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2-Silyloxy-1,2-oxazines, a New Type of Acetals of Conjugated Nitroso Alkenes

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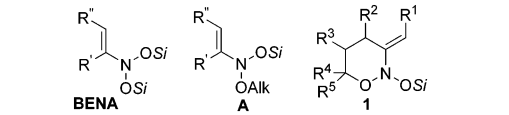
Abstract: 3-Alkyl-substituted 1,2-oxazine *N*-oxides **2** can be selectively transformed into 2-silyloxy-1,2-oxazines **1** upon treatment with silylating reagents. In the solid state derivatives **1** adopt a chair conformation with the pyramidal nitrogen atom, whereas in solution they exist as an equilibrating mixture of two conformers ($\Delta G^{\ddagger}$ 55−60 kJ/mol). A preliminary study of the reactivity of nitrosals **1** has shown that they react with *O*- and *N*-stabilized carbocations to yield 1,2-oxazine *N*-oxides with a functionalized alkyl substituent at the 3-position. Moreover, compounds **1** can rearrange into silyloxy-1,2-oxazines **5** and react with morpholine to produce 3-morpholinoalkyl-1,2-oxazines **7** existing in a tautameric equilibrium with open-chain oximes **6**.

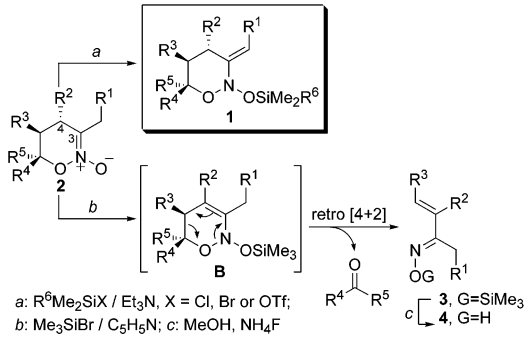
N,*N*-Bis(silyloxy)enamines (BENA), readily available acetals of conjugated nitroso alkenes,[1] exhibit ambident reactivity as moderate *β-C*-nucleophiles[2] and formal *β-C*-electrophiles.[3] This versatility of the reactivity of BENA allows one to consider them as promising reagents for organic synthesis. However, the instability of BENA, due to the presence of two *Si*O groups complicates their practical use, which prompted us to look for more stable analogues of these interesting compounds. Higher stability could be expected for the unknown enamines **A**, which contain one silyloxy and one alkyloxy group at the nitrogen atom (Chart 1).

These compounds could be synthesized by either silylation of alkyl nitronates or alkylation of silyl nitronates. Whereas the double alkylation of aliphatic nitro compounds is unknown, their double silylation is a well-developed protocol.[1] Therefore, the first approach to the synthesis of enamines **A** seems more attractive. Because many acyclic alkyl nitronates are relatively unstable,[4] we have chosen much more stable cyclic nitronates as objects for the silylation.

CHART 1



SCHEME 1



In this connection, we have synthesized hitherto unknown 2-silyloxy-1,2-oxazines **1a**−**j** with good yields by silylation of 1,2-oxazine *N*-oxides **2a**−**j** (Scheme 1), which are easily prepared employing the hetero Diels−Alder reaction between nitroalkenes and olefins.[5]

In principle, the silylation of 1,2-oxazine *N*-oxides **2** can lead to the formation of either *endo* or *exo* C=C isomers (Scheme 1). The control of regioselectivity is achieved by varying the bases of the silylating mixture. The conditions of silylation and results obtained are summarized in Table 1.

The mixture of Et_3N and various silylating agents (Me_3-SiBr, *t*-BuMe_2SiOTf, and EtMe_2SiCl) leads to the formation of the target nitroso acetals **1**. It is worthy of note that even 1,2-oxazine *N*-oxide **2j**, which possesses an electron-withdrawing 4-$NO_2C_6H_4$ substituent in the 4-position, can be selectively transformed into nitrosal **1j″**.

The use of pyridine in combination with Me_3SiBr dramatically changes the direction of the silylation. The immediate products of this reaction, 1,2-oxazines **B**, undergo [4 + 2] cycloreversion leading to α,β-unsaturated oximes **3** and carbonyl fragments.[6] The influence of the base on the regioselectivity of this reaction is likely connected with steric factors; however, this question requires more detailed study.

