Trimethylsilyl derivatives of aliphatic nitro compounds in α,α-carbon-carbon cross- coupling reactions

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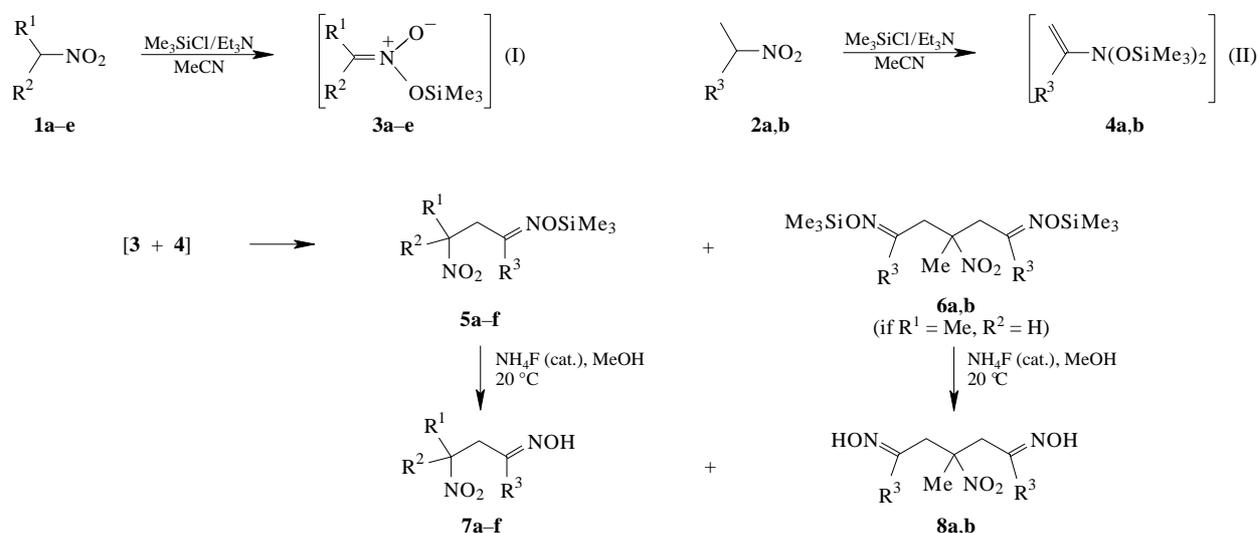
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A new coupling of the products of single silylation of nitro compounds (trimethylsilyl nitronates) with the products of double silylation of nitro compounds [*N,N*-bis(trimethylsilyloxy)enamines] is described as a new route to γ-nitro-substituted oximes by a one-pot procedure.

Aliphatic nitro compounds and their trialkylsilyl and lithium derivatives can be used as diverse building blocks for constructing carbon skeletons of polyfunctional compounds.[1] Trialkylsilyl nitronates have been used frequently and successfully for the formation of new C–C bonds, for

Our subsequent studies have shown that the reaction between trimethylsilyl nitronates and *N,N*-bis(trimethylsilyloxy)enamines resulting from single and double silylation of nitro compounds, respectively, is a general process and can be regarded as a new pathway to γ-nitroximes.[†]

Scheme 1 *Conditions:* (I) and (II) Preparation of a mixture of intermediates **3** + **4** from the same nitroalkane. For **1a**: 20 °C; molar ratio **1a**:Me₃SiCl:Et₃N = 1:2.1:2.3; stirring until the **3a**:**4a** molar ratio is 1.5:1 (NMR monitoring); for **1b**: keeping for 36 h at 5–15 °C, **1b**:Me₃SiCl:Et₃N = 1:1.5:1.5. Preparation of a mixture of intermediates **3** + **4** from different nitroalkanes [(**3a**, **3c** or **3d**) + **4b**]. Molar ratio **1**:**2**:Me₃SiCl:Et₃N = 1.2:1:3.3:3.4; first, **2** was stirred with a silylating agent for 3 h at 7–15 °C and for 70 h at 20 °C, then **1** was added, and the mixture was stirred for 20 h at 20 °C. **3e**[2] and **4b**[9] prepared separately were mixed. (III) Reaction of **3** with **4**: 2 h, 40–45 °C without solvent (or 4 h in the case of preparation of **5d** or **5f**).

