A Facile Synthesis of Saturated 2-Nitrosugar Derivatives

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Saturated 2-nitrosugar derivatives (**11**−**20** and **22**) are easily synthesized by oxidation with *m*-CPBA of readily available corresponding 2-aminosugars (**1**−**10** and **21**), in excellent yield. Alkyl 4,6-*O*-benzylidene-2-deoxy-2-nitro-D-hexopyranosides suffer *O*-alkylation and *O*-acylation in the usual conditions. These 3-*O*-acetyl-2-nitrosugar derivatives gave the corresponding 2-nitroalkene derivative, which reacts *in situ* with nuclephiles in high stereoselectivity.

Introduction

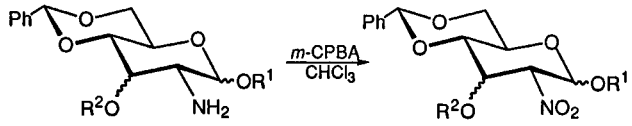
We are interested in the synthesis of saturated 2-nitrosugar derivatives as key intermediates to obtain D-glucosamine derivatives modified at positions 2 and/or 3 of the sugar ring. Many sugars with a nitro group have been synthesized, and their versatility as synthetic intermediates is widely accepted.[1] Nevertheless, although there are many articles about 3-nitrosugar derivatives synthesis, the number of references on the synthesis of saturated 2-nitrosugar derivatives is substantially more limited. Lemieux *et al.*[2,3] obtained alkyl 2-nitroglucopyranoside derivatives by treatment of glucal with N_2O_4 and then glycosidation of 2-nitroglucal by alcohols. These compounds represent the first cyclic carbohydrate bearing a nitro group on carbon 2.[1d]

Various types of 2-nitrosugars were synthesized by oxidation of the corresponding oximes with trifluoroperoxyacetic acid in which all hydroxyl groups were protected by an ether or acetal function.[4−7]

Another important synthetic route contains a long sequence of reactions with a 3-nitroalkene as intermediate, which gives 2-nitroalkene by isomerization with sodium nitrite.[8−11] This key reaction gives low yields (15−45%).

More recently, a different procedure for 2-nitroglycal synthesis from 2-deoxyglycal and NO_2BF_4 has been proposed.[12] These 2-nitroglycals were transformed into saturated 2-nitrosugar derivatives by different methods.

Scheme 1



1-10 **11-20**

1 and **11**	R^1 = β *n*-$C_{12}H_{25}$	R^2 = H	*Gluco*
2 and **12**	R^1 = β *c*-C_6H_{11}	R^2 = H	*Gluco*
3 and **13**	R^1 = β Ph	R^2 = H	*Gluco*
4 and **14**	R^1 = β Bn	R^2 = H	*Gluco*
5 and **15**	R^1 = α Bn	R^2 = H	*Gluco*
6 and **16**	R^1 = β *n*-$C_{12}H_{25}$	R^2 = H	*Allo*
7 and **17**	R^1 = β Bn	R^2 = H	*Allo*
8 and **18**	R^1 = β *c*-C_6H_{11}	R^2 = Bn	*Gluco*
9 and **19**	R^1 = β Ph	R^2 = Bn	*Gluco*
10 and **20**	R^1 = β Bn	R^2 = Bn	*Allo*

In summary, 2-nitroalkenes or 2-nitroglycals are the key intermediates for most saturated 2-nitrosugars syntheses. In general, these routes mean many reaction steps, mixtures of compounds, and low yields.

In this paper, we propose an alternative way to obtain alkyl (aryl) 2-deoxy-2-nitro-D-glucopyranosides from appropriately protected 2-aminoglycosides, by oxidation of the amino group. Although the oxidation of an amino compound to nitro compound is known,[13,14] this procedure has not been used previously in the case of 2-aminosugars.

