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Dedicated to Full Member of the Russian Academy of Sciences I.P. Beletskaya on Her Jubilee

Effects of Structural Factors in Silyl Ethers Derived from Terminal Acetylenic Alcohols on 1,4-O→C_{sp} Migration of the Silyl Group

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Abstract—Effects of structural factors in silyl ethers derived from terminal acetylenic alcohols on 1,4-O→C_{sp} migration of the silyl group in the Iotsitch reagent were studied. The effect of steric factor at the carbon atom neighboring to the reaction center was found to be stronger than that at the silicon atom in the migrating group.

In the preceding communications we reported on 1,4-O→C_{sp} migration of the trimethylsilyl group in 3-trimethylsiloxy-1-propyne by the action of ethylmagnesium bromide to give (after hydrolysis) 85% of 3-trimethylsilyl-2-propyn-1-ol [1–3]. An analogous X→C_{sp} migration of the R_3M group occurs by the action of Grignard compounds on propynes of the general formula $HC{\equiv}CCH_2XMR_3$, where M = Si, Ge; X = O, S [4, 5]. This reaction demonstrates a radically new procedure for introduction of Si(Ge)−C_{sp} bond into acetylenic alcohols and thiols. We previously found that the structure of trimethylsilyl alkynyl ethers strongly influences the efficiency of their isomerization into trimethylsilylacetylenic alcohols: The isomerization is considerably hindered when the trimethylsiloxy group occupies β- rather than α-position with respect to the triple bond or there are substituents at the carbon atom neighboring to the reaction center (O−Si) in 3-trimethylsiloxy-1-propyne. For example, trimethylsilyl 1,1-dimethyl-2-propynyl ether does not undergo isomerization into 4-trimethylsilyl-2-methyl-3-butyn-2-ol under the conditions optimal for isomerization of trimethylsilyl 2-propynyl ether [2].

While continuing our studies on 1,4-O→C_{sp} migration of the R_3Si group in silyl ethers derived from terminal acetylenic alcohols, we examined the effect of steric factors in the initial acetylenic alcohol and migrating group on the isomerization process. For this purpose, we have synthesized trimethylsilyl ethers of alicyclic terminal acetylenic alcohols **I** and **II**, 2-(1-trimethylsiloxycyclopentyl)ethyne (**III**) and 2-(1-trimethylsiloxycyclohexyl)ethyne (**IV**), as well as chloromethyl(dimethyl)silyl and *tert*-butyl(dimethyl)silyl 2-propynyl ethers **V** and **VI**.

We anticipated that steric hindrances to O→C_{sp} migration of the trimethylsilyl group in trimethylsilyl ethers derived from tertiary acetylenic alcohols of the alicyclic series would be lower than in the acyclic analog, trimethylsilyl 1,1-dimethyl-2-propynyl ether. The silylation of tertiary acetylenic alcohols was performed following the procedure developed by us previously; this procedure utilizes hexamethyldisilazane as silylating agent and a new catalyst, ethylenedinitramine (EDNA) [6]. As might be expected, the silylation of alcohols **I** and **II** was much more difficult than the silylation of 2-propynyl alcohol (**VII**). The latter reaction was complete in 5 min in the presence of 0.01 mol % of EDNA; the process was accompanied by strong heat evolution, and the yield of the product was quantitative. Trimethylsilyl ethers **I** and **II** were synthesized by the action of hexamethyldisilazane in the presence of 0.1 mol % of EDNA at elevated temperature. A considerable difference in the reactivities of alcohols **I** and **II** should be noted. Ether **III** was obtained in 95% yield in 3.5 h at 70°C, while previously unknown cyclohexyl analog **IV** was isolated in 60% yield after heating at 120–130°C for

