Alkaloids of *Tabernaemontana psychotrifolia* H.B.K.

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A new alkaloid $C_{20}H_{24}N_2O$ (taberpsychine) obtained from Venezuelan *T. psychotrifolia* is shown to have structure **5**. The Hofmann degradation products of taberpsychine and its dihydro derivative are discussed. Two other bases isolated are affinine and 16-epi-vobasinic acid, the latter for the first time as a natural product.

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Extraction of *Tabernaemontana psychotrifolia* H.B.K.[1] yielded three principal alkaloids but the abundance of the major base taberpsychine, $C_{20}H_{24}N_2O$, and the fact that it could not be readily placed in a "skeletal" group by mass spectrometry made it the principal area of interest.

The u.v. spectrum of taberpsychine shows absorption typical of an indole moiety, with no substituents other than the "normal" ones at position 2 and 3. The i.r. spectrum confirms the presence of the aromatic nucleus and of the indolic NH, but the absence of absorption due to hydroxyl or carbonyl groups fails to provide information concerning the nature of the oxygen atom present. Since neither acetylation nor mild oxidation reactions produced any change in the molecule, the oxygen atom was, by exclusion, assumed to be ethereal.

The n.m.r. spectrum affords evidence about the remainder of the molecule, including the functionality of the second nitrogen atom. A broad quartet at 5.38 δ (J = 6.5 Hz) integrating for one proton, accompanied by a doublet of doublets for three protons at 1.68 δ (J = 6.5 and 2.0 Hz respectively) is evidence for an ethylidene side chain. Decoupling experiments (Fig. 1) left no doubt about this and at the same time localized the origin of the small coupling observed in the methyl signal and also of the broadening of the quartet for the olefinic proton. Irradiating the methyl signal, the broad lower field part (H in Fig. 1) of an AB quartet (3.60 and 2.93 δ, J = 14 Hz) becomes a sharp doublet; while irradiating this broad doublet (3.60 δ) the disappearance of the small splitting of the methyl group signal is observed (this also sharpens the quartet for the olefinic proton). This AB quartet is found in a region typical for protons at carbon atoms adjacent to nitrogen, permitting the placing of the ethylidene side chain in the sequence shown in **1**, with the methylene group adjacent to the basic nitrogen atom responsible for the AB quartet discussed above. A singlet at 2.53 δ integrating for three protons must be assigned to a methyl group on the basic nitrogen (since the indolic nitrogen bears no substituent). The spectrum also confirms the presence of four aromatic protons (4H multiplet 7.07–7.66 δ) and the indolic NH (singlet 8.42 δ).

Another feature in the n.m.r. spectrum is a pair of doublets at 5.13 δ (J = 10 and 2 Hz) integrating for one proton. The signal is only ascribable to a proton adjacent both to an aromatic moiety and an oxygen atom. The splitting pattern suggests that it is also adjacent to a methylene.

Zinc dust distillation of taberpsychine, following a small scale method described by Biemann and Spiteller (1) coupled with gas-chromatographic analysis of the volatile distillate showed the major product to be 3-ethylpyridine (direct comparison in the gas chromatograph with an authentic sample and n.m.r. spectrometry of the material recovered). The product could only *be formed from the part of the molecule containing the basic nitrogen* and since the analogous pyridinium ion is observed as one of the major peaks in the fragmentation in the mass spectrum (122 m/e) the basic nitrogen atom is located in a six-membered ring.

Hydrogenation of taberpsychine afforded a dihydro derivative, $C_{20}H_{26}N_2O$, in which the ethylidene side chain was no longer present as shown by the n.m.r. spectrum, while a signal due to a methyl group on a saturated carbon appeared as a triplet at 0.98 δ (J = 7 Hz).

[1]The identification was made by, and a herbareum specimen is filed at, the Botanical Gardens, Caracas, Venezuela.

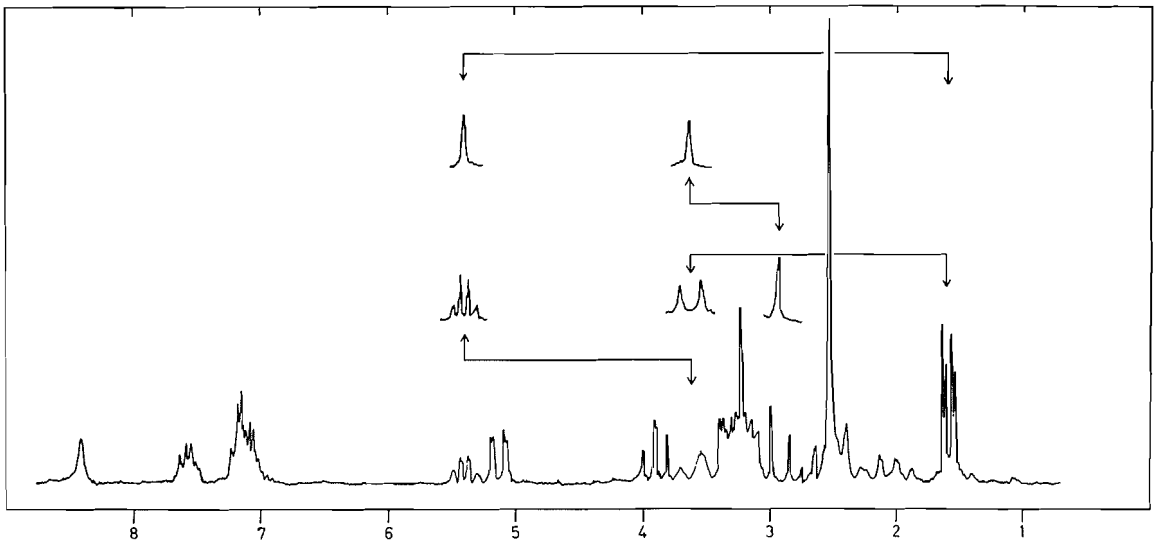
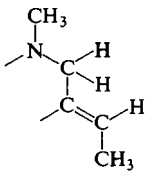


FIG. 1. The n.m.r. spectrum (100 MHz) of taberpsychine in deuteriochloroform (TMS = 0 p.p.m.). Double irradiations are indicated by the double headed arrows.



