

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

By R. CHATTERJEE.

Umbellatine is shown to possess an imino methyl group. Of the 8 atoms of oxygen, 4 were shown in a previous communication to be present in a methylenedioxy and two methoxy groups, the remaining 4 are now proved to be present as OH groups. A comparison of the properties, absorption curves and derivatives of umbellatine with those of berberine has been made; it has been concluded that methylenedioxy-tetrahydro-isoquinoline skeleton forms a part of the umbellatine nucleus.

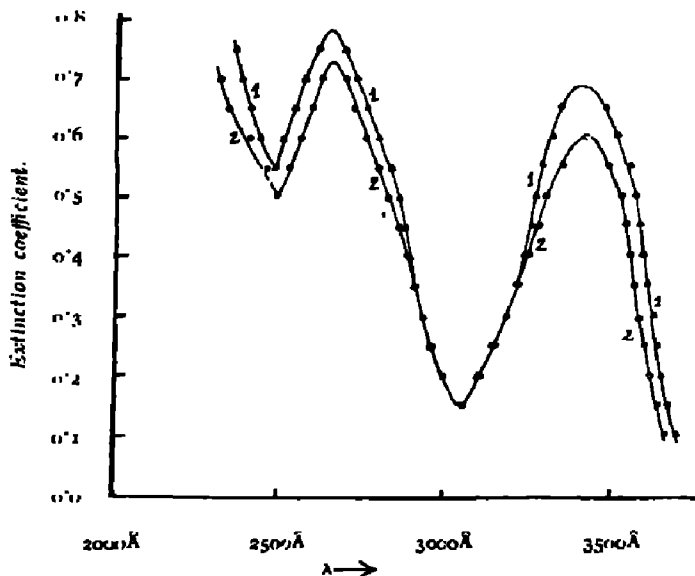
Umbellatine is mentioned to be the chief alkaloid of the Himalayan *Berberes*, e.g., *B. insignis*, *B. nepalensis*, *B. lycium* and *B. Wallichiana* etc., and some of its salts are described.

Umbellatine, the alkaloid first isolated from *Berberis umbellata*, Wall (*J. Indian Chem. Soc.*, 1940, 17, 289) is found to be present as the major alkaloid in other Himalayan *Berberes*. It has been reported to occur in *B. insignis* Hook. f. (Chatterjee, *J. Amer. Pharm. Assoc.*, 1941, 30, 247) and also in other species of the Himalayan *Berberes* like *B. nepalensis* Spreng., *B. lycium* Royle and *B. Wallichiana* D.C., an account of which has not yet been published. Berberine is the chief alkaloid of all European *Berberes*, investigated up till now, and since umbellatine is observed to occur commonly in the Himalayan species of the same genus *Berberis*, it is thought that most probably umbellatine is analogous to berberine in structure. A comparative study of the properties and derivatives of both umbellatine and berberine shows the close similarity of the two alkaloids (Table I).

In Fig. 1 are shown the near ultraviolet absorption curves of umbellatine and berberine. It is well known that such comparison of spectra serves as one of the physical methods to arrive at the essential central structure of complex organic compounds (Hartley, *Phil. Trans.*, 1865, 176A, 471; Dobbie, *J. Chem. Soc.*, 1903 83, 605; Brustier, *Bull. Soc. Chim.*, 1926, 39, 1527). It is evident from the figure that the absorption curves of these two alkaloids are extremely analogous. Only a slight hyperchromic effect is observed in the new base which might easily be attributed to the several phenolic OH groups it contains (Klingstedt and Brode, International Critical Tables). Kitasato's work (*Acta Phytöchim.*, 1927, 3, 175) on the absorption spectra of 42 alkaloids classifies the bases berberine, coptisine,

cotarnine, worenine and hydrastinine as showing very similar absorption spectra. They all show the strong band at *ca.* 3400-3500Å, which the author connects with the methylenedioxy-tetrahydroisoquinoline skeleton by a process of elimination. The identical position of this prominent band in umbellatine is a strong positive evidence for the presence of the same basic nucleus in this alkaloid, the evidence being of course as conclusive as is warranted by this statistical physical method of structure analysis.

FIG. 1.



Curves 1 & 2 refer respectively to berberine and umbellatine.

Umbellatine forms salts with acids like hydrochloric, hydriodic, nitric, sulphuric and picric acids mostly analogous to the corresponding salts of berberine, in their colour and solubility in water. With palladium-charcoal, umbellatine takes up successively 2 and 4 atoms of hydrogen, forming a yellow dihydroumbellatine and a lemon-yellow tetrahydro-umbellatine, m.p. 213-15° (decomp.). It had been already shown that umbellatine formed a yellow coloured, bright crystalline derivative with nitrous acid. From the estimation of nitrogen of the derivative, it was supposed to be a nitroso compound which pointed to the secondary character of the nitrogen atom in umbellatine. The analytical data are also in good

agreement with the formula $C_{21}H_{21}O_8N$, HNO_2 , where nitrous acid forms the nitrite of the base. It is not improbable, therefore, that the N atom in umbellatine molecule might be present as a tertiary amine. More than one example of alkaloids might be cited where a molecule of nitrous acid is added to the tertiary nitrogen group. The phenylthiocarbamide test for the secondary nitrogen fails in the case of umbellatine. The base forms a methiodide and its imino-methyl determination (Herzig and Meyer) is positive, elucidating the tertiary nature of the N atom of the base; so the molecular formula of umbellatine $C_{21}H_{21}O_8N$, can be extended to $C_{20}H_{19}O_8 (N \cdot CH_3)$.

