Cycloadditions, 55[◇]

Substituent Effects in Tandem Intramolecular Silyl Nitronate Olefin Cycloadditions (ISOC) Leading to Functionalized Tetrahydrofurans

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The intramolecular silyl nitronate olefin cycloaddition (ISOC) leading to substitued, fused-ring tetrahydrofurans **6** was examined with regard to optimum conditions and substituent effects. The required unsaturated nitro ethers **3** resulted from low-temperature, base-mediated Michael addition of allyl alcohols **2** to nitroolefins **1**, followed by conversion to unsaturated silyl nitronates **4**. Cycloaddition of the latter and elimination of silanol provided **6**. One-pot tandem reactions, starting with nitroolefins **1** and allyl alcohols **2** and involving four steps, sometimes proceeded in better yields but often gave unexpected side products. Terminal olefinic electron-donating substituents (Me, MeO) increased the rate of cycloaddition, while an internal olefinic methyl substituent slowed down the reaction. In the case of nitronates possessing ester or nitrile moieties as terminal olefin substituents, tandem Michael addition to produce substituted furans **14**, **15** occurred faster than trapping of the nitronate anion by TMSCl.

Introduction

Intramolecular dipolar cycloadditions have recently been of considerable synthetic and mechanistic interest[1,2]. Such reactions generate two new rings, one of which is a five-membered heterocyclic ring, which can be cleaved, thereby leading to the stereospecific introduction of two functional groups. Intramolecular nitrile oxide olefin cycloadditions (INOC) have shown considerable synthetic utility in natural products synthesis[3]. They proceed at room temperature but with a variable degree of stereoselectivity. Nitrone olefin cycloadditions including intramolecular oxime olefin cycloadditions (IOOC) proceeding via NH-nitrones[4–6], and silyl nitronate olefin cycloadditions[7], often require higher temperatures but are usually more stereoselective[8].

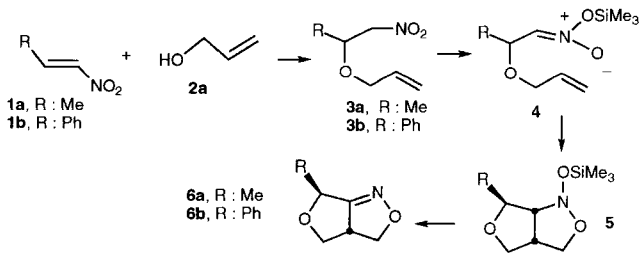
Silyl nitronates (cf. **4**) can be considered as synthetic equivalents of nitrile oxides in their reactions with alkenes[7,8], since the resulting *N*-silyloxyisoxazolidines (cf. **5**) are readily transformed into isoxazolines (see **6**) upon treatment with acid or TBAF.

In a preliminary communication, we reported on the intramolecular version of the silyl nitronate olefin cycloaddition (ISOC) and showed that the stereochemical results were very promising. However, several steps were required in the sequence, starting from nitro compounds[8].

Tandem reactions have emerged in recent years as powerful tools in organic synthesis, due to their operational simplicity and frequently observed selectivity[9]. Prominent in this family are Michael initiated reactions in which the enolate resulting from initial 1,4-addition can subsequently undergo a legion of other transformations in the same reaction vessel, including a facile intramolecular cyclization[9,10].

With this in mind we decided to examine the possibility of performing in one pot the sequence of four steps: Michael addition, silylation, cycloaddition and elimination of siloxane (**1** + **2** → **3** → **4** → **5** → **6**). For optimization, it was first necessary to examine each step in the above sequence in turn (see Scheme 1).

Scheme 1



Additionally, we report herein on the effect of olefinic substituents on the course of the intramolecular silyl nitronate olefin cycloaddition of ethers of type **4** and on the conditions affecting the intermediate steps such as formation of unsaturated silyl nitronates **4** via Michael addition of allyl alcohols **2** to nitroolefins **1**.

Reactions of 1-Nitropropene (1a)

First we examined the addition of allyl alcohol (**2a**) to 1-nitropropene (**1a**) and to β-nitrostyrene (**1b**) in the presence of potassium *tert*-butoxide. The base-catalyzed Michael ad-

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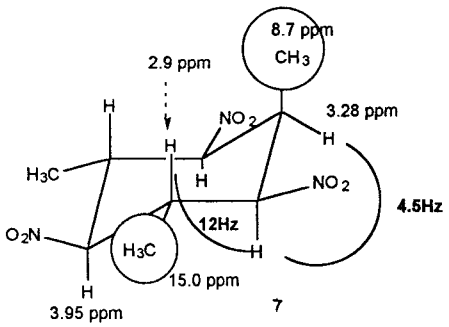
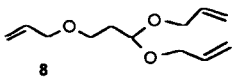
dition of allyl alcohol to β-nitrostyrene had been examined in the past but in order to proceed in good yield the reaction required the presence of at least 3 equivalents of both the alcohol and the base[10]. Obviously for less accessible alcohols a more efficient reaction is desirable.

When the reaction sequence **1a** + **2a** → **6a** was performed as a one-pot reaction (addition of the alcohol at −60 °C, followed after 30 min by addition of TMSCl and TEA, stirring for 2 h at room temp., and addition of TBAF), the yield of isolated isoxazoline (**6a**) was only 20%. This was improved to 41% by allowing the silylation to proceed at −60 °C for 1 h instead of at room temperature and increasing the cycloaddition time to 72 h. However, two minor side products, a trimethyltrinitrocyclohexane (**7**) and an allyl acetal (**8**) were isolated from this one-pot reaction.

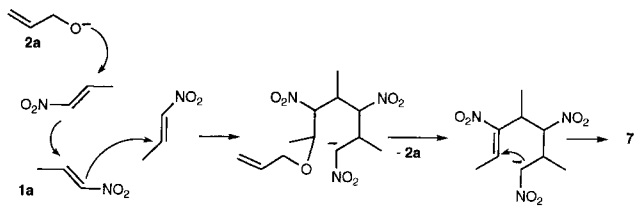
The structure of **7** as *cis,trans*-2,4,6-trimethyl-*cis,cis*-1,3,5-trinitrocyclohexane was elucidated by ^1H and ^{13}C NMR. The latter attested to a twofold symmetry in **7**, with one methyl group different from the other two, while the ^1H-NMR spectrum showed that all hydrogens except one (which was geminal to a Me group, $J_{Ha,Hb}$ = 4.5 Hz) were axial with $J_{H,H} \approx 12$ Hz. This indicated a configuration in which all three nitro groups were equatorial, while two methyl groups were equatorial and one axial.



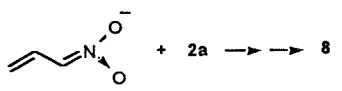


Only one method of preparation of 1,3,5-trinitrocyclohexanes has been reported, namely nucleophilic addition to 1,3,5-trinitrobenzene, i.e. $NaBH_4$ reduction or Grignard addition to 1,3,5-trinitrobenzene[11]. The stereochemistry of 1,3,5-trinitrocyclohexane was thought to be either all *cis* (equatorial) or *cis,trans* (diequatorial, axial) on the basis of dipole moments[12]. The product from MeMgBr addition to 1,3,5-trinitrobenzene was a 2,4,6-trimethyl-1,3,5-trinitrocyclohexane to which no stereochemistry was assigned[11b]. In our case, the formation of **7** could be due to addition of allyl alcoholate to the conjugated double bond of **1a** followed by conjugate addition of the resulting nitronate to two other molecules of **1a**; elimination of allyl alcohol and ring closure would lead to the trinitrocyclohexane **7** as shown in Scheme 2. The likelihood of such a process is indicated by the isolation of intermediate **10** (see below) in the reaction of allyl alcohol with β-nitrostyrene (**1b**). Reaction of 1-nitropropene with KO*t*Bu alone did not produce **7**.

Scheme 2



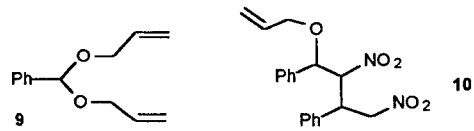
The second minor product in the one-pot formation of **6a** was shown by NMR spectra to be **8**, the diallyl acetal of 3-allyloxypropanal. The route to this product is still uncertain, but presumably involves a Michael addition of allyl alcohol (**2a**) to the nitronate derived from **1a**.



