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SYNTHESIS OF 5-AMINO-5-DEOXY-α-D-ALLOFURANURONIC ACID DERIVATIVE, A SUGAR COMPONENT OF POLYOXINS

SYNTHESIS IN NUCLEOSIDE ANTIBIOTICS, PART VII

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Polyoxins A - L, discovered by Suzuki, Isono and their coworkers[1] are a group of antifungal nucleoside antibiotics produced by Streptomyces cacaoi var. asoensis. These antibiotics, except polyoxins C and I, are highly active against phytopathogenic fungi such as Pellicuraria sasakii, and now in practical use in this country as an agricultural fungicide. Structures of these antibiotics have recently been firmly established by the above investigators, and a 5-amino-5-deoxy-D-allofuranuronic acid has been found to be a commonly occurring sugar component of polyoxins.[2] This paper deals with the first chemical synthesis of 5-amino-5-deoxy-α-D-allofuranuronic acid derivative. The sequence of reactions is shown in Chart 1.

The 1,2:5,6-di-O-isopropylidene-α-D-allofuranose[3] (I) derived from D-glucose was benzoylated to give 3-O-benzoate, m.p. 75-76°; $[\alpha]_D^{22}$ +116°(c 1.0 acetone). The 3-O-benzoate was then converted into 3-O-benzoyl-1,2-O-isopropylidene-α-D-allofuranose (II), m.p. 107-109°; $[\alpha]_D^{22}$ +117°(c 1.5 chloroform), by hydrolysis with 1.5% H_2SO_4-70% ethanol in 70% yield.

After mesylation of II with mesyl chloride in pyridine, treatment of the dimesyl compound, m.p. 102-104°; $[\alpha]_D^{22}$ +102°(c 1.5 chloroform), with sodium benzoate in boiling DMF[4] gave 1,2-O-isopropylidene-3,5,6-tri-O-benzoyl-β-L-talofuranose (III) in 55% yield, m.p. 156-158°; $[\alpha]_D^{22}$ +90°(c 1.0 chloroform).

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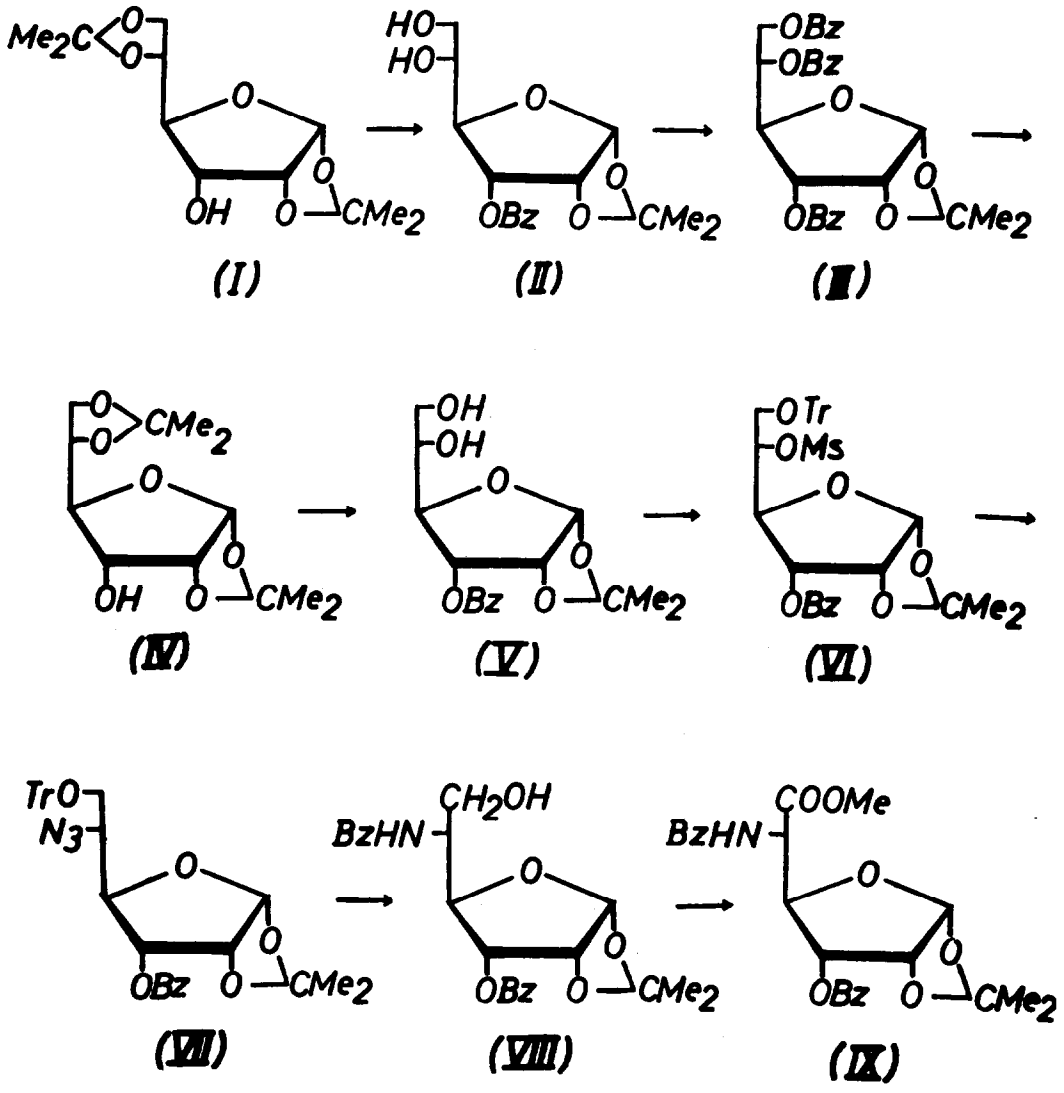
Me2C
HO
HO
OBz
OBz
OH
OBz
CMe2
(I)
(II)
(III)
OH
OTr
OMs
(IV)
(V)
(VI)
TrO
N3
BzHN
CH2OH
COOMe
(VII)
(VIII)
(IX)

