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THE STRUCTURE OF PIPERENONE, A NEW INSECT ANTIFEEDING SUBSTANCE FROM PIPER FUTOKADZURA

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During a search for insect antifeeding substances from plant, we found that the benzene extracts of the leaves of Piper futokadzura Sieb. et Zucc. showed an antifeeding activity against the larvae of Spodoptera litura F. An active principle has been isolated from the benzene extracts[1] and named piperenone. We wish to report here on the structure of piperenone.

Piperenone (I) had m.p. 86-88°, $[\alpha]_D$ -129° (c, 1.16, MeOH), $C_{22}H_{28}O_6$ (M^+ 388), ν_{max}[2] 1687, 1642, 1596 and 1515 cm^{-1} and λ_{max}[2] 232, 280 and 285(sh) nm (ε, 16600, 3640 and 3240). The spectral data suggested that I had a substituted benzene and an α,β-unsaturated carbonyl group. That the substituted benzene was a veratryl function was indicated by the NMR spectrum[2] of I (δ 3.85 and 3.87, each 3H, s and 6.8-6.9, 3H, overlap). This was confirmed by oxidation of I with potassium permanganate affording veratric acid. In addition to the veratryl function, the NMR spectrum of I revealed the presence of a moiety CH_3-CH-CH-(O)- (δ 0.98, 3H, d, J=7Hz; 2.90, 1H, dq, J=11, 7Hz and 4.12, 1H, d, J=11Hz), an isolated methylene group (δ 2.63 and 3.29, 2H, ABq, J=17Hz) and two aliphatic methoxy groups (δ 3.40 and 3.53, each 3H, s). The remaining six protons were interrelated by decoupling experiments, indicative of a moiety -CH=C-CH_2-CH=CH_2. Irradiation of an olefinic proton signal at δ 5.90 (1H, ddt, J=17, 9.5, 6.5Hz) collapsed a methylene doublet at δ 3.14 (2H, J=6.5Hz) to a singlet and simplified the overlapped signals of two olefinic protons at δ 5.0-5.3 to a AB-quartet (J=3Hz). Irradiation of the methylene doublet at δ 3.14 sharpened a broad singlet of an olefinic proton at δ 6.44 ($W_{\frac{1}{2}}$=3Hz). The presence of the allyl group in this moiety was confirmed by catalytic hydrogenation of I over 10%Pd-C in ethanol affording dihydropiperenone (II), m.p. 91-92°; $[\alpha]_D$ -107° (c, 0.90, MeOH); $C_{22}H_{30}O_6$ (M^+ 390); ν_{max} 1685, 1595 and 1516 cm^{-1}; δ 0.93 (3H, t, J=6.5Hz), 1.52 (2H, sex, J=6.5Hz) and 2.34 (2H, t, J=6.5Hz).

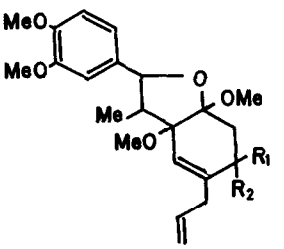
Reduction of I with lithium aluminium hydride in ether gave a mixture of epimeric alcohols, (IIIa) m.p. 141-142°; $C_{22}H_{30}O_6$ (M^+ 390); ν_{max} 3603 cm^{-1}; λ_{max} 232, 279 and 284(sh) nm (ε, 10800, 3480 and 3090) and (IIIb) oil; $C_{22}H_{30}O_6$ (M^+ 390); ν_{max} 3503 cm^{-1}; λ_{max} 232, 278 and 284(sh) nm (ε, 9950, 3200 and 2800), which regenerated I on oxidation with manganese dioxide. The NMR spectrum of IIIa showed the broad double doublet (δ 4.35, J=10, 6Hz) due to the resulting carbinol methin proton which was coupled to the methylene protons (δ 1.63, 1H, dd, J=12.5, 10Hz

and 2.82, 1H, dd, J=12.5, 6Hz). The olefinic proton singlet at δ 6.44 in I was shifted to δ 5.33 in IIIa, indicating that this proton was located at the β-position in the α,β-unsaturated carbonyl system in I. Thus, the moiety $-CH=\underset{|}{C}-CH_2-CH=CH_2$ was extended to $-CH=C(-CH_2-CH=CH_2)-CO-CH_2-\underset{\sim}{C}$.

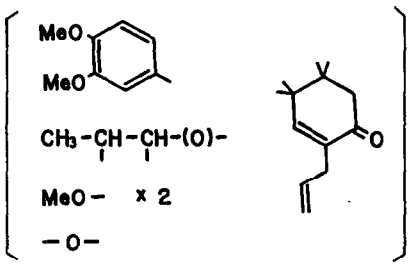
Catalytic hydrogenation of II over 10%Pd-C in methanol gave tetrahydropiperenone (IV), m.p. 86-87°; $C_{22}H_{32}O_6$ (M^+ 392); λ_{max} 233, 278 and 284(sh) nm (ε, 9870, 3140 and 2740). In the NMR spectrum of IV no olefinic proton signal was observed and its IR spectrum in carbon tetrachloride showed the carbonyl absorption at 1722 cm^{-1} due to a six-membered ketone. Therefore, I had a cyclohexenone ring system. One oxigen function remaining unassigned in I was an ether linkage. The all functional groups in I were represented as (A). Their arrangement was elucidated by the following evidence.