Reactions of β-Nitrostyrene with Allyl Alcohol (2a)

In order to gain more insight into these reactions and possibly to avert the formation of side products, each step in the sequence was examined in more detail with allyl alcohol (**2a**) and β-nitrostyrene (**1b**) as substrates. Reaction of the latter with 3 equiv. of allyl alcohol and 3 equiv. of KO*t*Bu at −20 °C produced **3b** in 77% yield. It was possible to increase the yield of this Michael addition step to 90% and at the same time to decrease the amount of reagents to 1 equiv. of alcohol and of 2 equiv. of base by carrying out the reaction at −98 °C for 30 sec. (see Table 1).

Reaction of **3b** with TMSCl-TEA in benzene for 12 h followed by treatment with aqueous HCl produced the cyclized isoxazoline **6b** in 77% yield. On the other hand, a one-pot reaction of **1b** at −20 °C with 3 equiv. of **2a** and 3 equiv. of KO*t*Bu for 30 min followed by TMSCl-TEA for 72 h and then TBAF afforded **6b** in only 30% yield, together with two side products, **9** and **10**.



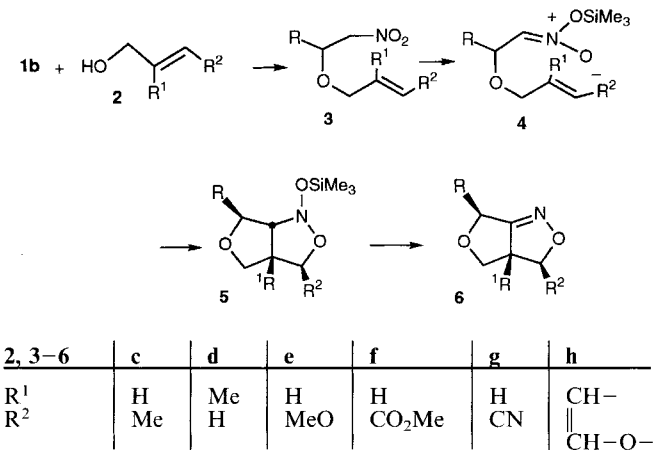
In order to prevent formation of side products and improve the yield of **6b**, different conditions were tried, first for the cycloaddition step and then for the one-pot reaction. When the cycloaddition (**4** → **5**) was carried out in different solvents (benzene and THF) it was found that the reaction required 16 h in benzene, whereas in THF it was complete in less than 1 h. Thus, by reducing the number of equivalents of allyl alcohol to one and replacing the solvent by THF, the yield of **6b** in the one-pot tandem sequence (1 h) was increased to 40%.

Finally, the one-pot tandem reaction of **1b** was performed with 1 equiv. of allyl alcohol and 2 equiv. of KO*t*Bu at a temperature of −98 °C and at 10-fold dilution (0.04 M in nitrostyrene, 0.02 M in allyl alcohol) so that, after desilyl-

Table 1. One pot tandem reactioans [**1b** + **2a–d** + KO*t*Bu (2 equiv.), −98 °C, then TMSCl–TEA, then TBAF 20 °C] to yield **6b–e**; vs. stepwise reactions (**1b** + **2a–d** → **3b–e** → **4** → **5** → **6b–e**)

	Tandem reaction yield of **6** (%)	time[a]	Stepwise reaction yield of **6** (%)	[yield of **3** (%)]
3b				[77[b]]
6b	74	1 h	74	[90]
6c	79	1 h	64	[84]
6d	40	48 h	69	[75]
6e	30	5 min	0	[79]

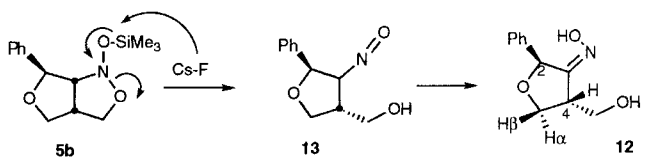
[a] Reaction time for formation of **3**. – [b] 3 equiv. of **2a**, 3 equiv. of KO*t*Bu, −20 °C.



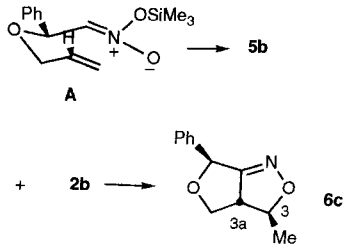
2, 3–6	c	d	e	f	g	h
R^1	H	Me	H	H	H	CH–
R^2	Me	H	MeO	CO_2Me	CN	‖ CH–O–

ation with TBAF, **6b** was isolated in 74% overall yield (slightly higher than in the stepwise reactions, see Table 1).

Concerning the silanol elimination step, i.e. conversion of **5b** to **6b**, we found that reaction of **5b** with anhydrous CsF, in contrast to that with TBAF, led to oxime alcohol **12**, apparently via the nitroso alcohol. CsF acts preferentially as a nucleophile on the silyl ether to produce **13**, whereas TBAF acts as a base causing elimination of silanol. The structure of **12** follows from NOE data. The *trans* stereochemistry of the 2- and 4-substituents (2% NOE between the benzylic proton (H-2) and H-5α but not H-5β, and 6% between H-5β and H-4) is the same as in the cyclic adducts. The stereochemistry of the oxime is (*Z*), as indicated by a 16% enhancement of the aromatic hydrogens upon irradiation of the oxime proton.



The *trans* stereochemistry in products **6** as well as in the *trans* 2,4-disubstituted furan **12** is probably the result of a preferred *endo* transition state A (Ph and H_a *exo*)[13] during the silyl nitronate olefin cycloaddition leading to **5b** (see also discussion of **B**, **C** later), in which the Ph substituent assumes a pseudoequatorial orientation[14]. In the nitrostyrene reaction with allyl alcohol, the yields of **6b** are comparable for the stepwise and the tandem 4-step reaction, and in both cases a low temperature of −95 °C is most beneficial.



Olefinic Substituent Effects in Dipolar Cycloaddition of Unsaturated Silyl Nitronates

Stepwise reaction of (*E*)-2-butenol (**2b**) with β-nitrostyrene (**1b**) proceeded in 84% yield, followed by ISOC and elimination of silanol (see Table 1) to produce the isoxazoline **6c** as a single isomer in 68% yield. Alternatively, the one-pot tandem procedure furnished **6c** in 79% yield. Again, NOE's were most useful in the structure elucidation (for instance, 6% enhancement of the bridge proton (H-3a) on irradiation of the C-3 Me group, 2% NOE between H-4a and the benzylic H, and 3% between the benzylic H and H-3). Three stereocenters had been formed stereospecifically in the ISOC process, with a preference for the *exo* methyl substituent.

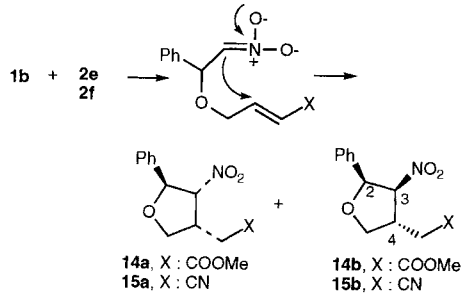
Formation of isoxazoline **6d**, obtained from 2-methyl-2-propenol (**2c**) and β-nitrostyrene (**1b**) either in the stepwise reactions (53% overall) or the one-pot reaction (40%), also proceeded stereospecifically to yield a single isomer, but the cycloaddition step required 48 h in contrast to 1 h for formation of **6c**. Similar rate differences reflecting the substitution pattern on the alkene moiety, have been observed in the IOOC reaction leading to substituted pyrrolidines[14].

Michael addition of furfuryl alcohol (**2g**) to β-nitrostyrene (**1b**) at 20 °C led to isolation of the nitro ether **3h** in only 8% yield, although this was improved to 72% when the reaction was carried out at −98 °C. However, attempts to perform the ISOC reaction on **3h** were unsuccessful and led only to decomposition.

Next we examined 3-methoxy-2-propenol (**2d**), possessing a methoxy substituent on the terminal position of the double bond, which was prepared from methyl propiolate by addition of MeOH and DIBAL reduction[14]. Michael addition of **2d** to **1b** took place readily at −98 °C to afford the unsaturated nitro ether **3e** in 79% yield. However, reaction of (**3e**) with TMSCl and TEA led only to decomposition. On the other hand, the one-pot tandem reactions provided **6e** as a single isomer [NOE of 7% between MeO protons and bridge hydrogen (H-3a)], albeit in only 30% yield.

