

Reaction of 3-Trimethylsilylprop-2-ynal with α -Hydroxyamino Oximes

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Received September 5, 2006

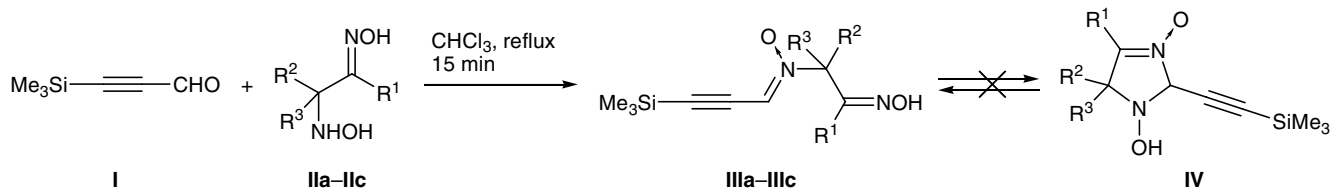
Abstract—3-Trimethylsilylprop-2-ynal reacted with aliphatic α -hydroxyamino oximes in a chemoselective fashion at the aldehyde group to give hitherto unknown open-chain 3-trimethylsilylprop-2-yn-1-ylideneamine oxides. The possibility for intramolecular hydrogen bonding with participation of OH, C $\equiv$ C, and N $\rightarrow$ O groups in the products was studied by IR spectroscopy.

DOI: 10.1134/S1070428007040033

Nitrones are widely used as 1,3-dipoles in inter- and intramolecular cycloadditions to activated double [1] or triple bond [2] with formation of the corresponding dihydroisoxazoles or isoxazoles. This approach was applied to the synthesis of analogs of natural compounds, such as monatin [3]. 1,2-Oxazolidines were obtained via cycloaddition of nitrones [generated *in situ* from aldehydes and hydroxylamines by the action of Yb(OTf)₃] with cyclopropane-1,1-dicarboxylates [4]. Linear and cyclic nitrones are effective radical traps *in vitro* and *in vivo* [5]. Published data on nitrones having an acetylenic fragment are very limited. For example, tricyclic conjugated nitrone containing a trimethylsilylethynyl group in the γ -position [6] and 2-(*m*- and *p*-ethynylphenyl)-4,4,5,5-tetramethyl-4,5-dihydroimidazol-1-oxyl 3-oxides were reported [7]. We have found no published data on α -acetylenic aldonitrones.

With a view to synthesize polyfunctional nitrones containing a trimethylsilylethynyl group in the α -position, we examined reactions of 3-trimethylsilylprop-2-ynal (**I**) with α -hydroxyamino oximes **IIa–IIc**. We anticipated that subsequent desilylation of the nitrones thus formed could give rise to their analogs with a terminal acetylenic bond. Reactions of α -hydroxyamino oximes with propynals were not reported previously. Theoretically, difunctional nucleophiles **IIa–IIc** are capable of adding at two reaction centers of ambident trimethylsilylpropynal [8]. Aromatic and aliphatic aldehydes are known to react with α -hydroxyamino oximes to give mainly 1-hydroxy-2,5-dihydroimidazole 3-oxides some of which in solution exist as tautomeric mixtures with open-chain form [9]. Ketone oximes were reported to add at the triple bond of ethyl prop-2-ynoate in the presence of triphenylphosphine with formation of *O*-vinyl oximes [10], while β,γ -ace-

Scheme 1.



II, III, $\text{R}^1 = \text{R}^2 = \text{Me}$, $\text{R}^3 = \text{H}$ (**a**); $\text{R}^1 = \text{R}^2 = \text{R}^3 = \text{Me}$ (**b**); $\text{R}^1\text{R}^2 = (\text{CH}_2)_4$, $\text{R}^3 = \text{H}$ (**c**).

tylenic oximes underwent cyclization to 3,5-disubstituted isoxazoles by the action of K_2CO_3 [11].

