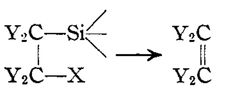
[CONTRIBUTION FROM THE WHITMORE LABORATORY OF THE SCHOOL OF CHEMISTRY AND PHYSICS, THE PENNSYLVANIA STATE COLLEGE]

γ-Eliminations Involving Silicon. A New Synthesis of the Cyclopropane Ring[1]

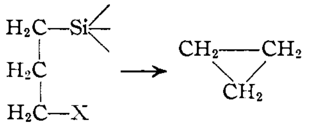
BY LEO H. SOMMER, RICHARD E. VAN STRIEN[2] AND FRANK C. WHITMORE[3]

In previous work[4] we found that the remarkable reactivity of halogen bound to carbon in the beta relation to silicon (X—C—C—Si≡) is associated with cleavage of the carbon–silicon bond. Many examples of this type of reaction have been found. All take place according to the general equation

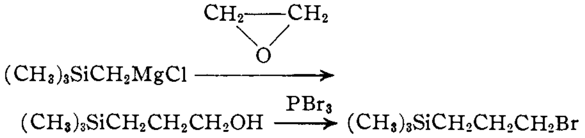

(1)

Equation (1) shows that these reactions are β-eliminations involving silicon, formally similar to the dehydrohalogenation of ordinary organic halides.

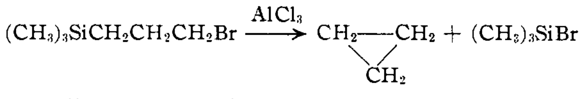
In extension of this work we have investigated the reactions of γ-haloalkyl silicon compounds and now report two γ-eliminations involving silicon which give cyclopropane.


(2)

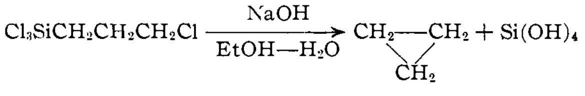
γ-Bromopropyltrimethylsilane was synthesized by the following sequence of reactions.



Warming with a catalytic amount of aluminum chloride gave a 92% yield of pure cyclopropane.



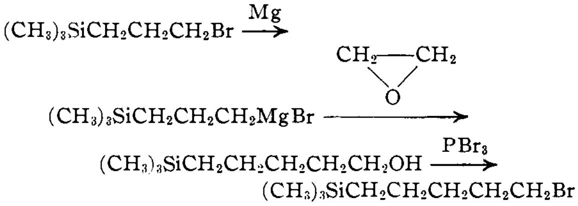
γ-Chloropropyltrichlorosilane also gave pure cyclopropane (31% yield) when heated with a solution of sodium hydroxide in aqueous ethanol.



In connection with a study of the reaction mechanisms of these γ-eliminations, it was found that when the reagents are interchanged, *i. e.*, γ-bromopropyltrimethylsilane is treated with base and γ-chloropropyltrichlorosilane is treated with aluminum chloride, no cyclopropane is formed. Furthermore, 5-bromopentyltrimethylsilane failed to give cyclopentane when treated with aluminum chloride in catalytic amounts.[5] Instead, somewhat impure 1-pentene was obtained in low yield. The other products were polymers, presumably polyamylenes, and trimethylbromosilane.

$$(CH_3)_3SiCH_2CH_2CH_2CH_2CH_2Br \xrightarrow{AlCl_3} (CH_3)_3SiBr + CH_2{=}CHCH_2CH_2CH_3 + (C_5H_{10})_n$$

5-Bromopentyltrimethylsilane was synthesized from γ-bromopropyltrimethylsilane by the reaction sequence



