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Rearrangement of 3-alkylidene-2-siloxy-tetrahydro-1,2-oxazines (ASENA). A new approach toward the synthesis of 3-α-hydroxyalkyl-5,6-dihydro-4*H*-1,2-oxazines

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ABSTRACT

A new approach toward the synthesis of 3-α-hydroxyalkyl-5,6-dihydro-4*H*-1,2-oxazines **1** from available 5,6-dihydro-4*H*-1,2-oxazine *N*-oxides **2** has been described. The key step of the process—the rearrangement of 3-alkiliden-2-siloxy-tetrahydro-1,2-oxazines **3** (ASENA)—was thoroughly investigated. Optimal experimental conditions were developed. A possible pathway of the ASENA rearrangement was proposed.

1. Introduction

1,2-Oxazine-*N*-oxides **2**—the products of [4+2]-cycloaddition of nitroalkenes to olefines—are useful intermediates in organic chemistry. They were used as convenient precursors of pyrrolidines,[1a,b] aminosugars,[1c] and other compounds. Silylation is one of the possible applications of 1,2-oxazine-*N*-oxides **2**.[2] It was found that they can be transformed into 3-halomethyl-derivatives of 1,2-oxazines,[2b] modified 1,2-oxazines,[2c] and tetrahydrooxazines[2d] (Scheme 1).

Recently, we have reported that 3-alkylidene-2-siloxy-tetrahydro-oxazines **3** (ASENA) obtained by silylation of 1,2-oxazine-*N*-oxides **2** can undergo the rearrangement affording 3-(1-silyloxy)alkyl-5,6-dihydro-4*H*-1,2-oxazines **4** (Scheme 1).[2a] On the one hand, this was the only example of this reaction. On the other hand, the reaction proceeded with a good yield and stereoselectivity. Also, the resulting 3-α-hydroxyalkyl-5,6-dihydro-4*H*-1,2-oxazines **1** can be considered as useful precursors of 2-hydroxyalkylpyrrolidines or 2-amino-1,5-dialcohols that possess different biological activity.[3]

Given the foresaid, the goal of this research was the detailed investigation of the rearrangement of **3** to **4** and elaboration of the method for the transformation of 5,6-dihydro-4*H*-1,2-oxazine-*N*-oxides **2** into 3-α-hydroxyalkyl-5,6-dihydro-4*H*-1,2-oxazines **1**, based on this rearrangement.[4]

2. Results and discussion

2.1. Rearrangement of 3-alkilidene-2-siloxy-tetrahydro-1,2-oxazines 3 (ASENA) to 3-(1-silyloxy)alkyl-1,2-oxazines 4

The reaction sequence **2**→**1** consists of three steps (Scheme 1). The first step—silylation of 1,2-oxazine-*N*-oxides **2** into ASENA **3**—has already been studied.[2a,b] The third step—desilylation of the siloxy derivative **4** of α-hydroxyoxime—has also been well-studied.[5,6] Thus, at first, we focused on the second step of the process, viz. the ASENA **3** rearrangement.

Previously it was reported that *N*,*N*-bis(silyloxy)enamines **5**, i.e., acyclic analogues of ASENA **3**, could undergo the acid-promoted rearrangement affording derivatives of α-oxyoximes **6** (Scheme 2). It was shown that the reaction proceeded with good yields both under the silylation conditions[7] and also upon treatment with catalytic amounts of a weak Lewis acid, e.g., AgOTf or $Zn(OTf)_2$.[6]

We attempted to use the same reaction conditions for the ASENA **3** rearrangement (Scheme 3, Table 1, entries 1–4). Since in the ASENA structure there are two non-equivalent oxy-groups bound with the nitrogen atom, two products were expected to form: the above-mentioned oxazines **4** (path a) and oximes of tetrahydropyrans **7** (path b) (Scheme 3, Table 1). Oxazines **4** were obtained under the non-nucleophilic conditions. In the case of the nucleophile catalysis we obtained pyranone oximes **7** (entry 12, vide infra). In all cases, yields of the rearrangement product did not exceed 40%. Interestingly, treatment of model compound **3a** with $Zn(OTf)_2$, successfully employed for the rearrangement of BENA **5** (Scheme 2), afforded **4a** in rather low yields (entry 1).

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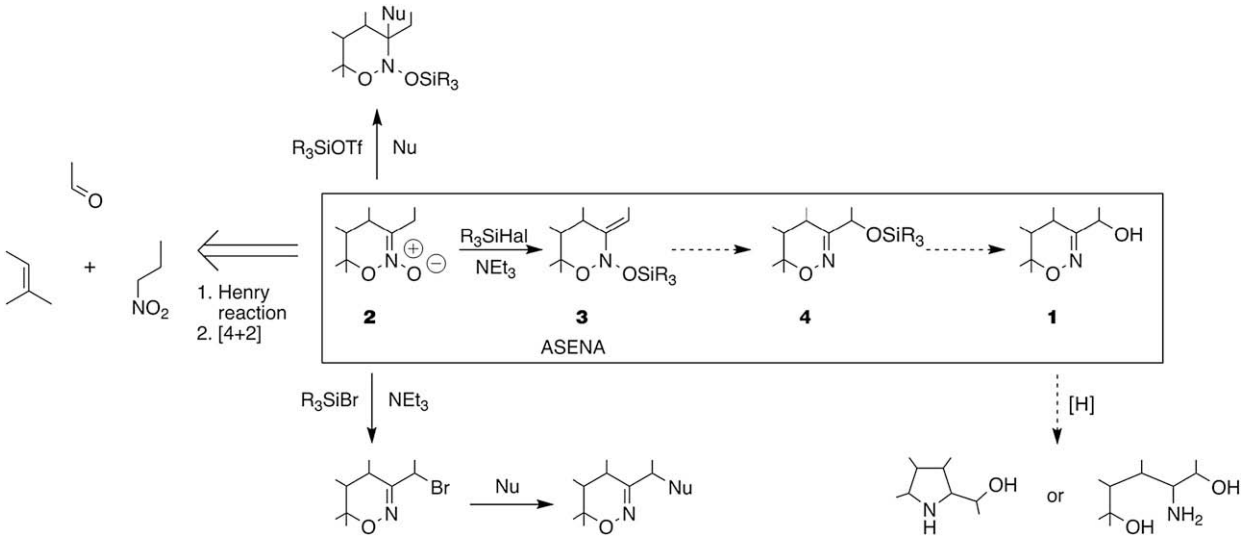
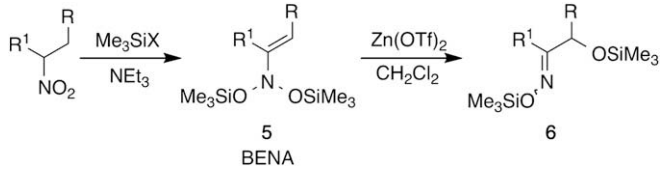
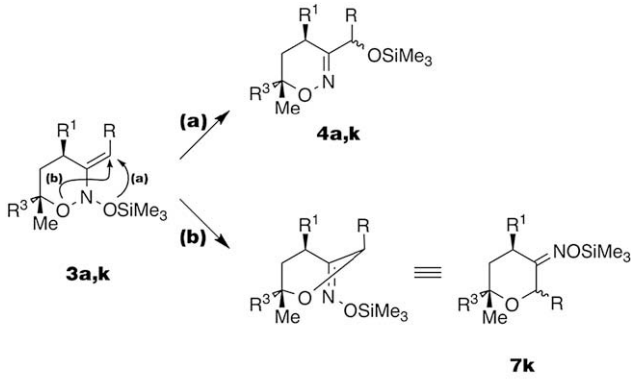


Scheme 1. Silylation of 1,2-oxazine-*N*-oxides **2**.



Scheme 2. Silylation of aliphatic nitro compounds.



Scheme 3. Rearrangement of ASENA **3**.

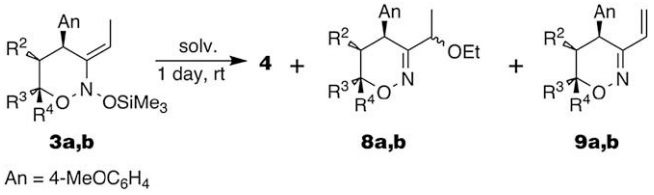
Table 1
Optimization of the conditions for the ASENA **3** rearrangement

Entry	Compound	Conditions	Product	Yield[a], %
1	**3a**	$Zn(OTf)_2$ (5%), 1 h	**4a**	16
2	**3k**	$Zn(OTf)_2$ (5%), 1 h	**4k**	15
3	**3a**	TsOH (10%), 1 h	**4a**	40
4	**3a**	TMSCl (10%), 1 h	**4a**	35
5	**3a**	$CHCl_3$, 24 h	**4a**	61
6	**3k**	$CHCl_3$, 24 h	—	0
7	**3a**	$CHCl_3/NEt_3$ (10%), 24 h	**4a**	53
8	**3a**	$CHCl_3$ (abs), 24 h	**4a**	15
9	**3a**	Hexane, 24 h	**4a**	11
10	**3a**	EtOAc, 24 h	**4a**	19
11	**3k**	$CHCl_3/H_2O$ (5%), 24 h	**4k**, **7k**	30 (**4k**), 30 (**7k**),
12	**3k**	TBAF (5%), 1 h	**7k**	27

[a] According to NMR with the internal standard ($CHCl{=}CCl_2$).

In contrast to it was found that several ASENA, when diluted in $CDCl_3$ and kept in the NMR tube for some time, rearranged to oxazines **4** in moderate to good yields. Also ASENA rearrangement occurred in other solvents such as ethyl acetate, hexane, tetrahydrofuran or dichloromethane though in lower yields than in chloroform. The highest yields were obtained where chloroform was distilled from P_2O_5 with subsequent water addition (5%).

While using commercially available chloroform (stabilized by ethanol) the formation of by-product **8** (13%) was observed (Scheme 4, Table 2).



Scheme 4. By-products of the ASENA **3** rearrangement.

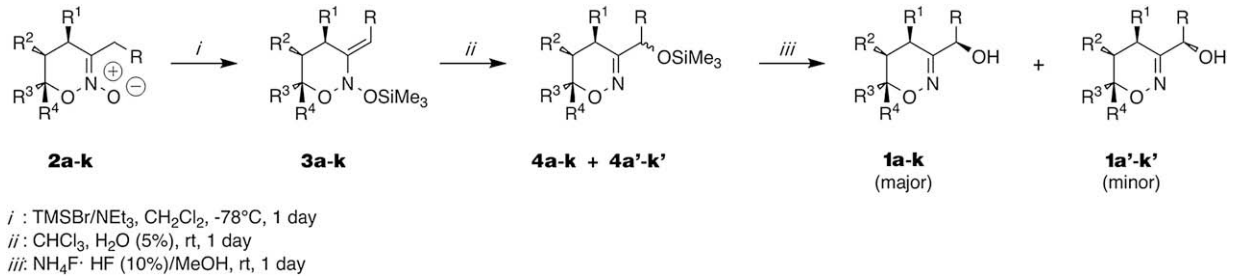
The other by-products obtained were 3-vinyl-5,6-dihydro-4*H*-1,2-oxazines **9** (Scheme 4, Table 2). Their yields generally did not exceed 15%, and they could be easily separated from the target derivatives **1** by column chromatography.

It was found that the nature of the substituent R at the double bond had the most significant influence on the process rate. The rearrangement of ASENA **3g** with the electron-donating 4-methoxyphenyl substituent occurred in situ, simultaneously with silylation of initial 1,2-oxazine-*N*-oxide **2g**. ASENA with less electron-donor substituents (R=Me, Et, Ph) underwent the rearrangement within 24 h. The ASENA rearrangement with $R{=}CH_2CO_2Me$ proceeded in 30 days affording the target product in 76% yield. ASENA with the terminal double bond (R=H) gave bad yields under the mentioned conditions (Scheme 5, Table 3). Desilylation of derivatives **4** afford the target oxazines **1**.

Table 2
By-products of the ASENA **3** rearrangement

Entry	**3**,**4**,**8**,**9**[a]	Solv.	Yield **4**, %	Yield **8**, %	Yield **9**, %
1	**a**	$CHCl_3$ (stab. EtOH)	47	13	10
2	**b**	$CHCl_3$, H_2O (5%)	74	—	14

[a] See Table 3.



Scheme 5. Synthesis of oxazines **1** from oxazine *N*-oxides **2** via the ASENA **3** rearrangement.

Table 3
Synthesis of oxazines **1** from oxazine *N*-oxides **2** via the ASENA **3** rearrangement

Entry	1-4	R	R^1	R^2	R^3	R^4	de, %	Yield **2**→**3**[a], %	Yield **3**→**4**,[a] %	Yield **4**→**1**, %	Yield **2**→**1**, %
1	**a**	Me	An	H	OMe	Me	>95	94	61	94	54
2	**b**	Me	An	$-(CH_2)_4-$		H	>95	66	74	94	46
3	**c**	Me	4-Cl-C_6H_4–	H	OMe	Me	>95	94	82	94	73
4	**d**	Me	Ph	H	OMe	Me	>95	95	61	90	52
5	**e**	Me	An	H	Me	Me	16[b]	24[c]	95	96	46
6	**f**	Et	An	H	OMe	Me	>95	98	62	95	58
7	**g**	An	An	H	OMe	Me	71	—[d]	61[e]	95	58
8	**h**	Ph	An	H	OMe	Me	88	85	67	95	54
9	**i**	CH_2CO_2Me	An	H	OMe	Me	>95	93	76[f]	94	66
10	**j**	Me	2-MeO-C_6H_4–	H	OMe	Me	83	90	75	95	64
11	**k**	H	4-Cl-C_6H_4–	H	Me	Me	—	97	32	96	30

[a] According to NMR with the internal standard ($CHCl{=}CCl_2$) unless otherwise mentioned.
[b] We cannot judge about the configuration of the major isomer.
[c] In a mixture with **4e**+**4e**′ (**3e**/**4e**+**4e**′=1:1) according to NMR. Procedure: TMSOTf/EtN(*i*-Pr)$_2$, CH_2Cl_2, −78 °C to −30 °C, 1 day.
[d] Compound **3g** was not detected due to the rearrangement in the reaction mixture (see in the text).
[e] Yield **2g**→**4g**+**4g**′, purified product.
[f] Reaction time **3i**→**4i**+**4i**′, 1 month.

The configuration of the CH(OH)R fragment in the obtained oxazines **1a**–**c**,**f** was determined by X-ray diffraction analysis (Fig. 1).[8] It was found that the ASENA **3** rearrangement generally proceeded with a high stereoselectivity and afforded a single isomer of siloxy derivative **4**. However the formation of both isomers in almost equal ratio was observed in one experiment (see Table 3, entry 5).

2.2. The pathway of the ASENA 3 rearrangement to derivatives 4

The ASENA rearrangement results could not be explained using the model proposed previously for the similar BENA process (Scheme 6).[6] It was demonstrated that the acidic impurities present in chloroform (hydrogen chloride, phosgene) had no influence on the process rate because triethylamine addition to the reaction mixture did not affect the outcome of the process. Moreover, the use of 'acidic' chloroform (pH<5) led to significant initial ASENA decomposition. We found that ASENA **3a** was rather stable in absolute chloroform at room temperature (the average conversion was estimated at 10% for 24 h according to NMR), whereas the addition of a small amount of water (5%) resulted in a 61% yield of the rearrangement product **4a**.

Considering high sensitivity of the reaction to the water we suggest the following reaction pathway. We suppose that it should

Scheme 6. The BENA **5** rearrangement mechanism.

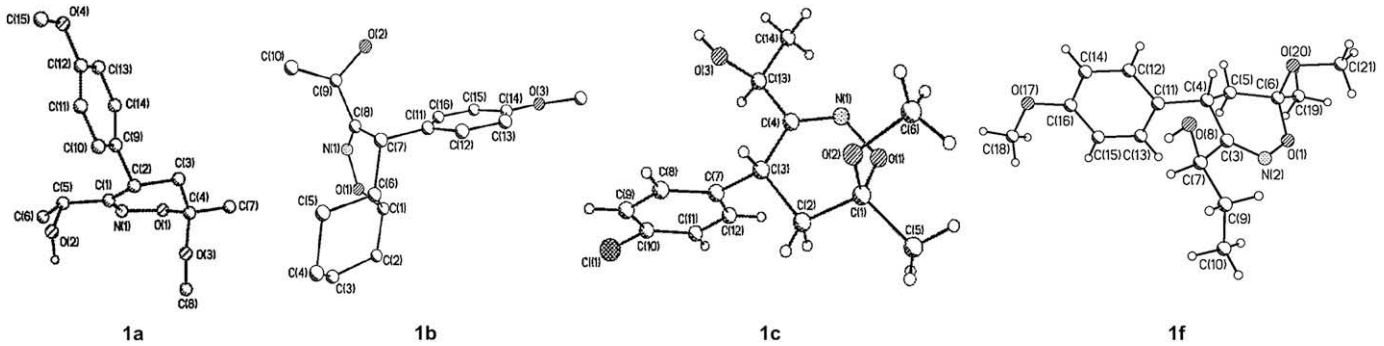
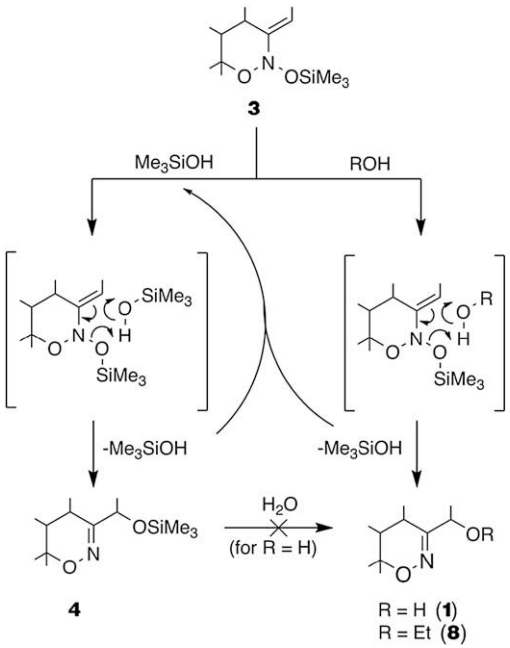


Figure 1. X-ray structure of oxazines **1a**–**c**,**f**.

occur via initial water interaction with ASENA affording TMSOH (Scheme 7). The obtained trimethylsilanol subsequently reacts with ASENA yielding target siloxy derivative **4** through the pericyclic transition state. Also ASENA can react with water through the similar transition state affording derivatives **1** directly. Indeed, we observed the formation of derivatives **1** in the rearrangement reaction with a large excess of water. It is noteworthy that **4** did not yield **1** under these reaction conditions. Unfortunately, we could not directly confirm the participation of TMSOH in the reaction due to instability of TMSOH.[9] However, the reaction with ethanol (see Scheme 4) can be similarly explained by this pathway that indirectly confirms the supposed pathway.



