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THE CONFIGURATION OF OXYLUBIMIN[1)]

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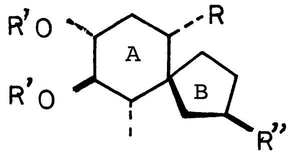
The configuration of oxylubimin was determined on the basis of the NMR spectrum in the presence of the shift reagent and the CD spectrum of oxylubimin derivatives.

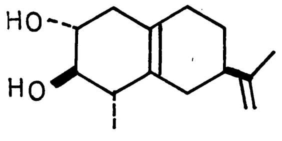
In a previous paper[2)] we reported the structure of oxylubimin (1), an antifungal metabolite from diseased potatoes. The chemical and spectral data in the paper evidently indicated that two hydroxy and methyl groups on the A ring of 1 possess equatorial conformations on the chair form ring. Later, Stoessl and coworkers[3)] deduced the same relative configuration for 1 on the same spectral ground as ours. However, the configuration of an isopropenyl group on the B ring, including the disposition to the A ring, has been left undecided. Only recently, they have completely defined the *relative* configuration of the whole molecule of 1 on the basis of the X-ray crystallography.[4)] This prompts us to publish our alternate approach, which leads to the same conclusion and also involves decision of the *absolute* configuration.

Hydride reduction of 1 gave triol (2),[5)] mp 170-171°C, which on hydrogenation formed the dihydro derivative (3), mp 163-165°C. Compound 3, when treated with *p*-bromobenzenesulfonyl chloride, underwent partial brosylation to give monobrosylate (4), mp 97-100°C, in a 44% over-all yield, which on treatment with potassium *t*-butoxide in *t*-butyl alcohol at 0°C for 30 min yielded oxolane (5), oil, quantitatively; m/e 238 (M^+) and 220; ν_{max} (film) 3420, 1390, 1372, 1079, and 1010 cm^{-1}; δ ($CDCl_3$) 0.88 (6H, d J = 6.5 Hz), 1.06 (3H, d J = 8, 4-$C\underline{H}_3$), 1.90 (1H, t J = 4.5, 10β-$\underline{H}$), 2.36 (1H, d J = 12, 1β-$\underline{H}$), 3.66 (1H, do d J = 8 and 4.5, 15a-$\underline{H}$), 3.78 (1H, d J = 5, 3α-$\underline{H}$), 3.87 (1H, d J = 8, 15b-$\underline{H}$), 4.18 (1H, t J = 5, 2β-$\underline{H}$). The NMR spectrum indicated the A ring to take a chair form with the three substituents at C_2, C_3, and C_4 all axial (note $J_{3\alpha,4\beta}$ = 0 Hz). 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. 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 ring. Only one exceptional signal at a low field, δ 9.34, was reasonably assigned to the 6β-proton (H_A), as the C_6 atom was disposed 1,3-diaxial to the 3β-hydroxy group (formula 5).[6)] Spin-decoupling studies (Table 1) confirmed that the 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 1. In view of the absolute configuration (R) of C_7 in naturally occurring vetispiranes,[7] oxylubimin is represented by formula 1, assuming that the three substituents on the A ring of 1 possess the same absolute configurations as those of rishitin[8] (6). This assumption was verified by measurement of the CD spectrum ("Benzoate rule")[9] of 2,3-dibenzoate (7), mp 58-59°C, of triol 2; $\Delta\varepsilon$ -19.2 (235 nm) and +5.9 (219) [cf., $\Delta\varepsilon$ -17.6 (235 nm) and +6.1 (218) for rishitin dibenzoate[8b)]]. All these results have completely defined the configuration of oxylubimin (1).

Table 1 The NMR spectrum of oxyoxolane (5) in the presence of the shift reagent $Eu(dpm)_3$ (CCl_4, 100 MHz) and spin-decoupling results

Irradiated proton	Observed proton (multiplicity change and splitting decoupled)
H_A (δ 9.34) do d	H_B do d → d (13 Hz); H_C sex → qui (8)
H_B (δ 6.08) do d	H_A do d → d (13 Hz); H_C sex → qui (9)
H_C (δ 4.69) sex	H_A do d → d (8 Hz); H_B do d → d (9); H_D change
H_D (δ 3.23) m	H_C sex → qui (8 Hz); $2CH_3$ (δ 2.05 and 1.96) each d → s (6.5)





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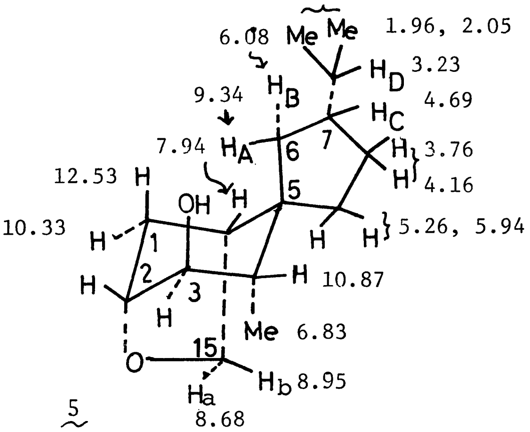
1 R=CHO, R'=H, R"=C(CH_3)=CH_2

2 R=CH_2OH, R'=H, R"=C(CH_3)=CH_2

4 R=CH_2OBs, R'=H, R"=CH(CH_3)$_2$

7 R=CH_2OH, R'=COC_6H_5, R"=C(CH_3)=CH_2



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References and Footnotes

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3) A. Stoessl, J. B. Stothers, and E. W. B. Ward, Chem. Commun., 1975, 431.
4) G. Birnbaum, C. P. Huber, M. L. Post, J. B. Stothers, J. R. Robinson, A. Stoessl, and E. W. B. Ward, Chem. Commun., 1976, 330.
5) All new compounds gave elementary analyses, Mass, IR, and NMR spectra in good accord with the assigned structures. Abbreviations "s, d, t, qui, sex, m, and do" in the NMR spectra denote " singlet, doublet, triplet, quintet, sextet, multiplet, and double," respectively.
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