Carbohydrate Research, 72 (1979) 272–275

Note

A convenient preparation of 2,3-unsaturated *N*-galactosyl derivatives

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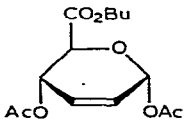
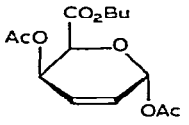
(Received May 30th, 1978; accepted for publication, July 17th, 1978)

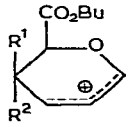
Pseudoglycals (hex-2-enopyranoses) are valuable intermediates for the synthesis of modified carbohydrates, glycosides, and oligosaccharides[1–3]. 2,3-Dideoxy-α-DL-*erythro*- and -*threo*-hex-2-enopyranuronates (**1** and **2**) are accessible[1] *via* a one-step reaction from 1,3-butadienylene diacetate and alkyl glyoxylates. The 1-*O*-acetyl-pseudoglycals are of value because, under mild acidic conditions, they are cleaved into acetate and the resonance-stabilised allyloxocarbonium-ion system[4–7] **3**, and thereby react easily with *O*-nucleophiles to give glycosides and oligosaccharides in high yield[1,2,8]. By-products were not observed under our experimental conditions[1].



1



2



3 $R^1 = H, R^2 = OAc$
$R^1 = OAc, R^2 = H$

The formulae denote only compounds of the D series

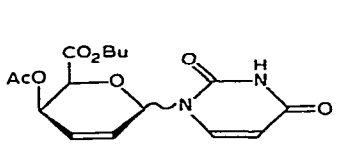
On the basis of the results of glycosidation[1] of **2**, similar results were expected for *N*-glycosylation[9]. *N*-Glycosyl derivatives having pseudoglycal structures have been obtained by reaction of glycals and heterocyclic bases under acid catalysis; 1,2-unsaturated C-3-nucleosides were obtained as by-products from tri-*O*-acetyl-glucal and di-*O*-acetylxylal[7,10–20]. A similar result was obtained with tri-*O*-acetyl-pseudoglucal[19], and di-*O*-acetylarabinal and tri-*O*-acetylgalactal also gave 2′-deoxy-nucleosides[7,10,11,13,16]. However, the 1-(2,3-dideoxy-D-*threo*-hex-2-enopyranosyl)-uracils were obtained[21] in reasonable yield from tri-*O*-acetylgalactal and bis-*O*-(trimethylsilyl)uracil (**4**), with only trace amounts of 3-uracilyl-3-deoxyglycal.

The reaction of **4** with **2** in ethyl acetate catalysed by antimony pentachloride gave >80% of the α- (**7α**) and β-nucleosides (**7β**) in the ratio ~3:2.

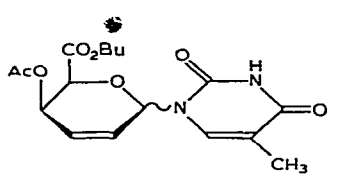
Formation of the α anomer is less preferred in *N*- than in *O*-glycosylation, which may be ascribed to a less-pronounced anomeric effect. Likewise, trimethylsilylated

thymine (**5**) reacted with **2** to give a 2:1 mixture of the α- (**8α**) and β-nucleosides (**8β**).

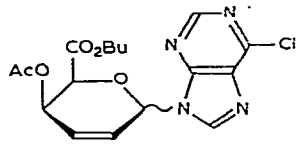
The reactivity of 1-*O*-acylpseudoglycals is emphasised by the reaction of **2** with 6-chloropurine (**6**) in boiling nitromethane in the absence of catalyst. A high yield of a 2:1 mixture of the α- (**9α**) and β-nucleosides (**9β**) was obtained*.



7 α,β (α:β 3 : 2)



8 α,β (α:β 2 : 1)



9 α,β (α:β 2:1)

The formulae denote only compounds of the D series

TABLE I

^{1}H-N.M.R. DATA[a]

Compound	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*OAc*	*Base*	*Coupling data (Hz)*
7α	6.56	6.05	6.50	5.48	4.71	2.08	5.72 (H-5'), 7.30 (H-6'), 9.86 (NH)	$J_{1,2}$ 2.5, $J_{1,3}$ 2, $J_{2,3}$ 10, $J_{3,4}$ 5, $J_{4,5}$ 3, $J_{5',6'}$ 8
7β	6.59	5.95	6.43	5.49	4.68	2.10	5.83 (H-5'), 7.35 (H-6'), 9.98 (NH)	$J_{1,2}$ 1.5, $J_{1,3}$ 1.5, $J_{2,3}$ 10, $J_{3,4}$ 5.5, $J_{4,5}$ 2.5, $J_{5',6'}$ 8
8α	6.53	6.02	6.45	5.48	4.73	2.05	7.06 (H-6'), 9.00 (NH), 1.93 (CH_3)	$J_{1,2}$ 2.5, $J_{1,3}$ 2, $J_{2,3}$ 10, $J_{3,4}$ 4.5, $J_{4,5}$ 3
8β	6.58	5.95	6.45	5.45	4.63	2.11	7.13 (H-6'), 9.65 (NH), 1.94 (CH_3)	$J_{1,2}$ 1.5, $J_{1,3}$ 2, $J_{2,3}$ 10, $J_{3,4}$ 5.5, $J_{4,5}$ 2.5,
9α	6.79	6.34	6.68	5.67	4.88	2.10	8.32 (H-8'), 8.76 (H-2')	$J_{1,2}$ 3, $J_{1,3}$ 2, $J_{2,3}$ 10, $J_{3,4}$ 5, $J_{4,5}$ 3
9β	6.76	6.23	6.60	5.62	4.88	2.12	8.35 (H-8'), 8.76 (H-2')	$J_{1,2}$ 1.5, $J_{1,3}$ 2, $J_{2,3}$ 10, $J_{3,4}$ 5.5, $J_{4,5}$ 3

[a]80 MHz, $CDCl_3$, δ scale.

