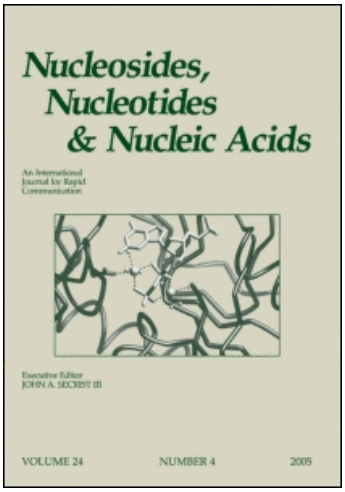

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NUCLEOSIDE ANALOGUES OF PURINE WITH A 1,2-DISUBSTITUTED CYCLOPENTENE RING

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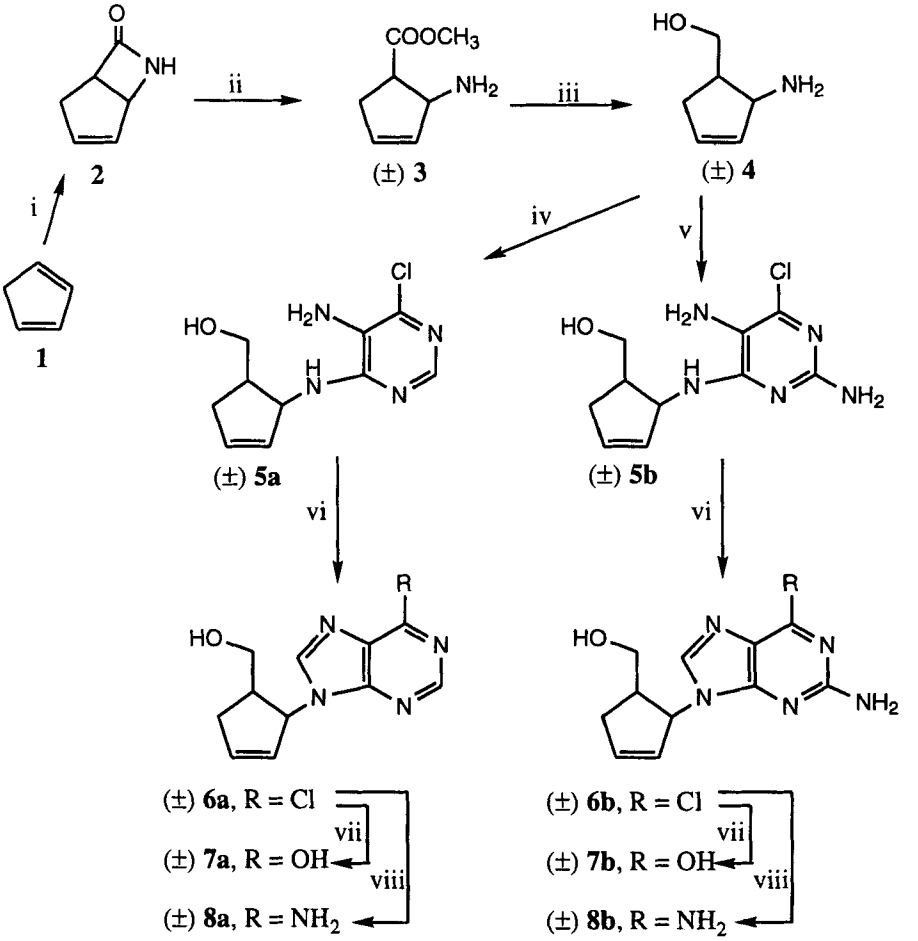
ABSTRACT. One, two-disubstituted carbonucleoside analogues of purine with unsaturated carbocyclic were synthesized by construction of the heterocyclic base about the primary amino group of the amino alcohol **4** intermediate, which was also synthesized in good yield starting from cyclopentadiene.

Following our previous work on carbocyclic nucleoside analogues **o**ne, **t**wo-disubstituted **c**arbonucleosides (OTCs-cyclopentanes with a hydroxymethyl group and the heterocyclic base attached to contiguous ring carbons), we describe here the preparation of compounds with an unsaturation in the 2',3' position of the carbocyclic ring. These compounds can be considered as analogues of carbovir and other nucleoside analogues with interesting pharmacological properties.

Racemic mixtures of compounds **6** - **8** with *cis* stereochemistry, were prepared as shown in scheme 1. The key intermediate (±) cis-2-amino-3-cyclopentenylmethanol (**4**) was synthesized in good yield from the cyclopentadiene in 4 steps: treatment of cyclopentadiene (**1**) with chlorosulfonyl isocyanate to obtain the lactame **2** corresponding to an 2+2 cycloaddition; hydrolysis of this lactame to 2-amino-3-cyclopentenecarboxylic acid; formation of the methyl ester via acid chloride; and final reduction of the resulting amino ester **3** with lithium borohydride. The purine base was then constructed about the primary amino group of these intermediates.[1] To obtain the 6-substituted purines (**6a** - **8a**), the amino alcohol **4** was reacted with 5-amino-4,6-dichloropyrimidine, which afforded **5a**, and to obtain the 2,6-disubstituted purines (**6b** - **8b**), the amino alcohol **4** was firstly reacted with 2-amino-4,6-dichloropyrimidine, and then a second amino group was introduced at position 5 of the pyrimidine ring by reaction with p-

chlorobenzenediazonium chloride followed by reduction to afford the compound **5b**. The fused imidazole ring was then formed in compound **5a** or **5b**, by reaction with ethylortoformate in acid medium, which afforded respectively 6-chloropurine **6a** and 2-amino-6-chloropurine **6b**.

The 6-hydroxy analogues **7a** and **7b** were prepared in good yield by treatment of **6a** and **6b** respectively with NaOH and similary good yields of the 6-amino analogues **8a** and **8b** were obtained by amination of **6a** and **6b** in metanol.[2]



i: CSI, ether dry. ii: a) HCl 12M; b) MeOH dry, Cl_2SO; c) amberlite IRA 420(OH)ion-exchange resin. iii: $LiBH_4$, THF dry. iv: 5-amino-4,6-dichloropyrimidine, n-BuOH, Et_3N. v: a) 2-amino-4,6-dichloropyrimidine, n-BuOH, Et_3N; b) p-chlorophenyldiazonium chloride, $AcONa.3H_2O$; c) Zn, AcOH, H_2O, EtOH. vi: $CH(EtO)_3$, HCl 12M. vii: NaOH 0,5M. viii: MeOH, NH_4OH.

SCHEME 1

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1. Vince, R.; Hua, M. *J. Med. Chem.*, **1990**, 33, 17-21.
2. All compounds had spectral and analytical data consistent with their structures.