Reactions of *N*-nitramines and their trimethylsilyl derivatives with *N,N*-bis(trimethylsilyloxy)enamines

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Trimethylsilyl derivatives of methyl- and ethylnitramine react as *N*-centered nucleophiles with 2-*N,N*-bis(trimethylsilyloxy)aminopropene to give trimethylsilyl derivatives of hitherto unknown α-(*N*-nitro)alkylamino-substituted acetone oximes. As an ambident nucleophile, nonsubstituted methylnitramine reacts with the same enamine to give both a product of N,C-cross-coupling and a product of O,C-cross-coupling, *viz.*, *N'*-methyl-*N*-[(2-trimethylsilyloxyimino)propoxy]diazene *N*-oxide.

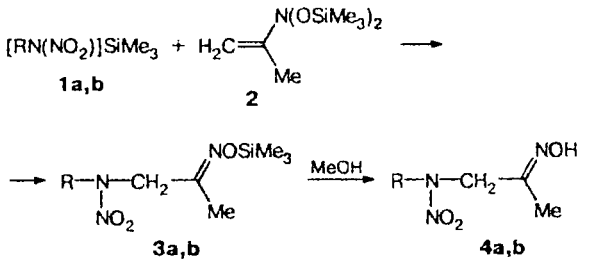
Key words: nitramines, silylation, N,C-cross-coupling, *N,N*-bis(trimethylsilyloxy)enamines.

N,N-Bis(trialkylsilyloxy)enamines (BSENA), obtained previously,[1–3] behave in chemical reactions as formal β-C-electrophiles. It is known that they undergo rearrangements into bis(trialkylsilyl) derivatives of α-hydroxy oximes,[1] are aminated by secondary amines at the β-C atom,[2] and enter into β,α-C,C-cross-coupling with trimethylsilyl nitronates.[4]

In the present paper, the reaction of alkylnitramines and their trimethylsilyl derivatives (**1a,b**)[5,6] with 2-*N,N*-bis(trimethylsilyloxy)aminopropene (**2**) as a model BSENA was discussed.

It turned out that derivatives **1a,b** smoothly react with enamine **2** as *N*-centered nucleophiles to give α,β-N,C-cross-coupling products, namely, the corresponding (*N*-nitro)alkylamino derivatives of acetone oxime (**3a,b**) (Scheme 1).

Scheme 1



R = Me (**a**), Et (**b**)

Mixing of the reagents at 15 °C without a solvent results in a weakly exothermic reaction. Methanolysis of derivatives **3a,b** yield the corresponding oximes **4a,b**. It should be noted that α-*N*-nitroalkylamino-substituted oximes have not been described in the literature.

The data from heteronuclear NMR and elemental analysis convincingly prove the structures of compounds **3** and **4**. In organic solvents, derivatives **3** and **4a** exist solely as *E*-isomers, whereas the NMR spectra of oxime **4b** exhibit two sets of signals, and two components were revealed by TLC. Thus, one can conclude that this oxime is formed as a mixture of *E/Z*-isomers in the ratio of *ca.* 3 : 1. Several recrystallizations from CCl_4 afford virtually pure *E*-isomer.

The isomers of oximes **4** and their derivatives **3** were assigned with consideration of the fact that the signals for the α-C atoms of *cis*-substituents with respect to the OH group are shifted upfield compared to similar signals for the *trans*-substituents in the ^{13}C NMR spectra of the oximes.[7] The chemical shifts of the Me group in the ^{13}C NMR spectra of oximes **4** and their derivatives **3** are quite close to those for the corresponding isomers of butan-2-one oxime.[7]

It should be specially emphasized that the reaction **1** + **2** affords good yields of derivatives **3** only in the absence of a solvent and when the initial enamine **2** has been isolated without washing the organic layer with sodium hydrogensulfate, contrary to what is recommended in the latest procedure for the synthesis of BSENA.[3] The use of aprotic organic solvents (MeCN, CH_2Cl_2, *etc.*) or BSENA washed with sodium hydrogensulfate results in the formation of by-products **5** and **6** (see below).

The reaction of BSENA with nonsubstituted alkylnitramines was studied using enamine **2** with methylnitramine as an example. This process is not chemoselective and yields a mixture of products **3a**, **5**, and **6** (Scheme 2).