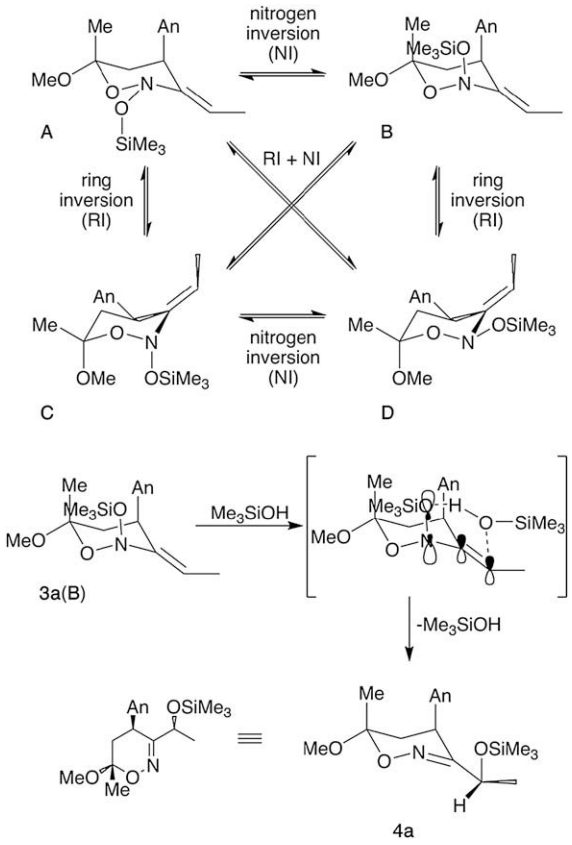
Scheme 7. The ASENA **3** rearrangement reaction pathway.

It is known that ASENA can easily undergo two dynamic processes at room temperature,[10] namely inversions of the nitrogen atom and cycle ($E \sim 60$ kJ/mol) (Scheme 8). As mentioned above, the rearrangement rate strongly depends on the nature of the substituent R at the double bond (Table 3). Thus only those conformations with the siloxy group that occupy the axial position should be considered as reacting ones (conformations **B** and **C**), whereas the axial position provides the required orbital overlap of the substituent R with the antibonding orbital of the N–O bond. Moreover, in these conformations the N–O bond is weaker due to the anomeric interaction with the lone pair of the cyclic oxygen atom.

Considering the configuration of the formed stereocentre CH(OH)R we suppose that reaction proceeded from conformation **B**. Thus conformation **C** should lead to another diastereomer of the derivative **4**. The preference for this conformation **B** can be explained in the following way. Where ASENA bear the alkoxy group at C-6 of the oxazine cycle, conformation **C** is significantly destabilized by the transannular interaction between the 6-alkoxy and *N*-siloxy groups.

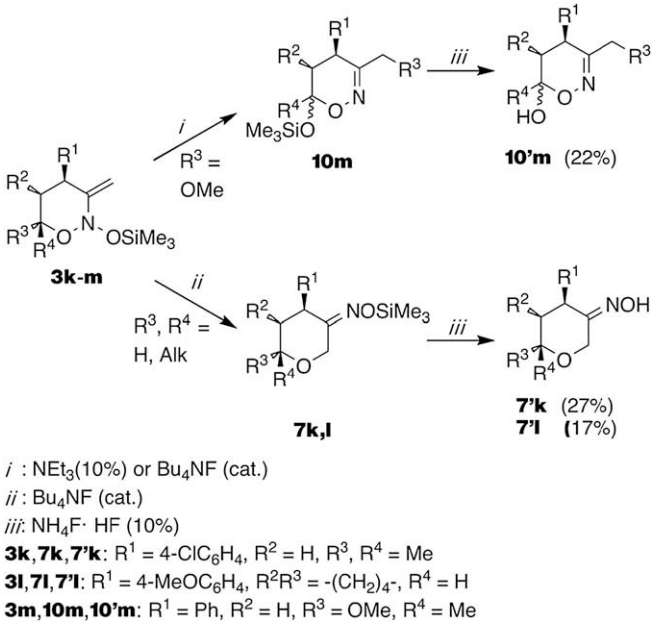
2.3. The rearrangement of 3-alkylidene-2-siloxy-tetrahydro-1,2-oxazines 3 (ASENA) under treatment with nucleophiles[11]

As it was demonstrated previously, *N*,*N*-bis(siloxy)enamines can be involved in the rearrangement by treatment with nucleophiles via the formation of conjugated nitroso alkene as a key reaction



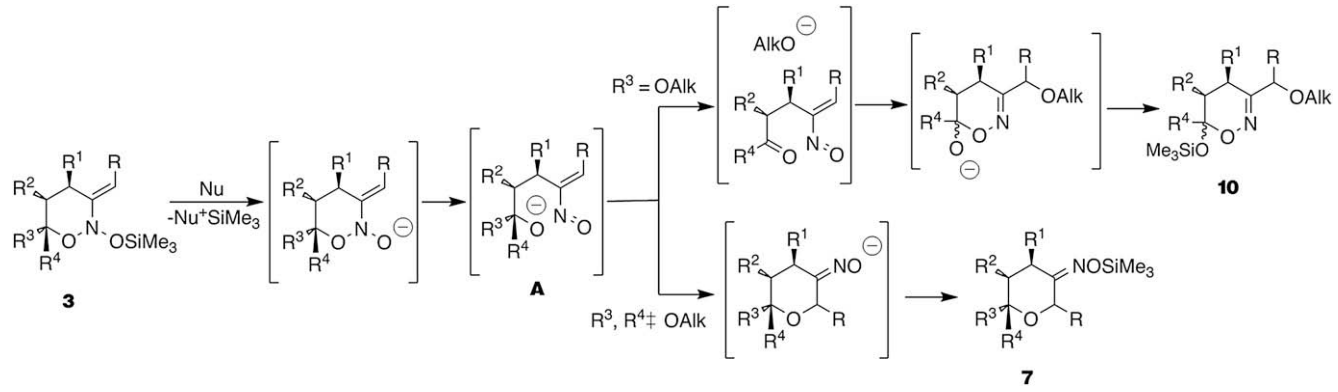
Scheme 8. Dynamic processes in ASENA **3** and stereochemistry of its rearrangement.

intermediate.[12] We also tried to induce the ASENA rearrangement by treatment with tetrabutylammonium fluoride or triethylamine. As a result, we observed the migration of the alkoxy group instead of the siloxy group leading to derivatives **7** and **10** (Scheme 9).



Scheme 9. Nucleophile-promoted rearrangement of ASENA **3**.

To explain this fact we may assume that the reaction includes the generation of a nitroso alkene similar to the process described for *N*,*N*-bis(siloxy)enamines (Scheme 10).[12] The rearrangement outcome significantly depends on the substituents R^3 and R^4 at C-6



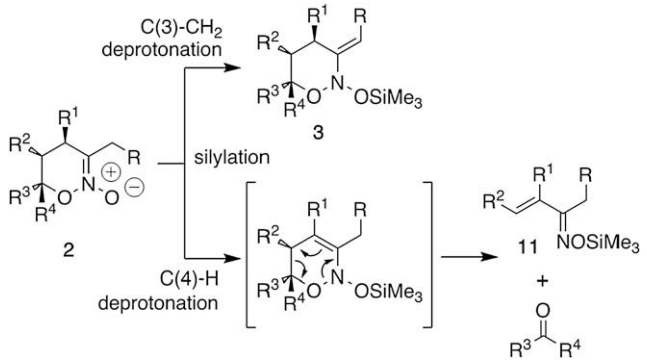
Scheme 10. The mechanism of the nucleophile-promoted rearrangement of ASENA **3**.

of the oxazine cycle. Where R^3 and $R^4 \neq$ OAlk, the intermediate **A** formed in the reaction course undergoes re-cyclization yielding tetrahydropyranone oxime **7**. If R^3=OAlk, elimination of the alkoxy anion occurs followed by its addition to the double bond and subsequent transformation into 1,2-oxazine **10**. A further hydrolysis of **7** and **10** affords derivatives **7′** and **10′**, respectively.

2.4. Synthesis of initial ASENA 3a–c,e,f,h–j

As mentioned above, the first step of the reaction sequence—silylation of *N*-oxides **2**—was thoroughly investigated in the case of 3-methyl-5,6-dihydro-4*H*-1,2-oxazine-*N*-oxides.

Since only ASENA with the substituent R at the C=C double bond underwent the rearrangement with good yields, it was necessary to synthesize previously non-described ASENA. It was found that silylation of 1,2-oxazin-*N*-oxides bearing an ethyl or even more bulky substituent at C-3 of the oxazine cycle was complicated by the formation of several by-products, primarily enoximes **11**, due to a competitive process of C-4 deprotonation of the oxazine cycle (Scheme 11).[2a]



Scheme 11. Silylation of 1,2-oxazine-*N*-oxides **2**.

The steric and electron properties of the substituent R^3 obviously have a significant influence on the ratio of products **3** and **11**. It was found that even in the case of R^3=Me (**2e**) silylation using triethylamine as a base afforded enoxime **11** as the single product. Fortunately, the use of a more sterically hindered base—the Hunig base[13]—was quite effective and gave an enhanced yield of target ASENA **3**.

However, our attempts to obtain siloxy derivative **3** of oxazine-*N*-oxides with more branched substituents at C-3 of the oxazine cycle (e.g., the 3-*i*-Pr derivative) failed.

Based upon the obtained results a conclusion was made on the necessary presence of the sterically unhindered substituent R at the C(3)-methyl group (R=H) for silylation of oxazine-*N*-oxides **2**. On the other hand, the ASENA **3** rearrangement proceeded efficiently where R≠H. This fact limits the number of oxazines **1** attainable by this method.

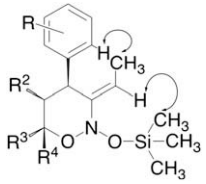


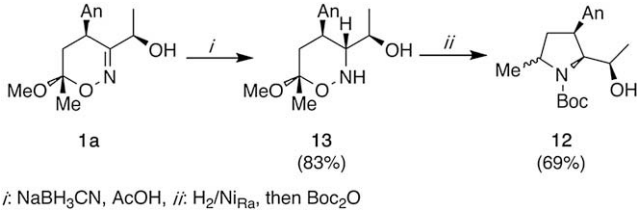
Figure 2. Selected NOE interactions in the ASENA **3**.

To perform a one-stage transformation **2**→**1** it was necessary to succeed in selective silylation of initial oxazine-*N*-oxides yielding ASENA **3**. The optimal conditions found for the silylation reaction are shown in Scheme 5. Subsequent treatment of the reaction mixture with water led to the formation of ASENA **3**. The double bond configuration in the products was determined by two-dimensional NOESY spectra revealing characteristic interactions presented in Figure 2. In all cases only (*E*)-isomers were obtained.

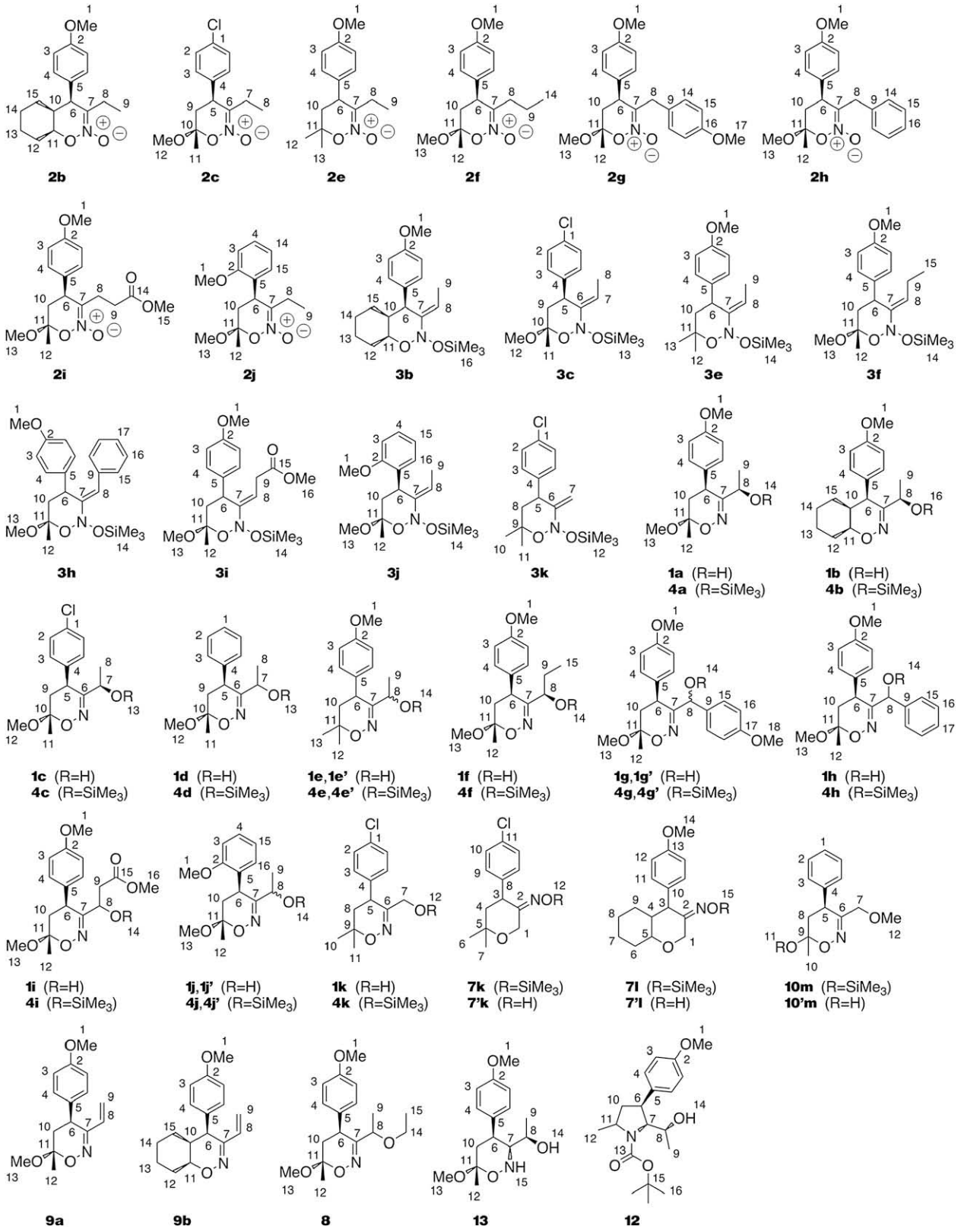
2.5. Application of 1,2-oxazines 1

5,6-Dihydro-4*H*-1,2-oxazines have found numerous applications in the total synthesis of natural and biologically active nitrogen-containing compounds, e.g., alkaloids, unnatural amino acids, and amino sugars. In these syntheses reduction of the oximino-fragment plays the key role that makes it possible to transform oxazines into a wide range of heterocyclic and acyclic products. Thus, depending on the structure of oxazines and reaction conditions, reduction can lead to substituted[14a] and fused[14b] pyrrolidines, pyrroles,[14c] five-membered cyclic nitrones,[14d] δ-aminoalcohols,[14e] and diketones.[14f]

To demonstrate an application of synthesized oxazines **1** we reduced **1a** to pyrrolidine **12** in two steps by a known procedure[15] via the formation of tetrahydrooxazine **13** (Scheme 12).



Scheme 12. Reduction of derivative **1a**.



Scheme 13. Structures of compounds **1**–**4**, **7**–**10**, **12**, **13**.

3. Conclusions

A new approach to the synthesis of 3-α-hydroxymethyl-5,6-dihydro-4*H*-1,2-oxazines **1** from 1,2-oxazin-*N*-oxides **2** via the formation and subsequent rearrangement of 3-alkiliden-2-siloxy-tetrahydrooxazines **3** was demonstrated. An efficient one-step procedure for the transformation **2**→**1** was developed without purifying intermediate products. The impact of different factors on the reaction outcome was evaluated. Basing on the results the pathway of the process was proposed.

4. Experimental section

4.1. General information

All silylation reactions were performed in oven-dried (150 °C) glassware under an argon atmosphere. Melting points were determined on a Koffler melting point apparatus and are uncorrected. Chromatographic separations were performed on silica gel (Merck Kieselgel 230–400 mesh) with analytical-grade solvents, driven by a positive pressure of air. Analytical thin-layer chromatography was performed on Merck silica gel plates with QF-254 indicator. Visualization was accomplished with UV light and/or anisaldehyde and/or ninhydrin. IR spectra were recorded on the spectrometer Bruker Vector22 in the thin layer, ν_{max} are reported in cm^{-1}. 1D and 2D NMR spectra were recorded on the NMR-spectrometers Bruker DRX-500 (^1H: 500.13 MHz, NOESY), Bruker AM-300 (^1H: 300.13 MHz, ^{13}C: 75.47 MHz, ^{29}Si: 59.63 MHz), and Bruker WM-250 (^1H: 250 MHz, ^{13}C: 62.5 MHz,) for $CDCl_3$ solutions with residual solvent peak as an internal standard.[16] The INEPT pulse sequence was used for observation of the ^{29}Si signals. Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad). Coupling constants, *J*, are reported in hertz. Atom numbering is shown in Scheme 13. Elemental analyses were performed by the analytical Centre of N.D. Zelinsky Institute of Organic Chemistry.

Hexane, EtOAc, toluene, EtOH, and MeOH were distilled without drying agents. Glacial acetic acid was recrystallized twice. The following reaction solvents and reagents were distilled from the indicated drying agents: methylene chloride (CaH_2), $CHCl_3$ (P_2O_5), triethylamine (CaH_2), ethyl-di-*iso*-propylamine (CaH_2), tin tetrachloride (CaH_2), cyclohexane (CaH_2). The following chemicals were purchased from the indicated sources: TMSBr (Acros), TMSOTf (Acros), $CaCl_2$ (Acros), 2-methoxypropene (Acros), ethylvinyl ether (Acros), isobutylene (Aldrich), 4-methoxybenzaldehyde (Acros), 4-chlorobenzaldehyde (Acros), 1-nitropropane (Acros), methyl-4-nitrobutyrate (Aldrich), butylamine (Acros), $NH_4F{\cdot}HF$ (Acros), $NaBH_3CN$ (Acros), Raney Nickel (50% slurry in water) (Acros), Boc_2O (Acros). Brine refers to a saturated aqueous solution of NaCl.

