Dichloro[TADDOLato(2−)-*O*,*O*′]titanium/Dichlorobis[1-methylethoxy]titanium-Mediated, Highly Diastereo- and Enantioselective Additions of Silyl Enol Ethers to Nitro Olefins and [3+2] Cycloadditions of Primary Adducts to Acetylenes

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The diastereoselective, Ti-*Lewis*-acid-mediated, low-temperature addition of silyl enol ethers to 1-aryl-2-nitroethenes (*Scheme 1*) occurs enantioselectively with dichloro[TADDOLato(2−)-O,O′]titanium **3** (TADDOL = α,α,α′,α′-tetraaryl-1,3-dioxolane-4,5-dimethanol) (*Scheme 2*). At least 3 equiv. of *Lewis* acid are required for high conversions (yields). However, the chiral *Lewis* acid **3** can be 'diluted' with the achiral $Cl_2Ti(OCHMe_2)_2$ analog (ratio 1:2.5), with hardly any loss of enantioselectivity! Both, the primary (4+2) cycloadducts (**B**, **9**) and the γ-nitro ketones (**A**, **1a**–**h**, **5**, **7**), formed by hydrolysis, can be isolated in good yields and with high configurational purities (*Schemes 3* and *4*, and *Table 1*). The relative and absolute configurations (2*S*,1′*R*) of the products **1** from cyclohexanone silyl enol ether and 1-aryl(including 1-heteroaryl)-2-nitroethenes (obtained with (*R*,*R*)-TADDOLate) are assigned by NMR spectroscopy, and optical comparison and correlation with literature data, as well as by anomalous-dispersion X-ray crystal-structure determination (nitro ketone **1c**; *Fig.*). The nitro ketone **7** from cyclohex-2-enone and 4-methoxy-β-nitrostyrene was cyclized (*via* a silyl nitronate **C**; *Scheme 5*) to the nitroso acetal **8**, and one of the bicyclic nitronate primary adducts **9** underwent a [3+2] cycloaddition to phenylacetylene and to ethyl 2-butynoate to give, after a ring-contracting rearrangement, tricyclic aziridine derivatives with five consecutive stereocenters (**10**, **11**; *Scheme 5* and *Table 2*), in enantiomerically pure form. With an aliphatic nitro olefin, the Ti-TADDOLate-mediated reaction with (silyloxy)cyclohexene led to a moderate yield, but the product **4** was isolated in a high configurational purity.

1. Introduction. – *Michael* addition of carbonyl compounds to nitro olefins is an efficient method of preparing γ-nitro-ketone derivatives (*cf.* **A** in *Scheme 1*), and therefrom a host of other products[3]). With Li-enolates as carbonyl derivatives, the reactions are diastereospecific, both with respect to the configuration of the enolate and of the nitro olefin [2]. As indicated in *Scheme 1*, the reaction can also be carried out enantioselectively. To this end, Li-enolate complexes with chiral Li amides, or enamines and enol ethers with covalently attached chiral auxiliary groups have been employed. The relative topicity [3], with which the trigonal centers are combined, may be *like* (X = OLi/LiNR$^*_2$, NR$^*_2$ in *Scheme 1*) or *unlike* (X = OR*/*Lewis* acid). Especially useful are those reagents and conditions that allow isolation or *in situ* trapping of intermediate [4+2] cycloadducts **B**. These cyclic nitronates[4]) are highly reactive 1,3-dipoles, which add *intra*- [4] or *inter*molecularly [5] to alkene [6] or alkyne double and triple bonds [7]. In this way, products with an array of up to five directly connected stereogenic centers

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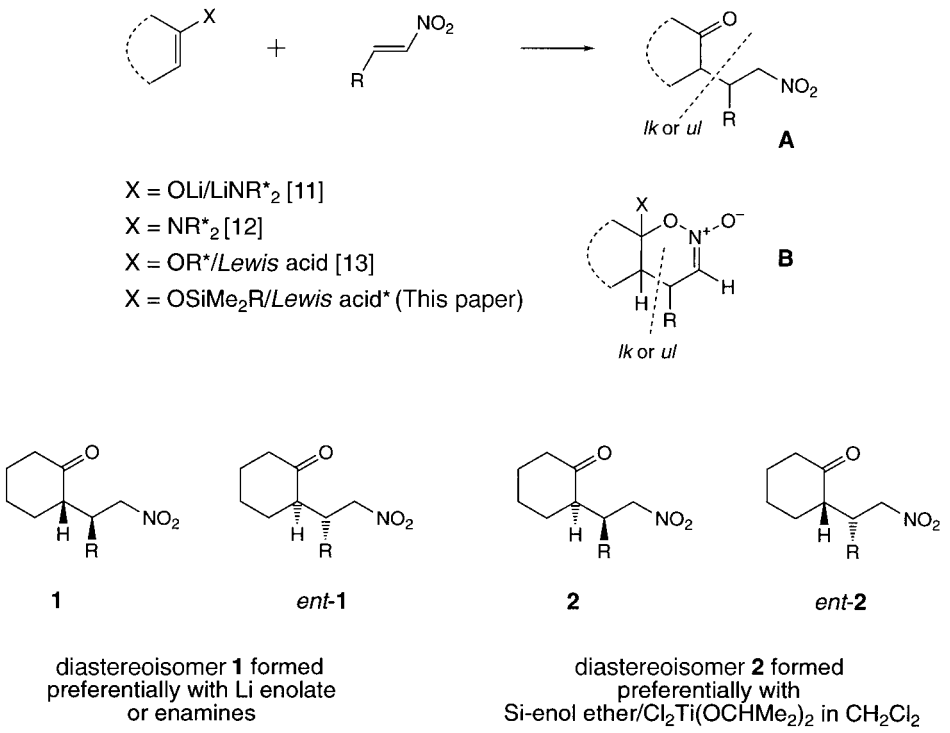
[3]) Nitroaliphatic Compounds – Ideal Intermediates in Organic Synthesis? [1].

[4]) Lactone analogs with an endocyclic electrophilic C=X group!

have been produced [8][9] in overall enantioselective processes [6][10]. In contrast to the reaction of nitro olefins with Li-enolates, which occurs spontaneously even at very low temperatures, the addition of enol ethers, including silyl enol ethers, is slow and, thus, requires catalysis by *Lewis* acids. Interestingly, the stereochemical course of addition to nitrostyrenes is reversed in going from cyclohexanone Li-enolate or enamines (→**1** in *Scheme 1*) to silyl enol ether/$Cl_2Ti(OCHMe_2)_2$ (→**2**) [8][9]. Although earlier attempts to use achiral enol ethers and chiral *Lewis* acids had failed to provide promising results[5]), and inspite of the fact that large excesses of *Lewis* acid are required, in order to achieve good conversion, and thus high yield, we decided some time ago[6]) to employ Ti-TADDOLates as chiral mediators for this reaction; the results are reported below.

Scheme 1. *Addition of Enolates, Enamines, and Enol Ethers to Nitro-olefins.* The asterisks indicate chiral groups or reagents causing enantioselective formation of products **A** and/or **B**.



2. Results. – The chiral *Lewis* acid dichloro-Ti-TADDOLate **3** (see *Scheme 2*) has been successfully applied to all-carbon *Diels-Alder* additions, as well as to [2+2] cycloadditions[7]). It is readily available in both enantiomeric forms[8]) from inexpensive

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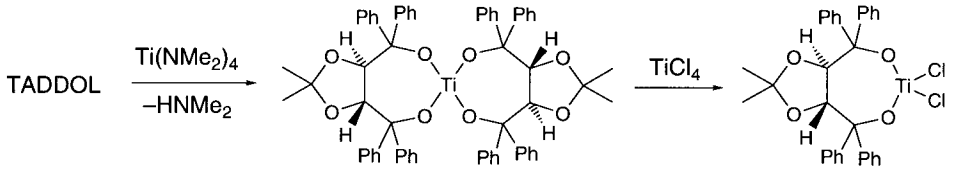
5) See comment on page 161 in [6].
6) See the Dissertation No. 11822 by *R. Dahinden*, ETH-Zürich, 1996.
7) For an early, short review article, see [14].
8) Thus, the enantiomers of all products described herein are also readily accessible!

Scheme 2. *Preparation of* **3** *from TADDOL*[9]). For a detailed procedure, see *Exper. Part.*



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commercial starting materials[9]). Thus, we used **3** for the present investigation of the reaction between silyl enol ethers and nitro olefins, formally a hetero-*Diels-Alder* addition. This reaction has been previously studied by us [8][9], with the achiral *Lewis* acid $Cl_2Ti(OCHMe_2)_2$ in CH_2Cl_2 solution. With 3 equiv. of the dichlorotitanate, the nitro ketone *rac*-**2** (R = Ph; *Scheme 1*) was obtained in good yield and in reasonable diastereoselectivity (72% ds) from cyclohexenyl trimethylsilyl ether and β-nitrostyrene. Thus, we chose this pair of reactants for testing the chiral *Lewis* acid **3**. In CH_2Cl_2 the reaction was fast at $-90°$, and, to our surprise, the course of the major reaction reversed with **3** ($\rightarrow$ **1a**), as compared to the achiral $Cl_2Ti(OCHMe_2)_2$ ($\rightarrow$ **2**, see *Scheme 1*). We were pleased to find that the nitro ketone **1** obtained with the TADDOLate was optically active, but the reaction had occurred with a disappointing stereoselectivity[10]). The situation improved greatly when we switched to toluene as the solvent (-90 to $-70°$, *Scheme 3* and *Table 1*)[11]): While the conversion with equimolar amount of **3** was low (33% after a reaction time of up to 36 h), both the diastereo- and the enantioselectivity rose above 90% (*Entry 1* of *Table 1*). The enantioselectivity was determined by chromatography on the chiral column *Chiralcel OD* (see *Exper. Part*), and the relative and absolute configuration of the major product **1a** was assigned as (2*S*,1′*R*) by comparison of its NMR spectrum and of the sign of its optical rotation with literature data [17]. An excess of 3.5 equiv. of the chiral *Lewis* acid was required to increase the conversion to nearly 90%, with concomitant increase of selectivity (96% ds, 99% es; see *Entries 1–4* of the *Table 1*).

