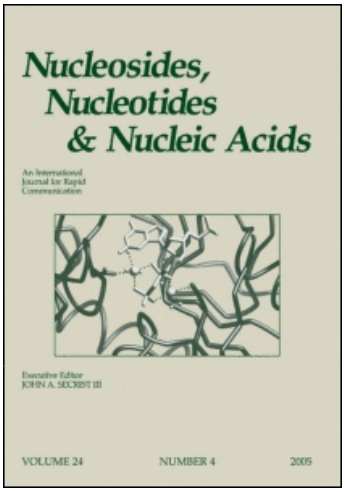

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Synthesis of Pyrrolo[3,2-c]pyridine and Pyrazolo[3,4-d]pyrimidine β-D-Arabinonucleosides via Nucleobase Anion Glycosylation

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SYNTHESIS OF PYRROLO[3,2-c]PYRIDINE AND PYRAZOLO[3,4-d]PYRIMIDINE β-D-ARABINONUCLEOSIDES VIA NUCLEOBASE ANION GLYCOSYLATION

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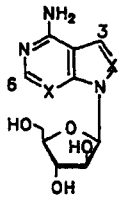
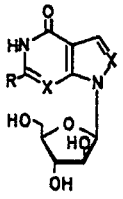
ABSTRACT: Ara-3,7-dideazaadenosine (**1a**), ara-8-aza-7-deazaadenosine (**1b**) and the corresponding inosine derivatives **2a,b** were synthesized. Nucleobase anion glycosylation was stereoselective but gave N-1 and N-2 regioisomers in case of pyrazolo[3,4-d]pyrimidines.

3,7-Dideazaadenine and 8-aza-7-deazaadenine β-D-arabinofuranoside (**1a,b**)[1,2] as well as the inosine derivatives **2a-c** were synthesized.

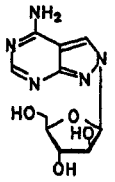


1a,b

	X	R
a	CH	H
b	N	H
c	CH	Cl



2a-c



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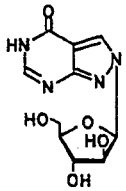

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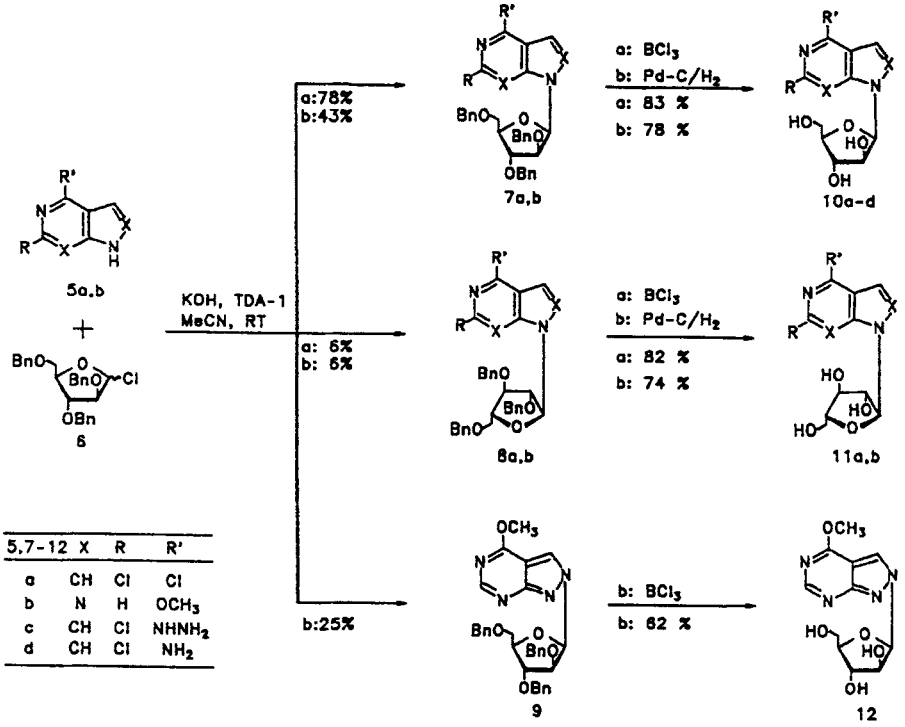
Phase-transfer glycosylation of the **5a** anion with the halogenose **6** (MeCN, KOH,TDA-1)[3] resulted in the N-1 isomer **7a**, stereoselectively. Under the same conditions the regioisomers **7b** and **9** were formed from **5b**. The formation of small amounts of α-anomers (**8a** and **8b** = 6%, each) is due to the anomeric mixture of **6** (α:β, 12:1) used for the glycosylation reaction.

Debenzylation of **7a,b**, **8a,b** and **9** afforded the arabinonucleosides **10a,b**, **11a,b** and **12**. Their anomeric configuration and the position of glycosylation were determined by ^{1}H NMR NOE-difference spectroscopy.[4]

Compound **10a** was converted into **10d** via the hydrazino derivative **10c** followed by treatment with Raney nickel catalyst. Catalytic hydrogenation of **10d** gave **1a**. The 4-chloro group of **10a** was also displaced with NaOH (**2c**) and the 6-chloro substituent removed by catalytic hydrogenation (**2a**). In case of **10b** and **12** the 4-methoxy group was converted into **1b**, **2b**, **3**, and **4** by NH_3 or NaOH treatment. Compound **2b** was also obtained from **1b** upon deamination with adenosine deaminase while the nucleosides **1a** and **3** are resistant.



5,7-12	X	R	R'
a	CH	Cl	Cl
b	N	H	OCH_3
c	CH	Cl	$NHNH_2$
d	CH	Cl	NH_2

REFERENCES AND NOTES

1. ^1H NMR (DMSO-d_6): **1a**: 6.01 (s, NH_2), 6.08 (d, J = 4.9 Hz, H-1'); **1b**: 7.76 (s, NH_2), 8.17 (s, H-3), **2a**: 6.09 (d, J = 5.1 Hz, H-1'); **2b**: 8.12 (s, H-3), 12.38 (d, J = 3.8 Hz, NH); **2c**: 6.07 (d, J = 5.4 Hz, H-1'); **3**: 7.76 (s, NH_2), 8.54 (s, H-3), **4**: 11.76 (s, NH), 8.59 (s, H-3); **10a**: 6.30 (d, J = 5.5 Hz, H-1'), 7.84 (s, H-7); **10b**: 8.32 (s, H-3), 8.61 (s, H-6); **10c**: 4.36 (br s, NH_2), 6.08 (d, J = 5.4 Hz, H-1'), 8.14 (s, NHNH$_2$); **10d**: 6.05 (d, J = 5.2 Hz, H-1'); **11a**: 5.94 (d, J = 5.2 Hz, H-1'); **11b**: 8.40 (s, H-3), 8.67 (s, H-6), **12**: 8.55 (s, H-6), 8.74 (s, H-3).

2. M.P.(°C): **1a**: 236; **1b**: 202; **2a**: 241-243; **2b**: 186-188; **2c**: 238-240; **4**: 176; **10a**: 204-205; **10b**: 215; **10c**: 205; **10d**: 205-206; **11a**: 198-199; **11b**: 153; **12b**: 134-136.

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4. H. Rosemeyer, G. Tóth, F. Seela, Nucleosides & Nucleotides, **8**, 587 (1989).