782. *The Mechanism of Decarboxylation. Part VII.* The Decarboxylation of α-Amino-acids in Benzaldehyde.*

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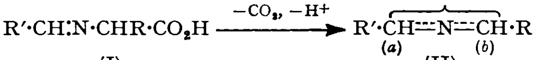
The decarboxylation of a number of α-amino-acids in benzaldehyde yields 2-hydroxy-1 : 2-diphenylethylamine. The reaction is interpreted as involving decarboxylation of azomethinecarboxylic acids, $\mathrm{R'{\cdot}CH{:}N{\cdot}CHR{\cdot}CO_2H}$ by a mechanism analogous to that of the decarboxylation reactions of picolinic and similar acids with carbonyl groups.

Schonberg, Moubasher, and Mostafa (*J.*, 1948, 176), Baddar (*J.*, 1949, S 163; 1950, 136), and Baddar and Iskander (*Nature*, 1951, **167**, 1069) have shown that the breakdown of α-amino-acids to amines and aldehydes by interaction with certain carbonyl compounds (the Strecker degradation) probably proceeds through the intermediate formation of azomethinecarboxylic acids of type (I), which lose carbon dioxide and a proton to give the mesomeric anion (II). Combination with a proton can occur at (*a*) or (*b*), and in fact mixtures of isomers are obtained after hydrolysis of the resulting Schiff bases.



$$\mathrm{R'{\cdot}CH{:}N{\cdot}CHR{\cdot}CO_2H} \xrightarrow{-\mathrm{CO_2},\ -\mathrm{H^+}} \mathrm{R'{\cdot}}\overbrace{\underset{(a)}{\mathrm{CH}}\!=\!\!=\!\mathrm{N}\!=\!\!=\!\underset{(b)}{\mathrm{CH}}}^{-}\mathrm{{\cdot}R}$$

(I) (II)

The extreme electronic forms of (II) are

$$\mathrm{R'{\cdot}}\underset{(a)}{\overset{-}{\mathrm{C}}\mathrm{H}}\mathrm{-N{=}}\underset{(b)}{\mathrm{CH}}\mathrm{{\cdot}R} \text{ and } \mathrm{R'{\cdot}}\underset{(a)}{\mathrm{CH}}\mathrm{{=}N-}\underset{(b)}{\overset{-}{\mathrm{C}}\mathrm{H}}\mathrm{{\cdot}R}$$

which in some respects resemble the anions apparently produced in the course of the decarboxylation of picolinic and similar acids in the presence of aldehydes and ketones,

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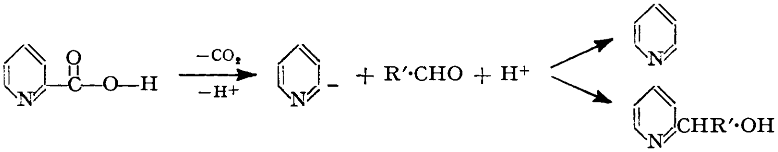
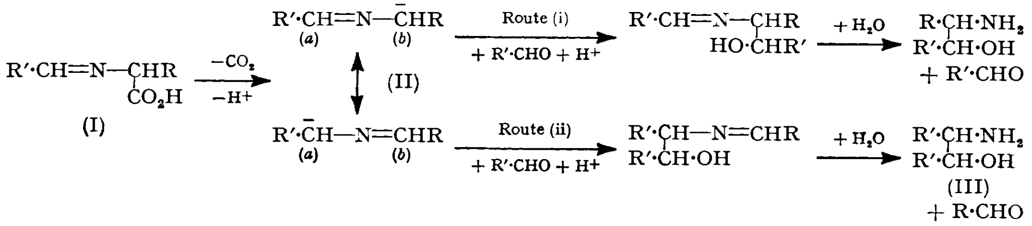
* Part VI, *J.*, 1951, 1384.