The product of methylation of the base by diazomethane could not be isolated; the methylating agent methyl iodide reacted only to form a methiodide; umbellatine could only be successfully methylated by dimethyl sulphate, producing a monomethyl ether, which indicates the phenolic character of one of the hydroxyl groups present. On boiling with acetic anhydride in presence of a few drops of pyridine, umbellatine yields a diacetyl derivative. Of the 8 oxygen atoms present, in one molecule of the base, 6 can now be accounted for—2 of them are in the methylenedioxy group and 2 in the methoxy groups in the molecule as has been previously recorded. The remaining 2 which are acetylated must be present in two free hydroxyl groups. Now the formula of umbellatine is further extended to $C_4H_8O_2 (CH_2O_2) (NCH_3) (OMe)_2 (OH)_2$. The function of the remaining 2 oxygen atoms of the molecule could not be determined directly as yet. Umbellatine does not undergo hydrolysis in presence of an acid or an alkali, eliminating the possibility of the 2 oxygen atoms being present in a lactone ring. Unlike berberine, it would neither form an oxime nor a semicarbazone which, in all probability, indicates the absence of a carbonyl group. The base contains 4 reactive hydrogen atoms (Zerewitinoff). It has already been mentioned (*loc. cit.*) that umbellatine retains half a molecule of water of crystallisation even when dried in *vacuo* over P_2O_5 at 110° . The experimental results show that the volumes of methane collected during the active hydrogen determinations are always greater than the calculated volumes. There the excess volume of methane can safely be considered to be formed from half a molecule of water reacting with magnesium methyl iodide, so the 4 atoms of hydrogen have been, in all probability, obtained from 4 hydroxyl groups of the base, 2 of which could be acetylated. Hence the formula of umbellatine can be written as :

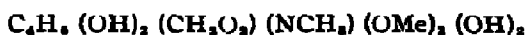


TABLE I.

Comparison of properties of umbellatine and berberine and their derivatives.

	Umbellatine.	Berberine.
Mol. formula	$C_{21}H_{21}O_5N$	$C_{20}H_{19}O_5N$
Colour	Yellow	Yellow
M.p.	206-7° (decomp.)	145°
Water of crystallisation	5.5 molecules; $\frac{1}{2}$ molecule is retained even on drying <i>in vacuo</i> at 110°.	5.5 molecules; $\frac{2}{3}$ molecules are retained on drying at 100°.
Solubility	Soluble in ethyl and methyl alcohols, sparingly soluble in acetone, chloroform and cold water. Insoluble in benzene.	Soluble in ethyl and methyl alcohols; sparingly soluble in acetone and chloroform, more soluble in water. Slightly soluble in benzene.
Optical activity	Inactive	Inactive
Acidified with conc. H_2SO_4 and brought in contact with chlorine water.	A blood-red ring at the junction of the layers of two liquids.	A blood-red ring at the junction of the layers of two liquids.
	Umbellatine chloroplatinate cannot be crystallised.	Berberine chloroplatinate can be crystallised from boiling anyl alcohol.
Functional groups	Contains 2 methoxy groups, 1 methylenedioxy group.	Contains 2 methoxy groups, 1 methylenedioxy group.
	Contains at least two active hydroxyl groups.	Does not contain any hydroxyl group.
	Contains an imino-methyl group	Contains an imino group.
	Does not form an oxime.	Forms an oxime under certain conditions.
Tetrahydro derivatives	Tetrahydroumbellatine	Tetrahydroberberine
	Lemon-yellow plates, crystalline, m.p. 213-15° (decomp.)	Crystalline, colourless prismatic needles m.p. 262° (decomp.).
Salts of the type B, HX with mineral acids.	Umbellatine, HCl etc.	Berberine, HCl etc.

EXPERIMENTAL.

Absorption Spectra of Umbellatine and Berberine.—Solutions of the bases having a concentration of 1 in 80,000 in water were used.

Tungsten steel spark was the source of light. The spectra were photographed with a Spekker spectrophotometer on a quartz spectrograph. The match points were marked by visual comparison and the wave-lengths read off approximately from a wave-length reading plate slipped behind the negative. Both the curves show two absorption maxima at 2650 and 3430, minima at 2490 and 3050 Å. (FIG. 1).

