Reversal of Regioselectivity of Nitrone Cycloadditions by *Lewis* Acids

by **Branislav Dugovič**[a]), **Lubor Fišera***[a]), **Michal K. Cyranski**[b]), **Christian Hametner**[c]), **Nada Prónayová**[d]), and **Marián Obranec**[a])

[a]) Department of Organic Chemistry, Slovak University of Technology, SK-812 37 Bratislava, Slovak Republic (phone: +42-1529-68560; fax: +42-1529-68560; e-mail: lubor.fisera@stuba.sk)

[b]) Department of Chemistry, University Warsaw, PL-02 093 Warsaw

[c]) Institute of Applied Synthetic Chemistry, University of Technology, A-1060 Vienna

[d]) Central Laboratory of Chemical Techniques, Slovak University of Technology, SK-812 37 Bratislava

This paper is dedicated to Professor *Rolf Huisgen* on the occasion of his 85th birthday

The regio- and stereoselectivity of cycloadditions of the nitrone **1a** and the chiral, sugar-derived nitrones **13a** and **13b** with 3-(prop-2-enoyl)-1,3-oxazolidin-2-one (**2**) depends on the nature of the *Lewis* acid catalyst used. Addition of *Lewis* acid reverses the regioselectivity of the cycloaddition, and improves the *anti*-diastereoselectivity in the case of chiral nitrones. The sterically favored isoxazolidin-5-yl-substituted adducts **3**, **4**, and **14**–**17** are produced as the major products in the absence of *Lewis* acid, while the electronically favored regioisomers with isoxazolidin-4-yl substituents (**5**, **6**, and **18**–**21**, respectively) are obtained as major products in the $[Ti(O^iPr)_2Cl_2]$ catalyzed reactions. The reactions of nitrone **13b** with **2** in the presence of other *Lewis* acids such as $ZnCl_2$, $ZnBr_2$, ZnI_2 and MgI_2/I_2 gave both regioisomeric pairs of the diastereoisomers, favoring the 4-substituted congeners. The diastereoisomeric isoxazolidines **3a**–**6a** were reduced with $NaBH_4$ in THF/H_2O with subsequent desilylation to yield the separable diols **9**–**12**. Reduction of the diastereoisomeric isoxazolidines **19a** and **18a** afforded the chiral alcohols **23** and **22**, the latter of which was analyzed by X-ray crystallography.

Introduction. – Over the years, nitrones have become important building blocks in organic synthesis. The nitrone–olefin 1,3-dipolar cycloaddition is a powerful reaction in that it can create as many as three new contiguous stereogenic centers in a single step [1]. Based on an evaluation of the nitrone cycloaddition, it was felt that the configuration of these new centers could be controlled if the reaction system were properly designed [2][3]. Regio- and stereoselective nitrone cycloaddition, followed by reduction of the NO bond to produce both an amino and a hydroxy function, allows the synthesis of many products of potential interest [4].

Lewis acids are often used as catalysts in 1,3-dipolar cycloadditions of nitrones [5], but strong binding of nitrones to the catalyst in the cycloadditions to electron-deficient alkenes is a serious problem, as the dipoles have a tendency to form inactive 1,3-dipole–*Lewis* acid complexes. To overcome this difficulty, bidentate dipolarophiles such as 3-(alk-2-enoyl)oxazolidin-2-ones have been used to secure the tight coordination of acceptors to the catalyst [5]. Recently, we have described that the addition of $[Ti(O^iPr)_2Cl_2]$ reverses the regioselectivity of cycloaddition of *N*-benzyl-*N*-[2-(benzyloxy)ethylidene]amine oxide (**1b**) with 3-prop-2-enoyl-1,3-oxazolidin-2-one (**2**; see *Table 1* below) [6].

In continuing our efforts to use 1,3-dipolar cycloadditions in (stereoselective) synthesis [7], and as an extension of our recent work [6], we herein report the effect of

the addition of *Lewis* acids on the regio- and stereoselectivity of cycloadditions between compound **2** and different nitrones such as **1a** and sugar-based analogues thereof.

Results and Discussion. – The application of a properly substituted nitrone in a 1,3-dipolar-cycloaddition strategy towards natural products is of interest because debenzylation/desilylation leads to the introduction of NH_2 and $HOCH_2$ functions in the molecule. We, thus, first investigated the cycloaddition of the sterically hindered nitrone **1a** with the 1,3-oxazolidin based olefin **2** (*Table 1*). Nitrone **1a** reacted smoothly with **2** in CH_2Cl_2 at ambient temperature within 28 h to afford a 75:25 mixture of the diastereoisomeric isoxazolidines **3a** and **4a** in 59% yield. The cycloaddition was found to be completely regioselective, with only the sterically favored 5-substituted[1]) compounds being detected (*Table 1*, *Entries 1* and *2*).When the reaction was performed in the presence of $[Ti(O^iPr)_2Cl_2]$, a slightly lower total yield was observed compared with the uncatalyzed reaction, but the regioselectivity was completely reversed (exclusive formation of the 4-substituted regioisomers **5a** and **6b**), the corresponding diastereoselectivity being unchanged (*Entry 3*). In the catalyzed reaction, the nitrone O-atom selectively attacks the β-C-atom of the α,β-unsaturated moiety of **2**. Moreover, the observed selectivity for nitrone **1a** was even better than that for the doubly benzyl substituted analogue **1b** (*Entries 4* and *5*) [6].

When the catalyzed reaction was carried out at ambient temperature for 19 h, beside the mixture **5a**/**6a** (57%), we also isolated the i-Pr esters **7a** and **8a** as side products in 7 and 11% yield, respectively.

Unfortunately, the chromatographic separation and, thus, unequivocal characterization of the 4- and 5-substituted, isomeric adducts **3a**–**6a** was not possible. Therefore, the inseparable product mixtures were reduced with $NaBH_4$ in THF/H_2O, followed by desilylation with Bu_4NF (TBAF) in THF, to yield the well-separable diols **9**–**12** (*Scheme 1*). The latter could be readily characterized spectroscopically. Based on ^{1}H-NOE experiments targeted at H–C(3), H–C(4), and H–C(5), we assigned the *trans* configuration to the major isomers **9** and **11**, respectively.

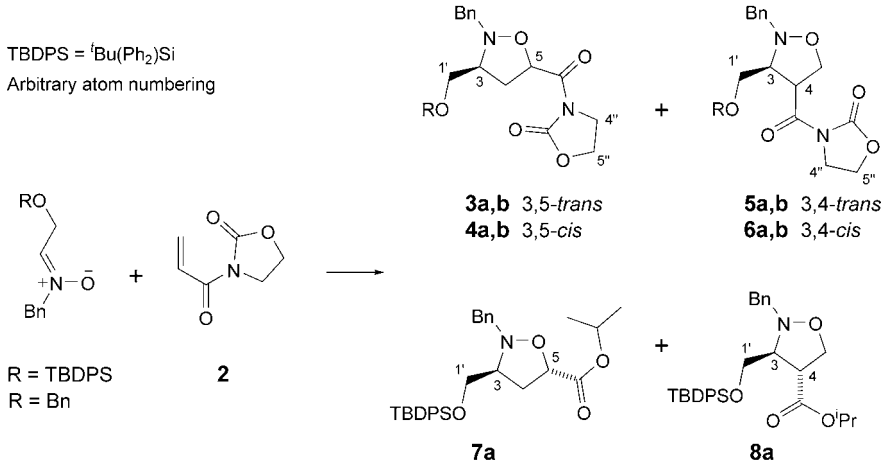
As mentioned previously, in the case of nitrones **1a** and **1b**, *Lewis* acids favor the electronically controlled formation of 4-substituted cycloadducts. Therefore, we next investigated the catalytic effects of *Lewis* acids on the regio- and diastereoselectivity of 1,3-dipolar cycloadditions of the chiral, sugar-derived nitrones **13** with substrate **2** (*Scheme 2*). The results are summarized in *Table 2*. Note that the reaction between **2** and **13** can, in principle, give rise to four isomers of *anti*,*trans*, *syn*,*trans*, *anti*,*cis*, and *syn*,*cis* configuration with respect to the 3,4′- and the 3,5-positions[1]), respectively.

