STUDIES RELATING TO ORGANIC GERMANIUM DERIVATIVES. V. REACTION OF SODIUM TRIPHENYL GERMANIDE WITH HALOGENATED METHANES IN LIQUID AMMONIA

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I. Introduction

Triphenylgermanium is an amphoteric group which forms non-salt-like compounds with the halogens and true salts with the alkali metals.[1] The latter compounds, of which sodium triphenyl germanide is an example, are valuable as reagents for introducing the triphenylgermanium group into combination with carbon and perhaps other elements. In principle, the reactions proceed as follows

$$R_{4-n}CX_n + nNaGe(C_6H_5)_3 = nNaX + R_{4-n}C[Ge(C_6H_5)_3]_n \qquad (Ia)$$
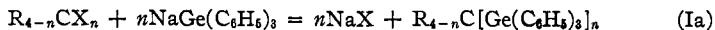
Here R represents hydrogen or a hydrocarbon group and X represents a halogen atom. With monohalides, the above reaction ordinarily proceeds quantitatively in liquid ammonia solution.

It might be expected that the same type of reaction would occur in the case of more highly halogenated organic derivatives. Thus, sodium trimethyl stannide reacts readily with methylene chloride in accordance with equation Ia[2] although complications result when it reacts with chloroform.[3] On the other hand, sodium triphenyl stannide reacts with chloroform in accordance with equation Ia while, in the case of carbon tetrachloride, coupling between tin and carbon fails to occur.[4]

In the present investigation, a study has been made of the reactions of liquid ammonia solutions of sodium triphenyl germanide with methyl iodide, ethyl bromide, methylene chloride, chloroform and carbon tetrachloride. The reactions with methylene chloride and ethyl bromide were found to proceed normally and quantitatively. On the other hand, in the case of both methylene chloride and chloroform, side reactions occur in which the solvent is involved. With methylene chloride, the chief product is di-triphenylgermanylmethane, along with some triphenylgermanylmethane and triphenylgermanylamine. In the case of chloroform, no tertiary substitution product is obtained. The products, in fact, are the same as those obtained with methylene chloride although in somewhat different proportions. With carbon tetrachloride a mixture of reac-

[1] W. H. Kahler has shown that sodium triphenyl germanide is more highly ionized in liquid ammonia than are ordinary inorganic salts, such as the alkali metal halides (Thesis, Brown University, 1930).

[2] Kraus and Neal, THIS JOURNAL, **52,** 695 (1930).

[3] Kraus and Neal, *ibid.,* **52,** 4426 (1930).

[4] Harry Eatough, Thesis, Brown University, 1929.

tion products was obtained that were not completely separated. Triphenylgermanylamine appeared to be formed and there was evidence of the formation of small quantities of di-triphenylgermanylmethane and triphenylmethylgermane.

II. Materials

Tetraphenylgermanium.—The source material for the present investigation was tetraphenylgermanium prepared by the method of Kraus and Foster.[5] After decomposing the excess reagent, the product was thoroughly washed with water and dried. The dry material was washed with low-boiling petroleum ether in order to remove diphenyl. The tetraphenylgermane was then extracted with trichloroethylene.

Triphenylgermanium Bromide.—This compound was prepared according to the method of Kraus and Foster.[5] Equivalent quantities of tetraphenylgermane and bromine were boiled for fifteen hours in twenty times their combined weight of carbon tetrachloride. No diphenylgermanium dibromide was formed and 80% of the tetraphenylgermane was converted to the desired bromide while the remainder was recovered as unreacted material. The triphenylgermanium bromide was freed from tetraphenylgermane by sublimation in a high vacuum at 150° (m. p. 138°).

The attempt was made to prepare triphenylgermanium bromide by the interaction of tetraphenylgermanium and germanium tetrabromide. According to Eatough,[4] the corresponding reaction proceeds readily in the case of tin. After heating to 265° for more than fifteen hours, only about 20% of the tetraphenylgermanium was converted to the bromide. Some dibromide was also formed.