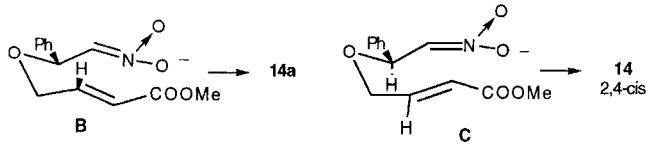
We then turned our attention to ISOC reactions in which the double bond carried an electron-withdrawing substituent. The one-pot reaction of methyl 4-hydroxy-2-butenoate

(**2e**)[15] with β-nitrostyrene (**1b**) in the presence of KO*t*Bu led, even in the absence of TMSCl, to the isolation of two diastereomers of 4-(methoxycarbonylmethyl)-3-nitro-2-phenyltetrahydrofuran (**14a**) and (**14b**) in 72% yield. Evidently, the nitronate formed on Michael addition of the alcoholate undergoes a tandem intramolecular Michael addition to the unsaturated ester in an *exo-trig* cyclization, before it can get trapped by TMSCl. The reaction occurs almost instantaneously at −98 °C to afford **14a** and **14b** in a 2:1 ratio. The structure of **14a** as 2,3-*trans*-3,4-*cis*-4-(methoxycarbonylmethyl)-3-nitro-2-phenyltetrahydrofuran, was clear from NOE and coupling data. The second isomer was only tentatively assigned as **14b**, the nitro epimer of **14a**.



While stereochemical determination in substituted 5-membered rings is complicated because of ring flexibility, NOE experiments rather than coupling constants can be useful tools for revealing stereochemistry[14b]. Thus, in **14a**, H-3 and H-4 are in a *cis*-orientation as indicated by a 7% NOE enhancement, as well as by a *J* value of 7.5 Hz. NOE between H-2 and H-3, as well as the 2.5 Hz coupling constant are consistent with a *trans* relationship of these protons.

If in the intermediate the C=N of the nitronate is almost parallel to the acceptor olefin, so as to facilitate best orbital overlap, then attack of the nitronate on the conjugated double bond in a transition state in which the Ph group is pseudoequatorial (see **B**) should lead to the 2,4-*trans*-disubstituted tetrahydrofuran **14a**. Transition state **C** would result in a 2,4-*cis*-disubstituted product.



A similar result was found with the cyano substituted unsaturated alcohol **2f**, obtained by $Pd(Ph_3P)_4$ catalyzed isomerization of the cyanohydrin derivative of acrolein[17]. Although **2f** was found to polymerize readily in the presence of KO*t*Bu, even at −50 °C, we succeeded in accomplishing the Michael addition of **2f** to nitrostyrene (**1b**) by lowering the temperature to −98 °C. The tandem addition − ring closure proceeded much more slowly (2 h) than the analogous reaction of the corresponding ester **2e** and led to two diastereomers **15a** and **15b** in 50% yield and in approximately 1:1 ratio. NOE's of both compounds indicated the structures shown, possessing the 2,4-*trans* stereochemistry as in the carbethoxy analogues **14**.

In **15b**, irradiation of H-2 results in a 7% enhancement of the H-3 signal, indicative of a *cis* relationship. A 2% NOE between H-3 and H-4, as well as a 3% NOE between H-3 and the CH_2 protons α-to the CN function are consistent with a *trans* relationship between H-3 and H-4. NOE of the second isomer (**15a**) indicated that H-2 and H-3 were *trans* to one another (0%), while H-3 and H-4 were *cis* (6%). Thus, both cyclization products **15a** and **15b** differ only in the stereochemistry of C-3 (due to epimerization at the NO_2 carbon), while the stereorelationship between C-2 and C-4 is the same. This is consistent with a preferred approach analogous to **B** in the ring closure.

In conclusion, the study reported herein establishes the utility of the ISOC reaction, starting with nitroolefins, for the stereoselective construction of fused tetrahydrofuro[3,4-*c*]isoxazolidines **6** or of substituted tetrahydrofurans **14**, **15**. Furthermore, light is shed on the comparative advantages of stepwise versus tandem one-pot procedures, on temperature effects in the formation of **6**, and on the effect exerted by double bond substituents in the unsaturated silyl nitronate **4** on the mode and relative rate of cycloaddition.

Support of this research by a grant from the *Israel Science Foundation* is gratefully acknowledged. We thank Dr. *H. E. Gottlieb* for valuable help with NMR spectra.

Experimental Section

^1H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ with a Bruker AC-200 or a Bruker AM-300 spectrometer. − High resolution mass spectra were recorded at 60−70 eV with a VG-Fisons "Autospec".

2-(Alloxy)-1-nitropropane (**3a**): Procedure (a), a described for the production of **3b**, was followed using 0.93 ml (812 mg, 1.43 mmol) of allyl alcohol **2a** in 20 ml of THF, potassium *tert*-butoxide (1.6 g, 14.3 mmol) and 1-nitropropene **1a** (500 mg, 5.7 mmol) in 10 ml of THF, to afford 446 mg (3.08 mmol) of **3a** as an oil (57%). The spectral data were identical to those reported previously[10a].

3a,6-trans-6-Methyl-3,3a,4,6-tetrahydrofuro[3,4-c]isoxazole (**6a**). − *a) One-Pot Reaction:* Allyl alcohol **2a** (0.46 ml, 400 mg, 7 mmol) in 10 ml of THF in a flame-dried flask under argon was cooled to −60 °C. After addition of 785 mg (7 mmol) of potassium *tert*-butoxide and stirring for 10 min, a solution of 203 mg (2.3 mmol) of 1-nitropropene **1a** in 5 ml of THF was added dropwise. After further stirring at this temperature for ca. 30 min, 0.883 ml (7 mmol) of TMSCl was added. After 1 h at −60 °C the mixture was brought to room temp. and stirred for an additional 72 h. TBAF, 7 ml (7 mmol) of a 0.1 M solution in THF was then added and after stirring for 1 h the solvent was evaporated and dichloromethane (50 ml) was added. Extraction with 2 × 20 ml of water, drying with $MgSO_4$, evaporation, and chromatography on silica [petroleum ether (PE)/ethyl acetate (EA), 1:1] afforded 120 mg (0.94 mmol) of **6a** as an oil (41% yield). Later fractions contained **7** and **8**.

b) Stepwise Reaction: The stepwise procedure as for the production of **6b** was followed using a solution of 2-(allyloxy)-1-nitropropane **3a** (70 mg, 0.482 mmol) in 10 ml of dry benzene, 0.08 ml (0.579 mmol) of Et_3N, and 0.067 ml (0.528 mmol) of TMSCl to give 35 mg (0.274 mmol) of **6a** (57% yield). − ^1H NMR ($CDCl_3$): δ = 4.72−4.5 (m, 2H), 4.31−4.15 (m, 2H), 4.05−3.92 (m, 1H),

3.74–3.59 (m, 1H), 1.46 (d, J = 6.5 Hz, 3H). The spectral data were in agreement with those reported previously[10].

cis,trans-2,4,6-Trimethyl-1,3,5-trinitrocyclohexane (**7**) was obtained as an oil (8%) by elution with PE/EA. – ^{1}H NMR ($CDCl_3$): δ = 4.4 (dd, J = 12, 4.5 Hz, 1H, $CHNO_2$), 3.95 (t, J = 11.5 Hz, 1H, $CHNO_2$), 3.28 (ddt, J = 14, 7, 4.5 Hz, 1H, $CHCH_3$), 2.99 (tq, J = 11.5, 6 Hz, 1H, $CHCH_3$), 1.1 (d, J = 6 Hz, 3H, CH_3), 1.02 (d, J = 7 Hz, 3H, CH_3). – ^{13}C NMR ($CDCl_3$): δ = 93.56 (d, $CHNO_2$), 88.43 (d, $CHNO_2$), 37 (d, $CHCH_3$), 32.5 (d, $CHCH_3$), 15 (q, CH_3), 8.6 (q, CH_3). – MS (CI; CH_4), *m/z* (%): 279 (10) [MH_2O^+], 263 (3.4) [M + 2 H^+], 262 (28) [MH^+], 216 (12) [$MH^+ - NO_2$], 215 (100) [$MH^+ - HNO_2$], 169 [$MH^+ - (HNO_2 + NO_2)$], 168 (43) [$MH^+ - (2 \times HNO_2)$], 121 (85) [$MH^+ - (3 \times HNO_2)$].

