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N.S. Zefirov on His 70th Anniversary

Synthesis of Trimethylsilylpropynoyl Chloride

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Abstract—Trimethylsilylpropynoic acid reacts with thionyl chloride to give a mixture of trimethylsilylpropynoyl chloride and 3-chloro-3-trimethylsilyl-2-propenoyl chloride whose ratio depends on the reaction conditions (temperature, reactant ratio). Dimethylformamide almost does not catalyze the reaction. Treatment of trimethylsilylpropynoic acid with oxalyl chloride in the presence of 0.04 equiv of DMF at room temperature ensures selective formation of trimethylsilylpropynoyl chloride (yield 80%).

Carboxylic acid chlorides are widely used in organic synthesis as efficient acylating agents toward various O-, N-, S-, and C-centered nucleophiles [1]. They are convenient reagents in the preparation of hydroxamic acids [2], multicomponent syntheses of 2-propynyl amides [3], and syntheses of various heterocyclic compounds, in particular substituted guanines [4], dihydropyrazolones [5], 1,2,4-oxadiazoles [6], thioxopiperidinones [7], etc. The presence of several reaction centers in silicon-containing acetylenic carboxylic acid chlorides considerably extends their synthetic potential. Electron-withdrawing effect of the trimethylsilylethynyl group and the absence of steric hindrances at the carbonyl carbon in such acid chlorides should facilitate acylation of various nucleophiles. When necessary, the trimethylsilyl group can be removed from the *sp*-hybridized carbon atom to afford the corresponding products with a terminal triple bond.

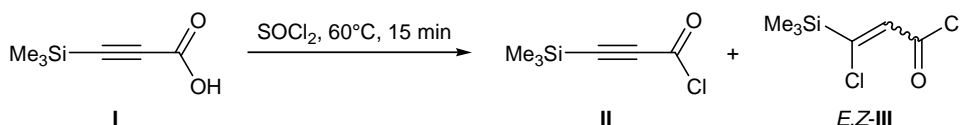
We previously studied 1,3-dipolar cycloaddition of diazoalkanes to 3-trimethylsilyl-2-propynoyl chloride [8] and acylation with the latter of butyl trimethylsilyl sulfide, sodium thiolate [9], and a wide series of amines [10]. Some α -silylated acetylenic amides thus obtained were found to exhibit fungicide, insecticide, and antiphlogistic activity [11].

The IR, UV, and ^{13}C NMR spectra and relative basicity of trimethylsilylpropynoyl chloride (**II**) were described in [12, 13]; however, the conditions for the synthesis of compound **II** were not given. We previously obtained trimethylsilylpropynoyl chloride (**II**) by treatment of trimethylsilylpropynoic acid with thionyl chloride [14], but the yield of **II** did not exceed 60%. In order to find optimal conditions for the preparation of acid chloride **II**, in the present work we examined the effects of the chlorinating agent nature and other factors on the yield of the target product.

When acid **I** was heated with thionyl chloride, apart from chloride **II** as the major product, we isolated ~20% of previously unknown 3-chloro-3-trimethylsilyl-2-propenoyl chloride (**III**) as a mixture of *E* and *Z* isomers (Scheme 1). The isomer ratio varied from 1:1 to 3:1, depending on the reaction conditions; however, we failed to reliably assign signals in the NMR spectra to particular isomers even using NOESY technique. Chlorides **II** and **III** were separated by vacuum distillation.

We examined the effects of such factors as reactant ratio, temperature, reaction time, and catalyst on the yields of the target product **II** and by-product **III**. The reaction mixtures were analyzed by ^1H NMR spectroscopy.

Scheme 1.



