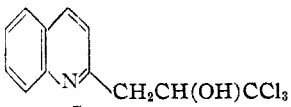
[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY AND THE LILLY RESEARCH LABORATORIES]

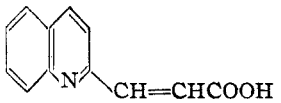
# The Action of Alkali on Chloral-quinaldine

BY R. B. WOODWARD AND EDMUND C. KORNFELD

By treatment of chloral-quinaldine (I) with alcoholic sodium hydroxide, Einhorn[1] obtained β-(2-quinolyl)-acrylic acid (II), and a *bright orange* sodium salt, $C_{12}H_{10}O_2NNa\cdot 3H_2O$, which was formulated as a derivative of the hydroxyacid (III).

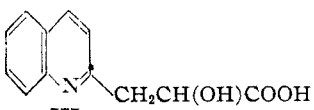



I

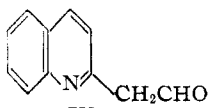



II

The salt was supposed to have been transformed by oxidation in turn to quinoline-2-acetaldehyde (IV) and quinoline-2-acetic acid (V). Borsche[2]

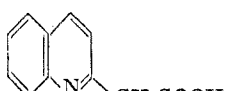



III

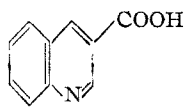



IV

noted that the properties of the acid obtained by oxidation were inconsistent with the formulation as (V), and was able to demonstrate that the substance was quinoline-3-carboxylic acid (VI), but did not challenge the expressions for the anterior substances.

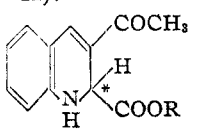



V

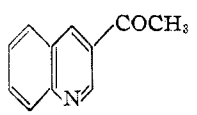



VI

In this communication it is shown that the orange sodium derivative is in fact a salt of 3-acetyl-1,2-dihydroquinoline-2-carboxylic acid (VII, R = H).

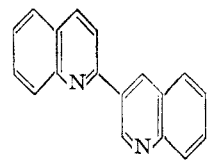



VII

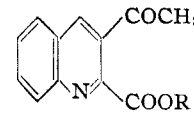



VIII

We were able to demonstrate first, by direct comparison, that the carbonyl derivative obtained on oxidation, and formulated by Einhorn as (IV), is 3-acetyl-quinoline[3] (VIII). The (erroneous) proof of the structure (IV) rested on the conversion of the substance, by condensation with *o*-aminobenzaldehyde, to 3-(2-quinolyl)-quinoline (IX); it is interesting to note that 3-acetylquinoline gives the same product (IX) in that reaction.[4] The orange salt, and the ethyl ester (VII, R = Et), m. p. 110.5–111.5°, obtained from it, were



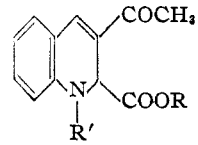
IX



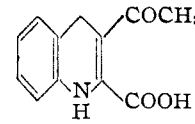

X

oxidized by potassium permanganate in aqueous pyridine to 3-acetylquinoline-2-carboxylic acid[3] (X, R = H) and the corresponding ester[3] (X, R = Et), respectively.

Further, the methyl ester (VII, R = Me) was transformed by benzoyl chloride in pyridine to an N-benzoyl derivative (XI, R = Me, R′ = $C_6H_4$-CO—), m. p. 140–141°, while the ethyl ester (VII, R = Et) gave with acetic anhydride the N-acetyl derivative (XI, R = Et, R′ = $CH_3CO$—), m. p. 130–131°. These facts necessitate the formulation of the original acid as (VII, R = H) or XII. An unequivocal decision in favor of (VII,



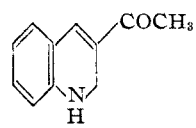

XI



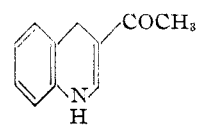

XII

R = H) was made possible through the isolation, through resolution by brucine, of an optically active sodium salt, $[\alpha]^{28}D$ −430°. Of the two possibilities, only VII possesses an asymmetric carbon atom (starred).

We turn now to a consideration of certain remarkable properties of the orange acid (VII, R = H). When this substance is pyrolyzed, 3-acetylquinoline and a *product*, $C_{11}H_{11}ON$, are formed. The latter was isolated by previous investigators,[1,2] but was not identified. We have found that the substance is oxidized by aqueous permanganate to 3-acetylquinoline, and that in turn, it may be resynthesized by the hydrogenation of the latter substance in the presence of Raney nickel. Since the compound is colorless, the expression (XIII) is excluded, and it seems probable that the structure (XIV) represents the




XIII




XIV

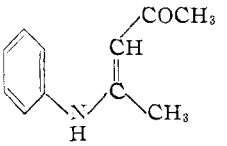
compound correctly. This conclusion is supported by the close similarity of the ultraviolet absorption spectrum of the substance (Fig. 1) to that of acetylacetone anil (XIVa) which contains the

(1) Einhorn, *Ber.*, **19**, 904 (1886); *cf.* also Einhorn and Sherman, *Ann.*, **287**, 38 (1895).

(2) Borsche and Manteuffel, *ibid.*, **526**, 22 (1936).

(3) Koller, *Monatsh.*, **52**, 59 (1929).

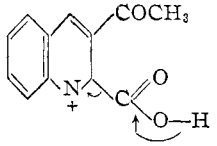
(4) Koller and Ruppersberg, *ibid.*, **58**, 238 (1931).



