The chemistry of *N,N*-bis(trialkylsilyloxy)enamines 2.* Alkylation of primary amines with *N,N*-bis(trimethylsilyloxy)enamines

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The reactions of primary amines with *N,N*-bis(trimethylsilyloxy)enamines can give products of both mono- and bis-α-oximinoalkylation of primary amines. The steric restrictions in both reactants substantially retard bis-α-oximinoalkylation. A general method for the synthesis of α-amino-substituted oximes from primary amines and bis-silyl derivatives of aliphatic nitro compounds was developed.

Key words: amines, *N,N*-bis(trimethylsilyloxy)enamines, alkylation of amines, oximes of α-amino-substituted ketones and aldehydes.

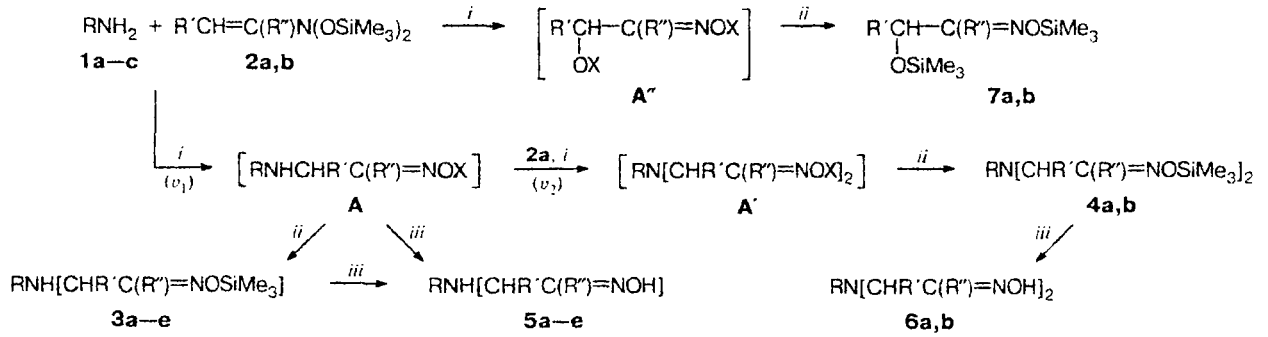
After a convenient method for the synthesis of *N,N*-bis(trialkylsilyloxy)enamines (BSENA) had been developed,[2] systematic study of the chemistry of these interesting and available derivatives of aliphatic nitro compounds became a topical line of research.

Recently, we reported successful C,C-cross-coupling of BSENA with derivatives of aliphatic nitro compounds[1,3] and N,C-cross-coupling of BSENA with derivatives of *N*-nitroamines.[4]

The possibility of α-oximinoalkylation of secondary amines by BSENA[5] was pointed out by the discoverer of BSENA, Professor Simchen. He attempted to extend this process to primary amines. However, according to ^{1}H NMR data, the target amino oxime is formed in the reaction of cyclohexylamine with *N,N*-bis(trimethylsilyloxy)aminoethylene in a yield not exceeding 16% and cannot be isolated from the reaction mixture in a pure state.[5] Meanwhile, α-*N*-alkylamino-substituted carbonyl compounds and their derivatives present considerable interest as intermediates for the synthesis of polyfunctional compounds.

The main purpose of this work was to study the reactions of primary amines RNH_2 (**1**) with BSENA (**2**); the model compounds chosen were *n*-hexylamine (**1a**) and BSENA **2a,b**, which are derivatives of 2-nitro- and 1-nitropropanes containing terminal and internal C=C double bonds, respectively.

Scheme 1



1: R = *n*-C_6H_{13} (**a**), MeCHEt (**b**), MeCHPh (**c**);
2, 7: R' = H, R" = Me (**a**); R' = Me, R" = H (**b**);
A, A', A": X = H, $SiMe_3$

Note. The substituents R, R', and R" for products **3—6** are given in Table 1.

Reagents and conditions: (*i*) 20 °C, without a solvent; (*ii*) 20 °C, PhH, Me_3SiCl/Et_3N; (*iii*) 20 °C, MeOH, NH_4F.

* For Part 1, see Ref. 1.

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Table 1. Synthesis of silyl derivatives **3** and **4** and amino oximes **5** and **6**

Products	R	R′	R″	Reaction conditions		The yield of the Me_3Si derivatives **3** or **4** (% based on **2** taken)	The yield of oximes **5** or **6** (% based on BSENA **2**)	
				The amine/BSENA molar ratio	τ[a]/h		crude	analytically pure
3a, **5a**	*n*-C_6H_{13}	H	Me	12 : 1	12	69[b]	85	64
3b, **5b**	*n*-C_6H_{13}	Me	H	2 : 1	24	60	—[c]	57
3c, **5c**	MeCHEt	Me	H	2 : 1	20	80[b]	~100	78
3d, **5d**	MeCHPh	H	Me	4 : 1	24	80	—[c]	76
3e,[d] **5e**	MeCHPh	Me	H	2 : 1	40	—[c]	~100[e]	66
4a, **6a**	*n*-C_6H_{13}	H	Me	1 : 1	12	79	—[c]	78
4b, **6b**	*n*-C_6H_{13}	H	Me[f]	2 : 1[g]	13	68	—[c]	67
		Me	H[f]		(at 50 °C)			

[a] Duration of cross-coupling, 20 °C. [b] After silylation of oxime **5a**. [c] Was not determined.
[d] MeCH(Ph)N(SiMe$_3$)[C(Me)CH=NOSiMe$_3$]. [e] After methanolysis of derivative **3e**. [f] See Scheme 2. [g] The **3b** : **2a** ratio.