Reactions of 3-trimethylsilyl-2-propynoic acid (**I**) with thionyl chloride and oxalyl chloride

Reagent (equiv)	Temperature, °C	Reaction time, h	Conversion, %	Yield, ^a %		Molar ratio II : III
				II	III	
SOCl ₂ (2.5)	25	1.5	45	35	10	3.5:1
SOCl ₂ (2.5) ^b	25	1.5	59	45	14	3.2:1
SOCl ₂ (1.5)	60	0.25	24	20	4	5:1
SOCl ₂ (1.5)	75	1	96	70	26	2.7:1
SOCl ₂ (2.5) ^c	60	0.25	96	36	33	1:1
SOCl ₂ (2.5)	45	0.1	86	64	22	2.9:1
SOCl ₂ (2.5)	60	0.25	98	75	23	3.3:1
SOCl ₂ (5.0)	60	0.25	99	75	24	3.1:1
(COCl) ₂ (1.1) ^b	25	0.5	100	100	–	–
(COCl) ₂ (1.1)	25	0.5	7	7	–	–
(COCl) ₂ (1.1)	25	20	76	76	–	–

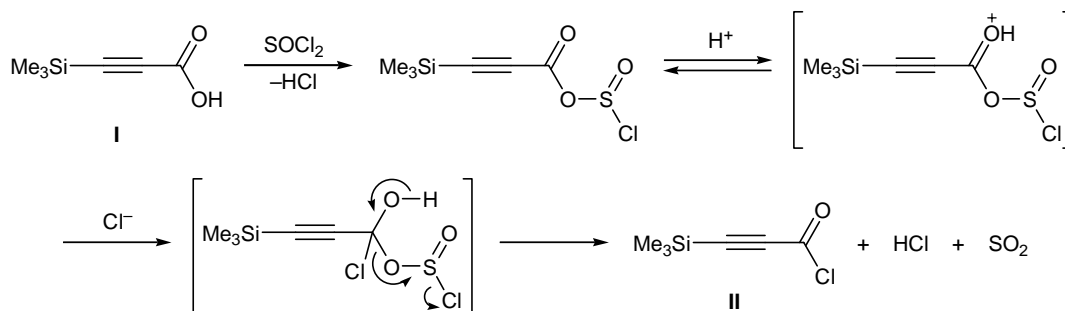
^a According to the ¹H NMR data.^b In the presence of 0.04 equiv of DMF.^c In the presence of 0.3 equiv of DMF.

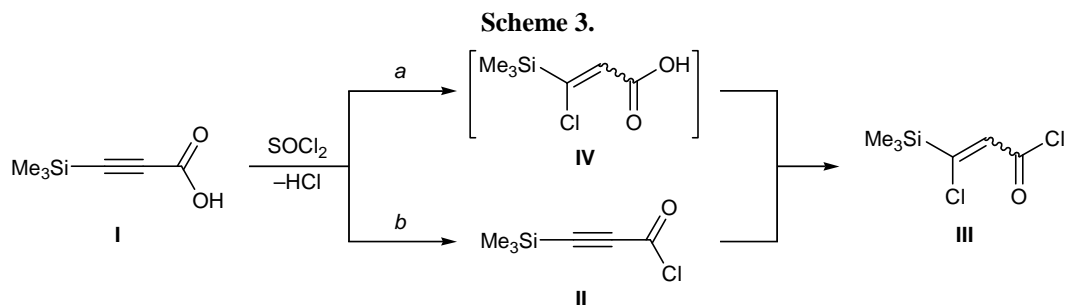
copy, and the results are collected in table. The reaction of acid **I** with thionyl chloride at room temperature was ineffective: in the presence of 2.5 equiv of SOCl₂, the conversion did not exceed 45% in 1.5 h. Raising the temperature strongly accelerates the process. At 60°C, the reactant ratio being the same, the conversion reached 98% in 15 min, and the yield of chloride **II** was 75%. An important factor affecting the efficiency of the process is the reactant ratio. Decrease in the amount of thionyl chloride to 1.5 equiv dramatically reduces the conversion. The conversion may be raised to 96% by heating at 75°C over a period of 1 h. It is known that dimethylformamide catalyzes chlorination of carboxylic acids with thionyl chloride [1]. However, no catalytic effect of DMF was observed in the reaction under study: the conversion of **I** increased only slightly in the presence of 0.04 equiv of DMF (at room temperature). Raising the amount of DMF to 0.3 equiv and the temperature to 60°C

