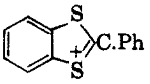
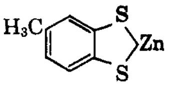
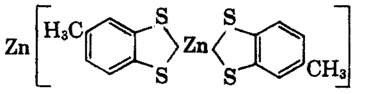
gents. The solid sugar is required when using anthrone as this reagent must be employed in the presence of very little water. With zinc dithiol an aqueous solution of the sugar may be used.



III



V



VI

Department of Chemistry
Cambridgeshire Technical College and School of Art
Cambridge, England

Synthesis of 4-Acetylphenylmethylsilanes Using 2-(4-Bromophenyl)-2-methyl-1,3-dioxolane

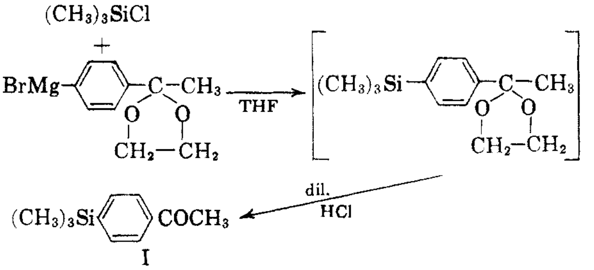
Roy G. Neville[1]

Received July 28, 1958

When acylation of trimethylphenylsilane is conducted under the usual Friedel-Crafts conditions the aryl-silicon bond is cleaved by the aluminum chloride used as catalyst.[2,3] This fact has limited the availability of 4-trimethylsilylacetophenone (I), and similar acetyl compounds of silicon.

Recently, Szmant and Skendrovich[4] obtained approximately 35% yields of I using a modification of the Friedel-Crafts reaction in which trimethylphenylsilane is treated with acetyl fluoride in chloroform saturated with boron trifluoride. Apart from the low yield, the method is disadvantageous in that acetyl fluoride boils at room temperature and requires special care in handling to achieve the maximum reaction.

Continuing our work on organosilanes,[5] in this paper we wish to report that yields of I approximating 80% may be obtained by avoiding a Friedel-Crafts reaction. The Grignard reaction of the ethylene ketal of 4-bromoacetophenone, *i.e.*, 2-(4-bromophenyl) - 2 - methyl - 1,3 - dioxolane, with trimethylchlorosilane produces I in excellent yield. In addition to the high over-all yield this method offers the advantage that the acetyl substituent is in a known position. The possibility of isomeric contaminants, as in the Friedel-Crafts procedure, is thereby eliminated. The reaction occurs smoothly in tetrahydrofuran, but attempts to form the Grignard reagent of the ketal in diethyl ether were unsuccessful.



I

The method has been extended to the preparation of the new compound di(4-acetylphenyl)dimethylsilane[6] in 50–60% yield. New derivatives of these compounds have also been prepared and are reported here.

EXPERIMENTAL

2-(4-Bromophenyl)-2-methyl-1,3-dioxolane (II). In a 3-l. flask, fitted with a Dean-Stark trap and reflux condenser, were placed 4-bromoacetophenone[7] (300 g., 1.5 moles), anhydrous ethylene glycol (93 g., 1.5 moles), 4-toluenesulfonic acid (1.2 g.), and anhydrous benzene (1500 ml.). The mixture was heated at brisk reflux until no more water distilled (20–25 hr.). Sodium acetate (1.2 g.) was added and the mixture stirred or shaken for 30 min., then filtered. The filtrate was washed thoroughly with water and dried over anhydrous sodium sulfate, and the benzene was distilled off at atmospheric pressure. The ketal was obtained as 300 g. (82%) of a colorless liquid, b.p. 175–180°/20–30 mm., which crystallized on standing in the receiver, m.p. 44–45°.[8] The infrared spectrum of the freshly prepared compound has a doublet at 1038 and 1078 cm.$^{-1}$ (C—O of a ketal) with no absorption in the carbonyl region.[9]

Anal. Calcd. for $C_{10}H_{11}BrO_2$: C, 49.34; H, 4.56; Br, 32.87. Found: C, 49.10; H, 4.51; Br, 32.90.