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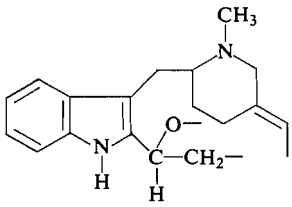

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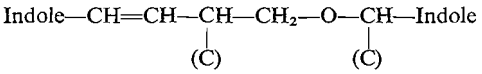
The methiodide of the dihydro derivative undergoes Hofmann degradation with potassium tertiobutoxide to give a major product, $C_{21}H_{28}N_2O$, whose u.v. spectrum indicates the presence of a double bond conjugated to the indole chromophore (2, 3). The presence of this new double bond is corroborated by the n.m.r. spectrum of the dihydrotaberpsychine-methine, in which one finds the signals for two olefinic protons at 6.69 (doublet J = 12 Hz) and 5.55 δ (doublet of doublets J = 12 and 8 Hz) as the low field AB part of an ABX system (see Fig. 2). The fact that the double bond introduced during this reaction is conjugated with the aromatic moiety and the assumption of a very likely tryptamine biogenesis allows the linkage of the two units as shown in partial structure **2** and also places the oxygen atom on the carbon attached to position 2 of the indolic portion. A methylene group can be placed adjacent to the carbon bearing the oxygen atom on the basis of the pattern for the proton adjacent to both the aromatic residue and oxygen (doublet of doublets J = 10 and 2 Hz).

Spin decoupling experiments (Fig. 2) on dihydrotaberpsychine-methine provided information concerning the missing linkage of the oxygen atom. In effect, it demonstrated that the X part (1H) of the ABX system involving the vinyl protons introduced by the degradation, is also coupled to an A′B′ system (doublet 4.21 δ, J = 11 Hz and triplet 3.79 δ, J = 11 Hz) appearing in a region typical for protons adjacent to oxygen. The Hofmann product must therefore contain the sequence:



and this observation is only compatible with the partial structure for the methine shown by **3**.

The molecular formula of the base indicates a pentacyclic structure. The additional ring must involve the methylene group shown and only one point of attachment remains (at the starred carbon) since the nature and number of protons at all other positions has been demonstrated in the discussion above, thus the complete structure for the major Hofmann product is given as **4** in which the configuration of the *C*-ethyl residue must be as shown, arising from hydrogen addition to the more exposed face of the molecule, and hence the

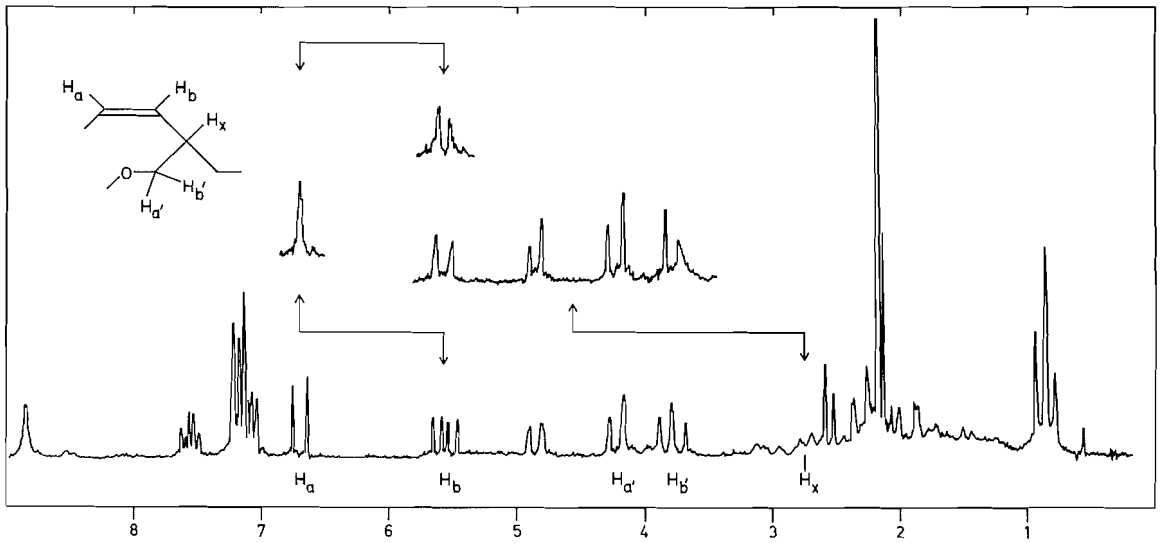
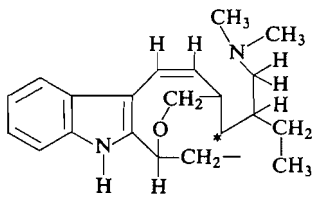


FIG. 2. The n.m.r. spectrum (100 MHz) of dihydrotaberpsychine methine in deuteriochloroform (TMS = 0 p.p.m.).



