Organic Chemistry

A novel general method for the synthesis of nitrones by reaction of nitroso compounds with anions of aliphatic nitro compounds*

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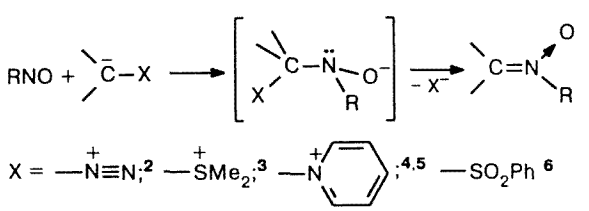
Anions of aliphatic nitro compounds $R^1R^2C{=}NO_2^-$ react with nitroso compounds RNO to give nitrones $R^1R^2C{=}N(O)R$. Salts of nitro compounds with metals and Et_3N, as well as trimethylsilyl nitronates in the presence of F^-, can serve as the sources of the anions. The structure of the nitrones was established by NMR spectroscopy. 1,3-Dipolar cycloaddition of a series of the nitrones obtained to olefins was investigated.

Key words: salts of nitro compounds; nitroso compounds; nitrones; trimethylsilyl nitronates; isoxazolidines; 1,3-dipolar cycloaddition; regioselectivity.

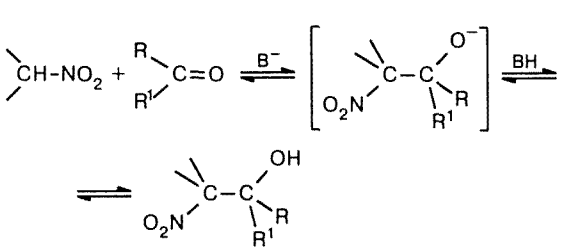
A known general method for the synthesis of nitrones is based on the interaction of nitroso compounds with carbanions. This reaction can be regarded as a two-step process that involves the addition of ambident carbanion, stabilized with a leaving group X, to the N atom of a nitroso group followed by elimination of a leaving group X (Scheme 1).[2–6]

In these reactions, anions of aliphatic nitro compounds can be used as carbanion components. An additional argument in favor of our proposal is the fact that the nucleophilic addition of primary and secondary nitroalkanes (involving functionally substituted ones) to carbonyl group under conditions of basic catalysis is well known[7] (Scheme 2).

Scheme 1



Scheme 2



* For a brief communication see Ref. 1.

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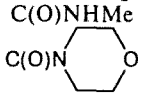
Table 1. Reagents, reaction conditions, and yields of nitrones **3**

Nitroso compound	R	Salt	R^1	R^2	M	Solvent	Reaction temperature/°C	Nitrone	Yield of nitrone (%)
1a	Bu^t	**2a**	Ph	H	K	DMF	20	**3a**	77
		2b	CO_2Me	H	K	DMF	50	**3b**	90
		2c	$C(O)NMe_2$	H	K	DMF	45	**3c***	65
		2d	C(O)NHMe	H	K	DMF	50	**3d***	40
1b	Ph	**2e**	Me	H	Na	MeOH	−10	**3e**	90
		2f	Me	Me	Na	MeOH	0	**3f**	90
		2c	$C(O)NMe_2$	H	K	DMF	−7	**3g***	94
		2d	C(O)NHMe	H	K	MeCN	5	**3h***	97
		2a	Ph	H	K	DMF	−15	**3i**	82
1c	*p*-$NO_2C_6H_4$	**2a**	Ph	H	K	MeOH	−30	**3j**	70
		2c	$C(O)NMe_2$	H	K	MeOH	−30	**3k***	50
		2g	C(O)NHMe	H	Et_3NH	MeOH	−50	**3l***	75
		2h		H	Et_3NH	MeOH	−40	**3m***	75
1d	*o*-$NO_2C_6H_4$	**2g**	C(O)NHMe	H	Et_3NH	MeOH	−40	**3n***	80

* Obtained for the first time.

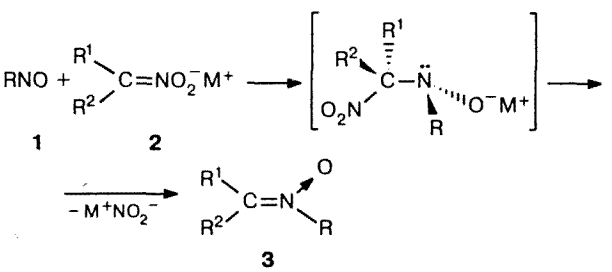
Taking into account the similarity of electronic structure of C=O and N=O groups, the nucleophilic addition of α-nitro carbanions to the nitroso group seems to be very likely. The elimination of NO_2^- anion from sp^3-hybridized C atom linked with the N atom that contains an unshared electron pair, is also known.[8]

However, there is still no data on reactions of nitroso compounds with aliphatic nitro compounds.

