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European Journal of Organic Chemistry

A Journal of
ChemPubSoc Europe

Accepted Article

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To be cited as: Eur. J. Org. Chem. 10.1002/ejoc.201600952

Link to VoR: http://dx.doi.org/10.1002/ejoc.201600952

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New six-membered cyclic nitroso acetals - *N*-silyloxy-3,6-dihydro-2*H*-1,2-oxazines: synthesis and studies of the nitrogen inversion process.

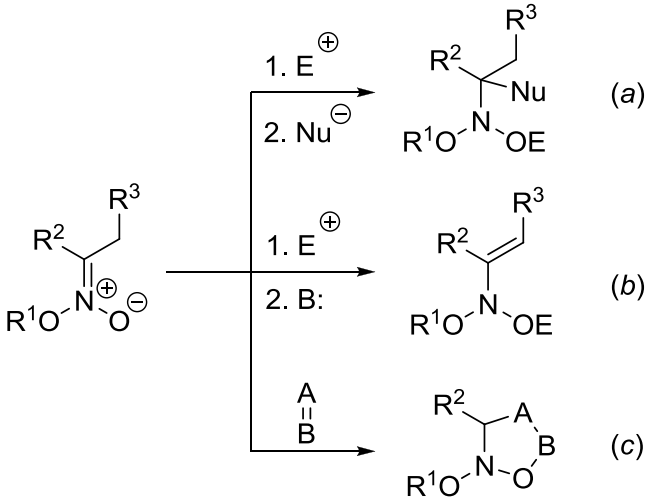
Alexander S. Shved,*[a,b] Andrey A. Tabolin,*[a] Roman A. Novikov,[c] Yulia V. Nelyubina,[d] Vladimir P. Timofeev,[c] and Sema L. Ioffe[a]

Abstract: Silyl nitronates undergo rhodium-catalyzed formal [3 + 3]-cycloaddition with enol diazoacetates giving rise to *N*-silyloxy-3,6-dihydro-2*H*-1,2-oxazines. Reaction scope and major side process were evaluated. Mechanistic scheme was proposed. Nitrogen inversion barrier in obtained nitroso acetals was estimated both by means of quantum calculations and kinetic measurements.

Introduction

Nitroso acetals constitute a interesting class of organic compounds from both theoretical and practical aspects.[1] Presence of two electronegative oxygens bonded to the central nitrogen is known to increase nitrogen inversion barrier thus encouraging investigations on asymmetric nitrogen atom.[2,3] Synthetic potential of nitroso acetals mostly arise from the presence of two relatively weak N-O bonds which rupture allows synthesis of various amino alcohol derivatives, including biologically active ones, *via* hydrogenolysis[4] or rearrangements.[5] The most common and convenient precursors for nitroso acetal syntheses are nitronates (Scheme 1) with three main transformation pathways are: consecutive electrophile and nucleophile addition (pathway *a*),[6] electrophile addition with subsequent proton elimination (pathway *b*)[7] and [3+2]-cycloaddition (pathway *c*).[1b,4,8] The latter possibility was the most exploited, however this was nearly the only type of cycloaddition investigated for nitronates. Consequently, only 5-membered isoxazolidine ring was accessible.

Expanding reactivity of nitronates to other cycloaddition types may give access to other N,O-containing heterocycles. Thus, [3+3]-cycloaddition can give access to such useful products as 1,2-oxazine derivatives.[9] Recently we reported the first examples of formal [3 + 3]-cycloaddition of nitronates with donor-acceptor cyclopropanes.[10] Herein we report [3 + 3]-cycloaddition of silyl nitronates **1** with rhodium enolcarbenoid species,[11] generated *in situ* from corresponding enol diazoacetates **2**.



Scheme 1. Pathways for the synthesis of nitroso acetals from nitronates.

Results and Discussion

Silyl nitronate **1a** and enol diazoacetate **2a** were chosen as substrates for optimization experiments (Table 1). 2 mol % of $Rh_2(OAc)_4$ in CH_2Cl_2 (Entry 1) gave the best results leading to target 1,2-oxazine **3aa** in 88% yield. Other tried metal (Cu, Ag) catalysts failed to promote desired reaction (Entries 17-20). Attempts to reduce the amount of catalyst gave increased amounts of side-product **4** even for more active catalyst $Rh_2(esp)_2$ (Entries 3-5).[12] Increase of reaction temperature also did not suppress formation of **4** completely (Entry 5). Use of more polar solvents also gave inferior results (Entries 6,7), presumably due to solvent coordination to the catalyst. Low yields obtained in aromatic solvents (toluene, p-fluorotoluene, perfluorobenzene, Entries 8-10) can be ascribed to low solubility of rhodium acetate in the reaction medium. Consequently, better soluble rhodium octanoate gave high yields of target product regardless of solvent used (cf. Entries 2, 11, 12). More Lewis acidic rhodium trifluoroacetate gave lower yields of target [3+3]-adduct **3aa** (Entry 16). Chiral complex Rh_2(*S*-PTA)$_4$ was able of catalyzing the reaction, but the asymmetric induction was low (Entries 13-15). [13]

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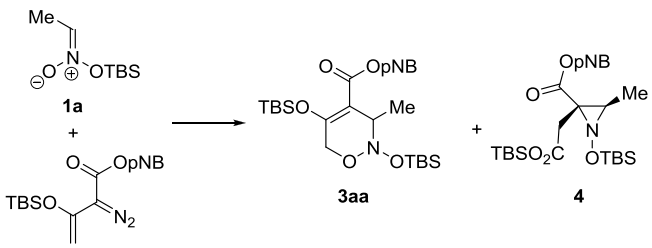


pNB = 4-$NO_2C_6H_4CH_2$

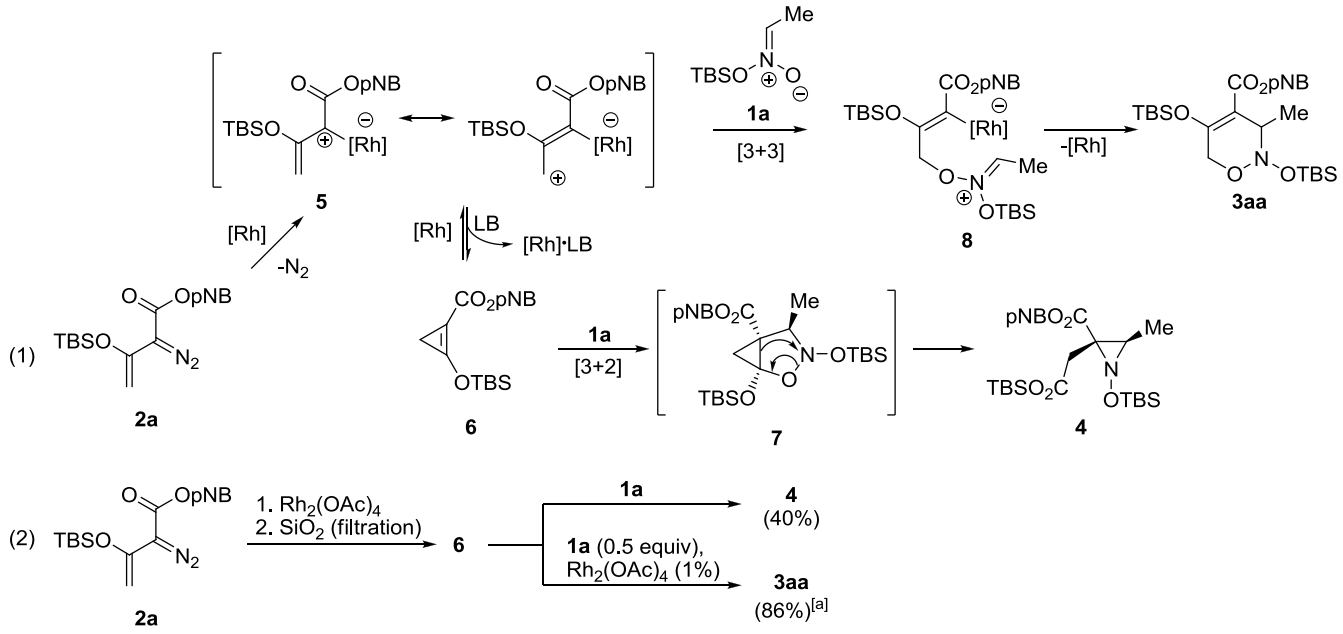
Table 1. Optimization of the conditions for formal [3+3]-cycloaddition.

Entry	Conditions	Yield **3aa**, % [a]	Yield **4**, % [a]
1	$Rh_2(OAc)_4$, 2 mol%, CH_2Cl_2, r.t., 1 h	88	0
2	$Rh_2(Oct)_4$, 2 mol%, CH_2Cl_2, r.t., 1 h	85	0
3	$Rh_2(OAc)_2$, 0.5 mol%, CH_2Cl_2, r.t., 1 d	17	45
4	$Rh_2(esp)_2$,[b] 0.5 mol%, CH_2Cl_2, r.t., 1 h	78	6
5	$Rh_2(OAc)_2$, 0.5 mol%, $ClCH_2CH_2Cl$, 65 °C, 1 h	40	29
6	$Rh_2(OAc)_4$, 2 mol%, THF, r.t., 1 d	20	33
7	$Rh_2(OAc)_4$, 2 mol%, MeCN, r.t., 1 d	0	34
8	$Rh_2(OAc)_4$, 2 mol%, toluene, r.t., 1 d	24	23
9	$Rh_2(OAc)_4$, 2 mol%, C_6F_6, r.t., 1 d	24	34
10	$Rh_2(OAc)_4$, 2 mol%, p-fluorotoluene, r.t., 1 d	27	23
11	$Rh_2(Oct)_4$, 2 mol%, toluene, r.t., 1 h	87	0
12	$Rh_2(Oct)_4$, 2 mol%, p-fluorotoluene, r.t., 1 h	78	0
13	Rh_2(*S*-PTA)$_4$,[c] 2 mol%, CH_2Cl_2, r.t., 1 h	77 (22)[d]	0
14	Rh_2(*S*-PTA)$_4$, 2 mol%, toluene, r.t., 1 h	78 (12)[d]	0
15	Rh_2(*S*-PTA)$_4$, 2 mol%, CH_2Cl_2, 0 °C, 2 h	80 (24)[d]	0
16	$Rh_2(OOCCF_3)_4$, 2 mol%, CH_2Cl_2, r.t., 1 d	7	23
17	$Cu(MeCN)_4PF_6$, 5 mol%, CH_2Cl_2, r.t., 1 d	0	0
18	$Cu(CF_3C(O)CHC(O)CH_3)_2$, 5 mol%, CH_2Cl_2, r.t., 1 d	0	0
19	CuOTf·PhH, 5 mol%, CH_2Cl_2, r.t., 1 d	0	0
20	AgOTf, 5 mol%, CH_2Cl_2, r.t., 2 h	0	0