resulted in increased conversion (96% in 15 min), but the conversion was 98% in 15 min in the absence of DMF. Moreover, the presence of DMF favors formation of the by-product: in the absence of catalyst, the ratio of products **II** and **III** was about 3:1, while in the presence of 0.3 equiv of DMF their ratio became approximately equimolar. These results are consistent with published data on the reactions of propynoic acids with SOCl₂ in DMF, which were reported to produce *E,Z*-isomeric 3-chloro-2-alkenoic acids, the *E* isomer prevailing [15]. The minimal concentration of 3-chloro-3-trimethylsilyl-2-propenoyl chloride (**III**) (ratio **II**:**III** = 5:1) was observed when the reaction was carried out with 1.5 equiv of SOCl₂, but in this case the conversion was as low as 24% (60°C, 15 min).

The structure of acid chlorides **II** and **III** was confirmed by the IR and ¹H, ¹³C, and ²⁹Si NMR spectra and elemental analyses. Compound **III** was isolated as

Scheme 2.

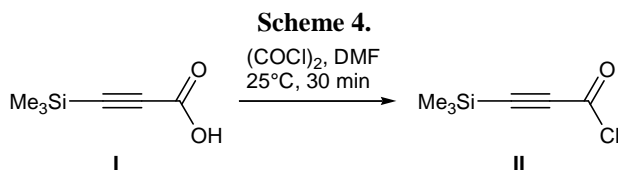




a colorless liquid; on storage, it undergoes slow hydrolysis by the action of atmospheric moisture to give previously unknown crystalline (*E/Z*)-3-chloro-3-trimethylsilyl-2-propenoic acid $\text{Me}_3\text{Si}(\text{Cl})\text{C}=\text{CHCOOH}$ (**IV**) (the fraction of one isomer is 98%).

In keeping with the known mechanism of formation of acid halides by the action of thionyl chloride [1], hydrogen chloride is released in both stages of the process (Scheme 2). Chloride **III** could be formed by addition of hydrogen chloride at the triple bond of trimethylsilylpropynoic acid **I** or chloride **II** (Scheme 3). Insofar as compound **III** was not detected by ^1H NMR spectroscopy when pure chloride **II** was heated with SOCl_2 for 1.5 h at 60°C , we presumed that hydrogen chloride adds at the triple bond of trimethylsilylpropynoic acid **I** according to pathway *a*. The mechanism of addition of hydrogen halides at the triple bond of propynoic acids was studied in [16].

With the use of oxalyl chloride as chlorinating agent, we succeeded in isolating trimethylsilylpropenoyl chloride (**II**) in 80% yield, the conversion being 100% (Scheme 4). The reaction was complete in 30 min at room temperature in the presence of a small excess (1.1 equiv of oxalyl chloride). In this case, unlike the reaction with thionyl chloride, the presence of 0.04 equiv of DMF as catalyst was necessary. As follows from the data in table, in the absence of catalyst the conversion sharply decreases (from 100 to 7% in 30 min). We succeeded in raising the conversion to 76% only by considerable increase of the reaction time (to 20 h).



Thus the reaction of trimethylsilylpropynoic acid with oxalyl chloride in the presence of DMF at room temperature ensures selective formation of trimethyl-

silylpropenoyl chloride in high yield. With the use of thionyl chloride as chlorinating agent, the yield of the target product does not exceed 60%, for the process is accompanied by formation of 3-chloro-3-trimethylsilyl-2-propenoic acid in ~20% yield.

EXPERIMENTAL

The IR spectra were recorded on a Specord 75IR spectrometer. The ^1H , ^{13}C , and ^{29}Si NMR spectra were measured on a Bruker DPX-400 instrument from solutions in CDCl_3 using cyclohexane as internal reference.

