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Rearrangements of *O*-Protected Glycosylenamines. A New and Efficient Route for the Synthesis of *O*-Protected 4-Aminoaldoses

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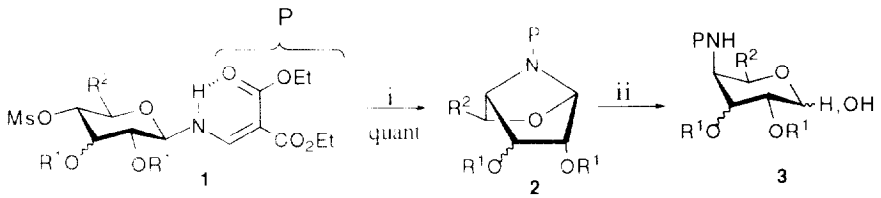
Abstract: *O*-Protected 4-deoxy-4-diethoxycarbonylvinylaminoaldoses with **D**-galacto, **L**-arabino and **L**-lyxo configurations (**3**) are prepared by a nucleophilic rearrangement of easily available glycosylamine derivatives.

Several aminosugars have been synthetized by nucleophilic displacement reactions of sulfonyloxy groups, such as *p*-toluenesulphonates[1,2] or triflates[3]. This displacement has most frequently been intermolecular using nitrogen functional groups as nucleophiles, and in some cases these reactions have been used in an intramolecular way to form five and six membered rings in carbohydrate derivatives[2]. At the same time the 4-amino-4-deoxysugars and their derivatives are important compounds which have been identified as constituents of several natural antibiotics and antifungal agents[2,4]. They are also interesting as synthetic precursors of glycocynamoylspermidines[5], a family of broad spectrum antibiotics, sugar isothiocyanates[6], and β-lactams[7].

To the best of our knowledge the glycosylamines or their *N*-protected derivatives have not been used to obtain aminodeoxy sugars in non anomeric positions. In this communication we report the migration of the enamino group of *N*-diethoxycarbonylvinyl-**D**-glycopyranosylamines (**1**) to the position 4 (**3**) via the intermediate aza-anhydrosugar **2**. The starting materials (**1**) were easily prepared from the corresponding glycosylenamines or partially protected glycosylenamines[8,9] and the transformations **1**→**2**→**3** took place in high yield.

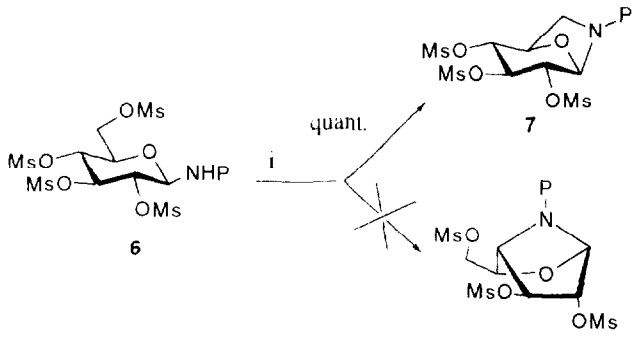


R^1 = Bz, Ms; R^2 = CH_2OBz, CH_2OTr, H

Conf. = **D**-gluco, **D**-xylo, and **D**-ribo

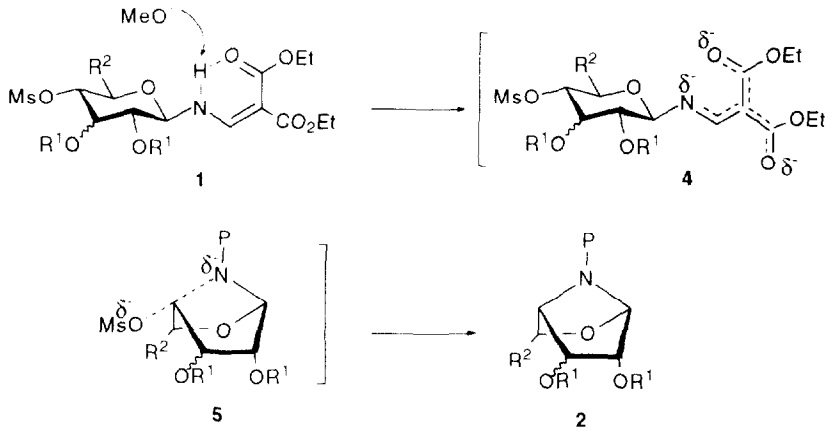
i: MeONa/HMPT; ii: F_3CCO_2H/H_2O (3:1)

Conf. = **D**-galacto, **L**-arabino, and **L**-lyxo



P = HC=C(CO$_2$Et)$_2$; i) MeONa/HMPT

The aza-anhydrosugars **2** were stable compounds whose analytical and spectroscopic data (IR, ^{1}H and ^{13}C-NMR) confirmed the proposed structure. Thus their ^{1}H-NMR spectra had no signals for NH and show a singlet at 7.37-7.76 ppm for the HC= of the diethoxycarbonylvinyl group (=CHNR$_2$) instead of the doublet (=CHNHR) of compounds **1** and **3**. The $^3J_{H,H}$ values of **2** were in agreement with that expected for a boat conformation[10].