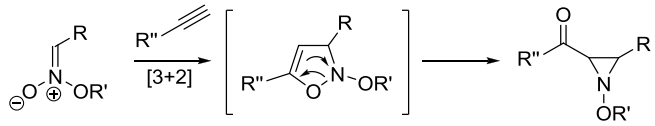
[a] determined by ^{1}H NMR with internal standard (1,4-dinitrobenzene). [b] esp = α,α,α′,α′-tetramethyl-1,3-benzenedipropionate. [c] *S*-PTA = *N*-phthaloyl-(*S*)-alaninate [d] ee value of **3aa** is indicated in parentheses. Determined on Chiralpak IA-3 column, eluent: Hexane-*i*-PrOH, 98:2, 1 mL/min.

Formation of product **4** deserves some additional attention (Scheme 2, eq. 1). Metal enol carbenoids **5** are known to exist in equilibrium with corresponding cyclopropenes **6**.[11d,14] Therefore competitive [3+2]-cycloaddition between nitronate **1a** and cyclopropene **6** might be expected leading to cyclopropane-annelated isoxazolidine **7**. However, obtained NMR-data was inconsistent with the structure of **7** and evidenced about occurred rearrangement and formation of aziridine **4**.[5b,15] Such cycloaddition-rearrangement process closely resembles reaction course of nitronates with acetylenes (Scheme 3).[16] Isolation of pure aziridine **4** was achieved after separation of steps of Rh-catalyzed cyclopropene formation **2**→**6** and addition of nitronate **1a** (Scheme 2, eq (2)). Filtration through a short plug of silica eliminated Rh-catalyst from cyclopropene **6** suppressing [3+3]-cycloaddition between **1a** and **5**. Addition of Rh-catalyst turned the reaction again to the formation of oxazine **3aa**.

Chemoselectivity of the reaction can be interpreted on the basis of position of equilibrium between **5** and **6** (Scheme 2).[17] Large Rh-catalyst loadings (e.g. 2 mol %, Table 1, Entries 1,2,11,12) shifted the equilibrium resulting in higher concentration of **5** thus leading to [3 + 3]-cycloaddition exclusively. Oppositely when the concentration of **5** was too low for fast [3 + 3]-cycloaddition, competitive uncatalyzed [3 + 2]-cycloaddition of **1a** with **6** became a significant process furnishing aziridine **4** (see Table 1, Entries 3-10,16). Lewis bases LB (e.g. coordinating solvents: THF, MeCN, Entries 6,7) were shown to decrease the activity of Rh-species presumably through displacement of bound carbene in ligand sphere of rhodium. This increases the rate of **5**→**6** transformation thus also decreasing concentration of **5**.[11d] Nitronates **1** should also be considered as Lewis base due to *N*-oxide moiety. Thus they are also able to deactivate Rh-species. The effect should be more significant in the case of Lewis acidic Rh-catalysts and was observed for rhodium trifluoroacetate (Entry 16).[11d] In accordance with the equilibrium between **5** and **6** is the formation of adduct **3aa** in the Rh-catalyzed reaction between nitronate **1** and preformed cyclopropene **6** (Scheme 2, eq (2)).

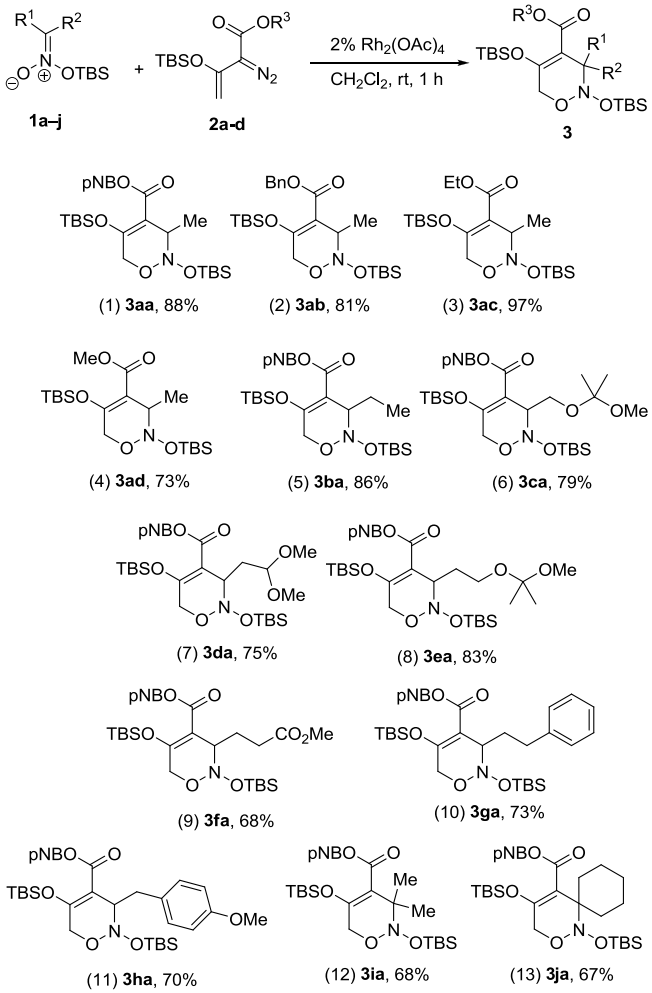


Scheme 2. Proposed mechanisms for the reactions of nitronate **1a** and enol diazoacetate **2a**. [a] Yield is based on nitronate **1a**, determined by ^{1}H NMR with internal standard (1,4-dinitrobenzene)



Scheme 3. Tandem [3+2]-cycloaddition/rearrangement of nitronates and alkynes.

After establishing the optimal conditions, the scope of nitronates **1** and enol diazoacetates **2** was tested (Scheme 4). All tried enol diazoacetates **2a–d** (R^1 = Me, Et, benzyl, *p*-nitrobenzyl, Entries 1–4) gave desired oxazines **3** in good yields. Similarly various silyl nitronates could be used (Entries 5-13). The reaction tolerated such functionalities as acetal (Entries 6-8), carboxylate (Entry 9) or aromatic ring (Entries 10,11) in initial silyl nitronate **1**. Silyl nitronates derived from both primary (Entries 1–11) and secondary (Entries 12,13) nitro compounds could be used. Structures of obtained dihydrooxazines **3** were supported by NMR, HRMS and elemental analysis data. For adduct **3ha** X-ray analysis was performed (Figure 1).[18]



Scheme 4. Formal [3+3]-cycloaddition of nitronates **1** and enol diaoacetates **2**.

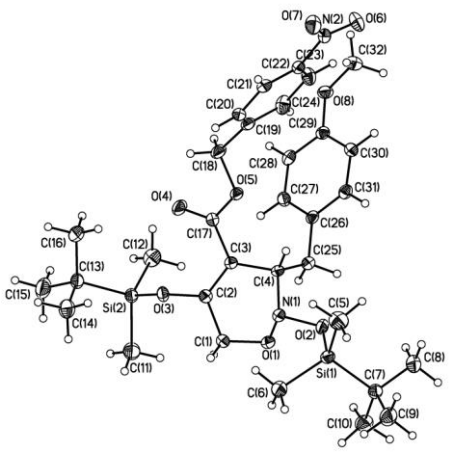
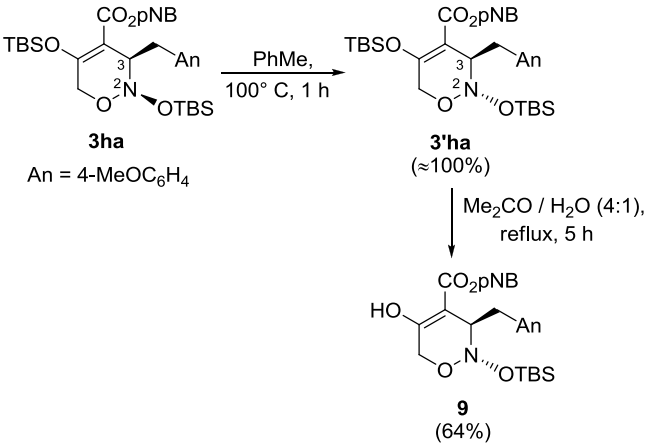


Figure 1. Single-crystal ORTEP drawing for **3ha**.

All nitroso acetals **3** were isolated as single diastereomers. While NOESY data were little informative for determination of relative configuration, considering the similarity of ^{15}N chemical shifts of N–OTBS moiety for adducts **3aa-3ha** (δ = 242-245 ppm) and X-ray data for **3ha** their configuration may be assumed as 2,3-*cis*. However, as was noted in the introduction, slow nitrogen inversion should also be taken in consideration. Indeed upon storage of adducts **3** in solution or neat in liquid appearance of a second sets of signals in NMR spectra was observed. To investigate the process the nitroso acetal **3ha** was chosen due to its X-ray analysis (*vide supra*) undoubtedly providing relative configuration of stereocenters at N-2 and C-3. Interestingly short heating of toluene solution of **3ha** at 100 °C gave complete conversion of starting material (Scheme 5)! NMR spectra (^{1}H, ^{13}C, ^{29}Si, ^{15}N, COSY, NOESY, HSQC, HMBC) as well as HRMS data were consistent with the occurrence of nitrogen inversion and formation of diastereomer **3'ha**. The most dramatic change in NMR spectra was observed for C$\underline{H}_2$-C(3) protons with two resolved doublets of doublets at 3.10 and 3.83 ppm turned into one multiplet at 2.92-2.98 ppm. One of the H-6 protons shifted from 3.98 to 3.75 ppm, while two $^{5}J_{H,H}$ coupling constants between two H-6 and H-3 remained unchanged (≈1.5 Hz and 0 Hz) indicating that H-3 remained in pseudoequatorial position. Of note is the change of ^{15}N chemical shift of N–OTBS moiety (δ (ppm) = 244 for **3ha**; 226 for **3'ha**). X-ray analysis of desilylated product **9** proved its 2,3-*trans* configuration (Figure 2).[18]



Scheme 5. Nitrogen inversion in oxazine **3ha**.

