formamidine which precipitated was collected. An additional 25-cc. of benzene was added to the filtrate and the aqueous layer was extracted with an additional 25-cc. portion of benzene. The combined benzene extracts were washed with 20 cc. of water, which was then added to the main aqueous acid solution. *m*-Chloroaniline (*ca.* 2.6 g.) was isolated from the aqueous solution and identified by conversion to the benzenesulfonamide, m. p. 118–119° (lit., 121°).[10]

The benzene solution was distilled at atmospheric pressure and finally at reduced pressure to remove the unchanged malonic ester. To the residue was added 10 cc. of ether and 25 cc. of low-boiling petroleum ether and the solution was cooled in an acetone–Dry Ice mixture. After one and one-half hours the mixture was filtered and 6.3 g. of very fine white needles were collected, m. p. 48–49°.

This product was shown to be ethyl α-carbethoxy-β-*m*-chloroanilinoacrylate (I), containing about 10% ethyl α-*m*-chlorocarbanilido-β-*m*-chloroanilinoacrylate (II), both by recrystallization (a) and by cyclization (b). Hence the conversion to the former (I) was about 38% neglecting the starting materials recovered. (In other experiments it was shown that the unreacted amidine could be recovered in good yield.)

A series of experiments indicated that the conditions above were about optimum. At shorter times, the conversion was considerably less. At longer times or higher temperatures, the yield of anilide (II) increased rapidly.

(a) **Recrystallization.**—A 1.0-g. sample of the product above was recrystallized from 12 cc. of ethanol. The crystals recovered amounted to 0.10 g. and melted at 102–103°. A second recrystallization from 5 cc. of ethanol brought the melting point to 112–113°; a mixed melting point with an authentic sample of ethyl α-*m*-chlorocarbanilido-β-*m*-chloroanilinoacrylate[5] (II) was 112–113°. The filtrate from the first recrystallization was evaporated to dryness at room temperature and the residue was recrystallized from 10 cc. of low-boiling petroleum ether to give fine white needles, m. p. 53–54°. A mixed melting point with an authentic sample of ethyl α-carbethoxy-β-*m*-chloroanilinoacrylate[4] (I) was 53–55°.

(b) **Cyclization.**—A 3.0-g. sample of the product was melted, added to 9 cc. of boiling "Dowtherm-A" and washed in with another cubic centimeter of hot solvent. The crystals which separated after three or four minutes soon filled the mixture, and the heating was continued for only fifteen minutes. The reaction mixture set to a solid light yellow mass on cooling. To this was added 10 cc. of 10% sodium hydroxide solution and the mixture was heated under reflux for twenty minutes. When the two-phase liquid mixture cooled, a precipitate appeared in the aqueous layer; this was collected by filtration and amounted to 0.3 g., m. p. 290–305° (uncor.). It was evidently 7-chloro-3-*m*-chlorocarbanilido-4-hydroxyquinoline.[5] Ether was added to the filtrate and the layers were separated. The aqueous layer was extracted with another 10-cc. portion of ether and then neutralized with 10% hydrochloric acid. The white precipitate was digested by heating to boiling, cooled and collected on a filter. After drying *in vacuo* the weight of the acid was 1.6 g. (79% of the theoretical amount, assuming the starting material to be 90% pure), m. p. 253° (uncor.) with loss of carbon dioxide. One gram of this acid was decarboxylated to 7-chloro-4-hydroxyquinoline in the usual way, and the recrystallized product was found to be identical with a sample prepared from ethoxymethylenemalonic ester.[4]

(10) Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1940, p. 195.

Summary

It has been found that, under the proper conditions, *bis*-(*m*-chlorophenyl)-formamidine will condense with malonic ester to produce ethyl β-(*m*-chloroanilino)-α-carbethoxyacrylate in excellent yield.

