GIBBANE METABOLITES FROM ENT-KAURA-2,16-DIEN-19-OL

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We have previously reported[1] that ent-Kaura-2,16-dien-19-ol(1) is converted to the gibbane (6) by Gibberella fujikuroi. Examination of the less polar methyl esters of the acidic metabolites derived from 1 or its hemisuccinate ester (2) has given a series of gibbanes, four of which are described here.

Of these the dimethyl ester (7), M^+ 358.2143($C_{22}H_{30}O_4$) had m.s. peaks at m/e 358, 326, 298 (base peak), 266, 239, 238 and i.r. max (CS_2) at 3050, 875cm^{-1}($C=CH_2$), 3010cm^{-1}(CH=CH), 1725cm^{-1}(C=O). The n.m.r. spectrum (CDCl$_3$, τ) showed singlets at 9.27, 8.72, 6.33, 6.27(2 tert. Me and 2CO$_2$Me resp), an AB quartet, characteristic of gibberellins[2] (7.78, 6.65; J=12.5Hz), due to the C-5 and C-6 protons and two proton signals at 5.12 and 4.35 ($C=CH_2$ and CH=CH resp).

Also isolated, was the related epoxy-dimethyl ester (13), M^+ 374.2099 ($C_{22}H_{30}O_5$); I.r. max (CS_2) at 3060, 875 cm^{-1} ($C=CH_2$) and 1730cm^{-1} (C=O). The n.m.r. spectrum (CDCl$_3$) showed singlets at 9.25, 8.64, 6.28 and 6.26 (2 tert Me and 2CO$_2$Me resp); an AB quartet at 7.78 and 6.68 (J=12.5Hz, C-5 and C-6 protons); a broad singlet at 5.13 ($C=CH_2$) and a complex multiplet centred at 6.54 (C-2 and C-3 protons).

Support for its structure came from the conversion of 13 into the known gibbane triol (10) by lithium aluminium hydride reduction. The triol (10), m.p. 185-186°C (lit[3] 182-184°C), thus obtained had i.r. spectrum identical with that of a sample derived from GA14 dimethyl ester[3] (11). The n.m.r. spectrum (d-5 pyridine) was consistent with the given structure showing singlets at 8.92 and 8.21 (2 tert Me), a doublet at 6.02 (J=8Hz, C-7⟩CH-CH$_2$OH); an AB quartet at 5.78 and 6.15 (J=11Hz, C-19 -C̦-CH$_2$OH) and two broad singlets at 5.00 and 5.17 ($C=CH_2$).

Metabolites 7 and 13 were interrelated by treating the dimethyl ester (7) with excess m-chlorperbenzoic acid, yielding the diepoxide (14). Selective reduction of the exocyclic epoxide was achieved by treating 14 with excess KSeCN[4], affording the epoxy-dimethyl ester (13).

The other two metabolites isolated were the aldehyde dimethyl ester (9) and the related trimethyl ester (8). The aldehyde-dimethyl ester (9) , M^+ 372.1947 ($C_{22}H_{28}O_5$) had i.r. max (CS_2) 3050, 880 cm^{-1} ($C=CH_2$), 3010 cm^{-1} ($CH=CH$), 2785 cm^{-1} (aldehyde function) and 1730 cm^{-1} (ester C=O). The presence of the aldehyde was further suggested by the loss of 28 mass-units from M^+ and from M-60 in the mass spectrum. The n.m.r. spectrum ($CDCl_3$) confirmed the presence of a tertiary aldehyde by showing a one proton singlet at 0.42. Other resonances occurred at 8.68, 6.35 and 6.23 (tert Me and 2 CO_2Me resp), at 8.10 ($C=CH_2$) and at 4.33 (multiplet, $CH=CH$). An AB quartet at 7.55 and 6.18 (J=13Hz) is typical of the C-5 and C-6 protons of C-20 gibberellins, where the C-6 proton is deshielded by carbonyl functionalities at C-19 and C-20[5,6]. The above data suggest two structural possibilities (9 and 16) for the aldehyde diester, the preferred assignment (9) being based on a comparison of the C-4 methyl chemical shift with the kaurene derivatives 3 and 4 (see table).

The trimethyl ester (8) m.p. and mixed m.p. 129.5-131°C (lit[5] 133-134.5°C) was found to be identical (m.s., n.m.r., i.r., g.l.c., and t.l.c. in two solvent systems) with the trimethyl ester obtained from GA13, by tosylation of GA13 trimethyl ester (12) and elimination of toluene sulphonic acid in refluxing collidine[5].

