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THE STRUCTURE OF CORIOLIN, A NEW SESQUITERPENE ANTIBIOTIC

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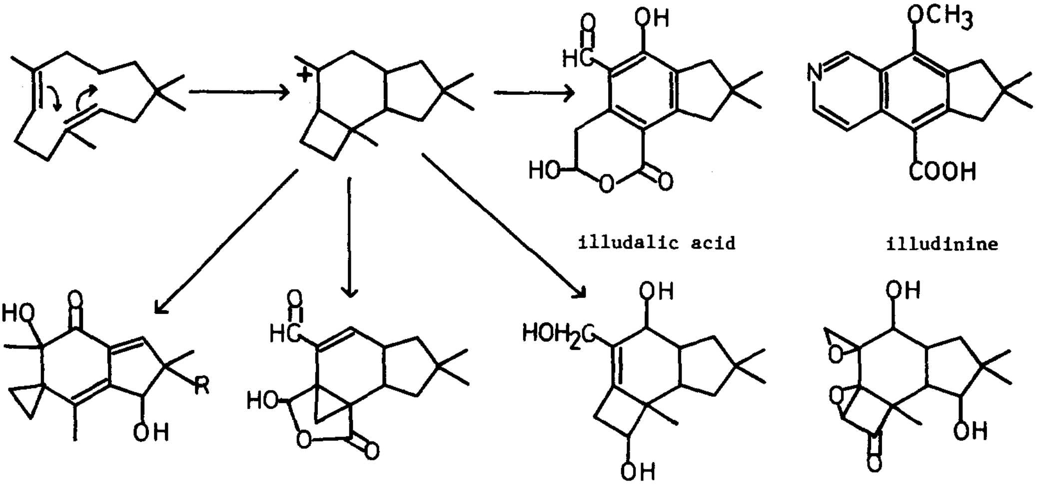
Coriolin (1) is a new sesquiterpene antibiotic isolated from a cultured broth of a Basidiomycetes, Coriolus consors (Japanese name, Nikuusuba-take). In this report the structure of coriolin is proposed as I based on spectroscopic data, chemical evidences, and biogenetic consideration.

M. Anchel et al. isolated illudin S and M (2), illudol (3), illudalic acid, and illudinine (4) from Clitocybe illudens and marasmic acid (5) from Marasmius congenus. A humulene type precursor and a tricyclic cation are involved in the biosyntheses of these compounds. We have obtained a new sesquiterpenoid dioxide, coriolin, with the same carbon skeleton as illudol.



illudalic acid

illudinine

illudin M:R=CH_3
S:R=CH_2OH

marasmic acid

illudol

I

Coriolin is a crystalline neutral substance, m.p. 175°. The molecular formula $C_{15}H_{20}O_5$ was established on the basis of analytical and mass spectral data. The mass spectrum shows major peaks at m/e 280 (molecular ion), 262 (M-18), 244 (M-2X18), 251 (M-29), 233 (M-18-29), and 205. The infrared absorption at 3450-3300 cm^{-1} and two deuterium exchangable protons in the NMR spectrum suggest the presence of two hydroxyl groups in the molecule. A ketone function is suggested by the absorption band at 1758 cm^{-1}, and a gem-dimethyl group is shown by absorption bands at 1192, 1218, 1369, and 1382 cm^{-1}.

The NMR spectrum (Fig. 1) of coriolin in D_6-dimethylsulfoxide was analyzed with aid of double resonance experiments.

Ha: 3.82(J_{af}=5.5, J_{a-OH}=6.0), Hb: 3.75(S), Hc: 3.47(J_{cg}=9.5, J_{c-OH}=3.8), Hd: 2.96(J_{de}=7.0), He: 2.87(J_{de}=7.0), Hf: 2.7(J_{af}=5.5, J_{fg}=12.0, J_{fh}=9.8, J_{fi}=9.0), Hg: 2.26(J_{gc}=9.5, J_{gf}=12.0), Hh: 1.70(J_{hf}=9.8, J_{hi}=12.5), Hi: 1.26(J_{if}=9.0, J_{ih}=12.5)