The components were made to react at room temperature without a solvent (Scheme 1) as this had been done in a previous study.[5]

The reaction between equimolar amounts of compounds gave a multicomponent mixture. According to NMR, it contained products of mono- and bis-oximinoalkylation of amine **1a** (**A** and **A′**, respectively) and 2-hydroxy oxime derivatives (**A″**), arising upon rearrangement of the initial BSENA **2**.*

The oximino fragments in products **A**, **A′**, and **A″** were partially silylated: the >C=NOH : >C=NOSiMe$_3$ ratio varied from one experiment to another. A similar pattern has been observed previously for the oximinoalkylation of secondary amines with BSENA.[5]

Note that we were the first to observe the rearrangement of BSENA in the presence of (or on treatment with) amines. Previously, this process was accomplished only on treatment with Lewis or Brønsted acids and on heating of BSENA.[2,5] At a stoichiometric ratio of the reactants **1** and **2**, the contribution of rearrangement products **A″** to the resulting mixture is quite substantial. To minimize this process, it is expedient to use at least a twofold molar excess of amine **1** with respect to BSENA **2**.

The v_1/v_2 ratio of the rates of mono- and bis-α-oximinoalkylation of amines **1** depends appreciably on the shielding of reaction sites. The introduction of substituents (Et or Ph) to the α-carbon atom of amine **1** and, especially, to the β-carbon atom of BSENA **2** sharply decreases the rate of bis-α-oximinoalkylation (v_2). Therefore, to perform smooth mono-α-oximinoalkylation of amines **1** with BSENA **2b** containing an internal double bond, it is sufficient to use only a twofold molar excess of amine **1**. However, successful mono-α-oximinoalkylation of sterically nonhindered amine **1a** with BSENA **2a** containing a nonhindered terminal double bond requires at least a tenfold molar excess of amine **1a**. When BSENA **2a** with the terminal double bond reacts with a more sterically hindered amine **1c**, selective monoalkylation proceeds with a fourfold molar excess of amine **1c**.

In the case of appreciable steric hindrance in the reactants, the reaction cannot be brought to a satisfactory yield of the target product due to the competing rearrangement **2b** → **7b** (for example, N,C-cross-coupling of amine **3b** with BSENA **2b**).

The main process parameters and the yields of the target oximes and their trimethylsilyl derivatives are summarized in Table 1.

The isolation of target oximes **5** or **6** from intermediates (**A** or **A′**) was performed either by their exhaustive silylation followed by fractionation of trimethylsilyl derivatives **3** or **4** (see Scheme 1, pathway *2*) and desilylation of purified substrates (see Scheme 1, pathway *3*) or, whenever possible, by exhaustive desilylation of the oximino group in **A** (see Scheme 1, pathway *3*).

When oximes **5a** and **5c** were prepared under optimized conditions, the reaction mixtures virtually did not contain trimethylsilyl derivatives and, after evaporation *in vacuo*, the target oximes were isolated in a virtually pure state (according to ^{1}H NMR data). Analytically pure samples were prepared by silylation of the prepared oximes **5a** and **5c** with subsequent fractionation and desilylation.

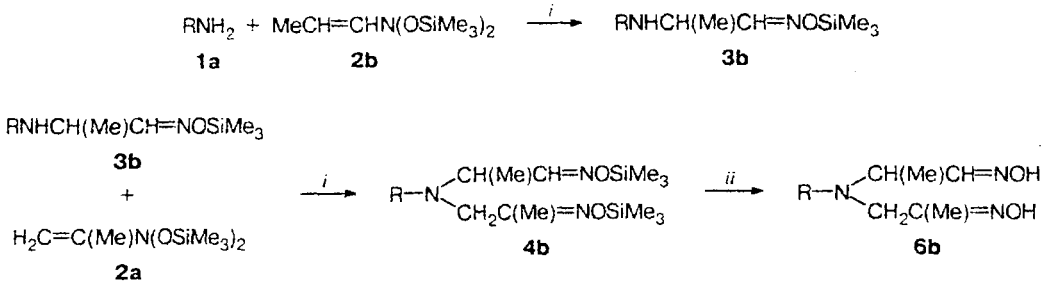
It follows from the data of Scheme 1 and Table 1 that N,C-cross-coupling of primary amines with BSENA is a convenient and efficient method of mono-α-oximinoalkylation of primary aliphatic amines. Thus a method for the synthesis of α-amino oximes from primary amines and aliphatic nitro compounds has been developed.

Apparently, this reaction can also be used for the design of bis(oximes) **6**, including "nonsymmetrical" ones (Scheme 2).

However, in this case, both the reaction pathway and the reaction conditions should be specially selected

* The rearrangement of BSENA is considered in detail in Refs. 2, 5.

Scheme 2



R = *n*-C_6H_{13}

Reagents and conditions: *i*) (*1*) 20 °C, without a solvent; (*2*) 20 °C, PhH, Me_3SiCl/Et_3N; *ii*) 0 °C, MeOH.

for each particular target product. For example, oxime **6b**, prepared by Scheme 2, cannot be synthesized *via* the alternative route

1a + **2a** ⟶ **3a**.

3a + **2b** ⟶ **4b**.

The reaction of derivative **3a** with the internal BSENA **2b** proceeds very slowly; therefore, the target product cannot be prepared in a satisfactory yield.

We did not specially study the mechanism of N,C-cross-coupling of amines with BSENA. However, the data obtained in this study, together with previous results,[4] suggest a scheme for this process whose key step is the formation of quite reactive α-nitroso alkenes (intermediates **C**, Scheme 3). This should be accompanied by silylation of the starting amines **1**.

The silylating activity of BSENA toward amines can be implemented by the initial electrophilic attack of the amine nitrogen atom by the silicon atom, which gives intermediate **B** (pathway *a*), or it is accompanied by elimination of silanol giving intermediate **B′** (pathway *b*). Both routes require electrophilic assistance and involve elimination of the same substrates. Naturally, the rate of the process should depend on the nucleophilicity of amine **1** and steric accessibility of the amine nitrogen atom.

