CHEMISTRY LETTERS, pp. 1285-1288, 1981. © The Chemical Society of Japan 1981

TWO NEW PYRONES, METABOLITES OF PENICILLIUM CITREO-VIRIDE BIOURGE

Masatake NIWA, Tetsuji ENDO, Shigeki OGISO, Hideyuki FURUKAWA, and Shosuke YAMAMURA*+

Faculty of Pharmacy, Meijo University, Tempaku-ku, Nagoya 468

+Department of Chemistry, Faculty of Science and Technology,
Keio University, Hiyoshi, Yokohama 223

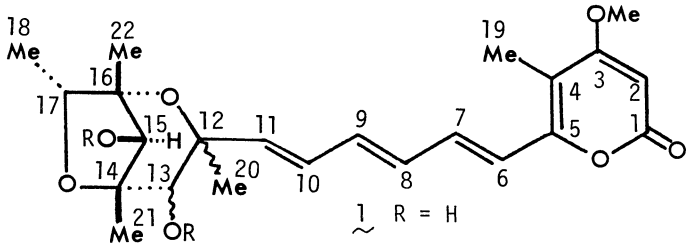
Two new pyrones, citreoviridinol and secocitreoviridin, have been isolated from the yellow rice, and their structures also been elucidated on the basis of their spectral data.

In connection with citreoviridin,[1] a potent inhibitor of ATP-synthesis and ATP-hydrolysis catalyzed by mitochondrial enzyme system, we have isolated citreopyrone,[2] a new metabolite of P. citreo-viride B. (IFO 6200). Recent investigation on several toxic substances related to citreoviridin (aurovertin B,[3] asteltoxin,[4] citreomontanin,[5] and citreoviridins B, C, D, E, and F[6]) prompted us to report some new results concerning the isolation of two new pyrones from the mycelium of P. citreo-viride B.

According to essentially the same procedure as reported in the previous paper,[2] the AcOEt extract (15.2 g) of the yellow rice (250 g)[8] was roughly separated by column chromatography [Mallinckrodt, 100 mesh; AcOEt] to give four fractions.[9] Citreopyrone has already been obtained from the second fraction.[2] The third fraction was further purified by preparative TLC [Kieselgel PF_{254}; $CHCl_3$ - AcOEt (1 : 1)] to afford secocitreoviridin as an amorphous solid (ca. 10 mg). The remaining fraction was also subjected to preparative TLC [Kieselgel PF_{254}; benzene - AcOEt (1 : 10)] to give citreoviridinol (45 mg) as a crystalline solid, in addition to citreoviridin (445 mg).

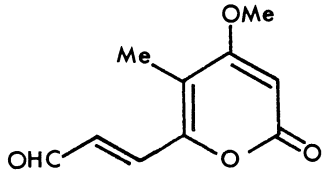
Citreoviridinol (1) is a yellow toxic substance with the following physical data: $C_{23}H_{30}O_7$ [m/e 418(M^+)]; ν_{max} (film) 3400br., 1695br., 1620, 1550, and 1540sh.cm^{-1}; ^1H NMR ($CDCl_3$): δ1.18(3H, d, J= 7Hz), 1.28(3H, s), 1.37(3H, s), 1.41(3H, s), 1.93(3H, s), 3.80(3H, s), 4.01(1H, s), 4.04 (1H, s), 4.14(1H, q, J= 7Hz), 5.44(1H, s), 6.1 - 6.6(6H, complex).

The IR spectrum of citreoviridinol (1) is similar to that of citreoviridin (2). However, remarkable differences between 1 and 2 are seen in the following points. The ^1H NMR spectrum of 1 has two singlets at δ 4.01 and 4.04, both of which are shifted to lower magnetic field (δ 4.93 and 5.04) on acetylation with Ac_2O - pyridine (1 : 10) (room temp., 2 days and then 50 °C, 3 h) giving

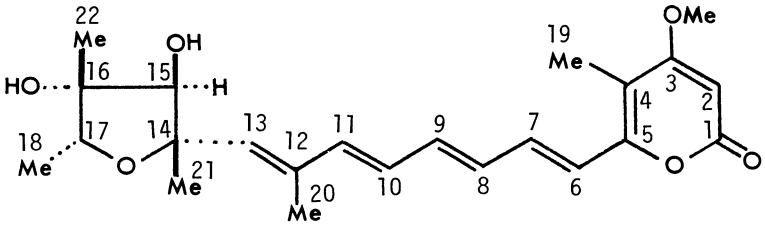


1 R = H

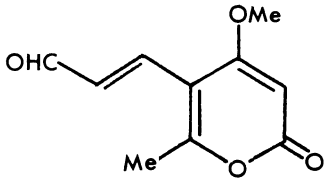
3 R = Ac



4a



2



4b

the corresponding diacetate (3), $C_{27}H_{34}O_9$ [m/e 502(M^+); ν_{max} (film) 1740 cm^{-1} and no OH band]. On the other hand, citreoviridin (2) has only one secondary OH group in addition to one tertiary OH group. Furthermore, 2 has a -CMe=CH- grouping [δ 1.96(3H, s) and 5.87(1H, s)], but instead an additional Me-C(-O)- group (δ 1.41) is present in 1. Finally, the structure of citreoviridinol (1), which is similar to that of aurovertin B,[3] was elucidated by comparing ^{13}C NMR spectra of 1, 2, and 3 (see Table 1). As expected from the stereostructure of the tetrahydrofuran moiety in 2, any

