

ANOMALOUS NUCLEOSIDES

X. Synthesis of 1-Benzotriazolylglycosides*

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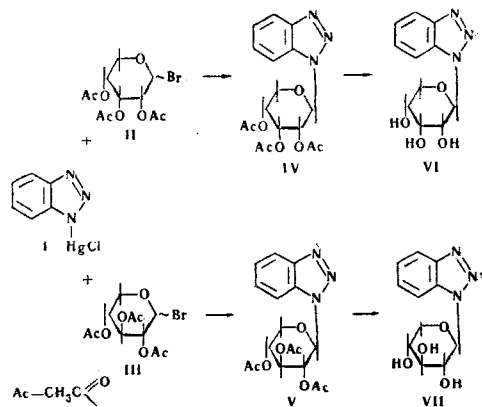
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By the condensation of the mercury salt of benzotriazole with acetylpenosyl bromides in xylene, we have synthesized 1-benzotriazolyl-2',3',4'-tri-O-acetyl- β -D-ribo- and -xylopranosides, the deacetylation of which has given anomalous nucleosides—antimetabolites of nucleic metabolism: 1-benzotriazolyl- β -D-ribo- and 1-benzotriazolyl- β -D-xylopyranoside.

It is known that nitrogen bases that are derivatives and analogs of the natural pyrimidines and purines exert their biological activity in many cases after their conversion in the organism into the corresponding nucleosides and nucleotides. Since the limiting stage in this is ribosidation, it is desirable to synthesize derivatives and analogs of the natural nucleosides and even use them as chemotherapeutic substances [1].

A structural analog of purine—benzotriazole—and a number of its derivatives possess biological activity [2, 3]. Their glycosidation may be expected to increase the activity and broaden the spectrum of their biological action.



The following compounds of this type are known: 1-benzotriazolyl-5,6-D-ribofuranoside [4], obtained via the silver salt of benzotriazole, and the benzotriazolynucleosides of gluco-, galacto-, and arabopyranoses, synthesized via N-trimethylsilylbenzotriazole [5, 6].

*For part IX, see [9].

In order to study their biological activity, we have synthesized, by the mercury salt method, 1-benzotriazolyl- β -D-ribo- and -xylopyranoside (VI) and 1-benzotriazolyl- β -D-xylopyranoside (VII).

The pyranose forms of VI and VII were shown by periodate oxidation. (In 12 hr, 1 mole of VI consumed 1.9 mole of NaIO_4 and 1 mole of VII consumed 2.05 mole of NaIO_4).

We may assume that VI and VII have the β -configuration [7], but this will be established accurately by experiment.

EXPERIMENTAL

Mercury salt of benzotriazole (I). A solution of 5.95 g (0.05 mole) of benzotriazole in a mixture of 50 ml of 1 N NaOH and 50 ml of ethanol was added, dropwise with stirring, to a solution of 13.8 g (0.05 mole) of mercury chloride in 800 ml of 25% ethanol solution. The white amorphous precipitate was filtered off and washed with 25% ethanol. Yield 16.5 g (91.5%).

Acetylribose bromide (II) and acetylxylose bromide (III) were obtained by treating the corresponding tetraacetylpenosides with 40% HBr in glacial acetic acid [8].

1-Benzotriazolyl-2',3',4'-tri-O-acetyl- β -D-ribo- and -xylopranosides (IV and V). A solution of 3.35 g (0.01 mole) of II (or III) in xylene was added with stirring to a suspension of 3.5 g (0.01 mole) of I in 800 ml of boiling xylene, after part of the solvent had been distilled off. The mixture was boiled for another 20-30 min, cooled, and filtered from the HgCl_2 . The filtrate was treated twice with 100 ml of a 30% solution of KI, washed with water, dried over Na_2SO_4 , and evaporated in vacuum to a syrup. The syrup was diluted with a small amount of absolute ethanol and left to crystallize in the cold. The precipitate of IV (or V) was filtered off, dried, and recrystallized.

1-Benzotriazolyl- β -D-ribo- and -xylopyranosides (VI, VII). A solution of 0.8 g (0.002 mole) of IV (or V) in absolute methanol was saturated with ammonia at 0° C for 1 hr 30 min and was left in the cold for two days, after which it was evaporated to dryness and the residue was recrystallized.

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1-Benzotriazolylglycosides

Compound	Mp, °C (ethanol)	[α] _D ²⁰	Empirical formula	Found, %			Calc., %			Yield, %
				C	H	N	C	H	N	
IV	156-158	-38	$\text{C}_{17}\text{H}_{19}\text{N}_3\text{O}_7$	54.11	5.04	11.14	—	—	11.24	52
V	161-163	-114	$\text{C}_{17}\text{H}_{19}\text{N}_3\text{O}_7$	54.11	5.04	11.14	54.63	5.03	11.03	38
VI	184-186	-32	$\text{C}_{11}\text{H}_{13}\text{N}_3\text{O}_4$	52.60	5.17	16.75	52.50	5.38	16.83	90
VII	207-209	-43	$\text{C}_{11}\text{H}_{13}\text{N}_3\text{O}_4$	52.60	5.17	16.75	52.97	5.06	16.75	92

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