Experimental

Synthesis of γ-Bromopropyltrimethylsilane.—Ethylene oxide, 10 moles, dissolved in 750 cc. of dry ether was added to the Grignard reagent prepared from 5 moles of chloromethyltrimethylsilane. The reaction mixture was stirred for three days and then 1 liter of ether was distilled and replaced by 1 liter of dry benzene. After refluxing for twenty hours, the product was treated with 500 cc. of water followed by 3 liters of 10% hydrochloric acid. The organic layer was separated and the water layer extracted once with ether. After washing the ether-benzene solution of the product with saturated salt solution and drying with sodium sulfate, the ether and most of the benzene were removed by fractionation in a column of about 15 theoretical plates and the remaining material was rapidly distilled from a 1-liter distillation flask. This distillate was then fractionated in a glass-helix packed column of about 15 theoretical plates. There was obtained 468 g., 3.57 moles, of γ-hydroxypropyltrimethylsilane, b. p. 83° at 27 mm., n^{20}_D 1.4290, d^{20} 0.8316, a yield of 71%.

Anal. Calcd. for $C_6H_{16}SiO$: Si, 21.2. Found: Si, 21.3.

In a 1-liter flask equipped with a stirrer, reflux condenser and dropping funnel there was placed 326 g. (2.47 moles) of γ-hydroxypropyltrimethylsilane. The flask was cooled in an ice-bath and 350 g., 1.29 moles, of phosphorus tribromide was slowly added to the alcohol. After completion of the addition, the reaction mixture was allowed to warm to room temperature. This was followed by heating (85–90°) for a period of four hours. After cooling to room temperature, the reaction product was poured on ice and the resulting layers were separated. The organic layer was washed with water and then with dilute potassium carbonate solution. Drying was effected with sodium sulfate. Fractionation gave 404 g., 2.07 moles, of γ-bromopropyltrimethylsilane, b. p. 70° (25 mm.), n^{20}_D 1.4541, d^{20} 1.1173, a yield of 84%.

Anal. Calcd. for $C_6H_{15}SiBr$: Si, 14.4; Br, 41.0. Found: Si, 14.6; Br, 41.3.

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[1] XXIII in a series on organosilicon chemistry. For XXII see THIS JOURNAL, **71**, 2746 (1949).

[2] Taken in part from a thesis submitted by R. E. Van Strien in partial fulfillment of the requirements for the Ph.D. degree.

[3] Deceased June 24, 1947.

[4] (a) Sommer, Goldberg, Dorfman and Whitmore, THIS JOURNAL, **68**, 1083 (1946); (b) Sommer, Bailey and Whitmore, *ibid.*, **70**, 2869 (1948).

[5] When cyclopentane (10 g.) is refluxed with aluminum chloride (3 g.) for eight hours no change takes place; see Cox, *Bull. soc. chim.*, **37**, 1549 (1925).

Cyclopropane Formation from γ-Bromopropyltrimethylsilane.—The procedure used was as follows: The γ-bromopropyltrimethylsilane was placed in a 100-cc. flask equipped with a reflux condenser and a dropping bottle for introduction of aluminum chloride. The exit end of the condenser led to a 5-liter flask filled with saturated salt solution which was used to measure the volume of gas evolved.

γ-Bromopropyltrimethylsilane, 19.1 g., 0.098 mole was placed in the reaction flask and treated with a few crystals of sublimed aluminum chloride (*ca.* 0.2 g.). Reaction was spontaneous and the reaction mixture became somewhat cooler than room temperature. After most of the reaction had taken place, gentle heating was applied by means of a water-bath held at 70°. Air was then passed into the reaction flask in order to sweep all of the gaseous product into the receiving flask. The gas mixture collected comprised 2960 cc. of which 670 cc. was shown to be air by gas analysis.

A sample of the gas mixture was condensed in a trap cooled in Dry Ice acetone mixture, and was then charged to the isothermal distillation apparatus of Zook, Oakwood and Whitmore.[6] After removal of air, a series of vapor pressure–temperature measurements were made and the data were plotted for comparison with cyclopropane and propylene.[7] Figure 1 shows that the gaseous product of the reaction is pure cyclopropane. The yield was 92%.

