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SYNTHESES OF ISOMALTOSE, ISOMALTOTETRAOSE, AND ISOMALTOÖCTAOSE

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Ethyl 2,3,4-tri-O-benzyl-1-thio-α-D-glucopyranoside (II-1) was converted into p-nitrobenzoyl derivative (I-1), which was then brominated to give the bromide (III-1). III-1 was condensed with II-1 in nitromethane in the presence of 2,6-lutidine to give ethyl 2,2',3,3',4,4'-hexa-O-benzyl-6'-O-p-nitrobenzoyl-1-thio-α-isomaltoside (I-2) in 92% yield. This synthetic cycle was repeated twice to synthesize isomaltotetraose and isomaltoöctaose as well as their related derivatives.

Recently, chemical syntheses of various kinds of oligosaccharides have been performed quite actively. Especially, in the last decade, the effort has focused upon the synthesis of α-linked oligosaccharides. Now, we wish to report the syntheses of isomaltose1), isomaltotetraose, and isomaltooctaose which contain α-glucoside linkage, by glycosidation in a homogeneous reaction system2) under mild conditions (Fig 1).

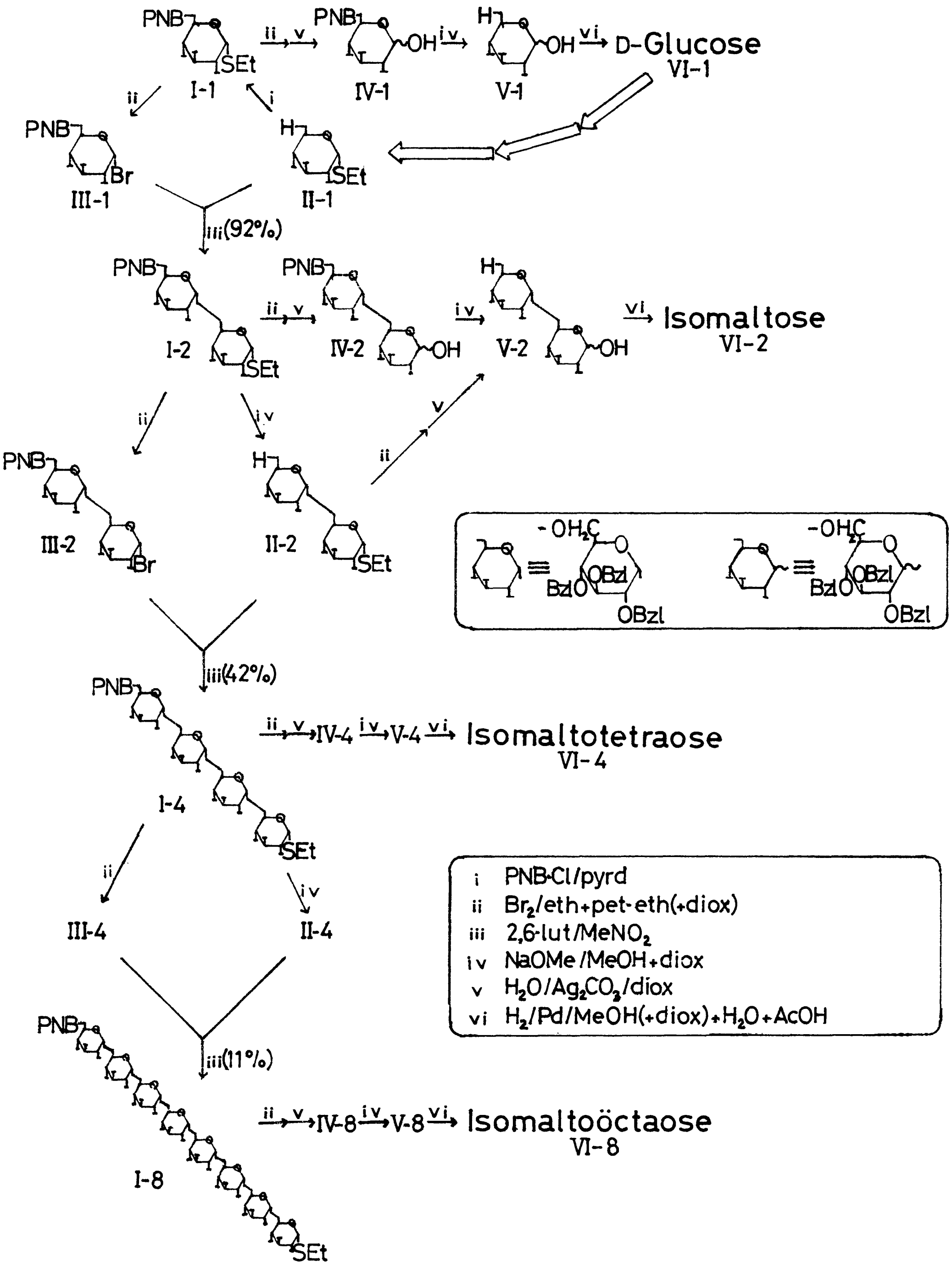
Tri-O-benzyl derivative of levoglucosan3) was treated with ethanethiol in the presence of zinc chloride at room temperature to give the starting material, ethyl 2,3,4-tri-O-benzyl-1-thio-α-D-glucopyranoside (II-1), mp 61—63.5°C, (40%), which was successively converted into p-nitrobenzoate (I-1), mp 91—92°C. An ethereal solution of I-1 was treated with a solution of bromine in petroleum ether4) to afford a nascent bromide (III-1)5), $[\alpha]_D^{25}$ 127° (c 2.9, $CHCl_3$). III-1 was condensed with slight excess of II-1 in the presence of 2,6-lutidine at room temperature for 20 hr to give the α-linked disaccharide (I-2) in 92% yield. I-2 was brominated, hydrolyzed, methanolyzed, and hydrogenolyzed to give isomaltose (VI-2) containing no trace of gentiobiose (paper chromatography). β-Octa-p-nitrobenzoyl derivative of VI-2 was identified with that of an authentic isomaltose6).

