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Note

Synthesis of a *C*-glycosyl amino acid analogue of *O*-(β-D-xylopyranosyl)serine

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C-Glycosyl analogues of naturally occurring compounds have been prepared for a variety of reasons, primarily as inhibitors of glycosidic bond hydrolases or to prepare a more stable form of an active principle. An interesting class of *C*-glycosyl compounds are the *C*-glycosyl amino acids. Previously prepared have been α-*C*-glycosyl-α-amino acids[1,2]. Especially interesting would be those *C*-glycosyl amino acids that are analogues of points of saccharide attachment in glycoproteins, proteoglycans, and protein–polysaccharides[3].

Herein, we describe the synthesis of intermediates related to one such compound, the *C*-glycosyl ($-CH_2-$) analogue (**7**) of *O*-(β-D-xylopyranosyl)-L-serine. Synthesis began with (β-D-xylopyranosyl)nitromethane[4] (**1**) *. (Glycopyranosyl)nitromethanes, also known as 2,6-anhydro-1-deoxy-1-nitroalditols, are convenient starting compounds for the preparation of *C*-glycosyl compounds via nitroaldol condensation with an appropriate aldehyde[5], a reaction analogous to the classical nitromethane synthesis. Another approach, the addition of *C*-nucleophiles to α,β-unsaturated nitro sugars, has been used to prepare branched-chain sugar derivatives from 2,3-dideoxy-3-nitro-olefins[6,7]. This communication extrapolates this approach to 2-glycopyranosyl-2-nitroethanols[8], other potential precursors of nitro-olefins, and describes a simple approach to **7**.

Nitroaldol addition of **1** to formaldehyde provided a mixture of epimeric 2-nitro-2-(β-D-xylopyranosyl)ethanols (**2**). Formation of their insoluble sodium salts was a decisive step in their synthesis, as normally all the acidic α-protons of primary nitroalkanes react with formaldehyde[9–14]. In fact, **1** does undergo double electrophilic addition of formaldehyde in aqueous alkaline solution (unpublished result). Simultaneous use of carbon dioxide buffering and a strongly acidic cation-

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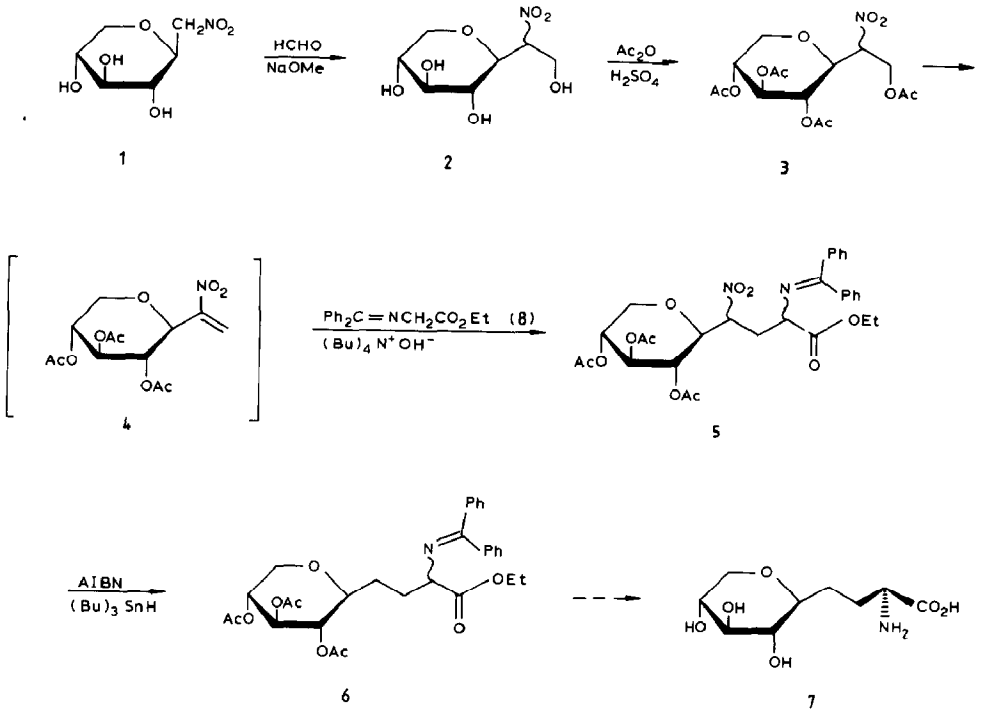
* Compound **1** is properly named as 2,6-anhydro-1-deoxy-1-nitro-D-gulitol.



exchange resin produced **2** from its sodium nitronate form and prevented further condensation.

Per-*O*-acetylation produced no change in the ratio of epimers.

Olefin **4**, expected as a dehydroacetoxylation product of **3**, could not be isolated. When isolation was attempted, a new product was formed, probably in a reaction sequence beginning with the opening of the anhydro ring. Therefore, **3** was allowed to react with a glycine nucleophile generated from ethyl *N*-diphenylmethyleneglycinate[15], but by a somewhat different procedure than that reported[16]. The coupling reaction afforded the expected product in 50% yield as a mixture of all four possible diastereomers. Crystallization gave one isomer (**5**), one of the principal ones. The configuration of this isomer at the $CH-NO_2$ and CH–N= centers is being determined by crystallographic analysis.