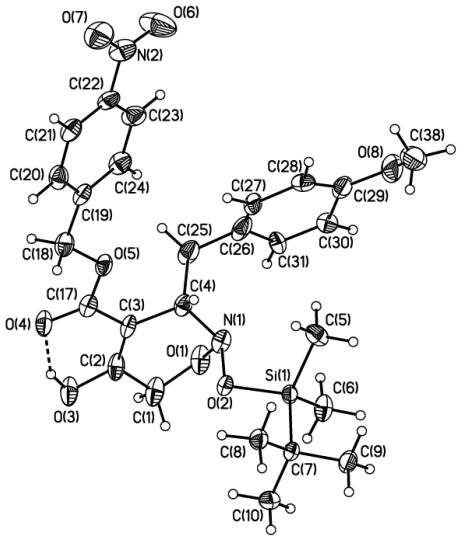
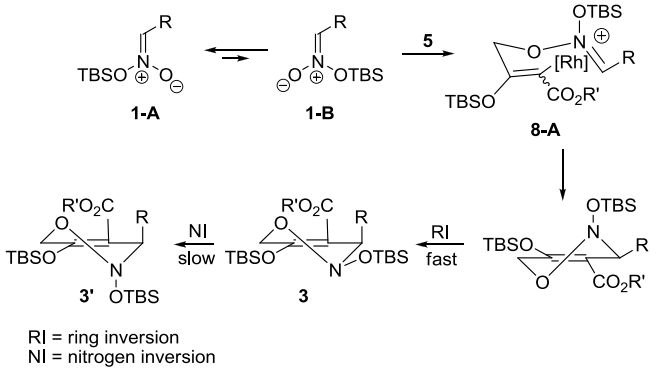


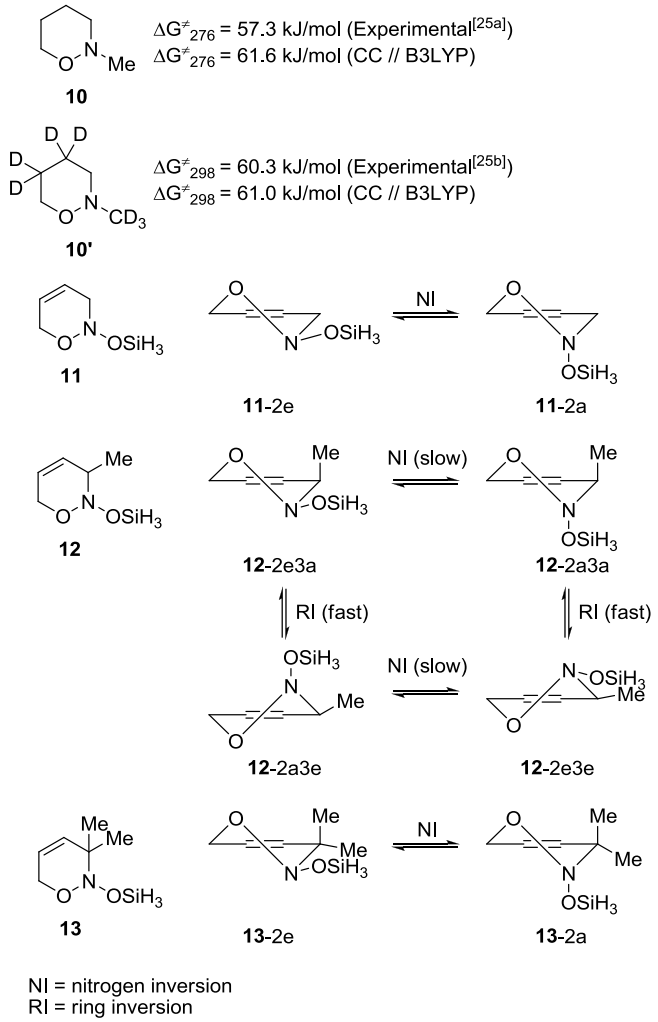
Figure 2. Single-crystal ORTEP drawing for **9**.

Assuming the mechanism for [3+3]-cycloaddition nitroso acetals **3** should be considered as kinetic products as exemplified in Scheme 6. Silyl nitronates are known to exist as equilibrating mixtures of *trans*- (**1-A**) and *cis*- (**1-B**) isomers.[19] *Trans*-isomer **1-A** is more stable than *cis*-isomer **1-B** due to sterical reasons. On the other hand approach to the *N*-oxide moiety in *trans*-isomer is blocked by R-substituent so *cis*-isomer **1-B** is considered to be more reactive.[10b,20] Therefore interaction of **1-B** with enol carbenoid **5** give zwitter-ion **8 (**see Scheme 2), which ring-closure should occur in twist-like conformation **8-A** due to stereoelectronic effects. Finally fast ring inversion leads to more stable conformation with bulky OTBS-group adopting a pseudoequatorial position. However bulky substituents OTBS at N-2 and R at C-3 are still in less sterically favoured *cis*-arrangement. Heating the nitroso acetal **3** allows nitrogen inversion leading to *trans*-arrangement of substituents at N-2 and C-3 in **3'**. Preference of their (pseudo)axial positions may be explained mainly by reduced sterical repulsion between these two particular substituents.[21] Distances between C(25) and Si(1) atoms (see Figures 1 and 2 for numbering) are 4.466 Å in **3ha** (2-equatorial-3-axial isomer) and 4.635 Å in **9** (2,3-diaxial isomer) thus supporting the thermodynamic preference of 2,3-*trans* isomer. At the same time these atoms should be located at only 4.044 Å distance in 2,3-diequatorial isomer (calculated data for **12**-2e3e, see Scheme 7) thus supporting the preference of 2,3-diaxial conformer over 2,3-diequatorial one. Additional advantage of 2,3-diaxial conformer may arise from anomeric effect in O–N–O system[22] and/or crystall packing.



Scheme 6. Rationale for stereochemical outcome of formal [3+3]-cycloaddition.

Firstly nitrogen inversion barrier in **3** was estimated by theoretical methods. Quantum chemical calculations were performed in ORCA 3.0.3 package.[23] Geometry optimizations were done at RIJCOSX-B3LYP/*def2*-TZVP level (briefly – B3LYP). Frequency run was done at this point to acquire thermochemical functions. Final single point energy was acquired at DLPNO-CCSD(T)/*def2*-TZVPP level of theory (briefly – CC)[24] at the geometries obtained from previous step (See supporting information for details). Calculations were performed for model oxazine derivatives **10-13** (Scheme 7, Figure 3). Firstly simple 2-methyl-oxazinane **10** and its deutero-derivative **10'** were tested to verify the quality of calculations by comparison with known experimental inversion barriers.[25] Indeed calculated data fit well with the experimental results (Scheme 7). After that variously 3-substituted *N*-silyloxy-3,6-dihydro-2*H*-1,2-oxazines **11-13** were examined. All three cases gave nearly the same nitrogen inversion barrier ≈115 kJ/mol (Figure 3). *A priori* it was rather tricky to predict the dominant conformation since preudoaxial position of OTBS-group allowed anomeric stabilization in O-N-O moiety, while pseudoequatorial position was considered to be less sterically demanded (see above). Indeed, 3-unsubstituted (**11**) and 3,3-dimethyl- (**13**) substituted derivatives showed negligible difference between axial and equatorial positions of $OSiH_3$ - group (# 1,3, Figure 3). For 3-monomethyl-derivative **12** the difference in conformer energies was more significant. Altogether four possible isomers/conformers (**12**-2a3a, **12**-2e3a, **12**-2a3e, **12**-2e3e) should be taken into account for oxazine **12** (Scheme 7). The preference of 2,3-diaxial isomer **12**-2a3a is in agreement with the structures of oxazines **3'ha** and **9** (Scheme 5, Figure 3). All four conformers of **12** are interconnected through ring and nitrogen inversion processes. Considering the fast nature of ring inversion conversion of 2,3-*cis*-isomer (cf. **3ha**) to 2,3-*trans*-isomer (cf. **3'ha**) may occur either *via* **12**-2e3a → **12**-2a3a or **12**-2a3e → **12**-2e3e pathway. Calculations indicated the former pathway being more favorable ($\Delta G^{\neq}_{298}$ = 114.7 vs. 124.3 kJ/mol).



Scheme 7. Oxazines used for quantum calculations of nitrogen inversion.

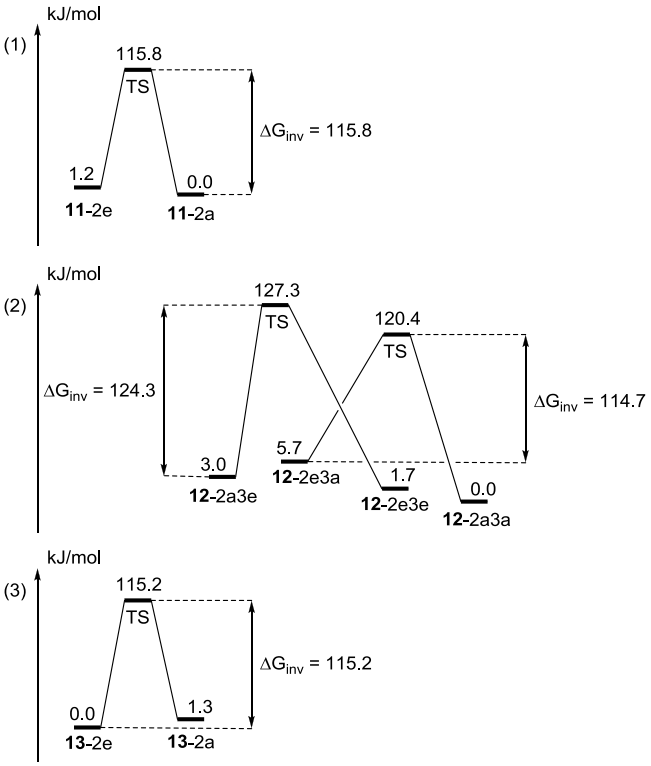


Figure 3. Calculated (CC //B3LYP) energy diagrams for nitrogen inversion in oxazines **11**-**13**. ΔG_{298} are given in kJ/mol relatively to more stable conformer.

