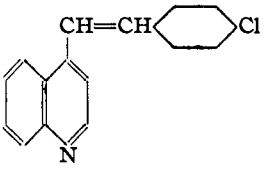
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

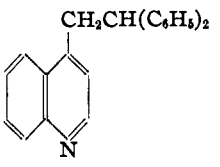
The Addition of Benzene to Benzalquinaldines and Benzallepidines

BY REYNOLD C. FUSON, L. L. ALEXANDER, ELLSWORTH ELLINGBOE AND ARNOLD HOFFMAN

The conversion of benzalquinaldines[1] and similarly constituted compounds[2] into the corresponding α-benzohydryl derivatives appears to involve a reversible 1,4-addition of aromatic compounds to conjugated systems. The principle of vinylogy[3] suggests that a similar result might be obtained with benzallepidines in which the reaction would depend on a reversible 1,6-addition. To test this, benzallepidine and *p*-chlorobenzallepidine (I) were prepared and subjected to the treatment with benzene in the presence of aluminum chloride and hydrogen chloride. A compound corresponding to the expected α-benzohydryllepidine (II) was produced. The action of phenylmagnesium bromide likewise converted benzallepidine into a compound with the same composition as II. The two products proved, however, to be isomeric rather than identical.



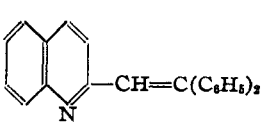
I



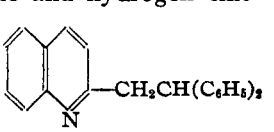
II

In view of this result, it became necessary to determine the structures of these isomers as well as that of α-benzohydrylquinaldine whose structure had been assigned upon the results of these two types of addition reactions which have now been called in question.

The structure of α-benzohydrylquinaldine (IV) was established by synthesis. β-Phenylbenzalquinaldine (III) was made from benzophenone and lithiumquinaldine according to the method of Ziegler and Zeiser[4] and reduced catalytically. The hydrogenation was also effected by the use of benzene, aluminum chloride and hydrogen chloride. Efforts to synthesize the corresponding chloro compound from 1-*p*-chlorophenyl-1-phenyl-2-(2-quinolyl)-ethanol were unsuccessful.

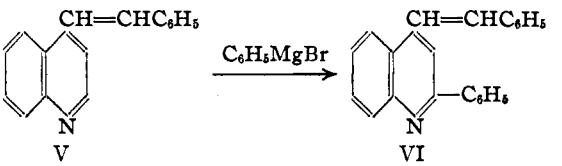


III



IV

The product obtained by the action of phenylmagnesium bromide on benzallepidine was shown to be 2-phenyl-4-styrylquinoline (VI). This compound was prepared by condensing α-phenyllepidine with benzaldehyde according to the method of John and Fischel.[5] From this result it became evident that the addition of phenylmagnesium bromide involved the 1,2- rather than the 1,6-positions



V VI

The isomer produced by the addition of benzene to benzallepidine is evidently α-benzohydryllepidine (II). This is indicated by the close analogy with α-benzohydrylquinaldine, the structure of which is now certain. The synthesis from the *p*-chlorobenzallepidine by the action of benzene, aluminum chloride and hydrogen chloride shows that the phenyl group takes the position adjacent to the *p*-chlorophenyl radical rather than that adjacent to the quinoline ring. Otherwise, the quinolyl rather than the *p*-chlorophenyl radical would have been replaced.

Experimental

***p*-Chlorobenzallepidine.**—Equivalent amounts of lepidine and *p*-chlorobenzaldehyde were heated for six hours at 125° in the presence of a small amount of anhydrous zinc chloride. The product was triturated with ammonium hydroxide, removed by filtration and washed with cold alcohol. It crystallized from alcohol in yellow fibrous needles melting at 127–128°; yield 70%. The benzal compound decolorized a solution of bromine in carbon tetrachloride and discharged the color of permanganate solutions in acetone.

Anal. Calcd. for $C_{17}H_{12}NCl$: C, 76.83; H, 4.56; Cl, 13.4. Found: C, 76.95; H, 4.61; Cl, 13.2.

α-Benzohydryllepidine

A. From Benzallepidine.—Following the general procedure of Fuson, Farlow and Hoffman,[1a] dry hydrogen chloride was passed into a mixture of 2 g. of benzallepidine, 4 g. of anhydrous aluminum chloride and 40 cc. of

(1) (a) Hoffman, Farlow and Fuson, THIS JOURNAL, **55**, 2000 (1933); (b) Fuson, Kozacik and Eaton, *ibid.*, **55**, 3799 (1933).

(2) For other references, see Woodward, Borcherdt and Fuson, *ibid.*, **56**, 2103 (1934).

(3) Fuson, *Chem. Rev.*, **16**, 1 (1935).

(4) Ziegler and Zeiser, *Ann.*, **485**, 174 (1931).