We have found that 3-trimethylsilylprop-2-ynal (**I**) reacts with α -hydroxyamino oximes **IIa–IIc** chemoselectively at the aldehyde fragment to give hitherto unknown crystalline *N*-(3-trimethylsilylprop-2-yn-1-ylidene)-2-hydroxyiminoalkanimine oxides **IIIa–IIIc** in 52–80% yield (Scheme 1). The reactions were carried out by heating the reactants in boiling chloroform for 15 min. The structure of compounds **IIIa–IIIc** was confirmed by analytical data and IR and NMR (1H , ^{13}C , ^{29}Si) spectra.

The 1H NMR spectra of compounds **IIIa** and **IIIb** contain a signal at δ 6.75–6.80 from proton in the $CH=N\rightarrow O$ fragment, signals in the region δ 1.57–1.62 ppm from protons in the methyl groups at the sp^3 -carbon atom, a signal at δ 1.84–1.95 ppm from the methyl group on the sp^2 -carbon atom, a group of signals in the regions δ 1.4–1.7, 1.8–2.0, 2.4–2.6, and 2.8–2.9 ppm from the cyclohexyl fragment, and a signal at δ 0.21–0.24 ppm from the trimethylsilyl group. The absence of signals in the region δ 5.0–5.2 ppm, typical of 2-H in dihydroimidazole oxides [12] indicates that cycloadducts like **IV** are not formed. In the ^{13}C NMR spectra of **IIIa–IIIc**, carbon atom in the oxime group ($C=N\rightarrow O$) gave rise to a signal at δ_C 154.59–159.51 ppm, while the $C=N\rightarrow O$ carbon signal appeared in the region δ_C 115.03–120.48 ppm. Signals from the triple-bonded carbon atoms were located at δ_C 111.86–117.38 (SiC) and 95.06–95.48 ppm ($\equiv CC$); the $C-N$ carbon atom had a chemical shift δ_C of 62.44–73.38 ppm, and signals in the δ_C range from -0.46 to -0.65 ppm were assigned to methyl carbon atoms in the $(CH_3)_3Si$ group. Signals from sp^3 -carbon atoms (methyl and cyclohexyl groups) occupy the δ_C range from 10.29 to 29.99 ppm. The chemical shifts of the ^{29}Si nuclei in **IIIa–IIIc** range from -15.66 to -15.89 ppm.

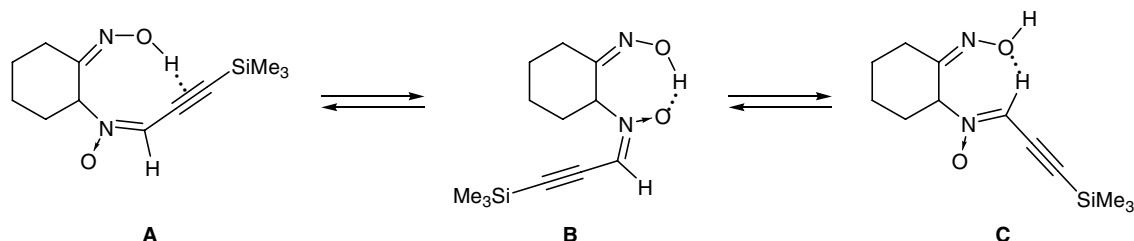
It should be noted that the difference $\Delta\delta_{C_{sp}}$ in the chemical shifts between the triple-bonded carbon atoms in **IIIa–IIIc** is 16.80–21.90 ppm, while $\Delta\delta_{C_{sp}}$

values for a large number of α,β -acetylenic silicon derivatives do not exceed 10 ppm [13–16]. These data indicate strong polarization of the triple bond in molecules **IIIa–IIIc**.

Compounds **IIIa–IIIc** displayed the following absorption bands in the IR spectra: $\nu(OH)$ 3200–3500, $\nu(C\equiv C)$ 2130 m, 2170 w, $\nu(C=N-OH)$ 1640, $\nu(C=N\rightarrow O)$ 1520–1580, $\nu_s(Si-CH_3)$ 1240–1250, ν_{as} 840–850 cm^{-1} . The $C=N\rightarrow O$ stretching vibration band was assigned with account taken of the IR spectra of initial α -hydroxyamino oximes **IIa–IIc**. Unlike previously described α,β -acetylenic organosilicon compounds like $Me_3SiC\equiv CX$ ($X = Alk, Ph$ [13], $CHROH$, $CHROSiMe_3$ [14], $CONHR$ [15], $C=NR$ [16]) which are characterized by absorption at 2160–2190 cm^{-1} due to stretching vibration band of the triple bond, the IR spectra of **IIIa–IIIc** contain an additional low-frequency band at 2130 cm^{-1} together with a band located at 2170 cm^{-1} .

