SYNTHESIS OF 1,4-ANHYDRO-2,5-DIDEOXY-D-*ERYTHRO*-3--(HYDROGEN PHOSPHATE)-5-AMINIUM-PENTITOL

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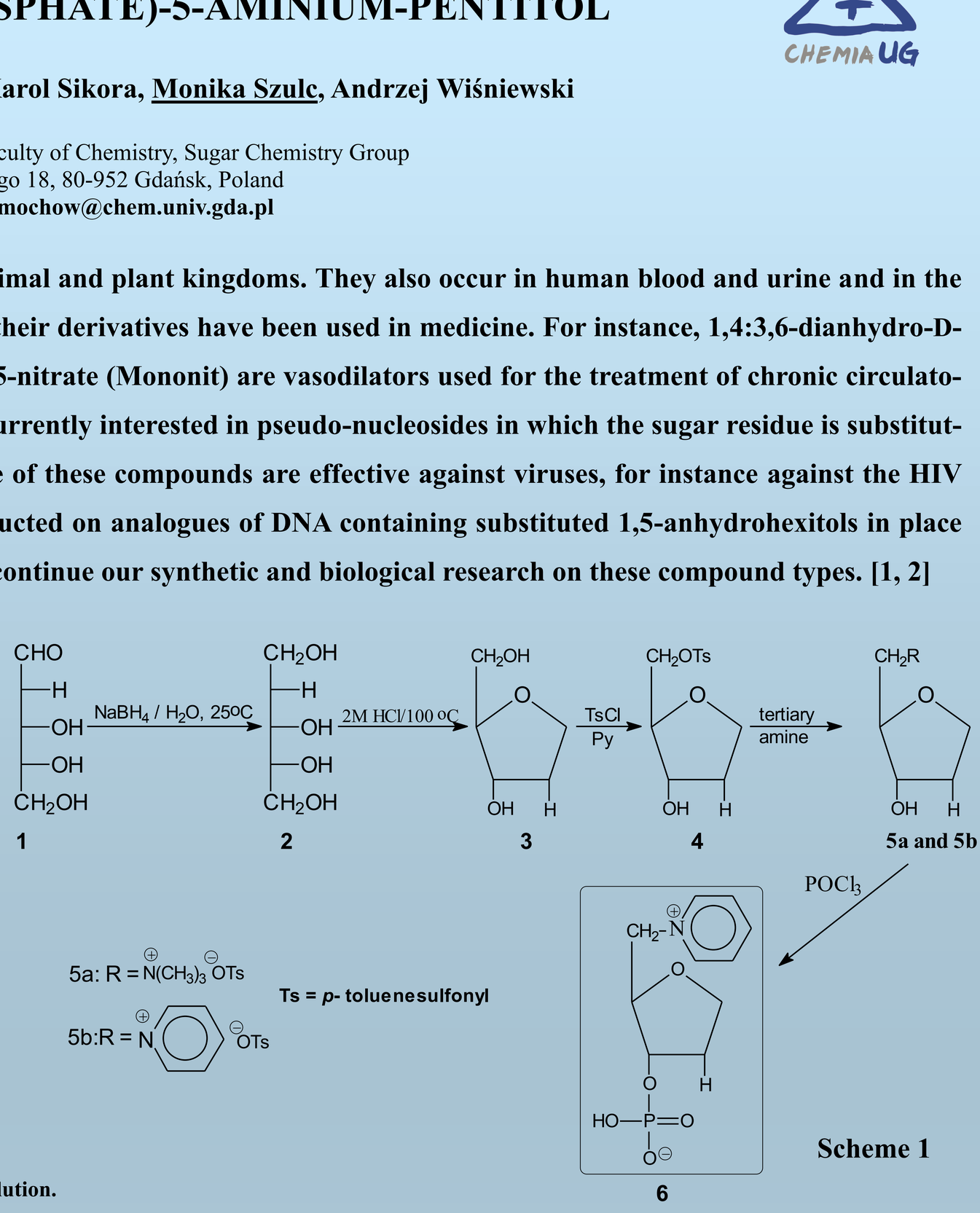
Alditols and anhydroalditols are widespread in both the animal and plant kingdoms. They also occur in human blood and urine and in the amniotic and cerebrospinal fluids. These compounds and some of their derivatives have been used in medicine. For instance, 1,4:3,6-dianhydro-D-glucitol 2,5-dinitrate (Sorbonit) and 1,4:3,6-dianhydro-D-glucitol 5-nitrate (Mononit) are vasodilators used for the treatment of chronic circulatory insufficiency and stenocardia. Both chemists and biologist are currently interested in pseudo-nucleosides in which the sugar residue is substituted by 1,4-anhydropentitol or 1,5-anhydrohexitol derivatives. Some of these compounds are effective against viruses, for instance against the HIV virus. Intense chemical and biological investigations are also conducted on analogues of DNA containing substituted 1,5-anhydrohexitols in place of 2-deoxy-D-ribose. In view of these developments, we decided to continue our synthetic and biological research on these compound types. [1, 2]