The target products **3** and side products **7** result from the reactions of nitrosoalkenes **C** with amines **1** or

Scheme 3

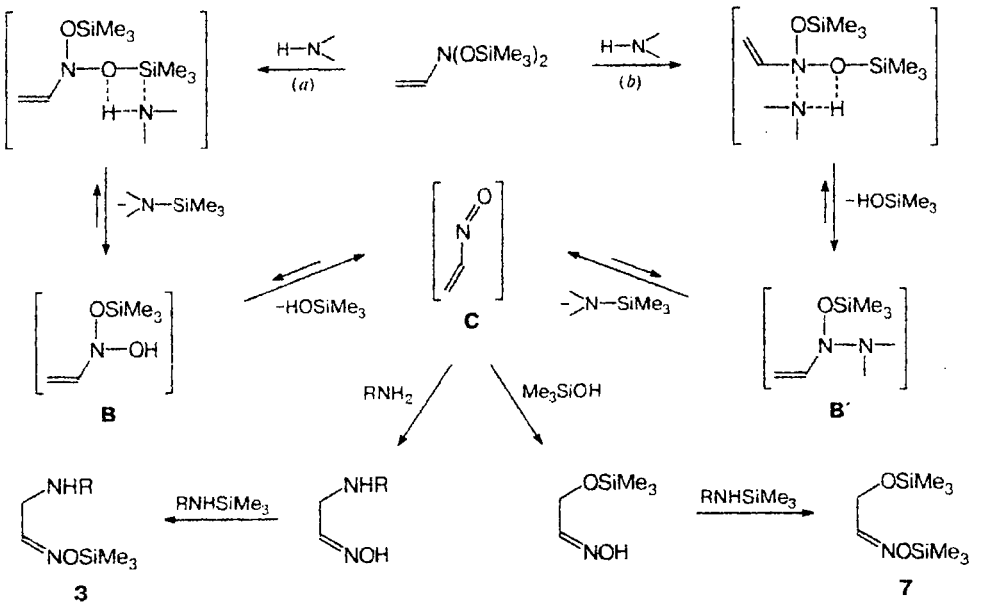


Table 2. Data of NMR for amino oximes and their trimethylsilyl derivatives

Compound (solvent)	^{1}H NMR (Me_4Si, δ, *J*/Hz)	^{13}C NMR (Me_4Si, δ)	^{29}Si NMR (Me_4Si, δ)	*E*/*Z* or Σ*E*/Σ*Z*
3a ($CDCl_3$)	*E isomer*: 0.21 (s, 9 H, $SiMe_3$); 0.89 (t, 3 H, $\underline{Me}CH_2$, ^3J = 6.7); 1.30 (m, 6 H, $(CH_2)_3$); 1.45 (m, 2 H, $\underline{CH_2}(CH_2)_3Me$); 1.87 (s, 3 H, $\underline{Me}$–C=); 2.56 (m, 2 H, CH_2–N); 3.32 (s, 2 H, CH_2) *Z isomer*: 1.92 (s, 3 H, Me–C=); 3.47 (s, 2 H, CH_2)	*E isomer*: −0.82 ($SiMe_3$); 12.86 ($\underline{Me}$–C=); 13.91 ($\underline{Me}$–CH_2); 22.52, 26.90, 29.87, 31.67 (–$(CH_2)_4$–); 49.15 (CH_2–N); 53.35 (CH_2–C); 159.97 (C=N) *Z isomer*: −0.90 ($SiMe_3$); 19.11 ($\underline{Me}$–C=); 47.24 ($\underline{CH_2}$–C=); 49.27 (CH_2–N)		~6 : 1
3b ($CDCl_3$)	*E isomer*: 0.21 (s, 9 H, $SiMe_3$); 0.89 (t, 3 H, $\underline{Me}CH_2$, ^3J = 6.7); 1.20 (d, 3 H, $\underline{Me}CH$, ^3J = 6.7); 1.27 (m, 6 H, $(CH_2)_3$); 1.45 (m, 2 H, $\underline{CH_2}(CH_2)_3$); 2.56 (m, 2 H, CH_2N); 3.39 (quint, 1 H, CH, ^3J = 6.7); 7.30 (d, 1 H, CH=N, ^3J = 6.7) *Z isomer*: 1.16 (d, 3 H, $\underline{Me}CH$, ^3J = 6.0); 6.73 (d, 1 H, CH=N, ^3J = 6.0)	*E isomer*: −0.81 ($SiMe_3$); 14.03 ($\underline{Me}$–CH_2); 19.78 ($\underline{Me}CH$); 22.60, 27.02, 30.19, 31.75 ($(CH_2)_4$); 47.42 (CH_2–N); 52.70 (CH); 158.40 (CH=)	25.11	>15 : 1
3c[a] ($CDCl_3$)	*E, E′ isomers*: 0.20 (s, 9 H, $SiMe_3$); 0.80–0.85 (m, 3 H, $\underline{Me}$–CH_2); 1.00 (m, 3 H, $\underline{Me}$–CHN); 1.20 (m, 3 H, $\underline{Me}$–CHC=); 1.25–1.35 (m, 2 H, CH_2); 2.55 (m, 1 H, Me$\underline{CH}$–N); 3.45 (m, 1 H, $\underline{CH}$–C=); 7.25 and 7.30 (both d, 1 H each, CH=, ^3J = 6.7) *Z, Z′ isomers*: 0.12 