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STRUCTURE OF SPARSIFLORINE, AN ALKALOID OF CROTON SPARSIFLORUS MORUNG.

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The isolation of a new alkaloid, sparsiflorine[1], as a white amorphous powder, $C_{17}H_{17}O_3N$, m.p. 230-32° (dec.) from the leaves of the shrub, Croton sparsiflorus Morung. (Fam. Euphorbiaceae), was reported earlier by one of the authors. Sparsiflorine formed a number of crystalline salts and was found to contain one methoxyl, three active hydrogens and no methylenedioxy group. The present communication deals with our structural studies on the alkaloid and structure (Ia) is proposed on the basis of the following evidences.

After repeated attempts now it has been possible to obtain sparsiflorine in silky fine needles (from alcohol), m.p. 228° (dec.). The free base suffers ready air oxidation and decomposes on standing for a long time or heating in solution. The mass number (283) confirms the above molecular formula. The alkaloid does not contain any N-methyl or carbonyl group (reported earlier[1]) as indicated from its nuclear magnetic resonance and infrared spectra. The ultraviolet absorption spectrum of sparsiflorine hydrochloride, $[\alpha]_D^{30}$ + 43° (H_2O) λ_{max}^{EtOH} 226 mμ (log ε, 4.54), 266 (4.09), 275 (4.23) and 310 (3.95); strong bathochromic shift of the

maxima in alkaline medium due to the presence of phenolic hydroxyl_7 suggests[2] the alkaloid to be an aporphine derivative containing phenolic group and oxygenated at C-1, C-2 and C-10 positions. The presence of one -NH and two phenolic hydroxyls (thus accounting for all three active hydrogens) was revealed in the following reactions : sparsiflorine readily formed an O,N-diacetate (Ib) (acetic anhydride/pyridine, room temperature), $C_{21}H_{21}O_5N$* (mass number 367), crystallising from chloroform-benzene mixture in rods, m.p. 245°; ν_{max}^{KBr} 1775 and 1258 cm^{-1} (phenolic acetate) and 1640 cm^{-1} (tertiary amide); the other phenolic hydroxyl in sparsiflorine (Ia) (probably C_1-OH which is not readily acetylated due to chelation with C_{11}-H) could also be acetylated (acetic anhydride/pyridine, room temperature, 7 days) to yield N,O,O-triacetyl sparsiflorine (Ic), $C_{23}H_{23}O_6N$ (mass number 409), m.p. 196-97°. With methyl iodide the base slowly formed an N-methylmethiodide derivative (IIa), $C_{19}H_{22}O_3NI$, m.p. 236-38° (dec.); its ultraviolet absorption spectrum λ_{max}^{EtOH} 225 mμ (log ε, 4.57), 267 (4.08), 277 (4.0) and 310 (3.85); bathochromic shift of the maxima in alkaline medium_7 also speaks of aporphine structure oxygenated at 1, 2 and 10 positions[2]. ν_{max}^{KBr} at 3223 cm^{-1} for -OH disappeared in the infrared spectrum of N,O,O-trimethylsparsiflorine methiodide (IIb), $C_{21}H_{28}O_3NI$, m.p. 218° (dec.) obtained from N-methylsparsiflorine methiodide (IIa) by treatment with diazomethane. The former (IIb) was found to be identical with N,O-dimethyltuduranine methiodide (obtained[3] from tuduranine (Id) by the action of dimethyl sulphate and alkali) by direct comparison (I.R.). It was further observed that compound (IIb) upon Hofmann elimination, furnished a basic compound, isolated as its

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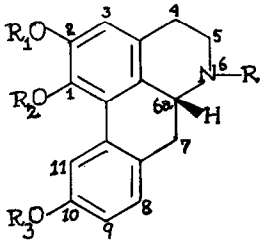
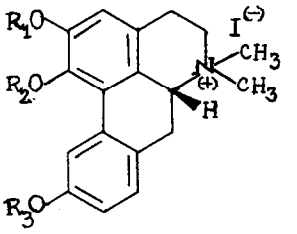
*Satisfactory elemental analyses were obtained for all compounds cited in this communication.

methiodide, m.p. 276-77° (dec.). This methiodide upon further Hofmann degradation gave a nitrogen-free compound, $C_{19}H_{18}O_3$ (mass number 294), m.p. 92°, having ultraviolet spectrum characteristic of a phenanthrene derivative [λ_{max}^{EtOH} 222 mμ (log ε, 4.18), 245 (inflex) (4.20), 263 (4.32), 318 (3.71) and 328 (3.75)]. These two compounds were shown to be identical (m.m.p. and I.R.) with the methine methiodide and 3,4,6-trimethoxy-1-vinyl phenanthrene respectively, obtained by similar Hofmann degradation[3] of N,O-dimethyltuduranine methiodide (IIb). These experiments establish that sparsiflorine possesses 1,2,10-oxygenated noraporphine structure and has the D (or R) configuration at C_{6a} like tuduranine (Id), the acid rearrangement product of stepharine[4].