Actually we are working on the synthesis of 1,4-anhydro-2,5-dideoxy-D-*erythro*-3-(hydrogen phosphate)-5-aminium-pentitol in reaction of *N*-(1,4-anhydro-2,5-dideoxy-D-*erythro*-pentitol-5-yl)aminium tosylates (QACs) with phosphoryl chloride and trimethyl phosphate (Scheme 1).

The structures of isolates were determined by spectral analysis including extensive 2D NMR (Table 1,2) analyses and X-ray crystallography (Fig. 1 and Fig. 2). QACs demonstrated mutagenic activity in bioluminescence mutagenicity assay based on *Vibrio harveyi* A16 strain (Fig. 3 and Fig. 4).



Scheme 1

Table 1. Chemical shifts (ppm) in the ^{1}H NMR spectra for ammonium salts in D_2O solution.

	H-1	H-1'	H-2	H-2'	H-3	H-4	H-5	H-5'	cation	anion
5a	3.99; **dd,** 1H	3.99; **dd,** 1H	1.90; **m**, 1H	2.17; **m**, 1H	4.14; **m**, 1H	4.18; **m**, 1H	3.38; **dd**, 1H	3.50; **dd**, 1H	3.14; **s**, 9H	2.34; **s**, 3H (MePh) 7.65-7.31; **2d**, 2H (Ph)
5b	4.01; **sextet,** 1H	3.94; **q**, 1H	1.95; **m**, 1H	2.11; **m**, 1H	4.34; **quintet**, 1H	4.16; **dt**, 1H	4.43; **dd**, 1H	4.80; **dd**, 1H	8.77-8.00; **m**, 5H	2.32; **s**, 3H (MePh) 7.63-7.28; **2d**, 2H (Ph)
6	4.01; **sextet**, 1H	3.91; **q**, 1H	2,11; **m**, 1H	2.11; **m**, 1H	4.63; **m**, 1H	4.32; **dt**, 1H	4.48 **dd**, 1H	4.86 **dd**, 1H	8.77-8.01; **m**, 5H	———

Table 2. Chemical shifts (ppm) in the ^{13}C NMR spectra for ammonium salts in D_2O solution.

	C-1	C-2	C-3	C-4	C-5	cation	anion
5a	67.79	33.14	74.46	79.41	67.62	54.36-54.29	142.70-125.64; 20,73
5b	67.77	33.66	73.10	83.97	62.84	146.41-128.38	142.60-125.59; 20.69
6	67.87	33.00	76.81	83.20	62.55	146.50-128.42	———

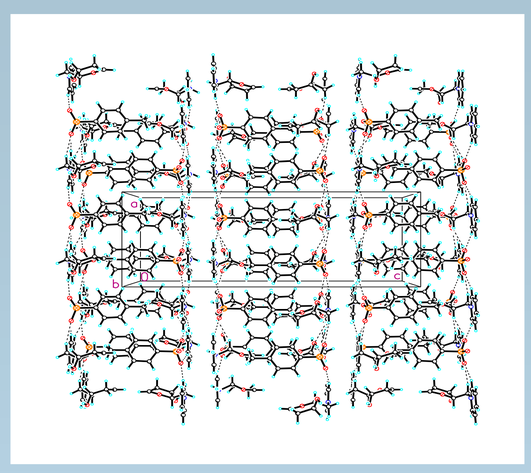


Fig. 1. The molecular packing of *N*-(1,4-anhydro-2,5-dideoxy-D-*erythro*-pentitol-5-yl) pyridinium tosylate (**5b**).

