2. Certain pharmacological properties of dihydroeugenol, eugenol and some of their derivatives have been studied.

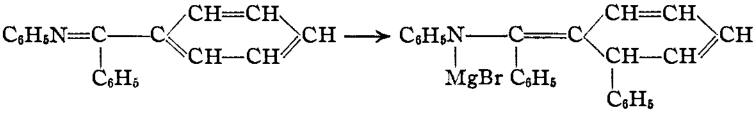
PITTSBURGH, PENNSYLVANIA
RECEIVED OCTOBER 3, 1932
PUBLISHED MAY 6, 1933

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

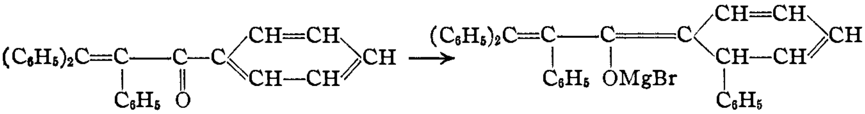
Ring–Chain Conjugation in the Quinoline Series

BY ARNOLD HOFFMAN, MARK W. FARLOW AND REYNOLD C. FUSON

There are many types of evidence which indicate that conjugation occurs between aromatic rings and their unsaturated side-chains containing suitably placed multiple linkages. The most convincing evidence of conjugation in this type of molecule is that in certain cases 1,4-addition of the Grignard reagent has been observed. This type of addition is characteristic of systems of conjugated double bonds in which a terminal position is occupied by an electronegative atom such as oxygen or nitrogen. It has recently been shown to take place even when one of the double bonds is situated in a benzene ring. Gilman, Kirby and Kinney[1] have found that phenylmagnesium bromide adds to benzophenone anil

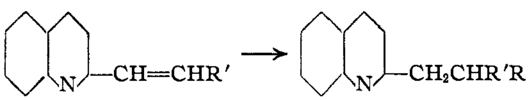


and similarly, Kohler and Nygaard[2] have observed the addition of phenylmagnesium bromide to tetraphenylpropenone



In both of these cases the ethylenic double bond involved in the addition reaction is situated in a benzene ring. The present paper deals with a similar case of ring–chain conjugation in which, however, the ethylenic double bond is in the side-chain and is conjugated with a nitrogen–carbon double bond situated in an aromatic ring.

The compounds which have been studied are benzalquinaldines and with RMgX they have been found to undergo the following transformation



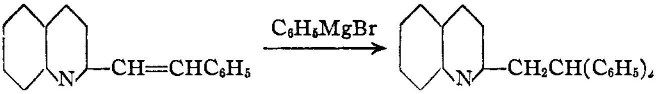
Benzalquinaldine when treated with a solution of phenylmagnesium

---

(1) Gilman, Kirby and Kinney, THIS JOURNAL, **51**, 2252 (1929).

(2) Kohler and Nygaard, *ibid.*, **52**, 4128 (1930).

bromide gave a 70% yield of the expected addition product, α-benzohydrylquinaldine



This compound was further characterized by the preparation of a monobromo derivative—presumably α-bromo-α-benzohydrylquinaldine—and the picrate.

In view of the fact that in the presence of aluminum chloride the addition of benzene is characteristic of conjugated systems of certain types, this reaction was tried with benzalquinaldine. The product was found to be identical with that obtained when phenylmagnesium bromide was used—namely, α-benzohydrylquinaldine.

In order to see if these reactions were general for benzalquinaldines, the behavior of *p*-chlorobenzalquinaldine was studied. This base was prepared by the interaction of *p*-chlorobenzaldehyde and quinaldine in the presence of zinc chloride. It was a solid melting at 139.5° and gave a dibromo derivative melting at 175°. The reaction of *p*-chlorobenzalquinaldine with phenylmagnesium bromide was similar to that observed with benzalquinaldine. α-(*p*-Chlorobenzohydryl)-quinaldine, melting at 91.5–92.5°, was obtained in a yield of 64% of the theoretical.