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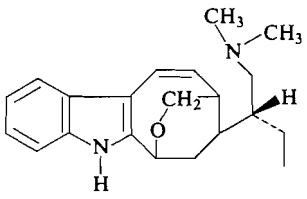

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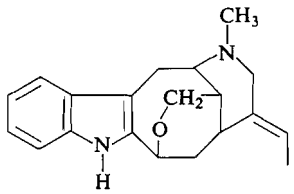

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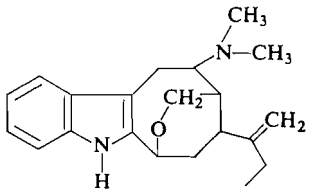


6

structure of taberpsychine is **5** which is compatible with all spectral data.[2]

A minor product from the Hofmann degradation of dihydrotaberpsychine methiodide was also isolated although it could not be induced to crystallize. The n.m.r. spectrum shows a pair of doublets (4.98 and 5.63 δ, J = 1 Hz) typical of a terminal methylene group, which together with the preceding evidence permitted the formulation of the material as structure **6**.

Once the structure of taberpsychine had been elucidated, the result obtained from the Hofmann degradation performed on the methiodide of taberpsychine itself could be rationalized, whereas before a rather complex n.m.r. spectrum had rendered its interpretation difficult. This degradation, effected using the same conditions as for the dihydro compound already discussed, af-

[2]After our preliminary report on taberpsychine (P. R. Benoin *et al.* (6)) we were informed that the alkaloid anhydrovobasindiol had been ascribed the same structure (M. Hesse, personal communication). In a subsequent publication (J. J. Dugan *et al.* (7)) the two alkaloids are shown to be identical.

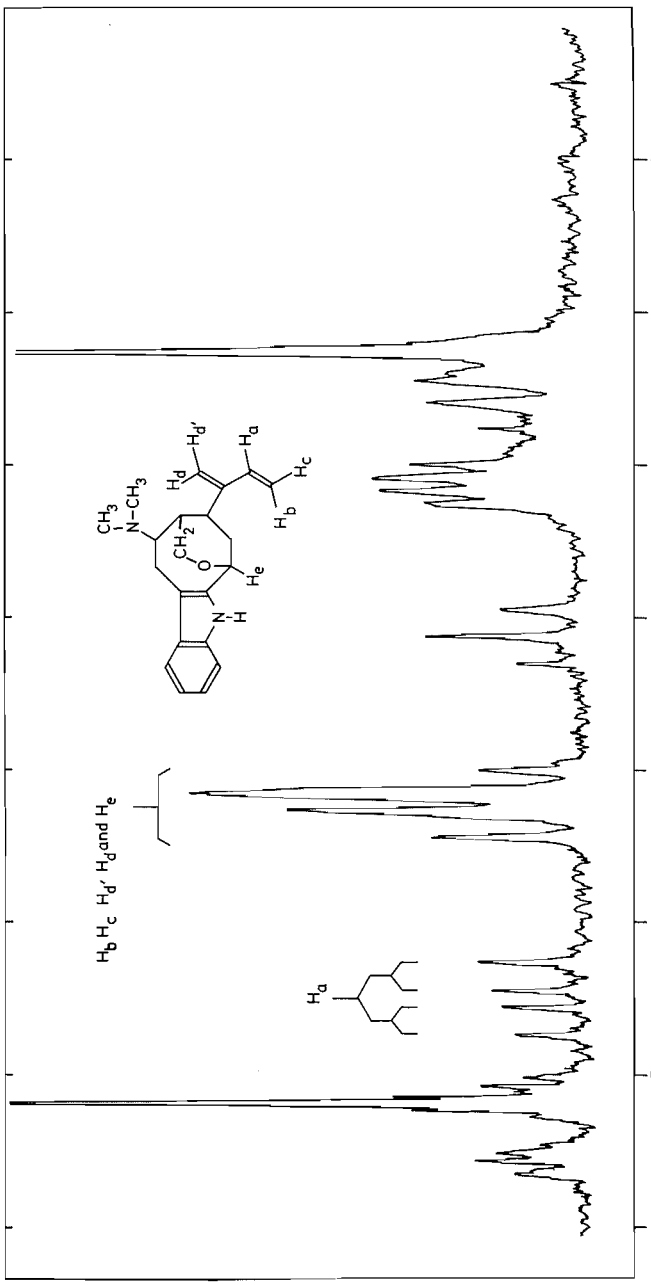
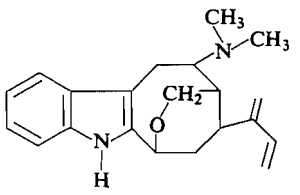


FIG. 3. The n.m.r. spectrum (60 MHz) of taberpsychine methine in deuteriochloroform (TMS = 0 p.p.m.).



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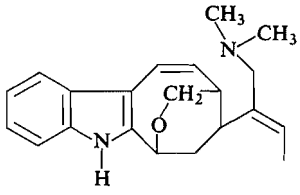

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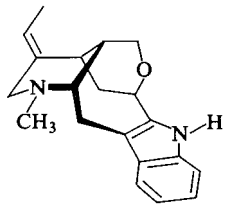

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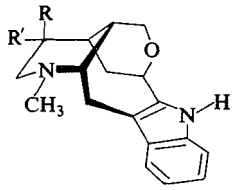


10

a R = H; R′ = Et
b R = Et; R′ = H

forded a major product, $C_{21}H_{26}N_2O$, whose u.v. spectrum shows the presence of a conjugated diene in addition to the original indole residue. The n.m.r. spectrum of this taberpsychine-methine shows a complex (5H) pattern in the region where the absorption for olefinic protons is expected (see Fig. 3). The pattern is further complicated by the presence in the same area, of the absorption due to the C-3 proton adjacent to the aromatic ring and the oxygen atom. The product obtained by hydrogenation of the methine showed two saturated *C*-methyl signals in the n.m.r. spectrum hence the conjugated diene could only be formed by elimination of one of the protons in the methyl group and migration of the double bond to open the piperidine ring, leaving the nitrogen attached to the eight-membered ring. The structure of this degradation product was assigned as shown in **7**. A very minor product of this Hofmann degradation was observed by t.l.c. but could not be isolated. This is probably the isomer of the diene as depicted in **8**.

