].

2-Bromopropanal *O*-(Trimethylsilyl)oxime (1ab): Compound **1ab** was obtained as a mixture with **8ab**[15] [ratios **1ab**/**8ab** = 1:2.9, (*E*)-**1ab**/(*Z*)-**1ab** = 6.7:1, (*E*)-**8ab**/(*Z*)-**1ab** = 3.9:1] by procedure *iii* employing K_2CO_3 instead of $NaHSO_4$ for the aqueous work-up, yield 13%. Characterized by ^{1}H NMR spectroscopy as a mixture with **8ab**.[15] ^{1}H NMR ($CDCl_3$, 300.13 MHz, *E* isomer): δ = 0.22 [s, 9 H, $Si(CH_3)_3$], 1.85 (d, *J* = 6.8 Hz, 3 H, CH_3), 4.71 (m, 1 H, C*H*I), 7.61 (d, *J* = 7.6 Hz, 1 H, *H*C=N) ppm. ^{1}H NMR ($CDCl_3$, 300.13 MHz, *Z* isomer): δ = 0.22 [s, 9 H, $Si(CH_3)_3$], 1.76 (d, *J* = 6.8 Hz, 3 H, CH_3), 5.34 (m, 1 H, C*H*I), 7.05 (d, *J* = 7.8 Hz, 1 H, *H*C=N) ppm. The ^{1}H NMR spectra of the *E*/*Z* isomers are in accordance with literature data.[8b]

Methanolysis of Silyl Ethers of α-Halo Oximes 1v–z: A solution of tetrabutylammonium fluoride (0.13 g, 0.5 mmol) in methanol (2.5 mL) was added to a stirred solution of the crude trimethylsilyl ether of the α-halo oxime (0.5 mmol) in methanol (2.5 mL). The mixture was kept at room temperature for 48 h, evaporated in vacuo, and the residue was subjected to column chromatography on silica gel (eluent EtOAc/hexane gradient).

Methyl 4-(Hydroxyimino)-5-methoxypentanoate (9v): Yield 70% (from **1v**), 72% (from **1y**). For analytical purposes **9v** was purified by vacuum bulb-to-bulb distillation (0.4 Torr). Colorless liquid. Mixture of isomers (ratio *E*/*Z* = 1.8:1). R_f = 0.4 (EtOAc/hexane = 1:1). ^{1}H NMR ($CDCl_3$, 300.13 MHz, *E* isomer): δ = 2.52–2.73 (m, 4 H, CH_2-CH_2), 3.30 (s, 3 H, CH_2OCH_3), 3.67 (s, 3 H, $COOCH_3$), 3.97 (s, 2 H, CH_2OCH_3), 9.01 (br., 1 H, O*H*) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, *E* isomer): δ = 21.5 and 29.6 (CH_2-CH_2), 51.7 (CO_2CH_3), 58.2 (OCH_3), 72.7 (CH_2OCH_3), 157.0 (*C*=N), 173.2 (*C*=O) ppm. ^{1}H NMR ($CDCl_3$, 300.13 MHz, *Z* isomer): δ = 2.52–2.73 (m, 4 H, CH_2-CH_2), 3.35 (s, 3 H, CH_2OCH_3), 3.66 (s, 3 H, $COOCH_3$), 4.29 (s, 2 H, CH_2OCH_3), 9.01 (br., 1 H, O*H*) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, *Z* isomer): δ = 25.8 and 30.4 (CH_2-CH_2), 51.7 (CO_2CH_3), 59.1 (OCH_3), 67.1 (CH_2OCH_3), 158.4 (*C*=N), 173.3 (*C*=O) ppm. $C_7H_{13}NO_4$ (175.18): C 47.99, H 7.48, N 8.00; found C 47.93, H 7.62, N 8.15.

