On standing for 48 hr. at room temperature, clusters of colorless crystals formed. The product was collected and recrystallized from hot ethanol.

The same reaction condition was applied for bromide and 2-bromobutane. Evolution of olefinic gas was detected in both cases and when cooled a large quantity of colorless crystals formed. Recrystallization from aqueous acetone and ether gave colorless crystals of m.p. 228°.

Both 2-bromoethylacetate and 4-bromopentan-1-ol were reacted in the same way in methanol solution. After methanol was removed, colorless hygroscopic crystals were obtained in large quantity. This was recrystallized from ethanol, m.p. 319° with decomposition. Mixed melting point with authentic sample of 1,4-dihydro-1,4-diazabicyclo[2.2.2]octane dibromide of m.p. 319° did not show depression.

Anal. Calcd. for $C_6H_{14}N_2Br_2$ C, 26.4; H, 5.15. Found: C, 26.63; H, 5.41.

The results of physiological tests indicate that 1,4-diazabicyclo[2.2.2]octane bis(hexadecylbromide) has some activity against microorganisms while 1,4-diazabicylo[2.2.2]-octane bis(tetradecylbromide) shows a little CNS depressant activity in mice.

The authors are indebted to Dr. Reuben G. Jones of the Lilly Research Laboratories for performing the physiological tests.

CHEMISTRY DEPARTMENT
DREXEL INSTITUTE OF TECHNOLOGY
PHILADELPHIA 4, PA.

Reaction of Triphenylsilyllithium and of Triphenylsilylpotassium with Benzaldehyde

DIETMAR WITTENBERG, T. C. WU,
AND HENRY GILMAN

Received February 20, 1959

It has been reported recently that silyllithium compounds add to the carbonyl group of aliphatic ketones to give α-silylcarbinols.[1] From the reaction of triphenylsilylpotassium and –lithium with aromatic ketones, however, "abnormal" addition products resulted, in which the silicon atom is bonded to oxygen.[2,3] Two reactions show that silylmetallic compounds add in a "normal" manner to aliphatic aldehydes. Triphenylsilylmethanol was obtained from the reaction of triphenylsilylpotassium with formaldehyde,[4] and 1-(triphenylsilyl)-ethanol was synthesized from acetaldehyde and the corresponding silyllithium reagent.[5] In an extension of these studies, the reaction of triphenylsilyllithium and of triphenylsilylpotassium with benzaldehyde has been investigated.

Rapid addition of one equivalent of benzaldehyde (II) to triphenylsilyllithium (I) at –60° yielded benzyloxytriphenylsilane (V) in fair yield. Prior to hydrolysis, the reaction mixture gave a strongly positive Color Test I.[6] When a second equivalent of benzaldehyde was added, Color Test I was negative, and no benzyloxytriphenylsilane was isolated. Instead, the monotriphenylsilyl ether of 1,2-dihydroxy-1,2-diphenylethane (VI, with hydrogen replacing lithium) was obtained as a mixture of isomers. At room temperature, using a slow rate of addition, triphenylsilyllithium reacted further with the alkoxysilane-type intermediate VI to give hexaphenyldisilane and 1,2-dihydroxy-1,2-diphenylethane, the latter compound as a mixture of its stereoisomers.

Whereas benzyl ethers, the carbon analogs of V, rearrange upon treatment with phenyllithium to give the corresponding carbinols,[7] Brook, in

$$C_6H_5CH_2OR \xrightarrow{C_6H_5Li} C_6H_5CH(Li)OR \longrightarrow C_6H_5CH(R)OLi$$

some attractive studies, observed that phenyl-substituted α-silylcarbinols in the presence of catalytic amounts of base undergo the reverse rearrangement to give the corresponding alkoxysilanes.[8] Diphenyl(triphenylsilyl)methanol was shown to form triphenyl(diphenylmethoxy)silane by rearrangement,[8] and, similarly, phenyl(triphenylsilyl)methanol yielded benzyloxytriphenylsilane.[9]

