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GMELOFURAN - AN UNUSUAL SESQUITERPENE

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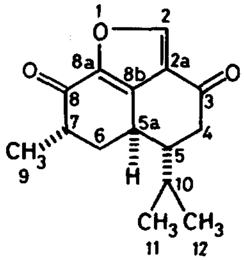
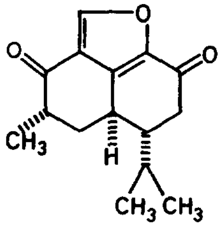
The heartwood of <u>Gmelina arborea</u> has already yielded several unusual lignans[1]. We now report the characterisation of a unique cadinane type furanosesquiterpenoid, gmelofuran (1), isolated from the roots of this plant[2]. Gmelofuran, (5-isopropyl-7-methyl-5,5a,6,7-tetrahydro-3H,8H-naphtho[1,8-bc]furan-3,8(4H)-dione) was isolated as needles m.p. 122-123°, $[\alpha]_D^{25}-900^{\circ}$ $(CHCl_3)$ by chromatography of the petroleum ether extract of the roots of <u>G.arborea</u>. The compound had the empirical formula, $C_{15}H_{18}O_3$(C, 73.37, H, 7.27%, $M^{\cdot +}$ 246.1256; required is C, 73.23, H, 7.38%, $M^{\cdot +}$ 246.12559). It gave a mono-DNP derivative ($M^{\cdot +}$ 427, N, 14.06%) reduced Tollens reagent and readily decolourised bromine water and alkaline permanganate. It had λ_{max}(EtOH) 230.5 (19,010) and 265.5nm (15,655) which underwent a profound, reversible change on addition of aq. NaOH to give peaks at 231(4,474), 260(5,220) and 417nm (32,615). The latter peak suggests the formation of a highly conjugated enolate or phenolate anion. The i.r. spectrum had ν_{max} 1675 and 1700 cm^{-1} showing carbonyl groups to be present, whilst a peak at 3110 cm^{-1} could be assigned to an aromatic type proton. No bonds due to hydroxy groups were evidenced.

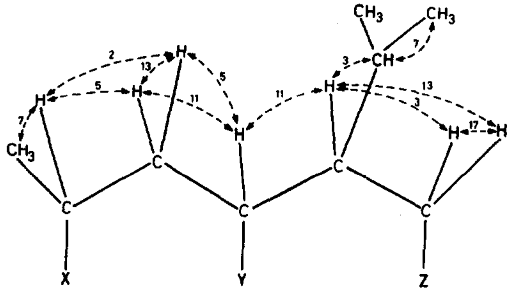


(1)



(2)

The 100MHz ^1H n.m.r. spectrum showed three $\underline{CH_3}$-CH doublets at δ0.95, 1.01 and 1.36 and a singlet at δ8.12(1H). The region between δ8.12 and 3.2 was clear, showing that there are no protons attached to simple alkene units, nor can there be any protons α to oxygen atoms. The remaining eight protons gave signals between δ3.2 and 1.8 and neither the multiplicity of the signals nor their relationships could be deduced from the 100MHz spectrum. However in the 300MHz spectrum[3] six of these signals appear as well resolved systems whilst two protons gave overlapping signals (Table 1). Extensive decoupling experiments allowed all the coupling constants to be uncovered, those for the overlapping signals at δ1.9 being assigned by reciprocal decoupling with systems in which the multiplicity was clear. Although the overlap of two signals allowed for some slight ambiguity, system A could be defined for seventeen of the eighteen protons of gmelofuran, leaving only the low field singlet at δ8.12 to be accounted for.



X, Y, Z = Carbon atoms bearing no protons

System A

Table 1

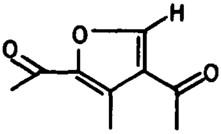
^{1}H n.m.r.* of gmelofuran

δ	mult.	J(Hz)	Integral	Proton assignment
0.95	d	7	3H	11
1.01	d	7	3H	12
1.36	d	7	3H	9
1.9	m	-	2H	6(ax) and 5(ax)
2.05	d.septet	3,7	1H	10
2.21	d.d.d.	2,5,13	1H	6(eq)
2.36	d.d.	13,17	1H	4(ax)
2.62	d.d.	3,17	1H	4(eq)
2.82	d.d.q.	2,5,7	1H	7(eq)
3.06	d.d.d.	5,11,11	1H	5a(ax)
8.12	s	-	1H	2

*Spectrum run at 300MHz in $CDCl_3$, TMS as internal standard

The chemical shifts indicate that H-7 and H-5a are adjacent to unsaturated systems and this also holds true for the signal at δ2.62 and hence for both protons at C-4.