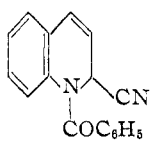
XIVa

same chromophore as XIV. The failure of the hydrogenation to proceed beyond the dihydro-stage, as well as the lack of carbonyl reactivity in (XIV) may be attributed to the interaction, through the double bond, between the imino and the carbonyl groups. The formation of (XIV) from (VII, R = H) takes place by decarboxylation, with simultaneous wandering of a double bond; it is worthy of note that not infrequently the decarboxylation of $\beta,\gamma$-unsaturated acids takes place with movement of the double bond to the $\alpha,\beta$-position.[5]

Another interesting transformation of the orange acid is its spontaneous air oxidation. When the acid is exposed to air, the color gradually fades, and changes from orange to buff. The conversion is remarkably accelerated by light, and the sole product is 3-acetylquinoline. No 3-acetylquinoline-2-carboxylic acid (X, R = H) can be isolated and, further, the latter acid is stable under the conditions of the experiment. It is clear that (X, R = H) cannot be an intermediate in the change and that another intermediate, more subsceptible to decarboxylation, must be involved. We suggest that the withdrawal of two electrons and a proton (probably in stages) from (VII, R = H) gives an intermediate (XV) in which the environment of the carboxyl group is favorable to the ready loss of carbon dioxide, with the electronic shift shown (XV, arrows); the



XV



XVI

change thus becomes fully analogous to the decarboxylation of $\beta$-keto-acids, $\beta$-bromo-acids, and other acids containing properly situated electron-accepting centers. A similar mechanism must be operative in the aqueous permanganate oxidation of (VII) since, again, 3-acetylquinoline is the sole product, and (X, R = H) is stable under the conditions of the experiment (presence of permanganate *and* manganese dioxide).

The behavior of the N-benzoyl derivative (XI, R = Me, R′ = $C_6H_5CO$—) on acid hydrolysis presents an interesting contrast to that of N-benzoyl-2-cyano-1,2-dihydroquinoline (XVI).[6] While the latter undergoes a remarkable cleavage to benzaldehyde and quinoline-2-carboxylic acid

(5) *Cf.* Wallach, *Ann.*, **365**, 258 (1909). The change is also formally similar to that which accompanies the decarboxylation of $\beta$-keto-acids.

(6) Reissert, *Ber.*, **38**, 1610 (1905).

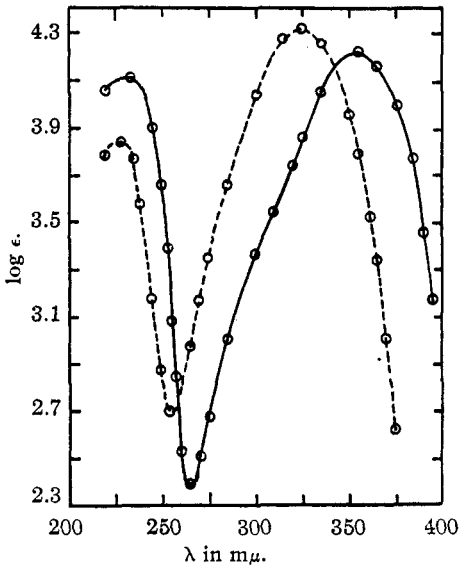
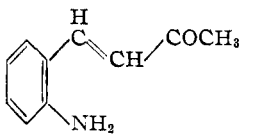


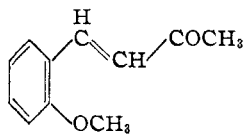

Fig. 1.— ----, Acetylacetone anil; —, 3-acetyl-1,4-dihydroquinoline.

(the reaction forms the basis of a general method for the preparation of aldehydes from acids), (XI, R = Me, R′ = $C_6H_5CO$—), under the same conditions, gave only the corresponding *acid* (XI, R = H, R′ = $C_6H_5CO$—), m. p. 198° (dec.) on more vigorous treatment, benzoic acid was split off, but in no instance could benzaldehyde be detected.

The color of the compound (VII) and its derivatives is consonant with the structure now assigned to it. It was, in fact, this property which revealed at once that the previous structure (III) could not be correct, since from the point of view of light absorption III is simply a 2-alkylquinoline, and consequently colorless. On the other hand (VII) possesses the absorbing system of *o*-aminobenzalacetone (XVII); unfortunately, the

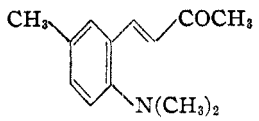


XVII

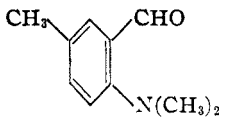


XVIII

latter substance does not appear to be capable of existence, in consequence of its ready conversion to quinaldine. However, there can be no doubt that it (and VII) should be colored. The corresponding methoxy compound (XVIII), for example, is bright orange. We have obtained absorption data which provide further support for these views. In view of the non-existence of (XVII), we had hoped to examine the spectrum of 2 - dimethylamino - 5 - methylbenzalacetone (XIX); the methyl group is (to a good approximation) irrelevant to the spectral discussion, and its presence offers preparative advantages (*vide infra*). It might be doubted that the spectrum of (XIX) and that of (VII) would be directly com-




XIX




XX

parable, in view of the considerable bulk of the N-methyl groups, which might force the dimethylamino group, or the adjacent side chain out of the plane, with consequent resonance damping; in any case, remarkably, and possibly for steric reasons, we were unable under any conditions to bring about the condensation of 2-dimethylamino-4-methylbenzaldehyde (XX) with acetone. On the other hand, we did determine the ultraviolet absorption spectrum of the aldehyde (XX) (Fig. 2), of *p*-dimethylaminobenzaldehyde (XXI) (Fig. 2)

