

Synthesis of novel 2-(2-(6-chloro-9H-purin-9-yl)ethoxy)-6-isobutoxy-tetrahydro-2H-pyran-3-ol as a potential antiviral agent

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Abstract : In this paper we propose the synthesis of 2-(2-(6-chloro-9H-purin-9-yl)ethoxy)-6-isobutoxy-tetrahydro-2H-pyran-3-ol as a new potential antiviral agent. Its structure has been confirmed by IR, ^1H -NMR, ^{13}C -NMR, UV and Mass spectroscopic data.

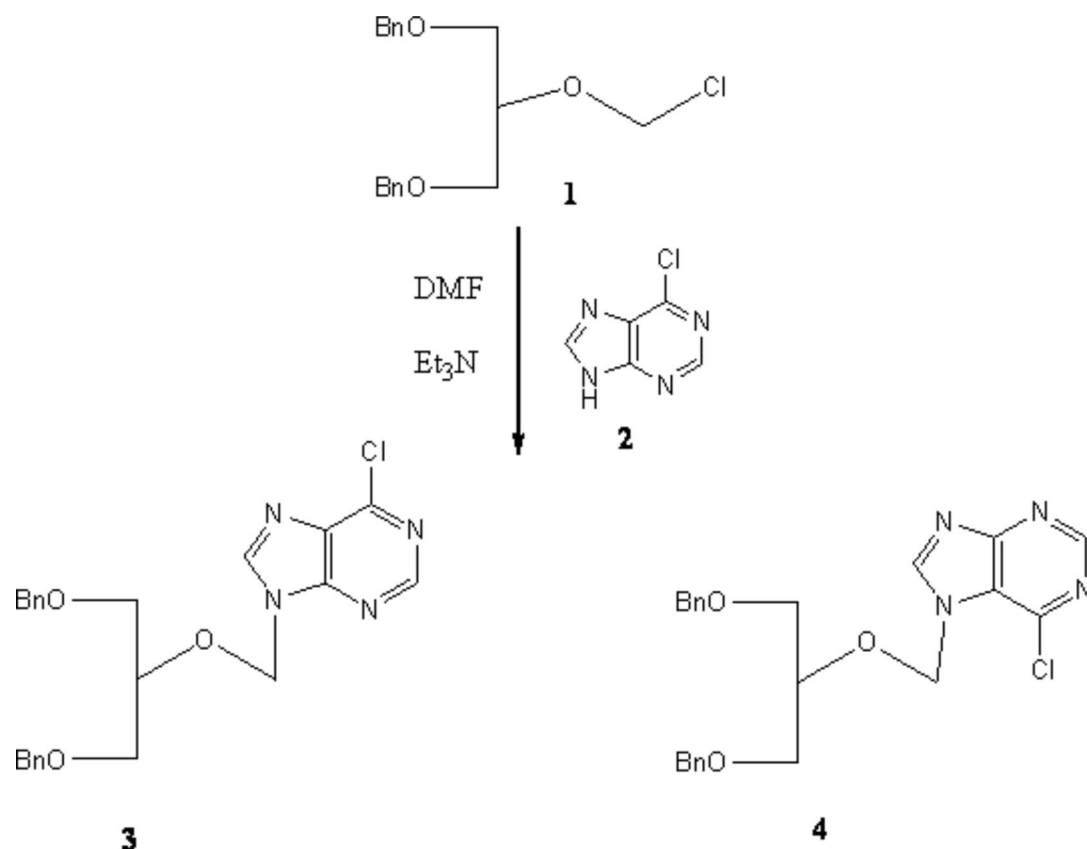
Keywords: nucleoside, 6-chloropurine, tetrahydropyran, bromoether.

Introduction

In keeping with the general antineoplastic and antileukemic properties of purine bases and their nucleosides [1-2], natural and synthetic nucleosides can have significant antitumor and/or antiviral activity [3-7]. Biological activity and importance of 6-substituted purine bases and nucleosides have been reported many times [8-11]. This led us to the synthesis of a new series of pyran nucleosides including the following one.

Results and Discussion

In principle, coupling condensation of the halo ethers with 6-chloropurine give the corresponding nucleosides as a mixture of N-7 and N-9 alkylated products. For example, 6-chloropurine **2** reacts with compound **4** in DMF to produce the 9-alkylated product **5** and N-7 isomer **6**. Heating the mixture of products results in the complete conversion of 7-alkylated isomer into 9-alkylated one (Scheme1) [12].