Analysis of the IR spectra of **IIIa–IIIc** shows that the stretching vibration frequencies of their OH and $C\equiv C$ groups are considerably lower than those usually observed for structurally related compounds [14–17]. Using nitron **IIIc** as an example, we revealed hydrogen bonding with participation of the OH, $C\equiv C$, and $N\rightarrow O$ moieties. Successive dilution ($CHCl_3$, layer thickness up to 1 cm) did not result in appreciable transformation of the spectral pattern in the corresponding regions. On the other hand, we observed a reversible temperature dependence of the intensity of absorption bands at 3640–3540, 3400–3000, 2170–2130, 1640–1520, and 1170–1150 cm^{-1} arising from the above free and H-bonded groups. As solvent we used 1,2-dichloroethane, and the temperature was varied from 25 to 60°C. Taking into account the presence of several functional groups in molecule **IIIc** and the possibility for rotation about the $C-N$ and $C-C$ bonds and isomerization with respect to the $C=N$ bond, we presumed several modes of intramolecular hydrogen bonding, e.g., as in structures **A–C** shown in Scheme 2.

Scheme 2.



Analogous intramolecular hydrogen bonds could be formed in compounds **IIIa** and **IIIb**. Although the initial α -hydroxyamino oximes **IIa–IIc** have *E* configuration of the oxime fragment, while the most favorable isomer of aldonitrone is *Z*, we presumed that the configurations of both oxime and *N*-oxide moieties in **IIIa** and **IIIb** can change during the process to give a structure stabilized by intramolecular hydrogen bond. The possibility for hydrogen bonding like $O-H\cdots\pi(C\equiv C)$ was discussed in [18].

Thus our results showed that α -hydroxyamino oximes react with 3-trimethylsilylprop-2-ynal under mild conditions in the absence of a catalyst; the reaction is chemoselective, and it occurs exclusively at the aldehyde center with participation of more nucleophilic hydroxyamino group, leading to previously unknown *N*-(3-trimethylsilylprop-2-yn-1-ylidene)-2-hydroxyiminoalkanamine oxides.

EXPERIMENTAL

The IR spectra were recorded on a Specord 75IR spectrometer from samples prepared as KBr pellets, dispersed in mineral oil, or dissolved in $CHCl_3$ or $C_2H_2Cl_2$ (cell path length 0.254 to 1 cm; temperature range 25–60°C). The 1H , ^{13}C , and ^{29}Si NMR spectra were measured on a Bruker DPX-400 spectrometer at 400.13, 100.62, and 79.49 MHz, respectively, using $CDCl_3$ as solvent and HMDS as internal reference. The progress of reactions was monitored by TLC on Silufol UV-254 plates using chloroform–acetonitrile as eluent; development with iodine vapor. 3-Trimethylsilylprop-2-ynal was prepared by oxidation of 3-trimethylsilylprop-2-yn-1-ol with neutral manganese dioxide (γ -modification) according to [19].

3-Hydroxyimino-*N*-(3-trimethylsilylprop-2-yn-1-ylidene)butan-2-amine *N*-oxide (IIIa). A solution of 0.28 g (2.2 mmol) of 3-trimethylsilylprop-2-ynal (**I**) in 2 ml of anhydrous chloroform was added under stirring to a suspension of 0.24 g (2 mmol) of 3-(hydroxyamino)butan-2-one oxime (**IIa**) in 2 ml of chloroform. The mixture was heated for 15 min under reflux, cooled, and slowly added dropwise to 50 ml of hexane. The precipitate was filtered off, washed with hexane, and dried under reduced pressure. Yield 0.24 g (52%), colorless crystalline substance, mp 94°C. IR spectrum (mineral oil), ν , cm^{-1} : 3250 (OH_{ass}), 3080 ($H-C\equiv$), 2130 m, 2170 w ($C\equiv C$), 1640 ($C=N-OH$), 1580, 1520 ($C=N\rightarrow O$), 1250, 850 ($SiMe_3$). 1H NMR spectrum ($CDCl_3$), δ , ppm: 0.21 s [9H, $(CH_3)_3Si$], 1.57 d (3H, CH_3CH), 1.94 s (3H, $CH_3C=N$), 4.64 q (1H,