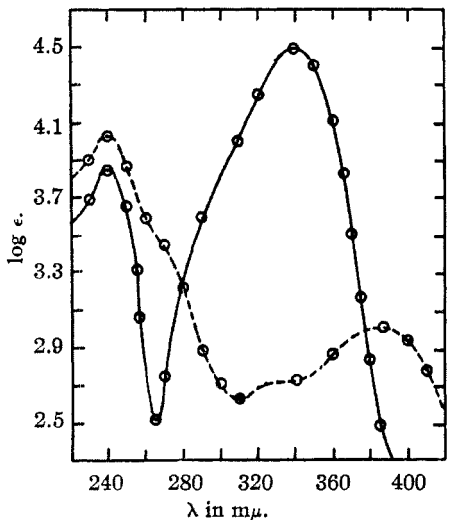



Fig. 2.— —*p*-Dimethylaminobenzaldehyde; ---, 2-dimethylamino-5-methylbenzaldehyde.

and *p*-dimethylaminobenzalacetone (XXII) (Fig. 3). It may be expected that the differences between the spectra of the *p*-substituted aldehyde and its condensation product will be reflected in the comparison of the spectrum of (XX) with that (Fig. 4) of the orange compound and its derivatives. The fact that this is the case provides confirmation of our view of the constitution of these substances; in the change XXI → XXII, a short wave length band (240 mμ) is displaced to 250 mμ (Δ = 10 mμ) and a long wave length band (338 mμ) moves to 385 mμ (Δ = 47 mμ). Correspondingly, in comparing (XX) with (VII), a shift of a short wave length band (240 mμ) to 250 mμ (Δ = 10 mμ), and of a long wave length band (370 mμ) to 415 mμ (Δ = 45 mμ) is observed. In the latter case, a third band, discernible only as a shoulder (~270 mμ) in the spectrum of (XX) appears as a well-defined maximum at 320 mμ in that of (VII). Furthermore, the relative intensities of the various bands, which differ markedly in the *ortho* as compared with the *para* series, are in each case comparable within the series. The greater complexity

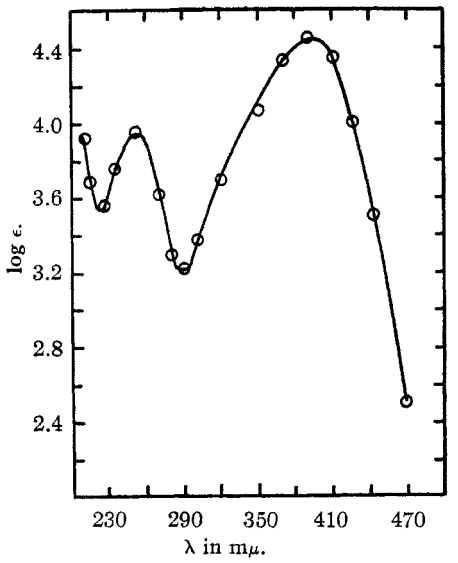



Fig. 3.—*p*-Dimethylaminobenzalacetone.

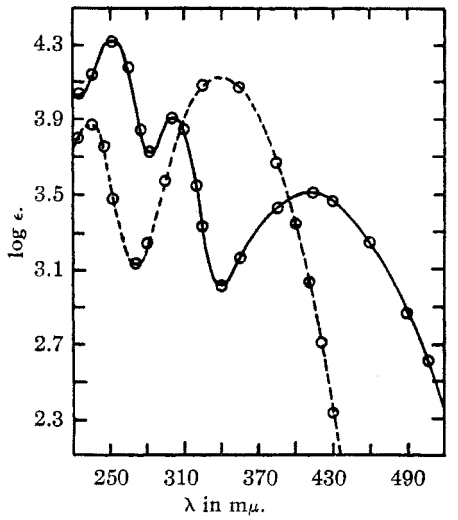
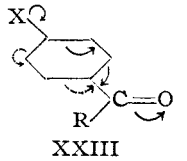
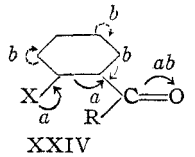



Fig. 4.— —Orange compound, sodium salt; ---, ethyl acetopyruvate-anil.

of the spectra of the *ortho* as compared with the *para* compounds is another example of a general effect[7] which probably has its origin in the greater symmetry of the latter; thus, while the available oscillatory paths in (XXIII) are indistinguishable, in (XXIV), two distinct oscillations of different




XXIII

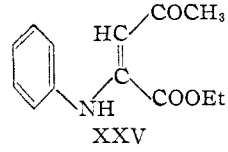



XXIV

length (*a* or *b*) may be envisaged, whose excitations should involve different energies and, corre-

(7) *Cf.* Dede and Rosenberg, *Ber.*, **67**, 147 (1934); Morton and Stubbs, *J. Chem. Soc.*, 1347 (1940); Blout and Gofstein, THIS JOURNAL, **67**, 15 (1945).

