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Preliminary communication

Stereospecific glycosylation by 1,2-*O*-cyanoethylidene derivatives of uronic acids

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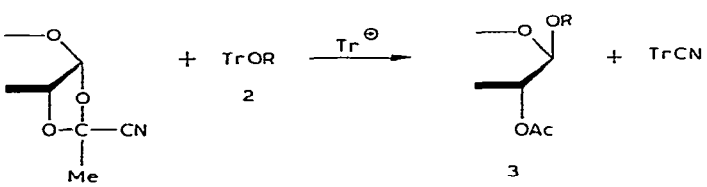
Uronic acids are components of various homo- and hetero-polysaccharides[1]. The directed synthesis of oligo- and poly-(glycosiduronic acids) requires glycosylating agents which ensure regio- and, especially, stereo-regularity of all the newly formed glycosidic linkages. We now report on the synthesis and glycosylating properties of 1,2-*O*-(1-cyanoethylidene) derivatives of methyl D-glucuronate and methyl D-galacturonate.

1,2-*O*-(1-Cyanoethylidene) derivatives of neutral sugars are 1,2-*trans*-glycosylating agents suitable for syntheses of di-[2–4] and poly-saccharides[5–9]. The reaction involves a 1,2-*O*-cyanoethylidene derivative (1) and a trityl ether (2) in the presence of a triphenylmethylium salt as catalyst, to give the glycoside 3.



1 2 3

For acetylated derivatives of 1,2-*O*-cyanoethylidene monosaccharides, the products were 1,2-*trans*-glycosides (3) containing <1% of the 1,2-*cis* anomers[4].

Syrupy methyl 3,4-di-*O*-acetyl-1,2-*O*-[(1-*exo*-cyano)ethylidene]-α-D-gluco- (4) and -galacto-pyranuronate (5) were obtained by treatment[10] of methyl (2,3,4-tri-*O*-acetyl-α-D-gluco-[11] and -galacto-pyranosyl bromide)uronate[12] with excess of silver cyanide in boiling xylene. The structures of 4 and 5 were established by analytical and spectral data (Table I).

Compounds 4 and 5 exhibited Raman absorption for nitrile at 2238 and 2240 cm^{-1}, respectively, and i.r. absorption at 2000–2300 cm^{-1} was practically absent. The ^{1}H-n.m.r. data (Table I) confirmed the presence in 4 and 5 of a dioxolane system fused to the 1,2-positions of the sugar moiety and the *exo*-configuration of the CN group. The spectral features of 4 and 5 are very similar to those of neutral–sugar analogues[15], for which chemical shifts in the n.m.r. spectra were shown to correlate with absolute configurations determined by X-ray analysis[16].

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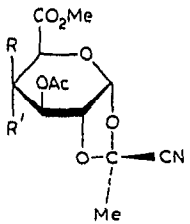
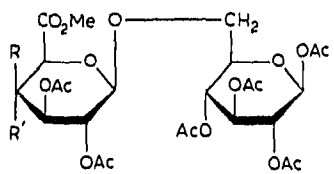
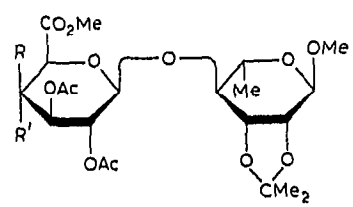
TABLE 1

DATA [a] FOR COMPOUNDS 4–9

Compound		Yield (%) [b] R	R'	$[\alpha]_D^{23}$ (degrees) (c, $CHCl_3$)	Chemical shifts [δ scale (J in Hz)] CMe	CMe_2	C(CN)Me	AcO	CO_2Me	H-1	OMe
	4	II (58)	OAc	−7.0 (2.1)	–	–	1.88	2.05, 2.07	3.72	5.85 (4.5)	–
	5	OAc (34)	II	+89.0 (1.7)	–	–	1.88	2.08 (x 2)	3.76	5.92 (4.0)	–
	6	H (43)	OAc	−8.5 [c] (2.3)	–	–	–	2.01–2.10 (7 AcO)	3.74	5.70 (7.5)	–
	7	OAc (54)	H	+14.0 (2.7)	–	–	–	2.00–2.10 (7 AcO)	3.75	5.70 (7.0)	–
	8	H (83)	OAc	−33.5 (2.1)	1.30 (5.5)	1.35, 1.51	–	2.03(x 2), 2.07	3.75	4.83 (0)	3.37
	9	OAc (81)	H	−8.9 [d] (2.5)	1.33 (5.5)	1.31, 1.48	–	1.97, 2.06, 2.10	3.73	4.08 (0)	3.35

[a] Varian DA-60-IL spectrometer ($CDCl_3$, Me_4Si); Perkin-Elmer 141 polarimeter; all compounds gave correct C, H (C,H,N for 4 and 5) microanalyses. [b] After column chromatography on silica gel (benzene→ethyl acetate). [c] M.p. 198–199°; lit.[13] m.p. 198–199°, $[\alpha]_D^{23}$ −11.0° (*c* 1, $CHCl_3$); lit.[14] m.p. 200–202°, $[\alpha]_D^{20}$ −11° (*c* 0.1, $CHCl_3$). [d] Compound 9 obtained as a white powder by Helferich glycosylation had $[\alpha]_D^{23}$ −8.8° (*c* 2.2, $CHCl_3$).

TABLE II

^{13}C-N.M.R. DATA [a] FOR DISACCHARIDE DERIVATIVES

Compound	*Chemical shifts (p.p.m.)*											
	Uronic acid residue						*Neutral sugar residue*					
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*
6	100.7	71.0	72.7	69.45	72.1	167.3	91.7	70.4	73.0	68.5	74.1	67.8
7	101.1	68.4	70.5	68.4	72.5	166.6	91.7	70.5	73.0	68.4	74.25	67.9
8	99.5	71.45	72.55	69.7	72.55	167.25	97.9	76.1	78.0	79.7	63.8	17.4
9	100.1	68.2	70.4	68.7	72.2	166.3	97.75	75.9	77.8	80.3	63.9	17.4

[a] Bruker WP-60 instrument ($CDCl_3$, Me_4Si); other resonances: CH_3CO-, 20.3–20.8; CH_3CO-, 167.8–170.1; $-CO_2CH_3$, 52.3–52.9; CH_3O-, 54.6–54.9; $>C(CH_3)_2$, 26.1–26.4 and 27.7–27.9; $>C<$, 109.3–109.5.

Glycosylation of 1,2,3,4-tetra-*O*-acetyl-6-*O*-triphenylmethyl-β-D-glucopyranose[17] and methyl 2,3-*O*-isopropylidene-4-*O*-triphenylmethyl-α-L-rhamnopyranoside[4] by **4** or **5** was performed for 18 h in the dark, as described earlier[4]. The yields and properties of the products (**6**–**9**, obtained as white powders) are noted in Tables I and II. The efficiency of these glycosylations is comparable to that for neutral analogues, and the reactions proceeded stereospecifically to give 1,2-*trans*-glycosiduronic acids only (^{13}C-n.m.r. spectroscopy).

Thus, 1,2-*O*-(1-cyanoethylidene) derivatives of uronic acids are highly stereospecific glycosylating agents in disaccharide synthesis and may be of value in the stereospecific synthesis of glycuronans.

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