The material remaining in the reaction flask consisted of 12.5 g., 82% yield, of trimethylbromosilane, b. p. 79° (732 mm.)[8]; Br, 52.4 (calcd., 52.3).

Formation of Cyclopropane from γ-Chloropropyltrichlorosilane.—In a 500-cc. flask equipped with a reflux condenser connected to a gas collector, and a dropping funnel, was placed a solution of 28 g., 0.50 mole, of potassium hydroxide dissolved in 100 cc. of absolute ethanol. Then 24.6 g., 0.116 mole of γ-chloropropyltrichlorosilane[9] was slowly added to this solution. An immediate reaction took place as each portion of γ-chloropropyltrichlorosilane was added, a precipitate of potassium chloride being formed. At the end of the addition, the reaction mixture was brought to reflux. However, the volume of gas collected amounted to only 70 cc. when the reaction mixture was cooled to room temperature. To the reaction flask were then added 150 cc. of water and an additional 28 g. of potassium hydroxide. The material was once more brought to reflux and the total volume of gas collected was 1320 cc. of which 410 cc. was shown to be air.

Following a procedure similar to that used above, the gaseous product of the reaction was shown to be pure cyclopropane (see Fig. 1). The yield was 31%.

Reaction of γ-Bromopropyltrimethylsilane with Potassium Hydroxide in 50% Aqueous Ethanol.—γ-Bromopropyltrimethylsilane (0.067 mole) was treated with a solution of potassium hydroxide (56 g., 1 mole) in 50% aqueous ethanol (260 cc.) at reflux temperature for five hours. No gas was evolved. Reaction was shown to be complete by treatment of the product with silver nitrate and weighing the silver bromide formed. Apparently, normal dehydrohalogenation and/or metathesis occurred. Since the major point under investigation was formation or non-formation of cyclopropane, and because of lack of material, a larger run was not made, and the organosilicon products were not identified.

Reaction of γ-Chloropropyltrichlorosilane with Aluminum Chloride.—In a 50-cc. flask was placed 9.7 g. of γ-chloropropyltrichlorosilane. Through the top of the reflux condenser was added a few crystals of aluminum chloride. No reaction was observed at room temperature. Upon heating by means of a water-bath held at 60°, the liquid turned brown. Heating was gradually increased and the reaction mixture was finally heated for two hours at 95–97°. Throughout the heating period there was no appreciable formation of a gaseous product. After cooling, the product was distilled at reduced pressure until the temperature reached 135° at 35 mm. Distillation of this material at atmospheric pressure gave only 2.7 g. of material boiling between 60° and 180°. A residue of about 3 g. of viscous material was also not identified. The complex mixture of products obtained in this reaction are characteristic of the reaction of many organic compounds with aluminum chloride at about 100° for a number of hours.

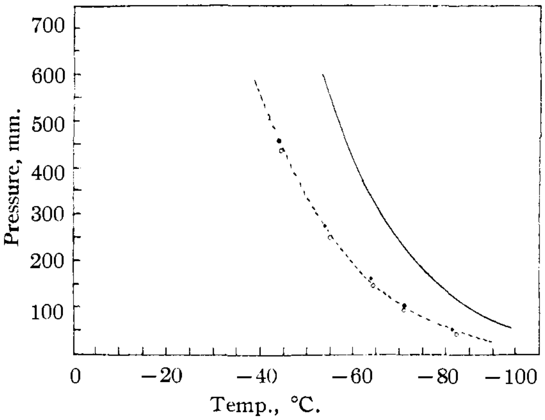

Fig. 1.—Vapor pressure curves: O, cyclopropane from γ-bromopropyltrimethylsilane; ●, cyclopropane from γ-chloropropyltrichlorosilane; ----, cyclopropane curve from the literature; —, propylene curve from the literature.