URBANA, ILLINOIS RECEIVED APRIL 5, 1946

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

Synthesis of 4-Hydroxyquinolines. V. A Direct Synthesis from β-Anilinoacrylates[1]

BY CHARLES C. PRICE,[2] NELSON J. LEONARD AND ROBERT H. REITSEMA

In spite of the report that ethyl β-*p*-anisidinoacrylate could not be cyclized to 6-methoxy-4-hydroxyquinoline,[3] the desirability of such a simple, direct synthesis of 4-hydroxyquinolines, coupled with the successful application to α-carbethoxy analogs,[4] has led to a careful reëxamination of this possibility.

After many preliminary experiments, the observation that the α-cyano- or α-carbanilidoacrylates would cyclize only at very high dilution[5] was applied successfully to the cyclization of methyl or ethyl β-anilino- and β-*m*-chloroanilinoacrylates. When the β-*m*-chloroanilinoacrylates (I) are boiled in relatively concentrated diphenyl ether solution the only crystalline product isolated was *bis*-(*m*-chlorophenyl)-urea (II). An acrid odor resembling acetaldehyde was noticed. At high dilution, three crystalline products were isolated. Two were identified as chlorohydroxyquinolines. The one formed in greater yield was identical with that obtained in the synthesis through ethoxymethylenemalonic ester, 7-chloro-4-hydroxyquinoline (III). Since no proof that this substance had the chlorine in the 7-position has appeared in the literature, its structure was established by conversion to 7-chloro-8-nitroquinoline.[6] The isomer was presumed to be 5-chloro-4-hydroxyquinoline, IV.

The third product from the cyclization had the correct analysis for 1,1-*bis*-(7-chloro-4-hydroxy-3-quinolyl)-ethane, V, which could conceivably be formed by condensation of III with acetaldehyde.

(1) The work described in this paper was carried out under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Illinois.

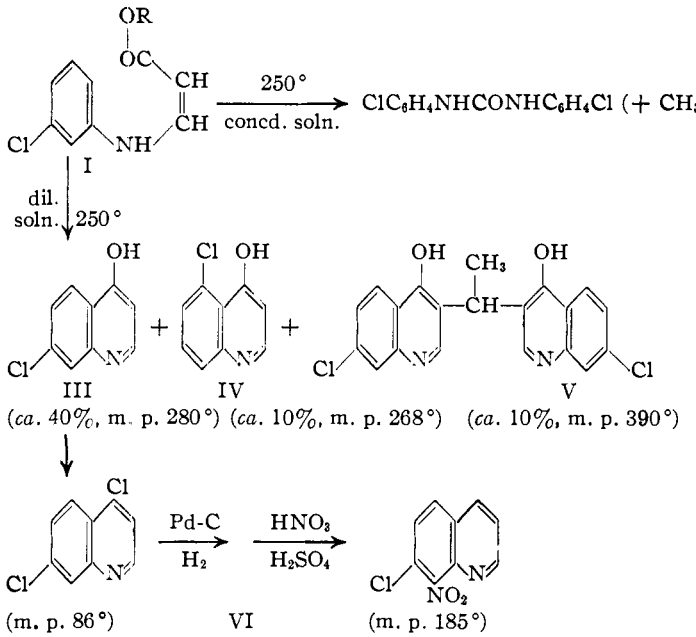
(2) Present address, University of Notre Dame, Notre Dame, Indiana.

(3) Rubtsov, *J. Gen. Chem.* (USSR), **7**, 1885 (1937); *C. A.*, **32**, 526 (1938).

(4) Price and Roberts, THIS JOURNAL, **68**, 1204 (1946).

(5) Price, Leonard and Herbrandson, *ibid.*, **68**, 1251 (1946).

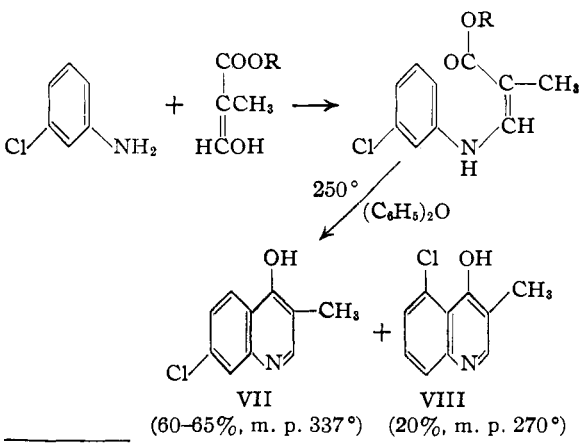
(6) Price and Guthrie, *ibid.*, **68**, in press (1946).