3-Allyloxypropanal Diallyl Acetal (**8**) was obtained on elution with PE/EA (1:1) as an oil (5%). – ^{1}H NMR ($CDCl_3$): δ = 5.91 (m, 3H, RHC=CH_2), 5.28 (dddd, J = 17, 6.5, 3, 1.5 Hz, 3H, RHC=CH_2), 5.17 (ddd, J = 10, 3, 1.5 Hz, 3H, RHC=CH_2), 4.78 (t, J = 5.5 Hz, 1H, OCHO), 4.12 (ddt, J = 12.5, 5.5, 1.3 Hz, 2H, CH_2C=C), 4.03 (ddt, J = 12.5, 5.5, 1.3 Hz, 2H, CH_2C=C), 3.96 (dt, J = 5.5, 1.3 Hz, 2H, CH_2C=C), 3.52 (t, J = 6.5 Hz, 2H, OCHCH_2), 1.96 (td, J = 6.5, 5.8 Hz, 2H, OCH_2CH_2). – ^{13}C NMR ($CDCl_3$): δ = 143.87 (d), 134.7 (d), 116.7 (t), 116.6 (t), 100 (d), 71.9 (t), 66.78 (t), 66.24 (t), 43 (t). MS (CI, CH_4), *m/z* (%), ($C_{12}H_{20}O_3$, MW 212): 213 (73) [MH^+], 212 (12) [MH^+ – H], 172 (10) [$MH^+ - CH_2$–CH=CH_2], 156 (97) [MH^+ – O–CH_2–CH=CH_2], 155 (100) [$MH^+ - HOCH_2CH$=CH_2], 99 (42) [$MH^+ - (2 \times OCH_2CH$=$CH_2)$].

1-(Allyloxy)-2-nitro-1-phenylethane (**3b**). – *a) At –20°C:* A solution of 1.74 g (30 mmol) of allyl alcohol **2a** in 20 ml of THF was stirred at –10 to –20°C while 3.36 g (30 mmol) of potassium *tert*-butoxide was added in small portions. After all the base had dissolved, a solution of 0.87 g (10 mmol) of β-nitrostyrene **1b** in 10 ml of THF was added dropwise over ca. 15 min. Stirring was continued for an additional 15 min, then 2 ml of acetic acid was added, followed by 50 ml of diethyl ether. The mixture was filtered, the inorganic salts were washed several times with diethyl ether, and the combined filtrates were concentrated. Chromatography of the product on silica gel with PE/EA (4:1) as the eluent gave 1.82 g (77%) of **3b** as a colourless oil.

b) Under Dilution and at Lower Temperature: Compound **2a** (0.13 ml, 2 mmol) in 40 ml of THF was placed at room temp. in a flame-dried flask under argon and cooled to –98°C. Potassium *tert*-butoxide (448 mg, 4 mmol) was added. After stirring for ca. 10 min a solution of β-nitrostyrene **1b** (298 mg, 2 mmol) in 50 ml of dry THF was slowly injected, followed immediately by 1 ml of glacial acetic acid. The reaction mixture was allowed to warm to room temp., whereupon it was filtered and the salt residue was rinsed with 20 ml of diethyl ether. The pooled organic phases were evaporated. Chromatography on silica gel with PE/EA (5:1) as the eluent gave 373 mg of **3b** as a yellow oil (90%). The spectral data were identical to those reported previously[10a]. HRMS (EI) *m/z* (MH^+): calcd. for $C_{11}H_{13}NO_3$ 207.0895; found 207.0331.

3a,6a-cis-6a,6-trans-6-Phenyl-1-(trimethylsilyloxy)perhydrofuro-[3,4-c]isoxazole (**5b**): The reaction was carried out in an NMR tube in $CDCl_3$ as described in method (b) for **6a**. The NMR spectrum of intermediate **5b** was obtained before addition of HCl. – ^{1}H NMR ($CDCl_3$): δ = 7.35 (m, 5H, Ar), 4.52 (d, J = 7 Hz, 1H, C_6H_5CH), 4.40 (t, J = 8.5 Hz, 1H, $NOCH_2$), 3.39 (dd, J = 8.5, 6.5 Hz, 1H, OCH_2), 4.01 (dd, J = 8, 7 Hz, 1H, CHCN), 3.87 (bd, J = 8.5 Hz, 1H, $NOCH_2$), 3.66 (dd, J = 9, 6.5 Hz, 1H, OCH_2), 3.44 (dddd, 9, 8.5, 8.5, 8 Hz, 1H, CH_2CHCH_2).

3a,6-trans-6-Phenyl-3-3a,4,6-tetrahydrofuro[3,4-c]isoxazole (**6b**). – *a) Stepwise reaction:* A solution of 100 mg (0.48 mmol) of 1-allyloxy-2-nitro-1-phenylethane **3b** in 10 ml of dry benzene was placed at room temp. in a flame-dried flask under argon. Et_3N (0.08 ml, 0.58 mmol) was added, followed immediately by 0.067 ml (0.528 mmol) of TMSCl. The mixture was stirred for about 12 h and worked-up by addition of 10 ml of 10% HCl(aq). After stirring for 30 minutes the phases were separated. The aqueous phase was extracted with dichloromethane (3 × 5 ml). The combined organic phases were dried with $MgSO_4$. After evaporation the product was purified on silica gel with PE/EA (2:1) as eluent, which afforded 64 mg (77% yield) of **6b** as an oil.

b) At –98°C: Allyl alcohol **2a** (0.13 ml, 2 mmol) in 50 ml of THF was placed in a flame-dried flask under argon and cooled to –98°C. At this stage 448 mg (4 mmol) of potassium *tert*-butoxide was added. After stirring for approx. 10 min, a solution of 290 mg (2 mmol) of β-nitrostyrene **1b** in 40 ml of THF was slowly injected, followed immediately by 0.76 ml (6 mmol) of TMSCl. After 1 h at –98°C the mixture was warmed to room temp. and 6 ml (6 mmol) of TBAF (1.0 M in THF) was slowly injected. After 1 h the mixture was filtered and evaporated. Chromatography on silica gel with PE/EA (2:1) afforded 280 mg (158 mmol) of **6b** as an oil (74%). The spectral data were identical to those reported previously[10b]. Further elution afforded **9** (8%) and **10** (4%).

Benzaldehyde Diallyl Acetal (**9**), obtained as an oil on chromatography after elution with PE/EA (2:1). – ^{1}H NMR ($CDCl_3$): δ = 7.50 (bd, J = 8 Hz, 2H, *ortho* Ar), 7.36 (m, 3H, Ar), 5.94 (ddt, J = 17, 10, 5.55 Hz, 2H, RHC=CH_2), 5.65 (br s, 1H, C_6H_5CH), 5.31 (ddd, J = 17, 3, 1.5 Hz, 2H, RHC=CH_2 *trans*), 5.17 (ddd, J = 10, 3, 1.5 Hz, 2H, RHC=CH_2 *cis*), 4.06 (dt, J = 5.2, 1.5 Hz, 4H, CH_2CH=CH_2). – ^{13}C NMR ($CDCl_3$): δ = 134.5 (d, RC=C), 129 (s, *ipso* Ar), 128.9 (d, CH Ar), 128.2 (d, CH Ar), 126.7 (d, CH Ar), 116.7 (t, C=CH_2), 100.5 (d, $C_6H_5CH_2$), 100.5 (d, C_6H_5CH), 66.2 (t, OCH_2).

1-Allyloxy-2,4-dinitro-1,3-diphenylbutane (**10**), obtained as an oil on elution with PE/EA (2:1). – ^{1}H NMR ($CDCl_3$): δ = 7.45–6.93 (m, 10H, Ar), 5.75 (ddd, J = 17, 11, 6.5, 5 Hz, 1H, HC=CH_2), 5.18 (dm, J = 17 Hz, 1H, HCCH_2), 5.16 (dm, J = 11 Hz, 1H, HC=CH_2), 4.99 (dd, J = 8, 6.5 Hz, 1H, $C_6H_5CHCHNO_2$), 4.92 (dd, J = 13.5, 10.5 Hz, 1H, CH_2NO_2), 4.81 (dd, J = 13.5, 4 Hz, 1H, CH_2NO_2), 4.67 (d, 8H, 1H, $C_6H_5CHCHNO_2$), 3.90 (ddd, J = 10.5, 6.5, 4 Hz, 1H, $C_6H_5CHCH_2NO_2$), 3.88 (ddm, J = 12.5, 5 Hz, 1H, OCH_2), 3.59 (ddt, J = 12.5, 6.5, 1 Hz, 1H, OCH_2). – ^{13}C NMR ($CDCl_3$): δ = 133.2 (d, R–C=C), 129.96 (s, *ipso* Ar), 129.72 (s, *ipso* Ar), 129.3 (d, CH Ar), 129.1 (d, CH Ar), 129 (d, CH Ar), 128.8 (d, CH Ar), 127.5 (d, CH Ar), 127.3 (d, CH Ar), 117.7 (t, C=CH_2), 94.9 (d, C_6H_5CHO), 79.5 (d, NO_2CH), 75.7 (t, CH_2NO_2), 70.0 (t, CH_2O), 43.2 (d, $C_6H_5CHCH_2NO_2$).