The silylation of 3-ethyl-1,2-oxazine *N*-oxide **2h** is stereoselective and produces only the *E*-isomer of 3-ethylidene-1,2-oxazine **1h** (by NOE measurements). Nitroso acetals **1** obtained as solids were purified by recrystal-

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(1) For the discovery of BENA, see: (a) Feger, H.; Simchen, G. *Liebigs Ann. Chem.* **1986**, 1456. For the improved procedure for preparation of BENA, see: (b) Dilman, A. D.; Tishkov, A. A.; Lyapkalo, I. M.; Ioffe, S. L.; Strelenko, Yu. A.; Tartakovsky, V. A. *Synthesis* **1998**, 181. (c) Dilman, A. D.; Tishkov, A. A.; Lyapkalo, I. M.; Ioffe, S. L.; Kachala, V. V.; Strelenko, Yu. A.; Tartakovsky, V. A. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2926.

(2) (a) Dilman, A. D.; Lyapkalo, I. M.; Ioffe, S. L.; Strelenko, Yu. A.; Tartakovsky, V. A. *J. Org. Chem.* **2000**, *65*, 8826. (b) Dilman, A. D.; Ioffe, S. L.; Mayr, H. *J. Org. Chem.* **2001**, *66*, 3196.

(3) (a) Dilman, A. D.; Lyapkalo, I. M.; Ioffe, S. L.; Strelenko, Yu. A.; Tartakovsky, V. A. *Synthesis* **1999**, 1767. (b) Lesiv, A. V.; Ioffe, S. L.; Strelenko, Yu. A.; Tartakovsky, V. A. *Helv. Chim. Acta* **2002**, *85*, 3489.

(4) Torssell, K. B. G. *Nitrile Oxides, Nitrones and Nitronates in Organic Synthesis*; VCH Publishers Inc.: New York, 1988; p 106.

(5) Denmark, S. E.; Thorarensen, A. *Chem. Rev.* **1996**, *96*, 137.

(6) This reaction, occurring upon silylation of C(3) unsubstituted 1,2-oxazine *N*-oxides, was discussed in a previous publication: Tishkov, A. A.; Lyapkalo, I. M.; Kozincev, A. V.; Ioffe, S. L.; Strelenko, Yu. A.; Tartakovsky, V. A. *Eur. J. Org. Chem.* **2000**, 3229.

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

entry	1,2-Oxazine *N*-oxide **2**	R^1	R^2	R^3	R^4	R^5	reagent R^6Me_2SiX/Et_3N	conditions *T*, °C/*t*, h	product (yield, %)
1	**2a**	H	4-$MeOC_6H_4$	H	OMe	Me	Me_3SiBr/Et_3N	−78/24	**1a** (67)
2	**2a**	H	4-$MeOC_6H_4$	H	OMe	Me	$EtMe_2SiCl/Et_3N$	20/72	**1a′** (62)
3	**2a**	H	4-$MeOC_6H_4$	H	OMe	Me	*t*-$BuMe_2SiOTf/Et_3N$	−78/1	**1a″** (71)
4	**2b**	H	4-$MeOC_6H_4$	H	OEt	H	Me_3SiBr/Et_3N	−78/24	**1b** (98)
5	**2c**	H	4-$MeOC_6H_4$	H	H	OEt	Me_3SiBr/Et_3N	−78/24	**1c** (98)
6	**2d**	H	C_6H_5	H	OMe	Me	Me_3SiBr/Et_3N	−78/24	**1d** (97)
7	**2d**	H	C_6H_5	H	OMe	Me	*t*-$BuMe_2SiOTf/Et_3N$	−78/1	**1d″** (94)
8	**2e**	H	C_6H_5	H	OBu-*n*	H	*t*-$BuMe_2SiOTf/Et_3N$	−78/1	**1e″** (95)
9	**2f**	H	C_6H_5	H	H	OBu-*n*	*t*-$BuMe_2SiOTf/Et_3N$	−78/1	**1f″** (93)
10	**2g**	H	C_6H_5	H	Me	Me	Me_3SiBr/Et_3N	−78/24	**1g** (95)
11	**2h**	Me	C_6H_5	H	OMe	Me	Me_3SiBr/Et_3N	−78/24	**1h** (95)
12	**2i**	H	4-$MeOC_6H_4$	$(CH_2)_4$	$(CH_2)_4$	H	Me_3SiBr/Et_3N	−78/24	**1i** (95)
13	**2j**	H	4-$NO_2C_6H_4$	$(CH_2)_4$	$(CH_2)_4$	H	*t*-$BuMe_2SiOTf/Et_3N$	−78/1	**1j″** (98)
14	**2a**	H	4-$MeOC_6H_4$	H	OMe	Me	Me_3SiBr/C_5H_5N	−30/24	**4a** (89)
15	**2d**	H	C_6H_5	H	OMe	Me	Me_3SiBr/C_5H_5N	−30/24	**4d** (81)
16	**2h**	Me	C_6H_5	H	OMe	Me	Me_3SiBr/C_5H_5N	−30/24	**4h** (64)