$$(C_6H_5)_3Si—CH(OH)—C_6H_5 \longrightarrow (C_6H_5)_3Si—O—CH_2—C_6H_5$$

The course of the reaction of I with II might therefore be explained by assuming that in the first step a "normal" addition takes place to give III, which immediately rearranges with the formation of IV. The organometallic reagent IV yields benzyloxytriphenylsilane (V) on hydrolysis, while treatment with another equivalent of benzaldehyde gives VI. Since alkoxytriphenylsilanes are reported[10] to react with triphenylsilylmetallic compounds with the formation of hexaphenyldisilane, the isolation of large amounts of the latter can be easily explained from the reaction of I and VI. To our surprise, large amounts of hexaphenyldisi-

---

[1] H. Gilman and G. D. Lichtenwalter, *J. Am. Chem. Soc.*, **80**, 2680 (1958).

[2] H. Gilman and T. C. Wu, *J. Am. Chem. Soc.*, **75**, 2935 (1953).

[3] H. Gilman and G. D. Lichtenwalter, *J. Am. Chem. Soc.*, **80**, 607 (1958).

[4] H. Gilman and T. C. Wu, *J. Am. Chem. Soc.*, **76**, 2502 (1954).

[5] D. Wittenberg and H. Gilman, *J. Am. Chem. Soc.*, **80**, 4529 (1958).

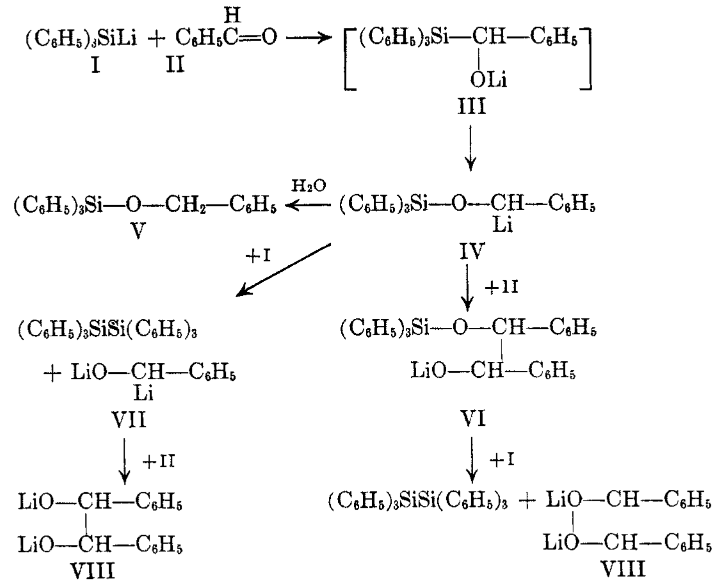
[6] H. Gilman and F. Schulze, *J. Am. Chem. Soc.*, **47**, 2002 (1925).

[7] G. Wittig and L. Löhmann, *Ann.*, **550**, 260 (1942); G. Wittig and W. Harpe, *Ann.*, **557**, 205 (1947); G. Wittig and R. Clausnizer, *Ann.*, **588**, 145 (1954); G. Wittig and E. Stahnecker, *Ann.*, **605**, 69 (1957).

[8] A. G. Brook, *J. Am. Chem. Soc.*, **80**, 1886 (1958). See also D. Wittenberg and H. Gilman, *J. Am. Chem. Soc.*, **80**, 4529 (1958); D. Wittenberg, M. V. George, T. C. Wu, D. H. Miles, and H. Gilman, *J. Am. Chem. Soc.*, **80**, 4532 (1958).

[9] A. G. Brook, C. M. Warner, and M. E. McGriskin, *J. Am. Chem. Soc.*, **81**, 981 (1959).

