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ALKALOID STUDIES LX[1]. THE STRUCTURES OF TWO NOVEL ASPIDOSPERMA ALKALOIDS, DEOXYASPIDODISPERMINE AND ASPIDODISPERMINE[2].

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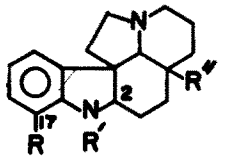
In continuation of our studies on the alkaloids of the genus Aspidosperma, we have so far isolated seven new alkaloids from Aspidosperma dispermum. Two of them, deoxyaspidodispermine and aspidodispermine were obtained in amorphous form by repeated preparative tlc on alumina of the neutral methylene chloride plant extract. The results presented below are most consistent with structures I and II, whose variation from the usual aspidospermine (V) substitution pattern is of considerable biogenetic significance.

Deoxyaspidodispermine (I), $[\alpha]_D$ -20° (MeOH), (picrate monohydrate m.p. 184-186°), has the molecular formula $C_{19}H_{24}N_2O_2$ (mol. wt. 312, by mass spec.). Its UV (λ_{max}^{MeOH} 207, 252, 279, 289 mμ, log ε 4.44, 3.98, 3.50, 3.45), IR ($\nu_{max}^{CHCl_3}$ 3610 cm^{-1} (OH), 1650 (amide)) and NMR spectra (2.26 δ (s, 3H, $NCO\underline{CH}_3$), 6.9-7.4 (m, 3 arom. H), 8.10 (d, J = 10c/s, 1H, C17-H)) are indicative of an N-acetyldihydroindole moiety.

The UV (λ_{max}^{MeOH} 219, 260, 290 mμ, log ε 4.36, 3.88, 3.49), IR ($\nu_{max}^{CHCl_3}$ 3580 cm^{-1} (OH), 1626 (amide)) and NMR spectra (2.30 δ(s, 3H, $NCO\underline{CH}_3$), 6.7-7.2 (m, 3 arom. H)) of aspidodispermine (II), $[\alpha]_D$ +119° (MeOH), $C_{19}H_{24}N_2O_2$ (by high resolution mass spec.) are also compatible with an N-acetyldihydroindole structure. The mass spectrum shows an intense molecular ion peak (m/e 328) and indole peaks at m/e 146 and 160, 16 mass units higher than the corresponding ones (m/e 130 and 144) in the spectrum of I, indicating that the extra hydroxylic group of II lies in the aromatic part of the molecule. This conclusion is supported by the observation of a bathochromic shift in its UV spectrum in alkaline solution ($\lambda_{max}^{NaOH-MeOH}$ 302 mμ, log ε 3.54). Acetylation of II with acetic anhydride in pyridine at room temperature gave an amorphous monoacetate (III) (M^+, 370;

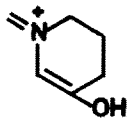
NMR, 2.20 δ (s, 3H, $OCOCH_3$ or $NCOCH_3$), 2.26 (s, 3H, $NCOCH_3$ or $OCOCH_3$) which shows phenolic acetate IR absorption at 1760 cm^{-1} and hydroxyl absorption at 3610 and 3550 cm^{-1}. Methylation of II with dimethyl sulfate yielded an O-methyl derivative (IV) ($C_{20}H_{26}N_2O_3$, m.p. 189-191°, $[\alpha]_D$ -43° (MeOH), IR $\nu_{max}^{CHCl_3}$ 3850 cm^{-1} (OH), 1630 (amide); NMR 2.18 δ(s, 3H, $NCOCH_3$), 3.84 (s, 3H, OCH_3)), with a molecular ion peak at m/e 342 and indole peaks now appearing at m/e 160 and 174, corresponding to the change OH → OCH_3. The location of the phenolic hydroxyl group at C-17 follows from the NMR signal at 10.82 δ in the spectrum of II associated with the hydrogen-bonded phenolic hydroxyl group.

Since I-IV show hydroxyl absorption in their IR spectra as well as an M-18 peak in their mass spectra, the remaining oxygen atom of I and II must be incorporated in a hydroxyl group.