Synthesis of 5-Bromopentyltrimethylsilane.—The Grignard reagent was prepared in the usual manner from 390 g., 2 moles, of γ-bromopropyltrimethylsilane and 48 g. of magnesium turnings in 1 liter of ether. To the Grignard reagent was added 200 cc. of ethylene oxide dissolved in 150 cc. of dry ether. On standing for a period of eighteen hours at room temperature the reaction mixture solidified. This was treated with 2 liters of water followed by addition of sufficient hydrochloric acid to render the mixture acid to litmus. The water layer was extracted with pentane and the combined organic layers were washed with potassium carbonate solution and then with water. After drying with anhydrous sodium sulfate, fractionation gave 206 g., 1.3 moles, of 5-hydroxypentyltrimethylsilane, b. p. 85° at 8 mm., $n^{20}{}_{D}$ 1.4371, 64% yield.

Anal. Calcd. for $C_8H_{20}SiO$: Si, 17.50. Found: Si, 17.45.

In a 100-cc. reaction flask equipped with a condenser and dropping funnel was placed 42.9 g., 0.27 mole, of 5-hydroxypentyltrimethylsilane. Phosphorus tribromide, 36 g., 0.13 mole, was then slowly added with frequent shaking of the flask. After standing at room temperature for eighteen hours, followed by heating at 95–99° for one hour, the layers were separated. Ether was added to the organic layer which was then washed twice with water and once with ammonium hydroxide. The product was dried over calcium chloride and fractionated under reduced pressure. There was obtained 47.1 g., 0.21 mole, of 5-bromopentyltrimethylsilane, b. p. 113° at 23 mm., $n^{20}{}_{D}$ 1.4570, 78% yield.

Anal. Calcd. for $C_8H_{19}SiBr$: Si, 12.57; Br, 35.81. Found: Si, 12.72; Br, 35.66.

Reaction of 5-Bromopentyltrimethylsilane with Aluminum Chloride.—A 200-cc. flask was equipped with a condenser arranged for distillation. 5-Bromopentyltrimethylsilane was placed in the flask and a few small crystals of aluminum chloride were added. Reaction was spontaneous, but heat was applied to distill any volatile

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[6] Design of the apparatus will be submitted for publication.

[7] (a) Ruehrwein and Powell, THIS JOURNAL, **68**, 1063 (1946); (b) Burrel and Robertson, *ibid.*, **37**, 2188 (1945).

[8] Gilliam, Meals and Sauer, THIS JOURNAL, **68**, 1161 (1946); Pray, Sommer, Goldberg, Kerr, DiGiorgio and Whitmore, *ibid.*, **70**, 433 (1948).

[9] Sommer, Dorfman, Goldberg and Whitmore, THIS JOURNAL, **68**, 488 (1946).

material which formed. Two runs, utilizing a total of 108 g., 0.485 mole, of the bromide were made.

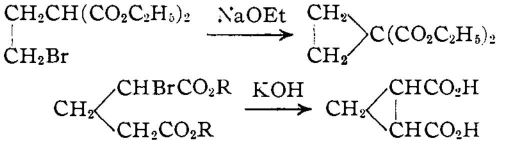
The combined distillate, 54 g., which contained trimethylbromosilane, was carefully washed with ice-water and then with potassium carbonate solution. All washings were made in capped bottles to prevent loss by volatilization. Drying was effected with sodium sulfate to give 34 g. of product. Fractionation in a column of 40 theoretical plates gave 6.0 g. of somewhat impure pentene-1, b. p. 28.6–29.5° at 732 mm., $n^{20}D$ 1.3702–1.3722, d^{20} 0.644,[10] which was identified by characterization of its ozonolysis products as formaldehyde (dimedone deriv., m. p., 189–190°) and butyraldehyde (2,4-dinitrophenylhydrazone deriv. m. p. 120–121°). The yield of impure pentene-1 was 17%. No evidence was found for formation of cyclopentane, b. p. 49.3° at 760 mm., $n^{20}D$ 1.40645, or ethylcyclopropane, b. p. 32.5°, $n^{20}D$ 1.379.[11]

In addition to pentene-1, there was also obtained from the fractionation 15.0 g., 0.098 mole, of hexamethyldisiloxane, b. p. 98°, $n^{20}D$ 1.3770, and a higher-boiling residue of 3.8 g.