2,4-trans-4-Hydroxymethyl-2-phenyltetrahydrofuran-3-one Oxime (**12**): To a solution of 90 mg (0.438 mmol) 1-allyloxy-2-nitro-1-phenylethane (**3b**) in 20 ml dry chloroform in a flame-dried flask under argon at room temp., a solution of 0.09 (0.65 mmol) of dry Et_3N and 0.66 ml (0.52 mmol) of dry TMSCl was injected. After stirring for 20 min the chloroform was evaporated by a stream of argon and was replaced by 20 ml of dry THF. After this change of solvent, 1 g (6.5 mmol) of CsF was added. The heterogeneous mixture was stirred at room temp. for 64 h. The reaction mixture was worked-up by adding 100 ml of dichloromethane, washing with 3 × 20 ml of water and extracting the combined aqueous phases with 3 × 15 ml of diethyl ether. The combined organic phases were dried with $MgSO_4$ and evaporated. The remaining oil was chromatographed on silica gel with PE/EA (1:1) to give 50 mg (0.26 mmol)

of oxime **12** (60%), m.p. 95–96°C. – ^{1}H NMR ($CDCl_3$): δ = 8.5 (br s, 1H, =NOH), 7.35 (m, 5H, Ar), 5.7 (bd, *J* = 1.5 Hz, 1H, C_6H_5CH), 4.22 (ddd, *J* = 8, 9, 0.5 Hz, 1H, H-5), 3.81 (ABX, m, 2H, CH_2OH), 3.80 (dd, *J* = 9, 7.5 Hz, 1H, OCH_2, H-5), 3.2 (dddd, 8, 7.5, 6, 1.5 Hz, 1H, H-4) and (br s, 1H, OH). – ^{13}C NMR ($CDCl_3$): δ = 164.5 (s, C=N), 137.3 (s, *ipso* Ar), 128.4 (d, CH Ar), 128.2 (d, CH Ar), 127.3 (d, CH Ar), 78.8 (d, C_6H_5CH), 68.5 (t, C-5), 61.5 (t, CH_2OH), 44.2 (d, C-4). – MS (CI, isobutane); *m/z* (%), ($C_{11}H_{13}NO_3$, MW 207): 208 (47) [MH^+], 190 (100) [$MH^+ - H_2O$], 160 (4) [$MH^+ - (CH_2OH + OH)$], 131 (1.3) [$MH^+ - C_6H_5$], 107 (30) [$C_6H_5-CH=OH^+$]. – HRMS (EI), *m/z* (M^+) calcd. for $C_{11}H_{13}NO_3$ 207.0895; found 207.0903.

1-(E-2'-Buten-1'-oxy)-2-nitro-1-phenylethane (**3c**). – *a) At −20°C:* Procedure (a) as for production of **3b** was followed using crotyl alcohol **2b** (0.51 ml (6 mmol), potassium *tert*-butoxide (732 mg, 6 mmol), and β-nitrostyrene **1b** (298 mg, 2 mmol) to afford 372 mg (0.168 mmol) of **3c** (84%) as an oil.

b) Under Dilution and at Low Temperature: Procedure (b) as for production of **3b** was followed using crotyl alcohol **2b** (0.17 ml, 2 mmol) in 40 ml of THF, potassium *tert*-butoxide (448 mg, 4 mmol), β-nitrostyrene **1b** (298 mg, 2 mmol) in 50 ml of THF and glacial acid (0.5 ml) to afford 372 mg (1.68 mmol) of **3c** (84%) as an oil. – ^{1}H NMR ($CDCl_3$): δ = 7.30–7.45 (m, 5H, Ar), 5.57 (m, 2H, HC=CH), 5.12 (dd, *J* = 10, 3.5 Hz, 1H, C_6H_5CH), 4.63 (dd, *J* = 12.5, 10 Hz, 1H, CH_2NO_2), 4.39 (dd, *J* = 12.5, 3.5 Hz, 1H, CH_2NO_2), 3.92 (ddm, *J* = 11.5, 5 Hz, 1H, CH_2O), 3.75 (ddm, *J* = 11.5, 5 Hz, 1H, CH_2O), 1.69 (dm, *J* = 6 Hz, 3H, CH_3). – ^{13}C NMR ($CDCl_3$): δ = 136.5 (s, *ipso* Ar), 130.2 (d, CH), 128.9 (d, CH), 126.8 (d, CH), 126.5 (d, CH), 80.4 (t, CH_2NO_2), 77.1 (d, C_6H_5CH), 69.7 (t, CH_2-O), 17.6 (q, CH_3). – MS (CI, isobutane), *m/z* (%), ($C_{12}H_{15}NO_3$, MW 221): 222 (10) [MH^+], 221 (0.5) [MH^+], 175 (3) [$MH^+ - HNO_2$], 174 (7) [$MH^+ - HNO_2$], 161 (100) [$MH^+ - CH_2-NO_2$]. – HRMS (EI), *m/z* (%): (MH^+ autoprotonation) calcd. for $C_{12}H_{15}NO_3$ 222.1130; found 222.1077.

3,3a-trans-3a,6-trans-3-Methyl-6-phenyltetrahydrofuro[3,4-c]-isoxazole (**6c**): a) The stepwise procedure for production of **6b** was followed using a solution of 100 mg (0.48 mmol) of **3c** in 10 ml of dry benzene, Et_3N (0.08 ml, 0.597 mmol), TMSCl (0.067 ml, 0.528 mmol), and 10% HCl(aq) (5 ml) to afford 66.2 mg (0.326 mmol, 68%) of **6c** as an oil. – b) The one-pot procedure as for production of **6b** was followed using a solution of 0.17 ml (2 mmol) of crotyl alcohol **2c** in 40 ml of THF, potassium *tert*-butoxide (448 mg, 4 mmol), β-nitrostyrene (298 mg, 2 mmol) in 50 ml of THF, TMSCl (0.76 ml, 6 mmol), and TBAF (3 ml, 3 mmol, 1.0 M in THF) to afford 319 mg (2.57 mmol, 79%) of **6c**. – ^{1}H NMR: δ = 4.46–3.28 (m, 5H, Ar), 5.57 (br s, 1H, C_6H_5CH), 4.65 (m, 1H, H-3a), 4.39 (m, 1H, CH_3CH), 3.83 (m, 2H, CH_2O), 1.51 (d, *J* = 6 Hz, 3H, CH_3). – ^{13}C NMR ($CDCl_3$): δ = 171.4 (s, C=N), 137.5 (s, *ipso* Ar), 128.7 (d), 128.4 (d), 125.6 (d), 84.1 (d, $CHCH_3$), 73.3 (d, C_6H_5CH), 69.2 (t, CH_2O), 59.4 (d, C-3a), 18.2 (q, CH_3). – MS (CI, isobutane), *m/z* (%), ($C_{12}H_{13}NO_2$, MW 203): 260 (8) [$MC_4H_4^+$], 205 (11) [$(M + 1)H^+$], 204 (100) [MH^+], 188 (<1) [$MH^+ - O$], 173 (<1) [$MH^+ - (O + Me)$], 159 (<1) [$MH^+ - (N-O + CH_2)$]. – HRMS (EI), *m/z*: (MH^+) calcd. for $C_{12}H_{13}NO_2$ 203.0946; found 203.0796.

1-(2'-Methyl-2'-propenoxy)-2-nitro-1-phenylethane (**3d**): a) Procedure (a) as for production of **3b** was followed using a solution of 2.54 ml (30 mmol) of 2-methyl-2-propen-1-ol **2c** in 25 ml of dry THF, potassium *tert*-butoxide (3.67 g, 30 mmol), β-nitrostyrene (1.49 g, 10 mmol) in 10 ml of THF, and glacial acetic acid (2.5 ml) to afford 1.723 g (7.8 mmol) of **3d** as an oil in 79% yield.

b) Procedure (b) as for production of **3b** was followed using 0.169 ml (2 mmol) of 2-methyl-2-propen-1-ol **2c** in 40 ml of dry THF, potassium *tert*-butoxide (448 mg, 4 mmol), and β-nitrostyrene (298 mg, 2 mmol) in 50 ml of THF to afford 331 mg (75%) of **3d**. – ^{1}H NMR ($CDCl_3$): δ = 7.30–7.45 (m, 5H, Ar), 5.11 (dd, *J* = 10, 3 Hz, 1H, C_6H_5CH), 4.88 (m, 2H, $C=CH_2$), 4.66 (dd, *J* = 13, 10 Hz, 1H, CH_2NO_2), 4.40 (dd, 13, 3.5 Hz, 1H, CH_2NO_2), 3.88 (br d, *J* = 12 Hz, 1H, CH_2O), 3.7 (br d, *J* = 12 Hz, 1H, CH_2O), 1.68 (br s, 3H, CH_3). – ^{13}C NMR ($CDCl_3$): δ = 141.0 (s, *ipso* Ar), 136.2 (s), 129 (d), 129.0 (d), 126.8 (d), 113.2 (t, $C=CH_2$), 80.4 (t, CH_2NO_2), 77.4 (t, CH_2O), 72.9 (t, C_6H_5CH), 19.4 (q, CH_3). – MS (CI, isobutane), *m/z* (%), ($C_{12}H_{16}NO_3$, MW 222): 222 (43) [MH^+], 176 (31) [$MH^+ - NO_2$], 161 (72) [$MH^+ - (NO_2 + CH_3)$], 104 (100) [$C_6H_5-C_2H_3^+$].