[10] H. Gilman and T. C. Wu, *J. Am. Chem. Soc.*, **73**, 4031 (1951); *J. Org. Chem.*, **18**, 753 (1953).



lane and 1,2-dihydroxy-1,2-diphenylethane were also obtained when the *reverse* addition was employed, *i.e.*, the slow addition of benzaldehyde to triphenylsilyllithium. Since the excess of I present during the addition should have diminished the formation of VI, hexaphenyldisilane and VII may have resulted from the attack of I upon IV. Compound VIII can arise from the reaction of II with the organolithium compound VII formed in this manner.

The reaction of triphenylsilylpotassium with benzaldehyde seems to take a different course. In addition to 1,2-dihydroxy-1,2-diphenylethane, tetraphenylsilane[11] was isolated in a 77% yield.

EXPERIMENTAL[12]

Reaction of triphenylsilyllithium with benzaldehyde. First experiment. Triphenylsilyllithium was prepared in tetrahydrofuran by lithium cleavage of hexaphenyldisilane according to a recently reported procedure.[13] Over a period of 10 min., a solution containing 0.050 mole of triphenylsilyllithium was added to a stirred solution of 5.3 g. (0.050 mole) of benzaldehyde in 10 ml. of tetrahydrofuran, cooled to −70°. During the addition, a temperature of −50 to −60° was maintained. Subsequent to the addition of 20 ml. of dilute sulfuric acid, the reaction mixture was allowed to warm to room temperature. The dried organic layer was distilled, and the oily residue was treated with 30 ml. of petroleum ether (b.p. 60–70°). A small amount of insoluble material was removed by filtration. The concentrated filtrate was cooled and deposited 8.3 g. (46%) of benzyloxytriphenylsilane, m.p. 78–82°. Recrystallization from the same solvent gave 6.8 g. (38%) of pure product, m.p. 83–84°. A mixed melting point with an authentic specimen was not depressed. The infrared spectra were superimposable.

Second experiment. A solution of 0.025 mole of triphenylsilyllithium was added to 5.3 g. (0.050 mole) of benzaldehyde in 10 ml. of tetrahydrofuran under the same conditions as in Experiment I. Low temperature hydrolysis with dilute acid, followed by the usual work-up of the organic layer, gave a viscous oil, which was subsequently chromatographed on alumina. Petroleum ether (b.p. 60–70°) and cyclohexane did not elute any product, indicating the absence of benzyloxytriphenylsilane. The use of benzene and ethyl acetate as eluents gave pale yellow viscous oils which could not be crystallized. These were insoluble in petroleum ether (b.p. 60–70°), but soluble in benzene and polar solvents. The infrared spectra showed absorption bands at 2.8, 3.3, 3.5, 9.0, and 9.5 μ, indicative of O—H, aromatic C—H, aliphatic C—H, the phenyl-silicon and the Si—O—C linkage, respectively. The oil is thought to consist of a mixture of stereoisomers of the monotriphenylsilyl ether of 1,2-dihydroxy-1,2-diphenylethane.

Third experiment. A solution containing 0.05 mole of triphenylsilyllithium was added dropwise to 5.3 g. (0.05 mole) of benzaldehyde. The mixture was subsequently stirred for 12 hr. at room temperature, at which time Color Test I[6] was still strongly positive. Subsequent to hydrolysis with dilute acid and addition of some ether, the reaction mixture was filtered to give 7.0 g. (60%) of hexaphenyldisilane, m.p. 356–358° (mixed m.p.). The layers of the filtrate were separated, the organic layer dried with sodium sulfate, and the solvents removed by distillation. The pale yellow residue was distilled at reduced pressure.

The spectrum of the first fraction (0.35 g., b.p. 50–60°/0.1 mm.) indicated the presence of benzyl alcohol. The alcohol was identified by its 3,5-dinitrobenzoate, m.p. 110–111.5°.