Derivative **6** is a product of the known rearrangement of the initial enamine **2**,[1,2] which is catalyzed by Lewis or Brønsted acids. Apparently, methylnitramine,

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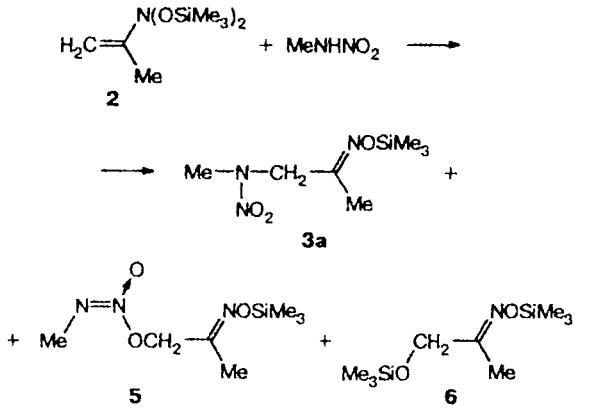
Scheme 2



as an N—H-acid, also catalyzes this rearrangement. The presence of diazene oxide **5** (a product of the O,C-cross-coupling of methylnitramine and enamine **2**) in the reaction mixture suggests that, unlike its trimethylsilyl derivative **1A**, methylnitramine itself is not an *N*-centered nucleophile in the strict sense, exhibiting ambident properties in the reaction with BSENA. Because of the side rearrangement **2**→**6**, a twofold (at least) molar excess of enamine **2** is necessary for satisfactory conversion of methylnitramine in this process.

Products **3a**, **5**, and **6** resulting from the reaction presented in Scheme 2 were separated by fractional crystallization followed by fractionation. The structures of compounds **3a** and **6** were unambiguously established by comparison of their spectral and physicochemical characteristics with those of authentic samples. The structure of diazene oxide **5** was confirmed by data from elemental analysis and heteronuclear NMR. The characteristics of the MeN=N(O)O— fragment in derivative **5** are close to similar characteristics of *O*-methyl derivative of methylnitramine.[8] In solutions of product **5**, only one stereoisomer was detected by NMR, although the formation of four isomers is theoretically possible. Taking into account the chemical shift value of the methyl group of the Me—C=N fragment in the ^{13}C NMR spectrum of product **5** (δ 12.01), *E*-configuration can be attributed to the silyloxyimino fragment. However, spectral data preclude any conclusion on the configuration of the N=N(O) fragment, because the signals for the carbon and nitrogen atoms of analogous fragments in a model compound MeN=N(O)OMe are quite similar for both stereoisomers.[8]

When methylnitramine is replaced by its anion generated upon addition of an equimolar amount of DBU to methylnitramine, the reaction with enamine **2** leads to the same products, but their overall yield decreases. It is significant that the product of rearrangement of enamine **2** is also present in the resulting mixture.

The results obtained allow us to propose a convenient preparative method for the synthesis of hitherto unknown oximes **4** from trimethylsilyl derivatives of the corresponding alkylnitramines and nitroparaffins. Obviously, the mechanism of this reaction is difficult to illustrate by simple formal schemes and its elucidation requires further investigations.

Experimental

NMR spectra were recorded on a Bruker AM-300 spectrometer (^1H (300.13 MHz), ^{13}C (75.47 MHz), ^{29}Si (INEPT, 59.63 MHz), and ^{14}N (21.69 MHz)).

4-Aza-4-nitro-2-(trimethylsilyloxyimino)pentane (3a). Derivative **1a** (0.85 g, 6.4 mmol) in 1 mL of hexane was added to a solution of enamine **2*** (1.3 g, 5.58 mmol) in 6.5 mL of hexane at 15 °C and stirred at this temperature for 30 min. 12 h after removal of the volatile products at 15 °C (10 Torr), derivative **3a** was obtained. Yield 0.87 g (71%), m.p. 40 °C (from hexane). ^1H NMR ($CDCl_3$, δ (Me_4Si)): 0.20 (s, 9 H, $SiMe_3$); 1.9 (s, 3 H, Me—C); 3.40 (s, 3 H, Me—N); 4.50 (s, 2 H, CH_2). ^{13}C NMR ($CDCl_3$, δ (Me_4Si)): −0.95 ($SiMe_3$); 12.54 (Me—C); 38.70 (Me—N); 55.30 (CH_2); 154.24 (C=). ^{29}Si NMR (INEPT, $CDCl_3$, δ (Me_4Si)): 26.17. ^{14}N NMR, δ ($MeNO_2$): −28.0 (Δν = 15.5 Hz). Found (%): C, 38.70; H, 7.53. $C_7H_{17}N_3O_3Si$. Calculated (%): C, 38.34; H, 7.81.

Similar reaction with enamine **2** purified according to the known procedure[3] yields a mixture of derivatives **3a**, **5**, and **6**, the rate of conversion of the initial **1a** being markedly lower.