Chart 1.

Debenzoylation of III with sodium methoxide in methanol afforded 1,2-O-isopropylidene-β-L-talofuranose in 75% yield, m.p. 100-101°; $[\alpha]_D^{22}$ +52°(c 1.1 methanol), which, after treatment with dimethoxypropane containing catalytic quantity of p-toluenesulfonic acid, yielded 1,2:5,6-di-O-isopropylidene-β-L-talofuranose (IV) in 65% yield, m.p. 86-87°; $[\alpha]_D^{22}$ +30°(c 1.0 acetone), [lit.[5] m.p. 85-86°; $[\alpha]_D$ +31°(c 0.5 chloroform)].

Benzoylation of IV and subsequent hydrolysis by the same procedure descrived above gave the product (V), m.p. 96-98°; $[\alpha]_D^{22}$ +107°(c 1.6 chloroform), which was in turn tritylated and mesylated in pyridine to give 3-O-benzoyl-1,2-O-isopropylidene-5-O-mesyl-6-O-trityl-β-L-talofuranose (VI), $[\alpha]_D^{22}$ +50°(c 1.4 chloroform).

Inversion of VI with sodium azide in refluxing DMF gave 5-azido allofuranose derivative (VII) in 85% yield, $[\alpha]_D^{22}$ +79°(c 1.1 chloroform). The 5-azido derivative (VII) was hydrogenated over 10% palladium on charcoal in methanol and then benzoylated to 5-benzamido-3-O-benzoyl-5-deoxy-1,2-O-isopropylidene-6-O-trityl-α-D-allofuranose, $[\alpha]_D^{22}$ +67°(c 1.1 chloroform).

Detritylation of 5-benzamido derivative with acetone containing equivalent quantity of p-toluenesulfonic acid instead of hydrogen chloride[6] afforded 5-benzamido-3-O-benzoyl-5-deoxy-1,2-O-isopropylidene-α-D-allofuranose (VIII) in 70% yield, m.p. 206-208°; $[\alpha]_D^{22}$ +100°(c 1.2 chloroform).

Oxidation of VIII with potassium permanganate in acetone-acetic acid followed by esterification with diazomethane afforded methyl(5-benzamido-3-O-benzoyl-5-deoxy-1,2-O-isopropylidene-α-D-allofuran)uronate (IX) in 50% yield, m.p. 152-154°; $[\alpha]_D^{22}$ +112°(c 0.3 chloroform).

The nmr parameters of IX are shown in Table 1. The sequence of above reactions and nmr data support the structure of IX.

Table 1. The nmr data of IX in $CDCl_3$ (60 MHz)

	Chemical shift (δ)*		Coupling constant (Hz)		Chemical shift (δ)*
H-1	5.88	doublet		$-COOCH_3$	3.75
			($J_{1,2}$= 3.6)		
H-2	4.96	quartet		$-O-O-C(CH_3)_2$	1.33, 1.55
			($J_{2,3}$= 5.0)		
H-3	5.55	quartet			
			($J_{3,4}$= 9.0)		
H-4	4.68	quartet			
			($J_{4,5}$= 3.5)		
H-5	5.50	quartet			
			($J_{5,NH}$= 8.5)		
-NH	7.11	doublet			

* ppm from internal TMS.

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