Nitrone **13a** reacted very slowly with **2** at ambient temperature to afford a 98:2 regioisomeric mixture of five diastereoisomeric isoxazolidines (**14a**–**17a** and **20a**) in 86% overall yield after 14 d (*Table 2*, *Entry 1*). The major *anti*,*trans*-adduct **14a** could be isolated by flash chromatography. Addition of $Mg(ClO_4)_2 \cdot Et_3N$ not only changed the regioselectivity, but also improved the *anti*-diastereoselectivity (*Entries 1 vs.* 6). The highest rate acceleration was achieved in the reaction with $[Ti(O^iPr)_2Cl_2]$, where the regioselectivity observed in the thermal reaction was completely reversed from

---

[1]) Arbitrary atom numbering. For systematic compound names, see *Exper. Part.*

Table 1. 1,3-Dipolar Cycloadditions of **1a** and **1b** with Alkene **2**



Entry	Nitrone	Conditions	*Lewis* acid	Yield [%][a]	Regio-selectivity [b]		Diastereo-selectivity [b]			
					3+**4**	**5**+**6**	**3**	**4**	**5**	**6**
1	**1a**	CH_2Cl_2, r.t., 28 h	–	59	100	n.d.[c]	75	25	n.d.	n.d.
2	**1a**	PhMe, reflux, 2.5 h	–	55	100	n.d.	74	26	n.d.	n.d.
3	**1a**	CH_2Cl_2, −10 to 0°, 48 h	$[Ti(O^iPr)_2Cl_2]$ (1.1 equiv.)	54	n.d.	100	n.d.	n.d.	77	23
4	**1b**	CH_2Cl_2, r.t., 2 d	–	84	96	4	70	30	100	n.d.
5	**1b**	CH_2Cl_2, −10°, 5 h	$[Ti(O^iPr)_2Cl_2]$ (1.0 equiv.)	60	2	98	100	n.d.	59	41

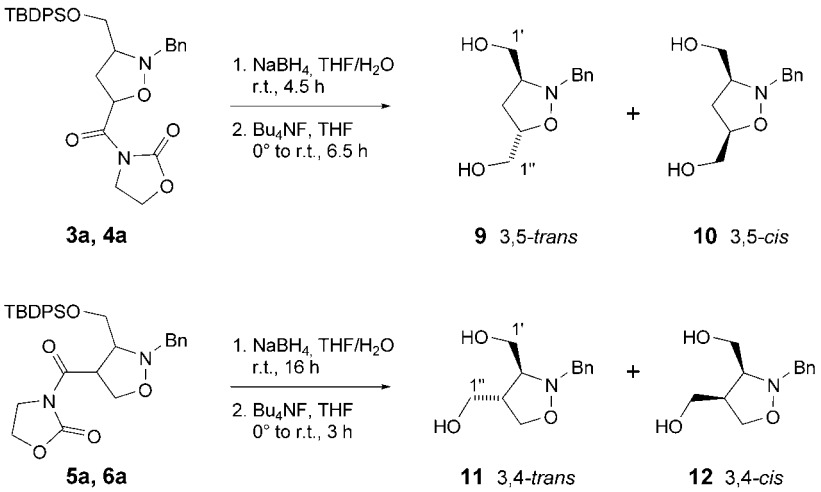
[a]) Total yield of isolated mixture of **3**–**6**. [b]) Ratio based on ^{13}C-NMR integration of the C(5) signals[1]). [c]) Not detected in the NMR spectrum of the crude product mixture.

98:2 to 6:94 (*Entries 1 vs. 7*). Moreover, the reaction in the presence of $[Ti(O^iPr)_2(OTs)_2]$[2]) as catalyst proceeded in a regioselective manner to give a mixture of the four diastereoisomeric, 4-substituted isoxazolidines **18a**–**21a** (*Entry 8*). This clearly is the first example of the reversal of the regioselectivity of a 1,3-dipolar cycloaddition caused by a *Lewis* acid in the case of chiral nitrones.

The chromatographic separation and characterization of the 4-substituted cycloadducts **18a**–**21a** was, again, impossible. Therefore, the product mixtures were reduced directly with $NaBH_4$ in THF/H_2O to yield the separable, chiral primary alcohols **22** and **23** (*Scheme 3*). The different isomers were assigned by straightforward analysis of the diagnostic ^{1}H-NMR chemical shifts of the isoxazolidine ring H-atoms. The ratio of the diastereoisomers was determined from quantitative ^{13}C-NMR integration of the isoxazolidine C(4) resonances. The structure of the separated major isomer **22** was unambiguously assigned 3,4-*trans*-configuration by means of a detailed NMR analysis, including 2D experiments. Finally, the relative 3,4′-*anti*-configuration of **22** was

[2]) Ts = Tosyl (= 4-methylbenzenesulfonyl).

Scheme 1



elucidated by X-ray crystal-structure analysis (*Figure*), which, at the same time, corroborated the suggested *trans* relationship between H–C(3) and H–C(4) for the major isomers **18a**. That compound **14a** has the same configuration as **18a** was inferred from the above diagnostic signals, NOEDS results, as well as by comparison with literature data of the cycloaddition of nitrone **13a** with methyl acrylate obtained by *Merino et al.* [8].

As shown in *Table 2* (*Entries 2–5*), the cycloaddition of the dipolarophile **2** with the chiral nitrone **13b** proceeded, in the absence of catalyst, completely regioselectively, providing a mixture of four diastereoisomers (**14b–17b**), with **14b** being the major adduct. When the reaction was performed in the presence of ZnI_2 as catalyst, the regioselectivity was changed, and the *anti*-diastereoselectivity was improved (*Entry 9*). Additionally, other *Lewis* acids such as $ZnCl_2$, $ZnBr_2$, or MgI_2/I_2 were also found to be efficient and to reverse the regioselectivity of this reaction compared with the noncatalyzed one (*Entries 10*, *11*, and *13*). However, $MgBr_2 \cdot OEt_2$ was found not to be efficient in this reaction, affording an inseparable mixture of decomposition products.

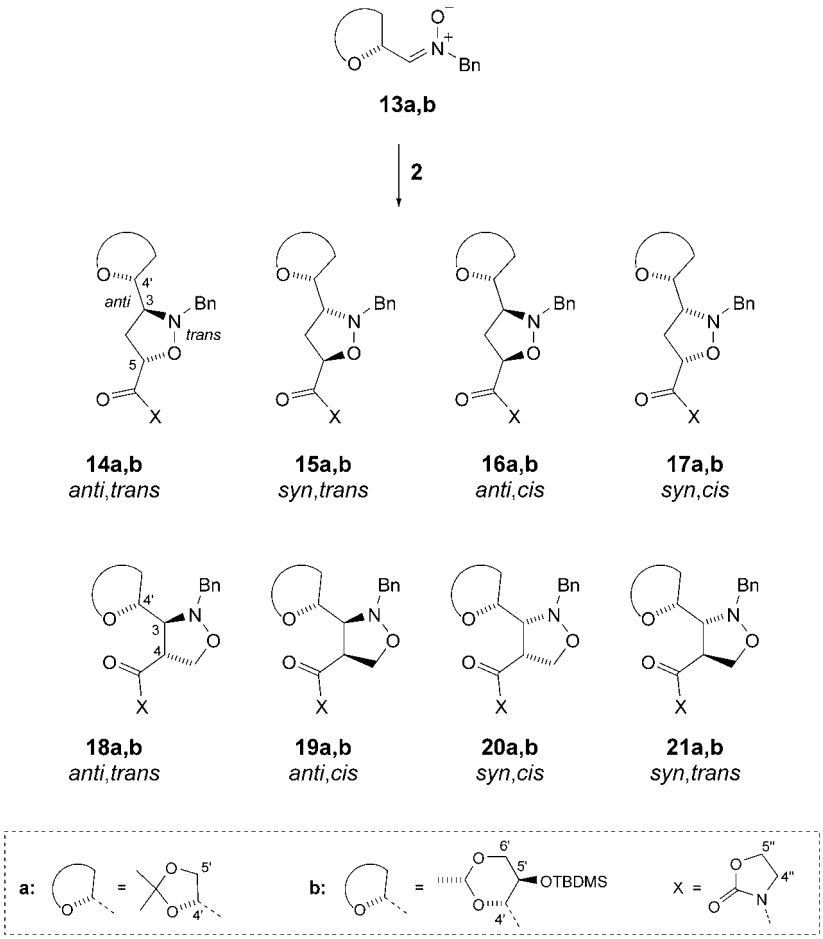
The highest rate acceleration was achieved with $[Ti(O^iPr)_2Cl_2]$, where the regioselectivity observed in the thermal reaction was reversed (*Table 2*, *Entry 14*). Purification by flash chromatography allowed the isolation of the pure adducts **14b** and **16b**, while the chromatographic separation of the isoxazolidines **15b** and **17b** was not possible. The structures and configurations of **14b–17b** were determined by ^{1}H-NMR, ^{13}C-NMR, 2D-COSY, C,H-HETCOR, and NOESY experiments. While the configuration at C(3)/C(5) and C(3)/C(4), respectively, was confirmed by NOE measurement of the cycloadducts, assignment of the relationship between stereogenic centers at C(3) and C(4′) was based on our previous results from 1,3-dipolar cycloadditions of sugar nitrones bearing a free as well as a protected OH group in α-position [7a–f], and on comparison with isoxazolidine **22**, whose structure was determined by X-ray analysis (see *Figure*).

