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STRUCTURE OF BULNESOL

STEREOCHEMISTRY OF GUAIOL, NEPETALINIC ACIDS AND IRIDOMYRMECINS

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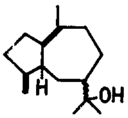
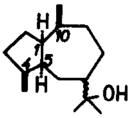
ON the basis of the facts presented in this paper, the structure I has been suggested for bulnesol, the sesquiterpenic alcohol $C_{15}H_{26}O$ which accompanies guaiol in guaiac wood oil (Bulnesia sarmienti Lor.).



I



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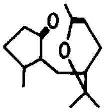

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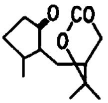

IV

In view of earlier investigations, bulnesol is a bicyclic tertiary alcohol containing one double bond.[1] On dehydration with thionyl chloride, bulnesol afforded a diene which on subsequent dehydrogenation with sulphur yielded guaiazulene, identified as the adduct with s-trinitrobenzene, m.p. 151°, undepressed on admixture of an authentic sample.

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[1] H. Wienhaus and H. Scholz, Ber. Schimmel 269 (1929).

The dihydroderivative of bulnesol, m.p. 74-76°, according to the infra-red spectrum, mixed melting point and optical rotation, is identical with the crystalline isomer of dihydroguaiol II.*

On oxidation with chromic acid in acetic acid, dihydrobulnesol afforded products identical with those from dihydroguaiol II. As a neutral material we obtained a ketone of molecular formula $C_{12}H_{20}O$ (Found: C, 80.15; H, 11.11. Calc.: C, 79.94; H, 11.18%), affording a semicarbazone, m.p. 203-208° and $[\alpha]_D^{20}$ -78.6° (AcOH) (Found: C, 65.62; H, 9.74; N, 17.69. $C_{13}H_{23}N_3O$ requires: C, 65.78; H, 9.77; N, 17.71%) and a benzylidene derivative of m.p. 147.5°. The acidic material formed a dicarboxylic acid of molecular formula $C_{12}H_{20}O_4$, m.p. 186-187° (Found: C, 63.14; H, 8.64. Calc.: C, 63.13; H, 8.83%).

Ozonolysis of bulnesol and subsequent hydrogenation of the resulting ozonide on palladized charcoal led to the enol ether III, m.p. 99-100° (Found: C, 76.14; H, 10.26. $C_{15}H_{24}O_2$ requires: C, 76.22; H, 10.24%). Infra-red spectrum of this substance exhibited absorption bands at 1744 cm^{-1} (γ (C = O) in a five-membered ring) and at 1685 cm^{-1} [γ (C = C) in enol ether].[2] Unlike bulnesol, the enol ether showed in its infra-red spectrum no frequencies for a hydroxyl group. The formation of a monosemicarbazone m.p. 174-175° (Found: C, 65.18; H, 9.32; N, 13.98. $C_{16}H_{27}N_3O_2$ requires: C, 65.49; H, 9.28; N, 14.32%) is in agreement with the presence of only one carbonyl group in III. The compound III gave iodoform at Legal test and gave a positive tetranitromethane reaction. The double bond, according to the ultra-violet spectrum, is not conjugated with the keto group. On

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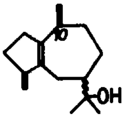
[*] Melting point of dihydroguaiol is 79°. We explain the lower melting point of dihydrobulnesol by the admixture of a stereoisomer.

[2] P. Wieland, K. Hausler, H. Ueberwasser and A. Wettstein, [Helv. Chim. Acta 41, 74 (1958)] found values about 1680 cm^{-1} for steroidal cyclic enol ethers.

ozonolysis and subsequent hydrolysis, the ether III afforded acetic acid, characterized by paper chromatography and by preparation of the p-bromophenacyl ester. The product of ozonolysis when oxidized with potassium permanganate in acetic acid, afforded acidic material from which was prepared a 2,4-dinitrophenylhydrazone, m.p. 173° insoluble in hydrogen carbonate solution (Found: N, 14.07. $C_{19}H_{24}N_4O_6$ requires: N, 13.86%). The sunstance obviously is the hydrazone of the keto-lactone IV. From the results follows the location of the double bond of bulnesol as shown in formula I.

Djerassi et al.[3] inferred for dihydroguaiol the absolute



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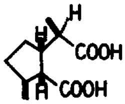
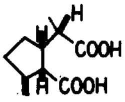


VI



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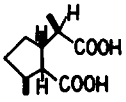
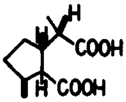


VIII



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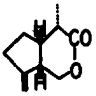
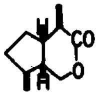


X



XI

configuration on carbon atoms C_1, C_4 and C_5.*

On the basis of the identity of dihydrobulnesol and dihydroguaiol, the

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* We wish to express our gratitude to Professor Djerassi who sent us the manuscript of his paper "On the Absolute Configuration of Guaiol. Correlation with Nepetalinic Acid" before publishing.

[3] E.J. Eisenbraun, T. George, B. Riniker and C. Djerassi, J. Amer. Chem. Soc. **82**, to be published (1960).

absolute configuration of bulnesol, expressed with formula I, may thus be inferred. Assuming the <u>cis</u>-addition of hydrogen at hydrogenation of bulnesol, we may infer also the obsolute configuration on C_{10} of guaiol and its crystalline dihydroderivative in the sense of structure V and II respectively. From the above follows even the absolute configuration on the side-chain methyl group of four isomeric nepetalinic acids[3 <u>cf.</u>4,6]; the particular acids possess following structures: the isomer of m.p. 85°: VI, the isomer of m.p. 117°: VII, the isomer of m.p. 115°: VIII and the isomer of m.p. 111°: IX. Iridomyrmecin and isoiridomyrmecin, the relationship of which to nepetalinic acids has been known[4], possess absolute configuration expressed by formulae X and XI, respectively.

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[4] R.B. Bates, E.J. Eisenbraun and S.M. McElvain, <u>J. Amer. Chem. Soc.</u> **80**, 3420 (1958).

[5] S.M. McElvain and E.J. Eisenbraun, <u>J. Amer. Chem. Soc.</u> 77, 1599 (1955).