2-Methoxy-1-phenylethanone Oxime (9w): Yield 71% (from **1w**), 62% (from **1x**). Crystallized from pentane as only the *E* isomer (m.p. 51–55 °C), which slowly isomerizes in $CDCl_3$ solution to give a mixture of *E*/*Z* isomers, ratio 1.0:3.0. R_f = 0.5 (EtOAc/hexane = 1:1). ^{1}H NMR ($CDCl_3$, 300.13 MHz, *E* isomer): δ = 3.39 (s, 3 H, OCH_3), 4.35 (s, 2 H, CH_2), 7.34–7.51 and 7.62–7.78 (2 m, 3 H and 2 H, *o*-, *m*-, *p*-C_6H_5), 9.40 (br., 1 H, O*H*) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, *E* isomer): δ = 58.1 (OCH_3), 73.5 (CH_2), 127.0, 128.3, and 129.4 (*o*-, *m*-, *p*-C_6H_5), 133.6 (*i*-C_6H_5), 154.3 (*C*=N) ppm. ^{1}H NMR ($CDCl_3$, 300.13 MHz, *Z* isomer): δ = 3.38 (s, 3 H, OCH_3), 4.72 (s, 2 H, CH_2), 7.34–7.51 and 7.62–7.78 (2 m, 3 H and 2 H, *o*-, *m*-, *p*-C_6H_5), 9.40 (br., 1 H, O*H*) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, *Z* isomer): δ = 58.7 (OCH_3), 64.0 (CH_2), 127.0, 128.4, and 129.4 (*o*-, *m*-, *p*-C_6H_5), 134.1 (*i*-C_6H_5), 156.4 (*C*=N) ppm. ^{1}H NMR spectra of the *E*/*Z* isomers are in accordance with literature data.[23]

1-Methoxy-3-phenylacetone Oxime (9z): Yield 74% (from **1z**). Colorless oil. Mixture of isomers (ratio *E*/*Z* = 17:1). R_f = 0.3 (EtOAc/hexane = 1:3). ^{1}H NMR ($CDCl_3$, 300.13 MHz, *E* isomer): δ = 3.30 (s, 3 H, OCH_3), 3.81 and 3.92 (2 s, 2 H and 2 H, CH_2Ph and CH_2OCH_3), 7.19–7.36 (m, 5 H, *o*-, *m*-, *p*-C_6H_5), 9.63 (br., 1 H, O*H*) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, *E* isomer): δ = 31.3 (CH_2Ph), 58.1 (OCH_3), 72.6 (CH_2OCH_3), 126.6, 128.6, and 129.3 (*o*-, *m*-, *p*-C_6H_5), 136.1 (*i*-C_6H_5), 157.0 (*C*=N) ppm. ^{1}H NMR ($CDCl_3$, 300.13 MHz, *Z* isomer): δ = 3.32 (s, 3 H, OCH_3), 3.63 (s, 2 H, CH_2Ph), 4.25 (s, 2 H, CH_2OCH_3), 7.19–7.36 (m, 5 H, *o*-, *m*-, *p*-C_6H_5), 9.63 (br., 1 H, O*H*) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz, DEPT, characteristic signals of *Z* isomer): δ = 36.8 (CH_2Ph), 58.1 (OCH_3), 66.0 (CH_2OCH_3), 126.8, 128.6, and 129.1 (*o*-, *m*-, *p*-C_6H_5) ppm. $C_{10}H_{13}NO_2$ (179.22): calcd. C 67.02, H 7.31, N 7.82; found C 66.81, H 7.34, N 7.89.

Methoxyacetaldehyde Oxime (9aa): A solution of tetrabutylammonium fluoride (0.20 g, 0.75 mmol) in methanol (3.8 mL) was added to a stirred solution of crude iodoacetaldehyde *O*-(trimethylsilyl)-oxime (**1aa**; 0.194 g, 0.75 mmol) in methanol (3.8 mL). The mixture

was kept at room temperature for 48 h and then evaporated under normal pressure. The residue was subjected to flash chromatography on silica gel (eluent pentane/Et_2O = 1:1). The resulting fraction was evaporated under normal pressure to give 0.046 g (69%) of **9aa** as a colorless volatile liquid. For analytical purposes **9aa** was additionally purified by vacuum bulb-to-bulb distillation (15 Torr). Colorless volatile liquid. Mixture of isomers (ratio *E*/*Z* = 1.4:1). R_f = 0.4 (EtOAc/hexane = 1:1). ^{1}H NMR ($CDCl_3$, 300.13 MHz, *E* isomer): δ = 3.38 (s, 3 H, OCH_3), 4.04 (d, *J* = 5.6 Hz, 2 H, CH_2), 7.49 (t, *J* = 5.6 Hz, 1 H, *H*C=N), 8.05 (br., 1 H, OH) ppm. ^{13}C NMR ($CDCl_3$, 300.13 MHz, DEPT, *E* isomer): δ = 58.4 (OCH_3), 69.0 (CH_2OCH_3), 148.2 (*C*=N) ppm. ^{1}H NMR ($CDCl_3$, 300.13 MHz, *Z* isomer): δ = 3.41 (s, 3 H, OCH_3), 4.29 (d, *J* = 3.1 Hz, 2 H, CH_2), 6.88 (t, *J* = 3.1 Hz, 1 H, *H*C=N), 8.05 (br., 1 H, OH) ppm. ^{13}C NMR ($CDCl_3$, 300.13 MHz, DEPT, *Z* isomer): δ = 59.0 (OCH_3), 66.4 (CH_2OCH_3), 151.0 (*C*=N) ppm. The ^{1}H NMR spectra of the *E*/*Z* isomers are in accordance with literature data.[24]

