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Reaction of Trimethylsilylpropiolyl Chloride with Diamines and 2-Aminoethanethiol

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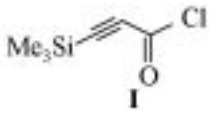
Abstract—Reaction of 3-trimethylsilyl-2-propiolyl chloride with ethylenediamine and hexamethylenediamine provided previously unknown bis(trimethylsilylpropiolyl)amides. Reactions of the acyl halide with 1,2-phenylenediamine and 2-aminoethanethiol proceeded regioselectively at a single reaction center to furnish amino- and thioamides of trimethylsilylpropiolic acid.

The development of propynamides chemistry is due to their high reactivity and to pharmacophoric character of the ethynylamide moiety as follows from the wide range of biological activity exhibited by compounds of this class [1–8]. They are also suitable for synthesis of natural amides, e.g., immunosuppressing rapamycin [9]. α,β-Siliconacetylene amides are less known. *N*-Benzyl-3-trimethylsilyl-2-propynamide prepared from lithium 2-propynamide dianion and trimethylchlorosilane took up phenyl isocyanate to afford *Z*-trimethylsilylhydantoin [10] and was selectively reduced on $Pd/CaCO_3$ into ethylenesilylamide or saturated silylamides [11]. Among the α,β-siliconacetylene amides we synthesized [12, 13], were found compounds with fungicidal, insecticidal, and antiphlogistic activity [14, 15].

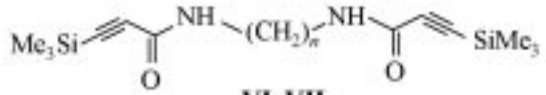
In the preceding communication [16] we reported on the preparation of trimethylsilylpropiolic acid N-hydroxyamides by reaction of trimethylsilylpropiolyl chloride with silyl ethers of aminoalcohols. By an example of monoethanolamine we demonstrated that, depending on the reaction conditions both NH and OH groups can be simultaneously involved into the reaction giving rise to 2-(3-trimethylsilylpropiolylamino)ethyl trimethylsilylpropiolate.

In extension of regular studies on reactions of trimethylsilylpropiolyl chloride (**I**) with functionally substituted amines we report here on reactions of compound **I** with ethylenediamine (**II**), hexamethylenediamine (**III**), 1,2-phenylenediamine (**IV**), and 2-aminoethanethiol (**V**).

It was established that the reaction direction depended on the character of nucleophile. For instance, the reaction between 3-trimethylsilyl-2-propiolyl chloride (**I**) with two moles of ethylenediamine (**II**) or hexamethylenediamine (**III**) gave rise only to diacyl derivatives in spite of excess diamine. The reaction readily occurs in ethyl ether at −10–0°C affording previously unknown trimethylsilylpropiolic acid *N*-2-(3-trimethylsilylpropiolylaminoethyl)amide (**VI**) and *N*-6-(3-trimethylsilylpropiolylaminohexyl)-amide (**VII**) in high yield.



I



VI, VII

n = 2 (**II, VI**), 6 (**III, VII**).

Yields, physical constants, and elemental analyses of compounds obtained are given in Table 1.

IR spectra of compounds **VI** and **VII** contain characteristic absorption bands of stretching vibrations of Si–Me bond at frequencies 735–760, 845–850, 1240–1260, of C=O bond at 1620–1630, triple bond Si–C≡C at 2170, and NH group in the region 3220–3280 cm^{-1}; to bending vibrations of N–H bond corresponds the absorption band at 1510–1550 cm^{-1} (Table 1). The structure of diamides **VI** and **VII** was also confirmed by ^1H, ^{13}C, and ^{29}Si NMR spectra listed in Table 2. Similar to the ^1H NMR spectrum of

Table 1. Yields, melting points, IR spectra, and elemental analyses of compounds **VI**–**IX**

Compd. no.	Yield, %	mp, °C	IR spectrum, ν, cm^{-1}					Found, %				Formula	Calculated, %			
			Si–C	C=O	C≡C	C=N, δNH	NH	C	H	N	Si		C	H	N	Si
VI	74	125-126	760, 850, 1260	1630	2170	1550	3280	54.31	7.73	9.16	18.37	$C_{14}H_{24}N_2O_2Si_2$	54.53	7.84	9.08	18.17
VII	83	117-119	735, 845, 1240	1620	2170	1510	3220	59.06	8.45	7.63	15.36	$C_{18}H_{32}N_2O_2Si_2$	59.31	8.85	7.68	15.37
VIII[a]	64	135-136	740, 847, 1251	1625	2175	1530	3230	61.76	6.75	12.09	11.95	$C_{12}H_{16}N_2OSi$	62.05	6.94	12.06	12.06
IX[b]	79	Viscosious liquid	750, 830, 1240	1630	2160	1520	3270	47.28	7.45	6.55	13.60	$C_8H_{15}NOSSi$	47.72	7.50	6.96	13.94

[a] IR spectrum (ν, cm^{-1}): 1580 (Ph), 3365 (NH_2). [b]IR spectrum (ν, cm^{-1}): 2540 (SH). Found, %: S 15.60. Calculated, %: S 15.92.