We have used some of these 2-aminoglucosides as starting products in other, previous aspects of our work.[15−17]

Results and Discussion

The synthesis of new saturated 2-nitrosugar derivatives (**11**−**20**, **22**) takes place by addition of *m*-CPBA to a chloroform refluxing solution of the corresponding 2-aminosugar (**1**−**10**, **21**) (Schemes 1 and 2). The

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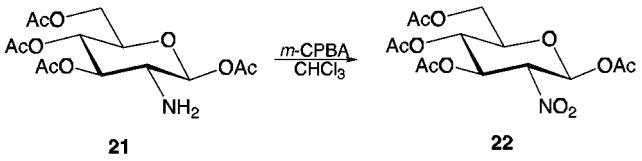
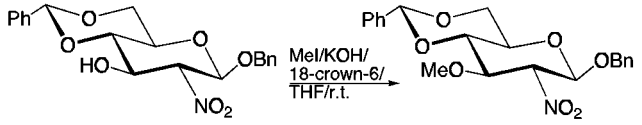
Scheme 2



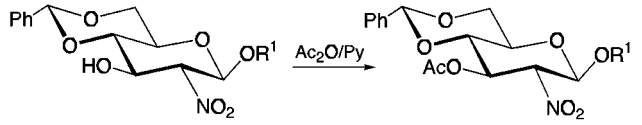
21 22

Scheme 3



14 23

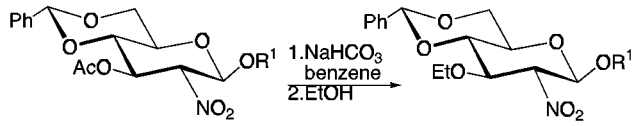
Scheme 4



12, 14 24, 25

R^1 = *c*-C_6H_{11}, Bn

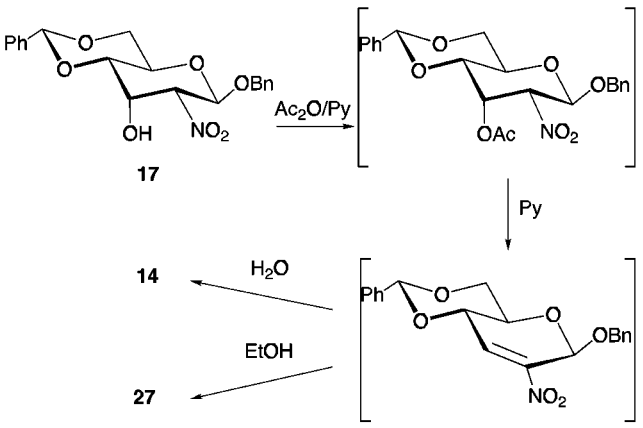
Scheme 5



24, 25 26, 27

R^1 = *c*-C_6H_{11}, Bn

Scheme 6



compounds were isolated in good yield. Analysis of the results reveals the general character of the procedure. It is noteworthy that the good results, besides being independent of the aglycon, are compatible with different configurations, with the stereochemistry on carbon 1 and carbon 3 and with the protection of the carbon 3 hydroxyl as an ether or ester in the starting 2-aminosugar. These starting compounds are readily available from commercial *N*-acetyl-D-glucosamine using procedures described in the literature[18,19] and give good yields.

The compounds obtained were characterized by their elemental analyses, MS (EI-HR, CI and FAB) data, and NMR (^{1}H and ^{13}C) data. In some cases, double resonance, DEPT, COSY, and CHCORR experiments have been performed in order to assign the different signals in the spectra.

The ^{1}H NMR chemical shift data from these 2-nitro compounds (**11**−**20**) included, as most-characteristic signals, a doublet about 5−5.5 ppm for H-1, a doublet of doublets about 4−5 ppm for H-2, and a triplet or doublet of doublets about 4−4.5 ppm for H-3. These three signals replace those of around 4.5, 3, and 3.5 ppm for H-1, H-2, and H-3, respectively, for the starting 2-amino compounds (**1**−**10**). The ^{13}C NMR spectra recorded for **11**−**20** showed a signal at about 90 ppm for C-2, while the resonance of this carbon appeared at about 60 ppm for **1**−**10**.

We studied the reaction of **14** with the MeI/KOH/18-crown-6/THF system[20] and obtained the corresponding 3-*O*-methyl derivative **23** (Scheme 3).[3] The methyl group of **23** appeared as a singlet at 3.52 ppm in the ^{1}H NMR and at 61.1 ppm in the ^{13}C NMR spectra.

