

Synthesis of 1-halo-*N,N*-bis(silyloxy)enamines

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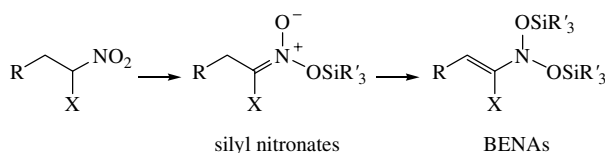
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1-Fluoro-, chloro-, bromo- and iodo-*N,N*-bis(silyloxy)enamines were obtained by the silylation of 1-halo nitro compounds.

Recently, 1-halo nitro compounds have attracted the attention of synthetic chemists as versatile reagents.^{1,2} In this respect, we have initiated studies on the silylation of 1-halo nitro compounds and found that the products of their monosilylation (1-halosilyl nitronates) demonstrated a reactivity that was quite different from that of non-halogenated analogues.²

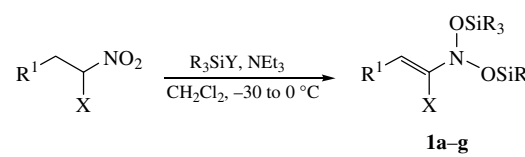


Scheme 1

At the same time, it would be of considerable interest to obtain the products of double silylation of 1-halo nitro compounds, corresponding *N,N*-bis(silyloxy)enamines (BENAs) (Scheme 1) since non-halogenated BENAs possess interesting stereochemical behaviour³ and can participate in a number of carbon–carbon⁴ and carbon–heteroatom⁵ bond forming reactions.

While many BENAs with functionalised double bonds were obtained,^{3,6} corresponding 1-halo-substituted derivatives, have not been reported. Here, we present a convenient procedure for the synthesis of a variety of 1-halo-substituted BENAs.[‡]

Table 1 Synthesis of enamines **1a–g**.



R ₃ SiY	Compound 1	R ¹	X	Yield of 1 (%)
Bu ^t Me ₂ SiOTf	1a	H	Br	72
Bu ^t Me ₂ SiOTf	1b	H	I	56
Bu ^t Me ₂ SiOTf	1c	Me	Br	90
Bu ^t Me ₂ SiOTf	1d	<i>n</i> -C ₈ H ₁₇	Cl	90
Bu ^t Me ₂ SiOTf	1e	<i>n</i> -C ₈ H ₁₇	I	75
Bu ^t Me ₂ SiOTf	1f	<i>n</i> -C ₈ H ₁₇	F	75
Me ₃ SiBr	1g	H	Br	85

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[‡] During the preparation of this manuscript, one BENA (**1a**) has been communicated, but for that species neither melting point nor microanalysis data were given, see ref. 7.

The silylation of 1-halo nitro compounds was carried out in methylene chloride in the presence of Bu^tMe₂SiOTf and triethylamine.[§] Under these conditions, BENAs **1a–f** bearing fluorine, chlorine, bromine and iodine substituents were obtained in moderate to good yields (Table 1).

It is known that BENAs bearing trimethylsilyl groups at oxygen atoms are less stable than their *tert*-butyldimethylsilyl counterparts. In particular, the silylation of nitro compounds to BENAs using Me₃SiOTf is frequently accompanied by the rearrangement of BENAs into α -silyloxyoximes.^{6,8} For this reason, we employed bromotrimethylsilane for the synthesis of enamine **1g**.⁹

All of the obtained compounds were characterised by ¹H and ¹³C NMR spectroscopy.[¶] Enamines **1c–f** containing internal double bonds were produced as single isomers. Unfortunately, attempts to determine the geometry of the double bond by NOE measurements were inconclusive. Nevertheless, based on the reported examples of BENAs with triply substituted double bonds,^{3,6} it would be expected that, in compounds **1c–f**, the alkyl group and *N,N*-bis(silyloxy)amino fragment are located in a *trans* orientation.

[§] General procedure for the preparation of BENAs **1a–g**. 1-Halo nitro compound (1 mmol) and NEt₃ (0.32 ml, 2.3 mmol) were mixed in dichloromethane (2.5 ml) at 0 °C. The reaction flask was placed in a cooling bath at –30 °C, and a silylating agent (2.2 mmol) was added dropwise. The mixture was kept at –30 °C for 30 min and at 0 °C (4 h for **1a–e**, 24 h for **1f** and 48 h for **1g**). The reaction mixture was diluted with cold hexane (5 ml) and poured into hexane–water (20 ml, 1:1). The organic phase was washed with an aqueous solution of NaHSO₄·H₂O (50 mg in 10 ml), water (2×10 ml) and brine, dried over Na₂SO₄ and concentrated in a vacuum.