Table 2. ^{1}H, ^{13}C and ^{29}Si NMR spectra of compounds **VI**–**IX**, δ, ppm

Compd. no.	^{1}H NMR spectrum				^{13}C NMR spectrum					^{29}Si NMR spectrum
	Me_3Si	NH	N–CH_2	CH_2–C	$(CH_3)_3Si$	Si<u>C</u>≡C	SiC≡<u>C</u>	C=O	C–NH	
VI	0.22 s (9H)	6.31 s (1H)	3.43 t (2H)	–	–0.49	92.73	97.42	153.93	40.07	–17.61
VII[a]	0.21 s 0.23 s (9H)	5.87 s 5.76 s (1H)	3.26 q 3.38 q (2H)	1.50 m 1.60 m (2H)	–0.26, –0.29	90.88	98.36	152.75	40.08	–17.78
VIII[b]	0.20 s (9H)	7.35 s (1H)	–	–	–0.58	90.13	–17.93	157.75	39.66	–17.93
IX[c]	0.21 s (9H)	6.99 br.s (1H)	3.45 q (2H)	2.68 q (2H)	–	–	–	–	–	–

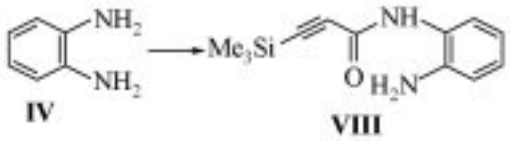
[a] Chemical shift, δ, ppm: 1.34 m (2H, $CH_2^{\gamma}C$). ^{13}C NMR signals, δ, ppm: 29.57 ($\underline{C}H_2CH_2$), 26.41 ($CH_2\underline{C}H_2$).

[b] Chemical shifts, δ, ppm: 3.75 s (2H, NH_2), 6.75 m (1H, H^3), 6.77 t (1H, H^5), 7.03 t (1H, H^4), 7.24 d (1H, H^6) of aromatic ring ^{13}C NMR signal, δ, ppm: 127.45 (Ph).

[c] Chemical shift, δ, ppm: 1.46 t (1H, SH).

hydroxyamide $Me_3SiC{\equiv}CCONHCH_2CH_2OH$ [16] in the corresponding spectrum of compound **VII** alongside the signals consistent with its assumed structure appear also weak signals from NH, NCH_2, $CH_2^{\beta}C$ and Me_3Si groups revealing the presence of the second rotary isomer that is stable due to hindered amide rotation [17] (Table 2).

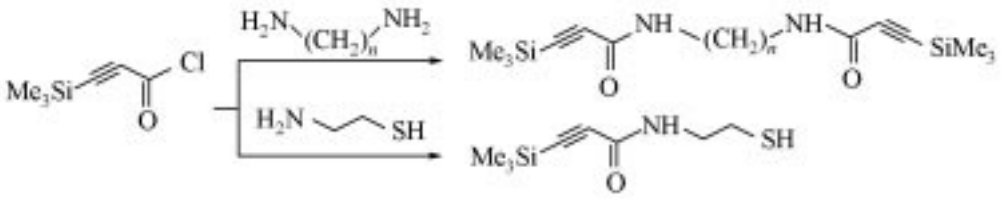
In contrast to aliphatic diamines **II, III** 1,2-phenylenediamine **IV** is acylated with trimethylsilylpropiolyl chloride at the same reagents ratio (2:1) regioselectively at one amino group. The previously unknown *N*-phenylamino-3-trimethylsilylpropiolamide (**VIII**), initial compound for further transformation into the corresponding trimethylsilylethynylbenzimidazole, was prepared in THF solution at –40°C in 64% yield. Its structure was proved by IR, ^{1}H, ^{13}C, and ^{29}Si NMR spectra presented in Tables 1 and 2.



IV VIII

In the IR spectrum of *N*-phenylamino-3-trimethylsilylpropiolamide (**VIII**) are present absorption bands in the region 740, 847, 1251 (Si–Me), 1620 (C=O), 1580 (Ph), 2175 (Si–C≡C) and 3230 (NH) and 3365 cm^{-1} (NH_2); to bending vibrations of N–H bond corresponds the absorption band at 1530 cm^{-1}.