Possibility of isolation of diastereomerically pure **3ha** and **3'ha** allowed to investigate nitrogen inversion barrier using kinetic measurements. NMR monitoring of **3ha** → **3'ha** transformation at different temperatures: 58 °C, 70 °C, 80 °C, 90 °C, 100 °C (Table 2, see Supporting information for full experimental details) – allowed to determine the rate constants and consequently the thermodynamic parameters using Eyring equation (Figure 4). Obtained inversion parameters ($\Delta H^{\neq}$ = 111.2 kJ/mol, $\Delta S^{\neq}$ = 0.6 J/(mol·K), $\Delta G^{\neq}_{298}$ = 111.0 kJ/mol) are in good agreement with quantum calculation data ($\Delta G^{\neq}_{298}$ = 114.7, see above). From practical point such barrier value means that exposure of the sample to elevated temperatures (including those during evaporation) should be minimized if the isolation of pure oxazine **3** is desired.

Found inversion barrier is close to the values of five-membered nitroso acetals **14** ($\Delta G^{\neq}$ = 106-121 kJ/mol) (Figure 5).[2d-f,26] Reasonably the barrier is higher than that of six-membered nitroso acetals **15** ($\Delta G^{\neq}_{298}$ = 56-60 kJ/mol),[7c] where barrier is lowered due to the conjugation. Similarly higher barrier in nitroso acetal **3ha** compared to the data for nitroso acetals **16** ($\Delta G^{\neq}_{298}$ = 84-103 kJ/mol),[2a-c] is in agreement with known regularity, that ring strain in transition state raise the barrier of cyclic compounds relatively to acyclic analogs.[3]

Table 2. Kinetic data for nitrogen inversion **3ha** → **3'ha**

Entry	T, °C	k, h^{-1}	$t_{1/2}$
1	58	0.067	10 h
2	70	0.343	2 h
3	80	1.15	36 min
4	90	2.79	15 min
5	100	7.89	5 min

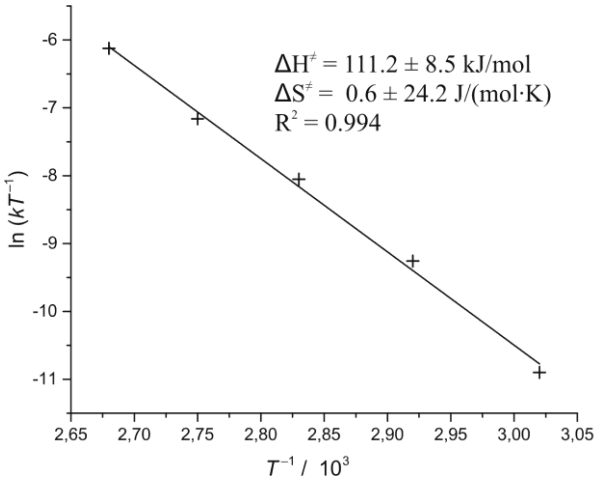
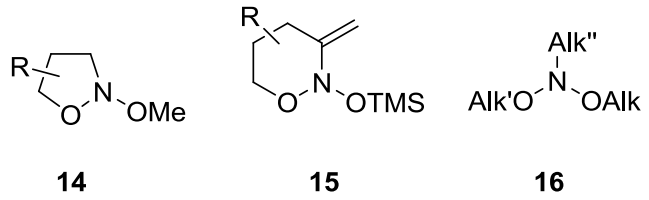


Figure 4. Eyring plot for nitrogen inversion **3ha** → **3'ha**.



14 **15** **16**

Figure 5. Nitroso acetals with known nitrogen inversion barriers.

Conclusions

In conclusion a new formal [3 + 3]-cycloaddition reaction between silyl nitronates **1** and enol diazoacetates **2** was discovered and its substrate scope was elaborated. Nitrogen inversion barrier in target nitroso acetals **3** was estimated. The investigation of chemistry of adducts **3** is currently underway.

Experimental Section

General procedure for dirhodium (II) catalyzed [3 + 3]-cycloadditions

Dirhodium (II) tetraacetate (0.02 equiv) and silyl nitronate **1** (1 equiv) were mixed in dichloromethane (2 mL / 1 mmol of nitronate) in the reaction vessel which was then purged with argon. A solution of enoldiazoacetate **2** (1 equiv) in dichloromethane (3 mL / 1 mmol of enoldiazoacetate) was added dropwise via syringe to the reaction vessel at ambient temperature under stirring. Immediate dinitrogen evolution was observed during the addition. The reaction was maintained for 1 h (TLC monitoring), the solvent was removed in vacuo and the residue was subjected to column chromatography (95:5 PE–EtOAc). Target compounds **3** were obtained as colorless viscous oils. Some of them could be recrystallized from methanol to afford crystalline adducts.

4-nitrobenzyl 2,5-bis((*tert*-butyldimethylsilyl)oxy)-3-methyl-3,6-dihydro-2*H*-1,2-oxazine-4-carboxylate (3aa)

Obtained according to general procedure from nitronate **1a** (284 mg, 1.5 mmol) and diazo compound **2a** (566 mg, 1.5 mmol). Yield: 710 mg (88 %), almost colorless viscous oil. R_f (SiO_2, 10:1 PE–EtOAc): 0.36. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 8.9 Hz, 2 H, CH(pNB)), 7.51 (d, *J* = 8.9 Hz, 2 H, CH(pNB)), 5.30 (d, *J* = 13.5 Hz, 1 H, CH_{2a}(pNB)), 5.25 (d, *J* = 13.6 Hz, 1 H, CH_{2b}(pNB)), 4.30 (dd, *J* = 15.9, 1.6 Hz, 1 H, H_a-6), 4.06 (dd, *J* = 15.9, 0.8 Hz, 1 H, H_b-6), 3.98 (qdd, *J* = 6.2, 1.6, 0.8 Hz, 1 H, H-3), 1.33 (d, *J* = 6.3 Hz, 3 H, Me-3), 0.92 (s, 9 H, *t*-BuSi), 0.90 (s, 9 H, *t*-BuSi), 0.16 (s, 12 H, 2×Me_2Si). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.4 (C=O), 159.0 (C-5), 147.8 (C-NO_2), 143.9 (C(pNB)), 128.6 (CH(pNB)), 123.9 (CH(pNB)), 109.8 (C-4), 67.9 (C-6), 64.3 (CH_2(pNB)), 61.1 (C-3), 26.1 ($\underline{Me}_3$CSi), 25.7 ($\underline{Me}_3$CSi), 18.6 ($Me_3\underline{C}$Si), 18.0 ($Me_3\underline{C}$Si), 12.4 (Me-3), –3.7 (Me_2Si), –5.1 (Me_2Si). ^{29}Si INEPT (60 MHz, $CDCl_3$): δ = 27.4, 24.2. ^{15}N NMR (30 MHz, $CDCl_3$, from {^{1}H–^{15}N}HMBC) δ = 242 (N–OTBS). HRMS (ESI) *m/z* calcd. for [$C_{25}H_{42}N_2O_7Si_2$ + Na^+]: 561.2423, found: 561.2424.

Benzyl 2,5-bis((*tert*-butyldimethylsilyl)oxy)-3-methyl-3,6-dihydro-2*H*-1,2-oxazine-4-carboxylate (3ab)

Obtained according to general procedure from nitronate **1a** (189 mg, 1.0 mmol) and diazo compound **2b** (332 mg, 1.0 mmol). Yield: 400 mg (81 %), colorless oil. R_f (SiO_2, 5:1 PE–EtOAc): 0.60. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.43 – 7.26 (m, 5 H, Ph), 5.20 (s, 2 H, CH_2(Bn)), 4.30 (dd, *J* = 15.8, 1.7 Hz, 1 H, H_a-6), 4.06 (dd, *J* = 15.8, 0.8 Hz, 1 H, H_b-6), 4.01 (qdd, *J* = 6.2, 1.7, 0.8 Hz, 1 H, H-3), 1.35 (d, *J* = 6.3 Hz, 3 H, Me-3), 0.94 (s, 9 H, *t*-BuSi), 0.92 (s, 9 H, *t*-BuSi), 0.17 (s, 3 H, MeSi), 0.16 (s, 3 H, MeSi), 0.16 (s, 3 H, MeSi), 0.16 (s, 3 H, MeSi). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.8 (C=O), 157.8 (C-5), 136.4 (C_{Ph}), 128.5, 128.4 and 128.2 (CH_{Ph}), 110.4 (C-4), 67.8 (C-6), 65.9 (CH_2(Bn)), 61.1 (C-3), 26.1 ($\underline{Me}_3$CSi), 25.8 ($\underline{Me}_3$CSi), 18.6 ($Me_3\underline{C}$Si), 18.0 ($Me_3\underline{C}$Si), 12.3 (Me–11), –3.8 (MeSi), –3.8 (MeSi), –5.0 (MeSi), –5.1 (MeSi). ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 27.2, 23.8. ^{15}N NMR (30 MHz, $CDCl_3$, from {^{1}H–^{15}N}HMBC) δ = 242 (N–OTBS). HRMS (ESI): *m/z* calcd. for [$C_{26}H_{44}N_2O_7Si_2$ + Na^+]: 553.2760, found: 553.2760.

