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Metal-assisted addition of a nitrate anion to bis(oxy)enamines. A general approach to the synthesis of α -nitroxy-oxime derivatives from nitronates[†]

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The synthesis of α -nitroxy-substituted oxime derivatives has been achieved by an unprecedented metalassisted addition of a nitrate anion to bis(oxy)enamines, which are readily available from nitronates or nitroalkanes. The method has a broad scope and provides access to α -nitroxy-oximes and their cyclic ethers including nitroxy-substituted isoxazolines and dihydro-1,2-oxazines, which are of interest as potential NO-donors and intermediates in the synthesis of bioactive molecules.

Introduction

Nitrate esters are widely used in pharmaceuticals as efficient NO donors¹ with vasodilative,^{1a} vasorelaxant,^{1b} and anti-tumor activities.^{1c} Since NO is associated with the cytotoxic and antimicrobial functions of the immune system, the introduction of a nitroxy group in natural molecules and pharmaceuticals significantly enhances their efficacy.^{1d} This strategy is widely applied in the design of hybrid drugs.^{1d-h}

In organic synthesis, nitrates are considered convenient substrates for nucleophilic substitution reactions, due to the good leaving group ability of the ONO_2 fragment.² Nitrates are employed as intermediates in the synthesis of alcohols³ and aldehydes⁴ from the corresponding halides. Furthermore, nitrates of small alcohols are also well-known high-energy materials and components of explosive compositions.⁵

Traditional methods for the introduction of the ONO_2 fragment in organic molecules are based either on the direct nitration of alcohols⁶ or on the nucleophilic S_N1-type substitution of halides in haloalkanes, upon the action of silver or mercury nitrate.⁷ Another method substantially less explored is nucleophilic addition of a nitrate anion to double carboncarbon bonds.^{8,9} Such processes are usually realized under oxidative conditions (Scheme 1, eqn (1)),⁸ or initiated by the addition of an electrophile to a C=C bond, followed by the nucleophilic attack of a nitrate anion on the carbocation or onium ion (Scheme 1, eqn (2)).⁹ However, examples of direct addition of a nitrate anion to an activated carbon–carbon double bond as well as its participation in S_N' type substitution reactions are, to the best of our knowledge, unprecedented to date.





Scheme 1 Addition of a nitrate anion to a C,C-double bond.



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The carbon–carbon double bond in bis(oxy)enamines **1**, readily available by silylation of nitronates,¹⁰ is easily attacked by some nucleophiles, thus forming α -substituted oximes and their ethers as a result of a formal S_N' substitution of the silyloxy group.¹¹ We were interested in employing nitrate anions as nucleophiles in reactions with bis(oxy)enamines, in order to obtain α -nitroxy-oximes and their cyclic ethers (Scheme 1, eqn (3)). These products are virtually unknown in the literature,¹² though first attempts to synthesize simple α -nitroxy-oximes (so-called "nitrosates") by nitration of some olefins with N₂O₄ date back to the 19th century in the studies of Guthrie,^{13a} Wallach^{13b} and Ipatiew.^{13c} However, in those times the structure of "nitrosates" could not be determined unambiguously.

Results and discussion

Recently, we have demonstrated that the reactions of bis(oxy) enamines with halide anions are promoted by Lewis acids, in particular transition metal and magnesium salts.¹⁴ Therefore, to achieve the desired transformation we studied the interactions of model cyclic bis(oxy)enamine **1a** with a series of

main and transition group metal nitrates (Table 1). In our experiments, crystal hydrates were usually used as they were the most readily available form of metal nitrates. The latter were dissolved in tetrahydrofuran (in the event of insolubility, dimethylformamide was used as a solvent instead) and treated with a solution of **1a** in dichloromethane.

As can be seen from the data in Table 1, almost all studied metal nitrates produced the target product 2a with full conversion of enamine 1a. An exception was lithium nitrate which gave low conversion of the starting material (Table 1, entry 1). The major by-products identified in experiments were 3-hydroxymethyl-substituted 1,2-oxazine 3a, its trimethylsilyl ether 4a, as well as formate 5a and 1,4-butanediol ether nitrate 6a. Products 5a and 6a arise from competitive addition of solvent to bis(oxy)enamine 1a (vide infra). In reactions with magnesium, aluminium and gallium nitrates, the desired nitro-ester 2a was obtained in 42-59% yields (Table 1, entries 2-4). The reaction of bis(oxy)enamine 1a with lead and bismuth nitrates (Table 1, entries 5 and 6) produced formiate 5a in addition to dihydrooxazines 2a, 3a and 4a. In the case of bismuth nitrate, formiate 5a was obtained as the major product (35% yield). Nitrates of early transition metals afforded nitrate ester 2a in

	$ \begin{array}{c} \begin{array}{c} \begin{array}{c} Ph \\ + \\ + \\ + \\ + \\ - \\ - \\ - \\ - \\ - \\ -$							
					Yields of by-products ^{<i>a</i>} (%)			
Entry	Metal nitrate $M(NO_3)_n$	Solvent	Time (h)	Yield of $2a^{a}$ (%)	3a	4a	5a	6a
1	LiNO ₃	THF/CH ₂ Cl ₂	2.5	17^b	_	8	_	
2	$Mg(NO_3)_2 \cdot 6H_2O$	THF/CH ₂ Cl ₂	2.5	42	17	7	_	_
3	$Al(NO_3)_3 \cdot 9H_2O$	DMF/CH ₂ Cl ₂	2.5	53	43	_	_	_
4	$Ga(NO_3)_3 \cdot 9H_2O$	THF/CH ₂ Cl ₂	2.5	59	19	_	_	_
5	$Pb(NO_3)_2$	DMF/CH ₂ Cl ₂	2.5	40	23	18	4	_
6	Bi(NO ₃) ₃ ·5H ₂ O	DMF/CH ₂ Cl ₂	2.5	22	_	_	35	_
7	$Mn(NO_3)_2 \cdot H_2O$	THF/CH ₂ Cl ₂	2.5	42	19	18	_	4
8	$Fe(NO_3)_3 \cdot 9H_2O$	THF/CH ₂ Cl ₂	2.5	43^c	_	_	_	_
9	$Co(NO_3)_2 \cdot 6H_2O$	THF/CH ₂ Cl ₂	2.5	59	32	_	_	6
10	$Co(NO_3)_2$	THF/CH ₂ Cl ₂	3	55	_	_	_	6
11	$Ni(NO_3)_2 \cdot 6H_2O$	THF/CH ₂ Cl ₂	3	60	29	_	_	6
12	$Cu(NO_3)_2 \cdot 3H_2O$	THF/CH ₂ Cl ₂	2.5	54	11	5	_	_
13	$Zn(NO_3)_2 \cdot 6H_2O$	THF/CH ₂ Cl ₂	3	53	32	7	_	_
14	$Cr(NO_3)_3 \cdot 9H_2O$	THF/CH ₂ Cl ₂	2.5	71	21	_	_	6
15	$Cr(NO_3)_3 \cdot 9H_2O$	DMF/CH ₂ Cl ₂	2.5	41	25	5	_	_
16	AgNO ₃	DMF/CH ₂ Cl ₂	2.5	10	6	_	_	_
17	$Y(NO_3)_3 \cdot 6H_2O$	THF/CH ₂ Cl ₂	3	24	56	_	_	7
18	$La(NO_3)_3 \cdot 6H_2O$	THF/CH ₂ Cl ₂	2.5	16	60	13	_	_
19	$Eu(NO_3)_3 \cdot 6H_2O$	THF/CH ₂ Cl ₂	2.5	21	56	4	_	6
20	NH_4NO_3	DMF/CH ₂ Cl ₂	1	35	24	14	_	_
21	HNO ₃	THF/CH ₂ Cl ₂	2.5	58	13	5	_	_
22	3 equiv. $KNO_3 + 1$ equiv. $BF_3 \cdot Et_2O$	DMF/CH ₂ Cl ₂	2.5	26	37	_	_	_
23	$LiNO_3 + 10 mol\% Cr(NO_3)_3 \cdot 9H_2O$	THF/CH ₂ Cl ₂	3	56^d	4	18	_	5

^{*a*} Yields of all products were determined by ¹H NMR with an internal standard. ^{*b*} Conversion – 27%. ^{*c*} By-products were not identified. ^{*d*} Conversion – 82%.

moderate to good yields, while by-product 3a was usually formed in 10–30% yield (Table 1, entries 7–16). It should be noted that employing anhydrous nitrates allows for the suppression of the formation of 3a, but does not lead to the increase of the yield of nitrate 2a due to the formation of unidentified by-products (*cf.* entries 9 and 10 in Table 1).

The best result was achieved with chromium(III) nitrate nonahydrate, which gave product 2a in 71% yield (Table 1, entry 14). Changing of solvent to dimethylformamide led to a decrease of nitrate 2a yield (Table 1, entry 15).

Yttrium, lanthanum and europium nitrates produced 3-hydroxymethyl-substituted 1,2-oxazine 3a as the major product, while the yield of target 2a did not exceed 24% (Table 1, entries 17–19). The formation of nitrate ester 2a was also observed in reactions of enamine 1a with ammonium nitrate and nitric acid (yield of 35% and 58% respectively, entries 20 and 21 in Table 1). Our attempts to use other non-metal based Lewis acids such as boron trifluoride to promote the addition of nitrate to enamine 1a were not successful and led to 3a as the major product (entry 22 in Table 1).

Reaction with chromium nitrate was subsequently studied in more detail. UV-Vis titration of chromium nitrate solution in THF with bis(oxy)enamine **1a** revealed that the majority of chromium is present in the form of the aqueous complex $[Cr(H_2O)_6]^{3+}$ (see the ESI†). This implies that a catalytic process could be designed using a catalytic amount of $Cr(NO_3)_3$, in combination with a cheaper nitrate source. Indeed, addition of 10 mol% of chromium nitrate in the reaction of **1a** with LiNO₃ led to a high conversion of the starting material (*cf*. entries **1** and 23 in Table 1). However, the yield of target **2a** was only 56% due to the formation of significant amounts of byproducts.

