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ALKALOIDS OF *ASPIDOSPERMA CUSPA* BLAKE

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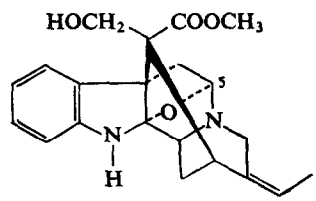
Abstract—The three principal alkaloids of Venezuelan *Aspidosperma cuspa* have been identified as burnamine (I), des-*O*-methylaspidocarpine (XV) and aspidodasycarpine (II). Several reaction products and derivatives of the latter are described.

Aspidosperma cuspa is found in the coastal regions of Venezuela close to Caracas, as a large shrub in contrast to the enormous trees which characterize the species *A. fendleri*.[2a] *A. vargasi*[2b] and particularly *A. excelsum*[2c] which we have previously examined in our survey of Venezuelan plants. The crude alkaloids were obtained from the aerial bark by a routine mild extraction procedure and separated by counter-current distribution. Three relatively stable alkaloids were isolated and characterized in this manner and all three are previously described but originating from other species of *Aspidosperma.*

By direct comparison, one of the bases has been identified as burnamine (I) (desacetylpicraline).[3] Of great help in the characterization of this compound is the absorption in the



(I)

nuclear magnetic resonance (NMR) spectrum at 4·75δ attributable to the lone proton at C-5 which is flanked on one side by the more basic nitrogen atom and on the other side by the ethereal oxygen atom. The infrared (i.r.) and ultraviolet (u.v.) spectra are in agreement with those given in the literature and a mixed melting point with an authentic sample showed no depression.

The major alkaloid of *A. cuspa* has now been shown to be aspidodasycarpine (II),[4] although originally this appeared unlikely due to an ostensibly different melting point of the *O,N*-diacetyl derivative (III) as described in the literature (m.p. 110°) and that obtained from the plant (m.p. 175°). The constancy of the melting point of our aspidodasycarpine on admixture with an authentic sample, superposable i.r. spectra and identical R_f values on TLC

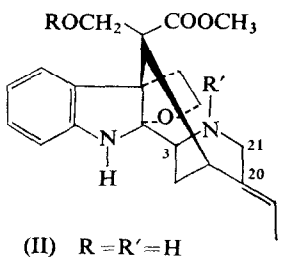
[1] The preliminary stages of this work were performed at I.V.I.C., Caracas, Venezuela.

[2] (*a*) R. H. BURNELL, J. D. MEDINA and W. A. AYER, *Can. J. Chem.* **44**, 28 (1966). (*b*) R. H. BURNELL and D. DELLA CASA, *Can. J. Chem.* **45**, 89 (1967). (*c*) P. R. BENOIN, R. H. BURNELL and J. D. MEDINA, *Can. J. Chem.* **45**, 725 (1967).

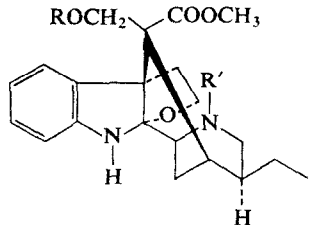
[3] A. Z. BRITTEN and G. F. SMITH, *J. Chem. Soc.* 3850 (1963).

[4] M. OHASHI, J. A. JOULE and C. DJERASSI, *Tetrahedron Letters* 3899 (1964).

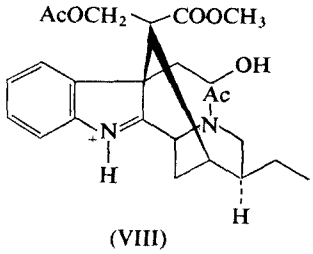
conclusively showed the *A. cuspa* base to be aspidodasycarpine. Our original uncertainty led us to prepare other derivatives and to undertake certain degradative reactions, thinking perhaps a structure elucidation would be necessary.