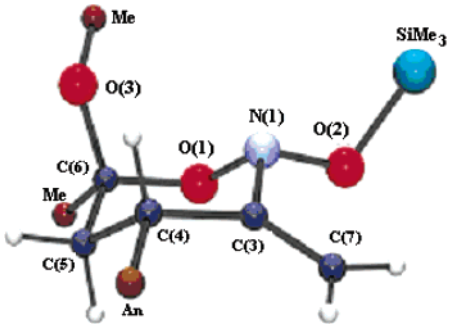


FIGURE 1. The structure of 3-methylene-1,2-oxazine **1a**.

lization, while oily products were either thoroughly evaporated in high vacuum or distilled in a short-path apparatus. The purity of all nitrosals **1** was proved by elemental analysis.

Compound **1a** was studied by means of X-ray analysis (Figure 1),[7] which revealed that in the solid state 2-silyloxy-1,2-oxazines **1** adopt a chair conformation with the pyramidal nitrogen atom (the sum of the valence angles at N is 317.3 grad) and an equatorial arrangement of the *Si*O group. The lengths of C═C and C−N bonds in nitrosal **1a** are similar with these parameters in BENA.[8]

According to the NMR analysis, nitroso acetals **1** exist in solution as equilibrium mixtures of two conformers, which quickly interconvert at room temperature (Table 2). A typical example of NMR spectra of nitrosals **1** at variable temperatures is presented in Figure 2.

The activation parameters of this dynamic process coincide with the $\Delta G^{\ddagger}$ for nitrogen inversion measured for BENA (50−60 kJ/mol).[8] However, in contrast to BENA, one can observe the second, faster dynamic process in DNMR spectra of nitrosals **1**. Unfortunately, the quantitative analysis of this dynamic process is complicated by the restriction of the rotation motion of the substituents in the ring of the 1,2-oxazine; the nature

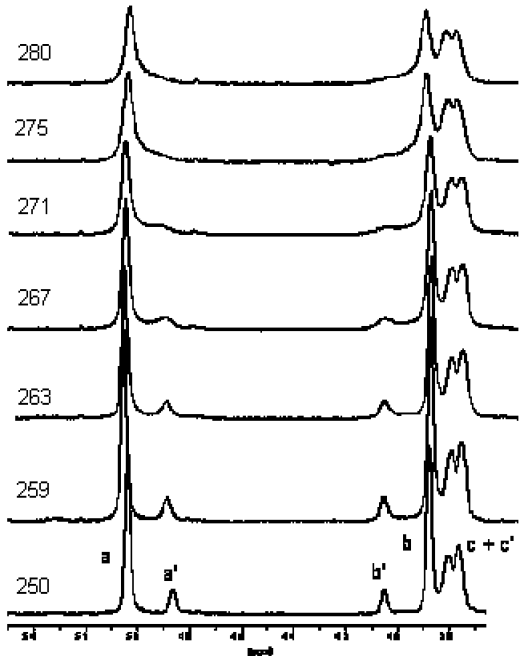


FIGURE 2. ^1H NMR spectra of nitrosal **1g** at variable temperatures. a, b, and c: signals of major conformer of **1g**. a′, b′, and c′: signals of minor conformer of **1g**. a,a′ and b,b′: signals of CH_2═C protons. c,c′: signals of HC(4) protons of **1g**.

of stereodynamics peculiar to nitroso acetals **1** is not completely clear now.