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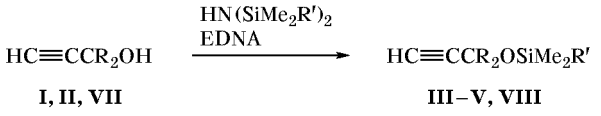
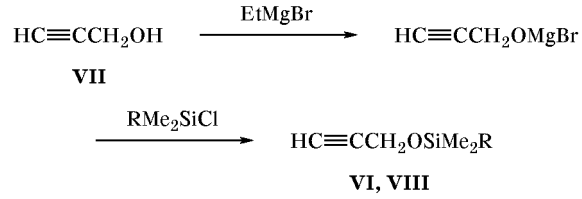
15 h. Presumably, the reason is the different steric structures of the substrates containing 5- and 6-membered rings. Due to planar structure of the five-membered ring in alcohol **I**, steric hindrances at the reaction center to attack by silylating agent are considerably lower than in cyclohexyl analog **II**. 3-Chloromethyl(dimethyl)siloxy-1-propyne (**V**) was obtained from 2-propynyl alcohol and bis(chloromethyl)tetramethyldisilazane in the presence of 0.01 mol % of EDNA (70–75°C, 2 h; yield 82%).



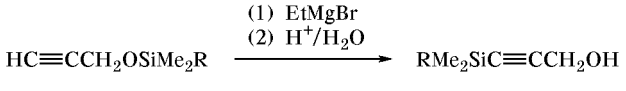
I, CR_2 = *cyclo*-C_5H_{11}; **II**, CR_2 = *cyclo*-C_6H_{13}; **III**, R′ = Me, CR_2 = *cyclo*-C_5H_{11}; **IV**, R′ = Me, CR_2 = *cyclo*-C_6H_{13}; **V**, R = H, R′ = CH_2Cl; **VII**, R = H; **VIII**, R = H, R′ = Me.

Our attempt to synthesize hitherto unknown 3-*tert*-butyl(dimethyl)siloxy-1-propyne (**VI**) by the action of *tert*-butyl(chloro)dimethylsilane on 2-propynyl alcohol (**VII**) in the presence of pyridine was unsuccessful. The reaction was accompanied by strong tarring, and the yield of silyl ether **VI** was poor. Therefore, we have developed a procedure for chemoselective metalation of the hydroxy group in **VII** by ethylmagnesium bromide to obtain 2-propynyloxymagnesium bromide. The subsequent treatment with chlorotrimethylsilane gave ether **VIII** which contained no impurity of isomeric 3-trimethylsilyl-2-propyn-1-ol (product of the reaction of the Iotsitch reagent with chlorotrimethylsilane). Following the same procedure, ether **VI** was obtained in 58% yield.



VI, R = *t*-Bu; **VIII**, R = Me.

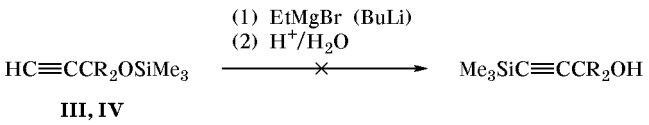
Ethers **III** and **IV** were subjected to isomerization under the conditions optimal for O→C_{sp} migration of the trimethylsilyl group in ether **VIII** (EtMgBr, THF, reflux, 9 h) [2–4], as well as by the action of butyllithium. However, after hydrolysis with 5% hydrochloric acid, we isolated only the corresponding terminal acetylenic alcohols **I** and **II** instead of the expected C_{sp}-silylated acetylenic alcohols. In the reaction with EtMgBr, initial silyl ether **III** was isolated in addition to alcohol **I** (ratio 1 : 1). These data indicate that ether **III** is relatively stable (as compared to trimethylsilyl ether **VIII**) under conditions of Si–O bond heterolysis by the action of both Iotsitch (Grignard) reagent and 5% hydrochloric acid.



V, **IX**, R = CH_2Cl; **VI**, **X**, R = *t*-Bu.

These results supplement our previous data on the high sensitivity of the rearrangement under study to steric effects at the carbon atom attached to oxygen in silyl ethers derived from acetylenic alcohols.

