Organosilicon Compounds IV. Synthesis of Organosilicon Substituted Bunte Salts and Mercaptoethylamines (1)

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Recent interest in the radiation-protective action of 2-aminoethanethiols and 2-aminoethanethiosulfuric acids (2) suggests that organosilicon-containing derivatives of these would be of interest as possible radiation-protective agents. Thus we have prepared, for the first time, a number of organosilicon-containing Bunte salts and tetra-alkylsilicon substituted mercaptoethylamines for evaluation as radioprotective agents.

Our initial and most direct route to the synthesis of N-substituted Bunte salts employed the reaction of a haloalkyl silane in a basic solution of aminoethanethio-sulfuric acid (3) (Scheme A).

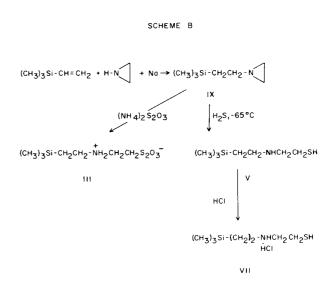
$$\begin{array}{c} R_1 \\ R_2 - \text{Si-(CH}_2)_n - \text{X+ NaOH+ } H_2 \text{NCH}_2 \text{CH}_2 \text{S}_2 \text{O}_3 \text{H} \\ \rightarrow R_2 - \text{Si-(CH}_2)_n - \text{NH}_2 \text{CH}_2 \text{CH}_2 \text{S}_2 \text{O}_3 \\ R_3 \\ \end{array}$$

$$\begin{array}{c} R_1 = R_2 - R_3 - \text{CH}_3 - \text{N}_3 - \text{CH}_2 - \text{CH}_2 \text$$

Reasonable yields were obtained in all cases except when a combination of n=2 with X=Cl or Br existed. The products obtained under these conditions were trimethylvinylsilane, identified by gas chromatography, and an unidentified product in relative yields of 52 and 48% respectively.

The preparation of 2-bromoethyltrimethylsilane was was accomplished by a peroxide catalyzed addition of hydrogen bromide to the corresponding vinyl silane (4). The synthesis of 2-hydroxyethyltrimethylsilane (5), which was subsequently transformed into 2-chloroethyltrimethylsilane (6) via treatment with thionyl chloride, was accomplished by the lithium aluminum hydride reduction of trimethylsilylacetic acid according to the procedure of Sommer, et al., (7).

The preparative difficulties encountered with the use of aminoethane thiosulfuric acid (Scheme A) were circumvented when III was prepared via an ethylenimine intermediate according to Scheme B.



The preparation of IX was accomplished according to the procedure of Nametkin, et al., (8) while ring opening to afford III was conducted in a methanol solution of ammonium thiosulfate according to the procedure of Klayman, Gilmore, and Sweeney (9).

The synthesis of V (Scheme B) and VI (Scheme C) was accomplished by ethylenimine ring opening of IX and X, respectively, with excess hydrogen sulfide at -65°. The preparation of X was conducted in fair yields from γ -chloropropyltrimethylsilane, aziridine, and potassium carbonate in refluxing absolute ethanol in the manner described by Westland, et al., (10).

The free base mercaptoethylamines (V,VI) were quite hygroscopic and we were therefore unable to obtain satisfactory elemental analyses; however, their structure was confirmed by infrared spectroscopy and supporting elemental analyses and infrared data for their derivatives VII and VIII, respectively.

Data suggest that ring opening of organosilicon substituted derivatives of ethylenimine with ammonium thiosulfate and hydrogen sulfide to produce Bunte salts and beta-mercaptoethylamines, respectively, is general and limited only to the availability of the aziridine substrate (11).

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SCHEME C

The preparation of XI and XII, in yield of 54 and 68% respectively, was accomplished by treatment of a refluxing p-dioxane solution of the trialkoxysilicon-containing amine with ethylene sulfide. This procedure appears to be quite superior, in yield and complexity, to that reported by Bulbenko (12) who obtained XI in 24% yield.

EXPERIMENTAL

The melting points reported were determined on a Fisher-Johns apparatus and are uncorrected. The infrared spectra were determined with a Beckman IR-5 spectrophotometer. Chromatograms were obtained on an Aerograph, Model A-700 "Autoprep" gas chromatograph using a Silicon GE, 30% SE-30, acid washed column. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee. All chlorosilanes were distilled prior to use. Distillations were carried out using a 15" Vigreux column. N-(3-Trimethylsilylpropyl)aminoethanethiosulfuric Acid (IV).

