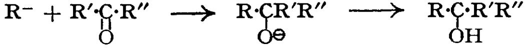
# 39. *The Mechanism of Decarboxylation. Part III. Further Evidence for the Occurrence of α-Quinolyl Anions during the Decarboxylation of Quinaldinic Acid.*

By B. R. Brown and D. Ll. Hammick.

By decarboxylating quinaldinic acid in quinoline (and also by the pyrolysis of calcium quinaldinate) αα′-diquinolyl has been obtained. In 1-chloro-2 : 4-dinitrobenzene, α-5-*chloro*-2-*nitrophenylquinoline* was formed, the reaction involving elimination of the 2-nitro-group and the substitution of the quinolyl group into the 3-position adjacent to it. In the presence of certain esters, decarboxylation of quinaldinic acid replaces the –OR group by the quinolyl group. Though in all cases yields are small, the fact that the reactions occur is taken as further evidence for the formation of quinolyl ions (anionoid and basic reagents) during the decarboxylation of quinaldinic acid.

In Parts I and II (Dyson and Hammick, *J.*, 1937, **1724**; Ashworth, Daffern, and Hammick, *J.*, 1939, 809) it has been shown that the decarboxylation of picolinic, quinaldinic, and *iso*quinaldinic acids in aldehydes and ketones yields carbinols of the type R·C(OH)R′R″ (where R is α-pyridyl, α-quinolyl, or 1-*iso*quinolyl; R′ is aryl; and R″ is hydrogen, alkyl or aryl). The course of the reaction was formulated in terms of an intermediate anion :

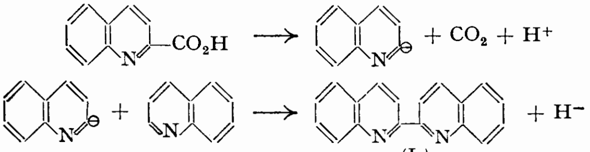
$$R\cdot CO_2H \longrightarrow R^- + CO_2 + H^+$$



$$R^- + R'\cdot\underset{\underset{O}{\|}}{C}\cdot R'' \longrightarrow R\cdot\underset{O^{\ominus}}{C}R'R'' \xrightarrow{H^+} R\cdot\underset{OH}{C}\cdot R'R''$$

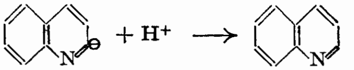
A similar mechanism of decarboxylation has been suggested for various acids on the basis of kinetic investigations (Verhoek, *J. Amer. Chem. Soc.*, 1934, **56**, 571; Fairclough, *J.*, 1938, 1186). However, direct chemical evidence for the occurrence of such anions is scarce, the only recorded examples being the rapid reactions of the anions from aliphatic α-nitro-carboxylic acids and from dibromomalonic acid with bromine (Pedersen, *J. Physical Chem.*, 1934, **38**, 559; Muus, *ibid.*, 1935, **39**, 343). A variety of chemical evidence is now presented to substantiate this ionic mechanism for the decarboxylation of quinaldinic acid.

By decarboxylating quinaldinic acid in quinoline, we have obtained a very small amount of αα′-diquinolyl (I), identified by the method of mixed m. p. We believe that this substance is produced by attack of the transitory α-quinolyl anion on the cationoid α-position of a quinoline molecule and liken this process to the reaction of quinoline with such reagents as sodamide, sodium hydroxide, lithiumalkyls, and sodium piperidine (Bradley and Robinson, *J.*, 1932, 1254) :



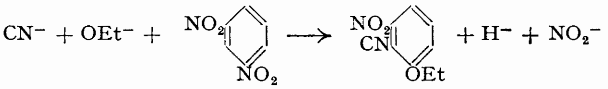
(I.)

It is recorded (Besthorn and Ibele, *Ber.*, 1904, **37**, 1243) that 2 : 7′-diquinolyl, m. p. 191°, is produced by heating calcium quinaldinate. We have reinvestigated this reaction, and have proved that the compound so obtained is the expected αα′-isomer. The better yield obtained from the calcium salt is probably due to the absence of the competing reaction :

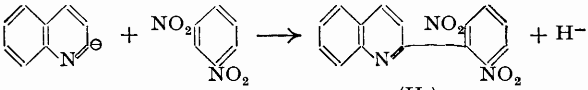


which occurs when the free acid decomposes. The production of αα′-dipyridyl by the distillation of copper picolinate (Blau, *Ber.*, 1888, **21**, 1077) probably occurs by the same mechanism.