	1 or 3			2 or 4		5 or 7					6 or 8	
	R¹	R²		R³		R¹	R²	R³	Yield 5 (%)[a]		R³	Yield 6 (%)[a]
a	Me	H	**a**	H	**a**	Me	H	H	22	**a**	H	33
b	Me	Me	**b**	Me	**b**	Me	H	Me	29	**b**	Me	20
c	Et	H			**c**	Me	Me	Me	60			
d	(CH₂)₂CO₂Me	H			**d**	Et	H	Me	35			
e	CO₂Me	H			**e**	(CH₂)₂CO₂Me	H	Me	43			
					f	CO₂Me	H	Me	31			

[a] Yield of oximes **7** and **8** 77–100%.

example, as 1,3-dipoles in concerted cycloaddition,[2,3] as α-C-nucleophiles in the Henry,[4] Mannich[5] and Michael[6] reactions and also as sources of electrophilic and radical intermediates in reactions with organolithium compounds[7] and nucleophilic alkenes,[8] respectively.

Recently we have found[9] that silylation of 2-nitropropane according to the standard procedure[10] involves cross-coupling of its two trimethylsilyl derivatives formed successively.

Silyl nitronates obtained from primary and secondary nitro derivatives **1**, including those with functional groups, can be used as the component **3** in this reaction.

Components **4** can be synthesised *via* double silylation of the nitro compounds **2** containing a methyl group at the α-carbon

[†] Up to now, no general method for the synthesis of γ-nitroximes has been reported. Only a few data on these compounds are known.[9,11,12]

Table 1 Main physical constants of new compounds **5**–**8**.

Compound (configuration)	Bp/°C (Torr)	n_D^{20}	Compound (yield, %, configuration)	Mp/°C
5a (*E*:*Z* 2:1)	60-6 2 (0.6)	1.445	**7a** (100, *E*:*Z* 1:1)	oil
5b (*E*)	45-4 8 (0.25)	1.442	**7b** (98, *E*)	68-7 2
5c (*E*)	62-6 4 (0.5)	1.450	**7c** (85, *E*)	63-6 4
5d (*E*)	60 (0.5)	1.445	**7d** (98, *E*)	51-5 6
5e (*E*)	95-9 7 (0.25)	1.455	**7e** (77, *E*)	oil
5f (*E*)	72-7 6 (0.2) part. decomp.	–	**7f** (100, *E*:*Z* 4:1)	oil
6a (*EE*:*EZ* 4:1)	114 (0.6)	1.459	**8a** (100, *EE*:*EZ*:*ZZ* 5:8:1)	oil
6b (*EE*)	100–102 (0.6); mp 24–30 °C	–	**8b** (87, *EE*:*EZ* 4:1)	128–136

atom by treating **2** with chlorotrimethylsilane in the presence of triethylamine in acetonitrile.

A significant advantage of the reaction outlined in Scheme 1 is that the trimethylsilyl derivatives of oximes **5** can be obtained by a 'one-pot' procedure without isolation of the intermediates **3** and **4**. It should be noted that the rearrangement of the intermediates **4** to 2-trimethylsilyloxy trimethylsilyloxy-iminoalkanes reported previously[13] does not occur under the conditions of reactions (I)–(II I) (Scheme 1).

Cross-coupling of **3** with **4** can formally be regarded as S_N2' substitution of the mild nucleophile **3** for the Me₃SiO group in **4**, *i.e.* as a process similar to the reaction of enamines **4** with secondary aliphatic amines described previously.[13] The reaction **3** + **4** could occur *via* cyclic transition state **A** or intermediate **B** which undergoes fast [3,3]-sigmatropic rearrangement (Scheme 2).[‡]
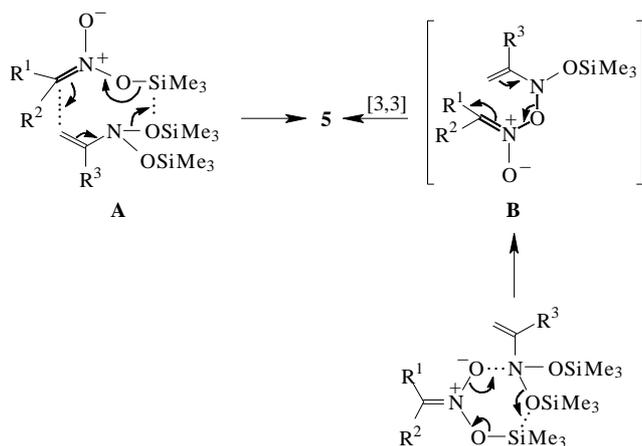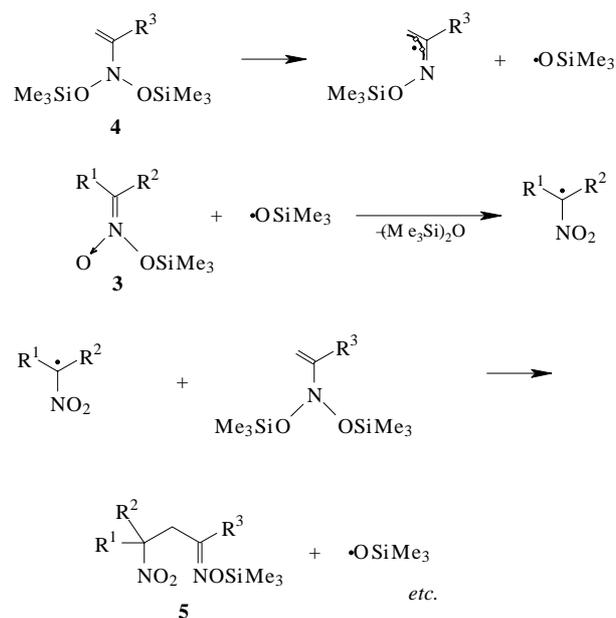
Scheme 2