An analogous condensation reaction was carried out by use of 3,5-dinitrobenzoyl derivative of I-2, mp 124—126°C, $[\alpha]_D^{25}$ 110° (c 1.4, $CHCl_3$), to give the amorphous α-linked disaccharide in 49% yield, which was deacylated into crystalline II-2, mp 97—99°C, and identified with that from I-2.

Next, I-2 was brominated to give III-2, which was condensed with II-2 by use of the aforementioned system at room temperature for 2 days to furnish α-linked tetraglucoside (I-4) in 42% yield. PMR spectrum and the value of $[M]_D$ (Fig 2) supported this structure. The removal of the blocking groups by the sequence of reactions as above gave isomaltotetraose (VI-4).

This reaction-cycle was then once more repeated to synthesize α-linked octaglucoside (I-8), (11%), from which the protecting groups were removed to result isomaltoöctaose (VI-8)

All the values of $[M]_D$'s and R_M's of the synthetic homologous compounds showed good linearity to the degree of polymerization[7] (Fig2 and Fig 3)



SCHEMA OF SYNTHESIS OF OLIGOSACCHARIDE

Fig 1

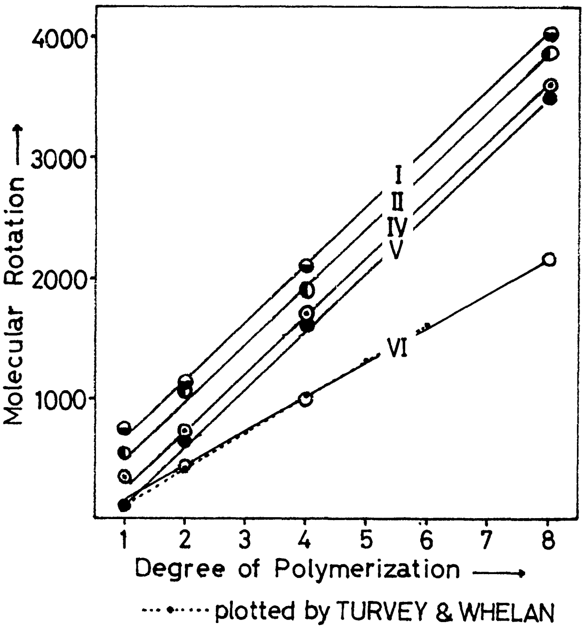


Fig 2

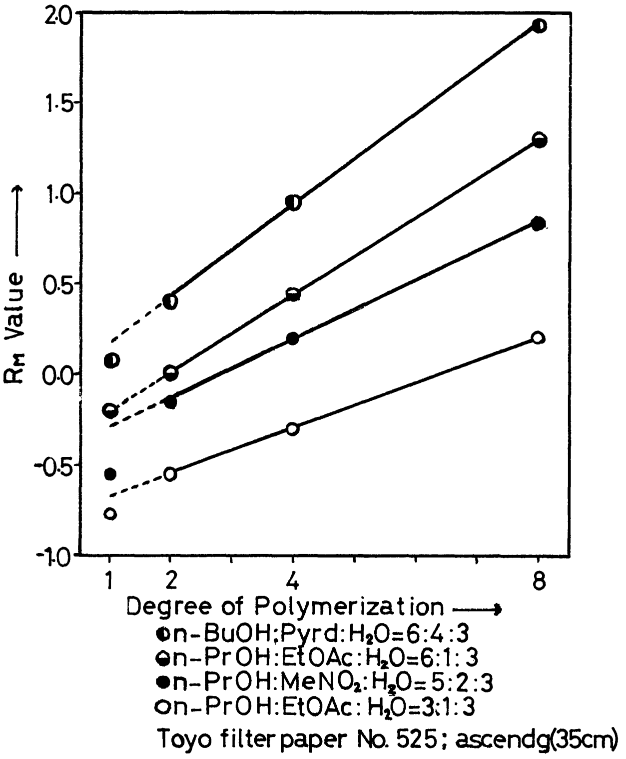


Fig 3

Table 1 Optical Rotational Data (deg.; measured at 25°C)

	I (%,$CHCl_3$)	II (%,$CHCl_3$)	IV (%,$CHCl_3$)	V (%,$CHCl_3$)	VI (%,H_2O)
-1	116 (1.0)	111 (1.8)	60 (1.6)	23 (0.6)	55 (1.0)
-2	105 (2.0)	114 (1.1)	72 (0.5)	73 (0.5)	126 (0.8)
-4	108 (1.0)	106 (1.0)	91 (1.0)	91 (1.0)	148 (0.3)
-8	110 (1.1)	110 (0.8)	99 (0.5)	102 (0.3)	165 (0.2)

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2) cf. N. K. Kochetkov, A. J. Khorlin, and A. F. Bochkov, Tetrahedron, 23, 693 (1967).

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6) cf. E. M. Montgomery, F. B. Weakley, and G. E. Hilbert, J. Amer. Chem. Soc., 71, 1682 (1949). Octa-p-nitrobenzoate prepared by their direction melted at 200—202°C and its value of $[\alpha]_D^{25}$ 99°(c 1.0, $CHCl_3$). The synthetic specimen had mp 199—201°C and $[\alpha]_D^{25}$ 97°(c 1.4, $CHCl_3$) [$\delta_{CDCl_3}^{TMS}$(ppm): 6.37 (1H, doublet; H-1, $J_{1,2}$ = 9.2 Hz)].

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