That the α-quinolyl anion can also react with cationoid centres in purely aromatic molecules has been established by decarboxylating quinaldinic acid in nitro-compounds. *m*-Dinitrobenzene yields α-2 : 6-*dinitrophenylquinoline* (II), the structure of which is inferred from analogy with the reaction between *m*-dinitrobenzene and alcoholic potassium cyanide (Lobry de Bruyn, *Rec. Trav. chim.*, 1883, **2**, 219; von Heteren, *ibid.*, 1901, **20**, 107) :

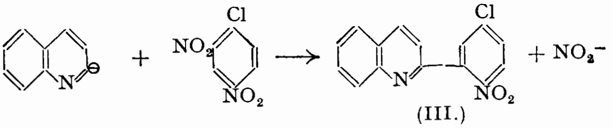


complications due to the presence of alcohol being absent :



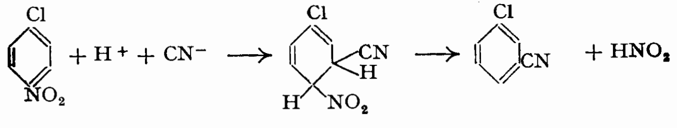
(II.)

Similarly, by decarboxylating in 1-chloro-2 : 4-dinitrobenzene, αα′-diquinolyl and α-5-*chloro*-2-*nitrophenylquinoline* (III) (identified by mixed m. p. with a synthetic specimen) were produced in small yield. (It was proved in separate experiments that neither of these products was obtained by heating quinoline with 1-chloro-2 : 4-dinitrobenzene for several hours at 180°.) The αα′-diquinolyl probably arose from the attack of the anion on the quinoline produced by straight decarboxylation. The formation of α-5-chloro-2-nitrophenylquinoline involves the elimination of a nitro-group with substitution by the quinolyl anion in the *adjacent* position :



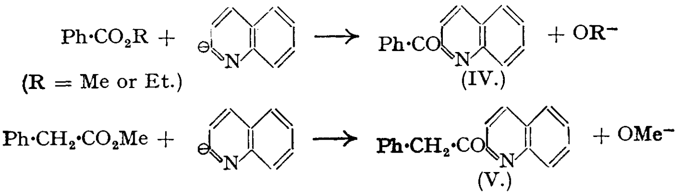
(III.)

Though the exact mechanism of such a reaction is obscure, it is analogous to the reaction of alcoholic potassium cyanide with *m*- and *p*-chloronitrobenzene, which von Richter (*Ber.*, 1875, **8**, 1418) formulated as an addition reaction, followed by elimination of nitrous acid :



Similar group displacements with substitution in adjacent positions have been studied by Gilman and his co-workers (*J. Amer. Chem. Soc.*, 1945, **67**, 349, 1479; 1946, **68**, 143), who, however, advance no mechanism.

In the reactions discussed above, the α-quinolyl anion apparently functions like a cyanide ion, behaviour remarked upon in Parts I and II (*locc. cit.*), and recently shown to extend to the γ-position of pyridine and quinoline (Mislow, *J. Amer. Chem. Soc.*, 1947, **69**, 2559; Brown, Hammick, and Thewlis, *Nature*, 1948, **162**, 73). Moreover, the quinolyl anion is the conjugate strong base of the " acid " quinoline, and as such should be able to displace other anionic bases (*e.g.*, O·Alk⁻) from esters. This reaction has been realised by decarboxylating quinaldinic acid in methyl and ethyl benzoates and in methyl phenylacetate :



(IV.)

(V.)

The yields obtained were small, the more facile reaction with hydrogen ions predominating. Phenyl α-quinolyl ketone (IV) was identified by analysis and mixed m. p., and benzyl α-quinolyl ketone (V) was separated from the αα′-diquinolyl formed as its 2 : 4-*dinitrophenylhydrazone*, and identified by mixed m. p. It was not possible to investigate the displacement of halide ions from aliphatic halides, since complications would arise from the attack of the halide on the quinoline produced during decarboxylation.

α-3-*Chlorophenylquinoline*, α-3-*chloro*-2-*nitrophenylquinoline*, and α-5-chloro-2-nitrophenylquinoline, needed for comparison with the decarboxylation products, were obtained in good yield from the corresponding substituted acetophenones (Waters, *J.*, 1945, 629) by the Friedländer synthesis.

## EXPERIMENTAL.

(Analyses are by Mr. F. C. Hall and Drs. Weiler and Strauss, Oxford. M. p.s are uncorrected.)