Ethyl 2,5-bis((*tert*-butyldimethylsilyl)oxy)-3-methyl-3,6-dihydro-2*H*-1,2-oxazine-4-carboxylate (3ac)

Obtained according to general procedure from nitronate **1a** (189 mg, 1.0 mmol) and diazo compound **2c** (270 mg, 1.0 mmol). Yield: 418 mg (97 %), colorless oil. R_f (SiO_2, 5:1 PE–EtOAc): 0.56. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.26 (dd, *J* = 15.7, 1.6 Hz, 1 H, H_a-6), 4.17-4.23 (m, 2 H, CH_2(Et)), 4.03 (dd, *J* = 15.7, 0.8 Hz, 1 H, H_b-6), 3.95 (qdd, *J* = 6.3, 1.7, 0.8 Hz, 1 H, H-3), 1.32 (d, *J* = 6.3 Hz, 3 H, Me-3), 1.28 (t, *J* = 7.1 Hz, 3 H, $OCH_2\underline{CH}_3$), 0.93 (s, 9 H, *t*-BuSi), 0.92 (s, 9 H, *t*-BuSi), 0.19 (s, 6 H, Me_2Si), 0.15 (s, 3 H, MeSi), 0.13 (s, 3 H, MeSi). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 165.1 (C=O), 157.0 (C-5), 110.9 (C-4), 67.8 (C-6), 61.2 (C-3),

60.1 (CH_2(Et)), 26.1 ($\underline{Me}_3CSi$), 25.9 ($\underline{Me}_3CSi$), 18.6 ($Me_3\underline{C}Si$), 18.1 ($Me_3\underline{C}Si$), 14.6 (Me–3), 12.2 ($OCH_2\underline{C}H_3$), –3.8 (MeSi), –5.0 (MeSi), –5.1 (MeSi). ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 27.1, 23.6. ^{15}N NMR (30 MHz, $CDCl_3$, from {^{1}H–^{15}N}HMBC) δ = 243 (N–OTBS). HRMS (ESI) *m/z* calcd. for [$C_{20}H_{41}NO_5Si_2$ + Na^+]: 454.2415, found: 454.2417.

Methyl 2,5-bis((*tert*-butyldimethylsilyl)oxy)-3-methyl-3,6-dihydro-2*H*-1,2-oxazine-4-carboxylate (3ad)

Obtained according to general procedure from nitronate **1a** (189 mg, 1.0 mmol) and diazo compound **2d** (256 mg, 1.0 mmol). Yield: 304 mg (73 %), colorless oil. R_f (SiO_2, 3:1 PE–EtOAc): 0.55. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.26 (dd, *J* = 15.8, 1.6 Hz, 1 H, H_a-6), 4.02 (dd, *J* = 15.8, 0.8 Hz, 1 H, H_b-6), 3.95 (qdd, *J* = 6.3, 1.7, 0.7 Hz, 1 H, H-3), 3.70 (s, 3 H, OMe), 1.31 (d, *J* = 6.3 Hz, 3 H, Me-3), 0.93 (s, 9 H, *t*-BuSi), 0.91 (s, 9 H, *t*-BuSi), 0.17 (s, 6 H, Me_2Si), 0.14 (s, 3 H, MeSi), 0.13 (s, 3 H, MeSi). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 165.6 (C=O), 157.4 (C-5), 110.6 (C-4), 67.8 (C-6), 61.2 (C-3), 51.2 (OMe), 26.1 ($\underline{Me}_3CSi$), 25.7 ($\underline{Me}_3CSi$), 18.5 ($Me_3\underline{C}Si$), 18.0 ($Me_3\underline{C}Si$), 12.2 (Me-3), –3.9 (MeSi), –5.04 (MeSi), –5.15 (MeSi). ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 27.1, 23.6. ^{15}N NMR (30 MHz, $CDCl_3$, from {^{1}H–^{15}N}HMBC) δ = 243 (N–OTBS). HRMS (ESI) *m/z* calcd. for [$C_{19}H_{39}NO_5Si_2$ + H^+]: 418.2440, found: 418.2421.

4-nitrobenzyl 2,5-bis((*tert*-butyldimethylsilyl)oxy)-3-ethyl-3,6-dihydro-2*H*-1,2-oxazine-4-carboxylate (3ba)

Obtained according to general procedure from nitronate **1b** (203 mg, 1.0 mmol) and diazo compound **2a** (377 mg, 1.0 mmol). Yield: 475 mg (86 %), almost colorless viscous oil. R_f (SiO_2, 3:1 PE–EtOAc): 0.55. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 7.52 (d, *J* = 9.0 Hz, 2 H, CH(pNB)), 5.32 (d, *J* = 13.4 Hz, 1 H, CH_{2a}(pNB)), 5.21 (d, *J* = 13.4 Hz, 1 H, CH_{2b}(pNB)), 4.29 (dd, *J* = 15.9, 1.6 Hz, 1 H, H_a-6), 4.05 (dd, *J* = 15.9, 0.7 Hz, 1 H, H_b-6), 3.88 (dddd, *J* = 5.9, 4.7, 1.6, 0.7 Hz, 1 H, H-3), 2.16 (dqd, *J* = 15.0, 7.5, 5.9 Hz, 1 H, H_a(Et-3)), 1.67 (dqd, *J* = 15.1, 7.6, 4.7 Hz, 1 H, H_b(Et-3)), 0.97 (t, *J* = 7.6 Hz, 3 H, Me), 0.93 (s, 9 H, *t*-BuSi), 0.91 (s, 9 H, *t*-BuSi), 0.17 (s, 3 H, Me_2Si), 0.16 (s, 6 H, Me_2Si), 0.15 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.7 (C=O), 158.3 (C-5), 147.8 (C-NO_2), 143.8 (C(pNB)), 128.7 (CH(pNB)), 123.9 (CH(pNB)), 109.3 (C-4), 68.0 (C-6), 66.7 (C-3), 64.5 (CH_2(pNB)), 26.1 ($\underline{Me}_3CSi$), 25.8 ($\underline{Me}_3CSi$), 21.6 (CH_2(Et)), 18.6 ($Me_3\underline{C}Si$), 18.03 ($Me_3\underline{C}Si$), 12.86 (CH_3(Et)), –3.71 (Me_2Si), –5.02 (Me_2Si), –5.17 (Me_2Si). ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 27.3, 24.1. ^{15}N NMR (30 MHz, $CDCl_3$, from {^{1}H–^{15}N}HMBC) δ = 369 (NO_2), 245 (N–OTBS). HRMS (ESI) *m/z* calcd. for [$C_{26}H_{44}N_2O_7Si_2$ + Na^+]: 575.2579, found: 575.2570.

4-nitrobenzyl 2,5-bis((*tert*-butyldimethylsilyl)oxy)-3-(((2-methoxypropan-2-yl)oxy)methyl)-3,6-dihydro-2*H*-1,2-oxazine-4-carboxylate (3ca)

Obtained according to general procedure from nitronate **1c** (277 mg, 1.0 mmol) and diazo compound **2a** (377 mg, 1.0 mmol). Yield: 492 mg (79 %), almost colorless viscous oil. R_f (SiO_2, 3:1 PE–EtOAc): 0.60. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 7.56 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 5.34 (d, *J* = 13.7 Hz, 1 H, CH_{2a}(pNB)), 5.18 (d, *J* = 13.8 Hz, 1 H, CH_{2b}(pNB)), 4.31 (dd, *J* = 15.8, 1.6 Hz, 1 H, H_a-6), 4.22 (ddd, *J* = 6.5, 5.5, 1.3 Hz, 1 H, H-3), 4.10 (dd, *J* = 9.5, 5.2 Hz, 1 H, CH_{2a}–C(3)), 4.06 (d, *J* = 16.1 Hz, 1 H, H_b-6), 3.71 (dd, *J* = 9.5, 6.1 Hz, 1 H, CH_{2b}–C(3)), 3.12 (s, 3 H, OMe), 1.26 (s, 3 H, CH_3), 1.23 (s, 3 H, CH_3), 0.93 (s, 9 H, *t*-BuSi), 0.90 (s, 9 H, *t*-BuSi), 0.16 (s, 12 H, 2×Me_2Si). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.7 (C=O), 157.5 (C-5), 147.8 (C-NO_2), 143.9 (C(pNB)), 128.5 (CH(pNB)), 123.8 (CH(pNB)), 108.1 (C-4), 100.2 (O-C-O), 68.2 (C-6), 65.0 (C-3), 64.5 (CH_2(pNB)), 58.9 ($\underline{CH}_2$-C(3)), 48.6 (OMe), 26.1 ($\underline{Me}_3CSi$), 25.7 ($\underline{Me}_3CSi$), 24.4 (2×$\underline{Me}$-C), 18.5 ($Me_3\underline{C}Si$), 18.0 ($Me_3\underline{C}Si$), –3.7 (Me_2Si), –5.0 (Me_2Si), –5.2 (Me_2Si). ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 27.9, 24.2. ^{15}N NMR (30 MHz, $CDCl_3$, from {^{1}H–^{15}N}HMBC) δ = 371 (NO_2), 243 (N–OTBS). HRMS (ESI) *m/z* calcd. for [$C_{29}H_{50}N_2O_9Si_2$ + Na^+]: 649.2947, found: 649.2940.