Compounds **1a,b,g** were purified by either recrystallization or distillation. BENAs **1c–f** were of >90% purity (NMR spectroscopy). The products contained only 5–10% Bu^tMe₂SiOH and traces of starting halo nitro compounds, while their purification failed owing to their propensity to decomposition.

[¶] NMR spectra were recorded on Bruker AM-300, WM-250 and AC-200 instruments in CDCl₃.

N,N-Bis(*tert*-butyldimethylsilyloxy)(1-bromovinyl)amine **1a**:⁷ mp 70–72 °C (from light petroleum). Found (%): C, 43.75; H, 8.27; N, 3.92. Calc. for C₁₄H₃₂BrNO₂Si₂ (%): C, 43.96; H, 8.43; N, 3.66.

N,N-Bis(*tert*-butyldimethylsilyloxy)(1-iodovinyl)amine **1b**: mp 55–57 °C (from light petroleum). ¹H NMR, δ : 0.22 (s, 12H, 2Me₂Si), 0.93 (s, 18H, 2Me₃C), 5.54 (s, 1H, CH), 6.19 (s, 1H, CH). ¹³C NMR δ : –4.3 (2Me₂Si), 17.9 (2CMe₃), 25.8 (2CMe₃), 119.6 (CH₂), 129.3 (CI).

N,N-Bis(*tert*-butyldimethylsilyloxy)(1-bromopropenyl)amine **1c**: ¹H NMR, δ : 0.16 and 0.21 (2s, 2×6H, 2Me₂Si), 0.91 (s, 18H, 2Me₃CSi), 1.74 (d, 3H, Me, *J* 6.8 Hz), 6.03 (q, 1H, CH, *J* 6.8 Hz). ¹³C NMR, δ : –5.0 and –4.3 (2Me₂Si), 14.2 (Me), 17.8 (2CMe₃), 25.6 (2CMe₃), 121.4 (CH), 140.4 (CBr).

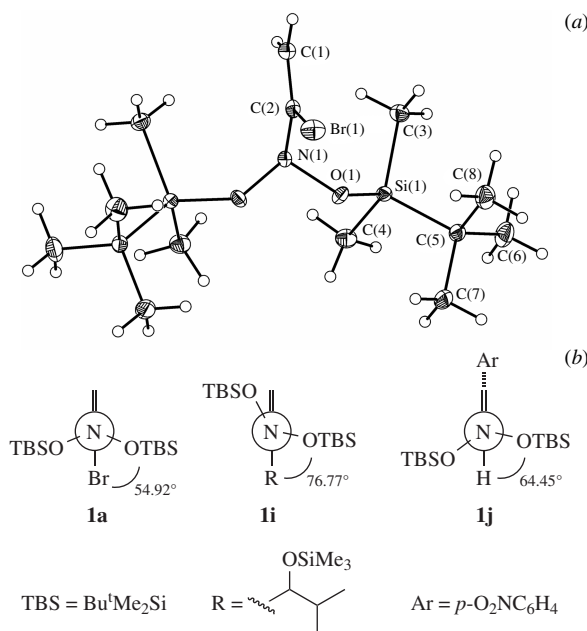


Figure 1 (a) Molecular structure of **1a** presented by thermal ellipsoids with 50% probability. Selected bond lengths (Å) and angles (°): C(1)–C(2) 1.316(2), N(1)–C(2) 1.433(2), N(1)–O(1) 1.436(2), Br(1)–C(2) 1.906(2), O(1)–N(1)–O(1) 103.66(12), C(2)–N(1)–O(1) 106.11(9), O(1)–N(1)–C(2) 125.08(8), Si(1)–O(1)–N(1)–C(2) –112.39(10). (b) Conformations of BENAs **1a,i,j**, view along C–N bond.

The crystal and molecular structures of **1a** were studied by X-ray diffraction analysis [Figure 1(a)].^{††} Previously, only two BENAs (**1i,j**) were structurally characterised.³ A comparison of the structures of **1a** and **1i**, which contains the (1-trimethylsilyloxy-2-methyl)propyl group instead of bromine, suggests that they reside in different conformations around the C–N bond [Figure 1(b)]. The preference of **1a** to adopt a staggered conformation may be tentatively ascribed to weak anomeric stabilization between a nitrogen lone pair and an antibonding orbital of the carbon–bromine bond (*n*–σ* interaction).¹⁰ This effect is supported by the shorter N–C bond distance in **1a** (1.433 Å) relative to **1i** (1.450 Å). However, in compound **1j** bearing hydrogen at the α-carbon atom, the distorted staggered orientation was observed with the N–C bond distance of 1.439 Å.

