## 172. *The Mechanism of Decarboxylation. Part II. The Production of Cyanide-like Ions from α-Picolinic, Quinaldinic, and* iso*Quinaldinic Acids.*

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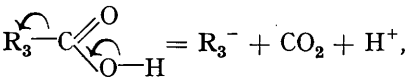
When α-picolinic, quinaldinic, and *iso*quinaldinic acids are decarboxylated in the presence of aldehydes and ketones, carbinols containing the pyridyl, quinolyl, and *iso*quinolyl radicals are obtained. This reaction is shown to be specific for the α-imino-acids mentioned above and it is suggested that the reason for this is that the anion-radicals produced when these acids lose carbon dioxide contain the modified cyanide ion structure $\left[\overset{\cdot\cdot}{\underset{\cdot\cdot}{N}}=\overset{\cdot\cdot}{\underset{\cdot\cdot}{C}}\right]^-$. The addition of such cyanide-like ions to the carbonyl group would thus be analogous to cyanohydrin formation.

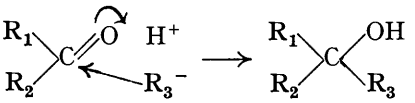
An explanation is suggested for the readiness with which α-imino-carboxylic acids lose carbon dioxide and of the action of carboxylase.

In a previous communication (Part I, J., 1937, 1724), it was shown that when quinaldinic and *iso*quinaldinic acids are heated with certain aldehydes and ketones (benzaldehyde, acetophenone, benzophenone), carbon dioxide is liberated and carbinols of the type $R_1R_2R_3C{\cdot}OH$ are obtained, in which $R_3$ is α-quinolyl or *iso*quinolyl and $R_1$ may be hydrogen. The view was put forward that the reaction consists essentially in the production of hydrogen ions, carbon dioxide and quinolyl or *iso*quinolyl ions, thus :



$$= R_3^- + CO_2 + H^+,$$

the ions subsequently (or simultaneously) attaching themselves to the carbinol group :



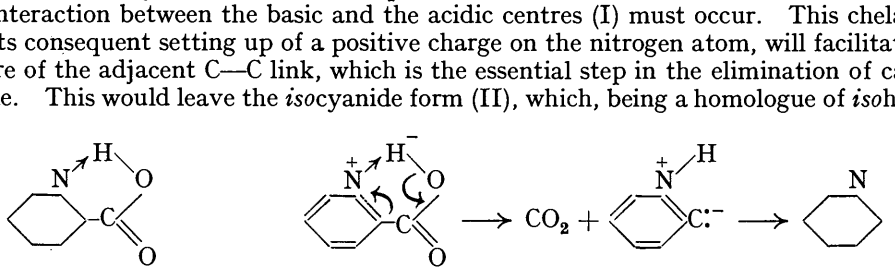
At first sight there does not appear to be any reason why, if the above mechanism were correct, any carboxylic acid that readily loses carbon dioxide should not yield, in the presence of carbonyl groups, products similar to those obtained from the quinaldinic acids. However, a thorough examination of the products of the decarboxylation of a wide variety of acids * in aldehydes and ketones (and also in unsaturated substances containing ethylenic

* Trichloroacetic, malonic, maleic, pyruvic, phenylacetic, propiolic, trinitrobenzoic, and anthranilic acids, glycine, 1 : 3-dimethylpyrrole-2 : 4-dicarboxylic, 1-phenyl-5-methylpyrazole-3-carboxylic, 1-phenyl-5-methyltriazole-4-carboxylic, indazolecarboxylic, indole-2-carboxylic, 3-methylindole-2-carboxylic, 5-methoxy-3-methylindole-2-carboxylic, 4-chloro-2 : 6-dimethylpyridine-3-carboxylic, 2-methylquinoline-3- and -4-carboxylic, 2-phenylquinoline-4-carboxylic, 2-methylquinoline-8-carboxylic, 3-methyl-2-ethylquinoline-8-carboxylic, 1 : 2 : 3 : 4-tetrahydroquinoline-2- and -9-carboxylic, 2-methyl-4 : 5-dihydrofuran-3-carboxylic, and chelidonic acids.

and acetylenic linkages and the nitrile group) has resulted in the addition of only one acid, α-picolinic, to those known to undergo the type of reaction under discussion. It therefore became necessary to discover some factor common to the three acids α-picolinic, quinaldinic, and *iso*quinaldinic, that could be connected with the fact that only when they, of all the acids examined, lose carbon dioxide, do the products of decarboxylation interact with the carbonyl group. It was at once apparent that the mere presence of a basic centre in the molecule was insufficient; the decarboxylation of pyridine and quinoline acids other than those containing the carboxyl group α to the nitrogen atom yielded no products of interaction with aldehydes and ketones. Furthermore, the nitrogen atom must be tertiary; thus tetrahydroquinaldinic acid and 1 : 3-dimethylpyrrole-2 : 4-dicarboxylic acid when decarboxylated in benzaldehyde or acetophenone yielded no products of interaction with the solvents.

