

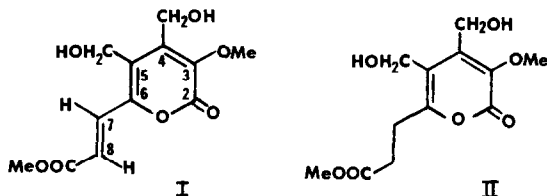
METABOLITES OF PYRENOMYCETES IV:<sup>1</sup> ROSELLISIN, AN ANTIBIOTIC  $\alpha$ -PYRONE FROM  
HYPOMYCES ROSELLUS

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(Received in USA 14th May, 1975; received in UK for publication 11th August, 1975)

Hypomyces rosellus (Alb. & Schw. ex Fr.) Tul. produces an antibacterial culture liquid from which a crystalline compound, rosellisin, was isolated.

Rosellisin has been assigned the novel structure I on the basis of chemical and spectral characteristics reported here.



Rosellisin, mp 110-112<sup>o</sup> (EtOAc), C<sub>12</sub>H<sub>14</sub>O<sub>7</sub> (elemental analysis), had MW 270 (ms),  $\lambda_{\max}$  (EtOH) 333 and 228 nm ( $\epsilon$  12,700 and 22,000),  $\nu_{\max}$  3430, 1720 (sh), 1703, 1669, 1600 and 1550 cm<sup>-1</sup> and ms peaks at 270 (M<sup>+</sup>, 40%), 239 (M-OMe, 45%), 211 (M-COOMe, 40%), 193 (211-H<sub>2</sub>O, 80%) and 165 (193-CO, 100%). The uv and ir spectra of I are very similar to those of nectriapyrone,<sup>2</sup> an extended  $\alpha$ -pyrone. On boiling with Ac<sub>2</sub>O-NaOAc, rosellisin formed a diacetate, mp 135-6<sup>o</sup> (EtOH),  $\lambda_{\max}$  333 and 228 nm,  $\nu_{\max}$  1750-1710 (broad), 1656, 1618 and 1567 cm<sup>-1</sup>. On hydrogenation (5% Pd on C), I gave a dihydro derivative, II, mp 101-2<sup>o</sup>,  $\lambda_{\max}$  291 and 206 nm ( $\epsilon$  7,500 and 18,000)  $\nu_{\max}$  ca. 3500, 1736, 1709, 1647 and 1563 cm<sup>-1</sup>. The uv and ir spectra of II were similar to those of an  $\alpha$ -pyrone.<sup>3</sup> The pmr spectrum<sup>4</sup> of rosellisin showed singlets at 2.85 (2H, exchanges with D<sub>2</sub>O) for the hydroxyls, 3.8 (3H) for the COOMe, 4.03 (3H) for the OMe, 4.53 (2H) and 4.56 (2H) for the two CH<sub>2</sub>-OH and an AB quartet centered at 6.62 and 7.67 (J 15.5 Hz) for the C-8 and C-7 protons, respectively. In the pmr spectrum of the acetate a singlet (6H) for the acetate methyls appeared at 2.12; the COOMe and OMe signals were shifted to 3.85 and 4.1, the methylene signals to 5.04 and 5.08, and the olefinic protons to 6.8 and 7.6. The pmr spectrum of II showed a singlet at 2.8 superimposed on a broad peak 2.7-2.9 integrating for a total of 4H, for the hydroxyls and C-8 protons, another broad peak at 3.0-3.3 (2H) for the C-7 protons, and singlets at 3.65 (3H), 4.1 (3H), 4.50 (2H broad), and 4.53 (2H) for the COOMe, OMe and C-5 and C-4 hydroxymethylenes, respectively. The appearance of a peak at 1736 cm<sup>-1</sup> in the ir spectrum of II, taken together with the pmr spectra, showed the presence of the carbomethoxy group in the side chain,

and the ms fragmentation pattern was in agreement. The chemical shifts of the olefinic protons,<sup>5</sup> and the high coupling constant,<sup>6</sup> defined the trans nature of the side chain double bond. Broadening of the signal ( $N \frac{1}{2} 3$  Hz) of one of the  $\text{CH}_2\text{-OH}$  in the pmr spectrum of II showed that it was on carbon 5 (long range coupling with the C-7 protons). In confirmation, 30% nuclear Overhauser effect enhancement, was observed between the C-7 proton and the acetoxy-methylene protons in the acetate of I. This left two possible structures for rosellisin: one with OMe in the 3-position and the other with OMe in the 4-position. The chemical shift of the OMe protons was lower field than that of comparable 4-methoxy  $\alpha$ -pyrones,<sup>2,3</sup> which suggested that the OMe was in the 3-position.  $^{13}\text{C}$  nmr spectrum of I was in agreement with this assignment: It showed signals at 52.2 (COOMe), 54.6 and 55.6 (2  $\text{CH}_2\text{-OH}$ ), 63.2 (OMe), 113.9 (C-4), 118.7 (C-5), 125.1 (C-7), 130.5 (C-8), 153.3 (C-6), 163.8 (COOMe), 166.2 (C-3) and 167.7 (C-2). Chemical shifts observed for the ring olefinic carbons in I were different from those typical for 4-oxy- $\alpha$ -pyrones.<sup>2,3,7</sup> This, taken together with the chemical shift of 63.2 for the OMe, compared to 56 and 56.2 of comparable 4-methoxy  $\alpha$ -pyrones,<sup>2,3</sup> showed that the OMe group was in the 3-position, and thus rosellisin has structure I. In further confirmation, the two sharp singlets for the hydroxy methylenes in the pmr spectrum of I collapsed to broad peaks on addition of copper acetylacetonate, and little or no broadening of the other peaks was observed. The bidentate complex formation with the reagent is possible only if these groups are in 4- and 5-positions.

Several oxy- $\alpha$ -pyrones occur in nature; but in all of them the oxy-group is in 4-position<sup>2</sup> as would be expected from the Birch acetate rules. To our knowledge, rosellisin is the only naturally-occurring  $\alpha$ -pyrone with a methoxyl in 3-position. This, in combination with the two hydroxy methylene groups on carbons 4 and 5, poses an interesting biogenetic problem which we plan to investigate.

Rosellisin was active against Staphylococcus aureus at a concentration of 30 ppm.

#### Acknowledgement:

This work was supported by a grant, Al-11233, from the Institute of Allergy and Infectious Diseases, and a General Research Support Grant, SOL-RR05621, from the Division of Research Resources, National Institutes of Health. We are grateful to Dr. C. T. Rogerson and Dr. G. J. Samuels for the cultures of Hypomyces roselius, to Dr. Marjorie Anchel for helpful discussions, and to Mr. I Miura for several of the nmr spectra. We thank Mr. Francis Manginelli and Mr. Thomas Amato for technical assistance.

#### Footnotes and References:

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