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Convenient Synthesis of Hex-5-enopyranosides

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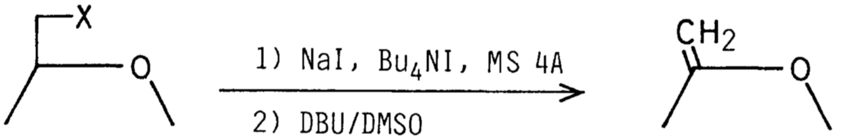
Hex-5-enopyranosides were prepared in an one-pot procedure from 6-bromo-6-deoxy- or 6-O-tosylhexopyranoside by the successive treatment with iodide anion and 1,8-diazabicyclo-[5.4.0]undec-7-ene in DMSO.

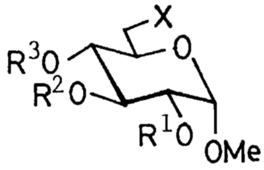
Hex-5-enopyranosides are very useful precursor of such biologically important compounds as 6-deoxy-L-hexose[1] and cyclitol,[2] and have been synthesized by treatment of 6-bromo- or 6-iodo-6-deoxyhexopyranosides with AgF/pyridine,[3] NaH/N,N-dimethylformamide,[4] or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)/CH_3CN-benzene.[5] These methods, however, are often accompanied with the formation of such by-products as 6-fluoro-6-deoxy derivatives.[6] We should like to report a facile and effective synthesis of hex-5-enopyranosides from easily available 6-bromo-6-deoxy- and 6-O-tosylhexopyranosides.



X=Br, OTs

The optimized conditions for this elimination reaction were as follows: A mixture of 6-bromo-6-deoxy or 6-O-tosylhexopyranoside (0.5 mmol), sodium iodide (2.5 mmol), tetrabutylammonium iodide (0.25 mmol) and molecular sieves 4A in dimethyl sulfoxide (DMSO, 10 ml), was stirred at 80-110 °C until the starting hexose disappeared on TLC. After DBU (0.6 mmol) was added, the mixture was stirred at 80 °C until the intermediary 6-iodide disappeared, poured into water (40 ml) and extracted with ethyl acetate several times. The combined organic layer was washed with a small amount of water, dried and evaporated to give crude hex-5-enopyranoside,[7] which was purified by preparative TLC. Under this condition (A in Table 1) five 6-bromo-6-deoxy-α-D-gluco (1) and -α-D-altrohexopyranosides (4–7) and two 6-O-tosyl-α-D-glucopyranosides (2 and 3) gave the expected hex-5-enopyranosides in 84-95% yields.

The addition of the molecular sieves caused a distinct improvement as was not always the case (see the yields under condition B in Table 1, where the reaction was carried out without molecular sieves 4A). Under the anhydrous conditions undesired hydrolysis may be prevented especially in the cases of the sluggishly eliminating substrates. The effect of the substitution with iodide was much more obvious as shown in the cases of α-D-glucopyranosides 1—3 (see the yields under condition C in Table 1, where the reaction was carried out without the iodides and molecular sieves). Thus the method proposed herein may promise a wide application to the preparation of hex-5-enopyranosides.



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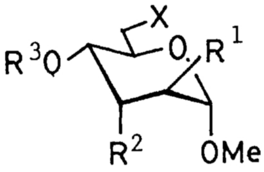

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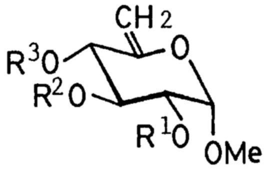

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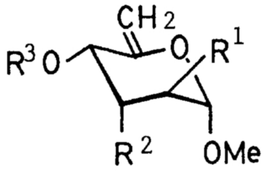

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Table 1. Yields of hex-5-enopyranosides under different reaction conditions

Substrate	R^1	R^2	R^3	X	Product	Yields/% A	Yields/% B	Yields/% C	Chemical shift of methylene proton /ppm	
1	Me	Me	Bz	Br	8	85	68	32	4.56t,	4.72t
2	Me	Me	Bn	OTs	9	88	84	28	4.72t,	4.87t
3	Bz	Bz	Ac	OTs	10	84	66	10	4.68t,	4.87t
4	OBz	OAc	Bz	Br	11	95	95	78	4.88d,	4.97d
5	OAc	NHAc	Bz	Br	12	84	81	80	4.81s,	4.91s
6	H	OBz	Me	Br	13	86	82	54	4.66s,	4.87s
7	H	OBz	Bz	Br	14	94	94	92	4.82d,	4.90d

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7) The structures of 5-enopyranosides 8—14 were clearly ascertained by disappearance of H-5 protons and exocyclic methylene protons on C-6 (see Table 1), which have characteristic small geminal coupling constants, if any.

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