112. *Some Degradation Studies of Carpaine.*

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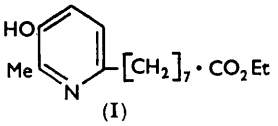
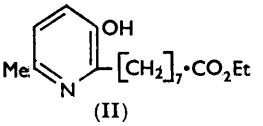
Degradation studies on carpaine lead to structure (I) for ethyl carpyrinate and confirm structure (III) for carpaine assigned by Rapoport *et al.*[1]

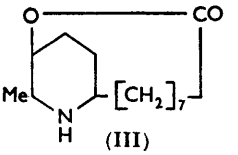
In a previous paper[2] it was shown that ethyl carpyrinate obtained from the lactonic alkaloid, carpaine, by hydrolysis, esterification, and dehydrogenation could be assigned structure (I) or (II). A choice between these in favour of (I) would confirm structure (III)



(I)



(II)



(III)

assigned to carpaine by Rapoport, Baldridge, and Volcheck[1] on the basis of Hofmann degradation. It was felt that this might be possible by elimination of the 2- or the 6-side-chain, leading to a simpler pyridine derivative. It was found that 3-methoxy-2 : 6-lutidine, on treatment with 1 mol. of benzaldehyde, yielded 3-methoxy-6-methyl-2-styrylpyridine in excellent yield. Oxidation with barium permanganate then gave an acid which was decarboxylated to 5-methoxy-2-picoline. 3-Methoxy-2 : 6-lutidine was also directly oxidised by 2 equivalents of potassium permanganate to an acid which was decarboxylated to 5-methoxy-2-picoline. Both procedures, however, when applied to

[1] Rapoport, Baldridge, and Volcheck, *J. Amer. Chem. Soc.*, 1953, **75** 5290.
[2] Govindachari and Narasimhan, *J.*, 1953, 2635.

ethyl *O*-methylcarpyrinate, gave no useful result, the ethoxycarbonyl group being apparently the complicating factor. The ethoxycarbonyl group of ethyl carpyrinate was therefore replaced by a methyl group by the following sequence :

carpaine ⟶ carpamodiol [2] ⟶ chlorocarpamol ⟶ carpamol ⟶ hexadehydrocarpamol ⟶ hexadehydro-*O*-methylcarpamol.

Hexadehydro-*O*-methylcarpamol did not yield a pure monobenzylidene derivative. Oxidation with two equivalents of aqueous potassium permanganate yielded an acid which was decarboxylated to 5-methoxy-2-octylpyridine, isolated as the picrate and identified by comparison with a synthetic specimen. This result assigns structure (I) to ethyl carpyrinate and confirms the previous structure (III) for carpaine.[1]

Experimental

3-Methoxy-6-methyl-2-styrylpyridine.—3-Methoxy-2 : 6-lutidine (2 g.), benzaldehyde (1·6 g.), and anhydrous zinc chloride (300 mg.) were heated in a sealed tube for 6 hr. at 180° then treated with water (20 ml.) and repeatedly extracted with ether. The ether extract was shaken with dilute hydrochloric acid, and the acid layer rendered alkaline with sodium carbonate and re-extracted with ether. The ether extract when dried (Na_2SO_4) and evaporated gave a viscous oil, which with hydrogen chloride in ether gave the *hydrochloride*, m. p. 115° (from alcohol–ether) (Found : C, 68·9; H, 6·1. $C_{15}H_{15}ON$,HCl requires C, 68·9; H, 6·1%).

Oxidation of the Styryl Compound with Barium Permanganate.—A solution of the foregoing compound (1 g.) in pyridine (20 ml.) was treated at 0° with barium permanganate (800 mg.) in small portions with stirring, then filtered, and the residue was washed with hot water. The filtrate was evaporated to dryness. The residue was dissolved in water (10 ml.), and barium precipitated as sulphate. After filtration the filtrate was evaporated *in vacuo*. The amino-acid (300 mg.) thus obtained was hygroscopic. It was characterised as the *copper salt* (Found : C, 46·2; H, 4·5. $C_{16}H_{16}O_6N_2Cu,H_2O$ requires C, 46·4; H, 4·3%).

Decarboxylation of the Amino-acid by Copper Powder.—The above acid (200 mg.) was heated with copper powder (1·5 g.) gradually to 300°, an oil distilling, whose picrate, crystallised from alcohol, had m. p. 135—138° (Found : C, 44·6; H, 3·7. Calc. for $C_{13}H_{12}O_8N_4$: C, 44·3; H, 3·4%). It did not depress the m. p. of 5-methoxy-2-picoline picrate.