Reaction of trimethylsilylpropiolyl chloride (**I**) with 2-aminoethanethiol (**V**) at reagents ratio 1:2 also occurred at a single reaction center providing previously unknown *N*-2-(mercaptoethyl)-3-trimethylsilylpropiolamide (**IX**). The reaction required more stringent conditions (benzene, 80°C, 9 h).



Thioamide **IX** was isolated by column chromatography on silica gel L 40/100, eluent chloroform–methanol, 10:1. IR spectrum of N-2(mercaptoethyl)-3-trimethylsilylpropiolamide (**IX**) contained absorption bands of stretching vibrations of Si–Me (750, 830, 1240 cm^{-1}), of C=O (1630 cm^{-1}), of triple bond Si–C≡C (2160 cm^{-1}), SH (2540 cm^{-1}), and of NH bond (3270 cm^{-1}); to the bending vibrations of N–H bond corresponded an absorption band at 1520 cm^{-1} (Table 1). In the ^{1}H NMR spectrum of amide **XI** appear a singlet of methyl groups protons (Me_3Si) at 0.21 ppm, a broadened singlet of NH group at 6.99 ppm, a triplet of SH group at 1.46 ppm, and a quartet of CH_2–N group at 3.45 ppm (Table 2).

Thus unlike hydroxyamines the acylation of diamines and 2-aminoethanethiol with trimethylsilyl-

propiolyl chloride occurs cleanly yielding silylated acetylene amides without preliminary silylation of amines. Whereas the aliphatic diamines were acylated at both amino groups, 1,2-phenylenediamine reacted at a single amino group apparently because of steric hindrances. With 2-aminoethanethiol the reaction occurred at the more basic center providing the corresponding trimethylsilylpropiolic acid mercaptoamide.

EXPERIMENTAL

IR spectra of compounds **VI–IX** were recorded on spectrophotometer Specord 75IR from thin films or KBr pellets. ^{1}H, ^{13}C, and ^{29}Si NMR spectra were registered on spectrometer Bruker DPX-400 from solutions in $CDCl_3$, internal reference HMDS.

Trimethylsilylpropiolic acid *N*-2-(3-trimethylsilylpropiolylaminoethyl)amide (VI). To a solution of 1.83 g (30 mmol) of ethylenediamine in 10 ml of anhydrous ethyl ether was added dropwise at −10 ÷ −5°C within 20 min 2.42 g (15 mmol) of acyl chloride (**I**) in 10 ml of ether. The stirring was continued for 1 h more at room temperature. The reaction mixture was quenched with water, the products were extracted into ether. The extract was washed in succession with 5% aqueous hydrochloric acid, 5% solution of $NaHCO_3$, with water, and then dried with $MgSO_4$. On removing the solvent we obtained 2.3 g (74%) of compound **VI**, mp 125–126°C (from cyclohexane).

Trimethylsilylpropiolic acid *N*-6-(3-trimethylsilylpropiolylaminohexyl)amide (VII). To a solution of 1.58 g (13.6 mmol) of hexamethylenediamine (**III**) in 10 ml of anhydrous ethyl ether was added dropwise at −5–0°C within 30 min 1.1 g (6.8 mmol) of acyl chloride (**I**) in 5 ml of ether. After usual workup and removal of solvent we separated 1.3 g (83%) of compound **VII**, mp 117–119°C (from carbon tetrachloride).

***N*-Phenylamino-3-trimethylsilylpropiolamide (VIII).** To a solution of 1.47 g (13.6 mmol) of 1,2-phenylenediamine (**IV**) in 10 ml of anhydrous THF at −40°C was added dropwise a solution of 1.1 g (6.8 mmol) of acyl chloride **I** in 5 ml of anhydrous THF. The reaction mixture was warmed to room temperature and quenched with 10 ml of water. After the usual workup and removal of the solvent we obtained 1 g (64%) of compound **VIII**, mp 135–136°C (from cyclohexane).

***N*-2-(Mercaptoethyl)-3-trimethylsilylpropiolamide (IX).** To a solution of 1.7 g (22 mmol) of 2-aminoethanethiol (**V**) in 10 ml of anhydrous benzene at 45°C was added dropwise a solution of 1.8 g (6.8 mmol) of acyl chloride **I** in 10 ml of benzene, then the mixture was heated at reflux for 9 h. The reaction mixture was cooled to room temperature and quenched with 10 ml of water. After the usual workup and removal of the solvent the residue was subjected to column chromatography on silica gel L 40/100, eluent chloroform–methanol, 10 : 1. We isolated 1.75 g (79%) of compound **IX**.

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