Lubimin and Oxylubimin. The Structure Elucidation[1]

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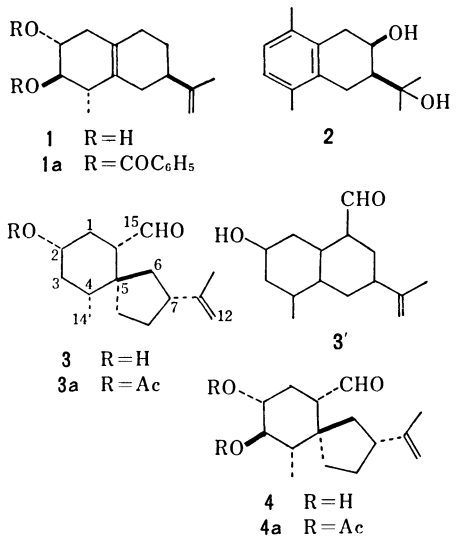
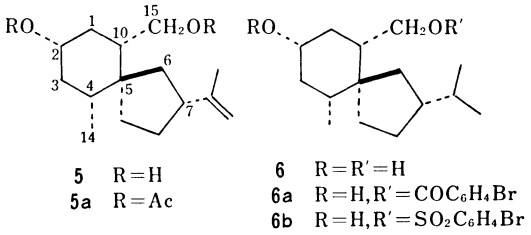
The isolation and structure elucidation of lubimin (**3**) and oxylubimin (**4**), stress metabolites from diseased white potato tubers, are described.

In continuing studies on phytoalexins produced by diseased potato tubers, we have isolated several new sesquiterpenes besides rishitin[2] (**1**) and rishitinol[3] (**2**) from white potato tubers (*Solanum tuberlosum* × *S. demissum*, "Rishiri") infected by an incompatible race of *Phytophthora infestans*. On the other hand, in 1971 Metlitskii and coworkers[4] reported the isolation of an antifungal metabolite, qualified as phytoalexin and designated as lubimin[4a] (**3**), along with rishitin (**1**) from white potato tubers (*S. tuberlosum*, "Lubimets") stressed with various pathogens. They presumed the metabolite to be sesquiterpene aldehyde and proposed formula **3'** on the basis of the spectral data.[4b] One of our new sesquiterpenes could immediately be identified as the Metlitskii lubimin, and one of the other sesquiterpenes was designated as oxylubimin (**4**). We recently reported in preliminary communications[5] that lubimin is represented more favorably by formula **3** rather than the proposed formula (**3'**),[4b] and oxylubimin correctly by formula **4**. The same structures and configurations for these stress metabolites have recently been reported independently by Stoessl and coworkers.[6]



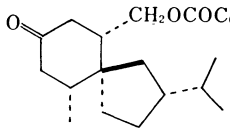
Lubimin. Planar Structure. Lubimin (**3**), colorless oil and $[\alpha]_D$ +36°, had the molecular formula $C_{15}H_{24}O_2$ and gave the monoacetate (**3a**), oil and $[\alpha]_D$ +35°. These compounds exhibited the following spectra: **3**, MS, *m/e* 236 (M^+); IR, ν_{max} 3410, 3085, 2740, 1715, 1640, and 890 cm^{-1}; NMR, δ 0.94 (3H, d, J=7 Hz), 1.68 (3H, s), 3.65 (1H, m, W_H=25 Hz), 4.65 (2H, s), and 9.74 (1H, d, J=3 Hz): **3a**, MS, *m/e* 278 (M^+); IR, ν_{max} 2715, 1735, 1720, 1640, 1238, and 888 cm^{-1}; NMR, δ 1.69 (3H, s) and 4.70 (1H, m, W_H=25 Hz). These spectral data were indistinguishable from the corresponding data reported by Metlitskii and coworkers[4b] and indicated that the following structural units are involved in the molecule, as had been pointed out by them;[4b] $-(CH_3)CH-$, $-C(CH_3)=CH_2$, $-CH(OH)-$, and $-CHO$.

Reduction of lubimin (**3**) with sodium borohydride in ethanol afforded unsaturated glycol, dihydrolubimin[7] (**5**), mp 129—130 °C; *m/e* 238 (M^+); δ 3.28 (1H, t, J= 10 Hz) and 3.90 (1H, do d, J=10 and 2.5 Hz), which formed the diacetate (**5a**), oil; ν_{max} 1743 and 1238 cm^{-1}; δ 2.04 and 2.07 (each 3H, s) 3.83 and 4.36 (each 1H, do ABq, J=11, 8 and 11, 4 Hz), and 4.69 (1H, br m, W_H=25 Hz). Compound **5**, when hydrogenated over Adams platinum in ethanol, gave saturated glycol, tetrahydrolubimin (**6**), mp 145—147 °C; *m/e* 240; ν_{max} 1387 and 1372 cm^{-1}; δ 0.86 (9H, d, J=7 Hz). All these spectra confirmed the presence of the four groupings in bicyclic lubimin.



Treatment of tetrahydrolubimin (**6**) with *p*-bromobenzoyl chloride (one mole) and pyridine resulted in monobenzoylation, giving the mono-*p*-bromobenzoate (**6a**), mp 106—108 °C; IR, ν_{max} 3400, 1718, 1594, and 847 cm^{-1}; NMR, δ 3.64 (1H, br m, W_H=25 Hz), 3.99 and 4.46 (each 1H, do ABq, J=11, 10 and 11, 2 Hz). Likewise, compound **6**, when treated with *p*-bromobenzenesulfonyl chloride (2 mole) and pyridine, underwent monobrosylation to give the monobrosylate (**6b**), oil; IR, ν_{max} 3400, 1372, and 1183 cm^{-1}; NMR, δ 3.64 (1H, br m, W_H=25 Hz), 3.70 and 4.15 (each 1H, do ABq, J=11, 8 and 11, 4 Hz). The NMR spectra revealed that the primary hydroxyl group, formed by reduction of the formyl group, was acylated but the secondary hydroxyl remained unchanged in each of the compounds (**6a** and **6b**). Oxidation of the benzoate (**6a**) with chromium(VI) oxide produced oxo-benzoate (**7**), mp 71—73 °C; MS, *m/e* 220 ($M^+-BrC_6H_4CO_2H$) and 177; IR, ν_{max} 1720 and 1705 cm^{-1} (sh). Treatment of the ketone (**7**) with sodium deuteroxide in a mixture of dioxane and deuterium oxide effected deuteration of

two methylene groups adjacent to the carbonyl group with concomitant hydrolysis to yield the d_5-derivative (**8**), $C_{15}H_{21}D_5O_2$; MS, *m/e* 243; IR, ν_{max} 1705 cm^{-1}. This result elucidated that a moiety $-CH_2CH(OH)CH_2-$ would be included in a six- or seven-membered ring but not in a five-membered ring. On the other hand, the monobrosylate (**6b**), on treatment with potassium *t*-butoxide in *t*-butyl alcohol, was converted into oxolane (**9**), oil. In accordance with the assigned structure, compound **9** exhibited parent and fragmentation peaks at *m/e* 222 and 179 in the mass spectrum and absorption maxima at 1105 and 912 cm^{-1},[8] and at δ 0.87, 0.89, and 1.10 (each 3H, d, J=7—7.5 Hz), 3.49 and 3.78 (each 1H, do ABq, J=10, 4.5 and 10, 0 Hz), and 4.19 (1H, narrow m, W_H=10 Hz). These results revealed the presence of a moiety $-CH_2CH(OH)CH_2CH(CHO)-$ in lubimin (**3**), implying that the proposed structure (**3'**) should be revised.