Hydrolysis of the ketal in the standard manner yielded 4-bromoacetophenone, m.p. 50°, which was characterized by its phenylhydrazone, m.p. 125°.[10]

4-Trimethylsilylacetophenone (I). Magnesium turnings (40 g., 1.65 g. atom), methyl iodide (5 ml.), and sodium-dried tetrahydrofuran (THF, 600 ml.), were placed in a 5-liter flask fitted with reflux condenser, motor-driven stirrer, thermometer, and dropping funnel. The mixture was heated at gentle reflux on the water bath and, after the methylmagnesium iodide had formed, a solution of the ketal (II) (334 g., 1.38 moles) dissolved in anhydrous THF (400 ml.) was run in, dropwise, during a period of about one hour. Gentle reflux was maintained for a further hour, then trimethylchlorosilane (150 g., 1.38 moles) was added with stirring to the solution cooled to 40°. After refluxing for an hour the mixture was allowed to cool overnight then 2 l. of water (containing 100 ml. of concentrated hydrochloric acid) was added to dissolve the crystalline magnesium salts. The lower aqueous layer was separated and the yellow oil was first washed several times with saturated calcium chloride

---

[1] For reprints: 783 Cereza Drive, Palo Alto, Calif.

[2] W. E. Evison and F. S. Kipping, *J. Chem. Soc.*, 2774 (1931).

[3] The phenyl-silicon bond of trimethylphenylsilane is also cleaved by bromine. See R. A. Benkeser and A. Torkelson, *J. Am. Chem. Soc.*, **76**, 1252 (1954).

[4] H. H. Szmant and S. Skendrovich, *J. Am. Chem. Soc.*, **76**, 2282 (1954).

[5] R. G. Neville, *J. Org. Chem.*, **23**, 937 (1958).

[6] Other acetylphenylsilanes are currently being synthesized in these laboratories.

[7] R. Adams and C. R. Noller, *Org. Syntheses*, Coll. Vol. I, 2nd edition, 109 (1951).

[8] All melting points are uncorrected.

[9] H. O. House and J. W. Blaker, *J. Org. Chem.*, **23**, 335 (1958).

[10] A. I. Vogel, "A Text-book of Practical Organic Chemistry," Longmans, Green and Co., London, 1956, p. 743.

solution,[11] then with water. After drying the oil over sodium sulfate the fraction of b.p. 150–175°/40–50 mm. was collected as a colorless liquid which solidified to 220 g. (83%) of white prisms, m.p. 41°.

Anal. Calcd. for $C_{11}H_{16}OSi$: C, 68.72; H, 8.39. Found: C, 68.99; H, 8.27.

This compound was characterized as the semicarbazone, oxime, phenylhydrazone, and 2,4-dinitrophenylhydrazone.

4-Trimethylsilylacetophenone semicarbazone. This derivative was formed in the standard manner. Two recrystallizations from isopropyl alcohol yielded colorless needles, m.p. 221°.

Anal. Calcd. for $C_{12}H_{19}N_3OSi$: N, 16.85. Found: N, 16.82.

4-Trimethylsilylacetophenone oxime. To a solution of hydroxylamine hydrochloride (5 g.) in water (10 ml.) were added I (12.8 g.) and a solution of sodium hydroxide (3 g.) in water (5 ml.). Isopropyl alcohol was cautiously added until, on warming to about 70°, the solution became clear and free from insoluble droplets. The mixture was heated at reflux on the water bath for 4 hr., then poured into water (100 ml.), and allowed to crystallize overnight. The stubby prismatic crystals were filtered, washed with water, and drained, m.p. 90–91°. Yield, 13.7 g. (99%). Two recrystallizations from alcohol raised the m.p. to 92°.

Anal. Calcd. for $C_{11}H_{17}NOSi$: N, 6.76. Found: N, 6.74.

4-Trimethylsilylacetophenone phenylhydrazone and 2,4-dinitrophenylhydrazone. The phenylhydrazone was prepared by the same procedure as that employed for acetophenone phenylhydrazone.[12] Recrystallization from alcohol yielded very pale yellow needles, m.p. 93°. On standing at room temperature for two to three days the crystals darkened considerably and began to decompose. It is well known that the acetophenone derivative behaves similarly.

The *2,4-dinitrophenylhydrazone*[4] was prepared in the usual manner and melted at 195°.

Anal. Calcd. for $C_{17}H_{20}N_4O_4Si$: N, 15.05. Found: N, 14.94.

