

II. C-NUCLEOSIDES AND RELATED COMPOUNDS

CARBOCYCLIC ANALOGUES OF C-NUCLEOSIDES:

A USEFUL INTERMEDIATE

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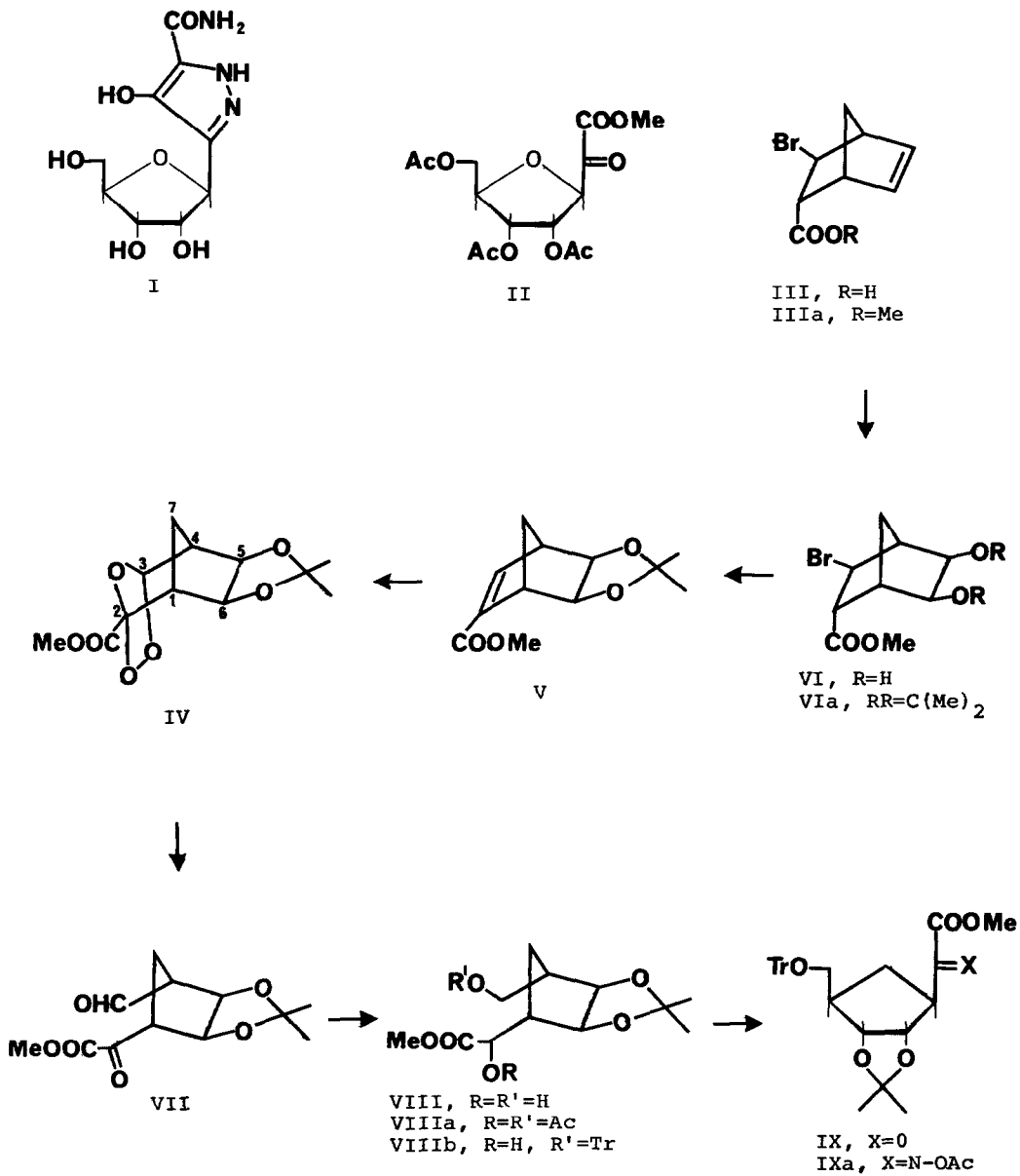
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Pyrazomycin (I)¹ and showdomycin², a closely related compound, have been recently synthesized starting from the ribose derivative II². We wish to report the synthesis of a carbocyclic analogue of II (IX), which should be a useful intermediate to prepare carbocyclic analogues of pyrazomycin. A somewhat similar approach has been used by Shealy and coworkers for the preparation of carbocyclic analogues of purine ribo and deoxyribonucleosides.^{3,4,5}

Diels-Alder adduct III^{6,7}, which can be obtained in good yield from cyclopentadiene and bromoacrylic acid, was esterified with diazomethane, and the methyl ester hydroxylated by catalytic osmylation.⁸ Diol VI, m.p. 144-5°, was obtained in 60% yield. The hydroxy groups in VI were assigned the exo configuration on the basis of analogous reactions in related systems.⁴ When VI was stirred in acetone-dimethoxypropane containing p-toluenesulphonic acid for 40 minutes and the resulting acetonide VIa (δ 1.39 (s, 3H), 1.52 (s, 3H)) treated with ethereal 1,5-diazabicyclo[5.4.0]undec-5-ene for 20 minutes at room temperature, olefinic acetonide V⁷, m.p. 60-62°, λ_{\max} 233 nm, was obtained in essentially quantitative yield.

Ozonolysis of V in methylene chloride at -50° gave a single⁹ oily ozonide IV. Its n.m.r. spectrum exhibited long range coupling between H₁ and H₄ (J = 3 Hz), a single sharp peak assigned to the methyl ester at 3.88 ppm, and a sharp doublet at δ 6.0, J = 7 Hz, assigned to H₃. Reduction of IV with dimethyl sulphide¹⁰ gave the keto aldehyde VII mainly in its hydrated form as a mixture of several isomers¹¹. It was characterized as its bis-dinitrophenyl-



hydrazone⁷, m.p. 205° dec. Attempts to reduce selectively the aldehyde function of VII failed. Reduction of VII with lithium tri-(t-butoxy)aluminum hydride gave a mixture of epimeric diols VIII in 70% yield, which was characterized as a mixture of oily diacetates VIIIa⁷. Reaction of VIII with trityl pyridinium fluoroborate, prepared from trityl fluoroborate and pyridine¹³, gave VIIIb in 75% yield. Oxidation of VIIIb with DMSO-based reagents¹⁴ gave unsatisfactory results. Oxidation of VIIIb with Collins' reagent¹⁵ or ruthenium tetroxide¹⁶ converted VIIIb to the α -keto ester IX in good yield. This compound was fully characterized as the oxime acetate IXa⁷. Work is in progress to assess the utility of this compound in elaborating carbocyclic analogues of nucleosides.

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