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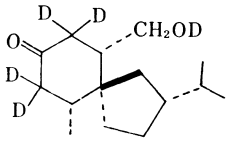

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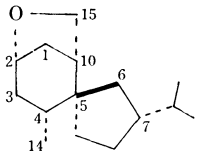

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The ^{13}C NMR spectra of diacetyldihydrolubimin (**5a**) were then obtained at 25.2 MHz under proton noise decoupled and single-frequency off-resonance decoupled conditions, and each signal was assigned, as summarized in Table 1, on the basis of the multiplicity and chemical shift.[9] As shown in Table 1, compound **5a** contained a quaternary carbon at δ 46.7[10] besides those of the isopropenyl and two acetoxyl groups, again excluding the proposed structure (**3'**). It is noted that the carbon in question would evidently be of spiro type

Table 1. The ^{13}C NMR spectra of dihydrolubimin (**5**), its diacetate (**5a**), and triacetyldihydrooxylubimin (**11a**)

Compound	**5**	**5a**	**11a**
Carbon no.	Chemical shift (δ, $CDCl_3$, 100 MHz)		
1	48.3	40.5	41.1
2	69.6	72.1	73.7
3	40.4	36.8	75.5
4	40.7 or 40.9	40.9 or 44.8	45.8 or 47.3
5	46.4	46.7	48.0
6	32.6	32.6	31.4
7	47.1	47.3	47.3 or 45.8
8	36.6	33.0	32.9
9	25.3	25.2	26.1
10	40.9 or 40.7	44.8 or 40.9	45.8 or 47.3
11	147.5	147.9	147.4
12	107.8	108.8	109.2
13	21.2	21.0	21.0
14	16.1	16.6	11.4
15	63.9	66.3	65.7

Table 2. The NMR spectrum of lubimin (**3**) in the presence of the europium shift reagent $Eu(fod)_3$ (CCl_4, 100 MHz) and spin-decoupling results

Run	Mole ratio **3** : $Eu(fod)_3$	Irradiated proton (δ, Hz)	Observed proton (δ) Multiplicity change and decoupled splitting (Hz)
1	2 : 1	11.13 (H_a at C_{15})	4.24 (H_b) br t ⟶ t (2.5)
2a	2 : 1	4.24 (H_b at C_{10})	11.13 (H_a) d ⟶ s (2.5)
b			7.30 (H_c) br t ⟶ br s
3a	2 : 1	7.30 (H_c at C_1)	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	10.36 (H_d at C_2)	7.30 (H_c) br t ⟶ br d
b			6.05 (H_e) br t ⟶ br d
5a	2 : 1	6.05 (H_e at C_3)	10.36 (H_d) m (W_H=25) ⟶ m (W_H=20)
b			≈3.4 (H_f) ch?
6a	2 : 1	3.38 (H_f at C_4)	6.05 (H_e) br t ⟶ br s
b			1.90 (H_g) d ⟶ s (7)
7	2 : 1	1.90 (H_g at C_{14})	≈3.4 (H_f) ch?
8a	2 : 1	3.82 (H_h at C_6)	≈3.2 (H_i) ch
b			≈2.3 (H_j) ch
9a	2 : 1	3.20 (H_i at C_6)	3.82 (H_h) do d ⟶ d (13)
b			≈2.3 (H_i) ch
10a	2 : 1	2.30 (H_j at C_7)	3.82 (H_h) do d ⟶ d (7)
b			≈3.2 (H_i) ch
11	1 : 1	4.54 (H_f at C_4)	2.50 (H_g) d ⟶ s (7)
12	1 : 1	2.50 (H_g at C_{14})	4.54 (H_f) br m ⟶ br d (J=11) (7)

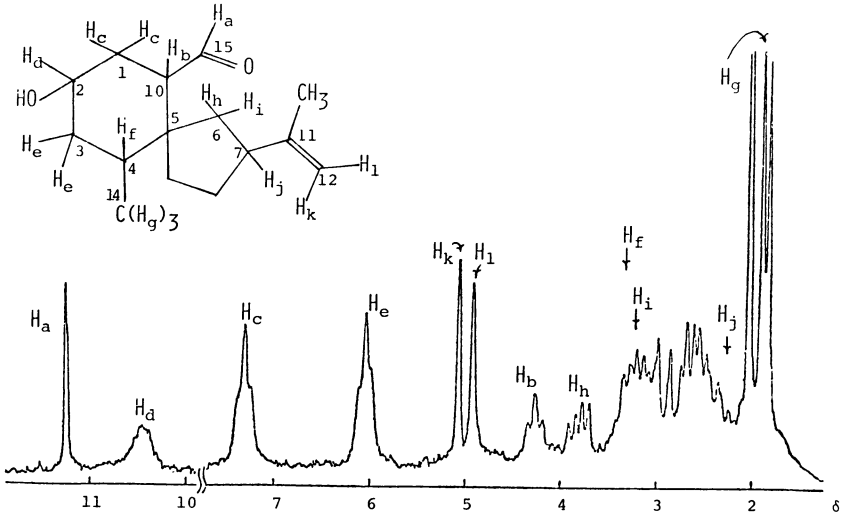
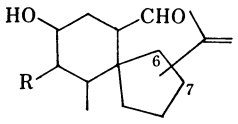


Fig. 1. The NMR spectrum of lubimin (**3**) in the presence of the shift reagent $Eu(fod)_3$ (CCl_4, 100 MHz, and the reagent: **3**=1 : 2).

owing to the absence of a methyl group attached to the quaternary carbon atom.

The whole structure of lubimin (**3**) was finally deduced from spin-decoupling studies of its NMR spectra of lubimin (**3**) in the presence of shift reagent $Eu(fod)_3$.[11] While the ring methylene and methine protons overlapped each other and appeared as a broad multiplet without the shift reagent, addition of 0.25—1.0 mole of $Eu(fod)_3$ per mole of the compound caused down-field shifts of all the signals. The down-field shifts were approximately linear with respect to concentration of the reagent and resulted in separation of most of the protons in question, as exemplified by Fig. 1. Decoupling studies were carried out on the europium-shifted spectra (the reagent : lubimin=1 : 2 and 1 : 1), the result being summarized in Table 2. In the spectrum (the reagent : lubimin=1 : 2, Fig. 1), signals centered at δ 11.13, 10.36, and 1.90 were readily assignable to the protons due to formyl, hydroxy-methine, and secondary methyl groups, respectively. Irradiation at δ 11.13 (C<u>H</u>O) collapsed a broad triplet at δ 4.24 [C<u>H</u>(CHO)] to a sharp triplet (run 1). Conversely, by irradiation at δ 4.24, the doublet (J=2.5 Hz) at δ 11.13 and a broad triplet at δ 7.30 [C<u>H</u>$_2$CH(CHO)] were simplified to a sharp singlet and a broad singlet, respectively (run 2). Further irradiation at δ 7.30 decoupled the broad triplet signal at δ 4.24 to a broad singlet and also narrowed a broad multiplet at δ 10.36 [C<u>H</u>(OH)CH$_2$CH-(CHO)] slightly but definitely (run 3). Similar change of the signal at δ 10.36 was also observed on irradiation at δ 6.05 [C<u>H</u>$_2$CH(OH)CH$_2$CH(CHO)], which simultaneously caused change of a signal pattern near δ 3.4 [C<u>H</u>CH$_2$CH(OH)CH$_2$CH(CHO)] (run 5). Inversely, irradiation at δ 3.38 collapsed the broad triplet at δ 6.05 to a broad singlet and also decoupled a doublet at δ 1.90 [CH(C<u>H</u>$_3$)] to a singlet (run 6), indicating the presence of a moiety -(CH$_3$)CHCH$_2$CH(OH)CH$_2$-CH(CHO)-. Fortunately, the methine protone (δ 3.38) adjacent to the methyl group appeared separately as a broad multiplet at δ 4.54 in the spectrum containing an equimolar shift reagent $Eu(fod)_3$. This multiplet signal was simplified to a broad doublet (J=11 Hz) by irradiation at δ 2.50, a center of a doublet due to the methyl protons (run 12). In view of the decoupling behaviors of the signals due to two relevant methine protons adjacent to the methyl and formyl groups (runs 12, 1, and 3a) as well as the presence of a quaternary carbon atom of spiro type, the quaternary carbon in question must be flanked by these two methine carbon atoms. Hence lubimin is represented either by (planar) formula **10a** or **10b**.