Using the procedure with chromium nitrate in THF (procedure i, Table 2), a series of 3-nitroxymethyl-substituted 1,2oxazines and isoxazolines **2a–j** from the corresponding bis(oxy)enamines **1a–j** were prepared. As can be seen from Table 2, the reaction is well-tolerated with various substituents in bis(oxy)enamines **1** and usually provides products in good yields. The structure of compound **2g** was confirmed by singlecrystal X-ray diffraction analysis.

Similar to **1a**, the major by-products in reactions with bis(oxy)enamines **1b–i** were 3-hydroxymethyl-substituted **1**,2-oxazines **3** (typically, not more than 15%) and products of tetrahydrofuran insertion **6** (5–10%), which in some cases were isolated and characterized. In the case of bis(oxy)enamine **1j**, ether **6j** was isolated in 18% yield. Furthermore, diether **7j** resulting from formal insertion of two tetrahydrofuran molecules was detected in trace amounts by high-resolution mass-spectrometry (Table 2).

The synthesis of nitrates 2 can be accomplished directly from the corresponding cyclic nitronates 8, which are synthetic precursors of bis(oxy)enamines 1 (Scheme 2, procedure ii). In this procedure, bis(oxy)enamines are generated *in situ* by silylation of nitronates 8 with trimethylsilyl triflate and triethylamine, followed by treatment of the reaction mixture with chromium nitrate solution in tetrahydrofuran. Such a one-pot

Table 2 Reaction of cyclic bis(oxy)enamines $1a\!-\!j$ with chromium nitrate



 a The product contains a small amount of the 4,6-*cis*-isomer (dr 13 : 1), probably formed *via* acid-promoted epimerization of acetal center C-6.¹⁴



Scheme 2 One-pot synthesis of nitrates 2 from nitronates 8.

process is operationally simpler, however the yield of product 2a is somewhat lower compared to a two-step procedure with isolation of bis(oxy)enamine 1a (*cf.* Scheme 2, eqn (1) and entry 14 in Table 1). Still, the application of a one-pot

procedure is beneficial in cases when bis(oxy)enamine **1** is labile upon isolation (for example bis(oxy)enamine generated from nitronate **8k**, see Scheme 2, eqn (2)).

Procedure i did not prove to be applicable to acyclic bis(silyloxy)enamines **11–o** (Schemes 3 and 4). In the corresponding experiments, only the formation of indecipherable product mixtures was observed. Interestingly, switching to anhydrous cobalt nitrate (procedure iii) in reaction with bis(oxy)enamine **11** produced the desired labile trimethylsilyl ether of α -nitroxyoxime **21** in 65% yield (Scheme 3). However, in reactions with acyclic bis(silyloxy)enamines **1m,o** the corresponding nitrates **2m,o** were identified in reaction mixtures by ¹H NMR and GC-MS in trace amounts (see the ESI[†]).

By conducting reactions with $Co(NO_3)_2$ in DMF, followed by desilylation with aqueous NaHSO₄ solution, labile α -nitroxyoximes **9** were obtained in reasonable yields (Scheme 4). In particular, by using this procedure, the simplest α -nitroxyoxime **9m** (2-(hydroxyimino)ethyl nitrate) was obtained from bis(oxy)enamine **1m** available from nitroethane. This product can be considered as a prospective intermediate in the synthesis of high-energy compounds. α -Nitroxy-oximes **9m–o** are viscous liquids, which are unstable upon heating and slowly decompose at room temperature.

The mechanism of α -nitroxy-oxime 2 formation deserves special discussion. In fact, depending on the nature of metal nitrate, the mechanism can be different. It is likely that the process involves initial Lewis acid-mediated cleavage of weak N–O bonds in initial bis(oxy)enamine **1**, and the subsequent addition of the nitrate anion to the resulting *N*-vinyl-*N*-alkoxynitrenium cation **A**¹⁵ (Scheme 5). This is confirmed by isolation of products **5** and **6**, which result from competitive addition of solvent to cation **A**. Thus, nitrates **2** are probably



Scheme 3 Synthesis of silyl ether 2l from bis(oxy)enamine 1l.



Scheme 4 Synthesis of α -nitroxy-oximes **9m–o** from enamines **1m–o**.



Scheme 5 Plausible mechanism for the formation of α -nitroxy-oxime ethers 2 from bis(oxy)enamines 1.

formed as a result of $S_N 1'$ substitution of the trimethylsilyloxy group in bis(oxy)enamines 1 for the nitrate anion.

The observed formation of α -hydroxy-oxime silvl ethers **4** can be explained by LA-mediated **1**,3-migration of the trimethylsilyloxy group in initial bis(oxy)enamines **1**.^{15d} On the other hand, α -hydroxy-oxime cyclic ethers **3** may originate from either the addition of water to cation **A** or the hydrolysis of the corresponding trimethylsilyl ethers **4** (Scheme 5). The formation of an open-chain oxime **5a** in the reaction of **1a** with bismuth and lead nitrates (Table **1**, entries **5** and **6**) demonstrates the possibility of competitive coordination of these metals by *endo-* and *exo*-cyclic oxygen atoms in cyclic bis(oxy) enamines **1**.

Nitrate esters are frequently employed as intermediates in the total synthesis of pharmacologically relevant compounds.^{3,4b,c,7b,c,8a,b,16} Recently, we developed the synthesis of oxazolidinone CMPO (a highly potent phosphodiesterase 4 inhibitor) via the nitrate intermediate 2p (Scheme 6).^{17a} The synthesis of nitrate 2p was achieved by the nucleophilic substitution of bromine in 3-bromomethyl-substituted 1,2-oxazine 10p. The latter was synthesized from cyclic nitronate 8p with poor yield and conversion, as well as a high degree of epimerization of the acetal center C-6 (Scheme 6).^{17a} Employing the process developed here, we were able to optimize the synthesis of nitrate 2p from nitronate 8p by the silvlation of the latter and treatment of the resulting bis(oxy)enamine 1p with chromium nitrate. In this sequence, the yield of product 2p is considerably higher and the degree of epimerization of C-6 is lower (cf. both approaches in Scheme 6). Unfortunately, onepot synthesis of nitrate 2p from nitronate 8p using procedure ii was less efficient than the two-step procedure via isolation of enamine **1p** (Scheme 6).

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Scheme 6 Two approaches to the synthesis of nitrate 2p - key precursor of the PDE 4b inhibitor CMPO.

Conclusions

In conclusion, we have demonstrated that the reaction of readily available N,N-bis(oxy)enamines with metal nitrates results in the addition of a nitrate anion to a double carboncarbon bond, with the elimination of the trimethylsilyloxygroup from the nitrogen atom. Using reactions of bis(oxy) enamines with chromium and cobalt nitrates, a general method for the synthesis of poorly accessible α-nitroxy-oximes of cyclic and acyclic structures was developed. These oximes are prospective NO donors and intermediates in the synthesis of bioactive molecules. The simplest α -nitroxy-oxime, 2-(hydroxyimino)ethyl nitrate, a potential intermediate in the synthesis of high energy materials, has been synthesized in two steps from nitroethane. The efficiency of the suggested method for the total synthesis of bioactive compounds was demonstrated by the optimization of the synthesis of the highly potent PDE 4 inhibitor.

Experimental

All reactions were performed in oven-dried (150 °C) glassware. Tetrahydrofuran was distilled first from LiAlH₄, stored under sodium benzophenone ketyl and distilled using the vacuum trap-to-trap technique prior to use. CH_2Cl_2 , MeCN, Et_3N , and $(CH_3)_3SiBr$ were distilled from CaH_2 . Hexane and EtOAc were distilled without drying agents. Pentane was commercial grade and used as received.

Inorganic reagents were commercial grade and were used as received. Anhydrous cobalt(II) nitrate was prepared by

thermal decomposition of the corresponding hexahydrate as described in ref. 18. Initial cyclic nitronates $8a^{10c}$ and $8p^{17b}$ were synthesized according to literature methods. Bis-(oxy)enamines 1a,^{10c} b,^{10h} c,^{10g} d,^{10f} e,^{10c} f,¹⁴ g,^{10c} h,^{10f} i,¹⁰ⁱ j,¹⁰ⁱ 1l,^{10e} and $1m-o^{10d}$ were obtained by silvlation of the corresponding nitronates according to previously published procedures.

Column chromatography was performed using Kieselgel 40–60 μ m 60A. Analytical thin-layer chromatography was performed on silica gel plates with QF-254. Visualization was accomplished with UV light and a solution of anisaldehyde/ H₂SO₄ in ethanol.

1D and 2D NMR spectra were recorded at room temperature in CDCl₃ on a Bruker AM 300 spectrometer. The chemical shifts (¹H, ¹³C) are given in ppm (δ) relative to the solvent signal, and liquid ammonia was used as a reference compound in the ¹⁴N NMR spectra. Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad). Trichloroethylene was used as an internal standard in quantitative NMR measurements.