and 0.21 (s, 9 H, $SiMe_3$); 0.80–0.85 (m, 3 H, $\underline{Me}$–CH_2); 1.00 (m, 3 H, $\underline{Me}$–CHN–); 1.15 (m, 3 H, $\underline{Me}$–CHC=); 1.53 (m, 2 H, CH_2); 2.60 (m, 1 H, Me$\underline{CH}$–N); 3.45 (m, 1 H, CH–C=); 6.67 and 6.72 (both d, 1 H each, CH=N, ^3J = 6.7)	*E, E′ isomers*: −0.87 ($SiMe_3$); 9.80 and 10.39 ($\underline{Me}$–CH_2); 19.54 and 20.16 ($\underline{Me}$–CH–C=); 20.57 and 20.65 ($\underline{Me}$–CHN–); 28.62 and 30.52 (CH_2); 49.72 and 50.06 (CH–N); 51.72 (CH–C=); 158.57 and 158.67 (CH=) *Z, Z′ isomers*: −0.47 and −0.36 ($SiMe_3$); 9.83 and 10.39 ($\underline{Me}$–CH_2); 18.80 and 19.71 ($\underline{Me}$–CHC=); 20.64 and 22.00 ($\underline{Me}$–CH–N); 28.85 and 30.43 (CH_2); 45.20 and 45.61 (CHC=); 52.50 (CH–N); 160.43 and 160.54 (CH=)	24.94 and 24.97 25.63	>10 : 1[b]
3d ($CDCl_3$)	*E isomer*: 0.21 (s, 3 H, $SiMe_3$); 1.37 (d, 3 H, $\underline{Me}CH$, ^3J = 6.6); 1.87 (s, 3 H, MeC=); 3.24 (m, 2 H, CH_2); 3.80 (m, 1 H, CH); 7.30–7.45 (m, 5 H, C_6H_5)	*E isomer*: −0.58 ($SiMe_3$); 13.19 ($\underline{Me}$C=); 24.27 ($\underline{Me}CH$); 51.42 (CH_2); 57.45 (CH); 126.75, 128.15 (C_6H_5, *ortho*- and *meta*-CH); 126.94 (C_6H_5, *para*-CH); 145.43 (C_6H_5, *ipso*-C); 160.15 (C=N)	—	—
4a ($CDCl_3$)	*E,E isomer*: 0.19 (s, 8 H, $SiMe_3$); 0.89 (m, 3 H, $\underline{Me}$–CH_2); 1.27 (m, 6 H, $(CH_2)_3$); 1.43 (m, 2 H, $\underline{CH_2}$–$(CH_2)_3$–Me); 1.87 (s, 6 H, MeC=) *E,Z isomer*: 1.88 and 1.90 (both s, 6 H, Me–C); 3.03 and 3.29 (s, 4 H, CH_2C=)	*E,E isomer*: −0.71 ($SiMe_3$); 12.93 ($\underline{Me}$–C=); 14.02 ($\underline{Me}$–CH_2); 22.66, 26.38, 26.97 (–$(CH_2)_3$–); 31.72 ($\underline{CH_2}$–CH_2N); 53.57 (CH_2N); 57.97 ($\underline{CH_2}$–C=); 160.74 (C=N) *E,Z isomer*: 12.19 and 18.30 ($\underline{Me}$–C=); 50.52, 53.56, 54.55, and 58.71 (CH_2–N and $\underline{CH_2}$–C=); 160.61 and 160.74 (C=N)	--	8 : 1 (*EE* : *EZ*)