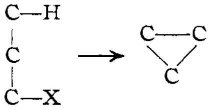
Fractionation of the material originally remaining in the reaction flask gave 20.1 g., 0.131 mole, of trimethylbromosilane, b. p. 77° at 725 mm., Br 52.6 (calcd. 52.3), and a residue of black tarry material, likely consisting of polymerized pentene. The yield of recovered material containing the trimethylsilyl group was 67%.

Discussion

Some Common Aspects of γ-Eliminations Involving Silicon and Other Syntheses of Cyclopropyl Compounds.—One of the methods for closing the cyclopropane ring involves γ-elimination of hydrogen halides from organic compounds. The following equations provide two examples of this type of synthesis.[12]

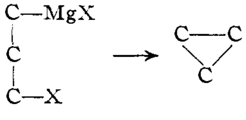


A large number of cyclopropane derivatives (but not cyclopropane itself) have been prepared by these reactions which take the general form



(3)

For the preparation of cyclopropane, reaction of an active metal such as magnesium or sodium with a 1,3-dihalopropane in an organic solvent may be used. In these reactions it seems probable that cyclopropane is formed from an organometallic intermediate.[13]



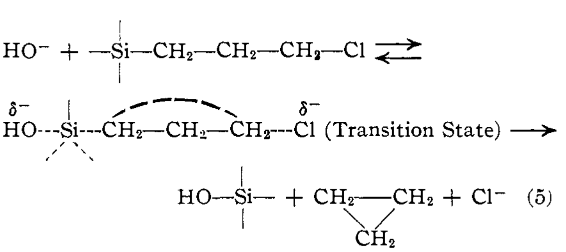
(4)

Comparison of equations (2), (3) and (4) indicates that the formation of cyclopropyl compounds from γ-haloalkyl silicon compounds and from purely organic halides are similar in three general ways: (1) Both give cyclopropyl compounds by 1:3 elimination reactions. (2) Both involve removal of an element more electropositive than carbon (silicon, hydrogen, or an active metal)[14] together with an element more electronegative than carbon (halogen). (3) Both types involve electron-release to carbon from an element more electropositive than carbon.

Similar considerations apply to a comparison of β-eliminations involving silicon with the dehydrohalogenation of purely organic halides to give olefins.[4b]

Mechanism.—β-Eliminations involving silicon are greatly accelerated by bases and take place by a one-stage mechanism involving initial nucleophilic attack on silicon. A study of the effect of structural variations in the β-haloalkylsilane on reaction velocity has shown that substitution of a single halogen on silicon by alkyl results in a tenfold decrease in rate. This relationship of structure to reactivity is the expected one for a mechanism involving nucleophilic attack on silicon since the presence of electronegative substituents should make the silicon a more effective center for nucleophilic attack.[4b]

If the mechanism of cyclopropane formation from compound II and alkali involves nucleophilic attack on silicon as the major driving force, it should follow that a decrease in the electrophilic activity of the silicon, *i. e.*, by replacement of halogen on silicon by alkyl, would result in a decrease of reaction velocity or in complete prevention of the reaction. The effect on γ-elimination should far exceed that on β-elimination because of the lesser ease of formation of cyclopropane as compared to olefin formation. The observed facts and the nucleophilic character of aqueous base are therefore in complete harmony with the following mechanism



(5)

The above mechanism is closely similar to the mechanism of γ-eliminations of purely organic compounds with bases which consist of 1:3 elimination of HX.[14a]

$$B^- + H—C—C—C—X \rightleftarrows$$

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[10] Physical constants for pentene-1 are b. p. 30.1° at 760 mm., $n^{20}D$ 1.3714, d^{20} 0.630. See Egloff, "Physical Constants of Hydrocarbons," Vol. I, Reinhold Publishing Corporation, New York, N. Y., 1940.