Table 2. *1,3-Dipolar Cycloadditions of the Chiral Nitrones* **13a** *and* **13b** *with Alkene* **2**. Isomer ratios were determined by NMR integration; values of 'zero', thus, mean that this specific isomer was not detected.

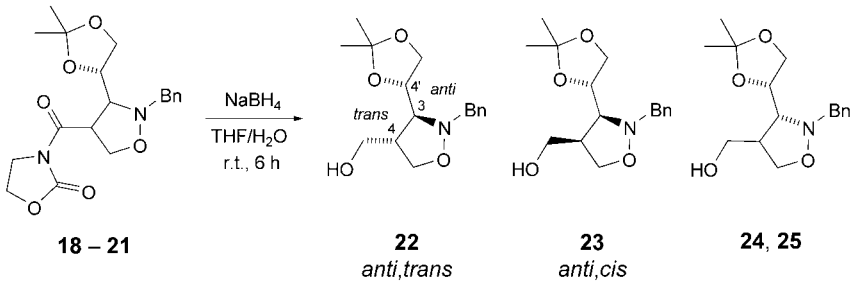
Entry	Nitrone	*Lewis* acid	Conditions	Yield [%][a])	Regioselectivity[b])	Diastereoselectivity[b])					
					(**14**–**17**)/(**18**–**21**)	**14/15/16/17**	*trans*/*cis*	*anti*/*syn*	**18/19/20/21**	*trans*/*cis*	*anti*/*syn*
1	**13a**	–	CH_2Cl_2, r.t., 14 d	86	98 : 2	46 : 16 : 22 : 16	62 : 38	68 : 32	0 : 0 : 100 : 0	0 : 100	0 : 100
2		–	CH_2Cl_2, r.t., 14 d	56	100 : 0	44 : 28 : 17 : 11	72 : 28	61 : 39	–	–	–
3		–	THF, r.t., 4 d	75	100 : 0	50 : 26 : 15 : 9	76 : 24	65 : 35	–	–	–
4		–	CCl_4, reflux, 7 h	78	100 : 0	50 : 32 : 14 : 4	82 : 18	64 : 36	–	–	–
5		–	PhMe, reflux, 6 h	83	100 : 0	51 : 36 : 13 : 0	87 : 13	64 : 36	–	–	–
6		$Mg(ClO_4)_2 \cdot Et_3N$ (0.1 equiv.)	CH_2Cl_2, r.t., 24 h	88	53 : 47	58 : 13 : 22 : 7	71 : 29	80 : 20	59 : 28 : 0 : 13	72 : 28	87 : 13
7		$[Ti(O^iPr)_2Cl_2]$ (1.1 equiv.)	CH_2Cl_2, −15 to 0°, 5 h	51	6 : 94	56: 0 : 44 : 0	56 : 44	100 : 0	53 : 40 : 3 : 4	57 : 43	93 : 7
8		$[Ti(O^iPr)_2(OTs)_2]$ (1.1 equiv.)	CH_2Cl_2, −20°, 12 d	n.d.[c])	0 : 100	–	–	–	40 : 39 : 4 : 17	57 : 43	79 : 21
9	**13b**	ZnI_2 (1.0 equiv.)	CH_2Cl_2, r.t., 20 d	51	18 : 82	100 : 0 : 0 : 0	100 : 0	100 : 0	30 : 45 : 0 : 25	55 : 45	75 : 25
10		$ZnCl_2$ (1.0 equiv.)	CH_2Cl_2, r.t., 20 d	80	44 : 56	61 : 28 : 0 : 11	89 : 11	61 : 39	31 : 45 : 0 : 24	55 : 45	76 : 24
11		$ZnBr_2$ (1.0 equiv.)	CH_2Cl_2, r.t., 20 d	57	22 : 78	77 : 23 : 0 : 0	100 : 0	77 : 23	28 : 72 : 0 : 0	28 : 72	100 : 0
12		$ZnBr_2$ (1.0 equiv.)	THF, r.t., 4d	53	100 : 0	50 : 27 : 15 : 8	77 : 23	65 : 35	–	–	–
13		MgI_2/I_2 (1.0 equiv.)	CH_2Cl_2, r.t., 12 d	69	46 : 54	66 : 34 : 0 : 0	100 : 0	66 : 34	100 : 0 : 0 : 0	100 : 0	100 : 0
14		$[Ti(O^iPr)_2Cl_2]$ (1.1 equiv.)	CH_2Cl_2, −15 to 0°, 21 h	82	22 : 78	43 : 24 : 33 : 0	67 : 33	76 : 24	69 : 0 : 0 : 31	100 : 0	69 : 31

[a]) Total yield of isolated mixture of **14**–**21**. [b]) Ratio based on ^{13}C-NMR integration of the C(4) signals[1]). [c]) Not determined.

Scheme 2



Scheme 3



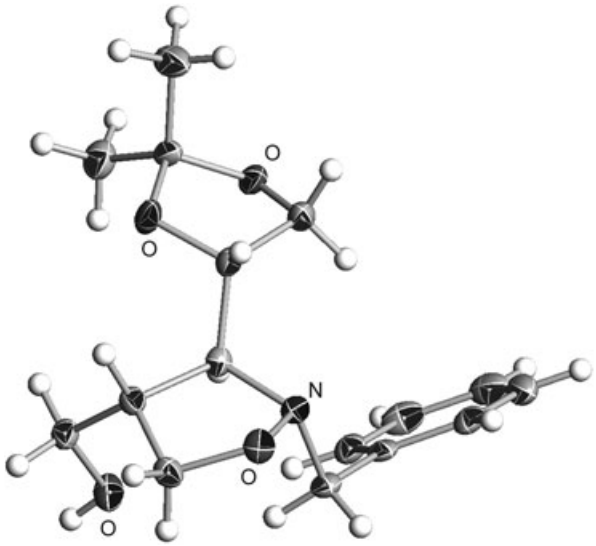


Figure. *X-Ray crystal structure of compound* **22**

Conclusions. – The regio- and stereoselectivity of cycloadditions of nitrone **1a** and chiral, sugar-derived nitrones **13a** and **13b** with alkene **2** depends on the nature of the *Lewis* acid catalyst. Addition of catalyst reverses the regioselectivity of the cycloaddition, and improves the *anti*-diastereoselectivity in the case of chiral nitrones. The sterically favored isoxazolidin-5-yl substituted oxazolidinones **3**, **4**, and **14**–**17** are formed as the major products in the absence of *Lewis* acids, while the electronically favored 4-congeners **5**, **6**, and **18**–**21**, respectively, are the dominant products in the $[Ti(O^iPr)_2Cl_2]$ catalyzed reactions. The reactions of nitrone **13b** with **2** in the presence of other *Lewis* acids such as $ZnCl_2$, $ZnBr_2$, ZnI_2 and MgI_2/I_2 afforded both regioisomeric pairs of diastereoisomers, favoring the 4-substituted adducts. The inseparable diastereoisomeric isoxazolidines **3a**–**6a** were reduced and desilylated to yield the separable diols **9**–**12**. Similarly, reduction of **18a** and **19a** gave the chiral alcohols **22** and **23**.

The authors are grateful to the *Slovak Grant Agency* (No. 1/0057/03).

Experimental Part

General. All commercially available starting materials and reagents (*Fluka*, *Merck*, *Acros*, *Avocado,* or *Aldrich*) were used without further purification. Solvents were dried before use. Nitrones **1a**, **1b**, **13a**, and **13b** were prepared from the corresponding aldehydes by reaction with *N*-(benzyl)hydroxylamine according to a procedure described earlier [7d–f][9]. The *Lewis* acid catalysts $ZnCl_2$, $ZnBr_2$, ZnI_2, and $Mg(ClO_4)_2$ are commercially available. The catalysts $MgBr_2 \cdot OEt_2$, MgI_2/I_2, $[Ti(O^iPr)_2Cl_2]$, and $[Ti(O^iPr)_2(OTs)_2]$ were freshly prepared prior to use. Thin-layer chromatography (TLC; *ALUGRAM Sil G/UV$_{254}$* from *Macherey-Nagel*) was used to monitor the course of the reactions. For flash chromatography (FC), *Silica Gel 60* (0.040–0.063 mm; *Merck*) was used. Melting points (m.p.) were determined on a *Kofler* hot-plate apparatus; uncorrected. Optical rotations $[\alpha]_D$ were measured on an *Polar-LμP* polarimeter (*IBZ Messtechnik*) in a 10-cm cell. IR Spectra were recorded on a *NICOLET MAGNA-750* FT-IR instrument; in cm^{-1}. ^1H- and ^{13}C-NMR Spectra were recorded on

Bruker DRX-400 (400/100 MHz) or *Varian VXR-300* (300/75 MHz) instruments in $CDCl_3$; chemical shifts δ in ppm rel. to Me_4Si, coupling constants J in Hz. Elemental analyses were conducted with a *Thermo FlashEA-1112* apparatus.

