Tetrahedron Letters No. 52, pp 4553 - 4556, 1977. Pergamon Press. Printed in Great Britain.

MUZIGADIAL AND WARBURGANAL, POTENT ANTIFUNGAL ANTIYEAST, AND AFRICAN ARMY WORM ANTIFEEDANT AGENTS

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(Received in USA 17 October 1977; received in UK for publication 31 October 1977)

We have previously reported the structure of warburganal 1, a potent antifeedant against the army worms Spodoptera littoralis and S. exempta[1]. The antifeedant activity of warburganal is much stronger than the related compounds polygodial[2] (structure 1 with no 9α-OH) and ugandensidial[3] (structure 1 with additional 6β-OAc). In the following, we report the structure of another equally potent antifeedant muzigadial 2, which has a rearranged drimedane skeleton[4].

The bark (500 g) of the East African tree Warburgia ugandensis ("Muziga" in Swahili), collected in Nairobi, Kenya, was extracted with hexane, and the solvent removed. The residue was chromatographed on silica gel using hexane/ether as the eluant, and the elute was submitted to high performance liquid chromatography (hplc) using a μ-Porasil column (4 mm x 30 cm) with ether-hexane (20:80 v/v) to give 50 mg of warburganal 1 and 48 mg of muzigadial 2.

The structure of muzigadial, m.p. 122-124°C is based on the following evidence: $C_{15}H_{22}O_3$: chemical ionization ms with iso-butane, 249 ($M^+ + 1$); uv(MeOH) 223 nm (ε 5,200); ir($CHCl_3$) 3480 (intramolecular H-bonded OH), 1682 and 1638 (enal, H-bonded), 2818 and 1719 (aldehyde), 1642 (sh.) and 892 cm^{-1} (exocyclic methylene) (see partial structure 3). The cmr data summarized in 4 showed the presence of two CH_3, three CH_2, two CH, two quarternary, four olefinic, and two carbonyl carbons. The pmr data, shown in 5, clarified the presence of blocks A and B depicted by the dotted areas in 2; a 10% NOE was induced on one of the exocyclic-olefinic protons upon irradiation of the 3-CH_3, thus indicating the equatorial

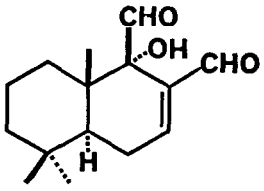
nature of the methyl group. Blocks A and B can be linked as shown because of the presence of the enal. Finally, decoupling experiments showed that the 3α-H had a neighboring CH_2, this, together with the absence of an isolated CH_2 (AB quartet), led to structure 2. The ring juncture is as depicted in 5 because, upon addition of $Eu(dpm)_3$, the 5α-H underwent a large shift in contrast to the 10β-CH_3 which did not shift. The cd spectrum of muzigadial 2 in MeOH, exhibiting two negative Cotton effects at 228 nm (Δε-0.76, π π* of enal) and 285 nm (Δε-2.06, overlapping n π* bands of the two aldehydes), was very similar to that of warburganal 1[1], 228 nm (Δε-1.54) and 285 nm (Δε-2.30) and hence the absolute configurations are identical.

According to electrophysiological tests employing S. exempta sensilla[5], the antifeedant activity of warburganal and muzigadial are comparable. These two compounds, together with azadirachtin[6], belong to the strongest group of antifeedants against the African army worm found so far. In addition, warburganal and muzigadial exhibit very potent antifungal, antiyeast and plant-growth regulatory activities[7]. For example, some minimum inhibitory concentrations of warburganal are as follows[8]: Candida albicans (2.5 μg/disk), Saccharomyces postorianus (2.0 μg/disk), and Trichophyton mentagrophytes (2.0 μg/disk).

Further studies into the significant biological activities of these two compounds are presently underway.[9]

The studies were supported by NIH grant AI 10187 and the International Centre of Insect Physiology and Ecology, Nairobi, Kenya.

One of the authors (I. Kubo) extends his gratitude to the Japan Society for the Promotion of Science for financial support.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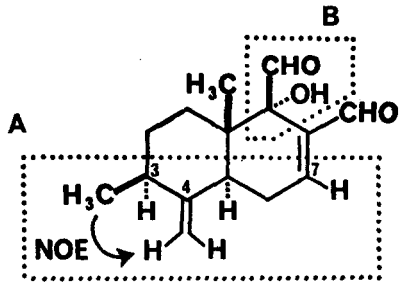
CHO
H

1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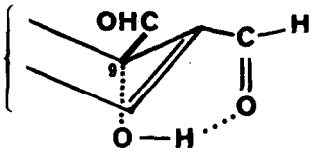
OH
CHO
3
4
7
H3C
H
H
H
NOE
H
H

2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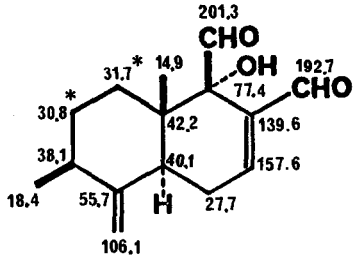
C
H
9
O
O
H

3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31.7
*
14.9
OH
192.7
77.4
CHO
*
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42.2
139.6
38.1
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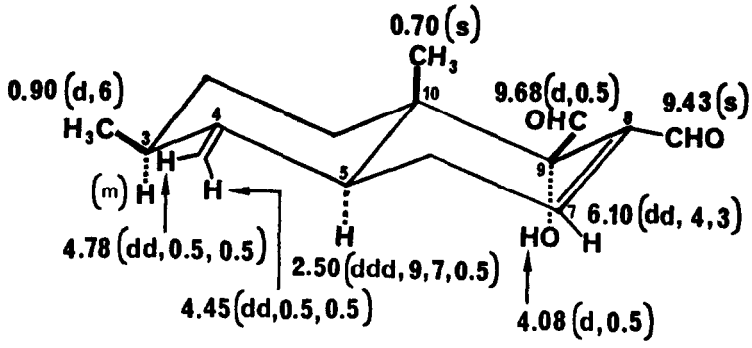
157.6
18.4
55.7
H
27.7
106.1

4


0.70 (s)
CH3
0.90 (d, 6)
H3C
10
9.68 (d, 0.5)
OHC
9.43 (s)
CHO
3
4
5
9
8
7
H
(m) H
H
6.10 (dd, 4, 3)
4.78 (dd, 0.5, 0.5)
H
2.50 (ddd, 9, 7, 0.5)
HO
H
4.45 (dd, 0.5, 0.5)
4.08 (d, 0.5)

5

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7. Details of various biological activities will be published elsewhere.

8. We are grateful to Dr. M. Taniguchi, Osaka City University, for this data.

9. Dr. F. S. El-Feraly, University of Mississippi, has isolated and characterized a compound identical (by direct comparison) with muzigadial: private communication.