A closer inspection of the structures of the anion-radicals that, on our view of the primary process in the decarboxylation, are produced when carbon dioxide is eliminated from α-picolinic, quinaldinic, and *iso*quinaldinic acids reveals the fact that they have in common the structure $\left[\overset{\diagdown}{\underset{\cdot\cdot}{N}}{=}\overset{\diagup}{\underset{\cdot\cdot}{C}}\right]^-$. This is the cyanide ion $[\underset{\cdot\cdot}{N}{\equiv}\underset{\cdot\cdot}{C}]^-$ with one of the three nitrogen-to-carbon bonds replaced by a ring. Since cyanide ions readily attack the carbonyl group, a similar reaction might reasonably be expected to occur with the modified ions $\left[\underset{\cdot\cdot}{N}{=}\underset{\cdot\cdot}{C}\right]^-$. It then follows that the production of carbinols from the three α-imino-acids mentioned above is nothing more or less than an analogue of cyanohydrin formation and the specific nature of the reaction receives a ready explanation.

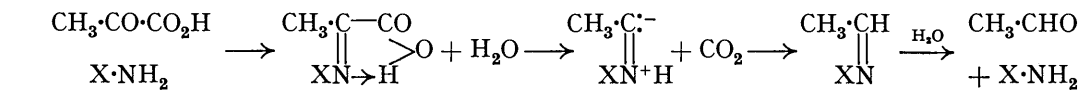
The carboxylic acids of the pyridine, quinoline, and *iso*quinoline series vary widely in the ease with which they lose carbon dioxide when heated. Examination of the data (Wieland and Berzel, *Annalen*, 1924, **439**, 196) and our own experience show, however, that the α-imino-acids are always much more easily decomposed than other isomers. This generalisation is illustrated by the behaviour on melting of quinoline-1 : 2-dicarboxylic acid, the carbonyl group α to the tertiary nitrogen atom alone being eliminated to give quinoline-2-carboxylic acid. It seems possible to connect this behaviour with the fact that interaction between the basic and the acidic centres (I) must occur. This chelation, with its consequent setting up of a positive charge on the nitrogen atom, will facilitate the rupture of the adjacent C—C link, which is the essential step in the elimination of carbon dioxide. This would leave the *iso*cyanide form (II), which, being a homologue of *iso*hydro-



(I.) (II.)

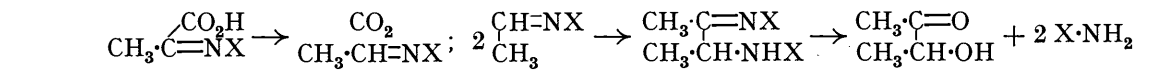
cyanic acid, might be expected to ionise and, in the absence of carbonyl groups to react with the ions, to revert to the ordinary form of the free base.

In this connection the catalytic effect of primary amines and amino-acids on the rates of decarboxylation of certain α-ketonic acids (pyruvic and phenylglyoxylic) investigated by Boklund (*Biochem. Z.*, 1930, **226**, 56) and by Langenbeck and Hutschenreuter (*Z. anorg. Chem.*, 1930, **118**, 1) is of interest. Formation of an intermediate anil by the action of the amine $X{\cdot}NH_2$ would give with, for instance, pyruvic acid,

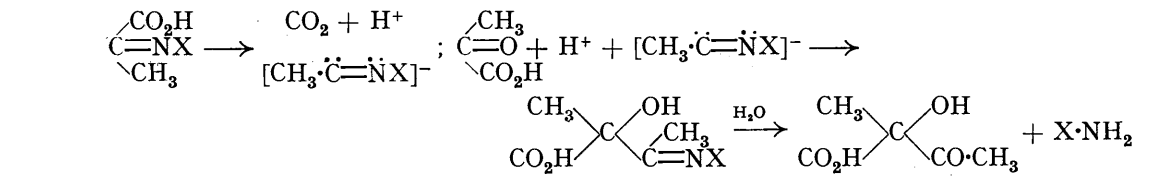


This mechanism makes it clear why secondary and tertiary bases (piperidine and pyridine) showed no catalytic effect (*loc. cit.*). The decarboxylation of the anil of pyruvic acid in boiling benzaldehyde ($X = C_6H_5$) failed to yield a cyanohydrin-like derivative, 2-styryl-quinoline-4-carboxylic acid being obtained as main product (Doebner and Peters,

*Ber.*, 1889, **22**, 3007). We would, however, call attention to the work of Langenbeck, Wrede, and Schlockermann (*Z. physiol. Chem.*, 1934, **227**, 263) on the decarboxylation of pyruvic acid by carboxylase with the production of α-acetylethyl alcohol. These authors proposed a mechanism which depends on the intermediate formation of an aldehyde-imine by the action of the enzyme, which is itself an amino-compound $X{\cdot}NH_2$, thus :



Our suggested mechanism for the decarboxylation of α-imino-carboxylic acids enables a reason to be given for the production of acetylethyl alcohol that does not require the unexplained second step in the above process, thus :



The product, α-hydroxy-α-methylacetoacetic acid, might be expected to lose carbon dioxide with the same ease as does acetoacetic acid, giving α-acetylethyl alcohol.