4-nitrobenzyl 2,5-bis((*tert*-butyldimethylsilyl)oxy)-3-(2,2-dimethoxyethyl)-3,6-dihydro-2*H*-1,2-oxazine-4-carboxylate (3da)

Obtained according to general procedure from nitronate **1d** (263 mg, 1.0 mmol) and diazo compound **2a** (377 mg, 1.0 mmol). Yield: 462 mg (75 %), almost colorless viscous oil. R_f (SiO_2, 3:1 PE–EtOAc): 0.44. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 7.57 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 5.33 (d, *J* = 13.7 Hz, 1 H, CH_{2a}(pNB)), 5.20 (d, *J* = 13.7 Hz, 1 H, CH_{2b}(pNB)), 4.76 (dd, *J* = 7.4, 4.3 Hz, 1 H, $C\underline{H}(OMe)_2$), 4.32 (dd, *J* = 15.8, 1.6 Hz, 1 H, H_a-6), 4.16 (ddd, *J* = 6.3, 4.5, 1.4 Hz, 1 H, H-3), 4.04 (d, *J* = 15.7 Hz, 1 H, H_b-6), 3.25 (s, 6 H, 2×OMe), 2.54 (ddd, *J* = 14.6, 6.6, 4.3 Hz, 1 H, CH_{2a}-C(3)), 1.87 (ddd, *J* = 14.7, 7.4, 4.4 Hz, 1 H, CH_{2b}-C(3)), 0.93 (s, 9 H, *t*-BuSi), 0.89 (s, 9 H, *t*-BuSi), 0.16 (s, 6 H, Me_2Si), 0.15 (s, 3 H, MeSi), 0.15 (s, 3 H, MeSi). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.2 (C=O), 158.2 (C-5), 147.7 (C-NO_2), 143.8 (C(pNB)), 128.5 (CH(pNB)), 123.7 (CH(pNB)), 109.6 (C-4), 103.4 ($\underline{C}(OMe)_2$), 68.5 (C-6), 64.5 (CH_2(pNB)), 61.8 (C-3), 53.3 (OMe), 52.7 (OMe), 32.1 ($\underline{CH}_2$-C(3)), 26.1 ($\underline{Me}_3CSi$), 25.7 ($\underline{Me}_3CSi$), 18.5 ($Me_3\underline{C}Si$), 18.0 ($Me_3\underline{C}Si$), –3.8 (MeSi), –5.1 (MeSi), –5.2 (MeSi). ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 27.9, 24.2. ^{15}N NMR (30 MHz, $CDCl_3$, from {^{1}H–^{15}N}HMBC) δ = 369 (NO_2), 245 (N–OTBS). HRMS (ESI) *m/z* calcd. for [$C_{28}H_{48}N_2O_9Si_2$ + Na^+]: 635.2791, found: 635.2786.

4-nitrobenzyl 2,5-bis((*tert*-butyldimethylsilyl)oxy)-3-(2-((2-methoxypropan-2-yl)oxy)ethyl)-3,6-dihydro-2*H*-1,2-oxazine-4-carboxylate (3ea)

Obtained according to general procedure from nitronate **1e** (291 mg, 1.0 mmol) and diazo compound **2a** (377 mg, 1.0 mmol). Yield: 533 mg (83 %), almost colorless viscous oil. R_f (SiO_2, 3:1 PE–EtOAc): 0.51. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 7.52 (d, *J* = 8.7 Hz, 2 H, CH(pNB)), 5.31 (d, *J* = 13.5 Hz, 1 H, CH_{2a}(pNB)), 5.21 (d, *J* = 13.5 Hz, 1 H, CH_{2b}(pNB)), 4.30 (dd, *J* = 15.9, 1.6 Hz, 1 H, H_a-6), 4.03 (d, *J* = 15.9 Hz, 1 H, H_b-6), 3.97 (ddd, *J* = 6.0, 3.4, 1.2 Hz, 1 H, H-3), 3.64 (td, *J* = 9.6, 5.7 Hz, 1 H, CH_{2a}–O), 3.55 – 3.42 (m, 1 H, CH_{2a}–O), 3.11 (s, 3 H, OMe), 2.41 (ddt, *J* = 14.3, 9.8, 6.0 Hz, 1 H, CH_{2a}–C(3)), 1.89 (dddd, *J* = 13.7, 9.6, 5.8, 3.5 Hz, 1 H, CH_{2b}–C(3)), 1.26 (s, 3 H, CH_3), 1.26 (s, 3 H, CH_3), 0.92 (s, 9 H, *t*-BuSi), 0.89 (s, 9 H, *t*-BuSi), 0.15 (s, 3 H, MeSi), 0.15 (s, 3 H, MeSi), 0.15 (s, 3 H, MeSi), 0.13 (s, 3 H, MeSi). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.2 (C=O), 159.0 (C-5), 147.8 (C-NO_2), 143.8 (C(pNB)), 128.6 (CH(pNB)), 123.8 (CH(pNB)), 109.1 (C-4), 99.9 (O-C-O), 68.3 (C-6), 64.4 (CH_2(pNB)), 63.2 (C-3), 59.8 (CH_2-O), 48.4 (OMe), 29.6 ($\underline{CH}_2$-C(3)), 26.0 ($\underline{Me}_3CSi$), 25.7 ($\underline{Me}_3CSi$), 24.6 (2×Me–14), 18.6 ($Me_3\underline{C}Si$), 17.9 ($Me_3\underline{C}Si$), –3.7 (MeSi), –5.1 (MeSi), –5.2 (MeSi). ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 27.8, 24.3. ^{15}N NMR (30 MHz, $CDCl_3$, from {^{1}H–^{15}N}HMBC) δ = 369 (NO_2), 244 (N–OTBS). HRMS (ESI) *m/z* calcd. for [$C_{30}H_{52}N_2O_9Si_2$ + Na^+]: 663.3104, found: 663.3097.

4-nitrobenzyl 2,5-bis((*tert*-butyldimethylsilyl)oxy)-3-(3-methoxy-3-oxopropyl)-3,6-dihydro-2*H*-1,2-oxazine-4-carboxylate (3fa)

Obtained according to general procedure from nitronate **1f** (261 mg, 1.0 mmol) and diazo compound **2a** (377 mg, 1.0 mmol). Title compound was recrystallized from methanol. Yield: 415 mg (68 %), off-white prisms. mp 76–77 °C (methanol). R_f (SiO_2, 3:1 PE–EtOAc): 0.51. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 7.53 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 5.30 (d, *J* = 13.3 Hz, 1 H, CH_{2a}(pNB)), 5.23 (d, *J* = 13.3 Hz, 1 H, CH_{2b}(pNB)), 4.30 (dd, *J* = 15.9, 1.6 Hz, 1 H, H_a-6), 4.03 (d, *J* = 15.9

Hz, 1 H, H_b-6), 3.97 (ddd, *J* = 5.3, 3.8, 1.3 Hz, 1 H, H-3), 3.61 (s, 3 H, OMe), 2.70 – 2.31 (m, 3 H, CH_2-CO_2Me + CH_{2a}-C(3)), 2.16 – 1.94 (m, 1 H, CH_{2b}-C(3)), 0.92 (s, 9 H, *t*-BuSi), 0.90 (s, 9H *t*-BuSi), 0.16 (s, 3 H, MeSi), 0.16 (s, 3 H, MeSi), 0.15 (s, 3 H, MeSi), 0.14 (s, 3 H, MeSi). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.0 (C–13), 164.3 (C=O), 159.6 (C-5), 147.8 (C-NO_2), 143.7 (C(pNB)), 128.7 (CH(pNB)), 123.9 (CH(pNB)), 108.4 (C-4), 68.3 (C-6), 64.5 (CH_2(pNB)), 64.5 (C-3), 51.5 (OMe), 32.9 (CH_2-CO_2Me), 26.1 (Me_3CSi), 25.7 (Me_3CSi), 23.9 (CH_2-C(3)), 18.6 (Me_3CSi), 18.0 (Me_3CSi), –3.6 (Me_2Si), –5.2 (Me_2Si). ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 28.03, 24.43. ^{15}N NMR (30 MHz, $CDCl_3$, from {^{1}H–^{15}N}HMBC) δ = 369 (NO_2), 245 (N–OTBS). Elem. anal. calcd. for $C_{28}H_{46}N_2O_9Si_2$: C, 55.06; H, 7.59; N, 4.59; Si, 9.20. Found: C, 55.08; H, 7.56; N, 4.60; Si, 9.18.

4-nitrobenzyl 2,5-bis((*tert*-butyldimethylsilyl)oxy)-3-phenethyl-3,6-dihydro-2*H*-1,2-oxazine-4-carboxylate (3ga)

Obtained according to general procedure from nitronate **1g** (276 mg, 1.0 mmol) and diazo compound **2a** (377 mg, 1.0 mmol). Yield: 461 mg (73 %), colorless oil. R_f (SiO_2, 3:1 PE–EtOAc): 0.51. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 7.49 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 7.25 – 7.06 (m, 5 H, Ph), 5.30 (d, *J* = 13.3 Hz, 1 H, CH_{2a}(pNB)), 5.21 (d, *J* = 13.3 Hz, 1 H, CH_{2b}(pNB)), 4.33 (dd, *J* = 15.9, 1.6 Hz, 1 H, H_a-6), 4.07 (dd, *J* = 15.9, 0.7 Hz, 1 H, H_b-6), 4.05 – 4.00 (m, 1 H, H-3), 2.87 (ddd, *J* = 13.5, 11.5, 5.3 Hz, 1 H, CH_{2a}–Ph), 2.77 – 2.63 (m, 1 H, CH_{2a}–Ph), 2.51 (ddt, *J* = 14.2, 11.4, 5.7 Hz, 1 H, CH_{2a}–C(3)), 1.88 (dddd, *J* = 14.2, 11.6, 5.4, 3.8 Hz, 1 H, CH_{2b}–C(3)), 0.96 (s, 9 H, *t*-BuSi), 0.93 (s, 9 H, *t*-BuSi), 0.20 (s, 3 H, MeSi), 0.19 (s, 3 H, MeSi), 0.18 (s, 3 H, MeSi), 0.18 (s, 3 H, MeSi). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.5 (C=O), 158.8 (C-5), 147.8 (C-NO_2), 143.7 (C(pNB)), 142.8 (C_{Ph}), 128.9 (CH(pNB)), 128.8 ($CH_{m\text{-}Ph}$), 128.6 ($CH_{p\text{-}Ph}$), 125.8 ($CH_{o\text{-}Ph}$), 123.9 (CH(pNB)), 109.3 (C-4), 68.1 (C-6), 65.2 (C-3), 64.4 (CH_2(pNB)), 34.9 (CH_2–Ph), 30.8 (CH_2–C(3)), 26.2 (Me_3CSi), 25.8 (Me_3CSi), 18.6 (Me_3CSi), 18.0 (Me_3CSi), –3.69 (MeSi), –4.97 (MeSi), –5.09 (MeSi). ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 27.7, 24.3. ^{15}N NMR (30 MHz, $CDCl_3$, from {^{1}H–^{15}N}HMBC) δ = 369 (NO_2), 245 (N–OTBS). HRMS (ESI) *m/z* calcd. for $C_{32}H_{49}N_2O_7Si_2$: 629.3073, found: 629.3071.

