STUDIES ON NUCLEOSIDE ANALOGS.XXIV. MONO- AND DISACCHARIDE ISOTHIOCYANATES[1)]

Haruo Ogura* and Hiroshi Takahashi
School of Pharmaceutical Sciences, Kitasato University
5-9-1 Shirokane, Minato-ku, Tokyo 108, Japan

Abstract- The reaction of mono- and disaccharide bromide with $Pb(SCN)_2$ or AgSCN in dry benzene or benzene-toluene gives the respective mono- and disaccharide isothiocyanates and the confirmation of their stereochemistry of mono- and disaccharide isothiocyanates is described.

Introduction of the isothiocyanate group in anomeric position of sugar derivatives is useful for the syntheses of nucleoside [2)] (thymine, thiothymine, and 5-azacytidine), modified nucleoside analogs,[3)] and glycoproteins.[4)]

We have recently reported convenient and general methods for the synthesis of nucleoside analogs, e. g., 1,2,4-triazole-, s-triazine or 1,2,4,6-thiatriazine-S-oxide glycosides.[5)] Khorlin et al.[6)] reported that the treatment of peracetylated lactosyl bromide with NH_4SCN at 50° for 5 min gave lactosyl isothiocyanate in 49% yield, but, from the result of IR spectrum (2120 cm^{-1}), their experiment suggested the possibility that lactosyl thiocyanate might be formed from their reaction mentioned above.

In this paper, we describe the synthesis and the confirmation of their stereochemistry of mono- and disaccharide isothiocyanates. In a general procedure, $Pb(SCN)_2$ (0.15 mol) or AgSCN (0.3 mol)(dried over silica gel at 90° for 3 days) was added to peracetylated D-glycosyl bromide (0.1 mol) in dry benzene or benzene-toluene (1:1, v/v)(300 ml). After heating at 80-90° for 3-6 hr, the reaction solution was filtered and evaporation of the solvent under reduced pressure left the products (1-6) as crystals except 2, which obtained as a syrup after chromatography (Table I).

The IR spectra of isothiocyanate (1-6) exhibited a strong absorption due to the isothiocyanate group. The ^{1}H-NMR spectra of 1 were well resolved at 90 MHz. The coupling constant of anomeric proton of β-D-glucopyranosyl isothiocyanate (1) is 6.0 Hz, while the corresponding values for 4, 5, and 6 are 10.0 Hz. Compound 1 exhibited the direct coupling[7] constant with 1-C of 165 Hz. The ^{13}C-NMR data lead to the assignment of the β-configuration at anomeric position to 4, 5, and 6 (Table II).

Table I. Monosaccharide Isothiocyanates (1-3) and Disaccharide Isothiocyanates(4-6)

Compd. (No.)[a]	Yield (%)	mp (°c)	IR ν_{max}^{KBr} cm^{-1} (NCS)
2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl (1)	86	113-115	2100
2,3,4-Tri-O-acetyl-α-D-arabinopyranosyl (2)	81	syrup[b]	2050[c]
2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl (3)	74	96-97	2000
2,2',3,3',4',6,6'-Hepta-O-acetyl-β-D-lactosyl (4)	85	157-159	1990
2,2',3,3',4',6,6'-Hepta-O-acetyl-β-D-maltosyl (5)	93	120-123	2025
2,2',3,3',4',6,6'-Hepta-O-acetyl-β-D-cellobiosyl (6)	84	191-195	2025

a: All products gave satisfactory microanalyses.
b: TLC Rf 0.85 [silica gel, benzene-acetone (3:2)]
c: film