We have found that nitroso compounds **1** react smoothly with anions of nitro compounds **2** to form, as expected, the corresponding nitrones **3** (Scheme 3). The preferable sources of α-nitrocarbanion are the salts of nitro compounds with alkaline metals or tertiary amines. This reaction is of rather general character, the yields of nitrones vary from moderate to high, and R, R^1, and R^2 radicals can be widely varied. The reaction conditions (temperature and solvent) depend strongly on the character of the substituents in the nitro and, especially, in the nitroso component. It is known that protic solvents (particularly, MeOH) stabilize anions of nitro compounds due to solvation; however, they also decrease the nucleophilicity of these anions. This is manifested in the fact that nitrosobenzene (**1b**) in MeOH at < 20 °C reacts only with the most nucleophilic substrates, *e.g.*, the salts of nitroalkanes **2e,f** (Table 1), with the formation of nitrones **3e,f**. Taking into account that these nitrones are readily isomerized into the corresponding vinylhydroxylamines[9] (see Experimental), the synthesis of these nitrones should be carried out under the mildest conditions possible.

The introduction of electron-withdrawing substituents (such as methoxycarbonyl or carbamoyl) into the α-position relative to the carbanionic center of the nitro component results in a significant decrease in the nucleophilicity of the corresponding nitro carbanion due to the additional delocalization of negative charge. Therefore, the salts **2c,d** do not react with PhNO in MeOH at 20 °C, and heating results in the formation of a mixture of nonidentified products, probably due to the instability of the corresponding nitrones **3g,h** under reaction conditions.

Scheme 3



However, these nitrones can be obtained in high yields under mild conditions, if the reaction of PhNO with salts **2c,d** is carried out in dipolar aprotic solvents (DMF and MeCN, respectively), which increase effectively the nucleophilicity of the anions of the nitro compounds due to a decrease in their solvation.

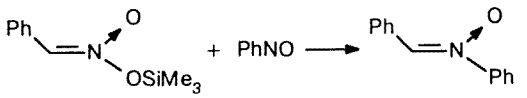
The increase in the electron-withdrawing character of the substituent R in 4- or 2-nitronitrosobenzenes **1c,d** (see Scheme 3) results in such a strong increase in the reaction rate that strong cooling of the reaction mixture is needed to obtain successfully nitrones **3j—n** in MeOH.

On the contrary, the least reactive Bu^tNO (**1a**) reacts with salts of nitro compounds at ~20 °C and at higher temperature only in DMF.

The reaction of PhNO with salt **2b** in DMF affords a mixture of nonidentified products of decomposition of the corresponding nitrone due to its lability.[10]

We have shown with trimethylsilyl *aci*-phenylmethane nitronate as an example that a similar reaction is possible for nitroso compounds with trimethylsilyl nitronates in the presence of $Bu_4N^+F^-$ (Scheme 4).

Scheme 4



The process is probably initiated by the attack of fluoride anion at the silicon atom[11] with the formation of the anion of the nitro compound.

However, the use of salts of nitro compounds is preferable since in this case the experimental procedure is easier and the yields of the final products are higher.

Nitrones **3** with R^2 = H have been isolated and characterized as one *Z*-isomer. This is confirmed by the fact that the nuclear Overhauser effect is observed between R^2 and the *ortho*-protons of the radical R. This indicates unambiguously the *cis*-orientation of R and R^2.

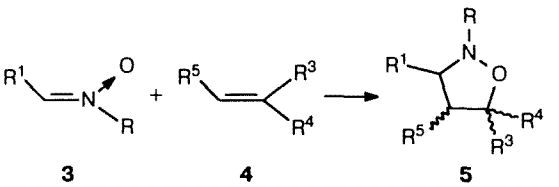
The high yields of nitrones **3** (see Table 1) confirm that ambident anions of aliphatic nitro compounds manifest themselves mainly as *C*-nucleophiles in the reaction with nitroso compounds.

The stability of the series of nitrones obtained is substantially higher in the crystalline state than in solutions and depends also on the nature of the substituents R and R^1. For example, nitrones **3g,h** melt without decomposition and can be stored without any changes for several days as solutions in DMSO.

The introduction of nitro group into the *ortho*- or *para*-position of the phenyl substituent at the *N*-oxide N atom decreases the stability of the corresponding nitrones. For example, nitrones **3k—n** melt with decomposition (see Experimental) and are unstable as solutions in DMSO, nitrone **3l** decomposing so fast that it was impossible to obtain its ^1H NMR spectrum.

Reactions of 1,3-dipolar cycloaddition to olefins **4** have been studied for a series of nitrones **3** (Table 2, Scheme 5).

Scheme 5

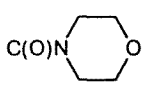


3 **4** **5**

The regularities of 1,3-dipolar cycloaddition of nitrones containing an electron-withdrawing carbamide group in the α-position to functionalized olefins are studied with nitrone **3g** as the example. The cycloaddition of unstable nitrones **3k—n** to methyl acrylate is used for additional proof of their structure.

In all cases, the corresponding isoxazolidines **5** were obtained whose structure was established by NMR spectroscopy and confirmed by elemental analysis data. It turned out that in the case of methyl acrylate the reaction proceeds regioselectively with the formation of 5-substituted isoxazolidines **5**, whereas the stereoselectivity of the process depends on the nature of nitrone **3**. Styrene and ethyl methacrylate also add regioselectively to nitrone **3g** to give the 5-substituted isoxazolidines. Although the rates of the cycloaddition of the olefins studied to nitrone **3g** differ substantially (see Scheme 4), all of them react smoothly with **3g** at 20 °C.

