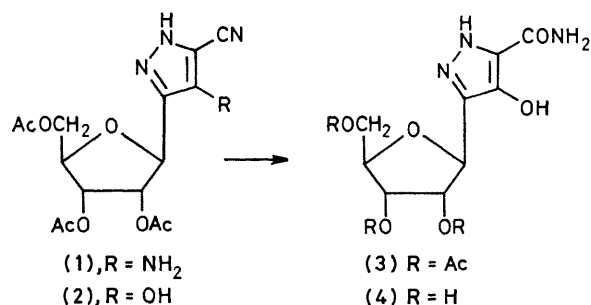


A New Synthesis of Pyrazofurin

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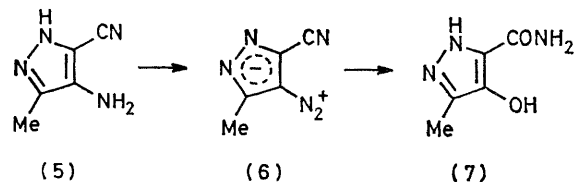
Summary Pyrazofurin (**4**) has been synthesised by a novel route, involving, as the key step, photochemical substitution of a diazopyrazole

THE C-nucleoside antibiotic pyrazofurin (pyrazomycin)¹ (**4**), isolated from the culture filtrate of a strain of *Streptomyces candidus*,² shows activity against a number of viruses³ and tumours,⁴ and is currently undergoing clinical trials



Pyrazofurin has previously been synthesised by two distinct routes,^{5,6} and we now report the application of our general method for C-nucleoside synthesis,⁷ involving acetylenic intermediates, to the synthesis of pyrazofurin, these methods have recently been successfully applied to the synthesis of the related antibiotic formycin⁸

Our earlier work⁸ had led to the synthesis of the 4-amino-pyrazole (**1**). Use of this intermediate for the synthesis of pyrazofurin clearly necessitates the replacement of nitrogen with oxygen at C-4 and a sequence involving diazotisation suggested itself. Use of this procedure for the synthesis of 4-hydroxypyrazoles is, however, not well documented, owing presumably to the known stability of pyrazole diazonium salts.⁹ Furthermore, it would be necessary to carry out a diazotisation prior to conversion of the nitrile into an amide, in order to avoid cyclisation to a pyrazolo-[4,3-*d*]triazinone.¹⁰ Diazotisation (NaNO₂, MeCO₂H, 0 °C) of the model compound 4-amino-5-cyano-3-methylpyrazole (**5**)¹⁰, and subsequent neutralisation (NaHCO₃), gave the



crystalline diazopyrazole (**6**) which was stable under a variety of hydrolytic conditions. When a solution of (**6**) in aqueous acetone was subjected to u v photolysis^{11,12} through Pyrex the 4-hydroxy compound (**7**) was produced in 62% overall yield. When a similar sequence was applied to (**1**) the hydroxypyrazole (**2**) was obtained in 87% yield.

Hydrolysis of the nitrile function was best achieved using nickel acetate tetrahydrate in boiling acetic acid,¹³ to give pyrazofurin triacetate (**3**) (65%); treatment of (**3**) with ammonia in aqueous methanol produced crystalline pyrazofurin (**4**) (75%), indistinguishable from an authentic sample.

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