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Preliminary communication

Stereospecific 1,2-*cis*-glycosylation: a modified thiocyanate method

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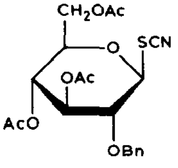
The development of a general stereospecific method for 1,2-*cis*-glycosylation remains an important problem of synthesis in carbohydrate chemistry. A new approach [1-3] for such glycosylation is based on the reaction of *O*-trityl derivatives of sugars with 1,2-*trans*-glycosyl thiocyanates having a non-participating group at C-2, in the presence of triphenylmethylium perchlorate. We now report a new modification of the method, namely, stereospecific 1,2-*cis*-glycosylation of sugar derivatives having unsubstituted hydroxyl groups with such a 1,2-*trans*-glycosyl thiocyanate in the presence of trimethylsilyl triflate (Me_3SiOTf) and molecular sieves.



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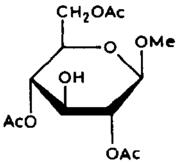

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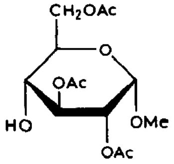

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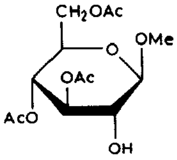

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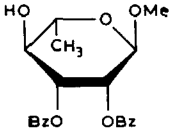

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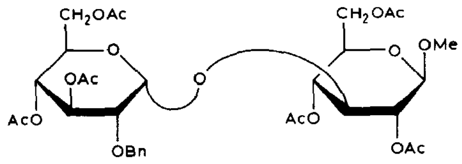
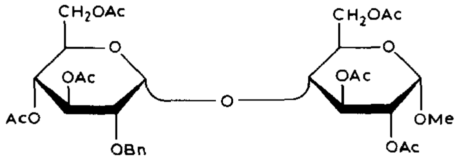
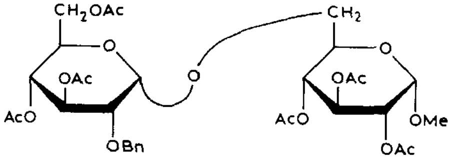
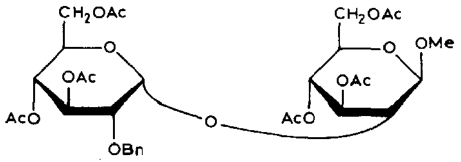
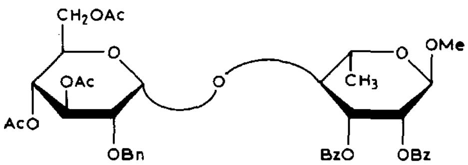
TABLE I

Glycosylation of **2–5** with **1**

Acceptor	Time (h)	Disaccharide derivatives (yield, %)		$[\alpha]_D$ (degrees)	NMR data[b] ^{1}H: H-1 ($J_{1,2}$) H-1′ ($J_{1',2'}$)	^{13}C: C-1 C-1′	C-2 C-2′	C-3 C-3′	C-4 C-4′	C-5 C-5′	C-6 C-6′
2	5		**6** (54)[a]	+23	4.28 (8) 4.86 (3.5)	101.63 99.00	72.60 78.04	81.88 71.37	67.89 67.89	71.92 68.76	62.10 61.22
3	8		**7** (40)	+104	4.81–4.88[c] 4.94 (3.5)	96.72 98.01	71.15 77.29	70.86 71.51	76.36 68.48	68.37 68.48	62.77 62.05
			**8** (25)	+132	4.77 (3.5) 4.94 (3.5)	96.70 96.45	71.10 76.85	70.17 71.75	68.71 68.04	69.66 67.50	66.97 62.12

4	10		**9** (73)	+72	4.46 (8) 5.55 (3.5)	103.92 95.50	74.61 76.10	73.23 71.40	68.98 68.36	71.56 67.60	61.92 [d] 61.66 [d]
5	13		**10** (61)	+105	4.80 (2) 4.90 (3.5)	98.42 98.84	70.72 77.75	71.47 71.96	80.62 68.33	68.13 67.14	18.35 61.45

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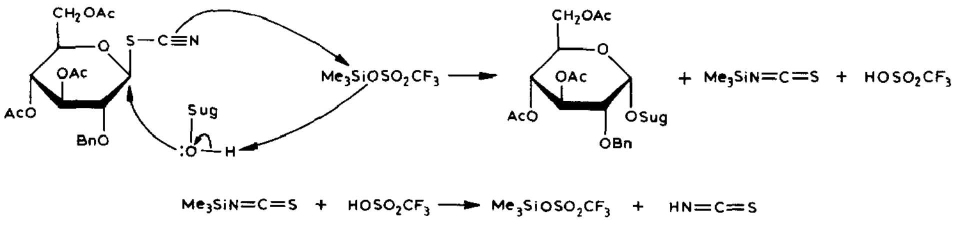
[a] Mp 143.5–145° (from ether). [b] Additional ^{13}C signals: 169.5–170.9 (C=O), 127.5–129.9 (C aromatic), 72.25–74.00 (CH_2), 55.42–57.14 (CH_3), and 20.26–21.04 ($COCH_3$). [c] Multiplet (2 H, H-1, 2). [d] Assignments may be reversed.



Scheme 1.

Thus, 3,4,6-tri-*O*-acetyl-2-*O*-benzyl-β-D-glucopyranosyl thiocyanate [2,3] (**1**) was reacted severally with the known [4–6] glucopyranose derivatives **2**–**4** and methyl 2,3-di-*O*-benzoyl-α-L-rhamnopyranoside (**5**). Compound **5** was synthesised by benzoylation of methyl 4-*O*-acetyl-α-L-rhamnopyranoside [7] followed by selective *O*-deacetylation by acidic methanolysis [8], and was obtained as a syrup, $[\alpha]_D^{22}$ +59° (*c* 1.64, $CHCl_3$).

Glycosylation involved the following general procedure. To a stirred solution of **1** (0.2 mmol) and **2**–**5** (0.2 mmol) in CH_2Cl_2 (2 mL) were added molecular sieves 4 A (100 mg) and a solution of Me_3SiOTf (0.04 mmol) in CH_2Cl_2. The mixture was stirred at room temperature for 5–12 h and the reaction was quenched with a drop of pyridine. Conventional work-up [3] followed by chromatography on silica gel gave the respective α-linked disaccharide derivatives **6**–**10** in yields of 50–75%. The results are summarised in Table I.

^1H- and ^{13}C-NMR spectroscopy of each whole disaccharide fraction indicated the absence of β-linked product.

The glycosylation of **3** gave two regioisomeric α-linked disaccharide derivatives (**7** and **8**) due to acetyl migration in the presence of Me_3SiOTf (cf. ref. 9). Hydrogenolysis of the disaccharide derivative **6** followed by hydrolysis gave methyl 3-*O*-α-D-glucopyranosyl-β-D-glucopyranoside (53% from **2**), $[\alpha]_D^{23}$ +71° (*c* 2.95, $CHCl_3$).

TLC showed that, during the reactions of **1**, there was partial isomerisation to yield the glycosyl isothiocyanate which could be isolated (cf. ref. 3). Therefore, more **1** and Me_3SiOTf (0.02–0.03 mmol) were added after 4–5 h.

The mechanism of this new glycosylation reaction may be tentatively represented as the concerted cyclic process shown in Scheme 1.

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