The following compounds were prepared according to literature procedures: tetra-*n*-butylammonium fluoride (TBAF),[17] methoxybenzaldehyde,[18] 2-phenylnitroethane, and 2-(4-methoxyphenyl)nitroethane,[19] 1-methoxy-4-((*E*)-2-nitro-1-pentenyl)-benzene,[20] ASENA **3a**,[2b] ASENA **3d**,**l**,**m**, oxazine *N*-oxide **2k**.[2c]

4.2. Preparation of oxazine *N*-oxides 2

4.2.1. Preparation of nitroalkenes

4.2.1.1. 1-Methoxy-4-((E)-2-nitro-1-butenyl)benzene.[21] The solution of 4-methoxybenzaldehyde (24 mL, 0.2 mol), 1-nitropropane (18 mL, 1 equiv, 0.2 mol), and butylamine (0.05 equiv, 1 mL) in toluene (30 mL) was refluxed for 12 h with a Dean–Stark trap. Then the Dean–Stark trap was replaced with the dropping funnel with anhydrous $CaCl_2$ (10 g). The reaction mixture was additionally refluxed for 12 h. The solvent was removed in vacuum. The residue was recrystallized from EtOH to give 24 g (58%) of title compound as a yellow solid. Mp=49–51 °C (lit.[21] mp=55–57 °C (MeOH)). ^1H NMR: 1.30 (t, *J*=7.4, 3H, CH_2CH_3), 2.91 (q, *J*=7.4, 2H, CH_2), 3.87 (s, 3H, O*Me*), 6.99 (d, *J*=8.5, 2H, $CH_{Ar,o\text{-}OMe}$), 7.43 (d, *J*=8.5, 2H, $CH_{Ar,m\text{-}OMe}$), 8.02 (s, 1H, =C*H*).

4.2.1.2. Methyl 5-(4-methoxyphenyl)-4-nitro-4-pentenoate. The solution of 4-methoxybenzaldehyde (12 mL, 0.1 mol), methyl-4-nitrobutyrate (14.7 g, 1 equiv, 0.1 mol), and butylamine (0.05 equiv, 0.5 mL) in toluene (15 mL) was refluxed for 12 h with a Dean–Stark trap. The solvent was removed in vacuum. The residue was recrystallized from EtOH to give 12 g (53%) of title compound as a yellow solid. R_f=0.68 (hexane/EtOAc, 1:1). Mp=55–56 °C. Anal. Calcd for $C_{13}H_{15}NO_5$: C, 58.86; H, 5.70; N, 5.28. Found: C, 58.87; H, 5.78; N, 5.25. ^1H NMR: 2.67 and 3.21 (t, *J*=7.3, both 2H, CH_2CH_2), 3.69 (s, 3H, CO_2Me), 3.85 (s, 3H, ArO*Me*), 6.97 (d, *J*=8.8, 2H, $CH_{Ar,o\text{-}OMe}$), 7.43 (d, *J*=8.8, 2H, $CH_{Ar,m\text{-}OMe}$), 8.08 (s, 1H, C=C*H*). ^{13}C NMR: 23.1 and 31.8 (CH_2CH_2), 52.0 (CO_2Me), 55.5 ArO*Me*), 114.8 ($CH_{Ar,o\text{-}OMe}$), 124.0 ($C_{Ar,p\text{-}OMe}$), 132.1 ($CH_{Ar,m\text{-}OMe}$), 135.2 (C=CH), 147.7 (*C*–NO_2), 161.6 (C_{Ar}–OMe), 172.5 (CO_2Me).

4.2.1.3. 1-Chloro-4-(2-nitro-1-butenyl)benzene.[22] The solution of 4-chlorobenzaldehyde (28 g, 0.2 mol), 1-nitropropane (18 mL, 1 equiv, 0.2 mol), and butylamine (0.05 equiv, 1 mL) in EtOH (20 mL) was refluxed for 16 h. The solution was cooled to 0 °C. The precipitate was filtered and washed with EtOH to give 10 g (23%) of title compound as a light yellow solid. Mp=72–73 °C. (lit.[22] mp=77.5 °C). ^1H NMR: 1.28 (t, *J*=7.3, 3H, CH_2CH_3), 2.85 (q, *J*=7.3, 2H, CH_2), 7.35 and 7.45 (d, *J*=8.8, both 2H, CH_{Ar}), 7.96 (s, 1H, =C*H*). ^{13}C NMR: 12.5 (CH_2CH_3), 20.7 (CH_2), 129.3 and 130.9 (CH_{Ar}), 130.8 and 136.1 (C_{Ar}), 131.8 (=CH), 153.7 (*C*–NO_2).

4.2.1.4. 1-Methoxy-4-(2-nitro-3-phenyl-1-propenyl)benzene. The solution of 4-methoxybenzaldehyde (12 mL, 0.1 mol), 2-phenylnitroethane (15 g, 1 equiv, 0.1 mol), and butylamine (0.05 equiv, 0.5 mL) in toluene (30 mL) was refluxed for 12 h with a Dean–Stark trap. The solvent was removed in vacuum. The residue was recrystallized from EtOH to give 24 g (90%) of title compound as a light yellow solid. Mp=53–58 °C. Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.37; H, 5.76; N, 5.20. ^1H NMR: 3.85 (s, 3H, O*Me*), 4.31 (s, 2H, CH_2), 6.95 (d, *J*=8.8, 2H, $CH_{Ar,o\text{-}OMe}$), 7.20–7.39 (m, 5H, *Ph*), 7.45 (d, *J*=8.8, 2H, $CH_{Ar,m\text{-}OMe}$), 8.35 (s, 1H,=C*H*(6)). ^{13}C NMR: 33.1 (CH_2), 55.5 (O*Me*(1)), 114.7 ($CH_{Ar,o\text{-}OMe}$), 124.2 ($C_{Ar,p\text{-}OMe}$), 126.9, 127.6, and 129.0 (*Ph*), 132.0 ($CH_{Ar,m\text{-}OMe}$), 135.8 (=CH), 136.4 (C_{Ph}), 147.4 (*C*–NO_2), 161.6 (*C*–OMe).

4.2.1.5. 1-Methoxy-4-(3-(4-methoxyphenyl)-2-nitro-1-propenyl)benzene.[23] The solution of 4-methoxybenzaldehyde (4.2 mL, 35 mmol), 2-(4-methoxyphenyl)nitroethane (6.4 g, 1 equiv, 35 mmol), and butylamine (0.08 equiv, 0.3 mL) in EtOH (4 mL) was refluxed for 16 h. The solvent was removed in vacuum. The residue was subjected to column chromatography (eluent: hexane/toluene, 1:1) to give 3.1 g (30%) of title compound as a yellow oil. R_f=0.62 (toluene). The spectral data (^1H and ^{13}C NMR) are identical to previously reported.[23]

4.2.1.6. 1-Methoxy-2-(2-nitro-1-butenyl)benzene.[24] The solution of 2-methoxybenzaldehyde (10 g, 73 mmol), 1-nitropropane (7 mL, 1 equiv, 73 mmol), and butylamine (0.07 equiv, 0.5 mL) in EtOH (8 mL) was refluxed for 16 h. The solvent was removed in vacuum. The residue was subjected to column chromatography (eluent: hexane/toluene, 1:1) to give 2.3 g (15%) of title compound as a yellow oil. R_f=0.45 (toluene). ^1H NMR: 1.26 (t, *J*=7.4, 3H, CH_2CH_3), 2.81 (q, *J*=7.4, 2H, CH_2), 3.87 (s, 3H, O*Me*), 6.95 (d, *J*=7.9, 1H, $CH_{Ar,o\text{-}OMe}$), 7.03 (t, *J*=7.9, 1H, $CH_{Ar,p\text{-}OMe}$), 7.30 (d, *J*=7.9, 1H, $CH_{Ar,o\text{-}CH=C}$), 7.41 (t, *J*=7.9, 1H, $CH_{Ar,p\text{-}CH=C}$), 8.23 (s, 1H, =C*H*). ^{13}C NMR: 12.6 (CH_2CH_3), 20.9 (CH_2), 55.6 (O*Me*), 110.9 ($CH_{Ar,o\text{-}OMe}$), 120.6 ($CH_{Ar,p\text{-}OMe}$), 121.5 ($C_{Ar,o\text{-}OMe}$), 129.3 and 129.4 ($CH_{Ar,m\text{-}OMe}$), 131.6 (=CH), 153.0 (*C*–NO_2), 158.1 (*C*–OMe).

4.2.2. [4+2]-Cycloaddition of nitroalkenes to olefins. General procedure for the preparation of oxazine N-oxides **2c,f–i**

$SnCl_4$ (0.65 mL, 1.1 equiv, 5.5 mmol) was added to a stirred solution of corresponding nitroalkene (5 mmol) in CH_2Cl_2 (25 mL) at −78 °C in dry argon. The temperature was decreased to −94 °C and 2-methoxypropene (0.96 mL, 2 equiv, 10 mmol) was added dropwise. The reaction mixture was stirred for 5 min and then poured

into a mixture of EtOAc (150 mL) and saturated aqueous solution of $NaHCO_3$ (100 mL). The organic layer was washed with saturated aqueous solution of $NaHCO_3$ (50 mL), H_2O (100 mL), and brine (2×50 mL), and dried over Na_2SO_4. The solvents were removed in vacuum and the residue was recrystallized from Hex/EtOAc=3:1 to give title compound as a white solid.

4.2.2.1. rel-(4S,4aR,8aR)-3-Ethyl-4-(4-methoxyphenyl)-4a,5,6,7,8,8a-hexahydro-4H-benzo[e][1,2]oxazine N-oxide ***2b****.* $SnCl_4$ (1.3 mL, 1.1 equiv, 11 mmol) was added to a stirred solution of 1-methoxy-4-(2-nitro-1-butenyl)benzene (2.07 g, 10 mmol) in CH_2Cl_2 (50 mL) at −78 °C in dry argon. The temperature was decreased to −94 °C and cyclohexene (1.9 mL, 2 equiv, 20 mmol) was added for 1 min. The reaction mixture was maintained for 1 day at −30 °C and then poured into a mixture of EtOAc (150 mL) and saturated aqueous solution of $NaHCO_3$ (100 mL). The organic layer was washed with a saturated aqueous solution of $NaHCO_3$ (50 mL), H_2O (100 mL), brine (2×50 mL), and dried over Na_2SO_4. The solvents were removed in vacuum and the residue was recrystallized from hexane/EtOAc, 3:1 to give 2.2 g (77%) of title compound as a white solid. R_f=0.26 (hexane/EtOAc, 1:1) (UV). Mp=105–106 °C (EtOAc). Anal. Calcd for $C_{17}H_{23}NO_3$: C, 70.56; H, 8.01; N, 4.84. Found: C, 70.63; H, 8.29; N, 4.89. ν_{max}: 2933, 2860, 1606, 1581, 1511, 1462, 1146, 1292, 1248, 1215, 1179, 1109, 1033, 965, 934, 885, 857, 733, 593 cm^{-1}. ^1H NMR: 1.26 (t, J=7.5, 3H, CH_3(9)), 1.20–1.83 (m, 8H, CH_2(12–15)), 1.98–2.13 (m, 2H, CH_2(8)), 2.60 (dq, J=13.9, 7.4, 1H, CH(10)), 3.35 (s, 1H, CH(6)), 3.79 (s, 3H, CH_3(1)), 4.58 (br s, 1H, CH(11)), 6.85 (d, J=8.5, 2H, CH(3)), 7.07 (d, J=8.5, 2H, CH(4)). ^{13}C NMR: 8.9 (CH_3(9)), 28.8, 27.4, 25.6, 24.8, 19.8 (all CH_2(8,12–15)), 39.7 (CH(10)), 47.7 (CH(6)), 55.4 (CH_3(1)), 75.0 (CH(11)), 110.7 (CH(11)), 114.4 (CH(3)), 124.1 (C(7)), 129.0 (CH(4)), 133.6 (C(5)), 159.0 (C(2)).

4.2.2.2. rel-(4S,6S)-4-(4-Chlorophenyl)-3-ethyl-6-methoxy-6-methyl-5,6-dihydro-4H-1,2-oxazine N-oxide ***2c****.* Oxazine *N*-oxide **2c** was prepared according to the general procedure from 1-chloro-4-(2-nitro-1-butenyl)benzene. Yield=69%. R_f=0.31 (hexane/EtOAc, 1:1) (UV). Mp=74–76 °C (hexane/EtOAc, 3:1). Anal. Calcd for $C_{14}H_{18}ClNO_3$: C, 59.26; H, 6.39; N, 4.94. Found: C, 58.97; H, 6.47; N, 4.87. ν_{max}: 2974, 2941, 1610, 1491, 1461, 1454, 1409, 1379, 1301, 1264, 1231, 1187, 1148, 1090, 1050, 1014, 852, 829, 771, 532 cm^{-1}. ^1H NMR: 0.97 (t, J=7.2, 3H, CH_3(8)), 1.51 (s, 3H, CH_3(11)), 1.94 (dd, J=13.8, 11.2, 1H, CH_{2a}(9)), 2.04 (dq, J=14.5, 7.2, 1H, CH_{2a}(7)), 2.29 (dd, J=13.8, 7.8, 1H, CH_{2e}(9)), 2.39 (dq, J=14.5, 7.2, 1H, CH_{2b}(7)), 3.47 (s, 3H, CH_3(12)), 3.87 (dd, J=11.2, 7.8, 1H, CH(5)), 7.13 (d, J=7.9, 2H, CH(3)), 7.32 (d, J=7.9, 2H, CH(2)). ^{13}C NMR: 8.6 (CH_3(8)), 20.9 (CH_3(11)), 24.3 (CH_2(7)), 40.3 (CH(5) and CH_2(9)), 50.2 (CH_3(12)), 103.9 (C(10)), 126.4 (CH(6)), 129.4 and 129.6 (CH(2) and CH(3)), 133.5 and 138.6 (C(1) and C(4)).

4.2.2.3. 3-Ethyl-4-(4-methoxyphenyl)-6,6-dimethyl-5,6-dihydro-4H-1,2-oxazine N-oxide ***2e****.* $SnCl_4$ (1.3 mL, 1.1 equiv, 11 mmol) was added to a stirred solution of 1-methoxy-4-(2-nitro-1-butenyl)benzene (2.07 g, 10 mmol) in CH_2Cl_2 (50 mL) at −78 °C in dry argon. The temperature was decreased to −94 °C and isobutylene (0.9 g, 2 equiv, 20 mmol) was added for 1 min. The reaction mixture was stirred for 5 min and then poured into a mixture of EtOAc (150 mL) and saturated aqueous solution of $NaHCO_3$ (100 mL). The organic layer was washed with a saturated aqueous solution of $NaHCO_3$ (50 mL), H_2O (100 mL), brine (2×50 mL), and dried over Na_2SO_4. The solvents were removed in vacuum and the residue was recrystallized from hexane/EtOAc, 5:1 to give 2.11 g (80%) of title compound as a white solid. R_f=0.18 (hexane/EtOAc, 1:1) (UV). Mp=80–81 °C (hexane/EtOAc, 5:1). Anal. Calcd for $C_{15}H_{21}NO_3$: C, 68.42; H, 8.04; N, 5.32. Found: C, 68.51; H, 8.29; N, 5.33. ν_{max}: 2977, 2933, 1602, 1512, 1462, 1372, 1297, 1247, 1177, 1033, 888, 856, 833, 529 cm^{-1}. ^1H NMR: 0.96 (t, J=7.4, 3H, CH_3(9)), 1.38 (s, 3H, CH_3(13)), 1.42 (s, 3H, CH_3(12)), 1.88–2.15 (m, 3H, CH_{2b}(8) and CH_2(10)), 2.42 (dq, J=14.4, 7.2, 1H, CH_{2a}(8)), 3.66 (dd, J=10.8, 8.1, 1H, CH(6)), 3.78 (s, 3H, CH_3(1)), 6.85 (d, J=8.5, 2H, CH(4)), 7.10 (d, J=8.5, 2H, CH(3)). ^{13}C NMR: 8.7 (CH_3(9)), 21.9 (CH_3(12)), 24.1 (CH_2(8)), 27.9 (CH(13)), 41.0 (CH(6)), 41.8 (CH_2(10)), 55.3 (CH_3(1)), 81.1 (C(11)), 114.5 (CH(3)), 126.5 (C(7)), 129.2 (CH(4)), 132.1 (C(5)), 159.0 (C(2)).

4.2.2.4. rel-(4S,6S)-6-Methoxy-4-(4-methoxyphenyl)-6-methyl-3-propyl-5,6-dihydro-4H-1,2-oxazine N-oxide ***2f****.* Oxazine *N*-oxide **2f** was prepared according to the general procedure from 1-methoxy-4-((*E*)-2-nitro-1-pentenyl)benzene. Yield=77%. R_f=0.23 (hexane/EtOAc, 1:1) (UV). Mp=92–93 °C (Et_2O). Anal. Calcd for $C_{16}H_{23}NO_4$: C, 65.51; H, 7.90; N, 4.77. Found: C, 65.60; H, 7.85; N, 4.70. ν_{max}: 2993, 2962, 2941, 1608, 1512, 1462, 1379, 1304, 1277, 1252, 1230, 1178, 1148, 1085, 1035, 872, 834, 798, 534 cm^{-1}. ^1H NMR: 0.84 (t, J=7.3, 3H, CH_3(14)), 1.48 (s, 3H, CH_3(12)), 1.56 (m, 1H, CH_{2b}(9)), 1.56 (m, 1H, CH_{2a}(9)), 1.88 (ddd, J=14.7, 8.8, 6.2, 1H, CH_{2b}(8)), 1.94 (dd, J=14.0, 11.5, 1H, CH_{2ax}(10)), 2.26 (dd, J=14.0, 8.1, 1H, CH_{2eq}(10)), 2.45 (ddd, J=14.7, 8.8, 6.2, 1H, CH_{2a}(8)), 3.44 (s, 3H, CH_3(13)), 3.77 (s, 3H, CH_3(1)), 3.79 (dd, J=11.5, 8.1, 1H, CH(6)), 6.83 (d, J=8.8, 2H, CH(3)), 7.07 (d, J=8.8, 2H, CH(4)). ^{13}C NMR: 13.6 (CH_3(14)), 17.6 (CH_2(9)), 20.8 (CH_3(12)), 32.2 (CH_2(8)), 40.3 (CH(6)), 40.5 (CH_2(10)), 50.0 (CH_3(13)), 55.3 (CH_3(1)), 103.7 (C(11)), 114.4 (CH(3)), 126.4 (C(7)), 129.1 (CH(4)), 131.9 (C(5)), 158.9 (C(2)).