The thermal stability of nitroso acetals **1** depends strongly on the substitution at the C═C bond (R^1): 3-methylene-1,2-oxazine **1e″** can be distilled at 120−125 °C (5×10^{-5} mmHg), whereas 3-ethylidene-1,2-oxazine **1h** rearranges chemo- and stereoselectively into silyloxy-1,2-oxazine **5** in 1 day at room temperature (Scheme 2).[9] Preliminary studies of the reactivity of nitroso acetals **1** revealed that these compounds as BENA can react with both electrophiles and nucleophiles.

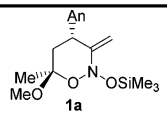
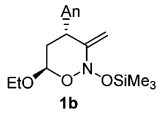
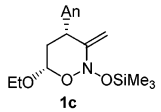
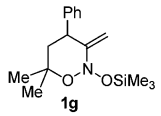
Usual alkylating agents, such as $MeOCH_2Cl$, do not react with 2-silyloxy 1,2-oxazines **1**. However, the nucleophilicity of the C═C bond of nitroso acetals **1** is sufficient to participate in reactions with more electro-

(7) The structure of 1,2-oxazine *N*-oxide **2a** was also studied by X-ray analysis (see Supporting Information). The configuration of the stereocenters in positions 4 and 6 of 1,2-oxazine's ring remains intact in the course of the silylation of *N*-oxides **2**.

(8) Tishkov, A. A.; Dilman, A. D.; Faustov, V. I.; Birukov, A. A.; Lysenko, K. S.; Belyakov, P. A.; Ioffe,S. L.; Strelenko, Yu. A.; Antipin, M. Yu. *J. Am. Chem. Soc.* **2002**, *124*, 11358−11367.

(9) The configuration of a new stereocenter was not established.

TABLE 2. Stereodynamics of Nitrosals 1

№	Compound[a]	Conformers ratio (T, K)	$\Delta G^{\ddagger}_{298}$, kJ/mol[b]
1	 **1a**	9 : 1 (236)	59.2 ± 3.3
2	 **1b**	4.6 : 1 (265)	55.7 ± 3.3
3	 **1c**	2.2 : 1 (250)	60.1 ± 2.7
4	 **1g**	3.3 : 1 (–)[c]	59.8 ± 2.9

[a] An = 4-MeOC$_6$H$_4$. [b] For a conversion of major conformer into minor. [c] The ratio of conformers varies only slightly within the studied temperature range.

SCHEME 2

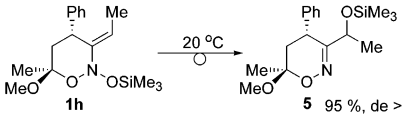
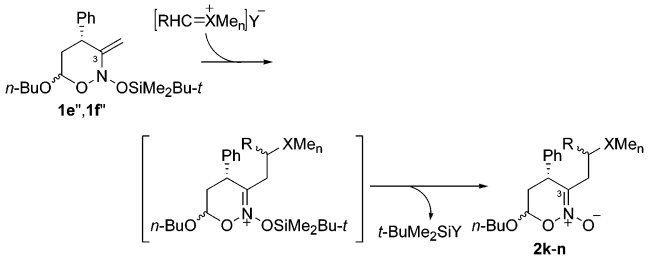


TABLE 3. Interaction of Nitrosals 1 with Electrophiles

entry		R	X	*n*	Y	conditions *T*, °C (*t*, h)	product (yield, %)
1	**1e″**	Ph	O	1	OTf	−78 (6)	**2k** (45)
2	**1f″**	Ph	O	1	OTf	−78 (6)	**2l** (55)
3	**1e″**	4-MeOC$_6$H$_4$	O	1	OTf	−78 (1.5)	**2m** (55)
4	**1e″**	H	N	2	Cl	0 (1)	**2n** (89)

