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FREELINGYNE, AN ACETYLENIC SESQUITERPENOID

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Freelingyne, $C_{15}H_{12}O_3$, is one of a series of related furano sesquiterpenes isolated from the wood oil of Eremophila freelingii. (I) is the most probable structure. Freelingyne is the most unsaturated furano sesquiterpene that has been found and is the first example of an acetylenic terpenoid. Oxygen is invariably located at the positions shown with an asterisk in compounds of this type (1,2). Freelingyne has presumably been oxygenated in all three positions the one adjacent to the furan ring having given rise to the acetylene group.

The compound was isolated from the acetone extract using chromatography on silica gel. Crystallisation from benzene and sublimation at 130°/0.02 mm gave yellow crystals, m.p. 164°. The infrared spectrum (nujol or chloroform) showed the presence of a conjugated disubstituted acetylene (2190 cm^{-1}) and an α,β-unsaturated γ-lactone (1755 cm^{-1}). Absorptions typical of a furan (1) were present at 1504, 1164, 874 cm^{-1}. The ultraviolet spectrum (ethanol) showed the presence of extended conjugation with λ_{max} 365 mμ (ϵ 45,000).

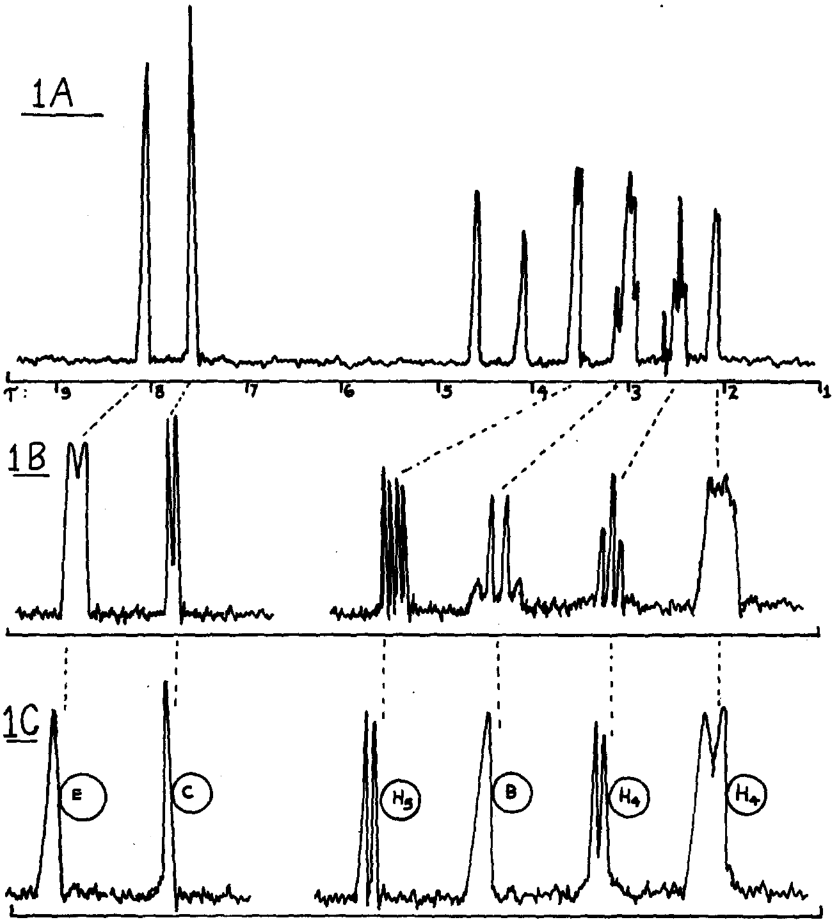
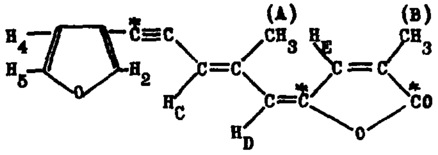


Figure 1A. N.M.R. spectrum of freelingyne in $CDCl_3$.
1B. Partial expanded spectrum.
1C. Spin-decoupled spectrum. Irradiated group ○.



(I)

TABLE 1

N.M.R. Spectrum of (1). (60 Mc, $CDCl_3$)

	Proton Count	Assignment	Appearance
7.97	3	B	Broad partly resolved doublet (J 1.35 cps.)
7.67	3	A	Sharp doublet (J 1.1 cps.)
4.38	1	D	Broad singlet
4.11	1	C	Broad singlet
3.53	1	4	Quartet (J 1.7, 0.7 cps.)
2.98	1	E	Quartet (J 1.35 cps.)
2.62	1	5	Apparent Triplet (J 1.7, 1.4 cps.)
2.35	1	2	Quartet (J 1.4, 0.7 cps.)

Chemical shifts are accurate to τ 0.005, coupling constants to 0.05 cps.

TABLE 2

Summary of Coupling Constants (cps.)

J_{24}	0.7	J_{AD}	0
J_{25}	1.4	J_{DE}	*ca.* 0.4
J_{45}	1.7	J_{DB}	0.6
J_{AC}	1.1	J_{EB}	1.35
J_{CD}	*ca.* 0.5		

The analytical data (3) and the integration of the N.M.R. spectrum support the formula $C_{15}H_{12}O_3$. The N.M.R. spectrum (Figure 1) showed the presence of two methyl groups attached to double bonds at τ 7.97 and 7.67, two olefinic protons in the normal region at τ 4.38 and 4.41, one strongly deshielded olefinic proton at τ 2.98, and three furan ring protons at τ 3.53, 2.62 and 2.35, giving a total count of twelve protons in agreement with the proposed molecular formula.