Hexaphenylgermanoethane.—This compound was prepared according to the method of Morgan and Drew[6] by the reduction of triphenylgermanium bromide with metallic sodium in boiling xylene. Histological xylene was purified by boiling with sodium previous to distillation. The reduction must be carried out under an atmosphere of nitrogen and with rigid exclusion of oxygen. In one preparation, 86% of hexaphenylgermanoethane (m. p. 336°) was obtained and 12% of triphenylgermanium bromide was recovered unconverted.

Sodium Triphenyl Germanide.—Sodium triphenyl germanide was prepared by the method of Kraus and Foster[5] by treating carefully purified hexaphenylgermanoethane with sodium in liquid ammonia. The sodium is introduced in small pieces so as to avoid a high concentration since, otherwise, phenyl groups are split off from the germanium atom. Reaction proceeds somewhat slowly on account of the low solubility of the germanoethane. The salt is very reactive toward oxygen, which needs to be excluded rigidly.

Apparatus and Procedure.—The apparatus employed in carrying out the reaction between sodium triphenyl germanide and the various halogenated organic derivatives is sketched in the accompanying figure (Fig. 1). The sodium triphenyl germanide is prepared in the reaction tube A and the reaction with the organic halide is carried out in the same tube. In preparing the sodium triphenyl germanide, the hexaphenylgermanoethane is introduced into the reaction tube while an equivalent quantity of sodium, cut in small pieces, is introduced into the addition tube B, which is fitted to the reaction tube by means of a ground glass joint C. By turning the addition tube through a suitable angle, the sodium may be added to the reaction mixture piece by piece. Ammonia is introduced into the reaction tube through the stirring tube D and is condensed under a pressure regulated by the height of mercury in the trap E. The reaction tube is surrounded by a bath of liquid ammonia contained in the Dewar tube F.

[5] Kraus and Foster, This Journal, **49**, 457 (1927).

[6] Morgan and Drew, *J. Chem. Soc.*, **127**, 1760 (1925).

The organic halide may be added directly from a pipet by replacing the addition tube B by the open end tube shown as 2b. Under these conditions, a stream of ammonia gas is kept issuing through the tube G. In most instances, however, with volatile organic halides, it is preferable to introduce the halide by means of a stream of ammonia vapor. The liquid is introduced into the tube H through the side arm I, which is then sealed off. By closing stopcocks J, K and L, ammonia vapor passes over the liquid in H and carries the vapors into the reaction tube A, where they are condensed.

The tube M is a buret for collecting any gases that may be formed in the course of the reaction. The bottom of this tube sets in a vessel containing freshly boiled water W. The reaction tube is attached to the system by means of de Khotinsky cement at N and O. If desired, the reaction tube may be detached and weighed. The ammonia system is provided with a safety trap P and the vacuum system is provided with a McLeod gage.
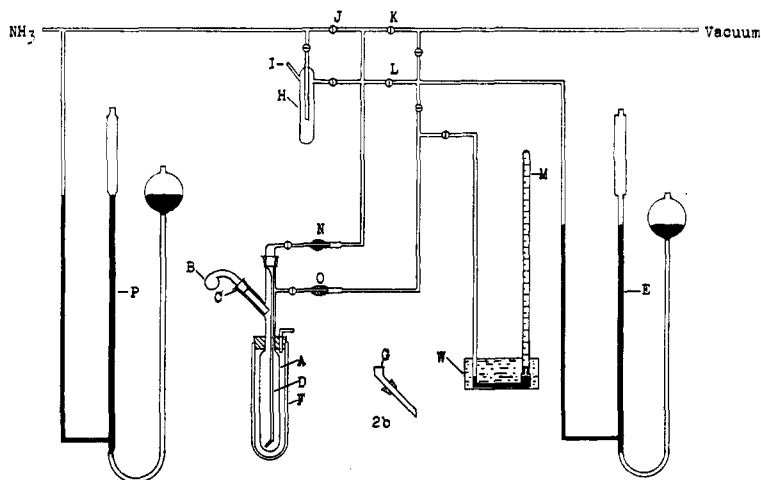

Fig. 1.—Sketch of apparatus.

When the sodium triphenyl germanide has been prepared, the organic halide is introduced into the reaction tube as described. After evaporating the solvent the reaction tube is detached and weighed and the contents are treated by various means, depending upon the nature of the product.