From the analytical data, V might have been a methyl homolog of III. However, 7-chloro-4-methyl-2-hydroxyquinoline is reported to melt at 272°,[7] and 7-chloro-2-methyl- and 7-chloro-3-methyl-4-hydroxyquinolines, m.p. 315 and 337°, respectively, were prepared in the course of the present investigation. It is difficult to see how 7-chloro-2-hydroxy-3-methylquinoline, the only other possibility, could be formed. The biquinolyl structure for V was substantiated by isolation of identical material by treatment of III with acetaldehyde under the conditions of the cyclization.

Cyclization of methyl β-anilinoacrylate at high dilution was also successful, yielding 44% of 4-hydroxyquinoline.

An extension of this procedure to the condensation product of *m*-chloroaniline with sodioformylpropionic esters, β-(*m*-chloroanilino)-α-methacrylates, produced 7-chloro-4-hydroxy-3-methylquinoline (VII) and the 5-chloro isomer (VIII) in 80 to 85% yield. About 65 to 75% of the crude mixture was the desired 7-chloro compound, of some interest as an intermediate in the preparation of the drug, Santochin, used by the Germans in North Africa.



The addition of 0.5 g. of *m*-chloroaniline to a cyclization of 10 g. of the acrylate reduced the yield of crude quinoline to 44%. It is perhaps significant in connection with the suggested structure for V, that no analogous high-melting product was formed in the cyclization of the α-methacrylate. In this instance, the reactive 3-position in the product is already occupied by a methyl group.

Experimental[8]

Ethyl β-*m*-Chloroanilinoacrylate.—Ethyl sodioformylacetate was prepared by the method described by Pechman.[9] In order to obtain an aqueous solution of the sodium salt, the flask containing the crude reaction mixture from the condensation of ethyl acetate and ethyl formate was placed in an ice-bath and about 150 cc. of water per mole of ester was added with stirring. The water was added slowly at first, rapidly toward the end. The aqueous layer was separated and the ether layer extracted with 50 to 100 cc. of water. The combined aqueous solutions were used in aliquot parts for subsequent condensations.

A solution of 40 g. (0.31 mole) of *m*-chloroaniline in 600 cc. of water containing 27.8 cc. (0.33 mole) of concentrated hydrochloric acid was stirred vigorously and 400 cc. of an aqueous solution containing ethyl sodioformylacetate from 0.33-mole quantities of ethyl formate and ethyl acetate was added dropwise. Only a lower layer of oil formed. Attempts to crystallize this oil by washing with dilute hydrochloric acid, or by dissolving in minimum amounts of various solvents were unsuccessful. Washing with 50% acetic acid similarly failed to produce a solid acrylate.

To check the aqueous solution of sodioformylacetate, it was added to a dilute acetic acid solution of aniline. Crude ethyl β-anilinoacrylate, m. p. 99–104°, was obtained directly. Pechman[9] reported that this ester melted at 106°.

Methyl β-*m*-Chloroanilinoacrylate.—Methyl sodioformylacetate was prepared from equal molar amounts of methyl formate and methyl acetate in the presence of sodium methoxide. As before, the salt was isolated from the ether suspension by extraction with water. A solution of 0.05 mole of methyl sodioformylacetate in 30 cc. of water was added dropwise with stirring to a solution of 5.8 g. (0.035 mole) of *m*-chloroaniline hydrochloride in 40 cc. of water containing 2 cc. of concentrated hydrochloric acid. The orange precipitate which formed was separated by filtration and was washed twice with 50 cc. of 5% acetic acid. After two recrystallizations from a minimum amount of methanol, 2.3 g. (31%) of methyl β-*m*-chloroanilinoacrylate was obtained as colorless soft crystals which melted at 153–154°.