Many of the peak splittings were of similar magnitude, and all were relatively small (Table 2), but the relationship between the protons was firmly established by field-sweep double irradiation experiments; the final assignments are given in Table 1, and the coupling constant data in Table 2.

The three furan ring protons formed an AMX system with $J_{4,5} = 1.7$ cps, $J_{2,5} = 1.4$ cps and $J_{2,4} = 0.7$ cps. The chemical shifts and coupling constants are in agreement with reported values (4,5) and the absence of the $J_{3,4}$ coupling of 3.2-3.8 cps. immediately established the β-position of the substituent. The low-field shift of H-2 relative to H-5 may be ascribed to the diamagnetic anistropy of the β-substituent.

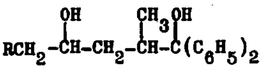
The proton H_E appeared as a 1:4:4:1 quartet at τ2.98 coupled to the methyl group (B) at τ 7.97 with J = 1.35 cps. The chemical shifts of these protons are in agreement with those reported for similar systems (6,7) and the coupling constant is of the order expected for allylic coupling (8). The olefinic proton H_E showed an additional small coupling (ca. 0.4 cps.) to H_D which was also coupled to the methyl group at τ 7.97 (J 0.6 cps.) over six bonds.

The methyl group (A) at τ 7.67 appeared as a sharp doublet (J 1.1 cps.) and was coupled only to H_C with no observable coupling to H_D or H_E.

The methyl group (A) is at lower field than expected for an allylic group β to an acetylenic bond (9) and is probably further deshielded by the double bond of the lactone ring.

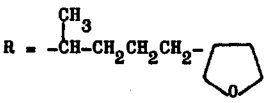
H_C and H_D appeared as broad partly resolved singlets with J_{CD} ca. 0.5 cps. The small coupling of 0.4 cps between H_D and H_E suggests the stereochemistry shown by analogy with cis-tagetone (± 0.5 cps.) (10) and this arrangement also accounts satisfactorily for the low-field shift of CH_3(A). The alternative arrangement about the double bond should give J_{DE} ca. 0.7 cps by analogy with trans-trans-muconic acid (10). However, the differences are small and the stereochemistry cannot be regarded as unequivocal.

The location and substitution pattern of the lactone was confirmed by the following degradations. Hydrogenation of freelingyne in ethyl acetate over palladium on charcoal gave the perhydro derivative,

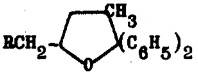


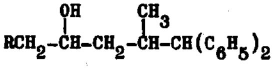
$RCH_2-\overset{OH}{\overset{|}{C}}H-CH_2-\overset{CH_3}{\overset{|}{C}}H-\overset{OH}{\overset{|}{C}}(C_6H_5)_2$

(II)



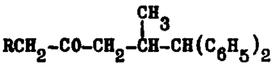
(III)





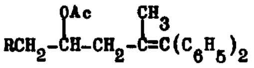
$RCH_2-\overset{OH}{\overset{|}{C}}H-CH_2-\overset{CH_3}{\overset{|}{C}}H-CH(C_6H_5)_2$

(IV)



$RCH_2-CO-CH_2-\overset{CH_3}{\overset{|}{C}}H-CH(C_6H_5)_2$

(V)



$RCH_2-\overset{OAc}{\overset{|}{C}}H-CH_2-\overset{CH_3}{\overset{|}{C}}=C(C_6H_5)_2$

(VI)

$C_{15}H_{26}O_3$ (uptake 7 moles) as an oil, b.p. 125°/0.4 mm. The infrared spectrum had carbonyl absorption at 1770 cm^{-1} (film) which is characteristic of a saturated γ-lactone. This lactone gave a diol (II), $C_{27}H_{38}O_3$, m.p. 123°, when treated with phenyl magnesium bromide.

When the diol was treated with iodine in benzene solution a quantitative yield of the tetrahydrofuran (III), $C_{27}H_{36}O_2$, b.p. 180° (0.05 mm) was obtained. Lithium and ammonia cleaved this benzylic ether to give an alcohol (IV), $C_{27}H_{38}O_2$, b.p. 175°, (0.05 mm) which was oxidised quantitatively with chromic oxide in pyridine to the ketone (V), $C_{27}H_{36}O_2$, b.p. 185° (0.05 mm). The N.M.R. spectrum revealed the presence of four protons adjacent to the carbonyl group (γ 7.95, 7.77).

Acetylation of the diol (II) with acetic anhydride and pyridine at room temperature gave the diacetate, $C_{31}H_{42}O_5$, m.p. 103°.

An unsaturated monoacetate (VI), $C_{29}H_{38}O_3$, b.p. 230°/25 mm was formed when this diactate was refluxed with toluenesulphonic acid in acetic acid solution. The ultraviolet spectrum (ethanol) had λ_{max} 242 mμ (ϵ 27,000) which was consistent with the loss of the benzylic acetate. In particular, the N.M.R. spectrum showed one methyl group attached to the double bond (τ8.2).

These reactions, together with the N.M.R. data and its probable biosynthesis, lead to the structure (I) for freelingyne. Full details of the chemistry of this substance and other members of this series will be published elsewhere.

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