The use of 3.5 equiv. of the Ti-TADDOLate **3** (M_r 583.3) in this reaction was, of course, not acceptable for any practical applications! In our search for improvement of this situation, we also tested mixtures of the chiral titanate **3** and the achiral titanate $Cl_2Ti(OCHMe_2)_2$. The exciting result was that we obtained high yields and excellent selectivities with 1 equiv. of **3** and 2.5 equiv. of the $Cl_2Ti(OCHMe_2)_2$ (*Scheme 3*), not only with our standard reactants (*Entry 5* of *Table 1*), but also with substituted β-

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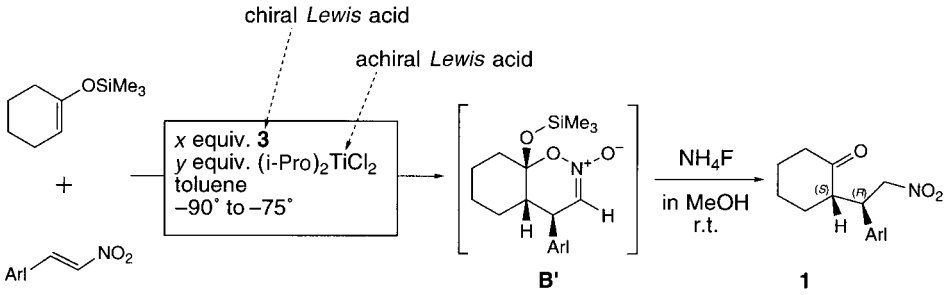
[9]) Solutions of pure **3** are best prepared by symproportionation from $TiCl_4$ and the 'spirotitanate' $Ti(TADDOLate)_2$ (*Scheme 2*) [15]. The latter is a useful, stable storage material and precursor of other Ti-TADDOLates. It is best prepared from $Ti(NMe_2)_4$ and TADDOL, with removal of Me_2NH (see *Exper. Part* and *Scheme 2*). TADDOL itself is commercially available, or can be prepared on large scale from commercial tartrate ester acetonide and phenyl *Grignard* reagent [16].

[10]) With 1 (3) equiv. of **3**, the total yield of the mixture of pure nitro ketones **1**, *ent*-**1**, **2**, and *ent*-**2** was 71% (84%), the **1**/**2** ratio was 63:37 (75:25), the enantiomer ratio **1**/*ent*-**1** 63:37 (90:10), and the enantiomer ratio **2**/*ent*-**2** 52:48 (91:9).

[11]) It is remarkable that the use of 3 equiv. of $Cl_2Ti(OCHMe_2)_2$ in PhMe led to a sluggish reaction (19% conversion after 24 h at $-78°$) with the preferential formation of the nitro ketone *rac*-**1a**, *i.e.*, the switch of solvent from CH_2Cl_2 to PhMe causes reversal of diastereoselectivity under otherwise identical conditions!

Scheme 3. *Enantio- and Diastereoselective Addition of the Trimethylsilyl Enol Ether of Cyclohexanone to* (E)*-1-Aryl-2-nitroethenes Induced by a Mixture of Cl_2Ti-TADDOLate* **3** *and $Cl_2Ti(OCHMe_2)_2$*. For conditions, yields and selectivities see Table 1.



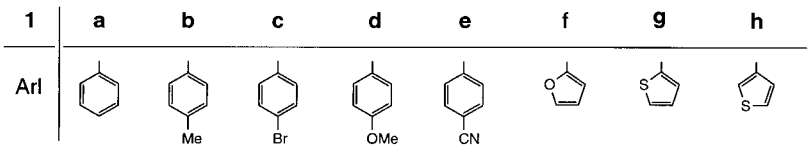


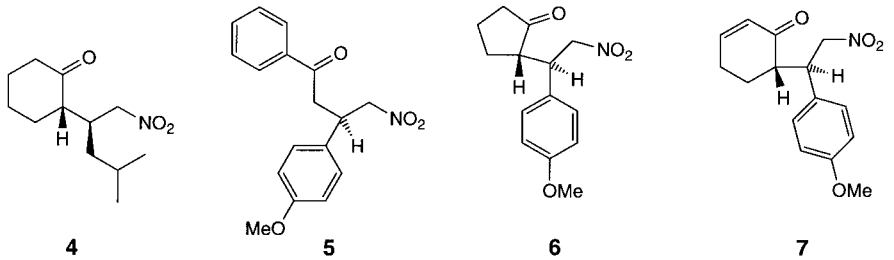
Table 1. *Yields and Stereoselectivities in the Cl_2Ti-TADDOLate-Induced Preparation of the Nitro Ketones* **1a**–**1h** *from Cyclohexenyl Silyl Ether and Nitro Olefins.* The reactions were carried out in toluene. The crude primary adducts **B′** were converted to the nitro ketones **1** without purification. The yields of **1** refer to chromatographed pure products, *x* and *y* refer to the number of equivs. of **3** and $Cl_2Ti(OCHMe_2)_2$ employed (*cf. Scheme 3*).

Entry	*x*	*y*	No.	M.p. [°]	Nitro ketone **1**		
	[equiv.]				Yield [%]	Diastereoselectivity [% ds]	Enantioselectivity [% es]
1	1.0	–	**1a**	132–134	33	91	95
2	1.5	–	**1a**		60	91	96
3	2.2	–	**1a**		68	97.8	95.6
4	3.5	–	**1a**		88	96	98.7
5	1.0	2.5	**1a**		79	97	89.4
6	1.5	–	**1b**		37	87	98
7	1.0	2.5	**1c**	123.5–125	77	99	> 99.5
8	3.5	–	**1d**	150–151	91	94.2	> 99.5
9[a])	1.0	2.5	**1d**		76	93.6	84.1
10	3.5	–	**1e**	150.6–152	75	96.2	> 99.5
11	1.0	2.5	**1e**		71	94	96
12	1.0	2.5	**1f**	80–81	82	93.6	95.4
13	1.0	2.5	**1g**	78–80	88	93.8	87
14	1.0	2.5	**1h**	110	73	96.6	89.8

[a]) The reaction was carried out with the *t*-$BuMe_2Si$ (TBDMS) enol ether instead of Me_3Si (TMS) ether, and the corresponding nitronate was isolated and characterized (see **9** in *Scheme 5*).

nitrostyrenes (products **1c**–**1e**; *Entries 7*, *9*, and *11*), and with heteroaromatic analogs (products **1f**–**1h**, *Entries 12–14*)! With an aliphatic nitro olefin (→ nitro ketone **4**) and with other silyl enol ethers (→ products **5**–**7**), we have, so far, carried out the reactions only with excess **3**, but again, we observed high stereoselectivities (see *Scheme 4*).

Scheme 4. *The Products of the Addition of Trimethylsilyl Enol Ethers of Cyclohexanone, Acetophenone, Cyclopentanone, and Cyclohex-2-enone to (*E*)-1-(4-Methoxyphenyl)-2-nitroethene and (*E*)-4-Methyl-1-nitropent-1-ene* (all reactions were carried out with 3.5 equiv. of **3**; in the case of **4**, conversion was poor).



4 (45% yield, 99.2% ds, 95% es) **5** (99% yield, 93% es) **6** (95% yield, 83% ds, >99.5% es) **7** (59%yield, 89% ds, 82% es)

All products (**1** and **5**–**7**) from (*E*)-1-aryl-2-nitroethenes are solid, and the data given in *Table 1* (m.p.) and in the *Exper. Part* (IR, NMR, MS, $[\alpha]_D^{r.t.}$, elemental analyses) were collected with recrystallized samples[12]). All nitro ketones (except for **5** and **7**) have a negative sign of optical rotation and are thus assigned the same absolute configuration as the known compound **1a** (2*S*,1′*R*). The relative configurations of the products **1b**–**1h**, **6**, and **7** were also deduced from common characteristic NMR patterns, again as compared to the known compound **1a**[13]). For the nitro ketone **4** with aliphatic side chain, and **5** with only one stereogenic center, we inferred the configuration by analogy: we assume that the enol ether attacks the trigonal center of the nitro olefin from the *Re* face in all cases.

Of the 2-[1′-(4-bromophenyl)-2′-nitroethyl]cyclohexanone **1c**, we could obtain an X-ray crystal structure using the *Bijvoet* anomalous-dispersion method [18a] for phasing[14]) (*Fig*). Thus, the relative and absolute configuration of this compound, and – considering the identity of sign of optical rotation and the similarity of the NMR spectra – that of all 2-(1′-aryl-2′-nitroethyl)cyclohexanones **1a**–**1h** was established.

Of many possible subsequent reactions with the nitro ketones of type **A** or their immediate precursors **B**, we investigated only two (see *Scheme 5*).

The product **7** from the reaction of cyclohex-2-enone with (*E*)-2-(4-methoxyphenyl)-1-nitroethene was converted to the silyl nitronate **C**, which, upon heating *in situ*, underwent *intra*molecular [3 + 2] cycloaddition to form the tricyclic nitroso acetal **8**, which was fully characterized.

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12) We did not analyze the enantiomer purity after recrystallization, except with compound **1d**, which turned out to be > 99% enantiomerically pure.

13) In previous work with chiral enamines (which also gave preferentially the diastereoisomers **1**), we had already described compounds **1a** and *ent*-**1a** [17].

14) See the extensive discussion of this method in Chapt. 3, p. 129 *ff.* of [18b].

