Removal of residual amine from this aqueous phase is necessary for the subsequent preparation of streptomycin suitable for clinical use. This may readily be accomplished by extracting the aqueous phase with a mixture of chloroform and acetone before any *p*H adjustments have been made. The *p*H of the aqueous phase is then adjusted to desirable limits for streptomycin stability with a suitable mineral acid and dried to give a purified streptomycin product.

### Experimental

The streptomycin used in the following example of this procedure was obtained by the process essentially as described by Vander Brook, *et al.*,[3] for the preparation of streptomycin sulfate. All assays were conducted by the paper-disc plate method[4] using *B. subtilis* as a test organism. One unit is equivalent to one microgram of streptomycin base.

**Purification of Streptomycin Sulfate by Solvent Extraction.**—Forty grams of streptomycin sulfate, assaying 580 units per mg., was dissolved in water to give 925 ml. of solution testing 25,000 units per ml. The *p*H of this solution was adjusted to 12 with dilute NaOH, and 3 g. of NaCl was added per 10 ml. of resulting solution. 2-Aminoheptane (465 ml.) was added, the mixture stirred one-half hour, and the two phases separated. The water phase containing less than 6% of the starting activity was discarded. The amine phase was concentrated *in vacuo* to approximately one-third volume, and filtered. To the filtered amine phase were added an equal volume of water and three volumes of $CHCl_3$. After stirring one hour, the mixture was allowed to separate. The $CHCl_3$ was discarded.

The water phase, 370 ml. at 57,000 units per ml., contained 21,000,000 units or 91% of the starting activity. The water phase was extracted with one-half volume of acetone and one volume of $CHCl_3$. After separation, the *p*H of the water phase was adjusted to 5.5 with dilute $H_2SO_4$ and the resulting solution dried to give 27 g. of streptomycin sulfate testing 748 units per mg., $[\alpha]^{25}D$ −73.5° (*c* 1 in $H_2O$), and representing 87% of the original activity.

**Acknowledgments.**—The authors are indebted to Dr. J. J. Stefaniak for the microbiological assays and to Mrs. Ruth St. John and Mrs. Margaret Wilson for technical assistance.

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[3] M. J. Vander Brook, A. N. Wick, W. H. DeVries, R. Harris and G. F. Cartland, *J. Biol. Chem.*, **165**, 463 (1946).

[4] Y. H. Loo, P. S. Skell, H. H. Thornberry, J. Erhlich, J. M. McGuire, G. M. Savage and J. C. Sylvester, *J. Bact.*, **50**, 701 (1945).

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## Propylgermanium Trichloride: The Question of Pyrolysis and Isomerization in the Direct Synthesis of Organogermanium Compounds

BY EUGENE G. ROCHOW, ROTISLAV DIDTSCHENKO AND ROBERT C. WEST, JR.

The action of methyl chloride[1] on elementary germanium intimately mixed with copper powder as catalyst results in dimethylgermanium dichloride as principal product, only one-tenth as much methylgermanium trichloride being formed. Under similar conditions ethyl chloride[2] yields principally diethylgermanium dichloride plus four-tenths as much ethylgermanium trichloride. If the alkyl groups are transferred first as copper alkyls and then as free radicals, as appears to be so in the reaction of methyl chloride with silicon,[3] larger alkyl groups may be expected to suffer some rearrangement and pyrolysis at the elevated temperatures necessary for the reaction. This in turn should place an upper limit on the size of the alkyl group that can successfully be transferred to germanium by the direct synthesis as ordinarily conducted.

To investigate these matters, the reaction of *n*-propyl chloride in the vapor phase with a contact mass of powdered metallic germanium and copper at 310 to 330° was studied. The only isolable product was found to be a propylgermanium trichloride. Pure isopropyl- and *n*-propylgermanium trichloride then were prepared by the Grignard reaction, since they had not previously been made, in order that the product of the direct reaction might be compared with these pure substances.

### Experimental

The apparatus for the experiments with metallic germanium consisted of a glass reaction tube 2.5 cm. in diameter and 50 cm. long, fitted with standard taper joints to an inlet system for *n*-propyl chloride and hydrogen at one end, and a condensing trap and drying tube at the other. The inlet system consisted of a vertical elbow bearing a small dropping funnel for the *n*-propyl chloride (which was delivered through a capillary tube) and a sealed-in stopcock leading from the hydrogen drier. The reaction tube was mounted in an electric furnace tilted downward at an angle of 15°, so that the *n*-propyl chloride ran into the hot tube and was vaporized before it entered the charge of powdered germanium.

The reaction tube was charged with a finely-ground mixture of 11.5 g. of germanium and 2.5 g. of copper, supported on glass wool to provide maximum contact area. A thermometer was embedded in the contact mass in such a way that it was totally enclosed in the reaction system but protruded from the exit end of the furnace sufficiently to be read.