Anal. Calcd. for $C_{10}H_{10}ClNO_2$: C, 56.74; H, 4.76. Found: C, 56.82; H, 4.70.

(7) German Patent 556,324, Feb. 23, 1930; *C. A.*, **26**, 5573 (1932).

(8) Analyses by Miss Theta Spoor and Miss Lillian Hruda. All melting points are corrected.

(9) Pechman, *Ber.*, **25**, 1040 (1892).

sym-bis-m-**Chlorophenylurea.**—(a) To 100 cc. of refluxing diphenyl ether was added 25 g. of the oil obtained in the attempted preparation of ethyl β-*m*-chloroanilinoacrylate. The solution was allowed to reflux for one hour. An acrid odor similar to acetaldehyde could be detected at the open end of the condenser. The gold, sparkling crystals obtained by cooling the solution to 30° were collected on a filter and washed twice with petroleum ether (b. p. 90–110°). The product (2 g.) melted at 245–246.5° after three recrystallizations from ethanol and proved to be *sym-bis-m*-chlorophenylurea. Jadhav reported that this compound melted at 245–246°,[10] and a mixture with an authentic sample prepared by the procedure of Hurst and Thorpe, melted at the same temperature.[11]

Anal. Calcd. for $C_{13}H_{10}Cl_2N_2O$: C, 55.53; H, 3.59; N, 10.00; Cl, 25.22. Found: C, 55.88, 55.63; H, 3.65, 3.85; N, 10.66, 10.74; Cl, 24.87.

(b) To 42 cc. of refluxing diphenyl ether was added 13 g. (0.06 mole) of methyl β-*m*-chloroanilinoacrylate.[12] Samples removed after twenty and forty minutes failed to yield a precipitate when cooled. After one hour crystalline material sublimed in the condenser. This was shown to be *sym-bis-m*-chlorophenylurea. After the diphenyl ether solution had stood overnight, no solid had formed.

7-Chloro-4-hydroxyquinoline (III).—A solution of 10.5 g. (0.05 mole) of methyl β-*m*-chloroanilinoacrylate in 50 cc. of warm diphenyl ether was added dropwise into 200 cc. of vigorously-refluxing diphenyl ether during twelve minutes and boiled an additional six minutes. The crude solid product weighed 5.0 g., m. p. 210–250°. Extraction of the diphenyl ether solution with sodium hydroxide yielded an additional 0.8 g. of 7-chloro-4-hydroxyquinoline, m. p. 267–270°. A similar experiment in which 100 g. of the acrylate was heated thirty-five minutes yielded 45 g. of precipitate plus 13 g. of solid by alkaline extraction; total, 58 g. (68%).

Two grams was crystallized from 400 cc. of boiling water to yield 1.0 g. of white needles, m. p. 272.5–277.5° (block, uncor.), giving no depression in the melting point of authentic 7-chloro-4-hydroxyquinoline.[4] This represented a 38% yield of purified product from the acrylate. Two more crystallizations from water raised the melting point to 277–279°.

Various other attempts to purify the crude 7-chloro-4-hydroxyquinoline from 95 to 50% ethanol or methanol, glacial acetic acid, or 50% acetic acid failed to yield a product that melted above 265°. The crude material was recrystallized also from a minimum amount of pyridine. After evaporation of a portion of the solvent the product melted at 265–273° with very slight softening at 233°.

The picrate of 7-chloro-4-hydroxyquinoline, prepared in an ethanol solution and recrystallized from an ethanol–water mixture, contained one mole of picric acid for every two moles of 7-chloro-4-hydroxyquinoline, m. p. 251.5–253.5° (dec.).

Anal. Calcd. for $C_{24}H_{15}Cl_2N_5O_9$: C, 48.99; H, 2.57; N, 11.91. Found: C, 49.24; H, 2.67; N, 12.55.