Umbellatine nitrate, prepared by the usual method, crystallised from alcohol as dull yellow needles. It charred without melting above 250°. (Found: N, 6.3. $C_{21}H_{21}O_2N$, HNO_3 requires N, 6.0 per cent).

Umbellatine sulphate, prepared by the usual method, crystallised from hot alcohol as glistening yellow needles, m.p. 274° (decomp.). [Found: S, 3.2. $(C_{21}H_{21}O_2N)_2H_2SO_4$ requires S, 3.4 per cent].

Umbellatine Picrate.—On treating a solution of umbellatine in alcohol with an alcoholic solution of picric acid, the picrate was precipitated at once. The picrate was crystallised from hot alcohol as brown feathery needles, m.p. 232° (decomp.). (Found: N, 8.9. $C_{27}H_{26}O_{11}N_4$ requires N, 8.7 per cent).

Tetrahydroumbellatine.—A solution of umbellatine base (0.23 g.) in methyl alcohol (20 c.c.) was mixed with palladium-charcoal catalyst (0.1 g.) and shaken with hydrogen until the yellow solution was practically colourless. Absorption was at first rapid but became slower after 20 minutes; 23 c.c. of hydrogen were absorbed in 45 minutes (Calc. for $C_{21}H_{21}O_2N$, $\frac{1}{2} H_2O$: 4 H, 25 c.c.). The solution was filtered from the charcoal; the charcoal was washed carefully with methyl alcohol (10 c.c.). The solution deposited on concentration a pale yellow powder which on recrystallisation yielded lemon-yellow transparent plates of tetrahydroumbellatine, m.p. 213–15° (decomp.). (Found: C, 59.5; H, 5.5; N, 3.3. $C_{21}H_{25}O_2N$ requires C, 60.0; H, 6.0; N, 3.34 per cent).

Dihydroumbellatine.—A solution of umbellatine (0.2 g.) in methyl alcohol (20 c.c.) was shaken with palladium-charcoal catalyst (0.1 g.) in hydrogen. Absorption was stopped after 20 minutes when 11 c.c. of hydrogen (equivalent to 2 atoms) had been taken up. The solution of the product was filtered from the catalyst and was concentrated to yield dihydroumbellatine as dull yellow rods, which charred without melting. (Found: C, 60.0; H, 5.34. $C_{21}H_{23}O_2N$ requires C, 60.43; H, 5.5 per cent).

The Imino-methyl in Umbellatine.—The imino-methyl was determined by the micro Herzig-Meyer method. (Found: N·Me, 5.3. $C_{21}H_{21}O_2N$, $\frac{1}{2} H_2O$ requires N·Me, 6.8 per cent).

Umbellatine Monomethyl ether.—An excess of dimethyl sulphate was added drop by drop to a solution of umbellatine (0.1 g.) in 10% potassium

hydroxide with constant shaking. After $\frac{1}{2}$ hour yellow, silky fine needles separated. The shaking and the addition of dimethyl sulphate were continued and the mixture was kept alkaline. After an hour the crystals were filtered, well washed with water, dried and then crystallised from alcohol as silky yellow needles, m.p. 265° . [Found: OMe, 21.1. $C_{21}H_{20}O_2N$ (OMe) requires, OMe 20.9 per cent; equiv. to 3 OMe groups of which 2 are already present in a molecule of umbellatine].

Diacetylumbellatine.—Umbellatine (0.1 g.) was mixed with acetic anhydride (20 c.c.) and pyridine (6 to 8 drops) and heated on a water-bath till the last traces of umbellatine went completely into solution, the time usually taken being $3\frac{1}{2}$ hours. On leaving overnight, yellow needles appeared which shrink at 187° and melt with decomposition at 193° . (Found: C, 59.72; H, 5.84; N, 1.98. $C_{22}H_{20}O_4N$ requires C, 59.8; H, 5.4; N, 2.8 per cent).

Reactive H atoms in Umbellatine.—A Zerewitinoff determination of the base liberated methane equivalent to 4 reactive hydrogen atoms.

0.48 G. of umbellatine, $C_{21}H_{21}O_2N$, $\frac{1}{2}$ H_2O , in pyridine treated at the ordinary temperature for 10 minutes with excess of methyl magnesium iodide, gave 13.2 c.c. of methane (theory requires 11.2 c.c. of methane, equiv. to 4 reactive hydrogen atoms).

0.454 G. of umbellatine gave 12.3 c.c. of methane (theory requires 10.6 c.c. of methane; equiv. to 4 reactive hydrogen atoms).

0.38 G. of umbellatine gave 10.4 c.c. of methane (theory requires 7.8 cc. of methane; equiv. to 4 reactive hydrogen atoms).

The author expresses his gratefulness to the Rector, the very Rev. Father C. A. Vrithoff, S.J., for affording him laboratory facilities, to Mr. G. Karmakar, M.Sc., for the absorption photographs and to Mr. N. Ghosh, M.Sc. for all the micro-analyses, recorded in this paper.

ST. JOSEPH'S COLLEGE,
DARJEELING.

Received February 23, 1942.