THE STRUCTURE OF FUTOENONE,

A NOVEL SPIRO-CYCLOHEXADIENONE DERIVATIVE

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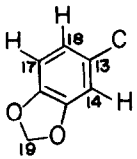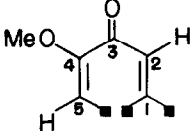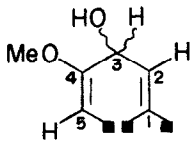(Department of Chemistry, Tohoku University, Sendai, Japan)

From the leaves and stem of _Piper futokadzura_ Sieb. et Zucc. we have isolated two new crystalline compounds designated futoenone, $C_{20}H_{20}O_5$ (M^+ 340), m. p. 197°, $[\alpha]_D^{CHCl_3}$ -58. 0°, and futoxide, $C_{18}H_{18}O_8$, m. p. 153°, $[\alpha]_D^{CHCl_3}$ +79. 5°, respectively.

Futoenone (I) [ν_{max}^{nujol} 1655, 1622, 1522 cm^{-1}, no OH absorption] exhibits in its NMR spectrum (Fig. 1) signals (H_{14}, H_{17}, H_{18}, H_{19}) assignable to a 3, 4-methylenedioxyphenyl moiety (IA), as well as low-field absorption from two isolated olefinic protons (H_2, H_5).   Double resonance experiments show H_5, at 5. 49[1], to be coupled (J = ca 0. 2)[1] to the OMe signal at 3. 63.

Hydrogenation of futoenone over PtO_2 in ethanol affords dihydrofutoenone (II) [$C_{20}H_{22}O_5$; m. p. 173°; ν_{max}^{nujol} 1650, 1630 cm^{-1}] which has only one olefinic proton (H_2 at 5. 59) in its NMR spectrum.   The remainder of the spectrum is very similar to that of futoenone, except for the presence of a new ABX-pattern (δ_4 = 3. 69, δ_{5a} = 2. 14, δ_{5b} = 2. 27; $J_{5a, 5b}$ = 15. 5, $J_{4, 5a}$ = 4. 1, $J_{4, 5b}$ = 9. 5) from which it may be deduced that futoenone contains a -CH=C(OMe)- grouping.

Reduction of futoenone with $LiAlH_4$ gave a 60:40 mixture of epimeric alcohols (IIIa, IIIb), the 100 Mc NMR spectrum of which was assigned in sufficient detail to establish the presence of part-structure (IIIA) from the chemical shifts of H_2, H_3, H_5, and the 4-OMe, and from the magnitudes of $J_{2, 3}$, $J_{3, 5}$, and $J_{5, OMe}$.


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(IA)   (IB)   (IIIA)

■ = oxygen or carbon bearing no proton.

	III a	III b
$J_{2,3}$	1. 8	6. 4
$J_{3,5}$	1. 0	0. 8
$J_{5,OMe}$	<u>ca</u> 0. 2	<u>ca</u> 0. 2
δ_2	4. 97	5. 12
δ_3	4. 80	<u>ca</u> 4. 7
δ_5	4. 64	4. 71
δ_{4-OMe}	3. 61	3. 57

Since the infrared spectra of futoenone (I) and dihydrofutoenone (II) show absorption due to a carbonyl group but no hydroxyl band, whereas those of the alcohols IIIa and IIIb show hydroxyl absorption near 3600 cm^{-1} but no strong band in the 1600-2000 cm^{-1} region, it is apparent that futoenone contains the part-structure (IB). Oxidation with MnO$_2$ reconverts the epimeric alcohols IIIa and IIIb to futoenone. The UV absorptions in ethanol of futoenone [λ_{max}: 257 (18,900), 285 (8,800)], dihydrofutoenone [259 (12,900), 288 (3,400)], the mixture of epimeric alcohols IIIa and IIIb [233 (6,000), 288 (4,500)], and methylenedioxybenzene [232 (2,900), 283 mμ (ε 3,300)][2] are also in accord with the presence of an α, β, α', β'-dienone moiety and a 3,5-methylenedioxyphenyl grouping in futoenone.