4.2.2.5. rel-(4S,6S)-6-Methoxy-3-(4-methoxybenzyl)-4-(4-methoxyphenyl)-6-methyl-5,6-dihydro-4H-1,2-oxazine N-oxide ***2g****.* Oxazine *N*-oxide **2g** was prepared according to the general procedure from 1-methoxy-4-(3-(4-methoxyphenyl)-2-nitro-1-propenyl)benzene. Yield=50%. R_f=0.30 (hexane/EtOAc, 1:1) (UV). Mp=79–80 °C (hexane/EtOAc, 1:1). Anal. Calcd for $C_{21}H_{25}NO_5$: C, 67.91; H, 6.78; N, 3.77. Found: C, 68.28; H, 6.80; N, 3.77. ν_{max}: 2995, 2941, 2918, 2837, 1609, 1511, 1458, 1301, 1248, 1178, 1139, 1082, 1065, 1035, 840, 534 cm^{-1}. ^1H NMR: 1.50 (s, 3H, CH_3(12)), 2.25 (dd, J=13.6, 11.0, 1H, CH_{2ax}(10)), 2.25 (dd, J=13.6, 8.1, 1H, CH_{2eq}(10)), 3.03 (d, J=15.1, 1H, CH_{2b}(8)), 3.46 (s, 3H, CH_3(13)), 3.77 and 3.80 (s, 6H, CH_3(1) and CH_3(17)), 3.74 (dd, J=11.0, 8.1, 1H, CH(6)), 4.05 (d, J=15.1, 1H, CH_{2a}(8)), 6.76 and 6.83 (d, J=8.8, 4H, CH(3) and CH(15)), 6.97 and 6.99 (d, J=8.8, 4H, CH(4) and CH(14)). ^{13}C NMR: 20.8 (CH_3(12)), 34.8 (CH_2(8)), 39.4 (CH(6)), 40.5 (CH_2(10)), 50.1 (CH_3(13)), 55.2 and 55.3 (CH_3(1) and CH_3(17)), 104.1 (C(11)), 113.8 and 114.5 (CH(3) and CH(15)), 126.1 (C(7)), 128.1 and 131.8 (C(5) and C(9)), 129.3 and 129.8 (CH(4) and CH(14)), 158.3 and 158.9 (C(2) and C(16)).

4.2.2.6. rel-(4S,6S)-3-Benzyl-6-methoxy-4-(4-methoxyphenyl)-6-methyl-5,6-dihydro-4H-1,2-oxazine N-oxide ***2h****.* Oxazine *N*-oxide **2h** was prepared according to the general procedure from 1-methoxy-4-(2-nitro-3-phenyl-1-propenyl)benzene. Yield=76%. R_f=0.29 (hexane/EtOAc, 1:1) (UV). Mp=80 °C (EtOAc). Anal. Calcd for $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10. Found: C, 69.94; H, 6.87; N, 4.09. ν_{max}: 3060, 3028, 2995, 2941, 2836, 1607, 1512, 1453, 1379, 1300, 1250, 1231, 1178, 1140, 1080, 1065, 1035, 984, 835, 798, 704, 536, 519 cm^{-1}. ^1H NMR: 1.51 (s, 3H, CH_3(12)), 1.99 (dd, J=13.7, 11.2, 1H, CH_{2ax}(10)), 2.26 (dd, J=13.7, 7.9, 1H, CH_{2eq}(10)), 3.10 (d, J=14.7, 1H, CH_{2b}(8)), 3.46 (s, 3H, CH_3(13)), 3.77 (dd, J=11.2, 7.9, 1H, CH(6)), 3.80 (s, 3H, CH_3(1)), 4.11 (d, J=14.7, 1H, CH_{2a}(8)), 6.83 (d, J=8.5, 2H, CH(3)), 6.99 (d, J=8.5, 2H, CH(4)), 7.06–7.09 and 7.19–7.27 (m, 5H, CH(14–16)). ^{13}C NMR: 20.8 (CH_3(12)), 55.3 (CH_3(1)), 50.1 (CH_3(13)), 35.6 (CH_2(8)), 40.0 (CH(6)), 40.5 (CH_2(10)), 104.2 (C(11)), 114.4 (CH(3)), 125.9 (C(7)), 131.7 (C(5)), 136.1 (C(9)), 128.4 and 129.3 (CH(14) and CH(15)), 128.8 (CH(3)), 159.0 (C(2)).

4.2.2.7. rel-(4S,6S)-6-Methoxy-3-(3-methoxy-3-oxopropyl)-4-(4-methoxyphenyl)-6-methyl-5,6-dihydro-4H-1,2-oxazine N-oxide ***2i****.* Oxazine *N*-oxide **2i** was prepared according to the general

procedure from methyl 5-(4-methoxyphenyl)-4-nitro-4-pentenoate. Yield=70%. R_f=0.12 (hexane/EtOAc, 1:1) (UV). Mp=60–62 °C (EtOAc). Anal. Calcd for $C_{17}H_{23}NO_6$: C, 60.52; H, 6.87; N, 4.15. Found: C, 60.37; H, 6.75; N, 4.17. ν_{max}: 2995, 2948, 2837, 1737, 1608, 1513, 1462, 1438, 1380, 1362, 1302, 1252, 1231, 1178, 1143, 1084, 1072, 1036, 856, 836, 798, 536 cm^{-1}. ^1H NMR: 1.50 (s, 3H, CH_3(12)), 1.99 (dt, J=13.5, 10.5, 1H, CH_{2a}(8)), 2.28 (dd, J=14.0, 8.1, 1H, CH_{2e}(10)), 2.30–2.41 (2H), 2.49–2.58 (1H) and 2.77–2.88 (1H) (all m, CH_{2b}(8), CH_2(9) and CH_a(10)), 3.44 (s, 3H, CH_3(13)), 3.80 (s, 3H, CH_3(1)), 3.64 (s, 3H, CH_3(15)), 3.91 (dd, J=11.0, 7.3, 1H, CH(6)), 6.87 (d, J=8.8, 2H, CH(3)), 7.11 (d, J=8.8, 2H, CH(4)). ^{13}C NMR: 20.8 (CH_3(12)), 27.7 and 26.2 (CH_2(8) and CH_2(9)), 40.3 (CH_2(10)), 40.8 (CH(6)), 50.1 (CH_3(13)), 51.7 (CH_3(15)), 55.3 (CH_3(1)), 104.2 (C(11)), 114.6 (CH(3)), 125.2 (C(7)), 129.3 (CH(4)), 131.4 (C(5)), 159.0 (C(2)), 173.0 ((C(14))).

4.2.2.8. rel-(4S,6S)-3-Ethyl-6-methoxy-4-(2-methoxyphenyl)-6-methyl-5,6-dihydro-4H-1,2-oxazine N-oxide ***2j***. Oxazine *N*-oxide **2j** was prepared according to the general procedure from 1-methoxy-2-(2-nitro-1-butenyl)benzene. Yield=61%. Mp=71–73 °C (hexane/EtOAc, 1:1) (UV). R_f=0.11 (hexane/EtOAc, 1:1). Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.50; H, 7.58; N, 5.01. Found: C, 64.07; H, 7.70; N, 4.96. ν_{max}: 2972, 2942, 2839, 1613, 1587, 1493, 1462, 1439, 1379, 1298, 1248, 1233, 1188, 1051, 1028, 828, 800, 756 cm^{-1}. ^1H NMR: 0.97 (t, J=7.3, 3H, CH_3(9)), 1.50 (s, 3H, CH_3(12)), 1.98–2.09 (m, 2H, CH_{2a}(10) and CH_{2a}(8)), 2.23 (dd, J=13.2, 8.1, 1H, CH_{2e}(10)), 2.45 (dq, J=14.0, 7.3, 1H, CH_{2a}(8)), 3.48 (s, 3H, CH_3(13)), 3.83 (s, 3H, CH_3(1)), 4.21 (dd, J=11.1, 8.1, 1H, CH(6)), 6.87–6.95 (m, 2H, CH(3) and CH(14)), 7.11 (d, J=8.1, 1H, CH(15)), 7.23–7.29 (m, 1H, CH(4)). ^{13}C NMR: 8.5 (CH_3(9)), 21.0 (CH_3(12)), 24.2 (CH_2(8)), 35.2 (CH(6)), 37.7 (CH_2(10)), 50.1 (CH_3(13)), 55.5 (CH_3(1)), 103.9 (C(11)), 110.9 and 121.0 (CH(3) and CH(14)), 127.7 and 127.8 (C(5) and C(7)), 128.8 and 129.6 (CH(4) and CH(15)), 157.2 (C(2)).

4.3. Silylation of oxazine *N*-oxides 2

4.3.1. General procedure for the preparation of ASENA ***3b,c,f,h–k***

NEt_3 (0.36 mL, 1.3 equiv, 2.6 mmol) was added to stirred solution of corresponding nitronate **2** (2 mmol) in CH_2Cl_2 (4 mL) at −78 °C. Then TMSBr (0.32 mL, 1.2 equiv, 2.4 mmol) was added. The reaction mixture was maintained at the same temperature for 16 h, diluted with hexane (15 mL) and poured into a mixture of hexane (30 mL) and $NaHSO_4$ aqueous solution (0.5 g in 30 mL of water). The organic layer was washed with H_2O (30 mL) and brine (2×30 mL) and dried over Na_2SO_4. The solvents were removed in vacuum to give title ASENA as colorless oil, which was used in the next step without additional purification. For yields see Table 3.

4.3.1.1. rel-(4S,4aR,8aR)-(E)-3-Ethylidene-4-(4-methoxyphenyl)-2-(trimethylsilyloxy)-octahydro-2H-benzo[e][1,2]oxazine ***3b***. Two conformers in a ratio 3:1. ^1H NMR: major conformer: 0.24 (s, 9H, CH_3(16)), 1.58 (d, J=7.2, 3H, CH_3(9)), 1.80–2.09 (m, 9H, CH_2(12–15) and CH(10)), 3.80 (s, 3H, CH_3(1)), 4.35 (br s, 1H, CH(6)), 4.82 (br s, 1H, CH(11)), 5.85 (q, J=7.2, 1H, CH(8)), 6.84 (d, J=9.2, 2H, CH(3)), 7.33 (d, J=8.6, 2H, CH(4)). Minor conformer: 0.16 (s, 9H, CH_3(16)), 1.58 (d, J=7.2, 3H, CH_3(9)), 1.80–2.09 (m, 9H, CH_2(12–15) and CH(10)), 3.71 (s, 3H, CH_3(1)), 4.35 (br s, 1H, CH(6)), 4.82 (br s, 1H, CH(11)), 5.93 (q, J=7.2, 1H, CH(8)), 7.03 (d, J=9.2, 2H, CH(3)), 7.41 (d, J=8.6, 2H, CH(4)). ^{13}C NMR (major conformer): −0.6 (CH_3(16)), 11.4 (CH_3(9)), 20.2, 25.8, 27.7, 30.0 (CH_2(12–15)), 42.5 (CH(10)), 45.8 (CH(6)), 55.2 (CH_3(1)), 71.8 (CH(11)), 108.1 (CH(8)), 113.4 (CH(3)), 129.0 (CH(4)), 135.2 (C(5)), 145.5 (C(7)), 157.8 (C(2)). Signals of the minor conformer could not be unambiguously identified due to low intensity.

4.3.1.2. rel-(4S,6S)-(E)-4-(4-Chlorophenyl)-3-ethylidene-6-methoxy-6-methyl-2-(trimethylsilyloxy)morpholine ***3c***. ^1H NMR: 0.25 (s, 9H, CH_3(13)), 1.12 (s, 3H, CH_3(11)), 1.34 (d, J=6.6, 3H, CH_3(8)), 2.30 (dd, J=13.2, 6.6, 1H, CH_{2a}(9)), 2.45 (dd, J=13.2, 7.3, 1H, CH_{2b}(9)), 3.27 (s, 3H, CH_3(12)), 4.08 (br t, J=7.0, 1H, CH(5)), 5.67 (q, J=6.6, 1H, CH(7)), 7.25 (d, J=8.1, 2H, CH(3)), 7.34 (d, J=8.1, 2H, CH(2)). ^{13}C NMR: −0.6 (CH_3(13)), 12.1 (CH_3(8)), 23.4 (CH_3(11)), 36.9 (CH(5)), 39.5 (CH_2(9)), 49.1 (CH_3(12)), 101.3 (C(10)), 115.2 (CH(7)), 128.4 and 129.3 (CH(3) and CH(2)), 131.8 (C(1)), 141.9 (C(4)), 146.3 (C(6)).

4.3.1.3. rel-(4S,6S)-(E)-6-Methoxy-4-(4-methoxyphenyl)-6-methyl-3-propylidene-2-(trimethylsilyloxy)morpholine ***3f***. ^1H NMR: 0.26 (s, 9H, CH_3(14)), 0.80 (t, J=7.3, 3H, CH_3(15)), 1.10 (s, 3H, CH_3(12)), 2.27 (dd, J=13.2, 6.6, 1H, CH_{2b}(10)), 2.41 (dd, J=13.2, 8.1, 1H, CH_{2a}(10)), 1.61–1.85 (m, 2H, CH_2(9)), 3.28 (s, 3H, CH_3(13)), 3.79 (s, 3H, CH_3(1)), 4.07 (br t, 1H, CH(6)), 5.52 (t, J=7.4, 1H, CH(8)), 6.81 (d, J=8.1, 2H, CH(3)), 7.31 (d, J=8.1, 2H, CH(4)). ^{13}C NMR: −0.6 (CH_3(14)), 13.3 (CH_3(15)), 20.0 (CH(9)), 23.3 (CH_3(12)), 37.4 (CH(6)), 39.8 (CH_2(10)), 49.1 (CH_3(13)), 55.2 (CH_3(1)), 101.6 (C(11)), 113.5 (CH(3)), 121.4 (CH(8)), 129.3 (CH(4)), 135.8 (C(5)), 145.6 (C(7)), 157.8 (C(2)).

4.3.1.4. rel-(4S,6S)-(E)-3-Benzylidene-6-methoxy-4-(4-methoxyphenyl)-6-methyl-2-(trimethylsilyloxy)morpholine ***3h***. ^1H NMR: 0.35 (s, 9H, CH_3(14)), 0.95 (s, 3H, CH_3(12)), 2.35 (br s, 2H, CH_2(10)), 3.30 (s, 3H, CH_3(13)), 3.79 (s, 3H, CH_3(1)), 4.33 (br s, 1H, CH(6)), 6.60 (s, 1H, CH(8)), 6.84 (d, J=8.5, 2H, CH(3)), 7.05–7.20 (m, 5H, CH(15–17)), 7.33 (d, J=8.5, 2H, CH(4)). ^{13}C NMR: −0.5 (CH_3(14)), 22.4 (CH_3(12)), 38.8 and 40.6 (CH(6) and CH_2(10)), 49.3 (CH_3(13)), 55.2 (CH_3(1)), 102.8 (C(11)), 113.8 (CH(3)), 115.9 (CH(8)), 126.6 (CH(17)), 128.2 and 129.3 (CH(15–16)), 128.8 (CH(4)), 135.4 and 135.1 (C(5) and C(9)), 149.0 (C(7)), 157.9 (C(2)).

4.3.1.5. rel-(4S,6S)-(E)-Methyl 3-(6-methoxy-4-(4-methoxyphenyl)-6-methyl-2-(trimethylsilyloxy)-morpholin-3-ylidene)propanoate ***3i***. ^1H NMR: 0.27 (s, 9H, CH_3(14)), 1.07 (s, 3H, CH_3(12)), 2.35 (br s, 2H, CH_2(10)), 2.76 (dd, J=18.0, 6.2, 1H CH_{2a}(9)), 2.85 (dd, J=18.0, 8.1, 1H, CH_{2b}(9)), 3.26 (s, 3H, CH_3(13)), 3.57 (s, 3H, CH_3(16)), 3.76 (s, 3H, CH_3(1)), 4.05 (br t, J=5.9, 1H, CH(6)), 5.72 (t, J=7.4, 1H, CH(8)), 6.79 (d, J=8.5, 2H, CH(3)), 7.25 (d, J=8.8, 2H, CH(4)). ^{13}C NMR: −0.7 (CH_3(14)), 22.9 (CH_3(12)), 32.1 (CH_2(9)), 37.7 (CH(6)), 40.0 (CH_2(10)), 49.1 (CH_3(13)), 51.6 (CH_3(16)), 55.2 (CH_3(1)), 102.1 (C(11)), 113.8 (CH(3)), 129.2 (CH(4)), 129.5 (CH(8)), 134.4 (C(5)), 149.4 (C(7)), 158.1 (C(2)), 171.6 (C(15)). ^{29}Si NMR: 25.98.

4.3.1.6. rel-(4S,6S)-(E)-3-Ethylidene-6-methoxy-4-(2-methoxyphenyl)-6-methyl-2-(trimethylsilyloxy)morpholine ***3j***. ^1H NMR: 0.26 (s, 9H, CH_3(14)), 0.95 (s, 3H, CH_3(12)), 1.29 (d, J=6.6, 3H, CH_3(9)), 2.23–2.35 (m, 2H, CH_2(10)), 3.28 (s, 3H, CH_3(13)), 3.86 (s, 3H, CH_3(13)), 3.79–3.86 (m, 1H, CH(6)), 4.44 (br s, 1H, CH(6)), 5.54 (q, J=6.6, 1H, CH(8)), 6.77–6.87 (m, 2H, CH(3) and CH(15)), 7.14–7.22 (m, 1H, CH(4)), 7.45 (d, J=6.6, 1H, CH(16)). ^{13}C NMR: −0.6 (CH_3(14)), 12.0 (CH_3(9)), 23.1 (CH_3(12)), 31.7 (CH(6)), 36.6 (CH_2(10)), 49.2 (CH_3(13)), 55.3 (CH_3(1)), 102.2 (C(11)), 109.8 and 120.3 (CH(3) and CH(15)), 111.8 (CH(8)), 127.1 and 129.9 (CH(4) and CH(16)), 128.9 (C(5)), 147.7 (C(7)), 156.7 (C(2)). ^{29}Si NMR: 24.59.

