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THE STRUCTURE OF LUBIMIN AND OXYLUBIMIN, ANTIFUNGAL METABOLITES FROM DISEASED POTATO TUBERS[1)]

N. Katsui, Akira Matsunaga, and T. Masamune*

Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo, Japan

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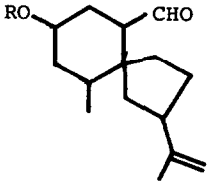
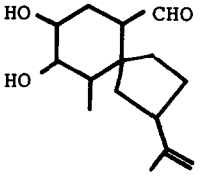
In a continuing study[2)] on phytoalexins produced by tuber tissues of white potatoes (Solanum tuberlosum and S. demissum) infected by an incompatible race of Phytophthora infestans, we isolated two antifungal sesquiterpenes, one being identified as lubimin (I), obtained recently from the same sources by Metlitskii et al.,[3a)] and the other being regarded as oxylubimin (II), in 2×10^{-5} and 5×10^{-5}% yields, respectively, along with rishitin[2a)] (1.5×10^{-4}%).[4)] We present here evidence that lubimin is represented more favorably by formula I, rather than a proposed formula (III),[3b)] and oxylubimin by formula II.

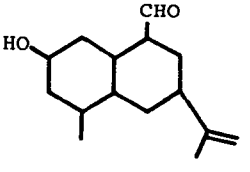
Lubimin (I), colorless oil, $[\alpha]_D$ +36°,[5)] $C_{15}H_{24}O_2$,[5)] gave monoacetate (Ia), oil, $[\alpha]_D$ +35°. These compounds exhibited the following spectra:[5)] (I); Mass, m/e 236 (M^+); IR (film), ν_{max} 3410, 3085, 2740, 1715, 1640, and 890 cm^{-1}; NMR,[4)] δ 0.94 (3H, d J = 7), 1.68 (3H, s), 3.65 (1H, m W_H = 25), 4.65 (2H, s), and 9.74 (1H, d J = 3): (Ia); Mass, m/e 278 (M^+); IR (film), ν_{max} 2715, 1735, 1720, 1640, 1238, and 888 cm^{-1}; NMR, δ 1.96 (3H, s) and 4.60 (1H, m W_H = 25). These spectra indicate that Metlitskii's[3a)] and our lubimin is identical and contains $CH_3\overset{|}{C}H-$, $CH_2=C(CH_3)-$, $HO\overset{|}{C}H-$, and CHO- groupings in the molecule.[3b)]



