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Carbocyclic Nucleosides: Synthesis of Analogues of Cyclobut-G

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CARBOCYCLIC NUCLEOSIDES : SYNTHESIS OF ANALOGUES OF CYCLOBUT-G

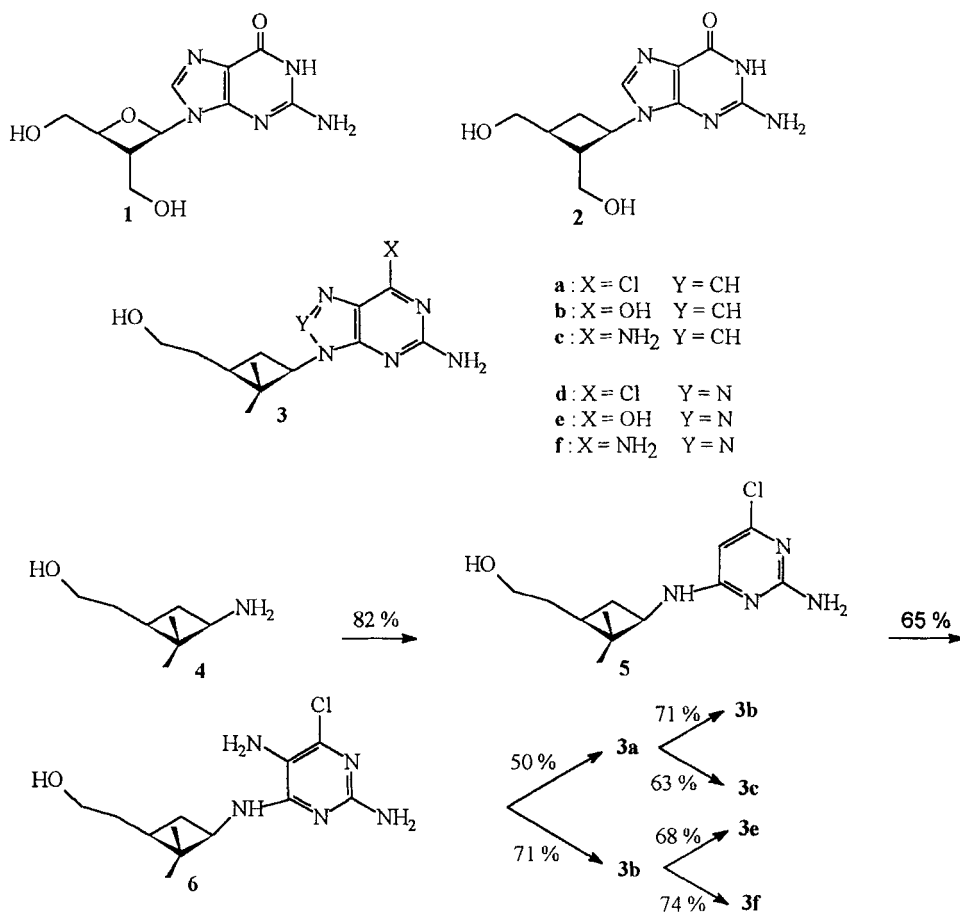
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ABSTRACT : Several carbocyclic nucleosides structurally related to Cyclobut-G have been synthesized from pinonic acid.

Oxetanocin-G (1) and its carbocyclic counter-part, Cyclobut-G (2) have received notable attention for their anti-HIV properties.¹ As part of a research programme aimed at determining the structural features of 2 required for its antiviral action and/or discovering other congeners with interesting biological properties, we have synthesized a family of carbocyclic nucleosides of type 3.

H₂NOSO₃H in AcOH was used to achieve the Beckmann rearrangement² of (*1R, cis*)-pinonic acid and was followed by CH₂N₂ esterification to give (*1R, cis*)-methyl (3-acetylamino-2,2-dimethylcyclobutyl)acetate. This amide ester was successively reduced by the NaBH₄-CaCl₂ method,³ and then acetylated with Ac₂O/pyridine for an easier purification of the product, and hydrolyzed by 2N HCl to afford amino alcohol 4 in 50% overall yield. Condensation of 4 with 2-amino-4,6-dichloropyrimidine⁴ gave 5, which upon diazo coupling with p-chlorobenzenediazonium chloride, followed by Zn-AcOH reduction gave 6 in a fair yield. Ring closure of 6 with triethyl orthoformate or with NaNO₂-AcOH afforded 3a or 3d, respectively. 3a was hydrolyzed by NaOH to the guanine derivative 3b, while its treatment with NH₃ yielded the diaminopurine derivative 3c. Similar procedures gave, when applied to 3d, the corresponding 8-azapurine analogues 3e and 3f.



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