III. Actions of Sodium Triphenyl Germanide on Methyl Iodide and Ethyl Bromide

Methyl Iodide.—Reaction takes place according to the equation

$$CH_3I + NaGe(C_6H_5)_3 = NaI + CH_3Ge(C_6H_5)_3 \qquad (I)$$
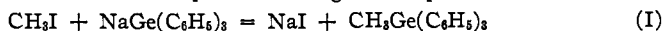
After preparing the solution of sodium triphenyl germanide in liquid ammonia, methyl iodide, in excess, was added through the addition tube 2b as described above. Reaction took place immediately with the formation of a voluminous white precipitate which slowly settled and agglomerated to a granular mass. The ammonia was then evaporated and the last traces removed by means of a pump. The dry white powder which remained was transferred to an extraction funnel and extracted with benzene. On evaporating the benzene under diminished pressure, colorless transparent crystals remained which, after washing with low-boiling petroleum ether, melted at 69–70°. Neglecting material contained in the washings, a yield of 86% was obtained. The compound was crystallized by dissolving in chloroform and precipitating with methyl alcohol.

Analysis for germanium was carried out by oxidizing with fuming sulfuric and nitric acids according to the method commonly used in this Laboratory.[7]

Anal. Subs., 0.2591, 0.1903, 0.1693: GeO_2, 0.0860, 0.0621, 0.0557. Calcd. for $(C_6H_5)_3GeCH_3$: Ge, 22.78. Found: Ge, 22.99, 22.65, 22.83, mean, 22.82.

The molecular weight of the compound was determined in benzene by the cryoscopic method.

Mol. wt. Solvent, 21.91; solute 0.1851, 0.3272; Δt, 0.142, 0.252°; mol. wt. calcd. for $(C_6H_5)_3GeCH_3$, 318.7; found: 304, 305.

Triphenylmethylgermane is very soluble in benzene, ether, petroleum ether, acetone and chloroform. It is slightly soluble in isopropyl alcohol and almost insoluble in cold methyl alcohol. It is quite insoluble in liquid ammonia. It melts at 70.5–71.0°. It does not react with sodium in liquid ammonia.

Ethyl Bromide.—Reaction takes place according to the equation

$$(C_6H_5)_3GeNa + C_2H_5Br = (C_6H_5)_3GeC_2H_5 + NaBr \qquad (II)$$
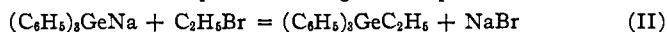
Triphenylethylgermane has been prepared previously by Orndorff, Tabern and Dennis[8] by the action of ethylmagnesium bromide on triphenylgermanium bromide.

Ethyl bromide reacts readily and quantitatively with sodium triphenyl germanide, the reaction being carried out as already described in connection with methyl iodide. The compound was recrystallized from isopropyl alcohol and melted at 78–78.5°, which is slightly higher than that recorded by Orndorff, Tabern and Dennis.

Anal. Subs., 0.2124, 0.2186: GeO_2, 0.0671, 0.0692. Calcd. for $(C_6H_5)_3GeC_2H_5$: Ge, 21.82. Found: Ge, 21.88, 21.97, mean, 21.92.

The molecular weight was determined in benzene solution by the cryoscopic method.

Mol. wt. Solvent, 19.75; solute, 0.2174, 0.4587, 0.5582; Δt, 0.174, 0.375, 0.456°; mol. wt. calcd. for $(C_6H_5)_3GeC_2H_5$, 332.7. Found, 324, 317, 317, mean, 319.

Triphenylethylgermane is very soluble in ether, petroleum ether, benzene, chloroform, acetone and trichloroethylene. It is slightly soluble in isopropyl acohol and almost insoluble in methyl alcohol; it melts at 78–78.5°.

Triphenylethylgermane reacts readily with bromine, apparently with the substitution of a phenyl group. On carrying out such bromination in carbon tetrachloride, a product was obtained that melted at 67–70°. It contained bromine and sublimed readily at 100° in vacuum. Had the ethyl group been substituted, the resulting triphenylgermanium bromide would have melted at 138°.

