

THE ALKALOID OF *BERBERIS UMBELLATA*, WALL. PART III.

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Umbellatine $C_{21}H_{27}O_3N$, the common alkaloid of the Himalyan species of *Berberis* yields on potassium permanganate oxidation hemipinic acid and on potassium hydroxide fusion, protocatechuic acid. These results show that the two methoxy groups are in adjacent positions in a benzene nucleus in umbellatine and that other groups, like the methylenedioxy and hydroxyl, are not present in the benzene ring containing the two methoxyl groups.

Umbellatine, $C_{21}H_{27}O_3N$, which is found to be present not only in *B. umbellata* (*J. Indian Chem. Soc.*, 1940, 17, 289; 1942, 19, 233) but also in other Himalyan species of *Berberis*, e.g., *B. insignis* (*J. Amer. Pharm. Assoc.*, 1941, 30, 247), *B. lycium*, *B. nepalensis* and *B. Wellichiana* (*Science & Culture*, 1942, 7, 619) yields hemipinic acid ($C_{10}H_{10}O_6$) on oxidation by potassium permanganate solution, like berberine $C_{20}H_{19}O_5N$, (Perkin, *J. Chem. Soc.*, 1889, 85, 63) the common alkaloid of the European species of *Berberis*, or other isoquinoline alkaloids, corydaline, $C_{22}H_{27}O_4N$, (Dobbie and Lauder, *J. Chem. Soc.*, 1902, 81, 145; 1903, 83, 605), and narcotine, $C_{22}H_{23}O_7N$ (Wöhler, *Annalen*, 50, 17). Hemipinic acid, thus obtained, melts at $177-78.5^\circ$, which does not eliminate its possibility of being *m*-hemipinic acid, m.p., 175° as obtained from papavarine, $C_{20}H_{21}O_4N$ (Goldschmidt, *Monatsh*, 1888, 9, 327; *ibid.*, 1888, 9, 778), and also from corydaline (*loc. cit.*). To elucidate its nature the ethylimide of the hemipinic acid is prepared and its melting point determined as 92° , which proves conclusively the nature of the hemipinic acid as 3 : 4-dimethoxyphthalic acid since the ethylimide of *m*-hemipinic acid melts at $226-27^\circ$.

The production of hemipinic acid shows conclusively that the two methoxy groups present in umbellatine are placed adjacent to each other and that they are present in a benzene ring in the umbellatine molecule. The two carboxyl groups next to the methoxy groups are in all probability produced by the fission of the linkings of a fused ring of the molecule, as in the case of the molecules of other bases, like berberine etc.

Like berberine, umbellatine also yields protocatechuic acid on fusion with solid potassium hydroxide above 250° . Protocatechuic acid might have been obtained by the production and subsequent demethylation and elimination of a molecule of carbon dioxide of one of the two carboxyl

groups of hemipinic acid, since Perkin (*loc. cit.*) has shown that hemipinic acid yields on potash fusion protocatechuic acid.

EXPERIMENTAL.

Permanganate Oxidation of Umbellatine.—Umbellatine hydrochloride (5 g.) was dissolved in warm water (150 c.c.), and treated with potassium carbonate (1.0 g.) solution and then oxidised by slowly running in a solution of potassium permanganate solution (25 g. in 500 c.c. of water). The decolourisation of the permanganate was very rapid at start, and as soon as about 330 c.c. of the solution were added, decolourisation slowed down appreciably, and continued warming was necessary to remove the last traces of the pink colour of the permanganate solution.

The solution was left overnight and then saturated with carbon dioxide gas and filtered from the manganese precipitate. The filtrate and the washings were evaporated completely to dryness on a water-bath, and the residue was soxhletted with absolute alcohol. The residue obtained after removal of the last traces of alcohol, was dissolved in water and the brown aqueous solution was treated with dilute sulphuric acid when a small quantity of sticky matter separated which could not be solidified. The sticky matter was removed by filtration and the filtrate was extracted continuously with ether (100 c.c. in 4 instalments) by shaking each time in a mechanical shaker for 8 hours. The ethereal solution on removal of ether yielded a pale yellow oily residue which solidified when kept in a vacuum desiccator over concentrated sulphuric acid for a week. It was then sublimed at 0.1 mm. pressure when a minute quantity of a yellow liquid separated first at 140-150°, and then a transparent crystalline solid, moist with the liquid, at 150-160°. The moist solid when dried on a porous plate melted at 125°-157°.