(*To be continued*)

Table 2. (*Continued*)

Compound (solvent)	^{1}H NMR (Me_4Si, δ, *J*/Hz)	^{13}C NMR (Me_4Si, δ)	^{29}Si NMR (Me_4Si, δ)	*E*/*Z* or Σ*E*/Σ*Z*
4b ($CDCl_3$)	*E,E isomer*: 0.19 and 0.22 (both s, 18 H, $SiMe_3$); 0.87 (t, 3 H, Me—CH_2, ^3J = 6.7); 1.17 (d, 3 H, Me—CH, ^3J = 7.3); 1.24 (m, 6 H, Me—(CH_2)$_3$); 1.38 (m, 2 H, CH_2—CH_2N); 1.87 (s, 3 H, Me—C=); 2.43 (m, 2 H, CH_2N); 3.00—3.20 (m, 2 H, CH_2C=); 3.47 (m, 1 H, CH—Me); 7.46 (d, 1 H, CH=N, ^3J = 5.5)	*E,E isomer*: −0.69 and −0.82 ($SiMe_3$); 12.61, 13.80, 14.06 (all Me); 22.70, 26.88, 27.98, 31.74 (Me—(CH_2)$_4$—); 50.05 (CH_2—CH_2N); 54.33 (N—CH_2—C=); 54.57 (N—CH); 156.60 (CH=); 161.19 (Me—C=N)	23.53 and 24.94	~5 : 1 (*EE* : *EZ*)
	E,Z isomer (*Z* at the *CH=NO— fragment*): 0.14 and 0.20 (both s, 18 H, $SiMe_3$); 0.87 (t, 3 H, Me—CH_2, ^3J = 6.7); 1.17 (d, 3 H, Me—CH, ^3J = 7.3); 1.24 (m, 6 H, Me(CH_2)$_3$); 1.38 (m, CH_2—CH_2N); 1.87 (s, 3 H, Me—C=); 2.46 (m, 2 H, CH_2N); 3.00—3.20 (m, 2 H, CH_2—C=); 4.22 (m, 1 H, CH—Me); 6.87 (d, 1 H, CH=N, ^3J = 6.7)	*E,Z isomer* (*Z* at the *CH=NO— fragment*): 1.17 and −0.20 ($SiMe_3$); 12.70, 12.92, 15.06 (all Me); 26.94, 27.67 ((CH_2)$_4$); 50.32 (N—CH); 50.99 (CH_2—N); 157.55 (CH=N); 161.13 (Me—C=N)	23.54 and 25.11	
5a ($CDCl_3$)	*E isomer*: 0.87 (m, 3 H, Me—CH_2); 1.28 (m, 6 H, (CH_2)$_3$); 1.47 (m, 2 H, CH_2—CH_2N); 1.87 (s, 3 H, Me—C=); 2.55 (m, 2 H, CH_2—N); 3.32 (s, 2 H, CH_2—C=)	*E isomer*: 12.45 (Me—C=); 13.98 (Me—CH_2); 22.57, 26.93, 29.62, 31.70 ((CH_2)$_4$); 49.14 (CH_2—N); 53.22 (N—CH_2—C=); 155.66 (C=N)	—	~4 : 1
	Z isomer: 1.90 (s, 3 H, Me—C=); 3.48 (s, 2 H, CH_2)	*Z isomer*: 19.77 (Me—C=); 47.15 (N—CH_2—C=); 49.61 (CH_2—N); 156.55 (C=N)		
5b ($CDCl_3$)	*E isomer*: 0.88 (m, 3 H, $MeCH_2$), 1.25 (d, 3 H, MeCH, ^3J =6.7); 1.28 (m, 6 H, (CH_2)$_3$); 1.50 (m, 2 H, CH_2CH_2N); 2.62 (m, 2 H, CH_2N); 3.43 (q, 1 H, CH, ^3J = 6.7); 7.28 (d, 1 H, CH=, ^3J = 6.7)	*E isomer*: 14.04 (Me—CH_2); 19.29 (MeCH); 22.59, 26.77, 29.66, 31.69 ((CH_2)$_4$); 47.27 (CH_2N); 52.88 (CH); 153.23 (C=N)	—	>10 : 1
	Z isomer: 6.66 (d, 1 H, CH=, ^3J = 6.7)			
5c[a] (DMSO-d_6)	*E, E′ isomers*: 0.80—0.85 (m, 3 H, Me—CH_2); 0.96 (m, 3 H, Me—CHN—); 1.10 (m, 3 H, Me—CHC—); 1.25—1.45 (m, 2 H, CH_2); 2.55 (m, 1 H, Me—CHN—); 3.40 (m, 1 H, CHC=); 7.08 and 7.12 (both d, 1 H, CH=N, ^3J = 7.8)	*E, E′ isomers*: 9.83 and 10.30 (Me—CH_2); 19.55 and 19.79 (Me—CHC=); 19.88 (Me—CHN); 28.51 and 29.63 (CH_2); 49.38 and 49.62 (CH—N); 50.99 and 51.16 (CH—C=); 152.68 and 152.75 (C=N)	[c,d]	~2.5 : 1[e]
	Z, Z′ isomers: 0.80—0.85 (m, 3 H, Me—CH_2); 0.96 (m, 3 H, Me—CHN—); 1.10 (m, 3 H, Me—CHC—); 1.25—1.45 (m, 2 H, CH_2); 2.55 (m, 1 H, Me—CHN—); 4.08 (m, 1 H, CHC=); 6.46 and 6.52 (both d, 1 H, CH=N, ^3J = 6.3)	*Z, Z′ isomers*: 9.90 and 10.30 (Me—CH_2); 18.70 and 18.83 (Me—CHC=); 19.88 (Me—CHN); 28.48 (CH_2); 44.51 and 44.81 (CH—C=); 51.85 and 52.04 (CH—N); 154.55 and 154.61 (C=N)		
5d ($CDCl_3$)	*E isomer*: 1.39 (d, 3 H, Me—CH, ^3J = 6.6); 1.84 (s, 3 H, MeC=); 3.18 (s, 2 H, CH_2); 3.77 (q, 1 H, CH, ^3J = 6.6); 7.20—7.25 (m, 5 H, C_6H_5)	*E isomer*: 12.95 (MeC=); 24.00 (Me—CH); 51.31 (CH_2); 57.65 (CH); 126.92 (C_6H_5, *ortho*-CH); 127.10 (C_6H_5, *para*-CH); 128.60 (C_6H_5, *meta*-CH); 144.92 (C_6H_5, *ipso*-C); 155.53 (C=N)		~6 : 1
	Z isomer: 1.40 (d, 3 H, Me—CH, ^3J = 6.6); 1.86 (s, 3 H, MeC=); 3.34 (s, 2 H, CH_2); 3.77 (q, 1 H, CH, ^3J = 6.6); 7.20—7.25 (m, 5 H, C_6H_5)	*Z isomer*: 19.62 (MeC=); 25.00 (Me—CH); 45.44 (CH_2); 58.24 (CH); 125.80 (C_6H_5, *ortho*-CH); 126.92 (C_6H_5, *para*-CH); 128.68 (C_6H_5, *meta*-CH); 147.00 (C_6H_5, *ipso*-C); 156.47 (C=N)		

(*To be continued*)

Table 2. (*Continued*)