5-Chloro-4-hydroxyquinoline.—Evaporation of the aqueous filtrate from the recrystallization of 4 g. of crude 7-chloro-4-hydroxyquinoline nearly to dryness yielded 0.24 g. of product which melted at 210–230°. This solid was boiled with a minimum amount of methanol and filtered from insoluble material. From the cold methanol solution yellowish needles were obtained which melted at 240–260°. After two additional recrystallizations from methanol, a small amount of 5-chloro-4-hydroxyquinoline, which melted at 266–268°, was recovered. The mixed melting point with 7-chloro-4-hydroxyquinoline was 214–243°.

Anal. Calcd. for C_9H_6ClNO: C, 60.18; H, 3.37. Found: C, 59.71; H, 3.47.

The picrate of this compound was much less soluble in ethanol than was the picrate of 7-chloro-4-hydroxyquinoline. As with the isomeric picrate, the analysis indicated that one mole of picric acid was associated with two moles of 5-chloro-4-hydroxyquinoline. After three recrystallizations from ethanol, it melted at 262–264°. The mixed melting point with the picrate of 7-chloro-4-hydroxyquinoline was 223–225°.

Anal. Calcd. for $C_{24}H_{15}Cl_2N_5O_9$: C, 48.99; H, 2.57. Found: C, 49.19; H, 2.67.

High-Melting Product from the Cyclization.—When the diphenyl ether solution of the acrylate was refluxed forty to sixty minutes, a solid precipitated from the hot solution. This material was isolated either by filtering the hot diphenyl ether solution or by dissolving the other products of the cyclization in methyl or ethyl alcohol. From each gram of acrylate, 0.05 to 0.1 g. was obtained. The material was insoluble in most organic solvents, soluble in warm alkali, from which it could be reprecipitated by acidification, and soluble to the extent of 0.4 g. in 100 cc. of glacial acetic acid. Recrystallization could be accomplished by dissolving the material in boiling glacial acetic acid or pyridine and adding water until a cloudiness persisted in the hot solution. After cooling, a white precipitate which melted at about 385–390° was obtained.

Anal. Calcd. for $C_{10}H_8ClNO$: C, 62.03; H, 4.16; Cl, 18.31; N, 7.23. $C_{20}H_{14}Cl_2N_2O_2$: C, 62.35; H, 3.64; Cl, 18.41; N, 7.27. Found: C, 62.12; H, 3.89; Cl, 18.41; N, 7.31.

When heated under reflux for two hours with 25% sodium hydroxide, the material was recovered unchanged by acidification of the solution.

A sample of this product was prepared by sweeping acetaldehyde through a refluxing solution of Dowtherm containing 7-chloro-4-hydroxyquinoline in a concentration comparable to that in the cyclizations. The material was isolated as before by washing the crude precipitate several times with boiling ethanol. The small amount of insoluble residue melted at about 385–390° and did not depress the melting point of an authentic sample of the high melting material.

7-Chloro-8-nitroquinoline.—The structure of 7-chloro-4-hydroxyquinoline, m. p. 277–279°, was demonstrated by conversion to 7-chloro-8-nitroquinoline. A mixture of 7.0 g. (0.035 mole) of 4,7-dichloroquinoline, m. p. 81–84°, obtained from 7-chloro-4-hydroxyquinoline, 3.0 g. of palladium–charcoal (10%) catalyst, 4.0 g. of potassium hydroxide, and 125 cc. of ethanol was shaken under a pressure of 2 to 3 atmospheres of hydrogen at room temperature. The reaction was very rapid and one equivalent of hydrogen was absorbed within ten minutes. The catalyst was removed by filtration and washed with 20 cc. of ethanol. The filtrate and wash solutions were combined and evaporated under a jet of air to remove the ethanol. From the reaction, 3.3 g. of reddish oil was obtained. Nitration[6] of this oil yielded white crystals of 7-chloro-8-nitroquinoline, m. p. 184–185°, which did not depress the melting point of an authentic sample of 7-chloro-8-nitroquinoline.[6] The isomeric 5-chloro-8-nitroquinoline melts at 135–136°.[13]

Methyl β-Anilinoacrylate.—A solution of 0.23 mole of methyl sodioformylacetate in 140 cc. of water was added dropwise to a stirred solution of 16 g. (0.17 mole) of aniline in 160 cc. of 20% acetic acid. The solution was filtered and the orange solid was washed with 100 cc. of 5% acetic acid and with water. The crude product, which melted at 107–114°, weighed 7.9 g. (26%). After recrystallization from a minimum amount of ethanol, methyl β-anilinoacrylate melted at 137.5–139°.