The moist solid was well washed with small quantities of ether, dried and powdered and warmed with concentrated hydrochloric acid and kept overnight and filtered from the acid solution and repeatedly washed with cold water in small amount. The filtrate and the washings yielded a very small quantity of a semi-solid which could not be successfully handled. The residue was then dried, m.p. 155°-60°. The melting point further rose to 177-178.5°, on slow crystallisation of the solid from boiling water. (Found in the sample dried in *vacuo* over P₂O₅ at 100°: C, 52.96; H, 4.75. Calc. for C₁₀H₁₀O₈: C, 53.1; H, 4.43 per cent). To identify the hemipinic acid thus obtained, the m.p. of the sample was compared with that of hemipinic acid prepared from opianic acid. The hemipinic acid, as

obtained from narcotine melted at 179-80°, and when mixed with that obtained from umbellatine melted at 179°.

The *ethylimide* derivative of hemipinic acid was prepared according to Liebermann (*Ber.*, 1886, 19, 2275), by dissolving the purified acid obtained from umbellatine in an aqueous solution of ethylamine (30%) and evaporating it to dryness. The residue, thus obtained, was heated carefully over a naked flame, and then exhausted with boiling methyl alcohol. On cooling, the ethylimide separated as needles, m.p. 90°. The melting point did not change even on high vacuum sublimation of the ethylimide at 125-135° under 0.15 mm. pressure. The ethylimide of hemipinic acid, obtained from narcotine, was purified by the author by high vacuum sublimation and by repeated crystallisation from water, and was found to melt sharply at 92° (mixed m.p. with the ethylimide of the hemipinic acid from umbellatine). This shows that the hemipinic acid thus obtained is 3 : 4-dimethoxyphthalic acid. (Found in the vacuum dried sample : N, 5.63. Calc. for $C_{10}H_8O_4N$: N, 5.9 per cent).

Fusion of Umbellatine with Potassium Hydroxide.—Umbellatine (1 g.) and potassium hydroxide (6 g.) were heated rapidly with constant stirring in a nickel crucible on a metal-bath. When the temperature reached 270-280°, bubbles of a pungent smelling gas resembling methyl or ethylamine were evolved. The foaming mass was stirred and kept at the above temperature for 10 minutes. The mass was then cooled down quickly to room temperature, and treated with water (30 c.c.) and the dark aqueous solution was saturated with solid ammonium chloride and filtered. On treatment with animal charcoal a clear dark brown coloured filtrate was obtained. The filtrate was extracted with ether, the ethereal solution was washed twice with water and then dried over anhydrous sodium sulphate. On removal of ether, a brown syrupy residue was obtained, which crystallised immediately as needles contaminated with resinous matter. The needles could not be freed from the associated impurities by crystallisation. The aqueous solution of the needles was acidic, and produced a deep emerald green colouration with ferric chloride solution. On adding a solution of sodium carbonate the green colour changed first to blue, then violet and finally red. Like protocatechuic acid, it reduced an ammoniacal solution of silver nitrate and gave with lead acetate solution a white precipitate soluble in acetic acid.

The needles were then purified by high vacuum sublimation at 0.1 mm. pressure. Two fractions were obtained—the one as a slightly brownish coloured crystalline solid at 140-160°, and the other which was the main fraction as colourless crystals, at 160-170°. The first fraction

melted at 103° . The fraction did not depress the m.p. of pyrocatechol and in fact responded to the reactions of pyrocatechol.

The second fraction, the colourless crystals, melted with decomposition at $196-98^{\circ}$, the m.p. of protocatechuic acid. When mixed with an authentic sample of protocatechuic acid the m.p. did not change. (Found: C, 50.1; H, 4.8. Calc. for $C_7H_6O_4$, H_2O : C, 49.0; H, 4.7 per cent).

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