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ABSOLUTE STEREOCHEMISTRY OF THE TRIOL MOIETY OF GYMNOPRENOLS

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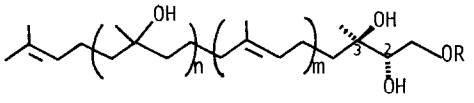
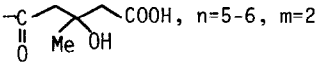
Summary: Absolute configuration of the triol portion in gymnoprenols, the polyisoprenepolyols obtained from mushroom Gymnopilus spectabilis, has been established as 2S and 3R by a stereocontrolled synthesis of the enantiomer of a chemical degradation product of gymnoprenol.

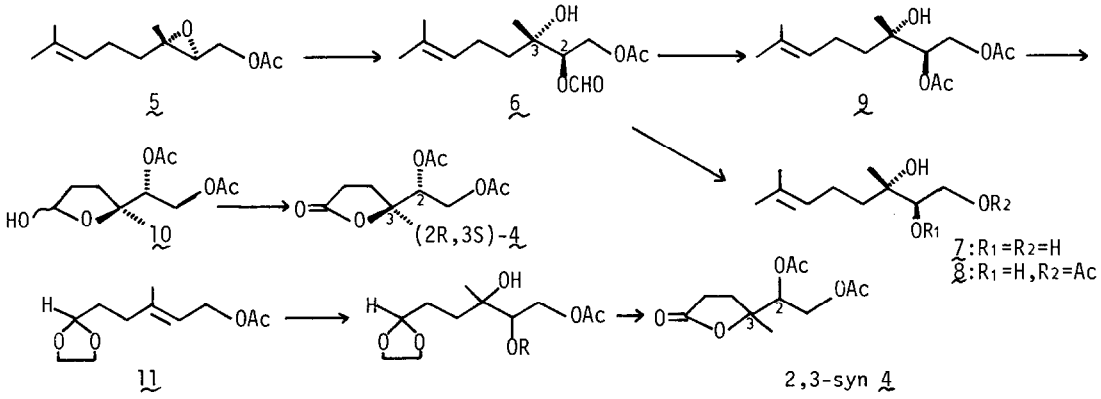
We recently reported the isolation of gymnoprenol-A (1), -B (2) and gymnopilin (3) from the fruiting bodies of a hallucinogenic mushroom, Gymnopilus spectabilis[1)2)]. The plane structure of these substances was determined by chemical degradation and spectroscopic analysis. It was found that these compounds belong to a novel type of polyisoprenepolyols occurring as a mixture of isoprene homologs with 45 to 60 carbon atoms. The relative stereochemistry of the triol moiety located at a terminal position of the chain was shown to be anti as to C-2 and C-3[3)], but the absolute configuration of this and other chiral centers remains to be elucidated. In the present paper we describe the absolute stereochemistry at C-2 and C-3 on the basis of the stereocontrolled synthesis of the (2R,3S) lactone 4, the enantiomer of a degradation product of natural gymnoprenol.



2: R=H, n=7-9, m=1
: R=H, n=5-6, m=2
3: R=  COOH, n=5-6, m=2

E-Geraniol was transformed to the (2S,3S) epoxy alcohol by the Sharpless asymmetric epoxidation[4)](78% yield, $[\alpha]_D$-5.89°,$CHCl_3$). The epoxide ring of the corresponding acetate 5 was cleaved with perchloric acid in DMF to give a formate 6 (73% yield) along with recovered 5 ; 6, $[\alpha]_D$-12.24°(c,0.9), m/e 248 (M^+), nmr 1.22 (3H,s), 1.62 (3H,s), 1.68 (3H,s), 2.02 (3H,s), 4.10 (1H,dd,8.6,12.3Hz) 4.55 (1H,dd,2.9,12.3 Hz), 5.17 (1H,dd,2.9,8.6Hz), 4.96-5.21 (1H,m), 8.14 (1H,s). Hydrolysis of 6 afforded triol 7 of which the nmr spectrum was identical with that of the specimen prepared from linalool.[5)] That this epoxide opening reaction proceeded with high stereo- and regioselectivity giving rise to the product 6 was confirmed by selective hydrolysis[6)] of the formate ester (NH_3 in MeOH, half-saturated at 0°C, 5min) to the acetate 8 as well as by alternative synthesis of (±)-syn isomer of

4 (vide infra). Oxidation of the diacetate 9, $[\alpha]_D$-11.5°(c, 0.93), m/e 273.1735 (M^++1) which was obtained by mild basic hydrolysis of 6 followed by acetylation, with OsO_4 and $NaIO_4$ (aq dioxane at rt) afforded a hemiacetal 10 as an epimeric mixture. The product 10 was then converted by Jones oxidation into (2R,3S) anti-γ-lactone 4; $[\alpha]_D$-7.6°(c, 0.52), m/e 245.1058 (M^++1), pmr 1.44 (3h,s), 2.04 (3h,s), 2.09 (3H,s), 4.10 (1H,dd,6.9,12.0Hz), 4.41 (1H,dd,3.0,12.0Hz), 5.18 (1H,dd,3.0,6.9Hz), cmr 20.7(q), 20.8(q), 23.1(q), 28.5(t), 30.0(t), 62.2(t), 74.0(d), 84.8(s), 169.8(s), 170.4(s), 175.7(s). On the other hand, racemic syn-4 (2,3-syn isomer) was prepared from E-geranyl acetate through the dioxolane derivative 11 which was submitted to OsO_4 oxidation followed by acetylation, deprotection and oxidation. The pmr and cmr of the (±)-syn-4 [pmr 1.51 (3H,s), 2.06 (3H,s), 2.16 (3H,s), 4.04 (1H,dd,8.0,12.3Hz), 4.51 (1H,dd,2.9,12.3Hz), 5.18 (1H,dd,2.9,8.0Hz), cmr 20.7(q), 20.8(q), 23.6(q), 28.7(q), 31.1(t), 62.2(t), 74.8(d), 84.9(s), 170.0(s), 170.6(s), 175.7(s)] were found to be different from those of (2R,3S)- and natural-derived 4.[1] The natural-derived γ-lactone($[\alpha]_D$+8.8°) was found to be identical with the synthetic (2R,3S)-4 in all respects excepting the sign of optical rotation. Thus the absolute configuration of 4 of natural origin was regarded as 2S,3R. In conclusion, 2S,3R stereochemistry, as depicted in the structure 1, 2 and 3, was proposed for gymnoprenol-A, -B and gymnopilin. The stereochemistry of other chiral centers is under investigation.



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Reference and Notes:

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