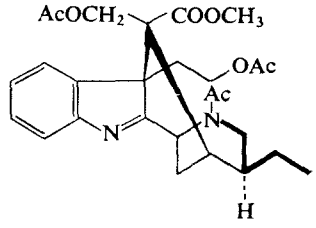
(II) R = R' = H
(III) R = R' = $COCH_3$
(IV) R = H R' = $COCH_3$



(V) R = R' = H
(VI) R = R' = $COCH_3$
(VII) R = H R' = $COCH_3$



(VIII)



(IX)

Pyrolysis of aspidodasycarpine in vacuum in the presence of zinc powder produced, as expected, 3-ethylpyridine as the major volatile product as shown by direct vapour phase chromatographical comparison and by the NMR spectrum of the principal volatile fraction. A much smaller quantity of 3- or 4-methylpyridine was observed but the yield was too low to obtain a clear NMR spectrum.

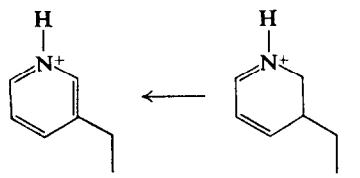
A neutral *N*-acetyl derivative (IV) of aspidodasycarpine was prepared by reacting the base with 1 mole of acetic anhydride in pyridine at low temperature and this same product was obtained by the hydrolysis of the *O,N*-diacetyl derivative (III) in dry methanol containing a small amount of sulfuric acid. Catalytic reduction of aspidodasycarpine in acetic acid gave rise to a dihydro compound (V) in which the exocyclic double-bond is reduced. The configuration of the newly formed asymetric center is assumed to be as shown in V with the C-ethyl residue *cis* to the ester-bearing bridge since examination of models reveals considerable hindrance to the approach of a hydrogen-bearing catalyst from the same side of the molecule as the bridge. The NMR spectrum of the dihydro derivative confirms the saturation of the double bond since the peaks of the ethylidene residue in aspidodasycarpine (quartet: 1H, 5·52δ; J = 6·5 c.p.s. and doublet of doublets 1·7δ; J = 6·5, J = 2 c.p.s.) are no longer observed and a resonance for a methyl grouping is now found at 1·0δ (doublet: J = 6 c.p.s.). Acetylation of the dihydro base (V) afforded the expected *O,N*-diacetyldihydro derivative (VI) which proved to be a remarkably insoluble but clearly crystalline substance. The latter could also be prepared by hydrogenation of *O,N*-diacetylaspidodasycarpine (III). Hydrolysis of the diacetyl dihydro compound (VI) using the conditions described above led to *N*-acetyldihydroaspidodasycarpine (VII) which, again, was more readily prepared by

controlled partial acetylation of the dihydro base (V). Catalytic reduction of *N*-acetyl-aspidodasycarpine (IV) also afforded the dihydro compound VII. The spectral characteristics of these various acetyl derivatives are in agreement with their proposed functionality (see Experimental).

The carbinolamine ether structure of aspidodasycarpine suggests that in acid solution the five-membered ethereal ring should open, affording an indolenium structure comparable to VIII. Djerassi used this protonated form of the alkaloid to explain the degradation products obtained by reduction with zinc in hydrochloric acid.[4] We felt it would be of interest to characterize the indolenine, the acetyl derivative of which we found to be readily obtained by acetylation of dihydroaspidodasycarpine (V), or its acetyl derivatives (VI and VII) in acetic anhydride containing small quantities of concentrated sulfuric acid. The product (IX) absorbs in the u.v. spectrum at 222 and 261 nm reflecting the change in chromophore and the i.r. and NMR spectra now show the absence of the indoline N–H moiety. All attempts to hydrogenate the indolenine double bond met with failure, however reduction with sodium borohydride afforded *N*-acetyldihydroaspidodasycarpine (VII) showing that the ethereal ring is very readily reestablished.

The mass spectra of aspidodasycarpine (II), the dihydro base (V) and the indolenine (IX) deserve some comment, although no detailed analysis of the fragmentations will be presented due to the lack of suitably deuterated substrates.