FTIR spectra were recorded on a Bruker Alpha-T spectrometer. Peaks in IR-spectra data are reported in cm⁻¹ with the following relative intensities: s (strong), m (medium), w (weak), br (broad), and sh (shoulder). UV-VIS spectra were recorded on a Shimadzu UVmini-1240 spectrometer (data are reported in nm). Elemental analysis (average of two combustions) was performed by the Analytical Laboratory of the Institute of Organic Chemistry. HRMS were measured on an electrospray ionization (ESI) instrument with a time-of-flight (TOF) detector. GC-MS was performed on a Chromatec 5000 with the Agilent DB-1MS column 122-0132. EI mass spectra were recorded on a Finnigan MAT Incos 50 spectrometer (70 eV). Optical rotation angles were measured on a JASCO P2000 polarimeter. Concentrations *c* are given in g per 100 mL. $[\alpha]_D$ values are given in $10^{-1} \text{ deg cm}^2 \text{ g}^{-1}$.

rel-(4*S*,6*S*)-4-(3-(Cyclopentyloxy)-4-methoxyphenyl)-3-methylene-6-((1*S*,2*R*)-2-phenylcyclohexyloxy)-2-(trimethylsilyloxy)morpholine (1p)

To a stirred solution of nitronate $rac-8p^{17b}$ (0.20 g, 0.416 mmol) and Et₃N (0.14 mL, 1.0 mmol) in 4.8 mL of CH₂Cl₂ was added Me₃SiBr (0.12 mL, 0.91 mmol) at -78 °C under an argon atmosphere. The mixture was kept at -78 °C for 60 h, then diluted with hexane (5 mL) and poured into a mixture of hexane (50 mL) and 0.25 M aqueous NaHSO₄ solution (50 mL). The aqueous layer was back-extracted with hexane (20 mL). Combined organic layers were washed with water (30 mL), and brine (30 mL), dried (Na₂SO₄), and evaporated in a vacuum. The residue was dried in a vacuum until constant weight to give 0.202 g (88%) of bis(oxy)enamine 1p as colorless oil (unstable at r.t.). ¹H NMR (CDCl₃, 300.13 MHz, COSY, HSQC): 0.31 (s, 9 H, (CH₃)₃Si), 1.25-1.47, 1.50-1.63 and 1.72-2.00 (3 m, 16 H, CH-5, CH2-9, CH2-10, CH2-11, CH-12, CH_2 -22, CH_2 -23), 2.10 (ddd, J = 12.0, 8.9, 4.3 Hz, 1 H, HC-5), 2.40 (m, 1 H, HC-12), 2.67 (ddd, J = 11.5, 10.3, 2.9 Hz, 1 H, H_{ax}C-8), 3.53 (br s, 1 H, HC-4), 3.84 (s, 3 H, OCH₃), 3.94 (br s, 1 H, HC-13), 4.09 (ddd, J = 10.3, 10.1, 3.5 Hz, 1 H, H_{ax}C-7), 4.75 (br m, 2 H, HC-13 and HC-21), 5.42 (dd, J = 4.6, 4.3 Hz, 1 H, H_{eq} C-6), 6.68 (d, J = 8.0 Hz, 1 H, HC-19), 6.69 (s, 1 H, HC-15), 6.81 (d, J = 8.0 Hz, 1 H, HC-18), 7.19-7.37 (m, 5 H, o-, m-, p-C₆H₅). ²⁹Si NMR (CDCl₃, 59.63 MHz): 25.9. ¹³C NMR (CDCl₃, 75.47 MHz, HSQC): -0.51 (CH₃)₃Si), 24.0, 24.8 and 26.2 (CH2-9, CH2-10 and CH2-23), 30.6 (CH2-12), 32.8 (CH2-22), 34.5 and 36.9 (CH2-5 and CH2-11), 40.0 (br, CH-4), 50.2 (CH-8), 56.1 (OCH₃), 76.2 (CH-7), 80.4 (CH-21), 93.9 (CH-6), 96.9 (br, CH₂-3), 111.9 (CH-18), 116.0 (CH-15), 120.7 (CH-19), 125.8, 127.9 and 128.0 (o-, m-, p-C₆H₅), 132.3 (br, C-14), 144.2 (i-C₆H₅), 147.4 and 149.0 (C-16 and C-17), 159.3 (br, C-13). ²⁹Si NMR (CDCl₃, 59.63 MHz): 26.0. HRMS: m/z Calcd for $[C_{32}H_{46}NO_5Si^+]$ 552.3140 ($[M + H]^+$). Found: 552.3136.

rel-(4*S*,5*S*)-5-(Ethoxycarbonyl)-4-(4-methoxyphenyl)-3-methyl-4,5-dihydroisoxazole 2-oxide (8k)

To a stirred solution of sulfonium ylide¹⁹ (5 mL in CHCl₃, c = 0.14 g mL⁻¹, 4.8 mmol) derived from carbethoxymethyldimethylsulfonium bromide and K₂CO₃ was added (*E*)-1methoxy-4-(2-nitroprop-1-enyl)benzene (0.776 g, 4 mmol). After 2.5 h at r.t., an additional 2.5 ml of sulfonium ylide solution in CHCl₃ was added (c = 0.14 g mL⁻¹, 2.4 mmol). After 2 h the resulting solution was poured into a mixture of EtOAc (100 mL) and water (100 mL). The aqueous layer was backextracted with EtOAc (50 mL). Combined organic layers were washed with water (50 mL), and brine (50 mL), dried (Na₂SO₄), and evaporated in a vacuum. The residue was triturated with an Et₂O/pentane (1:10) mixture and dried in a vacuum until constant weight to give 0.992 g (89%) of nitronate **8k** as a white solid. Mp = 93–95 °C. ¹H NMR (CDCl₃, 300.13 MHz, HSQC, NOESY): 1.36 (t, J = 7.1 Hz, 3 H, CH_3 CH₂), 1.90 (s, 3 H, CH₃), 3.85 (s, 3 H, OCH₃), 4.34 (q, J = 7.1 Hz, 2 H, CH₃CH₂), 4.51 (br d, J = 4.0 Hz, 1 H, CH-4), 4.81 (d, J = 4.0 Hz, 1 H, CH-5), 6.96 (d, J = 8.6 Hz, 2 H, o-C₆H₄OCH₃), 7.21 (d, J =8.6 Hz, 2 H, m-C₆H₄OCH₃). ¹³C NMR (CDCl₃, 75.47 MHz, HSQC): 10.6 (CH₃), 14.0 (CH₃CH₂), 55.3 (OCH₃ and CH-4), 62.2 (CH₃CH₂), 78.5 (CH-5), 113.3 (C=N), 114.9 (o-C₆H₄OCH₃), 128.6 (m-C₆H₄OCH₃), 128.9 (p-C₆H₄OCH₃), 159.9 (C–O), 168.7 (C=O). Characteristic 2D NOESY correlations: CH-5/ m-C₆H₄OCH₃. Anal. Calcd for C₁₄H₁₇NO₅: C, 60.21; H, 6.14; N, 5.02. Found: C, 60.43; H, 6.07; N, 5.05.

General procedure for the synthesis of nitrates 2a-j,p (procedure i)

To a stirred solution of $Cr(NO_3)_3 \cdot 9H_2O$ (0.8 g, 2.0 mmol) in THF (4 mL) was added 2 mL of 0.5 M solution of bis(oxy)enamines **1a–j,p**. The resulting solution was stirred for 2 h at room temperature and poured into a mixture of EtOAc (50 mL) and 0.25 M NaHSO₄ solution (50 mL). The aqueous layer was backextracted with EtOAc (50 mL). Combined organic layers were washed with 0.25 M NaHSO₄ solution (50 mL), water (50 mL), and brine (50 mL), dried (Na₂SO₄), and evaporated in a vacuum. The residue was subjected to column chromatography on silica gel to give nitrates **2a–j,p**. For determining analytical properties, products were recrystallized from pentane/Et₂O mixtures.

General procedure for the synthesis of nitrates 2a,k from cyclic nitronates 8 (procedure ii)

To a stirred solution of nitronates **8a,k** (1.0 mmol) and triethylamine (0.17 mL, 1.2 mmol) in CH₂Cl₂ (3 mL) was added trimethylsilyl triflate (0.2 mL, 1.1 mmol) at -78 °C under an argon atmosphere. After stirring the reaction mixture for 2 h at -78 °C, a solution of Cr(NO₃)₃·9H₂O (0.8 g, 2.0 mmol) in THF (4 mL) was added *via* a syringe and the cooling bath was removed. After 2 h the resulting dark-colored solution was poured into a mixture of EtOAc (50 mL) and 0.25 M NaHSO₄ solution (50 mL). The aqueous layer was back-extracted with EtOAc (50 mL). Combined organic layers were washed with 0.25 M NaHSO₄ solution (50 mL), water (50 mL), and brine (50 mL), dried (Na₂SO₄), and evaporated in a vacuum. The residue was subjected to column chromatography on silica gel to give nitrates **2a,k** as well as by-products **6a** and **3k**, **6k**, respectively.

(6,6-Dimethyl-4-phenyl-5,6-dihydro-4*H*-1,2-oxazin-3-yl)methyl nitrate (2a). Yields: 71% (procedure i), 62% (procedure ii). White solid. Mp 50–51 °C. $R_{\rm f}$ = 0.7 (EtOAc/hexane = 1:1). ¹H NMR (CDCl₃, 300.13 MHz): 1.31 and 1.41 (2 s, 6 H, 2 *CH*₃), 1.95 (dd, *J* = 12.0, 13.5 Hz, 1 H, $H_{\rm ax}$ C-5), 2.13 (dd, *J* = 7.8, 13.5 Hz, 1 H, $H_{\rm eq}$ C-5), 3.51 (dd, *J* = 7.8, 12.0 Hz, 1 H, $H_{\rm ax}$ C-4), 4.75 (d, *J* = 12.4 Hz, 1 H, *H*C–ONO₂), 4.84 (d, *J* = 12.4 Hz, 1 H, *H*C–ONO₂), 7.22 (d, *J* = 6.7 Hz, 2 H, *o*-C₆H₅), 7.32–7.38 (m, 3 H, *m*- and *p*-C₆H₅). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 22.6 and 28.3 (2 *C*H₃), 37.8 (*C*H-4), 39.7 (*C*H₂-5), 72.0 (*C*H₂–ONO₂), 75.7 (*C*-6), 127.9, 128.1 and 129.4 (*o*-, *m*- and *p*-C₆H₅), 138.6 (i-C₆H₅), 151.3 (*C*=N). ¹⁴N NMR (CDCl₃, 21.69 MHz): -45.0. FTIR (KBr): 1643 (s, $\nu_{\rm as}$ ONO₂). UV-VIS (CH₂Cl₂): $\lambda_{\rm max}$, nm 203,