4-Aza-4-nitro-2-(trimethylsilyloxyimino)hexane (3b). Under similar conditions, the reaction of enamine **2** (1.33 g, 5.7 mmol) in 7 mL of hexane and derivative **1b** (1.15 g, 7.1 mmol) in 2 mL of hexane yields derivative **3b** (1.2 g, 90%), b.p. 70 °C (0.9 Torr). ^1H NMR ($CDCl_3$, δ (Me_4Si)): 0.19 (s, 9 H, $SiMe_3$); 1.25 (t, 3 H, Me, J = 7 Hz); 1.89 (s, 3 H, Me—C=); 3.78 (q, 2 H, CH_2); 4.48 (s, 2 H, CH_2). ^{13}C NMR ($CDCl_3$, δ (Me_4Si)): −0.70 ($SiMe_3$); 11.80 (Me—CH_2); 12.43 (Me—C); 48.30 (CH_2—Me); 53.29 (N—CH_2—C=); 154.70 (C=). ^{29}Si NMR (INEPT, $CDCl_3$, δ (Me_4Si)): 25.85. ^{14}N NMR δ, (CH_3NO_2): −29.6 (Δν = 20 Hz).

Methanolysis of compounds 3a,b. Compound **3** (for amount, see below) was mixed with 15—20 mL of methanol and left at 20—22 °C for 12 h, whereupon the reaction mixture was concentrated *in vacuo* and dried to constant weight.

4-Aza-2-hydroxyimino-4-nitropentane (4a). Oxime **4a** (0.3 g, (100%) was obtained from derivative **3a** (0.43 g, 1.96 mmol). M.p. 95 °C (from CCl_4). Found (%): C, 32.64; H, 6.25; N, 28.57. $C_4H_9N_3O_3$. Calculated (%): C, 32.65; H, 6.17; N, 28.56. ^1H NMR (CD_2Cl_2, δ (Me_4Si)): 1.90 (s, 3 H, Me—C); 3.40 (s, 3 H, Me—N); 4.49 (s, 2 H, CH_2). ^{13}C NMR (CD_2Cl_2, δ (Me_4Si)): 12.25 (Me—C); 39.10 (Me—N); 55.73 (CH_2); 152.25 (C=). ^{14}N NMR δ (CH_3NO_2): −28.1 (Δν = 20.0 Hz). IR, ν/cm^{-1}: 1300 (ν_s NO_2); 1530 (ν_{as} NO_2); 3350—3400 br. (OH).

4-Aza-2-hydroxyimino-4-nitrohexane (4b). Oxime **4b** (0.07 g, 77%) was obtained as a mixture of *E*/*Z*-isomers, ~3 : 1 (TLC, Silufol-UV, ether—hexane (4 : 1)) from derivative **3b** (0.13 g, 0.56 mmol). M.p. 95—98 °C (from CCl_4). Found (%): C, 37.05; H, 6.48; N, 25.96. $C_5H_{11}N_3O_3$. Calculated (%): C, 37.26; H, 6.88; N, 26.07. ^1H NMR (acetone-d_6, δ (Me_4Si)): major isomer, 1.25 (t, 3 H, Me—C, J = 7 Hz);

* Compound **2** was obtained according to the procedure in Ref. 3, but without washing the organic layer with an aqueous solution of $NaHSO_4$.

1.85 (s, 3 H, Me—C=); 3.80 (q, 2 H, CH_2); 4.51 (s, 2 H, CH_2); 9.95 (br.s, 1 H, OH); minor isomer, 1.30 (t, 3 H, Me—C, J = 7 Hz); 1.80 (s, 3 H, Me—C=); 3.92 (q, 2 H, CH_2); 4.68 (s, 2 H, CH_2); 9.95 (br.s, 1 H, OH). ^{13}C NMR (acetone-d_6, δ (Me_4Si)): major isomer, 11.82 (Me—CH_2); 11.95 (Me—C=); 47.32 (CH_2—Me); 54.23 (CH_2—C=); 151.13 (C=); minor isomer, 11.58 (Me—CH_2); 17.50 (Me—C=); 48.33 (CH_2—Me); 49.28 (CH_2—C=); 152.56 (C=). ^{14}N NMR, δ ($MeNO_2$): −29.0 (Δν = 20.0 Hz).

Reaction of enamine 2 with methylnitramine. Methylnitramine (1.52 g, 20 mmol) was added with stirring to enamine **2** (10.2 g, 43.6 mmol) at 15—20 °C. The reaction mixture was stirred for an additional 15 min and then evacuated with stirring at 10 Torr for 1.5 h (the temperature increased to 26 °C and then slowly decreased to ~20 °C). Concentration of the mixture at 20 °C (1 Torr) gave an oil (6.52 g) containing methylnitramine, derivative **3a**, *O*-derivative **5**, and a rearrangement product **6** in a molar ratio 1 : 1.5 : 2.5 : 5 (according to ^1H, ^{13}C, and ^{14}N NMR spectroscopic data). The oil was diluted with 10 mL of light petroleum (b.p. 50—70 °C) and cooled to −20 °C. The mixture of methylnitramine with *N*-derivative **3a** that precipitated upon cooling was filtered off. The filtrate was concentrated at 20 °C (20 Torr) and the residue was fractionated to give derivatives **6** and **5**.

