[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

The Reactivity with Alkali of Chlorine–Carbon Bonds Alpha, Beta and Gamma to Silicon[1,2]

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We have previously reported that the chlorination of ethyltrichlorosilane with sulfuryl chloride gives the alpha and beta mono-chlorinated products in a ratio of 1 to 2.5, and that the beta C—Cl bond in the latter is remarkably active, giving quantitative reaction on titration with dilute alkali, whereas the alpha C–Cl bond cannot be titrated in this manner.[1] To determine the ease of chlorination of gamma carbon in comparison to analogous alpha and beta carbon atoms, and to determine also the activity of a gamma C–Cl bond in comparison to analogous alpha and beta C–Cl bonds, we have synthesized and studied the chloro-*n*-propyltrichlorosilanes.

Refluxing of *n*-propyltrichlorosilane[3] with sulfuryl chloride in the presence of a small amount of benzoyl peroxide gave a 90% yield of monochlorinated products. There were obtained, (I) α-chloro-*n*-propyltrichlorosilane, CH_3—CH_2—$CHCl$—$SiCl_3$, b. p. 157°, (II) β-chloro-*n*-propyltrichlorosilane, CH_3—$CHCl$—CH_2—$SiCl_3$, b. p. 162°, and (III) γ-chloro-*n*-propyltrichlorosilane, CH_2Cl—CH_2—CH_2—$SiCl_3$, b. p. 178°. The ratio of I to II to III was 1 to 3.5 to 3.1. Thus the gamma carbon is somewhat less easily chlorinated than the beta carbon. The alpha carbon, like that in ethyltrichlorosilane, shows the inactivation toward chlorination which is caused by proximity of the —$SiCl_3$ group.

Activity of Alpha, Beta and Gamma C–Cl Bonds with Alkali

Titration of organo-silicon chlorides with dilute alkali gives a neutral equivalent corresponding to quantitative hydrolysis of Si–Cl bonds. Titration of I gave a value corresponding to chlorine attached only to silicon. *The alpha C–Cl bond was left intact.* Titration of II gave a value corresponding to chlorine attached to both carbon and silicon. *The beta C–Cl bond reacted as completely as the Si–Cl bonds.* Titration of III gave a value corresponding to chlorine attached only to silicon. *The gamma C–Cl bond was left intact.*

The above clearly shows that activity toward alkali is greatest when the carbon holding the chlorine atom is in the beta relation to the silicon atom. In order to complete the picture of changing activity of a C–Cl bond with change in the position of the chlorine atom, compounds I and III above, α-chloroethyltrichlorosilane and *n*-hexyl chloride were treated with ethanolic potassium hydroxide for one hour at room temperature. The gamma C–Cl bond in III gave 100% reaction. The alpha C–Cl bond in I and in α-chloroethyltrichlorosilane as well as the C–Cl bond in *n*-hexyl chloride gave zero reaction. These data show the striking difference between the activity of gamma and alpha C–Cl bonds. While neither can be titrated with alkali, the gamma C–Cl bond is still remarkably active in comparison to alpha C–Cl bonds and to the C–Cl bond in *n*-hexyl chloride. The gamma C–Cl bond is less reactive than the beta C–Cl bond, but both are far more reactive with alkali than analogous alpha C–Cl bonds and ordinary organic chlorides. The significance of the formation of propylene and of cyclopropane in the reaction with alkali of the beta and gamma C–Cl bonds in II and III, respectively, will be considered in later papers.

Compound I and α-chloroethyltrichlorosilane were compared with *n*-hexyl chloride by treatment with ethanolic potassium hydroxide for two hours at reflux temperature. The alpha C–Cl bonds in the silicon compounds reacted to the extent of 99%, while *n*-hexyl chloride gave 56% reaction.