Besides signals attributable to part structures IA and IB, the NMR spectrum of futoenone contains a broad doublet of doublets (H$_{8\alpha}$ at 5.01), a three-proton doublet at 0.59 (secondary methyl), and a complex group of signals in the 1.5 to 3.0 ppm region due to six-protons. By means of double resonance experiments using several different solvents it was possible to unambiguously assign[3] all of these proton-signals (see FIG. 1) and to establish which proton is coupled to which. From the NMR data it is apparent that the structural sequence (IC) must be present in futoenone.

(IC)
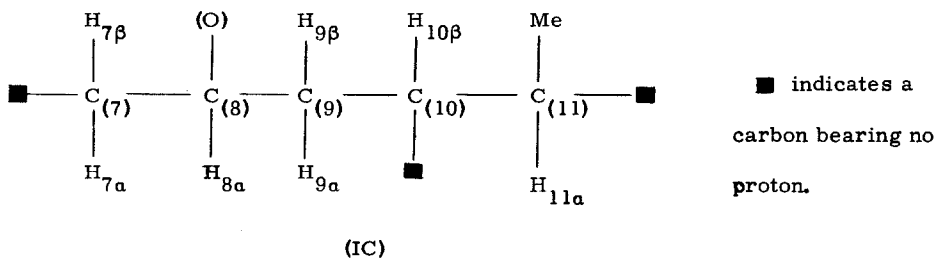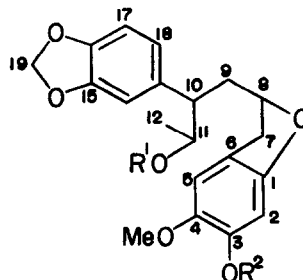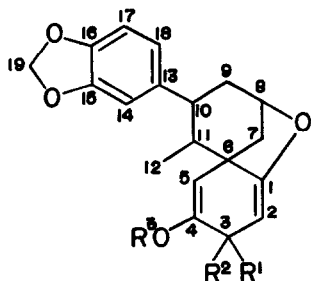
I: $R_1R_2=O$; $R_3=Me$

II = 4,5-dihydro-I

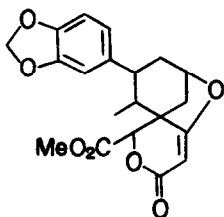IIIa, b: R_1, $R_2=H$, OH; $R_3=Me$
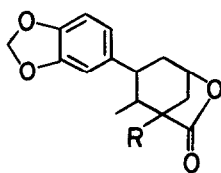
XI: $R_1R_2=O$; $R_3=H$

IV: $R_1=R_2=Ac$

V: $R_1=R_2=H$

VI: $R_1=H$; $R_2=CH_2Ph$

VII: $R_1=Tosyl$; $R_2=CH_2Ph$

VIII: $R_1=Tosyl$; $R_2=H$

IX

X: $R=CO_2Me$

XII: $R=CH_2CO_2Me$

XIII = Futoenone

δ_2	5.75	$\delta_{10\beta}$	2.52	$J_{5,OMe}$	ca 0.2	$J_{9a,9\beta}$	13.5
δ_5	5.49	δ_{11a}	2.03	$J_{7a,7\beta}$	11.5	$J_{9a,10\beta}$	11.5
δ_{7a}	2.17	δ_{11-Me}	0.59	$J_{7a,8a}$	ca 0.0	$J_{9\beta,10\beta}$	6.0
$\delta_{7\beta}$	2.35	δ_{14}	6.68	$J_{7\beta,8a}$	6.0	$J_{10\beta,11a}$	11.2
δ_{8a}	5.01	δ_{17}	6.72	$J_{7\beta,9\beta}$	ca 1.5	$J_{11a,12}$	6.4
δ_{9a}	1.70	δ_{18}	6.63	$J_{8a,9a}$	ca 0.5	$J_{14,18}$	1.8
$\delta_{9\beta}$	2.26	δ_{19}	5.91	$J_{8a,9\beta}$	5.0	$J_{17,18}$	8.0
		δ_{OMe}	3.63				
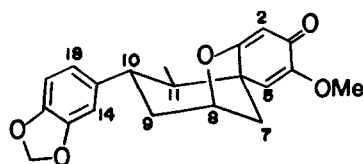
85% $C_6D_6CDCl_3$ CDCl$_3$ OMe   11-Me

FIG. 1. 100 Mc NMR spectrum of futoenone (I).