Table 2. Reagents, reaction conditions, yields, and ratio of stereoisomers of isoxazolidines **5**

Nitrone	R	R^1	Olefin	R^3	R^4	R^5	Isoxazolidine	Reaction time /h	Yield (%)	**3**:**4** molar ratio	Ratio of stereoisomers **5**
3g	Ph	$C(O)NMe_2$	**4a**	CO_2Me	H	CO_2Me	**5a**	1.5	98	1:1.2	One stereoisomer
3g	Ph	$C(O)NMe_2$	**4b**	CO_2Et	Me	H	**5b**	3	97	1:15	6.7:1
3g	Ph	$C(O)NMe_2$	**4c**	Ph	H	H	**5c**	8	92	1:20	10:1
3k	*p*-$NO_2C_6H_4$	$C(O)NMe_2$	**4d**	CO_2Me	H	H	**5d**	3	90	1:25	4.5:1*
3l	*p*-$NO_2C_6H_4$	C(O)NHMe	**4d**	CO_2Me	H	H	**5e**	4	95	1:25	3:1
3m	*p*-$NO_2C_6H_4$		**4d**	CO_2Me	H	H	**5f****	5	90	1:25	5:1
3n	*o*-$NO_2C_6H_4$	C(O)NHMe	**4d**	CO_2Me	H	H	**5g**	2	86	1:25	3:1

* According to ^1H and ^{13}C NMR spectral data, the product contains ~9 % of an admixture, probably, 4-substituted isoxazolidine (^{13}C NMR, δ: 37.60 (4-CH); 69.97 (5-CH_2)). ** The reaction was carried out in CH_2Cl_2.

In this work we did not determine the configuration of the products **5**.

Experimental

^1H, ^{13}C, and ^{14}N NMR spectra were recorded on a Bruker AM-300 spectrometer (300.13, 75.5, and 21.5 MHz, respectively) in DMSO-d_6 at 27 °C. ^1H and ^{13}C signals were assigned using $^1H-^1H$ and $^1H-^{13}C$ two-dimensional correlation spectra and selective transfer of polarization. $SiMe_4$ was used as an internal standard (^1H and ^{13}C NMR) and $MeNO_2$ as an external standard (^{14}N NMR).

The syntheses of nitrones were carried out in absolute solvents in an atmosphere of dry argon.

The initial nitro and nitroso compounds are described in the literature. *N*-Methyl- and *N,N*-dimethylnitroacetamides were prepared using the known procedure by refluxing methyl nitroacetate with saturated aqueous solutions of the corresponding amines.[12] Salts **2a—d** were obtained in ~90 % yields by the addition of an equimolar amount of saturated methanolic solution of KOH to nitro compounds on cooling. The solution obtained was stirred for 10 min and then diluted with ten volumes of Et_2O. The salt precipitated was filtered off, washed several times with Et_2O, and dried. In the case of **2b**, the mixture was not diluted with ether since this salt is poorly soluble in MeOH.

***N*-(Nitroacetyl)morpholine** was obtained by boiling of methyl nitroacetate (2 g, 16.81 mmol) in a mixture of morpholine (7.3 mL, 84.05 mmol) and EtOH (8 mL) for 2 h. The mixture was then evaporated *in vacuo*, and the residue was dissolved in H_2O and acidified with 20 % HCl to pH 2—3 at ~0 °C. The *N*-(nitroacetyl)morpholine precipitated was filtered off, washed with H_2O until neutral reaction, and dried. The yield was 68 %, m.p. 107—109 °C.

Nitrones **3a**,[13] **3b**,[14] **3e,f**,[9] **3i** [15] and **3j** [16*] were described earlier. The elemental analysis data and melting points of the nitrones that have been obtained for the first time are given in Table 3. The procedures for the synthesis of nitrones **3** (see Scheme 2) are arbitrarily divided into four types according to the peculiarities of the reaction conditions and the isolation of the products.

Method *A*: synthesis of nitrones **3a—d**. DMF (2 mL per mmol of Bu^tNO) was added to an equimolar mixture of the corresponding salt and crystalline dimer of Bu^tNO. The mixture was vigorously stirred in a hermetically sealed flask. The reaction time and temperatures were as follows: **3a**: 22 h, 20 °C; **3b**: 2 h, 20 °C, then 12 h, 50 °C; **3c**: 8 h, 20 °C, then 4 h, 45 °C; **3d**: 2 h, 20 °C, then 8 h, 50 °C. For the isolation of **3a**, the mixture was poured into ice water and extracted with $CHCl_3$, the extract was washed with H_2O, dried with Na_2SO_4, filtered, and evaporated *in vacuo*. The solid product was crystallized from *n*-hexane.