Supporting Information (see footnote on the first page of this article): ^{1}H, ^{13}C, ^{29}Si, 2D NMR, IR, and UV spectra for all compounds.

Acknowledgments

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[1] a) W. Oppolzer, M. Petrzilka, K. Battig, *Helv. Chim. Acta* **1977**, *60*, 2964; b) W. Oppolzer, K. Battig, T. Hudlicky, *Tetrahedron* **1981**, *37*, 4359; c) E. J. Corey, M. Petrzilka, Y. Ueda, *Helv. Chim. Acta* **1977**, *60*, 2294; d) Y. Feng, M. M. Majirek, S. M. Weinreb, *J. Org. Chem.* **2014**, *79*, 7; e) P. S. Chauhan, S. M. Weinreb, *J. Org. Chem.* **2014**, *79*, 6389; f) T. Tsuritani, K. Yagi, H. Shinokubo, K. Oshima, *Angew. Chem. Int. Ed.* **2003**, *42*, 5613; *Angew. Chem.* **2003**, *115*, 5771; g) H. Kakiya, K. Yagi, H. Shinokubo, K. Oshima, *J. Am. Chem. Soc.* **2002**, *124*, 9032; h) W. D. Shipe, E. J. Sorensen, *Org. Lett.* **2002**, *4*, 2063; for reviews on the applications of α-halo oximes and their ethers, see: i) T. L. Gilchrist, *Chem. Soc. Rev.* **1983**, *12*, 53; j) T. L. Gilchrist, J. E. Wood, in: *Comprehensive Heterocyclic Chemistry II*, vol. 6 (Ed.: A. J. Boulton), Pergamon Press, Oxford, UK, **1996**, p. 279; k) I. M. Lyapkalo, S. L. Ioffe, *Russ. Chem. Rev.* **1998**, *67*, 467; l) B. G. Gowenlock, G. B. Richter-Addo, *Chem. Rev.* **2004**, *104*, 3315; m) R. Zimmer, M. Collas, M. Roth, H.-U. Reissig, *Liebigs Ann. Chem.* **1992**, *7*, 709; n) R. Zimmer, H.-U. Reissig, *J. Org. Chem.* **1992**, *57*, 339; o) R. Zimmer, J. Angermann, U. Hain, F. Hiller, H.-U. Reissig, *Synthesis* **1997**, *12*, 1467.

[2] a) S. E. Denmark, M. S. Dappen, *J. Org. Chem.* **1984**, *49*, 798; b) S. E. Denmark, M. S. Dappen, J. A. Sternberg, *J. Org. Chem.* **1984**, *49*, 4741; c) S. E. Denmark, M. S. Dappen, N. L. Sear, R. T. Jacobs, *J. Am. Chem. Soc.* **1990**, *112*, 3466.

[3] a) I. Korbouch, P. Kumar, S. M. Weinreb, *J. Am. Chem. Soc.* **2007**, *129*, 10342; b) P. Kumar, P. Li, I. Korboukh, T. L. Wang, H. Yennawar, S. M. Weinreb, *J. Org. Chem.* **2011**, *76*, 2094; c) J. A. Witek, S. M. Weinreb, *Org. Lett.* **2011**, *13*, 1258; d) S. Shatzmiller, S. Bercovici, *Liebigs Ann. Chem.* **1992**, 1005; e) K. Wimalasena, D. C. Haines, *J. Org. Chem.* **1994**, *59*, 6472; f) A. Yu. Sukhorukov, M. S. Klenov, P. E. Ivashkin, A. V. Lesiv, Yu. A. Khomutova, S. L. Ioffe, *Synthesis* **2007**, 97; g) M. S. Klenov, A. V. Lesiv, Yu. A. Khomutova, I. D. Nesterov, S. L. Ioffe, *Synthesis* **2004**, 1159; h) A. A. Tishkov, A. V. Lesiv, Yu. A. Khomutova, Yu. A. Strelenko, I. D. Nesterov, M. Yu. Antipin, S. L. Ioffe, S. E. Denmark, *J. Org. Chem.* **2003**, *68*, 9477.