The assigned structures of the chloro-*n*-propyltrichlorosilanes are based on the following: (a) The —$SiCl_3$ group is known to hinder chlorination of alpha carbon with sulfuryl chloride.[1] Thus, the alpha compound is the one formed in lesser amount than the other two isomers. (b) The beta C–Cl bond in β-chloroethyltrichlorosilane gives complete reaction on titration with dilute alkali.[1] Therefore the beta compound should be the one whose C–Cl bond undergoes this titration. (c) The C–Cl bond in the compound assigned the gamma structure is more reactive than the corresponding bond in α-chloroethyltrichlorosilane and less reactive than that in β-chloroethyltrichlorosilane.

Investigation of the properties of C–Cl bonds beta and gamma to silicon is being continued.

Experimental[4]

***n*-Propyltrichlorosilane.**[3]—This intermediate was prepared from 9.2 equivalents of *n*-propylmagnesium bromide. The product was fractionated in a 30-plate glass-helix packed column. There was obtained 670 g. (3.78 moles) of *n*-propyltrichlorosilane, b. p. 122–124° (734 mm.), a yield of 41%. This was analyzed for chlorine content by the usual titration with 0.5 *N* alkali.

Anal. Calcd. for $C_3H_7SiCl_3$: Cl, 59.9. Found: Cl, 59.6, 59.5.

Chlorination of *n*-Propyltrichlorosilane.—In a 2-liter round-bottomed flask there was placed 671 g. (3.78 moles)

(1) Paper IV on Organo-silicon compounds. For Paper III, see Sommer and Whitmore, THIS JOURNAL, **68**, 485 (1946).

(2) Presented before the Division of Organic Chemistry at the New York Meeting of the American Chemical Society, September 12, 1944.

(3) Melzer, *Ber.*, **41**, 3390 (1908).

(4) Boiling points are uncorrected.

of *n*-propyltrichlorosilane and 546 g., 4 moles, of sulfuryl chloride activated by 1 g. of benzoyl peroxide. The flask was fitted with an efficient reflux condenser connected to a phosphorus pentoxide tube and the reaction mixture heated on the steam-bath. Reaction started immediately as evidenced by a vigorous evolution of hydrogen chloride and sulfur dioxide. The reaction mixture was refluxed for twelve hours, at the end of which time evolution of hydrogen chloride and sulfur dioxide had ceased. The product, 797 g., was then fractionated in a column of 30 theoretical plates. There were obtained: (I) crude α-chloro-*n*-propyltrichlorosilane, 110 g., b. p. 153–158°, which on refractionation gave 78 g. (0.37 mole) of pure α-chloro-*n*-propyltrichlorosilane, b. p. 157° (739 mm.); (II) β-chloro-*n*-propyltrichlorosilane, 273 g. (1.3 moles) b. p. 162° (729 mm.); and (III) γ-chloro-*n*-propyltrichlorosilane, 242 g. (1.15 moles), b. p. 178.5° (732 mm.). In addition, 180 g. (1 mole) of unreacted *n*-propyltrichlorosilane was obtained. The chloro-*n*-propyltrichlorosilanes were analyzed for chlorine content by peroxide fusion in a Parr bomb.

Anal. Calcd. for $C_3H_8SiCl_4$: Cl, 66.9. Found: for the α-chloro compound, 66.7; for the β-chloro compound, 67.0; for the γ-chloro compound, 67.0.

Alkali Titration of the Chloro-*n*-propyl-trichloro-silanes.—Weighed samples, about 0.7 g., were added to 20 cc. of methanol. Addition of distilled water, 50 cc., was followed by titration with 0.5 *N* sodium hydroxide using phenolphthalein.

Titration of α-chloro-*n*-propyltrichlorosilane gave: Cl, 50.1. Calcd. for Cl attached only to silicon, 50.2.

Titration of β-chloro-*n*-propyltrichlorosilane gave: Cl, 67.0. Calcd. *total Cl* for $C_3H_6SiCl_4$ is 66.9.

Titration of γ-chloro-*n*-propyltrichlorosilane gave: Cl, 50.2. Calcd. for Cl attached only to silicon, 50.2.