Partial Oxidation and Decarboxylation of 3-Methoxy-2 : 6-lutidine.—A mixture of 3-methoxy-2 : 6-lutidine (1 g.) and potassium permanganate (2·3 g.) in water (250 ml.) was stirred on a water-bath until the permanganate was consumed. The precipitated manganese dioxide was filtered off and washed twice with hot water (50 ml.). The combined filtrates were concentrated to 50 ml. After removal of suspended impurities the solution was acidified to Congo-red with hydrochloric acid and evaporated to dryness. The residue was extracted with dry acetone. The acetone extract was evaporated to dryness, and the residue passed in water (20 ml.) through De-acidite E (The Permutit Co. Ltd.). The column was eluted with distilled water (100 ml.), and the eluate evaporated to dryness. The residue was heated with copper powder (500 mg.) gradually to 300° (metal-bath) during 15 min. The distillate was converted into the picrate, m. p. 138° (from alcohol–water), alone or mixed with 5-methoxy-2-picoline picrate.

Chlorocarpamol.—A solution of carpamodiol [2] hydrochloride (5 g.) in absolute chloroform (40 ml.) was treated at 0° with thionyl chloride (1·45 ml.), kept overnight, and evaporated to dryness *in vacuo*. The residue was dissolved in water (20 ml.), basified with saturated sodium hydrogen carbonate solution, and extracted with ether. The ether extract, when dried (Na_2SO_4), evaporated, and distilled, gave *chlorocarpamol* (3 g.), b. p. 150°/0·4 mm. (Found : C, 63·8; H, 10·4. $C_{14}H_{28}ONCl$ requires C, 64·3; H, 10·7%).

Carpamol.—A solution of chlorocarpamol (3 g.) in tetrahydrofuran (20 ml.) was added dropwise with stirring to a suspension of lithium aluminium hydride (3 g.) in tetrahydrofuran (30 ml.). The mixture was stirred and refluxed for an additional 6 hr. Next morning sufficient moist ether was added to decompose the complex. The solvent was decanted and the residue repeatedly extracted with ether. The combined extracts, after drying (Na_2SO_4) and removal of solvent, gave an oil which on distillation furnished *carpamol* (2·5 g.), b. p. 114°/0·4 mm. (Found : C, 73·7; H, 12·8. $C_{14}H_{29}ON$ requires C, 74·0; H, 12·8%).

Hexadehydrocarpamol.—This *compound* was obtained in quantitative yield by the dehydrogenation of carpamol according to the usual procedure (cf. dehydrogenation of ethyl carpamate [2]).

Crystallised from benzene–light petroleum it had m. p. 114—115° (Found : C, 75·8; H, 10·1. $C_{14}H_{23}ON$ requires C, 76·0; H, 10·4%).

Hexadehydro-O-methylcarpamol.—Hexadehydrocarpamol (1·8 g.) in methyl alcohol (40 ml.) was treated with a solution of excess of diazomethane (from 15 g. of nitrosomethylurea) in ether at 0°, kept overnight, and evaporated to an oil (1·8 g.) which on distillation gave the *methyl ether*, b. p. 168°/9 mm. (Found : C, 76·3; H, 10·5. $C_{15}H_{25}ON$ requires C, 76·6; H, 10·6%).

Partial Oxidation and Decarboxylation of Hexadehydro-O-methylcarpamol.—A mixture of hexadehydro-*O*-methylcarpamol (210 mg.) and potassium permanganate (300 mg.) in water (250 ml.) was refluxed until the permanganate was completely consumed, then worked up as described for the oxidation and decarboxylation of 3-methoxy-2 : 6-lutidine, yielding an oil which was converted into the picrate, m. p. 72° alone or mixed with 5-methoxy-2-octylpyridine picrate.

5-Methoxy-2-octylpyridine.—To a vigorously stirred solution of potassium amide in liquid ammonia (from 1·7 g. of potassium, 200 mg. of ferric chloride, and 100 ml. of liquid ammonia) was added 5-methoxy-2-picoline (3·6 g.). An intense red colour developed. The mixture was stirred and then heptyl chloride (4 g.) was added as rapidly as possible with continued stirring. Next morning the mixture was decomposed with water and extracted with ether. The ether extract was shaken with N-hydrochloric acid, and the acid extract was cooled, and rendered alkaline with solid sodium carbonate, and extracted repeatedly with ether. The combined ether extracts furnished an oil which on distillation gave, first, 5-methoxy-2-picoline (1·5 g.) and then *5-methoxy-2-octylpyridine* (1·8 g.), b. p. 156°/5 mm. (Found : C, 75·5; H, 10·2. $C_{14}H_{23}ON$ requires C, 76·0; H, 10·4%). The *picrate* had m. p. 72° (from alcohol) (Found : C, 53·5; H, 6·0. $C_{20}H_{26}O_8N_4$ requires C, 53·3; H, 5·8%).

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