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STRUCTURE OF MUKAADIAL, A MOLLUSCICIDE FROM THE WARBURGIA PLANTS

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The structure of a new sesquiterpene dialdehyde, mukaadial, isolated from Warburgia stuhlmannii and W. ugandensis and possessing molluscicidal property, has been established by means of spectroscopic and chemical data.

The barks of the East African medicinal trees, Warburgia stuhlmannii and W. ugandensis (Canellaceae) have recently yielded a series of sesquiterpene dialdehyde as insect antifeedant against the African armyworm Spodoptera exempta[1,2] with a leaf disk assay.[3] These insect antifeedants have been shown to possess a wide spectrum of biological activity including molluscicidal property.[4] Hence, these sesquiterpene dialdehydes are currently receiving considerable attention as potential molluscicides for the control of schistosomiasis.[5] However, the isolation of the Warburgia extracts was not guided by a molluscicide assay. For this reason further purification of the hexane extract of W. stuhlmannii (Mukaa in Swahili) has been carried out. Molluscicidal activity was monitored as described previously.[4] This has now led to the isolation of an additional new molluscicidal sesquiterpene dialdehyde, mukaadial (1),[6] which is closely related to warburganal (2).[1] The molluscicidal activity of mukaadial (LD_{50}=20 ppm within 24 h against the South American snail Biomphalaria glabratus) is about one tenth of warburganal (LD_{50}=2 ppm within 24 h).

The structure of mukaadial, mp 173°C (sublime) is based on the following evidence: $C_{15}H_{22}O_4$, (CI-MS with iso-butane and elemental analysis): λ_{max}(EtOH) 210 and 235(sh) nm (ε 4300 and 2000); ν_{max}($CHCl_3$) 3550(OH), 3450(intramol. H-bonded OH), 2850(CHO), 1720(CHO), 1685 and 1650 cm^{-1}(enal). The ^{13}C NMR($CDCl_3$) spectrum showed the presence of 3 CH_3, 3 CH_2, 3 quaternary C, 2 olefinic C, and 2 carbonyl C atoms.[7] Pertinent 400 MHz ^1H NMR($CDCl_3$) data are; δ 9.70(1H, s, 9-CHO), 9.47 (1H, s, 8-CHO), 7.04(1H, d, J=2 Hz, 7-H), 4.57(1H, dd, J=10, 2 Hz, 6-H), 4.1(OH), 1.90(1H, d, J=10 Hz, 5-H), 1.13(s, CH_3), 1.16(s, CH_3), 1.20 ppm(s, CH_3). The ^1H NMR spectrum is closely similar to that of warburganal, except for the additional low field signal at δ 4.57 ppm due to a new hydroxy group at C-6. The stereochemistry of this new hydroxy group was established as equatrial because the large coupling (J=10 Hz) was observed between the 6-H and 5-H.

The stereochemistry at C-9 was confirmed by conversion of mukaadial into

6-oxo-lactone (4). Mukaadial was treated with 1 mol dm^{-3} NaOH aq soln. at room temp to yield the lactone (3) $C_{15}H_{22}O_4$, M 266 through intramolecular Cannizzaro reaction. The ^1H NMR($CDCl_3$) of this lactone (3) shows the AB q at δ 4.38 ppm (J=11 Hz, 11-H) instead of dialdehyde groups. Jones' oxidation of 3 gave the 6-oxo-lactone (4). The treatment of ugandensidial (cinnamodial) (5) by the similar manner gave 6-oxo-lactone (4) which was identical in all respects with the aforementioned 6-oxo-lactone (4).

The absolute configuration of mukaadial was established by the CD(EtOH), Δ_ε(335) -0.4 and Δ_ε(291) -0.7 which was almost identical with those of warburganal. Since the absolute configuration of warburganal was confirmed by the synthesis of the optically active warburganal from l-abietic acid,[8] the absolute configuration of mukaadial is that shown in 1. This also established the absolute configuration of ugandensidial.

The structure-activity relationships among the sesquiterpene dialdehydes seem to be of interest since polygodial,[1] warburganal and muzigadial[2] exhibit potent antimicrobial[9,10] and anticomplemental[11] activity -- mukaadial dose not show these properties.

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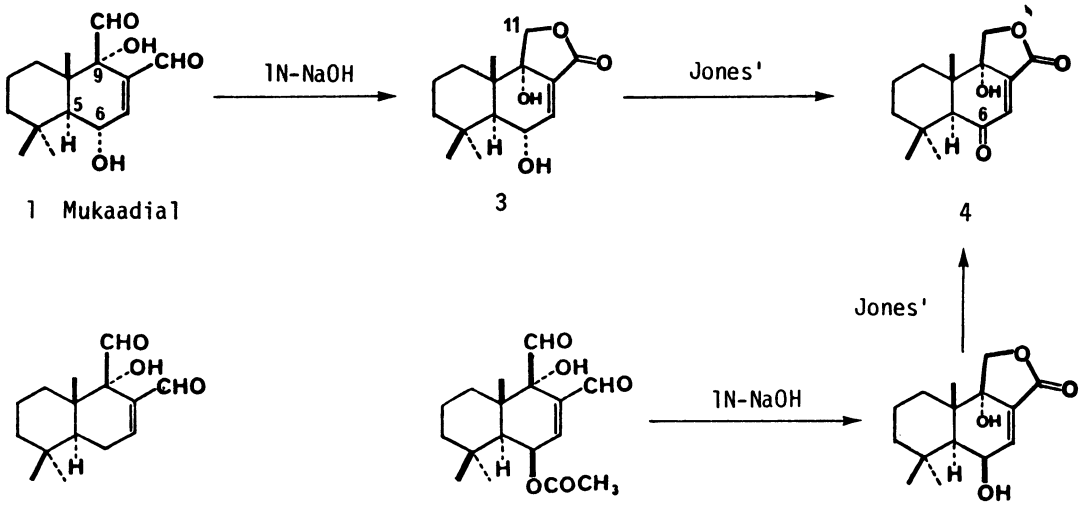

1 Mukaadial 3 4

2 Warburganal 5 Ugandensidial (Cinnamodial)

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