described in previous Parts of this series (Dyson and Hammick, *J.*, 1937, **1724**; Ashworth, Daffern, and Hammick, *J.*, 1939, 809; Brown and Hammick, *J.*, 1949, 173; see also Mislow, *J. Amer. Chem. Soc.*, 1947, **69**, 2559; Brown, Hammick, and Thewlis, *Nature*, 1948, **162**, 73; Brown, *J.*, 1949, 2577). For these reactions we may write :



and it occurred to us that the anils from α-amino-acids (I) might react in the same way. If they did, two reaction paths could be followed, according as to which carbon atom (*a*) or (*b*) in (II) attacks the carbon atom of the carbonyl group. Thus, for the decarboxylation of the amino-acid $R{\cdot}CH(NH_2)CO_2H$ in the presence of the aldehyde $R'{\cdot}CHO$, we might expect :



By route (i), differently substituted hydroxyethylamines should be expected from different amino-acids, whereas route (ii) should give, for a particular carbonyl compound, always the same amine. Decarboxylation of a series of α-amino-acids in benzaldehyde, including the dibasic glutamic acid, has given a mixture of the stereoisomerides of 2-hydroxy-1 : 2-diphenylethylamine (III; R′ = Ph). We have not obtained any products indicating that route (i) has been followed to any appreciable extent, nor has the reaction so far been successful with aromatic ketones or aromatic aldehydes other than benzaldehyde and anisaldehyde.

EXPERIMENTAL

All the decarboxylations were carried out under similar conditions, which are described for the typical case of DL-alanine.

Decarboxylation of DL-*Alanine in Benzaldehyde.*—DL-Alanine (10 g., 0·11 mole) and freshly distilled benzaldehyde (100 c.c., 1 mole) were heated in a 200-c.c. Claisen flask (thermometer in liquid), fitted so that gases evolved were passed through a trap cooled by solid carbon dioxide and alcohol into a test-tube containing lime-water. At about 120° the alanine dissolved with effervescence, and heating was continued so as to distil off water formed but as far as possible retain the benzaldehyde (2—5° below the b. p.). After 5—10 min. evolution of carbon dioxide practically ceased; in the trap were found ice, acetaldehyde, and a little benzaldehyde. The cooled deep red reaction mixture was shaken with 6N-hydrochloric acid (200 c.c.) and distilled in steam to remove all the benzaldehyde. The hot acid solution was boiled with 2 g. of animal charcoal, then filtered, and the boiling filtrate was cautiously made alkaline with pellets of sodium hydroxide. This treatment was necessary in order to ensure the precipitation of the bases in a crystalline and filtrable form. After several hours the solid was collected, washed with water, and dried to give 2 g. of crude product (8·4%).

The two racemic forms of 2-hydroxy-1 : 2-diphenylethylamine were separated from the crude product by shaking with ether (150 c.c.), in which the *iso* is much more soluble than the normal isomer. The residue, recrystallised from benzene, had m. p. 163—164° (Found : C, 78·8; H, 6·8; N, 6·7. Calc. for $C_{14}H_{15}ON$: C, 78·8; H, 7·0; N, 6·6%), unaltered by admixture with an authentic specimen of normal 2-hydroxy-1 : 2-diphenylethylamine (Weijlard, Pfister, Swanezy, Robinson, and Tishler, *J. Amer. Chem. Soc.*, 1951, **73**, 1216). The *N*-acetyl derivative (from ethanol) had m. p. 196°; Söderbaum (*Ber.*, 1896, **29**, 1210) gives m. p. 196—197°.

The ethereal filtrate was evaporated and the sticky residue taken up in hydrochloric acid, boiled with charcoal, and made alkaline with sodium hydroxide. The solid which separated was recrystallised three times from boiling water until a constant m. p. (128°) was obtained (Found: C, 78·9; H, 7·1; N, 6·5%). The m. p. was undepressed on admixture with an authentic specimen of the *iso*-amine (Weijlard *et al.*, *loc. cit.*). The *N*-benzoyl derivative (from light petroleum, b. p. 60—80°) had m. p. 221—222°. Auwers and Sonnenstuhl (*Ber.*, 1904, **37**, 3937) give m. p. 223°.

The yields of crude hydroxydiphenylethylamine obtained with other amino-acids were: glycine 5, alanine 8·4, α-amino*iso*butyric acid 5, tyrosine 21, norleucine 34, methionine 18, and glutamic acid 22%.

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