3-Trimethylsilyl-2-propenoyl chloride (**II**).

a. A mixture of 5.7 g (40 mmol) of acid **I** and 8.5 g (71 mmol) of thionyl chloride was heated for 15 min. Excess thionyl chloride was removed under reduced pressure, and the residue was distilled at $53\text{--}55^\circ\text{C}$ (17 mm). Yield 3.5 g (55%). IR spectrum (film), ν , cm^{-1} : 860, 1250 (SiMe_3); 1750 ($\text{C}=\text{O}$); 2170 ($\text{C}\equiv\text{C}$). ^1H NMR spectrum (CDCl_3), δ , ppm: 0.30 s (9H, CH_3Si). ^{13}C NMR spectrum (CDCl_3), δ_{C} , ppm: 149.40 ($\text{C}=\text{O}$); 103.40, 97.10 ($\text{C}\equiv\text{C}$). ^{29}Si NMR spectrum (CDCl_3): δ_{Si} -12.50 ppm. Found, %: C 44.61; H 5.65; Cl 22.10; Si 17.20. $\text{C}_6\text{H}_9\text{ClOSi}$. Calculated, %: C 44.85; H 5.65; Cl 22.07; Si 17.48.

b. A mixture of 2.9 g (20 mmol) of trimethylsilylpropynoic acid (**I**), 2.8 g (22 mmol) of oxalyl chloride, and 0.04 equiv of DMF was kept for 30 min at room temperature. The mixture was then distilled under reduced pressure to isolate 2.7 g (80%) of chloride **II**, bp $49\text{--}51^\circ\text{C}$ (16 mm).

(*E,Z*)-3-Chloro-3-trimethylsilyl-2-propenoyl chloride (**III**) was isolated by distillation of the high-boiling fraction (obtained as described above in *a*) at $88\text{--}90^\circ\text{C}$ (11 mm). Yield 1.6 g (20%). IR spectrum (film), ν , cm^{-1} : 830, 1250 (SiMe_3); 1640, 1660 ($\text{C}=\text{C}$); 1740, 1770 ($\text{C}=\text{O}$). ^1H NMR spectrum (CDCl_3), δ , ppm: 0.30 s and 0.32 s (9H, CH_3Si), 6.68 s and 7.02 s (1H, $\text{C}=\text{CH}$). ^{13}C NMR spectrum (CDCl_3), δ_{C} , ppm: 159.75, 159.07 ($\text{C}=\text{CH}$); 137.33, 130.41 ($\text{C}=\text{CH}$); 167.67, 163.27 ($\text{C}=\text{O}$); -2.98 , -2.09 (CH_3Si). ^{29}Si NMR

spectrum (CDCl₃), δ_{Si} , ppm: 5.01, 3.95. Found, %: C 36.40; H 5.68; Cl 35.70; Si 14.03. C₆H₁₀Cl₂OSi. Calculated, %: C 36.56; H 5.11; Cl 35.96; Si 14.25.

(E,Z)-3-Chloro-3-trimethylsilyl-2-propenoic acid (IV) (isomer ratio 98:2) was formed from chloride **III** on storage. mp 91–92°C. IR spectrum (KBr), ν , cm⁻¹: 830, 1220 (SiMe₃); 1570 (C=C); 1680 (C=O). ¹H NMR spectrum (CDCl₃), δ , ppm: major isomer: 0.33 s (9H, CH₃Si), 6.77 s (1H, C=CH), 11.04 br.s (1H, OH); minor isomer: 0.38 s (9H, CH₃Si), 6.43 s (1H, C=CH). ¹³C NMR spectrum (CDCl₃), δ_{C} , ppm: 170.56, 165.73, 132.23, -0.62. ²⁹Si NMR spectrum (CDCl₃): δ_{Si} 3.37 ppm. Found, %: C 39.91; H 6.09; Cl 19.28; Si 15.29. C₆H₁₁ClO₂Si. Calculated, %: C 40.33; H 6.20; Cl 19.84; Si 15.72.

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