The problem of the stereochemistry of taberpsychine is almost reduced to a question of absolute stereochemistry, since once the configuration at one of the asymmetric centers is fixed, the closing of the rings determines the configuration at the other centers. Thus the alkaloid has either the stereochemistry shown in structure **4** or its complete mirror image. The vinylogous Hofmann degradation of taberpsychine methiodide to give the diene **7** is understandable since the two activated "benzylic" protons at C-6 are not suitably disposed to allow facile *trans*-elimination. Examination of molecular models of taberpsychine suggests that the hydrogenation of the exocyclic double bond would be specifically from that face of the molecule which would lead to an equatorial ethyl group as in **10***a*. Hydrogenation from the other face, which should give the axial ethyl residue (as in **10***b*) is seriously hindered by the eight-membered ring and the aromatic system. The results of the Hofmann degradation of the methiodide of the dihydrotaberpsychine **10***a* show that the predominant reaction involves the elimination of one of the protons at C-6 adjacent to the indole ring. It would be difficult to rationalize this observation on the basis of structure **10***b* where the equatorial hydrogen substituent, introduced by hydrogenation, is stereochemically well situated for a *trans*-elimination.[3]

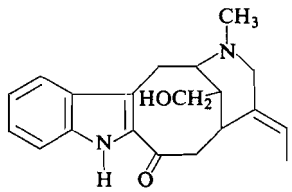
Another alkaloid obtained from *T. psychotrifolia* analyzed for $C_{20}H_{24}N_2O_2$ and its particular u.v. spectrum [λ_{max} 224 (10 000) and 318 (12 000)] permitted its classification as an α-acyl indole.

The i.r. spectrum confirms the presence of the

[3]We realize that the structural elucidation of taberpsychine is based almost entirely on spectral evidence. Although we had a large amount of alkaloid available for degradative studies, some 40 different experiments aimed at the isolation of other degradation products failed (J. D. Medina (8)).

carbonyl group (strong band 1650 cm^{-1}) as well as that of the aromatic moiety and the indolic NH. This spectrum also shows the presence of a hydroxyl group. The n.m.r. spectrum was difficult to perform due to the only slight solubility of the base in most organic solvents, but the problem was partly solved by the use of a hot saturated chloroform solution. The spectrum showed the presence of a methyl group attached to the basic nitrogen (singlet 2.53 δ) and of a methyl group on a tri-substituted double bond (1H quartet 5.40 δ, J = 6 Hz and 3H triplets 1.68 δ, J = 6 Hz).

Acetylation of the base with acetic anhydride in pyridine at room temperature gives a monoacetate (molecular weight by mass spectrometry 366) and while this product is rather unstable it could be characterized spectrally. The i.r. spectrum proves that it is an *O*-acetyl derivative (peaks at 1745 and 1235 cm^{-1}) and the n.m.r. spectrum reveals that the acetyl methyl is unusually shielded (3H singlet 1.77 δ). The most useful information, however, is given by the mass spectra since that of the base itself shows two major peaks at 152 and 122 *m/e* while in the acetate one finds a new peak at 194 *m/e* (42 mass units from 152 *m/e*).



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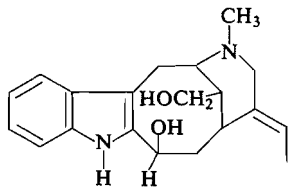
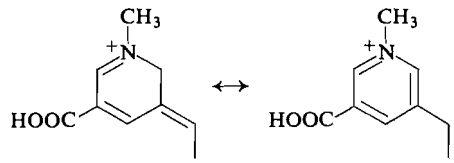


12

The structure proposed, which is justified by the mass spectrum is identical with that proposed for affinine **11**, (4) and although the physical constants given in the literature for the latter were misleading, the base is in fact affinine and this was confirmed by reduction by sodium borohydride to vobasinediol **12**.

That the stereochemistry at C-16 is as shown can be readily seen from the extreme shielding of the acetyl methyl (3H singlet 1.77 δ) observed in the n.m.r. spectrum of the *O*-acetyl derivative. In vobasine, the same shielding is observed for the methyl of the ester group, this appearing at 2.63 δ.

A third alkaloid, $C_{20}H_{22}N_2O_3$, is a high melting compound (m.p. 295° dec.) only sparingly soluble in most organic solvents which suggested it to be a salt. However, no anion was detectable pointing to an internal salt or amino acid. The u.v. spectrum of the base [λ_{max} 238 (13 100) and 316 (20 000) mμ] is that of an α-acyl indole and the i.r. spectrum presents two very typical bands in the region for carbonyl groups. One of them at 1650 cm^{-1} is assigned, in agreement with the u.v. spectrum, to a keto group on C-3 conjugated to the indole moiety and the other at 1610 cm^{-1}, a very strong band which is only compatible with a carboxylate carbonyl. The n.m.r. spectrum (performed in 2% D_2SO_4 in D_2O solution) shows the presence of an *N*-methyl group (3H singlet at 3.00 δ, displaced to lower field due to the quaternization of the basic nitrogen) and of an exocyclic ethylidene chain (1H quartet 5.93 δ and 3H doublet 1.68 δ, J = 7 Hz) in addition to the absorption expected from the indolic residue.