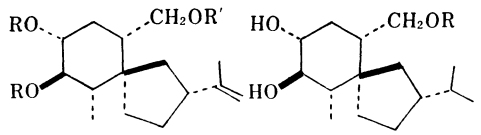
10a R=H, 6-isopropenyl
10b R=H, 7-isopropenyl
10c R=OH, 7-isopropenyl

In the NMR spectrum shown in Fig. 1, a clearly separated signal centered at δ 3.82 must be a methine or one of a methylene protons in a five-membered ring. The multiplicity (do d, J=13 and 7 Hz) revealed that the proton would probably be coupled to only two protons, one being a geminal proton and another a proton on the adjacent carbon atom. In fact, irradiation at δ 3.20 and 2.30 decoupled the signal to two doublets with coupling constants of 7 and 13 Hz, respectively. Thus the proton in question (δ 3.82) must be one of the methylene protons at C_6. The remarkable europium-induced down-field shift of this proton, as compared with the other five-membered ring protons, suggested that the proton would be disposed in the neighborhood of the formyl group. This result was not compatible with formula **10a** but only with formula **10b**. On the analogy of the structure and configuration of oxylubimin (**4**) described later, lubimin is represented most favorably by the stereostructure **3**, because the three substituents, formyl, hydroxyl, and methyl groups at C_{10}, C_2, and C_4 in the A ring would evidently be oriented

equatorial.

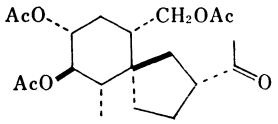
Oxylubimin. Planar Structure. The titled compound (**4**), mp 85—86 °C and $[\alpha]_D$ +27°, had the molecular formula $C_{15}H_{24}O_3$ and gave the diacetate (**4a**), oil and $[\alpha]_D$ +22°. Reduction of oxylubimin (**4**) with sodium borohydride afforded unsaturated triol, dihydrooxylubimin (**11**), mp 170—171 °C, which formed the triacetate (**11a**), oil, and, on hydrogenation over Adams platinum, yielded saturated triol, tetrahydrooxylubimin (**12**), mp 163—165 °C. Likewise, the diacetate (**4a**) was reduced with sodium borohydride to give diacetyldihydrooxylubimin (**11b**), oil, which was converted into the triacetate (**11a**). The IR and NMR spectra of these compounds indicated that oxylubimin (**4**) contained the following structural units: $-CH(CH_3)-$ [**4** and **11b**, δ 1.08 and 0.89 (each 3H, d, J=7 Hz)]: $-CH(CHO)-$ [**4**, ν_{max} 2715 and 1715 cm^{-1}, δ 2.38 (1H, do do d, J=10, 4, and 2.5 Hz) and 9.80 (1H, d, J=2.5 Hz); **11b**, ν_{max} 3460 cm^{-1}, δ 3.34 and 3.92 (each 1H, do ABq, J=11, 8 and 11, 3 Hz)]: $-CH(CH_3)=CH_2$ [**4**, ν_{max} 1645 and 895 cm^{-1}, δ 1.72 (3H, s) and 4.75 (2H, br s); **11b**, ν_{max} 1643 and 885 cm^{-1}, δ 1.73 (3H, s) and 4.68 (2H, br s); **12**, ν_{max} 1388 and 1372 cm^{-1}]: $-CH(OH)CH(OH)-$ [**4**, positive to the HIO_4 test,[12] ν_{max} 3560, 3300, and 3080 cm^{-1}, δ 3.01 (1H, t, J= 10 Hz), 3.48 (1H, br t, J=10 Hz, W_H=20 Hz), and 3.90 (2H, br s, disappeared on addition of D_2O); **11b**, ν_{max} 3460, 1745, and 1250 cm^{-1}, δ 2.00, 2.04 (each 3H, s), and 4.76 (2H, m).

These results and the spin-decoupling studies on the NMR spectra of oxylubimin (**4**) in the absence and also in the presence of the shift reagent Eu(fod)$_3$, the results being summarized in Table 3, elucidated the presence of a moiety ■(quaternary carbon)–$CH(CH_3)$–$CH(OH)$–$CH(OH)$–CH_2–$CH(CHO)$–■ and hence oxylubimin (**4**) could be regarded as a 3β-hydroxyl derivative of lubimin (**3**). In good accord with this presumption, triacetyldihydrooxylubimin (**11a**) exhibited the ^{13}C NMR spectra (Table 1) closely similar to that of diacetyldihydrolubimin (**5a**), apart from a signal due to the 3-carbon atom, in which a quaternary carbon of spiro type was observed as a singlet peak at δ 48.0. Moreover, oxidation of triacetate (**11a**) by the Lemieux-Johnson procedure[13] gave methyl ketone (**13**), oil, which displayed a three-proton singlet and a broad one-proton peak (W_H=25 Hz) due to the acetyl and acetyl-methine protons at δ 2.16 and 2.83 in the NMR spectrum. The wide half-width of the methine proton signal indicated that the acetyl group, derived from the isopropenyl group in oxylubimin (**4**), would not be located on the carbon atom adjacent to the spiro-carbon. Hence oxylubimin must be represented by (planar) formula **10c**.



11 R=R'=H
11a R=R'=Ac
11b R=Ac, R'=H
11c R=COC_6H_5, R'=H

12 R=H
12a R=$SO_2C_6H_4Br$



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Stereochemistry. The four substituents in the A ring

