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STRUCTURE OF DENDROBINE[1] (Supplement)

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RECENTLY, the structure of dendrobine, an alkaloid first isolated from Dendrobium Nobile by Suzuki et al.[2], has been investigated independently by three groups[1),3),4)] and the formula (I) including the absolute stereostructure has been proposed for this alkaloid. However, the chemical evidences reported so far could not conclusively eliminate two alternative structures (II) or (III)[*1] because that A ring in the molecule would be a six membered one was inferred mainly from the formation of alkyl benzenes by selenium dehydrogenation of dendrobine and dendrobinediol, and from the absorption band of the carbonyl group in IR spectrum which originated from the hydroxyl group forming a lactone ring.

In this communication the authors wish to present the decisive evidence which leads firmly to the formula (I) for dendrobine.

It was reported that all attempts to get the nitrogen free substance by the second stage Hofmann degradation of the methine base (IV) and dihydromethine (V, R=H) had failed[1)]. Then, cis-elimination was applied to a N-oxide derived

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*1 Dr. C. E. Edwards, National Research Council, Canada, also pointed out this ambiguity in his private communication to the authors, and we are grateful for his valuable discussions.

from dihydromethine diacetate. Treatment of dihydromethine with acetic anhydride in pyridine gave the diacetate (VI, R=Ac), mp. 99°, $C_{21}H_{37}NO_4$,[*2] ν_{max}[*3] 1724cm^{-1} (OAc), NMR[*3] τ : 7.98 (3H, singlet, OAc), 7.93 (3H, singlet, OAc), 5.51-6.39 (2H, octet, >CH-C<u>H</u>$_2$-CAc), 4.62-4.88 (1H, multiplet, >C<u>H</u>-CAc). Oxidation of the compound (VI) with monoperphthalic acid in ether furnished a N-oxide (VII), mp. 144-147° (decomp.), $C_{21}H_{37}NO_5 \cdot 4H_2O$ (hygroscopic) which was then submitted to pyrolysis under reduced pressure to give, in excellent yield, an expected des-N compound (VIII), mp. 78°, $C_{19}H_{30}O_4$, ν_{max} 1718 (OAc), 1642cm^{-1} (>C=CH$_2$), δ_{max} 890cm^{-1} (>C=CH$_2$), NMR τ : 5.16-5.39 (2H, multiplet, >CH=CH$_2$).

Osmolation of (VIII) and lead tetraacetate cleavage of the resulting glycol (amorphous), ν_{max} 3356, 3247 (OH), 1724cm^{-1} (OAc) gave norketone diacetate (IX), mp. 109-111°, $C_{18}H_{28}O_5$, ν_{max} 1727cm^{-1} (OAc and ketone group). Formation of a ketone group was proved by its positive Cotton effect in the ORD curve [RD in dioxane, [ϕ]$_{287}$ -2130 (trough), [ϕ]$_{319}$ -558 (peak)] and by the disappearance of olefinic proton signals in the NMR spectrum.

Bromination of the compound (IX) gave bromonorketone diacetate (X), mp. 141-143°, $C_{18}H_{27}O_5Br$, ν_{max} 1721cm^{-1} (OAc and ketone group). That the bromine atom introduced has α configuration was proved by its strong negative Cotton effect in the ORD curve [RD in dioxane, [ϕ]$_{290}$ +1454 (peak), [ϕ]$_{342}$ -4210 (trough)] in contrast to the compound (IX) which gave a weak positive Cotton effect[*4]. The NMR spectrum of (IX) exhibited a multiplet (1H) at 4.70 τ and an octet (2H) at

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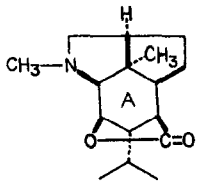
* 2 All compounds given by formula in this communication gave correct elementary analysis.

* 3 All NMR spectra were taken on Varian A-60 machine in $CDCl_3$ with $SiMe_4$ as an internal standard; UV spectra were measured in ethanol and IR spectra on Nujol mull unless otherwise stated.