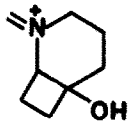


	R	R'	R''		R	R'	R''
I	H	Ac	OH	VI	H	Et	OH
II	OH	Ac	OH	VII	OMe	H	OH
III	OAc	Ac	OH	VIII	H	Ac	OAc
IV	OMe	Ac	OH	IX	OMe	Ac	OAc
V	OMe	Ac	Et	X	OMe	Ac	$OCOCF_3$

Two peaks at m/e 112 (75-100% relat. intensity) and 140 appearing in the mass spectra of I-IV have compositions of $C_6H_{10}NO$ and $C_8H_{14}NO$, respectively (high resolution mass spec.) and are assigned structures a and b, by analogy to the m/e 124 and 152 peaks of aspidospermine (V) (4).



a



b

The NMR spectra of I-IV show that the C-2 hydrogen signal appears as a quartet centered at 4.04, 4.03, 4.10 and 4.53 δ respectively, characteristic of the aspidospermine (V) type alkaloids (5). However, there is no signal due to an ethyl side chain typical of V and its congeners.

On the basis of these spectral data it is reasonable to conclude that I and II possess an aspidospermine skeleton with one hydroxyl group on the piperidine ring but lacking an ethyl side chain.

Reduction of I with $LiAlH_4$ in tetrahydrofuran provided the N-ethyl derivative (VI) with a molecular ion peak at m/e 298 as well as intense peaks at m/e 112 and 140, while the same reduction of IV gave the deacetyl derivative (VII)* as the only isolatable product, whose mass spectrum displayed peaks at m/e 112 and 140 in addition to the molecular ion at m/e 300. These results preclude the existence of a carbinolamine moiety (6). The nature of the hydroxyl group in the aliphatic portion of the molecule is shown to be tertiary by the following observations. Acetylation of I and IV with acetic anhydride in pyridine under reflux gave the corresponding O-acetyl derivatives VIII (amorphous; M^+, 354; IR $\nu_{max}^{CHCl_3}$ 1725 cm^{-1} (OAc), 1645 (NAc); NMR, 1.48 δ(s, 3H, $OCOCH_3$), 2.25 (s, 3H, $NCOCH_3$); 4.06 (q, 1H, C-2H)) and IX (m.p. 169-171°; M^+, 384 $C_{22}H_{28}N_2O_4$ (by high resolution mass spec.); IR $\nu_{max}^{CHCl_3}$ 1724 cm^{-1} (OAc), 1630 (NAc); NMR, 1.48 δ (s, 3H, $OCOCH_3$), 2.21 (s, 3H, $NCOCH_3$), 3.86 (s, 3H, OCH_3), 4.58 (2, 1H, C-2H)). Neither VIII or IX show a signal due to $\diagdown$CHOAc in their NMR spectra. Since hydrolysis of VIII regenerated I, no skeletal change took place during the acetylation. Attempted Moffatt oxidation (7) using trifluoracetic acid led to an amorphous trifluoroacetate (X) (M^+, 408; IR $\nu_{max}^{CHCl_3}$ 1780 cm^{-1} ($OCOCF_3$), 1645 (amide); NMR, 2.25 δ(s, 3H, $NCOCH_3$), 4.07 (q, 1H, C-2H)) but no ketonic substance, thus supporting the existence of a tertiary hydroxyl group.

In the light of this cumulative evidence we formulate tentatively deoxyaspidodispermine and aspidodispermine as I and II, which would be the first aspidospermine-type alkaloids lacking the angular ethyl group. The unusually high field location of the O-acetyl methyl signals of VIII and IX is consistent with a stereochemical arrangement identical to that of aspidospermine (V).

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* Reduction of aspidospermine (V) with $LiAlH_4$ in tetrahydrofuran gave deacetylaspidospermine, m.p. 109-110°, as the major and N-ethyldeacetylaspidospermine as the minor product. However, if ether was substituted for tetrahydrofuran, the product composition was reversed,

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1. For paper LIX see S. H. Brown, C. Djerassi and P. G. Simpson, J. Am. Chem. Soc., 90, 2445 (1968).

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3. Postdoctorate fellow, 1966-1968.

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