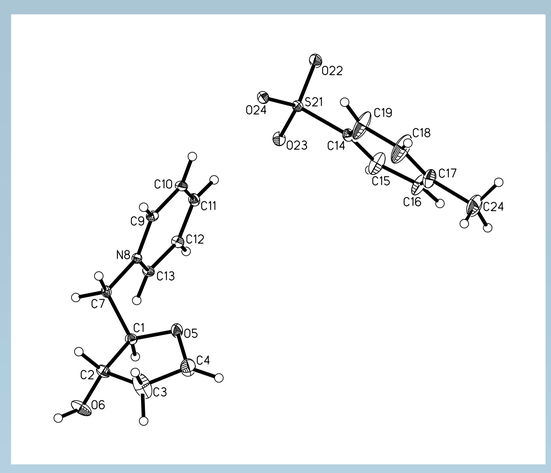


Fig. 2. The molecular structure of *N*-(1,4-anhydro-2,5-dideoxy-D-*erythro*-pentitol-5-yl) pyridinium tosylate (**5b**).

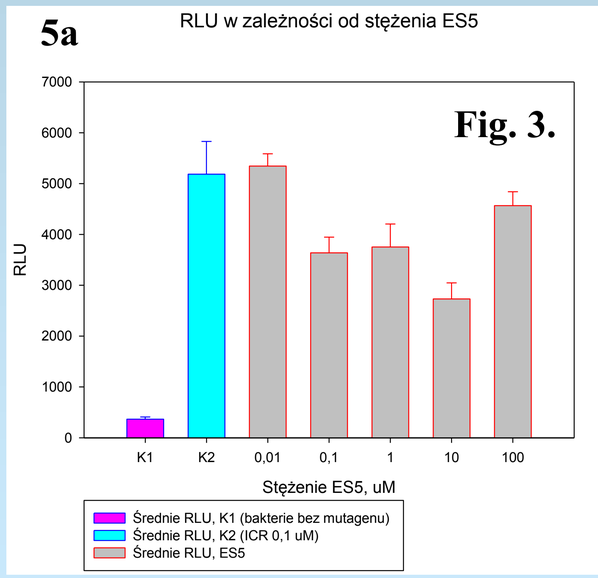


Fig. 3.

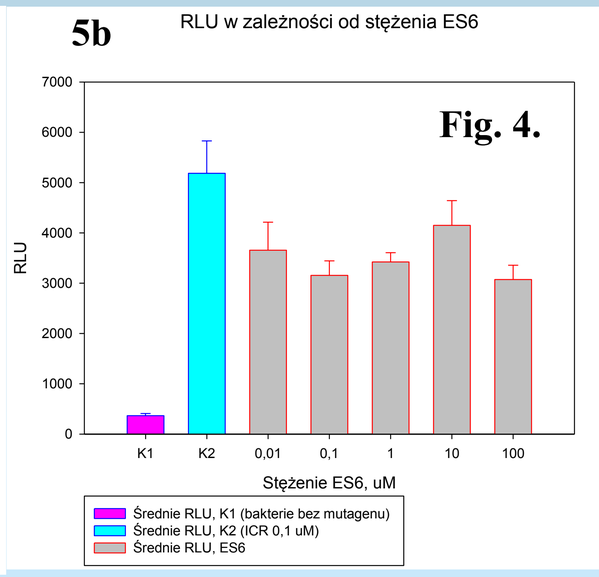


Fig. 4.

K1 – control 0; **K2** – control MeIQ, 0.1μM

References:

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[2] M. Thomas, D. Montenegro, A. Castano, L. Friedman, J. Leb, M. Lace Hung, L. Rothman, H. Lee, C. Capodiferro, D. Ambinder, E. Care, J. Galante, J.L. Rizzo, K. Melkonian, R. Engel, *Carbohydr. Res.* **2009**, 344, 1620-1627.

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