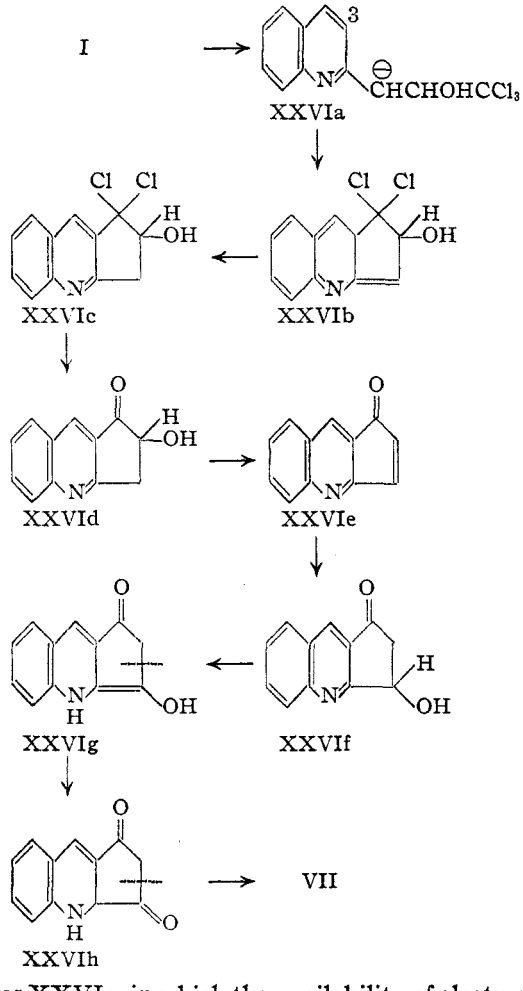
spondingly, different absorption bands. A final spectrographic check on our structural conclusions is provided by the absorption spectrum (Fig. 4) of (XXV), which contains the absorbing system



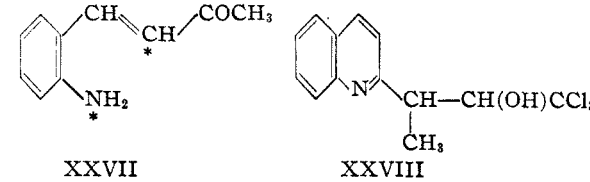
XXV

of (XII). It is clear that this spectrum bears no resemblance to those of the orange acid and its esters, and that consequently the expression (XII) is excluded for these substances.

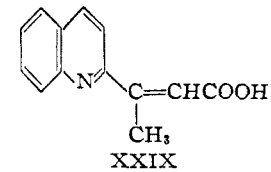
There remains only a consideration of the mechanism of the remarkable change, I → VII. The following mechanistic scheme is a reasonable one; it is intended as an outline only, and in particular, the sequence of steps, and the exact nature of the various intermediates may be varied considerably. Thus, the removal of a proton by base



gives XXVIa, in which the availability of electrons at C.3 permits attack on the trichloromethyl group, with loss of halide ion and cyclization. The $\alpha,\gamma$ shift (XXVIb → XXVIc) with aromatization, and the hydrolysis of the remaining chlorine atoms are unexceptional. The loss of water (XXVId → XXVIe) is permissible in view of the $\beta$-position of the hydroxyl group with respect to the quinoline nucleus and its subsequent readdition in the opposite sense (XXVIe → XXVIf) is characteristic of $\alpha,\beta$-unsaturated carbonyl compounds. The change XXVIf → XXVIg is reminiscent of the familiar $\alpha$-methylpyridine–$\alpha$-pyridone methide equilibrium, which in this case is rendered irreversible by the ketonization, XXVIg → XXVIh. Normal cleavage of the $\beta$-diketone (XXVIh) then leads to VII. Complicated as the suggested sequence is, it is difficult to conceive of a simpler series to account for so deep-seated a change. We have considered one other possibility, namely, that in effect the chloral-quinaldine (I) breaks down to give *o*-aminobenzalacetone (XXVII) and chloral, or equivalents of these fragments; subsequent re-condensation of the aldehyde group of chloral at the starred positions, followed by hydrolysis could lead to (VII). It will be noted that a prerequisite for the mechanism outlined above is the presence of *two* hydrogen atoms on the carbon $\alpha$ to the quinoline nucleus. On the other hand, the second mechanism possesses no such feature. Consequently, the chloral-$\alpha$-ethylquinoline condensation product (XXVIII) should undergo an analogous rearrangement to 3-propionyl-1,2-dihydroquinoline-2-carboxylic acid, if the second mechanism is operative, but no such change is possible in the event that the alternative sequence is correct. We have prepared XXVIII and observed that it is smoothly converted by alcoholic sodium hydroxide to $\beta$-($\alpha$-quinolyl)-crotonic acid (XXIX); no evidence of the formation of a rearrangement product analogous to (VII) could be obtained. Consequently, we reject the cleavage–recondensation mechanism, and its equivalents.



XXVII XXVIII

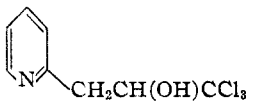


XXIX

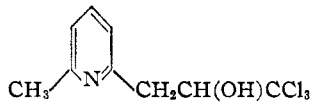
In conclusion, we may point out that we have prepared the chloral condensation products XXX,[8] XXXI,[9] XXXII[10] and XXXIII[11] and subjected them to the conditions which bring about the change I → VII. In none of these cases

(8) Tullock and McElvain, THIS JOURNAL, **61**, 961 (1939).
(9) Einhorn and Gilbody, *Ber.*, **26**, 1414 (1893).
(10) Koenigs and Menzel, *ibid.*, **37**, 1330 (1904).
(11) Clemo and Hoggarth, *J. Chem. Soc.*, 1241 (1939).

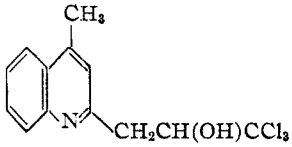
have we observed any reaction other than the normal conversion to the corresponding substituted acrylic acid.



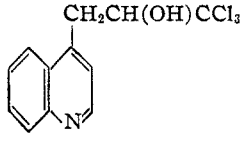

XXX




XXXI




XXXII




XXXIII

## Experimental

**Chloralquinaldine (I).**—The method of Bachman[12] was used. It was found to be essential that the initial exothermic reaction be moderated so that the temperature did not exceed 100°. Dark-colored by-products were formed if the mixture was allowed to overheat; yield, 71%, m. p. 145–146°.