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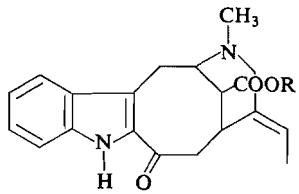

14

a R = H
b R = CH_3

The mass spectrum of the base presents its principal peak at 122 *m/e*, very typical fragmentation in the mass spectrometric degradation of vobasine-like alkaloids. Another important peak is that at 166 *m/e* (44 mass units = COO from

122) which coupled to the evidence for the presence of an acidic residue in the molecule, leads to the conclusion that the latter is attached to the six-membered ring producing the pyridinium ion **13** in the fragmentation.

Based on this evidence the alkaloid was assigned structure **14*a***, which is that of 16-epi-vobasinic acid previously prepared by Renner (5) but never before reported as a natural product. All spectral data are in agreement with this structure, including the fragmentation in the mass spectrum.

Confirmation for the structure is provided by methylation of the base by prolonged treatment with diazomethane. The i.r. spectrum of the product obtained shows the absorption typical of esters (1740 cm^{-1}), while the n.m.r. spectrum shows it is a methyl ester (3H singlet 3.53 δ). The position of the absorption for the methyl group of the ester in the spectrum determines the stereochemistry at C-16, as being epimeric to that in vobasine where the same absorption shows the methyl group of the ester to be very shielded (3H singlet 2.63 δ) presumably because it lies immediately above the electronic cloud of the aromatic ring.

The methylated derivative **14*b*** presents the same physical properties, and the i.r., n.m.r., and mass spectra are identical with those of *16-epi-vobasine* given in the literature (5).

Experimental

Melting points are uncorrected. Unless otherwise stated, the conditions and instruments employed for the various spectra were as follows: u.v., ethanol solutions (ε in parentheses); i.r., KBr pellets, Beckmann I.R.4; n.m.r., deuteriochloroform solutions with tetramethylsilane protons taken as 0 p.p.m., Varian A 60; mass spectra, AEI MS-9 and Varian M-66 spectrometers.

Extraction and Isolation of the Alkaloids

The ground trunk bark (6.5 kg) was extracted with methanol, until the alcoholic extract gave a negative reaction with Vassler's reagent. Evaporated to dryness this extract yielded a brown tar, which was triturated five times with 200 ml fractions of 2% hydrochloric acid. The acidic solution was then continuously extracted with chloroform to separate non-basic materials. From this chloroform, after concentration and cooling, was obtained the soluble hydrochloride of *taberpsychine* (6.627 g).

The aqueous solution was then basified with ammonia and again continuously extracted with chloroform. The chloroform containing the basic material yielded, on cooling, a black powder (1.505 g) which was filtered, redissolved in 2% hydrochloric acid, and extracted once with chloroform. This chloroform was discarded and the aqueous solution neutralized with ammonia then extracted with chloroform four times. The chloroform was taken to dryness and the white amorphous *16-epi-vobasinic* acid (454 mg) was obtained.

The chloroform solution containing the bases was evaporated to dryness to give a semi-solid tar (61 g; total crude bases: 68.08 g). Part of the crude bases (10 g) was dissolved in acetone–ethanol and on slow evaporation a fine precipitate was obtained. Filtered and washed with cold acetone, it resulted in a mixture of 16-epi-vobasinic acid and affinine (300 mg). Both materials are virtually insoluble in all solvents, but affinine is slightly soluble in hot methanol and so the mixture was separated by boiling the solid in methanol and filtering while hot. Affinine (180 mg) precipitated from the methanol solution as an amorphous solid.

Another portion of the crude base (25 g) was submitted to a countercurrent distribution with acetate buffer, p*H* 3.4 (25 ml), using chloroform as stationary phase (25 ml), for a total of 50 transfers.

Fractions 1 to 7 (10 g) contained only neutral material and were not investigated further. Fractions 18 to 40 (12.7 g) yielded taberpsychine. Fractions 41 to 50 (1.22 g) yielded affinine.

Taberpsychine

The base was recrystallized from acetone and sublimed for analysis, m.p. 208° (dec.), $[\alpha]_D$ −243°; λ_{max} 222 (33 100), 272 (sh. 6500), 280 (7500), and 286 mμ (6650); ν_{max} 3241 (NH), 2747 (*N*-methyl), 744 and 728 cm^{-1} (aromatic).

The n.m.r. spectrum δ: 1H singlet 8.42 (NH); 4H multiplet 7.07–7.66 (aromatic); 1H broad quartet 5.38, J = 6.5 Hz, and 3H doublet of doublets, J = 6.5 and 2.0 Hz (ethylidene side chain); 3H singlet 2.53 (*N*-methyl); 1H doublet of doublets 5.13, J = 10 and 2 Hz (C_3—H); 2H AB quartet 2.93 and 3.60, J = 14 Hz (C-21 methylene). Mass spectrum: 308.1849 (M^+; $C_{20}H_{24}N_2O$ requires 308.1887), 293, 279, 154, 130, 122, 121, 108, 107 *m/e*.

Anal. Calcd. for $C_{20}H_{24}N_2O$: C, 77.9; H, 7.8; N, 9.1; O, 5.2. Found: C, 77.9; H, 8.0; N, 9.0; O, 5.2.

Taberpsychine Methiodide

Taberpsychine (409 mg) was dissolved in acetone (10 ml) and methyl iodide (0.5 ml) added. The solution was refluxed for a few min and then cooling gave white needles of taberpsychine methiodide which was recrystallized from acetone, m.p. 272–274° (dec.); λ_{max} 222 (34 400), 276 (sh. 7200) and (7800) mμ; ν_{max} 3170 (NH), 2830 (*N*-methyl), and 780 (aromatic) cm^{-1}.