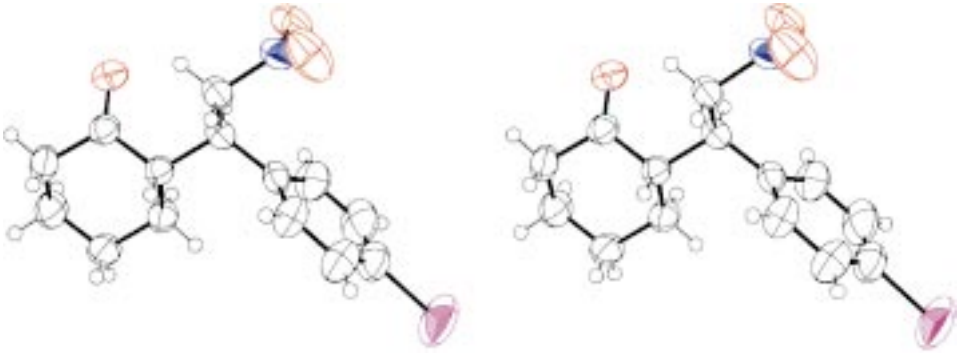
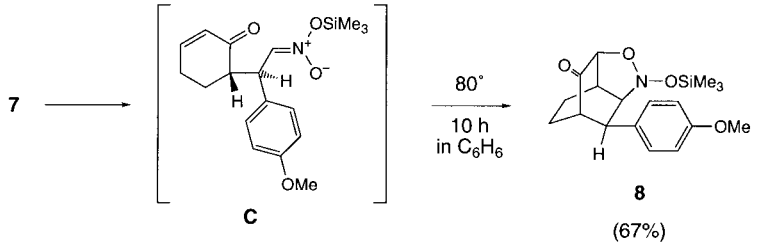
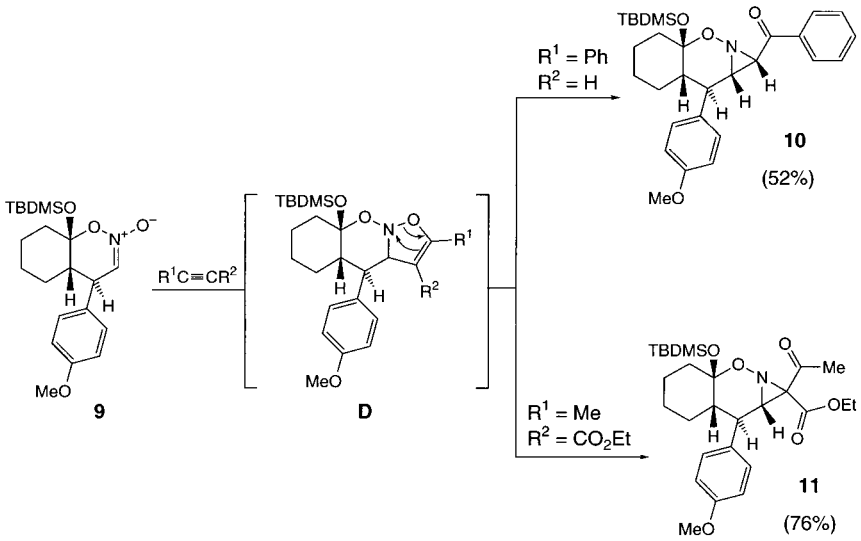


Fig. 1. *ORTEP Stereo plot of the crystal structure of the 2-[1′-(4-bromophenyl)-2′-nitroethyl]cyclohexanone* (**1c**), showing the relative and absolute configuration (2S,*1′*R). The structure was determined (*Bijvoet* method) by *W. B. Schweizer*. For details, see the *Exper. Part*.

Scheme 5. *Intra- and Intermolecular [3+2] Cycloaddition of Nitronate Groups to C=C and C≡C Bonds* (The configuration of the tertiary stereogenic center of the aziridine ring of **11** is unknown).





The second reaction studied was the *inter*molecular [3 + 2] cycloaddition of the bicyclic nitronate[15]) **9** to acetylenes, a process which had been carried out before with achiral, acyclic, and monocyclic alkyl nitronates to provide aziridine derivatives which have been proposed to form *via in situ* rearrangement of the primarily produced dihydro-1,2-oxazoles [7].

We employed phenylacetylene and ethyl 2-butynoate as dipolarophiles and isolated the tricyclic compounds **10** and **11** as single regio- and diastereoisomers (*Scheme 5*). The structures of these products with five consecutive stereogenic centers (not counting the pyramidalized N-atom [19]) were established unambiguously by NOE measurements (see *Table 2* in the *Exper. Part*). The only configuration we were not able to assign is that of the tertiary center of the aziridine ring in the β-keto ester **11**. As indicated in formula **D**, the formation of the aziridinyl-carbonyl moiety in **10** and **11** is formally the reversal of a vinylcyclopropane/cyclopentene rearrangement.

3. Conclusion. – The results described herein demonstrate that the overall *Michael*-type addition of Si-enol ethers to β-nitrostyrenes can be achieved highly enantioselectively in the presence of a chiral *Lewis* acid.

There are several surprising aspects of this process: *i*) The diastereoselectivity of the addition in CH_2Cl_2 reverses with the closely related $Cl_2Ti(OCHMe_2)_2$ and Cl_2Ti-TADDOLate. *ii*) In toluene, however, both *Lewis* acids give rise to preferential formation of the same diastereoisomer. *iii*) The more bulky Cl_2Ti-TADDOLate **3** is a more active *Lewis* acid than the diisopropoxy analogue: $\geq$ 95% conversion (36 h at $-90°$) with 3.5 equiv. of **3** *vs.* 19% with 3 equiv. of the $Cl_2Ti(OCHMe_2)_2$ (24 h at $-78°$)[11][16]). *iv*) 'Dilution' of the chiral *Lewis* acid (1 equiv.) with 2.5 equiv. of the achiral *Lewis* acid leads to much higher conversion than observed with the same amount of the separate *Lewis* acids (*cf. Footnote 11* and *Entry 1* of the *Table 1*)[17][18]). *v*) In view of the fact that TADDOL derivatives can form inclusion compounds enantioselectively [22][23], it is important to point out that all reactions of silyl enol ethers with nitro olefins described here occur in homogeneous solutions, and that we made sure that no epimerization takes place during workup steps[15]).

In view of the complexity of the system studied, and inspite of the fact that some effects observed here have been seen before with other Ti-TADDOLate mediated reactions[16])[17]), we refrain from discussing possible mechanisms.

Apart from mechanistic aspects, it is evident that the enantioselective reaction is far more effective with 2-aryl-1-nitroethenes than it is with aliphatic 1-nitroalk-1-enes (*cf.*

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[15]) The bicyclic intermediates **B′** were all identified by ^{1}H-NMR spectroscopy before cleavage to the nitro ketones. The spectra confirmed that the *cis*-fused bicyclic nitronates are formed (see formula **B′** in *Scheme 3*) in all cases (comparison with previously assigned characteristic NMR data [9]; see *GP 2* and *GP 3* in the *Exper. Part*). Furthermore, the *cis*-fusion of the six-membered ring of **9** was confirmed by NOE measurement (see the *Exper. Part*).

[16]) In the addition of Et_2Zn to PhCHO, the ratio of catalytic activity of $(Me_2CHO)_2$Ti-TADDOLate and $(Me_2CHO)_4Ti$ is *ca.* 70 : 1 [20].

[17]) In the case of the addition of Et_2Zn to PhCHO, the same type of 'dilution' also gave better results than with the pure TADDOLate catalyst, and it was shown that this is due to a 'cleansing' effect on the chiral catalyst [21].

[18]) Upon inspection of *Table 1*, it appears that the enantioselectivity drops slightly when **3** is 'diluted' with $Cl_2Ti(OCHMe_2)_2$.

yields in *Table 1* with yield of product **4** in *Scheme 4*). On the other hand, the products **8**, **10**, and **11** of subsequent conversions of the enantiomerically pure nitro ketones and nitronates demonstrate the synthetic potential of the method described here.

We are indebted to the *Fonds Ostkontakte of ETH-Zürich* for the partial financial support of *I. M. L.* We thank Dr. *W. B. Schweizer* for the determination of the X-ray crystal structure of **3c** and *Novartis Pharma AG*, Basel, for continuing support.

Experimental Part

1. *General*. Abbrevation: BSA: *N*,*O*-bis(trimethylsilyl)acetamide. Toluene and $(i\text{-}Pr)_2NEt$ were freshly distilled over a Na-suspension under Ar before use. CH_2Cl_2 was freshly distilled over CaH_2 under Ar before use. The solvents for FC and workup procedures were distilled over P_2O_5 (*Merck*). $(i\text{-}PrO)_4Ti$ was received from *Hüls* and distilled prior to use. All reactions were carried out in a dry Ar atmosphere. $TiCl_4$, 1-(trimethylsilyloxy)cyclohexene, 1-(trimethylsilyloxy)cyclopentene, BSA, phenylacetylene, ethyl 2-butynoate were used as purchased from *Fluka*. 1-Phenyl-1-(trimethylsilyloxy)ethylene [24], 2-(trimethylsilyloxy)cyclohexa-1,3-diene [25], 1-[(*tert*-butyl)dimethylsilyloxy]cyclohexene [26], $Ti(NMe_2)_4$ [27], (*E*)-2-aryl-1-nitro- and 2-heteroaryl-1-nitroethenes [12], and (*E*)-4-methyl-1-nitropent-1-ene [28] were prepared according to literature procedures. All long-term reactions at below $-78°$ were carried out using a *Lauda Ultra Kryomat® RUK90*. TLC: *Merck* silica gel *60* F_{254} plates; detection with UV or dipping into a soln. of phosphomolybdic acid (25 g), $Ce(SO_4)_2 \cdot H_2O$ (10 g), conc. H_2SO_4 (60 ml) in H_2O (940 ml), followed by heating. FC: *Fluka* silica gel *60* (40–63 μm); at *ca*. 0.3 bar. Anal. HPLC: *Knauer* HPLC system (pump type *64*, *EuroChrom 2000* integration package, degaser, UV detector (variable-wavelength monitor, detection at $\lambda = 220$ nm); *Chiralcel OD* (*Daicel Chemical Industries, Ltd.*; 4.6 × 250 mm, 10 μm) connected consecutively with *WHELK* (*Regis*; 4.6 × 250 mm, 5 μm); t_R in min, described only for the major stereoisomer. M.p.: *Büchi-510* apparatus; uncorrected. Optical rotations: *Perkin-Elmer 241* polarimeter (10 cm, 1 ml cell) at r.t. IR Spectra: *Perkin-Elmer-782* spectrophotometer. NMR Spectra (only for the major stereoisomer): *Bruker AMX 500* (^1H: 500 MHz, ^{13}C: 125 MHz), *AMX 400* (^1H: 400 MHz, ^{13}C: 100 MHz), *Varian Gemini 300* (^1H: 300 MHz, ^{13}C: 75 MHz), or *Gemini 200* (^1H: 200 MHz, ^{13}C: 50 MHz); chemical shifts (δ) in ppm downfield from $SiMe_4$ (= 0 ppm); *J* values in Hz; unless stated otherwise, $CDCl_3$ solns. MS: *VG Tribrid* (EI) or *Finnigan-MAT-TSQ 7000* (ESI) spectrometer; in *m*/*z* (% of basis peak). Elemental analyses were performed by the Microanalytical Laboratory of the Laboratorium für Organische Chemie, ETH-Zürich.

