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FUNGAL EXTRACTIVES—XI[1]

ON THE BIOGENETIC INTERRELATIONSHIP BETWEEN THE MARSMANE- AND VELLERANE SESQUITERPENE SKELETONS

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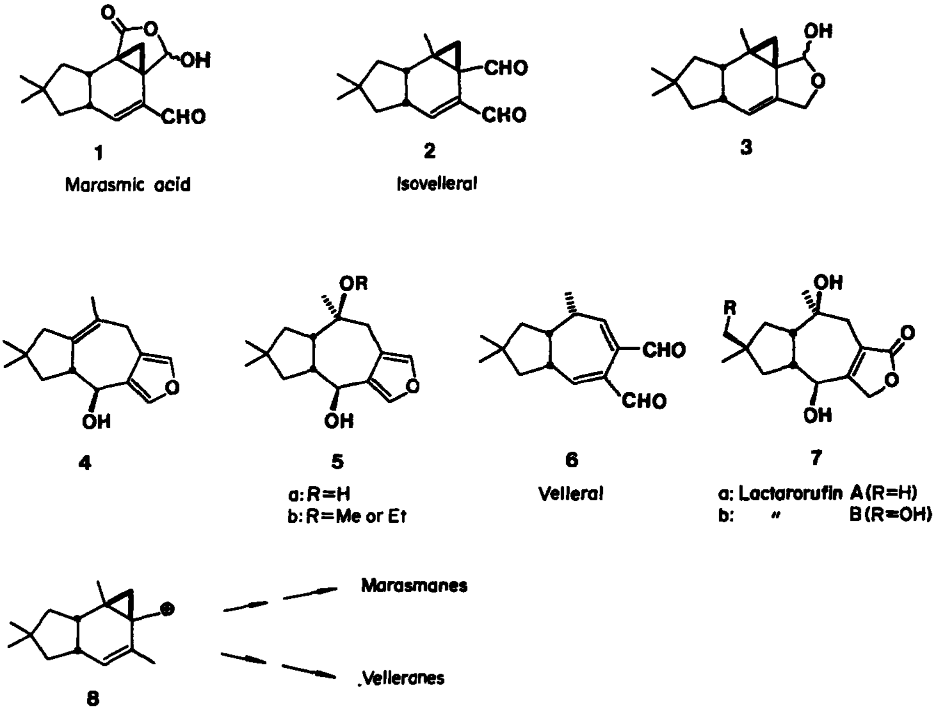
Abstract—The cyclopropane ring of isovelleral (marsmane skeleton) opens by a thermal rearrangement giving a hydroazulenic furan with vellerane skeleton.

During the last decade, a number of fungal sesquiterpenes with marasmane (**1**[2], **2**[3] and **3**[4]) and vellerane skeletons (e.g. **4**[4–6], **5**[4–8], **6**[9] and **7**[10]) have been reported (Scheme 1). Several authors[4,11,12] have suggested biosynthetic routes to these compounds with the cation **8** (or some equivalent species) as a common precursor to both the marasmanes and the velleranes. Experimental proof seems however to be lacking (investigation is reported to be in progress, *cf* Ref. 4). Compound **5a** has also been suggested[7] to be the biosynthetic precursor to lactarorufin A (**7a**).

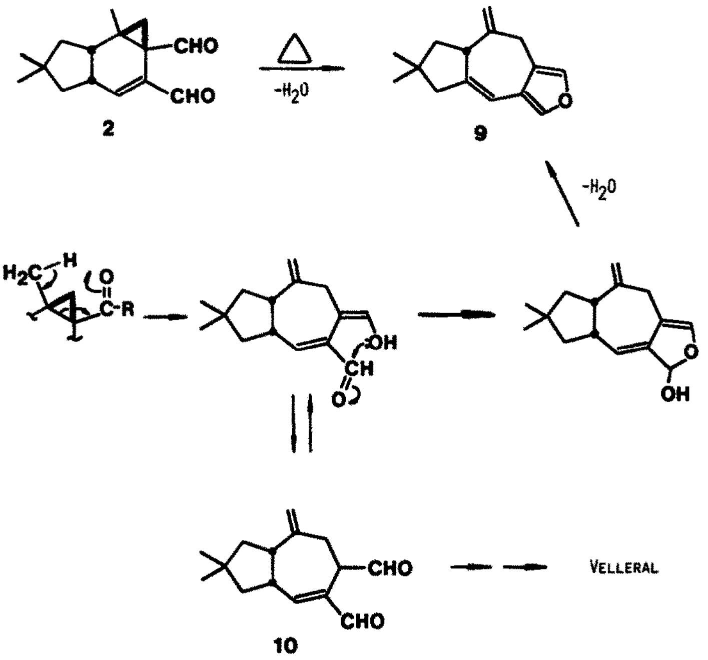
Cyclopropyl ketones of the type shown in Scheme 2 (R = methyl or *n*-hexyl) are known to undergo a thermal ring opening reaction leading to λ,δ-unsaturated ketones.[13,14] We now wish to report that isovelleral **2** undergoes a smooth thermal transformation (210°/30 min or 110°/several days) to the dienofuran **9** (suggested name: pyrovellerofuran) via a transient intermediate (TLC; presumably the dialdehyde **10**; the ring-forming reaction can of course occur via enolisation of either of the two aldehyde groups). Compound **9** appears to be a very reasonable biosynthetic precursor to the furan alcohols **4** and **5** and furthermore, compound **10** would provide a precursor to velleral **6**.