SCHEME 3

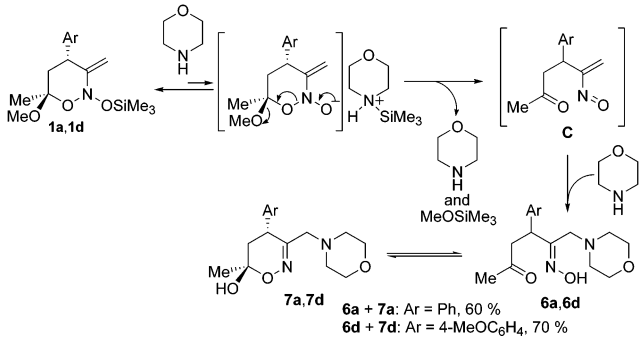


philic *O*- and *N*-stabilized carbocations (Scheme 3, Table 3). These processes afford 1,2-oxazine *N*-oxides **2k**−**n** with a functionalized substituent at C(3) position.

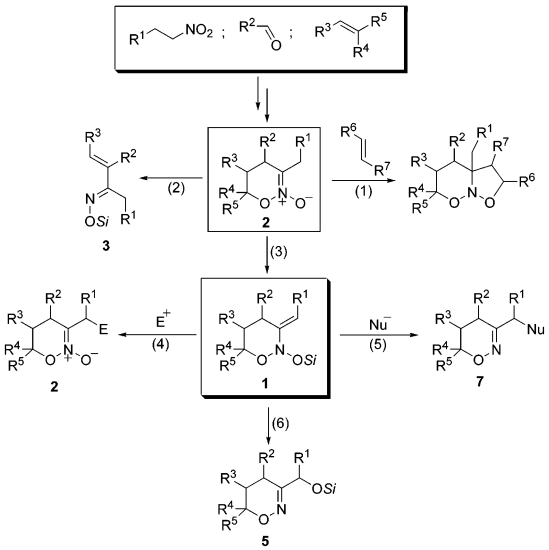
The action of nucleophiles on nitrosals **1** brings about the formation of different products. For example, interaction of compounds **1a** or **1d** with morpholine produces in solution a tautomeric mixture of compounds **6** and **7** (Scheme 4). By analogy with BENA,[10] one can propose that the mechanism of this reaction includes the generation of strongly electrophilic nitroso alkenes **C**, which react with the nucleophilic amine.

(10) Makarenkova, L. M.; Bliznets, I. V.; Ioffe, S. L.; Strelenko, Yu. A.; Tartakovsky, V. A. *Russ. Chem. Bull.* **2000**, *49*, 1261 (English ed.); **2000**, *49*, 1265 (Russian ed.).

SCHEME 4



SCHEME 5



In conclusion, we have developed a method for the transformation of 3-alkyl-1,2-oxazine *N*-oxides **2** into previously unknown 2-silyloxy-1,2-oxazines **1**, a new type of acetals of conjugated nitroso alkenes. This preliminary study of their reactivity demonstrated the promising synthetic potential of these new derivatives.

Moreover, our results have expanded the traditional palette of reactions of cyclic alkyl nitronates **2**, readily available substrates, which are easily built from simple molecules (Scheme 5). Previously the application of 1,2-oxazine *N*-oxides **2** was mainly limited by their involvement in the inter- and intramolecular dipolar cycloadditions [reaction 1].[4,5] At the same time, now we can functionalize the position 3 of nitronates **2** [reactions 3 and 4], synthesize the *Si*-derivatives of conjugated enoximes **3** [reaction 2] and various types of 1,2-oxazines **5** and **7** [reactions 5 and 6]. According to our preliminary results, reactions 3, 5, and 6 can be expected to be highly diastereoselective. Our following publications will contain the convenient protocols as well as scopes and limitations for the transformations of cyclic alkyl nitronates **2**, presented in Scheme 5.