For denitration, a radical process employing tributyltin hydride and azobis(isobutyronitrile) (AIBN) was used[17]. Proof of the structure of **6** was given by mass and ^{13}C-NMR spectra. The overall yield of **6** (single isomer) from **1** was 4.2%.

EXPERIMENTAL

Addition of (β-D-xylopyranosyl)nitromethane (**1**) *to formaldehyde.*—Formaldehyde (0.6 g, generated by thermal decomposition of paraformaldehyde) was intro-

duced to a solution of **1** (1.93 g, 10.0 mmol)[2] in Me_2SO (10 mL). A solution of sodium methoxide (prepared from 0.35 g of Na) in MeOH (10 mL) was added. The mixture containing a precipitate was stirred (1 min). Then, 1-butanol (70 mL) was added. (This mixture could be kept several days at 5° without changes.) The precipitate was collected by filtration, washed with 1-butanol (5 × 10 mL), and added under vigorous stirring to a suspension of a strongly acidic cation-exchange resin (H^+ form, 50 mL, exchange capacity 1.5 mequiv/mL) and crushed solid CO_2 (100 g) in water (200 mL). Filtration and evaporation of the filtrate provided a syrup (2.14 g, 96%) containing **2** (epimeric ratio, 2:1 by ^{13}C-NMR spectroscopy) and starting material (~ 5%).

Acetylation of **2**.—Compound **2** (syrupy mixture, 1.40 g, 6.28 mmol) was dissolved in MeOH (3 mL) and added dropwise into acetic anhydride (50 mL) containing concentrated H_2SO_4 (4 drops) at 30–40° with stirring. After the final addition, the mixture was stirring an additional 2 h. The clear solution was then poured into ice and water (300 mL), and the mixture was stirred 3 h. Extraction of the water with $CHCl_3$, drying (Na_2SO_4), and evaporation afforded tetraacetate **3** (1.69 g, 69%, epimeric ratio, 2:1) (identity confirmed by ^{13}C-NMR spectroscopy).

Reaction of **3** *and* **8**.—A solution of *N*-diphenylmethyleneglycine ethyl ester (**8**) (0.53 g, 2.0 mmol)[15] and tetrabutylammonium bromide (0.64 g, 2.0 mmol) in $CHCl_3$ (50 mL) was shaken with aq M NaOH (50 mL) for 10 min. The $CHCl_3$ layer was removed and dried (Na_2SO_4), and to it was added **3** (0.78 g, 2.0 mmol). The mixture was stirred 16 h at room temperature. Column chromatography (Silica Gel-60, 4:3 v/v hexane–EtOAc) provided a fraction from which a crystalline diastereoisomer of ethyl 2-(diphenylmethyleneamino)-4-nitro-4-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)butanoate (**5**, 0.16 g, 13%) was obtained: mp 149–151°; $[\alpha]_D^{25}$ −103° (*c* 1.65, $CHCl_3$); *m/z* 599 $[M + H]^+$ (FAB mass spectrum). ^{13}C-NMR (50.309 MHz, $CDCl_3$, internal Me_4Si), δ: 14.10 (ethyl CH_3), 20.51, 20.67 (acetyl CH_3), 29.58 (C-3), 60.96 (ethyl CH_2), 61.38 (C-5′), 66.81 (C-2), 68.46 (C-2′), 69.15 (C-4′), 73.76 (C-3′), 78.89 (C-1′), 83.45 (C-4), 127.76, 128.08, 128.55, 128.82, 130.76, 135.56, 138.74 (aryl C), 169.16, 169.68, 170.27, 170.60 (C-1, acetyl C=O), 172.74 (C=N).

Anal. Calcd for $C_{30}H_{34}N_2O_{11}$: C, 60.19; H, 5.73; N, 4.68. Found: C, 60.34; H, 5.83; N, 4.52.

Denitration of **5**.—A mixture of **5** (122 mg, 0.2 mmol), AIBN (33 mg, 0.2 mmol), tributyltin hydride (0.55 mL, 2 mmol), and toluene (0.3 mL) was stirred at 110° under an atmosphere of N_2 for 1 h[17]. Column chromatography (Silica Gel-60, 5:3 v/v hexane–EtOAc) afforded ethyl 2-(diphenylmethyleneamino)-4-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)butanoate (**6**, 26 mg, 24%; overall yield from **1** 2.1%); $[\alpha]_D^{25}$ −84.1° (*c* 1.35, $CHCl_3$); *m/z* 554 $[M + H]^+$ (FAB mass spectrum). ^{13}C-NMR (50.309 MHz, $CDCl_3$, internal Me_4Si), δ: 14.21 (ethyl CH_3), 20.56, 20.73 (acetyl CH_3), 27.59 (C-4), 28.89 (C-3), 60.93 (ethyl CH_2), 64.52 (C-1′), 66.65 (C-2), 69.36 (C-5′), 72.07 (C-4′), 73.82 (C-2′), 77.52 (C-3′), 128.03, 128.49, 128.80, 130.03, 130.40, 136.27, 139.37 (aryl C), 169.59, 169.82, 170.40, 170.53 (C-1, acetyl C=O),

171.95 (C=N). As the (β-D-xylopyranosyl)methyl group is identical to the 1,5-anhydro-6-deoxy-L-glucitol-6-yl group, assignment of the xylopyranosyl carbon atoms was made from data for 1,5-anhydro-D-glucitol and methyl 6-deoxy-α-D-glucopyranoside[18].

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