2. *Modified Procedure for the Preparation of [*T-*4-(4*R-trans*)]-Bis[2,2-dimethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanolato(2–)-*O^{α},$O^{\alpha'}$*]titanium* ('*Spirotitanate*')[19]). $Ti(NMe_2)_4$ (10.9 g, 48.8 mmol) was added dropwise *via* syringe to a precooled (5–10°), vigorously stirred soln. of 2,2-dimethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanol (TADDOL) [16] (43.46 g, 93 mmol) in CH_2Cl_2 (150 ml). Most of the volatile components were distilled off at atmospheric pressure. The residual amount of solvent was removed carefully *in vacuo*. The residue was dried (98°/0.01 Torr) for 12 h to yield 45.41 g (99%) of the 'spirotitanate' as a yellow microcrystalline solid, which was then dissolved in 180 ml of toluene and used as a stock soln. for the generation of the chiral *Lewis* acid **3** (see below).

3. *Preparation of the Solution of Dichloro[2,2-dimethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanolato(2–)-*O,O′*]titanium* (Cl_2Ti-TADDOLate; **3**). *General Procedure 1* (*GP 1*). A soln. of the 'spirotitanate' (1.05 equiv.) in toluene (0.025M) was cooled to $-92°$ (EtOH/liquid N_2), and $TiCl_4$ (1.00 equiv.) was added. The vigorously stirred mixture was allowed to warm to 20° for 2 h, resulting in a clear yellow-to-orange soln. of **3**, which was used as the chiral *Lewis* acid for subsequent addition reactions.

4. Michael *Addition of Silyl Enol Ethers to Nitro Olefins Using* **3**/$Cl_2Ti(OCHMe_2)_2$. *General Procedure 2* (*GP 2*). A soln. of **3** (1.0 equiv.) (see *GP 1*) was cooled to $-40°$, and a soln. of the nitro olefin (1.0 equiv.) in toluene (0.15M) was added. The colored soln. (varying from yellow to deep red, depending on the nitro olefin) was cooled to $-92°$ (EtOH/liquid N_2), and the silyl enol ether (1.2–1.3 equiv.) was added. The mixture was allowed to warm to $-75°$ for 1 h then recooled to $-92°$ (EtOH/liquid N_2). A soln. of $Cl_2Ti(OCHMe_2)_2$ (*ca*. 2.5 equiv.) in toluene (*ca*. 0.25M; freshly prepared by addition of $TiCl_4$ (1.3 equiv.) to a precooled (5–10°) soln. of $(i\text{-}PrO)_4Ti$ (1.45 equiv.) in toluene, followed by stirring at 20° for 0.5 h) was added at temps. below $-90°$ for *ca*. 20 min, using a syringe pump. The resulting mixture was allowed to warm to $-75°$ for 0.5 h and stirred at this

[19]) For the synthesis of 'spirotitanate' by the reaction of TADDOL with $(i\text{-}PrO)_4Ti$, see [29].

temp. (dry ice/acetone) for 24 h. It was then poured into a vigorously stirred Et_2O/sat. aq. $NaHCO_3$ bilayer (2 : 1; a threefold excess with respect to the volume of the reaction mixture) and filtered through a pad of *Celite*. The H_2O layer was re-extracted twice with Et_2O, and the combined org. phases were washed with H_2O and dried at 0° with $NaHCO_3/MgSO_4$ 1 : 1. After filtration, the solvents were removed *in vacuo* (the H_2O-bath temp. should be below 20°), and the residue[20]) was dissolved in MeOH (0.02M), and NH_4F (3.0 equiv.) was added. The resulting soln. was stirred at 20° for *ca.* 12 h, poured into twice the volume of H_2O/ice mixture, and extracted three times with Et_2O. The combined org. phases were dried ($MgSO_4$) and evaporated *in vacuo*. The residue was separated by FC (hexane/Et_2O from 6 : 1 up to 1 : 1) to afford the TADDOL (92–96% recovery) and the γ-nitro ketone **1**.

5. Michael *Addition of Silyl Enol Ethers to Nitro Olefins Using Only* **3**. *General Procedure 3* (*GP 3*). A soln. of **3** (3.5 equiv.; see *GP 1*) was cooled to −40°, and a soln. of the nitro olefin (1.0 equiv.) in toluene (0.15M) was added. The colored soln. (varying from yellow to deep red, depending on the nitro olefin) was cooled to −92° (EtOH/liquid N_2), and a soln. of the silyl enol ether (1.2–2.0 equiv.) in toluene (0.25M) was added at temps. below −90° (EtOH/liquid N_2) for *ca.* 1 h, using a syringe pump. The resulting mixture was allowed to warm to −88° (kryostat) and stirred at this temp. for 12 h. The mixture was then poured into a vigorously stirred Et_2O/sat. aq. $NaHCO_3$ bilayer (2 : 1; a threefold excess with respect to the volume of the reaction mixture) and filtrated through a pad of *Celite*. The H_2O layer was re-extracted twice with Et_2O, and the combined org. phases were washed with H_2O and dried at 0° with $NaHCO_3/MgSO_4$ 1 : 1. After filtration, the solvents were removed *in vacuo* (the H_2O-bath temp. should be below 20°), and the residue[20]) was dissolved in MeOH (0.02M), and NH_4F (3.0 equiv.) was added. The resulting soln. was stirred at 20° for *ca.* 12 h, poured into twice the volume of H_2O/ice mixture and extracted three times with Et_2O. The combined org. phases were dried ($MgSO_4$) and evaporated *in vacuo*. The residue was recrystallized (MeOH) in order to separate up to 50% of the TADDOL as the inclusion compound with MeOH [31]. The mother liquor was evaporated *in vacuo*. The residue was separated by FC (hexane/Et_2O from 6 : 1 up to 1 : 1) to afford the TADDOL (92–96% recovery altogether with the previously crystallized amount) and the γ-nitro ketone **1**.

6. *[3+2] Cycloaddition to Acetylenes Followed by Ring Contraction to Aziridines. General Procedure 4* (*GP 4*). A soln. of the cyclic nitronate **9** (1.0 equiv.), (i-Pr)$_2$NEt (a few drops), and the corresponding acetylene (3.0–4.0 equiv.) in benzene (0.4M) was stirred at 50°, until the nitronate was completely consumed (TLC, ^{1}H-NMR). The volatile components were removed *in vacuo*, and the residue was purified by FC (hexane/Et_2O from 20 : 1 to 10 : 1) to give the aziridines **10** and **11**.

*(2*S*)-2-[(1*R*)-1-Phenyl-2-nitroethyl]cyclohexanone* (**1a**). [(*E*)-2-Nitroethenyl]benzene (0.19 g, 1.28 mmol) was allowed to react with 1-(trimethyl-silyloxy)cyclohexene (0.30 ml, 1.52 mmol) according to *GP 2* or *GP 3*. FC (hexane/Et_2O) yielded **1a** (0.249 g, 79%, or 0.277 g, 88% according to *GP 2* or *GP 3*, resp.). White crystals. HPLC (hexane/i-PrOH 97 : 3; flow 3.0 ml/min): t_R 21.06 min. M.p. 132–134° (hexane) ([17]: 133–134°). $[\alpha]_D^{r.t.} = -26.3$ ($c = 0.93$, $CHCl_3$) ([17]: $[\alpha]_D^{r.t.} = -28$). ^{1}H-NMR (200 MHz): 1.13–1.34 (*m*, 1 H, CH_2); 1.50–1.84 (*m*, 2 CH_2); 2.01–2.14 (*m*, 1 H, CH_2); 2.29–2.55 (*m*, CH_2); 2.61–2.77 (*m*, CHC=O); 3.76 (*dt*, $^3J = 4.6$, $^3J = 10.0$, PhC*H*); 4.64 (*dd*, $^2J = 12.5$, $^3J = 10.0$, 1 H, CH_2NO_2); 4.94 (*dd*, $^2J = 12.5$, $^3J = 4.6$, 1 H, CH_2NO_2); 7.18 (*m*, 2 arom. H); 7.29 (*m*, 3 arom. H). ^{13}C-NMR (50 MHz): 24.9, 28.4, 33.1 (CH_2); 42.6 (*C*H_2C=O); 43.9 (Ph*C*H); 52.5 (*C*HC=O); 78.9 (CH_2NO_2); 127.8 (arom. C_p); 128.2, 129.0 (arom. CH); 137.9 (arom. C); 212.1 (C=O).