Fragmentation of aspidodasycarpine is characterized by an intense peak at 108 *m/e*, presumably arising from the ethylpyridinium ion X. The only other significant peak is at 14 mass units lower. The dihydro derivative (V) also shows a tendency to produce similar stable ions but, as expected, the base peak is now at 110 *m/e* (XI) with a much smaller peak at 108 *m/e* (X). Relatively pronounced peaks also appear at 130 and 144 *m/e* (from the indole moiety).



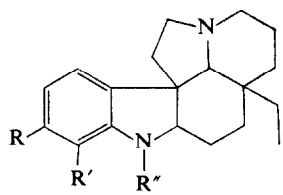
(X) 108 m/e (XI) 110 m/e

The indolenine also shows the dihydropyridinium ion (XI) but as a relatively weak peak, while the major fragments arise from loss of the various oxygenated groupings. The cleavage of the acetyl groups (as ketene) and the ester function is reflected by the M-42 and M-59 peaks respectively but the most intense peak by far arises from the expulsion of —CH_2—O—CO—CH_3. The other alkyl chain —CH_2CH_2—O—CO—CH_3 is also extruded as judged by the significant peak at M-87. One other intense peak at 385 *m/e* (M-113) is postulated as arising from rupture of the piperidine ring and release of the C-ethyl residue and carbon atoms C-20 and C-21 with the nitrogen atom and the accompanying acetyl residue (heavy lines in IX).

The third alkaloid obtained from *A. cuspa* belongs to a different group of *Aspidosperma* bases and this was evident at an early stage. Absorption in the u.v. showed the aromatic portion of the molecule to be an hydroxylated *N*-acyl indoline. The *N*-acyl carbonyl group which produces an intense peak at 1635 cm^{-1} in the i.r. spectrum is presumably strongly

hydrogen bonded and the spectrum also shows an unbonded hydroxyl at 3360 cm^{-1}. Despite many attempts to dry the sample a peak of variable intensity at 1715 cm^{-1} persisted in the i.r. spectrum. This peak was felt to be due to acetone of crystallization and this was indeed shown to be the case by analysis and mass spectral determination of the molecular weight. Elemental analysis of the base, although somewhat variable, had indicated $C_{24}H_{34}N_2O_4$ (mol. wt. 414) as the molecular formula but the mass spectrum showed the molecular ion to be at 356 *m/e* corresponding to $C_{21}H_{28}N_2O_3$, the difference between the two formulae being essentially the elements of acetone.[5] The possibility of a facile fragmentation in the mass spectrometer could not be ruled out so the NMR spectrum was examined and the expected peak arising from the methyl groups of a molecule of acetone was observed at 2·14δ. The sample was taken to dryness and redissolved in deuterioacetone and then taken to dryness again. This procedure was repeated twice and the NMR spectrum then taken revealed the absence of the 2·14δ peak. Other features of the NMR spectrum included absorption arising from a saturated C-methyl grouping which gave a doublet at 0·7δ ($J=6$ c.p.s.), an *N*-acetyl three-proton singlet at 2·25δ, a complex pattern around 2·8δ reminiscent of that considered diagnostic of the aspidospermine skeleton,[6] a quartet centered at 4·0δ also observed in aspidospermine type bases (C–H adjacent to the indoline nitrogen atom), a single peak at 6·36δ integrating for two aromatic protons and, finally, a low-field singlet at 10·85δ attributed to the chelated phenolic hydroxyl group. The latter disappeared on shaking with deuterium oxide.