Relative Activity of C-Cl Bonds Alpha and Gamma to Silicon toward Alcoholic Alkali.—Weighed samples (0.5 g.) of I, III, α-chloroethyltrichlorosilane, and *n*-hexyl chloride were placed in 50-cc. flasks containing 18 cc. of 1.5 *N* ethanolic potassium hydroxide and the flasks were quickly stoppered for reaction at room temperature, or quickly fitted with reflux condensers if the reactants were to be refluxed. Half of these solutions were allowed to stand at room temperature for one hour. The others were refluxed for two hours. Extent of reaction was then determined by Volhard titration for chloride ion.

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Summary

1. The three chloro-*n*-propyltrichlorosilanes have been synthesized by the peroxide-catalyzed chlorination of *n*-propyltrichlorosilane with sulfuryl chloride.

2. The gamma carbon in *n*-propyltrichlorosilane is somewhat less easily chlorinated than the beta carbon atom. The alpha carbon is chlorinated with relative difficulty due to the proximity of the $-SiCl_3$ group.

3. The reactivity of a C–Cl bond gamma to silicon is far greater than that of primary alkyl chlorides. At room temperature, it reacts completely with alcoholic alkali in one hour.

4. The beta C–Cl bond in β-chloro-*n*-propyltrichlorosilane reacts quantitatively on titration with 0.5 *N* alkali.

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Antibacterial Substances from *Asarum canadense*. I. Isolation, Physical Properties and Antibacterial Action

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Although considerable chemical work has been done with constituents of species of *Asarum*,[1] it is only recently that screening tests for antibiotic activity in plants have shown that some members of this genus demonstrate weak activity against Gram positive bacteria.[2,3]

From *Asarum canadense* var. *reflexum* (Wild Ginger) there have been isolated two antibiotic substances, A, a very potent colorless compound of tentative empirical formula $C_{21}H_{20}O_8N_2S$, and B, a lemon-yellow acid of tentative formula $C_{16}H_{11}O_7N$, which shows considerably less activity. The activity has been observed against only Gram positive organisms. Each product has been obtained in a yield of approximately 20 milligrams per kilogram of fresh leaves and stems (moisture content about 85%).

Substances A and B are soluble in ethanol, acetone, chloroform, ethyl acetate and dioxane, almost insoluble in water, benzene and the Skellysolves; B forms water-soluble salts. Both compounds are readily inactivated by cysteine[3] and fall in line with the mode of action theories postulated for antibiotics.[4] The inactivation of A by cysteine shows similar time–concentration–*p*H effects as demonstrated for penicillin. Product A may be readily adsorbed from aqueous solutions by means of activated charcoal.

Product A is neutral in aqueous ethanol solutions and cannot be removed from a chloroform solution by extraction with aqueous sodium bicarbonate solution or by tenth normal hydrochloric acid. Treatment of A with alkalies (*p*H 10) and back titration with acid demonstrates the liberation of acidic groups and formation of a highly greenish-fluorescent product. Vapors from the hydrolysis solution darken lead acetate paper indicating formation of hydrogen sulfide.

Although pure B was prepared readily, A was

(1) Kaku, *et al.*, *C. A.*, **33**, 546 (1939); Nomura, *et al.*, *ibid.*, **24**, 2445 (1930); Takahashi, *ibid.*, **25**, 4975 (1931); Chou and Chu, *ibid.*, **30**, 241 (1936); Gerö, *ibid.*, **24**, 2235 (1930); Orient, *ibid.*, **28**, 6247 (1934); Bruckner and Szeki, *J. prakt. Chem.*, **134**, 107 (1932).

(2) Osborn, *Brit. J. Exp. Path.*, **24**, 227 (1943).

(3) Cavallito and Bailey, *Science*, **100**, 390 (1944).

(4) Cavallito, Bailey, Haskell, McCormick and Warner, *J. Bact.*, **50**, 61 (1945).