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ISOLATION AND STRUCTURE OF CITREOPYRONE, A METABOLITE OF PENICILLIUM CITREO-VIRIDE BIOURGE

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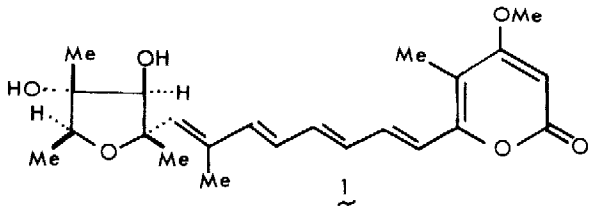
Summary. Citreopyrone isolated from the mycelium of Penicillium citreo-viride B. has been found to be 5-crotonoyl-4-methoxy-6-methyl-2-pyrone. This is the first naturally occurring pyrone with an acyl group at C_5-position.

Of many substances produced by mould and fungus, pyrones which are regarded as masked β-polyketo carboxylic acids are quite interesting from view points of their chemical reactivity[1] as well as of biological activity.[2] Citreoviridin, a toxic yellow metabolite of P. citreo-viride B., was first isolated by Hirata,[3] and its structure was also elucidated to be 1.[4] In the present paper, we wish to describe the isolation and structure of a new pyrone (2), called citreopyrone. This is the first naturally occurring pyrone with an acyl group at C_5-position.

Polished rice (250 g) in deionized water (800 ml) was allowed to stand at room temperature for 30 min, then cooked using an electric rice cooker (99 °C, 17 min) and transfered into an Erlenmyer flask (3 l), which was pasteurized (120 °C, 20 min at 2 atom), then inoculated with a suspension of mycelium of P. citreo-viride B. (IFO 6200) in a sterilized water and incubated stationarily at 24 °C for 32 days. The yellow rice thus obtained was extracted with AcOEt and then with acetone. The combined extracts were concentrated under reduced pressure, and then separated by a combination of column chromatography (Mallinckrodt, 100 mesh; AcOEt)[5] and repeated preparative TLC [Kieselgel PF_{254}; $CHCl_3$ - AcOEt (1 · 1)] to afford citreopyrone (2) (17 mg) as colorless columns [mp 109 - 109.5 °C; $C_{11}H_{12}O_4$ (m/e 208(M^+))]. The IR and UV spectra [ν_{max}(Nujol) 1735, 1635 and 1565 cm^{-1}; λ_{max}(MeOH) 273 nm (ε 7300)] of 2 indicate the presence of an α-pyrone, which has three substituents: Me [δ2.18(3H, s)], MeO [δ3.80(3H, s)] and $MeCH{=}^{E}CHCO$ [ν_{max}(Nujol) 1680 and 1610 cm^{-1}; δ1.97(3H, dd, J= 7, 1.5Hz), 6.26(1H, dq, J= 16, 1.5Hz) and 6.76(1H, dq, J= 16,

7Hz)].[6] Particularly, the presence of the crotonoyl group was confirmed by $NaBH_4$ reduction of 2 in THF (0 °C, 50 min) leading to the formation of the corresponding tetrahydro compound (3) as a colorless oil [$C_{11}H_{16}O_4$ (m/e 212(M^+)); ν_{max}(film) 3400 cm^{-1}; δ0.93(3H, t, J= 7Hz), 1.1 - 1.9(4H, complex) and 4.61(1H, t, J= 7Hz)]. The methine triplet at δ4.61 in 3 was shifted to δ5.76 in the ^1H NMR spectrum of the corresponding acetate (4) which was readily obtained on acetylation of the former with Ac_2O - pyridine.

Finally, the positions of each substituent on the α-pyrone ring were based on a comparison of ^{13}C NMR spectra between 2 and 5 [2: δ162.7(s) (C^a), 87.5(d) (C^b), 168.3(s) (C^c), 113.7(s) (C^d), 161.0(s) (C^e), 18.4(q) (C^f), 56.2(q) (C^g), 190.0(s) (C^h), 132.7(d) (C^i), 146.4(d) (C^j) and 18.2 (q) (C^k). 5: δ163.1(s) or 163.3(s) (C^a), 87.5(d) (C^b), 167.9(s) (C^c), 108.8(s) (C^d), 162.1(s) (C^e), 18.6(q) (C^f), 56.5(q) (C^g), 163.3(s) or 163.1(s) (C^h), 61.6(t) and 14.1(q) (Et)].[7] In the ^1H NMR spectra, furthermore, both 2 and 5 have a singlet assignable to C_3-H at δ5.45 and 5.44, respectively. Biogenetically, citreopyrone (2) may be derived from a plausible intermediate (6).



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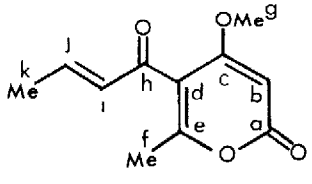

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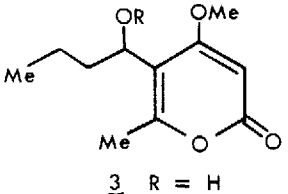

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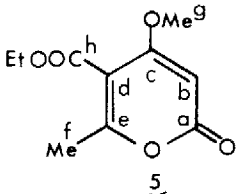
4 R = Ac



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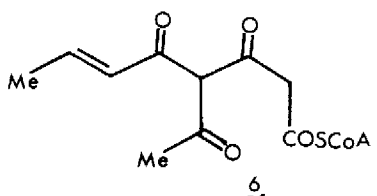

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References and Notes

1. T. Money, Chem. Rev., 70, 553 (1970), T. M. Harris and C. M. Harris, Tetrahedron, 33, 2159 (1977) and many references cited therein.
2. T. Goto and S. Yamamura, "Pyran Compounds" in Methodicum Chimicum Vol. 11-3 (F. Korte and M. Goto ed.) p. 134, Academic Press, New York (1978).
3. Y. Hirata, J. Chem. Soc. Japan, 68, 63, 74 and 104 (1947).
4. N. Sakabe, T. Goto, and Y. Hirata, Tetrahedron Lett., 1964, 1825; Tetrahedron, 33, 3077 (1977).
5. After elution of 2, citreoviridin (1) (237 mg) was obtained.
6. ^1H and ^{13}C NMR spectra of these pyrones were measured on a JEOL PS-100 or FX-100 NMR spectrometer using $CDCl_3$ as the solvent and TMS as the internal standard.
7. The chemical shifts of each corresponding signal in both 2 and 5 are quite similar to each other except for the chemical shifts assignable to C^d (δ113.7 in 2; δ108.8 in 5). Clearly, this difference is explained well by remarkable differences of the two different types of CO group in their effects on the C atom directly attached to them.

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