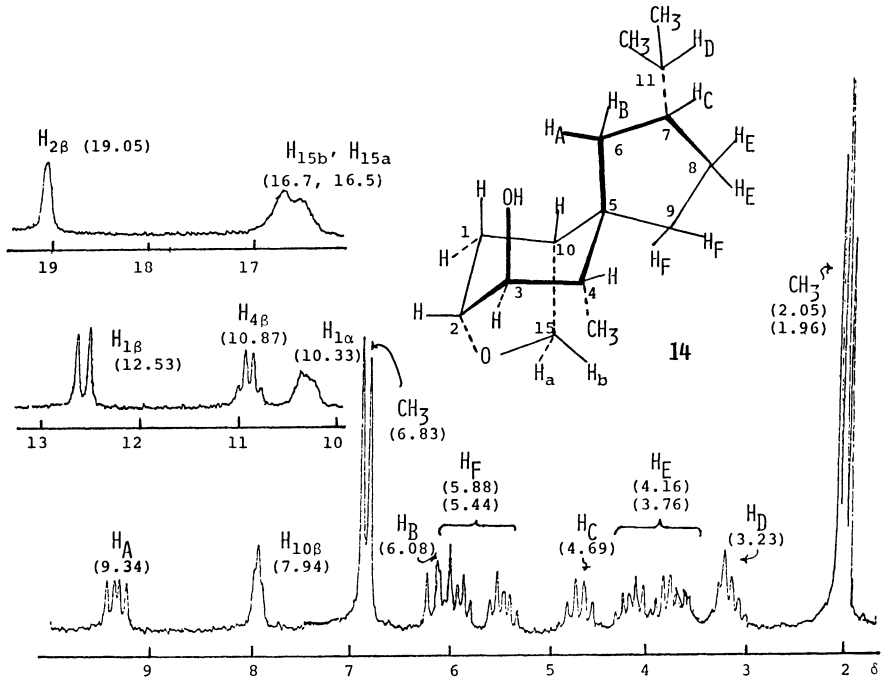
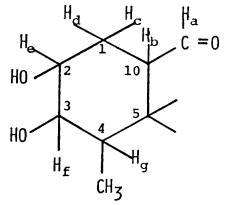


Fig. 2. The NMR spectrum of hydroxyoxolane (**14**) in the presence of the shift reagent Eu(dpm)$_3$ (CCl_4, 100 MHz, and the reagent: **14**=0.8 : 1).

Table 3. The NMR spectra of oxylubimin (**4**) in the absence [A] and in the presence of the shift reagent $Eu(fod)_3$ [B] and spin-decoupling results

Irradiated proton (δ, Hz)	Observed proton (δ) Multiplicity change and decoupled splitting (Hz)			
[A] (CCl_4, 100 MHz)				
9.80 (H_a) CH(CHO) (d, J=2.5)	2.38 (H_b)	do t	⟶	do d (2.5)
2.38 (H_b) CH(CHO) (do do d, J=10, 4, and 2.5)	9.80 (H_a)	d	⟶	s (2.5)
1.76 (H_c) H (ax) at C_1 (not clearly obsd)	2.38 (H_b)	do do d	⟶	br s (10)
	3.48 (H_e)	br t	⟶	br d (10)
2.08 (H_d) H (eq) at C_1 (not clearly obsd)	2.38 (H_b)	ch		
	3.48 (H_e)	br t	⟶	t (small)
3.48 (H_e) CH(OH) at C_2 (br t, J=10)	3.01 (H_f)	t	⟶	d (10)
3.01 (H_f) CH(OH) at C_3 (t, J=10)	3.48 (H_e)	br t	⟶	br d (10)
1.60 (H_g) CH(CH_3) (not clearly obsd)	3.01 (H_f)	t	⟶	d (10)
	1.08 (CH_3)	d	⟶	s (7)
[B] (CCl_4, 100 MHz; the shift reagent: **4**=1 : 1)				
8.86 (H_b) CH(CHO) (br d, J=10)	11.38 (H_c)	br q	⟶	do t (10)
	10.77 (H_d)	br d	⟶	do d (small)
11.38 (H_c) H (ax) at C_1 (br q, $J\approx$10)	8.86 (H_b)	br d	⟶	br s (10)
	10.77 (H_d)	br d	⟶	br s (12)
10.77 (H_d) H (eq) at C_1 (br d, J=12)	8.86 (H_b)	br d	⟶	d (small)
	11.38 (H_c)	ch		
11.20 (H_g) CH(CH_3) (br m)	5.68 (CH_3)	d	⟶	s (7)
5.68 (CH_3) (d, J=7)	11.20 (H_g)	br m	⟶	d (J=10) (7)



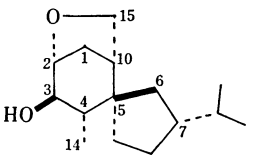
of oxylubimin (**4**) were presumed to be all equatorial on the basis of the magnitudes of the vicinal coupling constants for each of the methine, methylene, and hydroxy-methine protons ($J_{b,c}$, $J_{b,d}$, $J_{e,c}$, $J_{e,d}$, $J_{e,f}$, and $J_{f,g}$ =10, 4, 10, small, 10, and 10 Hz), estimated from the data in Table 3. Since the A ring would probably adopt a chair conformation, the relative configurations of the four substituents at C_{10}, C_2, C_3, and C_4 must be *cis*, *trans*, and *trans*, respectively. Moreover, the *trans*-diequatorial disposition between the C_3-hydroxyl and C_4-methyl groups was also deduced from the ^{13}C NMR specrum of triacetyldihydrooxylubimin (**11a**), in which the 14-methyl carbon atom was observed at a higher field (δ 11.4) as compared with the corresponding carbon (δ 16.6) in diacetyldihydrolubimin (**5a**). This high-field shift of the methyl carbon atom could be explained well as a neighboring effect due to the diequatorially-oriented acetoxyl group at C_3.[14] The absolute configrations of these substituents were decided by application of "exciton chirality method"[15] to dibenzoyldihydrooxylubimin (**11c**), mp 58—59 °C. This dibenzoate was obtained by benzoylation of oxylubimin followed by sodium borohydride reduction and exhibited a characteristic split curve in the CD spectrum (ethanol); $\Delta\varepsilon$ −19.2 (235 nm) and +5.9 (219) [*cf.*, rishitin dibenzoate, $\Delta\varepsilon$ −17.6 (235 nm) and +6.1 (218)].[16] The negative sign of the first splitting effect indicated a left-hand helix for the vicinal dibenzoate moiety, leading to assignment of α-, α-, β-, and α-configurations to the four substituents at C_{10}, C_2, C_3, and C_4 in the A ring.

Tetrahydrooxylubimin (**12**), when treated with *p*-bromobenzenesulfonyl chloride, underwent partial brosylation to give monobrosylate (**12a**), mp 98—100 °C, which on treatment with potassium *t*-butoxide in *t*-butyl alcohol at 0 °C for 30 min yielded hydroxyoxolane (**14**), oil. The mass [*m/e* 238 (M^+) and 220] and IR spectra (ν_{max} 3420, 1390, 1372, 1079, and 1010 cm^{-1}) were consistent with the assigned structure, and the NMR spectrum [δ 0.88 (6H, d, J=6.5 Hz, 12- and 13-CH_3), 1.06 (3H, d, J=8 Hz, 14-CH_3), 1.90 (1H, t, J=4.5 Hz, β-H at C_{10}), 2.36 (1H, d, J=12 Hz, β-H at C_1), 3.66 (1H, do d, J=8 and 4.5 Hz, a-H at C_{15}), 3.78 (1H, d, J=5 Hz, α-H at C_3), 3.87 (1H, d, J=8 Hz, b-H at C_{15}), and 4.18 (1H, t, J=5 Hz, β-H at C_2)], indicated the A ring to take a slightly deformed chair-form with the four substituents at C_{10}, C_2, C_3, and C_4 all axial; $J_{1\beta,1\alpha}$, $J_{1\beta,2\beta}$, $J_{1\alpha,2\beta}$, $J_{2\beta,3\alpha}$, $J_{3\alpha,4\beta}$, $J_{10\beta,1\beta}$, $J_{10\beta,1\alpha}$, $J_{10\beta,15a}$, $J_{10\beta,15b}$, and $J_{15a,14b}$=12, 0, 5, 5, 0, 0, 4.5, 4.5, 0, and 8 Hz, respectively (see formula **14**). Addition of 0.8 mol equiv of the shift reagent $Eu(dpm)_3$ effected complete separation of the NMR signals due to individual protons which were correlated to the respective signals by spin-decoupling studies (Fig. 2). As expected, most of the protons on the B ring were observed at higher fields (below δ 7.00) as compared with those on the A