**Sodium Salt of 2-Carboxy-3-acetyl-1,2-dihydroquinoline (VII, R = Na).**—This product was obtained in 35–45% yield by the method of Einhorn.[1] The free acid, m. p. 123–125° (dec.), was obtained by neutralizing a concentrated aqueous solution of the sodium salt with hydrochloric acid.

The acid was resolved in the following way: the orange sodium salt (32.8 g., 0.112 mole) and brucine sulfate (56 g.) were dissolved together in 500 ml. of hot water. The product which separated slowly from the cooled solution was collected and recrystallized twice from water, with considerable loss. The salt was then decomposed by taking up in 50 ml. of water and adding a solution containing 1.8 g. of sodium hydroxide. Brucine was removed by three extractions with chloroform. The aqueous layer was cooled, and the *l*-sodium salt which separated was recrystallized from dilute ethanol, m. p. 187–191°; $[\alpha]^{26}D$ −430° ($l$ = 2 dcm, $C$ = 0.5 g./100 ml. $H_2O$). A sample for analysis was dried at 125°.

*Anal.* Calcd. for $C_{12}H_{10}O_3NNa$: C, 60.25; H, 4.21; N, 5.86. Found: C, 60.33; H, 4.51; N, 5.61.

**2-Carbethoxy-3-acetyl-1,2-dihydroquinoline (VII, R = Et).**—The sodium salt trihydrate of 3-acetyl-1,2-dihydroquinoline-2-carboxylic acid (4.0 g.) was suspended in 40 ml. of absolute ethanol, the solution was immersed in ice, and saturated with dry hydrogen chloride. After twelve hours the solvent was removed *in vacuo*, the residue was stirred with ice and water and neutralized with sodium bicarbonate. After addition of cold 10% sodium hydroxide (25 ml.) the product was removed, washed with water and dried; yield, 2.16 g. (65%). Recrystallized from dilute ethanol, it formed bright-yellow needles, m. p. 110.5–111.5°. *Anal.* Calcd. for $C_{14}H_{15}O_3N$: C, 68.55; H, 6.16. Found: C, 68.63; H, 5.75.

The ester was obtained in like yield by direct esterification of the free acid (VII, R = H). The corresponding **methyl ester (VII, R = Me)** was obtained in a similar manner. After repeated recrystallization from dilute methanol, it formed golden-yellow prisms, m. p. 140–141°. It is undoubtedly identical with the ester, m. p. 145°, obtained by Borsche[2] from the acid and diazomethane. *Anal.* Calcd. for $C_{13}H_{13}O_3N$: C, 67.52; H, 5.67. Found: C, 67.22; H, 5.21.

**N-Benzoyl-2-carbomethoxy-3-acetyl-1,2-dihydroquinoline (XI, R = Me, R′ = $C_6H_5CO$—).**—The above methyl ester (VII, R = Me, 0.95 g.) and benzoyl chloride (0.62 g.) were dissolved in 10 ml. of dry pyridine. After standing several days the solvent was removed *in vacuo* and the residue was made alkaline with dilute sodium bicarbonate solution. The product which oiled out was washed by decantation with water and recrystallized from methanol; yield, 0.4 g., pale yellow crystals, m. p. 140–141°. *Anal.* Calcd. for $C_{20}H_{17}O_4N$: C, 71.63; H, 5.11. Found: C, 71.84; H, 4.87.

When this benzoyl derivative (0.1 g.) was allowed to stand for two days with 1 ml. of concentrated hydrochloric acid, addition of water gave the crystalline free *acid* (XI, R = H; R′ = $C_6H_5CO$—) which was recrystallized from dioxane; m. p. 198–199° (dec.). *Anal.* Calcd. for $C_{19}H_{15}O_4N$: C, 71.02; H, 4.71. Found: C, 70.33; H, 4.89.

More drastic hydrolysis of the N-benzoyl ester (XI, R = Me, R′ = $C_6H_5CO$—) with concentrated hydrochloric acid at 100° gave benzoic acid in 55% yield and an unidentified oil. No benzaldehyde could be detected.

**2-Carbethoxy-1,3-diacetyl-1,2-dihydroquinoline (XI, R = Et, R′ = $CH_3CO$—).**—2-Carbethoxy-3-acetyl-1,2-dihydroquinoline (VII, R = Et, 0.6 g.) was dissolved in 2 ml. of pyridine and 3 ml. of acetic anhydride; the solution was warmed on the steam-bath for three hours. The excess solvents were removed *in vacuo* and ice-water was added to the residue. The oil soon solidified and was collected, washed and recrystallized from ethanol; yield of pale-yellow prisms, 50%; m. p. 131–132°. *Anal.* Calcd. for $C_{16}H_{12}O_4N$: C, 66.88; H, 5.96. Found: C, 67.32; H, 5.69.

**3-Acetylquinoline (VIII).**—This ketone was prepared by permanganate oxidation of the sodium salt (VII, R = Na) according to Borsche and Manteuffel[2] (yield, 85%), by chromic acid oxidation (A) of the salt or by the action of light and air on the free acid (VII, R = H) (B).

(A) The sodium salt (VII, R = Na, 5 g.) was dissolved in a mixture of 150 ml. of glacial acetic acid and 100 ml. of water. Concentrated sulfuric acid (2 ml.) was added followed by a solution of 1.85 g. of potassium dichromate in 30 ml. of water. The solution which turned green was concentrated *in vacuo* and the residue was made alkaline with ammonium hydroxide. The solution of the residue in ethanol was filtered and evaporated *in vacuo*. The residue was crystallized twice from water. It then had m. p. 96–98° and mixed with a sample from the permanganate oxidation of (VII, R = Na) or with an authentic sample of 3-acetylquinoline (see below) melted at 96–99°.

