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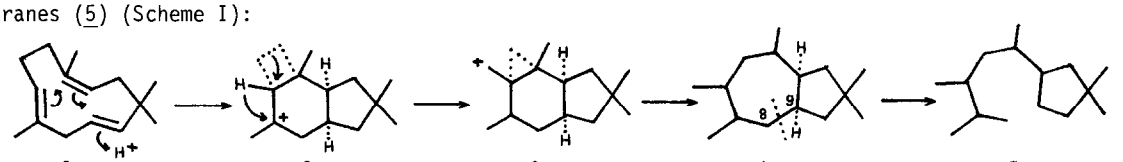
BIOGENESIS-LIKE CONVERSION OF MARASMANE TO LACTARANE AND SECO-LACTARANE SKELETON

Maria De Bernardi, Giovanni Vidari and Paola Vita-Finzi
Istituto di Chimica Organica - Università di Pavia - Via Taramelli 10 - 27100 Pavia (Italy)

Katia Gluchoff Fiasson
Université Claude Bernard Lyon-1 - Departement de Biologie Vegetale - Service de Mycochimie
F-69622 Villeurbanne Cedex (France)

Summary: Some sesquiterpene furans with lactarane and seco-lactarane skeletons which previously have been isolated from many Lactarius and Russula species, were chemically derived from stearyl velutinal via a transformation similar to the biosynthetic pathway.

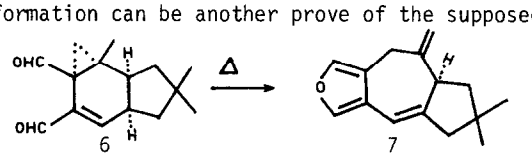
Lactaranes and seco-lactaranes are two classes of sesquiterpenes often containing furan or lactone rings which have been found in many mushrooms of the genus Lactarius and Russula[1]. They have been thought[2] to be biosynthesized from humulene (1) via protoilludyl cation (2) to the marasmane skeleton (3) which through cation (3) (or an equivalent ion) rearranges to the lactarane skeleton (4). C(8)-C(9) bond cleavage of the lactaranes gives rise to the seco-lactaranes (5) (Scheme I):



1 2 3 4 5

Scheme I

Biosynthetic studies to confirm this general scheme have not yet been published but the co-occurrence in few cases of marasmane, lactarane and seco-lactarane sesquiterpenes in the same mushroom[1] gives a support to this hypothesis. Moreover isovelleral (6) was thermally converted, albeit in quite drastic conditions, to a synthetic furane lactarane, pyrovellerofuran (7)[3] and this "biomimetic" transformation can be another prove of the supposed biogenesis.



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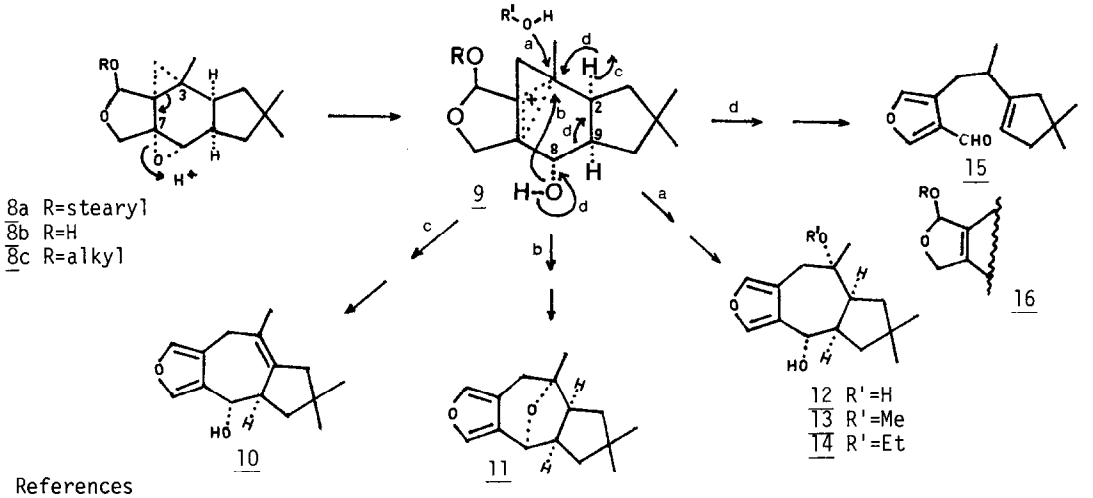
We wish to report here a chemical conversion of a marasmane compound to some furolactaranes and seco-lactaranes which occurs in very mild conditions along the biosynthetic pathway. We have observed that in the recently isolated stearyl velutinal[4] (8a) three structural features, i.e. the epoxide and the cyclopropane rings and the acetal function are strategically placed in such a way that the molecule becomes extremely reactive towards electrophilic attack. This leads to the easy loss of a molecule of stearic acid and to the stereospecific rearrangement of the fused cyclopropane-cyclohexane system forming the seven membered ring of the lactarane skeleton.

In fact when (8a) is stirred in wet acetone for few hours or is adsorbed on silica gel, it readily decomposes to a mixture of products among which furanol[5] (10), furanether A[6,7] (11), furandiol[5] (12) and lactaral[8] (15) were isolated and identified by comparison of their spectral and physical data with those of authentic samples. Similarly when (8a) is treated with absolute MeOH or EtOH overnight, 3-alkoxy derivative (13) or (14)[9] were formed in high yields along with

furanol (10) and other not yet identified sesquiterpenes. The possible mechanism of these transformations is depicted in Scheme II.

The cyclopropyl assisted opening of the epoxide in (8) leaves a vacant orbital at C(7) which is approximately parallel to the bent orbitals in the cyclopropane ring: electron delocalization in the cyclopropylmethyl cation can be depicted as the non-classical ion (9)[10]. Nucleophilic attack by any reactive at C(3) occurs with formation of a seven membered ring and gives an unstable 2,5-dihydrofuran (16) which readily eliminates a molecule of ROH[11] yielding the heteroaromatic ring. Thus intermolecular attack by H_2O or alcohols from the less hindered concave face of (9) leads to (12-14) while intramolecular attack by the hydroxyl at C(8) gives the internal ether (11). Loss of a proton from C(2) can explain the formation of furanol (10). On the other hand examination of molecular models reveals that the carbonium ion (9) can assume a conformation where the H-C(2) bond and the vacant orbital at C(3) are parallel and the H-C(2) and the C(8)-C(9) bonds have the trans anti-parallel stereochemistry. Therefore (9) is expected to undergo an easy 1,2-hydride shift with fragmentation of the C(8)-C(9) bond leading to the seco-furan (15).

This "biomimetic" transformation of stearyl velutinal to lactarane and seco-lactarane terpenes indicates that stearyl velutinal can be a key intermediate in the biosynthesis of this kind of sesquiterpenes giving rise to a cation equivalent to (3). On this respect it is interesting to note that the lactaranes so far isolated from Basidiomycetes and bearing an OH at C(8) have the same stereochemistry at C(8) as in stearyl velutinal (8a).[12]



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6. In these conditions furandiol (12) does not dehydrate to (10) or (11).
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11. Stearic acid (R=stearyl) is always present in the reaction mixture. It can be formed either during the aromatization of (16) or by hydrolysis of the acetalic function.
12. The only exception is furanether B (see note 7).

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