3a. M.p. 73—76 °C (*cf.* Ref. 13: m.p. 75—77 °C). ^1H NMR ($CDCl_3$), δ: 1.58 (s, 9 H, Me_3); 7.37 (m, 3 H, 2 H_m + 1 H_p); 7.54 (s, 1 H, CH=N); 8.30 (m, 2 H, 2H_o). ^{13}C NMR, δ: 28.2 (Me_3); 70.7 (C—N); 128.3 (C_m); 128.8 (C_o); 129.6 (C=N); 130.0 (C_p); 131.0 ($\underline{C}_{Ar}$—CH). ^{14}N NMR, δ: −77 ($\Delta\nu_{1/2}$ = 200 Hz, =N→O).

Nitrones **3b—d** were isolated by evaporation of DMF *in vacuo* followed by treatment of the nonvolatile residue with MeCN. KNO_2 was filtered off, MeCN was evaporated *in vacuo*; **3b** was distilled, and **3c,d** were crystallized from *n*-heptane.

* For **3j**, only ^1H and ^{13}C NMR spectral data are given.[16]

Table 3. Elemental analysis data and melting points of nitrones **3c,d,g,h,j—n**

Nitrone	M.p./°C	Found / Calculated (%)			Molecular formula
		H	C	N	
3c	83—86	9.29 / 9.36	55.84 / 55.79	16.28 / 16.27	$C_8H_{16}N_2O_2$
3d	59—62	8.87 / 8.92	53.22 / 53.15	17.65 / 17.71	$C_7H_{14}N_2O_2$
3g	91—92	6.33 / 6.29	62.55 / 62.49	14.61 / 14.57	$C_{10}H_{12}N_2O_2$
3h	145—146	5.50 / 5.66	60.60 / 60.66	15.76 / 15.72	$C_9H_{10}N_2O_2$
3j	182—190 (decomp.)	4.04 / 4.16	64.45 / 64.46	11.51 / 11.56	$C_{13}H_{10}N_2O_2$
3k	157—160 (decomp.)	4.61 / 4.67	50.59 / 50.63	17.68 / 17.71	$C_{10}H_{11}N_3O_4$
3l	142—148 (decomp.)	3.90 / 4.06	48.47 / 48.43	18.74 / 18.83	$C_9H_9N_3O_4$
3m	147—155 (decomp.)	4.72 / 4.69	51.70 / 51.58	14.98 / 15.04	$C_{12}H_{13}N_3O_5$
3n	139—144 (decomp.)	3.93 / 4.06	48.52 / 48.43	18.86 / 18.83	$C_9H_9N_3O_4$

3b. B.p. 84—87 °C/0.35 Torr (*cf.* Ref. 14: b.p. 110—120 °C/0.55 Torr). ^1H NMR, δ: 1.46 (s, 9 H, Me_3); 3.69 (s, 3 H, Me); 7.54 (s, 1 H, CH=N). ^{13}C NMR, δ: 27.5 (Me_3); 51.2 (Me); 74.1 (C—N); 121.0 (C=N); 160.9 (C=O). ^{14}N NMR, δ: −48 ($\Delta\nu_{1/2}$ = 400 Hz, =N→O).

3c. ^1H NMR, δ: 1.42 (s, 9 H, Me_3); 2.86 (s, 6 H, Me_2N); 7.44 (s, 1 H, CH=N). ^{13}C NMR, δ: 27.2 (Me_3); 33.6 (Me); 35.3 (Me); 70.1 (C—N); 125.5 (C=N); 162.2 (C=O). ^{14}N NMR, δ: −70 ($\Delta\nu_{1/2}$ = 300 Hz, =N→O).

3d. ^1H NMR, δ: 1.46 (s, 9 H, Me_3); 2.77 (d, 3 H, MeNH, $^3J_{H,H}$ = 4.8 Hz); 7.31 (s, 1 H, CH=N); 9.94 (br.s, 1 H, NH). ^{13}C NMR, δ: 27.2 (Me_3); 25.1 (Me); 72.6 (C—N); 126.7 (C=N); 161.3 (C=O). ^{14}N NMR, δ: −61 ($\Delta\nu_{1/2}$ = 300 Hz, =N→O); −275 ($\Delta\nu_{1/2}$ = 400 Hz, MeNHC(O)).

Method *B*: synthesis of nitrones **3g—i**. A solution of PhNO (~0.5 *M*) was added to a suspension of the corresponding salt in the corresponding solvent (see Table 1) for 10 min and the mixture was kept for the following times and at the following temperatures: **3g**: 0.5 h (−7 °C), then the temperature was raised to ~20 °C in 0.5 h; **3h**: 1 h, 5 °C; **3i**: 1 h, −15 °C, 2 h, 0 °C. Then DMF was evaporated, the residue was treated with MeCN (nitrone **3g**) or benzene (nitrone **3i**) and filtered, the filtrate was concentrated, and the residue was crystallized from Et_2O or from a $CHCl_3$—hexane mixture, respectively.

In the isolation of **3h**, it was sufficient to filter the reaction mixture, evaporate MeCN *in vacuo*, and crystallize the residue from Et_2O.

3g. ^1H NMR, δ: 2.96 (s, 3 H, Me); 3.04 (s, 3 H, Me); 7.56 (m, 3 H, 2 H_m + H_p); 7.89 (m, 2 H, 2 H_o); 8.20 (s, 1 H, CH=N). ^{13}C NMR, δ: 33.8 (Me); 35.6 (Me); 121.3 (C_o); 129.2 (C_m); 130.7 (C_p); 129.0 (C=N); 146.4 (C—N); 161.3 (C=O). ^{14}N NMR, δ: −91 ($\Delta\nu_{1/2}$ = 350 Hz, =N→O).