Decoupling experiments showed $H_{10\beta}$ to be weakly coupled to H_{14} and H_{18} ($J_{14,\,10\beta}$ = ca 0. 1;

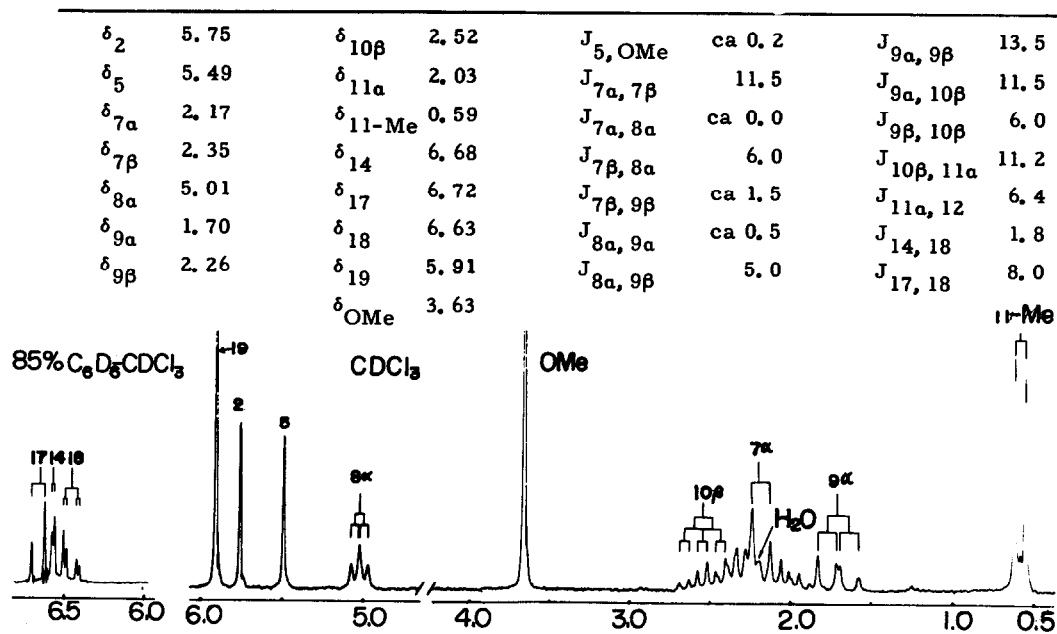$J_{10\beta,\,18}$ = ca 0. 2), which means that $C_{(10)}$ in IC must be joined to $C_{(13)}$ of the aromatic ring (IA).

Since partial structures IA, IB, and IC, together account for all twenty protons, all five

oxygens, and nineteen of the twenty carbons present in the futoenone molecule, this means that

$C_{(1)}$, $C_{(5)}$, $C_{(7)}$ and $C_{(11)}$ must be connected to one and the same carbon atom (C_6), which leads

immediately to the full structure (I) for futoenone (cf. Stereostructure XIII). The oxygen bridge

can only be across $C_{(8)}$ to $C_{(1)}$. The relative stereochemistry follows from the magnitudes of

$J_{11\alpha,\,10\beta}$, $J_{10\beta,\,9\alpha}$ (both about 11. 5 cps) and from the presence of the oxygen-bridge, the other

coupling constants being in complete accord with the proposed stereochemistry. An alternative

possible stereochemistry in which the six-membered carbocyclic-ring is constrained to a boat

form, with quasi-equatorial methyl and aromatic groups (i. e., inverted configurations at C_{10}

and C_{11}), is rejected for two reasons (1) $J_{7\beta,\,9\beta}$ = ca 2 cps which is in accord with the coupling

frequently observed[4] across four-bonds in a W-arrangement, as occurs in I but not in the

alternative boat-shaped six-membered ring, and (2) interaction between the quasi-axial protons

$C_{(7)}$ and $C_{(10)}$ in a boat form would be expected to reduce the values of $J_{10,\,11}$ and $J_{9,\,10}$ below

that of the observed values of 11. 5 cps.