4.3.1.7. 4-(4-Chlorophenyl)-3-methylidene-6,6-dimethyl-2-(trimethylsilyloxy)morpholine ***3k***. ^1H NMR: 0.24 (s, 9H, CH_3(12)), 1.31 (s, 3H, CH_3(10 or 11)), 1.50 (br s, 3H, CH_3(10 or 11)), 1.73 (dd, J=12.6, 4.7, 1H, CH_{2a}(8)), 1.96 (t, J=12.6, 1H, CH_{2e}(8)), 3.79 (br t, J=12.6, 1H, CH(5)), 3.90 (s, 1H, CH_{2a}(7)), 5.00 (s, 1H, CH_{2a}(7)), 7.21 (d, J=8.5, 2H, CH(6 or 7)), 7.31 (d, J=8.5, 2H, CH(6 or 7)). ^{13}C NMR: −0.7 (CH_3(12)), 23.9 (br) and 28.9 (CH_3(10) and CH_3(11)), 42.3 (CH(5)), 43.5 (CH_2(8)), 76.8 (C(9)), 97.3 (CH(7)), 128.6 and 130.2 (CH(2) and CH(3)), 132.6 (C(4)), 139.4 (C(1)), 158.0 (C(6)).

4.3.1.8. (E)-3-Ethylidene-4-(4-methoxyphenyl)-6,6-dimethyl-2-(trimethylsilyloxy)morpholine ***3e***. $EtN(i\text{-}Pr)_2$ (0.78 mL, 1.5 equiv, 4.5 mmol) was added to a stirred solution of the oxazine *N*-oxide **2e**

(0.79 g, 3 mmol) in CH_2Cl_2 (6 mL) at −78 °C. Then TMSOTf (0.63 mL, 1.1 equiv, 3.3 mmol) was added. The reaction mixture was maintained at −30 °C for 16 h, diluted with hexane (20 mL) and then poured into a mixture of hexane (30 mL) and aqueous solution of $NaHSO_4$ (0.5 g in 30 mL of water). The organic layer was washed with H_2O (50 mL), brine (2×50 mL), and dried over Na_2SO_4. The solvents were removed in vacuum to give mixture of **3e** with **4e** and **4e′**. Overall yield **3e**+**4e**+**4e′**=48% (according to NMR). Two conformers in a ratio 1:1. Characteristic signals in ^{1}H NMR: 4.01 (br t, *J*=7.3, 1H, CH(6)), 5.63 (q, *J*=6.6, 1H, CH(8)) and 5.75 (q, *J*=7.2, 1H, CH(8)).

4.4. Preparation of siloxy derivatives 4a–f,h–k

*4.4.1. General procedure for the rearrangement of ASENA **3a–f,h–k***

Crude ASENA was dissolved in $CHCl_3$ (10 mL). H_2O (0.5 mL) was added. The reaction mixture was maintained for 24 h, and the solvents were removed in vacuum to give crude oxazine **4** as colorless or slightly yellow oil, which was used in the next step without additional purification. For yields see Table 3.

*4.4.1.1. rel-(4S,6S)-6-Methoxy-4-(4-methoxyphenyl)-6-methyl-3-((1R)-1-(trimethylsilyloxy)ethyl)-5,6-dihydro-4H-1,2-oxazine **4a**.* Title compound can be additionally purified by column chromatography (eluent: hexane/EtOAc, 10:1). R_f=0.57 (hexane/EtOAc, 1:1) (UV). ^{1}H NMR: −0.09 (s, 9H, CH_3(14)), 1.30 (d, *J*=6.6, 3H, CH_3(9)), 1.42 (s, 3H, CH_3(12)), 1.84 (dd, *J*=13.2, 12.5, 1H, CH_{2ax}(10)), 2.25 (dd, *J*=13.2, 8.1, 1H, CH_{2eq} (10)), 3.28 (s, 3H, CH_3(13)), 3.72–3.80 (m, 1H, CH(6)), 3.78 (s, 3H, CH_3(1)), 4.25 (q, *J*=6.7, 1H, CH(8)), 6.83 (d, *J*=8.4, 2H, CH(3)), 7.07 (d, *J*=8.4, 2H, CH(4)). ^{13}C NMR: 0.3 (CH_3(14)), 20.5 (CH_3(12)), 21.6 (CH_3(9)), 35.6 (CH(6)), 40.3 (CH_2(10)), 49.4 (CH_3(13)), 55.3 (CH_3(1)), 68.4 (CH(8)), 97.4 (C(11)), 114.2 (CH(3)), 129.7 (CH(4)), 132.9 (C(5)), 158.6 (C(2)), 162.5 (C(7)).

*4.4.1.2. rel-(4S,4aR,8aR)-4-(4-Methoxyphenyl)-3-((1R)-1-(trimethylsilyloxy)ethyl)-4a,5,6,7,8,8a-hexahydro-4H-benzo[e][1,2]oxazine **4b**.* ^{1}H NMR: −0.12 (s, 9H, CH_3(16)), 1.37 (d, *J*=6.6, 3H, CH_3(9)), 1.21–1.74 (m, 9H, CH(10) and CH_2(12–15)), 3.36 (s, 1H, CH(6)), 3.79 (s, 3H, CH_3(1)), 4.00 (br s, 1H, CH(11)), 4.37 (q, *J*=6.6, 1H, CH(8)), 6.85 (d, *J*=8.5, 2H, CH(4)), 7.03 (d, *J*=8.5, 2H, CH(3)). ^{13}C NMR: −0.1 (CH_3(16)), 19.9, 25.2, 27.6, and 29.5 (CH_2(12–15)), 21.7 (CH_3(9)), 38.7 (CH(10)), 41.8 (CH(6)), 55.3 (CH_3(1)), 68.0 and 68.8 (CH(8) and CH(11)), 113.9 (CH(3)), 129.3 (CH(4)), 134.6 (C(5)), 157.3 and 158.4 (C(2) and C(7)). ^{29}Si NMR: 17.35.

*4.4.1.3. rel-(4S,6S)-4-(4-Chlorophenyl)-6-methoxy-6-methyl-3-((1R)-1-(trimethylsilyloxy)ethyl)-5,6-dihydro-4H-1,2-oxazine **4c**.* ^{1}H NMR: −0.09 (s, 9H, CH_3(13)), 1.33 (d, *J*=6.6, 3H, CH_3(8)), 1.43 (s, 3H, CH_3(11)), 1.84 (dd, *J*=13.3, 12.5, 1H, CH_{2ax}(9)), 2.28 (dd, *J*=13.3, 8.1, 1H, CH_{2eq}(9)), 3.29 (s, 3H, CH_3(12)), 3.81 (dd, *J*=12.5, 8.1, 1H, CH(5)), 4.28 (q, *J*=6.6, 1H, CH(7)), 7.11 (d, *J*=8.8, 2H, CH(3)), 7.29 (d, *J*=8.8, 2H, CH(2)). ^{13}C NMR: 0.2 (CH_3(13)), 20.7 (CH_3(11)), 21.4 (CH_3(8)), 35.8 (CH(5)), 40.4 (CH_2(9)), 49.4 (CH_3(12)), 68.6 (CH(7)), 97.2 (C(10)), 128.8 and 129.9 (CH(2) and CH(3)), 132.6 (C(4)), 139.7 (C(1)), 162.0 (C(6)). ^{29}Si NMR: 17.11.

*4.4.1.4. rel-(4S,6S)-4-Phenyl-6-methoxy-6-methyl-3-(1-(trimethylsilyloxy)ethyl)-5,6-dihydro-4H-1,2-oxazine **4d**[2a].* ^{1}H NMR: 0.12 (s, 9H, CH_3(13)), 1.33 (d, *J*=6.6, 3H, CH_3(8)), 1.44 (s, 3H, CH_3(11)), 1.88 (dd, *J*=13.1, 12.5, 1H, CH_{2a}(9)), 2.29 (dd, *J*=13.1, 8.1, 1H, CH_{2e}(9)), 3.31 (s, 3H, CH_3(12)), 3.84 (dd, *J*=12.5, 8.1, 1H, CH(5)), 4.29 (q, *J*=6.6, 1H, CH(7)), 7.15–7.28 (m, 5H, CH(1–3)). ^{13}C NMR: 0.2 (CH_3(6)), 20.6 and 21.5 (CH_3(8) and CH_3(11)), 36.4 (CH(5)), 40.5 (CH_2(9)), 49.4 (CH_3(12)), 68.4 (CH(7)), 97.3 (C(10)), 126.8 (CH(1)), 128.8 and 128.9 (CH(2) and CH(3)), 141.1 (C(4)), 162.3 (C(6)).

*4.4.1.5. 4-(4-Methoxyphenyl)-6,6-dimethyl-3-(1-(trimethylsilyloxy)-ethyl)-5,6-dihydro-4H-1,2-oxazines **4e** and **4e′**.* Mixtures **4e** and **4e′** in a ratio 1:1. ^{1}H NMR: −0.09 and 0.15 (s, 9H, CH_3(14)), 0.99 (d, *J*=6.6, 3H, CH_3(9)), 1.26 and 1.32 (both s, both 3H, CH_3(12) and CH_3(13)), 1.79–2.10 (m, 3H, CH_2(10)), 3.51 and 3.60 (*J*=10.8, 8.8, 1H, CH(6)), 3.80 (s, 3H, CH_3(1)), 4.23 and 4.35 (both q, *J*=6.6, both 1H, CH(8)), 6.86 (both d, both *J*=8.5, both 2H, CH(3)), 7.07 and 7.13 (d, *J*=8.4, 2H, CH(4)). ^{13}C NMR: 0.1 and 0.3 (CH_3(14)), 22.6 and 22.9 (CH_3(9) and CH_3(12)), 28.5 and 29.7 (CH_3(13)), 36.2 and 36.3 (CH(6)), 41.9 and 42.0 (CH_2(10)), 55.3 (CH_3(1)), 68.2 and 70.0 (CH(8)), 74.2 (C(11)), 114.1 and 114.4 (CH(3)), 129.5 and 130.0 (CH(4)), 132.6 and 133.3 (C(5)), 158.7 (C(2)), 160.2 and 161.8 (C(7)).

*4.4.1.6. rel-(4S,6S)-6-Methoxy-4-(4-methoxyphenyl)-6-methyl-3-((1R)-1-(trimethylsilyloxy)propyl)-5,6-dihydro-4H-1,2-oxazine **4f**.* ^{1}H NMR: −0.07 (s, 9H, CH_3(14)), 0.84 (t, *J*=7.3, 3H, CH_3(15)), 1.44 (s, 2H, CH_3(12)), 1.60–1.74 (m, 2H, CH_2(9)), 1.93 (dd, *J*=13.5, 11.5, 1H, CH_{2ax}(10)), 2.27 (dd, *J*=13.5, 8.2, 1H, CH_{2eq}(10)), 3.27 (s, 3H, CH_3(13)), 3.70 (dd, *J*=11.5, 8.2, 1H, CH(6)), 3.78 (s, 3H, CH_3(1)), 4.06 (t, *J*=6.6, 1H, CH(8)), 6.83 (d, *J*=8.5, 2H, CH(3)), 7.08 (d, *J*=8.5, 2H, CH(4)). ^{13}C NMR: 0.1 (CH_3(14)), 9.7 (CH_3(15)), 21.5 (CH_3(12)), 27.8 (CH_2(9)), 35.9 (CH(6)), 40.9 (CH_2(10)), 49.3 (CH_3(13)), 55.3 (CH_3(1)), 74.5 (CH(8)), 97.5 (C(11)), 114.1 (CH(3)), 129.8 (CH(4)), 132.8 (C(5)), 158.5 (C(2)), 162.1 (C(7)).

*4.4.1.7. rel-(4S,6S)-6-Methoxy-4-(4-methoxyphenyl)-6-methyl-3-(phenyl(trimethylsilyloxy)methyl)-5,6-dihydro-4H-1,2-oxazine **4h**.* ^{1}H NMR: −0.15 (s, 3H, CH_3(14)), 1.40 (s, 3H, CH_3(12)), 1.95 (dd, *J*=13.2, 10.8, 1H, CH_{2ax}(10)), 2.19 (dd, *J*=13.2, 8.2, 1H, CH_{2eq}(10)), 3.28 (s, 3H, CH_3(13)), 3.53 (dd, *J*=10.8, 8.6, 1H, CH(6)), 3.81 (s, 3H, CH_3(1)), 5.31 (s, 1H, CH(8)), 6.83 (d, *J*=7.9, 2H, CH(3)), 6.99 (d, *J*=7.9, 2H, CH(4)), 7.20–7.30 (m, 5H, CH(15–17)). ^{13}C NMR: −0.3 (CH_3(14)), 21.4 (CH_3(12)), 35.5 (CH(6)), 40.9 (CH_2(10)), 49.3 (CH_3(13)), 55.3 (CH_3(1)), 75.3 (CH(8)), 97.8 (C(11)), 113.7 (CH(3)), 126.6 and 130.1 (CH(15) and CH(16)), 127.4 (CH(17)), 127.8 (CH(4)), 132.6 (C(5)), 141.0 (C(9)), 158.5 (C(2)), 163.3 (C(7)).

*4.4.1.8. rel-(4S,6S)-Methyl 3-(6-methoxy-4-(4-methoxyphenyl)-6-methyl-5,6-dihydro-4H-1,2-oxazin-3-yl)-3-(trimethylsilyloxy)propanoate **4i**.* Oxazine **4i** was prepared according to the general procedure from ASENA **3i** with one change: the reaction mixture was maintained not for 1 day, but for 1 month. ^{1}H NMR: −0.08 (s, 9H, CH_3(14)), 1.43 (s, 3H, CH_3(12)), 1.82 (dd, *J*=13.2, 12.5, 1H, CH_{2a}(10)), 2.27 (dd, *J*=13.2, 8.1, 1H, CH_{2e}(10)), 2.59 (dd, *J*=16.1, 6.6, 1H, CH_{2a}(9)), 2.91 (dd, *J*=16.1, 8.8, 1H, CH_{2b}(9)), 3.30 (s, 3H, CH_3(13)), 3.66 (s, 3H, CH_3(16)), 3.75 (dd, *J*=12.5, 8.1, 1H, CH(6)), 3.80 (s, 3H, CH_3(1)), 4.67 (t, *J*=6.6, 1H, CH(8)), 6.89 (d, *J*=8.4, 2H, CH(3)), 7.11 (d, *J*=8.4, 2H, CH(4)). ^{13}C NMR: 0.2 (CH_3(14)), 21.4 (CH_3(12)), 35.5 (CH(6)), 38.8 and 40.2 (CH_2(9) and CH_2(10)), 49.5 (CH_3(13)), 51.5 (CH_3(16)), 55.3 (CH_3(1)), 68.7 (CH(8)), 97.5 (C(11)), 114.4 (CH(3)), 129.7 (CH(4)), 132.0 (C(5)), 158.7 (C(2)), 160.0 (C(7)), 171.6 (C(15)).

*4.4.1.9. rel-(4S,6S)-6-Methoxy-4-(2-methoxyphenyl)-6-methyl-3-(1-(trimethylsilyloxy)ethyl)-5,6-dihydro-4H-1,2-oxazine **4j**.* ^{1}H NMR: −0.14 (s, 9H, CH_3(14)), 1.33 (d, *J*=6.5, 3H, CH_3(9)), 1.43 (s, 3H, CH_3(12)), 1.94 (dd, *J*=13.1, 11.8, 1H, CH_{2ax}(10)), 2.17 (dd, *J*=13.1, 7.9, 1H, CH_{2eq} (10)), 3.31 (s, 3H, CH_3(13)), 3.79 (s, 3H, CH_3(1)), 4.09 (dd, *J*=11.8, 7.9, 1H, CH(6)), 4.25 (q, *J*=6.6, 1H, CH(8)), 6.84–6.94 (m, 2H, CH(3) and CH(15)), 7.09 (d, *J*=7.2, 1H, CH(16)), 7.23 (t, *J*=7.2, 1H, CH(4)). ^{13}C NMR: 0.1 (CH_3(14)), 20.6 (CH_3(12)), 21.7 (CH_3(9)), 31.5 (CH(6)), 37.5 (CH_2(10)), 49.4 (CH_3(13)), 55.4 (CH_3(1)), 68.5 (CH(8)), 97.3 (C(11)), 110.7 (CH(3)), 120.8 (CH(5)), 128.1 and 130.4 (CH(4) and CH(16)), 129.1 (C(5)), 157.1 (C(2)), 162.5 (C(7)). ^{29}Si NMR: 20.6.

*4.4.1.10. 4-(4-Chlorophenyl)-6,6-dimethyl-3-((trimethylsilyloxy)methyl)-5,6-dihydro-4H-1,2-oxazine **4k**.* Oxazine **4k** was prepared according to the general procedure from ASENA **3k**. R_f=0.63 (hexane/EtOAc, 1:1) (UV). Purity was approximately 50% according to NMR. Spectroscopically pure sample was obtained from purified desilylated product **1k** (see Section 4.5.12) by the following procedure: NEt_3 (0.063 mL, 3 equiv, 0.45 mmol) was added to a stirred solution of the oxazine **1k** (0.038 g, 0.15 mmol) in CH_2Cl_2 (1 mL) at 0 °C in dry argon. Then TMSCl (0.029 mL, 1.5 equiv, 0.23 mmol) was added. After 10 min the cooling bath was removed and the reaction mixture was maintained for 24 h and then the solvent was removed in vacuum. The solid residue was washed with hexane (2×10 mL) and hexane phase was evaporated in vacuum to give title oxazine **4k** (0.05 g, ca. 100%), which was NMR spectroscopically pure. ^{1}H NMR: −0.03 (s, 9H, CH_3(12)), 1.30 and 1.35 (both s, 3H, CH_3(10) and CH_3(11)), 1.84 (dd, *J*=13.2, 11.7, 1H, CH_{2ax}(8)), 2.05 (dd, *J*=13.2, 8.1, 1H, CH_{2eq}(8)), 3.63 (dd, *J*=11.8, 8.1, 1H, CH(5)), 3.91 (d, *J*=11.7, 1H, CH_{2a}(7)), 4.02 (d, *J*=11.7, 1H, CH_{2b}(7)), 7.13 and 7.31 (both d, *J*=8.8, both 2H, CH(2) and CH(3)). ^{13}C NMR: −0.7 (CH_3(12)), 22.7 and 28.5 (CH_3(10) and CH_3(11)), 36.2 (CH(5)), 40.3 (CH_2(8)), 62.8 (CH_2(7)), 74.4 (C(9)), 125.0 (C(4)), 128.9 and 129.9 (CH(2) and CH(3)), 138.9 (C(1)), 157.3 (C(6)).