IV. Action of Sodium Triphenyl Germanide on Methylene Chloride

It might be expected that the reaction between sodium triphenylgermanide and methylene chloride would take place according to the equation

$$2(C_6H_5)_3GeNa + CH_2Cl_2 = [(C_6H_5)_3Ge]_2CH_2 + 2NaCl \qquad (III)$$
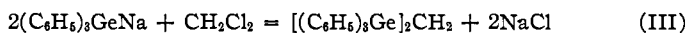
The corresponding reaction has been shown to take place in the case of sodium triphenyl stannide[4] as well as sodium trimethyl stannide.[2]

When methylene chloride or bromide is added to a solution of sodium triphenyl germanide in liquid ammonia, reaction takes place in the main according to equation III. However, a side reaction occurs, inasmuch as there are recovered, along with di-triphenylgermanylmethane, smaller

[7] Kraus and Brown, THIS JOURNAL, **52**, 3693 (1930).

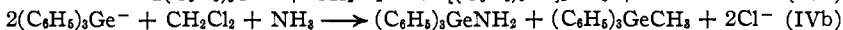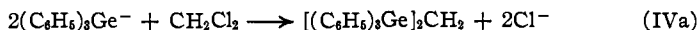[8] Orndorff, Tabern and Dennis, *ibid.*, **47**, 2039 (1925).

quantities of triphenylmethylgermane and triphenylgermanium oxide. The latter compound is a secondary product resulting from the hydrolysis of triphenylgermanyl amine, $(C_6H_5)_3GeNH_2$.

It may be pointed out that a reaction such as III is an ionic one and involves mutual oxidation and reduction between several of the molecular species. In ionic form the reaction would be written as follows

$$2(C_6H_5)_3Ge^- + CH_2Cl_2 = [(C_6H_5)_3Ge]_2CH_2 + 2Cl^-$$
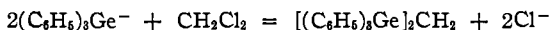
The sodium ion takes no actual part in the reaction. What happens is that chlorine, being much more electronegative than germanium, takes over the electrons from the germanium ions to form chloride ions, while the germanium groups combine with the residual carbon valences.

Owing to the affinity of germanium for nitrogen on the one hand and the affinity of carbon for hydrogen on the other, reactions may occur in which ammonia is concerned, the amino group of the ammonia combining with germanium and the hydrogen combining with carbon. In the case of simple carbon groups, as, for example, methyl or ethyl groups, the germanium is coupled quantitatively to carbon. When, however, we come to the more highly halogenated carbon derivatives, only one of the halogens is substituted quantitatively by the germanyl group, while the others are substituted only incompletely. The reaction of sodium triphenyl germanide with methylene chloride in liquid ammonia may be formulated as follows

$$2(C_6H_5)_3Ge^- + CH_2Cl_2 \longrightarrow [(C_6H_5)_3Ge]_2CH_2 + 2Cl^- \qquad (IVa)$$
$$2(C_6H_5)_3Ge^- + CH_2Cl_2 + NH_3 \longrightarrow (C_6H_5)_3GeNH_2 + (C_6H_5)_3GeCH_3 + 2Cl^- \quad (IVb)$$

In the case of methylene chloride and bromide, reaction takes place in the main according to equation IVa. Comparatively small amounts of triphenylmethylgermane and triphenylgermanylamine are formed. The proportion of reaction IVb seemed to be somewhat greater in the case of methylene chloride than in that of methylene bromide. In the reactions as carried out, triphenylgermanylamine was not recovered as such, since the reaction products were handled in the atmosphere and, as Wooster has shown, the amine is completely hydrolyzed under these conditions.[9] The corresponding oxide, however, was recovered in all cases.

While reaction IVb is not of any considerable consequence in the case of methylene chloride, it becomes of great importance in the case of chloroform, as will be described in the next section.