Experimental Section

Typical Procedures for Preparation of Nitroso Acetals 1. (a) *rel*-(4*R*,6*R*)-6-Methoxy-6-methyl-2-trimethylsilyloxy-3-methylene-4-(4-methoxyphenyl)-2,3,5,6-tetrahydro-1,2-oxazine (1a). To a stirred solution of nitronate **2a** (0.27 g,

1 mmol) in CH_2Cl_2 (2 mL) were added at −78 °C NEt_3 (0.17 mL, 1.2 mmol) and Me_3SiBr (0.15 mL, 1.1 mmol). The reaction mixture was stirred for 24 h at −78 °C, diluted with hexane (5 mL), and poured in a mixture of hexane (15 mL) and H_2O (5 mL). The organic layer was washed with a solution of $NaHSO_4 \cdot H_2O$ (0.12 g, 0.87 mmol) in H_2O (6 mL), H_2O (6 mL), and brine (5 mL), treated with activated charcoal, and dried over Na_2SO_4. Solvents were evaporated in a vacuum, and the residue was recrystallized from hexane to give title compound **1a** as colorless prisms (0.23 g, 67%). Mp: 68−70 °C.

(b) *rel*-(4*R*,6*R*)-6-Methoxy-6-methyl-2-(*tert*-butyldimethylsilyloxy)-3-methylene-4-(4-methoxyphenyl)-2,3,5,6-tetrahydro-1,2-oxazine (1a″). To a stirred solution of nitronate **2a** (0.27 g, 1 mmol) in CH_2Cl_2 (2 mL) were added at −78 °C NEt_3 (0.21 mL, 1.5 mmol) and *t*-$BuMe_2SiOTf$ (0.28 mL, 1.2 mmol). The reaction mixture was stirred for 1 h at −78 °C, diluted with hexane (5 mL), and poured in a mixture of hexane (15 mL) and H_2O (5 mL). The organic layer was washed with H_2O (2 × 6 mL) and brine (5 mL), treated with an activated charcoal, and dried over Na_2SO_4. Solvents were evaporated in a vacuum, and the residue was recrystallized from hexane to give title compound **1a″** as colorless prisms (0.27 g, 71%). Mp: 62−65 °C. Analytical data for **1a** and **1a″** are presented in Supporting Information.

Typical Procedure for Preparation of Conjugated Enoximes 4. 2-Phenyl-but-1-en-3-one Oxime (4d). To a stirred solution of nitronate **2d** (0.24 g, 1 mmol) in CH_2Cl_2 (2 mL) were added at − 30 °C pyridine (0.12 mL, 1.5 mmol) and Me_3SiBr (0.16 mL, 1.2 mmol). The reaction mixture was stirred for 24 h at −30 °C, diluted with hexane (5 mL), and poured in a mixture of hexane (15 mL) and H_2O (5 mL). The organic layer was washed with a solution of $NaHSO_4 \cdot H_2O$ (0.35 g, 2.54 mmol) in H_2O (15 mL), H_2O (10 mL), and brine (5 mL), treated with activated charcoal, and dried over Na_2SO_4. Solvents were evaporated in a vacuum, the residue was dissolved in MeOH (5 mL), and NH_4F (5 mg, 0.14 mmol) was added. After being stirred for 3 h, the mixture was filtered though a pad of Celite and evaporated. The residue was recrystallized from EtOAc/hexane mixture to give title compound **4d** as a white crystals (0.12 g, 81%). Mp: 100−101 °C (hexane/EtOAc, 10/1). ^{1}H NMR (300.13 MHz, 300 K, $CDCl_3$): δ 9.30 (br, 1 H), 7.32 (m, 5 H), 5.61 (s, 1 H), 5.43 (s, 1 H), 2.06 (s, 3 H). ^{13}C NMR (75.47 MHz, 300 K, $CDCl_3$): δ 156.8, 146.7, 139.1, 128.3, 128.2, 127.7, 117.8, 12.0. R_f 0.68 (silica gel, hexane/EtOAc, 1/1, UV).