4-nitrobenzyl *rel*-(2R,3R)-2,5-bis((*tert*-butyldimethylsilyl)oxy)-3-(4-methoxybenzyl)-3,6-dihydro-2*H*-1,2-oxazine-4-carboxylate (3ha)

Obtained by a modified general procedure: solution of nitronate **1h** (590 mg, 2.0 mmol) and diazo compound **2a** (1131 mg, 3.0 mmol) in CH_2Cl_2 (4 mL) was added dropwise during 15 min. to the stirring suspension of $Rh_2(OAc)_4$ (18 mg, 0.04 mmol) in CH_2Cl_2 (1 mL). Title compound was recrystallized from methanol (10 mL). Yield: 897 mg (70 %), off-white prisms. mp 95–97 °C (methanol). R_f (SiO_2, 3:1 PE–EtOAc): 0.50. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 8.7 Hz, 2 H, CH(pNB)), 7.32 (d, *J* = 8.7 Hz, 2 H, CH(pNB)), 7.08 (d, *J* = 8.5 Hz, 2 H, CH(PMP)), 6.68 (d, *J* = 8.6 Hz, 2 H, CH(PMP)), 5.04 (d, *J* = 13.6 Hz, 1 H, CH_{2a}(pNB)), 4.66 (d, *J* = 13.6 Hz, 1 H, CH_{2b}(pNB)), 4.37 (dd, *J* = 15.9, 1.5 Hz, 1 H, H_a-6), 4.20 (ddd, *J* = 6.6, 4.8, 1.4 Hz, 1 H, H-3), 4.08 (d, *J* = 15.9 Hz, 1 H, H_b-6), 3.71 (s, 3 H, OMe), 3.57 (dd, *J* = 13.9, 4.8 Hz, 1 H, CH_{2a}–C(3)), 2.85 (dd, *J* = 13.9, 7.0 Hz, 1 H, CH_{2b}–C(3)), 0.91 (s, 9 H, *t*-BuSi), 0.90 (s, 9 H, *t*-BuSi), 0.16 (s, 6 H, Me_2Si), 0.15 (s, 3 H, MeSi), 0.14 (s, 3 H, MeSi). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.1 (C=O), 158.4 (C-5), 157.9 (C(PMP)), 147.7 (C-NO_2), 143.6 (C(pNB)), 132.2 (C(PMP)), 130.7 (CH(PMP)), 128.4 (CH(pNB)), 123.7 (CH(pNB)), 113.6 (CH(PMP)), 109.9 (C-4), 68.9 (C-6), 67.1 (C-3), 64.4 (CH_2(pNB)), 55.3 (OMe), 33.6 (CH_2-C(3)), 26.1 (Me_3CSi), 25.7 (Me_3CSi), 18.5 (Me_3CSi), 18.0 (Me_3CSi), –3.7 (MeSi), –5.0 (MeSi), –5.2 (MeSi). ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 27.8, 24.4. ^{15}N NMR (30 MHz, $CDCl_3$, from {^{1}H–^{15}N}HMBC) δ = 369 (NO_2), 244 (N–OTBS). ^{1}H NMR (200 MHz, toluene-d_8): δ = 7.73 (d, *J* = 8.5 Hz, 2 H), 7.15 (d, *J* = 8.3 Hz, 2 H), 6.72 (d, *J* = 8.5 Hz, 2 H), 6.62 (d, *J* = 8.2 Hz, 2 H), 4.94 (d, *J* = 13.5 Hz, 1 H, CH_{2a}(pNB)), 4.47-4.53 (m, 1 H, H-3), 4.42 (dd, *J* = 15.9, 1.4 Hz, 1 H, H_a-6), 4.39 (d, *J* = 13.5, 1 H, CH_{2b}(pNB)), 3.98 (d, *J* = 15.9 Hz, 1 H, H_b-6), 3.83 (dd, *J* = 14.0, 4.6 Hz, 1 H, CH_{2a}–C(3)), 3.33 (s, 3 H, OMe), 3.10 (dd, *J* = 14.0, 6.5 Hz, 1 H, CH_{2b}–C(3)), 0.97 (s, 9 H, *t*-BuSi), 0.86 (s, 9 H, *t*-BuSi), 0.25 (s, 3 H, MeSi), 0.19 (s, 3 H, MeSi), 0.13 (s, 3 H, MeSi), 0.09 (s, 3 H, MeSi). ^{13}C NMR (50 MHz, toluene-d_8): δ = 163.3 (C=O), 158.2 and 158.0 (C-5 and C(PMP)), 147.4 (C-NO_2), 142.9 (C(pNB)), 132.0 (C(PMP)), 130.7 (CH(PMP)), 128.1 (CH(pNB)), 127.9 (CH(pNB)), 123.0 (CH(PMP)), 110.0 (C-4), 68.7, 67.2 and 63.9 (C-3, C-6 and CH_2(pNB)), 54.3 (OMe), 33.9 (CH_2-C(3)), 25.7 (Me_3CSi), 25.4 (Me_3CSi), 18.2 (Me_3CSi), 17.8 (Me_3CSi), -4.2 (MeSi), -4.3 (MeSi), –5.3 (MeSi), –5.5 (MeSi). ^{15}N NMR (30 MHz, toluene-d_8, from {^{1}H–^{15}N}HMBC) δ = 244 (N–OTBS). Signal of NO_2 was not observed due to broadening and low intensity. Elem. anal. calcd. for $C_{32}H_{48}N_2O_8Si_2$: C, 59.60; H, 7.50; N, 4.34; Si, 8.71. Found: C, 59.85; H, 7.51; N, 4.28; Si, 8.52.

4-nitrobenzyl 2,5-bis((*tert*-butyldimethylsilyl)oxy)-3,3-dimethyl-3,6-dihydro-2*H*-1,2-oxazine-4-carboxylate (3ia)

Obtained according to general procedure from nitronate **1i** (203 mg, 1.0 mmol) and diazo compound **2a** (377 mg, 1.0 mmol). Yield: 375 mg (68 %), colorless oil. Crystallized spontaneously upon storage at 4 °C. mp 50–53 °C (not recrystallized). R_f (SiO_2, 3:1 PE–EtOAc): 0.60. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 7.53 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 5.30 (d, *J* = 13.5 Hz, 1 H, CH_{2a}(pNB)), 5.23 (d, *J* = 13.4 Hz, 1 H, CH_{2b}(pNB)), 4.21 (d, *J* = 15.5 Hz, 1 H, H_a-6), 3.91 (br d, *J* = 15.6 Hz, 1 H, H_b-6), 1.36 (s, 3 H, Me-3), 1.23 (s, 3 H, Me-3), 0.92 (s, 9 H, *t*-BuSi), 0.89 (s, 9 H, *t*-BuSi), 0.19 (s, 6 H, Me_2Si), 0.15 (s, 6 H, Me_2Si). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.0 (C=O), 151.2 (C-5), 147.8 (C-NO_2), 143.6 (C(pNB)), 128.6 (CH(pNB)), 123.9 (CH(pNB)), 112.6 (br, C-4), 65.2 (C-3), 64.6 (CH_2(pNB)), 61.5 (br, C-6), 27.3 (Me-3), 26.1 (Me_3CSi), 25.7 (Me_3CSi), 22.5 (Me-3), 18.4 (Me_3CSi), 18.0 (Me_3CSi), –3.83 (Me_2Si), –4.77 (Me_2Si). ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 27.1, 23.7. ^{15}N NMR (30 MHz, $CDCl_3$, from {^{1}H–^{15}N}HMBC) δ = 240 (N–OTBS). HRMS (ESI) *m/z* calcd. for [$C_{26}H_{44}N_2O_7Si_2$ + H^+]: 553.2760, found: 553.2760.

4-nitrobenzyl 1,4-bis((*tert*-butyldimethylsilyl)oxy)-2-oxa-1-azaspiro[5.5]undec-4-ene-5-carboxylate (3ja)

Obtained according to general procedure from nitronate **1j** (243 mg, 1.0 mmol) and diazo compound **2a** (377 mg, 1.0 mmol). Title compound crystallized spontaneously upon storage. Yield: 400 mg (67 %), white solid. mp 51–53 °C (not recrystallized). R_f (SiO_2, 3:1 PE–EtOAc): 0.57. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 7.54 (d, *J* = 8.7 Hz, 2 H, CH(pNB)), 5.32 (d, *J* = 13.6 Hz, 1 H, CH_{2a}(pNB)), 5.20 (d, *J* = 13.6 Hz, 1 H, CH_{2b}(pNB)), 4.18 (d, *J* = 15.4 Hz, 1 H, H_a-6), 3.73 (d, *J* = 15.4 Hz, 1 H, H_b-6), 1.97 – 1.02 (m, 10 H, CH_2(c-Hex)), 0.92 (s, 9 H, *t*-BuSi), 0.87 (s, 9 H, *t*-BuSi), 0.24 (s, 3 H, MeSi), 0.21 (s, 3 H, MeSi), 0.13 (s, 3H, MeSi), 0.13 (s, 3H, MeSi). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.0 (C=O), 147.8 (C-5), 147.7 (C-NO_2), 143.5 (C(pNB)), 128.5 (CH(pNB)), 123.8 (CH(pNB)), 113.0 (C-4), 66.7 (C-3), 64.8 (CH_2(pNB)), 59.0 (C-6), 36.6 (CH_2-C(3)), 31.4 (CH_2-C(3)), 26.1 (Me_3CSi), 25.7 (Me_3CSi), 21.8 (CH_2), 21.4 (CH_2), 18.2 (Me_3CSi), –3.8 (MeSi), –4.1 (MeSi), –4.9 (MeSi). ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 27.8, 23.3. ^{15}N NMR (30 MHz, $CDCl_3$, from {^{1}H–^{15}N}HMBC) δ = 235 (N–OTBS). Elem. anal. calcd. for $C_{29}H_{48}N_2O_7Si_2$: C, 58.75; H, 8.16; N, 4.73; Si, 9.47. Found: C, 58.70; H, 8.17; N, 4.72; Si, 9.36.