All the evidence accumulated was consistent with the formulation of this base as a dihydroxy-*N*-acetyl derivative of aspidospermidine (XII) and the mass spectral fragmentation was typical for this type of skeleton. The loss of a fragment of mass 28 (ethylene) is now well



(XII) $R=R'=R''=H$
(XIII) $R=R'=CH_3O$ $R''=COCH_3$
(XIV) $R=R'=OCOCH_3$ $R''=COCH_3$
(XV) $R=R'=OH$ $R''=COCH_3$

established as the first step in the degradation of aspidospermine derivatives and the peak at M-43 is in keeping with the presence of an acetyl residue. The principal indole ions appear at 190, 176 and 162 *m/e* as opposed to 144 and 130 *m/e* in alkaloids bearing no substituents in the indoline moiety which confirms the placing of the two hydroxyl groups on the aromatic ring. The remainder of the molecules gives rise to significant peaks at 152 and 138 *m/e* with by far the most intense peak at 124 *m/e*. These three peaks and especially the latter are found in the spectra of all bases embodying this skeleton.[7] To fully describe the structure of the alkaloid the substitution pattern on the aromatic moiety needed clarification. The confusion

[5] The $C_{21}H_{28}N_2O_3$ formula was obtained by analysis after several weeks of drying—see Experimental.
[6] C. DJERASSI, A. A. P. G. ARCHER, T. GEORGE, B. GILBERT, J. N. SCHOOLERY and L. F. JOHNSON, *Experientia* **16**, 532 (1960).
[7] K. BIEMANN, M. FRIEDMANN-SPITELLER and G. SPITELLER, *J. Am. Chem. Soc.* **85**, 631 (1963).

arising from the apparent singlet for the two aromatic protons in the NMR spectrum of the base was cleared up by methylating the two phenolic hydroxyls by prolonged treatment with diazomethane and the NMR spectrum of the product (XIII) now showed not only the two intense singlets for the methoxyl residues (3·67 and 3·59δ) but also a clear AB quartet for the aromatic protons (6·49 and 6·68δ: $J=8$ c.p.s.).

This limits the possible structures for the base to XV which is in fact *O*-demethylaspidocarpine and has been prepared from aspidocarpine[8] and isolated later from *A. album* as one of the minor bases.[9] Direct comparison of the *O*-methylated compound (XIII) with an authentic sample established the identity.

EXPERIMENTAL[10]

Extraction and Separation of the Bases

The *Aspidosperma cuspa* bark[11] was air dried and finely divided (12·6 kg) and extracted by percolation with ethanol until the percolate no longer gave positive tests with the usual alkaloid reagents. The ethanolic solution was concentrated under reduced pressure to give a tar which was triturated with 2 per cent aq. HCl several times. The aqueous extracts were combined and extracted continuously with $CHCl_3$ to remove non-basic material and then rendered alkaline with NH_3 and the crude basic fraction (80 g) obtained by $CHCl_3$ extraction. The crude bases were redissolved in dil. HCl and, after removing neutrals (as above), the crude base (54 g) was again obtained by $CHCl_3$ extraction.

The crude basic material (54 g) was distributed between a stationary $CHCl_3$ phase and acetate buffer (pH 3·72) in a fifty-tube countercurrent distribution apparatus. The most advanced aqueous phases (tubes 37–50) showed by paper chromatography one principal alkaloid in quantity and aspidodasycarpine (II, 12·5 g) was obtained from these tubes by normal manipulation. The crude base from the remaining tubes was combined and distributed again between $CHCl_3$ (stationary) and acetate buffer (pH 3·42) for fifty transfers and tubes 40–48 afforded more aspidodasycarpine (1·5 g). Tubes 6–8 contained essentially one base, which was shown later to be des-*O*-methylaspidocarpine (XV, 978 mg), and tubes 9–15 gave a crystalline alkaloid (1·089 g) shown to be burnamine (I). Further countercurrent distribution of the mother liquors afforded more I (371 mg) and XV (210 mg).