In carrying out the reaction between sodium triphenyl germanide and methylene halide, the method was much the same as that described in the preceding section except that the methylene chloride was introduced by means of ammonia vapor passing over the liquid contained in tube H. The reaction with methylene chloride and bromide takes place immediately, a white, curdy precipitate being formed. After evaporating the solvent and pumping off the ammonia, a pasty mass remained which was converted to a dry white powder on exposure to the air. On extracting the organic materials with

⁹ Kraus and Wooster, THIS JOURNAL, **52**, 372 (1930).

benzene and subjecting the resulting product to sublimation at 100° under a pressure of 0.05 mm., about 20% of the material was obtained as a sublimate, melting at 70–71°. In three cryoscopic determinations of the molecular weight in benzene, the values 328.6, 327.3 and 318.6 were obtained, which corresponds closely with the molecular weight of triphenylmethylgermane, 318.7. The melting point of a mixture of this sublimate with known triphenylmethylgermane served to identify it definitely as the latter compound.

Di-triphenylgermanylmethane.—The main portion of the reaction product remained after the sublimation at lower pressures at a temperature of 100°. This residue was found to melt, for the most part, at 143–147°, although some remained solid up to 160°. A great deal of difficulty was experienced in purifying this material, which might have been expected to be a nearly pure substance. The melting point varied from 139 to 180°. Finally, by careful fractional crystallization from a mixture of chloroform and methyl alcohol, two substances were separated. The one had a melting point of 180–182° and was shown to be triphenylgermanium oxide, while the other had a melting point of approximately 139°. By recrystallization, large, transparent, prismatic crystals were obtained from the 139° product which melted at 134.5°, and, on further purification, a few crystals were obtained that melted at 132–133°. The lower-melting crystals were identified as di-triphenylgermanylmethane.

Anal. Subs., 0.2410, 0.4814: GeO₂, 0.0806, 0.1617. Calcd. for [(C₆H₅)₃Ge]₂CH₂: 23.36. Found: Ge, 23.20, 23.31, mean, 23.26.

The molecular weight of the compound was determined in benzene by the cryoscopic method.

Mol. wt. Solvent, 18.77; solute, 0.1731, 0.2471, 0.3183; Δt, 0.073, 0.105, 0.142°; mol. wt. calcd. for [(C₆H₅)₃Ge]₂CH₂: 621.4; found: 647, 642, 611, mean, 633.
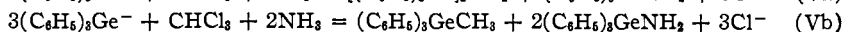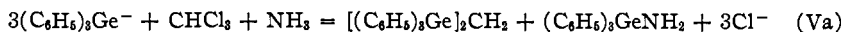
Di-triphenylgermanylmethane is very soluble in ether, petroleum ether, benzene, chloroform and trichloroethylene. It is quite insoluble in liquid ammonia and the lower acohols. It forms large transparent prisms when allowed to crystallize slowly from a chloroform–methyl alcohol mixture.

Di-triphenylgermanylmethane forms a series of solid solutions with triphenylgermanium oxide from which it is separated with difficulty. The existence of these solid solutions was shown by taking the melting point of known mixture. With di-triphenylgermanyl methane melting at 134° and triphenylgermanium oxide melting at 183°, mixtures were made up in the ratios of 3.4:1, 1:1, and 1:2. These melted, respectively, in the ranges 135–160, 145–170 and 170–181°. The two compounds appear to be miscible in all proportions and with rather slight difference between the composition of the liquid and solid phases.

V. Action of Sodium Triphenyl Germanide on Chloroform

While one might expect that, on treating chloroform with sodium triphenyl germanide, an appreciable amount of the tertiary substituted methane would be produced, there were actually obtained the same products as in the methylene chloride reaction. The proportion of di-triphenylgermanylmethane and of triphenylgermanylamine was, however, much greater than in the case of methylene chloride. A relatively small amount of triphenylmethylgermane is also formed.

It is evident that of the three chlorine atoms attached to carbon in chloroform, one is quantitatively substituted by a triphenylgermanyl group; · a second halogen atom is largely substituted while the third is completely replaced by hydrogen. The reactions may be formulated as follows

$$3(C_6H_5)_3Ge^- + CHCl_3 + NH_3 = [(C_6H_5)_3Ge]_2CH_2 + (C_6H_5)_3GeNH_2 + 3Cl^-   (Va)$$
$$3(C_6H_5)_3Ge^- + CHCl_3 + 2NH_3 = (C_6H_5)_3GeCH_3 + 2(C_6H_5)_3GeNH_2 + 3Cl^-   (Vb)$$

For the most part, reaction takes place according to equation Va.

