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THE ABSOLUTE CONFIGURATION OF THE SIDE CHAIN DIOL MOIETY OF THE POISON-FROG ALKALOID PUMILIOTOXIN B

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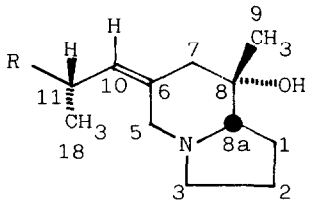
Summary: The absolute configuration of the diol moiety in the side chain of pumiliotoxin B has been established by comparison of the ozonolysis product from pumiliotoxin B diacetate with the synthetic 3,4-diacetoxy-2-pentanone derived from L-(+)-tartaric acid. This indicates the absolute configuration (R, R) of C-15, C-16 diol of pumiliotoxin B.

Pumiliotoxin B (1) was first isolated from the Panamanian frog Dendrobates pumilio together with a close analog pumiliotoxin A (2).[1] The key to the structure of pumiliotoxin A class of dendrobatid alkaloids was obtained through X-ray analysis of a relatively simple member, pumiliotoxin 251D (3), isolated from Ecuadorian frog, Dendrobates tricolor.[2] The structure of pumiliotoxin A and B were deduced from magnetic resonance studies to be as in Fig. 1 with a single hydroxyl group in the side chain of pumiliotoxin A (2) and a diol moiety in the side chain for pumiliotoxin B (1). A recent study revealed the E-configuration for the Δ^{13}-double bond and threo-relation for the C-15, C-16 diol of the pumiliotoxin B side chain.[3] Independently, Overman and McCready also defined the threo-configuration for the diol moiety of pumiliotoxin B.[4] The present communication reports the absolute configuration of the C-15, C-16 diol group of pumiliotoxin B.

2,3-Isopropylidene-2,3-dihydroxylbutanal (4) was obtained from L-(+)-

tartaric acid according to the reported procedures[5] and then converted to methyl ketone (5) $[\alpha]_D$ +75° (c 1.6 $CHCl_3$) by the treatment of CH_3MgBr and subsequent DMSO-$(COCl)_2$ oxidation. Treatment of the methyl ketone (5) with p-TsOH in MeOH, and acetylation with Ac_2O gave 3,4-diacetoxy-2-pentanone (6) $[\alpha]_D$ -36° (c 0.5 $CHCl_3$).

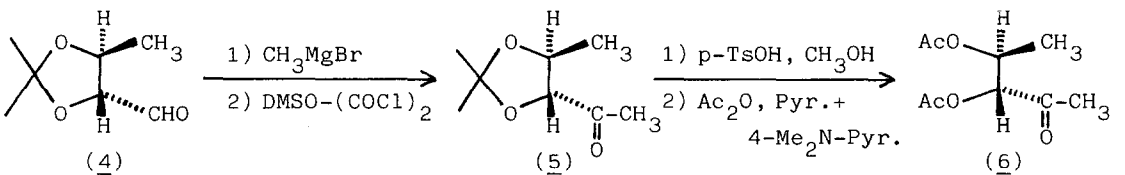
Fig. 1



(1) R^1: $-CH_2-CH=CCH_3-CHOH-CHOH-CH_3$ (12 13 19 15 16 17)

(2) R^2: $-CH_2-CH=CCH_3-CHOH-CH_2-CH_3$

(3) R^3: $-CH_2-CH_2-CH_2-CH_3$



(4) (5) (6)

Ozonolysis in methanol of pumiliotoxin B diacetate (m/z 407(27), 348(100), 288(26), 194(72), 166(63), 70(69); δ_H of the acetyls, 2.03, 2.04; $[\alpha]_D$ +17.8° (c 0.47 CH_3OH) gave 3,4-diacetoxy-2-pentanone identical with the synthetic sample (6) in ir and nmr. The ozonolysis product shows $[\alpha]_D$ +42° (c 0.09 $CHCl_3$) and a positive maximum at 280 nm in CD spectrum, while the synthetic sample shows a negative maximum at the same wavelength. The present data complete the total structure assignment of pumiliotoxin B by defining the absolute configuration of the C-15, C-16 diol group.

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