237. Anal. Calcd for $C_{13}H_{16}N_2O_4$: C, 59.08; H, 6.10; N, 10.60. Found: C, 59.12; H, 6.22; N, 10.53.

4-((6,6-Dimethyl-4-phenyl-5,6-dihydro-4H-1,2-oxazin-3-yl)methoxy)butyl nitrate (6a). Yield: 5% (procedure ii). Oil. Isolated as a by-product to nitrate 2a by column chromatography. $R_{\rm f} = 0.65$ (EtOAc/hexane = 1 : 1). ¹H NMR (CDCl₃, 300.13 MHz): 1.31 and 1.35 (2 s, 6 H, 2 CH₃), 1.58 and 1.74 (2 m, 4 H, CH_2 - CH_2), 1.91 (dd, J = 12.3, 13.3 Hz, 1 H, H_{ax} C-5), 2.09 (dd, J = 7.9, 13.3 Hz, 1 H, H_{eq} C-5), 3.18 and 3.40 (2 m, 2 H, CH_2-CH_2-O , 3.56 (dd, J = 7.9, 12.3 Hz, 1 H, CH-4), 3.81 (s, 2 H, CH₂-O), 4.43 (t, J = 6.5 Hz, 2 H, CH₂-CH₂-ONO₂), 7.19 $(d, J = 6.7 \text{ Hz}, 2 \text{ H}, o-C_6H_5), 7.27-7.38 \text{ (m, 3 H}, m- \text{ and } p-C_6H_5).$ ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 22.8 and 28.5 (2 CH₃), 23.8 and 25.7 (CH₂-CH₂), 37.4 (CH-4), 40.2 (CH₂-5), 69.6, 70.6 and 73.1 (3 CH2-O), 74.6 (C-6), 127.2, 128.4 and 128.9 (o-, m- and $p-C_6H_5$), 140.1 (i- C_6H_5), 156.1 (C=N). ¹⁴N NMR (CDCl₃, 21.69 MHz): -41.1. FTIR (thin layer): 1636 (s, ν_{as} ONO₂). HRMS: m/z Calcd for $[C_{17}H_{24}N_2O_5Na^+]$ 359.1577 $([M + Na]^{+})$. Found: 359.1577.

(4-(4-Methoxyphenyl)-6,6-dimethyl-5,6-dihydro-4H-1,2-oxazin-3-yl)methyl nitrate (2b). Yield: 72% (procedure i). White solid. Mp 43-45 °C (pentane/Et₂O = 5:1). $R_{\rm f}$ = 0.7 (EtOAc/hexane = 1:1). ¹H NMR (CDCl₃, 300.13 MHz): 1.28 and 1.38 (2 s, 6 H, 2 CH₃), 1.91 (dd, J = 12.1, 13.5 Hz, 1 H, H_{ax}C-5), 2.09 (dd, J = 7.8, 13.5 Hz, 1 H, H_{eq} C-5), 3.47 (dd, J = 7.8, 12.1 Hz, 1 H, H_{ax} C-4), 3.80 (s, 3 H, OC H_3), 4.74 (d, J = 12.2 Hz, 1 H, $HC-ONO_2$, 4.80 (d, J = 12.2 Hz, 1 H, $HC-ONO_2$), 6.94 (d, J =8.7 Hz, 2 H, $o-C_6H_4OCH_3$), 7.11 (d, J = 8.7 Hz, 2 H, *m*-C₆*H*₄OCH₃). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 22.6 and 28.3 (2 CH₃), 37.0 (CH-4), 39.6 (CH₂-5), 55.3 (OCH₃), 71.9 (CH₂-ONO₂), 75.8 (C-6), 114.7 (o-C₆H₄OCH₃), 129.2 (*m*-*C*₆H₄OCH₃), 130.3 (*p*-*C*₆H₄OCH₃), 151.6 (*C*-O), 159.2 (C=N). ¹⁴N NMR (CDCl₃, 21.69 MHz): -45.0. FTIR (KBr): 1644 (s, *v*_{as} ONO₂). Anal. Calcd for C₁₄H₁₈N₂O₅: C, 57.13; H, 6.16; N, 9.52. Found: C, 57.02; H, 6.05; N, 9.44.

(4-(4-Chlorophenyl)-6,6-dimethyl-5,6-dihydro-4*H*-1,2-oxazin-3-yl)methyl nitrate (2c). Yield: 70% (procedure i). White solid. Mp 59–61 °C (pentane/Et₂O = 5 : 1). $R_{\rm f}$ = 0.7 (EtOAc/hexane = 1 : 1). ¹H NMR (CDCl₃, 300.13 MHz): 1.29 and 1.39 (2 s, 6 H, 2 CH₃), 1.89 (dd, *J* = 12.0, 13.3 Hz, 1 H, $H_{\rm ax}$ C-5), 2.14 (dd, *J* = 7.8, 13.3 Hz, 1 H, $H_{\rm eq}$ C-5), 3.52 (dd, *J* = 7.8, 12.0 Hz, 1 H, $H_{\rm ax}$ C-4), 4.72 (d, *J* = 12.5 Hz, 1 H, HC–ONO₂), 4.84 (d, *J* = 12.5 Hz, 1 H, HC–ONO₂), 7.16 (d, *J* = 8.3 Hz, 2 H, C₆H₄Cl), 7.35 (d, *J* = 8.3 Hz, 2 H, C₆H₄Cl). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 22.6 and 28.2 (2 CH₃), 37.2 (CH-4), 39.6 (CH₂-5), 71.8 (CH₂-7), 75.7 (C-6), 129.5 and 129.6 (o- and m-C₆H₄Cl), 133.8 and 137.1 (*p*-C₆H₄Cl and *C*-Cl), 150.7 (*C*==N). ¹⁴N NMR (CDCl₃, 21.69 MHz): -45.6. FTIR (thin layer): 1629 (s, $\nu_{\rm as}$ ONO₂). Anal. Calcd for C₁₃H₁₅ClN₂O₄: C, 52.27; H, 5.06; N, 9.38. Found: C, 52.35; H, 5.06; N, 9.30.

4-((4-(4-Chlorophenyl)-6,6-dimethyl-5,6-dihydro-4*H*-1,2-oxazin-3-yl)methoxy)butyl nitrate (6c). Yield: 8% (procedure i). Oil. Isolated as a by-product to nitrate 2c by column chromatography. $R_{\rm f} = 0.6$ (EtOAc/hexane = 1:1). ¹H NMR (CDCl₃, 300.13 MHz): 1.29 and 1.37 (2 s, 6 H, 2 CH₃), 1.59 and 1.75 (2 m, 4 H, CH₂-CH₂), 1.86 (dd, J = 12.1, 13.3 Hz, 1 H, $H_{\rm ax}$ C-5), 2.08 (dd, J = 7.8, 13.3 Hz, 1 H, $H_{eq}C$ -5), 3.20 and 3.38 (2 m, 2 H, CH₂-CH₂-O), 3.55 (dd, J = 7.8, 12.1 Hz, 1 H, CH-4), 3.80 (s, 2 H, CH₂-O), 4.44 (t, J = 6.4 Hz, 2 H, CH₂-CH₂-ONO₂), 7.14 (d, J = 8.3 Hz, 2 H, C₆H₄Cl), 7.32 (d, J = 8.3 Hz, 2 H, C₆H₄Cl). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 22.7 and 28.4 (2 CH₃), 23.8 and 25.7 (CH₂-CH₂), 36.8 (CH-4), 40.0 (CH₂-5), 69.6, 70.5 and 73.0 (3 CH₂-O), 74.6 (C-6), 129.1 and 129.7 (*o*- and m-C₆H₄Cl), 133.1 and 138.6 (*p*-C₆H₄Cl and *C*-Cl), 155.5 (C=N). ¹⁴N NMR (CDCl₃, 21.69 MHz): -40.9. FTIR (KBr): 1641 (s, ν_{as} ONO₂). HRMS: m/z Calcd for [C₁₇H₂₃ClN₂O₅Na⁺] 393.1188 ([M + Na]⁺). Found: 393.1182.

(rel-(4S,6S)-4-(4-Methoxyphenyl)-6-phenyl-5,6-dihydro-4H-1,2-oxazin-3-yl)methyl nitrate (2d). Yield: 69% (procedure i). White solid. Mp 73-75 °C (pentane/Et₂O = 5:1). $R_{\rm f}$ = 0.7 (EtOAc/hexane = 1:1). ¹H NMR (CDCl₃, 300.13 MHz): 2.13 $(ddd, J = 13.6, 2.1, 1.5 Hz, 1 H, H_{eq}C-5), 2.38 (ddd, J = 13.6, 1.5 Hz, 1 H, H_{eq}C-5), 2.38 (ddd, J = 13.6, 1.5 Hz, 1 H, H_{eq}C-5), 2.38 (ddd, J = 13.6, 1.5 Hz, 1 H, H_{eq}C-5), 2.38 (ddd, J = 13.6, 1.5 Hz, 1 H, H_{eq}C-5), 2.38 (ddd, J = 13.6, 1.5 Hz, 1 H, H_{eq}C-5), 2.38 (ddd, J = 13.6, 1.5 Hz, 1 H, H_{eq}C-5), 2.38 (ddd, J = 13.6, 1.5 Hz, 1 H, H_{eq}C-5), 2.38 (ddd, J = 13.6, 1.5 Hz, 1 H, H_{eq}C-5), 2.38 (ddd, J = 13.6, 1.5 Hz, 1 H, H_{eq}C-5), 2.38 (ddd, J = 13.6, 1.5 Hz, 1.5 Hz, 1 H, H_{eq}C-5), 2.38 (ddd, J = 13.6, 1.5 Hz, 1.5 H$ 11.3, 6.3 Hz, 1 H, H_{ax} C-5), 3.66 (dd, J = 6.3, 1.5 Hz, 1 H, H_{eq}C-4), 3.84 (s, 3 H, OCH₃), 4.91 (dd, J = 11.1, 2.1 Hz, 1 H, H_{ax} C-6), 4.96 (d, J = 12.8 Hz, 1 H, HC-ONO₂), 5.09 (d, J =12.8 Hz, 1 H, *H*C-ONO₂), 6.96 (d, *J* = 8.3 Hz, 2 H, *o*-C₆*H*₄OCH₃), 7.17 (d, J = 8.3 Hz, 2 H, $m - C_6 H_4 OCH_3$), 7.31–7.42 (m, 5 H, o-, m-, p-C₆H₅). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 34.2 (CH₂-5), 36.7 (CH-4), 55.4 (OCH₃), 71.8 (CH₂-ONO₂), 74.0 (CH-6), 114.8 (o-C₆H₄OCH₃), 126.6, 128.5 and 128.6 (o-, m-, p-C₆H₅), 129.3 $(m-C_6H_4OCH_3)$, 132.0 $(p-C_6H_4OCH_3)$, 138.7 $(i-C_6H_5)$, 150.6 (C-O), 159.2 (C=N). ¹⁴N NMR (CDCl₃, 21.69 MHz): -45.8. FTIR: 1643 (s, ν_{as} ONO₂). Anal. Calcd for C₁₈H₁₈N₂O₅: C, 63.15; H, 5.30; N, 8.18. Found: C, 62.63; H, 5.26; N, 7.97.

