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ABSOLUTE CONFIGURATION OF BOURGEANIC ACID: X-RAY CRYSTAL STRUCTURE OF A 4-BROMOPHENACYL DERIVATIVE OF HEMIBOURGEANIC ACID.

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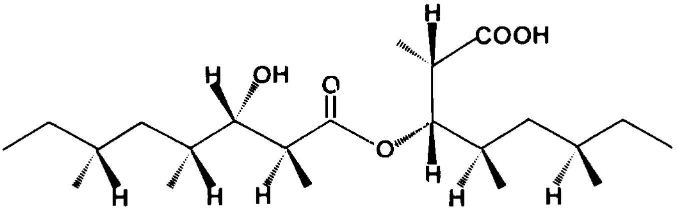
Summary: *The absolute configuration of the asymmetric centers of bourgeanic acid has been determined from an X-ray crystallographic analysis of the 4-bromophenacyl ester of hemibourgeanic acid, which is thus 3S-hydroxy-2S,4R,6R-trimethyl-octanoic acid.*

Bourgeanic acid 1, an unusual lichen metabolite, isolated from several *Ramalina* species, is formed by *O*-acylation of a molecule of the hydroxy acid 2 (hemibourgeanic acid) by a second molecule, appearing thus to be the unique "aliphatic depside" in lichens (1-3). An absolute configuration of bourgeanic acid has been proposed previously (2), based mainly on spectroscopic evidence and chemical transformations. The relative configuration of 1 was verified by an *X*-ray analysis of the crystalline natural product, but the absolute configuration could not be determined as no crystalline heavy atom containing derivative was available (4). Alkaline hydrolysis of 1 gave the non cristalline hemibourgeanic acid 2 (2), which gave the *p*-bromophenacylate 3 upon treatment with *p*-bromophenacyl bromide; 3 was then purified by column chromatography (SiO_2 gel-hexane with increasing proportion of acetone) and crystallized from methanol-water mixture. Mp = 61-62°C; $[\alpha]_D$= +4.7° (c=1.05, MeOH). 3: $C_{19}H_{27}BrO_4$. Elemental analysis (Calcd, C 57.15 %, H 6.83 %, O 16.03 % and Br 20.00 %; Found, C 57.16 %, H 6.85 %, O 15.73 % and Br 20.26 %). MS (16 eV) *m/z*: 401 and 399 $(M+H)^+$. IR (KBr disk) ν_{max} (cm^{-1}): 3460 (OH), 1740, 1723, 1703 and 1682 (C=O), and 1587 (C=C).



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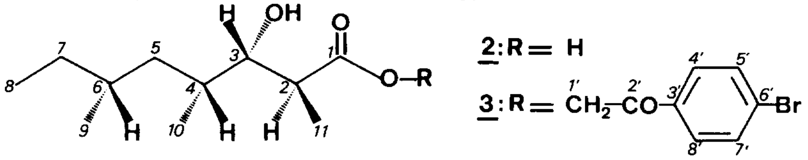


2: R= H

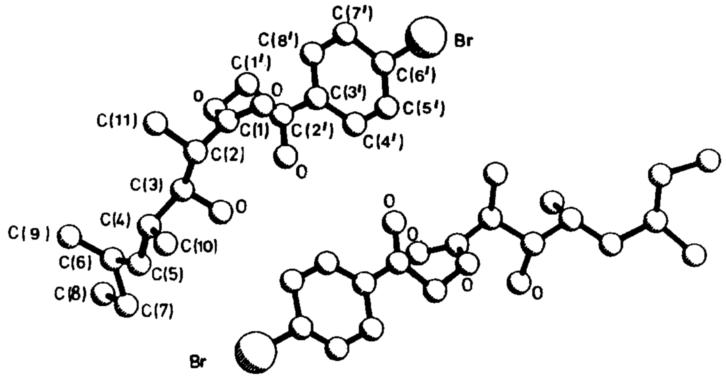
3: R= CH_2-CO-C6H4-Br

The ^1H NMR spectrum of 3 ($CDCl_3$, 400 MHz) is consistent with the structure (δ ppm): 7.66 (4H, m,arom.), 5.38 (1H,d,*J*= 16.5 Hz) and 5.32 (1H,d,*J*= 16.5 Hz) CH_2-1', 3.69 (1H,dd,*J*= 2.7 and 9.0 Hz) H-3, 3.37 (1H,br.s) OH, 2.78 (1H,dq,*J*= 9.0 and 7.0 Hz) H-2, 1.75 (1H,dtq,*J* = 2.7, 6.9 and 6.9 Hz) H-4, 1.48 (1H,m) H-5, 1.43 (1H,m) H-6, 1.33 (1H,m) H-7, 1.16 (3H,d,*J*= 7.0 Hz) CH_3-11, 1.08 (2H,m) H-5 and H-7, 0.87 (3H,d,*J*= 6.9 Hz) CH_3-10, 0.84 (3H,t,*J*= 7.4 Hz) CH_3-8, 0.84

(3H,d,*J* = 6.4 Hz) CH$_3$-9. The signals of the ^{13}C NMR spectrum of 3 have been assigned using selective proton decoupling experiments (δ ppm): 191.2 (2'), 176.1 (1), 132.9 (3'), 131.9 (5'), 131.9 (7'), 129.8 (4'), 129.8 (8'), 124.2 (6'), 91.1 (3), 65.7 (1'), 44.8 (2), 39.0 (5), 35.5 (4), 31.4 (6), 30.0 (7), 19.7 (9), 17.0 (10), 14.6 (11), and 11.4 (8).

Crystal data: C$_{19}$H$_{27}$BrO$_4$, molecular weight 399.32, space group $P2_12_11$, a = 1500.8(10), b = 4436.6(23), c = 599.6(3) pm, Z = 8, D_{ber} = 1.325 g.cm^{-3}, 2139 observed of 2892 independent reflections ($I > 2.0\sigma(I)$), R = 0.104. Synthex-P2$_1$-diffractometer, Cu-K_α-radiation (154.178 pm), $2\Theta_{max}$ = 115°. Full crystallographic data have been deposited with the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England. Complex form factors (5) were used for the refinement of the compound. The assignment of the absolute configuration was based on two independent methods, a statistical significance test ("Hamilton-test")(6), and a comparison of observed and calculated values of both configurations for the reflections most sensible to a change of the absolute configuration. The comparison of the two R_G-values ($\Sigma\ [w(F_o - F_c)^2/\ wF_o^2]^{\frac{1}{2}}$ of the two enantiomers supported the assumed configuration on a high significance level. The assumption of the opposite configuration could be rejected on the 0.005 level. Of the 100 reflections most sensible to a change of absolute configuration 70 supported the mentioned one and only 30 the opposite one. The figure shows a perspective view of the molecule, which has the *S*-configuration for carbons 2 and 3, and the *R*-configuration for carbons 4 and 6. Thus bourgeanic acid is 2*S*,4*R*,6*R*-trimethyl-3*S*-(3'*S*-hydroxy-2'*S*,4'*R*,6'*R*-trimethyl octanoyloxy)-octanoic acid in agreement with the previously proposed structure.

Figure: Perspective view of the crystal structure of 3.



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