(B) A sample of the orange acid (VII, R = H) was allowed to stand in air for eleven days with frequent stirring of the crystals. The bright orange color gradually faded and finally a buff-colored crystalline solid remained. The decomposition was markedly favored by sunlight; exposure in thin layers was best. The product was stirred with 10% sodium bicarbonate solution, removed by filtration and washed with water. Recrystallization from water gave 3-acetylquinoline, m. p. 96–98°. From the sodium bicarbonate solution a small further quantity of 3-acetylquinoline, but no 3-acetylquinoline-2-carboxylic acid was obtained.

For comparison authentic samples of 3-acetylquinoline (VIII), m. p. 97–99°, 3-acetylquinoline-2-carboxylic acid (X, R = H), m. p. 142–143° (dec.), and the corresponding ethyl ester (X, R = Et), m. p. 93–94.5°, were prepared by the condensation of *o*-aminobenzaldehyde (Raney nickel reduction of *o*-nitrobenzaldehyde[13]) with ethyl acetopyruvate followed by hydrolysis and decarboxylation, according to Koller.[3]

**Oxidation of (VII, R = Na) and (VII, R = Et) with Permanganate in Aqueous Pyridine.**—While permanganate oxidation of (VII, R = Na) according to Borsche's procedure gives only 3-acetylquinoline, careful oxidation in aqueous pyridine gives some 3-acetylquinoline-2-carboxylic acid:

One hundredth of a mole (2.96 g.) of the sodium salt was suspended in 140 ml. of pyridine. A solution of 1.2 g. in potassium permanganate in 140 ml. of warm pyridine was then added. Little evidence of reaction was noted until 50 ml. of water was added. After a few minutes the pre-

(12) Alberts and Bachman, THIS JOURNAL, 57, 1284 (1935).

(13) Ruggli and Schmid, *Helv. Chim. Acta*, 18, 1235 (1935).

cipitated manganese dioxide was removed and the filtrate was concentrated to a very small volume. Addition of a little sodium acetate caused the crude acid to separate (m. p. 120° (dec.)). The product was stirred with 2 ml. of 10% sodium bicarbonate and the mixture was filtered to remove 3-acetylquinoline. The filtrate was first acidified with hydrochloric acid and further concentrated *in vacuo*. The pure acid, m. p. 141–142° (dec.), separated as white needles from the cooled solution. The mixed melting point with authentic 3-acetylquinoline-2-carboxylic acid, m. p. 142–143° (dec.) (see above), was likewise 141–142° (dec.).

The ethyl ester (VII, R = Et) (2.0 g.) was dissolved in 200 ml. of pyridine and 200 ml. of water. The solution was cooled in ice to 2°. Potassium permanganate (1.4 g.) in 80 ml. of pyridine and 80 ml. of water was added dropwise, with stirring and cooling in ice. After the addition which took about twenty minutes the solution was warmed to room temperature and the manganese dioxide was removed. The filtrate was treated with 0.75 ml. of concd. hydrochloric acid and concentrated *in vacuo* to a very small volume. The residue which crystallized was suspended in a little ice water and was filtered and washed with water; yield, 50%. Recrystallization from ethanol gave white needles, m. p. 93–94°, mixed with an authentic sample (see above) of (X, R = Et), m. m. p. 93–94.5°.

**Stability of (X, R = H) under Conditions of Aqueous Permanganate Oxidation.**—A solution containing 5 ml. of 1% potassium permanganate, 0.5 ml. of 10% sodium bicarbonate and 4 ml. of water was cooled in ice and 5 ml. of 1% sodium bisulfite was added. 3-Acetylquinoline-2-carboxylic acid (0.1 g.) was added and the solution was heated to boiling. Manganese dioxide was removed and the filtrate was concentrated *in vacuo*. Acidification with one drop of concd. hydrochloric acid yielded the unchanged acid, m. p. 142–143° (dec.).

**3-Acetyl-1,4-dihydroquinoline (XIV). (a) By Pyrolysis of (VII, R = H).**—3-Acetyl-1,2-dihydroquinoline-2-carboxylic acid (8.1 g.) was placed in a 200-ml. round-bottom flask and heated in a metal-bath for twenty minutes at 180–190°. (Nitrogen was bubbled through the flask during the pyrolysis.) The resultant red oil was cooled and taken up in ethanol. From the cooled solution colorless plates separated which after recrystallization from dilute ethanol melted at 177–181°.

**(b) By Catalytic Hydrogenation of 3-Acetylquinoline.**—One gram of the ketone was hydrogenated at atmospheric pressure in 100 ml. of absolute ethanol using about 2 g. of Raney nickel catalyst. The theoretical volume of hydrogen was absorbed in two hours. The catalyst was removed and the filtrate concentrated *in vacuo* to *ca.* 15 ml. From the cooled solution the product (XIV) separated in 40% yield, m. p. 174–180°.

**Permanganate Oxidation of 3-Acetyl-1,4-dihydroquinoline (XIV).**—A sample of the dihydro-compound (XIV) (200 mg.) was dissolved in a hot mixture of 50 ml. of water and 10 ml. of acetone. A solution of 122 mg. of potassium permanganate in 10 ml. of water was then added dropwise and with shaking in the course of ten minutes. The resulting mixture was reheated to boiling, filtered and the filtrate concentrated *in vacuo* to about 10 ml. The product crystallized on cooling and was recrystallized from water; yield, 50%; m. p. 97–98°; mixed with authentic 3-acetylquinoline, m. m. p. 98–99°.