Compound (solvent)	^{1}H NMR (Me_4Si, δ, *J*/Hz)	^{13}C NMR (Me_4Si, δ)	^{29}Si NMR (Me_4Si, δ)	*E*/*Z* or Σ*E*/Σ*Z*
5e[a] (DMSO-d_6)	*E, E' isomers*: 1.10 and 1.20 (both d, 3 H, Me—CHC=, ^3J = 6.7); 1.30 (d, 3 H, Me—CHPh, ^3J = 6.0); 3.10 and 3.35 (both m, 1 H, CH—(Me)C=); 3.80—3.90 (m, 1 H, CH—Ph); 7.30 (m, 5 H, C_6H_5); 7.20 and 7.30 (both d, 1 H, CH=N) *Z, Z' isomers*: 1.10—1.30 (d, 6 H, Me in two isomers); 3.70 and 4.40 (m, 1 H, CH(Me)Ph); 3.75 and 4.05 (both m, 1 H, CH(Me)C=); 6.55 and 6.73 (both d, 1 H, CH=N, ^3J = 6.7)	*E, E' isomers*: 18.75 and 19.99 (Me—CHC=); 23.45 and 24.64 (Me—CHPh); 49.78 and 50.74 (CH—Me); 54.37 and 54.80 (CH—Ph); 125.44, 126.09, 126.37, 126.45, 126.52, 128.10, 128.32 (all signals CH fragments Ph); 145.54 and 145.67 (C_6H_5, *ipso*-C); 152.58 (C=N) *Z, Z' isomers*: 17.45 and 18.19 (Me—CH—C=); 21.42 and 24.03 (Me—CHPh); 49.78 and 50.81 (CH—Me); 54.94 and 55.70 (CH—Ph); 125.44, 126.09, 126.37, 126.45, 126.52, 128.10, 128.32 (all signals CH fragments Ph); 145.54 (C_6H_5, *ipso*-C); 152.76 and 154.34 (C=N)	—	3 : 1[f]
6a ($CDCl_3$)	*E,E isomer*: 0.88 (t, 6 H, Me—CH_2, ^3J = 6.7); 1.27 (m, 6 H, $(CH_2)_3$); 1.45 (m, 2 H, $CH_2(CH_2)_3$—Me); 1.90 (s, 6 H, MeC=); 2.40 (m, 2 H, CH_2—N); 3.00 (s, 4 H, CH_2—C=) *E,Z isomer*: 3.02 and 3.30 (s, 4 H, CH_2—C=)	*E,E isomer*: 12.39 (Me—C=N); 14.04 (Me—CH_2); 22.60, 26.76, 26.92 ($(CH_2)_3$); 31.70 (CH_2CH_2N); 54.04 (CH_2—N); 58.07 (CH_2C=); 157.08 (C=N) *E,Z isomer*: 18.72 (MeC=); 54.82 and 58.76 (CH_2C=); 156.50 and 156.90 (C=N)	—	>10 : 1
6b ($CDCl_3$)	*E,E isomer*: 0.85 (t, 3 H, $MeCH_2$, ^3J = 6.7); 1.15 (m, 3 H, MeCH); 1.27 (m, 6 H, Me(CH_2)$_3$—); 1.40 (m, 2 H, CH_2CH_2—N); 1.87 (s, 3 H, MeC=); 2.40 (m, 2 H, CH_2CH_2N); 3.10 (m, 2 H, CH_2—C=); 3.42 (d.q, 1 H, CH—Me, ^3J = 6.0); 7.40 (d, 1 H, CH=, ^3J = 6.0); 9.50 (br.s, 2 H, OH) *E,Z isomer (Z at the CH=N—O fragment)*: 0.85 (t, 3 H, $MeCH_2$, ^3J = 6.7); 1.15 (m, 3 H, MeCH); 1.27 (m, 6 H, Me(CH_2)$_3$—); 1.40 (m, 2 H, CH_2CH_2N—); 1.87 (s, 3 H, MeC=); 2.40 (m, 2 H, CH_2CH_2N); 3.15 (m, 2 H, CH_2C=); 4.40 (d.q, 1 H, CHMe, ^3J = 6.7); 6.70 (d, 1 H, CH=, ^3J = 6.7); 9.50 (br.s, 2 H, OH)	*E,E isomer*: 12.17, 13.48, 14.04 (all Me); 22.64, 26.90, 27.90, 31.71 (Me(CH_2)$_4$); 49.97 (CH_2CH_2—N); 54.28 (CH—C=); 54.42 (N—CH_2C=); 152.68 (CH=N); 157.50 (C(Me)=N) *E,Z isomer (Z at the CH=N— fragment)* : 12.32, 13.83, 14.40 (all Me); 27.88, 31.76 $(CH_2)_4$); 50.28 (N—CH); 51.42 (CH_2N or NCH_2C=); 152.68 (CH=N); 157.41(C(Me)=N)	—	~4 : 1[g] (*EE* : *EZ*)

[a] Designations *Z,Z'* and *E,E'* refer to diastereomers having identical configurations of the oximino group. Exact correspondence between the configurations of diastereomers and the oximino groups was not established.

[b] The *E/E'* and *Z/Z'* isomer ratio ~1 : 1.

[c] ^{15}N (INEPT): −18.62 and −19.48 (C=N, *Z, Z'* isomers); −20.16 and −20.37 (C=N, *E, E'* isomers); −317.93 and −318.45 (NH, *E, E'* isomers); for the CH=N—O fragments in the *Z, Z'* isomers, $^2J_{H,15N}$ = 16.6 and 16.3; $^1J_{H,13C}$ = 173; for the CH=N—O fragment in *E, E'* isomers, $^2J_{H,15N}$ = 4.5 and 4.8; $^1J_{H,13C}$ = 162.

[d] Contaminated by HO—CH(Me)CH=NOH (~10—15%).

[e] The *E/E'* and *Z/Z'* isomer ratio ~1 : 1.

[f] The distilled product exhibited only signals of *E,E'* isomers. The *E/E'* isomer ratio ~1 : 1.

[g] The product contained up to 10% *Z,E*- or *Z,Z* isomer (^{13}C NMR data).

with trimethylsilanol, respectively. Note that reactions of amines with α-nitrosoalkenes are fairly well studied (for example, see review[6]). The nucleophilicity of amine **1** and steric accessibility of reaction sites should determine the rate and chemoselectivity of this process. In particular, it is known that the efficiency of α-nitrosoalkenes as β-C-electrophiles decreases upon introduction of substituents to the β-carbon atom.[1,6]

Thus, although Scheme 3 has not been proven, it nevertheless explains adequately the effects of the concentration, the reactant ratio, and the steric effects on the rate and selectivity of N,C-cross-coupling of amines **1** with BSENA **2**. From this standpoint, *N*-trimethylsilyl derivatives of amines should not enter actively into N,C-cross-coupling with BSENA **2** due to its relatively low nucleophilicity and steric hindrance. Indeed, Et_2NSiMe_3 does not react noticeably with BSENA **2a** even at 50 °C. The reaction of the trimethylsilyl derivative of amine **1a** (**1d**) can be performed under rigorous conditions but this reaction is not chemoselective (Scheme 4).*

Scheme 4

$$\underset{\mathbf{1d}}{RNHSiMe_3} + \underset{\mathbf{2a}}{H_2C{=}C(Me){-}N(OSiMe_3)_2} \xrightarrow{i}$$

$$\rightarrow \underset{\mathbf{5a}}{RNH[CH_2C(Me){=}NOH]} + \underset{\mathbf{6a}}{RN[CH_2C(Me){=}NOH]_2} +$$

$$+ \underset{\mathbf{1a}}{RNH_2}$$

R = *n*-C_6H_{13}

Reagents, conditions, and yields: *i*) (*1*) 50 °C, without a solvent; (*2*) MeOH, catalyst NH_4F. The yield of **5a**+**6a** is 50%; molar ratio **5a** : **6a** ≈ 1 : 2.5; the yield of **1a** is 50%.