rel-[(4S,4aR,8aR)-4-(4-Methoxyphenyl)-4a,5,6,7,8,8a-hexahydro-4H-1,2-benzoxazin-3-yl]methyl nitrate (2e). Yield: 74% (procedure i). White solid. Mp 78–80 °C (pentane/Et₂O = 5 : 1). $R_{\rm f}$ = 0.8 (EtOAc/hexane = 1 : 1). ¹H NMR (CDCl₃, 300.13 MHz, COSY, HSQC): 1.22-1.53, 1.54-1.69 and 1.70-1.82 (3 m, 4 H, 2 H and 2 H, HC-5, HC-7, H₂C-8, H₂C-9, H₂C-10), 2.03-2.12 (m, 1 H, HC-7), 3.12 (br s, 1 H, H_{eq}C-4), 3.80 (s, 3 H, H₃CO), 4.06 (br m, 1 H, HC-6), 4.86 (d, J = 12.7 Hz, 1 H, HC-ONO₂), 5.02 (d, J =12.7 Hz, 1 H, *H*C–ONO₂), 6.89 (d, *J* = 8.6 Hz, 2 H, *o*-C₆*H*₄OCH₃), 7.07 (d, J = 8.6 Hz, 2 H, $m-C_6H_4OCH_3$). ¹³C NMR (CDCl₃, 75.47 MHz, COSY, HSQC, DEPT): 19.9 and 24.8 (CH2-9 and CH2-10), 27.5 (CH2-8), 29.0 (CH2-7), 38.8 (CH-5), 43.5 (CH-4), 55.3 (OCH₃), 69.7 (CH-6), 72.1 (CH₂-ONO₂), 114.5 $(o-C_6H_4OCH_3)$, 129.1 $(m-C_6H_4OCH_3)$, 132.1 $(p-C_6H_4OCH_3)$, 148.9 (C-O), 159.0 (C-3). ¹⁴N NMR (CDCl₃, 21.69 MHz): -45.1. FTIR (KBr): 1639 (s, ν_{as} ONO₂). Anal. Calcd for C₁₆H₂₀NO₅: C, 59.99; H, 6.29; N, 8.74. Found: C, 60.03; H, 6.36; N, 8.73.

((1*R*,2*S*,4*S*,4′*S*)-3,3-Dimethyl-4′-phenyl-4′,5′-dihydrospiro-[bicyclo[2.2.1]heptane-2,6′-[1,2]oxazine]-3′-yl)methyl nitrate (2f). Yield: 72% (procedure i). White solid. Mp 65–72 °C (pentane). $R_f = 0.8$ (EtOAc/hexane = 1 : 1). $[a]_D = +48.1$ (EtOAc, c = 1.0, 24 °C). ¹H NMR (CDCl₃, 300.13 MHz, COSY, HSQC): 0.91 (s, 3 H, CH₃), 1.16 (s, 3 H, CH₃), 1.19 (d, J = 10.1 Hz, 1 H, HC-7), 1.24–1.46 (m, 2 H, CH₂-6), 1.48–1.64 (m, 2 H, CH₂-5), 1.83 (dd, J = 13.6, 12.7 Hz, 1 H, H'_{ax} C-5′), 1.85 (br s, 1 H, HC-4), 2.18 (d, J = 10.1 Hz, 1 H, HC-7), 2.33 (dd, J = 13.6, 7.0 Hz, 1 H, H''_{eq} C-5′), 2.38 (d, J = 4.4 Hz, 1 H, HC-1), 3.42 (dd, J = 12.7, 7.0 Hz, 1 H, H_{ax} C-4′), 4.74 (d, J = 12.4 Hz, 1 H, HC-ONO₂),

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4.80 (d, J = 12.4 Hz, 1 H, HC-ONO₂), 7.22 (d, J = 7.7 Hz, 2 H, o-C₆ H_5), 7.30–7.42 (m, 3 H, m- and p-C₆ H_5). ¹³C NMR (CDCl₃, 75.47 MHz, HSQC, DEPT): 22.3 and 24.2 (2 CH_3), 22.3 and 23.8 (CH_2 -5 and CH_2 -6), 30.8 (CH_2 -5'), 34.6 (CH_2 -7), 39.9 (CH-4'), 42.7 (CH-1), 44.7 (C-3), 49.3 (CH-4), 72.0 (CH_2 -8), 87.8 (C-2), 127.9, 128.1 and 129.4 (o-, m-, p- C_6H_5), 138.8 (i- C_6H_5), 151.9 (C-3'). ¹⁴N NMR (CDCl₃, 21.69 MHz): -45.0. FTIR (KBr): 1647 (s, ν_{as} ONO₂). Anal. Calcd for C₁₉H₂₄N₂O₄: C, 66.26; H, 7.02; N, 8.13. Found: C, 66.28; H, 7.00; N, 8.03.

[rel-(4S,6S)-6-ethoxy-4-(4-methoxyphenyl)-5,6-dihydro-4H-1,2oxazin-3-yl]methyl nitrate (2g). Yield: 54% (procedure i). White solid. Mp 61–62 °C (pentane/Et₂O = 5:1). $R_{\rm f}$ = 0.7 (EtOAc/hexane = 1:1). ¹H NMR (CDCl₃, 300.13 MHz): 1.25 (t, J = 7.1 Hz, 3 H, CH₃), 2.12 (ddd, J = 2.6, 12.0, 13.5 Hz, 1 H, H_{ax} C-5), 2.28 (ddd, J = 2.4, 7.6, 13.5 Hz, 1 H, H_{eq} C-5), 3.68 (dd, J = 7.6, 12.0 Hz, 1 H, H_{ax} C-4), 3.63 and 3.90 (2 m, 2 H, OCH_2CH_3 , 3.82 (s, 3 H, OCH_3), 4.73 (d, J = 13.2 Hz, 1 H, HC-ONO₂), 4.81 (d, J = 13.2 Hz, 1 H, HC-ONO₂), 5.20 (dd, J = 2.4 and 2.6 Hz, 1 H, H_{eq} C-6), 6.91 (d, J = 8.6 Hz, 2 H, $o-C_6H_4OCH_3$, 7.13 (d, J = 8.6 Hz, 2 H, $m-C_6H_4OCH_3$). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 15.0 (CH₃CH₂-O), 32.4 (CH₂-5), 34.0 (CH-4), 55.3 (OCH₃), 64.0 (CH₃CH₂-O), 71.4 (CH₂-ONO₂), 96.1 (CH-6), 114.8 (o-C₆H₄OCH₃), 129.3 (m-C₆H₄OCH₃), 130.0 $(p-C_6H_4OCH_3)$, 154.3 (C-O), 159.2 (C=N). ¹⁴N NMR (CDCl₃, 21.69 MHz): -45.8. FTIR (KBr): 1643 (s, vas ONO₂). Anal. Calcd for C14H18N2O6: C, 54.19; H, 5.85; N, 9.03. Found: C, 54.22; H, 5.89; N, 8.98. Single crystals for X-ray analysis (CCDC 1419082) were obtained by crystallization from pentane/Et₂O = 5:1 at -30 °C. Minor 4,6-cis-isomer: ¹H NMR (CDCl₃, 300.13 MHz, characteristic signals): 2.45 (ddd, J = 3.1, 7.8, 13.8 Hz, 1 H, H_{ax} C-5), 4.80 (d, J = 12.6 Hz, 1 H, HC-ONO₂), 4.90 (d, J = 12.6 Hz, 1 H, HC-ONO₂), 5.10 (dd, J = 2.9, 5.7 Hz, 1 H, $H_{eq}C-6$).

6,6-Dimethyl-3-(nitrooxymethyl)-5,6-dihydro-4*H***-1,2-oxazin-4-yl benzoate (2h).** Yield: 64% (procedure i). Oil. $R_{\rm f} = 0.7$ (EtOAc/hexane = 1:1). ¹H NMR (CDCl₃, 300.13 MHz): 1.43 and 1.44 (2 s, 6 H, 2 CH₃), 2.08 (dd, J = 5.8, 14.3 Hz, 1 H, *H*C-5), 2.33 (dd, J = 6.6, 14.3 Hz, 1 H, *H*C-5), 5.16 (d, J = 12.7 Hz, 1 H, *H*C-ONO₂), 5.30 (d, J = 12.7 Hz, 1 H, *H*C-ONO₂), 5.30 (d, J = 12.7 Hz, 1 H, *H*C-ONO₂), 5.62 (dd, J = 5.8, 6.6 Hz, 1 H, *H*C-4), 7.51 (dd, J = 7.5, 7.6 Hz, 2 H, *m*-C₆H₅), 7.66 (t, J = 7.5 Hz, 1 H, *p*-C₆H₅), 8.06 (d, J = 7.6 Hz, 2 H, *m*-C₆H₅). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 25.2 and 25.9 (2 CH₃), 35.9 (CH₂-5), 60.1 (CH-4), 70.7 (CH₂-ONO₂), 75.8 (C-6), 128.7, 129.7 and 133.8 (*o*-, *m*-, *p*-C₆H₅ and i-C₆H₅), 147.6 (C=N), 165.3 (C=O). ¹⁴N NMR (CDCl₃, 21.69 MHz): -46.6. FTIR (thin layer): 1724 (s, C=O), 1643 (s, $\nu_{\rm as}$ ONO₂). Anal. Calcd for C₁₄H₁₆N₂O₆: C, 54.54; H, 5.23; N, 9.09. Found: C, 54.40; H, 4.88; N, 8.90.