6-Methoxy-6-methyl-4-phenyl-3-(1-trimethylsilyloxyethyl)-5,6-dihydro-4*H*-1,2-oxazine (5). 1,2-Oxazine **1h** (0.32 g, 1 mmol) was maintained for 24 h at room temperature. The resulting title compound **5** was purified by column chromatography on silica gel in hexane/EtOAc 3:1 to give title compound **5** (0.30 g, 92%) as an oil. ^{1}H NMR (300.13 MHz, 300 K, $CDCl_3$): δ 7.35−7.15 (m, 5 H), 4.29 (q, J = 5.8,1 H), 3.84 (dd, J = 8.1, 12.5, 1 H), 3.31 (s, 3 H), 2.29 (dd, J = 13.1, 8.1, 1 H), 1.88 (dd, J = 13.1, 12.5, 1 H), 1.44 (s, 3 H), 1.33 (d, J = 5.8, 3 H), 0.12 (s, 9 H). ^{13}C NMR (75.47 MHz, 300 K, $CDCl_3$): δ 162.5, 141.3, 128.9, 128.8, 126.9, 96.4, 68.6, 49.6, 40.6, 36.6, 21.7, 20.7, 0.3. ^{29}Si NMR (59.63 MHz, 300 K, $CDCl_3$): δ 17.09. R_f 0.71 [hexane/EtOAc 3:1].

Typical Procedure for Reactions of Compounds 1 with Acetals. *rel*-(4*R*,6*R*)-6-Butoxy-3-(2-methoxy-2-phenyl-ethyl)-4-phenyl-5,6-dihydro-4*H*-1,2-oxazine *N*-Oxide (2k). To a cold (−78 °C) solution of pyridine (3 μL, 0.037 mmol) in CH_2Cl_2 (0.7 mL) were added successively Me_3SiOTf (0.15 mL, 0.799 mmol) and a solution of benzaldehyde dimethyl acetal (0.122 g, 0.803 mmol) in CH_2Cl_2 (0.7 mL). Then a solution of nitrosal **1e″** (0.25 g, 0.66 mmol) in CH_2Cl_2 (1.3 mL) was added dropwise. The resultant mixture was stirred at −78 °C for 6 h, and a solution of $BnEt_3NCl$ (0.27 g, 1.187 mmol) in CH_2Cl_2 (2 mL) followed by Et_3N (0.26 mL, 1.871 mmol) were added successively. After 5 min of stirring the mixture was poured into a mixture of H_2O (20 mL) and ether, the organic layer was separated, and the aqueous phase was diluted with brine (5 mL) and back-extracted with ether (2 × 10 mL). The combined organic layers were washed with H_2O (15 mL), saturated aqueous NH_4Cl solution (10 mL), H_2O (15 mL), saturated aqueous $NaHCO_3$ solution (10 mL), H_2O (15 mL), and brine (10 mL) and dried over Na_2SO_4. The solvents were evaporated in a vacuum, and the yellow residue was separated on preparative MPLC (Rexchrom 5/100 silica, 25 cm × 21.1 mm, flow rate 15 mL/min, eluent hexane/*i*-PrOH 1:30). The upper product was distilled and recrystallized to give the major isomer of the title compound **2k** (0.08 g, 30%), and the lower product was recrystallized (Et_2O/hexane) to give the minor isomer of the title compound **2k** (0.03 g, 15%) of white crystals. Analytical data for both isomers are in Supporting Information.