Noncatalyzed Cycloadditions: General Procedure (*GP 1*). A soln. of **2** and the appropriate nitrone was stirred until complete consumption of the nitrone. The solvent was removed *in vacuo* (rotary evaporator), and the residue was purified by FC. Further exper. details and yields of isolated mixtures of cycloadducts are given in *Tables 1* and *2*.

Lewis *Acid Catalyzed Cycloadditions: General Procedure* (*GP 2*). All reactions were carried out under Ar atmosphere. Alkene **2** was added at r.t. to a stirred soln. of the *Lewis* acid in CH_2Cl_2, and the mixture was stirred for 15 min. A CH_2Cl_2 soln. of the nitrone (**1** or **13**) was then added in one portion. For details, see *Tables 1* and *2*. The mixture was stirred until complete consumption of the nitrone, quenched with sat. aq. NH_4Cl soln., and extracted with CH_2Cl_2. The combined org. layers were washed with brine, dried (Na_2SO_4), filtered through *Celite*, and evaporated *in vacuo* (rotary evaporator). The resulting residue was purified by FC. Further exper. details and yields of isolated mixtures of cycloadducts are given in *Tables 1* and *2*.

Noncatalyzed Reaction of **1a** *with* **2**. According to *GP 1*, with **1a** (0.100 g, 0.25 mmol) and **2** (0.035 g, 0.25 mmol) in toluene (5 ml) at r.t., followed by FC (SiO_2 (12 g); 12.5 × 2 cm; CH_2Cl_2/AcOEt/hexanes 40:10:50): inseparable mixture (0.079 g, 59%) of **3a**/**4a** (*ca.* 75:25). The diastereoisomeric ratio was determined by means of quant. ^{13}C-NMR integration of the C(4) resonances at δ(C) 35.8 (**3a**) and 35.6 (**4a**) of the isoxazolidine moieties.

Reduction and Desilylation of **3a**/**4a**. A soln. of the above mixture **3a**/**4a** (0.121 g, 0.22 mmol) in THF/H_2O 3:1 (4 ml) was stirred at r.t. with $NaBH_4$ (0.018 g, 0.47 mmol) for 6 h. The reaction was quenched with sat. aq. NH_4Cl soln. The mixture was extracted with CH_2Cl_2, the org. layer was dried (Na_2SO_4) and evaporated. The resulting residue was dissolved in THF (2 ml), and Bu_4NF (0.061 g, 0.23 mmol) in THF (1 ml) was added dropwise at 0°. The temp. was gradually increased to r.t. over 3 h with stirring. Then, sat. aq. $NaHCO_3$ soln. was added, the mixture was extracted with CH_2Cl_2, the org. layer was dried (Na_2SO_4) and evaporated. The crude was purified by FC (SiO_2 (13 g); 13.5 × 2 cm; CH_2Cl_2/MeOH 98:2) gave pure **10** (0.010 g, 20%), a mixture of **9**/**10** (0.017 g, 35%), and pure **9** (0.017 g, 35%).

trans-*2-(Phenylmethyl)isoxazolidine-3,5-dimethanol* (**9**). Colorless oil. R_f (CH_2Cl_2/MeOH 94:6) 0.16. IR (film): 3384, 3087, 3063, 3030, 2928, 2875, 1496, 1454, 1387, 1342, 1288, 1041. ^{1}H-NMR (400 MHz, $CDCl_3$)[1]): 7.42–7.29 (*m*, Ph); 4.21 (*dddd*, *J* = 8.0, 8.0, 5.0, 3.2, H–C(5)); 4.11 (*d*, *J* = 13.4, 1 H of PhCH_2); 4.06 (*d*, *J* = 13.4, 1 H of PhCH_2); 3.78 (*dd*, *J* = 12.1, 3.2, H_a–C(1″)); 3.59 (*dd*, *J* = 12.1, 5.1, H_b–C(1″)); 3.57–3.56 (*m*, CH_2(1′)); 3.29–3.23 (*m*, H–C(3)); 2.56 (br., 2 OH); 2.30 (*ddd*, *J* = 12.4, 8.3, 8.3, H_a–C(4)); 2.18 (*ddd*, *J* = 12.4, 7.7, 4.7, H_b–C(4)). ^{13}C-NMR (100 MHz, $CDCl_3$)[1]): 136.3, 129.2, 128.5, 127.7 (Ph); 79.1 (C(5)); 66.3 (C(3)); 63.7 (C(1″)); 62.2 (C(1′)); 62.1 (PhCH_2); 32.3 (C(4)). Anal. calc. for $C_{12}H_{17}NO_3$ (223.27): C 64.55, H 7.67, N 6.27; found: C 64.26, H 7.38, N 6.41.

cis-*2-(Phenylmethyl)isoxazolidine-3,5-dimethanol* (**10**). Colorless oil. R_f (CH_2Cl_2/MeOH 94:6) 0.18. IR (film): 3388, 3063, 3030, 2928, 2874, 1496, 1455, 1380, 1286, 1045. ^{1}H-NMR (400 MHz, $CDCl_3$)[1]): 7.41–7.32 (*m*, Ph); 4.48–4.22 (*m*, H–C(5)); 4.14 (*d*, *J* = 13.1, 1 H of PhCH_2); 3.98 (*d*, *J* = 13.1, 1 H of PhCH_2); 3.82 (*dd*, *J* = 12.2, 2.7, H_a–C(1″)); 3.64 (*dd*, *J* = 12.4, 4.9, H_b–C(1″)); 3.61 (*dd*, *J* = 11.3, 7.6, H_a–C(1′)); 3.53 (*dd*, *J* = 11.4, 4.2, H_b–C(1′)); 3.42–3.35 (*m*, H–C(3)); 2.63 (br., 2 OH); 2.51 (*ddd*, *J* = 12.7, 8.5, 8.5, H_a–C(4)); 1.98 (*ddd*, *J* = 12.0, 6.9, 4.8, H_b–C(4)). ^{13}C-NMR (100 MHz, $CDCl_3$)[1]): 135.9, 129.3, 128.6, 127.9 (Ph); 77.7 (C(5)); 66.5 (C(3)); 63.2 (C(1′), C(1″)); 60.9 (PhCH_2); 31.5 (C(4)). Anal. calc. for $C_{12}H_{17}NO_3$ (223.27): C 64.55, H 7.67, N 6.27; found: C 64.52, H 8.14, N 6.63.

Catalyzed Cycloaddition of **1a** *with* **2**. According to *GP 2*, with **1a** (0.245 g, 0.61 mmol), a 0.5M CH_2Cl_2 soln. of [Ti(O^{i}Pr)$_2$Cl$_2$] (1.3 ml, 0.65 mmol), and **2** (0.094 g, 0.67 mmol) in CH_2Cl_2 (7 ml). FC (SiO_2 (30 g); 13.5 × 3 cm; AcOEt/hexanes 30:70) gave an inseparable mixture (0.180 g, 54%) of **5a**/**6a** (*ca.* 75:25). The diastereoisomer ratio was determined by quant. ^{13}C-NMR integration of C(4) at δ(C) 51.5 (**5a**) and 51.0 (**6a**) of the isoxazolidine moieties.

Reduction and Desilylation of **5a**/**6a**. A soln. of the above mixture **5a**/**6a** (0.180 g, 0.33 mmol) in THF/H_2O 3:1 (4 ml) was stirred at r.t. with $NaBH_4$ (0.025 g, 0.66 mmol) for 16 h. The reaction was quenched with sat. aq. NH_4Cl soln., the mixture was extracted with CH_2Cl_2, and the org. layer was dried (Na_2SO_4) and evaporated. The resulting residue was dissolved in THF (3 ml). Then., Bu_4NF (0.084 g, 0.32 mmol) in THF (2 ml) was added dropwise at 0°. The temp. was gradually increased to 10° over 3 h with stirring. Then, sat. aq. $NaHCO_3$ soln. was added, the mixture was extracted with Et_2O, and the combined org. extracts were dried (Na_2SO_4) and evaporated. FC (SiO_2 (5 g); 10.5 × 1.5 cm; CH_2Cl_2/MeOH 98:2) gave almost pure **12** (0.009 g, 12%) and pure **11** (0.041 g, 56%).