[4] a) B. Noverges, C. Mollar, M. Media-Simon, G. Asensio, *Adv. Synth. Catal.* **2013**, *355*, 2327; b) O. L. Eliseev, P. E. Ivashkin, A. G. Ostapenko, A. V. Lesiv, Y. A. Khomutova, S. L. Ioffe, A. L. Lapidus, *Synlett* **2006**, 2239; c) M. Shimizu, T. Toyoda, *Org. Biomol. Chem.* **2004**, *2*, 2891; d) M. Shimizu, M. Tanaka, T. Itoh, *Synlett* **2006**, 1687; e) R. Sengupta, S. M. Weinreb, *Synthesis* **2012**, *44*, 2933.

[5] A. Yu. Sukhorukov, S. L. Ioffe, *Chem. Rev.* **2011**, *111*, 5004.

[6] a) A. Yu. Sukhorukov, A. V. Lesiv, Yu. A. Khomutova, S. L. Ioffe, *Synthesis* **2009**, 741; b) A. Yu. Sukhorukov, A. V. Lesiv, O. L. Eliseev, Yu. A. Khomutova, S. L. Ioffe, *Synthesis* **2009**, 2570; c) A. Yu. Sukhorukov, A. V. Lesiv, O. L. Eliseev, Yu. A. Khomutova, S. L. Ioffe, A. O. Borissova, *Eur. J. Org. Chem.* **2008**, 4025; d) A. Yu. Sukhorukov, A. V. Lesiv, O. L. Eliseev, Yu. A. Khomutova, T. N. Bondarenko, A. L. Lapidus, S. L. Ioffe, *Mendeleev Commun.* **2007**, *17*, 122; e) A. Yu. Sukhorukov, A. V. Lesiv, Yu. A. Khomutova, S. L. Ioffe, V. A. Tartakovsky, *Synthesis* **2009**, 1999; f) A. Yu. Sukhorukov, A. V. Lesiv, Yu. A. Khomutova, S. L. Ioffe, Yu. V. Nelyubina, *Synthesis* **2008**, 1205.

[7] For other applications of cyclic α-halo oxime ethers in total synthesis, see: a) A. Yu. Sukhorukov, Y. D. Boyko, Yu. A. Khomutova, Yu. V. Nelyubina, S. L. Ioffe, V. A. Tartakovsky, *J. Org. Chem.* **2011**, *76*, 7893; b) P. A. Zhmurov, A. Yu. Sukhorukov, V. I. Chupakhin, Yu. A. Khomutova, S. L. Ioffe, V. A. Tartakovsky, *Org. Biomol. Chem.* **2013**, *11*, 8082.

[8] a) A. Hassner, K. S. K. Murthy, *Tetrahedron Lett.* **1987**, *28*, 683; b) A. Hassner, K. S. K. Murthy, *J. Org. Chem.* **1988**, *53*, 5063; c) A. Hassner, K. S. K. Murthy, *J. Org. Chem.* **1989**, *54*, 5277; d) A. Hassner, K. S. K. Murthy, *Tetrahedron Lett.* **1987**, *28*, 4097; e) A. Hassner, R. Maurya, E. Mesko, *Tetrahedron Lett.* **1988**, *29*, 5313.

[9] For some recent patents on the application of α-halo oxime ethers in the synthesis of pharmaceuticals, see: a) T. Biftu, M. Wyvratt, M. Fisher (Merck), U.S. Patent 20060293303 A1, Dec. 28, **2006**; *Chem. Abstr. 143*: 115554, **2005**; b) U. Saha, G. H. Posner, M. Kahraman, Johns Hopkins University, U.S. Patent 20090082317 A1, Apr. 26, **2009**; *Chem. Abstr. 145*: 471757, **2006**; c) D. A. Guthrie, Johns Hopkins University, W.O. Patent 2013059194 A1, Apr. 15, **2013**; *Chem. Abstr. 158*: 620863, **2013**; d) G. D. Artman, R. C. Gadwood, S. D. Larsen, T. Parker, S. P. Tanis, J. R. Zeller, MSDC, W.O. Patent 2012021467 A1, Feb. 16, **2012**; *Chem. Abstr. 156*: 284871, **2012**; e) D. W. Brooks, A. O. Steward, J. G. Martin, Abbott Labs, U.S. Patent, 5183818 A1, Feb. 2, **1993**; *Chem. Abstr. 118*: 212868u, **1993**.

