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REACTION OF TRIETHYLSILYLMETHYLAMINE AND SOME SECONDARY ORGANOSILICON AMINES WITH FORMALDEHYDE AND SULFUR

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The reaction of **3-alky1-** and 3-alkoxysilylpropylamines $R_3Si(CH_2)_3NH_2$ (I) with CH_2O and elemental sulfur [1, 2], and with thiourea in the presence of $(NH_4)_2SO_4$ [2], has been investigated by means of the easily available N_N '-bis(3-trialkylsilyl)- and N_N '-bis(3-trialkoxy-silylpropyl)thiourea.

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In this investigation we studied the reaction of sulfur and CH_2O (or paraformaldehyde) with triethylsilylmethylamine (II) and with $[Et_3Si(CH_2)_n]_2NH$ (where n = 1 or 3). In aqueous ethanol the main reaction product of II with CH_2O and sulfur is triethylsilylmethyl isothiocyanate (III). Also formed are (triethylsilymethyl)formamide (IV) and (triethylsilylmethyl)thioformamide (V). It can be suggested that in contrast to amines I, the aldimine $Et_3SiCH_2N=CH_2$ (VI) that is formed in one of the intermediate steps of this reaction is not converted to a trimer, and the process proceeds by the scheme

$$\begin{array}{c} \underset{(II)}{\text{Et}_{\vartheta}\text{SiCH}_{2}\text{NH}_{2} + \text{CH}_{2}\text{O} \rightarrow [\text{Et}_{\vartheta}\text{SiCH}_{2}\text{NHCH}_{2}\text{OH}] \rightarrow \begin{pmatrix} s \\ -\text{H}_{z}\text{S} \end{pmatrix} \xrightarrow{\text{Et}_{\vartheta}\text{SiCH}_{2}\text{NHCHO} & (IV) \\ s \\ -\text{H}_{z}\text{O} \end{pmatrix} \xrightarrow{\text{Et}_{\vartheta}\text{SiCH}_{2}\text{NHCHS} & (V) \\ \hline -\text{H}_{z}\text{O} \longrightarrow [\text{Et}_{\vartheta}\text{SiCH}_{2}\text{N=CH}_{2}] \xrightarrow{S} \xrightarrow{\text{Et}_{\vartheta}\text{SiCH}_{2}\text{NCS}} \\ \xrightarrow{-\text{H}_{z}\text{O}} \xrightarrow{\text{(VI)}} (\text{III)} \end{array}$$

The trimer of aldimine VI, 1,3,5-tris(triethylsilylmethyl)hexahydrotriazine, also could not be obtained by the reaction of II with paraformaldehyde and sulfur under the conditions of [2]. In this case the formation of N,N'-bis(triethylsilylmethyl)thiourea (VII) along with isothiocyanate III, formamide IV, and thioformamide V is explainable, by analogy with [3], by the reaction of aldimine VI with the starting amine II and sulfur:

$$(VI) + (II) \xrightarrow{S} (Et_3SICH_2NH)_2C = S$$

$$(VII)$$

or by the reaction of amine II with isothiocyanate III.

Compounds III-V are formed as a mixture that is hard to separate by ordinary methods, and its composition was determined by PMR. Using preparative GLC, only a 4:1 mixture of III and IV could be separated from the reaction product. The individual substance VII was obtained by the reaction of amine II with thiourea in the presence of a catalytic amount of $(NH_4)_2SO_4$:

$$2(II) + \mathrm{NH}_{2}\mathrm{C}(\mathrm{S})\mathrm{NH}_{2} \xrightarrow{(\mathrm{NH}_{4})_{2}\mathrm{SO}_{4}}_{-2\mathrm{NH}_{3}} (\mathrm{VII})$$

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But in contrast to the amines I, for which N,N'-bis(3-trialkylsilyl)- and N,N'-bis(3-trialkoxysilylpropyl)thiourea are the natural products of the analogous reaction, in the case of amine II, besides thiourea there were separated **isothiocyanate** III and hexaethyldisiloxane; this is explainable by the thermal decomposition of VII to III and II, and the hydrolysis of silane II by traces of water in the reaction mixture [4, 5].

