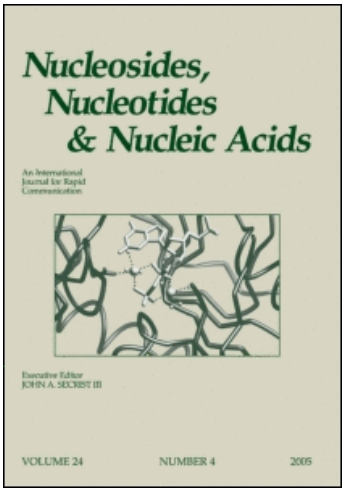

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The Synthesis of Derivatives of 2-Arylamino *ara*-Carbocyclic Purine Nucleosides as Potential Anti-Viral Agents

Masakazu Koga[a]; Stewart W. Schneller[a]
[a] Department of Chemistry, University of South Florida, Tampa, FL

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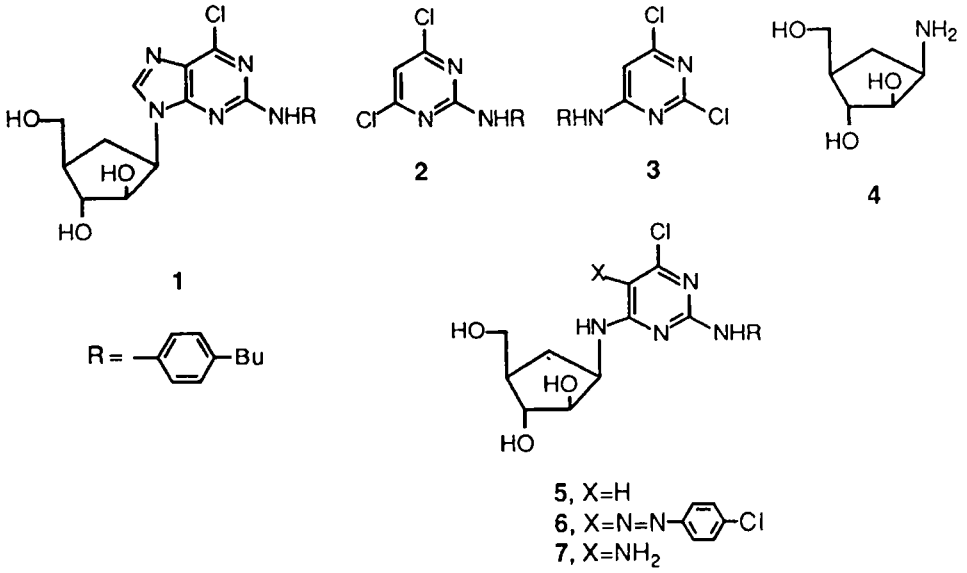
THE SYNTHESIS OF DERIVATIVES OF 2-ARYLAMINO *ara*-CARBOCYCLIC PURINE NUCLEOSIDES AS POTENTIAL ANTI-VIRAL AGENTS

Masakazu Koga and Stewart W. Schneller*
Department of Chemistry
University of South Florida
Tampa, FL 33620-5250

Abstract: A general synthetic method into 2-arylamino *ara*-carbocyclic purine nucleosides from 2,4,6-trichloropyrimidine is described.

Wright and his co-workers have described purine nucleosides that possess a C-2 arylamino side chain and are inhibitory towards DNA polymerase alpha.[1] In an effort to extend these observations to the development of antiviral agents that can act at the viral DNA polymerase level, similar derivatives of carbocyclic nucleosides have been established in our laboratory as target molecules. This paper is a preliminary account of a route into the *ara*-carbocyclic series as represented by **1**.

Reaction of 2,4,6-trichloropyrimidine with 2 eq. of 4-(1-butyl)aniline gave a mixture, which was subjected to flash column chromatography to give **2** (35%, mp 59-60 °C, colorless needles) upon elution with $CHCl_3$:hexane (1:1) and **3** (54%, mp 77-78 °C, colorless needles) following elution with $CHCl_3$.[2,3] Treatment of **2** with **4**[4] in refluxing 1-butanol with triethylamine under Argon resulted in **5** (76% yield, based on the tetra-acetyl precursor of **4**, following flash chromatography using MeOH:$CHCl_3$ (10:90) and then recrystallization from AcOEt; mp 114-116 °C, colorless needles). Compound **5** was converted into the diazo product **6** (83%, mp 203-205 °C, as a yellow powder following washing with MeOH) with 4-chlorobenzenediazonium chloride. Reduction of **6** with zinc in MeOH containing AcOH produced a 93% yield of **7** (mp 106-109 °C, pale pink needles), following flash chromatography using MeOH:$CHCl_3$ (5:95). Ring closure of **7** with diethoxymethyl acetate in MeOH containing a small amount of HCl resulted in **1** (75%, mp 172-173 °C, colorless needles following flash chromatography with MeOH:$CHCl_3$ (5:95) and then recrystallization from $CHCl_3$/MeOH).



Due to the lability of the 6-Cl group of purine nucleosides towards nucleophilic substitution, **1** offers a convenient entry into a large number of carbocyclic derivatives of interest, particularly when done in tandem with varying the arylamino unit of **2**. This is currently being pursued.

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REFERENCES

(1) For a leading reference, see Wright, G. E.; Dudycz, L. W.; Kazimierczuk, Z.; Brown, N. C.; Khan, N. N., *J. Med. Chem.*, **1987**, *30*, 109.

(2) Pyrimidine ring ^{13}C-NMR (DMSO-d_6) for **2**: δ 160.90, 158.95, and 109.71; for **3**: δ 162.25, 158.89, 158.14, and 103.20.

(3) All compounds reported herein gave satisfactory spectral data (including ^{13}C NMR).

(4) Vince, R.; Brownell, J.; Daluge, S., *J. Med. Chem.*, **1984**, *27*, 1358.