4-nitrobenzyl (2*R,3*S**)-1-((*tert*-butyldimethylsilyl)oxy)-2-(2-((*tert*-butyldimethylsilyl)oxy)-2-oxoethyl)-3-methylaziridine-2-carboxylate (4)**

Dirhodium (II) tetraacetate (2.2 mg, 0.005 mmol) was added to a solution of diazo compound **2a** (377 mg, 1.0 mmol) in dichloromethane (1 mL) at ambient temperature. The mixture was maintained until full conversion of **2a** (completion of nitrogen evolution, ca. 30 min) and was filtered through a short plug of silica. Then nitronate **1a** (208 mg, 1.1 mmol) was added. The reaction was maintained for 24 hours, then evaporated and subjected to column chromatography on silica to give 206 mg (40 %) of title compound **4** as colorless oil. R_f (SiO_2, 3:1 PE–EtOAc): 0.53. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 7.48 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 5.30 (d, *J* = 13.6 Hz, 1 H, CH_{2a}(pNB)), 5.16 (d, *J* = 13.8 Hz, 1 H, CH_{2b}(pNB)), 3.02 (d, *J* = 18.1 Hz, 1 H, CH_{2a}–CO_2TBS), 2.81 (d, *J* = 18.2 Hz, 1 H, CH_{2b}–CO_2TBS), 2.79 (q, *J* = 6.3 Hz, 1 H, CH–N), 1.27 (d, *J* = 6.2 Hz, 3 H, Me–C), 0.89 (s, 18 H, 2×*t*-BuSi), 0.24 (s, 3 H, MeSi), 0.23 (s, 3 H, MeSi), 0.13 (s, 3 H, MeSi), 0.10 (s, 2 H, MeSi). Characteristic NOESY-interactions: CH_2–CO_2TBS / Me–C, CH–N / Me–C. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.2 (C=O), 170.4 (C=O), 147.8 (C-NO2), 143.2 (C(pNB)), 128.0 (CH(pNB)), 123.9 (CH(pNB)), 65.3 (CH_2(pNB)), 45.8 (CH-N), 45.3 (C-N), 29.9 (CH_2–CO_2TBS), 26.3 (Me_3CSi), 25.63 (Me_3CSi), 18.3 (Me_3CSi), 17.7 (Me_3CSi), 6.7 (Me–C), –3.5 (MeSi), –4.7 (MeSi), –5.1 (MeSi), –5.2 (MeSi). ^{15}N NMR (30 MHz, $CDCl_3$, from {^{1}H–^{15}N} HMBC) δ = 369 (NO_2), 135 (N–OTBS). HRMS (ESI) *m/z* calcd. for [$C_{25}H_{42}N_2O_7Si_2$ + Na^+]: 561.2423, found: 561.2412.

4-nitrobenzyl *rel*-(2S,3R)-2,5-bis((*tert*-butyldimethylsilyl)oxy)-3-(4-methoxybenzyl)-3,6-dihydro-2*H*-1,2-oxazine-4-carboxylate (3'ha)

Solution of oxazine **3ha** (89 mg, 0.14 mmol) in toluene (1.1 mL) was maintained at 100 °C for 1 h and evaporated to give 89 mg (ca. 100%) of oxazine **3'ha** as colorless oil. ^{1}H NMR (400 MHz, toluene-d_8): δ = 7.77 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 7.20 (d, *J* = 8.6 Hz, 2 H, CH(PMP)), 6.90 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 6.75 (d, *J* = 8.7 Hz, 2 H, CH(PMP)), 4.86 (d, *J* = 13.4 Hz, 1 H, CH_{2a}(pNB)), 4.76 (d, *J* = 13.4 Hz, 1 H, CH_{2b}(pNB)), 4.40 (dd, *J* = 16.3, 1.7 Hz, 1 H, H_a-6), 4.16 (ddd, *J* = 7.9, 5.5, 1.4 Hz, 1 H, H-3), 3.74 (d, *J* = 16.3 Hz, 1 H, H_b-6), 3.37 (s, 3 H, OMe), 2.92-2.98 (m, 2 H, CH_2–C(3)), 0.92 (s, 9 H, *t*-BuSi), 0.88 (s, 9 H, *t*-BuSi), 0.18 (s, 3 H, Me_2Si), 0.14 (s, 3 H, MeSi), 0.08 (s, 3 H, MeSi), -0.09 (s, 3 H, MeSi). ^{13}C NMR (101 MHz, toluene-d_8): δ = 163.9 (C=O), 158.6 (C(PMP)), 157.5 (C-5), 147.6 (C-NO_2), 143.1 (C(pNB)), 131.2 (C(PMP)), 130.7 (CH(PMP)), 128.1 (CH(pNB)), 123.2 (CH(pNB)), 113.5 (CH(PMP)), 105.0 (C-4), 69.1 (C-3), 63.8 (CH_2(pNB)), 59.8 (C-6), 54.4 (OMe), 40.1 (CH_2-C(3)), 25.7 (Me_3CSi), 25.5 (Me_3CSi), 18.3 (Me_3CSi), 17.8 (Me_3CSi), –4.2 (MeSi), –4.4 (MeSi), –5.7 (MeSi), –5.9 (MeSi). ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 26.7, 23.7. ^{15}N NMR (30 MHz, $CDCl_3$, from {^{1}H–^{15}N}HMBC) δ = 369 (NO_2), 226 (N–OTBS). HRMS (ESI) *m/z* calcd. for [$C_{32}H_{48}N_2O_8Si_2$ + Na^+]: 667.2841, found: 667.2841.

(*rel*)-(2S,3*R*)-4-nitrobenzyl 2(*tert*-butyldimethylsilyloxy)-5-hydroxy-3-(4-methoxybenzyl)-3,6-dihydro-2*H*-1,2-oxazine-4-carboxylate (9)

Water (0.75 mL) was added to the solution of oxazine **3'ha** (97 mg, 0.15 mmol) in acetone (3 mL). The reaction mixture was refluxed for 5 h, evaporated and recrystallized from EtOH to give 51 mg (64%) of oxazine **9** as slightly beige powder. Alternatively: Crystalls of **9** were obtained during attempted crystallization of **3'ha** for X-ray analysis from the MeOH/toluene, ca. 10:1, at open air. mp 109–111 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.66 (br s, 1 H, OH), 8.26 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 7.52 (d, *J* = 8.8 Hz, 2 H, CH(pNB)), 7.05 (d, *J* = 8.7 Hz, 2 H, CH(PMP)), 6.76 (d, *J* = 8.7 Hz, 2 H, CH(PMP)), 5.31 (s, 2 H, CH_2(pNB)), 4.49 (dd, *J* = 16.9, 1.1 Hz, 1 H, H_a-6), 3.99 (d, *J* = 16.9 Hz, 1 H, H_b-6), 3.78 (s, 3 H, OMe), 3.69 (td, *J* = 6.9, 1.1 Hz, 1 H, H-3), 2.79 (d, *J* = 6.9 Hz, 2 H, CH_2–C(3)), 0.80 (s, 9 H, *t*-BuSi), -0.05 (s, 3 H, Me_2Si), -0.15 (s, 3 H, MeSi). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.2 (C=O), 168.3 (C-5), 158.2 (C(PMP)), 148.0 (C-NO_2), 142.7 (C(pNB)), 131.2 (C(PMP)), 130.5 (CH(PMP)), 128.5 (CH(pNB)), 124.0 (CH(pNB)), 113.6 (CH(PMP)), 95.0 (C-4), 66.8 (C-3), 64.9 (CH_2(pNB)), 57.3 (C-6), 55.3 (OMe), 40.2 (CH_2-C(3)), 25.8 (Me_3CSi), 17.9 (Me_3CSi),–5.5 (MeSi), –5.7 (MeSi). ^{29}Si NMR (60 MHz, $CDCl_3$): δ = 27.4. ^{15}N NMR (30 MHz, $CDCl_3$, from {^{1}H–^{15}N}HMBC) δ = 228 (N–OTBS) Signal of NO_2 was not observed due to broadening and low intensity. HRMS (ESI) *m/z* calcd. for [$C_{26}H_{34}N_2O_8Si$ + H^+]: 531.2157, found: 531.2150.

Acknowledgements

Research was supported by Russian Science Foundation (grant 14-50-00126).

Keywords: nitroso acetals • cycloaddition • nitrogen heterocycles • nitrogen inversion • diazo compounds

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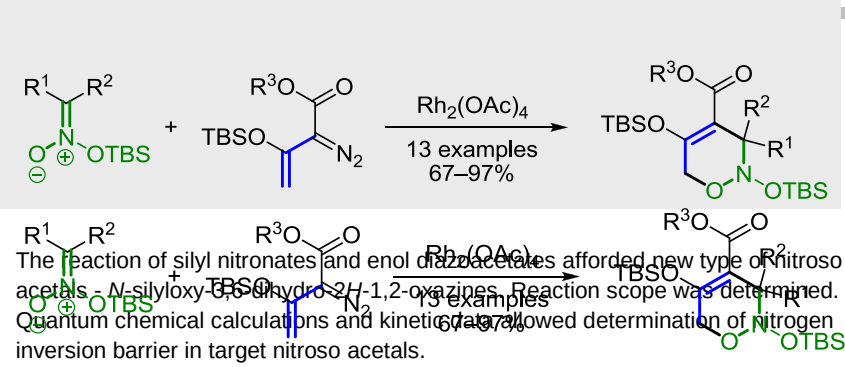

The reaction of silyl nitronates and enol diazoacetates afforded new type of nitroso acetals - *N*-silyloxy-3,6-dihydro-2*H*-1,2-oxazines. Reaction scope was determined. Quantum chemical calculations and kinetic data allowed determination of nitrogen inversion barrier in target nitroso acetals.

N,O-heterocycles

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New six-membered cyclic nitroso acetals - *N*-silyloxy-3,6-dihydro-2*H*-1,2-oxazines: synthesis and studies of the nitrogen inversion process.