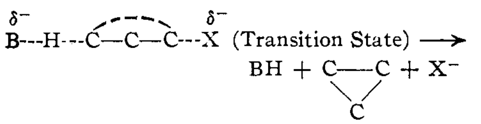
[11] See ref. 10, Vol. II.

[12] See Fuson in Gilman, "Organic Chemistry," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 65–67.

[13] Hass, *Ind. Eng. Chem.*, **28**, 1178 (1936).

[14] Pauling, "Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1940, p. 60.

[14a] Hauser, THIS JOURNAL, **62**, 933 (1940).

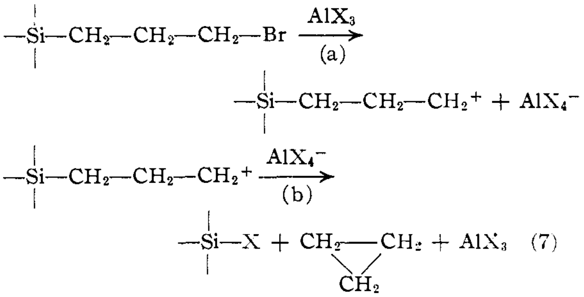


(6)

In these latter syntheses of cyclopropyl compounds nucleophilic attack on γ-hydrogen is facilitated by the activating effect of a carbonyl group adjacent to the hydrogen atom.

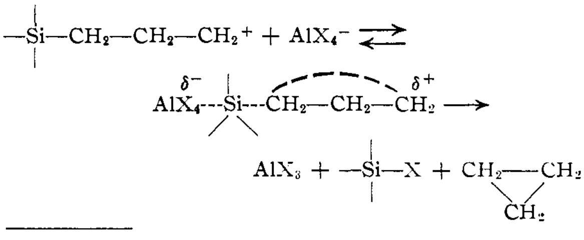
The only difference between the mechanisms is that in (5) the base attacks electropositive silicon instead of the protonic part of an activated hydrogen atom.

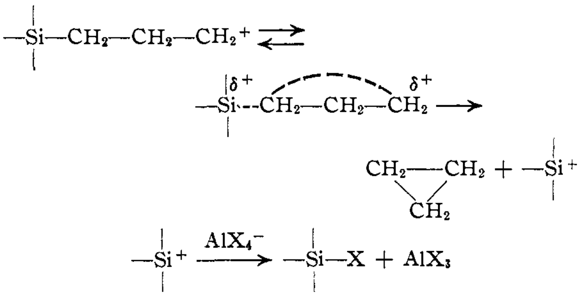
Previous work has shown that electron-release from silicon to electronically deficient carbon in the beta relation to silicon constitutes a general mechanism whereby cleavage of the carbon–silicon bond can occur in a variety of organosilicon structures.[4b] β-Eliminations involving silicon which take place with electrophilic reagents such as aluminum chloride are examples of reactions proceeding by this mechanism. The electropositive nature of silicon and the ability of aluminum chloride to cause ionization of the carbon–halogen bond make a similar mechanism seem probable for the reaction of γ-bromopropyltrimethylsilane with aluminum chloride.[15]



(7)

There are two reaction paths for the silicon in (7b) which comprise possible extremes of mechanism: (1) A transition state in which the siliconium ion is transferred to the new linkage with halogen without being set free. (2) A reaction process in which a siliconium ion is actually set free prior to combination with halogen from AlX_4^-.