It is most likely that, under these conditions, derivative **1d** undergoes desilylation and the greater part of the resulting derivatives of oximes **5a** and **6a** are formed from free amine **1a** rather than from **1d**.

The N,C-cross-coupling of amines **1b,c** with **2b** has been studied in order to elucidate the possibility of a diastereoselective process at the two chiral atoms marked by asterisks $Me(Y)C^*H{-}NH{-}C^*H(Me)CH{=}N{-}OH$, where Y = Et (**5c**) or Ph (**5e**).

It was found that cross-coupling of both amines with BSENA **2b** does not provide a noticeable diastereomeric excess of the target oximes. However, to draw ultimate conclusions, it is necessary to study the behavior in this process of BSENA **2** containing asymmetric centers near the C=C bond and of cyclic amines containing asymmetric centers.

Development of the chemistry of amino oximes **5** and **6** is the subject of our subsequent studies.

The structures of the target products **3**—**6** were confirmed by the data of heteronuclear NMR; for stable substrates **4b**, **5a**—**e**, and **6a** satisfactory data of elemental analysis were obtained.

In addition to the confirmation of the molecular formula and the presence of functional groups and substituents, we determined the spatial configuration of the oximino group.

Derivatives **3**—**6** contain Me—C=N—O— or H—C=N—O— fragments.
| |

The configurations of ketoximes and their silyl derivatives were determined from the ^{13}C NMR data relying on the postulate that signals of α-substituents located in the *cis*-position relative to the lone electron pair of the oximino group nitrogen atom are shifted downfield with respect to those of substituents located in the *trans*-position relative to this lone pair (for example, in the case of the Me group, the difference between the chemical shifts is 5—7 ppm[7a]).

The configurations of aldoximes and their derivatives were determined based on two criteria: (1) $^2J(^1H,^{15}N(syn)) >> {}^2J(^1H,^{15}N(anti))$ [7b] and (2) $^1J(^1H,^{13}C(syn)) > {}^1J(^1H,^{13}C(anti))$ (by ~10 Hz).[8]

These facts and analysis of the ^1H NMR data (Table 2) allow one to derive one more rule for establishing the configuration of the aldoxime group from the chemical shift of the α-proton in the ^1H NMR spectra. The signal for the CH=N protons in the *E* isomer is shifted 0.5—0.7 ppm downfield with respect to the corresponding signal for the *Z* isomer. This rule is most useful for determining the configurations of aldoxime fragments in products **4b** and **6b** and in monooximes **5c,e** and silyl derivatives **3c,e**, having diastereomers.

We did not perform detailed interpretation of all signals in the complex spectra of the reaction products. In addition, we did not match all signals to particular diastereomers but only determined the configuration of the oximino group. Exact assignment requires rather cumbersome NMR studies, which do not appear justified until essential diastereoselectivity of the **1** + **2** reaction has been revealed.

The main NMR data for products **3**—**6** are presented in Table 2.

Experimental

NMR spectra were recorded on Bruker AM-300 (operation frequency 300.3 MHz for ^1H, 75.47 MHz for ^{13}C, 59.63 MHz for ^{29}Si, INEPT, and 30.42 MHz for ^{15}N, INEPT) and Bruker DRX-500 (operation frequency 500.13 MHz for ^1H, 125.69 MHz for ^{13}C, 99.31 MHz for ^{29}Si, INEPT, and 50.69 MHz for ^{15}N, INEPT) spectrometers.

All operations with BSENA were performed in anhydrous solvents prepared using standard procedures. DL-α-Methylbenzylamine, (±)-*sec*-butylamine, and *n*-hexylamine were commercial reagents (Fluka) with ≥98% purity.

* However, trimethylsilyl derivatives of *N*-nitroamines are known [4] to be more efficient in N,C-cross-coupling than free *N*-nitroamines.

Table 3. Conditions of N,C-cross-coupling of amines **1a—c** with BSENA **2a,b** and of the isolation of the target products

Cross-coupling	Amine /g (mmol)	BSENA 2 /g (mmol) petroleum ether/mL	A+A′+A″ /g	Silylation of the reaction mixture or oxime			Methanolysis		
				Me_3SiCl	Et_3N	C_6H_6	Derivative /g (mmol)	Oxime	Yield of oxime[a] (%)
				g (mmol)		/mL			
1a+2a	36.36 (360)	6.99 (30) 30	4.4	27.84 (256.6)	26 (257.4)	63	**3a** 5.02 (20.6)	**5a**	94
1a+2b	1.41 (14)	1.62 (6.9) 15	1.47	0.76 (70)	0.71 (7.03)	22	**3b** 1.0 (4.1)	**5b**	96
1b+2b	0.93 (12.8)	1.5 (6.4) 20	0.92	0.69 (6.36)	0.65 (6.43)	15	**3c** 1.1 (5.0)	**5c**	98
1c+2a	1.0 (8.24)	0.48 (2.1) 6	0.52	0.19 (1.75)	0.18 (1.78)	7.0	**3d** 0.44 (1.66)	**5d**	94
1c+2b	2.42 (20)	2.33 (10) 15	2.51	2.14 (19.72)	2.02 (20.0)	50	**3e**[b] 2.79 (10.5)	**5e**	63
1a+2a	0.92 (9.1)	2.11 (9.1) 20	1.42	1.3 (11.98)	1.21 (11.98)	11	**4a** 1.38 (3.6)	**6a**	99

[a] Based on the trimethylsilyl derivative taken.
[b] *N,O*-Bis-trimethylsilyl derivative.