Burnamine (I)

The material obtained after recrystallizing from acetone gave m.p. 190–191° (dec.), $[\alpha]_D -151°$. (Found: C, 68·4; H, 6·7; N, 7·5; O, 17·5. Calc. for $C_{21}H_{24}N_2O_4$: C, 68·5; H, 6·6; N, 7·6; O, 17·4 per cent.) U.v. spectrum: λ_{max} 233 (8800) and 283 (3660) nm; $\lambda_{max}^{HClO_4\ 70\%}$ 247·5 and 302 nm. I.r. spectrum: 1747 (ester), 3550 (—OH), 3050 (NH), 1615 (arom.) cm^{-1}. NMR spectrum: complex 4H multiplet (aromatic) centered at 7·06δ; 1H singlet 5·16δ (NH); 1H quartet 5·38δ, $J=7·5$ c.p.s. (1 olefinic proton); 3H doublet 1·56δ, $J=7·5$ c.p.s. (C-methyl); 1H doublet 4·75δ, $J=2·5$ c.p.s. (C_5—H); 3H singlet 3·60δ (methyl ester).

Des-O-methylaspidocarpine (*XV*)

The base crystallized from acetone to give a substance containing acetone of crystallization, m.p. 139–140°, $[\alpha]_D +97°$. For analysis the sample was dried *in vacuo* for several weeks during which time the analysis changed from that corresponding to the hydrate to that of the base alone. (Found: C, 70·4; H, 8·0; mol. wt. (by mass spectrometry) 356·1978. $C_{21}H_{28}N_2O_3$ required: C, 70·7; H, 8·0 per cent; mol. wt. 356·2022.) U.v. spectrum: λ_{max} 224·5 (18,800) and 259·5 (7300) nm; λ_{max}^{NaOH} 236·5 (15,800) and 300 (3000) nm. I.r. spectrum: 3250 (—OH), 1635 (N-acyl) cm^{-1}. NMR spectrum: 1H singlet 10·85δ (chelated phenolic hydroxyl); 2H singlet 6·36δ (aromatic protons); 1H quartet 4·0δ, $J=5$ c.p.s. (C_2—H); 3H singlet 2·25δ (N-acetyl); 3H doublet 0·7δ, $J=4$ c.p.s. (saturated C-methyl).

Methylation of the base. Dimethyl sulfate, K_2CO_3 in dry acetone afforded (−)-pyrifolidine, m.p. 148–150°, $[\alpha]_D -83·5°$ ($[\alpha]_D -95°$, $CHCl_3$). U.v. spectrum: λ_{max} 224 (28,900), 252 (11,700) and 288 (2800) nm. I.r. spectrum: 1680 (*N*-acetyl) and 1610 (OCH_3) cm^{-1}. NMR spectrum: 2H AB quartet 6·49 and 6·68δ, $J=8$ c.p.s. (adjacent aromatic protons); 3H singlets at 3·67 and 3·59δ (two methoxyls); 3H singlet 2·05δ (*N*-acetyl); 3H triplet 0·73δ, $J=6$ c.p.s. (methyl of ethyl side-chain).

[8] S. McLean, K. Palmer and L. Marion, *Can. J. Chem.* **38**, 1547 (1960).

[9] C. Ferrari, S. McLean, L. Marion and K. Palmer, *Can. J. Chem.* **41**, 1531 (1963).

[10] Melting points are uncorrected. Unless otherwise stated, the conditions and instruments employed for the various spectra were as follows. Ultraviolet: ethanol solutions (ε in parenthesis); infrared: KBr pellets, Beckmann i.r. 4; nuclear magnetic resonance: deuteriochloroform solutions with tetramethylsilane protons taken as 0 p.p.m., Varian A. 60; mass spectra: AEI MS-9 spectrometer.

[11] R. E. Woodson, *Ann. Missouri Botan. Garden* **38**, 162 (1951).

Comparison of this product with an authentic sample by spectral and chromatographic methods confirmed their identity.

The di-*O*-acetyl derivative (XIV) was also prepared, m.p. 138–140° $[\alpha]_D$ −19° and showed the expected functionality, in particular the AB quartet in the NMR (6·99 and 6·88δ, J=8·5 c.p s.) ascribable to two adjacent aromatic protons.