In an attempt to add benzene to *p*-chlorobenzalquinaldine in the presence of anhydrous aluminum chloride an unexpected result was obtained. Instead of the expected α-(*p*-chlorobenzohydryl)-quinaldine there was obtained a good yield of α-benzohydrylquinaldine. The chlorine atom had been smoothly removed during the reaction. It is interesting to note that when the reactants are kept free from moisture this condensation does not take place. Apparently, the addition of a little water brings about the reaction by liberating hydrogen chloride from the aluminum chloride by hydrolysis. It was, in fact, later found that the reaction could be made to proceed rapidly if dry hydrogen chloride was run into the reaction flask. These experiments suggest that the condensation involves the hydrochloride of the base rather than the free base itself. This is in harmony with the mechanism of Vorländer and Friedberg[3] proposed to explain certain similar cases of the addition of aromatic hydrocarbons to conjugated systems of this type. This unusual behavior is being investigated further.

Experimental

α-Benzohydrylquinaldine (First Method).—A solution of benzalquinaldine in dry ether was slowly added to an equimolecular amount of phenylmagnesium bromide in ether. Reaction was indicated by the appearance of a deep red color. The addition was carried out at room temperature and was completed in an hour. The mixture was then heated for an hour under reflux and after being cooled was decomposed by an ice–

---

(3) Vorländer and Friedberg, *Ber.*, **56**, 1144 (1923).

hydrochloric acid mixture. The gummy material was separated from the ether by decantation. It was then treated with boiling concentrated hydrochloric acid whereby it was converted into an oil which solidified on being cooled. The solid was treated with ammonium hydroxide and recrystallized from 80% alcohol. It separated in the form of large, colorless crystals melting at 121–121.5°. The yield was about 70% of the theoretical.

Anal. Calcd. for $C_{23}H_{19}N$: C, 89.3; H, 6.2; N, 4.5. Found: C, 89.6; H, 6.5; N, 4.6.

α-Benzohydrylquinaldine (Second Method). A mixture of 20 g. of anhydrous aluminum chloride and 8 g. of benzalquinaldine in 100 cc. of dry benzene was allowed to stand twelve hours in a flask protected by a calcium chloride drying tube. The color of the solution changed gradually from yellow to dark brown. The reaction mixture was decomposed with ice and hydrochloric acid. The brown semi-solid mass which resulted was washed with benzene, heated with ammonium hydroxide solution, cooled to room temperature and filtered. The solid thus obtained was treated with boneblack to remove the color and was recrystallized from alcohol. It melted at 120–121° and was shown by the mixed melting point method to be identical with the α-benzohydrylquinaldine described above.

Monobromide.—Bromination was carried out by means of a modification of the method of Hammick.[4] Four and eight-tenths grams of α-benzohydrylquinaldine was dissolved in a mixture of 13 g. of glacial acetic acid and 7 g. of sodium acetate. Two cubic centimeters of bromine dissolved in 30 cc. of glacial acetic acid was then added and the reaction mixture was heated for some time. In this way a small amount of a monobromo derivative was obtained. After several recrystallizations from alcohol, it melted at 131.5–132.5°.

Anal. Calcd. for $C_{23}H_{18}NBr$: Br, 20.6. Found: Br, 20.7.

Picrate.—Alcoholic solutions of equivalent amounts of picric acid and α-benzohydrylquinaldine were mixed at 70°. The picrate separated at once in the form of yellow needles. It decomposed above 200°. The yield was nearly quantitative. When treated with a hot dilute solution of sodium hydroxide the picrate was decomposed and the original base was recovered.

Anal. Calcd. for $C_{29}H_{22}N_4O_7$: N, 10.5. Found: N, 10.3.

p-Chlorobenzalquinaldine.—Equimolecular amounts of quinaldine and *p*-chlorobenzaldehyde were mixed with a small amount of zinc chloride and heated for four hours at 140–160°. The hard brown mass was cooled and washed with cold alcohol to remove unchanged reactants. In this way the base was obtained in shining yellow scales which when purified by recrystallization from alcohol melted at 139.5°. The yield was 75% of the theoretical.

