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THE STRUCTURE OF PSEUDOANISATIN[1]

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Lane et al.[2] isolated a convulsant principle, anisatin $C_{15}H_{20}O_8$ from the Japanese star anise, Illicium anisatum Linn. (Magnoliaceae, Japanese name is shikimi). The structure (I) was later established by the extensive studies of Hirata et al.[3] together with the isolation and the structure (II) of another toxic component, neoanisatin $C_{15}H_{20}O_7$. We now report the structure (III) of pseudoanisatin, a non-toxic compound reported by Lane et al.

Pseudoanisatin, m.p. 207-208°,[4] $C_{15}H_{22}O_6$ gave a triacetate $C_{21}H_{28}O_9$ (IV) on acetylation and showed the NMR signals (ppm, pyridine) corresponding to three methyl groups [0.89 d (J=7 cps, H_{13}), 1.59 s (H_{11}) and 1.71 s (H_{10})], three methylene groups [2.75 d & 3.22 d (J=16, H_8), 2.70 d & 3.86 d (J=15, H_7) and 3.94 d & 6.00 d (J=13, H_{12})] and a proton attached to an oxygenated carbon [4.74 q (J=5, 1, H_3)]. The presence of a δ-lactone ring was suggested by the IR spectra of III (1710 cm^{-1}) and its barium salt (1545 and 1400 cm^{-1}).

On periodate oxidation III afforded a diketone $C_{15}H_{20}O_6$ (V), which gave a monoacetate (VI) and NMR signals [2.18, 3H, s, $CDCl_3$ and 5.58, 1H, d (J=4), DMSO] due to a methyl ketone and a secondary hydroxyl group. An ether oxygen should be involved in III because the IR spectra of IV and VI showed no hydroxyl group.

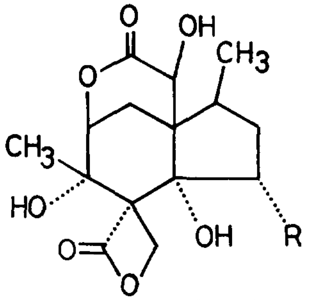
When treated with sodium methoxide in methanol III isomerized to a translactonization product (VII), which gave a monoacetate (VIII) but was unchangable against periodate oxidation. A γ-lactone ring was suggested by the IR spectrum (1770 cm^{-1}) and a partial structure (A) was proposed by using NMDR (double resonance) techniques. The NMR signals of all hydrogens other than three hydroxyl groups in VII were as follows (pyridine): three methyl groups [0.87 d (J=7, H_{13}), 1.44 s (H_{11}) and 1.69 s (H_{10})], four methylene groups [1.90 octet (J=13, 6, 1) & 1.50 q (J=13, 4, H_2), 2.36 d & 2.71 d (J=13, H_7), 2.90 d & 3.21 d (J=18, H_8) and 3.74 d & 4.21 d (J=10, H_{12})] and two protons [4.41 q (J=4, 1, H_3) and ca. 2.8 m (H_1)].

On oxidation with Jones reagent VII gave a five membered ring ketone (IX), the structure of which was deduced by the IR [1780 (γ-lactone) and 1740 cm^{-1} (ketone)] and the NMR [the H_3 proton (4.41 q) of VII was lost] spectra. The protons of VIII showed almost similar chemical shifts (pyridine) to those of the corresponding protons of VII except the H_3 signal(5.52 q) suggesting an acetoxyl group attached to the C_3 of VIII and an ether oxygen attached to the C_{12} atom.

When treated with thionyl chloride in pyridine VII afforded a cyclic sulfite $C_{15}H_{20}O_7S$ (X, calcd.: 344.093, found: 344.096), whereas such a sulfite was not obtained from III on the same treatment. X was not acetylated under usual condition. These facts were compatible with the structure (X). Similarly, VII reacted with phosgene to give a cyclic compound (XI), the IR spectrum of which showed an absorption band [1750 (KBr), 1773 cm^{-1}($CHCl_3$)] corresponding to a six membered ring carbonate besides the γ-lactone [1795 (KBr), 1780 cm^{-1} ($CHCl_3$)]. On reduction with sodium borohydride V gave a diol (XII), which showed another methyl doublet [1.57 d (J=7)] and a new proton signal [5.79 q (J=7)] indicating the acetyl group of V attached to a quaternary carbon atom. Besides an acetyl group $-CH_2COO-$ group was postulated in V from the results of the high resolution mass spectrum which showed fragment ions corresponding to $C_{11}H_{13}O_3$ and $C_{11}H_{12}O_2$ besides $C_{13}H_{17}O_5$, $C_{13}H_{16}O_4$ and $C_{13}H_{14}O_3$.