(5) John and Fischel, *Ber.*, **59**, 722 (1926).

dry benzene until the gas was no longer absorbed. The mixture was stirred for three hours and then poured into an ice–hydrochloric acid mixture. The semi-solid product was heated with ammonium hydroxide for a short time, cooled and extracted with ether. The crystalline product remaining after the evaporation of the ether was recrystallized from alcohol; m. p. 130–131°.

Anal. Calcd. for $C_{28}H_{19}N$: C, 89.28; H, 6.19; N, 4.53. Found: C, 89.18; H, 6.21; N, 4.60.

B. From *p*-Chlorobenzallepidine.—α-Benzohydryllepidine was obtained from *p*-chlorobenzallepidine by a procedure similar to the preceding one.

β-Phenylbenzalquinaldine (III).—This compound was prepared by the method of Ziegler and Zeiser.[4] Its structure was confirmed by oxidation. With chromic acid it gave benzophenone.

α-Benzohydrylquinaldine (IV).—This compound was prepared by the reduction of β-phenylbenzalquinaldine. The reduction was carried out in two ways.

(a) By the Friedel–Crafts Method.—A mixture of 5.5 g. of β-phenylbenzalquinaldine, 50 cc. of dry benzene and 15 g. of anhydrous aluminum chloride was saturated at room temperature with dry hydrogen chloride gas. The mixture was shaken in a closed container for twenty hours. The color changed from bright red to brown. The reaction mixture was decomposed in an ice–hydrochloric acid mixture. The semi-solid hydrochloride was separated on a filter, washed with benzene and with water and finally heated with ammonium hydroxide for one hour to regenerate the free amine. The solid was recrystallized from alcohol; m. p. 119–121°. The yield was 92%. A mixed melting point determination with α-benzohydrylquinaldine showed no depression.

(b) By Catalytic Reduction.—Hydrogenation in the presence of a platinum–platinum oxide catalyst converted the β-phenylbenzalquinaldine into α-benzohydrylquinaldine. The samples prepared by methods (a) and (b) and that of Hoffman, Fuson and Farlow proved to be identical.

1-*p*-Chlorophenyl-1-phenyl-2-(2-quinolyl)-ethanol.—The method of Ziegler and Zeiser for the halogen-free carbinol was used. From 30 g. of *p*-chlorobenzophenone was obtained 43 g. of carbinol melting at 127–130°. The pure compound (from alcohol) melted at 140.5–141°.

Anal. Calcd. for $C_{28}H_{18}ONCl$: C, 76.75; H, 5.02. Found: C, 76.60; H, 5.18.

Attempts to dehydrate this carbinol by treatment with sulfuric acid, iodine, potassium bisulfate or acetic anhydride were unsuccessful. The only solid product which was isolated was *p*-chlorobenzophenone.

2-Phenyl-4-styrylquinoline (VI).—To an ether solution of benzallepidine an excess of phenylmagnesium bromide was added. The mixture was heated, with stirring, for five hours. Decomposition with ice and hydrochloric acid gave a gummy mass which, when treated with ammonium hydroxide, gave the free base. The pure compound (from alcohol) melted at 102.5–103.5°.

Anal. Calcd. for $C_{23}H_{17}N_3$: N, 4.56. Found: N, 4.74.

A mixture of this compound with a specimen of 2-phenyl-4-styrylquinoline, prepared by the method of John and Fischel,[5] melted at 102–103°.

Summary

1. Benzallepidine and *p*-chlorobenzallepidine react with benzene in the presence of aluminum chloride and hydrogen chloride to give α-benzohydryllepidine.

2. Benzallepidine reacts with phenylmagnesium bromide to give 2-phenyl-4-styrylquinoline.

3. The structure of α-benzohydrylquinaldine has been confirmed by synthesis.

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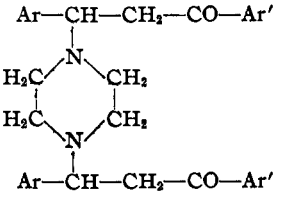
[CONTRIBUTION FROM THE ORGANIC CHEMICAL LABORATORY OF THE UNIVERSITY OF FLORIDA]

Derivatives of Piperazine. IX. Addition to Conjugate Systems. I

BY VINCENT E. STEWART AND C. B. POLLARD

Additive compounds of benzalacetophenone (chalcone) with ammonia and primary aromatic amines were prepared by Tambor and Wildi.[1] The reaction goes readily in the cold, generally with or without alkali. They were not successful in adding secondary aromatic or mixed secondary bases. An addition compound of benzalacetophenone with piperidine was prepared by Georgi and Schwyzer;[2] upon heating with water it splits into the original substances. Bain[3] reported that he obtained an addition compound of benzalacetophenone with piperazine. We have verified his results, and have endeavored to determine the generality of this addition.

Chalcone and most substituted chalcones readily add piperazine to yield a compound of the type



The addition is effected readily by refluxing the

(1) Tambor and Wildi, *Ber.*, **31**, 349 (1898).
(2) Georgi and Schwyzer, *J. prakt. Chem.*, **86**, 273–276 (1912).
(3) Bain, unpublished work, University of Florida.