

A Simple Synthesis of the Pyrazofurins

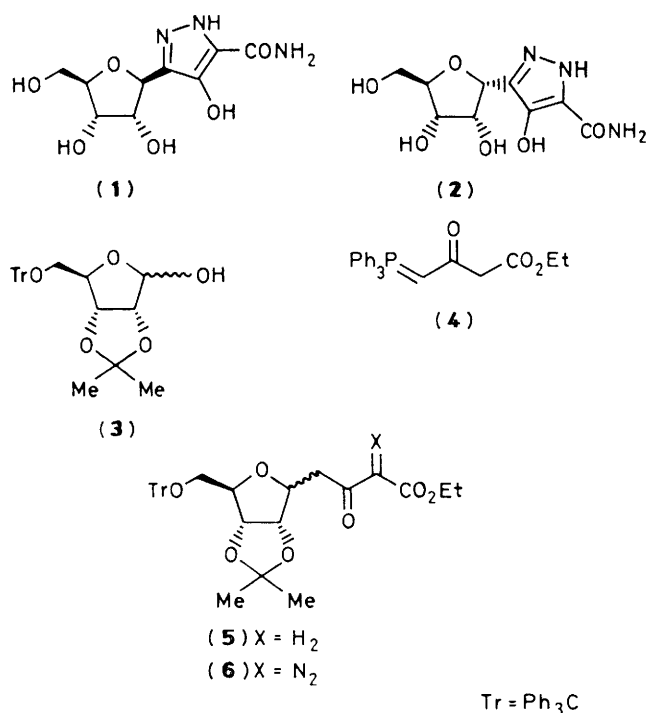
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Pyrazofurin (**1**) and pyrazofurin B (**2**) have been synthesised from the β -keto ester (**5**), which can be readily prepared by Wittig reaction of the protected D-ribose (**3**) with the phosphorane (**4**).

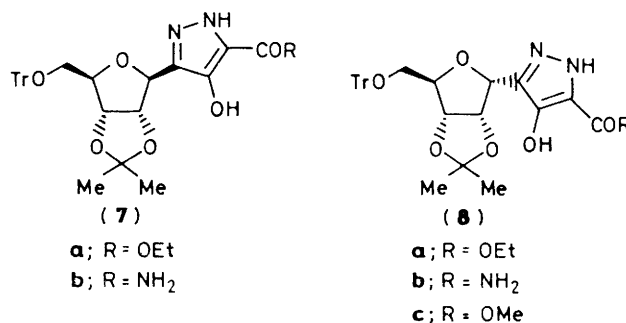
Pyrazofurin (pyrazomycin)¹ (**1**) is a C-nucleoside, isolated from fermentations of a strain of *Streptomyces candidus*,²

having antitumour³ and antiviral⁴ activities. Pyrazofurin B (**2**),⁵ the α -epimer of (**1**), was also isolated from the same



fermentations. There have been three reports concerning the synthesis of (1).⁶⁻⁸ We now report a simple synthesis of (1) and (2) from the β -keto ester (5).

Our starting material (5), the analogue of which has already been prepared by Claisen condensation of methyl D-ribofuranosylacetate with lithio-t-butyl acetate,⁹ was easily obtained by Wittig reaction of the protected D-ribose (3)¹⁰ with the phosphorane (4).¹¹ Treatment of (3) with (4) in acetonitrile under reflux for 90 h gave an anomeric mixture (ca. 2:1, β : α) of (5) in 95% yield. Compound (5) was treated with tosyl azide in the presence of triethylamine to afford the diazo-compound (6) (ca. 1:1, β : α) in 94% yield. Compound (6), on treatment with sodium hydride in 1,2-dimethoxyethane at 20 °C for 3 h, cyclized to form the pyrazole (7a) (42%), m.p. 159–160 °C, and its α -epimer (8a) (21%). Treatment of (7a) with ammonia in methanol at 90–95 °C for 7 h gave the amide (7b) in 94% yield. In a similar manner (90–95 °C; 2 h), compound (8a) was transformed into the amide (8b) and the methyl ester (8c) in 46 and 25% yields, respectively. Com-



pound (8c) was also treated with ammonia to give (8b) in 71% yield. Deprotection of (7b) and (8b) with 90% trifluoroacetic acid at 20 °C for 45 min gave pyrazofurin (1) (85%), m.p. 108–110 °C (C₉H₁₃N₃O₆·H₂O), and pyrazofurin B (2) (84%), m.p. 69–70 °C (C₉H₁₃N₃O₆·2H₂O), respectively. The i.r. spectra of our synthetic (1) and (2) were identical in every respect with those of authentic samples of pyrazofurin and pyrazofurin B, respectively.

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