The reaction tube and its charge were brought to 300° with a slow stream of hydrogen passing through, in order to reduce any copper oxide. The temperature was then raised to 320°, the stream of hydrogen stopped and 50 ml. of *n*-propyl chloride admitted over a period of seven hours. During this time the temperature was maintained at 320 to 330°. High-boiling liquid was seen to condense after a lapse of 45 minutes, and was collected in the trap along with unchanged *n*-propyl chloride.

The condensate from the reaction was distilled, yielding 30 ml. of unchanged *n*-propyl chloride and 2 ml. of clear viscous liquid boiling above 145° with some decomposition. The high-boiling material from a second run, conducted at the somewhat reduced temperature of 310 to 320°, was combined with the distillate of the first run, and the mixture distilled at reduced pressure through a packed column 40 cm. long and 6 mm. in diameter. The main fraction of 3.5 ml. was collected at 43 to 45° at 12 mm. pressure. This was analyzed for carbon and hydrogen by combustion, and for chlorine by hydrolysis and titration.

*Anal.* Calcd. for $C_3H_7GeCl_3$: Cl, 47.8; C, 16.2; H, 3.2. Found: Cl, 47.5, 47.9; C, 16.7, 16.7; H, 3.3, 3.4.

Propylgermanium trichloride prepared this way is a colorless, viscous oil with a sharp, unpleasant odor. It hydrolyzes to a white gelatinous precipitate which dissolves in alkalies. The boiling point is 167° at 763 mm., 43 to 45° at 12 mm. and the density at 20° is 1.513.[4] The index of refraction at 20° is 1.4779 and at 25° is 1.4720.

Isopropylgermanium trichloride was prepared by the action of one equivalent of isopropylmagnesium chloride on germanium tetrachloride in anhydrous ether, and was purified by fractional distillation. Its boiling point was found to be 164.5 at 767 mm., and the refractive index was 1.4760 at 20° and 1.4700 at 25°.

*n*-Propylgermanium trichloride was prepared by the action of 1.5 equivalents of *n*-propylmagnesium chloride on germanium tetrachloride in ether. The purified product

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[1] E. G. Rochow, THIS JOURNAL, **69**, 1729 (1947).

[2] E. G. Rochow, *ibid.*, **72**, 198 (1950).

[3] D. T. Hurd and E. G. Rochow, *ibid.*, **67**, 1057 (1945).

[4] The densities at 20° of the entire propyl series now are known:

| | | | | | |
|---|---|---|---|---|---|
| *n*-$Pr_4Ge$ | 0.9539 | *n*-$Pr_2GeCl_2$ | 1.227 | $GeCl_4$ | 1.879 |
| *n*-$Pr_3GeCl$ | 1.106 | *n*-$PrGeCl_3$ | 1.513 | | |

was found to boil at 167.0° at 767 mm. and the refractive index at 20° was 1.4780 and at 25° was 1.4718.

Infrared spectrograms of *n*-propyl- and isopropylgermanium trichlorides, and of the product from the direct reaction of *n*-propyl chloride on germanium, were obtained by means of a Baird recording spectrophotometer, using solutions of the substances in chloroform. Comparison of the spectrograms showed marked similarity between those for *n*-propylgermanium trichloride and the product of direct reaction, especially in the region of wave numbers 1350 to 1230 cm.$^{-1}$ and 1000 to 1100 cm.$^{-1}$. The band at wave numbers 880 to 910 cm.$^{-1}$ which is characteristic[5] of isopropyl groups was lacking in the pattern for the product of direct reaction. The spectrogram of *n*-propyl bromide resembled that of the product of direct reaction as well as that of *n*-propylgermanium trichloride.

### Discussion

Comparison of the physical constants and the infrared absorptions indicates that the substance from the vapor-solid reaction of *n*-propyl chloride and germanium is principally *n*-propylgermanium trichloride, and that rearrangement of the propyl groups occurred only to a minor degree during their transfer to germanium. Rearrangement of *n*-propyl to isopropyl groups has been observed as a result of the pyrolysis of *n*-propyl bromide at 280°,[6] but the time required for the rearrangement may have been longer than the time involved in transfer of the *n*-propyl groups to germanium. The results obtained here indicate that most of those *n*-propyl groups which ultimately become bonded to germanium are protected from rearrangement during transfer, probably because they are in the form of *n*-propyl copper[3] most of the time instead of in the form of free radicals. Those propyl groups which are completely lost (and which outnumber those which become attached to germanium) may, of course, suffer rearrangement during the course of their decomposition.

[5] N. B. Colthup, *J. Optical Soc. Am.*, **40**, 397 (1950).

[6] Michael and Lenpold, *Ann.*, **379**, 263 (1911); Aronstein, *Ber.*, **14**, 607 (1881); *Rec. trav. chim.*, **1**, 134 (1882).