However, some experimental facts cannot be explained adequately within the framework of these models. In particular, although anhydrous solvents and an inert atmosphere have been used, the initial nitro compound **1** has always been detected in the resulting mixture (in a yield of *ca.* 20%), whereas, according to NMR spectroscopy, the mixture of the intermediates **3** and **4** did not contain this compound. In addition, when the solvent was removed *in vacuo* from the mixture of intermediates **3** and **4**, they interact spontaneously with heat evolution. All these facts could be explained in terms of the chain radical mechanism shown in Scheme 3, although we have not observed formation of any radical intermediates in this process.[§]

When silyl nitronate **3a**, the use of which results in the most exothermal reactions, is involved in the cross-coupling **3** and **4**, products of double cross-coupling **6** are formed, in addition to the usual products **5**. Compounds **6** could arise *via* silylation of the derivatives **5a,b**, formed initially by the silyl nitronate **3a** followed by the interaction of the resulting intermediates with **4**.

Scheme 3

The main physical constants of the new compounds are given in Table 1. The structures and configurations of the derivatives **5a**–**f** and **6a,b** were confirmed by ^{1}H, ^{13}C, ^{14}N and ^{29}Si NMR data and also by conversion into oximes **7a**–**f** and **8a,b**, which were isolated by standard procedures. The structures and configurations of the oximes were confirmed by ^{1}H, ^{13}C and ^{14}N NMR spectroscopy and by elemental analysis.[¶]

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‡ An ionic mechanism for the reaction **3** + **4** can, apparently, be ruled out, since all attempts to model this reaction by the interaction between the anions derived from nitro compounds **3** and derivatives **4** failed, and the reaction **3** + **4** itself occurs efficiently only when a polar solvent (acetonitrile) and the base (triethylamine) were removed from the reaction mixture.
§ Radical reactions are known both for silyl nitronates[8] and for analogues of **4**, *N*,*N*-dialkoxyamines,[14] capable of homolytic cleavage of the N–O b ond.

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¶ The typical NMR data [NMR spectra were recorded on a Bruker AM 300 spectrometer at 300.13 MHz (^{1}H), 75.47 MHz (^{13}C), 59.63 (^{29}Si, INEPT), 21.69 (^{14}N, MeNO$_2$ as external standard), 30.42 (^{15}N, INEPT, MeNO$_2$ as external standard). Chemical shifts except ^{14}N and ^{15}N were measured relative to tetramethyl silane as internal standard. For the minor isomers only characteristic signals have been presented. The estimation of configuration of oximes has been made according to the literature data.[15]]:

5a. *E*-isomer, ^{1}H NMR (CDCl$_3$) δ: 0.20 (s, 9H, Me$_3$Si), 1.57 (d, 3H, Me), 2.65 (dt, 1H, CH_AH$_B$), 2.95 (ddd, 1H, CH$_A H_B$), 4.80 (m, 1H, CH–NO$_2$), 7.49 (t, 1H, CH); ^{13}C NMR (CDCl$_3$) δ: –1.35 (Me$_3$Si), 18.80 (Me), 34.14 (CH$_2$), 79.61 (CH), 149.21 (C=N). The Z-isomer, ^{1}H NMR (CDCl$_3$) δ: 0.23 (s, 9H, Me$_3$Si), 1.55 (d, 3H, Me), 6.92 (t, 1H, CH); ^{13}C NMR (CDCl$_3$) δ: –1.25 (Me$_3$Si), 18.69 (Me), 30.34 (CH$_2$), 79.86 (CH), 148.88 (C=N); ^{14}N NMR (CDCl$_3$) δ: 12.17 (NO$_2$).