Methyl 5-methyl-3-(nitrooxymethyl)-4,5-dihydroisoxazole-5carboxylate (2i). Yield: 47% (procedure i). Oil. $R_{\rm f} = 0.4$ (EtOAc/ hexane = 1:3). ¹H NMR (CDCl₃, 300.13 MHz): 1.66 (s, 3 H, CH₃), 2.92 (d, J = 17.6 Hz, 1 H, CHH), 3.57 (d, J = 17.6 Hz, 1 H, CHH), 3.81 (s, 3 H, OCH₃), 5.22 (s, 2 H, CH₂ONO₂). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 23.2 (CH₃), 44.4 (CH₂), 53.1 (OCH₃), 66.4 (CH₂ONO₂), 86.8 (C–O), 151.7 (C=N), 171.6 (C=O). ¹⁴N NMR (CDCl₃, 21.69 MHz): -47.1. FTIR (thin layer): 1647 (s, ν_{as} ONO₂). HRMS: Calcd for $[C_7H_{10}N_2O_6K^+]$: m/z 257.0170 ($[M + K]^+$). Found: 257.0171.

[5-(4-Bromophenyl)-4,5-dihydroisoxazol-3-yl]methyl nitrate (2j). Yield: 65% (procedure i). White solid. Mp 49–51 °C (pentane/Et₂O = 5 : 1). $R_{\rm f}$ = 0.7 (EtOAc/hexane = 1 : 1). ¹H NMR (CDCl₃, 300.13 MHz): 2.99 (dd, J = 17.3, 8.5 Hz, 1 H, HC), 3.49 (dd, J = 17.3, 11.0 Hz, 1 H, HC), 5.27 (s, 2 H, CH_2 –ONO₂), 5.66 (dd, J = 11.0, 8.5 Hz, 1 H, HC–Ar), 7.20 (d, J = 8.2 Hz, 2 H, C₆H₄Br), 7.52 (d, J = 8.2 Hz, 2 H, C₆H₄Br). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 42.7 (CH_2), 66.6 (CH_2 –ONO₂), 82.4 (CH), 122.5 (p- C_6H_4 Br), 127.4 and 132.0 (o- C_6H_4 Br and m- C_6H_4 Br), 139.0 (C–Br), 151.4 (C=N). ¹⁴N NMR (CDCl₃, 21.69 MHz): -47.0. FTIR (KBr): 1640 (s, $\nu_{\rm as}$ ONO₂), 525 (m, C–Br). Anal. Calcd for C₁₀H₉BrN₂O₄: C, 39.89; H, 3.01; N, 9.30. Found: C, 39.71; H, 3.01; N, 9.11.

4-{[5-(4-Bromophenyl)-4,5-dihydroisoxazol-3-yl]methoxy}butyl nitrate (6j). Yield: 18% (procedure i). Characterized in a mixture with 2j (ratio 6j/2j = 4.1:1). Oil. $R_f = 0.6$ (EtOAc/hexane = 1:1). ¹H NMR (CDCl₃, 300.13 MHz): 1.60–2.99 (m, 4 H, CH2-CH2), 2.96 (dd, J = 17.3, 8.0 Hz, 1 H, HC), 3.46 (dd, J = 17.3, 10.5 Hz, 1 H, HC), 3.47 (dd, J = 6.2, 5.1 Hz, 2 H, CH₂- CH_2 -O), 4.26 (s, 2 H, CH_2 -O), 4.46 (dd, J = 6.2, 6.2 Hz, 2 H, CH₂-ONO₂), 5.58 (dd, J = 10.5, 8.0 Hz, 1 H, HC-Ar), 7.22 (d, J = 8.2 Hz, 2 H, C_6H_4Br), 7.50 (d, J = 8.2 Hz, 2 H, C_6H_4Br). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 23.8 and 25.8 (CH₂-CH₂), 43.4 (CH2), 65.2, 70.0 and 73.0 (CH2-O, CH2-CH2-O and CH₂-ONO₂), 81.3 (CH), 122.1 (*p*-C₆H₄Br), 127.4 and 131.9 (*o*-*C*₆H₄Br and *m*-*C*₆H₄Br), 139.9 (*C*-Br), 156.0 (*C*=N). ¹⁴N NMR $(CDCl_3, 21.69 \text{ MHz})$: -41.4. IR: 1627 (s, ν_{as} ONO₂). HRMS: m/z Calcd for $[C_{14}H_{17}BrN_2O_5Na^{\dagger}]$: 395.0213 and 397.0193 ([M + Na]⁺). Found: 395.0216 and 397.0194. Contains diether 7 in trace amounts: Calcd for $[C_{18}H_{25}BrN_2O_6Na^{\dagger}]$: 467.0794 and 469.0776 ([M + Na]⁺). Found: 467.0789 and 469.0775.

rel-(4S,5S)-Ethyl 4-(4-methoxyphenyl)-3-(nitrooxymethyl)-4,5dihydroisoxazole-5-carboxylate (2k). Yield: 65% (procedure ii). Oil. $R_f = 0.6$ (EtOAc/hexane = 1:1). ¹H NMR (CDCl₃, 300.13 MHz): 1.32 (t, J = 7.1 Hz, 3 H, OCH₂CH₃), 3.81 (s, 3 H, OCH_3 , 4.29 (q, J = 7.1 Hz, 2 H, OCH_2CH_3), 4.63 (d, J = 5.3 Hz, 1 H, CH-4), 4.95 (d, J = 13.9 Hz, 1 H, HC-ONO₂), 4.97 (d, J = 5.3 Hz, 1 H, CH-5), 5.21 (d, J = 13.9 Hz, 1 H, HC-ONO₂), 6.91 $(d, J = 8.6 Hz, 2 H, o-C_6H_4OCH_3), 7.12 (d, J = 8.6 Hz, 2 H,$ *m*-C₆*H*₄OCH₃). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 14.0 (OCH₂CH₃), 55.4 (OCH₃), 57.1 (CH-4), 62.2 and 64.8 (2 CH₂), 86.4 (CH-5), 115.0 (o-C₆H₄OCH₃), 127.5 (p-C₆H₄OCH₃), 128.7 $(m-C_6H_4OCH_3)$, 154.1 (C-O), 159.9 (C=N), 169.9 (C=O). ¹⁴N NMR (CDCl₃, 21.69 MHz): -47.6. FTIR (thin layer): 1741 (s, C=O), 1650 (s, ν_{as} ONO₂). HRMS: m/z Calcd for $[C_{14}H_{17}N_2O_7^+]$ 325.1030 ($[M + H]^+$). Found: 325.1021. Anal. Calcd for C14H16N2O7: C, 51.85; H, 4.97; N, 8.64. Found: C, 51.86; H, 4.90; N, 8.60.

rel-(4*S*,5*S*)-Ethyl 3-(hydroxymethyl)-4-(4-methoxyphenyl)-4,5dihydroisoxazole-5-carboxylate (3k). Yield: 19% (procedure ii). Isolated as a by-product to nitrate 2k by column chromatography. Characterized in a mixture with 6k (ratio 3k/6k = 7.6:1.0). Oil. $R_f = 0.5$ (EtOAc/hexane = 1:1). ¹H NMR (CDCl₃, 300.13 MHz): 1.30 (t, J = 7.1 Hz, 3 H, OCH₂CH₃), 2.76 (br, 1 H, OH), 3.79 (s, 3 H, OCH₃), 4.11 (d, J = 14.3 Hz, 1 H, CH–OH), 4.25 (q, J = 7.1 Hz, 2 H, OCH₂CH₃), 4.37 (d, J = 14.3 Hz, 1 H, CH–OH), 4.68 (d, J = 5.2 Hz, 1 H, CH-4), 4.87 (d, J = 5.2 Hz, 1 H, CH-5), 6.89 (d, J = 8.6 Hz, 2 H, o-C₆H₄OCH₃), 7.13 (d, J =8.6 Hz, 2 H, m-C₆H₄OCH₃). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 14.0 (OCH₂CH₃), 55.3 (OCH₃), 57.5 (CH-4), 56.3 and 62.0 (2 CH₂), 85.5 (CH-5), 114.8 (o-C₆H₄OCH₃), 128.7 (m-C₆H₄OCH₃ and p-C₆H₄OCH₃), 159.6 and 160.5 (C–O and C=N), 169.8 (C=O). HRMS: m/z Calcd for [C₁₄H₁₈NO₅⁺] 280.1179 ([M + H]⁺). Found: 280.1179.