1-Trimethylsilyloxy-2-(trimethylsilyloxyimino)propane (6), b.p. 45 °C (7 Torr) or 26 °C (0.3 Torr) (*cf.* Ref. 1: b.p. 72 °C (9 Torr)). ^1H NMR ($CDCl_3$, δ (Me_4Si)): 0.15 and 0.22 (s, 18 H, $SiMe_3$); 1.88 (s, Me, *Z*-isomer); 1.92 (s, Me, *E*-isomer); 4.18 (s, CH_2, *E*-isomer); 4.52 (s, CH_2, *Z*-isomer), this corresponds to the data from Ref. 1. ^{13}C NMR ($CDCl_3$, δ (Me_4Si)): −0.68 and −0.45 ($SiMe_3$, *E*-isomer); −0.45 and −0.17 ($SiMe_3$, *Z*-isomer); 11.54 (Me, *E*-isomer); 16.50 (Me, *Z*-isomer); 58.72 (CH_2, *Z*-isomer); 64.86 (CH_2, *E*-isomer); 160.82 (C=, *E*-isomer); 163.4 (C=, *Z*-isomer). ^{29}Si NMR (INEPT, $CDCl_3$, δ (Me_4Si)): 19.54 ($OSiMe_3$, *Z*-isomer); 20.00 ($OSiMe_3$, *E*-isomer); 23.63 (NO—$SiMe_3$, *Z*-isomer); 24.14 (NO—$SiMe_3$, *E*-isomer). The ratio of *E*/*Z*-isomers ≈ 4 : 1 (^1H NMR spectroscopic data).

***N*'-Methyl-*N*-[(2-trimethylsilyloxyimino)propoxy]-diazene *N*-oxide (5)**, b.p. 50 °C (0.015 Torr). Found (%): C, 39.06; H, 8.05; N, 19.17. $C_7H_{17}N_3O_3Si$. Calculated (%): C, 38.34; H, 7.81; N, 19.17. ^1H NMR ($CDCl_3$, δ (Me_4Si)): 0.19 (s, 9 H, $SiMe_3$); 1.92 (s, 3 H, Me—C=); 3.22 (s, 3 H, Me—N); 4.89 (s, 2 H, CH_2). ^{13}C NMR ($CDCl_3$, δ (Me_4Si)): −0.92 ($SiMe_3$); 12.01 (Me—C=); 40.41 (Me—N); 71.14 (CH_2); 155.42 (C=). ^{29}Si NMR (INEPT, $CDCl_3$, δ (Me_4Si)): 25.89. ^{14}N NMR, δ (CH_3NO_2): −55.5 (Δν = 200 Hz, N(O)); −104 (Δν = 800 Hz, N=).

The reaction of methylnitramine (0.076 g, 1 mmol) with enamine **2** (0.23 g, 1 mmol) in 3 mL of CH_2Cl_2 at 20 °C for 24 h leads, according to NMR data (benzene as the internal standard), to derivative **6** (yield 47%) and derivatives **3a** and **5** (overall yield 33%, ratio 1 : 1.36). The conversion of methylnitramine amounted to 39%.

The reaction of enamine 2 with methylnitramine in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). DBU (0.15 g, 0.98 mmol) was added with stirring to a solution of methylnitramine (0.076 g, 1 mmol) in 1.5 mL of CH_2Cl_2 at 0 °C and stirred for 30 min. Then, enamine **2** (0.23 g) in 0.5 mL of CH_2Cl_2 was added at 0 °C, and stirring was continued for an additional 30 min. The reaction mixture was diluted with equal volume of CH_2Cl_2 and washed with a solution of sodium hydrogensulfate hydrate (0.13 g) in 1 mL of water. The organic layer was separated, washed with water (0.5 mL), dried with magnesium sulfate, and concentrated *in vacuo*. To the residual oil (0.47 g) benzene (0.06 mL) was added as the internal standard, and the resulting mixture was analyzed by ^1H and ^{29}Si NMR spectroscopy. The starting methylnitramine (20%), derivatives **3a** (6.5%) and **5** (6.5%), and 1-trimethylsilyloxy-2-trimethylsilyloxyiminopropane, the rearrangement product of the initial enamine **2** (19%), were identified.

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