The second fraction (3.95 g., b.p. 145–150°/0.1 mm.) was recrystallized from a mixture of benzene and petroleum ether (b.p. 60–70°) to give 2.7 g. (49%) of 1,2-dihydroxy-1,2-diphenylethane as a mixture of isomers, m.p. 114–125°. The spectrum of this solid showed no absorption band at 9.0μ, indicating the absence of the phenyl-silicon linkage, and was almost identical with the spectrum of *meso*-1,2-dihydroxy-1,2-diphenylethane, m.p. 135–136° (hydrobenzoin). Several recrystallizations from aqueous methanol and from a mixture of benzene and petroleum ether gave a small amount of crystals, m.p. 133–135°, which showed no depression in melting point when admixed with an authentic sample of the *meso*-isomer.

No crystalline product was isolated from the highest boil-

---

[11] For the formation of tetraphenylsilane from various reactions involving triphenylsilylpotassium, see H. Gilman and T. C. Wu, *J. Am. Chem. Soc.*, **75**, 2509 (1953); A. G. Brook and H. Gilman, *J. Am. Chem. Soc.*, **76**, 2333, 2338 (1954).

[12] Melting points and boiling points are uncorrected. Reactions involving organometallic compounds were carried out in an atmosphere of dry, oxygen-free nitrogen.

[13] H. Gilman and G. D. Lichtenwalter, *J. Am. Chem. Soc.*, **80**, 608 (1958).

ing fraction (0.4 g., b.p. 190–210°/0.05 mm.) or from the dark brown distillation residue.

Fourth experiment. A solution of 5.3 g. (0.05 mole) of benzaldehyde in 15 ml. of tetrahydrofuran was added dropwise, over a period of 3 hr., to a stirred solution of 0.050 mole of triphenylsilyllithium in the same solvent. Heat was evolved during the addition, and the solution gave only a weak Color Test I[6] after the addition was complete. Subsequent to hydrolysis with dilute acid and addition of ether, the mixture was filtered to give 7.92 g. (62%) of hexaphenyldisilane, m.p. 355–358°. The organic layer of the filtrate was worked up in the same manner as in the third experiment. There was obtained 3.2 g. (58%) of 1,2-dihydroxy-1,2-diphenylethane, m.p. 105–117° (mixture of isomers, identified by their infrared spectrum), and 0.6 g. (4.1%) of benzyloxytriphenylsilane, m.p. 83–84°, identified by a mixed melting point. No crystalline compound was isolated from the distillation residue.

When in two more experiments, benzaldehyde was added rapidly to triphenylsilyllithium (1:1 ratio), hexaphenyldisilane was isolated in 21 and 40% yields, respectively.

Reactions of triphenylsilylpotassium.[14] *A. With benzaldehyde.* A solution of 2.1 g. of benzaldehyde in 20 ml. of ether was added rapidly to 0.02 mole of a triphenylsilylpotassium suspension in ether in which the excess of alloy had been removed by amalgamation.[15] Some heat was evolved during the addition. After 48 hr. of stirring, the brown mixture was hydrolyzed and filtered to separate 2.6 g. (77%) of tetraphenylsilane, m.p. 232–234° (mixed m.p.). From the ethereal solution there was obtained a solid residue, melting over the range 85–125°. Several recrystallizations from ethanol gave 0.34 g. (16%) of 1,2-dihydroxy-1,2-diphenylethane, m.p. 138–139° and 0.6 g. (11%) of triphenylsilanol, m.p. 150–151°.

The experiment was repeated using 1,2-dimethoxyethane as the solvent. Under these conditions, a 77% yield of tetraphenylsilane was obtained.

B. With other carbonyl compounds. No addition products have been isolated so far from the reaction of triphenylsilylpotassium with hexamethylacetone, Michler's ketone, benzalacetophenone, paraldehyde, and benzalaniline. From the reaction of triphenylsiylpotassium with formaldehyde the products were triphenylsilylmethanol[4] and a small amount of a compound, m.p. 119–120°. The infrared spectrum of the compound indicated the presence of a carbonyl group and aliphatic hydrogen in the molecule, and the absence of hydroxyl and Si—O groups. Duplicate analyses gave 75.69 and 75.82% carbon and 5.70 and 5.67% hydrogen. The structure of this product has not yet been determined.