Using 3-*tert*-butyl(dimethyl)siloxy-1-propyne (**VI**) and 3-chloromethyl(dimethyl)siloxy-1-propyne (**V**) as examples, we examined the effect of the migrating group (R_3Si) structure. The isomerization of ether **VI** under the above conditions in the presence of EtMgBr gave the expected product, previously unknown 3-*tert*-butyl(dimethyl)silyl-2-propyn-1-ol (**X**) in 27% yield. When one methyl group in the Me_3Si substituent of ether **VIII** was replaced by chloromethyl group, the yield of the rearrangement product, 3-chloromethyl-(dimethyl)silyl-2-propyn-1-ol (**IX**) under the optimal conditions was considerably lower (48%). These data may be explained by electron-acceptor properties of the chloromethyl group, which facilitate heterolysis of the Si–O bond by the action of Grignard reagent.



Thus the results of our study show much stronger effect of steric environment of the carbon atom nearest to the reaction center on O→C_{sp} migration of the silyl group in silyl alkynyl ethers, as compared to the corresponding steric effect of the silicon-containing moiety. In keeping with our concept implying intermolecular mechanism of the process [2], the rate-determining stage is heterolytic dissociation of the Si–O bond. It might be expected *a priori* that steric hindrances at the reaction center, created by both acetylenic and silicon-containing fragments, would hamper formation of transition complex and hence the isomerization process. However, the greater contribution of steric hindrances at the α-carbon atom rather than at the silyl group to nucleophilic attack on the silicon atom was not obvious.

EXPERIMENTAL

The IR spectra were recorded on a Specord 75IR spectrometer. The ^1H and ^{13}C NMR spectra were obtained on a Bruker DPX-400 instrument using $CDCl_3$ as solvent and HMDS as internal reference. Analysis by GLC was performed using an LKhM-80 chromatograph equipped with a thermal conductivity detector; carrier gas helium; 1500 × 3.0-mm column; stationary phase 10% of polymethylsiloxane on Chromaton.

1-Ethynylcyclopentanol (**I**) [7] and 1-ethynylcyclohexanol (**II**) [8] were synthesized by the Favorsky reaction.

(1-Trimethylsiloxycyclopentyl)ethyne (III). A mixture of 3.56 g (0.032 mol) of alcohol **I**, 2.6 g (0.016 mol) of hexamethyldisilazane, and 0.1 mol % of EDNA was stirred for 3.5 h at 70°C. Vacuum distillation gave 4.9 g (95%) of ether **III**, bp 64–65°C (16 mm), n_D^{20} 1.4410 [9].

(1-Trimethylsiloxycyclohexyl)ethyne (IV). A mixture of 6.2 g (0.05 mol) of alcohol **II**, 4.04 g (0.025 mol) of hexamethyldisilazane, and 0.1 mol % of EDNA was stirred for 15 h at 120–130°C. Vacuum distillation gave 6.1 g (60%) of ether **IV**, bp 69.5–72°C (14 mm), n_D^{20} 1.4550. IR spectrum (film), ν, cm^{-1}: 1250 (Si–C), 2102 (C≡C), 3310 (≡C–H). ^1H NMR spectrum, δ, ppm: 0.19 s [9H, $(CH_3)_3Si$]; 1.27 m (2H), 1.56 m (4H), and 1.83 m (4H, *cyclo*-C_6H_{10}), 2.44 s (1H, HC≡). ^{13}C NMR spectrum, δ_C, ppm: 2.31 [$(CH_3)_3Si$]; 23.12 (C^4), 25.45 (C^3), 39.97 (C^2), 72.16 (C^1) (*cyclo*-C_6H_{10}); 73.38 (HC≡); 88.23 (HC≡**C**).

3-Chloromethyl(dimethyl)siloxy-1-propyne (V). A mixture of 5.6 g (0.1 mol) of 2-propynyl alcohol, 11.5 g (0.05 mol) of bis(chloromethyl)tetramethyldisilazane, and 0.01 mol % of EDNA was stirred for 2 h at 70–75°C. According to the GLC data, the yield of silyl ether **V** was 82%. Vacuum distillation gave 12.7 g (78%) of ether **V**, bp 64.5–65°C (25 mm), n_D^{20} 1.4494. IR spectrum (film), ν, cm^{-1}: 2105 (C≡C), 3280 (≡C–H). Published data [10]: bp 78–79°C (25 mm), n_D^{20} 1.4488.

