Tetrahedron Letters,Vol.26,No.43,pp 5343-5344,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

MELLEDONAL AND MELLEDONOL, SESQUITERPENE ESTERS FROM *ARMILLARIA MELLEA*

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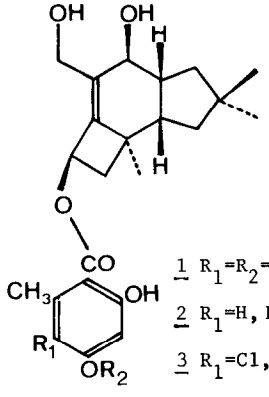
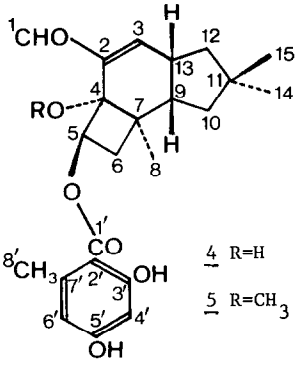
Summary: Isolation of two new sesquiterpene aryl esters melledonal (6) and melledonol (8) from culture broth extract of *Armillaria mellea* are reported. Their structures were deduced from spectral and chemical data.

The pathogenic basidiomycete *Armillaria mellea* produces a range of sesquiterpenoid aryl esters with the protoilludane skeleton[1-5] including armillyl orsellinate (1)[1], armillyl evernin-ate (2)[2], arnamiol (3)[2], melleolide (4)[3,4] and 4-O-methylmelleolide (5)[3]. In the course of continuing studies on the fungus in search of additional biologically active constituents, we have isolated from the culture broth two new sesquiterpenoid aryl esters for which the names melle-donal (6) and melledonol (8) are proposed.

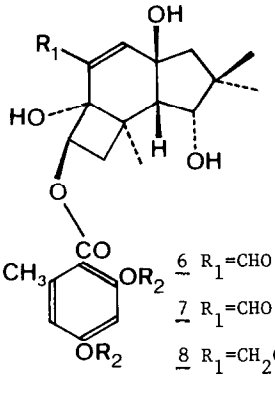
The molecular formula $C_{23}H_{28}O_8$ of melledonal (6) (m.p. 136-137°; $[\alpha]_D^{21}$ + 195.3° (c, 0.1, MeOH) was established by elemental analysis and by FAB mass spectrometry ($|MH|^+$ m/z 433). The i.r. spectrum (KBr) showed two carbonyl bands at 1678 (unsatd. aldehyde) and 1638 cm^{-1} (chelated ester) and hydroxyl bands at 3400 cm^{-1}. The eims displayed $|M-H_2O|^+$ at m/z 414 and the base peak at m/z 151 $[C_6H_2(OH)_2MeCO]^+$ indicated[1] the presence of an orsellinate ester. The 270 MHz ^1H n.m.r. spectrum ($CDCl_3$-CD_3OD) showed signals due to three aliphatic and one aromatic methyl groups (δ1.00, 1.17, 1.40 and 2.28) and an α,β unsaturated aldehyde group (δ9.49,s(CHO); 6.86,s(vinylic)). Decoupling experiments allowed the assignments of the other protons: δ1.88, 1.94 (2H,2xd,J=13.9,H-12α,12β), 2.05(1H,dd,J=11.4,8.3,H-6α), 2.15(1H,dd,J=11.4,9.1,H-6β), 2.51(1H,d,J=3.3,H-9), 3.72(1H,d,J=3.3, H-10), 5.72(1H,dd,J=9.1,8.3,H-5), 6.15(1H,d,J=2.4,H-4'), 6.21(1H,d,J=2.4,H-6').