Anal. Calcd. for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.23. Found: C, 67.90; H, 6.42.

4-Hydroxyquinoline.—Two grams (0.011 mole) of methyl β-anilinoacrylate in 15 cc. of warm Dowtherm, was added to 35 cc. of refluxing Dowtherm and boiled for twelve minutes. No additional material was obtained by

(10) Jadhav, *J. Ind. Chem. Soc.*, **10**, 391 (1933).

(11) Hurst and Thorpe, *J. Chem. Soc.*, **107**, 934 (1915).

(12) The β-*m*-chloroanilinoacrylate used in these experiments was kindly furnished by the Calco Chemical Division of the American Cyanamid Company, Bound Brook, N. J.

(13) Fourneau, Tréfouel, Tréfouel and Wancolle, *Bull. soc. chim.*, **47**, 738 (1930).

extraction of the diphenyl ether mother liquor with dilute alkali. The solid product weighed 0.7 g. (44%) and melted at 199–201° after recrystallization from methanol. Bobranski reported that 4-hydroxyquinoline melted at 201°.[14]

Ethyl α-Methyl-β-*m*-chloroanilinoacrylate.—To 255.2 g. (2.0 moles) of *m*-chloroaniline in 1200 cc. of water containing 166.8 cc. (2.0 moles) of concentrated hydrochloric acid (sp. gr. 1.187) was added 50 cc. (0.6 mole) of concentrated hydrochloric acid. The solution was stirred and the aqueous solution of ethyl α-sodioformylpropionate from 5.0 moles of ester was added dropwise over a three-hour period. During the same period, 367 cc. (4.4 moles) of concentrated hydrochloric acid was added. Light yellow solid appeared very soon after the first drops had been added, and stirring was continued for one hour. The solid acrylate was isolated by filtration, and washed once with water. The major part of occluded *m*-chloroaniline was removed by washing with 500 cc. of petroleum ether (b. p. 90–110°) and filtration. After thorough drying, 261.7 g. (21.9%) of ethyl α-methyl-β-*m*-chloroanilinoacrylate, m. p. 93–96°, was obtained as long shiny white needles. The ester was not completely stable and decomposed when dried at 65°. It turned slightly yellow when dried over phosphorus pentoxide at room temperature for two days.

Anal. Calcd. for $C_{12}H_{14}ClNO_2$: C, 60.13; H, 5.89. Found: C, 59.57; H, 5.93.

Methyl α-Methyl-β-*m*-chloroanilinoacrylate.—The methyl ester was prepared by the same method outlined above in which methyl propionate was condensed with ethyl or methyl formate to produce methyl α-sodioformylpropionate. The methyl α-methyl-β-*m*-chloroanilinoacrylate melted at 113.5–115.5°.

Anal. Calcd. for $C_{11}H_{12}ClNO_2$: C, 58.54; H, 5.36. Found: C, 58.73; H, 5.55.

7-Chloro-4-hydroxy-3-methylquinoline.—Ten grams (0.445 mole) of methyl α-methyl-β-*m*-chloroanilinoacrylate was boiled for twenty minutes in 30 cc. of Dowtherm. The solid product weighed 7.3 g. (85%), m. p. 255–312°. On recrystallization from ethanol, 65 to 75% of the crude material was recovered as white needles of 7-chloro-4-hydroxy-3-methylquinoline, m. p. 334–337°.

Anal. Calcd. for $C_{10}H_8ClNO$: C, 62.03; H, 4.16. Found: C, 62.08; H, 4.17.