3-*tert*-Butyl(dimethyl)siloxy-1-propyne (VI). A solution of 2.8 g (0.05 mol) of 2-propynyl alcohol in 10 ml of THF was added over a period of 5 min at 10°C to the Grignard compound prepared from 1.22 g (0.05 mol) of magnesium and 5.45 g (0.05 mol) of ethyl bromide in 20 ml of THF. The mixture was stirred for 40 min on cooling with ice water, a solution of 7.5 g (0.05 mol) of *tert*-butyl(chloro)dimethylsilane in 10 ml of THF was added over a period of 0.5 h, and the mixture was stirred for 50 min. A finely crystalline solid precipitated. After appropriate treatment and removal of the solvent, the residue (9.5 g) was distilled under reduced pressure. Yield of ether **VI** 5.3 g (54%), bp 102–105°C (16 mm). IR spectrum (film), ν, cm^{-1}: 1250 (Si–C), 2119 (C≡C), 3300 (≡C–H). ^1H NMR spectrum, δ, ppm: 0.08 s [6H, $(CH_3)_2Si$], 0.91 s (9H, *t*-BuSi), 2.40 t (1H, HC≡, J = 2.5 Hz), 4.31 d (2H, CH_2O, J = 2.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: –5.04 [$(CH_3)_2Si$], 18.40 [$(CH_3)_3C$], 25.93 [$(CH_3)_3C$], 51.55 (CH_2O), 73.02 (H**C**≡C), 82.50 (HC≡**C**).

3-Trimethylsiloxy-1-propyne (VIII). *a*. A solution of 5.6 g (0.1 mol) of 2-propynyl alcohol in 10 ml of THF was quickly added at 10°C (cooling with ice water) to the Grignard compound prepared from 2.4 g (0.1 mol) of magnesium and 10.9 g (0.1 mol) of ethyl bromide in 40 ml of THF. The mixture was stirred for 25 min at 18–20°C, and 10.9 g (0.1 mol) of chlorotrimethylsilane in 10 ml of THF was added over a period of 5 min. The mixture was stirred for 50 min and diluted with 50 ml of dry hexane. An abundant fine precipitate separated, the solvent was removed by decanting, the precipitate was washed with hexane, and the filtrate was concentrated under reduced pressure. Yield of ether **VIII** 43% (GLC).

b. A mixture of 5.6 g (0.1 mol) of 2-propynyl alcohol, 8.1 g (0.05 mol) of hexamethyldisilazane, and 0.01 mol % of EDNA was stirred for 5 min at 18–20°C. According to the GLC data, the yield of ether **VIII** was 96%.

Attempted isomerization of (1-trimethylsiloxycyclopentyl)ethyne (III) by the action of EtMgBr. A solution of 1.82 g (0.01 mol) of ether **III** in 10 ml of THF was added to the Grignard compound prepared from 0.24 g (0.01 mol) of magnesium and 1.1 g (0.01 mol) of ethyl bromide in 20 ml of THF. The mixture was heated under reflux for 16 h with stirring. It was then treated with a saturated solution of NH_4Cl and extracted with chloroform, and the organic phase was dried over $MgSO_4$. The solvent was removed under reduced pressure. According to the GLC data, the residue, 1.8 g, was a mixture of 1-ethynylcyclopentanol (**I**) and initial ether **III** at a ratio of 1 : 1.

Attempted isomerization of (1-trimethylsiloxycyclohexyl)ethyne (IV) by the action of EtMgBr. A solution of 1.96 g (0.01 mol) of ether **IV** in 10 ml of THF was added to the Grignard compound prepared from 0.24 g (0.01 mol) of magnesium and 1.1 g (0.01 mol) of ethyl bromide in 20 ml of THF. The mixture was heated under reflux for 7 h with stirring. After appropriate treatment, 1.6 g of 1-ethynylcyclohexanol (**II**) was isolated.

