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DITERPENOID CONSTITUENTS OF *CALLICARPA MACROPHYLLA* VAHL

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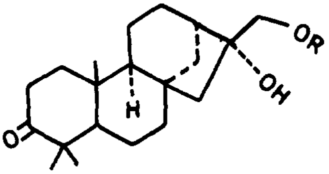
The occurrence of a number of alcohols and ketones[1,2] based on the kaurane skeleton has been reported in recent years. Kaurane structures were also assigned by A.Chatterjee *et al*.[3] to calliterpenone and calliterpenone monoacetate, the diterpenes of *Callicarpa macrophylla*, in a report which appeared while our own work on the constituents of this plant was in progress. Their findings are not in accord with the results obtained by us which lead us to propose structures (I) and (II) for calliterpenone[4] and its acetate, showing them to be derivatives of phyllocladane. We present here evidence in support of these structures:

Calliterpenone (I), $C_{20}H_{32}O_3$, m.p. 151-52° $[\alpha]_D^{19}$ + 30° ($CHCl_3$) showed in its IR spectrum carbonyl and hydroxyl absorption at 1708 and 3300-3400 cm^{-1}. The NMR spectrum (60 Mc, τ values) indicated the presence of three tertiary methyls at 9.00, 8.97, 8.90 and two mutually coupled protons $\underline{CH}_2$-OH at 6.38, 6.16 (J_{gem} = 11 cps). The mass spectrum showed M^+ at 320 followed by peaks at m/e 302 (7%), 289, (100%) and 271 (20%) corresponding to $M^+ - H_2O$, $M^+ - CH_2{=}\dot{O}H$, $M^+ - CH_2{=}\dot{O}H - H_2O$.

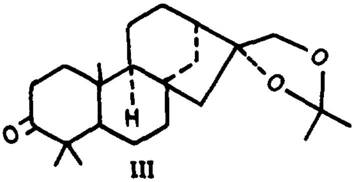
Acetylation afforded a product $C_{22}H_{34}O_4$ (M^+, m/e 362) m.p. 124°, found to be identical with naturally occurring calliterpenone monoacetate (II) which still showed absorption of the tertiary hydroxyl at 3400 cm^{-1} and could be hydrolysed back to the starting material. The NMR spectrum of the acetate differed from that of the alcohol in that the resonance of the $\underline{CH}_2$-OAc protons occurs in it as a sharp singlet at 5.79 which is in contrast to the behaviour of diterpenes having a CH_2-OH group, axial or equatorial, at C-4[5].

Periodate oxidation of (I) afforded a diketone $C_{19}H_{28}O_2$ (M^+, m/e 288) m.p.180° showing carbonyl absorption in the IR spectrum at 1710 and 1750 cm^{-1}, establishing the formation of a 5 membered ketone in the reaction.

These features can be accommodated by the 16,17-diol system in a phyllocladane or kaurane skeleton. To decide between these two alternatives (I) was subjected to Huang Minlon reduction under conditions normally used for this reaction.^{6} TLC of the reaction mixture showed formation of three products which were separated by chromatography over silica gel. The major component of the mixture, m.p.171-72° displayed no carbonyl absorption in its IR spectrum. It formed a monoacetate m.p.135-40° and could be oxidised with periodate to a ketone m.p.98-100°. The melting points agree closely with those reported in literature^{7} for phyllocladane-16,17-diol, its 17-monoacetate and 17-nor-phyllocladane-16-one.



I, R = H
II, R = Ac

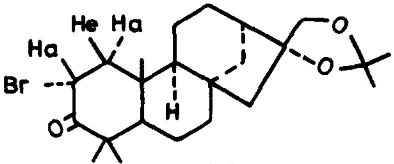


III

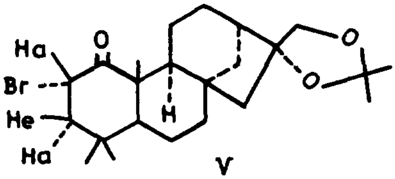
These identifications were very kindly confirmed for us by Prof.R.C.Cambie through mixed m.p. determinations with authentic phyllocladane-16,17-diol and the 17-monoacetate. Similarly the ketone obtained above was found identical (mixed m.p.) with a sample of 17-nor-phyllocladane-16-one also provided by Prof.Cambie. This firmly established the presence of a phyllocladane nucleus in (I) and (II).

The position assigned to the carbonyl function in (I) is based on the results of the following reactions. Treatment of (I) with acetone/HCl gave crystals m.p. 164-65° whose TLC showed that the main product of the reaction was accompanied by traces of a second from which it was freed by chromatography over silica gel. The purified product, m.p.175°, was shown by elemental analysis and spectral data [IR (KBr) 1720 cm^{-1}, NMR 8.63, 8.66, 8.95, 9.0, 9.05 (5 tertiary methyls) and 6.13, 5.95, (ds J = 9 cps $\underline{CH_2}$OR)] to be the acetonide (III).

Bromination of (III) with bromine-ether complex^{8} afforded a crystalline bromide m.p.192° which analysed for $C_{23}H_{35}BrO_3$ (IV). IR (KBr) 1730 cm^{-1} indicated formation of an α-bromoketone. In the NMR spectrum the C$\underline{H}$-Br proton appears as a quartet centered at 4.96 showing diaxial and axial-equatorial couplings (J = 14 and 6 cps respectively) with the adjacent methylene protons. The equatorial proton of the latter gives rise to a quartet centered at 7.4 (J_{gem} = 13 cps ; $J_{e,a}$ = 6 cps). This leaves only two possible formulations, (IV) and (V), for the bromide. The spectrum in the regions discussed above is strikingly similar to that of 2α-bromocholestan-3-one[9] which, along with biogenetic considerations favours (IV).

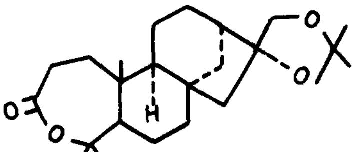


IV



V

As in the structure elucidation of abbeokutone[2] final confirmation for the position of the carbonyl could be obtained by the application of Baeyer Villiger oxidation. Treatment of (III) with perbenzoic acid in chloroform over five days resulted in its partial conversion to the lactone (VI) $C_{23}H_{36}O_4$ m.p. 158-64° [IR (KBr) 1740cm.$^{-1}$ NMR 8.93, 8.66, 8.55 (s, 3H each) 8.63 (s 6H)] showing in effect deshielding of the methyls attached to C-4 by 0.5τ and 0.37τ as required by structure (VI). In abbeokutone, using m-chloroperbenzoic acid, the product of this reaction was an unsaturated acid but the lactone appears to be the only product in this case.



VI

In view of these results it is difficult to understand the structures assigned earlier to calliterpenone and its acetate. Though no explanation can be advanced for the identification of the kaurane skeleton, failure of the H.M.reduction may have been due to the mild conditions, not involving hydrazine and water distillation, reportedly used.

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