Table II. ^{1}H- and ^{13}C-NMR data for 1-6

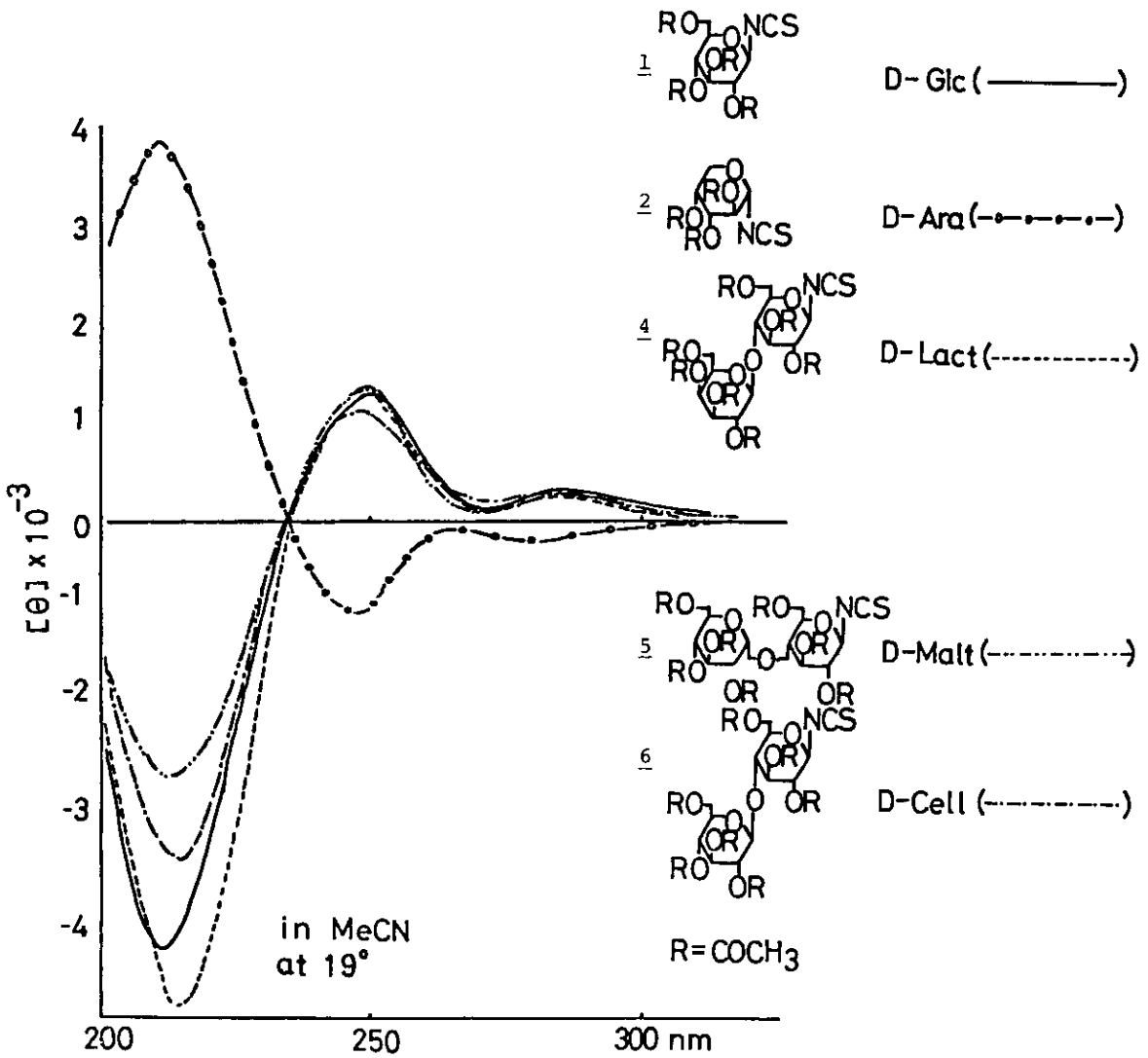
Compd. (No.)	^{1}H-NMR (C_6D_6, δ)	^{13}C-NMR ($CDCl_3$, δ)	
	(1-H)	(1-C)	(NCS)
1	5.15 (d, 6.0 Hz)[a]	83.5 (165 Hz)	144.1
2	4.46 (d, 6.0)	83.3 (168)	142.2
3	5.15 (d, 1.8)	88.5 (180)	144.4
4	5.13 (d, 10.0)	78.5 (165)	144.0
5	5.07 (d, 10.0)	83.0 (165)	144.2
6	5.15 (d, 10.0)	83.3 (165)	144.0

a: $CDCl_3$

As shown in Fig.1, β-isomers (1, 4, 5, and 6) showed similar CD curves around their absorption regions except 2 which exhibited the opposite Cotton effect curves. These results confirm that the configuration of the anomeric position in disaccharide isothiocyanates is β.

Application to syntheses of modified nucleoside analogs will be reported elsewhere.

Fig. 1. CD Curves of Glycosyl Isothiocyanates (1-6)



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