Table 4. Physicochemical properties of compounds **3a—e**, **4a**, **5a—e**, and **6a** and data of elemental analysis of oximes **5a—e** and **6a**

Derivative	B.p. /°C (*p*/Torr)	Molecular formula	Oxime	M.p. /°C	Found (%) / Calculated			Molecular formula
					C	H	N	
3a	55 (0.08)	$C_{12}H_{28}N_2OSi$	**5a**	40	62.19 62.79	11.42 11.62	16.12 16.28	$C_9H_{20}N_2O$
3b	58 (0.08)	$C_{12}H_{28}N_2OSi$	**5b**	70	62.80 62.79	11.63 11.62	15.66 16.28	$C_9H_{20}N_2O$
3c	38 (0.08)	$C_{10}H_{24}N_2OSi$	**5c**	60	57.41 58.33	11.05 11.11	19.81 19.44	$C_7H_{16}N_2O$
3d	75 (0.1)	$C_{14}H_{24}N_2OSi$	**5d**	Oil	68.75 68.75	8.50 8.33	14.38 14.58	$C_{11}H_{16}N_2O$
3e	105 (0.25)	$C_{17}H_{32}N_2OSi_2$	**5e**	71—75	68.57 68.75	8.31 8.33	14.24 14.58	$C_{11}H_{16}N_2O$
4a	105 (0.1)	$C_{18}H_{41}N_3O_2Si_2$	**6a**	Oil	59.20 59.25	10.20 10.29	17.09 17.28	$C_{12}H_{25}N_3O_2$

N,C-Cross-coupling of amines 1 with BSENA 2 (general procedure). A specified amount of BSENA **2**, prepared by a known procedure,[2] was added with stirring, either in petroleum ether or neat, to a specified amount of amine **1** at 20 °C (see Table 3). The solvent was evaporated at 20 °C (40 Torr). The residue was kept at 20 °C for the period indicated in Table 1 and the volatile components were removed at 20—50 °C (1 Torr) to give a certain amount of an A+A′+A″ mixture (see Scheme 1 and Table 3). The oximes **5a** and **5c** thus isolated were almost pure (according to NMR data, they contained less than 10% impurities). Oxime **5e** of the same quality was isolated after treatment of the A+A′+A″ mixture obtained with excess MeOH and subsequent removal of the volatile products *in vacuo*.

Preparation of trimethylsilyl derivatives 3 and 4 from the reaction mixture A+A′+A″ or from oximes 5a,c,e (general procedure). The silylating agent Me_3SiCl/Et_3N, in an amount calculated from ^1H NMR data (see Table 3), in anhydrous benzene was added with vigorous stirring (20—35 °C) to the specified amount of the A+A′+A″ mixture, prepared by the above procedure, or of oxime **5a,c,e** in anhydrous benzene (see Table 3). The mixture was kept for 12 h at 20 °C and diluted with an approximately equal volume of anhydrous petroleum ether, the precipitate was filtered off under argon, and the filtrate was concentrated at 20 °C (5—10 Torr). The target derivatives **3** or **4** were isolated by fractionation under argon (see Table 3).

Isolation of oximes 5 and 6 in an analytically pure state from their derivatives 3 or 4 (general procedure). A 15—20 weight excess of MeOH was added to a specified amount of derivative **3** or **4** (see Table 3); the mixture was kept for 12 h at 20 °C (or for 2 h after addition of 5 mg of NH_4F) and concentrated at 20 °C (1 Torr) to a constant weight

(the yields and the characteristics of the target products are presented in Table 3).

3-*n*-Hexyl-2-methyl-1,5-bis(oximino)-3-azahexane (6b) and its bis(trimethylsilyl) derivative 4b. Amine **3b** (0.8 g, 33 mmol) and BSENA **2a** (0.38 g, 1.63 mmol) were heated for 13 h at 50 °C (or kept for 10 days at 20 °C) and concentrated at 20 °C (0.2 Torr) to give 0.97 g of an oil. Anhydrous benzene (5 mL) was added and a mixture of Me_3SiCl (5.41 g, 50 mmol) and Et_3N (5.05 g, 50 mmol) in anhydrous benzene (10 mL) was added with vigorous stirring at 20 °C under dry argon. The mixture was kept for 12 h at 20 °C and diluted with anhydrous petroleum ether (30 mL), the precipitate was filtered off under argon, and the filtrate was concentrated at 20 °C (5 Torr) to give 1.14 g of an oil, which was fractionated in dry argon. This gave 0.44 g of derivative **3b**, b.p. 60 °C (0.08 Torr), and 0.43 g (68%) of 3-*n*-hexyl-2-methyl-1,5-bis(trimethylsilyloximino)-3-azahexane (**4b**), b.p. 90 °C (0.04 Torr). Found (%): C, 56.09; H, 10.62; Si, 14.51. $C_{18}H_{41}N_3O_2Si_2$. Calculated (%): C, 55.81; H, 10.59; Si, 14.51.

A solution of **4b** (0.1 g, 0.26 mmol) in MeOH (2 mL) was kept for 12 h at 0 °C and the volatile components were evaporated at 20 °C (0.1 Torr) to give 0.062 g (98%) of compound **6b** as an oil (spectroscopic characteristics are listed in Table 2); when stored in a refrigerator, the substance rapidly grew dark and decomposed.

Reaction of derivative 1d with BSENA 2a. Compound **1d** was prepared by a previously described procedure[9] in 34% yield, b.p. 56 °C (15 Torr), ^1H NMR (Me_4Si, $CDCl_3$), δ: 0.05 (s, 9 H, $SiMe_3$); 0.89 (t, 3 H, Me, J = 6.7 Hz); 1.30 (m, 8 H, $(CH_2)_4$); 2.70 (t, CH_2N, J = 6.0 Hz). Derivative **1d** (0.35 g, 2 mmol) and BSENA **2a** (0.48 g, 2 mmol) were kept for 1 h at 50 °C until the BSENA **2a** was entirely converted. The resulting mixture was analyzed by NMR; oximes **5a** and **6a** and amine **1a** were identified (see Scheme 4).

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