Concerning the carbon–bromine bond in **1a**, its value of 1.906(2) Å falls within a typical range for organic bromides (1.87–1.97 Å).¹¹ At the same time, an analysis of the Cambridge Structural Database indicated only one structure possessing a 1-bromoenamine fragment as the part of a polycyclic molecule with the C–Br bond distance of 1.912 Å.¹²

N,N-Bis(tert-butyltrimethylsilyloxy)(1-chlorohept-1-enyl)amine 1d: ¹H NMR, δ: 0.16 and 0.20 (2s, 2×6H, 2Me₂Si), 0.75–1.03 and 1.20–1.48 [2m, 27H, 2Me₃CSi + Me(CH₂)₃], 2.15 (q, 2H, CH₂CH=CBr, *J* 7.2 Hz), 5.75 (t, 1H, CH=CCl, *J* 7.2 Hz). ¹³C NMR, δ: –4.8 and –4.1 (2Me₂Si), 14.0, 18.0, 22.4, 26.9, 27.7, 31.5 [CSi + Me(CH₂)₄], 25.8 (2CMe₃), 123.4 (CH), 143.3 (CCl).

N,N-Bis(tert-butyltrimethylsilyloxy)(1-iodohept-1-enyl)amine 1e: ¹H NMR, δ: 0.16 and 0.22 (2s, 2×6H, 2Me₂Si), 0.78–1.04 and 1.20–1.50 [2m, 27H, 2Me₃CSi + Me(CH₂)₃], 2.14 (q, 2H, CH₂CH=CBr, *J* 7.4 Hz), 5.95 (t, 1H, CH=CI, *J* 7.4 Hz). ¹³C NMR, δ: –4.4 and –3.9 (2Me₂Si), 14.0, 18.0, 22.4, 26.0, 27.5, 31.4 [CSi + Me(CH₂)₄], 25.9 (2CMe₃), 127.6 (CH), 131.7 (CI).

N,N-Bis(tert-butyltrimethylsilyloxy)(1-fluorohept-1-enyl)amine 1f: ¹H NMR, δ: 0.16 and 0.21 (2s, 2×6H, 2Me₂Si), 0.70–1.07 and 1.20–1.50 [2m, 27H, 2Me₃CSi + Me(CH₂)₃], 1.94–2.15 (m, 2H, CH₂CH=CF), 4.84 (dt, 1H, CH=CF, *J* 7.9 Hz, *J* 28.9 Hz). ¹³C NMR, δ: –4.8 and –4.2 (2Me₂Si), 14.0, 18.0, 22.4, 23.1, 28.7, 31.3 [CSi + Me(CH₂)₄], 25.8 (2CMe₃), 98.8 (d, CH, *J* 20.4 Hz), 157.7 (d, CF, *J* 277.4 Hz).

N,N-Bis(trimethylsilyloxy)(1-bromovinyl)amine 1g: bp 48 °C (0.5 Torr). ¹H NMR, δ: 0.22 (s, 18H, 2Me₃Si), 5.27 (d, 1H, CH, *J* 1.5 Hz), 5.75 (d, 1H, CH, *J* 1.5 Hz). ¹³C NMR, δ: –0.1 (Me₃Si), 112.7 (CH₂), 144.1 (CBr).

Thus, we found that various 1-halo-*N,N*-bis(silyloxy)enamines can be obtained by the double silylation of 1-halo nitro compounds.

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^{††} Crystallographic data for **1a**: crystals of C₂₀H₂₀Br₂N₂O₂Si₂ are orthorhombic, space group *Pnma*, *a* = 12.8935(6), *b* = 23.1323(10) and *c* = 6.7096(3) Å, *V* = 2001.2(2) Å³, *Z* = 4, *M* = 536.38, *d*_{calc} = 1.780 g cm^{–3}, μ(MoKα) = 41.91 cm^{–1}, *F*(000) = 1072. Intensities of 28 137 reflections were measured with a Smart APEX II diffractometer at 100 K [λ(MoKα) = 0.71072 Å, ω-scans, 2θ < 64.1°] and 3562 independent reflections (*R*_{int} = 0.0543) were used in a further refinement. Absorption correction was carried out semi-empirically on the basis of equivalents intensities (*T*_{min} and *T*_{max} are 0.679 and 0.818, respectively). The structure was solved by a direct method and refined by the full-matrix least-squares technique against *F*² in the anisotropic approximation. Hydrogen atoms were calculated and refined in the rigid body approximation with the *U*(H) = 1.5 *U*_{eq}(C) and *U*(H) = 1.2 *U*_{eq}(C) for others. The refinement converged to *wR*₂ = 0.0754 and *GOF* = 0.983 for all independent reflections [*R*₁ = 0.0280 was calculated against *F*² for 2810 observed reflections with *I* > 2σ(*I*)].

Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk). Any request to the CCDC for data should quote the full literature citation and CCDC reference number 637866. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2007.