3a,6-cis-3a-Methyl-6-phenyl-3,3a,4,6-tetrahydrofuro[3,4-c]isoxazole (**6d**): a) The stepwise procedure as for production of **6b** was followed using 1-(2'-methyl-2'-propenoxy)-2-nitro-1-phenylethane **3d** (106 mg, 0.48 mmol) in 10 ml of dry benzene, Et_3N (0.08 ml, 0.59 mmol), and TMSCl (0.067 ml, 0.528 mmol). The solution was stirred at room temp. for 47 h. A solution of 5 ml of 10% HCl(aq) was injected to afford 70 mg (0.33 mmol) of **6d** as an oil in a yield of 69%.

b) The one-pot procedure as for production of **6b** was followed using 2-methyl-2-propenol **2c** (0.169 ml, 2 mmol) in 40 ml of dry THF, potassium *tert*-butoxide (448 mg, 4 mmol), β-nitrostyrene (298 mg, 2 mmol) in 50 ml dry THF, TMSCl (0.76 ml, 6 mmol) and TBAF (3 ml, 3 mmol, 1.0 M in THF) to afford 163 mg (0.803 mmol, 40%) of **6d**. – ^{1}H NMR ($CDCl_3$): δ = 7.50–7.25 (m, 5H, Ar), 5.63 (br s, 1H, C_6H_5CH), 4.21 (ABX m, 2H, CH_2O), 4.06 (dd, *J* = 8.5, 0.9 Hz, 1H, CH_2O), 3.98 (d, *J* = 8.5 Hz, 1H, CH_2O), 1.33 (s, CH_3). – ^{13}C NMR ($CDCl_3$): δ = 173.9 (s, C=N), 137.5 (s, *ipso* Ar), 128.6 (d), 128.0 (d), 125.4 (d), 80.3 (t, CH_2O), 76.1 (t, CH_2O), 73.1 (d, C_6H_5CH), 61.3 (s, C-3a), 20.4 (q, CH_3). – MS (CI, isobutane), *m/z* (%): ($C_{12}H_{13}NO_2$, MW 203), 204 (43) [MH^+], 174 (2.6) [$MH^+ - NO$], 145 (17) [$MH^+ - (CH_2ON + CH_3)$], 105 (40) [$C_6H_5CO^+$], 104 (100) [$C_6H_5C_2H_3^+$], 91 (53) [$C_6H_5CH_2^+$]. – HRMS (EI), *m/z* (MH^+): calcd. 203.0946; found 203.0944.

1-(Furfuryloxy)-2-nitro-1-phenylethane (**3h**): a) Procedure (a) as for production of **3b** was followed using a solution of furfuryl alcohol **2g** (2.6 ml, 30 mmol) in 25 ml of THF. The mixture was cooled to 0°C. Potassium *tert*-butoxide (3.67 g, 30 mmol), β-nitrostyrene (1.49 g, 10 mmol) in 10 ml of THF, and glacial acetic acid (2.5 ml) were added. The ^{1}H-NMR spectrum indicated formation of only 8% of **3h**.

b) Procedure (b) as for production of **3b** was followed using furfuryl alcohol **2g** (0.172 ml, 2 mmol) in 40 ml of dry THF, potassium *tert*-butoxide (448 mg, 4 mmol), β-nitrostyrene (298 mg, 2 mmol) in 50 ml of dry THF, and glacial and acetic acid (0.5 ml). Chromatography on silica gel with PE/EA (2:1), afforded 355 mg (1.43 mmol) of **3h** as an oil in 78% yield. – ^{1}H NMR ($CDCl_3$): δ = 7.45–7.31 (m, 6H, $C_6H_5OCH=$), 6.30 (dd, *J* = 3, 2 Hz, 1H, = CH), 6.23 (d, *J* = 3 Hz, 1H, C=CH), 5.14 (dd, *J* = 9.8, 3.5 Hz, 1H, C_6H_5CH), 4.64 (dd, *J* = 13, 9.8 Hz, 1H, CH_2NO_2), 4.46 (d, *J* = 13 Hz, 1H, CH_2O), 4.36 (dd, *J* = 13, 3.5 Hz, 1H, CH_2NO_2), 4.31 (d, *J* = 13 Hz, 1H, CH_2O). – ^{13}C NMR ($CDCl_3$): δ = 150.6 (s, $C=CR_2$), 142.9 (d, C=CH), 136.0 (s, *ipso* Ar), 129.0 (d, CH), 110.2 (d, C=CH), 109.7 (d, C=CH), 80.1 (t, CH_2NO_2), 77.4 (d, C_6H_5CH), 62.9 (t, CH_2O). – MS (EI), *m/z* (%), ($C_{13}H_{18}NO_4$, MW 247): 247 (14) [MH^+], 210 (8.4) [$MH^+ - NO_2$], 200 (1.2) [$MH^+ - HNO_2$], 105 (23) [$C_6H_5-CO^+$], 104 (79) [$C_6H_5-C_2H_3^+$], 97 (26) [furfuryl alcohol$^+$ – H], 77 (5) [$C_6H_5^+$]. – HRMS (EI), *m/z*: (MH^+) calcd. for $C_{13}H_{18}NO_4$ 247.060; found 247.0785.

1-(3'-Methoxy-2'-propenoxy)-2-nitro-1-phenylethane (**3e**): A modification of procedure (b) as for production of **3b** was followed using a solution of (*E*)-3-methoxy-2-propenol **2d**[14], 200 mg (2.27 mmol) in 40 ml of dry THF. At 0 °C, potassium *tert*-butoxide (305 mg, 2.72 mmol) was added. After stirring for 5 min, the mixture was cooled to −98 °C. Thereafter, subsequent reaction steps were carried out as in the procedure for preparing **3b**, using β-nitrostyrene **1b** (338.2 mg, 2.27 mmol) in 50 ml of THF and quenching with glacial acetic acid (0.25 ml, 9.16 mmol). Chromatography on silica gel with PE/EA (1:5) afforded 400 mg (1.68 mmol) of **3e** (74%) as a yellowish oil. – ^{1}H NMR ($CDCl_3$): δ = 7.45–7.34 (m, 5H, Ar), 6.42 (d, *J* = 12.5 Hz, 1H, CC*H*OMe), 5.15 (dd, *J* = 10, 3.5 Hz, 1H, C_6H_5–CH), 4.78 (ddd, *J* = 12.5, 8, 6.5 Hz, 1H, *H*C=CHOMe), 4.62 (dd, *J* = 12.5, 10 Hz, 1H, CH_2NO_2), 4.39 (dd, *J* = 12.5, 3.5 Hz, 1H, CH_2NO_2), 3.95 (ddd, *J* = 11.5, 6.5, 1H, 1H, CH_2O), 3.75 (ddd, *J* = 11.5, 8, 1 Hz, 1H, CH_2O), 3.54 (s, 3H, CH_3O). – ^{13}C NMR ($CDCl_3$): δ = 151.8 (d, C=*C*HOMe), 136.6 (s, *ipso* Ar), 128.9 (d, Ar CH), 128.8 (d, Ar CH), 126.8 (d, Ar CH), 97.9 (d, *H*C=CHOMe), 80.3 (t, CH_2–NO_2), 76.2 (d, C_6H_5CH), 66.5 (t, CH_2O), 55.8 (q, CH_3O). – MS (CI, NH_4), *m/z* (%), ($C_{12}H_{15}NO_4$, MW 237.3): 255 (16) [MNH_4^+], 238 (3.3) [MH^+], 223 (17.6) [$MNH_4^+ - CH_3OH$], 88 (74) [$MH^+ - C_6H_5$–CH=$CHNO_2$]. $C_{12}H_{15}NO_4$ (237): calcd. C 60.75, H 6.37, N 5.90; found C 60.45, H 6.63, N 6.04. – Reaction of **3e** with a trace of Et_3N led to decomposition.