An alcoholic solution (95%, 300 ml.) of sodium hydroxide (10.0 g., 0.25 mole) was treated with 2-aminoethanethiosulfuric acid (39.3 g., 0.25 mole) dissolved in a minimum amount of water and the resulting solution was heated to reflux. γ -Chloropropyltrimethylsilane (30.1 g., 0.2 mole) was added dropwise to

the refluxing solution over 1.5 hours and refluxing was maintained for an additional 5.0 hours, at which time ethanol (250 ml.) was removed by distillation and replaced with an equal volume of water. After neutralization with glacial acetic acid, the mixture was allowed to stand overnight in the cold to give 11.6 g. (21.4%) of IV, melting at $194\text{-}197^{\circ}$ dec. Purification by recrystallization from water afforded the pure product melting at $215\text{-}216^{\circ}$ dec.

Anal. Calcd. for $C_8H_{2\,1}NO_3S_2Si\colon C, 35.39;\ H, 7.79;\ Si, 10.35;\ N, 5.16;\ S, 23.62.$ Found: C, 35.59; H, 7.77; Si, 10.56; N, 5.17; S, 23.43.

The above procedure will serve as an example for the preparation of the following compounds.

N-(Trimethylsilylmethyl)aminoethanethiosulfuric Acid (1).

Chloromethyltrimethylsilane (15.0 g., 0.12 mole), 2-aminoethanethiosulfuric acid (23.6 g., 0.15 mole), and sodium hydroxide (6.0 g., 0.15 mole) were allowed to react to give 10.1 g. (34.8%) of the pure product melting at $195\text{-}196^{\circ}$ dec.

Anal. Calcd. for $C_6H_{17}NO_3S_2Si\colon C,29.61;\ H,7.03;\ N,5.76;\ Si,\ 11.53;\ S,\ 26.35.$ Found: C, 29.67; H, 7.03; N, 5.74; Si, 11.38; S, 26.15.

N-(Dimethylvinylsilylmethyl)aminoethanethiosulfuric Acid (II).

Chloromethyldimethylvinylsilane (20.0 g., 0.15 mole), 2-aminoethanethiosulfuric acid (39.3 g., 0.25 mole), and sodium hydroxide (10.0 g., 0.25 mole) gave, after concentrating the neutralized solution to one-half volume, 13.9 g. (36.3%) of product melting at 131-135°. Two recrystallizations from absolute ethanol gave the pure product melting at 155-156°.

Anal. Calcd. for $C_7H_{17}NO_3S_2Si$: C, 32.92; H, 6.71; Si, 10.99; N, 5.48; S, 25.11. Found: C, 33.02; H, 6.65; Si, 10.77; N, 5.50; S, 24.97.

Trimethyl- β -(N-ethylenimino)ethylsilane (IX).

The above-named compound was prepared by the method of Nametkin, Perchenko, and Grushevenko (5) in a (58%) yield, boiling at $53^{\circ}/27$ mm.; $n^{24} = 1.4288$. Literature reports $40-41^{\circ}/18$ mm., $n^{20} = 1.4300$.

N-(2-Trimethylsilylethyl)aminoethanethiosulfuric Acid (III).

Ammonium thiosulfate (10.4 g., 0.07 mole) and X (8.2 g., 0.058 mole) were placed in methanol (150 ml.) in a 250 ml. flask, equipped with thermometer, reflux condenser, and nitrogen inlet. The mixture was heated at reflux for 24 hours, and filtered hot to remove excess ammonium thiosulfate. The methanol was removed in vacuo to give, after recrystallization from absolute ethanol and drying, 9.0 g. (60.8%) of product melting at $172-175^{\circ}$ dec. Three recrystallizations afforded the pure product melting at $194-195^{\circ}$ dec.

Anal. Calcd. for $C_7H_{19}NO_3S_2Si$: C, 32.65; H, 7.44; Si, 10.91; N, 5.44; S, 24.90. Found: C, 32.63; H, 7.63; Si, 10.89; N, 5.65; S, 24.80.

Trimethyl- γ -(N-ethylenimino)propylsilane (X).

Ethylenimine (43.0 g., 1.0 mole), γ -chloropropyltrimethylsilane (15.1 g., 0.1 mole), and potassium carbonate (41.4 g., 0.3 mole) were placed in absolute ethanol (300 ml.) in a 500 ml. flask equipped with thermometer, reflux condenser, and nitrogen inlet. The mixture was heated at reflux for 67 hours, filtered, and the ethanol removed in vacuo. The last traces of inorganic materials were removed from the filtrate by treatment with anhydrous ether and subsequent filtration. Solvent removal in vacuo and fractionation of the residue gave 8.4 g. (53.5%) of X

boiling at $70^{\circ}/21$ mm., $n^{23} = 1.4322$.