Table 4. Conditions of synthesis of nitrones **3j—n**

Nitrone	Amount of salt/g (mmol)	V_{MeOH}/mL	Amount of ArNO/g (mmol)	V_{DMF}/mL	t_1[a]/h	T_1/°C	t_2[b]/h	T_2/°C
3j	0.50 (2.86)	20	0.43 (2.86)	12[c]	1	−30	0.5 1	−30 0
3k	0.45 (2.63)	20	0.4 (2.63)	8	1	−30	1.5	−30
3l	0.58 (2.63)	17[d]	0.4 (2.63)	7	1	−50	1	−50
3m	0.54 (1.97)	15[d]	0.3 (1.97)	6	0.75	−40	1	−30
3n	1.30 (5.93)	30[d]	0.9 (5.93)	12	0.67	−40	1	−20

[a] Duration of addition at T_1. [b] Duration of subsequent storage at T_2. [c] The solvent was $(MeOCH_2)_2$. [d] Obtained *in situ* by the addition of an equimolar amount of Et_3N to a solution of the corresponding nitro compound in MeOH followed by storage at 20 °C for 15 min.

3h. ^{1}H NMR, δ: 2.85 (d, 3 H, MeNH, $^3J_{H,H}$ = 4.5 Hz); 7.58 (m, 3 H, 2 H_m + H_p); 7.88 (m, 2 H, 2 H_o); 7.95 (s, 1 H, CH=N); 9.93 (br.s, 1 H, NH). ^{13}C NMR, δ: 25.3 (Me); 121.6 (C_o); 129.2 (C_m); 131.3 (C_p); 129.9 (C=N); 146.8 (C—N); 160.8 (C=O). ^{14}N NMR, δ: −83 ($\Delta\nu_{1/2}$ = 300 Hz, =N→O).

3i. M.p. 112—113 °C (*cp.* Ref. 15: m.p. 112—114 °C). ^{1}H NMR ($CDCl_3$), δ: 7.37 (m, 6 H); 7.69 (m, 2 H); 7.89 (s, 1 H, CH=N); 8.38 (m, 2 H). ^{13}C NMR, δ: 121.6; 128.5; 129.0; 129.8 and 130.8 (C_{Ar}H); 130.7 (C_{Ar}—CH); 134.4 (C=N); 148.9 (C—N). ^{14}N NMR, δ: −97 ($\Delta\nu_{1/2}$ = 250 Hz, =N→O).

Method *C*: synthesis of nitrones **3e,f**. To a 0.5 *M* methanolic solution of MeONa at a temperature below 0 °C was added an equimolar amount of the corresponding nitroalkane and the mixture was stirred for 10 min. Then the equimolar amount of PhNO in the form of crystalline dimer was added to the homogeneous solution of the Na salt and the mixture was kept for the following times and at the following temperatures: **3e**: 1.5 h, −10 °C; **3f**: 1 h, 0 °C. MeOH was then evaporated *in vacuo*, the residue was treated with Et_2O and filtered, the filtrate was evaporated *in vacuo*, the residue was dissolved in $CDCl_3$, and its NMR spectra were immediately recorded.*

3e: light-yellow oil. ^{1}H NMR ($CDCl_3$, 0 °C), δ: 2.22 (d, 3 H, Me, $^3J_{H,H}$ = 5.8 Hz); 7.36 (m, 1 H, CH=N); 7.42 (m, 3 H, 2 H_m + H_p); 7.64 (m, 2 H, 2 H_o). ^{13}C NMR, δ: 13.5 (Me); 121.5 (C_o); 129.1 (C_m); 130.0 (C_p); 136.3 (C=N); 147.3 (C—N). ^{14}N NMR, δ: −94 ($\Delta\nu_{1/2}$ = 300 Hz, =N→O).

3f: light-yellow oil. ^{1}H NMR ($CDCl_3$), δ: 1.97 (s, 3 H, Me); 2.35 (s, 3 H, Me); 7.39 (m, 5 H, Ph). ^{13}C NMR, δ: 19.3 (Me); 21.9 (Me); 123.4 (C_o); 129.5 (C_m); 129.2 (C_p); 145.3 (C—N); 148.6 (C=N). ^{14}N NMR, δ: −106 ($\Delta\nu_{1/2}$ = 450 Hz, =N→O).

Method *D*: synthesis of nitrones **3j—n**. To a solution of the salt in MeOH a solution of an equimolar amount of the corresponding nitroso compound (Table 4) was added dropwise.

As the nitroso compound was added, the products formed precipitated from the reaction mixture. The nitrones were isolated in a pure state by filtration under cooling followed by washing with MeOH at a temperature not higher than that at the end of the reaction.