Several reactions were carried out in a two-legged reaction tube in which bromoform was added to the solution of sodium triphenyl germanide in liquid ammonia. After evaporating the ammonia, the material was treated with various dry solvents in the absence of air in order to separate the organic product from the sodium bromide formed in the reaction. There was evidence that two soluble organic products were formed, one of which melted at 60–70° and was undoubtedly triphenylmethylgermane, although this product was present in very small amount. The reaction was finally carried out with the apparatus shown in Fig. 1, passing the chloroform into the reaction tube by means of ammonia vapor as already described.

A voluminous white precipitate resulted which resembled that formed in the methylene chloride reaction. It was slightly pasty when the ammonia was first evaporated but became dry upon standing in air. This was probably due to the conversion of triphenylgermanylamine to oxide by hydrolysis. On recrystallization, the product showed the same properties as did that of the methylene chloride reaction. The melting point varied with the treatment and extended over a considerable temperature range. After several recrystallizations from chloroform–alcohol mixtures, a product was separated that melted at 139–141°. Molecular weight determinations with this product in benzene by the cryoscopic method yielded the values 551 and 565, respectively; the molecular weight of di-triphenylgermanylmethane is 621.5 and that of tri-triphenylgermanylmethane is 924.2. The molecular weight indicated that tertiary substitution does not occur in the case of chloroform. An analysis of the product melting at 139° showed 23.57% of germanium as against 23.57% required for the tertiary derivative, and 23.36 for the di-substitution product. The composition of the two compounds is so nearly the same that analysis cannot be depended upon in distinguishing between them. The molecular weight, however, gives conclusive results.

By repeated recrystallization of the 139° product, crystals were finally obtained that melted at 132–134°. On comparing the melting point of this compound with that of known di-triphenylgermanylmethane and mixtures of the two, it was established that the 132–134° product was, in fact, di-triphenylgermanylmethane.

In the case of the methylene chloride reaction, a small quantity of a higher melting material was obtained which was identified as triphenylgermanium oxide by comparison of its melting point with that of known oxide and of mixtures of the two. In the chloroform reaction, relatively greater quantities of the same material were obtained and were similarly identified as triphenylgermanium oxide. As a further check on the identity of this material, it was treated with aqueous hydrobromic acid and petroleum ether. After removing the ether, the product was sublimed in a vacuum at 150°. The sublimate melted at 135–136°, which corresponds to the melting point of impure triphenylgermanium bromide. The high melting product is triphenylgermanium oxide which results from the hydrolysis of triphenylgermanylamine due to the moisture present in the atmosphere and in the solvents used in recrystallization.

VI. Action of Sodium Triphenyl Germanide on Carbon Tetrachloride

It might be expected that on treating carbon tetrachloride with sodium ·triphenyl germanide a quaternary substituted carbon compound would result. On the other hand, since the tertiary substituted product is not formed in the case of chloroform, the quaternary product is scarcely to be

expected in the case of carbon tetrachloride. Foster[10] carried out a reaction between sodium triphenyl germanide and carbon tetrachloride in benzene solution and found that hexaphenylgermanoethane was formed, together with a small amount of triphenylgermanium oxide. He did not study the reaction in detail and did not determine what becomes of the carbon atom of the original tetrachloride.

When carbon tetrachloride was treated with sodium triphenyl germanide in liquid ammonia solution, a pasty mass was obtained. On extracting with benzene and evaporating the solvent, crystals were obtained along with adhering liquid material. After washing with petroleum ether, the residue was found to melt at 156–160°. This material was recrystallized from chloroform–methyl alcohol solution and from petroleum ether, which raised the melting point to 178–179°. By comparison with known triphenylgermanium oxide, the compound was identified as this oxide.

From the petroleum ether washings, various crystalline products were obtained melting at 139–150, 63–69, 88–95 and 91–93°. The quantities were not sufficient for purification and identification. They probably comprised some triphenylmethylgermane and di-triphenylgermanylmethane.

When sodium triphenyl germanide reacts with carbon tetrachloride in liquid ammonia, no triphenylgermanium results. The large amount of triphenylgermanium oxide formed indicates that a large part of the germanium is converted to triphenylgermanylamine, corresponding to which the carbon atom must have been hydrogenated. The low-melting products doubtless contain this hydrogen.