5-Chloro-4-hydroxy-3-methylquinoline.—The isolation of the isomeric quinoline from the cyclization of methyl or ethyl β-*m*-chloroanilinomethacrylate was accomplished by recrystallization from acetic acid. From 4.8 g. of crude cyclization product dissolved in 50 cc. of hot glacial acid, 2.1 g. of the 7-chloro isomer was obtained upon cooling. Addition of 50 cc. of water to the heated filtrate produced 0.9 g. of a mixture, chiefly of the 7-chloro isomer. Addition of 200 cc. of water to the hot filtrate in turn yielded 1.4 g. of product, m. p. 215–220°. Numerous recrystallizations of this material from ethanol gave white needles of 5-chloro-4-hydroxy-3-methylquinoline, m. p. 268–269.5°.

Anal. Calcd. for $C_{10}H_8ClNO$: C, 62.03; H, 4.16; N, 7.23. Found: C, 61.89; H, 4.20; N, 7.33.

7-Chloro-4-hydroxy-2-methylquinoline.—The general method of Limpach[15] was utilized to prepare this quinoline. Twenty-six grams (0.2 mole) of acetoacetic ester and 25.5 g. (0.2 mole) of *m*-chloroaniline were mixed and allowed to stand at room temperature overnight. No water layer had formed so two drops of concentrated hydrochloric acid were added. Within five minutes a definite lower layer of water appeared. After standing five hours the water layer was removed and the organic layer was dried over magnesium sulfate. To 200 cc. of refluxing Dowtherm was added 20 g. (0.084 mole) of the oily crotonate. Heating was continued for one-half hour. The product which precipitated from the cooled Dowtherm weighed 11.6 g. (72%). After three recrystallizations from dilute ethanol, 7-chloro-4-hydroxy-2-methylquinoline melted at 313.5–315°.

Anal. Calcd. for $C_{10}H_8ClNO$: C, 62.03; H, 4.16; N, 7.23. Found: C, 62.31; H, 4.37; N, 7.41.

This compound is not identical with the high-melting product from the cyclization of the *m*-chloroanilinoacrylate, which was not appreciably soluble in warm ethanol or methanol and melted at a much higher temperature (390°).

Summary

Methyl β-anilinoacrylate has been cyclized to 4-hydroxyquinoline by heating at high dilution in boiling diphenyl ether solution. The *m*-chloroanilinoacrylate and methacrylate gave mixtures of 5- and 7-chloro-4-hydroxyquinoline and its 3-methyl homolog, respectively.

(14) Bobranski, *Ber.*, **69**, 1113 (1936).

(15) Limpach, *ibid.*, **64**, 969 (1931).

URBANA, ILLINOIS RECEIVED APRIL 5, 1946

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

Experiments on the Synthesis of 4-Hydroxy- and 4-Chloroquinolines from β-Anilinopropionic Acids[1]

BY ROBERT C. ELDERFIELD, WALTER J. GENSLER, THOMAS H. BEMBRY, CHESTER B. KREMER, FREDERICK BRODY, HOWARD A. HAGEMAN AND JAMES D. HEAD

The observation of Clemo and Perkin,[2,3] that certain β-anilinopropionic acids as their N-*p*-toluenesulfonyl (tosyl) derivatives undergo ring closure to dihydro-4-quinolone derivatives when treated with phosphorus pentoxide suggests the possibility that these acids might serve as a convenient source of 4-hydroxyquinolines and 4-chloroquinolines, the latter having assumed importance as intermediates in the synthesis of the members of the highly active 4-aminoquinoline group of antimalarial drugs. Clemo and Perkin also reported the formation of 1-tosyl-3-chlorodihydroquinolones when the anilinopropionic acid derivatives were subjected to the action of phosphorus oxychloride. Backeberg[4] reinterpreted the experimental observations of Clemo and Perkin on the latter reaction and showed that the product of the ring closure of N-tosyl-β-anilino-

(1) The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Columbia University.

(2) Clemo and Perkin, *J. Chem. Soc.*, **125**, 1608 (1924).

(3) Clemo and Perkin, *ibid.*, **127**, 2297 (1925).

(4) Backeberg, *ibid.*, 618 (1933).