Data of trans-*2-(Phenylmethyl)isoxazolidine-3,4-dimethanol* (**11**). Colorless oil. R_f (CH_2Cl_2/MeOH 96:4) 0.27. IR (film): 3385, 3087, 3063, 3031, 2930, 2873, 1496, 1455, 1379, 1334, 1079, 1043. ^{1}H-NMR (400 MHz, $CDCl_3$)[1]): 7.40–7.28 (*m*, Ph); 4.06 (*d*, *J* = 13.4 , 1 H of PhC*H*$_2$); 4.01 (*d*, *J* = 13.4, 1 H of PhC*H*$_2$); 3.98 (*dd*, *J* = 8.3, 8.3, H_a–C(5)); 3.79 (*dd*, *J* = 8.7, 6.2, H_b–C(5)); 3.71 (*dd*, *J* = 10.5, 6.3, H_a–C(1″)); 3.64 (*dd*, *J* = 10.5, 7.4, H_b–C(1″)); 3.59 (*dd*, *J* = 11.2, 5.5, H_a–C(1′)); 3.54 (*dd*, *J* = 11.1, 5.4, H_b–C(1′)); 3.18 (br., 2 OH); 2.91 (*ddd*, *J* = 5.5, H–C(3)); 2.62 (*m*, H–C(4)). ^{13}C-NMR (100 MHz, $CDCl_3$)[1]): 136.6, 129.1, 128.4, 127.6 (Ph); 70.2 (C(3)); 68.2 (C(5)); 63.1, 63.0 (C(1′), C(1″)); 61.3 (Ph*C*H$_2$); 49.4 (C(4)). Anal. calc. for $C_{12}H_{17}NO_3$ (223.27): C 64.55, H 7.67, N 6.27; found: C 64.14, H 8.06, N 6.67. Some relevant signals corresponding to the minor isomer **12** were also clearly observed in the other enriched fraction with **11**.

Data of cis-*2-(Phenylmethyl)isoxazolidine-3,4-dimethanol* (**12**). Colorless oil. R_f (CH_2Cl_2/MeOH 96:4) 0.34. IR (film): 3389, 3087, 3063, 3030, 2929, 2876, 1496, 1455, 1378, 1288, 1107, 1044. ^{1}H-NMR (400 MHz, $CDCl_3$)[1]): 7.42–7.30 (*m*, Ph); 4.21 (*dd*, *J* = 8.3, 8.3, H_a–C(5)); 4.11 (*d*, *J* = 13.3, 1 H of PhC*H*$_2$); 3.96 (d, *J* = 13.2, 1 H of PhC*H*$_2$); 3.86 (*dd*, *J* = 11.1, 7.9, H_a–C(1″)); 3.77 (*dd*, *J* = 11.1, 5.4, H_b–C(1″)); 3.73 (*dd*, *J* = 8.1, 6.8, H_b–C(5)); 3.72–3.69 (*m*, CH_2(1′)); 3.32 (*ddd*, *J* = 7.8, 5.7, 5.7, H–C(3)); 3.09–3.02 (*m*, H–C(4)); 2.89 (br., 2 OH). ^{13}C-NMR (100 MHz, $CDCl_3$)[1]): 136.1, 129.3, 128.5, 127.8 (Ph); 68.6 (C(5)); 67.1 (C(3)); 61.1 (Ph*C*H$_2$); 60.3, 60.2 (C(1′), C(1″)); 46.2 (C(4)).

When the [Ti(O^{i}Pr)$_2$Cl$_2$] catalyzed reaction was carried out at r.t. for 19 h, in addition to the mixture of **5a**/**6a** (57%), the esters **7a**/**8a** were isolated in 7 and 11% yield, resp.

Data of Isopropyl trans-*2-(Phenylmethyl)-3-({[*tert*-butyl(diphenyl)silyl]oxy}methyl)isoxazolidine-5-carboxylate* (**7a**). Colorless oil. R_f (CH_2Cl_2/hexanes 90:10) 0.13. IR (film): 3070, 3049, 3031, 2958, 2931, 2858, 1731, 1471, 1464, 1454, 1428, 1387, 1375, 1361, 1275, 1207, 1188, 1111, 1029, 1008. ^{1}H-NMR (400 MHz, $CDCl_3$)[1]): 7.68–7.27 (*m*, 3 Ph); 5.11 (*sept.*, *J* = 6.3, *C*HMe$_2$); 4.43 (*dd*, *J* = 7.4, 7.4, H–C(5)); 4.25 (*d*, *J* = 13.4, 1 H of PhC*H*$_2$); 4.11 (*d*, *J* = 13.3, 1 H of PhC*H*$_2$); 3.76 (*dd*, *J* = 10.4, 6.4, H_a–C(1′)); 3.63 (*dd*, *J* = 10.4, 6.5, H_b–C(1′)); 3.39 (*dddd*, *J* = 6.4, 6.4, 6.3, 6.3, H–C(3)); 2.54 (2*dd*, *J* = 8.4, 6.7, 6.6, 6.3, CH_2(4)); 1.31 (*d*, *J* = 6.3, CH*Me*$_2$); 1.07 (s, *t*-Bu). ^{13}C-NMR (100 MHz, $CDCl_3$)[1]): 171.9 (C=O); 135.6, 135.5, 133.1, 129.7, 129.0, 128.3, 127.7, 127.2 (3 Ph); 76.1 (C(5)); 68.9 (*C*HMe$_2$); 65.9 (C(3)); 64.9 (C(1′)); 62.8 (Ph*C*H$_2$); 35.7 (C(4)); 26.8 (*Me*$_3$C); 21.7 (CH*Me*$_2$); 19.2 (Me$_3$*C*). Anal. calc. for $C_{31}H_{39}NO_4Si$ (517.73): C 71.92, H 7.59, N 2.71; found: C 71.51, H 7.97, N 2.33.

Data of Isopropyl trans-*2-(Phenylmethyl)-3-({[*tert*-butyl(diphenyl)silyl]oxy}methyl)isoxazolidine-4-carboxylate* (**8a**). Colorless oil. R_f (CH_2Cl_2/hexanes 90:10) 0.19. IR (film): 3070, 3049, 3031, 2979, 2958, 2931, 2858, 1729, 1471, 1456, 1428, 1386, 1374, 1363, 1312, 1267, 1191, 1111, 1029, 1008. ^{1}H-NMR (400 MHz, $CDCl_3$)[1]): 7.70–7.28 (*m*, 3 Ph); 5.09 (*qq*, *J* = 6.3, 6.2, C*H*Me$_2$); 4.29 (*dd*, *J* = 8.7, 6.0, H_a–C(5)); 4.17 (*d*, *J* = 13.3, 1 H of PhC*H*$_2$); 4.10 (*dd*, *J* = 8.7, 8.7, H_b–C(5)); 4.07 (*d*, *J* = 13.3, 1 H of PhC*H*$_2$); 3.80 (*dd*, *J* = 10.3, 6.5, H_a–C(1′)); 3.69 (*dd*, *J* = 10.3, 6.6, H_b–C(1′)); 3.55 (*ddd*, *J* = 6.4, 6.4, 5.0, H–C(3)); 3.34 (*ddd*, *J* = 8.7, 5.9, 5.0, H–C(4)); 1.28, 1.27 (2*d*, *J* = 6.1, CH*Me*$_2$); 1.07 (*s*, *t*-Bu). ^{13}C-NMR (100 MHz, $CDCl_3$)[1]): 172.3 (C=O); 135.5, 135.5, 134.8, 133.2, 133.1, 129.7, 129.7, 129.0, 128.3, 127.7, 127.3 (3 Ph); 69.6 (C(3)); 68.7 (*C*HMe$_2$); 68.2 (C(5)); 65.0 (C(1′)); 60.8 (Ph*C*H$_2$); 51.0 (C(4)); 26.8 (*Me*$_3$C); 21.7 (OCH*Me*$_2$); 19.2 (Me$_3$*C*). Anal. calc. for $C_{31}H_{39}NO_4Si$ (517.73): C 71.92, H 7.59, N 2.71; found: C 71.53, H 7.87, N 3.13.

Noncatalyzed Cycloaddition of **13a** *with* **2**. According to the *GP 1*, with **13a** (0.196 g, 0.83 mmol) and **2** (0.118 g, 0.83 mmol) in CH_2Cl_2 (20 ml) at r.t. FC (SiO_2 (35 g); 11.5 × 3 cm; AcOEt/hexanes 35:65) gave pure **14a** (0.064 g, 20%) and an inseparable mixture of **14a**–**17a** (0.271 g, 66%).