rel-(4S,5S)-Ethyl 4-(4-methoxyphenyl)-3-((4-(nitrooxy)butoxy)methyl)-4,5-dihydroisoxazole-5-carboxylate (6k). Yield: 13% (procedure ii). Isolated as a by-product to nitrate 2k by column chromatography. Characterized in a mixture with 2k (ratio 6k/2k = 2.5:1). Oil. $R_f = 0.55$ (EtOAc/hexane = 1:1). ¹H NMR (CDCl₃, 300.13 MHz): 1.35 (t, J = 7.1 Hz, 3 H, OCH₂CH₃), 1.65 and 1.77 (2 m, 4 H, CH2-CH2), 3.37 and 3.48 (2 m, 2 H, CH2-CH₂-O), 3.84 (s, 3 H, OCH₃), 4.04 (d, J = 13.0 Hz, 1 H, CH₂-O), 4.20 (d, J = 13.0 Hz, 1 H, CH_2 -O), 4.31 (q, J = 7.1 Hz, 2 H, OCH₂CH₃), 4.46 (t, J = Hz, 2 H, CH₂-CH₂-ONO₂), 4.64 (d, J = 5.0 Hz, 1 H, CH-4), 4.92 (d, J = 5.0 Hz, 1 H, CH-5), 6.93 (d, J = 8.6 Hz, 2 H, $o-C_6H_4OCH_3$), 7.16 (d, J = 8.6 Hz, 2 H, *m*-C₆*H*₄OCH₃). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 14.1 (OCH₂CH₃), 23.7 and 25.6 (CH₂-CH₂), 55.3 (OCH₃), 57.6 (CH-4), 62.0, 63.3, 69.7 and 73.0 (4 CH₂-O), 85.4 (CH-5), 114.7 (o-C₆H₄OCH₃), 128.7 (m-C₆H₄OCH₃ and p-C₆H₄OCH₃), 158.4 (C-O), 159.6 (C=N), 169.7 (C=O). ¹⁴N NMR (CDCl₃, 21.69 MHz): -41.4. FTIR (thin layer): 1740 (s, sh, C=O), 1649 (s, sh, ν_{as} ONO₂). HRMS: m/z Calcd for $[C_{18}H_{25}N_2O_8^+]$ 397.1605 $([M + H]^{+})$. Found: 397.1606.

rel-((4S,6S)-4-(3-(Cyclopentyloxy)-4-methoxyphenyl)-6-((1S,2R)-2-phenylcyclohexyloxy)-5,6-dihydro-4H-1,2-oxazin-3-yl)methyl nitrate (rac-2p). Yields: 46% (procedure i), 35% (procedure ii). Obtained in a mixture with rel-(1S,2R,4S,6R)-2p' (ratio 2p/2p' =6.1:1 (procedure i), 5.8:1 (procedure ii), HPLC). Oil. Pure 2p can be obtained by crystallization from pentane/Et₂O mixtures (Mp = 110–114 °C). ¹H NMR (CDCl₃, 300 MHz, COSY, HSQC): 1.22-1.45, 1.49-1.75 and 1.77-2.10 (3 m, 17 H, H₂C(5), H₂C(9), $H_2C(10), H_2C(11), HC(12), H_2C(22)$ and $H_2C(23)), 2.40$ (m, 1 H, HC(12)), 2.61 (dd, J = 11.2, 10.7 Hz, 1 H, $H_{ax}C(8)$), 2.90 (dd, J =10.9, 7.9 Hz, 1 H, H_{ax}C(4)), 3.84 (s, 3 H, H₃C(20)), 3.99 (dd, J = 10.7, 9.9 Hz, 1 H, $H_{ax}C(7)$, 4.22 (d, J = 13.3 Hz, 1 H, HC(13)), 4.39 (d, J = 13.3 Hz, 1 H, HC(13)), 4.73 (br m, 1 H, HC(21)), 5.41 (br s, 1 H, $H_{eq}C(6)$), 6.54 (s, 1 H, HC(15)), 6.58 (d, J = 7.1 Hz, 1 H, HC(19)), 6.79 (d, J = 7.1 Hz, 1 H, HC(18)), 7.16–7.39 (m, 5 H, C₆H₅). ¹³C NMR (CDCl₃, 75.47 MHz, HSQC): 24.0 and 24.6 (CH2-9 and CH2-23), 26.1 (CH2-10), 30.5 (CH2-5), 31.8 (CH2-12), 32.7 and 32.8 (CH2-22), 33.6 (CH-4), 34.0 (CH2-11), 50.9 (CH-8), 56.1 (CH₃-20), 70.6 (CH₂-13), 76.3 (CH-7), 80.6 (CH-21), 91.1 (CH-6), 112.4 (CH-18), 114.8 (CH-15), 120.6 (CH-19), 125.9 (p-C₆ H_5), 127.9 and 128.1 (*o*- and m-C₆ H_5), 130.1 (C-14), 144.5 (i-C₆H₅), 148.2 and 149.7 (C-16 and C-17), 153.1 (C-3). ¹⁴N NMR (CDCl₃, 21.69 MHz, rac-2p): -44.2. ¹H NMR spectra of *rac*-2**p** are in accordance with previously published data. ¹H NMR (CDCl₃, 300.13 MHz, rac-2p', characteristic signals): 3.20 (dd, J = 8.3, 8.1 Hz, 1 H, $H_{eq}C$ -4), 3.84 (s,

3 H, OC H_3), 4.28 (dd, J = 6.5, 2.8 Hz, 1 H, H_{eq} C-6), 4.68 (d, J = 12.9 Hz, 1 H, HC-ONO₂), 4.80 (d, J = 12.9 Hz, 1 H, HC-ONO₂).

Reactions of model bis(oxy)enamine 1a with metal nitrates

To a stirred solution of metal nitrate (0.5 mmol) in 1 mL of solvent indicated in Table 1 was added 0.5 ml of 0.5 M solution of bis(oxy)enamine (0.25 mmol) in CH₂Cl₂. The mixture was stirred at r.t. for the time indicated in Table 1, and then poured into a mixture of EtOAc (25 mL) and 0.25 M NaHSO₄ solution (25 mL). The aqueous layer was back-extracted with EtOAc (25 mL). Combined organic layers were washed with 0.25 M NaHSO₄ solution (25 mL), water (25 mL), and brine (25 mL), dried (Na₂SO₄), and evaporated in a vacuum. The residue was analyzed by ¹H NMR with an internal standard. ¹H NMR of by-product 3a is in accordance with published data.^{10h} A sample of pure 4a was prepared by standard silylation (r.t., 18 h) of 3a (0.3 mmol) with (CH₃)₃SiCl (0.6 mmol)/ Et₃N (0.75 mmol) in CH₂Cl₂ (1 mL) followed by evaporation and extraction of the product with pentane (yield: 99%). M.p. = 51-55 °C. ¹H NMR (CDCl₃, 300.13 MHz): -0.04 (s, 9 H, (CH₃)₃Si), 1.33 and 1.37 (2 s, 6 H, 2 CH₃), 1.90 (dd, J = 12.8, 12.2 Hz, 1 H, HC-5), 2.11 (dd, J = 12.8, 8.1 Hz, 1 H, HC-5), 3.66 (dd, J = 12.2, 8.1 Hz, 1 H, HC-4), 3.95 (d, J = 11.7 Hz, 1 H, CHO), 4.03 (d, J = 11.7 Hz, 1 H, CHO), 7.10-7.38 (m, 5 H, o-, m-, p-C₆H₅). ¹³C NMR (CDCl₃, 75.47 MHz, HSQC): -0.37 ((CH₃)₃Si), 22.9 and 28.6 (2 CH₃), 36.9 (CH-4), 40.6 (CH2-5), 63.0 (CH2-O), 74.5 (C-6), 127.1, 128.6 and 128.8 (o-, m-, p-C₆H₅), 140.5 (i-C₆H₅), 158.0 (C=N). ²⁹Si NMR (CDCl₃, 59.63 MHz): 19.9. HRMS: m/z Calcd for $[C_{16}H_{26}NO_2Si^+]$ 292.1727 ([M + H]⁺). Found: 292.1725.

5-Hydroxy-2-(hydroxyimino)-5-methyl-3-phenylhexyl formate (5a). To a stirred solution of $Bi(NO_3)_3 \cdot 5H_2O$ (0.485 g, 1.0 mmol) in DMF (2.0 mL) was added 1.0 mL of 0.5 M solution of bis(oxy)enamine **1a** (0.5 mmol) in CH_2Cl_2 at r.t. The mixture was stirred for 2.5 h at r.t. and then diluted with AcOEt (5 mL) and poured into a mixture of AcOEt (50 mL) and 0.25 M aqueous solution of NaHSO₄ (50 mL). The aqueous layer was back-extracted with AcOEt (50 mL). Combined organic layers were washed with water (30 mL), and brine (30 mL), dried (Na₂SO₄), and evaporated in a vacuum. The residue was subjected to column chromatography on silica gel (eluent: hexane/AcOEt = $10: 1 \rightarrow 5: 1 \rightarrow 1: 1$) to give 0.045 g (34%) of 5a. Colorless oil. A mixture of E,Z-isomers, ratio 12:1.0. $R_f = 0.38$, 0.32 (2 isomers, EtOAc/hexane = 1:1). E-Isomer: ¹H NMR (CDCl₃, 300.13 MHz,): 1.26 and 1.30 (2 s, 6 H, 2 CH₃), 1.84 (dd, J = 15.0, 3.8 Hz, 1 H, HC-5), 2.1 (br, 1 H, OH), 2.48 (dd, J = 15.0, 10.9 Hz, 1 H, HC-5), 3.98 (dd, J = 10.9, 3.8 Hz, 1 H, HC-4), 4.58 (d, J = 14.6 Hz, 1 H, HC-O), 5.17 (d, J = 14.6 Hz, 1 H, HC-O), 7.12-7.38 (m, 5 H, o-, m-, p-C₆H₅), 7.91 (s, 1 H, HC=O), 10.7 (br, 1 H, NOH). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 27.9 and 31.5 (2 CH₃), 45.1 (CH-4), 47.3 (CH2-5), 57.4 (CH2O), 70.6 (C-6), 127.2, 127.9 and 129.2 (o-, m-, *p*-*C*₆H₅), 141.6 (i-*C*₆H₅), 156.9 (*C*=N), 160.0 (H*C*=O). *Z*-Isomer: ¹H NMR (CDCl₃, 300.13 MHz): 1.39 and 1.47 (2 s, 6 H, 2 CH₃), 2.1 (br, 1 H, OH), 2.14 (dd, J = 12.8, 3.8 Hz, 1 H, HC-5), 2.58 (dd, J = 12.8, 12.6 Hz, 1 H, HC-5), 3.53 (m, 1 H, HC-4), 4.76

(d, J = 14.7 Hz, 1 H, HC-O), 5.53 (d, J = 14.7 Hz, 1 H, HC-O), 7.12–7.38 (m, 5 H, *o*-, *m*-, *p*-C₆H₅), 7.91 (s, 1 H, HC=O), 10.7 (br, 1 H, OH). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT, characteristic signals): 40.3 and 43.7 (CH-4 and CH₂-5), 63.3 (CH₂O). Both isomers: HRMS: m/z Calcd for $[C_{14}H_{20}NO_4^+]$ 266.1387 ($[M + H]^+$). Found: 266.1377.