*4.4.1.11. rel-(4S,6S)-6-Methoxy-4-(4-methoxyphenyl)-3-((4-methoxyphenyl)(trimethylsilyloxy)methyl)-6-methyl-5,6-dihydro-4H-1,2-oxazine **4g** and **4g′**.* NEt_3 (0.36 mL, 2 equiv, 2.6 mmol) was added to a stirred solution of the oxazine *N*-oxide **2g** (0.48 g, 1.3 mmol) in CH_2Cl_2 (5.2 mL) at −78 °C in dry argon. Then TMSBr (0.22 mL, 1.3 equiv, 1.7 mmol) was added. The reaction mixture was maintained at the same temperature for 4.5 h, diluted with hexane (20 mL), and then poured into a mixture of hexane (30 mL) and aqueous solution of $NaHSO_4$ (0.5 g in 30 mL of water). The organic layer was washed with H_2O (30 mL), brine (2×30 mL), and dried over Na_2SO_4. The solvents were removed in vacuum, and the residue was subjected to column chromatography (eluent: hexane/EtOAc, 3:1) to give 0.35 g (61%) of title oxazines **4g** and **4g′** (mixture of two diastereomers, de=71%) as colorless oil. R_f=0.63 (hexane/EtOAc, 1:1) (UV). Compound **4g**: ^{1}H NMR: −0.17 (s, 3H, CH_3(14)), 1.40 (s, 3H, CH_3(12)), 1.94 (dd, *J*=13.9, 11.8, 1H, CH_{2ax}(10)), 2.19 (dd, *J*=13.9, 8.1, 1H, CH_{2eq}(10)), 3.28 (s, 3H, CH_3(13)), 3.57 (dd, *J*=11.8, 8.1, 1H, CH(6)), 3.79 and 3.80 (s, 6H, CH_3(1) and CH_3(18)), 5.24 (s, 1H, CH(8)), 6.84 (d, *J*=8.5, 4H, CH(3) and CH(16)), 7.00 and 7.12 (d, *J*=8.5, 4H, CH(4) and CH(15)). ^{13}C NMR: −0.3 (CH_3(14)), 21.4 (CH_3(12)), 35.5 (CH(6)), 40.9 (CH_2(10)), 49.3 (CH_3(13)), 55.2 and 55.3 (CH_3(1) and CH_3(18)), 75.3 (CH(8)), 97.7 (C(11)), 113.2 and 113.7 (CH(3) and CH(16)), 127.8 and 130.0 (CH(4) and CH(15)), 132.6 and 133.0 (C(5) and C(9)), 158.4 and 158.9 (C(2) and C(17)), 163.4 (C(7)). Compound **4g′**: ^{1}H NMR: 0.09 (s, 3H, CH_3(14)), 1.45 (s, 3H, CH_3(12)), 1.92 (dd, *J*=13.9, 11.8, 1H, CH_{2ax}(10)), 2.16 (dd, *J*=13.9, 8.1, 1H, CH_{2eq}(10)), 3.33 (s, 3H, CH_3(13)), 3.52 (dd, *J*=11.8, 8.1, 1H, CH(6)), 3.75 and 3.80 (s, 6H, CH_3(1) and CH_3(18)), 5.19 (s, 1H, CH(8)), 6.61 and 6.65 (d, *J*=8.5, 4H, CH(3) and CH(16)), 6.78 and 6.94 (d, *J*=8.5, 4H, CH(4) and CH(15)). ^{13}C NMR: −0.3 (CH_3(14)), 21.3 (CH_3(12)), 39.6 (CH(6)), 41.0 (CH_2(10)), 49.3 (CH_3(13)), 55.2 and 55.3 (CH_3(1) and CH_3(18)), 74.9 (CH(8)), 97.5 (C(11)), 113.1 and 113.5 (CH(3) and CH(16)), 126.9 and 130.2 (CH(4) and CH(15)), 131.1 and 133.1 (C(5) and C(9)), 158.6 and 158.9 (C(2) and C(17)), 162.5 (C(7)).

4.5. General procedure for desilylation. Preparation of hydroxy derivatives 1a–k

Crude oxazine **4** was dissolved in MeOH (4 mL). $NH_4F{\cdot}HF$ (11 mg, 0.1 equiv, 0.2 mmol) was added. The reaction mixture was maintained for 24 h, the solvents were removed in vacuum, and the residue was separated by column chromatography (eluent: hexane/EtOAc, from 10:1 to 3:1) to give title oxazines **1** as colorless oil unless otherwise mentioned. For yields see Table 3.

*4.5.1. rel-(1R)-1-((4S,6S)-6-Methoxy-4-(4-methoxyphenyl)-6-methyl-5,6-dihydro-4H-1,2-oxazin-3-yl)ethanol **1a***

Oxazine **1a** was prepared according to the general procedure from oxazine **4a**. Yield=94% (total yield from oxazine **2a** on three steps=54%). R_f=0.26 (hexane/EtOAc, 1:1) (UV). Mp=63–64 °C (hexane/EtOAc, 3:1). Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.50; H, 7.58; N, 5.01. Found: C, 64.42; H, 7.59; N, 4.83. ν_{max}: 3442, 2987, 2938, 2835, 1612, 1513, 1463, 1378, 1302, 1245, 1198, 1178, 1151, 1082, 1070, 1036, 905, 876, 834, 797, 553 cm^{-1}. ^{1}H NMR: 1.23 (d, J=6.7, 3H, CH_3(9)), 1.45 (s, 3H, CH_3(12)), 1.94 (dd, *J*=13.3, 12.6, 1H, CH_{2ax}(10)), 2.06 (d, *J*=6.7, 1H, OH(14)), 2.27 (dd, *J*=13.3, 8.1, 1H, CH_{2eq}(10)), 3.28 (s, 3H, CH_3(13)), 3.79 (s, 3H, CH_3(1)), 3.83 (dd, *J*=12.6, 8.1, 1H, CH(6)), 4.12 (m, *J*=6.7, 1H, CH(8)), 6.87 (d, *J*=8.5, 2H, CH(3)), 7.13 (d, *J*=8.5, 2H, CH(4)). ^{13}C NMR: 20.8 (CH_3(12)), 21.5 (CH_3(9)), 36.3 (CH(6)), 39.2 (CH_2(10)), 49.5 (CH_3(13)), 55.3 (CH_3(1)), 67.7 (CH(8)), 97.7 (C(11)), 114.5 (CH(3)), 129.7 (CH(4)), 131.5 (C(5)), 158.8 (C(2)), 162.9 (C(7)).

*4.5.2. rel-(1R)-1-((4S,4aR,8aR)-4-(4-Methoxyphenyl)-4a,5,6,7,8,8a-hexahydro-4H-benzo[e][1,2]oxazin-3-yl)ethanol **1b***

Oxazine **1b** was prepared according to the general procedure from oxazine **4b**. Yield=94% (total yield from oxazine **2b** on three steps=46%). R_f=0.46 (hexane/EtOAc, 1:1) (UV). Mp=116–120 °C (hexane/EtOAc, 3:1). Anal. Calcd for $C_{17}H_{23}NO_3$: C, 70.56; H, 8.01; N, 4.84. Found: C, 70.58; H, 8.05; N, 4.85. ν_{max}: 3411, 2932, 2858, 1610, 1511, 1462, 1445, 1299, 1248, 1180, 1110, 1034, 968, 941, 890, 876, 833 cm^{-1}. ^{1}H NMR: 1.26 (d, *J*=6.6, 3H, CH_3(9)), 1.20–1.75 (m, 8H, CH_2(12–15)), 2.05 (m, 1H, CH(10)), 2.58 (d, *J*=6.6, 1H, OH(16)), 3.29 (s, 1H, CH(6)), 3.76 (s, 3H, CH_3(1)), 4.01 (br s, 1H, CH(11)), 4.23 (m, *J*=6.6, 1H, CH(8)), 6.83 (d, *J*=8.8, 2H, CH(3)), 7.03 (d, *J*=8.8, 2H, CH(4)). ^{13}C NMR: 19.9, 25.1, 27.5 and 29.4 (CH_2(12–15)), 21.2 (CH_3(9)), 38.7 and 42.9 (CH(6) and CH(10)), 55.3 (CH_3(1)), 68.5 and 69.0 (CH(8) and CH(11)), 114.2 (CH(3)), 129.2 (CH(4)), 133.7 (C(5)), 156.6 (C(7)), 158.6 (C(2)).

*4.5.3. rel-(1R)-1-((4S,6S)-4-(4-Chlorophenyl)-6-methoxy-6-methyl-5,6-dihydro-4H-1,2-oxazin-3-yl)ethanol **1c***

Oxazine **1c** was prepared according to the general procedure from oxazine **4c**. Yield=94% (total yield from oxazine **2c** on three steps=73%). R_f=0.45 (hexane/EtOAc, 1:1) (UV). Mp=74–75 °C (hexane/EtOAc, 5:1). Anal. Calcd for $C_{14}H_{18}ClNO_3$: C, 59.26; H, 6.39; N, 4.94. Found: C, 59.36; H, 6.45; N, 4.87. ν_{max}: 3415, 2987, 2939, 2835, 1672, 1491, 1454, 1409, 1378, 1311, 1239, 1198, 1182, 1152, 1089, 1063, 1015, 941, 907, 877, 835, 776 cm^{-1}. ^{1}H NMR: 1.25 (d, *J*=6.6, 3H, CH_3(11)), 1.45 (s, 3H, CH_3(8)), 1.84 (dd, *J*=13.8, 12.1, 1H, CH_{2ax}(9)), 1.91 (d, *J*=6.6, 1H, OH(12)), 2.28 (dd, *J*=13.8, 7.9, 1H, CH_{2eq}(9)), 3.28 (s, 3H, CH_3(8)), 3.87 (dd, *J*=12.1, 7.9, 1H, CH(5)), 4.08 (m, *J*=6.6, 1H, CH(10)), 7.15 and 7.31 (both d, *J*=8.6, both 2H, CH(2) and CH(3)). ^{13}C NMR: 20.6 (CH_3(7)), 21.5 (CH_3(11)), 36.5 (CH(5)), 39.3 (CH_2(9)), 49.5 (CH_3(8)), 67.8 (CH(10)), 97.8 (C(6)), 129.2 and 130.0 (CH(2) and CH(3)), 133.2 (C(4)), 138.6 (C(1)), 162.1 (C(13)).

*4.5.4. rel-1-((4S,6S)-6-Methoxy-6-methyl-4-phenyl-5,6-dihydro-4H-1,2-oxazin-3-yl)ethanol **1d***

Oxazine **1d** was prepared according to the general procedure from oxazine **4d**. Yield=90% (total yield from oxazine **2d** on three steps=52%). R_f=0.50 (hexane/EtOAc, 1:1) (UV). Mp=86–87 °C (hexane/EtOAc, 7:1). Anal. Calcd for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62; Found: C, 64.40; H, 7.67; N, 5.59. ν_{max}: 3427, 3028, 2987, 2939, 2834, 1602, 1494, 1454, 1378, 1311, 1239, 1198, 1184, 1150, 1097, 1073, 1038, 1008, 944, 916, 900, 876, 837, 758, 704, 551 cm^{-1}. ^{1}H NMR: 1.17 (d, *J*=5.9, 3H, CH_3(8)), 1.39 (s, 3H, CH_3(11)), 1.90 (dd, *J*=13.3, 12.5, 1H, CH_{2ax}(9)), 1.99 (d, *J*=7.3, 1H, OH(13)), 2.24 (dd, *J*=13.3, 8.1, 1H, CH_{2eq}(9)), 3.23 (s, 3H, CH_3(12)), 3.81 (dd, *J*=12.5, 8.1, 1H, CH(5)),

4.04 (m, J=5.9, 1H, CH(7)), 7.14–7.29 (m, 5H, CH(1–3)). ^{13}C NMR: 20.8 and 21.6 (CH_3(8) and CH_3(11)), 37.3 (CH(5)), 39.5 (CH_2(9)), 49.6 (CH_3(12)), 67.8 (CH(7)), 97.8 (C(10)), 127.6 (CH(1)), 128.8 and 129.3 (CH(2) and CH(3)), 140.1 (C(4)), 162.8 (C(6)).

4.5.5. 1-(4-(4-Methoxyphenyl)-6,6-dimethyl-5,6-dihydro-4H-1,2-oxazin-3-yl)ethanol **1e**

Oxazine **1e** was prepared according to the general procedure from the mixture of oxazines **4e** and **4e′**. Yield=40% (total yield from oxazine **2e** on three steps=19%). R_f=0.46 (hexane/EtOAc, 1:1) (UV). Mp=92–94 °C (hexane/EtOAc, 10:1). Anal. Calcd for $C_{15}H_{21}NO_3$: C, 68.42; H, 8.04; N, 5.32. Found: C, 68.32; H, 8.27; N, 5.28. ν_{max}: 3470, 2975, 2930, 1612, 1513, 1462, 1385, 1370, 1304, 1263, 1248, 1179, 1130, 1111, 1035, 960, 926, 898, 833, 554 cm^{-1}. ^{1}H NMR: 1.24 (d, J=6.6, 3H, CH_3(9)), 1.26 and 1.36 (both s, both 3H, CH_3(12) and CH_3(13)), 1.86 (dd, J=13.7, 11.8, 1H, CH_{2ax}(10)), 2.05 (dd, J=13.7, 7.4, 1H, CH_{2eq}(10)), 3.39 (J=11.8, 7.4, 1H, CH(6)), 3.80 (s, 4H, CH_3(1) and OH(14)), 4.09 (m, J=6.6, 1H, CH(8)), 6.87 (d, J=8.5, 2H, CH(3)), 7.09 (d, J=8.5, 2H, CH(4)). ^{13}C NMR: 21.9 and 22.4 (CH_3(9) and CH_3(12)), 28.4 (CH_3(13)), 36.5 (CH(6)), 41.1 (CH_2(10)), 55.3 (CH_3(1)), 66.5 (CH(8)), 75.1 (C(11)), 114.6 (CH(3)), 129.3 (CH(4)), 131.5 (C(5)), 158.9 and 159.2 (C(2) and C(7)).

4.5.6. 1-(4-(4-Methoxyphenyl)-6,6-dimethyl-5,6-dihydro-4H-1,2-oxazin-3-yl)ethanol **1e′**

Oxazine **1e′** was prepared according to the general procedure from the mixture of oxazines **4e** and **4e′**. Yield=56% (total yield from oxazine **2e** on three steps=27%). R_f=0.37 (hexane/EtOAc, 1:1) (UV). ν_{max}: 3384, 2976, 2933, 2839, 1711, 1682, 1609, 1512, 1462, 1444, 1421, 1383, 1371, 1304, 1250, 1179, 1129, 1111, 1034, 953, 926, 833 cm^{-1}. ^{1}H NMR: 1.24 (d, J=6.5, 3H, CH_3(9)), 1.25 and 1.33 (both s, both 3H, CH_3(12) and CH_3(13)), 1.89 (dd, J=13.7, 11.8, 1H, CH_{2ax}(10)), 2.00–2.08 (m, 2H, CH_{2eq}(10) and OH(14)), 3.63 (J=11.8, 7.8, 1H, CH(6)), 3.78 (s, 3H, CH_3(1)), 4.09 (m, J=6.6, 1H, CH(8)), 6.85 (d, J=8.5, 2H, CH(3)), 7.11 (d, J=8.5, 2H, CH(4)). ^{13}C NMR: 20.5 and 22.6 (CH_3(9) and CH_3(12)), 28.6 (CH_3(13)), 37.0 (CH(6)), 40.9 (CH_2(10)), 55.3 (CH_3(1)), 67.5 (CH(8)), 74.4 (C(11)), 114.5 (CH(3)), 129.5 (CH(4)), 132.0 (C(5)), 158.6 (C(2)), 160.7 (C(7)).

4.5.7. rel-(1R)-1-((4S,6S)-6-Methoxy-4-(4-methoxyphenyl)-6-methyl-5,6-dihydro-4H-1,2-oxazin-3-yl)propan-1-ol **1f**

Oxazine **1f** was prepared according to the general procedure from oxazine **4f**. After column chromatography title compound was obtained as a slightly brown solid. Yield=95% (total yield from oxazine **2f** on three steps=58%). R_f=0.27 (hexane/EtOAc, 1:1) (UV). Mp=92–93 °C. Anal. Calcd for $C_{16}H_{23}NO_4$: C, 65.51; H, 7.90; N, 4.77. Found: C, 65.67; H, 8.13; N, 4.66. ν_{max}: 3454, 2964, 2938, 2877, 2835, 1611, 1513, 1462, 1378, 1302, 1246, 1178, 1151, 1105, 1083, 1066, 1035, 899, 834, 796, 553 cm^{-1}. ^{1}H NMR: 0.81 (t, J=7.5, 3H, CH_3(15)), 1.44 (s, 2H, CH_3(12)), 1.43–1.72 (m, 2H, CH_2(9)), 1.79 (d, J=7.2, 1H, OH(14)), 1.96 (t, J=13.1, 1H, CH_{2ax}(10)), 2.27 (dd, J=13.1, 7.9, 1H, CH_{2eq}(10)), 3.30 (s, 3H, CH_3(13)), 3.79 (m, 1H, CH(6)), 3.79 (s, 3H, CH_3(1)), 3.88 (dd, J=7.2, 5.9, 1H, CH(8)), 6.86 (d, J=8.5, 2H, CH(3)), 7.13 (d, J=8.5, 2H, CH(4)). ^{13}C NMR: 9.8 (CH_3(15)), 21.5 (CH_3(12)), 27.3 (CH_2(9)), 36.4 (CH(6)), 39.5 (CH_2(10)), 49.4 (CH_3(13)), 55.3 (CH_3(1)), 73.2 (CH(8)), 97.7 (C(11)), 114.5 (CH(3)), 129.7 (CH(4)), 131.5 (C(5)), 158.9 (C(2)), 162.0 (C(7)).