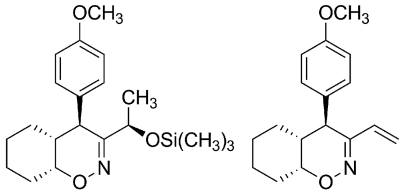
[10] a) A. D. Dilman, A. A. Tishkov, I. M. Lyapkalo, S. L. Ioffe, Yu. A. Strelenko, V. A. Tartakovsky, *Synthesis* **1998**, 181; b) A. D. Dilman, S. L. Ioffe, H. Mayr, *J. Org. Chem.* **2001**, *66*, 3196; c) A. Yu. Sukhorukov, I. V. Bliznets, A. V. Lesiv, Yu. A. Khomutova, S. L. Ioffe, *Synthesis* **2005**, 1077.

[11] a) A. A. Tabolin, A. V. Lesiv, Yu. A. Khomutova, Yu. V. Nelyubina, S. L. Ioffe, *Tetrahedron* **2009**, *65*, 4578; b) A. A. Tabolin, Yu. A. Khomutova, Yu. V. Nelyubina, S. L. Ioffe, V. A. Tartakovsky, *Synthesis* **2011**, 2415; c) A. A. Tabolin, A. V. Lesiv, S. L. Ioffe, *Synthesis* **2009**, 3099; d) A. A. Mikhaylov, A. D. Dilman, R. A. Kunetsky, Yu. A. Khomutova, M. I. Struchkova, A. A. Korlyukov, S. L. Ioffe, V. A. Tartakovsky, *Tetrahedron Lett.* **2010**, *51*, 1038.

[12] a) J. Hicks, C. Jones, *Inorg. Chem.* **2013**, *52*, 3900; b) A. Asadi, C. Eaborn, M. S. Hill, P. B. Hitchcock, J. D. Smith, *J. Organomet. Chem.* **2005**, *690*, 944.

[13] It is likely that due to a high affinity towards silicon, the fluoride anion attacks the trimethylsilyl group but not the carbon atom. This leads to the generation of highly reactive nitrosoalkenes, which easily undergo oligomerization reactions (for a detailed discussion of such processes see ref.[11b]).

[14] Silyl ether **10m** (5%) and ene-1,2-oxazine **11m** (4%) were obtained as byproducts. For selective syntheses of these products, see ref.[11a]



10m (5%) **11m** (4%)

[15] A. A. Tabolin, A. V. Lesiv, Yu. A. Khomutova, P. A. Belyakov, Yu. A. Strelenko, S. L. Ioffe, *Synthesis* **2005**, 1656.
[16] To the best of our knowledge, trimethylsilyl ethers of α-iodo oximes are hitherto unknown. One example of a TBS ether of an α-iodo oxime has been reported, see patent.[9e]
[17] These products also decompose under HRMS-ESI processing conditions.
[18] The reaction of **3a** with a mixture of $CoBr_2$ and $CoCl_2$ produced a 1.2:1.0 mixture of **1a** and **1q** in an overall yield of 93%.
[19] R. A. Kunetsky, A. D. Dilman, S. L. Ioffe, M. I. Struchkova, Yu. A. Strelenko, V. A. Tartakovsky, *Org. Lett.* **2003**, *5*, 4907.
[20] A. A. Mikhaylov, A. D. Dilman, M. I. Struchkova, Yu. A. Khomutova, A. A. Korlyukov, S. L. Ioffe, V. A. Tartakovsky, *Tetrahedron* **2011**, *67*, 4584.
[21] T. Ohwada, T. Ohta, K. Shudo, *Tetrahedron* **1987**, *43*, 297.
[22] P. Rupani, A. Singh, A. K. Rai, R. C. Mehrotra, *Synth. React. Inorg. Met.-Org. Chem.* **1979**, *9*, 565.
[23] J. E. Oatis Jr., H. P. Schultz, *Org. Magn. Reson.* **1978**, *11*, 40.
[24] M. I. Kemp, Pfizer, W.O. Patent 2008135830 A8, Dec. 10, **2009**; *Chem. Abstr. 149*: 534259, **2008**.

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