A SIMPLE SYNTHESIS OF NEW PYRIMIDINYL PURINE DIONES

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ABSTRACT:
One-pot facile synthesis of three novel unusual pyrimidinyl purine diones viz. 8-[1-(4-Amino-2-oxo-1,2-dihydropyrimidin-1-yl)-ethyl]-3-methyl-3,7-dihydro-1*H*-purine-2,6-dione **3a**, 8-[1-(4-Amino-2-oxo-1,2-dihydropyrimidin-1-yl)-ethyl]-1,3-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione **3b**, and 8-[1-(4-amino-2-oxo-1,2-dihydropyrimidin-1-yl)ethyl]-3,7-dihydro-1*H*-purine-2,6-dione **3c** using $BF_3.Et_2O$ have been reported.

Key Words : Cyclodehydration, unusual, pyrimidinyl purine diones, imidazole, deacylation.

INTRODUCTION

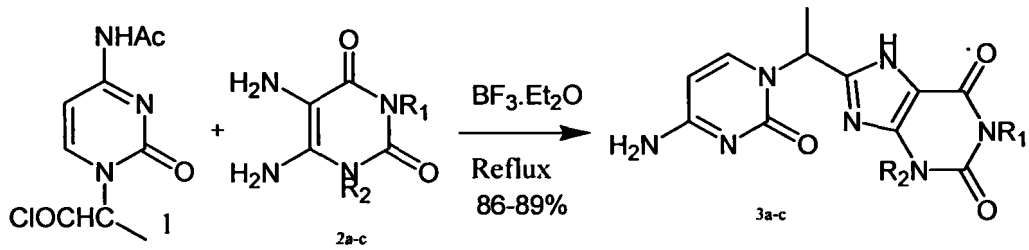
A number of fused system diones [1a-d] have been synthesized for their broad spectrum of biological activity. Various novel reagents[1e-m] have been used for the construction of imidazole rings on to aromatic hydrocarbons/heterocyclic systems. An α-nucleic acid base substituted propanoic acid has been used in the preparation of optically active polynucleotide analogs with synthetic polymer back bones,[2-5] polyethylenimine , polyvinylamine , poly(vinyl alcohol) and polytrimethylenimine .Some of these compounds possess antiviral activity [6-9].

RESULTS AND DISCUSSION

In this paper we report one-pot synthesis of three novel pyrimidinyl purine-2,6- diones using $BF_3.Et_2O$ for cyclodehydration of N- acyl derivatives. An imdazole ring was constructed onto substituted 5,6-Diaminopyrimidin-2,4-diones $\mathbf{2}_{a-c}$ using $BF_3.Et_2O$, a new and selective reagent for cyclodehydration of N- acyl derivatives. This reaction has many advantages over previous known methods. The acyl derivatives need not to be isolated for cyclodehydration and deacylation reaction.

An α-nucleic acid base substituted propanoic acid has been widely used as pendant group. It is one of the simplest derivatives of nucleic acid base possessing a chiral center and a carboxylic group. The synthesis of such compounds encouraged us to prepare some new pyrimidinyl purine-2,6-diones.

The three compounds **3a, 3b, and 3c** have been prepared by taking the advantage of this cyclodehydration reaction and such nucleic acid analogues having a carboxyl group essential for the following reaction.



a: R_1=H, R_2=Me,. b: R_1=R_2=Me,. c: R_1=R_2=H

Scheme1. Synthesis of pyrimidinyl purine-2,6-diones

The compounds **3a, 3b** and **3c** were characterized by IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectral data. In the IR spectrum, C=N appeared between 1588-1620 cm^{-1}where as NH at 3390-3425 cm^{-1}.