5d. *E*-isomer, ^{1}H NMR (CDCl$_3$) δ: 0.25 (s, 9H, Me$_3$Si), 0.99 (t, 3H, Me), 1.87 (s, 3H, MeC=N), 1.85–1.89 (m, 2H, CH$_2$), 2.58 (dd, 1H, CH_AH$_B$), 2.95 (dd, 1H, CH$_A H_B$), 4.76–4.86 (m, 1H, CHNO$_2$); ^{13}C NMR (CDCl$_3$) δ: –0.88 (Me$_3$Si), 10.10 (Me), 14.55 (*Me*C=N), 27.45 (CH$_2$), 38.59 (*C*H$_2$C=N), 85.61 (CH), 156.53 (C=N); ^{14}N NMR (CDCl$_3$) δ: 11.46 (NO$_2$); ^{29}Si NMR (CDCl$_3$) δ: 24.92.

6a. *EE*-isomer, ^{1}H NMR (CDCl$_3$) δ: 0.20 (s, 18H, Me$_3$Si), 1.63 (s, 3H, Me), 2.78–2.86 (dd, 2H, CH_AH$_B$), 2.88–2.95 (dd, 2H, CH$_A H_B$), 7.44 (t, 2H, CH=N); ^{13}C NMR (CDCl$_3$) δ: –1.13 (Me$_3$Si), 23.24 (Me), 38.16 (CH$_2$), 87.79 (C), 149.03 (C=N); ^{14}N NMR (CDCl$_3$) δ: 10.64 (NO$_2$). *EZ*-isomer, ^{1}H NMR (CDCl$_3$) δ: 0.22 (s, 18H, Me$_3$Si), 6.80 (t, 2H, CH=N); ^{13}C NMR (CDCl$_3$) δ: –1.06 (Me$_3$Si), 23.33 (Me), 33.75 (CH$_2$, Z), 38.32 (CH$_2$, E), 87.62 (C), 148.33 (C=N, Z) 149.14 (C=N, E).

7a. ^{1}H NMR (CDCl$_3$) δ: 1.55 (d, 3H, Me), 1.57 (d, 3H, Me), 2.60–3.10 (m, 4H, 2CH$_2$) 4.71–4.90 (m, 2H, 2CHNO$_2$), 6.80 (t, 1H, CH=N), 7.51 (t, 1H, CH=N), 8.3–9.3 (broad., 2H, OH); ^{13}C NMR (CDCl$_3$) δ: 19.13 and 19.22 (CH$_3$), 30.24 and 34.30 (CH$_2$), 79.88 and 80.31 (CH), 146.12 and 146.50 (C=N).

8a. *EE*-isomer, ^{1}H NMR ([^{2}H$_6$]acetone) δ: 1.65 (s, 3H, Me), 2.79–3.14 (m, 4H, CH$_2$), 7.38 (t, 2H, CH=N); ^{13}C NMR (CDCl$_3$) δ: 23.09 (Me), 39.20 (CH$_2$), 89.42 (C), 144.71 (C=N). *EZ*-isomer, ^{1}H NMR ([^{2}H$_6$]acetone) δ: 1.69 (s, 3H, Me), 2.79–3.14 (m, CH$_2$ groups in *EE*-, *EZ*- and *ZZ*-isomers), 7.51 (t, 2H, CH=N); ^{13}C NMR (CDCl$_3$) δ: 23.36 (Me), 34.28 (CH$_2$), 89.09 (C), 144.71 [C=N (*E*-conf.)], 145.17 [C=N (Z-conf.)]. *ZZ*-isomer, ^{1}H NMR ([^{2}H$_6$]acetone) δ: 1.73 (s, 3H, Me), 2.79–3.14 (m, 4H, CH$_2$), 6.88 (t, 2H, CH=N); ^{13}C NMR (CDCl$_3$) δ: 23.60 (Me), 34.41 (CH$_2$), 89.09 or 89.42 (C), 145.17 (C=N).