Scheme 1

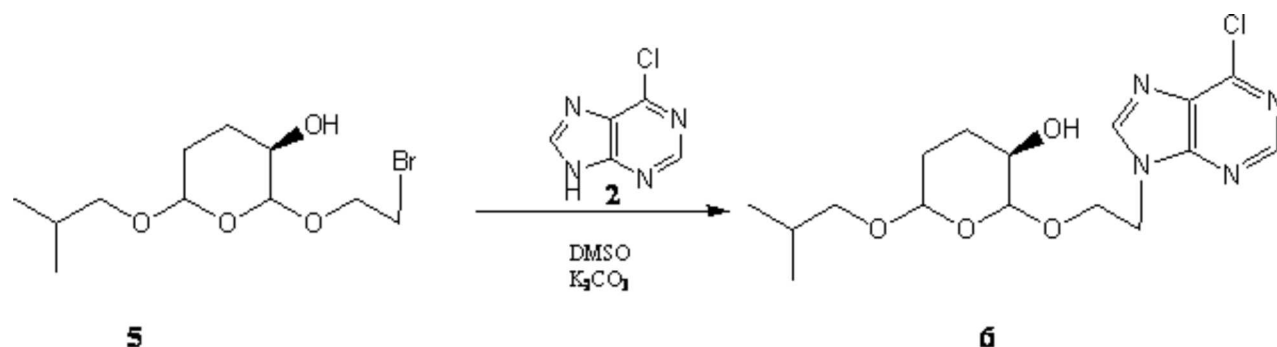
Experimental

General

All needed chemicals were purchased from Merck, Fluka chemical companies, and triethylamine. IR spectra were run on a Shimadzu FT-IR 8300 spectrophotometer. ¹H-NMR and ¹³C-NMR spectra were recorded in DMSO-d₆ and CDCl₃ using a Bruker Avance DPX instrument (¹H-NMR 250 MHz, ¹³C-NMR 62.9 MHz). Chemical shifts were reported in ppm (δ) downfield from TMS. The mass spectra were recorded on a Shimadzu GC-MS QP 1000 EX instrument. Thin-layer chromatography was carried out on silica gel 254 analytical sheets obtained from Fluka. Column chromatography was carried out on silica gel 60 Merck (230-270 mesh).

Synthesis of 2-(2-(6-chloro-9H-purin-9-yl)ethoxy)-6-isobutoxy-tetrahydro-2H-pyran-3-ol

To a mixture of bromoether **5** (5.94 g, 20.00mmol) and 6-chloropurine **2** (3.09g, 20.00mmol) in DMSO (50 mL) was added potassium carbonate (3.45g, 25.00mmol) and the mixture was stirred at room temperature for 39 hours. The reaction mixture was filtered and the mother liquor poured into ice water, acidified to pH 5 by acetic acid and then was extracted with ethyl acetate (4x200 mL). The organic layer was washed with water (800 mL) and extracted. It then was dried (Na₂SO₄), filtered, and then freed from solvent under reduced pressure. The residue was purified by column chromatography on silica gel and gave **6** as a yellow oil product in 50% (3.85g) yield (Scheme2).



Scheme 2

Boiling point: 153 °C

R_f = 0.58

¹H-NMR (CDCl₃): δ = 0.8 (d, 6H, C (CH₃)₂), J = 5 Hz); 1.6 (s, 5H, 2CH₂, CH); 2.7-4.00 (m, 7H, 2CH₂O, CH₂N, CH); 4.2-4.7 (m, 3H, 2CH, OH); 8.2 (s, 1H, Ar-H); 8.5 (s, 1H, Ar-H).

IR (neat, cm⁻¹): 3500; 3100; 2960; 2880.

UV (EtOH; λ_{max} nm; ε dm³.mol⁻¹.cm⁻¹): 267 (ε 16692); 201 (ε 20500).

MS (m/e): 118 (C₅H₂N₄); 100 (C₅H₈O₂); 99 (C₅H₇O₂); 83 (C₅H₇O); 47 (C₃H₇).

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Sample Availability: Available from MDPI.

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