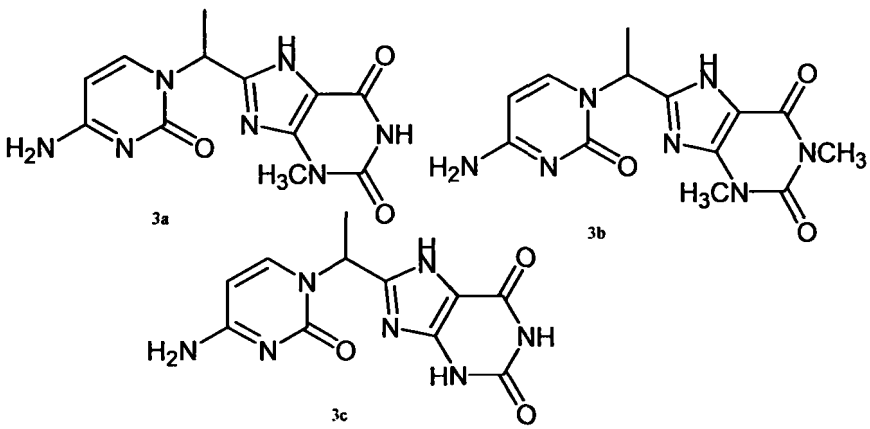


Figure 1. Structure of pyrimidinyl purine-2,6-diones

In conclusion, $BF_3.Et_2O$ has been used for the first time as efficient cyclodehydration and deacylation reagent for the synthesis of these novel pyrimidinyl purine-2,6-diones.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra of the three synthetic compounds were measured at 300 MHz and 100 MHz respectively using Bruker (Avance) NMR instrument in $CDCl_3$ and the chemical shifts referenced to tetramethylsilane. Microanalysis was carried on a Carlo Erba 1108 instrument. Mass Spectra was taken on Jeol SX 102 spectrometer. All the chemicals used were of AR grade (Sigma, BDH, & E. Merck).

Synthesis of Pyrimidinyl purine-2,6-diones ; General Procedure

2-(4-Amino-2-oxo-3,4-dihydro-2H-pyrimidin-1-yl)-propionic acid was prepared by the literature procedure.[2] The ethyl ester of the compound $[\alpha]_D$=70.2(C=0.25, TFE) after hydrolysis with 5N-HCl afforded the desired acid in 60% yield. The acid chloride **1** was prepared by treatment with $SOCl_2$ after acetylation.

To a stirred solution of 2-(4-Amino-2-oxo-3,4-dihydro-2H-pyrimidin-1-yl)-propionic acid chloride **1** (1mmol) in dry dioxane (8 mL) was added drop-wise 5,6-Diamino-1-methyl-1H-pyrimidin-2,4-dione **2a** (1mmol) dissolved in dry dioxane (2 mL) at 0^{0}C and stirred for 45min at r.t. $BF_3.Et_2O$ (0.5 mmol) in dry dioxane (2mL) was added to the

above reaction mixture and refluxed for 1.5-2.5 h at 130°C. The resulting content was concentrated in vacuo, cooled to 0°C and 0.1-NaOH aq. solution added till pH 6. The crude product was filtered and crystallized with suitable solvent to give 8-[1-(4-Amino-2-oxo-3,4-dihydro-2H-pyrimidin-1-yl)-ethyl]-3-methyl-3,7-dihydro-purin-2,6-dione **3a**.The other two compounds **3b** and **3c** were prepared following the above procedure. The TLC analysis ($CHCl_3$ - MeOH, 8:2) and Column Chromatography on Silica Gel ($CHCl_3$ -MeOH, 8:2) afforded the analytically pure compound **3a**, **3b** and **3c** in 86-89% yield, representative compound 3a, Yield (0.23g, 89%); ^{1}H NMR ($CDCl_3$): δ 7.98 (1H, d, J= 7.4 Hz), 8.1 (1H, d, J= 7.2), 1.62 (3H, d, J= 7.0), 4.8 (1H, q, J= 7.0), 2.71(3H, s); ^{13}C NMR (100MHz, $CDCl_3$): δ 166.8, 157.8, 157.6, 155.2, 136.2, 135.5, 121.9, 107.8, 62.1, 51.8, 35.8, 20.1; MS (FAB): m/z= 303 [M^+]; Anal. Calc for $C_{12}H_{13}N_7O_3$: C, 47.52; H, 4.29; N, 32.34. Found: C, 47.45; H, 4.27; N 32.29. Such analytical data for 3b and 3c were also found in conformity with their structures.

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