The n.m.r. spectrum δ : 1H singlet 8.35 (NH); 4H multiplet 7.00–7.87 (aromatic); 1H broad quartet 5.43, J = 7 Hz, and 3H broad doublet 1.65, J = 7 Hz (ethylidene side chain); 3H singlet 3.28, and 3H singlet 3.03 (2 *N*-methyls); 1H doublet of doublets 5.23, J = 10 and 2 Hz (C_3—H). Anal. Calcd. for $C_{21}H_{27}N_2OI$: C, 56.0; H, 6.0; N, 6.2; O, 3.6; I, 28.2. Found: C, 55.7; H, 5.8; N, 6.4; O, 3.9; I, 28.1.

3-Ethyl Pyridine from Taberpsychine

Sublimed taberpsychine (194 mg) was mixed with dried zinc dust (1 g) and heated in a sealed tube at 280° for 3 h. A yellow distillate obtained in the cooler part of the tube protruding from the block was dissolved in methanol and analyzed in the gas chromatograph [Apiezon L 10%]. The spectrum shows two peaks (3:1 ratio) with retention times of 6 and 12.5 min respectively at a column temperature of 130° and increasing at the rate of 1°/min, which were identified by direct comparison as corresponding to 3-ethyl pyridine and 3-methyl-5-ethyl pyridine respectively. The major fraction was recovered and dissolved in deuterated chloroform. The n.m.r. spectrum δ : 2H multiplet 8.27–8.47 (H-2 and -6); 1H broad doublet 7.40, J = 8 Hz (H-4); 1H quartet 7.03 and 7.13 J = 8 Hz (H-5); 2H quartet 2.62, J = 7 Hz, and 3H triplet 1.22, J = 7 Hz (ethyl chain).

Dihydrotaberpsychine

Taberpsychine (1.210 g) was dissolved in ethanol (100 ml) and platinum oxide (500 mg) added together with glacial acetic acid (10 ml). After shaking for 50 h in an atmosphere of hydrogen (50 p.s.i.), the catalyst was filtered off and the alcoholic solution evaporated to dryness under reduced pressure. The resulting brown foam was redissolved in 2% hydrochloric acid, basified with ammonia, and extracted four times with chloroform which was evaporated to dryness. The product (1.150 g) was dissolved in acetone and the dihydrotaberpsychine obtained as white crystals, m.p. 191–193°; λ_{max} 223 (34 100), 277 (sh. 9000), 284 (9800), and 293 (8300) mμ; ν_{max} 3271 (indole NH), 2788 (*N*-methyl), 745 and 726 aromatic cm^{-1}

The n.m.r. spectrum δ : 4H multiplet 7.00–7.80 (aromatic); 1H doublet of doublets 5.12, J = 10 and 2 Hz (C_3—H); 3H singlet 2.53 (*N*-methyl); 3H triplet 0.98, J = 7 Hz (methyl in saturated ethyl side chain). Mass spectrum: 310 (M^+), 295 (M-15), 279 (M-31), 265, 251, 195, 180, 170, 168, 155 *m/e*. (M^{++}), 144, 138, 130, 124, 122, 108 *m/e*.

Anal. Calcd. for $C_{20}H_{26}N_2O$: C, 77.4; H, 8.4; N, 9.0; O, 5.2. Found: C, 77.2; H, 8.4; N, 8.9; O, 5.4.

Dihydrotaberpsychine Methiodide

Dihydrotaberpsychine (650 mg) was dissolved in acetone (15 ml) and methyl iodide (2.5 ml) was added to the warm solution. The mixture was boiled for 5 min and then allowed to cool. The amorphous dihydrotaberpsychine methiodide obtained was recrystallized from acetone, m.p. 255–258° (dec.); λ_{max} 221 (55 200), 275 (sh. 10 900), 284 (11 700), and 292 (10 400) mμ.

Anal. Calcd. for $C_{21}H_{29}N_2OI$: C, 55.8; H, 6.5; N, 6.2; O, 3.5; I, 28.1. Found: C, 55.7; H, 6.5; N, 6.3; O, 3.6; I, 28.3.

Dihydrotaberpsychine-methine

Dihydrotaberpsychine methiodide (550 mg) was suspended in *tert*-butyl alcohol (15 ml) and a solution (25 ml) of potassium (1 g) in *tert*-butyl alcohol added slowly. The mixture was refluxed for 24 h, then evaporated to dryness under reduced pressure, the residue was redissolved in water and the aqueous solution extracted four times with chloroform. The dihydrotaberpsychine-methine (418 mg) was obtained as a pale yellow foam which was crystallized from acetone and sublimed for analysis, m.p. 153–155°; λ_{max} 229.5 (38 500), 271 (12 000), 284 (11 400), and 294 (sh. 9000) mμ; ν_{max} 3250 (indole NH), 2820 and 2760 (*N*-methyl), 745 and 730 (aromatic) cm^{-1}.

The n.m.r. spectrum δ : 1H singlet 8.84 (indole NH); 4H multiplet 7.00–7.64 (aromatic); 1H doublet 6.69, J = 12 Hz (C_6—H) and 1H doublet of doublets 5.55, J = 12 and 8 Hz (C_5—H), both being the low field portion of an ABX system; 1H doublet of doublets 4.84, J = 12 and 2Hz (C_3—H); AB part of a second ABX system; 1H doublet 4.21, J = 11 Hz and 1H triplet 3.79, J = 11 Hz (methylene adjacent to oxygen in the oxide ring); 6H singlet 2.20 (*N*-dimethyl); 3H triplet 0.87, J = 7 Hz (methyl on saturated ethyl side chain). Mass spectrum: 324 (M^+), 310, 295, 280, 266, 194, 185, 180, 169, 168, 162 (M^{2+}), 156, 137, 130, 124, 58 *m/e*. Mol. wt. by mass spectrometry: 324.2175. $C_{21}H_{28}N_2O$ requires: 324.2202.