Aspidodasycarpine (II)

Recrystallized from acetone, m p 207–209° $[\alpha]_D$ −130°, $[\alpha]_D$ −114° ($CHCl_3$). (Found: C, 68·2; H, 7·0; N, 7·8; O, 17·5. Calc. for $C_{21}H_{26}M_2O_4$: C, 68·1; H, 7·1; N, 7·6; O, 17·3 per cent.) U.v. spectrum: λ_{max} 239 (10,000) and 292 (4300) nm. I.r. spectrum: 3360 (—OH), 3580 (indoline NH), 3300 (N_b—H), 1610 (arom.) and 1720 (ester) cm^{-1}. Mixed m.p. with aspidodasycarpine showed no depression and i.r. spectra were identical. NMR spectrum: 4H multiplet 7·08δ (aromatic); 1H quartet 5·52δ, J=6·5 (olefinic); 3H doublet of doublets 1·7δ, J=6·5 c.p.s., J=2 c p.s. (unsaturated C-methyl); 3H singlet 3·76δ (methyl ester).

N,O-*Diacetylaspidodasycarpine (III)*

(*a*) To aspidodasycarpine (3·02 g) in pyridine (20 ml) was added acetic anhydride (10 ml). After 48 hr excess methanol was added with cooling and the solution then evaporated to dryness *in vacuo*. The residue was recrystallized from acetone (2·85 g), m.p. 175°, $[\alpha]_D$ −161°, $[\alpha]_D$ −174° ($CHCl_3$). (Found: C, 66·2; H, 6·8; O, 21·0; N, 6·0. $C_{25}H_{30}N_2O_6$ required: C, 66·1; H, 6·7; O, 21·1; N, 6·2 per cent.) U.v. spectrum: λ_{max} 241·5 (8900) and 297·5 (3100) nm. I.r. spectrum: 3450 (indoline NH), 1750 (—$OCOCH_3$), 1715 (—$COOCH_3$), 1630 (N—$COCH_3$), 1230 (—$OCOCH_3$) cm^{-1}. NMR spectrum: 4H multiplet 7·08δ (aromatic); 1H quartet 5·67δ, J=7 c p s. (olefinic); 1H singlet 4·85δ (indoline NH); 3H singlet 3·78δ (—$COOCH_3$), 3H singlet 2·17δ (N—$COCH_3$); 3H singlet 1·92δ (—O—$COCH_3$); 3H doublet 1·73δ, J=7 c.p s. (unsaturated C-methyl).

(*b*) The same *N,O*-diacetyl derivative (III) was obtained by similar acetylation of *N*-acetylaspidodasycarpine (IV).

N-*Acetylaspidodasycarpine (IV)*

(*a*) To aspidodasycarpine (500 mg) dissolved in pyridine (10 ml) was slowly added a cold solution of acetic anhydride (100 μl) in pyridine. After 6 hr at 5° the solution was allowed to warm up to room temperature and then evaporated to dryness *in vacuo* without heating. The residue afforded crystals of the *N*-acetyl derivative from acetone (302 mg) and from the mother liquors a further quantity (103 mg) was obtained by extraction of the neutral components in the usual manner. A small amount of unchanged aspidodasycarpine (47 mg) was obtained from the basic impurities obtained by washing with dil. HCl.

The pure *N*-acetyl derivative showed m p. 250–253°, $[\alpha]_D$ −147°. (Found: C, 66·8; H, 7·1; O, 19·2; N, 7·0. $C_{23}H_{28}N_2O_5$ required: C, 67·0; H, 6·8; O, 19·4; N, 6·8 per cent.) U.v. spectrum: λ_{max} 241·5 (8000) and 298·5 (2800) nm. I.r. spectrum: 3250 (indoline NH), 1760 (—$COOCH_3$), 1620 (N—$COCH_3$) cm^{-1}. NMR spectrum: 4H multiplet 6·75δ (aromatic); 1H quartet 5·38δ, J=7 c p.s. (olefinic proton); 3H singlet 2·05δ, (N—$COCH_3$); 3H doublet 1·65δ, J=7 c.p.s. (unsaturated C-methyl).