*(2*S*)-2-[(1*R*)-1-(4-Methylphenyl)-2-nitroethyl]cyclohexanone* (**1b**). 1-Methyl-4-[(*E*)-2-nitroethenyl]benzene (0.41 g, 2.5 mmol) was allowed to react with 1-(trimethylsilyloxy)cyclohexene (0.54 ml, 2.75 mmol) in the presence of **3** (3.75 mmol, 1.5 equiv.) for 48 h at −90°, according to *GP 3*. The product **1b** was separated from the TADDOL by bulb-to-bulb distillation (145°/0.03 Torr) and isolated (0.24 g, 37%) as a yellow solid. HPLC (hexane/i-PrOH 97 : 3, flow 3.0 ml/min): t_R 21.8 min. The spectroscopic data matched those of the literature [9][17].

*(2*S*)-2-[(1*R*)-1-(4-Bromophenyl)-2-nitroethyl]cyclohexanone* (**1c**). 1-Bromo-4-[(*E*)-2-nitroethenyl]benzene (0.32 g, 1.4 mmol) was allowed to react with 1-(trimethylsilyloxy)cyclohexene (0.33 ml, 1.7 mmol) according to *GP 2*. FC (hexane/Et_2O) yielded **1c** (0.352 g, 77%). White crystals. HPLC (hexane/i-PrOH 97 : 3, flow 1.4 ml/min): t_R 68,6 min. M.p. 123.5–125° (hexane) ([32]: *rac*-**1c**: M.p. 108–110°). $[\alpha]_D^{r.t.} = -24.1$ ($c = 1.5$, $CHCl_3$). ^{1}H-NMR (300 MHz): 1.15–1.30 (*m*, 1 H, CH_2); 1.49–1.82 (*m*, 2 CH_2); 2.02–2.14 (*m*, 1 H, CH_2);

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[20]) According to the ^{1}H-NMR spectra, the residue consists of TADDOL [30] and cyclic nitronate **B′** (typical signals ($CDCl_3$): 0.1–0.2 (*s*, Me_3Si); 5.9–6.5 (*d*, $^3J = 4.0$–4.5, CH=N); 3.2–3.6 (br. *d*, $^3J = 4.0$–4.5, Arl–C*H*)).

2.30–2.51 (*m*, CH_2); 2.59–2.70 (*m*, CHC=O); 3.75 (*dt*, ^3J = 4.5, ^3J = 10.0, 1 H, Arl–C*H*); 4.60 (*dd*, ^2J = 12.8, ^3J = 10.0, 1 H, CH_2NO_2); 4.93 (*dd*, ^2J = 12.8, ^3J = 4.5, 1 H, CH_2NO_2); 7.07 (*d*, ^3J = 8.4, 2 arom. H); 7.45 (*d*, ^3J = 8.4, 2 arom. H). ^{13}C-NMR (75 MHz): 24.9, 28.3, 33.0 (CH_2); 42.6 (*C*H_2C=O); 43.3 (ArlCH); 52.2 (*C*HC=O); 78.5 (CH_2NO_2); 121.8 (BrC); 130.0, 132.2 (arom. CH); 136.9 (arom. C); 211.7 (C=O).

(2S)-2-[(1R)-1-(4-Methoxyphenyl)-2-nitroethyl]cyclohexanone (**1d**). 1-Methoxy-4-[(*E*)-2-nitroethenyl]-benzene (0.25 g, 1.4 mmol) was allowed to react with 1-[(*tert*-butyl)dimethylsilyloxy]cyclohexene (0.39 g, 1.8 mmol) according to *GP 2* or with 1-(trimethylsilyloxy)cyclohexene (0.33 ml, 1.67 mmol) according to *GP 3*. FC (hexane/Et_2O) yielded **1d**[21]) (0.295 g, 76%, or 0.353 g, 91% according to *GP 2* or *GP 3*, resp.). White crystals. HPLC (hexane/i-PrOH 97:3, flow 3.0 ml/min): t_R 39.13 min. M.p. 150–151° (hexane/$CHCl_3$) ([8]: *rac*-**1d**: m.p. 125.1–126.5°). $[\alpha]_D^{r.t.} = -37.2$ (*c* = 1.21, $CHCl_3$). ^{1}H-NMR (300 MHz): 1.15–1.30 (*m*, 1 H, CH_2); 1.49–1.84 (*m*, 2 CH_2); 2.02–2.13 (*m*, 1 H, CH_2); 2.31–2.51 (*m*, CH_2); 2.58–2.71 (*m*, CHC=O); 3.71 (*dt*, ^3J = 4.5, ^3J = 10.0, Arl–C*H*); 3.78 (*s*, MeO); 4.59 (*dd*, ^2J = 12.5, ^3J = 10.0, 1 H, CH_2NO_2); 4.90 (*dd*, ^2J = 12.5, ^3J = 4.5, 1 H, CH_2NO_2); 6.85 (*d*, ^3J = 8.7, 2 arom. H); 7.08 (*d*, ^3J = 8.7, 2 arom. H). ^{13}C-NMR (75 MHz): 25.0, 28.5, 33.1 (CH_2); 42.7 (*C*H_2C=O); 43.2 (ArlCH); 52.6 (*C*HC=O); 55.2 (MeO); 79.1 (CH_2NO_2); 114.2, 129.1 (arom. CH); 129.5 (arom. C); 159.0 (*C*OMe); 212.0 (C=O).

4-[(1R)-2-Nitro-1-[(2S)-2-oxocyclohexyl]ethyl]benzonitrile (**1e**). 4-[(*E*)-2-Nitroethenyl]benzonitrile (0.24 g, 1.4 mmol) was allowed to react with 1-(trimethylsilyloxy)cyclohexene (0.34 ml, 1.8 mmol) according to *GP 2* or *GP 3*. FC (hexane/Et_2O), yielded **1e** (0.263 g, 71%, or 0.278 g, 75% according to *GP 2* or *GP 3*, resp.). White crystals. HPLC (hexane/i-PrOH 80:20, flow 3.0 ml/min): t_R 25.57 min. M.p. 150.6–152° (hexane/$CHCl_3$) ([12]: *rac*-**1e**: m.p. 124.8–126.2°). $[\alpha]_D^{r.t.} = -29.4$ (*c* = 1.27, $CHCl_3$). ^{1}H-NMR (300 MHz): 1.17–1.32 (*m*, 1 H, CH_2); 1.51–1.75 (*m*, 3 H, CH_2); 1.76-1.86 (*m*, 1 H, CH_2); 2.04–2.17 (*m*, 1 H, CH_2); 2.31–2.53 (*m*, CH_2); 2.64–2.75 (*m*, CHC=O); 3.87 (*dt*, ^3J = 4.4, ^3J = 9.7, Arl–C*H*); 4.67 (*dd*, ^2J = 13.1, ^3J = 9.7, 1 H, CH_2NO_2); 4.97 (*dd*, ^2J = 13.1, ^3J = 4.4, 1 H, CH_2NO_2); 7.34 (*d*, ^3J = 8.4, 2 arom. H); 7.64 (*d*, ^3J = 8.4, 2 arom. H). ^{13}C-NMR (75 MHz): 25.1, 28.3, 33.1 (CH_2); 42.7 (*C*H_2C=O); 43.9 (ArlCH); 52.1 (*C*HC=O); 78.0 (CH_2NO_2); 111.8 (*C*–C≡N); 118.3 (C≡N); 129.1, 132.6 (arom. CH); 143.5 (arom. C); 210.9 (C=O).

(2S)-2-[(1R)-1-(furan-2-yl)-2-nitroethyl]cyclohexanone (**1f**). 2-[(*E*)-2-Nitroethenyl]furan (0.20 g, 1.4 mmol) was allowed to react with 1-(trimethylsilyloxy)cyclohexene (0.36 ml, 1.9 mmol) according to *GP 2*. FC (hexane/Et_2O) yielded **1f** (0.280 g, 82%). Yellowish crystals. HPLC (hexane/i-PrOH 97:3, flow 1.0 ml/min): t_R 52.74 min. M.p. 80–81° (hexane). $[\alpha]_D^{r.t.} = -15.4$ (*c* = 1.27, $CHCl_3$). IR ($CHCl_3$): 3008*w*, 2945*m*, 2868*w*, 1708*s*, 1555*s*, 1448*w*, 1432*w*, 1377*m*, 1149*w*, 1131*w*, 1015*w*. ^{1}H-NMR (300 MHz): 1.21–1.36 (*m*, 1 H, CH_2); 1.56–1.69 (*m*, CH_2); 1.69–1.90 (*m*, CH_2); 2.02–2.18 (*m*, 1 H, CH_2); 2.30–2.50 (*m*, CH_2); 2.69–2.81 (*m*, CHC=O); 3.97 (*dt*, ^3J = 4.7, ^3J = 9.3, Arl–C*H*); 4.68 (*dd*, ^2J = 12.5, ^3J = 9.3, 1 H, CH_2NO_2); 4.79 (*dd*, ^2J = 12.5, ^3J = 4.7, 1 H, CH_2NO_2); 6.18 (*dd*, ^3J = 3.1, ^4J = 0.6, 1 arom. H); 6.29 (*dd*, ^3J = 1.9, ^3J = 3.1, 1 arom. H); 7.35 (*dd*, ^3J = 1.9, ^4J = 0.6, arom. CH–O). ^{13}C-NMR (75 MHz): 24.9, 28.0, 32.3 (CH_2); 37.4 (ArlCH); 42.4 (*C*H_2C=O); 51.0 (*C*HC=O); 76.6 (CH_2NO_2); 108.9, 110.3 (arom. CH); 142.4 (arom. CH–O); 151.1 (arom. C–O); 211.1 (C=O). EI-MS: 237 (0.06, M^+), 203 (0.09), 190 (82), 161 (100), 147 (15), 94 (26), 81 (17). Anal. calc. for $C_{12}H_{15}NO_4$ (237.25): C 60.75, H 6.37, N 5.90; found: C 60.62, H 6.32, N 5.96.