**α-Anilinoacetopyruvic Ester (XXV).**—One tenth of a mole each of aniline and ethyl acetopyruvate were mixed with 40 ml. of ether. After three days the ether was evaporated and the product distilled twice *in vacuo;* yield, 65%; b. p. 170–171° (8 mm.). *Anal.* Calcd. for $C_{13}H_{15}O_3N$: C, 66.93; H, 6.48. Found: C, 67.22; H, 6.38. The corresponding *o*-toluidino ester was prepared similarly from *o*-toluidine and ethyl acetopyruvate; yield, 57%, b. p. 154–155° (3 mm.). *Anal.* Calcd. for $C_{14}H_{17}O_3N$: C, 67.99; H, 6.93. Found: C, 68.07; H, 6.40.

**2-Dimethylamino-5-methylbenzaldehyde (XX).**—2-Dimethylamino-5-methylbenzyl alcohol was prepared by the method of von Braun and Kruber[14] in 45% yield, b. p. 125–127° (8 mm.). Oxidation to the aldehyde was carried out by the modified Oppenauer procedure of Woodward, Wendler and Brutschy.[15]

Potassium (20 g.) was dissolved in 400 ml. of *t*-butanol and the excess alcohol was removed completely *in vacuo*. To the dry potassium *t*-butoxide was added 33 g. of 2-dimethylamino-5-methylbenzyl alcohol, 2 liters of dry benzene and 260 g. of dry benzophenone. The mixture was refluxed in an atmosphere of nitrogen for twenty-three hours, after which it was extracted with dilute hydrochloric acid (150 ml. concd. acid and 500 ml. of water). The acid extract was made alkaline with sodium hydroxide and the product was extracted with 300 ml. of ether in three portions. The ether was removed and the residue was fractionated through a 30-cm. Podbielniak column. About 35% of dimethyl-*p*-toluidine (b. p. 90–97° (12–15 mm.)) and 40% of the bright-yellow desired aldehyde, b. p. 138–142° (16 mm.), were obtained.

The *p*-nitrophenylhydrazone, prepared in hot ethanol containing a few drops of glacial acetic acid, crystallized from ethanol in deep red-orange prisms, m. p. 185–186°. *Anal.* Calcd. for $C_{16}H_{18}O_2N_4$: C, 64.41; H, 6.08. Found: C, 64.50; H, 5.69.

The **azine** was prepared by allowing a solution of 0.7 g. of the aldehyde, 2.5 ml. of ethanol, 2.0 ml. of water and 0.1 g. of hydrazine hydrate to stand at room temperature for twenty-four hours. It crystallized from ethanol in lemon-yellow elongated plates, m. p. 147–148°. *Anal.* Calcd. for $C_{20}H_{26}N_4$: C, 74.49; H, 8.13. Found: C, 74.83; H, 7.92. In several attempts to effect condensation of the aldehyde with acetone, the starting material was recovered unchanged.

**2-Ethylquinoline.**—This compound was prepared by a method similar to that used by Ziegler[16] in the preparation of 2-butylquinoline.

Lithium metal (28 g.) was pounded into a thin sheet and the sheet was cut with scissors into small pieces, which were added quickly to 1200 ml. of dry ether. The mixture was stirred and cooled in ice while 200 g. of ethyl bromide was added dropwise during thirty minutes. The addition was conducted at such a rate that a steady reflux of the ether was maintained. Quinoline (200 ml.) was then added dropwise during fifteen minutes with stirring and cooling in ice. Unreacted lithium was then skimmed off and water was added cautiously with stirring to the mixture. The ether layer was separated, washed with water and dried over sodium sulfate. After the solvent was evaporated the residue of crude 1,2-dihydro-2-ethylquinoline was dissolved in 500 ml. of nitrobenzene. The mixture was heated slowly to 200° and was kept at that temperature five minutes. The solution was cooled, diluted with ether and the bases were extracted with dilute hydrochloric acid containing 175 ml. of the concd. acid. The acid extract was made alkaline with sodium hydroxide, and the product was taken up in ether. The ether extract was dried over potassium hydroxide after which the solvent was distilled. The residue was fractionated carefully *in vacuo*, and the 2-ethylquinoline was obtained as a yellow oil, b. p. 125–130° (15 mm.); yield 30%. The picrate was prepared, m. p. 147–149°. Doebner[17] reports a melting point of 148°.

**Chloral-2-ethylquinoline (XXVIII).**—To 58 g. of ethylquinoline was added 40 ml. of pyridine and 54.5 g. of chloral. The mixture was heated on a steam-bath for one and one-half hours. During the early part of the heating period, the reaction was exothermic, and the temperature was kept below 105° by periodic cooling. The product was then poured into water and was washed several times with water by decantation. Addition of a little ethanol caused the product to crystallize slowly. The adduct was filtered and washed with cold alcohol to remove dark-colored impurities, yield, 57%. A sample was recrystallized for analysis from methanol; m. p. 117–118°. *Anal.*

(14) von Braun and Kruber, *Ber.*, **45**, 2980 (1912).

(15) Woodward, Wendler and Brutschy, THIS JOURNAL, **67**, 1425 (1945).

(16) Ziegler, *Ann.*, **485**, 182 (1931).

(17) Doebner, *ibid.*, **242**, 272 (1887).

Calcd. for $C_{13}H_{12}ONCl_3$: C, 51.26; H, 3.97. Found: C, 51.02; H, 4.11.

