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SYNTHESIS OF PYRENOCINE A AND B

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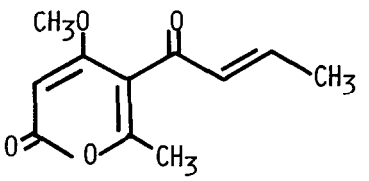
Summary. From 5-acetyl-4-hydroxy-6-methyl-α-pyrone, two phytotoxins, pyrenocine A and B, were synthesized and erroneous γ-pyrone structure of the starting compound was corrected on the basis of spectroscopic data.

Pyrenocine A (1) and B (2) are phytotoxins isolated from the culture filtrate of Pyrenochaeta terrestris (onion pink root disease), and showed inhibitory effects for lettuce germination at 50 ppm and 500 ppm, respectively.[1] In this communication, we would like to report the synthesis of these phytotoxins.



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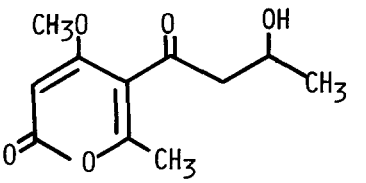
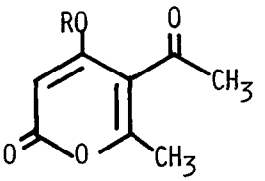


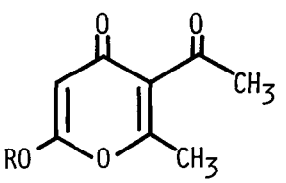
2

Condensation of acetylacetone and malonyl chloride according to the known procedure[2] afforded a pyron[3], mp 159.5~161.5°C, IR ν_{max}^{KBr} 1695, 1665, 1600, 1620 cm^{-1}; ^{1}H-NMR $\delta_{TMS}^{CDCl_3}$ 2.62 (3H, s, CH_3), 2.65 (3H, s, CH_3), 5.52 (1H, s, =C-H), 11.93~12.33 (1H, br.s, OH), to which γ-pyrone structure was assigned erroneously by Butt et al.[2] Validity of α-pyrone structure was confirmed by the IR spectrum, in which a broad absorption due to intramolecular hydrogen bonding was observed at 3200~3000 cm^{-1} under high dilute conditions (0.6 x 10^{-3} mole). In the ^{13}C-NMR spectrum of 3, a signal at δ162.5l due to C-2 was observed and no signals characteristic to γ-pyrone carbonyl appeared near 180 ppm.[4] Therefore, α-pyrone structure was assigned. Methylation of 3 with methyl iodide in the presence of silver oxide gave a single product 4, mp 103.5 ~104.5°C, IR ν_{max}^{KBr} 1760, 1700, 1620 cm^{-1}; ^{1}H-NMR $\delta_{TMS}^{CDCl_3}$ 2.28 (3H, s, CH_3), 2.42 (3H, s, CH_3), 3.87 (3H, s, OCH_3), 5.47 (1H, s, =C-H) in 96.3% yield. On the other hand, treatment of 3 with diazomethane afforded the α-pyrone 4 and a γ-pyrone 5, mp 114~116°C, IR ν_{max}^{KBr} 1700, 1670, 1630 cm^{-1}; ^{1}H-NMR $\delta_{TMS}^{CDCl_3}$ 2.31 (3H, s, CH_3), 2.52 (3H, s, CH_3), 3.87 (3H, s, OCH_3), 5.52 (1H, s, =C-H) in a ratio of 7.6 : 1. Aldol condensation of 4 with acetaldehyde in the presence of LDA yielded a mixture of 2 and 6,[5] which are unable to separate each other by usual silica gel chromatography. In order to obtain pyrenocine B (2) as a single product, the reactions were carried out under various conditions adding zinc

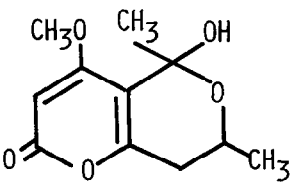
chloride[6], which is able to form a chelated intermediate 4a. The best result was obtained by the reaction carried out in dimethoxyethane at -70°C to -40°C adding zinc chloride in ether and we obtained 2 and 6 as a mixture (7.3 : 1), from which pyrenocine B was isolated as a crystalline material in low yield. Therefore, the pyrone 4 was treated with trimethylsilyl chloride to yield silyl enol ether 7, ^{1}H-NMR $\delta^{CDCl_3}_{TMS}$ 0.20 (9H, s, $OSi(CH_3)_3$), 2.32 (3H, s, CH_3), 3.81 (3H, s, OCH_3), 4.30 (1H, d, J=1.5Hz, =C-H), 4.66 (1H, d, J=1.5Hz, =C-H), 5.44 (1H, s, =C-H). Aldol condensation of 7 with acetaldehyde using titanium tetrachloride[7] in methylene chloride at -76°C afforded pyrenocine B, mp 103.0 ~ 103.5°C, in 40.7% yield (corrected). Synthetic pyrenocine B (2) was identical with natural sample in all respects. Treatment of 2 with acetic anhydride in pyridine gave quantitatively pyrenocine A (1)[1].



3 R=H
4 R=CH_3



3a R=H
5 R=CH_3



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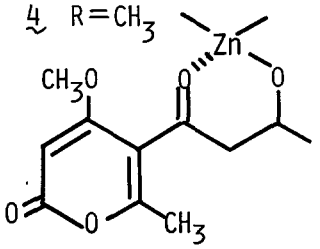
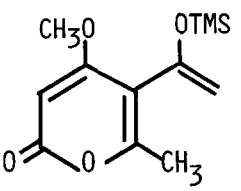


4a



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References and Notes

1) H. Sato, K. Konoma and S. Sakamura, Agric. Biol. Chem., 43, 2409 (1979). H. Sato, K. Konoma, S. Sakamura, A. Furusaki, T. Matsumoto and T. Matsuzaki, Agric. Biol. Chem., 45, 795 (1981). Pyrenocine A is identical with citreopyrone recently isolated from P. citreo-viride B: M. Niwa, S. Ogiso, T. Endo, H. Furukawa and S. Yamamura, Tetrahedron Lett., 4481 (1980).

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3) Satisfactory elemental composition was obtained on all new compounds.

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5) ^{1}H-NMR $\delta^{CDCl_3}_{TMS}$ 1.27 (3H, d, J=7Hz, CH_3), 1.69 (3H, s, CH_3), 2.40 (2H, d, J=7Hz, CH_2), 3.18 (1H, bs, OH), 3.82 (3H, s, OCH_3), 4.07~4.40 (1H, m, CH), 5.43 (1H, s, =C-H).

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