N,N-Bis(triethylsilylpropyl)amine, VIII, reacts with CH_2O and sulfur in aqueous ethanol analogously to primary amine I, to form N,N,N',N'-tetrakis(3-triethylsilylpropyl)thiourea IX as the main product. But this reaction is significantly slower, and in contrast to amine I there are obtained along with thiourea IX not only the formamide $[Et_3Si(CH_2)_3]_2NCHO$, X, but also the thioformamide $[Et_3Si(CH_2)_3]_2NCHS$, XI. When the reaction was carried out in benzene, besides compounds IX-XI, N,N,N',N'-tetrakis(3-triethylsilylpropyl)urea, XII, was also identified. The formation of all these products is explainable by the following conversions of amine VIII:

$$\begin{split} [\mathrm{Et}_{3}\mathrm{Si}(\mathrm{CH}_{2})_{3}]_{2}\mathrm{NH} &+ \mathrm{CH}_{2}\mathrm{O} \rightarrow [\mathrm{Et}_{3}\mathrm{Si}(\mathrm{CH}_{2})_{3}]_{2}\mathrm{NCH}_{2}\mathrm{OH} \rightarrow \\ & (\mathrm{VIII}) \\ & \underbrace{-\mathrm{H}_{2}\mathrm{S}}_{-\mathrm{H}_{2}\mathrm{O}} \xrightarrow{[\mathrm{Et}_{3}\mathrm{Si}(\mathrm{CH}_{2})_{3}]_{2}\mathrm{NCHO}} (\mathrm{X}) \\ & (\mathrm{XI}) & \underbrace{-\mathrm{H}_{2}\mathrm{O}}_{-\mathrm{H}_{2}\mathrm{O}} \xrightarrow{[\mathrm{Et}_{3}\mathrm{Si}(\mathrm{CH}_{2})_{3}]_{2}\mathrm{NCHS}} (\mathrm{XI}) \\ & (\mathrm{XI}) & + (\mathrm{VIII}) \xrightarrow{\mathrm{S}}_{-\mathrm{H}_{2}\mathrm{S}} \xrightarrow{} \{[\mathrm{Et}_{3}\mathrm{Si}(\mathrm{CH}_{2})_{3}]_{2}\mathrm{N}\}_{2}\mathrm{C} = \mathrm{S} \\ & (\mathrm{IX}) \\ & (\mathrm{X}) & + (\mathrm{VIII}) \xrightarrow{\mathrm{S}}_{-\mathrm{H}_{2}\mathrm{S}} \xrightarrow{} \{[\mathrm{Et}_{3}\mathrm{Si}(\mathrm{CH}_{2})_{3}]_{2}\mathrm{N}\}_{2}\mathrm{C} = \mathrm{O} \\ & (\mathrm{XII}) \end{split}$$

The reaction of N,N-bis(triethylsilylmethyl)amine, XIII, with formaldehyde and sulfur is even more complicated. Of the numerous products, only the formamide (Et₃SiCH₂)₂NCHO, XIV, could be identified by PMR, and only hexaethyldisiloxane could be separated.

EXPERIMENTAL

GLC analysis was carried out on an LKhM-8 MD-II apparatus using a column 1 m \times 3 mm with 10% PMS-100 on Chromaton N-AW, and on an LKhM-8 MD-V apparatus using a column 2 m \times 2 mm with 10% lucoprene on Chromaton N-AW; program, 50-200°C. The reaction products were separated by preparative GLC on a Chrom-3 chromatograph, using a column 1.2 m \times 3 mm with 1ucoprene G-1000 on Chemosorb. PMR spectra were obtained on a Tesla 80 MHz spectrometer for 20% solutions in CCl₄, with TMS as the internal standard. IR spectra were obtained on a UR-20 spectrometer in a microlayer.