4.5.8. rel-((4S,6S)-6-Methoxy-4-(4-methoxyphenyl)-6-methyl-5,6-dihydro-4H-1,2-oxazin-3-yl)(4-methoxyphenyl)methanol **1g** *and* **1g′**

Oxazines **1g** and **1g′** were prepared according to the general procedure from the mixture of oxazines **4g** and **4g′**. Yield=95% (total yield from oxazine **2g** on three steps=58%). R_f=0.43 (hexane/EtOAc, 1:1) (UV). Anal. Calcd for $C_{21}H_{25}NO_5$: C, 67.91; H, 6.78; N, 3.77. Found: C, 68.05; H, 6.74; N, 3.85. ν_{max}: 3458, 2993, 2937, 2835, 1611, 1585, 1513, 1463, 1443, 1421, 1379, 1358, 1303, 1248, 1176, 1153, 1112, 1083, 1072, 1034, 951, 899, 832, 798, 770, 736, 551 cm^{-1}. **1g** (major isomer): ^{1}H NMR: 1.47 (s, 3H, CH_3(12)), 1.98 (t, J=13.9, 1H, CH_{2ax}(10)), 2.20 (dd, J=13.9, 7.9, 1H, CH_{2eq}(10)), 2.85 (d, J=7.2, 1H, OH(14)), 3.33 (s, 3H, CH_3(13)), 3.71 (dd, J=13.9, 7.9, 1H, CH(6)), 3.76 (s, 6H, CH_3(1) and CH_3(18)), 5.03 (d, J=7.2, 1H, CH(8)), 6.67 and 6.70 (d, J=8.6, 4H, CH(3) and CH(16)), 6.85 and 6.95 (d, J=8.6, 4H, CH(4) and CH(15)). ^{13}C NMR: 21.5 (CH_3(12)), 36.8 (CH(6)), 39.1 (CH_2(10)), 49.5 (CH_3(13)), 55.3 (CH_3(1) and CH_3(18)), 74.6 (CH(8)), 98.1 (C(11)), 113.6 and 114.1 (CH(3) and CH(16)), 127.8 and 130.1 (CH(4) and CH(15)), 132.8 (C(5) and C(9)), 158.9 (C(2) and C(17)), 162.1 (C(7)). **1g′** (minor isomer): ^{1}H NMR: 1.47 (s, 3H, CH_3(12)), 1.90 (dd, J=13.9, 11.8, 1H, CH_{2ax}(10)), 2.17 (dd, J=13.9, 7.9, 1H, CH_{2eq}(10)), 3.20 (dd, J=11.8, 8.5, 1H, CH(6)), 3.44 (s, 3H, CH_3(13)), 3.81 (s, 6H, CH_3(1) and CH_3(18)), 4.37 (br s, 1H, OH(14)), 4.82 (br s, 1H, CH(8)), 6.67 and 6.70 (d, J=8.6, 4H, CH(3) and CH(16)), 6.85 and 6.97 (d, J=8.6, 4H, CH(4) and CH(15)). ^{13}C NMR: 21.5 (CH_3(12)), 36.2 (CH(6)), 40.5 (CH_2(10)), 50.3 (CH_3(13)), 55.3 (CH_3(1) and CH_3(18)), 72.6 (CH(8)), 98.2 (C(11)), 114.0 and 114.5 (CH(3) and CH(16)), 129.0 and 129.8 (CH(4) and CH(15)), 132.1 (C(5) and C(9)), 158.9 (C(2) and C(17)), 160.7 (C(7)).

4.5.9. rel-((4S,6S)-6-Methoxy-4-(4-methoxyphenyl)-6-methyl-5,6-dihydro-4H-1,2-oxazin-3-yl)(phenyl)methanol **1h**

Oxazine **1h** was prepared according to the general procedure from oxazine **4h**. Yield=95% (total yield from oxazine **2h** on three steps=54%). R_f=0.45 (hexane/EtOAc, 1:1) (UV). Anal. Calcd for $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10. Found: C, 70.30; H, 6.42; N, 4.20. ν_{max}: 3444, 3061, 3030, 2991, 2939, 2908, 2835, 1611, 1513, 1454, 1378, 1303, 1246, 1178, 1152, 1083, 1072, 1035, 900, 835, 797, 733, 710, 700, 551 cm^{-1}. ^{1}H NMR: 1.48 (s, 3H, CH_3(12)), 1.99 (dd, J=13.8, 12.5, 1H, CH_{2ax}(10)), 2.21 (dd, J=13.8, 7.9, 1H, CH_{2eq}(10)), 2.88 (d, J=7.6, 1H, OH(14)), 3.34 (s, 3H, CH_3(13)), 3.71 (dd, J=12.5, 7.9, 1H, CH(6)), 3.76 (s, 3H, CH_3(1)), 5.11 (s, 1H, CH(8)), 6.67 (d, J=8.6, 2H, CH(3)), 6.85 (d, J=8.6, 2H, CH(4)), 7.05 (br s, 2H, CH(15)), 7.17 (br s, 3H, CH(16–17)). ^{13}C NMR: 21.4 (CH_3(12)), 36.8 (CH(6)), 39.1 (CH_2(10)), 49.5 (CH_3(13)), 55.3 (CH_3(1)), 75.1 (CH(8)), 98.2 (C(11)), 114.2 (CH(3)), 126.5 and 129.9 (CH(15) and CH(16)), 127.4 (CH(17)), 127.7 (CH(4)), 129.9 (C(5)), 140.5 (C(9)), 158.9 (C(2)), 162.0 (C(7)).

4.5.10. Methyl rel-3-hydroxy-3-((4S,6S)-6-methoxy-4-(4-methoxyphenyl)-6-methyl-5,6-dihydro-4H-1,2-oxazin-3-yl)propanoate **1i**

Oxazine **1i** was prepared according to the general procedure from oxazine **4i**. Yield=94% (total yield from oxazine **2i** on three steps=66%). R_f=0.42 (hexane/EtOAc, 1:1) (UV). Anal. Calcd for $C_{17}H_{23}NO_6$: C, 60.52; H, 6.87; N, 4.15. Found: C, 60.78; H, 7.01; N, 3.99. ν_{max}: 3479, 2991, 2942, 2836, 1737, 1612, 1514, 1462, 1439, 1379, 1302, 1246, 1203, 1178, 1153, 1080, 1065, 1035, 902, 834, 797, 552 cm^{-1}. ^{1}H NMR: 1.39 (s, 3H, CH_3(12)), 1.86 (dd, J=13.2, 12.5, 1H, CH_{2ax}(10)), 2.24 (dd, J=13.2, 8.1, 1H, CH_{2eq}(10)), 2.67 (d, J=5.9, 2H, CH_2(9)), 3.21 (s, 3H, CH_3(13)), 3.37 (d, J=6.5, 1H, OH(14)), 3.59 (s, 3H, CH_3(16)), 3.73 (s, 3H, CH_3(1)), 3.86 (dd, J=12.5, 8.1, 1H, CH(6)), 4.25 (q, J=6.5, 1H, CH(8)), 6.81 (d, J=8.5, 2H, CH(3)), 7.09 (d, J=8.5, 2H, CH(4)). ^{13}C NMR: 21.2 (CH_3(12)), 35.6 (CH(6)), 37.0 and 39.1 (CH_2(9) and CH_2(10)), 49.3 (CH_3(13)), 51.6 (CH_3(16)), 55.2 (CH_3(1)), 67.1 (CH(8)), 97.6 (C(11)), 114.4 (CH(3)), 129.6 (CH(4)), 131.8 (C(5)), 158.7 (C(2)), 160.1 (C(7)), 173.2 (C(15)).

4.5.11. rel-1-((4S,6S)-6-Methoxy-4-(2-methoxyphenyl)-6-methyl-5,6-dihydro-4H-1,2-oxazin-3-yl)ethanol **1j** *and* **1j′**

Oxazines **1j** and **1j′** were prepared according to the general procedure from the mixture of oxazines **4j** and **4j′**. Yield=95% (total yield from oxazine **2j** on three steps=64%, de=83%). Major isomer: R_f=0.35 (hexane/EtOAc, 1:1) (UV). Mp=38–42 °C. Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.50; H, 7.58; N, 5.01. Found: C, 64.88; H, 7.60; N, 4.77. Minor isomer: R_f=0.46 (hexane/EtOAc, 1:1) (UV). Major

diastereomer **1j**: ν_{max}: 3442, 2987, 2940, 2836, 1745, 1599, 1587, 1494, 1463, 1446, 1377, 1377, 1290, 1245, 1198, 1183, 1151, 1082, 1052, 1028, 907, 877, 842, 756 cm^{-1}. ^1H NMR: 1.24 (d, J=6.5, 3H, CH_3(9)), 1.45 (s, 3H, CH_3(12)), 2.04–2.22 (m, 3H, CH_{2ax}(10), CH_{2eq}(10) and OH(14)), 3.30 (s, 3H, CH_3(13)), 3.82 (s, 3H, CH_3(1)), 4.08 (m, J=6.5, 1H, CH(8)), 4.17 (dd, J=11.7, 8.1, 1H, CH(6)), 6.88–6.96 (m, 2H, CH(3) and CH(15)), 7.15 (dd, J=7.3, 1.5, 1H, CH(16)), 7.26 (td, J=6.5, 1.5, 1H, CH(4)). ^{13}C NMR: 20.3 and 21.8 (CH_3(9) and CH_3(12)), 31.9 (CH(6)), 36.8 (CH_2(10)), 49.5 (CH_3(13)), 55.5 (CH_3(1)), 68.0 (CH(8)), 97.8 (C(11)), 111.3 (CH(3)), 121.4 (CH(15)), 127.9 (C(5)), 128.9 and 130.3 (CH(4) and CH(16)), 157.4 (C(2)), 162.8 (C(7)). Minor diastereomer **1j′**: ν_{max}: 3472, 2981, 2972, 2940, 2836, 1599, 1587, 1494, 1463, 1441, 1377, 1319, 1290, 1245, 1183, 1152, 1118, 1086, 1061, 1029, 948, 906, 840, 796, 757 cm^{-1}. ^1H NMR: 1.19 (d, J=6.5, 3H, CH_3(9)), 1.47 (s, 3H, CH_3(12)), 2.00 (dd, J=13.1, 11.2, H, CH_{2ax}(10)), 2.15 (dd, J=13.1, 8.1, 1H, CH_{2eq}(10)), 3.31 (s, 3H, CH_3(13)), 3.82 (s, 3H, CH_3(1)), 3.94 (dd, J=11.2, 8.1, 1H, CH(6)), 4.05 (m, J=6.5, 1H, CH(8)), 6.87–6.96 (m, 2H, CH(3) and CH(15)), 7.11 (d, J=7.9, 1H, CH(16)), 7.23–7.29 (m, 1H, CH(4)). ^{13}C NMR: 21.5 and 22.0 (CH_3(9) and CH_3(12)), 31.6 (CH(6)), 36.8 (CH_2(10)), 49.4 (CH_3(13)), 55.4 (CH_3(1)), 66.7 (CH(8)), 98.0 (C(11)), 111.1 (CH(3)), 121.2 (CH(15)), 127.4 (C(5)), 128.8 and 130.2 (CH(4) and CH(16)), 157.1 (C(2)), 162.1 (C(7)).

4.5.12. (4-(4-Chlorophenyl)-6,6-dimethyl-5,6-dihydro-4H-1,2-oxazin-3-yl)methanol **1k**

Oxazine **1k** was prepared according to the general procedure from oxazine **4k**. Yield=96% (total yield from oxazine **2k** on three steps=30%). R_f=0.38 (hexane/EtOAc, 1:1) (UV). Mp=53–57 °C. Anal. Calcd for $C_{13}H_{16}ClNO_2$: C, 61.54; H, 6.36; N, 5.52. Found: C, 61.48; H, 6.33; N, 5.67. ν_{max}: 3360, 2976, 2930, 2875, 1492, 1454, 1410, 1385, 1370, 1315, 1271, 1228, 1181, 1123, 1093, 1045, 1015, 995, 976, 941, 923, 860, 829, 783, 736, 714, 541 cm^{-1}. ^1H NMR: 1.27 and 1.36 (both s, 3H, CH_3(10) and CH_3(11)), 1.86 (dd, J=13.8, 11.8, 1H, CH_{2ax}(8)), 2.07 (dd, J=13.8, 7.6, 1H, CH_{2eq}(8)), 3.06 (br s, 1H, OH(12)), 3.52 (dd, J=11.8, 7.6, 1H, CH(5)), 3.93 (br s, 2H, CH(7)), 7.12 and 7.31 (both d, J=8.3, both 2H, CH(2) and CH(3)). ^{13}C NMR: 22.6 and 28.2 (CH_3(10) and CH_3(11)), 36.8 (CH(5)), 40.0 (CH_2(8)), 62.1 (CH_2(7)), 74.8 (C(9)), 129.1 and 129.5 (CH(2) and CH(3)), 133.2 (C(4)), 137.8 (C(1)), 156.3 (C(6)).

4.6. General procedure for the preparation of pyranone oximes 7′k,l

The solution of the corresponding ASENA (3 mmol) in CH_2Cl_2 (6 mL), was added dropwise for 10 min at −78 °C to the stirred solution of catalytic amount of TBAF in CH_2Cl_2 (12 mL). After 40 min the cooling bath was removed. The mixture was stirred for an additional 1 h and then poured into a mixture of EtOAc (100 mL)/brine (50 mL). The organic layer was dried over Na_2SO_4. The solvents were removed in vacuum to give crude **7k**,**l** (purity was approximately 40–50% according to NMR). The residue was dissolved in MeOH (24 mL) and $NH_4F{\cdot}HF$ (0.02 g, 0.1 equiv, 0.3 mmol) was added. The reaction mixture was maintained for 24 h, the solvent was removed in vacuum, and the residue was subjected to column chromatography (eluent: hexane/EtOAc, 3:1) to give title pyranone oximes **7′k**,**l** as colorless oils (yields: **7′k**—27%, **7′l**—17%).

4.6.1. Spectroscopically pure samples of **7k**,**l** were obtained from purified desilylated product **7′k**,**l** by the following procedure

NEt_3 (0.056 mL, 2 equiv, 0.4 mmol) was added to a stirred solution of the pyranone oximes **7′** (0.2 mmol) in CH_2Cl_2 (1.5 mL) at 0 °C in dry argon. Then TMSCl (0.038 mL, 1.5 equiv, 0.3 mmol) was added. After 15 min the cooling bath was removed and the reaction mixture was maintained for 24 h and then the solvent was removed in vacuum. The solid residue was washed with hexane (2×5 mL) and hexane phase was evaporated in vacuum to give title *O*-trimethylsilyl pyranone oximes **7** (yields: **7k**—85%, **7l**—67%), which were NMR spectroscopically pure.

4.6.2. 4-(4-Chlorophenyl)-6,6-dimethyl-dihydro-2H-pyran-3(4H)-one O-trimethylsilyl oxime **7k**

R_f=0.71 (hexane/EtOAc, 1:1) (UV). ^1H NMR: 0.05 (s, 9H, CH_3(12)), 1.10 and 1.26 (both s, both 3H, CH_3(6) and CH_3(7)), 1.97 (dd, J=14.7, 6.6, 1H, CH_{2a}(4)), 2.09 (dd, J=14.7, 7.3, 1H, CH_{2b}(4)), 4.27 (d, J=13.6, 1H, CH_{2a}(1)), 4.32 (dd, J=7.3, 6.6, 1H, CH(3)), 4.45 (d, J=13.6, 1H, CH_{2b}(1)), 7.11 and 7.27 (both d, J=8.0, both 2H, CH(9) and CH(10)). ^{13}C NMR: −1.0 (CH_3(12)), 27.7 and 28.2 (CH_3(6) and CH_3(7)), 37.1 (CH(3)), 41.3 (CH_2(4)), 62.2 (CH_2(1)), 72.6 (C(5)), 128.4 and 128.6 (CH(9) and CH(10)), 131.7 (C(8)), 140.1 (C(11)), 160.5 (C(2)).

4.6.3. rel-(4S,4aR,8aR)-4-(4-Methoxyphenyl)-hexahydro-2H-chromen-3(4H)-one O-trimethylsilyl oxime **7l**

R_f=0.73 (hexane/EtOAc, 1:1) (UV). Mixture of two isomers in a ratio 4:3 (cis:trans). cis-Isomer: ^1H NMR: 0.24 (s, 9H, CH_3(15)), 1.27–1.91 (m, 8H, CH_2(6–9)), 2.15–2.25 (m, 1H, CH(4)), 3.53 (br s, 1H, CH(3)), 3.80 (s, 3H, CH_3(14)), 3.80 (br s, 1H, CH(5)), 3.83 (d, J=14.0, 1H, CH_{2a}(1)), 5.23 (d, J=14.0, 1H, CH_{2b}(1)), 6.87 (d, J=8.8, 2H, CH(12)), 7.17 (d, J=8.8, 2H, CH(11)), 8.91 (br s, 1H, OH(15)). trans-Isomer: ^1H NMR: 0.21 (s, 9H, CH_3(15)), 1.27–1.91 (m, 8H, CH_2(6–9)), 2.15–2.25 (m, 1H, CH(4)), 3.80 (s, 3H, CH_3(14)), 3.90 (br s, 1H, CH(5)), 4.13 (d, J=12.8, 1H, CH_{2a}(1)), 4.29 (d, J=12.8, 1H, CH_{2b}(1)), 4.48 (br s, 1H, CH(3)), 6.87 (d, J=8.8, 2H, CH(12)), 7.13 (d, J=8.8, 2H, CH(11)), 8.91 (br s, 1H, OH(15)). ^{13}C NMR (cis+trans): −0.7 and −0.6 (CH_3(15)), 20.0 and 20.1, 25.8 and 26.1, 27.1 and 27.4, 31.0 and 31.2 (CH_2(6–9)), 41.0, 41.2, 42.2 and 47.5 (CH(3) and CH(4)), 55.2 (CH_3(14)), 60.3, 67.2, 70.6 and 71.5 (CH_2(1) and CH(5)), 113.8 and 114.0 (CH(12)), 128.6 (CH(11)), 132.1 and 132.6 (C(10)), 158.0 (C(2)), 159.3 and 159.7 (C(2) and C(13)).