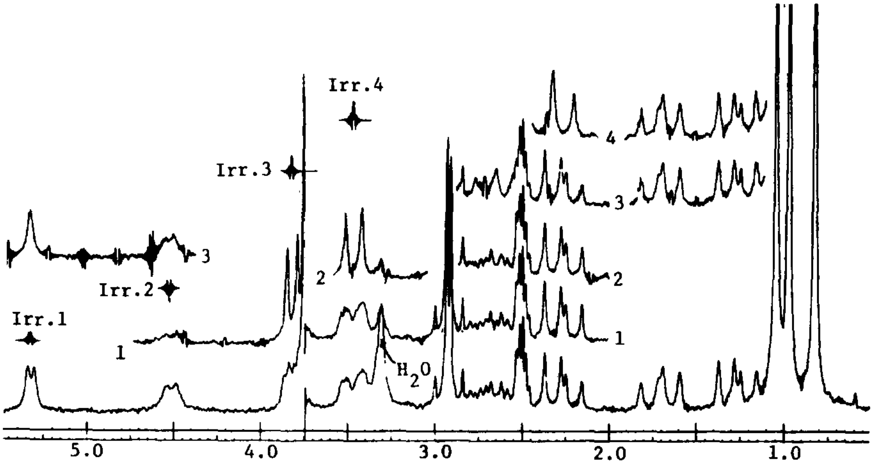
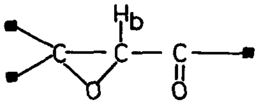


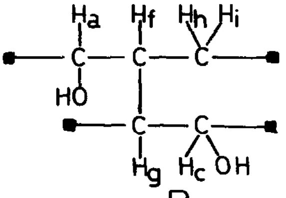
Fig. 1 NMR and NMDR spectra of Coriolin (D_6-DMSO)

The NMR spectrum shows the presence of three tertiary methyl groups (0.81, 0.97, and 1.04δ) and an exocyclic ethylene oxide (δH_d=2.96, δH_e=2.87, J=7.0 Hz, AB type quartet) (6). Two doublet signals at 5.33 (J=3.8) and 4.52 δ(J=6.0) disappeared by addition of deuterium oxide and coupled with carbinol protons H_a and H_c respectively. Among possible arrangements for a remaining oxygen only partial structure A can explain a singlet proton at 3.75 δ(H_b). The lower shift of the hydrogen, compared with a hydrogen on a usual epoxide ring, is apparently due to the effect of the adjacent carbonyl group (7).

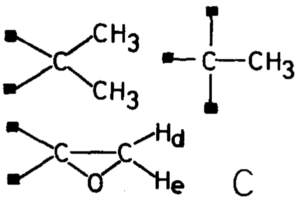
Double resonance experiments revealed that H_f coupled with H_a and H_g, and methylene protons H_h and H_i. And H_g coupled with H_c and H_f. Partial structure B can be deduced from these observations.



A

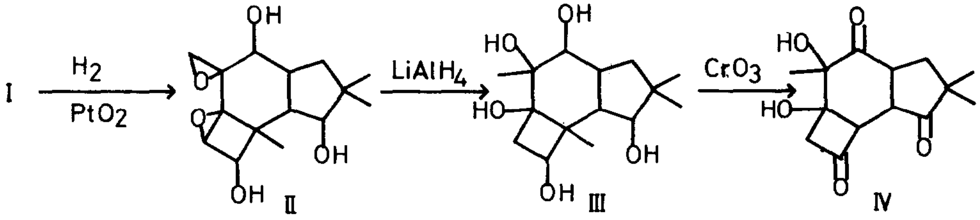


B



C

Partial structures A, B, and C account for fifteen carbons, twenty protons, and five oxygens, that is, all elements present in the molecule. From above-mentioned results, the structure of coriolin (I) can be deduced by the biogenetic consideration. The structure was confirmed by following chemical evidences.