Triethyl (aminomethyl)silane, II, and bis(triethylsilylmethyl)amine, XIII, were obtained by heating triethyl(chloromethyl)silane and an equimolar mixture of Et_3SiCH_2Cl and Et_3SiCH_2I with ammonia in an autoclave at 90-100°C for 14 h, and 100°C for 6 h, respectively. Bis(triethylsilylpropyl)amine, VIII, was obtained by hydrosilylation of diallylamine with triethylsilane in the presence of $H_2PtCl_6.6H_2O$ at 150°C for 7 h. After drying over alkali, amines with the following properties were obtained: II, bp 58-59°C (10 mm), $n_D^{2°}$ 1.4469. PMR spectrum (δ , ppm): 0.64 (CH_2Si), 0.96 (CH_3), 2.22 (α -CH_2), 3.89(NH). VIII, bp 183°C (3 mm), $n_D^{2°}$ 1.4680. PMR spectrum (δ , ppm): 0.55 (CH_2Si), 0.95 (CH_3), 2.72 (α -CH_2), 1.6 (β -CH_2), 0.5 (γ -CH₂), 7.11 (NH). XIII, bp 131-133°C (5 mm), $n_D^{2°}$ 1.4602. PMR spectrum (δ , ppm): 0.44 (CH_2Si), 0.94 (CH_3), 2.55 (α -CH_2).

The starting thiourea was dried by heating for 7 h at $110^{\circ}C$, and then kept over P_2O_5 .

Reaction of Organosilylalkylamines II, VIII, and XIII with CH_2O and Sulfur in Aqueous Alcohol. To a solution of 3.1 g (0.02 mole) of II in 4-5 ml of ethanol and 1.5 ml of H_2O were added with cooling 2.1 g of 30% aqueous CH_2O , then at 20°C, 2.6 g (0.06 mole) of sulfur. The mixture was boiled for 5 h with vigorous stirring and cooled. Unreacted sulfur (1.29 g) was filtered off and washed with ether and alcohol. The alcohol-ether washings were combined with the filtrate, the solvent was distilled off, and the residue was separated into two fractions by vacuum distillation: (1) bp 102-131°C (8 mm), 1.21 g; (2) bp 135-136°C (8 mm), 0.69 g. By preparative GC there was separated from fraction (1) a mixture of (triethylsilylmethyl)formamide, IV, and triethylsilylmethyl isothiocyanate, III in 1:4 ratio (by PMR). Found: C 52.13; H 9.79; S 12.38; Si 15.34%. $4C_8H_{17}NSSi + C_8H_{19}NOSi$. Calculated: C 52.06; H 9.50; S 13.90; Si 15.22%. PMR spectrum of mixture (δ , ppm): III: 3.05 (α -CH₂); IV: 2.80 (α -CH₂), 6.80 (NH), 8.05 (CHO). IR spectrum (ν , cm⁻¹): 2120, 2190 (NCS), 3070, 3270 (NH). According to PMR, fraction (2) contained, besides compounds III and IV, (triethylsilyl-methyl)thioformamide, V. Spectrum of V (δ , ppm): 9.13 (CHS).

Similarly, by the reaction of 2.35 g (0.007 mole) of VIII, 0.7 ml of 30% aqueous CH₂O, and 0.7 g (0.02 mole) of sulfur two fractions were obtained: 1) 193-205°C (3 mm), 0.32 g; 2) 205-208°C (3 mm), 0.75 g. The composition of fraction (1), by PMR was: $\sim90\%$ N,N,N',N'-tetrakis(3-triethylsilylpropyl)thiourea, IX: $\sim5\%$ formamide X: and $\sim5\%$ thioformamide XI. Found: C 60.97; H 11.80; N 4.98; S 6.35; Si 14.84%. $18C_{37}H_84N_2SSi_4 + C_{19}H_{43}NOSi_2 + C_{19}H_{43}NSSi_2$. Calculated: C 63.28; H 12.08; N 3.98; S 4.56; Si 15.98%. PMR spectrum of IX (δ , ppm): 0.95 (CH₃), 0.5 (CH₂Si), 3.47 (α -CH₂), 1.61 (β -CH₂), 0.5 (γ -CH₂). Fraction (2) by PMR consists of a \sim 12:1:3 mixture of IX, X, and XI. The presence of X and XI is confirmed by the following PMR signals (δ , ppm): 8.31 (CHO) and 9.01 (CHS).

