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STRUCTURE AND SYNTHESIS OF A NEW HYPOTENSIVE VASODILATOR ISOLATED FROM STREPTOMYCES AUREOFACIENS

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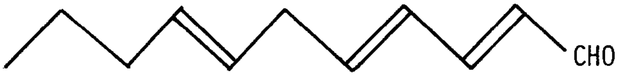
Summary: The structure elucidation and synthesis of WS-1228 A, produced by *Streptomyces aureofaciens*, were described.

As reported in a previous paper[1], *Streptomyces aureofaciens* produces several hypotensive vasodilators. In this report, we deal with the structure elucidation and synthesis of one of the compounds, the trivial name of which is WS-1228 A.

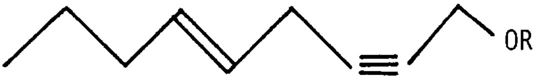
WS-1228 A(1), $C_{11}H_{17}N_3O$, mp 100-2°C(dec.),has ν_{max}^{nujol} 3300-2200, 1612 and 1580 cm^{-1}; λ_{max}^{MeOH} 300 nm (ε= 44,000); nmr($CDCl_3$)δ 0.90(3H,t,J=6.5Hz), 1.35(2H,m),2.00(2H,m), 2.88(2H,m), 5.45(2H,m), 5.9-7.1(4H,m), 8.36(1H,d,J=8Hz,C$\underline{H}$=N) and 11.3(1H, br.s, disappeared with D_2O); m/e 207(M^+), 177 and 162. It gave a brown color with ferric chloride indicating an oxime group.

Catalytic hydrogenation of 1 over 10% Pd-C afforded n-undecylamine. Treatment of 1 with p-toluenesulfonic acid in aqueous acetone at room temperature over night gave the aldehyde(2)[$C_{11}H_{16}O$, M^+=164, ν_{max}^{film} 1680, 1640, 990 and 970 cm^{-1}, δ 0.89(3H,t,J=6.5Hz), 1.40(2H,m), 2.00(2H,m), 2.92(2H,m), 5.45(2H,m), 6.08(1H,dd, J=8 and 16Hz), 6.2-6.45(2H,m), 7.10(1H,m) and 9.53(1H,d,J=8Hz)]. Decoupling experiment using the pseudo-contact shift with $Eu(DPM)_3$ as a shift reagent provided that the diene system conjugated with the aldehyde group has E-E configuration($J_{1,2}$=8Hz, $J_{2,3}$=16Hz, $J_{3,4}$=10.5Hz and $J_{4,5}$=15Hz.). In order to confirm the configuration and location of the isolated double bond in 2, synthesis of (E,E,E)-2,4,7-undecatrienal was undertaken as follow.

(1)

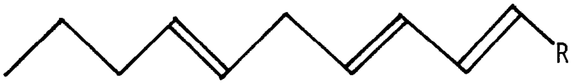


(2)



(3) R = THP
(4) R = H

(5) R = CH_2OH
(6) R = CHO



(7) R = $COOC_2H_5$
(8) R = $CH{=}NNH_2$
(9) R = CH=NNH-TMS

The copper catalyzed coupling reaction[2] of <u>trans</u>-hexenyl bromide[3] with propargyl tetrahydropyranyl ether[3] using ethylmagnesium bromide and cuprous cyanide in tetrahydrofuran gave the ether(3)[4] which was smoothly hydrolyzed to the alcohol(4)[4] with 2% oxalic acid in methanol at room temperature. Reduction of 4 with sodium in liquid ammonia gave nonadienol(5)[4] which was converted to nonadienal(6)[4] [$C_9H_{14}O$, $M^+=138$, ν_{max}^{film} 1687 and 970 cm^{-1}, δ 6.17(1H,dd,J=8 and 15Hz), assigned to C_2-H] with manganese dioxide in chloroform. Treatment of 6 with triethyl phosphonoacetate in the presence of sodium hydride in benzene[5] gave (E,E,E)-2,4,7-undecatrienoate(7)[4] [ν_{max}^{film} 1710 and 970 cm^{-1}, δ 5.80(1H,d,J=15Hz), assigned to C_2-H].

Reduction of 7 with lithium aluminum hydride in ether followed by oxidation with manganese dioxide in chloroform gave (E,E,E)-2,4,7-undecatrienal in 10% overall yield which was identical with the aldehyde(2) obtained from natural sources. Reaction of the aldehyde(2) with hydrazine hydrate in ethanol afforded the unstable hydrazone(8) which was, without purification, treated with trimethyl silyl chloride in the presence of triethylamine in ether to give the silyl hydrazone(9). Exposure of 9 to dinitrogen trioxide in methylene chloride at -20°C gave WS-1228 A. All the spectral data of synthetic WS-1228 A were identical with those of natural WS-1228 A, confirming the structure of 1.

To our knowledge, WS-1228 A is the first naturally occuring compound possessing a triazene group.

References and Notes

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