$CHN\rightarrow O$), 6.80 s (1H, $N=CH$), 8.48 br.s (1H, NOH). ^{13}C NMR spectrum ($CDCl_3$), δ_C , ppm: –0.65 (Me_3Si), 10.49 ($CH_3C=N$), 15.70 ($CH_3CHN\rightarrow O$), 73.38 ($CHN\rightarrow O$), 95.06 ($\equiv CCH$), 111.86 ($SiC\equiv$), 116.60 ($C=N\rightarrow O$), 154.59 ($C=NOH$). ^{29}Si NMR spectrum ($CDCl_3$): δ_{Si} –15.66 ppm. Found, %: C 52.93; H 7.96; N 12.27; Si 10.51. $C_{10}H_{18}N_2O_2Si$. Calculated, %: C 53.06; H 8.02; N 12.38; Si 12.41.

Compounds **IIIb** and **IIIc** were synthesized in a similar way.

3-Hydroxyimino-2-methyl-*N*-(3-trimethylsilylprop-2-yn-1-ylidene)butan-2-amine *N*-oxide (IIIb). Yield 0.37 g (79%), mp 99°C. IR spectrum (mineral oil), ν , cm^{-1} : 3200 (OH_{ass}), 2130 m, 2170 w ($C\equiv C$), 1640 ($C=N-OH$), 1580, 1530 ($C=N\rightarrow O$), 1250, 850 ($SiMe_3$). 1H NMR spectrum ($CDCl_3$), δ , ppm: 0.21 s [9H, $(CH_3)_3Si$], 1.62 s [6H, $(CH_3)_2C$], 1.85 s (3H, $CH_3C=N$), 6.75 s (1H, $N=CH$). ^{13}C NMR spectrum ($CDCl_3$), δ_C , ppm: –0.61 (Me_3Si), 10.29 ($CH_3C=N$), 24.49 [$(CH_3)_2C$], 62.44 ($CN\rightarrow O$), 93.22 ($\equiv CCH$), 112.03 ($SiC\equiv$), 115.03 ($C=N\rightarrow O$), 156.23 ($C=NOH$). ^{29}Si NMR spectrum ($CDCl_3$): δ_{Si} –15.83 ppm. Found, %: C 54.35; H 8.40; N 12.09; Si 11.43. $C_{11}H_{20}N_2O_2Si$. Calculated, %: C 54.96; H 8.39; N 11.65; Si 11.69.

2-Hydroxyimino-*N*-(3-trimethylsilylprop-2-yn-1-ylidene)cyclohexan-1-amine *N*-oxide (IIIc). Yield 0.39 g (80%), mp 102°C. IR spectrum (mineral oil), ν , cm^{-1} : 3290 (OH_{ass}), 2130 m, 2170 w ($C\equiv C$), 1640 ($C=N-OH$), 1580, 1520 ($C=N\rightarrow O$), 1240, 840 ($SiMe_3$). 1H NMR spectrum ($CDCl_3$), δ , ppm: 0.23 s [9H, $(CH_3)_3Si$], 1.48–2.87 br.m [8H, $(CH_2)_4$], 4.52 t (1H, $CHN\rightarrow O$), 6.76 s (1H, $N=CH$). ^{13}C NMR spectrum ($CDCl_3$), δ_C , ppm: –0.46 [$(CH_3)_3Si$], 21.58–29.99 (C^3 , C^4 , C^5 , C^6), 72.50 ($CHN\rightarrow O$), 95.48 ($\equiv CCH$), 117.38 ($SiC\equiv$), 120.48 ($CH=N\rightarrow O$), 159.51 ($C=NOH$). ^{29}Si NMR spectrum ($CDCl_3$): δ_{Si} –15.89 ppm. Found, %: C 56.67; H 8.24; N 11.25; Si 10.77. $C_{12}H_{20}N_2O_2Si$. Calculated, %: C 57.10; H 7.99; N 11.10; Si 11.13.

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