In addition, we acetylated the 2-nitro compounds **12** and **14** with acetic anhydride/pyridine to give the 3-*O*-acetyl derivatives **24** and **25** (Scheme 4), which present a doublet of doublets at 5.8−6.2 ppm for H-3 and a singlet at 2.05 ppm for the methyl of the acetyl group in the ^{1}H NMR spectra. Each ^{13}C NMR spectrum (**24** and **25**) showed two signals, at 169 and 20 ppm, for acetyl group.

We also studied the reaction of **24** and **25** with $NaHCO_3$/benzene[8] to obtain the 2-nitroalkenes, which can react *in situ* with nucleophiles. For example, when the elimination reaction finished (TLC), ethanol (some drops) was added. After workup, TLC showed only one product (75%), with the structure of a 3-*O*-ethylglucopyranoside derivative (**26** and **27**) (Scheme 5). Its ^{1}H NMR spectrum gave a doublet of doublets (J = 8.8 and 10.0 Hz) at 4.1 ppm for H-3 and a triplet (J = 7 Hz) at 1.11 ppm for the methyl of the ethyl group, as most-characteristic signals. The ^{13}C NMR spectrum is in agreement with the structures (15.2 ppm for methyl of ethyl group). We did not observe other stereoisomers in the reaction products.

The acetylation of **17**, under the same conditions as for **12** and **14**, yielded compound **14** (81%). That is, the configuration on carbon 3 changed from *allo* to *gluco*. We think that the 3-*O*-acetyl derivative obtained from **17** suffered elimination in the reaction medium by pyridine, giving the corresponding 2-nitroalkene. When the reaction mixture was added to water, compound **14** (*gluco* configuration) was obtained (Scheme 6).

This reaction sequence was confirmed when the acetylation reaction was terminated by addition of ethanol to the reaction mixture before water precipitation. In this case, compound **27** was obtained, which comes from addition of ethanol on 2-nitroalkene postulated as an intermediate (Scheme 6).

A broad discussion on the course of the reaction, the isolation and stability of the nitrous intermediates, and the reactivity on carbon 2 of the 2-nitrosugars will be submitted in the near future.

Experimental Section

Melting points are uncorrected. ^{1}H NMR spectra were recorded at 200 and 500 MHz. ^{13}C NMR spectra were recorded at 50 and 125 MHz. MS spectra were recorded at 70 eV for EI-HR (resolution 12000/10%) and 150 eV for CI. FAB spectra were recorded with a thioglycerol matrix. The specific rotations were obtained at 25 °C.

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General Procedure for Oxidation of 2-Aminosugar Compounds (1−10 and 21). A solution of alkyl (phenyl) 2-amino-4,6-*O*-benzylidene-2-deoxy-D-hexopyranoside (**1**−**7**), alkyl (phenyl) 2-amino-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-*β*-D-hexopyranoside (**8**−**10**), or 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-*β*-D-glucopyranose (**21**) (1 mmol) in $CHCl_3$ (20 mL) and solid Na_2SO_4 (2 g) was heated under reflux with stirring, and *m*-CPBA (Aldrich 57−86%) (2 g) was added. The suspension was stirred until completion of the reaction (TLC) (1−2 h). It was then left to cool to room temperature and diluted with CH_2Cl_2. When the starting material was **1**−**10**, the organic phase was washed successively with 0.1 M aqueous NaOH and water, then dried (Na_2SO_4), and evaporated *in vacuo* to dryness. The solid obtained (**11**−**20**) was crystallized from ethanol or ethanol−water.