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# Small-Ring Compounds. IX. The Reaction of Silver Cyclobutanecarboxylate with Iodine

By John D. Roberts and Howard E, Simmons, Jr.

Cyclobutanol was first reported by Perkin[1] in 1894 as the product of the reaction between cyclobutylamine and nitrous acid. However, it was later shown[2,3] that Perkin's material was actually a mixture of roughly equal amounts of cyclobutanol and cyclopropylcarbinol along with a small amount of allylcarbinol. In 1907, Demjanow and Dojarenko[4] reported the synthesis of presumably authentic cyclobutanol by hydrolysis of cyclobutyl cyclobutanecarboxylate obtained from the reaction of silver cyclobutanecarboxylate with iodine or the electrolysis of potassium cyclobutanecarboxylate. The product was characterized as the N-phenylcarbamate, m.p. 110–111°. In 1949, cyclobutanol prepared by the lithium aluminum hydride reduction of cyclobutanone[5] was found to yield a N-phenylcarbamate of m.p. 130.6–131.2°. This discrepancy in melting points has prompted us to repeat one of the earlier cyclobutanol preparations.

The reaction of silver cyclobutanecarboxylate with iodine was carried out following the procedure of Demjanow and Dojarenko[4] as closely as possible. The infrared spectrum for the ester product is given in Fig. 1 along with those of pure samples of the cyclobutylcarboxylate esters of cyclobutanol, cyclopropylcarbinol and allylcarbinol which were prepared by the reaction of the alcohols with cyclobutanecarboxylic acid chloride in pyridine. The infrared spectra indicate that the reaction product is a mixture of ~32% cyclobutyl, ~65% cyclo-

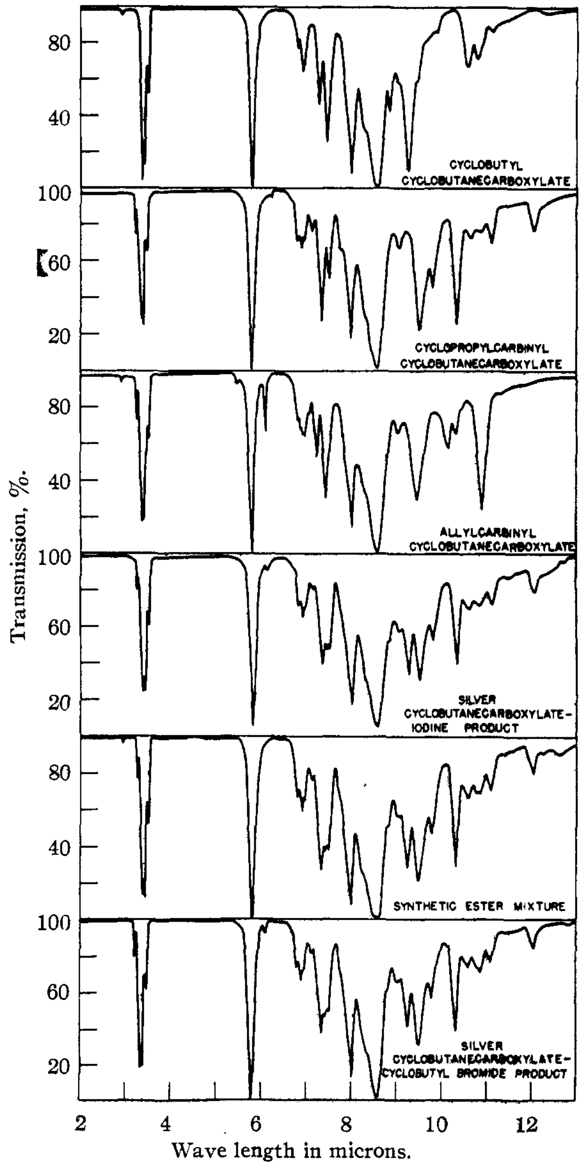

Fig. 1.—Infrared spectra: Baird Spectrograph with NaCl prism, solutions of 50 mg. of compounds in 0.50 ml. of carbon disulfide except in the regions 4.2–5.0 μ and 6.2–7.2 μ where carbon tetrachloride was used as solvent.

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[1] W. H. Perkin, Jr., *J. Chem. Soc.*, **65**, 950 (1894).

[2] (a) N. J. Demjanow, *Ber.*, **40**, 4393, 4961 (1907); (b) R. Skrabal, *Monatsh.*, **70**, 420 (1937).

[3] J. D. Roberts and R. H. Mazur, This Journal, **73**, 2509 (1951).

[4] N. J. Demjanow and M. Dojarenko, *Ber.*, **40**, 2594 (1907); *cf.* also N. J. Demjanow, *J. Russ. Phys. Chem. Soc.*, **61**, 1861 (1929).

[5] J. D. Roberts and C. W. Sauer, This Journal, **71**, 3925 (1949).