α-3-*Chlorophenylquinoline*.—A mixture of *m*-chloroacetophenone (0·8 g.) (Evans, Morgan, and Watson, *J.*, 1935, 1172), *o*-aminobenzaldehyde (0·6 g.), alcohol (40 c.c.), and 2N-sodium hydroxide (2 c.c.) was refluxed for 6½ hours. Water (60 c.c.) was added to the cooled solution, and the white solid precipitate separated, washed with water, and dried (1·1 g., 92%). Two recrystallisations from aqueous alcohol (1 : 10) yielded α-3-*chlorophenylquinoline* in the form of small colourless needles, m. p. 64—65° (Found : C, 75·45; H, 4·2; N, 5·85. $C_{15}H_{10}NCl$ requires C, 75·2; H, 4·2; N, 5·85%). The compound is readily soluble in light petroleum. It is soluble in dilute hydrochloric acid whence it is precipitated by alkali. The *picrate* separated from alcohol as small yellow prisms, m. p. 184—185° (Found : N, 11·75. $C_{21}H_{13}O_7N_4Cl$ requires N, 11·95%).

α-3-*Chloro*-2-*nitrophenylquinoline*.—3-Chloro-2-nitroacetophenone (1·0 g.) (Waters, *loc. cit.*) and *o*-aminobenzaldehyde (0·6 g.) were dissolved in a mixture of alcohol (50 c.c.), water (40 c.c.), and 2N-sodium hydroxide (10 c.c.), and refluxed for 2 hours. On cooling overnight, long flat golden-yellow crystals (0·5 g., 35%, m. p. 128—129°) separated. Two recrystallisations from light petroleum (b. p. 80—100°) yielded α-3-*chloro*-2-*nitrophenylquinoline* in the form of colourless needles, m. p. 129—130° (Found : C, 63·4; H, 3·15; Cl, 11·9. $C_{15}H_9O_2N_2Cl$ requires C, 63·3; H, 3·1; Cl, 12·4%). The compound is fairly soluble in cold alcohol, almost insoluble in water, but easily soluble in cold mineral acids. The *picrate* separated from alcohol as small chrome-yellow prisms, m. p. 144—145° (Found : C, 49·4; H, 2·5. $C_{21}H_{12}O_9N_5Cl$ requires C, 49·1; H, 2·3%).

α-5-*Chloro*-2-*nitrophenylquinoline* (III).—A mixture of 5-chloro-2-nitroacetophenone (0·6 g.) (Waters, *loc. cit.*), *o*-aminobenzaldehyde (0·4 g.), alcohol (40 c.c.), and 2N-sodium hydroxide (2 c.c.) was refluxed for 8 hours. Water (50 c.c.) was added to the cold solution, and the precipitated yellow solid (0·4 g., 47%) dried at 100° and recrystallised from aqueous acetone (1 : 1). The colourless feathery needles (m. p. 139—150°) which separated were crystallised 4 times from light petroleum (b. p. 80—100°); the product then had m. p. 156° (Found : C, 63·1; 63·7; H, 3·65, 3·5; Cl, 11·9. $C_{15}H_9O_2N_2Cl$ requires C, 63·3; H, 3·1; Cl, 12·4%). The compound is very soluble in cold alcohol or acetone but can be recrystallised from aqueous alcohol. It is almost insoluble in water, but easily dissolves in dilute mineral acids. The *picrate* separated from alcohol in the form of small yellow plates, m. p. 166—167° (Found : N, 12·6. $C_{21}H_{12}O_9N_5Cl,C_2H_6O$ requires N, 12·5%).

αα′-*Diquinolyl* (I) (Smirnoff, *Helv. Chim. Acta*, 1921, **4**, 807).—This formed colourless irregular plates, m. p. 192·5—193·5°, from alcohol. The picrate separated from alcohol as fine yellow needles, m. p. 211—212°.

*Benzyl α-Quinolyl Ketone* (V) (Kaufmann, Dändliker, and Burkhardt, *Ber.*, 1913, **46**, 2933).—This separated from aqueous alcohol as colourless silky needles, m. p. 78—79°. The 2 : 4-*dinitrophenylhydrazone* (prepared in alcohol) separated from glacial acetic acid as fine orange-coloured needles, m. p. 247° (Found : N, 16·0. $C_{23}H_{17}O_4N_5$ requires N, 16·4%).

*Decarboxylation of Quinaldinic Acid in Quinoline*.—The acid (10 g.) was decarboxylated by being heated at 160—180° in redistilled quinoline (50 c.c.) for 4 hours. The resulting dark brown solution was treated with dilute aqueous potassium hydroxide and distilled in steam. When all the quinoline had been removed, a tarry crystalline mass was isolated by ether extraction of the residual aqueous liquid. Two recrystallisations from alcohol (plus charcoal) yielded almost colourless, long narrow plates (6 mg.), m. p. 191—192°. The mixed m. p. with αα′-diquinolyl was 191—193°.