3j. ^{1}H NMR, δ: 7.53 (m, 3 H, 2 H_m + H_p); 8.22 (d, 2 H, $^3J_{H,H}$ = 9 Hz); 8.37 (d, 2 H); 8.51 (m, 2 H, 2 H_o); 8.61 (s, 1 H, CH=N). ^{13}C NMR, δ: 123.0 and 124.5 (C_{Ar}H); 128.5 (C_m); 129.2 (C_o); 130.7 (C_{Ar}—CH); 131.2 (C_p); 135.3 (C=N); 147.2 and 152.4 (C—N and C—NO_2). ^{14}N NMR, δ: −12 ($\Delta\nu_{1/2}$ = 500 Hz, NO_2); −100 ($\Delta\nu_{1/2}$ = 180 Hz, =N→O).

3k. ^{1}H NMR, δ: 2.96 (s, 3 H, Me); 3.04 (s, 3 H, Me); 8.15 (d, 2 H); 8.33 (s, 1 H, CH=N); 8.38 (d, 2 H). We failed to obtain ^{13}C NMR spectra due to the decomposition of the product in solution. ^{14}N NMR, δ: −94 ($\Delta\nu_{1/2}$ = 250 Hz, =N→O).

3m. ^{1}H NMR, δ: 3.64 (m, 8 H, $(CH_2)_4$); 8.16 (d, 2 H); 8.34 (s, 1 H, CH=N); 8.38 (d, 2 H). ^{13}C NMR, δ: 41.5 (CH_2N); 45.7 (CH_2N); 65.8 (CH_2O); 66.6 (CH_2O); 123.1; 124.6; 148.4 and 150.3 (C—N and C—NO_2); 130.1 (C=N); 159.3 (C=O). ^{14}N NMR, δ: −13 ($\Delta\nu_{1/2}$ = 750 Hz, NO_2); −93 ($\Delta\nu_{1/2}$ = 260 Hz, =N→O).

3n. ^{1}H NMR, δ: 2.64 (d, 3 H, Me); 7.87 (m, 3 H); 8.01 (s, 1 H, CH=N); 8.16 (m, 1 H); 9.58 (br.d, 1 H, NH). ^{13}C NMR, δ: 25.4 (Me); 125.5; 125.6; 131.9; 134.3 (C=N); 134.5; 140.4 and 142.4 (C—N and C—NO_2); 160.0 (C=O). ^{14}N NMR, δ: −13 ($\Delta\nu_{1/2}$ = 350 Hz, NO_2); −89 ($\Delta\nu_{1/2}$ = 600 Hz, =N→O).

* Nitrones of this type undergo reversible isomerization into vinylhydroxylamines followed by cycloaddition with the formation of 5-(*N*-hydroxy-*N*-phenyl)aminoisoxazolidines.[9]

Table 5. Elemental analysis data and melting points of isoxazolidines **5a—g**

Isoxazolidine	M.p./°C	Found / Calculated (%)			Molecular formula
		H	C	N	
5a	96	5.92 5.99	57.18 57.14	8.34 8.33	$C_{16}H_{20}N_2O_6$
5b	90—96	7.30 7.24	62.76 62.73	9.17 9.14	$C_{16}H_{22}N_2O_4$
5c	81—90	6.72 6.80	72.89 72.95	9.42 9.45	$C_{18}H_{20}N_2O_2$
5d	98—107	5.25 5.30	51.98 52.01	12.96 13.00	$C_{14}H_{17}N_3O_6$
5e	89—103	4.96 4.89	50.44 50.49	13.59 13.59	$C_{13}H_{15}N_3O_6$
5f	105—118	5.19 5.24	52.66 52.60	11.44 11.50	$C_{16}H_{19}N_3O_7$
5g	85—104	4.84 4.89	50.41 50.49	13.55 13.59	$C_{13}H_{15}N_3O_6$

Table 6. ^{1}H NMR data ($CDCl_3$) for predominant isomers of isoxazolidines **5**, δ (*J*/Hz)

Isoxazolidine	MeN	MeO	H_A(C(4))	H_B(C(4))	H_X(C(3))	H_M(C(5))	H_{Ar}	Other signals
5a	2.98 (s); 3.06 (s)	3.60 (s); 3.66 (s)	4.36 (dd, $^3J_1$ = 6.7, $^3J_2$ = 8.3)	—	5.06 (2 d, 2 H)		7.03 (t, 1 H_p); 7.13 (d, 2 H_o); 7.27 (t, 2 H_m)	—
5b	2.98 (s); 3.08 (s)	—	2.67 (dd, J_{AB} = 12.5, J_{AX} = 5.8)	3.15 (dd, J_{BX} = 8.0)	4.77 (dd, 1 H)	—	6.92 (t, 1 H_p); 7.02 (d, 2 H_o); 7.11 (t, 2 H_m)	3.90 (m, 2 H, OCH_2); 1.06 (t, 3 H, Me); 1.67 (s, 3 H, Me at C(5))
5c	3.00 (s); 3.13 (s)	—	2.72 (m)	2.89 (m)	4.78 (dd, J_{AX} = 5.1, J_{BX} = 8.1)	4.94 (t, 1 H, $J_{AM} \approx J_{BM} \approx 8$)	6.99 (t, 1 H_p); 7.13 (d, 2 H_o); 7.31 (m, 2 H_m)	CH–Ph: 7.31 (m, 2 H_m + H_p); 7.54 (d, 2 H_o)
5d*	2.94 (s); 3.22 (s)	3.68 (s)	2.90 (m, 2 H)		4.96 (dd, $^3J_1$ = 6.5, $^3J_2$ = 7.9)	5.32 (dd, $^3J_3$ = 4.3, $^3J_4$ = 7.2)	7.13 (d, 2 H); 8.10 (d, 2 H)	—
5e	2.90 (d, ^3J = 5.1)	3.68 (s)	2.93 (m, 2 H)		4.50 (dd, J_{AX} = 5.0, J_{BX} = 8.2)	4.76 (m, 1 H)	7.13 (d, 2 H); 8.14 (d, 2 H)	7.03 (br.s, 1 H, NHC(O))
5f	—	3.70 (s)	2.92 (m, 2 H)		4.92 (m, 2 H)		7.04 (d, 2 H); 8.13 (d, 2 H)	3.71 (m, 8 H, $(CH_2)_2N$ + $(CH_2)_2O$)
5g	2.93 (d)	3.80 (s)	2.52 (m, J_{AB} = 12.6, J_{AM} =10.7, J_{AX} = 7.3)	3.15 (m, J_{BM} = 6.5)	4.36 (d, 1 H)	4.62 (dd, 1 H)	—	7.36 (br.s, 1 H, NHC(O))