Anal. Calcd. for $C_{17}H_{12}NCl$: C, 76.8; H, 4.5; Cl, 13.4; N, 5.3. Found: C, 76.9; H, 4.8; Cl, 13.5; N, 5.3.

The Dibromide.—The base was dissolved in cold carbon tetrachloride and an equivalent amount of bromine in carbon tetrachloride was added. The dibromide separated at once. It was filtered and recrystallized from alcohol. The crystals melted at 175°.

Anal. Calcd. for $C_{17}H_{12}NBr_2Cl$: N, 3.3. Found: N, 3.5. Equivalents of halogen per gram of substance calculated for $C_{17}H_{12}NBr_2Cl$: 0.00705. Found: 0.00712.

α-(p-Chlorobenzohydryl)-quinaldine.—Twelve grams (0.045 mole) of *p*-chlorobenzalquinaldine was added in one portion to a solution of 0.19 mole of phenylmagnesium bromide in 70 cc. of ether. The mixture immediately became dark red. Two hundred cubic centimeters of ether was then added and the mixture was heated under re-

---

[4] Hammick, *J. Chem. Soc.*, **123**, 2882 (1923).

flux, with stirring, for twelve hours. To the cooled mixture a solution of 30 g. of ammonium chloride in 75 cc. of water was added dropwise; the dark red color changed to a light yellow during this decomposition. The entire mixture was then subjected to steam distillation until all volatile materials had been removed. The residue, which contained a yellow oil, was cooled and was then extracted with ether. The filtered ether layer was placed in a round-bottomed porcelain evaporating dish and the ether was allowed to evaporate at reduced pressure in a vacuum desiccator. The residue crystallized as a light brown, slightly sticky solid. The solid was pulverized under low-boiling petroleum ether, after which it was no longer sticky and was almost colorless. The yield of crude product was 10 g., or 64% of the theoretical. The solid crystallized readily from low-boiling petroleum ether; the melting point after each of two successive recrystallizations was 91.5–92.5°.

Anal. Calcd. for $C_{23}H_{18}NCl$: C, 80.4; H, 5.2; N, 4.1; Cl, 10.3. Found: C, 80.5; H, 5.3; N, 4.1; Cl, 10.2.

Conversion of *p*-Chlorobenzalquinaldine into *α*-Benzohydrylquinaldine (First Method).—A mixture of 10 g. of *p*-chlorobenzalquinaldine, 20 g. of anhydrous aluminum chloride and 100 cc. of benzene was allowed to stand for twelve hours. Only a slight amount of heat developed when the reactants were mixed. The color changed slowly from yellow to dark brown. The reaction mixture was decomposed with an ice–hydrochloric acid mixture. The product was washed with benzene, heated with ammonium hydroxide solution, cooled and filtered. After several recrystallizations from alcohol to which animal charcoal had been added, the compound formed in large, colorless crystals melting at 120–121.5°. The Beilstein test showed halogen to be absent. A mixed melting point taken with *α*-benzohydrylquinaldine showed no depression. This preparation of *α*-benzohydrylquinaldine from *p*-chlorobenzalquinaldine was checked repeatedly but failed to take place when great care was exercised in keeping the reactants dry. The following directions were found to be more satisfactory.