The results of the present investigation illustrate the propensity of the lighter elements of the fourth group to combine with nitrogen. This tendency appears again and again in the case of various reactions in which organic germanium derivatives are involved and to a still greater extent in the case of silicon, as will be shown in subsequent papers.

Summary

The reaction of sodium triphenyl germanide with various organic halides in liquid ammonia has been studied. The monohalogen derivatives react quantitatively according to the equation

$$(C_6H_5)_3GeNa + RX = NaX + (C_6H_5)_3GeR$$
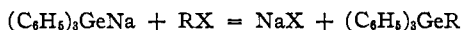
In the case of methylene chloride, the final products obtained are triphenylgermanylmethane, triphenylgermanium oxide and di-triphenylgermanylmethane. The last-named compound is the normal substitution product due to reaction of the two chlorine atoms of methylene chloride with the weakly negative ions of sodium triphenyl germanide. The other two compounds are due to the fact that one of the carbon valences reacts with ammonia. A hydrogen atom of ammonia combines with one of the carbon valences while the remaining amino group combines with the triphenylgermanium group. The resulting triphenylgermanylamine is hydrolyzed to oxide in the course of separation. The reaction as it takes place in liquid ammonia is as follows

$$2(C_6H_5)_3GeNa + H_2CCl_2 + NH_3 = 2NaCl + (C_6H_5)_3GeCH_3 + (C_6H_5)_3GeNH_2$$
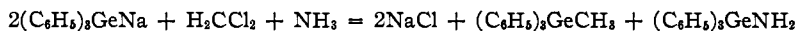
[10] Foster, Thesis, Brown University, 1927.

In the reaction between sodium triphenyl germanide and chloroform, the products are the same as in that with methylene chloride, but the proportion in which the compounds are formed is different. Larger quantities of triphenylgermanylamine (ultimately recovered as oxide) are obtained while the amount of triphenyl methyl germane is relatively smaller. Very considerable quantities of di-triphenylgermanylmethane are formed.

Di-triphenylgermanylmethane and triphenylgermanium oxide form a series of solid solutions that may be separated with some difficulty.

Sodium triphenyl germanide reacts readily with carbon tetrachloride. The reaction is evidently similar to that with chloroform and methylene chloride although apparently more complex. No free triphenylgermanium is formed. Triphenylgermanium oxide was obtained from the reaction mixture as well as a number of lower melting compounds that have not been separated and identified. Without doubt, ammonia takes part in this reaction.

PROVIDENCE, RHODE ISLAND

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l-p-METHOXYPHENYLALANINE[1]

BY LETHA DAVIES BEHR AND H. T. CLARKE

The methyl ether of racemic tyrosine has been prepared, by purely synthetic methods, by Dakin.[2] Need having arisen for an optically active variety of this acid, its preparation from natural tyrosine was indicated. The action of diazomethane upon tyrosine has been shown[3] to lead to a mixture of methyl esters which includes that of methoxyphenylalanine, but the process is obviously unsuitable for preparative purposes.

Methylation by means of methyl sulfate has proved eminently satisfactory, protection of the amino group being secured by acetylation. For this purpose it is desirable to select conditions in which only the amino group is acetylated, the phenolic hydroxyl group remaining intact. It has recently been shown that, in general, both the amino group and the phenolic hydroxyl group are readily acetylated by treatment in cold alkaline solution with acetic anhydride[4] or with ketene;[5] the hydroxyl group of tyrosine

[1] Work supported by a research grant from the Chemical Foundation.

[2] H. D. Dakin, J. Biol. Chem., 8, 11 (1910); A. J. Wakeman and H. D. Dakin, ibid., 9, 148 (1911).

[3] E. Abderhalden and E. Schwab, Z. physiol. Chem., 148, 16 (1925).

[4] F. D. Chattaway, J. Chem. Soc., 2495 (1931); C. P. Berg, W. C. Rose and C. S. Marvel, J. Biol. Chem., 85, 207 (1929).

[5] M. Bergmann, and F. Stern, Ber., 63B, 437 (1930).