4.6.4. 4-(4-Chlorophenyl)-6,6-dimethyl-dihydro-2H-pyran-3(4H)-one oxime **7′k**

R_f=0.48 (hexane/EtOAc, 1:1) (anisaldehyde). Mp=42–47 °C. Anal. Calcd for $C_{13}H_{16}ClNO_2$: C, 61.54; H, 6.36; N, 5.52. Found: C, 61.51; H, 6.56; N, 5.40. ν_{max}: 3317, 3103, 2973, 2931, 1492, 1462, 1446, 1408, 1384, 1369, 1257, 1234, 1215, 1178, 1126, 1091, 1014, 947, 827, 751, 530 cm^{-1}. ^1H NMR: 1.07 and 1.25 (both s, both 3H, CH_3(6) and CH_3(7)), 2.00 (dd, J=14.7, 6.6, 1H, CH_{2a}(4)), 2.09 (dd, J=14.7, 7.3, 1H, CH_{2b}(4)), 4.19 (d, J=13.9, 1H, CH_{2a}(1)), 4.33 (dd, J=7.3, 6.6, 1H, CH(3)), 4.40 (d, J=13.9, 1H, CH_{2b}(1)), 7.13 and 7.29 (both d, J=8.5, both 2H, CH(9) and CH(10)), 8.66 (br s, 1H, OH(12)). ^{13}C NMR: 27.5 and 28.3 (CH_3(6) and CH_3(7)), 36.5 (CH(3)), 41.3 (CH_2(4)), 62.0 (CH_2(1)), 72.7 (C(5)), 128.5 and 128.9 (CH(9) and CH(10)), 132.2 (C(8)), 139.3 (C(11)), 156.7 (C(2)).

4.6.5. rel-(4S,4aR,8aR)-4-(4-Methoxyphenyl)-hexahydro-2H-chromen-3(4H)-one oxime **7′l**

R_f=0.58 (hexane/EtOAc, 1:1) (anisaldehyde). Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 70.22; H, 8.00; N, 4.71. Mixture of two isomers in a ratio 4:3 (cis:trans) ν_{max}: 3287, 3101, 3001, 2932, 2854, 1610, 1582, 1512, 1462, 1444, 1298, 1248, 1181, 1111, 1087, 1051, 1035, 1007, 982, 946, 930, 920, 897, 837, 737 cm^{-1}. cis-Isomer: ^1H NMR: 1.25–1.95 (m, 8H, CH_2(6–9)), 2.14–2.21 (m, 1H, CH(4)), 3.49 (br s, 1H, CH(3)), 3.81 (s, 3H, CH_3(14)), 3.88 (br s, 1H, CH(5)), 4.05 (d, J=15.0, 1H, CH_{2a}(1)), 5.12 (d, J=15.0, 1H, CH_{2b}(1)), 6.87 (d, J=8.8, 2H, CH(12)), 7.17 (d, J=8.8, 2H, CH(11)), 8.91 (br s, 1H, OH(15)). trans-Isomer: ^1H NMR: 1.25–1.95 (m, 8H, CH_2(6–9)), 2.14–2.21 (m, 1H, CH(4)), 3.81 (s, 3H, CH_3(14)), 3.90 (br s, 1H, CH(5)), 4.17 (d, J=12.8, 1H, CH_{2a}(1)), 4.29 (d, J=12.8, 1H, CH_{2b}(1)), 4.41 (br s, 1H, CH(3)), 6.87 (d, J=8.8, 2H, CH(12)), 7.17 (d, J=8.8, 2H, CH(11)), 8.91 (br s, 1H, OH(15)). ^{13}C NMR (cis+trans): 19.8 and 20.2, 25.1 and 25.9, 27.1 and 27.4, 30.4 and 31.0 (CH_2(6–9)), 41.1, 41.3, 41.9 and 47.3 (CH(3) and CH(4)), 55.1 (CH_3(14)), 59.9, 68.9, 70.7 and 71.3

(CH_2(1) and CH(5)), 113.8 and 114.0 (CH(12)), 128.4 and 128.5 (CH(11)), 130.3 and 132.2 (C(10)), 156.2 (C(2)), 158.0 (C(13)).

4.7. Preparation of oxazines 10

*4.7.1. 3-(Methoxymethyl)-6-methyl-4-phenyl-6-(trimethylsilyloxy)-5,6-dihydro-4H-1,2-oxazine **10m***

The solution of ASENA **3m** (3 mmol) in CH_2Cl_2 (3 mL) was added dropwise to the stirred solution of NEt_3 (0.042 mL, 0.03 equiv, 0.1 mmol) in CH_2Cl_2 (3 mL), looking for the temperature didn't exceed 30 °C. The reaction mixture was stirred for an additional 20 min. The solvent was removed in vacuum, and then the residue was subjected to column chromatography (eluent: hexane/EtOAc, 10:1) to give 0.20 g (22%) of title oxazine **10m** as colorless oil. R_f=0.73 (hexane/EtOAc, 1:1) (UV). ^{1}H NMR: 0.02 (s, 9H, CH_3(11)), 1.21 (s, 3H, CH_3(10)), 2.17 (dd, J=13.9, 8.1, 1H, CH_{2a}(8)), 2.29 (dd, J=13.9, 7.3, 1H, CH_{2b}(8)), 3.26 (s, 3H, CH_3(10)), 4.37–4.51 (m, 3H, CH(5) and CH_2(7)), 7.17–7.30 (m, 5H, CH(1), CH(2) and CH(3)). ^{13}C NMR: −1.0 (CH_3(11)), 23.4 (CH_3(10)), 37.4 (CH(5)), 41.1 (CH_2(8)), 48.4 (CH_3(12)), 62.2 (CH_2(7)), 98.9 (C(9)), 126.1 (CH(1)), 127.7 and 128.2 (CH(2) and CH(3)), 141.5 (C(4)), 161.6 (C(6)).

*4.7.2. 3-(Methoxymethyl)-6-methyl-4-phenyl-5,6-dihydro-4H-1,2-oxazin-6-ol **10′m***

The solution of the ASENA **3m** (3 mmol) in CH_2Cl_2 (6 mL), was added dropwise in 10 min at −78 °C to the stirred solution of catalytic amount of TBAF in CH_2Cl_2 (12 mL). After 40 min the cooling bath was removed. The mixture was stirred for an additional 1 h and poured into a mixture of EtOAc (100 mL)/brine (50 mL). The organic layer was dried over Na_2SO_4. The solvents were removed in vacuum to give crude **10m**, which was dissolved in MeOH (24 mL) and $NH_4F\cdot HF$ (0.02 g, 0.1 equiv, 0.3 mmol) was added. The reaction mixture was maintained for 4 h, the solvent was removed in vacuum, and then the residue was subjected to column chromatography (eluent: hexane/EtOAc, 3:1) to give 0.16 g (23%) of title oxazine **10′m** as colorless oil. R_f=0.48 (hexane/EtOAc, 1:1) (ninhydrin). ν_{max}: 3333, 3086, 3060, 2987, 2940, 2858, 2831, 1601, 1494, 1451, 1379, 1230, 1213, 1181, 1150, 1112, 1099, 1056, 1002, 943, 878, 832, 745, 699 cm^{-1}. ^{1}H NMR: 1.15 (s, 3H, CH_3(10)), 2.17 (dd, J=14.3, 7.3, 1H, CH_{2a}(8)), 2.30 (dd, J=14.3, 7.3, 1H, CH_{2b}(8)), 3.24 (s, 3H, CH_3(10)), 4.31–4.48 (m, 3H, CH(5) and CH_2(7)), 7.20–7.34 (m, 5H, CH(1), CH(2) and CH(3)), 8.83 (br s, 1H, OH(11)). ^{13}C NMR: 23.4 (CH_3(10)), 36.8 (CH(5)), 41.1 (CH_2(8)), 48.4 (CH_3(12)), 61.9 (CH_2(7)), 99.1 (C(9)), 126.5 (CH(1)), 127.4 and 128.5 (CH(2) and CH(3)), 140.7 (C(4)), 157.4 (C(6)).

4.8. By-products of the synthesis of oxazines 1

*4.8.1. rel-(4S,6S)-6-Methoxy-4-(4-methoxyphenyl)-6-methyl-3-vinyl-5,6-dihydro-4H-1,2-oxazine **9a***

Vinyloxazine **9a** was obtained as a by-product in the preparation of oxazine **1a** from ASENA **3a** via oxazine **4a** with one change—in the stage **3a**→**4a** $CHCl_3$ (tech. grade) was used instead of mixture $CHCl_3$(anhydrous)/water. The product was purified by column chromatography (eluent: hexane/EtOAc, from 10:1 to 3:1). Yield=10%. R_f=0.61 (hexane/EtOAc, 1:1) (UV). ^{1}H NMR: 1.48 (s, 3H, CH_3(13)), 1.86 (dd, J=13.2, 12.5, 1H, CH_{2a}(10)), 2.35 (dd, J=13.2, 8.5, 1H, CH_{2e}(10)), 3.30 (s, 3H, CH_3(12)), 3.79 (s, 3H, CH_3(1)), 3.81 (dd, J=12.5, 8.5, 1H, CH(6)), 5.21 (d, J=11.0, 1H, CH_{2cis}(9)), 5.26 (d, J=17.6, 1H, CH_{2trans}(9)), 6.20 (dd, J=17.6, 11.0, 1H, CH(8)), 6.85 (d, J=8.1, 2H, CH(3)), 7.06 (d, J=8.1, 2H, CH(4)).

*4.8.2. rel-(4S,4aR,8aR)-4-(4-Methoxyphenyl)-3-vinyl-4a,5,6,7,8,8a-hexahydro-4H-benzo[e][1,2]oxazine **9b***

Vinyloxazine **9b** was obtained as a by-product in the preparation of oxazine **1b** from ASENA **3b** via oxazine **4b**. Yield=14%. R_f=0.67 (hexane/EtOAc, 1:1) (UV). ^{1}H NMR: 1.26–1.78 (m, 8H, CH_2(12–15)), 2.10 (br d, J=14.7, 1H, CH(10)), 3.44 (s, 1H, CH(6)), 3.79 (s, 3H, CH_3(1)), 4.04 (br s, 1H, CH(11)), 5.23 (d, J=11.0, 1H, CH_{2cis}(9)), 5.23 (d, J=17.7, 1H, CH_{2trans}(9)), 6.45 (dd, J=17.7, 11.0, 1H, CH(8)), 6.85 (d, J=8.5, 2H, CH(3)), 7.08 (d, J=8.5, 2H, CH(4)). ^{13}C NMR: 19.8, 25.3, 27.6, 29.4 (CH_2(12–15)), 39.1, 42.3 (CH(6,10)), 55.3 (CH_3(1)), 68.9 (CH(11)), 114.1 (CH(3)), 118.3 (CH_2(9)), 129.0 (CH(4)), 134.2 (CH(8)), 134.5 (C(5)), 153.3 (C(7)), 158.3 (C(2)).

*4.8.3. rel-(4S,6S)-3-(1-(Ethyloxy)ethyl)-6-methoxy-4-(4-methoxyphenyl)-6-methyl-5,6-dihydro-4H-1,2-oxazine **8***

Oxazine **8** was obtained as a by-product in the preparation of oxazine **1a** from ASENA **3a** via oxazine **4a** with one change—in the stage **3a**→**4a** $CHCl_3$ (tech. grade) was used instead of mixture $CHCl_3$(anhydrous)/water. The product was purified by column chromatography (eluent: hexane/EtOAc, from 10:1 to 3:1). Yield=13%. R_f=0.57 (hexane/EtOAc, 1:1) (ninhydrin). ν_{max}: 2974, 2937, 2837, 1713, 1689, 1681, 1666, 1602, 1512, 1463, 1454, 1443, 1423, 1373, 1360, 1302, 1248, 1174, 1113, 1084, 1065, 1032, 899, 833, 548 cm^{-1}. ^{1}H NMR: 1.05 (t, J=7.0, 3H, CH_3(15)), 1.27 (d, J=6.2, 3H, CH_3(9)), 1.45 (s, 3H, CH_3(12)), 1.92 (dd, J=13.2, 12.5, 1H, CH_{2ax}(10)), 2.27 (dd, J=13.2, 8.1, 1H, CH_{2eq}(10)), 2.99 (m, J=7.4, 1H, CH_{2a}(14)), 3.29 (s, 3H, CH_3(13)), 3.31 (m, J=7.4, 1H, CH_{2b}(14)), 3.77 (dd, J=12.5, 8.1, 1H, CH(6)), 3.79 (s, 3H, CH_3(1)), 4.12 (q, J=6.2, 1H, CH(8)), 6.85 (d, J=8.5, 2H, CH(3)), 7.11 (d, J=8.5, 2H, CH(4)). ^{13}C NMR: 15.4 and 16.2 (CH_3(9) and CH_3(15)), 21.5 (CH_3(12)), 36.4 (CH(6)), 39.7 (CH_2(10)), 49.4 (CH_3(13)), 55.3 (CH_3(1)), 62.8 (CH_2(14)), 74.2 (CH(8)), 97.5 (C(11)), 114.2 (CH(3)), 129.7 (CH(4)), 132.5 (C(5)), 158.6 (C(2)), 161.5 (C(7)).

4.9. Reduction of oxazine 1a

*4.9.1. rel-(1R)-1-((3R,4S,6S)-6-Methoxy-4-(4-methoxyphenyl)-6-methyl-1,2-oxazinan-3-yl)-1-ethanol **13***

$NaBH_3CN$ (0.19 g, 3 equiv, 3 mmol) was added to a stirred solution of oxazine **1a** (0.29 g, 1 mmol) in AcOH (4.4 mL). The reaction mixture was stirred for 1 h and then poured into a mixture of EtOAc (100 mL) and K_2CO_3 (aqueous solution) (100 mL). The aqueous phase was washed with EtOAc (2×30 mL). Combined organic layer was washed with brine (50 mL) and dried over Na_2SO_4. The solvents were removed in vacuum, and then the residue was subjected to column chromatography (eluent: hexane/EtOAc, 1:2) to give 0.24 g (83%) of title oxazine **13** as colorless oil. R_f=0.11 (hexane/EtOAc, 1:1). Mp=63–64 °C. Anal. Calcd for $C_{15}H_{23}NO_4$: C, 64.03; H, 8.24; N, 4.98. Found: C, 64.32; H, 8.25; N, 4.76. ν_{max}: 3417, 3261, 2987, 2930, 2835, 1611, 1513, 1462, 1443, 1377, 1304, 1271, 1246, 1236, 1180, 1147, 1107, 1068, 1051, 1035, 885, 845, 831, 799, 783, 736, 550 cm^{-1}. ^{1}H NMR: 1.15 (d, J=6.6, 3H, CH_3(9)), 1.30 (s, 3H, CH_3(12)), 1.82 (t, J=13.2, 1H, CH_{2ax}(10)), 2.01 (dd, J=13.1, 4.4, 1H, CH_{2eq}(10)), 2.88 (dd, J=11.1, 2.0, 1H, CH(7)), 3.18 (td, J=12.1, 4.4, 1H, CH(6)), 3.27 (s, 3H, CH_3(13)), 3.57 (qd, J=6.6, 2.0, 1H, CH(8)), 3.74 (s, 3H, CH_3(1)), 6.81 (d, J=8.5, 2H, CH(3)), 7.09 (d, J=8.5, 2H, CH(4)). ^{13}C NMR: 21.1 and 21.6 (CH_3(9)) and (CH_3(12)), 37.9 (CH_2(10)), 42.5 (CH(6)), 48.6 (CH_3(13)), 55.2 (CH_3(1)), 65.2 and 65.6 (CH(7) and CH(8)), 99.1 (C(11)), 114.1 (CH(3)), 128.6 (CH(4)), 134.4 (C(5)), 158.2 (C(2)).

*4.9.2. rel-tert-Butyl (2R,3S)-2-((1R)-1-hydroxyethyl)-3-(4-methoxyphenyl)-5-methyl-tetrahydro-1H-pyrrole-1-carboxylate **12***

One milliliter of 50% slurry Raney Nickel in water was washed with anhydrous methanol (5×5 mL), diluted with methanol (1 mL) and added to the solution of oxazine **13** (68 mg, 0.26 mmol) in MeOH (2.5 mL). The suspension was hydrogenated at 50 bar H_2 at room temperature with intensive stirring for 8 h, filtered and concentrated in vacuum. The residue was dissolved in CH_2Cl_2 (2 mL) and Boc_2O (0.17 mL, 3 equiv, 0.8 mmol) was added. The reaction mixture was stirred for 2 h, concentrated in vacuum and then the residue was subjected to column chromatography (eluent: hexane/EtOAc, from

5:1 to 3:1) to give 54 mg (67%) of title pyrrolidine **12** as colorless oil. R_f=0.45 (major diastereomer) and 0.41 (minor diastereomer) (hexane/EtOAc, 1:1). Mp=72–74 °C. Anal. Calcd for $C_{19}H_{29}NO_4$: C, 68.03; H, 8.71; N, 4.18. Found: C, 67.98; H, 8.72; N, 3.84. ν_{max}: 3443, 2973, 2931, 1690, 1666, 1613, 1514, 1455, 1395, 1367, 1251, 1177, 1120, 1095, 1078, 1035, 832 cm^{-1}. ^1H NMR: 1.13–1.16 (m, 6H, CH_3(9) and CH_3(12)), 1.15 (s, 9H, CH_3(16)), 1.70 (dt, J=12.8, 3.7, 1H, CH_{2a}(10)), 2.54 (dt, J=12.8, 8.0, 1H, CH_{2b}(10)), 3.10–3.15 (m, 1H, CH(6)), 3.79 (s, 3H, CH_3(1)), 3.86–3.99 (m, 1H, CH(7) and CH(11)), 4.26 (dd, J=7.4, 2.8, 1H, CH(8)), 6.85 (d, J=8.2, 2H, CH(3)), 7.19 (d, J=8.2, 2H, CH(4)). ^{13}C NMR: 20.8 and 21.5 (CH_3(9)) and (CH_3(12)), 28.5 (CH_3(16)), 41.5 and 43.6 (CH(6) and (CH_2(10)), 54.1 (CH(11)), 55.2 (CH_3(1)), 69.1 and 71.1 (CH(7) and CH(8)), 80.2 (C(15)), 114.0 (CH(3)), 128.2 (CH(4)), 136.2 (C(5)), 158.1 (C(2)).

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Supplementary data

NMR spectra for compounds **1–4**, **7–10**, **12**, **13**. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.03.082.

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