* The spectrum was recorded in $(CD_3)_2CO$.

Synthesis of isoxazolidines 5a–g. An excess of olefin was added to a suspension of the corresponding nitrone in an inert solvent (0.5–0.6 mol L^{-1}) and the mixture was stirred for the time indicated in Table 2. Then the mixture was concentrated *in vacuo*, and the nonvolatile residue in the form of a dense colorless or light-yellow transparent oil was crystallized from Et_2O, *n*-pentane, or their mixture (Table 5).

^{1}H and ^{13}C NMR spectroscopy data in $CDCl_3$ for the major isomers of isoxazolidines **5** are given in Tables 6 and 7, respectively.

Below are given those signals of minor isomers in the ^{1}H and ^{13}C NMR spectra which we were able to assign in the spectra of the mixtures.

5b. ^{1}H NMR, δ: 1.31 (t, 3 H, Me, ^3J = 7.1 Hz); 1.53 (s, 3 H, Me at C(5)); 2.39 (dd, 1 H, H_A, J_{AB} = 12.5, J_{AX} = 8.2 Hz); 2.96 (s, 3 H, MeN); 3.06 (s, 3 H, MeN); 3.27 (dd, 1 H, H_B, J_{BX} = 5.1 Hz); 4.26 (q, 2 H, CH_2O); 4.53 (dd, 1 H, H_X); 7.13 (m, 5 H, Ph). ^{13}C NMR, δ: 14.2 (Me); 24.5 (Me at C(5)); 36.5 (MeN); 37.0 (MeN); 42.2 (C(4)); 61.4 (CH_2O); 65.6 (C(3)); 83.6 (C(5)); 115.7 (C_o); 122.8 (C_p); 128.8 (C_m); 150.0 (C–N); 168.8 (C=O); 172.9 (C=O).

5c. ^{1}H NMR, δ: 2.46 (m, 1 H, H_A); 2.90 (m, 1 H, H_B); 3.05 (s, 3 H, MeN); 4.62 (dd, 1 H, H_X, J_{XA} = 9.4, J_{XB} = 3.0 Hz); 5.45 (dd, 1 H, H_M, J_{MB} = 9.0, J_{MA} = 7.2 Hz). ^{13}C NMR, δ: 36.2 (MeN); 37.1 (MeN); 40.2 (C(4)); 65.4 (C(3)); 80.5 (C(5)); 115.8; 122.4; 126.7; 128.1; 128.7; 150.3 (C–N); 169.7 (C=O).

5d. ^{1}H NMR, δ: 2.90 (m, 2 H, H_A + H_B); 2.88 (s, 3 H, MeN); 3.24 (s, 3 H, MeN); 3.74 (s, 3 H, MeO); 4.88 (dd, 1 H, H_X, $^3J_1$ = 9.0, $^3J_2$ = 5.8 Hz); 5.17 (dd, 1 H, H_M, $^3J_3$ = 4.0, $^3J_4$ = 7.7 Hz); 7.16 (d, 2 H); 8.13 (d, 2 H). ^{13}C NMR, δ: 35.8 (C(4)); 36.3 (MeN); 37.4 (MeN); 52.5 (MeO); 64.2 (C(3)); 76.7 (C(5)); 114.3 (C_o); 126.0 (C_m); 155.6 (C–N); 170.0 (C=O); 172.2 (C=O).

5e. ^{1}H NMR, δ: 2.92 (m, 2 H, H_A + H_B); 4.41 (dd, 1 H, H_X, J_{AX} = 8.5, J_{BX} = 4.6 Hz); 7.09 (d, 2 H); 8.16 (d, 2 H). ^{13}C NMR, δ: 36.9 (C(4)); 52.9 (MeO); 67.7 (C(3)); 75.8 (C(5)); 114.0 (C_o); 125.5 (C_m); 142.9 (C–NO_2); 154.5 (C–N); 169.3 (C=O); 169.7 (C=O).