The question as to whether a siliconium ion is set free for a period of time sufficient for the designation of such an ion as an actual reaction intermediate, or is transferred to the new linkage without acquiring the full status of an ion, is an interesting one. However, we wish to make it clear that the important general aspects of the mechanism given in equation (7) in no way depend upon the degree of freedom of the siliconium ion involved. These aspects are adequately summarized by the concept that the major driving force for these reactions derives from the ability of electropositive silicon to release an electron-pair to electronically deficient carbon within the molecule, regardless of whether the silicon has started to combine with an anion at substantially the same time. Similar considerations apply to β-eliminations involving silicon which result from reaction with electrophilic reagents.[16]

The failure of 5-bromopentyltrimethylsilane to give cyclopentane when treated with aluminum chloride is in accord with the mechanism for cyclopropane formation given in (7). In 5-bromopentyltrimethylsilane the deficiency on carbon is created at a distance from silicon which is great enough to prevent an intramolecular transmission of charge sufficient for cyclization, despite the lesser strain involved in a 5-membered ring.

Summary

1. A synthesis of pure cyclopropane has been found which results from γ-elimination of silicon and halogen from two organosilicon compounds.

2. Proposed mechanisms for these γ-eliminations involve as major driving forces (1) nucleophilic attack on silicon, and (2) electrophilic attack on halogen in the group being cleaved from silicon.

3. The latter type of γ-elimination extends the applicability of the concept of electron-release from silicon to electronicallydeficient carbon as constituting *one* major factor in eliminations involving silicon. Formation of free siliconium ions

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[15] The failure of γ-chloropropyltrichlorosilane to give cyclopropane with aluminum chloride is very likely due to the inhibiting effect of chlorine substituents on silicon (relative to alkyl) toward electron-release from silicon to electronically deficient carbon. For example, work on intramolecular rearrangements has shown that the replacement of only one alkyl group on silicon by a chlorine substituent completely prevents intramolecular rearrangement with aluminum chloride of $(CH_2)(CH_3)_2SiCl$ as compared to $(CH_2Cl)(CH_3)_3Si$: paper presented before the Organic Division in Chicago, April 22, 1948. These effects are readily explained on an inductive effect basis.

[16] Swain, Esteve and Jones, THIS JOURNAL, **71**, 965 (1949), have recently shown that a siliconium ion intermediate is unlikely in the reaction of triphenylfluorosilane with the relative weak electrophilic reagent, 50% water–50% acetone solution. These authors further point out, however, that their work does not preclude the possibility of siliconium ion intermediates with more powerful electrophilic reagents such as aluminum chloride.

as reaction intermediates is not a necessary condition for reactions proceeding by this mechanism. The greater or lesser degree of freedom of such ions must depend upon the organosilicon compound undergoing reaction, the attacking reagent, and the reaction medium, whereas the only essential requirement for reactions proceeding by the above mechanism is the creation of electron-deficiency at a carbon atom which is sufficiently close to the silicon so as to cause release of an electron-pair from silicon to carbon.

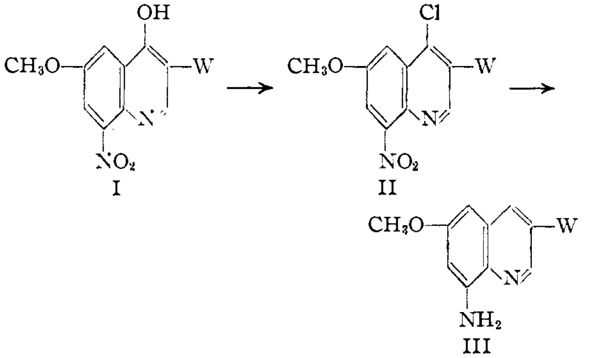
State College, Pa. Received February 25, 1949

[Contribution from the Chemical Laboratory of Northwestern University]

6-Methoxy-8-nitroquinolines with Substituents in the 3- and 4-Positions[1]

By Robert H. Baker, J. G. Van Oot, Samuel W. Tinsley, Jr., Dorothy Butler and Byron Riegel