I R=H
Ia R=Ac

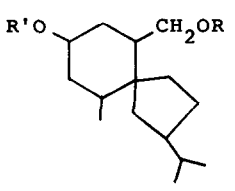


II



III

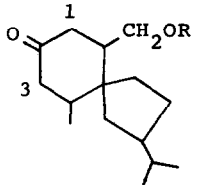
Reduction of I with $NaBH_4$ produced unsaturated glycol (IV), mp 128-130°, $[\alpha]_D$ +28°; Mass, m/e 238 (M^+), which on hydrogenation over Pt afforded saturated glycol (V), mp 145-147°, $[\alpha]_D$ +35°; Mass, m/e 240 (M^+); IR, ν_{max} 1387 and 1372 cm^{-1}; NMR, δ 0.86 (9H, d J = 7, $3CH_3CH$-), 3.30 and 3.89 (each 1H, do d J = 11, 8 and 11, 3, $HOCH_2CH$-), and 3.63 (1H, m W_H = 25, $HOCH$-). Glycol V was converted into monobenzoate (Va), mp 105-108°; IR, ν_{max} 3400, 1718, 1594, and 847 cm^{-1}; NMR, δ 3.64 (1H, m W_H = 25, $HOCH$-), 3.99 and 4.64 (each 1H, do d J = 11, 10 and 11, 2, $BrC_6H_4COOCH_2CH$-), which on oxidation with CrO_3 afforded keto-ester (VI) in 50% yield, mp 70-73°; Mass; m/e 220 (M^+ -199) and 177 (220-43); IR, ν_{max} 1720, 1705 (sh), 1598, and 842 cm^{-1}. Treatment of VI with NaOD in a refluxing mixture of D_2O and dioxane led to deuteration of two CH_2 groups adjacent to the CO group with concomitant hydrolysis, giving the d_5-derivative (VII), $C_{15}H_{21}D_5O_2$; Mass, m/e 243 (M^+) ; IR (film), ν_{max} 1705 cm^{-1}. Compound V, when treated with p-$BrC_6H_4SO_2Cl$ (2 moles), produced monobrosylate (Vb), oil, in 50% yield; IR (film), 3400, 1580, 1372, and 1183 cm^{-1}; NMR (CCl_4), δ 3.64 (1H, m W_H = 25, $HOCH$-), 3.70 and 4.15 (each 1H, do d J = 11, 8 and 11, 4, $BrC_6H_4SO_2OCH_2CH$-), which was converted spontaneously into cyclic ether (VIII), oil, $C_{15}H_{26}O$; Mass, m/e 222 (M^+); IR (film), ν_{max} 1105 and 912 cm^{-1};[6] NMR (CCl_4), δ 0.87 and 0.89 [total 6H, each d J = 7, $(CH_3)_2CH$-], 1.10 (3H, d J = 7.5, CH_3CH-), 3.49 and 3.78 (each 1H, do d J = 10, 4.5 and d J = 10, $-CHOCH_2CH$-), and 4.19 (1H, m W_H = 10, $-CHOCH_2CH$-). These facts strongly suggested the presence of a moiety $-CH_2CH(OH)CH_2CH(CHO)-$ in a 6- or 7-membered ring of lubimin (I). The whole structure was deduced from spin-decoupling studies on the NMR spectrum of I in the presence of shift reagent Eu(fod)$_3$[7] (Table 1 and Fig. 1).



V R=R'=H

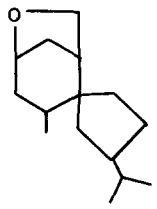
Va R=p-BrC_6H_4CO, R'=H

Vb R=p-$BrC_6H_4SO_2$, R'=H



VI R=p-BrC_6H_4CO

VII R=D and D_2 at C_1 and C_3



VIII

Table 1 The NMR spectrum of lubimin (I) in the presence of the europium shift reagent $Eu(fod)_3$ (CCl_4, 100 MHz) and spin-decoupling results

Run	Mole ratio I:$Eu(fod)_3$	Proton (δ) Irradiated			Observed		Multiplicity change	Splitting decoupled (Hz)
1	2:1	H-A	(C-15)	11.13	4.24	(H-B)	br t -- t	2.5
2a	2:1	H-B	(C-10)	4.24	11.13	(H-A)	d -- s	2.5
b					7.30	(H-C)	ch (br t -- br s)	
3a	2:1	H-C	(C-1)	7.30	4.24	(H-B)	br t -- br s	8 and 8
b					10.36	(H-D)	m (W_H 25) -- m (W_H 20)	
4a	2:1	H-D	(C-2)	10.36	7.30	(H-C)	ch (br t -- br d)	
b					6.05	(H-E)	ch (br t -- br d)	
5a	2:1	H-E	(C-3)	6.05	10.36	(H-D)	m (W_H 25) -- m (W_H 20)	
b					~3.4	(H-F)	ch ?	
6a	2:1	H-F	(C-4)	3.38	6.05	(H-E)	ch (br t -- br s)	
b					1.90	(H-G)	d -- s	7
7	2:1	H-G	(C-14)	1.90	3.4	(H-F)	ch ?	
8a	2:1	H-H	(C-6)	3.82	~3.2	(H-I)	ch	
b					~2.3	(H-J)	ch	
9a	2:1	H-I	(C-6)	3.20	3.82	(H-H)	do d -- d	13
b					~2.3	(H-I)	ch	
10a	2:1	H-J	(C-7)	2.30	3.82	(H-H)	do d -- d	7
					~3.2	(H-I)	ch	
11	1:1	H-F	(C-4)	4.54	2.50	(H-G)	d -- s	7
12	1:1	H-G	(C-14)	2.50	4.54	(H-F)	br m -- br d with J = 11	