(*b*) *N,O*-Diacetylaspidodasycarpine (III) (200 mg) was dissolved in dry methanol (10 ml) and conc. H_2SO_4 (0·25 ml) was added. 18 hr of reflux afforded a neutral product (80 mg) shown to be the *N*-acetyl derivative (IV) and a basic fraction (65 mg) identified as aspidodasycarpine.

(*c*) *N,O*-Diacetylaspidodasycarpine (III) (200 mg) was reacted with $NaBH_4$ in methanol (15 ml) at room temperature. Water was added to the reaction after 18 hr and the foam obtained by $CHCl_3$ extraction (185 mg) crystallized from acetone. The product was identical in all respects to the *N*-acetyl derivative (IV) obtained previously.

Dihydroaspidodasycarpine (V)

Aspidodasycarpine (500 mg) was dissolved in methanol (50 ml) containing conc. HCl (3 ml) and Pt_2O (90 mg) was added. The mixture was shaken with H_2 at 50 p.s.i. for 22 hr, filtered and part of the methanol was removed *in vacuo*. After diluting with water and basifying with NH_3 the product (500 mg) was obtained by $CHCl_3$ extraction. Only one component was present as shown by TLC and this crystallized slowly from acetone, m.p. 209–211°, $[\alpha]_D$ −212°. (Found: C, 67·6; H, 7·7; O, 17·4; N, 7·7. $C_{21}H_{28}N_2O_4$ required: C, 67·7; H, 7·6; O, 17·2; N, 7·5 per cent.) U.v. spectrum: λ_{max} 241 (9500) and 297 (3700) nm. I.r spectrum: 3550 (indoline NH), 3400 (—OH), 3170 (N—H), 1723 (—$COOCH_3$), 1610 (aromatic) cm^{-1}. NMR spectrum: 4H multiplet 7·43δ (aromatic); 3H singlet 3·96δ (—$COOCH_3$); 3H doublet 1·0δ, J=6 c.p.s. (saturated C-methyl).

N,O-*Diacetyldihydroaspidodasycarpine (VI)*

(*a*) Dihydroaspidodasycarpine (350 mg) was acetylated using acetic anhydride (1 ml) in pyridine (5 ml) for 20 hr. Crystals which appeared in the solution during the reaction were filtered (129 mg) and washed with, and then recrystallized from, ethanol, m.p. 321–324° (decomp.), $[\alpha]_D$ −168°. (Found: C, 64·6; H, 6·8; O, 22·6; N, 6·2. $C_{25}H_{32}N_2O_6\frac{1}{2}$ H_2O required: C, 64·5; H, 7·1; O, 22·4; N, 6·0 per cent.) U.v. spectrum: λ_{max}

240 (6000) and 295 (1800) nm. I.r. spectrum: 3200 (indoline NH), 1755 (—O—$COCH_3$), 1735 (—$COOCH_3$), 1645 (N—$COCH_3$), 1230 (—O—$COCH_3$) cm^{-1}. NMR spectrum: could not be performed due to the limited solubility of the compound.

(*b*) *N,O*-Diacetylaspidodasycarpine (III) (500 mg) was hydrogenated over Adam's catalyst (100 mg) in ethanol (100 ml) containing acetic acid (50 ml). After 24 hr the catalyst was removed by filtration and the solution evaporated to dryness *in vacuo*. The residue crystallized from methanol (414 mg), m.p. 321–324°, and was readily identified as the same *N,O*-diacetyldihydro derivative obtained above.

N-Acetyldihydroaspidodasycarpine (VII)

(*a*) By partial acetylation of dihydroaspidodasycarpine.