5f. ^{1}H NMR, δ: 3.64 (s, 3 H, MeO); 7.11 (d, 2 H, 2 H_m). ^{13}C NMR, δ: 35.6 (C(4)); 52.8 (MeO); 64.8 (C(3)); 76.0 (C(5)); 113.6 (C_o); 125.5 (C_m); 142.3 (C–NO_2); 154.4 (C–NO_2); 166.7 (C=O); 169.0 (C=O).

5g. ^{1}H NMR, δ: 2.70 (m, 1 H, H_A, J_{AB} = 13.4, J_{AM} = 10.5 Hz); 3.13 (m, 1 H, H_B); 4.23 (d, 1 H, H_X, J_{AX} = 8.1, J_{XB} = 0.0 Hz); 5.04 (dd, 1 H, H_M, J_{MB} = 3.2 Hz). ^{13}C NMR, δ: 30.9 (MeN); 34.4 (C(4)); 69.7 (C(3)); 77.0 (C(5)); 119.3; 125.2; 126.3; 134.3; 140.2 (C–NO_2); 144.6 (C–N); 169.1 (C=O); 169.9 (C=O).

Table 7. ^{13}C NMR data ($CDCl_3$) for predominant isomers of isoxazolidines **5**, δ

Isoxazolidine	MeN	MeO	C(3)	C(4)	C(5)	C_{Ar}	C=O	Other signals
5a	36.6; 37.3	52.4; 52.5	66.4	54.4	77.7	116.7 (C_o); 123.9 (C_p); 128.8 (C_m); 149.1 (C—N)	167.7; 169.1; 169.3	—
5b	36.6; 37.2	—	65.6	40.4	84.5	114.8 (C_o); 122.1 (C_p); 128.7 (C_m); 149.9 (C—N)	169.5; 172.8	61.4 (OCH_2); 13.7 (Me); 22.4 (Me at C(5))
5c	36.7; 37.2	—	66.6	39.7	80.4	114.4 (C_o); 122.2 (C_p); 129.2 (C_m); 150.5 (C—N)	169.9	CH—Ph: 127.6 (C_o); 128.4 (C_p); 128.4 (C_m); 137.5 (CH—C)
5d*	36.2; 37.3	52.7	62.7	36.0	77.8	113.9 (C_o); 125.7 (C_m); 141.6 (C—NO_2); 154.9 (C—N)	168.5; 171.4	—
5e	26.3	52.7	67.2	36.7	77.1	113.9 (C_o); 125.1 (C_m); 142.4 (C—NO_2); 154.85 (C—N)	169.4; 169.9	—
5f	—	52.7	62.9	36.0	76.8	113.2 (C_o); 125.3 (C_m); 141.5 (C—NO_2); 153.9 (C—N)	166.9; 170.4	43.0 (CH_2N); 46.1 (CH_2N); 66.5 (CH_2O); 66.8 (CH_2O)
5g	26.4	52.7	70.7	34.8	77.3	121.3; 125.1; 125.8; 134.3; 140.5 (C—NO_2); 145.1 (C—N)	169.0; 170.4	—

* The spectrum was recorded in $(CD_3)_2CO$.

Reaction of trimethylsilyl nitronate PhCH=N(O)OSiMe$_3$ with PhNO. *A.* Synthesis of trimethylsilyl phenylmethane nitronate. Et_3N (1.48 g, 14.61 mmol) and Me_3SiCl (1.58 g, 14.60 mmol) were added to a solution of phenylnitromethane (2.00 g, 14.60 mmol) in PhH (15 mL), and the mixture was stirred for 6 h. Then $[Et_3NH]^+Cl^-$ was filtered off in inert atmosphere, the solvent was evaporated *in vacuo*, and the product was distilled: b.p. 63—65 °C/0.35 Torr (*cf.* Ref. 17: b.p. 85—87 °C/0.5 Torr).

B. Preparation of a solution of Bu_4NF in THF. To a 10 % aqueous solution of Bu_4NOH an equimolar amount of NH_4F was added. NH_3 and H_2O were evaporated, and the product was dried for 12 h at 55—60 °C/0.2 Torr. The crystalline Bu_4NF was then dissolved in THF (concentration 1.15 mol L^{-1}).

C. A solution of Bu_4NF (0.77 mmol) in THF was added to a solution of PhCH=N(O)OSiMe$_3$ (1.6 g, 7.66 mmol) in THF (10 mL) at −78 °C and the mixture was kept at −78 °C for 10 min. Then a solution of PhNO (0.82 g, 7.66 mmol) in THF (11 mL) was added for 0.5 h at the same temperature. The temperature was raised to 0 °C in 40 min, and the mixture was stirred under these conditions for 0.5 h. Then the solvent was evaporated *in vacuo*, the residue was dissolved in PhH (50 mL), and the solution was washed with H_2O (3×15 mL) and dried with Na_2SO_4. Then PhH was evaporated *in vacuo*, and the residue was crystallized from $CHCl_3$—hexane mixture to afford 0.65 g (43 %) of PhCH=N(O)Ph (nitrone **3i**).

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