***rel*-(4*R*,6*R*)-6-Butoxy-3-(2-(dimethylamino)-ethyl)-4-phenyl-5,6-dihydro-4*H*-1,2-oxazine *N*-Oxide (2n).** To a cold (0 °C) solution of nitrosal **1e″** (0.38 g, 1.01 mmol) in CH_2Cl_2 (2 mL) was added solid methylenedimethylammonium chloride (0.19 g, 2.03 mmol). The mixture was allowed to warm to 20 °C in 1 h with stirring and poured into a mixture of Et_2O (20 mL) and H_2O (10 mL). The organic layer was separated, and the water phase was back-extracted with Et_2O (3 × 15 mL). The combined organic layers were washed with H_2O (15 mL), saturated aqueous solution of $NaHCO_3$ (10 mL), H_2O (15 mL), and brine (10 mL), dried over Na_2SO_4, and evaporated in a vacuum. The residue was recrystallized from hexane to give title compound **2n** as white crystals (0.29 g, 89%). Mp: 40−42 °C (hexane). ^{1}H NMR (500 MHz, 300 K, $CDCl_3$): δ 7.34 (tt, J = 1.3, 6.9, 2 H), 7.28 (tt, J = 1.3, 6.0, 1 H), 7.21 (dt, J = 2.1, 7.1, 2 H), 5.33 (t, J = 2.6, 1 H), 4.00 (dt, J = 6.6, 9.4, 1 H), 3.96 (dd, J = 7.7, 11.2, 1 H), 3.64 (dt, J = 6.4, 9.4, 1 H), 2.62−2.53 (m, 2 H), 2.29−2.21 (m, 2 H), 2.16−2.06 (m, 8 H), 1.65−1.58 (m, 2 H), 1.43−1.38 (m, 2 H), 0.94 (t, J = 7.5, 3 H). ^{13}C NMR (126 MHz, 300 K, $CDCl_3$): δ 140.5, 129.5, 128.5, 128.0, 125.8, 101.5, 69.3, 53.9, 45.4, 40.4, 34.8, 31.7, 29.1, 19.5, 14.1. R_f 0.28 [silica gel, Et_2O/*i*-PrOH, 2/1, anisaldehyde].

6-Methyl-3-morpholin-4-ylmethyl-4-phenyl-5,6-dihydro-4*H*-1,2-oxazin-6-ol (6a) and 1-Morpholin-4-yl-3-phenyl-hexane-2,5-dione 2-Oxime (7a). To a solution of nitrosal **1d** (0.31 g, 1 mmol) in CH_2Cl_2 (1 mL) was added simultaneously at ambient temperature morpholine (0.13 mL, 1.5 mmol). The reaction mixture was stirred for 5 min, and CH_2Cl_2 was carefully evaporated at 300 mmHg. The resulting solution was maintained at ambient temperature for 24 h, diluted with MeOH (3 mL), and after 3 h of stirring evaporated in a vacuum. The residue was recrystallized from a mixture of EtOAc and hexane 1:10 to give a mixture of title compounds **6a** and **7a** (0.18 g, 60%) as white powder. The ratio of tautomers **6a** and **7a** in DMSO is 1:1 at 20 °C and 1:3 at 70 °C. Mp: 99−103 °C (hexane/EtOAc, 10:1). **6a**: ^{1}H NMR (300.13 MHz, 300 K, DMSO-d_6): δ 7.4−7.2 (m, 5 H), 6.44 (s, 1 H), 3.79 (dd, J = 5.2, 12.5, 1 H), 3.56 (m, 4 H), 2.80 (d, J = 12.3, 1 H), 2.56 (d, J = 12.3, 1 H), 2.4−2.0 (m, 5 H), 1.89 (dd, J = 12.4, 12.5, 1 H), 1.49 (s, 3 H). ^{13}C NMR (75.47 MHz, 300 K, DMSO-d_6): δ 156.6, 140.6, 128.5, 128.1, 126.6, 94.6, 66.2, 59.7, 52.6, 37.9, 37.0, 26.8. **7a**: ^{1}H NMR (300.13 MHz, 300 K, DMSO-d_6): δ 10.81 (s, 1 H), 7.4−7.2 (m, 5 H), 4.79 (dd, J = 7.8, 7.3, 1 H), 3.51 (m, 4 H), 3.28 (dd, J = 7.8, 17.1, 1 H), 3.05 (dd, J = 7.3, 17.1, 1 H), 2.93 (d, J = 12.5, 1 H), 2.69 (d, J = 12.5, 1 H), 2.4−2.0 (m, 4 H), 2.12 (s, 3 H). ^{13}C NMR (75.47 MHz, 300 K, DMSO-d_6): δ 205.8, 154.7, 140.7, 128.4, 127.9, 126.1, 66.0, 59.7, 53.0, 44.6, 37.6, 29.8. For both: R_f 0.11 (silica gel, EtOAc, UV).

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Supporting Information Available: Full experimental procedures, analytical data for all compounds, CIF files and complete crystal structure data for **1a** and **2a**; general procedure for measurement of $\Delta\Delta G^{\ddagger}$ by dynamic NMR; rate constants and activation parameters of dynamic process **1a**−**d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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