(2S)-2-[(1R)-2-Nitro-1-(thiophen-2-yl)ethyl]cyclohexanone (**1g**). 2-[(*E*)-2-Nitroethenyl]thiophene (0.24 g, 1.55 mmol) was allowed to react with 1-(trimethylsilyloxy)cyclohexene (0.39 ml, 2.0 mmol) according to *GP 2*. FC (hexane/Et_2O) yielded **1g** (0.345 g, 88%). White crystals. HPLC (hexane/i-PrOH 97:3, flow 1.0 ml/min): t_R 64.5 min. M.p. 78–80° (hexane). $[\alpha]_D^{r.t.} = -21.1$ (*c* = 1.13, $CHCl_3$). IR ($CHCl_3$): 3008*w*, 2942*m*, 2867*w*, 1708*s*, 1556*s*, 1448*w*, 1431*w*, 1378*m*, 1128*w*, 1045*w*. ^{1}H-NMR (300 MHz): 1.25–1.39 (*m*, 1 H, CH_2); 1.54–1.73 (*m*, CH_2); 1.77–1.95 (*m*, CH_2); 2.02–2.14 (*m*, 1 H, CH_2); 2.29–2.50 (*m*, CH_2); 2.62–2.73 (*m*, CHC=O); 4.13 (*dt*, ^3J = 4.7, ^3J = 9.3, Arl–C*H*); 4.66 (*dd*, ^2J = 12.5, ^3J = 9.3, 1 H, CH_2NO_2); 4.89 (*dd*, ^2J = 12.5, ^3J = 4.7, 1 H, CH_2NO_2); 6.88 (*d*, ^3J = 3.4, 1 arom. H); 6.93 (*dd*, ^3J = 3.4, ^3J = 5.0, 1 arom. H); 7.21 (*d*, ^3J = 5.0, 1 arom. CHS). ^{13}C-NMR (75 MHz): 24.9, 28.1, 32.6 (CH_2); 39.2 (ArlCH); 42.4 (*C*H_2C=O); 53.2 (*C*HC=O); 79.2 (CH_2NO_2); 125.0, 126.6, 126.9 (arom. CH); 140.6 (arom. CS); 211.4 (C=O). EI-MS: 253 (0.18, M^+), 219 (0.18), 206 (98), 177 (100), 163 (13), 110 (38), 97 (26). Anal. calc. for $C_{12}H_{15}NO_3S$ (253.32): C 56.90, H 5.97, N 5.53; found: C 56.78, H 5.70, N 5.60.

(2S)-2-[(1R)-2-Nitro-1-(thiophen-3-yl)ethyl]cyclohexanone (**1h**). 3-[(*E*)-2-Nitroethenyl]thiophene (0.22 g, 1.4 mmol) was allowed to react with 1-(trimethylsilyloxy)cyclohexene (0.36 ml, 1.8 mmol) according to *GP 2*. FC (hexane/Et_2O) yielded **1h** (0.264 g, 73%). White crystals. HPLC (hexane/i-PrOH 97:3, flow 1.0 ml/min): t_R

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[21]) Cleavage of (*t*-Bu)Me_2SiO group of the intermediate cyclic nitronate (*GP 2*) requires stirring with the sat. soln. of NH_4F in MeOH for 12 h at ambient temp.

79.8 min. M.p. 110° (hexane). $[\alpha]_D^{r.t.} = -23.8$ ($c = 1.12$, $CHCl_3$). IR ($CHCl_3$): 3008*w*, 2943*m*, 2868*w*, 1707*s*, 1555*s*, 1448*w*, 1433*w*, 1378*m*, 1130*w*, 1045*w*, 877*w*. ^{1}H-NMR (300 MHz): 1.19–1.33 (*m*, 1 H, CH_2); 1.52–1.68 (*m*, CH_2); 1.74–1.83 (*m*, CH_2); 2.00–2.12 (*m*, 1 H, CH_2); 2.30–2.48 (*m*, CH_2); 2.61–2.72 (*m*, CHC=O); 3.97 (*dt*, $^3J = 4.7$, $^3J = 9.3$, C*H*); 4.63 (*dd*, $^2J = 12.5$, $^3J = 9.3$, 1 H, CH_2NO_2); 4.85 (*dd*, $^2J = 12.5$, $^3J = 4.7$, 1 H, CH_2NO_2); 6.94 (*d*, $^3J = 5.0$, 1 arom. H); 7.08 (*d*, $^3J = 3.1$, 1 arom. CH–S); 7.30 (*dd*, $^3J = 3.1$, $^3J = 5.0$, 1 arom. H). ^{13}C-NMR (75 MHz): 24.8, 28.1, 32.5 (CH_2); 39.0 (ArlC*H*); 42.4 (CH_2C=O); 52.3 (C*H*C=O); 78.6 (CH_2NO_2); 123.1, 126.4, 126.5 (arom. CH); 138.2 (arom. CS); 211.6 (C=O). EI-MS: 253 (0.56, M^+), 219 (0.23), 206 (100), 189 (11), 177 (97), 163 (15), 110 (33), 97 (33). Anal. calc. for $C_{12}H_{15}NO_3S$ (253.32): C 56.90, H 5.97, N 5.53; found: C 56.93, H 5.81, N 5.59.

*(2*S*)-2-[(1*S*)-3-Methyl-1-(nitromethyl)butyl]cyclohexanone* (**4**). According to *GP 3*[22]), (*E*)-4-methyl-1-nitropent-1-ene (0.18 g, 1.4 mmol) was allowed to react[23]) with 1-(trimethylsilyloxy)cyclohexene (0.36 ml, 1.8 mmol). After desilylation, most of the TADDOL (*ca.* 3.4 equiv.) was separated by recrystallization from CCl_4 as a clathrate [21]. FC (hexane/Et_2O) of the residue yielded **4** (0.143 g, 45%). Colorless oil. HPLC (hexane/i-PrOH 99.5:0.5, flow 0.4 ml/min): t_R 100.0 min. $[\alpha]_D^{r.t.} = -0.9$ ($c = 0.87$, $CHCl_3$). IR ($CHCl_3$): 3011*m*, 2960*s*, 2868*s*, 1706*s*, 1556*s*, 1466*s*, 1449*s*, 1435*m*, 1384*s*, 1339*m*, 1315*m*, 1125*m*, 1067*m*. ^{1}H-NMR (200 MHz): 0.90 (*d*, $^3J = 6.2$, Me); 0.95 (*d*, $^3J = 6.2$, Me); 1.11–1.38 (*2* H), 1.43–1.75 (4 H), 1.90–2.17 (3 H), 2.30–2.68 (4 H) (all *m*, 5 CH_2 + 3 CH); 4.38 (*dd*, $^2J = 12.5$, $^3J = 6.6$, 1 H, CH_2NO_2); 4.58 (*dd*, $^2J = 12.5$, $^3J = 5.4$, 1 H, CH_2NO_2). ^{13}C-NMR (50 MHz): 21.6, 22.9 (Me); 25.1 (CH_2); 25.4 (Me_2C*H*); 27.4, 30.1 (CH_2); 35.1 (C*H*CH_2NO_2); 38.5 (CH_2); 42.5 (CH_2C=O); 51.4 (C*H*C=O); 77.2 (CH_2NO_2); 211.3 (C=O). EI-MS: 228 (0.08, $[M+1]^+$), 210 (0.05), 197 (2.5), 137 (9.5), 123 (27.5), 98 (100), 83 (21). Anal. calc. for $C_{12}H_{21}NO_3$ (227.3): C 63.41, H 9.31, N 6.16; found: C 63.38, H 9.38, N 6.20.

*(*R*)-3-(4-Methoxyphenyl)-4-nitro-1-phenylbutan-1-one* (**5**). 1-Methoxy-4-[(*E*)-2-nitroethenyl]benzene (0.244 g, 1.36 mmol) was allowed to react with 1-phenyl-1-(trimethylsilyloxy)ethylene (0.36 ml, 1.77 mmol) according to *GP 3*. FC (hexane/Et_2O) yielded **5** (0.402 g, 99%). White crystals. HPLC (hexane/i-PrOH 90:10, flow 2.0 ml/min): t_R 56.81 min. M.p. 76–77.5° (hexane/benzene) ([33]: *rac*-**5**: m.p. 66° (benzene)). $[\alpha]_D^{r.t.} = +20.7$ ($c = 1.79$, $CHCl_3$). ^{1}H-NMR (300 MHz): 3.41 (*dd*, $^2J = 17.4$, $^3J = 7.2$, 1 H, CH_2C=O); 3.42 (*dd*, $^2J = 17.4$, $^3J = 6.8$, 1 H, CH_2C=O); 3.76 (*s*, MeO); 4.17 (*quint.*, Arl–C*H*); 4.64 (*dd*, $^2J = 12.1$, $^3J = 8.1$, 1 H, CH_2NO_2); 4.79 (*dd*, $^2J = 12.1$, $^3J = 6.5$, 1 H, CH_2NO_2); 6.85 (*d*, $^3J = 8.7$, 2 arom. H); 7.19 (*d*, $^3J = 8.7$, 2 arom. H); 7.42–7.48 (*m*, 2 H_m of Ph); 7.53–7.60 (*m*, H_p of Ph); 7.89–7.93 (*m*, 2 H_o of Ph). ^{13}C-NMR (75 MHz): 38.5 (ArlC*H*); 41.5 (CH_2C=O); 55.2 (MeO); 79.8 (CH_2NO_2); 114.5, 128.1, 128.6, 128.8 (arom. CH); 131.1 (arom. C); 133.6 (arom. CH); 136.5 (arom. C); 159.2 (*C*–OMe); 197.2 (C=O).