1 R_1=R_2=H
2 R_1=H, R_2=CH_3
3 R_1=Cl, R_2=CH_3



4 R=H
5 R=CH_3



6 R_1=CHO, R_2=H
7 R_1=CHO, R_2=Ac
8 R_1=CH_2OH, R_2=H

The appearance of H-3 as a singlet and H-12α,β as doublets, necessitates a hydroxyl substituent at position 13. The small coupling constant (3.3Hz) between H-9 and H-10 indicates that these protons are *cis*. The ^{13}C n.m.r. spectrum (CD_3CN) was consistent with the proposed structure (6), the relevant signals being at δ195.2(d,C-1), 152.2(d,C-3), 134.5(s,C-2), 81.2(d, C-10),72.9(d,C-5), 54.2(d,C-9), 76.0(s,C-4), 74.5(s,C-13), 54.2(d,C-9), 53.8(t,C-12) and 31.2 (t,C-6). The eight resonances of the orsellinate group compared well with those of methyl orsellinate[2].

Melledonal (6) formed a diacetate (Ac_2O/pyr; 0°,3hr) (7) (oil; $[\alpha]_D^{21}$ + 20.9°(c,0.2,$CHCl_3$); i.r.($CHCl_3$) 3400, 1750, 1730 and 1680 cm^{-1}). The 270MHz ^1H n.m.r. spectrum of 7 resembled that of 6 except for signals due to two additional methyl groups (δ2.23,2.27,ArOCOMe) and the downfield shifted aromatic protons (δ6.75,J=2.2Hz,H-6'; δ6.85,J=2.2Hz,H-4'). The ^{13}C spectrum ($CDCl_3$) supported the proposed structure 3',5'-O-diacetylmelledonal (7).

The relative configuration of 7 and hence of melledonal (6), was established by NOE experiments (Fig. 2). Large NOE enhancements on CH_3-14 and H-12α (with no NOE on H-12β) upon irradiation of H-3, revealed the *cis* hydrindane skeleton. The cyclobutane ring is *cis* to H-9, corroborated by the large NOE between H-6β and H-9 and the lack of an NOE between CH_3-8 and H-9.

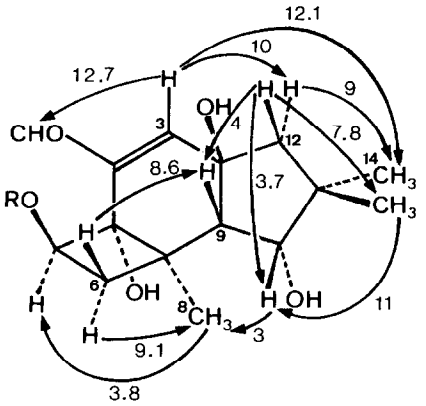


Fig. 2: NOE(→,%) values of 7. R = $-COC_6H_2(OAc)_2Me$.

Melledonol (8) (m.p. 216-218°; $[\alpha]_D^{21}$+44.6°(c,0.1,MeOH) had a molecular formula of $C_{23}H_{30}O_8$, established by elemental analysis and FAB mass spectrometry ($|MH|^+$ m/z 435). The i.r. spectrum (KBr) with hydroxyl (3400 cm^{-1}) and ester (1640 cm^{-1}) bands and the eims $|M-H_2O|^+$ at m/z 416 and base peak at m/z 151 suggested a dihydro derivative of melledonal (6). The 270MHz ^1H n.m.r. spectrum ($CDCl_3$-CD_3OD) was very similar to that of 6. An allylic CH_2OH group (δ3.96, 4.27, 2xd,J=4.1,H-1β,H-1α) and an upfield shifted vinylic proton (δ6.02,s,H-3) and decoupling experiments indicated an alcohol derivative of the aldehyde (6). The ^{13}C n.m.r. spectrum (CD_3OD) was consistent with the proposed structure (8) and has a marked resemblance to that of 6 except for a CH_2OH (δ62.6,t) and the alkene (δ135.7,s; 132.9,d; C-2,C-3) resonances. The other resonances compared well with those of 6. Reduction of 6 with $NaBH_4$ produced 8.

Acknowledgement: We thank Mr. P. Varenne for the FAB measurements.

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(Received in UK 23 August 1985)