Table 4. The NMR spectrum of hydroxyoxolane (**14**) in the presence of the shift reagent $Eu(dpm)_3$ (CCl_4, 100 MHz; the reagent; **14**=0.8 : 1) and spin-decoupling results

Irradiated proton (δ, Hz)	Observed proton (δ) Multiplicity change and decoupled splitting (Hz)
9.34 (H_A) (do d, J=13 and 8)	6.08 (H_B) do d ⟶ d (13); 4.69 (H_C) sex ⟶ qui (8)
6.08 (H_B) (do d, J=13 and 9)	9.34 (H_A) do d ⟶ d (13); 4.69 (H_C) sex ⟶ qui (9)
4.69 (H_C) (sex, $J\approx8$)	9.34 (H_A) do d ⟶ d (8); 6.08 (H_B) do d ⟶ d (9); 3.23 (H_D) ch
3.23 (H_D) (m)	4.69 (H_C) sex ⟶ qui (8); 2.05 and 1.96 (11- and 12-CH_3) each d ⟶ s (6.5)

ring. Only one exceptional signal at a low field, δ 9.34, was reasonably assigned to the β-proton at C_6 (H_A), because the 6-carbon atom was disposed 1,3-diaxial to the 3β-hydroxyl group.[17] Spin-decoupling studies (Table 4) confirmed that the relevant proton (H_A) and the isopropyl group were located on the vicinal carbon atoms, establishing the relative disposition of the isopropenyl group to the A ring in oxylubimin (**4**). Unfortunately, no assignments could be made to the configuration of the isopropyl group from the coupling constants ($J_{A,C}$ and $J_{B,C}$=8 and 9 Hz). However, in view of the absolute configuration (R) of the 7-carbon atom in naturally occurring vetispiranes,[18] oxylubimin must be represented correctly by formula **4**. Recently, Stoessl and coworkers[6b] completely defined the relative configruation of the whole molecule of oxylubimin on the basis of the X-ray crystallography. The present result leads to the same conclusion and also invloves decision of the absolute cofiguration.



14

Experimental

All the melting points were uncorrected. The purity of each compound was always checked by TLC over silica gel (Wakogel B-5 or Merck GF-254) with various solvent systems, and the spots were developed with cerium(IV) sulfate in dil sulfuric acid, iodine, vanilin–sulfuric acid and/or the Ehrlich reagent. The vanilin–sulfuric reagent was prepared by dissolving vanilin (250 mg) in concd sulfuric acid (100 ml), and the Ehrlich reagent by dissolving *p*-dimethylaminobenzaldehyde (100 mg) in acetone (9 ml) and concd hydrochloric acid (1 ml). The optical rotations, UV, and IR spectra were measured in 95% ethanol, in 95% ethanol, and in liquid state (oil) or in Nujol (crystals), respectively, unless otherwise stated. The NMR spectra were obtained in chloroform-*d*, unless otherwise stated, at 100 MHz, tetramethylsilane being used as an internal reference. The abbreviations "s, d, t, q, qui, sex, m, br, do, ch, and sh" in the spectral data denote "singlet, doublet, triplet, quartet, quintet, sextet, multiplet, broad, double, changed, and shoulder," respectively. The preparative TLC was carried out over silica gel (Merck GF-254), and the column chromatography over silica gel (Mallinckrodt AR-100) or alumina (Merck Active I, neutral).

*Isolation of Lubimin (**3**), Oxylubimin (**4**), and Lubiminol[7] (**5**).* The fraction E (4.8 g), yellow oil, described in the section of "Isolation of rishitin,"[1] was dissolved again in ether and shaken with 10% aq sodium carbonate to remove acidic components. The ether soln was washed with 0.1 M hydrochloric acid and water, dried, and evaporated to leave neutral substances (3.8 g), which consisted of two main components and showed two pink spots with the Ehrlich reagent on TLC, the R_f values being 0.54 and 0.47 (benzene : ether= 2 : 1). These were separated into two fractions by chromatography over silicic acid with benzene–ether (3 : 1). The less polar fraction (0.75 g) with R_f 0.54, oil, was further purified by preparative TLC, showing two bands, detected by spraying a soln of iodine in hexane, on TLC with benzene–ether (1 : 2). The more polar fraction on TLC was extracted with ethyl acetate containing a small volume of methanol to give crude lubimin, which was purified by TLC to give lubimin (**3**, 400 mg), in pure state, oil and $[\alpha]_D$ +39°; MS, *m/e* 236 (M^+), 218, 203, 193, and 175; IR and NMR, in the text; GLC, Silicone SE-52 (Chromosorb W, DMCS, 80—100 mesh), injection temp 200 °C, carrier gas nitrogen, 45 ml/min, retention time 5.8 min. Found: C, 76.65; H, 10.19%. Calcd for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24%.

The fraction H (2.42 g), oil,[1] was dissolved in ether and shaken with 10% aq sodium carbonate. The ether soln was washed with 0.1 M hydrochloric acid and water, dried, and evaporated to leave oily neutral substances (2.37 g), which were again dissolved in ether and separated roughly into two fractions by chromatography over silicic acid (130 g) with ether, ether–acetone, and acetone. Fractions, eluted later with ether and then with acetone, showed a magenta spot with the Ehrlich reagent on TLC and were combined and concentrated to leave oily residue (1.34 g), showing two spots on TLC with cerium(IV) sulfate. The residue was rechromatographed over silicic acid (120 g) with mixtures of ether–ethyl acetate. Early fractions eluted with ether–ethyl acetate (9 : 1, 400 ml) gave oily materials (378 mg). Subsequent fractions eluted with the same solvent mixture (220 ml) gave a crystalline material (670 mg), showing a single spot on TLC (R_f 0.50, ether). This was purified by recrystallization from isopropyl ether to give oxylubimin (**4**, 330 mg), needles, mp 85—86 °C and $[\alpha]_D$ +27°; MS, *m/e* 252 (M^+), 234, 209, and 191; IR and NMR, in the text. Found: C, 71.48; H, 9.59%. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59%. Further fractions eluted with ether–ethyl acetate (9 : 1, 80 ml and 4 : 1, 100 ml) afforded a crude crystalline material (122 mg), which was again purified by chromatography over silicic acid (1.2 g) with a 4 : 1 mixture of ether and ethyl acetate to give a crystalline substance (92 mg), showing a single spot on TLC. This was recrystallized from ether to give lubiminol[7] (**5**, 56 mg) in pure state, mp 129—130 °C and $[\alpha]_D$ +33°; MS, *m/e* 238 (M^+), 220, 202, 187, and 107 (base); IR, ν_{max} 3410, 3140, 1642, 1048, 1036, 1009, and 884 cm^{-1}; NMR, δ 0.89 (3H,

d, J=6.5 Hz, 14-C$\underline{H}_3$), 1.70 (3H, s, 13-C$\underline{H}_3$), 2.49 (2H, br s, 2O$\underline{H}$), 3.28 (1H, t, J=10 Hz, $\underline{H}$ at C_{15}), 3.60 (1H, br m, W_H=25 Hz, $\underline{H}$ at C_2), 3.90 (1H, do d, J=10 and 2.5 Hz, $\underline{H}$ at C_{15}), and 4.66 (2H, br s, 2$\underline{H}$ at C_{12}). Found: C, 75.77; H, 11.00%. Calcd for $C_{15}\underline{H}_{26}O_2$: C, 75.58; H, 11.00%.