*(2*S*)-2-[(1*R*)-1-(4-Methoxyphenyl)-2-nitroethyl]cyclopentanone* (**6**). 1-Methoxy-4-[(*E*)-2-nitroethenyl]-benzene (0.255 g, 1.42 mmol) was allowed to react with 1-(trimethylsilyloxy)cyclopentene (0.33 ml, 1.85 mmol) according to *GP 3*. FC (hexane/Et_2O) yielded **6** (0.356 g, 95%). White crystals. HPLC (hexane/i-PrOH 90:10, flow 0.6 ml/min): t_R 113.5 min. M.p. 79.5–80.5° (hexane) ([34]: *rac*-**6**: m.p. 70–71°). $[\alpha]_D^{r.t.} = -105.1$ ($c = 1.71$, $CHCl_3$). ^{1}H-NMR (300 MHz, C_6D_6): 0.84–1.08 (2 H), 1.18–1.32 (2 H), 1.49–1.73 (2 H), 1.78–1.88 (1 H) (all *m*, 3 CH_2 + CH); 3.27 (*s*, MeO); 3.53 (*ddd*, $^3J = 5.6$, $^3J = 9.0$, $^3J = 10.0$, Arl–C*H*); 4.28 (*dd*, $^2J = 12.5$, $^3J = 10.0$, 1 H, CH_2NO_2); 5.01 (*dd*, $^2J = 12.5$, $^3J = 5.6$, 1 H, CH_2NO_2); 6.66 (*d*, $^3J = 8.7$, 2 arom. H); 6.81 (*d*, $^3J = 8.7$, 2 arom. H). ^{13}C-NMR (75 MHz, C_6D_6): 20.2, 28.0 (CH_2); 38.3 (CH_2C=O); 43.7 (ArlC*H*); 50.5 (C*H*C=O); 54.9 (MeO); 78.7 (CH_2NO_2); 114.7, 129.7 (arom. CH); 130.4 (arom. C); 159.8 (*C*–OMe); 217.3 (C=O).

*(6*S*)-6-[(1*R*)-1-(4-Methoxyphenyl)-2-nitroethyl]cyclohex-2-enone* (**7**). 1-Methoxy-4-[(*E*)-2-nitroethenyl]-benzene (0.485 g, 2.7 mmol) was allowed to react with 2-(trimethylsilyloxy)cyclohexa-1,3-diene (1.00 ml, 5.4 mmol) according to *GP 3*. FC (hexane/Et_2O) yielded **7** (0.440 g, 59%). White crystals. HPLC (hexane/i-PrOH 90:10, flow 2.0 ml/min): t_R 40.89 min. M.p. 115–117° (hexane). $[\alpha]_D^{r.t.} = +31.1$ ($c = 1.05$, $CHCl_3$). IR ($CHCl_3$): 3009*w*, 2934*w*, 2838*w*, 1674*s*, 1611*w*, 1554*s*, 1514*s*, 1429*w*, 1380*m*, 1305*w*, 1128*w*, 1036*w*, 833*m*. ^{1}H-NMR (300 MHz, C_6D_6): 0.98–1.11 (1 H), 1.21–1.31 (1 H), 1.40–1.66 (2 H), (all *m*, 2 CH_2); 2.02 (*ddd*, $^3J = 4.4$, $^3J = 8.7$, $^3J = 10.4$, CHC=O); 3.26 (*s*, MeO); 3.85 (*ddd*, $^3J = 5.6$, $^3J = 8.7$, $^3J = 10.0$, Arl–C*H*); 4.30 (*dd*, $^2J = 12.8$, $^3J = 10.0$, 1 H, CH_2NO_2); 4.79 (*dd*, $^2J = 12.8$, $^3J = 5.6$, 1 H, CH_2NO_2); 5.82 (*ddd*, $^3J = 10.0$, $^4J = 2.5$, $^4J = 1.6$, 1 H, =C*H*–C=O); 6.15 (*dt*, $^3J = 3.7$, $^3J = 10.0$, 1 H, CH_2–C*H*=); 6.65 (*d*, $^3J = 8.7$, 2 arom. H); 6.83 (*d*, $^3J = 8.7$, 2 arom. H). ^{13}C-NMR (75 MHz, C_6D_6): 24.9, 26.1 (CH_2); 42.9 (ArlCH); 48.8 (CHC=O); 55.0 (MeO); 79.6 (CH_2NO_2); 114.7 (arom. CH); 129.7 (=CH–C=O); 129.8 (arom. CH); 130.1 (arom. C); 149.3 (CH_2C*H*=);

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[22]) After the addition of the solution of (*E*)-4-methyl-1-nitropent-1-ene to the soln. of **3** at −40°, the temp. was allowed to rise to −10°, then the resulting mixture was recooled to −95°.

[23]) Reaction conditions: 17 h at −75°, and 19 h at −55°.

159.7 (*C*–OMe); 198.9 (C=O). EI-MS: 275 (0.5, M^+), 241 (6.1), 228 (66), 200 (35), 161 (95), 134 (100), 121 (37), 91 (32). Anal. calc. for $C_{15}H_{17}NO_4$ (275.30): C 65.44, H 6.22, N 5.09; found: C 65.41, H 6.17, N 5.06.

*Synthesis of (5*R*,6*S*)-3-(Trimethylsilyloxy)-5-(4-methoxyphenyl)-2-oxa-3-azatricyclo[4.3.1.0^{4,9}]decan-10-one* (**8**). (i-Pr)$_2$NEt (3 drops) and BSA (0.68 ml, 2.76 mmol) were added consecutively to a soln. of **7** (0.38 g, 1.38 mmol) in benzene (10 ml). The resulting mixture was stirred at 20° for 1 h and then at 80° for 10 h. The volatile components were removed *in vacuo* (0.01 Torr, 5 h). The residue was recrystallized (hexane) to give **8** (0.32 g, 67%). Off-white crystals. M.p. 110–125° (dec.). $[\alpha]_D^{rt} = -57.1$ ($c = 1.56$, $CHCl_3$). IR ($CHCl_3$): 3008*m*, 2958*m*, 2838*w*, 1750*s*, 1674*w*, 1612*m*, 1554*m*, 1514*s*, 1464*m*, 1441*m*, 1304*m*, 1035*s*, 893*s*, 870*s*, 846*s*, 826*s*. ^{1}H-NMR (300 MHz): 1.54–1.67 (*m*, 1 H, CH_2); 1.89 (*ddd*, $^2J = 15.0$, $J_1 = 2.5$, $J_2 = 6.5$, 1 H, CH_2); 2.24–2.45 (*m*, 3 H, CH_2 + CH); 3.03 (*d*, $J = 2.5$, CH); 3.45 (*ddd*, $J_1 = 1.9$, $J_2 = 5.9$, $J_3 = 9.0$, CH); 3.78 (*s*, MeO); 3.87 (*dd*, $J_1 = 2.5$, $J_2 = 5.9$, CH); 5.16 (br. *d*, $J = 9.3$, CH–O); 6.83 (*d*, $^3J = 8.7$, 2 arom. H); 6.98 (*d*, $^3J = 8.7$, 2 arom. H). ^{13}C-NMR (75 MHz): –0.8 (Me_3Si); 22.4, 33.4 (CH_2); 49.7, 51.6, 55.2 (CH); 55.2 (MeO); 82.2 (NCH); 88.9 (CH–O); 114.4 (arom. CH); 127.4 (arom. CH); 136.9 (arom. C); 158.5 (*C*–OMe); 217.2 (C=O). ESI-MS: 386 (26, $[M + K]^+$), 370 (45, $[M + Na]^+$), 348 (6, $[M + 1]^+$). Anal. calc. for $C_{18}H_{25}NO_4Si$ (347.48): C 62.22, H 7.25, N 4.03; found: C 62.21, H 7.34, N 4.02.

*(4*R*,4a*S*,8a*R*)-8a-[(*tert*-Butyl)dimethylsilyloxy]-4-(methoxyphenyl)-4a,5,6,7,8,8a-hexahydro-4*H*-benz[*e*][1,2]-oxazine 2-Oxide* (**9**). 1-Methoxy-4-[(*E*)-2-nitroethenyl]benzene (1.13 g, 6.3 mmol) was allowed to react with 1-[(*tert*-butyl)dimethylsilyloxy)cyclohexene (1.61 g, 7.6 mmol) according to *GP 2*. Separation of the mixture by FC (hexane/Et_2O) yielded the TADDOL (97% recovery) and **9** (1.98 g) as a slightly yellowish oil, which crystallized upon the addition of hexane (10 ml) and (i-Pr)$_2$NEt (3 drops). Filtration (–20°) and rinsing with precooled (–20°) hexane gave **9** (1.88 g, 76%) as a white crystalline material, which is stable[24]) for several months at –18° in the absence of moisture. M.p. 82–86° (dec.). $[\alpha]_D^{rt} = -45.6$ ($c = 1.59$, $CHCl_3$). IR ($CHCl_3$): 3007*m*, 2933*s*, 2858*m*, 1627*s*, 1513*s*, 1463*m*, 1368*m*, 1317*m*, 1133*m*, 1107*m*, 1035*m*, 999*m*, 926*m*, 872*m*, 841*s*. ^{1}H-NMR (300 MHz): 0.20 (*s*, 3 H, Me_2Si); 0.26 (*s*, 3 H, Me_2Si); 0.78 (*s*, *t*-Bu); 1.30–1.43 (1 H), 1.48–1.74 (5 H), 1.78–1.89 (1 H), 2.05–2.15 (2 H) (all *m*, 4 CH_2 + CH); 3.45 (*dd*, $^3J = 3.7$, $^3J = 4.1$, Arl–C*H*); 3.79 (*s*, MeO); 6.49 (*d*, $^3J = 4.1$, CH=N); 6.86 (*d*, $^3J = 8.7$, 2 arom. H); 7.19 (*d*, $^3J = 8.7$, 2 arom. H). ^{13}C-NMR (75 MHz): –3.2 (MeSi); –3.0 (MeSi); 17.4 (Me_3C); 22.6, 22.7 (CH_2); 25.3 (*Me*$_3$C); 29.9, 35.5 (CH_2); 43.2, 43.8 (CH); 54.9 (MeO); 104.9 (COSi); 113.2 (CH=N); 113.8, 128.5 (arom. CH); 132.4 (arom. C); 158.5 (*C*OMe). ESI-MS: 430 (24, $[M + K]^+$), 414 (100, $[M + Na]^+$), 392 (36, $[M + 1]^+$). Anal. calc. for $C_{21}H_{33}NO_4Si$ (391.58): C 64.41, H 8.49, N 3.58; found: C 64.34, H 8.34, N 3.58.