Similarly, by the reaction of 7.6 g (0.029 mole) of amine XIII with 3ml of 30% aqueous CH_2O and 2.9 g (0.067 mole) of sulfur, 2.4 g of hexaethyldisiloxane was obtained with properties in agreement with the literature [6]. Also a wide boiling fraction of bp 112-154°C (3 mm), 3.8 g, was separated, which according to PMR was a complex mixture; only bis(triethyl-silylmethyl)formamide could be identified, by the PMR signal with a chemical shift δ of 8.82 ppm (CHO).

Reaction of Organosilylalkylamines II and VIII with Paraformaldehyde and Sulfur in Benzene. Into a three-necked flask provided with a dropping funnel, a stirrer, and a waterentrainment separator were placed 0.6 g of paraformaldehyde and 10 ml of benzene. To the stirred boiling mixture was added 2.9 g (0.02 mole) of amine II dropwise. The mixture was cooled, dried over MgSO₄, and filtered. The filtrate was treated with 0.6 g of sulfur and boiled with stirring for 5 h. Unreacted sulfur was filtered off, and benzene was distilled off. Vacuum distillation yielded two fractions: 1) bp 127-128°C (6 mm), 0.19 g; 2) bp 130-166°C (6 mm), 0.67 g.

According to PMR, fraction (1) consisted mainly of III and VII with a small amount of II. PMR spectrum of mixture (δ , ppm): III, 3.02 (α -CH₂); VII, 2.92 (α -CH₂); II, 2.24 (α -CH₂). IR spectrum (ν , cm⁻¹): 2120, 2190 (NCS).

According to PMR, fraction (2) contained, besides III and VII, also IV and V. PMR spectrum of mixture (δ , ppm): 3.02, 2.92, 2.77 (α -CH₂), 8.01 (CHO), 3.30 (α -CH₂). The first, second, and last signals indicate the presence of III, VIII, and V; the others indicate IV.

Similarly, by the reaction of 2.35 g (0.07 mole) of VIII, 0.2 g of paraformaldehyde, and 0.2 g of sulfur in 5 ml of dry benzene a fraction was obtained with bp 140°C (3 mm), 0.22 g, which according to PMR was a 2:1:1 mixture of starting amine VIII, IX, and N,N,N',N'-tetra-kis(3-triethylsilylpropyl)urea, XII. Found: C 62.50; H 13.60; S \sim 1; Si 16.42%. 2C₁₀H₄₃NSi₂ + C₃₇H₈₇N₂OSi₄+C₃₇H₈₇N₂SSi₄. Calculated: C 64.35; H 12.79; S 1.56; Si 15.90%. PMR spectrum (δ , ppm): VIII, 2.86 (α -CH₂); IX, 3.5 (α -CH₂); XII, 3.1 (α -CH₂). IR spectrum has absorption band at 1650 cm⁻¹ that is typical for $v_{C=0}$ in ureas.

<u>Reaction of Amine II with Thiourea.</u> a) A mixture of 2.6 g (0.019 mole) of II and 0.68 g (0.009 mole) of thiuorea was heated in an ampul at 170-175°C for 7 h in the presence of a catalytic amount of ammonium sulfate. The mixture was then filtered and vacuum distilled. There were separated 0.24 g of hexaethyldisiloxane (identified by GLC with a standard sample), and 1.23 g of a fraction with bp 136-147°C (6 mm), consisting according to PMR of a 1:4 mix-ture of III and VII. Found: C 53.72; H 10.50; Si 16.43%. $C_8H_{1.7}NSSi + 4C_{1.5}H_{3.6}N_2SSi_2$. Calculated: C 53.78; H 10.71; Si 16.65%. From this fraction, VII was separated by crystallization, mp 64-66°C. PMR spectrum (δ , ppm): 1.00 (CH₃), 0.66 (CH₂Si), 2.92 (α -CH₂), 5.94 (NH).