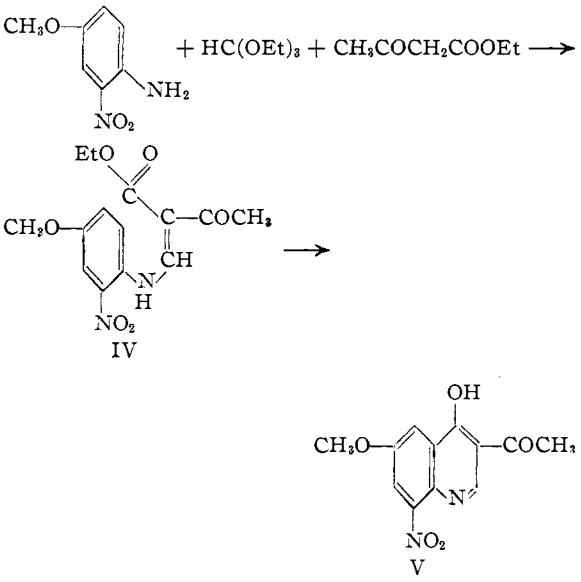
A common procedure for the replacement of hydroxyl by hydrogen in 4-quinolinols is conversion to the halide followed by reduction. Although this sequence of reactions had not been studied when other groups were in the 3-position, it appeared to be an attractive route to the 3-substituted-6-methoxy-8-aminoquinolines, III.



(W = CN, COOEt, C_6H_5 or CH_3CO)

The conversion to the halide, II, was difficult but could be accomplished with a mixture of phosphorus oxychloride and pentachloride.[2] However, none of a variety of conditions of hydrogenation over palladium, platinum or Raney nickel catalysts would effect reductive dehalogenation of II to III.

The preparation of 3-acetyl-6-methoxy-8-nitro-4-quinolinol (V) was accomplished by cyclization of the "anil" (IV) which in turn could be made by three methods. Direct combination of the nitroanisidine, ortho ester and keto ester is simpler but gives poorer yields than the reaction of the anisidine with ethoxymethyleneacetoacetic ester (formed by prior reaction of the latter two reagents). The third method involves reaction of the ortho ester and anisidine to give the substituted diphenylformamidine which in turn reacts with the keto ester.[3] Attempts were also made to produce ethoxymethylene-*m*-nitroanisidine which would be expected to be a useful intermediate but generally the diarylformamidine was the product.



Considerable difficulty has been encountered during "anil" formation in the use of α-formyl esters for quinolinol syntheses.[4] With formylphenylacetic ester and *m*-nitroanisidine, this difficulty is overcome by the use of zinc chloride to catalyze the reaction.

Successful attempts to prepare plasmochin-type drugs with blocking groups in the 3-position will be described in forthcoming publications.

Experimental[5]

3-Acetyl-6-methoxy-8-nitro-4-quinolinol.—Equimolar quantities of *m*-nitroanisidine and ethyl ethoxymethyleneacetoacetate were heated at 150° for fifteen minutes, cooled and the "anil" crystallized from ethanol in quantitative yield, m. p. 153–154°. This material was added to fifteen times its weight of boiling Dowtherm (a mixture of biphenyl and diphenyl ether). Eighteen minutes of

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(1) This work was supported by a grant from the National Institute of Health, U. S. Public Health Service.

(2) C. C. Price, N. J. Leonard and H. F. Herbrandson, This Journal, **68**, 1251 (1946), used thionyl chloride for this conversion on simpler compounds but we were unable to use it in this work.

(3) These combinations of reactants were previously studied by H. R. Snyder and R. E. Jones, *ibid.*, **68**, 1253 (1946).

(4) Because of this, we have previously used the α-oxalyl esters and subsequent decarboxylation, R. H. Baker and R. M. Dodson, *ibid.*, **68**, 1283 (1946); B. Riegel, C. J. Albisetti, Jr., G. R. Lappin and R. H. Baker, *ibid.*, **68**, 2685 (1946).

(5) Microanalyses by Jane Gibbs, Rosalind Guy and Virginia Hobbs.