Ia $R_1 = CH_3$; $R_2=R_3=R=H$
Ib $R_1 = CH_3$; $R_2=H$; $R=R_3=OAc$
Ic $R_1 = CH_3$; $R=R_2=R_3=OAc$
Id $R_1 = R_2 = CH_3$; $R=R_3=H$
Ie $R_1 = R = CH_3$; $R_2=R_3=H$
If $R_2 = CH_3$; $R_1=R_3=R=H$



IIa $R_1=CH_3$; $R_2=R_3=H$
IIb $R_1=R_2=R_3=CH_3$

As regards the relative positions of the two phenolic hydroxyls in sparsiflorine it is definite that they are not vicinal since characteristic catechol colour test[5] with ferric chloride was negative and it could not be condensed with methylene iodide to yield any product containing methylenedioxy group. One of the two hydroxyls must, therefore, be located at C_{10}.

The site of the methoxyl group has been settled to be at C_2 [thereby putting the second hydroxyl at C_1 as in apoglaziovine[6] (Ie)] from a comparative study of the N.M.R. spectra of the base hydrochloride and other aporphine bases of similar structure as illustrated in Table I. The spectrum resembles closely that of tuduranine (showing one more signal for

TABLE I

N.M.R. Spectra of 1,2,10-Oxygenated Aporphines

Group	No. of protons	τ-values			
		Sparsiflorine (Ia) [a]	Tuduranine (Id) [a]	[b][6]	Apoglaziovine (Ie) [c][6]
C_{11}-H	1, doublet[d]	1.96	1.95	2.14	1.92
C_8-H	1, doublet[d]	2.81	2.73	3.06	2.82
C_9-H	1, quartet	3.12[e]	3.00[e]	3.43	3.38
C_3-H	1, singlet	3.22	3.07	3.48	3.23
C_2-OCH_3	3, singlet	6.00	5.99	6.18	6.08
C_1-OCH_3	3, singlet	--	6.17	6.38	--
N-CH_3	3, singlet	--	--	--	7.43

[a]The base hydrochloride measured in CF_3COOH at 60 Mc. using TMS (τ=10) as internal standard. [b]Measured in $CDCl_3$ at 60 Mc. using TMS as internal standard. [c]Measured in D_2O-NaOD at 60 Mc. using benzene as external standard. [d]J_{HH} for C_{11}-H, C_9-H = 2.5 c.p.s. in Ia; for C_8-H, C_9-H = 8.5 c.p.s. in Ia. [e]The high field component of quartet due to C_9-H is buried under the signal of C_3-H.

methoxyl at C_1) run in the same solvent and that of apoglaziovine (showing an extra signal for N-CH_3 which is absent in sparsiflorine) giving allowance for the different solvent and standard used in case of apoglaziorine[6]. The noraphorphine structure thus proposed for sparsiflorine is in excellent accord with the N.M.R. spectrum.

It might be noticed that the aromatic protons at C_3, C_8 and C_9 are appearing at a higher field in sparsiflorine than in case of tuduranine (spectra run in the same solvent, CF_3COOH). This high field shift is apparently caused by the replacement of the methoxyl at C_1 by hydroxyl and the effect is found to be maximum on the proton in the same ring (C_3-H). Thus, the N.M.R. spectral pattern in the aromatic region as found in the case of above alkaloids (Table I) in conjunction with the characteristic U.V. absorption[2] is an important diagnostic tool for 1,2,10-oxygenated aporphines. The highly deshielded[6,7] aromatic proton at C_{11} must appear around 1.96τ region as a doublet (J = 2.5 c.p.s.) in any such aporphine.

Sparsiflorine (Ia) should, therefore, structurally correspond to N-nor-apoglaziovine and is a position isomer of apocrotonosine (If)[8], and N-methyl sparsiflorine methiodide (IIa) should be identical with apoglaziovine methiodide. However, a direct comparison could not be made due to nonavailability of an authentic sample of the latter or glaziovine[6] itself.

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