Treatment of II with ethanolic potassium hydroxide under reflux gave an α,β-α',β'-unsaturated ketone (V), oil; $C_{21}H_{26}O_5$ (M^+ 358); ν_{max} 1660 cm^{-1}. In the NMR spectrum of V the signal of an olefinic proton newly appeared as the singlet at δ 5.79 and the AB-quartet (δ 2.57 and 3.21, 2H, J=16Hz) of the methylene protons adjacent to the carbonyl function in II disappeared. One of the two aliphatic methoxy singlets in II also disappeared and another was shifted to higher field, δ 2.99 in V. V was further treated with zinc powder in acetic acid at room temperature to give an aromatized derivative (VI), oil; $C_{20}H_{24}O_4$ (M^+ 328); ν_{max} 3503 cm^{-1}; λ_{max} 228 and 287 nm (ε, 13400 and 7120); δ 3.91 (6H, s, $-OCH_3$ x 2), 4.31 (1H, br, OH), 6.36 (1H, s, aromatic proton) and 6.8-7.0 (4H, overlap, aromatic protons). The above data indicated that VI no longer contained an aliphatic methoxy group. Therefore, the two aliphatic methoxy groups must be attached to the different quaternary carbons in the cyclohexenone ring system in I. Moreover, the veratryl function was attached to the carbon bearing the oxigen in the moiety $CH_3-\underset{|}{C}H-\underset{|}{C}H-O-$, for the signal of the secondary methyl protons appeared at δ 0.98 in the NMR spectrum of I. Accordingly, I had a tetrahydrofuran ring system.

When treated with acetic anhydride and sodium acetate anhydrous under reflux[3], II gave an acetyl derivative (VII), oil; $C_{24}H_{32}O_7$ (M^+ 432); ν_{max} 1736 and 1661 cm^{-1}; δ 1.96 (3H, s, $-OCOCH_3$). The NMR spectrum of VII showed an olefinic proton singlet at δ 5.58 instead of the AB-quartet (δ 2.57 and 3.21) of the methylene protons in II. In addition, the doublet at δ 4.08 (J=10.5Hz) due to the α-proton in the tetrahydro furan ring system in II was shifted to δ 5.63 (d, J=4Hz) in VII. This finding indicated that the tetrahydrofuran ring in II was cleaved with an accompanying formation of an α,β-α',β'-unsaturated carbonyl system in VII which was supported from the carbonyl absorption at 1661 cm^{-1} in the IR spectrum of VII. This was verified by further treatment of VII with zinc powder in acetic acid affording an aromatized derivative (VIII), oil; $C_{23}H_{30}O_6$ (M^+ 402); ν_{max} 3600 and 1730 cm^{-1}; λ_{max} 227 and 282 nm (ε, 14000 and 5500); δ 2.05 (3H, s, $-OCOCH_3$), 3.61, 3.75 and 3.79 (each 3H, s, $-OCH_3$), 4.82 (1H, br, OH), 6.21 (1H, s, aromatic proton) and 6.6-6.8 (4H, overlap, aromatic protons), and with aqueous potassium hydroxide in ethanol affording a diastereoisomer of II (IX)[3], m.p. 104-105°; $[\alpha]_D$ + 60.9° (c, 0.55, MeOH); $C_{22}H_{30}O_6$ (M^+ 390); ν_{max} 1681 cm^{-1}; δ 0.69 (3H, d, J=7.5Hz, $-CH-C\underline{H}_3$), 2.66 and 3.36 (2H, ABq, J=16.5Hz, $-CO-CH_2-$), 3.36, 3.46, 3.76 and 3.82 (each 3H, s, $-OCH_3$), 5.16 (1H, d, J=10Hz, $-CH-C\underline{H}-O-$) and 6.23 (1H, brs, olefinic proton). Therefore, one end of the ether linkage



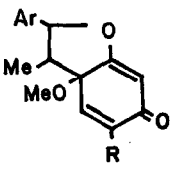
(I) R_1 , R_2 = O
(IIIa) R_1 = OH R_2 = H
(IIIb) R_1 = H R_2 = OH



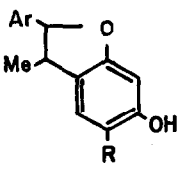
(A)

(II), (IX)

(IV)

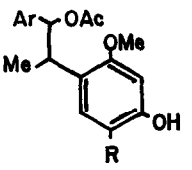


(V)

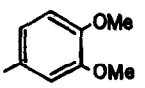


(VI)

(VII)



(VIII)

Ar = 

R = $-CH_2-CH_2-CH_3$

in the tetrahydrofuran ring system must be β-position to the carbonyl group in I. Thus, the structure of piperenone should be represented as I.

Piperenone is classified as a neolignan[4] containing a hexahydrooxobenzofuran ring system. However, the location of its allyl function is different from those for the compounds of this type, e.g., porosin[5] and canellin-B[6]. On a biogenetic point of view, piperenone is interesting.

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Footnotes and References

1) The biological study will be reported in detail elsewhere.
2) IR, UV and NMR spectra were measured in chloroform, ethanol and deuteriochloroform, respectively unless otherwise state.
3) T. Kubota and T. Matsuura, J. Chem. Soc. Japan, 78, 385 (1955)
4) O. R. Gottlieb, Phytochemistry, 11, 1537 (1972)
5) C. J. Aiba, R. Braz Filho and O. R. Gottlieb, ibid., 12, 413 (1973)
6) A. M. Giesbrecht, N. C. Franca and O. R. Gottlieb, ibid., 13, 2285 (1974)