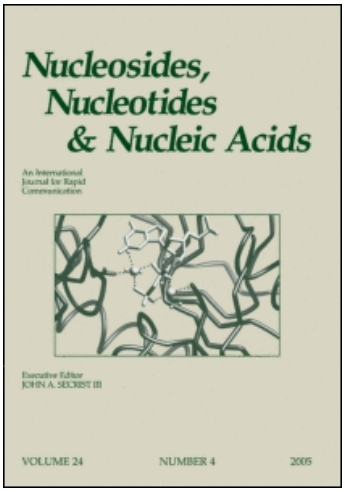

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A NEW METHOD FOR SYNTHESIZING ACYCLONUCLEOSIDES

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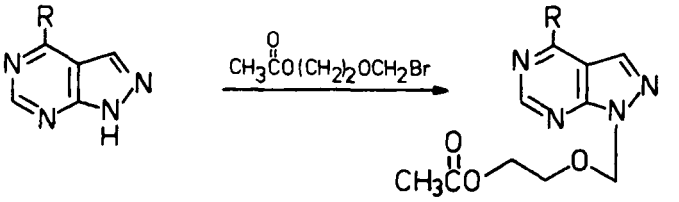
Abstract: We prepared, using a phase transfer catalyst liquid-liquid or solid-liquid, a new series of acyclonucleoside analogues of allopurinol, where the ribose moiety is replaced by (hydroxy-2-ethoxy)-methyl.

The synthesis method of Acyclonucleosides described in the literature (1) via silylation and subsequent alkylation or alkylation in presence of sodium hydride gives nucleosides 1A and 1B (scheme I) with low yield (table 1).

Then we used phase transfer catalyst (P.T.C.) to prepare our products. The P.T.C. liquid-liquid (2) reaction resulted in selective N_1 isomer and 30 to 60 % yield depending on the substitution at C_4 (serie A). The reaction in serie B afforded two isomers with 30 to 60 % yield.

In direction to have a high selectivity we made the alkylation reaction with P.T.C. solid-liquid using as catalyst 18 Crown 6 or tetraglyme. The yield increase (table 2) and the reaction became



A R = SCH_3; SC_2H_5; $SCH_2Ø$ 1A

B R = $NHCH_3$; $N(CH_3)_2$; $NHCH_2Ø$ 1B

Scheme I

Table 1

S = Silylation
Y = Silylation/$HgCN_2$ or TBAI
U = No Isomer N_1
Z = No reaction

	S	Y	NaH
1A	10-20%	Z	30-40%
1B	U	Z	30-40%

TBAI: Tetrabutylammoniumiodide
TBABr: " " bromide
T: Tetraglyme
C: 18 Crown 6
W: CH_2Cl_2 / THF
1Ad; 1-6BAP, 1U: acyclonucleosides
*: two isomers.

Table 2

	1 A	1 B	1 A	1 B	1 Ad	1 6BAP	1 U
Solv.	W	W	THF	THF	THF	THF	THF
Catal.	TBABr	TBABr	T / C	T / C	T / C	T / C	T / C
Yield	30-60%	30-60%*	50-80 % / 50-70 %	50-80 % / 50-70 %	70 % / 60 %	70 % / 80 %	60 % / 70 %

regioselective in serie B because only the isomers substituted at N_1 are obtained.

For comparison we applied the P.T.C. solid-liquid to obtain acyclonucleosides of adenine (Ad), 6-benzylamino purine (6-BAP), uracil (U), etc...

We remark that 18 Crown 6 and tetraglyme as catalyst lead to high yield (table 2) and good regioselectivity (only N_1 and N_9 are obtained respectively in serie pyrimidine and purine).

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