*(3*S*,3a*S*,4*R*,4a*S*,8a*R*)-{8a-[1-(*tert*-Butyl)dimethylsilyloxy]-4-(4-methoxyphenyl)perhydroazireno[1,2-*b*]benz[*e*][1,2]oxazin-3-yl}(phenyl)methanone* (**10**). Nitronate **9** (0.30 g, 0.77 mmol) was allowed to react with phenylacetylene (0.25 ml, 2.28 mmol) for 27 h according to *GP 4*. FC yielded **10** (0.197 g, 52%). White amorphous solid. $[\alpha]_D^{rt} = +134.7$ ($c = 0.65$, $CHCl_3$). IR ($CHCl_3$): 3007*m*, 2934*s*, 2858*s*, 1685*s*, 1612*m*, 1582*w*, 1513*s*, 1462*m*, 1450*s*, 1368*m*, 1304*m*, 1170*s*, 1146*m*, 1093*s*, 1034*s*, 1004*s*, 952*s*, 932*m*, 906*m*, 873*s*, 838*s*. ^{1}H-NMR (300 MHz): 0.03 (*s*, 3 H, Me_2Si); 0.29 (*s*, 3 H, Me_2Si); 0.91 (*s*, *t*-Bu); 1.14–1.45 (*m*, 4 CH_2); 2.24 (br. *d*, $^3J = 12.8$, CH); 2.67 (*dd*, $^3J = 7.5$, $^3J = 8.4$, CHN); 3.20 (*d*, $^3J = 7.5$, CHC=O); 3.28 (*dd*, $^3J = 8.4$, $^3J = 12.8$, Arl–C*H*); 3.82 (*s*, MeO); 6.95 (*d*, $^3J = 8.7$, 2 arom. H); 7.36 (*d*, $^3J = 8.7$, 2 arom. H); 7.46–7.52 (*m*, 2 H_m of Ph); 7.56–7.62 (*m*, 1 H_p of Ph); 8.18–8.22 (*m*, 2 H_o of Ph). ^{13}C-NMR (75 MHz): –3.4 (Me_2Si); 17.9 (Me_3C); 20.6, 21.6, 23.2 (CH_2); 25.8 (*Me*$_3$C); 33.0 (CH_2); 36.1, 43.6, 49.3, 52.9 (CH); 55.2 (MeO); 103.2 (COSi); 114.4, 128.5, 129.0, 129.7 (arom. CH); 132.7 (arom. C); 133.4 (arom. CH_p of Ph); 137.3 (arom. C); 158.7 (*C*OMe); 192.2 (C=O). ESI-MS: 532 (11, $[M + K]^+$), 516 (100, $[M + Na]^+$), 494 (4, $[M + 1]^+$). Anal. calc. for $C_{29}H_{39}NO_4Si$ (493.72): C 70.55, H 7.96, N 2.84; found: C 70.39, H 7.99, N 2.87.

*Ethyl (3a*S*,4*R*,4a*S*,8a*R*)-3-Acetyl-8a-[1-(*tert*-butyl)dimethylsilyloxy)-4-(4-methoxyphenyl)perhydroazireno[1,2-*b*]benz[*e*][1,2]oxazine-1-carboxylate* (**11**). Nitronate **9** (0.30 g, 0.77 mmol) was allowed to react with freshly distilled ethyl but-2-ynoate (0.26 ml, 2.24 mmol) for 14.5 h according to *GP 4*. FC yielded **11** (0.293 g, 76%). White amorphous solid. $[\alpha]_D^{rt} = +75.3$ ($c = 1.05$, $CHCl_3$). IR ($CHCl_3$): 3006*m*, 2936*s*, 2858*s*, 1717*s*, 1612*m*, 1514*s*, 1463*m*, 1448*m*, 1390*m*, 1368*m*, 1304*m*, 1171*s*, 1141*m*, 1104*s*, 1081*s*, 1048*s*, 1012*s*, 950*m*, 932*m*, 904*m*, 871*m*, 835*s*. ^{1}H-NMR (300 MHz, C_5D_5N): 0.35 (*s*, 3 H, Me_2Si); 0.53 (*s*, 3 H, Me_2Si); 0.95 (*t*, $^3J = 7.2$, Me); 1.02 (*s*, *t*-Bu); 1.14–1.25 (1 H), 1.31–1.53 (6 H), 1.63–1.74 (1 H) (all *m*, 4 CH_2); 2.49 (br. *d*, $^3J = 12.8$, 1 H, CH); 2.61 (*s*, MeC(O)); 3.21 (*dd*, $^3J = 8.4$, $^3J = 12.8$, Arl–C*H*); 3.45 (*d*, $^3J = 8.4$, CHN); 3.66 (*s*, MeO); 3.93 (*dq*, $^2J = 10.9$, $^3J = 7.2$, 1 H, CH_2O); 4.02 (*dq*, $^2J = 10.9$, $^3J = 7.2$, 1 H, CH_2O); 7.02 (*d*, $^3J = 8.7$, 2 arom. H); 7.43 (*d*, $^3J = 8.7$,

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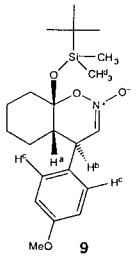
[24]) It is noteworthy that the solns. of **9** can be efficiently stabilized by the addition of few drops of tertiary amines (in particular, (i-Pr)$_2$NEt).

2 arom. H). ^{13}C-NMR (75 MHz, C_6D_6): −2.5 (MeSi); −2.4 (MeSi); 13.8 (Me); 18.6 (Me_3C); 21.1, 22.4, 23.8 (CH_2); 26.5 (Me_3C); 30.7 (*Me*C=O); 34.4 (CH_2); 37.5, 44.4 (CH); 55.1 (MeO); 58.9 (CN); 60.5 (CH); 62.3 (CH_2O); 104.3 (COSi); 115.3, 130.3 (arom. CH); 132.3 (arom. C); 159.9 (*C*OMe); 167.1 (CO_2Et); 197.0 (C=O). ESI-MS: 542 (30, $[M+K]^+$), 526 (100, $[M+Na]^+$), 504 (15, $[M+1]^+$). Anal. calc. for $C_{27}H_{41}NO_6Si$ (391.58): C 64.38, H 8.20, N 2.78; found: C 64.25, H 8.14, N 2.81.

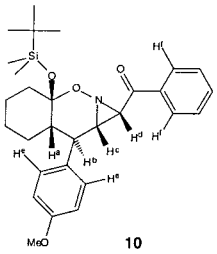
Nuclear Overhauser *Effect Measurements with Compounds* **9**–**11** (for assignment of H^a–H^f, see accompanying *Formulae*). The enlargement of the H^d signal (δ 0.20 ppm) upon irradiation with the H^c frequency (δ 7.19 ppm) in nitronate **9**, together with the finding that the configuration of CH^a–CH^b centers is *unlike* (**9** → **3d**; see *Scheme 3* and *Table 1*), confirms the *cis*-fision of the six-membered rings in **9**.

Table 2. *Nuclear* Overhauser *Effects Resulting from Irradiation with the Frequency of H^c of Oxaziridines* **10** *and* **11** (δ 2.67 and 3.45 ppm, respectively). For assignment of the H-atoms H^a–H^f, see accompanying *Formulae.*

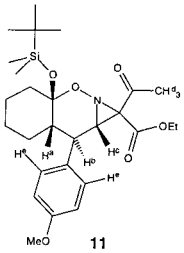
Compound	Enlargement of the signal (δ [ppm])					
	H^a	H^b	H^d	H^e	H^f	EtO
10	2.24; yes	3.28; no	3.20; yes	7.36; yes	8.18–8.22; no	–
11	2.49; yes	3.21; no	2.61; no	7.43; yes	–	0.95, 3.93, 4.02; no



9



10



11

The relative configurations at the stereogenic centers of **10** and **11** were deduced from the NOE measurement as listed in *Table 2*. Unfortunately, the irradiation of the protons of Ac or EtO groups in **11** gave no enlargement of any other signals, so we were not able to assign the configuration of the tertiary stereogenic center of the aziridine ring.

X-Ray Crystal-Structure Determination of **1c** (see *Fig.*). From a crystal of size 0.30 × 0.20 × 0.15 mm, 2848 reflexions were measured on an *Enraf Nonius CAD-4* Diffractometer with CuK_α radiation (graphite monochromator, $\lambda = 1.54184$ Å). Since the absolute structure had to be determined, the *Friedel* pair of every reflection was measured as well. The structure was solved by direct method with SIR97. The non-H-atoms were refined anisotropically with SHELXL-97. H-Atoms were calculated at idealized positions and included in the structure factor calculation with fixed isotropic displacement parameters. Drawings of the molecule were accomplished with PLUTO, ORTEP. $C_{14}H_{16}BrNO_3$, Mol.-wt. 326.19, crystallized from MeOH, temp. 293(2) K, orthorhombic, space group $P2_12_12_1$, $a = 5.5390(8)$ Å, $b = 8.4950(12)$ Å, $c = 30.777(3)$ Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$, $V = 1448.2(3)$ Å^3, $Z = 4$, $\rho_{calc.} = 1.496$ g·cm^{-3}, $\mu = 3.909$ mm^{-1}, $F(000) = 664$. Number of reflections collected 2848 (ω scan, $5.7 < 2\theta < 134.5$), 2348 independent reflections, 1945 reflections observed, criterion $I > 3\sigma(I)$, number of variables 173, final $R = 4.08\%$, $wR_2 = 13.29\%$, goodness of fit 1.209, $\Delta\rho$ (max, min) 0.511 eÅ^{-3}, −0.561 eÅ^{-3}. Crystallographic data (excluding structure factors) for the structure of **1c** have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC-127631. Copies of the Data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ UK (fax: +44(1233) 336033; e-mail: deposit@ccdc.cam.ac.uk).

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