*Acetyllubimin (**3a**), Diacetyloxylubimin (**4a**), and Diacetyloxylubiminol (**5a**).* (*i*) Lubimin (**3**, 39 mg) was treated with acetic anhydride (Ac_2O, 0.5 ml) and pyridine (Py, 0.5 ml) at room temp for 16 h. After addition of ethanol, the reaction mixture was worked up as usual to leave oily residue, which was purified by preparative TLC to give **3a** (23 mg), colorless oil and $[\alpha]_D$ +35°; MS, *m/e* 278 (M^+), 236, 218, 203, 191, 190, 189, and 175; IR, ν_{max} 3060, 2715, 1735, 1640, 1235, 1029, and 888 cm^{-1}; NMR, 0.95 (3H, d, J=7 Hz, 14-C$\underline{H}_3$), 1.69 (3H, s, 13-C$\underline{H}_3$), 4.65 (2H, s, 12-C$\underline{H}_2$), 4.70 (1H, m, W_H=25 Hz, $\underline{H}$ at C_2), and 9.76 (1H, d, J=3 Hz, C$\underline{H}$O).

(*ii*) Oxylubimin (**4**, 28 mg) was acetylated with Ac_2O (0.5 ml) and Py (0.5 ml) at room temp for 15 h to give **4a** (35 mg), colorless oil and $[\alpha]_D$+22°; MS, *m/e* 336 (M^+) and 276; IR, ν_{max} 3080, 2720, 1745, 1720, 1643, 1250, 1030, and 885 cm^{-1}; NMR, δ 0.90 (3H, d, J=7 Hz, 14-C$\underline{H}_3$), 1.69 (3H, s, 13-C$\underline{H}_3$), 1.96 and 1.99 (each 3H, s, 2OCOC$\underline{H}_3$), 2.35 (1H, m, $\underline{H}$ at C_{10}), 4.65 (2H, br s, 12-C$\underline{H}_2$), 4.65 (2H, m, 2$\underline{H}$ at C_2 and C_3), and 9.85 (1H, d, J=3 Hz, C$\underline{H}$O).

(*iii*) Lubiminol[7] (**5**, 30 mg) was treated with Ac_2O (0.2 ml) in Py (1.0 ml) at room temp for 23 h under stirring. The reaction mixture was worked up as usual to leave oily residue (39 mg), which was purified by chromatography over silica gel (3.0 g) with benzene-ether (30 : 1) to give **5a** (35 mg), oil and $[\alpha]_D$+43°; MS, *m/e* 262 ($M^+-C_2H_4O_2$) and 202; IR, ν_{max} 2970, 2890, 1743, 1642, 1465, 1432, 1365, 1238, 1027, and 886 cm^{-1}; NMR, 0.94 (3H, d, J=6.5 Hz, 14-C$\underline{H}_3$), 1.74 (3H, s, 13-C$\underline{H}_3$), 2.04 and 2.07 (each 3H, s, 2OCOC$\underline{H}_3$), 3.83 and 4.36 (each 1H, do ABq, J=11, 8, and 4 Hz, 2$\underline{H}$ at C_{15}), 4.69 (1H, br m, W_H=25 Hz, $\underline{H}$ at C_2), and 4.70 (2H, br s, 12-C$\underline{H}_2$).

*Dihydrolubimin (**5**) and Its Acetate (**5a**).* A soln of crude lubimin (**3**, 180 mg) in ethanol (3 ml) was treated with sodium borohydride (18 mg) at room temp for 1.5 h under stirring. The mixture was worked up as usual to leave amorphous residue (196 mg), which crystallized on trituration with isopropyl ether and was collected by filtration to give crude **5** (55 mg), mp 123—126 °C. The mother liquors were evaporated to leave oil, showing four spots on TLC, which was separated by preparative TLC over silica gel. A fraction with the smallest R_f value gave a crystalline substance (28 mg), which was recrystallized from isopropyl ether to give crude **5**, mp 124—127 °C. Both the samples **5** were combined and recrystallized from isopropyl ether to give **5** (75 mg) in pure state, mp 128—130 °C and $[\alpha]_D$ +28°. The mass, IR, and NMR spectra were identical with the corresponding spectra of lubiminol, isolated from the natural sources.

Compound **5** (83 mg), described above, was treated with Ac_2O (1 ml) and Py (1 ml) at room temp for 16 h. After being worked up as usual, the reaction mixture gave an oily product, which was purified by preparative TLC over silica gel to give **5a** (86 mg), oil and $[\alpha]_D$+35°. This sample was identical with that obtained from lubiminol in the mass, IR, and NMR spectra.

*Tetrahydrolubimin (**6**), Its 15-p-Bromobenzoate (**6a**), and Its 15-Brosylate (**6b**).* (*i*) Compound **5** (33 mg) was hydrogenated over Adams platinum (10 mg as $PtO_2 \cdot 2H_2O$) in ethanol (20 ml) at room temp for 3.5 h, when 2 mol of hydrogen had been consumed. After removal of the catalyst and solvent, the mixture gave a crystalline substance (33 mg), which was recrystallized from isopropyl ether to give **6** (27 mg), mp 145—147 °C and $[\alpha]_D$+35°; MS, *m/e* 240 (M^+), 222, 204, 197, 179, and 161; IR ($CHCl_3$), ν_{max} 3640 (sh), 3400, 1387, 1372, 1045 (sh), 1030, and 916 cm^{-1}; NMR, δ 0.86 (9H, d, J=7 Hz, 12-, 13-, and 14-C$\underline{H}_3$), 0.88 (2H, s, 2O$\underline{H}$), 3.32 and 3.90 (each 1H, do ABq, J=11, 8 and 11, 4 Hz, 2$\underline{H}$ at C_{15}), and 3.64 (1H, br m, W_H=25 Hz, $\underline{H}$ at C_2).

(*ii*) To a soln of **6** (17 mg, 7.8×10^{-5} mol) in Py (1 ml) was added dropwise a soln of *p*-bromobenzoyl chloride (14 mg, 6.3×10^{-5} mol) in Py (2.5 ml) at 0 °C under stirring. The mixture was stirred at room temp for 20 h, and then diluted with dichloromethane (25 ml) and poured slowly into 0.6 M sulfuric acid (40 ml) cooled with ice. The whole mixture was separated into two layers, and the aq layer was extracted with dichloromethane (2×30 ml). The combined organic soln was washed successively with 0.6 M sulfuric acid (2×30 ml), 10% aq sodium carbonate (2×30 ml) and water, dried, and evaporated to leave gummy solid, which was submitted to preparative TLC over silica gel with chloroform–ether (7 : 1). A fraction eluted with a low R_f value was extracted with ether containing methanol and gave a solid substance (14 mg), which was again purified by preparative TLC with benzene-ethyl acetate (5 : 1). Extraction of a band with a lower R_f value afforded a crystalline substance (11 mg), which was recrystallized from ethanol to give **6a** (10 mg), mp 106—108 °C; MS, *m/e* 424 (M^++2), 422 (M^+), 222, 204, 179, and 161; IR ($CHCl_3$), ν_{max} 3400, 1718, 1594, 1389, 1372, 1277, 1270, 1118, 1103, 1012, 963, and 847 cm^{-1}; NMR, δ 0.89 (9H, d, J=7 Hz, 12-, 13-, and 14-C$\underline{H}_3$), 3.64 (1H, br m, W_H=25 Hz, $\underline{H}$ at C_2), 3.99 and 4.46 (each 1H, do ABq, J=11, 10 and 11, 2 Hz, 2$\underline{H}$ at C_{15}), 7.73 and 7.81 (each 2H, ABq, J=8 Hz, Br$C_6\underline{H}_4$CO), and 1.60 (1H, br s, O$\underline{H}$). Extraction of a band with higher R_f value gave the 2,15-dibenzoate (8 mg), on trituration with hexane, mp 112—114 °C