Attempted isomerization of (1-trimethylsiloxycyclopentyl)ethyne (III) by the action of BuLi. A solution of 1.56 g (0.01 mol) of silyl ether **III** in 30 ml of THF was cooled to –36°C, 6 ml of a 1.6 M solution of butyllithium (0.01 mol) was added, and the mixture was stirred for 1 h in an inert atmosphere. The mixture was treated with 10 ml of a saturated solution of NH_4Cl and 10 ml of 5% hydrochloric acid and extracted with chloroform. The extract was dried over $MgSO_4$, and the solvent was removed under reduced pressure. According to the GLC data, the residue, 1.3 g, was initial ether **III**.

Attempted isomerization of (1-trimethylsiloxycyclohexyl)ethyne (IV) by the action of BuLi. A solution of 1.96 g (0.01 mol) of silyl ether **IV** in 30 ml of THF was cooled to –36°C, 7 ml of a 1.6 M solution of butyllithium (0.01 mol) was added, and the mixture was stirred for 1 h in an inert atmosphere. Appropriate treatment gave 1.5 g of a residue which, according to the GLC data, was initial ether **IV**.

Isomerization of 3-chloromethyl(dimethyl)siloxy-1-propyne (V). A solution of 6.5 g (0.04 mol) of ether **V** in 10 ml of THF was added to the Grignard compound prepared from 0.97 g (0.04 mol) of magnesium and 4.36 g (0.04 mol) of ethyl bromide in 40 ml of THF. The mixture was heated under reflux for 9 h with stirring and was subjected to standard treatment. The residue, 4.89 g, was distilled under reduced pressure to isolate 3.12 g (48%) of 3-chloromethyl(dimethyl)silyl-2-propyn-1-ol (**IX**), bp 81–82°C (5 mm), n_D^{20} 1.4598. IR spectrum (film), ν, cm^{-1}: 1240 (Si–C), 2174 (C≡C), 3350 (O–H). ^1H NMR spectrum, δ, ppm: 4.30 s (2H, CH_2O), 1.89 br.s (1H, OH), 0.26 s (2H, CH_2Cl), 0.19 s [6H, $(CH_3)_2Si$]. ^{13}C NMR spectrum, δ_C, ppm: 106.06 (Si**C**≡C), 86.04 (SiC≡**C**), 51.23 (CH_2O), 30.47 (CH_2Cl), –1.33 (CH_3Si).

Isomerization of 3-*tert*-butyl(dimethyl)siloxy-1-propyne (VI). A solution of 1.7 g (0.01 mol) of ether **VI** in 10 ml of THF was added to the Grignard compound prepared from 0.27 g (0.01 mol) of magnesium and 1.2 g (0.01 mol) of ethyl bromide in 20 ml of THF. The mixture was heated under reflux for 9 h with stirring and was subjected to standard treatment. The residue, 1.2 g, was distilled under reduced pressure to isolate 0.46 g (27%) of 3-*tert*-butyl(dimethyl)-silyl-2-propyn-1-ol (**X**), bp 91–92°C (10 mm), n_D^{20} 1.4600. IR spectrum (film), ν, cm^{-1}: 1240 (Si–C), 2175 (C≡C), 3350 (O–H). ^1H NMR spectrum, δ, ppm: 4.24 s (2H, CH_2O), 1.99 br.s (1H, OH), 0.91 s (9H, *t*-BuSi), 0.08 s [6H, $(CH_3)_2Si$]. ^{13}C NMR spectrum, δ_C, ppm: 104.54 (Si**C**≡C), 88.81 (SiC≡**C**), 51.56 (CH_2O), 26.00 [$(CH_3)_3$**C**], 16.39 [(**C**$H_3)_3$C], –4.70 (CH_3Si).

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