*3-({(3*S*,5*S*)-3-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-2-(phenylmethyl)isoxazolidin-5-yl}carbonyl)-1,3-oxazolidin-2-one* (**14a**). Colorless solid. M.p. 161–162°. R_f (AcOEt/hexanes 50:50) 0.12. $[\alpha]_D^{25} = +36.7$ (*c* = 0.1, $CHCl_3$). IR (KBr): 3065, 3031, 2999, 2982, 2936, 2892, 1772, 1709, 1484, 1381, 1271, 1244, 1207, 1153, 1115, 1068, 1036, 1016. ^{1}H-NMR (400 MHz, $CDCl_3$)[1]): 7.42–7.26 (*m*, Ph); 5.63 (*dd*, *J* = 8.3, 8.3, H–C(5)); 4.50–4.40 (m, CH_2(5″)); 4.33 (*d*, *J* = 12.9, 1 H of PhC*H*$_2$); 4.08–4.02 (*m*, CH_2(4″), H_a–C(5′), H–C(4′)); 3.82 (*d*, *J* = 12.9, 1 H of PhC*H*$_2$); 3.57 (*dd*, *J* = 7.5, 4.3, H_b–C(5)); 3.29 (*ddd*, *J* = 7.7, 7.6, 1.9, H–C(3)); 2.99 (*ddd*, *J* = 13.0, 8.7, 2.1, H_a–C(4)); 2.68 (*ddd*, *J* = 13.0, 7.5, 7.5, H_b–C(4)); 1.36, 1.23 (2*s*, *Me*$_2$C). ^{13}C-NMR (100 MHz, $CDCl_3$)[1]): 172.6 (C=O); 152.9 (OC(O)N); 137.1, 129.2, 128.3, 127.5 (Ph); 109.4 (C(2′)); 77.3 (C(5)); 75.5 (C(4′)); 68.0 (C(5′)); 67.5 (C(3)); 62.6 (Ph*C*H$_2$, C(5″)); 42.7 (C(4″)); 34.0 (C(4)); 26.7, 25.1 (*Me*$_2$C). Anal. calc. for $C_{19}H_{24}N_2O_6$ (376.40): C 60.63, H 6.43, N 7.44; found: C 60.30, H 6.51, N 7.83.

Catalyzed Cycloaddition of **13a** *with* **2**. According to *GP 2* with (0.500 g, 2.1 mmol) of **13a**, a 0.5M CH_2Cl_2 soln. of [Ti(O^{i}Pr)$_2$Cl$_2$] (4.4 ml, 2.3 mmol), and **2** (0.330 g, 2.3 mmol) in CH_2Cl_2 (15 ml). FC (SiO_2 (50 g); 22 × 3 cm; AcOEt/hexanes 30:70) gave an inseparable mixture of **18a**–**21a** (0.408 g, 51%).

Reduction of **18a**–**21a**. A soln. of the above mixture of **18a**–**21a** (*ca.* 53:40:3:4; 0.540 g, 1.4 mmol) in THF/H_2O 3:1 (8 ml) was stirred at r.t. with $NaBH_4$ (0.109 g, 2.9 mmol) for 6 h. The reaction was quenched with sat. aq. NH_4Cl soln., the mixture was extracted with CH_2Cl_2, and the org. layer was dried (Na_2SO_4) and

evaporated. FC (SiO_2 (45 g); 15 × 3 cm; CH_2Cl_2/AcOEt/hexanes 40 : 20 : 40 → 40 : 30 : 30) gave pure **22** (0.091 g, 22%), a mixture of **22** – **25** (0.031 g, 7%), and pure **23** (0.085 g, 20%).

{(3S,4S)-3-[(4S)-2,2-Dimethyl-1,3-dioxolan-4-yl]-2-(phenylmethyl)isoxazolidin-4-yl}methanol (**22**). Colorless solid. M.p. 152 – 153°. R_f (CH_2Cl_2/AcOEt/hexanes 40 : 30 : 30) 0.17. $[\alpha]_D^{25} = -34.7$ ($c = 0.1$, $CHCl_3$). IR (KBr): 3251, 3065, 3027, 2981, 2956, 2902, 2883, 1453, 1380, 1370, 1263, 1240, 1205, 1157, 1100, 1071, 1050, 1037. ^{1}H-NMR (400 MHz, $CDCl_3$)[1]): 7.29 – 7.29 (*m*, Ph); 4.01 (*d*, *J* = 12.9, 1 H of PhCH_2); 4.01 – 3.95 (*m*, H–C(4′), H_a–C(5)); 3.91 (*dd*, *J* = 8.4, 6.2, H_a–C(5′)); 3.86 (*d*, *J* = 13.3, 1 H of PhCH_2); 3.82 (*dd*, *J* = 8.6, H_b–C(5)); 3.72 (*dd*, *J* = 10.5, 6.2, 1 H of HOCH_2); 3.67 (*dd*, *J* = 10.4, 6.8, 1 H of HOCH_2); 3.34 (*dd*, *J* = 8.4, 5.9, H_b–C(5′)); 2.87 (*dd*, *J* = 8.2, 4.8, H–C(3)); 2.74 (*m*, H–C(4)); 2.35 (br., OH); 1.30, 1.25 (2*s*, Me_2C). ^{13}C-NMR (100 MHz, $CDCl_3$)[1]): 136.7, 129.3, 128.4, 127.6 (Ph); 109.2 (C(2′)); 77.8 (C(4′)); 69.8 (C(3)); 68.0 (C(5)); 67.7 (C(5′)); 63.3 (HO*C*H$_2$); 61.5 (Ph*C*H$_2$); 50.7 (C(4)); 26.6, 25.2 (Me_2C). Anal. calc. for $C_{16}H_{23}NO_4$ (293.36): C 65.51, H 7.90, N 4.77; found: C 65.66, H 8.03, N 4.81.

{(3S,4R)-3-[(4S)-2,2-Dimethyl-1,3-dioxolan-4-yl]-2-(phenylmethyl)isoxazolidin-4-yl}methanol (**23**). Colorless oil. R_f (CH_2Cl_2/AcOEt/hexanes 40 : 30 : 30) 0.32. $[\alpha]_D^{25} = -1.2$ ($c = 0.1$, $CHCl_3$). IR (film): 3491, 3087, 3063, 3030, 2984, 2933, 2880, 1496, 1455, 1381, 1372, 1257, 1215, 1156, 1064. ^{1}H-NMR (400 MHz, $CDCl_3$)[1]): 7.38 – 7.29 (*m*, Ph); 4.31 (*dd*, *J* = 8.9, 8.0, H_a–C(5)); 4.26 – 4.17 (*m*, H–C(4′), H_a–C(5′)); 4.08 (*d*, *J* = 12.5, 1 H of PhCH_2); 3.91 (*dd*, *J* = 12.0, 9.4, 1 H of HOCH_2); 3.81 (*dd*, *J* = 12.1, 4.3, 1 H of HOCH_2); 3.78 (*d*, *J* = 12.6, 1 H of PhCH_2); 3.64 (*dd*, *J* = 7.7, 7.7, H_b–C(5)); 3.56 (*dd*, *J* = 8.1, 6.0, H_b–C(5′)); 3.41 (br., OH); 3.34 – 3.22 (*m*, H–C(4), H–C(3)); 1.37, 1.34 (2*s*, Me_2C). ^{13}C-NMR (100 MHz, $CDCl_3$)[1]): 136.5, 129.2, 128.5, 127.7 (Ph); 109.9 (C(2′)); 74.2 (C(4′)); 69.2 (C(5′)); 67.9 (C(5)); 67.9 (C(3)); 61.1 (Ph*C*H$_2$); 60.1 (HOCH$_2$); 46.8 (C(4)); 26.4, 25.5 (Me_2C). Anal. calc. for $C_{16}H_{23}NO_4$ (293.36): C 65.51, H 7.90, N 4.77; found: C 65.48, H 8.33, N 4.94.

Noncatalyzed Cycloaddition of **13b** *with* **2**. According to *GP 1*, with **13b** (0.500 g, 1.4 mmol) and **2** (0.195 g, 1.4 mmol) in toluene (10 ml). FC (SiO_2 (80 g); 25 × 3 cm; AcOEt/hexanes 25 : 75) gave pure **14b** (0.040 g, 6%), almost pure **15b** (0.054 g, 8%), pure **16b** (0.078 g, 11%), and an inseparable mixture of **14b** – **17b** (0.399 g, 58%).