(*iii*) A soln of **6** (33 mg, 1.4×10^{-4} mol) and *p*-benzenesulfonyl chloride (85 mg, 3.4×10^{-4} mol) in dry Py (1 ml) was allowed to stand at 0 °C for 10 h. The mixture was poured into ice-water and extracted with ether and then with chloroform. Both the solns were washed successively with 0.5 M hydrochloric acid (2×15 ml), 5% aq sodium hydrogencarbonate (2×15 ml), and saturated brine, combined, dried, and evaporated to leave colorless oil (45 mg), showing two spots with a UV lamp on TLC, which was separated into two fractions by preparative TLC over silica gel with benzene–ethyl acetate (9 : 1). A less polar fraction afforded colorless oil (19 mg), which showed a single spot on TLC and was presumed to be the dibrosylate; NMR, δ 0.86 (9H, d, J=7 Hz), 3.70 and 4.17 (each 1H, do ABq, J=11, 8 and 11, 4 Hz), 4.36 (1H, br m, W_H=25 Hz), and 7.67 (8H, s). A more polar fraction gave **6b** (23 mg), colorless oil, showing a single spot on TLC; MS, *m/e* 238 and 236 ($BrC_6H_4SO_3H^+$), 222 (M^+-236), 204, 189, and 161; IR ($CHCl_3$), ν_{max} 3400, 1580, 1393, 1372, 1183, 1095, 1070, 1012, 962, 945, and 820 cm^{-1}; NMR (CCl_4), δ 0.86 (9H, d, J=7 Hz, 12-, 13-, and 14-C$\underline{H}_3$), 3.64 (1H, br m, W_H=25 Hz, $\underline{H}$ at C_2), 3.70 and 4.15 (each 1H, do ABq, J=11, 8 and 11, 4 Hz, 2$\underline{H}$ at C_{15}), 7.62 and 7.73 (each 2H, ABq, J=8 Hz, Br$C_6\underline{H}_4SO_4$).

*Oxidation of **6a** into the 2-Dehydro Derivative (**7**) Followed by Deuteration.* (*i*) A soln of **6a** (7 mg) in Py (0.3 ml) was added to a slurry, prepared by adding chromium(VI) oxide (30 mg) to vigorously stirred Py (0.3 ml), under cooling with ice-bath during 15 min. The mixture was stirred at the temp for 1 h and then allowed to stand at room temp for 16 h. The reaction mixture was poured into water

(10 ml) and extracted with ether. The ether soln was worked up as usual to leave oil (6 mg), showing two spots, which was purified by preparative TLC over silica gel with benzene–ethyl acetate (10 : 1). A fraction with a higher R_f value gave a crystalline material, which on recrystallization from hexane yielded **7** (3 mg), mp 71—73 °C; MS, *m/e* 220 ($M^+ - BrC_6H_4CO_2H$), 205, 195, 193, and 177: IR, ν_{max} 1720, 1705, 1387, 1370, 1598, 1265, and 842 cm^{-1}; NMR, δ 0.90 (9H, d, J=7 Hz, 12-, 13-, and 14-C$\underline{H}_3$), 3.99 and 4.40 (each 1H, do ABq, J=11, 9 and 11, 3 Hz, 2$\underline{H}$ at C_{15}), 7.67 and 7.77 (each 2H, ABq, J=8 Hz, $BrC_6\underline{H}_4SO_2$).

(*ii*) A soln of **7** (5 mg) in a sodium deuteroxide soln, which had been prepared by adding sodium (50 mg) to a 2 : 1 mixture (3.2 ml) of dry dioxane and deuterium oxide, was heated at 70 °C for 15 min under a stream of nitrogen. After removal of the solvents *in vacuo*, the mixture was extracted with ether. The ether extracts, oil, were again treated in the same manner as described above. The resulting oil was dissolved in chloroform, and the chloroform soln, after being dried, and evaporated, afforded a mixture of deuterated ketones including the d_5-derivative (**8**). The mixture showed the following spectra: MS, *m/e* 243 (M^+ of **8**), 242, 241, 240, 239, 238, 225, 224, 223, 181, and 180; IR, ν_{max} 3450, 2230, 1705, 1388, and 1372 $cm.^{-1}$

*Conversion of **6b** into Oxolane (**9**).* A soln of **6b** (24 mg) in *t*-butyl alcohol (0.4 ml) was stirred with potassium *t*-butoxide in *t*-butyl alcohol (0.2 ml), which had been prepared by dissolving potassium (29.7 mg) into *t*-butyl alcohol (1 ml), at room temp for 150 min under nitrogen. The reaction mixture was poured into water and extracted with ether. The ether soln, after being worked up as usual, left oil, showing two spots, which was separated into two fractions by preparative TLC over silica gel with benzene–ethyl acetate (5 : 1). A less polar fraction gave **9** (9.5 mg), showing a single spot, oil; MS, *m/e* 222 (M^+), 207, 191, 179, 161, and 152; IR, ν_{max} 1388, 1372, 1205, 1170, 1105, 1072, 1052, 1000, 912, 895, 860, and 815 cm^{-1}; NMR, in the text.

*The Periodic Acid Test for Oxylubimin (**4**) and Its Derivatives.* To a soln of periodic acid (50 mg as H_5IO_6) in water (10 ml) were added a drop of concd nitric acid and then a soln of sample in dioxane, and the whole soln was kept at room temp for 10—15 s. To the resulting soln were added two drops of 5% aq silver nitrate: oxylubimin (**4**), dihydrooxylubimin (**11**), and rishitin (**1**) formed white ppts of silver iodate, but lubimin (**3**) and methyl palmitate formed no ppt with the reagent.

*Dihydrooxylubimin (**11**), Its 2,3,15-Triacetate (**11a**), 2,3-Diacetate (**11b**), and 2,3-Dibenzoate (**11c**).* (*i*) A soln of **4** (150 mg) in ethanol (7 ml) was treated with sodium borohydride (30 mg) at room temp for 5 h under stirring. The reaction mixture was worked up as usual to leave crystalline residue (160 mg), which was recrystallized from isopropyl ether containing methanol to give **11** (107 mg), mp 170—171 °C; MS, *m/e* 254 (M^+), 236, and 218; IR, ν_{max} 3340, 3080, 1645, 1090, 1072, 1033, 1002, and 890 cm^{-1}; NMR, δ 1.01 (3H, d, J=7 Hz, 14-C$\underline{H}_3$), 1.71 (3H, s, 13-C$\underline{H}_3$), and 4.66 (2H, br s, 12-C$\underline{H}_2$). Found: C, 70.59; H, 10.28%. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30%.

