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# STRUCTURE OF PENICILLIDE, A NEW METABOLITE PRODUCED BY A *PENICILLIUM* SP.

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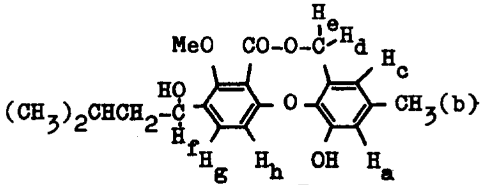
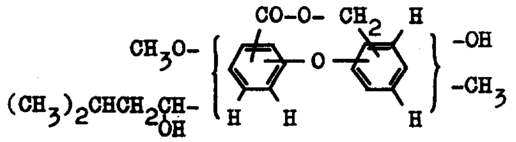
Recently, a novel highly methylated fatty acid(radiclonic acid) has been isolated from the mycelial extracts of a fungus(*Penicillium* sp.) as a new root-growth stimulant[1]. In this paper, we wish to report the structure of the new metabolite named penicillide(I). It was found that the monomethyl ether (II) markedly inhibited the growth of Chinese cabbage seedlings.

I and its derivatives exhibited the following physical properties:I;IR[2] $\nu_{max}$:3450, 1740, 1600 $cm^{-1}$, UV $\lambda_{max}$:285($\varepsilon$ 6000) nm, MS m/e:372($M^+$), 315($M^+$-57), monomethyl ether(II);mp 128-9.5°C, $C_{22}H_{26}O_6$, $[\alpha]_D^{27}$ +14.4°(MeOH), IR $\nu_{max}$: 3580, 1752 $cm^{-1}$, NMR $\delta(C_6D_6)$:0.93, 0.95(each 3H, d, J=6.0 Hz), ca. 1.65(2H, m), ca. 1.8(1H, m), 1.99($H_b$, br. s), 1.78(OH), 3.42, 3.80(each 3H, s), 4.64($H_e$), 4.74($H_d$, $J_{d,e}$=15 Hz), 4.99($H_f$, m), 5.92($H_c$), 6.45($H_a$, $J_{a,c}$=2.0 Hz), 6.95($H_h$), 7.44($H_g$, $J_{g,h}$=8.5 Hz), diacetate(III);IR $\nu_{c=o}$:1752, 1764 $cm^{-1}$(no hydroxyl band), NMR $\delta(CDCl_3)$:6.12($H_f$, m), 2.37, 2.06(each OAc), MS m/e:456($M^+$). The spectral data of I, II and III indicated that I is a monohydric phenol with one secondary hydroxyl, one methoxyl and three methyl groups.

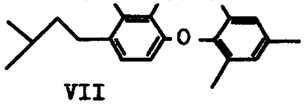
I was treated with bromine in $CCl_4$ to give a dibromide(MS m/e:510, 512, 514(1:2:1)). Its NMR spectrum showed no signals of the meta-coupling protons ($H_a$ and $H_c$) and displayed a sharp three-proton singlet of $H_b$. Oxidation of II with Jones reagent gave a conjugated ketone(IV), mp 128-9°C, $C_{22}H_{24}O_6$, IR $\nu_{c=o}$:



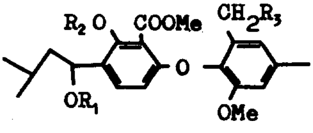
I



A



VII



VIII $R_1$ =$R_2$ =H
$R_3$ =Cl
IX $R_1$ =Me, $R_2$ =H
$R_3$ =Cl
X $R_1$ =Me, $R_2$ =Ac
$R_3$ =OAc

1756, 1683 cm$^{-1}$. Its NMR spectrum revealed the presence of isobutyl group in IV(0.93(6H, d, J=6.5 Hz), 2.25(1H, m), 2.85(2H, m)). The carbonyl function of I was clarified as that of an ester group by methanolysis of I. Treatment of I with KOH in MeOH afforded a hydroxy methyl ester(V);IR $\nu_{c=o}$:1710 cm$^{-1}$, UV $\lambda_{max}$:285($\varepsilon$ 6100) nm, MS m/e:404(M$^{+}$), its triacetate(VI);IR $\nu_{c=o}$:1784, 1743 cm$^{-1}$ (no hydroxyl band), NMR $\delta(CCl_4)$:1.85, 1.94, 1.97(each OAc), 3.86, 3.90(each OMe). In the NMR spectrum of VI, there were two signals of acylated shift at $\delta$ 5.00($H_d$ and $H_e$) and 5.98($H_f$). Therefore, one oxygen function remaining unassigned in I must be an ether linkage. From the above facts, the partial structure of I is represented as A.

The substitution pattern on benzene nuclei was elucidated by the following evidence. Hydrogenolysis product of V(10% Pd-C/MeOH) was hydrolyzed with aqueous NaOH, followed by treatment with $(CF_3CO)_2O$ to give a depsidone(VII)[3]; IR $\nu_{c=o}$:1757 cm$^{-1}$(no hydroxyl band), NMR $\delta(CCl_4)$:2.25, 2.37(each 3H, s), 2.57 (2H, m), UV $\lambda_{max}$:245(inflexion, $\varepsilon$ 6300), 279($\varepsilon$ 2500), 297($\varepsilon$ 2500) nm, MS m/e: 340(M$^{+}$). Treatment of II with $BCl_3$ in $CH_2Cl_2$ at -70°C, followed by methylation with ethereal diazomethane, yielded methyl esters with one chlorine atom. One(VIII;$FeCl_3$(EtOH):purple, IR $\nu_{max}$:3500, 3200-2800, 1660 cm$^{-1}$, NMR $\delta$:11.8 (-OH)) showed two O-methyl resonaces at $\delta$ 3.67 and 3.95 in the NMR spectrum. The other(IX;$FeCl_3$:purple, IR $\nu_{max}$:3200-2800, 1660 cm$^{-1}$, NMR $\delta$:11.6(-OH)) indicated the presence of three O-methyl groups in the NMR spectrum;$\delta$ 3.12, 3.67 and 3.93. Position of the methoxyl groups of IX was confirmed by derivation to X(IR $\nu_{max}$:1782, 1742 cm$^{-1}$, NMR $\delta(CCl_4)$:1.73, 2.22(each OAc), 4.98($H_d$ and $H_e$), MS m/e:502(M$^{+}$)). The abnormal reaction product IX could be formed by methyl migration to neighboring oxygen atom of the secondary hydroxyl group under the reaction conditions. Furthermore, the position of the substituents on benzene nuclei was supported by the intramolecular nuclear Overhauser effect on II. Decoupling experiments on II revealed the presence of long-range couplings;$J_{b,c}$=0.7 Hz, $J_{e,c}$=0.6 Hz, $J_{a,b}$=$J_{f,g}$=0.5 Hz and $J_{f,h}$= 0.4 Hz($J_{d,c}$=0.6 Hz).

From a biosynthetic point of view, penicillide may be analogous to the *Aspergillus terreus* metabolites, diphenyl ethers and geodoxin[4].

## REFERENCES

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