$J_{2,\,5}$ = ca 0. 2; $J_{2,\,7a}$ = ca 0. 1; $J_{2,\,7b}$ = ca 0. 1; $J_{5,\,OMe}$ = ca 0. 2; $J_{5,\,7a}$ = 0. 8

$J_{5,\,7b}$ = 0. 8; $J_{8,\,7a}$ = 8. 0; $J_{8,\,7b}$ = 8. 8; $J_{7a,\,7b}$ = 15. 5; $J_{8,\,9a}$ = 3. 2; $J_{8,\,9b}$ = 9. 5;

$J_{9a,\,9b}$ = 13. 5; $J_{9a,\,10}$ = 11. 5; $J_{9b,\,10}$ = 3. 5; $J_{10,\,11}$ = 9. 0; $J_{11,\,12}$ = 6;

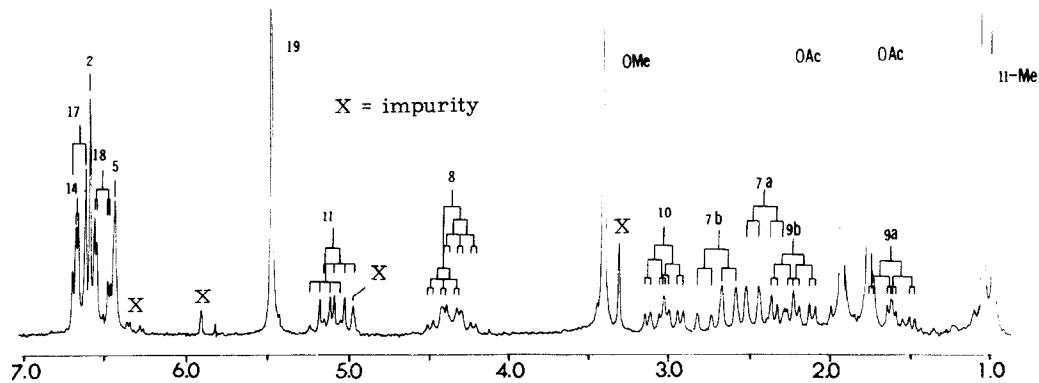$J_{10,\,14}$ = ca 0. 1 ?; $J_{10,\,18}$ = ca 0. 2; $J_{14,\,18}$ = 1. 6; $J_{17,\,18}$ = 7. 8

FIG. 2. 100 Mc NMR spectrum of the diacetate IV in 87% C_6D_6-$CDCl_3$

Confirmation of the presence of a spiro-ring junction and a bridged oxygen ring in futoenone is provided by the following reactions.

Treatment of futoenone with acetic anhydride in the presence of H_2SO_4 or BF_3 furnished the diacetate (IV) [$C_{24}H_{26}O_8$, m. p. 110-112°, $[\alpha]_D^{CHCl_3}$ -137°, ν_{max}^{nujol} 1710, 1755 cm^{-1}, λ_{max}^{EtOH} 232 (9, 400), 292 mμ (ε 7, 300)]. The 100 Mc spectrum (Fig. 2) of IV has been completely assigned[3], and deduction of structure IV from the NMR data (Fig. 2) is straightforward; in particular, the presence of the following small couplings, $J_{5, OMe}$ = ca 0. 2, $J_{5, 7a}$ = $J_{5, 7b}$ = 0. 8, and $J_{2, 7a}$ = $J_{2, 7b}$ = ca 0. 1 cps, establishes the structure of the aromatic ring bearing the methoxyl group and provides good evidence for the presence of an oxygen bridge between $C_{(1)}$ and $C_{(8)}$ and for the part structure IB.

Hydrolysis of the diacetate IV and benzylation of the resulting diol V, followed by treatment of the benzyl ether VI with tosyl chloride in pyridine, afforded a mixture of futoenone (I) and the tosylate VII. Hydrogenolysis of VII gave the corresponding phenol VIII which cyclized under basic conditions to afford futoenone (I) through Ar_1-6 participation[5], (Fig. 3).