(*ii*) Compound **11** (120 mg) was stirred with Ac_2O (2.5 ml) and Py (2.5 ml) at room temp for 19 h. The mixture was worked up as usual to leave oily residue (187 mg), which was purified by preparative TLC over silica gel with benzene–ethyl acetate (9 : 1) to give **11a** (161 mg) in pure state, colorless oil and $[\alpha]_D$+21°; MS, *m/e* 380 (M^+), 320, 260, and 200; IR, ν_{max} 3080, 1750, 1650, and 895 cm^{-1}; NMR, δ 0.90 (3H, d, J=7 Hz, 14-C$\underline{H}_3$), 1.73 (3H, s, 13-C$\underline{H}_3$), 2.00 and 2.04 (3H and 6H, s, 3OCOC$\underline{H}_3$), 3.86 and 4.25 (each 1H, do ABq, J=11, 9 and 11, 4 Hz, 2$\underline{H}$ at C_{15}), 4.70 (2H, br s, 12-C$\underline{H}_2$), and 4.76 (2H, br m, W_H=30 Hz, 2$\underline{H}$ at C_2 and C_3).

(*iii*) A soln of **4a** (33 mg) in ethanol (1.5 ml) was stirred with sodium borohydride (4 mg) at room temp for 4 h. The reaction mixture was worked up as usual to give oil, which was purified by preparative TLC over silica gel to yield **11b** (18 mg) in pure state, colorless oil and $[\alpha]_D$+24°; MS, *m/e* 320 ($M^+ - H_2O$), 295, 278, 260, 218, 200, 187, and 159; IR and NMR, in the text.

(*iv*) A soln of **4** (10 mg) in chloroform (0.3 ml) and Py (0.2 ml) was stirred with benzoyl chloride (25 mg) at room temp for 3.5 h. The mixture was diluted with chloroform, washed with 0.5 M sulfuric acid, water, 5% aq sodium carbonate, and water, dried, and evaporated to leave amorphous residue, which was treated with sodium borohydride (15 mg) at room temp for 3 h. The reaction mixture was worked up as usual to leave oily residue, (19 mg), which was purified by preparative TLC over silica gel with benzene–ethyl acetate (5 : 2) to give **11c** (8.5 mg), mp 58—59 °C (from hexane): CD, $\Delta\varepsilon$ −19.2 at 235 nm and +5.9 at 219 nm (c 1.6×10^{-3} in ethanol, cell length 0.01 dm); MS, *m/e* 462 (M^+), 340 ($M^+ - C_7H_6O_2$), 322, 218, and 105 (base); IR ($CHCl_3$), ν_{max} 3480, 3080, 1720, 1643, 1607, 1452, 1315, 1280, 1175, 1115, 1024, 975, and 890 cm^{-1}; NMR, δ 0.99 (3H, d, J=7 Hz, 14-C$\underline{H}_3$), 1.75 (3H, s, 13-C$\underline{H}_3$), 3.45 and 3.99 (each 1H, do ABq, J=11, 8 and 11, 3 Hz, 2$\underline{H}$ at C_{15}), 5.15 (1H, t, J=10 Hz, $\underline{H}$ at C_3), 5.21 (1H, m, $\underline{H}$ at C_2), 7.47 and 7.93 (6H and 4H, m, $2COC_6\underline{H}_5$).

*Tetrahydrooxylubimin (**12**) and Its 15-Brosylate (**12a**).* (*i*) Compound **4** (40 mg) was hydrogenated over Adams platinum (50 mg) in ethanol (10 ml) at room temp for 3 h, when 2 mol of hydrogen had been absorbed. After being worked up as usual, the reaction mixture left amorphous residue (39 mg), which crystallized on trituration with isopropyl ether–methanol. This was recrystallized from the same solvent mixture to give **12** (18 mg), mp 163—165 °C; MS, *m/e* 256 (M^+), 238, 220, 195, and 177, IR, in the text. This compound was also obtained by hydrogenation of **11**.

(*ii*) Compound **12** (63 mg) was stirred with *p*-bromobenzenesulfonyl chloride (89 mg, 1.4 equiv) in Py (1.2 ml) at 5 °C for 22 h. The mixture was worked up as usual to leave oily residue (97 mg), which was purified by preparative TLC over silica gel with benzene–ethyl acetate (5 : 1) to give **12a** (51 mg), mp 97—100 °C. This was recrystallized from isopropyl ether for analysis: mp 98—100 °C; MS, *m/e* 458 (M^++2), 456 (M^+), 440, 438, and 236 ($M^+ - BrC_6H_4SO_3H$); IR ($CHCl_3$), ν_{max} 3360, 1583, 1373, and 1183 cm^{-1}; NMR, δ 0.84 and 0.99 (6H and 3H, each d, J=7 Hz, 12-, 13-, and 14-C$\underline{H}_3$), 2.93 (1H, do d, J=10 and 8 Hz, $\underline{H}$ at C_3), 3.41 (1H, br m, W_H=24 Hz), 3.41 and 4.27 (each 1H, do ABq, J=11, 8 and 11, 4 Hz, 2$\underline{H}$ at C_{15}), and 7.75 (4H, s, $BrC_6\underline{H}_4SO_4$).

*The Lemieux-Johnson Oxidation of **11a** to Methyl Ketone (**13**).* To a soln of **11a** (31 mg, 8.2×10^{-4} mol) in distilled dioxane (2ml) and water (0.6 ml) was added osmium tetraoxide (5 mg) at room temp under stirring. The soln became dark brown. To this soln was added sodium metaperiodate (60 mg, 2.8×10^{-3} mol) at 27 °C (bath temp) under stirring. After being kept for 2 h, the reaction mixture was diluted with water (10 ml), and the aq soln was extracted with ether (30 ml) and chloroform (20 ml). Both the solns were combined, washed with water, dried, and evaporated to leave oily residue (32 mg), which was purified by preparative TLC over silica gel with benzene–ethyl acetate (2 : 1). A main fraction gave **13** (27 mg), colorless oil and $[\alpha]$ +27 °; MS, *m/e* 382 (M^+), 367, 325, 322, 307, 280, 262, 220, 219, 160,

and 159; IR, ν_{max} 1745, 1713, 1435, 1370, 1230, 1053, and 1030 cm^{-1}; NMR δ 0.90 (3H, d, J=7 Hz, 14-C$\underline{H}_3$), 2.00 and 2.06 (3H and 6H, s, 3OCOC$\underline{H}_3$), 2.16 (3H, s, COC$\underline{H}_3$), 2.83 (1H, br m, W_H=25 Hz, $\underline{H}$ at C_7), 3.82 and 4.29 (each 1H, do ABq, J=11, 8 and 11, 3 Hz, 2$\underline{H}$ at C_{15}), 4.69 (1H, t, J=10 Hz, $\underline{H}$ at C_3), and 4.75 (1H, m, $\underline{H}$ at C_2).

Conversion of ***12a*** *into Hydroxyoxolane (****14****).* Compound **12a** (51 mg) in *t*-butyl alcohol (0.8 ml) was stirred with potassium *t*-butoxide (0.15 ml), which had been prepared by dissolving potassium (37.5 mg) into *t*-butyl alcohol (1 ml), at 0 °C for 30 min under nitrogen. The mixture was mixed with water (4 ml) and extracted with ether. The ether soln was washed with water, dried, and evaporated to leave **14** (26 mg), showing a single spot on TLC. This was purified by preparative TLC to give **14** in pure state, oil; MS, *m/e* 238 (M^+), 220, 195, 177, 151, 109, and 95 (base); IR and NMR, in the text.

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