Table 1. ^{13}C NMR spectral data of citreoviridinol and related compounds

C-atom	1	2[10]	3¢	C-atom	1	2	3
C-1	163.7(s)	163.9(s)	163.1(s)	C-13	76.3(d)	141.9(d)*	78.7(d)
C-2	88.4(d)	88.2(d)	88.7(d)	C-14	84.0(s)	84.1(s)	83.4(s)
C-3	170.5(s)	170.6(s)	170.2(s)	C-15	79.7(d)+	85.5(d)+	80.9(d)+
C-4	107.6(s)	107.6(s)	107.8(s)	C-16	82.7(s)	80.7(s)	81.5(s)
C-5	154.3(s)	154.4(s)	154.0(s)	C-17	80.9(d)+	77.3(d)+	79.8(d)+
C-6	118.5(d)	118.1(d)	119.2(d)	C-18	13.5(q)	12.5(q)	12.8(q)
C-7	135.9(d)*	135.9(d)*	135.4(d)*	C-19	8.8(q)	8.8(q)	8.8(q)
C-8	127.0(d)	126.6(d)	128.5(d)	C-20	32.4(q)	21.4(q)	29.8(q)
C-9	138.1(d)*	138.6(d)*	137.2(d)*	C-21	17.6(q)#	17.9(q)	16.6(q)#
C-10	130.5(d)	130.7(d)	131.7(d)	C-22	17.4(q)#	13.4(q)	16.4(q)#
C-11	141.1(d)*	140.9(d)*	139.2(d)*	MeO	56.1(q)	56.1(q)	56.0(q)
C-12	78.0(s)	133.5(s)	78.0(s)				

*,+,# These assignments may be interchanged.
¢ Signals due to two AcO groups are not cited.

long-range coupling between C_{15}-H and C_{17}-H was not observed in the ^{1}H NMR spectrum of citreoviridinol (1).

Biogenetically, citreoviridinol (1) may be produced on epoxidation of the tri-substituted double bond of the conjugated system in 2 followed by ring-opening of the resulting epoxide together with intramolecular etherification.[11]

Secocitreoviridin (4) is a minor component[12] with the following physical data: $C_{10}H_{10}O_4$ [m/e 194(M^+)]; ν_{max} (KBr) 1720, 1675, 1600, and 1545 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ2.11(3H, s), 3.84(3H, s), 5.60(1H, s), 6.86(1H, dd, J= 15, 6Hz), 7.24(1H, d, J= 15Hz), and 9.64(1H, d, J= 6Hz).

On the basis of the ^{1}H NMR spectrum, the structure of secocitreoviridin, which has a $CH\overset{E}{=}CH$-CHO grouping (δ 6.86, 7.24, and 9.64), can be represented by 4a or 4b. Of these two possible structures, however, the former (4a) is more favorable, as judged from its UV spectrum [λ_{max} (MeOH) 334 nm (ε, 13500)] which is quite similar to that of rosellisin [λ_{max} (EtOH) 333 nm (ε, 12700)].[13] On addition of $NaBH_4$, this absorption band at 334 nm was shifted to 315 nm: both radicinol[14] and coarctatin[15] have the UV absorption bands in the same region [radicinol: λ_{max} (EtOH) 318 nm (ε, 10800); coarctatin: λ_{max} (MeOH) 313 nm (ε, 7800)].

Presumably, secocitreoviridin (4) is formed on catabolic oxidation of citreoviridin (2). Further study on this point is in progress.

The authors wish to thank Dr. M. Toda, Ono Central Research Institute, for measurements of high resolution mass spectra of the compounds cited herein.

References

1. N. Sakabe, T. Goto, and Y. Hirata, Tetrahedron Lett., 1964, 1825; Tetrahedron, 33, 3077 (1977).
2. M. Niwa, S. Ogiso, T. Endo, H. Furukawa, and S. Yamamura, Tetrahedron Lett., 1980, 4481.
3. L. J. Mulheirn, R. B. Beechey, D. P. Leworthy, and M. D. Osselton, J. C. S. Chem. Comm., 1974, 874.
4. G. J. Kruger, P. S. Steyn, R. Vleggar, and C. J. Rabie, J. C. S. Chem. Comm., 1979, 440.
5. S. Rebuffat, D. Davoust, L. Molho, and D. Molho, Phytochemistry, 19, 427 (1980).
6. B. Franck and H. P. Gehrken, Angew. Chem. Int. Ed., 1980, 461.
7. A part of this work was presented at the 43rd Annual Meeting of the Chemical Society of Japan (Tokyo, March, 1981), Abstract II, p 717.
8. Incubated stationarily at 24 °C for 8 weeks.
9. The first fraction contains paraffinic alcohols and higher fatty acids.

10. δ-Values in the ^{13}C NMR spectrum of 2 are almost identical with those cited in reference 6.

11. Citreoviridin (2) is biosynthesized from nine acetate moieties and four methionine molecules; D. W. Nagel, P. S. Steyn, and N. P. Ferreira, Phytochemistry, 11, 3215 (1972); see also reference 6.

12. It is pretty difficult to obtain this pyrone in a considerable amount, although we have attempted to find optimum conditions for the incubation.

13. M. S. Nair and S. T. Carey, Tetrahedron Lett., 1975, 3517; M. S. Nair, Phytochemistry, 15, 1090 (1976).

14. M. Nukina and S. Marumo, Tetrahedron Lett., 1977, 3271.

15. B. F. Burrows, W. B. Turner, and E. R. H. Walker, J. C. S. Perkin I, 1975, 999.

(Received July 8, 1981)