A 2,3-Dihydroxygermacrene and Other Stress Metabolites of *Datura stramonium*

By A. STOESSL,[*†] J. B. STOTHERS,[§] and E. W. B. WARD[†]

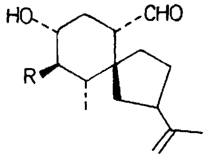
([†] *Agriculture Canada Research Institute and* [§] *Chemistry Department, University of Western Ontario, University Sub Post Office, London, Ontario* N6A 5B7, *Canada*)

Summary A 2,3-dihydroxygermacrene (**3**) has been isolated together with lubimin, hydroxylubimin, and capsidiol from *Datura stramonium* and is of interest as a possible biogenetic precursor for several stress metabolites of the *Solanaceae*.

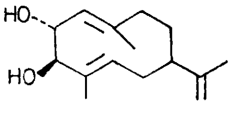
IN a recent report[1] on the structure and distribution of the phytoalexin lubimin[2] (**1**), we outlined a biogenetic scheme linking most of the known, bicyclic, sesquiterpenoidal stress compounds of the *Solanaceae*. Further definition can now be added to these proposals by the isolation from *Datura stramonium* of 4-hydroxylubimin[3] (**2**) and a previously unknown 2,3-dihydroxygermacrene (**3**), as stress metabolites induced together with (**1**) by inoculation with *Monilinia fructicola* and other fungi. A small amount of capsidiol (**4**), already established as a stress compound from *Capsicum frutescens*[4] and *Nicotiana* spp.,[5] was also isolated and identified.

4-Hydroxylubimin, $C_{15}H_{24}O_3$ (precise mass measurement) had m.p. 96—98 °C, $[\alpha]^{32}_{589}$ + 55° (*c*, 0·5 EtOH), λ_{max} 293 (log ϵ 1·48), ν_{max} ($CHCl_3$) 3585, 3420, 3090, 2745, 1725, and 900 cm^{-1}, which, with the ^1H and ^{13}C n.m.r. data led to structure (**2**). The ^{13}C n.m.r. spectrum in $CDCl_3$ contained the usual signals[1,4] for the isopropenyl group (21·2, 109·0, and 147·0), an aldehydic carbonyl at 204·3, two –CHOH– signals at 74·1 and 76·8, three methine carbons (57·6, 47·3, and 47·1), a quaternary carbon at 48·3 and a methyl carbon at 11·2 as well as four –CH_2– groups (42·2, 32·7, 30·5, and

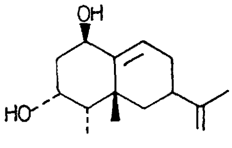
26·8 p.p.m.). In the ^{1}H n.m.r. spectrum, signals for carbinyl protons at δ 3·42 (m, $\nu_{\frac{1}{2}}$ *ca.* 25 Hz) and 2·98 (dd, $\nu_{\frac{1}{2}}$ *ca.* 20 Hz) were shown to arise from those protons bonded to the carbons at 74·1 and 76·8 p.p.m. respectively, by selective decoupling. Further, the carbinyl protons were mutually coupled (*J ca.* 10 Hz) and the remaining coupling of *ca.* 10 Hz for the carbinyl absorption at δ 2·98 was eliminated by simultaneous irradiation at δ 1·58, which also collapsed the methyl doublet (δ 1·06) to a singlet. Double irradiation of the formyl proton absorption (δ 9·78, d, *J ca.* 3 Hz) showed this proton to be coupled with a proton at δ 2·33 whose absorption contained a large coupling of *ca.* 10 Hz. Other decoupling experiments indicated that the protons at δ 2·33 and 3·42 were coupled to the same two other protons. These results are accommodated by the fragment $\geqslant$C–CH(Me)–CH(OH)–CH(OH)–CH$_2$–CH(CHO)–C$\leqslant$ and the magnitudes of the vicinal coupling constants for each of the methine and carbinyl protons indicate that each is axial. Upon comparison with the data for lubimin,[1] these results clearly point to (**2**) as the most probable formulation.



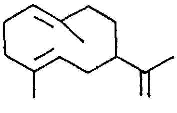
(1) R = H
(2) R = OH



(3)



(4)



(5)

Compound (**3**), $C_{15}H_{24}O_2$ (precise mass measurement) was a syrup, $[\alpha]^{32}_{589}$ + 103 (*c*, 1·0 EtOH), ν_{max} (liquid) 3370, 3080, 1670, 1650, 890, and 842 cm^{-1}, with no apparent carbonyl absorption and only end absorption in the u.v. [*cf.* germacrene A (**5**),[6] ν_{max} (liquid) 3060, 1660, 1640, 880, and 840 cm^{-1}]. The ^{13}C n.m.r. spectrum ($CDCl_3$) contained the signals characteristic of the isopropenyl group (20·2, 107·7, and 153·1), four olefinic signals (–CH=, 127·2 and 131·3; =C<, 130·9 and 140·6), two carbinyl carbon resonances (–CHOH–) at 74·9 and 84·4, two methyl carbons (12·5 and 17·4), one methine (51·4) and three methylene signals (34·2, 34·4, and 41·6 p.p.m.). The ^{1}H n.m.r. spectrum ($CDCl_3$) displayed three methyl singlets (δ 1·49, 1·59, and 1·73), four olefinic proton patterns and two carbinyl protons [δ 3·92 (d), *J ca.* 8 Hz and δ 4·35 (dd), *J ca.* 8 and *ca.* 10 Hz] which were shown to be bonded to the carbons at 84·4 and 74·9 p.p.m., respectively, by selective decoupling. ^{1}H–^{1}H decoupling experiments showed that the carbinyl proton at δ 4·35 was coupled to the other carbinyl proton (δ 3·92) and an olefinic proton at δ 4·95 (d), *J ca.* 10 Hz. These findings gave the part structure, –(Me)C=CH–CH(OH)–CH(OH)–C(Me)=CH–CH$_2$– which, with the isopropenyl group, accounted for 12 of the 15 carbons with one methine and two methylene groups remaining. Thus, on biogenetic grounds, we propose the 2,3-dihydroxygermacrene (**3**) structure for this compound.

Lubimin and 4-hydroxylubimin have the same absolute configuration at C-1, as shown by their well defined Cotton effects in EtOH at 32 °C [(**1**), $[\alpha]_{322}$ + 712°, $[\alpha]_{299}$ 0°, $[\alpha]_{280}$ −390°; (**2**), $[\alpha]_{322}$ + 1010°, $[\alpha]_{302}$ 0°, $[\alpha]_{279}$ −820°]. This is consistent with a common origin and a hydroxygermacrene could serve as an almost direct precursor for these as well as other sesquiterpenes found in *D. stramonium* and other solanaceous plants.

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[3] During the preparation of this manuscript, N. Katsui, A. Matsunga, and T. Masamune, *Tetrahedron Letters*, 1974, 4486 reported the isolation, from infected potatoes, of a compound regarded as 'oxylubimin.' Their compound seems likely to be the same as (**2**) although they gave no stereochemical assignments but we have isolated (**2**) from inoculated potatoes.

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