Conversion of *p*-Chlorobenzalquinaldine into *α*-Benzohydrylquinaldine (Second Method).—A mixture of 20 g. of anhydrous aluminum chloride, 10 g. of benzalquinaldine and 200 cc. of dry benzene was placed in a 500-cc. 3-necked flask fitted with a mercury-sealed stirrer, a calcium chloride tube and a tube for conducting dry hydrogen chloride into the flask. The hydrogen chloride tube was placed so as to deliver the gas above the surface of the reaction mixture. The stirrer was started and a slow stream of hydrogen chloride was passed into the flask. The gas was readily absorbed and produced a yellow precipitate which caused the mixture to become a paste. After a few minutes the absorption of gas ceased and the yellow color gradually gave way to a dark green. Heat was evolved by the reaction, making it necessary to cool the mixture by immersing the flask in an ice-bath. The disappearance of the yellow color was complete in about thirty minutes and during the latter part of this time the evolution of hydrogen chloride was noted. The stirring was continued for two and one-half hours longer, at the end of which time the evolution of hydrogen chloride had practically ceased. The reaction mixture, which now consisted of two liquid layers, was poured into a mixture of 200 g. of ice and 50 cc. of concentrated hydrochloric acid. The colorless semi-solid product was freed from the liquid layer by decantation. It was then heated with 100 cc. of concentrated ammonium hydroxide solution until it was converted into an oil. This mixture was cooled and extracted with ether and the resulting ether solution was allowed to evaporate spontaneously. The crystalline mass obtained as a residue was freed from the accompanying oil by being washed with a small amount of cold methyl alcohol. The crystals were dissolved in a mixture of methyl alcohol and ethyl alcohol and the solution was filtered to remove a small amount of insoluble material. When the solution was allowed to cool, it deposited 5 g. of a colorless solid melting at 118.5–121°. A Beilstein test showed the compound to be halogen-free.

Summary

Benzalquinaldine and *p*-chlorobenzalquinaldine react with phenylmagnesium bromide to give α-benzohydrylquinaldine and α-(*p*-chlorobenzohydryl)-quinaldine, respectively.

In the case of benzalquinaldine the same transformation is effected by the use of benzene in the presence of anhydrous aluminum chloride.

p-Chlorobenzalquinaldine, however, reacts with benzene in the presence of anhydrous aluminum chloride to give not the expected α-(*p*-chlorobenzohydryl)-quinaldine but the corresponding chlorine-free compound, α-benzohydrylquinaldine. This dehalogenation is being investigated.

URBANA, ILLINOIS RECEIVED OCTOBER 3, 1932
PUBLISHED MAY 6, 1933

[CONTRIBUTION NO. 115 FROM THE EXPERIMENTAL STATION OF E. I. DU PONT DE NEMOURS AND COMPANY]

Acetylene Polymers and their Derivatives. XI. Dichloro-2,3-butadiene-1,3 and Trichloro-1,2,3-butadiene-1,3

BY GERARD J. BERCHET AND WALLACE H. CAROTHERS

Chloroprene (I) under ordinary conditions polymerizes to a rubber-like product about 700 times as rapidly as isoprene (or butadiene).[1] Hence in the diene polymerization a chlorine atom at the β-position has a powerful activating influence. A bromine atom in the same position has an even greater positive effect.[2] On the other hand α-chlorobutadiene polymerizes not much more rapidly than isoprene, and the product, though elastic, has very little strength.[3] The corresponding bromine compound also polymerizes spontaneously but no rubber-like properties have been ascribed to it.[4] Hence the activation produced by the halogen atom is very sensitively related to its position, and multiple substitution does not modify this conclusion, for tetrachloro-1,2,3,4-butadiene-1,3 has been described without any indication that it polymerizes at all.[5] The effect of a single β-halogen atom on diene behavior is in fact unique so far as recorded facts go. No other type of substitution has yielded a compound that greatly exceeds butadiene in the speed of its spontaneous polymerization and at the same time leads to a rubber-like product. In the methyl series isoprene polymerizes somewhat more rapidly than butadiene, and β,γ-dimethylbutadiene perhaps yet faster;[6] and the product from the latter, though somewhat inferior in snap and extensibility, is still rubber-like. On the other hand,

---

[1] Carothers, Williams, Collins and Kirby, THIS JOURNAL, **53**, 4203 (1931).

[2] Carothers, Collins and Kirby, *ibid.*, **55**, 789 (1933).

[3] Unpublished results.

[4] Willstätter and Bruce, *Ber.*, **40**, 3979 (1907).

[5] Müller and Hüther, *ibid.*, **64**, 589 (1931). *Cf.* also pentachloro and hexachlorobutadiene-1,3, Beilstein, 4th ed., Vol. 1, p. 250.

[6] Whitby and Crozier, *Canadian J. Research* **6**, 203 (1932); Whitby and Katz, *ibid.*, **6**, 398 (1932).