3,3a-trans-3a,6-trans-6-Phenyl-3-methoxy-3,3a,4,6-tetrahydrofuro[3,4-c]isoxazole (**6e**): The one-pot procedure as for production of **6b** was followed using 3-methoxy-2-propenol **2d** (200 mg, 2.27 mmol) in 40 ml of dry THF. At 0 °C, potassium *tert*-butoxide (254 mg, 2.27 mmol) was added followed by β-nitrostyrene **1b** (338.2 mg, 2.27 mmol) in 50 ml of THF, TMSCl (0.57 ml, 4.54 mmol), and TBAF (4.54 ml, 4.54 mmol of a 1.0 M solution in THF). The reaction was monitored by TLC, the plates being developed with 5% (aq) $KMnO_4$. The isoxazole **6e** (148 mg, 0.681 mmol, 30%), was isolated as an oil. – ^{1}H NMR ($CDCl_3$): δ = 7.3 (m, 5H, Ar), 5.67 (d, *J* = 5.5 Hz, 1H, OCHO), 5.55 (br s, 1H, C_6H_5CH), 4.38 (dd, *J* = 8, 8 Hz, 1H, OCH_2), 4.00 (dddd, *J* = 10, 8, 5.5, 1 Hz, 1H, H-3a), 3.77 (dd, *J* = 10, 8 Hz, 1H, OCH_2). – ^{13}C NMR ($CDCl_3$): δ = 168.34 (s, CN), 137.4 (s, *ipso* Ar), 128.7 (d, Ar, CH), 128.4 (d, Ar, CH), 125.6 (d, CH), 110.3 (d, OCHO), 73.2 (d, C_6H_5CH), 66.8 (t, O–CH_2), 57.9 (q, OCH_3), 57.1 (d, C-3a). – MS (CI, NH_4), *m/z* (%), ($C_{12}H_{13}NO_3$, MW 219.2): 237 (100) [MNH_4^+], 220 (100) [MH^+], 207 (1.7) [MNH_4^+ – NO], 206 (1) [MNH_4^+ – OMe], 189 (3) [MH^+ – OMe], 190 (17) [MNH_4^+ – (OMe + O)]. – $C_{12}H_{13}NO_3$ (219): calcd. C 65.74, H 5.98, N 6.39; found C 65.30, H 5.81, N 6.30.

Methyl 4-Hydroxy-2-butenoate (**2e**): Methyl γ-bromocrotonate (17.9 g, 0.1 mol) was added to a well-stirred mixture of water (105 ml) and silver oxide (116 g, 0.05 mol). The mixture was stirred for 24 h at 25 °C and then heated for 6 h at 60 °C. Filtration and evaporation of the water under reduced pressure gave a liquid residue which was distilled in vacuo. **2e** was obtained as a clear liquid, 6.0 g (51%), b.p. 77–80 °C/0.3 mm Hg. – ^{1}H NMR ($CDCl_3$): δ = 7.05 (dt, *J* = 15.5, 3.5 Hz, 1H, CH_2C=C), 6.12 (dt, *J* = 15.5, 2 Hz, 1H, C*H*CO_2Me), 4.35 (m, 2H, HOCH_2), 3.75 (s, 3H, CH_3O), 2.5 (br s, 1H, OH). – ^{13}C NMR ($CDCl_3$): δ = 167 (s, CO), 147.3 [d, C=*C*C(O)R], 119.7 (d, C=C*H*CH_2OH), 61.8 (t, CH_2O), 51.6 (q, OCH_3). – MS (EI), *m/z* (%), ($C_5H_9O_3$, MW 116): 117 (40) [MH^+, (autoprotonation)], 116 (80) [MH^+], 101 (3.8) [$MH^+ - CH_3$], 99 (2) [$MH^+ - H_2O$], 87 (100) [$MH^+ - (CH_2 + O)$], 85 (50) [$MH^+ - (CH_3 + OH)$], 84 (25) [$MH^+ - (CH_3 + OH)$], 83 (25) [$MH^+ - (CH_3 + H_2O)$].

4-Methoxycarbonylmethyl-3-nitro-2-phenyltetrahydrofuran (**14**): Methyl 4-hydroxy-2-butenoate **2e** 232 mg (2 mmol) in 40 ml of THF was placed in a flame-dried flask under argon and cooled to −98 °C, and then potassium *tert*-butoxide (448 mg, 4 mmol) was added. After 5 min of stirring, a solution of β-nitrostyrene 209 mg (2 mmol) in 50 ml dry THF was quickly injected. Subsequently, 1 ml of glacial acetic acid was added and the mixture was allowed to warm to room temp. After filtration of the residues, evaporation, and chromatography on silica gel with PE/EA (1:1), two diastereomers **14a** and **14b** in a ratio of 2:1 were isolated in a total yield of 72%.

2,3-trans-3,4-cis-4-Methoxycarbonylmethyl-3-nitro-2-phenyltetrahydrofuran (**14a**): ^{1}H NMR ($CDCl_3$): δ = 7.35 (m, 5H, Ar), 5.53 (br d, *J* = 2.5 Hz, 1H, C_6H_5CH), 5.08 (dd, *J* = 7.5, 2.5 Hz, 1H, $CHNO_2$), 4.48 (t, *J* = 8 Hz, 1H, CH), 3.97 (dd, *J* = 8.5, 11 Hz, 1H), 3.68 (s, 3H, CH_3), 3.08 (dq, *J* = 11, 7.5 Hz, 1H, C*H*CH_2CO_2Me), 2.54 (dd, *J* = 17, 7.5 Hz, 1H, CHCH_2CO_2Me), 2.46 (dd, *J* = 17, 7.5 Hz, 1H, $CHCH_2CO_2$Me). – ^{13}C NMR ($CDCl_3$): δ = 171 (s, CO), 139.0 (s, *ipso* Ar), 128.9 (d, Ar), 128.5 (d, Ar), 125.3 (d, Ar), 94.3 (d, NO_2CH), 84.6 (d, C_6H_5CH), 72.1 (t, CH_2O), 52.0 (q, OMe), 39.3 (d, C*H*CH_2CO), 30.5 [t, CH_2C(O)]. – MS (CI, NH_3), *m/z* (%), ($C_{13}H_{15}NO_5$, MW 265): 283 (100) [MNH_4^+], 266 (3.4) [MH^+], 252 (5) [MNH_4^+ – OMe], 251 (7) [$MH^+ - CH_3$], 235 (3) [MH^+ – OMe], 204 (10.5) [$MH^+ - (Me + HNO_2)$]. – HRMS (EI), *m/z* (MH^+) calcd. for $C_{13}H_{15}NO_5$ 265.0950; found 265.0688.

2,3-cis-3,4-trans-4-Methoxycarbonylmethyl-3-nitro-2-phenyltetrahydrofuran (**14b**): – ^{1}H NMR ([D$_6$]acetone): δ = 7.38–7.23 (m, 5H, Ar), 5.38 (dd, *J* = 6, 3 Hz, 1H, $CHNO_2$), 5.31 (d, *J* = 6 Hz, 1H, C_6H_5CH), 4.59 (t, 8.5 Hz, 1H, OCH_2), 3.64 (s, 3H, OCH_3), 3.62 (dd, *J* = 7.5, 9.5 Hz, 1H, OCH_2), 3.56–3.44 (m, 1H, H-4), 2.85 (dd, *J* = 17.5, 8.5 Hz, 1H, OCH_2), 2.75 (dd, *J* = 17.5, 6.5 Hz, 1H, CH_2CO). – ^{13}C NMR ([D$_6$]acetone): δ = 172.4 (s, C=O), 136.1 (s, *ipso* Ar), 129.0 (d, Ar-*m*), 128.8 (d, Ar-*p*), 127.0 (d, Ar-*o*), 95.5 (d, $CHNO_2$), 84.0 (d, C_6H_5CH), 73.0 (t, CH_2O), 52.0 (q, CH_3O), 42.1 (d, C-4), 35.5 (t, CH_2C=O). – MS (EI), *m/z* (%), ($C_{13}H_{15}NO_5$, MW 265): 265 (2) [MH^+], 264 (8) [MH^+ – H], 219 (100) [$MH^+ - NO_2$], 218 (14) [$MH^+ - HNO_2$], 188 (13.9) [$MH^+ - (NO_2 + OCH_3)$], 187 (3.3) [$MH^+ - (HNO_2 + OCH_3)$], 105 (95) [C_6H_5–CO], 77 (41) [C_6H_5]. – MS (CI, NH_3), *m/z* (%): 283 (100) [MNH_4^+], 266 (1.7) [MH^+], 236 (10.5) [$MNH_4^+ - HNO_2$], 219 (19) [$MH^+ - NO_2$], 251 (2.5) [$MH^+ - CH_3$], 235 (2.1) [$MH^+ - OCH_3$].