A minor product which could not be induced to crystallize was identified by means of its n.m.r. spectrum as the other isomer of dihydrotaberpsychine-methine (structure **6**). The n.m.r. spectrum δ : principal feature was a pair of doublets at 4.97 and 5.63, J = 2 Hz due to a terminal methylene.

Hydrogenation of Dihydrotaberpsychine-methine

Dihydrotaberpsychine-methine (400 mg) was dissolved in ethanol (50 ml), platinum oxide (150 mg) and glacial acetic acid (15 ml) were added, and the mixture left hydrogenating for 24 h (50 p.s.i.). The reaction mixture was then filtered and evaporated to dryness under reduced pressure. The residue was dissolved in water, basified with ammonia, and extracted with chloroform yielding a yellow foam (340 mg). This foam was dissolved in acetone and the crystalline derivative obtained was recrystallized from the same solvent, m.p. 184–186°; λ_{max} 224.5 (46 000), 279 (sh. 11 050), 285 (12 000), and 293 (10 300) mμ; ν_{max} 3250 (indole NH), 2750 (*N*-methyl) and 740 (aromatic) cm^{-1}.

The n.m.r. spectrum δ : 1H broad singlet 9.23 (indole NH); 4H multiplet 6.92–7.73 (aromatic); 1H broad doublet 5.10, J = 10 Hz (C_3—H); 6H singlet 2.20 (*N*-methyls); 3H triplet 0.85, J = 7 Hz (methyl in saturated ethyl side chain). Mass spectrum: 326.2362 (M^+; $C_{21}H_{30}N_2O$ requires: 326.2358), 282, 281, 268, 226, 225, 180, 168, 156, 144, 130 *m/e*.

Anal. Calcd. for $C_{21}H_{30}N_2O$: C, 77.3; H, 9.3; N, 8.6; O, 4.9. Found: C, 77.5; H, 9.2, N, 8.4; O, 5.1.

Taberpsychine-methine

Taberpsychine methiodide (1.687 g) was suspended in *tert*-butyl alcohol and a solution (25 ml) of potassium (1 g) in *tert*-butyl alcohol added. The suspension was refluxed for 18 h and then taken to dryness under reduced pressure, redissolved in water and extracted with ether to give a brown foam (1.200 g). After redissolving the foam in ether and reducing the solution to a small volume, taberpsychine-methine crystallized selectively (589 mg). Recrystallization was from ether, m.p. 194–196° (dec.); λ_{max} 224 (46 300), 278 (sh. 8800), 284 (9200), and 292.5 (8100) mμ; ν_{max} 3270 (indole NH), 3075 (aromatic), 2766 (*N*-methyl), 1590, 740 and 725 (aromatic) cm^{-1}.

The n.m.r. spectrum δ : 1H broad singlet 8.18 (NH);

4H multiplet 6.98–7.64 (aromatic); 1H doublet of doublets 6.40 and 6.51, $J = 18$ and 11 Hz (H_a); 1H doublet 5.28, $J = 18$ Hz (H_b); 1H doublet 5.21, $J = 11$ Hz (H_c); 2H doublet 5.22, $J = 8$ Hz (2-H_d); 1H doublet 5.09, $J =$ 11 Hz (C_3—H); 6H singlet 2.27 (2-*N*-methyl). Mass spectrum: 322 (M^+), 278 (M-N(CH_3)$_2$), 215, 194, 183, 180, 168, 156, 136, 130 *m/e*.

Anal. Calcd. for $C_{21}H_{26}N_2O$: C, 78.2; H, 8.1; N, 8.7; O, 5.0. Found: C, 78.1; H, 8.0; N, 8.5; O, 5.0.

A minor product was observed by t.l.c. but could not be isolated. This is probably the other isomer formed in small quantity.

Hydrogenation of Taberpsychine-methine

Taberpsychine-methine (429 mg) was dissolved in ethanol (50 ml) containing acetic acid. Platinum oxide (200 mg) was added and the mixture shaken for 18 h under hydrogen (50 p.s.i.). The solution was then filtered, evaporated to dryness under reduced pressure, and the residue redissolved in water, basified with ammonia, and extracted with ether. The ether was evaporated to dryness and a white foam (400 mg) was obtained. The tetrahydro compound was crystallized from acetone–ether and sublimed, m.p. 153–155°; λ_{max} 225 (29 300), 278 (7500). 284.5 (8100), and 293 (7050) mμ; ν_{max} 3250 (indole NH), 2766 (*N*-methyl), 740 and 730 (aromatic) cm^{-1}.

The n.m.r. spectrum δ : 1H broad singlet 8.82 (indole NH); 4H multiplet 6.97–7.73 (aromatic); 1H broad doublet 5.12, $J = 10$ Hz (C_3—H); 6H singlet 2.35 (*N*-methyls); 3H triplet 1.25, $J = 9$ Hz, and 3H doublet 0.93, $J = 6$ Hz (saturated methyls).

Anal. Calcd. for $C_{21}H_{30}N_2O$: C, 77.3; H, 9.3; N, 8.6; O, 4.9. Found: C, 77.2; H, 9.3; N, 8.3; O, 4.9.

Affinine

The very insoluble base was recrystallized from a large volume of ethanol and sublimed for analysis, m.p. 273–275° (dec.); λ_{max} 236 (sh. 13 200) and 320 (13 400) mμ; ν_{max} 3150 (broad, NH and OH), 2800 (*N*-methyl), 1650 (3-keto), 740 (aromatic) cm^{-1}.