The ^{13}C n.m.r. spectrum is shown in Table 2, all assignments being in accord with the off-resonance spectrum, T_1 measurements and with comparisons with known compounds[4,5]. Two of the three oxygen atoms are present in ketone groups, and the presence of esters and lactones is excluded. The remaining oxygen atom is not present as a hydroxy or methoxy group leaving only ethers to be considered. For a benzene ring to be present it would have to be penta-substituted and this is impossible in view of system A, the two carbonyl groups and the lack of aromatic C-Me or $C-CH_2$- groups. As only one proton at low field can be associated with the remaining systems, epoxide, oxetane and hydrofurans are excluded, leaving only a tri-substituted furan for consideration. The chemical shift of the proton is very close to that found for H-2 of a furan doubly substituted with carbonyl groupings. Given the requirement of system A, the remaining carbon atoms together with the carbonyl groups and the last oxygen atom and proton can only be accommodated in system B, which fits exactly the above considerations, and also the ^{13}C n.m.r. data.



System B

Systems (A) and (B) can be linked to give either (1) or (2) but on biogenetic grounds structure (1) with a cadinane skeleton would be favoured. To our knowledge this structure represents a unique cadinane sesquiterpenoid and indeed the furan ring linking peri-positions is a hitherto unknown feature of sesquiterpene chemistry. Given structure (1) the coupling constants allow the signals in the ^{1}H n.m.r. to be assigned as in Table 1. One unusual feature that results is the presence of a C-7 axial-methyl group.

Table 2

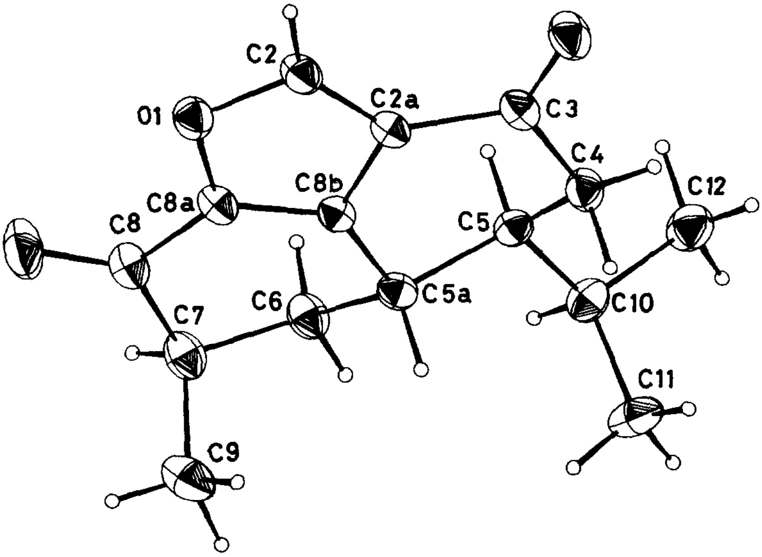
^{13}C N.m.r. spectrum of gmelofuran (CDCl$_3$)

δ	mult.	T_1	Carbon Assignment
15.47	q	1.31	11
16.38	q	1.26	12
20.87	q	1.36	9
35.98	t	0.96	6
40.04	t	0.87	4
26.63	d	1.98	10
30.03	d	2.26	5
42.77	d	2.00	7
47.93	d	2.42	5a
123.23	s		8b[*]
144.40	s		2a
144.88	s		8a
147.67	d		2
188.57	s		8
193.30	s		3[†]

[*] This assignment is based on the doublet seen in the fully coupled spectrum run in CCl$_4$, in which solvent peaks due to H-2a are well separated.

[†] Confirmed by the coupled spectrum.

To finally settle the structure an X-ray examination of gmelofuran was carried out. Single crystals for X-ray work were obtained by recrystallisation from methanol. The space group is orthorhombic with cell dimensions: a = 1686.3(4), b = 1081.9(5), c = 726.2(5) pm, Z = 2, M = 246.3 and D_c = 1.24 g cm^{-3}. 1328 independent reflections ($4.6^\circ \leqslant \theta \leqslant 70^\circ$) were measured on a Siemens diffractometer with Ni-filtered Cu-K$_\alpha$ radiation ($\theta/2\theta$ scan), and corrected in the usual way; 88 were coded unobserved($J \leqslant 2\sigma$). The structure was solved by direct methods and refined to R = 3.5% (MULTAN 77[6], X-RAY-76[7]). Mean standard deviations of bond lengths and bond angles between non-hydrogen atoms are 0.6 pm and 0.4° respectively. The structure for gmelofuran so obtained is shown below. It conforms in all details to formula (1).



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3. The 300MHz spectrum was run by Dr. R. Warren, University of Manchester to whom we are greatly indebted.

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