4-Cyanomethyl-3-nitro-2-phenyltetrahydrofuran (**15**): To a solution of 4-hydroxy-2-butenenitrile **2f**[16] (2 mmol) in 40 ml of dry THF at −98 °C was added 250 mg (2.23 mmol) of potassium *tert*-butoxide. After stirring for 5 min, a solution of 298 mg (2 mmol) of β-nitrostyrene **1b** in 20 ml of THF was injected. After two hours at this temperature, 1 ml of glacial acetic acid was injected into the solution. The mixture was allowed to warm to room temp. Chromatography on silica gel with PE/EA (3:1) gave two distinct diastereomers **15a** and **15b** in a 1:1 ratio and in a total yield of 50%.

2,3-trans-3,4-cis-4-Cyanomethyl-3-nitro-2-phenyltetrahydrofuran (**15a**) was eluted last and isolated as an oil. – ^{1}H NMR ($CDCl_3$): δ = 7.28–7.44 (m, 5H, Ar), 5.3 (d, *J* = 6.5 Hz, 1H, C_6H_5CH), 5.18 (dd, *J* = 6.5 Hz, 1H, $CHNO_2$), 4.7 (dd, *J* = 9, 7.5 Hz, 1H, CH_2O), 3.80 (dd, *J* = 9, 7.5 Hz, 1H, CH_2O), 3.53 (m, 1H, C*H*CH_2CN), 2.7 (m, 2H, CH_2CN). – ^{13}C NMR ($CDCl_3$): δ = 133.5 (s, *ipso* Ar), 129.9, 129.5, 128.9 (d, CH Ar), 116.5 (s, CN), 93.2 (d, C*H*NO_2), 83.6 (d, C_6H_5CH), 71.3 (t, OCH_2), 40.2 (d, C*H*CH_2CN), 18.8 (t, CH_2CN).

2,3-cis-3,4-trans-4-Cyanomethyl-3-nitro-2-phenyltetrahydrofuran (**15b**) was eluted first and obtained as an oil. – ^{1}H NMR ($CDCl_3$): δ = 7.44–7.28 (m, 5H, Ar), 5.59 (d, *J* = 3 Hz, 1H, C_6H_5CH), 5.04 (dd, *J* = 7.5 Hz, 1H, $CHNO_2$), 4.54 (dd, *J* = 8.5, 7.5 Hz, 1H, CH_2O), 4.07 (dd, *J* = 9.5, 8.5 Hz, 1H, CH_2O), 3.05 (m, 1H, C*H*CH_2CN), 2.56 (m, 2H, CH_2CN). – ^{13}C NMR ($CDCl_3$): δ = 137.9 (s, *ipso* Ar), 128.7, 125.9, 125.1 (d, CH Ar), 116.3 (s, CN), 93 (d, $CHNO_2$), 84.4 (d, C_6H_5CH), 71.4 (t, OCH_2), 39.2 (d, C*H*CH_2CN), 14.7 (t, CH_2CN). MS (CI, NH_3), *m/z* (%), ($C_{12}H_{12}N_2O_3$, MW 232): 251 (1) [(M + 1)NH_4^+], 250 (100) [MNH_4], 210 (1) [$MNH_4^+ - CH_2CN$], 204 (2.1) [$MNH_4^+ - NO_2$], 203 (18) [$MNH_4^+ - HNO_2$], 186 (1.2) [$MH^+ - HNO_2$].

[1] [1a]N. A. LeBel, *J. Am. Chem. Soc.* **1959**, *81*, 6334-6335. – [1b]W. Oppolzer, K. Keller, *Tetrahedron Lett.* **1970**, 1117–1120. – [1c]E. Breuer in *Nitrones, Nitronates, and Nitroxides* (Eds.: S. Patai, Z. Rappaport), John Wiley + Sons, Chichester, **1989**. – [1d]H. G. Aurich, G. Frenzen, C. Gentes, *Chem. Ber.* **1993**, *126*, 787–795.

[2] J. J. Tufariello, *Acc. Chem. Res.* **1979**, *12*, 396–403.

[3] For instance [3a]A. Padwa (Ed.), in *1,3-Dipolar Cycloaddition Chemistry*, J. Wiley, New York, **1984**, vol 2. – [3b]V. Jaeger, R. Schohe, *Tetrahedron* **1984**, 2199–2210. – [3c]A. P. Kozikowski, *Acc. Chem. Res.* **1984**, *17*, 410–416; – [3d]D. P. Curran, *J. Am. Chem. Soc.* **1982**, *104*, 4024–4026.

[4] M. H. Norman, C. H. Heathcock, *J. Org. Chem.* **1987**, *52*, 226–235.

[5] [5a]A. Hassner, R. Maurya, E. Mesko, *Tetrahedron Lett.* **1988**, *29*, 5313–5316. – [5b]A. Hassner, R. Maurya, *Tetrahedron Lett.* **1989**, *30*, 2289–2291.

[6] R. Grigg, *Chem. Soc. Rev.* **1987**, *16*, 89–121.

[7] [7a]K. B. G. Torssell, S. C. Sharma, *Acta Chem Scand B*, **1979**, *33*, 379–383. – [7b]B. G. Torssell, *Nitrile Oxides, Nitrones, and Nitronates in Organic Synthesis*, VCH Publishers, **1988**.

[8] A. Hassner, W. Dehaen, *Tetrahedron Lett.* **1990**, *31*, 743–746.

[9] [9a] G. H. Posner, *Chem. Rev.* **1986**, *86*, 831–844. – [9b] T.-L. Ho. *Tandem Organic Reactions*, J. Wiley, New York, **1992**. – [9c]L. F. Tietze, U. Beif uss, *Angew. Chem.* **1993**, *105*, 137–169; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 131–163. – [9d]R. A. Bunce, *Tetrahedron* **1995**, *51*, 13103–13159. – [9e] D. Enders, H. J. Scherer, G. Raabe, *Angew. Chem.* **1991**, *103*, 1676–1678; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1664–1666. – [9f] R. D. Little, J. R. Dawson, *Tetrahedron Lett.* **1980**, *21*, 2609–2612. – [9g] S. E. Denmark, A. Thorarensen, *Chem. Rev.* **1996**, *96*, 137–165.

[10] [10a]A. Hassner, W. Dehaen, *Chem. Ber.* **1991**, *124*, 1181–1186. – [10b]A. Hassner, K. S. K. Murthy, A. Padwa, U. Chiacchio, D. C. Dean, A. M. Schoffstall, *J. Org. Chem.* **1989**, *54*, 5277–5286.

[11] [11a]J. Dale, L. Vikersveen, *Acta Chem. Scand. B*, **1988**, *42*, 354–357. – [11b]T. Severin, M. Bohn, *Chem. Ber.* **1967**, *100*, 2532–2536. – [11c]L. I. Bagal, M. D. Boldyrev, G. D. Georgievskaya, *Zh. Org. Khim.* **1970**, *6*, 1342–1346.

[12] [12a]P. G. Hall, G. S. Horsfall, *J. Chem. Soc., Perkin Trans 2*, **1973**, 1280–1284. – [12b]J. W. Smith, *Electric Dipole Moments*, Butterworths, London, **1955**, p. 60.

[13] P. Armstrong, R. Grigg, F. Heaney, S. Surendrakumar, W. J. Warnock, *Tetrahedron* **1991**, *47*, 4495–4518.

[14] [14a]A. Hassner, R. Maurya, O. Friedman, H. E. Gottlieb, A. Padwa, D. Austin, *J. Org. Chem.* **1993**, *58*, 4539–4546. – [14b]I. N. N. Namboothiri, A. Hassner, H. E. Gottlieb, *J. Org. Chem.* **1997**, *62*, in press.

[15] R. E. Ireland, P. R. Wipf, J.-N. Xiang, *J. Org. Chem.* **1991**, *56*, 3572–3582.

[16] J. J. Tufariello, J. P. Tette, *J. Org. Chem.* **1975**, *40*, 3866–3869.

[17] A. Nudelman, E. Keinan, *Synthesis* **1982**, 687–689.

[96215]