*3-({(3S,5S)-3-[(2R,4S,5R)-5-{[(*tert*-Butyl)(diphenyl)silyl]oxy}-2-methyl-1,3-dioxan-4-yl]-2-(phenylmethyl)-isoxazolidin-5-yl}carbonyl)-1,3-oxazolidin-2-one* (**14b**). Yellowish oil. R_f (AcOEt/hexanes 50 : 50) 0.41. $[\alpha]_D^{25} = -418.9$ ($c = 0.1$, $CHCl_3$). IR (film): 3088, 3064, 3030, 2956, 2929, 2857, 1779, 1709, 1471, 1463, 1410, 1387, 1363, 1263, 1225, 1157, 1109, 1043, 1007. ^{1}H-NMR (400 MHz, $CDCl_3$)[1]): 7.45 – 7.43, 7.34 – 7.23 (2*m*, Ph); 5.63 (*dd*, *J* = 8.5, 6.7, H–C(5)); 4.69 (*q*, *J* = 5.0, H–C(2′)); 4.50 – 4.45 (*m*, CH_2(5″)); 4.38 (*d*, *J* = 13.2, 1 H of PhCH_2); 4.12 – 4.01 (*m*, CH_2(4″)); 3.98 (*dd*, *J* = 10.7, 4.9, H_e–C(6′)); 3.97 (*d*, *J* = 12.9, 1 H of PhCH_2); 3.57 – 3.54 (*m*, H–C(3)); 3.53 (*dd*, *J* = 9.2, 1.0, H–C(4′)); 3.45 (*ddd*, *J* = 9.4, 9.2, 4.9, H–C(5′)); 3.31 (*dd*, *J* = 10.6, 9.7, H_a–C(6′)); 3.05 (*ddd*, *J* = 13.0, 8.7, 4.5, H_a–C(4)); 2.43 (*ddd*, *J* = 12.5, 7.6, 6.8, H_b–C(4)); 1.35 (*d*, *J* = 5.0, H–C(7′)); 0.77 (*s*, Me_3C); 0.01, −0.04 (2*s*, $SiMe_2$). ^{13}C-NMR (100 MHz, $CDCl_3$)[1]): 172.8 (C=O); 152.9 (OC(O)N); 137.3, 129.1, 128.4, 127.3 (C(Ph)); 98.6 (C(2′)); 82.3 (C(4′)); 77.5 (C(5)); 71.0 (C(6′)); 63.7, 63.6 (C(3), C(5′)); 63.1 (Ph*C*H$_2$); 62.6 (C(5″)); 42.6 (C(4″)); 32.3 (C(4)); 25.5 (Me_3C); 20.4 (C(7′)); 17.6 (Me_3*C*); −4.37, −5.02 (Me_2Si). Anal. calc. for $C_{25}H_{38}N_2O_7Si$ (506.66): C 59.26, H 7.56, N 5.53; found: C 59.23, H 87.26, N 5.41. Some relevant signals corresponding to the minor isomer **15b** were also observed in the other enriched fraction with **14b**.

*3-({(3R,5R)-3-[(2R,4S,5R)-5-{[(*tert*-Butyl)(diphenyl)silyl]oxy}-2-methyl-1,3-dioxan-4-yl]-2-(phenylmethyl)-isoxazolidin-5-yl}carbonyl)-1,3-oxazolidin-2-one* (**15b**). Colorless oil. R_f (AcOEt/hexanes 50 : 50) 0.39. $[\alpha]_D^{25} = +16.0$ ($c = 0.1$, $CHCl_3$). IR (film): 3064, 3031, 2954, 2928, 2856, 1779, 1705, 1496, 1471, 1463, 1456, 1387, 1361, 1325, 1260, 1224, 1161, 1108, 1041, 1007. ^{1}H-NMR (400 MHz, $CDCl_3$)[1]): 7.52 – 7.50, 7.35 – 7.23 (2*m*, Ph); 5.58 (*dd*, *J* = 8.5, 6.1, H–C(5)); 4.70 (*q*, *J* = 5.0, H–C(2′)); 4.46 – 4.36 (*m*, CH_2(5″)); 4.30 (*d*, *J* = 13.6, 1 H of PhCH_2); 4.11– 4.07 (*m*, H_e–C(6′), 1 H of PhCH_2); 4.04 – 4.00 (*m*, CH_2(4″)); 3.93 (*ddd*, *J* = 9.7, 8.5, 4.2, H–C(5′)); 3.54 – 3.48 (*m*, H–C(4′), H–C(3)); 3.39 (*dd*, *J* = 10.4, 10.4, H_a–C(6′)); 2.86 (*ddd*, *J* = 13.5, 8.6, 5.2, H_a–C(4)); 2.66 (*ddd*, *J* = 13.1, 7.2, 6.0, H_b–C(4)); 1.36 (*d*, *J* = 5.0, H–C(7′)); 0.89 (*s*, *t*-Bu); 0.11, 0.09 (2*s*, Me_2Si). ^{13}C-NMR (100 MHz, $CDCl_3$)[1]): 172.8 (C=O); 152.9 (OC(O)N); 138.4, 129.2, 128.1, 126.9 (*Ph*CH$_2$)); 99.1(C(2′)); 84.0 (C(4′)); 76.9 (C(5)); 71.2 (C(6′)); 65.1 (C(3)); 64.6 (C(5′)); 63.5 (Ph*C*H$_2$); 62.6 (C(5″)); 42.6 (C(4″)); 36.8 (C(4)); 25.7 (Me_3C); 20.4 (C(7′)); 17.8 (Me_3*C*); −3.8, −4.6 (Me_2Si).

*3-({(3S,5R)-3-[(2R,4S,5R)-5-{[(*tert*-Butyl)(diphenyl)silyl]oxy}-2-methyl-1,3-dioxan-4-yl]-2-(phenylmethyl)-isoxazolidin-5-yl}carbonyl)-1,3-oxazolidin-2-one* (**16b**). Yellowish oil. R_f (AcOEt/hexanes 50 : 50) 0.22. $[\alpha]_D^{25} = -51.3$ ($c = 0.1$, $CHCl_3$). IR (film): 3064, 3029, 2956, 2930, 2885, 2858, 1778, 1717, 1472, 1463, 1410, 1389, 1363, 1262, 1226, 1158, 1116, 1042, 1007. ^{1}H-NMR (400 MHz, $CDCl_3$)[1]): 7.49 – 7.47, 7.35 – 7.25 (2*m*, Ph); 5.44 (*dd*, *J* = 9.8, 5.2, H–C(5)); 4.67 (*q*, *J* = 5.0, H–C(2′)); 4.50 – 4.46 (*m*, CH_2(5″)); 4.16 (*d*, *J* = 14.0, 1 H of PhCH_2); 4.12 – 4.05 (*m*, H–C(4″)); 4.02 – 3.95 (*m*, H_e–C(6′), H–C(4″)); 4.09 (*d*, *J* = 13.7, 1 H of PhCH_2); 3.49 (*dd*, *J* = 8.9, 0.7, H–C(4′)); 3.41 – 3.35 (*m*, H–C(3), H–C(5′)); 3.32 (*dd*, *J* = 9.9, 9.9, H_a–C(6′)); 2.83 (*ddd*, *J* = 12.8, 9.4, 9.4, H_a–C(4)); 2.67 (*ddd*, *J* = 12.8, 5.4, 5.4, H_b–C(4)); 1.29 (*d*, *J* = 5.0, H–C(7′)); 0.82 (*s*, *t*-Bu); 0.03, −0.01 (2*s*,

Me_2Si). ^{13}C-NMR (100 MHz, $CDCl_3$)[1]): 170.2 (C=O); 153.5 (OC(O)N); 136.5, 129.1, 128.3, 127.3 (Ph); 98.4 (C(2′)); 80.6 (C(4′)); 76.3 (C(5)); 71.1 (C(6′)); 64.1, 62.9 (C(3), C(5′)); 62.9 (C(5″)); 61.0 (Ph*C*H$_2$); 42.5 (C(4″)); 32.6 (C(4)); 25.6 (*Me*$_3$C); 20.4 (C(7′)); 17.7 (Me$_3$*C*); −4.4, −4.9 (Me_2Si). Anal. calc. for $C_{25}H_{38}N_2O_7Si$ (506.66): C 59.26, H 7.56, N 5.53; found: C 59.25, H 7.92, N 5.67.

