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PARAHERQUONIN, A NEW MEROTERPENOID FROM *PENICILLIUM PARAHERQUEI*

Emi Okuyama and Mikio Yamazaki*
Research Institute for Chemobiodynamics, Chiba University,
8-1, Inohana-1-chome, Chiba, 280, Japan
Kimiko Kobayashi and Tosio Sakurai
the Institute of Physical and Chemical Research,
2-1, Hirosawa, Wako-shi, Saitama-ken, 351, Japan

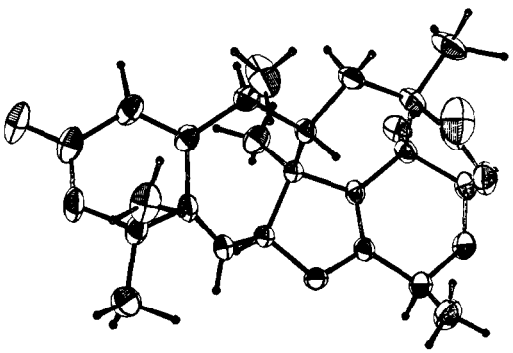
Summary: Paraherquonin, a new meroterpenoid was isolated from *Penicillium paraherquei* IFO 6234 and the structure was determined by X-ray diffraction analysis.

Isolation and structure determination of a toxic metabalite, paraherquamide from *Penicillium paraherquei* IFO 6234 were reported.[1] A new metabolite was isolated along with paraherquamide from the same fungi and designated as paraherquonin. The structure of paraherquonin and its biosynthetic relationship to some meroterpenoids are now reported.

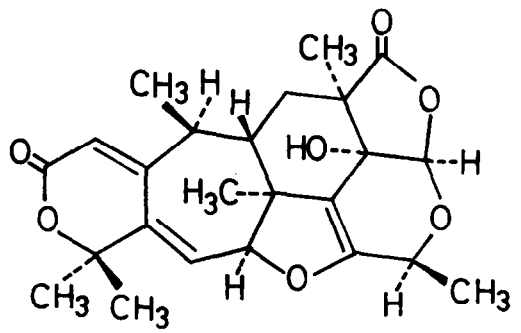
Paraherquonin (1), colorless prisms, mp 290-293°C (acetone), $C_{24}H_{28}O_7$, $[\alpha]_D^{26}$ +341° (c=0.20, $CHCl_3$); m/z 428(M^+, 69%), 370($M^+-C_3H_6O$, 100%); λ_{max}(ethanol) 211.5(ε11200), 265(ε9200) nm; ν_{max}(KBr) 3445(OH), 1770(γ-lactone C=O), 1692(conjugated C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$) 1.29(3H,s), 1.31(3H,d,7Hz), 1.32 (3H,s), 1.44(3H,d,7Hz), 1.55(3H,s), 1.67(3H,s), 1.42-1.72(2H), 2.18(1H,dd, 11,3 Hz), 2.22(1H,s), 2.47(1H,dq,10,7Hz), 4.54(1H,q,7Hz), 4.92(1H,d,3Hz), 5.74(1H,s), 5.87(1H,br.s), 6.08(1H,dd,3,2Hz); ^{13}C-NMR ($CDCl_3$) 19.89(q), 20.17(q, 2), 22.75 (q), 26.02(q), 26.23(q), 31.99(t), 41.65(d), 42.52(d), 46.61(s), 50.17(s), 67.09 (d), 73.32(s), 82.93(s), 91.40(d), 102.68(d), 108.00(s), 118.60(d), 127.04(d), 134.13(s), 153.96(s), 159.41(s), 163.62(s), 175.72(s). These data suggested that paraherquonin was highly oxidized and complicatedly condensed ring system. The detailed structure as well as the relative stereochemistry of this compound was established therefore by X-ray diffraction analysis.

Recrystallization of paraherquonin from pyridine-water gave well formed prisms; monoclinic, space group $P2_1$, a=11.208(3), b=11.185(3), c=8.891(2) Å, β=106.78(2)°, V=1067.1Å^3, Dx=1.33 g/cm^3, Z=2. The intensity data were collected up to 2θ=135° with a Rigaku automated four circle diffractometer with graphic monochromated CuKα radiation; 1869 independent reflections ($I>3\sigma I$) were measured The structure was solved by direct method. The block-diagonal least-squares refinements of the positional and anisotropic temperature parameters reduced the R value to 0.057. All hydrogen atoms were located by difference Fourier synthesis. Calculations were performed using the UNICS III program system for the crystallographic calculations.[2] For additional crystallographic details consult reference 3.

Paraherquonin seems to be biosynthetically related to the meroterpenoids such as austin[4], austinol[5], dehydroaustinol[6], terretonin[7], andilesins and andibenins[8]. These meroterpenoids have been shown to be formed via the same key intermediate which was derived from farnesyl pyrophosphate and a bis-C-methylated tetraketide.[9] The pathway of paraherquonin biosynthesis seems to be branched in the course of austin-pathway, and to form paraherquonin through further modification with oxidative cleavage, migration, decarboxylation and recyclization. The biosynthetic study on paraherquonin is undertaken in our laboratory. The intravenous injection of this compound 100 mg/kg to mice has shown no lethal effect.



Computer Generated Perspective Drawing of Paraherquonin



Structure of Paraherquonin

References

1) M.Yamazaki, E.Okuyama, M.Kobayashi, H.Inoue, Tetrahedron Letters, 22, 135 (1981).

2) T.Sakurai, K.Kobayashi, Rikagaku Kenkyusho Hokoku, 55, 69 (1979).

3) Final crystallographic coordinates have been deposited with the Cambridge Crystallographic Data Center.

4) K.K.Chexal, J.P.Springer, J.Clardy, R.J.Cole, J.W.Kirksey, J.W.Dorner, H.G.Cutler, B.J.Strawter, J.Am.Chem.Soc., 98, 6748 (1976).

5) K.Fukuyama, Y.Katsube, H.Ishido, M.Yamazaki, Y.Maebayashi, Chem.Pharm.Bull., 28, 2270 (1980); T.J.Simpson, D.J.Stenzel, A.J.Bartlett, E.O'Brien, J.S.E.Holker, J.C.S.Perkin I, 1982, 2687.

6) Y.Maebayashi, E.Okuyama, M.Yamazaki, Y.Katsube, Chem.Pharm.Bull., 30, 1911 (1982).

7) J.P.Springer, J.W.Dorner, R.J.Cole, R.H.Cox, J.Org.Chem., 44, 4852 (1979).

8) A.W.Dunn, R.A.W.Johnstone, B.Sklarz, T.J.King, J.C.S.Chem.Comm., 1976, 270; A.W.Dunn, R.A.W.Johnstone, B.Sklarz, L.Lessinger, T.J.King, J.C.S.Chem.Comm., 1978, 533; A.W.Dunn, R.A.W.Johnstone, T.J.King, L.Lessinger, B.Sklarz, J.C.S.Perkin I, 1979, 2113; T.J.Simpson, J.C.S.Perkin I, 1979, 2118.

9) T.J.Simpson, D.J.Stenzel, J.C.S.Chem.Comm., 1981, 1042; C.R.McIntyre, T.J.Simpson, J.C.S.Chem.Comm.,1981, 1043; J.S.E.Holker, T.J.Simpson, J.C.S. Chem.Comm., 1978, 626.

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