From the reaction of triphenylsilylpotassium with paraformaldehyde, a compound was obtained, m.p. 128–130°. Its infrared spectrum indicated the presence of a Si—O grouping and the absence of —OH in the molecule. The structure has not yet been established.

Anal. Found: C, 78.68, 78.58; H, 6.42, 6.29; Si, 9.82.

C. With di-p-tolylcarbinol. A solution of 2.1 g. (0.01 mole) of di-*p*-tolylcarbinol in 30 ml. of ether was added rapidly to an amalgamated suspension of 0.02 mole of triphenylsilylpotassium[15] in ether. After 48 hr. of stirring the reaction mixture was hydrolyzed and filtered to separate 3.2 g. of insoluble residue. Two recrystallizations from benzene yielded 2.2 g. (65%) of tetraphenylsilane,[11] m.p. 233–235°. (mixed m.p.). From the ethereal layer 0.5 g. (9%) of triphenyl silanol was isolated, m.p. 148–150°.

Under corresponding conditions, the reaction of benzhydrol with triphenylsilylpotassium yielded 80% of tetraphenylsilane.[11]

Acknowledgment. This research was supported in part by the United States Air Force under Contract AF 33(616)-3510 monitored by Materials Laboratory, Directorate of Laboratories, Wright Air Development Center, Wright-Patterson Air Force Base, Ohio. Infrared analyses were obtained through the courtesy of the Institute for Atomic Research, Iowa State College, and special acknowledgment is made to Dr. V. A. Fassel, M. Margoshes, and R. Kniseley for the spectra.

DEPARTMENT OF CHEMISTRY
IOWA STATE COLLEGE
AMES, IOWA

---

[14] Experiments of T. C. Wu.

[15] H. Gilman and T. C. Wu, *J. Org. Chem.*, **18**, 753 (1953).

Synthesis of 2-Isopropyl-4-methoxyphenol[1]

NICOLAS ZENKER[2] AND EUGENE JORGENSEN

Received February 23, 1959

Alkyl-4-methoxyphenols are important intermediates in the synthesis of alkyl-substituted thyroxine analogs. Although 2-isopropyl-4-methoxyphenol has been reported,[3] its synthesis and properties have not been described.

Using the conditions of Meyer and Bernhauer[4] as well as lower temperatures, our attempts at alkylation of 4-methoxyphenol with isopropyl alcohol in the presence of sulfuric acid resulted in a low yield (3%) of 2-isopropyl-4-methoxyphenol. Alkylation with isopropyl alcohol in the presence of 85% phosphoric acid[5] yielded a mixture from which pure 2-isopropyl-4-methoxyphenol, as characterized by ultraviolet absorption spectra, could not be separated by fractional distillation.

Because of the low yields and side reactions obtained in acid-catalyzed alkylations, a more specific synthesis of the compound and its 2-alkyl congeners was sought. 4-Aminophenols have been obtained from phenols by nitrosation and ammonium sulfide reduction[6] or by coupling with diazotized sulfanilic acid followed by sodium hydrosulfite reduction.[7] Oxidative hydrolysis of the diazonium salts of aminophenols yielded quinones[6] which have been reduced to hydroquinones with

---

[1] Supported by grant-in-aid funds from Smith Kline and French Laboratories and by Research Funds of the Academic Senate, University of California.

[2] In partial fulfillment of the requirements for the degree of Doctor of Philosophy, University of California, September 1958.

[3] R. H. Rosenwald and J. A. Chenicek, *J. Am. Oil Chemists' Soc.*, **28**, 185 (1951).

[4] H. Meyer and K. Bernhauer, *Monatsh.*, **53–54**, 751 (1929).

[5] N. G. Sidorova, *J. Gen. Chem. U.S.S.R.* (*Eng. Transl.*), **22**, 1015 (1952).

[6] E. Kremers, N. Wakeman, and R. M. Hixon, *Org. Syntheses*, **Coll. Vol. I**, 511 (1941).

[7] L. F. Fieser, *Org. Syntheses*, **Coll. Vol. II**, 39 (1943).