**Hydrolysis of Chloral-2-ethylquinoline.**—This hydrolysis was conducted using the same molar proportions and conditions as those used for chloral-quinaldine.

Five hundredths of a mole of the adduct was warmed with 67 ml. of ethanol, and 56 ml. of water was added slowly. The mixture was heated to boiling, and to it was added, as quickly as the vigorous ebullition would permit, a solution of 11.7 g. of sodium hydroxide in 37 ml. of water. After the reaction had subsided the solution was kept hot for five minutes and 100 ml. of hot ethanol was added. After the mixture had cooled overnight, no crystalline product had separated, so the solvents were removed *in vacuo*, and the residue was dissolved in water. The product was precipitated with 11 ml. of concd. hydrochloric acid and 5 ml. of acetic acid: yield, 79%, m. p. 190–195° (dec.). Recrystallization from dilute dioxane gave the colorless β-2-quinolylcrotonic acid, m. p. 204–206° (dec.). *Anal.* Calcd. for $C_{13}H_{11}O_2N$: C, 73.22; H, 5.20. Found: C, 72.85; H, 5.18.

## Summary

The action of alcoholic sodium hydroxide on chloral-quinaldine gives 3-acetyl-1,2-dihydroquinoline-2-carboxylic acid.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

# The Reaction of Benzophenone β-Naphthil with Phenylmagnesium Bromide and with Phenyllithium

BY HENRY GILMAN AND JOHN MORTON

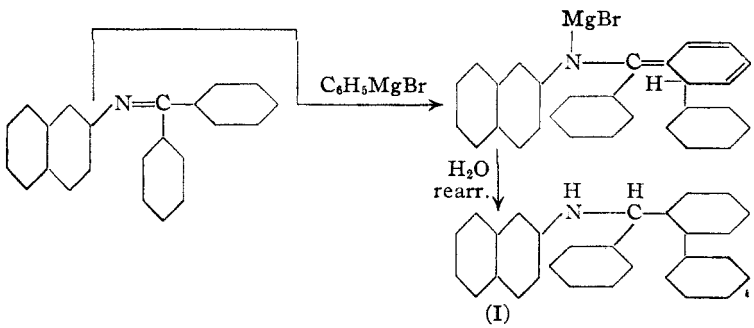
The forced reaction of phenylmagnesium bromide with benzophenone anil was reported earlier from this Laboratory.[1] It was found that the Grignard reagent undergoes a lateral-nuclear 1,4 addition to the conjugated system consisting of the anil linkage and an unsaturated linkage of one benzohydrylidene phenyl group to produce, after hydrolysis and a hydrogen shift, *o*-phenylbenzohydrylaniline. Similar lateral-nuclear additions, in which Grignard reagents add 1,4 to ketones whose carbonyl groups are conjugated with unsaturated linkages in aromatic nuclei, have since been described[2]; also, it has been demonstrated that benzalquinaldine adds phenylmagnesium bromide in a lateral-nuclear sense.[3]

Further work in this Laboratory[4] established that phenyllithium adds to benzophenone anil at the anil linkage only, yielding triphenylmethylaniline. This reaction proceeds at the temperature of refluxing ether, whereas phenylmagnesium bromide has no detectable effect upon the anil at this temperature.

The present study of the reaction of benzophenone β-naphthil with phenylmagnesium bromide and with phenyllithium, has been carried out to discover whether the substitution of an N-β-naphthyl group for the N-phenyl group of benzophenone anil could affect the course of reaction with either of the organometallic compounds, and particularly whether any addition involving the naphthyl group itself could be observed.

We find that the naphthil behaves quite similarly to the anil with respect to both organometallic compounds. With phenylmagnesium bromide at the temperature of refluxing ether, no reaction occurs; when ether–toluene is used and the temperature is raised to 90–100°, a compound melting at 185–186° and having a nitrogen content corresponding to that of *o*-phenylbenzohydryl-β-naphthylamine (I) is obtained in pure yields as high as 71%. Like the similarly substituted aniline described earlier,[1] this substance yields 9-phenylfluorene when refluxed with alcoholic hydrochloric acid.

The compound melting at 185–186° has been shown to be identical with the product of the forced reaction between *o*-biphenylylmagnesium iodide and benzal-β-naphthylamine, and was thus identified as (I). The reaction leading to the formation of compound (I) from the naphthil is shown.




(I)

We find that phenyllithium, on the other hand, reacts with the naphthil at the temperature of refluxing ether to produce a compound which melts at 185° but which gives a large depression of melting point when mixed with (I). The product from the RLi reaction proved to be identical with the product of the condensation of triphenylcarbinol with β-naphthylamine in glacial acetic acid. The

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

(2) Kohler and Nygaard, *ibid.*, **52**, 4128 (1930); Allen and Overbaugh, *ibid.*, **57**, 1322 (1935); Koelsch and Rosenwald, *ibid.*, **59**, 2166 (1938); Lutz and Reveley, *ibid.*, **63**, 3178 (1941); Geissman and Morris, *ibid.*, **66**, 716 (1944); Fuson, McKusick and Spangler, *ibid.*, **67**, 597 (1945); Koelsch and Rosenwald, *J. Org. Chem.*, **3**, 462 (1938); Koelsch and Anthes, *ibid.*, **6**, 558 (1941); Fuson, Kaiser and Speck, *ibid.*, **6**, 845 (1941); Fuson, Armstrong and Speck, *ibid.*, **7**, 297 (1942).

(3) Hoffman, Farlow and Fuson, THIS JOURNAL, **55**, 2000 (1933).

(4) Gilman and Kirby, *ibid.*, **55**, 1625 (1933).