Hydrogenation of coriolin over PtO_2 in methanol affords dihydrocoriolin (II) [$C_{15}H_{22}O_5$; m.p. 205-7°; mol wt 282 (mass spectrum)], which has no carbonyl absorption in the IR spectrum. The NMR spectrum of II is very similar to coriolin, except for appearance of a new hydroxy proton at 4.16 δ and a proton at 4.38 δ, which couple with each other with 8.0 Hz. The latter proton further couples with a proton at 3.38 δ with 2.0 Hz. The proton at 3.38 δ of II corresponds to a singlet proton H_b (3.75 δ) of I.

Reduction of II with $LiAlH_4$ in THF gives a hexahydro compound (III) [$C_{15}H_{26}O_5$; m.p. 189°]. The NMR spectrum of III (Fig. 2) shows the presence of four tertiary methyl groups (singlets at 0.78, 0.91, 1.02, and 1.06 δ in D_6-DMSO) and five hydroxy groups (3.23 δ(singlet), 3.76 δ(singlet 4.05 δ(doublet, J=6.0), 4.24 δ(doublet, J=7.5), and 4.42 δ(doublet, J=3.0) in D_6-DMSO), indicatin that an exocyclic ethylene oxide was reduced, yielding a tertiary methyl and a tertiary hydroxy groups and another oxide was also reduced, yielding another tertiary hydroxy group. A doublet proton after deuterium exchange at 4.38 δ(J=2.0) of II corresponds to a triplet at 3.82 δ(J=9.0) of III in the same condition (3).

Oxidation of III with CrO_3 in acetic acid gives a triketone (IV) which shows IR absorptions at 1782 (cyclobutanone), 1740 (cyclopentanone), and 1710 cm^{-1} (cyclohexanone). These absorptions strongly support that coriolin has a tricyclic carbon skeleton composed of four, five, and six membered rings.

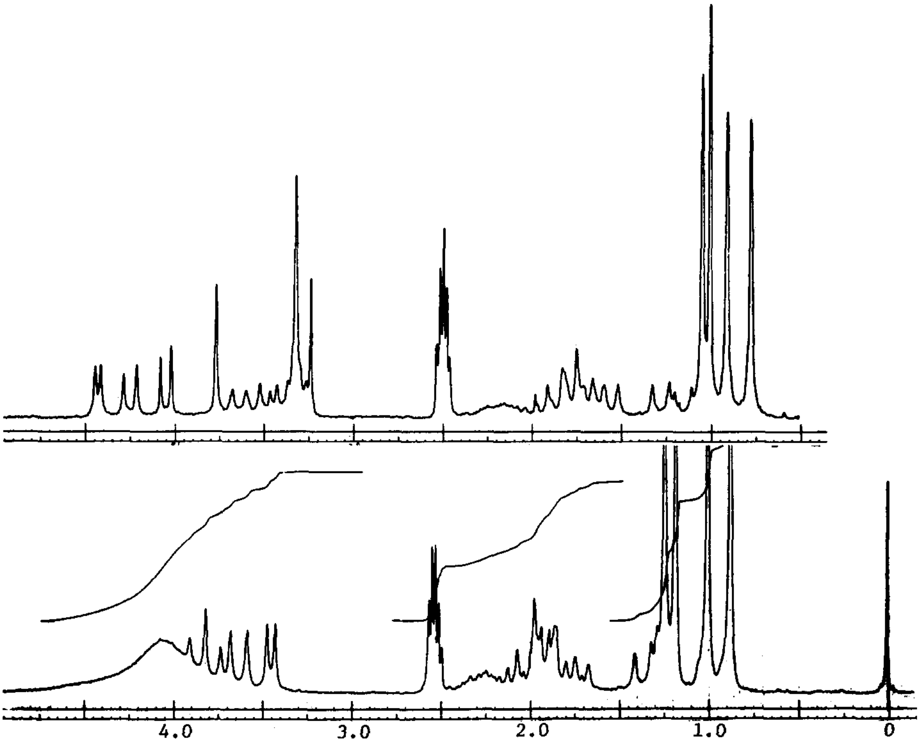


Fig. 2 NMR spectra of hexahydro compound (III)
Upper: D_6-DMSO, Lower: D_6-DMSO + D_5-Pyridine + D_2O

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