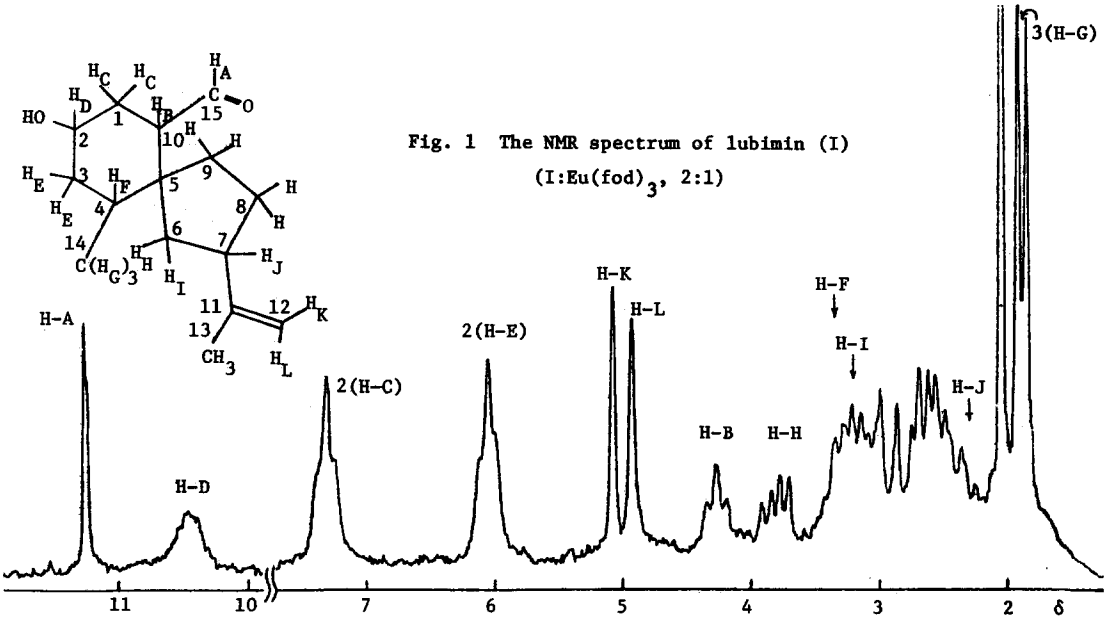


Fig. 1 The NMR spectrum of lubimin (I) (I:$Eu(fod)_3$, 2:1)

The decoupling studies, especially runs 3a, 12, 9a and 10a, indicated the presence of two partial structures; ■(quarternary carbon)-CH(CHO)-CH_2-CH(OH)-CH_2-CH(CH_3)-X (X, not CH_2 but probably ■), and ■-CH_2CH[C(CH_3)=CH_2]-$(CH_2)_n$- (n, probably 2). In view of the presence of a quarternary carbon, supported by appearance of a singlet signal at δ 47.6 ppm in an off-resonance decoupled CMR spectrum of diacetate of IV in $CDCl_3$, combination of these structures has elucidated the whole structure (I) with an agarospirane (vetispirane) skeleton.[8)]

Oxylubimin (II), mp 85-86° (isopropyl ether), $[\alpha]_D$ +27°, $C_{15}H_{24}O_3$, showed the following spectra; Mass, m/e 252 (M^+); IR, ν_{max} 3380, 3080, 2750, 1717, 1650, and 885 cm^{-1}; NMR, δ 1.06 (3H, d J = 7), 1.67 (3H, s), 2.87 (2H, br s, 20H), 2.98 (1H, t J = 10), 3.42 (1H, m W_H = 20), and 9.78 (1H, d J = 3), and was assigned formula II in essentially the same manner as lubimin.

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4 We are grateful to Mr. N. Sato for the preparation of raw materials and to Mrs. T. Okayama for the measurement of NMR spectra.

5 Optical rotations, IR and NMR spectra were measured in EtOH, $CHCl_3$ and $CDCl_3$, unless otherwise stated. Abbreviations "s, d, t, m, br, do, ch, and sh" in the spectral data denote singlet, doublet, triplet, multiplet, broad, double, change, and shoulder, respectively. Coupling constants J (Hz) were estimated by first-order approximations. All new compounds gave elementary analyses in good accord with the assigned structures.

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