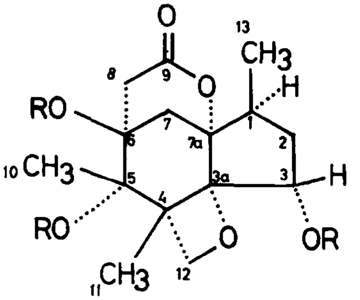
It will be noteworthy that the chemical shift difference (Δ 2.06 ppm) between the two H_{12} protons of III is much greater than that (Δ 0.47) of VII, whereas such difference is not observed in the case of the H_8 protons (III: Δ 0.48 and VII: Δ 0.31). This fact suggests that one of the H_{12} protons are near the lactone carbonyl group in the molecule of III receiving more deshielding effect than the other.

Nuclear Overhauser effects (NOE) When irradiated at the C_{11} methyl protons of V an increase (10 %) was found in the H_3 proton signal and the irradiation of



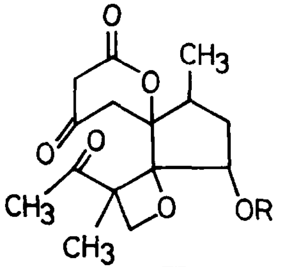
I R=OH

II R=H



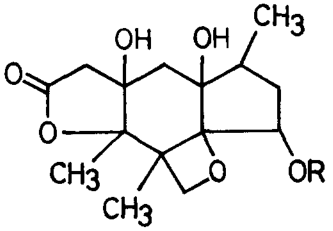
III R= H

IV R = Ac



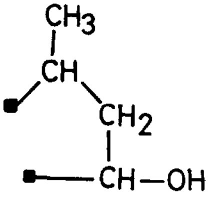
V R=H

VI R =Ac

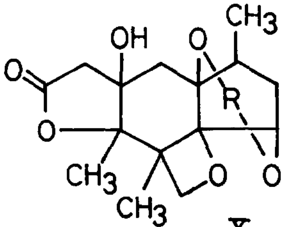


VII R=H

VIII R=Ac

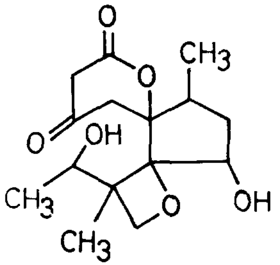


[A]

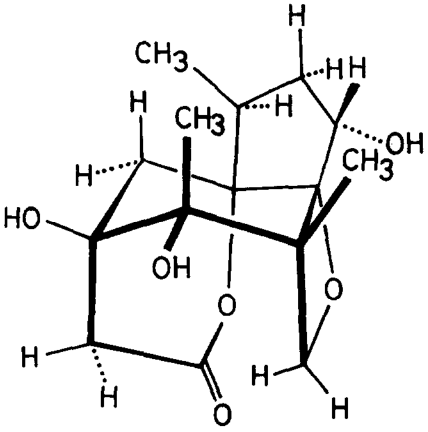


X R=SO

XI R=CO



XII



XIII

C_{13} methyl protons of the benzoate of VII caused 11 % increase of one of the H_7 proton signals. To sum up these findings the structure (III) was proposed as the most relevant structure for pseudoanisatin having a similar carbon skeleton to anisatin (I). The relative configuration of C_1, C_3, C_{3a}, C_4, C_5, C_6 and C_{7a} were determined on the basis of the NOE results, the evidence of translactonization and the formation of cyclic compounds (X and XI).

Absolute configuration The molecular rotation difference[5] between V (+285°) and its 3-monobenzoate (+370°) was observed as +85° indicating S-configuration at the C_3 atom. Consequently, the structure of pseudoanisatin is represented by the formula III or XIII including the absolute configuration. The negative sign of the ORD and CD curves of VII also supported this formula when the lactone sector rule of Klyne et al.[6] was applied.

References

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