The n.m.r. spectrum δ : 1H broad singlet 9.80 (indole NH); 4H multiplet 7.00–7.83 (aromatic); 1H broad quartet 5.40, $J = 6$ Hz, and 3H broad doublet 1.68, $J = 6$ Hz (ethylidene side chain); 3H sharp singlet 2.53 (*N*-methyl). Mass spectrum: 324 (M^+), 293 (M-CH_2OH), 158, 152, 122, 108 *m/e*.

Anal. Calcd. for $C_{20}H_{24}N_2O_2$: C, 74.0; H, 7.5; N, 8.6; O, 9.9. Found: C, 73.8; H, 7.5; N, 8.5; O, 10.0.

Affinine Acetate

Affinine (150 mg) was dissolved in pyridine (5 ml) and an excess of acetic anhydride (1 ml) added. The mixture was left standing overnight at room temperature. Methanol was then added to hydrolyze the excess anhydride and the solution evaporated to dryness under reduced pressure. The residue was redissolved in water, basified with ammonia, and the aqueous solution extracted with chloroform. The product is very unstable and decomposes while in solution, so crystallization was not possible. However i.r., n.m.r., and mass spectra indicate that it is indeed monoacetate of the base; λ_{max} (qualitative) 223 (shoulder), 237 (shoulder), and 319 mμ; ν_{max} 3300 (indole NH), 1745 and 1235 (O-acetyl), 1650 (3-keto), 1575 and 740 (aromatic) cm^{-1}.

The n.m.r. spectrum δ : 1H singlet 9.80 (indole NH); 4H multiplet 7.00–7.84 (aromatic); 1H broad quartet 5.40, $J = 6$ Hz and 3H doublet 1.67, $J = 6$ Hz (ethylidene side chain); 3H singlet 2.53 (*N*-methyl); 3H singlet 1.77 (*O*-acetyl). Mass spectrum: 366 (M^+), 306 (M-acetic acid), 293 (M-CH_3COOCH_2), 263, 194, 158, 122 *m/e*.

Vobasinediol (from Affinine)

Affinine (110 mg) was suspended in absolute methanol (25 ml), an excess of sodium borohydride (100 mg) was added, and the mixture left standing overnight at room temperature. Water (200 ml) was then added and the aqueous solution extracted with ether. After evaporation to a small volume, colorless needles of vobasinediol (100 mg) were obtained and sublimed for analysis, m.p. 244–245° (dec.), $[\alpha]_D$ −60° (methanol); λ_{max} 224 (21 600), 283 (6100), and 291 (5400) mμ; ν_{max} 3300 (NH and OH), 2280 (*N*-methyl), 740 (aromatic) cm^{-1}.

The n.m.r. spectrum δ : 1H singlet 9.75 (indole NH); 4H multiplet 6.90–7.62 (aromatic); 1H broad quartet 5.47, $J = 7$ Hz and 3H broad doublet 1.68, $J = 7$ Hz (ethylidene side chain); 1H broad doublet 5.27, $J = 6$ Hz C_3—H); 3H singlet 2.43 (*N*-methyl). Mass spectrum: 326 (M^+), 308 (M-H_2O), 293 (M-H_2O-15), 277 (M-H_2O-CH_2-OH), 183, 180, 154, 152, 136, 130, 122 *m/e*.

Anal. Calcd. for $C_{20}H_{26}N_2O_2$: C, 73.6; H, 8.0; N, 8.6; O, 9.8. Found: C, 73.6; H, 8.0; N, 8.4; O, 9.7.

16-epi-Vobasinic Acid

The base was recrystallized several times from large volumes of hot ethanol, m.p. 295° (dec.); λ_{max} 238 (13 100) and 316 (20 000) mμ; ν_{max} 3105 (indole NH), 1650 (3-keto), 1610 (carboxylate), and 753 (aromatic) cm^{-1}.

The n.m.r. spectrum δ : (in 2% D_2SO_4/D_2O solution) 4H multiplet 6.88–7.77 (aromatic); 1H broad quartet 5.93, $J = 7$ Hz and 3H broad doublet 1.68, $J = 7$ Hz (exocyclic ethylidene); 3H singlet 3.00 (*N*-methyl on quaternary nitrogen. Mass spectrum: 338 (M^+), 293 (M-COOH), 180, 166, 158, 122 *m/e*.

Anal. Calcd. for $C_{20}H_{22}N_2O_3$: C, 71.0; H, 6.6; N, 8.3; O, 14.2. Found: C, 70.8; H, 6.6; N, 8.0; O, 14.4.

16-epi-Vobasine (from 16-epi-Vobasinic Acid)

16-epi-Vobasinic acid (200 mg) was suspended in dry methanol (20 ml) and ethereal diazomethane solution (20 ml) added. The mixture was refluxed overnight on a water bath. The solution was then evaporated to dryness and redissolved in ether. 16-epi-Vobasine (190 mg) crystallized on slow evaporation and was recrystallized from ether, m.p. 185–187°; λ_{max} 237 (10 550) and 320 (12 000) mμ; ν_{max} 3300 (indole NH), 2750 (*N*-methyl), 1740 (methyl ester), 1645 (3-keto) and (aromatic) cm^{-1}.

The n.m.r. spectrum δ : 1H broad singlet 9.57 (indole NH); 4H multiplet 7.00–7.83 (aromatic); 1H broad quartet 5.51, $J = 7$ Hz and 3H broad doublet 1.73, $J = 7$ Hz (exocyclic ethylidene); 3H singlet 3.53 (methyl ester); 3H singlet 2.52 (*N*-methyl). Mass spectrum: 352 (M^+), 293 (M-$COOCH_3$), 180, 166, 158, 122 *m/e*.

Anal. Calcd. for $C_{21}H_{24}N_2O_3$: C, 71.6; H, 6.9; N, 8.0; O, 13.6. Found: C, 71.5; H, 6.8; N, 8.0; O, 13.6.

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