*Pyrolysis of Calcium Quinaldinate* (Besthorn and Ibele, *loc. cit.*).—The calcium salt (0·6 g.), heated over a free flame for several minutes, yielded a sublimate of yellow crystals. Two recrystallisations from alcohol yielded colourless plates (10 mg.), m. p. 192—193°, unchanged by admixture with synthetic αα′-diquinolyl.

*Decarboxylation of Quinaldinic Acid in* m-*Dinitrobenzene.*—Quinaldinic acid (10 g.) and recrystallised *m*-dinitrobenzene (100 g.) were kept at 155—175° until decarboxylation was complete (3 hours). Extraction by means of 15% hydrochloric acid with addition of charcoal yielded a yellow solution, which was made alkaline and distilled in steam to remove quinoline (about 4 c.c.). The remaining yellow solid was separated and recrystallised from aqueous acetic acid. The fine pale yellow needles of α-2 : 6-*dinitrophenylquinoline* (0·2 g., m. p. 140—142°) were recrystallised from the same solvent and were then colourless and had m. p. 140—141° (Found : C, 60·8; H, 3·0. $C_{15}H_9O_4N_3$ requires C, 61·0; H, 3·05%). The *picrate* separated from alcohol as yellow prisms, m. p. 183—184° (Found : N, 15·4. $C_{21}H_{12}O_{11}N_6$ requires N, 16·0%).

*Decarboxylation of Quinaldinic Acid in* 1-*Chloro*-2 : 4-*dinitrobenzene.*—The quantities and conditions used were as described for *m*-dinitrobenzene above. When the quinoline had been removed, the remaining dark brown solid was extracted with light petroleum, and yielded a pale yellow solid (0·25 g.), m. p. 145—160°. Recrystallisation from acetone (5 c.c.) gave pale yellow long narrow plates (10 mg.), m. p. 190—191°. On crystallisation from acetone and then from alcohol, the m. p. was 192—193°, unchanged by mixing with an authentic specimen of αα′-diquinolyl. The picrate separated from alcohol as yellow needles, m. p. 210—211°, alone or mixed with the picrate of αα′-diquinolyl.

The acetone mother liquor from the original crystallisation of the diquinolyl was evaporated and the white solid residue crystallised from aqueous acetone. The colourless feathery needles (m. p. 147—150°) which separated were twice recrystallised from light petroleum, and then had m. p. 157° (Found : C, 62·9, 63·2; H, 3·0, 3·2; N, 9·8. Calc. for $C_{15}H_9O_2N_2Cl$ : C, 63·3; H, 3·1; N, 9·8%). The mixed m. p. with synthetic α-5-chloro-2-nitrophenylquinoline was 156—157°.

*Decarboxylation of Quinaldinic Acid in Methyl Benzoate.*—Quinaldinic acid (5·0 g.) was dissolved in redistilled methyl benzoate (50 c.c.) and heated (gently at first, finally refluxing) for 2 hours. A steady evolution of carbon dioxide was maintained and the solution became red. The cold liquid was extracted with 15% hydrochloric acid (50 c.c.) and ether (50 c.c.). The acid layer was shaken with ether, separated, made alkaline, and distilled in steam. Quinoline (about 2 c.c.) collected in the distillate, and then colourless needles (several mg.). These were recrystallised from aqueous acetic acid and then had m. p. 107—108° (Found : C, 82·1; H, 5·1. Calc. for $C_{16}H_{11}ON$ : C, 82·4; H, 4·7%). On admixture with authentic phenyl α-quinolyl ketone (Dyson and Hammick, *loc. cit.*) the m. p. was unchanged.

Decarboxylation in ethyl benzoate yielded the same product.

*Decarboxylation of Quinaldinic Acid in Methyl Phenylacetate.*—A solution of the acid (10 g.) in the ester (100 c.c.) was heated until decarboxylation was complete (6 hours). Extraction and steam distillation as described in the previous examples removed quinoline. The residual brown solid was separated, washed with water, dried, and recrystallised from alcohol with addition of charcoal. The yellow crystals (several mg.) which separated were recrystallised from alcohol and were then obtained as colourless plates, m. p. 192—193°, alone or mixed with αα′-diquinolyl.

The alcoholic mother liquor from the original extraction was evaporated to small bulk and filtered into a hot solution of 2 : 4-dinitrophenylhydrazine sulphate in alcohol. A red precipitate (several mg.), m. p. 240°, separated on cooling. Recrystallisation from glacial acetic acid yielded orange micro-crystals, m. p. 245°. The mixed m. p. with the dinitrophenylhydrazone of benzyl α-quinolyl ketone was 246°.

The authors express their thanks to Dr. W. A. Waters for gifts of chemicals.

DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, April* 21*st*, 1948.]