* 4 Details of the stereochemistry of these compounds are now established by another series of experiments, these will be presented in elswhere.



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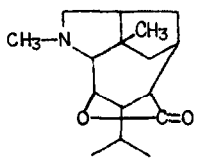

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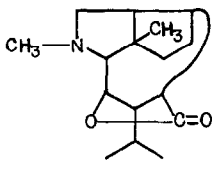

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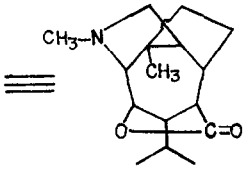

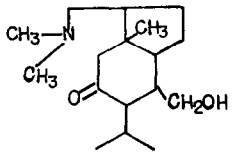

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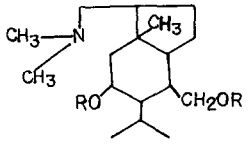
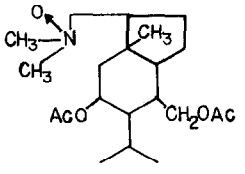


(Ⅴ) R=H

(Ⅵ) R= Ac



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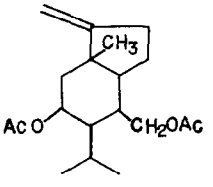

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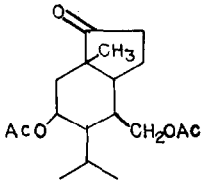

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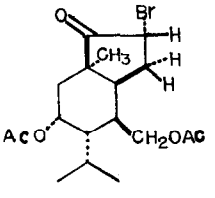

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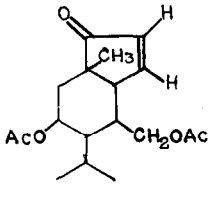

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5.45-6.22 τ, each originated from >C<u>H</u>-OAc and >CH-C<u>H</u>$_2$-OAc respectively, whereas the compound (X) showed one additional proton signal overlapping with the latter, which appeared centered at 5.56 τ in $CDCl_3$ and at 5.88 τ in $CDCl_3$-benzene mixture. Since this signal is undoubtedly attributable to the proton geminal to the bromine atom, the structure (III) for dendrobine is ruled out. Further examination on this signal in two solvent systems suggested that it was probably a quartet resulting from a X component of an ABX-system. Although the analysis is not conclusive since the peak separation of this signal from the octet due to >CH-C<u>H</u>$_2$-OAc is rather poor to distinguish definitely each other, this evidence suffices to assume that there are two protons present adjacent to the proton concerned, thus suggesting the structure (I) for dendrobine. The validity of this assumption was proved as follows.

Dehydrobromination of the compound (X) with lithium chloride-lithium carbonate in dimethylformamide afforded an α,β-unsaturated ketone (XI), mp. 75-78°, $C_{18}H_{26}O_5$, ν_{max} 1730 (OAc), 1701 (conjugated five membered ketone), 1575cm^{-1} (>C=C<), UV λ_{max} 226 mμ (log ε, 3.9). NMR τ: 8.91-9.22 (6H, two doublets, an isopropyl group), 8.73 (3H, singlet, >C-C<u>H</u>$_3$), 7.94 (3H, singlet, OAc), 7.89 (3H, singlet, OAc), 5.32-6.00 (2H, octet, >CH-C<u>H</u>$_2$-OAc), 4.61-4.88 (1H, multiplet, >C<u>H</u>-OAc), 3.83 (1H, quartet, $|J_1|$ =6.0 c.p.s., $|J_2|$ =2.4 c.p.s., olefinic proton), 2.40 (1H, quartet, $|J_1|$ =6.0 c.p.s., $|J_2|$ =1.8 c.p.s., olefinic proton). Hydrogenation of (XI) regenerated the saturated ketone (IX), eliminating the possiblity of skeletal rearrangement during the bromination and dehydrobromination process. Thus, the α,β-unsaturated ketone must be represented by the formula (XI).

From the evidence descrived above the structure of dendrobine was firmly established as the formula (I) including the absolute stereostructure.

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