The aldehyde-dimethyl ester (9) was related to the trimethyl ester (8) by lithium aluminium hydride reduction of eachto the same triol (15), m.p. 146-147.5°C. I.r. (mull) showed 3350 and 1025 cm^{-1} (OH), 3060, 1650 and 875 cm^{-1} ($C=CH_2$) and 3050 cm^{-1} ($CH=CH$). The n.m.r. spectrum (d-5 pyridine) showed a singlet at 8.51 (tert Me); a singlet at 5.72 (C-20 $-\overset{|}{C}-CH_2OH$) a doublet at 5.92 (J=8Hz, C-7 $>CH-CH_2OH$); an AB quartet at 5.65 and 6.07 (T=11Hz, C- 19 $-\overset{|}{\underset{|}{C}}-CH_2OH$); two broad singlets at 5.00 and 5.17 ($C=CH_2$) and a multiplet centred at 4.22 ($CH=CH$).

The above metabolites were recognized as such since they showed the required specific activity when derived from 17-$^3H_2$-labelled 1 or 2.
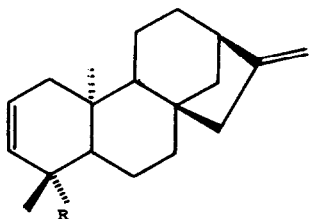
<u>Table</u>

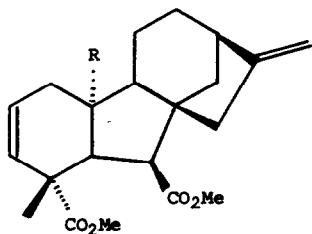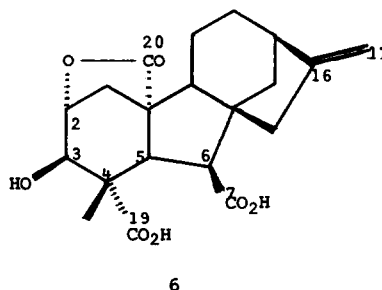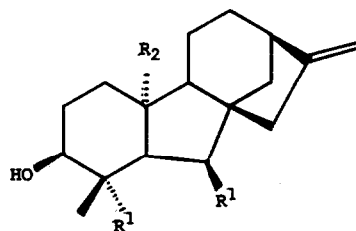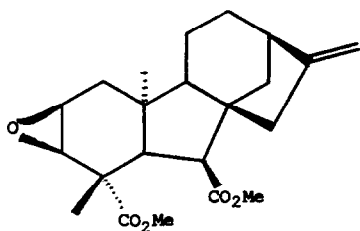|	C-4 Me (τ)
Aldehyde (3)[7]	9.01
Methyl ester (4)*	8.72
Dimethyl ester (7)	8.72
Aldehyde-dimethyl ester (9)	8.68
Trimethyl ester (8)	8.68

*Prepared from <u>ent</u>-Kaura-2,16-dien-19-oic acid (5)[7]

1 R = CH$_2$OH   4 R = CO$_2$Me
2   = CH$_2$OCO(CH$_2$)$_2$CO$_2$H   5   = CO$_2$H
3   = CHO

6

7 R = CH$_3$
8   = CO$_2$Me
9   = CHO

10 R$_1$ = CH$_2$OH, R$_2$= Me
11 R$_1$ = CO$_2$Me, R$_2$= Me
12 R$_1$ = R$_2$ = CO$_2$Me

13
14   16,17 epoxide
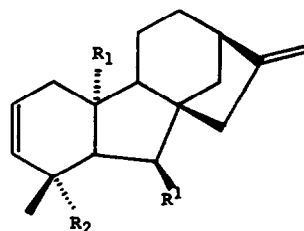
15 R$_1$ = R$_2$ = CH$_2$OH
16 R$_1$ = CO$_2$Me , R$_2$= CHO

References:-

1. I.F. Cook, P.R. Jefferies and J.R. Knox, Tetrahedron Letters, 2157 (1971).

2. M. Sheppard, J. Chem. Soc., 3040 (1960).

3. B.E. Cross, K. Norton and (in part) J.C. Stewart, J. Chem. Soc., 1054 (1968).

4. P.R. Jefferies and W. Schockoff, unpublished results.

5. R.H.B. Galt, J. Chem. Soc., 3143 (1965).

6. R.J. Pryce and J. MacMillan, Tetrahedron Letters, 4173 (1967).

7. E.L. Ghisalberti, P.R. Jefferies and E.J. Middleton, Aust. J. Chem.,22, 455 (1969).