The conversion of futoenone (I) into the diacetate (IV) can be considered to proceed via a dienone-phenol type rearrangement involving fission of the $C_{(6)}$— $C_{(11)}$ bond[6]. (See Fig. 3).
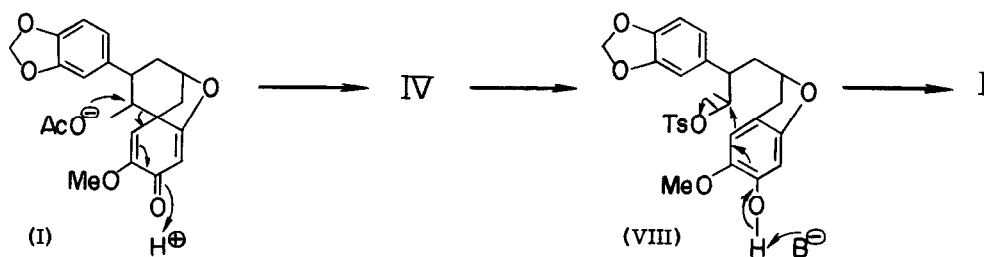

FIG. 3

Finally, Lemieux oxidation of futoenone and methylation of the product gave the unsaturated δ-lactone IX [$C_{20}H_{20}O_7$, m. p. 246°, ν_{max}^{nujol} 1735, 1700, 1660 cm^{-1}] and the γ-lactone X [$C_{17}H_{18}O_6$, m. p. 125-126°, ν_{max}^{nujol} 1795, 1700 cm^{-1}], whereas oxidation of the demethyl derivative (XI) with alkaline peroxide afforded, after methylation, the γ-lactone XII [$C_{18}H_{20}O_6$, m. p. 140°, ν^{nujol} 1765, 1730 cm^{-1}]. The 100 Mc spectrum of the γ-lactone XII (Fig. 4), which has been unambiguously assigned[3] in some detail by the use of double resonance techniques[3], is in complete accord with the proposed structure and stereochemistry of futoenone.

$$J_{5a, 5b} = 16.7; \quad J_{7\beta, 8a} = 6; \quad J_{7a, 8a} = ca\ 0.0; \quad J_{7a, 7\beta} = 11.6; \quad J_{7\beta, 9\beta} = 1.9;$$

$$J_{8a, 9\beta} = 4; \quad J_{8a, 9a} = 1; \quad J_{9a, 9\beta} = 14; \quad J_{9\beta, 10\beta} = 6; \quad J_{9a, 10\beta} = 11.5; \quad J_{10\beta, 11a} = 11.5;$$

$$J_{11a, 12} = 6.3; \quad J_{10\beta, 14} = ca\ 0.1; \quad J_{10\beta, 18} = ca\ 0.3$$
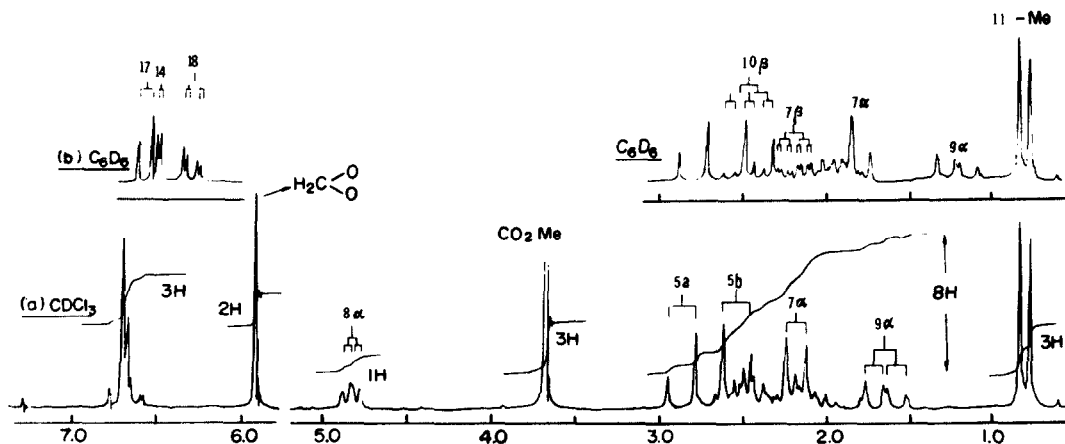
FIG. 4.   100 Mc NMR spectrum of the γ-lactone XII

ACKNOWLEDGEMENT

REFERENCES

1) Chemical shifts are for $CDCl_3$ solutions, unless otherwise stated, and are expressed in ppm down-field from internal TMS. Coupling constants were determined by first-order analyses and are expressed in cps.

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3) See following paper: Tetrahedron Letters

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6) P. J. Kropp, Ibid, 85, 3280 (1963).