*If the reaction is carried out in the presence of trace amounts of acid, a by-product is formed in low yield, which could not be isolated. Because of a ^{1}H-n.m.r. signal of the sugar moiety at δ 7.02 (d, *J* 6.0 Hz), a C-3-nucleoside structure is ascribed to this compound in agreement with the findings of Tam and Fraser-Reid[4] with pseudoglucals.

The structures of the nucleosides **7α,β** and **9α,β** were assigned on the basis of ^{1}H-n.m.r. data (see Table I); the $J_{3,4}$ value for each compound was ~5 Hz, which is in agreement with a pseudoequatorial position for H-4 in the $^0H_5$(D) half-chair conformation[2]. Thus, when both anomers are present, the larger $J_{1,2}$ value is due to the α anomer[12,20,21].

The foregoing results show that butyl 1-*O*-acetyl-2,3-dideoxy-α-DL-*threo*-hex-2-enopyranuronate (**2**) yields *N*-glycosyl derivatives (**7–9**) conveniently, and almost exclusively, under mild conditions of reaction; 1,2-unsaturated C-3-nucleosides or 2′-deoxynucleosdes were not detected when an excess of strong protic acid was avoided. Also, there was no tendency[22] for the uronates to undergo β-elimination. These results are also of importance for a modified synthesis[21] of the antibiotic Blasticidin S.

Tam and Fraser-Reid[4] recently reported the formation of a 1-*O*-acylpseudoglucal *via* a 1-*O*-alkylpseudoglucal. Reaction with 6-chloropurine then gave the anomeric pseudoglucal-nucleosides in reasonable yield. Thus, regiospecific glycosidation of 1-*O*-acylpseudoglycals appears to be a general reaction.

EXPERIMENTAL

General. — Melting points are uncorrected. ^{1}H-N.m.r. spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si) with a Bruker CW-80 spectrometer.

*1-(Butyl 4-O-acetyl-2,3-dideoxy-*DL-threo-*hex-2-enopyranosyluronate)uracil* (**7α,β**). — To a solution of **2** (1.2 g, 4 mmol) and **4** (3 g, 13 mmol) in anhydrous ethyl acetate (40 ml) was added antimony pentachloride (3 ml) at room temperature. After 15 min, the reaction was terminated by adding dichloromethane (90 ml) and pouring the mixture into saturated, aqueous sodium hydrogen carbonate (200 ml). After filtration, the organic layer was separated, washed thrice with saturated, aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and concentrated to dryness. The residue was eluted from silica gel with chloroform–methanol (95:5) to give, first, **7β** (440 mg, 32%) as an amorphous solid, λ_{max}^{MeOH} 259 nm (ε 10,000).

Anal. Calc. for $C_{16}H_{20}N_2O_7$: C, 54.54; H, 5.72; N, 7.95. Found: C, 54.15; H, 5.54; N, 7.81.

Eluted second was **7α** (750 mg, 53%), m.p. 186° (dec.), λ_{max}^{MeOH} 259 nm (ε 10,500).

Anal. Found: C, 54.46; H, 5.61; N, 7.83.

See Table I for ^{1}H-n.m.r. data.

*1-(Butyl 4-O-acetyl-2,3-dideoxy-*DL-threo-*hex-2-enopyranosyluronate)thymine* (**8α,β**). — Using the method described above, **2** (1.2 g, 4 mmol) and **5** (3.2 g, 13 mmol) were reacted. Elution of the product from silica gel with chloroform–methanol (96:4) gave, first, **8β** (510 mg, 35%), m.p. 125°, λ_{max}^{MeOH} 263 nm (ε 9000).

Anal. Calc. for $C_{17}H_{22}N_2O_7$: C, 55.73; H, 6.05; N, 7.65. Found: C, 55.64; H, 6.14; N, 7.44.

Eluted second was **8α** (830 mg, 55%), m.p. 206° (dec.), λ_{max}^{MeOH} 263 nm (ε 9000).

Anal. Found: C, 55.82; H, 6.19; N, 7.56.

See Table I for ^{1}H-n.m.r. data.

*9-(Butyl 4-O-acetyl-2,3-dideoxy-*DL-threo-*hex-2-enopyranosyluronate)-6-chloropurine* (**9α,β**). — A solution of **2** (0.6 g, 2 mmol) and **6** (0.42 g, 3 mmol) in anhydrous nitromethane (20 ml) was boiled under reflux for 4 h under rigorously anhydrous conditions. The mixture was then concentrated to dryness, and the residue was eluted from silica gel with chloroform–methanol (97:3) to give, first, **9β** (190 mg, 24%), m.p. 129°, λ_{max}^{EtOH} 265 nm (ε 9000).

Anal. Calc. for $C_{17}H_{19}ClN_4O_5$: C, 51.72; H, 4.85; N, 14.19; Cl, 8.98. Found: C, 51.83; H, 4.94; N, 14.14; Cl, 8.85.

Eluted second was **9α** (400 mg, 51%), m.p. 163°, λ_{max}^{EtOH} 265 nm (ε 9000).

Anal. Found: C, 51.64; H, 4.89; N, 14.16; Cl, 9.14.

See Table I for ^{1}H-n.m.r. data.

ACKNOWLEDGMENTS

This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

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