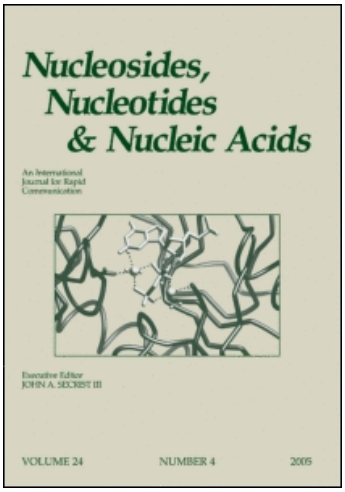

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Carbocyclic Nucleosides: Synthesis of Analogues of Cyclobut-G

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CARBOCYCLIC NUCLEOSIDES : SYNTHESIS OF ANALOGUES OF CYCLOBUT-G

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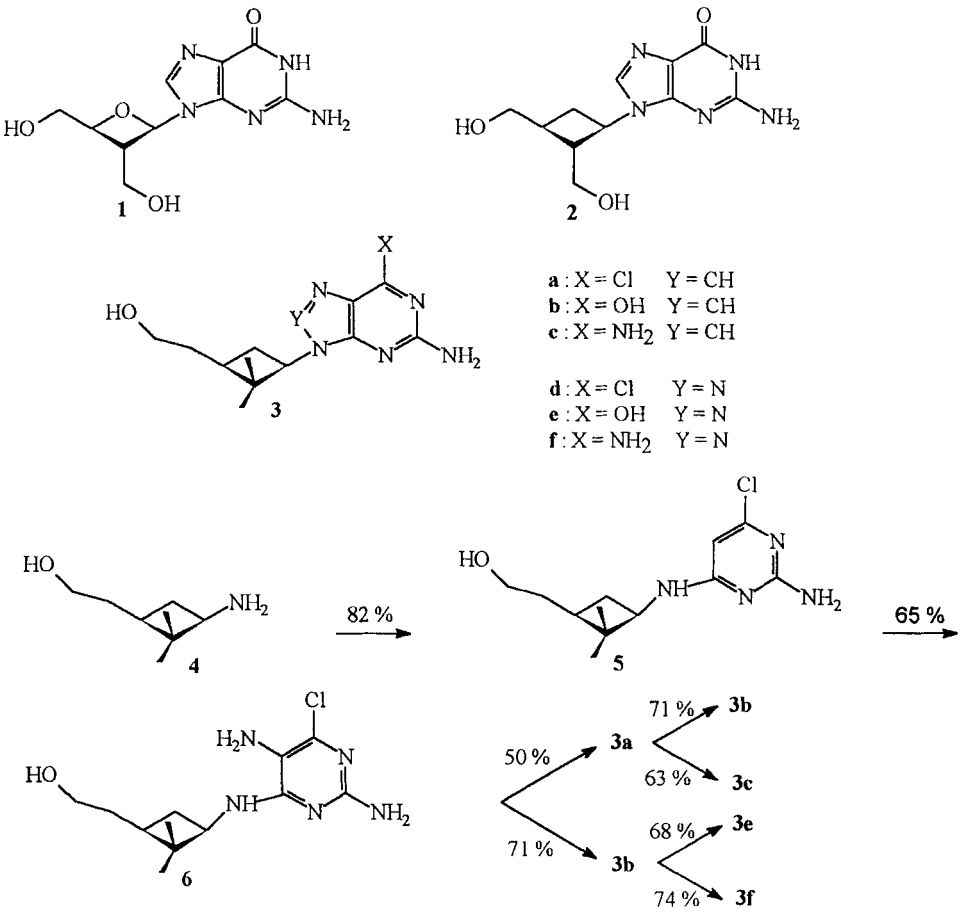
ABSTRACT : Several carbocyclic nucleosides structurally related to Cyclobut-G have been synthesized from pinonic acid.

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**.

H_2NOSO_3H in AcOH was used to achieve the Beckmann rearrangement[2] of (*1R, cis*)-pinonic acid and was followed by CH_2N_2 esterification to give (*1R, cis*)-methyl (3-acetylamino-2,2-dimethylcyclobutyl)acetate. This amide ester was successively reduced by the $NaBH_4$-$CaCl_2$ method,[3] and then acetylated with Ac_2O/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-dichloropyrimidine[4] 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 $NaNO_2$-AcOH afforded **3a** or **3d**, respectively. **3a** was hydrolyzed by NaOH to the guanine derivative **3b**, while its treatment with NH_3 yielded the diaminopurine derivative **3c**. Similar procedures gave, when applied to **3d**, the corresponding 8-azapurine analogues **3e** and **3f**.



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