Scheme 1

Scheme 1 shows a possible mechanism for the formation of products **2**. The methoxide ion elicits the formation of the stabilized ion **4**, which produces the nucleophilic displacement of the mesyloxy group.

When the reaction was performed starting from glycosylenamines bearing a mesyloxy group at C-6, such as **6**, the corresponding 1,6-aza-anhydro sugar (**7**)[11] was quantitatively formed, and there was no reaction at C-4. Consequently the method is useful to move the amino group from the anomeric position to position 4, when there is no MsO group in the position 6, that is in D-ribo and D-xylo compounds (**1**, R^2=H) and in 6-*O*-protected D-gluco compounds (**1**, R^2=CH$_2$OBz, CH$_2$OTr). Related nucleophile induced rearrangement involving the sulphur atom of thioglycosides have been recently described[12].

The treatment of **2** with trifluoracetic acid:water 3:1 yielded **3** as mixture of anomers[13], as their ^{13}C-NMR spectra show. In compounds **3** the configuration of C-4 has been inverted with respect to **1**. In order to prepare free aminosugars the *N*-protecting ethoxycarbonylvinyl group of **3** is easy to remove under mild conditions[6,14], but the facile decomposition of 4-amino-4-deoxy sugars by way of pyrrole derivatives[2] must be taken into account.

In conclusion we describe an efficient method to introduce one amino group in the position 4 of an aldose derivative. This method provides a valuable alternative to the S_N2 displacement of the mesyloxy group by sodium azide[15] and further reduction, because in this case the elimination reaction (of MsOH for **1**[15]) competes with the substitution.

The scope and limitations of this method are currently under study in our laboratory.

ACKNOWLEDGMENTS

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10. Selected data for **2** (R^1=OBz, R^2=CH_2OBz, conf. D-gluco): amorphous solid, $[\alpha]_D^{24}$ +43° (*c* 0.6, dichloromethane); IR ν_{max} 2959, 2872, 1724, 1601, 1451, 1267, 1026, 712 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.08-7.43 (m, 15 H, Ph), 7.76 (s, 1 H, HC=), 5.90 (d, 1 H, $J_{1,2}$ = 2.1, H-1), 5.19-5.18 (m, 1 H, H-2), 5.16 (s, 1 H, H-3), 4.95 (bs, 1 H, H-4), 4.38 (m, 1 H, H-6a), 4.30-4.26 (m, 4 H, H-5, H-6b, CH_2CH_3), 4.18 (q, 2 H, $J_{H,H}$ =7.1, CH_2CH_3), 1.25, 1.16 (each t, each 3 H, 2 CH_2CH_3); ^{13}C (75.4 MHz, $CDCl_3$) δ 166.0 (2 CO), 165.7 (2 CO), 165.6 (CO), 145.3 (HC=), 133.6-

128.3 (18 C, Ph), 100.3 (=C), 88.5 (C-1), 79.7 (C-2), 76.8 (C-3), 74.2 (C-5), 64.7(C-4), 63.4 (C-6), 60.9, 60.6 (2 CH_2CH_3), 14.1, 13.9 (2 $CH_2(CH_3)$; FABMS *m/z* 666 (65, $[M+Na]^+$).

Compounds **2** gave satisfactory microanalysis (C, H, N).

11. Selected data for **7**: amorphous solid, $[\alpha]_D^{24}$ -33° (*c* 1.0, dichloromethane); IR ν_{max} 3028, 2984, 1709, 1691, 1599, 1366, 1267, 1177, 1090, 961 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.59 (s, 1 H, HC=), 5.55 (s, 1 H, H-1), 5.01 (m, 1 H, H-2), 4.92 (m, 1 H, H-5), 4.76 (m, 2 H, H-3, H-4), 4.27-4.22 (m, 2 H, CH_2CH_3), 4.20 (q, 2 H, $J_{H,H}$ =7.1, CH_2CH_3), 3.72 (m, 1 H, H-6a), 3.48 (m, 1 H, H-6b), 3.23, 3.22, 3.20 (each s, each 3 H, 3 Ms), 1.32, 1.28 (each t, each 3 H, 2 CH_2CH_3); ^{13}C (75.4 MHz, $CDCl_3$) δ 166.5, 166.1 (2 CO), 144.9 (HC=), 98.7 (=C), 88.6 (C-1), 75.6, 72.0 (C-3, C-4), 73.6 (C-5), 72.6 (C-2), 61.1, 60.6 (2 $CH_2(CH_3)$), 48.4 (C-6), 38.5 (2 C, 2 Ms), 38.4 (1 C, Ms), 14.2, 14.0 (2 $CH_2(CH_3)$; FABMS *m/z* 588 (100, $[M+Na]^+$).

Compoun **7** gave satisfactory microanalysis (C,H,N,S).

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13. The microanalytical data (C, H, N) of **3** were satisfactory.
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