Anal. Calcd. for $C_8H_{19}NSi:\ C, 61.07;\ H, 12.17;\ Si, 17.86.$ Found: $C, 60.93;\ H, 12.09;\ Si, 17.62.$

N-(3-Trimethylsilylpropyl)-2-aminoethanethiol Hydrochloride (VIII).

Absolute ethanol (250 ml.) was placed in a 500 ml. flask equipped with dispersion tube, reflux condenser, and thermometer and cooled to -65° in a dry ice-acetone bath. The pre-cooled alcohol was saturated with hydrogen sulfide over a 1-hour period, at which time trimethyl- γ -(N-ethylenimino)propylsilane, X, (6.3 g., 0.04 mole) in 75 ml. of absolute ethanol was added in a dropwise manner over a 30-minute period. After addition was complete, the solution was stirred for 2.5 hours with hydrogen sulfide being passed through the reaction mixture. During this time the temperature rose to 25°. The ethanol was removed in vacuo and the residue fractionated to give 5.8 g. (75.7%) of VI boiling at $124^{\circ}/0.23$ mm.; $1^{9} = 1.4710$.

An ether solution (100 ml.) of VI (3.6 g., 0.19 mole) was treated with anhydrous hydrogen chloride until precipitation was complete. Filtration gave 4.3 g. (97.7%) of product, melting at 223-224° and 13.5% thiol by iodometric titration. Recrystallization from absolute ethanol or sublimation did not produce an increase in melting point.

Anal. Calcd. for $C_8H_{22}CINSSi$: C, 42.17; H, 9.73; Si, 12.33; N, 6.14; S, 14.07; Cl, 15.56. Found: C, 42.00; H, 9,58; Si, 12.08; N, 6.20; S, 13.49; Cl, 15.35.

The preparation of VII was conducted in the manner described above.

N-(2-Trimethylsilylethyl)-2-aminoethanethiol Hydrochloride (VII).

Trimethyl- β -(N-ethylenimino)ethylsilane, IX, (27.5 g., 0.19 mole) was allowed to react with hydrogen sulfide in the above manner to give 27.5 g. (81.6%) of V boiling at $108^{\circ}/22$ mm., n^{21} = 1.4731; which upon standing solidified to give a solid melting at $23\cdot24^{\circ}$. Treatment with anhydrous hydrogen chloride afforded VII in 97.7% yield, melting at $233\cdot234^{\circ}$, and $15\cdot10\%$ thiol by iodometric titration.

Anal. Calcd. for $C_7H_{20}CINSSi$: C, 39.32; H, 9.43; Si, 13.13; N, 6.55; S, 15.00; Cl, 16.57. Found: C, 39.55; H, 9.41; Si, 13.29; N, 6.76; Cl, 16.57.

N-(3-Triethoxysilylpropyl)-2-aminoethanethiol (XI).

Into a 250 ml. flask equipped with thermometer, reflux condenser, and nitrogen inlet was placed 3-aminopropyltriethoxysilane (22.1 g., 0.1 mole) and 150 ml. of p-dioxane. Ethylene sulfide (6.0 g., 0.1 mole) was added slowly over a 30 minute period. After refluxing the mixture overnight 5.0 g. of white solid, presumed to be hydrated starting material, was removed by filtration. The p-dioxane was removed in vacuo, and the residue was fractionated giving 8.1 g. of 3-aminopropyltrimethoxysilane boiling at 69-71°/0.5 mm. and 9.5 g. (53.7%), based on recovered starting material, of XI boiling at 96°/0.1 mm., $n^{23} = 1.4500$. Anal. Calcd. for $C_{11}H_{27}NSSi: C, 46.94$; H, 9.66; S, 11.39.

Found: C, 46.82; H, 9.67; S, 10.28.

 $N-{\rm Methyl-} N-(3-{\rm trimethoxy silyl propyl})-2-a minoeth an ethiol~XII.$

N-Methyl-3-aminopropyltrimethoxysilane (19.2 g., 0.1 mole) and ethylene sulfide (12.0 g., 0.2 mole) were allowed to react, as

described for the preparation of XI, to give 17.3 g. (68.1%) of XII boiling at $88^{\circ}/0.2$ mm., $n^{24} = 1.4567$.

Anal. Calcd. for $C_9H_{23}NO_3SSi: C$, 42.65; H, 9.15; O, 18.94; Si, 11.08; N, 5.53; S, 12.65. Found: C, 42.57; H, 9.05; O, 18.84; Si, 11.33; N, 5.75; S, 12.82.

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