Di(4-acetylphenyl)dimethylsilane. This compound was prepared in a manner similar to that employed for the preparation of I, using the following amounts of reactants: magnesium turnings (60 g., 2.47 g. atoms), ketal (II) (486 g., 2.0 moles), dimethyldichlorosilane (129 g., 1.0 mole). After addition of dilute hydrochloric acid, ether extraction and washing with saturated calcium chloride followed by water, the ether solution was dried over sodium sulfate, then distilled. The colorless liquid (172 g., 58%) of b.p. 287–290°/40 mm. was collected and crystallized in the receiver. Two recrystallizations from alcohol gave white needles, m.p. 130°.

Anal. Calcd. for $C_{18}H_{20}O_2Si$: C, 72.95; H, 6.80. Found: C, 72.77; H, 6.58.

Di(4-acetylphenyl)dimethylsilane disemicarbazone was prepared in the usual manner. Recrystallization from alcohol gave white needles, m.p. 137°.

Anal. Calcd. for $C_{20}H_{26}N_6O_2Si$: N, 20.48. Found: N, 20.37.

Acknowledgment. The author thanks Mr. Richard G. Tonkyn for helpful discussions concerning this work. Thanks are also due to Miss Ethel Schiavon and Mr. Joseph Wirth for their experimental assistance.

RESEARCH LABORATORIES
NON-METALS UNIT
BOEING AIRPLANE COMPANY
SEATTLE, WASH.

---

(11) A stable emulsion results if water is used as the first wash liquid.

(12) H. Reisenegger, *Ber.*, **16**, 662 (1883); R. L. Shriner, W. C. Ashley, and E. Welch, *Org. Syntheses*, **Coll. Vol. III**, 726, (1955); F. G. Mann and B. C. Saunders, "Practical Organic Chemistry," Longmans, Green and Co., London, 1949, p. 177.

Alkali Metal Complexes of Phenylalanine Derivatives[1,2]

MURRAY GOODMAN AND KENNETH C. STUEBEN

Received June 30, 1958

During the course of our work on the synthesis of peptides, we noted disagreement in the literature as to the correct melting point of benzyloxycarbonyl-L-phenylalanine. Bergmann[3] and Smith[4] reported 126–128° for the L- and D-isomers respectively but Holley[5] pointed out that this material possessed abnormally high neutralization equivalents. In addition, Holley[5] found that the neutralization equivalent could be lowered considerably by treating the product with dilute hydrochloric acid. Recently, Kenner[6] and coworkers, employing countercurrent distribution, were able to isolate a fraction which had the correct neutralization equivalent and melted at 87°. In this communication we wish to report that the high melting materials previously isolated were complexes of benzyloxycarbonyl-L-phenylalanine with its sodium salt. Conclusive evidence for the nature of these complexes was initially obtained in our laboratories using the DL-isomer.

When we prepared benzyloxycarbonyl-DL-phenylalanine, we observed the appearance of a side product which melted at 168°, much higher than the recorded 103° of the desired product. Elemental analyses, molecular weight, and infrared spectra indicated that the side product was a 1:1 complex of benzyloxycarbonyl-DL-phenylalanine with its sodium salt. This substance was subsequently shown to be identical with that obtained by half-neutralizing a sample of the pure acid with standard sodium hydroxide.

In the case of the corresponding L-isomer the product prepared in the usual way consists of varying quantities of the free acid and its sodium salt as evidenced from the neutralization equivalents reported.[5,6] These crude products can be converted to pure benzyloxycarbonyl-L-phenylalanine melting at 87° by extended treatment with hydrochloric acid. It is possible, however, to isolate a substance corresponding almost exactly to a 1:1 complex by acidifying the Schotten-Baumann reaction mixture to *p*H 5. Further acidification

---

(1) Presented before the Organic Section of the American Chemical Society at the 133rd meeting, San Francisco, Calif., April 1958.

(2) This research was supported by a grant from the National Science Foundation.

(3) M. Bergmann, L. Zervas, H. Rinke, and H. Schleich, *Z. physiol. chem.*, 224, 33 (1934).

(4) C. S. Smith and A. E. Brown, *J. Am. Chem. Soc.*, **63**, 2605 (1941).

(5) R. W. Holley and A. D. Holley, *J. Am. Chem. Soc.*, **74**, 3069 (1952).

(6) D. W. Clayton, J. A. Farrington, G. W. Kenner, and J. M. Turner, *J. Chem. Soc.*, 1398 (1957).