To a cooled solution of dihydroaspidodasycarpine (134 mg) in pyridine (5 ml) was added acetic anhydride (25 μl). After 2 hr at 5° and standing at room temperature overnight, the solution was evaporated to dryness *in vacuo* and the white residue redissolved in chloroform. Washing the $CHCl_3$ with dil. HCl afforded some unreacted dihydroaspidodasycarpine (28 mg) and the residue obtained by evaporating the washed (NH_3, water) $CHCl_3$ solution crystallized from acetone (68 mg), m.p. 262–264°, $[\alpha]_D$ −193°. (Found: C, 66·8; H, 7·1; O, 19·2; N, 7·0. $C_{23}H_{30}N_2O_5$ required: C, 66·6; H, 7·3; O, 19·3; N, 6·8 per cent.) U.v. spectrum: λ_{max} 241 (8000) and 298 (2800) nm. I.r. spectrum: 3550 (—OH), 3200 (indoline NH), 1740 (—$COOCH_3$), 1640 (N—$COCH_3$) cm^{-1}. NMR spectrum: 4H multiplet 7·04δ (aromatic); 3H singlet 3·75δ (—$COOCH_3$); 3H singlet 2·15δ (N—$COCH_3$); 3H doublet 0·99δ, J=5 c.p.s. (saturated C-methyl).

(*b*) By hydrogenation of *N*-acetylaspidodasycarpine.

N-Acetylaspidodasycarpine (200 mg) was dissolved in methanol (50 ml) containing HCl (3·5 ml). The solution was shaken under H_2 (50 p.s.i.) with Adam's catalyst (90 mg) for 48 hr and then filtered. Some methanol was removed on a rotary evaporator and the solution then diluted with H_2O (200 ml). $CHCl_3$ extraction gave a quantitative yield of a pale yellow foam which crystallized on contact with acetone, m.p. 262–264° (identical with the material obtained in (*a*) above).

(*c*) By hydrolysis of *N,O*-diacetyldihydroaspidodasycarpine.

N,O-Diacetyldihydroaspidodasycarpine (100 mg) dissolved in dry methanol (10 ml) containing conc. HCl (0·25 ml) was refluxed for 20 hr. The foam (87 mg) obtained by $CHCl_3$ extraction afforded a crystalline product identical with that obtained above.

$\Delta^{1,2}$Dehydro-4,5,17-Triacetyldihydroaspidodasycarpine (IX)

To *N,O*-diacetyldihydroaspidodasycarpine (254 mg) suspended in acetic anhydride (15 ml) was added conc. H_2SO_4 (9 drops) which sufficed to dissolve the suspended material. After 5 hr at room temperature the mixture was poured onto crushed ice and dilute NH_3 and then extracted with $CHCl_3$. The latter was washed with water and dried (Na_2SO_4) and on evaporation yielded a foam (227 mg) extremely soluble in acetone but which crystallized from acetone–ether (148 mg), m.p. 166–168° $[\alpha]_D$ −31°. (Found: C, 64·9; H, 6·8; O, 22·6; N, 5·9; mol. wt. 498·2368 (by mass spectrometry). $C_{27}H_{34}N_2O_7$ required: C, 65·0; H, 6·9; O, 22·5; N, 5·5 per cent; mol. wt. 498·2366.) U.v. spectrum: λ_{max} 222 (24,200) and 261 (6800) nm. I.r. spectrum: 1755 (—$COOCH_3$ and —O—$COCH_3$), 1655 (N—$COCH_3$), 1230 (—O—$COCH_3$) cm^{-1}. NMR spectrum: 4H multiplet 7·55δ (aromatic); 3H singlet 3·77δ (—$COOCH_3$); 3H singlet 2·27δ (N—$COCH_3$); 6H singlet 1·77δ (2O—$COCH_3$); 3H doublet 1·08δ, J=8 c.p.s. (saturated C-methyl).

Sodium Borohydride Reduction of the Indolenine (IX)

The indolenine (102 mg) was reacted with $NaBH_4$ (25 mg) in methanol (10 ml) for 24 hr. A crystalline product, which had separated from the solution, was collected by filtration (15 mg) and shown by the normal methods to be *N,O*-diacetyldihydroaspidodasycarpine, m.p. 325–327° (decomp.). The mother liquors were diluted with water and the product isolated by chloroform extraction. The resulting foam gave a further quantity of the diacetyldihydro derivative (8 mg) and then the more soluble *N*-acetyldihydroaspidodasycarpine (VII) (54 mg) identified in the usual manner.

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