2-Phenyl-2-(trimethylsilyloxyimino)ethyl nitrate (21) (procedure iii). To a stirred solution of anhydrous $Co(NO_3)_2$ (0.366 g, 2.0 mmol) in THF (4 mL) was added 2 mL of 0.5 M solution of bis(trimethysilyloxy)enamine 1l. The resulting solution was stirred for 2 h at room temperature and poured into a mixture of EtOAc (50 mL) and saturated aqueous solution of K₂CO₃ (50 mL). The aqueous layer was back-extracted with EtOAc (50 mL). Combined organic layers were washed sequentially with saturated aqueous solution of K₂CO₃ (50 mL), water (50 mL), and brine (50 mL), dried (Na₂SO₄), and evaporated in a vacuum. The residue was dissolved in diethyl ether and filtered through a short column filled with charcoal (0.5 cm) and Celite (0.5 cm) layers to remove polymer products and traces of inorganic salts. The filtrate was evaporated to give 202 mg (65%) of oxime 2l as vellowish oil unstable at r.t. Purity ca. 85% (according to ¹H NMR with internal standard). A mixture of Z/E-isomers, ratio 9:1. Z-Isomer: ¹H NMR (CDCl₃, 300.13 MHz): 0.35 (s, 9 H, (CH₃)₃Si), 5.69 (s, 2 H, CH₂-ONO₂), 7.39-7.46 and 7.63-7.67 (2 m, 4 H and 1 H, o-, m-, p-C₆H₅). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): -0.76 ((CH₃)₃Si), 64.3 (CH2-ONO2), 126.8, 128.6 and 129.9 (o-, m-, p-C6H5), 132.9 (i-C₆H₅), 154.8 (C=N). ²⁹Si NMR (CDCl₃, 59.63 MHz): 28.4. ¹⁴N NMR (CDCl₃, 21.69 MHz): -44.7. E-Isomer: ¹H NMR (CDCl₃, 300.13 MHz, characteristic signals): 0.34 (s, 9 H, $(CH_3)_3Si)$, 5.37 (s, 2 H, CH_2 -ONO₂). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT, characteristic signals): -0.64 ((CH₃)₃Si), 62.2 (CH2-ONO2). Both isomers: FTIR (thin layer): 1644 (s, ν_{as} ONO₂). MS (EI): m/z (%) = 268 (8) [M]^{+•}, 207 (95) $[M - CH_3 - NO_2]^+$, 192 (73) $[M - CH_2ONO_2]^+$, 103 (20) $[M - Ph - CH_2ONO_2]^+$, 77 (26) $[Ph]^+$, 73 (100) $[(CH_3)_3Si]^+$.

Synthesis of acyclic α-nitroxyoximes 9m-o (procedure iv)

To a stirred solution of anhydrous $Co(NO_3)_2$ (0.732 g, 4.0 mmol) in a mixture of DMF (4 mL) and CH₂Cl₂ (4 mL) was added 4 mL of 1 M solution of bis(trimethysilyloxy)enamines 1m-o (4.0 mmol) in CH₂Cl₂ at r.t. under an argon atmosphere. The mixture was stirred for 2.5 h at r.t., then poured into a mixture of AcOEt (100 mL) and 0.25 M aqueous solution of NaHSO₄ (100 mL) and intensively shaken for ca. 5 min. The aqueous layer was back-extracted with EtOAc (50 mL). The combined organic layers were washed with a 0.25 M aqueous solution of NaHSO₄ (70 mL), water (70 mL), and brine (70 mL), dried (Na₂SO₄), and concentrated in a vacuum. The residue was dissolved in 5 mL of Et₂O. Water (1 mL) was added and the mixture was intensively shaken for 1 min. The organic layer was separated and the water phase was washed with 5 mL of Et₂O. Combined organic layers were dried over Na₂SO₄ and the volatiles were evaporated. The residue was dried in a vacuum (10 Torr) to give a-nitroxyoximes 9m-o. Caution! Low molecular weight organic nitrates are explosive. No attempts to prepare more than 0.2 g were made.

2-(Hydroxyimino)ethyl nitrate (9m). A yellowish volatile liquid unstable upon heating and chromatography (purity ca. 90% determined by ¹H NMR with internal standard). Yield: 32% (with respect to purity). A mixture of E/Z-isomers, ratio 1.4:1. E-Isomer: ¹H NMR (CDCl₃, 300.13 MHz): 5.05 (d, J =5.5 Hz, 2 H, CH₂ONO₂), 7.54 (t, J = 5.5 Hz, 1 H, ==CH), 8.39 (br, 1 H, NOH). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 68.6 (CH_2ONO_2) , 143.7 (C=N). Z-Isomer: ¹H NMR $(CDCl_3)$ 300.13 MHz): 5.29 (d, J = 3.7 Hz, 2 H, CH_2ONO_2), 6.91 (t, J =3.7 Hz, 1 H, ==CH), 8.74 (br, 1 H, NOH). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 65.8 (CH₂ONO₂), 145.1 (C=N). Both isomers: ¹⁴N NMR (CDCl₃, 21.69 MHz): -45.8. FTIR (thin layer): 3306 (s, br, OH), 2917 (m, CH), 1645 (s, v_{as} ONO₂), 1426 (m), 1277 (s), 935 (m, sh), 852 (s). MS (EI): m/z =76 $[CH_2ONO_2]^+$, 58 $[M - NO_3]^+$, 57 $[M - HNO_3]^{+*}$, 46 $[NO_2]^+$, $44 [M - CH_2ONO_2]^+$.

2-(Hydroxyimino)propyl nitrate (9n). A yellowish volatile liquid unstable upon heating and chromatography (purity *ca.* 80% determined by ¹H NMR with internal standard). Yield: 25% (with respect to purity). A mixture of *E/Z*-isomers, ratio 6.3 : 1. *E*-Isomer: ¹H NMR (CDCl₃, 300.13 MHz): 1.98 (s, CH₃), 4.98 (s, CH₂ONO₂), 9.12 (br, 1 H, NOH). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 12.0 (CH₃), 73.1 (CH₂ONO₂), 151.2 (*C*==N). *Z*-Isomer: ¹H NMR (CDCl₃, 300.13 MHz): 1.96 (s, CH₃), 5.33 (s, CH₂ONO₂), 9.12 (br, 1 H, NOH). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT, characteristic signals): 15.7 (CH₃), 64.5 (CH₂ONO₂). Both isomers: ¹⁴N NMR (CDCl₃, 21.69 MHz): -45.2. FTIR (thin layer): 3272 (s, br, OH), 2923 (m, CH), 1730 (m), 1644 (s, ν_{as} ONO₂), 1438 (m), 1288 (s), 945 (m, sh), 921 (m), 851 (s). MS (EI): *m/z* = 135 [M + H]⁺, 76 [CH₂ONO₂]⁺, 58 [M - NO₃]⁺, 46 [NO₂]⁺, 44 [M - CH₂ONO₂]⁺.

Methyl 4-(hydroxyimino)-5-(nitrooxy)pentanoate (90). Yellowish oil unstable upon heating and chromatography (purity ca. 70% determined by ¹H NMR with internal standard). Yield: 27% (with respect to purity). Column chromatography (hexane/EtOAc = 5:1) on silica gel at -15 °C provided a sample of individual 12c, which was used for further analysis. A mixture of E/Z-isomers, ratio 3.8 : 1. $R_f = 0.55$ (EtOAc/hexane = 1:1). E-Isomer: ¹H NMR (CDCl₃, 300.13 MHz): 2.50-2.70 (m, 4 H, CH₂-CH₂), 3.70 (s, 3 H, OCH₃), 5.07 (s, 2 H, CH₂ONO₂), 9.18 (br, 1 H, NOH). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 22.0 and 29.7 (CH2-CH2), 52.0 (OCH3), 72.5 (CH₂ONO₂), 153.0 (C=N), 173.2 (C=O). Z-Isomer: ¹H NMR (CDCl₃, 300.13 MHz): 2.50-2.70 (m, 4 H, CH₂-CH₂), 3.80 (s, 3 H, OCH₃), 5.33 (d, J = 3.7 Hz, 2 H, CH₂ONO₂), 9.03 (br, 1 H, NOH). ¹³C NMR (CDCl₃, 75.47 MHz, DEPT): 25.7 and 29.9 (CH2-CH2), 52.0 (OCH3), 66.8 (CH2ONO2), 155.1 (C=N), 173.9 (C=O). Both isomers: ¹⁴N NMR (CDCl₃, 21.69 MHz): -45.2. FTIR (thin layer): 3382 (s, br, OH), 2957 (m, sh, CH), 1733 (s, C=O), 1644 (s, v_{as} ONO₂), 1440 (m), 1368 (m), 1283 (s, sh), 1203 (m), 1176 (m), 983 (m, sh), 851 (s), 640 (w). HRMS: m/z Calcd for $[C_6H_{10}N_2O_6Na^+]$ 229.0431 ($[M + Na]^+$). Found: 229.0434. MS (EI): m/z =206 [M]^{+•}.

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