X-Ray Crystal-Structure Analysis of (**22**)[3]). The analysis was performed at 100 ± 2 K on a *KUMA CCD* k-axis diffractometer with graphite-monochromated MoK_α radiation ($\lambda = 0.71073$ Å). The crystal was positioned 62.2 mm away from the *KM4CCD* camera. A total of 1332 frames were measured at 0.9° intervals on a counting time of 10 s. Data collection, cell refinement, and data reduction were carried out with the *Kuma* diffraction programs CrysAlis CCD and CrysAlis RED [10]. The data were corrected for *Lorentz* and polarization effects, but no absorption correction was applied. The structures were solved by direct methods [11], and refined with SHELXL [12]. The absolute configuration was assigned by reference to a stereogenic center conserved during the synthetic procedure. The refinement was based on F^2 for all reflections, except for those with very negative F^2 values. The *wR* and all goodness-of-fit *S* values were based on F^2. The non-H-atoms were refined anisotropically, and the H-atoms were placed in the calculated positions. The atomic scattering factors were taken from [13]. Crystallographic data: colorless crystal (0.1 × 0.25 × 0.3 mm) from EtOH; formula, $C_{16}H_{23}NO_4$; M_r 293.35; orthorhombic, space group $P2_12_12_1$, with $a = 6.448$ (1), $b = 13.778$ (1), $c = 17.087$ (2) Å; $V = 1518.0$ (3) Å^3; $Z = 4$; $D_x = 1.284$ Mg/m^3; $F(000) = 632$; $\mu = 0.092$ mm^{-1}; data range, $4.33° < \Theta < 24.99°$; $-7 \le h \le 7$, $-16 \le k \le 15$, $-20 \le l \le 20$; 17185 reflections collected, 1555 unique reflections (R(int) = 0.0503); 193 refined parameters; goodness-of-fit on F^2, 1.072; final $R = 0.0324$, $wR^2 = 0.0810$ (for all 1462 $F_0 > 4\,\sigma(F_0)$); $R = 0.0347$, $wR^2 = 0.0826$ (for all data), weight $= 1/[\sigma^2(F_0^2) + (0.0516P)^2 + 0.29P]$, where $P = (F_0^2 + 2\,F_c^2)/3$; maximum and minimum difference electron densities of 0.132 and −0.203 e Å^{-3}.

REFERENCES

[1] J. J. Tufariello, in '1,3-Dipolar Cycloaddition Chemistry', Ed. A. Padwa, Wiley Interscience, New York, 1984, Chapt. 9, p. 83; K. V. Gothelf, K. A. Jørgensen, *Chem. Rev.* **1988**, *98*, 863.

[2] M. Frederickson, *Tetrahedron* **1997**, *53*, 403.

[3] E. G. Baggiolini, J. A. Iacobelli, B. M. Hennesy, A. D. Batcho, J. F. Sereno, M. R. Uskovic, *J. Org. Chem.* **1986**, *51*, 3098; A. Brandi, S. Cicchi, A. Goti, K. M. Pietrusiewicz, *Tetrahedron: Asymmetry* **1991**, *2*, 1063; S. Saito, T. Ishikawa, N. Kishimoto, T. Kohara, T. Moriwake, *Synlett* **1994**, 282; T. Kametani, S. D. Chu, T. Honda, *Heterocycles* **1987**, *25*, 241; P. Merino, E. Castillo, S. Franco, F. L. Merchan, T. Tejero, *J. Org. Chem.* **1998**, *63*, 2371; B. Bernet, A. Vasella, *Helv. Chim. Acta* **1979**, *62*, 2411.

[4] K. B. G. Torssell, 'Nitrile Oxides, Nitrones, and Nitronates', VCH Publishers Inc., New York, 1988; P. Grünanger, P.Vita-Finzi, 'Isoxazoles: Part One', in 'The Chemistry of Heterocyclic Compounds', Ed. E. C. Taylor, E. Weissberger, J. Wiley & Sons, New York, 1991.

[5] K. B. Jensen, K. V. Gothelf, K. A. Jørgensen, *Helv. Chim. Acta* **1997**, *80*, 2039; K. V. Gothelf, K. A. Jørgensen, *J. Org. Chem*. **1994**, *59*, 5687; D. Seebach, R. E. Marti, T. Hintermann, *Helv. Chim. Acta* **1996**, *79*, 1710; K. Hori, H. Kodama, T. Ohta, I. Furukawa, *Tetrahedron Lett.* **1996**, *37*, 5947; K. Jensen, K. V. Gothelf, R. G. Hazell, K. A. Jørgensen, *J. Org. Chem*. **1997**, *62*, 2471; S. Kobayashi, M. Kawamura, *J. Am. Chem. Soc.* **1998**, *120*, 5840; K. Hori, H. Kodama, T. Ohta, I. Furukawa, *J. Org. Chem*. **1999**, *64*, 5017; G. Desimoni, G. Faita, A. Mortoni, P. Righetti, *Tetrahedron Lett*. **1999**, *40*, 2001; H. Kodama, J. Ito, K. Hori, T. Ohta, I. Furukawa, *J. Organomet. Chem*. **2000**, *603*, 6; S. Iwasa, S. Tsushima, T. Shimada, H. Nishiyama, *Tetrahedron Lett*. **2001**, *42*, 6715; M. Shirahase, S. Kanemasa, Y. Oderaotoshi, *Org. Lett*. **2004**, *6*, 675; X. Li, H. Takahashi, H. Ohtake, S. Ikegami, *Heterocycles* **2003**, *59*, 547; B. Dugovič, L. Fišera, C. Hametner, N. Prónayová, *ARKIVOC* **2003**, *xiv*, 162; B. Dugovič, T. Wiesenganger, L. Fišera, C. Hametner, N. Prónayová, *Heterocycles* **2005**, *65*, 591; O. Tamura, N. Mita, K. Gatanda, K. Yamada, T. Nakano, R. Katagiri, M. Sakamoto, *Heterocycles* **1997**, *46*, 95; K. B. Jensen, R. G. Hazell, K. A. Jørgensen, *J. Org. Chem*. **1999**, *64*, 2353; K. V. Gothelf, K. A. Jørgensen, *Chem. Commun*. **2000**, 1449.

[6] B. Dugovič, L. Fišera, C. Hametner, *Synlett* **2004**, 1569.

[7] a) L. Fišera, U. A. R. Al-Timari, P. Ertl, in 'Cycloadditions in Carbohydrate Chemistry', Ed. E. Gulliano, American Chemical Society, Washington, 1992, p. 158; b) U. A. R. Al-Timari, L. Fišera, P. Ertl, I. Goljer, N.

---

[3]) The crystallographic data for **22** were deposited at the *Cambridge Crystallographic Data Centre* as publication number CCDC-263463. The data can be obtained, free of charge, *via* http://www.ccdc.cam.ac.uk/data_request/cif.

Prónayová, *Monatsh. Chem*. **1992**, *123*, 999; c) J. Kubán, I. Blanáriková, L. Fišera, N. Prónayová, *Chem. Papers* **1997**, *51*, 378; d) J. Kubán, I. Blanáriková, L. Fišera, L. Jarošková, M. Fengler-Veith, V. Jäger, J. Kožíšek, O. Humpa, N. Prónayová, V. Langer, *Tetrahedron* **1999**, *55*, 9501; e) J. Kubán, A. Kolarovič, L. Fišera, V. Jäger, O. Humpa, N. Prónayová, P. Ertl, *Synlett* **2001**, 1862; f) J. Kubán, A. Kolarovič, L. Fišera, V. Jäger, O. Humpa, N. Prónayová, *Synlett* **2001**, 1866; g) I. Blanáriková-Hlobilová, Z. Kopaničáková, L. Fišera, M. K.Cyrański, P. Salanski, J. Jurczak, N. Prónayová, *Tetrahedron* **2003**, *59*, 3333; h) R. Fischer, A. Drucková, L. Fišera, A. Rybár, C. Hametner, M. K. Cyránski, *Synlett* **2002**, 1113; i) R. Fischer, E. Hýrošová, A. Drucková, L. Fišera, C. Hametner, M. K. Cyránski, *Synlett* **2003**, 2364.

[8] P. Merino, J. A. Mates, J. Revuelta, T. Tejero, U. Chiacchio, G. Romeo, D. Iannazzo, R. Romeo, *Tetrahedron: Asymmetry* **2002**, *13*, 173.

[9] A. Fiumana, M. Lombardo, C. Trombini, *J. Org. Chem.* **1997**, *62*, 5623; D. Iannazzo, A. Piperno, V. Pistara, A. Rescifina, R. Romeo, *Tetrahedron* **2002**, *58*, 581; P. DeShong, M. Dicken, J. M. Leginus, R. R. Whittle, *J. Am. Chem. Soc.* **1984**, *106*, 5598.

[10] Oxford Diffraction (2001), CrysAlis CCD and CrysAlis RED, *Oxford Diffraction Poland*, Wrocław, Poland.

[11] G. M. Sheldrick, *Acta Crystallogr., Sect. A* **1990**, *46*, 467.

[12] G. M. Sheldrick, SHELXL93, Program for the Refinement of Crystal Structures, University of Göttingen, Germany.

[13] 'International Tables for Crystallography', Ed. A. J. C. Wilson, Kluwer, Dordrecht, 1992, Vol. C.

Received February 24, 2005