b) When the above reagents were boiled together under reflux for 1.5 h, there were found hexaethyldisiloxane, 54.3%, separated and identified by GLC (with standard sample), and III (30%), bp 104-111°C (7 mm), $n_D^{2^\circ}$ 1.5042. Found: C 53.28; H 9.97; Si 15.80%. C₈H₁₇NSSi. Calculated: C 51.27; H 9.17; S 14.99%. PMR spectrum (δ , ppm): 3.05 (α -CH₂). IR spectrum (ν , cm⁻¹): 2090, 2170 (NCS).

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CONCLUSIONS

1. The reaction of triethylsilylmethylamine with formaldehyde and sulfur yields in aqueous ethanol mainly triethylsilylmethyl **isothiocyanate**, and in benzene a mixture of that compound with N,N'-bis(triethylsilylmethyl)thiourea. In a similar reaction, bis(3-triethylsilylpropyl)amine yields N,N,N',N'-tetrakis(3-triethylsilylpropyl)thiourea, while bis(triethylsilylmethyl)amine yields a complex mixture of products.

2. The reaction of triethylsilylmethylamine with thiourea in the presence of ammonium sulfate yields N,N'-bis(triethylsilylmethyl)thiourea.

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TRANSFORMED STEROIDS.

COMMUNICATION 130. EFFECT OF THE SUBSTITUENT AT POSITION 21 ON THE

REACTION OF Δ^{16} -20-KETOSTEROIDS WITH DIPHENYLSULFYLIMINE

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The presence of oxygen-containing functional groups at position 21 of steroids is apparently a necessary condition for the manifestation of cortisone activity. But such 21-functionalization frequently encounters great difficulty, especially with compounds that are multi substituted in the D ring. In continuation of our investigations of 16,17-heterosubstituted pregnanes, we have attempted to synthesize $16,17\alpha$ -epimino-21-hydroxy1(acetoxy)-20-ketopreg- α nanes, using the two-step method [1] that had been used previously to synthesize 16.17α -epiminopregnenolone (IX). It turned out that the nature of the substituent at position 21 substantially affects both steps of the process. Thus, Michael condensation of pregn-5,16-dien- 3β ,21-diol-20-one diacetate (III) with methylhydroxylamine is better defined than in the case of the 21-methyl analog (I) that leads to the 16α -methoxyamine (VI). But the second step of the process, viz., ring closure to aziridine with removal of the 17α proton, which requires prolonged heating of amine VI with CH3ONa to t-BuOK in DMFA, yields a complex mixture of products, in which aziridine was not detected. The only compound that was separated was the 16,20-diketone VIII, formed by the removal of the 168 proton. Seeking to moderate the cyclization conditions by carrying out the two reactions in one step, we replaced methylhydroxylamine by S,S-diphenylsulfylimine (DPSI) [2]; as recently discovered [3-6], this compound can react with electrophilic olefins by a kind of Michael reaction to form aziridines. Investigation of the reaction with ketones I and II in CH₃OH, C₆H₆, and C₆H₅CH₃ showed that it proceeds only with prolonged heating. The presence of another nucleophilic reagent that competes with the bulky DPSI at the step of addition to the sterically hindered $\Delta^{1.6}$ bond is undesirable. Thus, when I is heated with DPSI in CH₃OH, along with aziridine IX there is obtained the product of solvent addition, 16α -methoxypregn-5-en-3β-ol-20-one [7]. The optimum yield of IX was obtained (80%) when II was boiled with DPSI in C_6H_6 for 65-70 h. In order to accelerate the reaction we used high pressure (6000 atm). In this case IX was obtained in quantitative yield by heating II with excess DPSI in toluene for 6 h at 80°C in an ampul. The analogous reaction with 21-acetoxy(hydroxy)- Δ^{16} -steroids III-V is more complicated, and without high pressure does not take place at all: heating the reaction mixture thoroughly destroys the steroid molecule. Typical of the behavior of the 21-acetoxysteroids

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