This "biomimetic" transformation of isovelleral **2** to pyrovellerofuran **9** thus indicates that isovelleral (and possibly also compound **3**), because of the methyl-formyl substituted cyclopropane ring, is a key intermediate in the biosynthesis of vellerane sesquiterpenes.

Structure of pyrovellerofuran **9**. Mass spectrometry ($M^+ = 214$) and ^{13}C NMR (15 C, 18 H) gave the molecular formula ($C_{15}H_{18}O$). IR, ^{1}H and ^{13}C NMR showed a 3,4-disubstituted furan. Extensive ^{1}H NMR decoupling experiments (see experimental) in combina-



Scheme 1.



Scheme 2.

tion with the other spectroscopic data permitted an unconditional construction of the structure 9. Furthermore, the ^{1}H NMR chemical shifts of the furan and vinyl protons are in accord with those of very similar furan compounds prepared in this laboratory.[15]

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on Jeol MH-100 and Jeol FX-60 instruments respectively.

Pyrovellerofuran 9. Isovelleral (2; 400 mg) was heated (210°: 30 min) in a sealed glass tube (both Pyrex and soda glass gave the same result) filled with N_2. The crude product was chromatographed (SiO_2, 60 g; CH_2Cl_2) giving almost pure pyrovellerofuran (yield 62%). This was rechromatographed on a preparative TLC plate (SiO_2, 20 × 20 × 0.2 cm; EtOAc/hexane: 1/20) which had been pre-eluted with ether in order to remove possible impurities. The pure material had n_D^{23} 1.5500; $[\alpha]^{25}$ + 189.4° (589 nm), + 199.0° (578 nm), + 230.8° (546 nm), + 444.0° (436 nm), (c 0.72, ethanol); UV (ethanol): λ_{max} 241 nm (log ϵ 4.2); IR (film): 3140, 3088, 3032, 1735, 1650, 1535, 1390, 1373, 1058, 914, 900, 880, 860, 787, 740 cm^{-1}; ^{1}H NMR ($CDCl_3$, TMS) δ: 7.18, 7.13 (m, 1 H each, furan-*H*), 6.06 (m, 1 H, =*CH*-furan), 4.87 (m, 2 H, =CH_2), 3.48, 3.32 (ABq, 1 H each, J_{AB} = 15.0 Hz, = C-CH_2-furan), 3.0–3.5 (m, 1 H, *CH*-CH_2, X part of ABX system), 2.27 (m, 2 H, CH = C-CH_2), 1.86, 1.61 (AB part of ABX system, 1 H each, J_{AB} = 12.0 Hz, J_{AX} = 12.2 Hz, J_{BX} = 7.0 Hz, CH_2-CH), 1.08, 0.98 (s, 3 H each, $C(CH_3)_2$) ppm; ^{13}C NMR ($CDCl_3$, TMS) δ: 145.7 (s), 145.0 (s), 139.8 (d), 138.7 (d), 123.4 (s), 120.8 (s), 110.9 (d), 108.9 (t), 49.0 (t + d), 45.5 (t), 36.2 (s), 34.8 (t), 29.4 (q), 27.7 (q) ppm; mass spectrum *m/e* (rel intensity) 215 (19), 214 (M^+, 86, $C_{15}H_{18}O$), 199 (38), 158 (34), 128 (15), 115 (18), 58 (100, base peak).

In a separate experiment, isovelleral 2 was heated at 110° in an open tube under nitrogen. The reaction was followed by TLC (SiO_2, CH_2Cl_2). The starting material (2; R_f = 0.35) slowly disappeared and a transient compound (probably 10; R_f = 0.42) was formed together with pyrovellerofuran (9; R_f = 0.85) which finally was the only compound detected (except for some unidentified tailing substances). All isovelleral was consumed after seven days.

^{1}H NMR double resonance experiments. The following conclusions could be drawn. The AB quartet at 3.48 and 3.32 ppm and the multiplet at 6.06 ppm are coupled (long-range) to the signals at 7.18 and 7.13 ppm. The signal at 6.06 ppm is coupled (long-range) to the signals at 2.27 and 3.0–3.5 ppm. The multiplet at 3.0–3.5 ppm is coupled (vicinal) to the signals at 1.86 and 1.61 ppm (ABX system).

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