## Experimental.

*Diphenyl-2-quinolylcarbinol*, $C_9H_6N{\cdot}CPh_2{\cdot}OH$.—2·5 G. of quinaldinic acid were heated with 25 g. of benzophenone for 2 hours at 175°; evolution of carbon dioxide had then ceased. The cold reaction mixture was shaken with equal parts of 15% hydrochloric acid and ether. The aqueous layer, containing basic substances, was made alkaline with sodium hydroxide and distilled in steam to remove a small quantity of quinoline. The insoluble brown *carbinol* remaining (3 g.) was twice recrystallised from ligroin (b. p. 100—120°); m. p. 189° (Found : C, 84·4; H, 5·7. $C_{22}H_{17}ON$ requires C, 84·6; H, 5·8%). No acetyl or benzoyl derivative could be obtained and the substance formed no urethane with phenyl *iso*cyanate.

*Phenyl-2-pyridylcarbinol*, $C_5H_4N{\cdot}CHPh{\cdot}OH$.—5 G. of picolinic acid were dissolved in 30 g. of freshly distilled benzaldehyde and maintained at 140° for 1¼ hours (cessation of evolution of carbon dioxide). Treatment as above with hydrochloric acid and ether and liberation of bases by the addition of alkali gave 5 c.c. of a brown oil, which was washed with water to remove pyridine, dried in ether over sodium sulphate, and distilled under diminished pressure. The colourless liquid obtained (3 c.c.), b. p. 181—183°/16 mm., solidified on standing and after two crystallisations from ligroin (b. p. 80—100°) and one from ligroin–benzene (1 : 1) had m. p. 78° (Tschitschibabin, *Ber.*, 1904, **37**, 1371, gives m. p. 82°) (Found : C, 77·9; H, 6·0. Calc. for $C_{12}H_{11}ON$ : C, 77·8; H, 5·9%). The picrate had m. p. 169°, and the *phenylurethane*, m. p. 143·5° (Found : N, 9·5. $C_{19}H_{16}O_2N_2$ requires N, 9·2%). Unlike the corresponding phenyl-2-quinolylcarbinol (Dyson and Hammick, *loc. cit.*), this carbinol is not oxidised to the ketone in air.

*Phenyl-2-pyridylmethylcarbinol*, $C_5H_4N{\cdot}CPhMe{\cdot}OH$.—5 G. of picolinic acid and 25 g. of freshly distilled acetophenone were maintained at 25° for 2 hours. Working up as above yielded 7 c.c. of a basic oil free from pyridine. On distillation 5 c.c. of a colourless oil were obtained at 152·5°/745 mm.; this did not crystallise on keeping. The *picrate*, m. p. 176°, was crystallised from ethyl alcohol (Found : N, 13·4. $C_{13}H_{13}ON,C_6H_3O_7N_3$ requires N, 13·1%), and the *phenylurethane*, m. p. 151°, from light petroleum (b. p. 40—60°) (Found : C, 75·2; H, 5·6; N, 8·8. $C_{20}H_{18}O_2N_2$ requires C, 75·5; H, 5·7; N, 8·8%). The *p*-nitrobenzoate had m. p. 225°.

*Diphenyl-2-pyridylcarbinol*, $C_5H_4N{\cdot}CPh_2{\cdot}OH$.—6·5 G. of picolinic acid and 30 g. of benzophenone were heated for 4½ hours at 160°; no more carbon dioxide was then evolved. The cold product was acidified and extracted with ether. On neutralisation of the acid layer a red solid separated, which was crystallised from alcohol and from ligroin (b. p. 80—100°); yield, 1·6 g. of colourless crystals, m. p. 105°. The picrate had m. p. 173° (decomp.) (cf. diphenyl-2-pyridylcarbinol, m. p. 105°; picrate, m. p. 173° : Tschitschibabin and Benewolenskaja, *Ber.*, 1928, **61**, 547).

p-*Methoxyphenyl-2-pyridylcarbinol*, $C_6H_4(OMe)\cdot CH(OH)\cdot C_5H_4N$.—3·5 G. of picolinic acid in 30 g. of anisaldehyde ceased to give off carbon dioxide after 2 hours' heating at 175°. After working up as in the above preparations, 2·2 g. of colourless crystals, m. p. 131·5°, were obtained from ethyl alcohol (Found: N, 6·5. $C_{13}H_{13}O_2N$ requires N, 6·5%). The *phenylurethane* formed white needles, m. p. 145°, from ligroin (Found: N, 8·3. $C_{20}H_{18}O_3N_2$ requires N, 8·4%). The acetyl derivative had m. p. 82°.

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