Dodecyl 4,6-*O*-benzylidene-2-deoxy-2-nitro-*β*-D-glucopyranoside (11): yield 85%; mp 115−117 °C; $[\alpha]_D$ −37.0 (*c* 0.8, $CHCl_3$); MS (CI) *m*/*z* 466 (5%) (MH^+); MS (FAB) *m*/*z* 488 (52%) (MNa^+); ^{1}H NMR (500 MHz, DMSO-d_6) *δ* 7.4 (m, 5H), 6.25 (d, 1H, *J* = 4.3 Hz), 5.62 (s, 1H), 5.07 (d, 1H, *J* = 8.2 Hz), 4.42 (dd, 1H, *J* = 8.2, 10.0 Hz), 4.22 (dd, 1H, *J* = 4.7, 10.0 Hz), 4.18 (td, 1H, *J* = 4.3, 9.8 Hz), 3.75 (m, 2H), 3.67 (td, 1H, *J* = 4.8, 9.9 Hz), 3.57 (t, 1H, *J* = 9.6 Hz), 3.46 (m, 1H), 1.6−1.1 (20H), 0.85 (t, 3H, *J* = 7 Hz); ^{13}C NMR (125 MHz, DMSO-d_6) *δ* 137.3, 129.0, 128.0, 126.3, 100.9, 99.2, 91.5, 79.7, 70.3, 69.3, 67.4, 66.0, 31.3, 29.0, 28.9, 28.7, 28.5, 25.0, 22.1, 13.9; EI-HR calcd for $C_{25}H_{39}NO_7$ 465.2727, found 465.2731. Anal. Calcd for $C_{25}H_{39}NO_7$: C, 64.49; H, 8.44; N, 3.01. Found: C, 64.60; H, 8.20; N, 2.96.

Cyclohexyl 4,6-*O*-benzylidene-2-deoxy-2-nitro-*β*-D-glucopyranoside (12): yield 87%; mp 224−226 °C; $[\alpha]_D$ −55.3 (*c* 0.8, $CHCl_3$); IR (KBr) 1559 cm^{-1}; MS (CI) *m*/*z* 380 (12%) (MH^+); MS (FAB) *m*/*z* 402 (55%) (MNa^+); ^{1}H NMR (500 MHz, DMSO-d_6, D_2O) *δ* 7.4 (m, 5H), 5.60 (s, 1H), 5.15 (d, 1H, *J* = 8.2 Hz), 4.39 (dd, 1H, *J* = 8.2, 10.0 Hz), 4.21 (dd, 1H, *J* = 4.7, 10.0 Hz), 4.15 (t, 1H, *J* = 9.7 Hz), 3.73 (t, 1H, *J* = 10.0 Hz), 3.65 (m, 2H), 3.55 (t, 1H, *J* = 9.3 Hz), 1.8−1.0 (10H); ^{13}C NMR (50 MHz, DMSO-d_6) *δ* 137.6, 129.4, 128.4, 126.6, 101.2, 97.8, 92.2, 79.9, 76.6, 70.7, 67.8, 66.3, 32.9, 30.7, 25.2, 23.3, 23.0. EI-HR calcd for $C_{19}H_{25}NO_7$ 379.1631, found 379.1636. Anal. Calcd for $C_{19}H_{25}NO_7$: C, 60.15; H, 6.64; N, 3.69. Found: C, 59.97; H, 6.51; N, 3.49.

Phenyl 4,6-*O*-benzylidene-2-deoxy-2-nitro-*β*-D-glucopyranoside (13): yield 82%; mp 180−182 °C; $[\alpha]_D$ −349.4 (*c* 0.5, $CHCl_3$); MS (FAB) *m*/*z* 396 (100%) (MNa^+); ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 7.6−6.9 (m, 10H), 5.57 (s, 1H), 5.48 (d, 1H, *J* = 8.1 Hz), 4.76 (dd, 1H, *J* = 8.1, 10.0 Hz), 4.4 (m, 2H), 3.7 (m, 3H), 2.9 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 156.1, 136.3, 129.7, 128.5, 126.2, 124.2, 117.5, 102.3, 98.9, 89.9, 80.0, 71.2, 68.2, 66.5. Anal. Calcd for $C_{19}H_{19}NO_7$: C, 61.12; H, 5.13; N, 3.75. Found: C, 60.95; H, 5.11; N, 3.65.

Benzyl 4,6-*O*-benzylidene-2-deoxy-2-nitro-*β*-D-glucopyranoside (14): yield 78%; mp 178−180 °C; $[\alpha]_D$ −81.8 (*c* 0.7, $CHCl_3$); IR (KBr) 1559 cm^{-1}; MS (CI) *m*/*z* 388 (2%) (MH^+); MS (FAB) *m*/*z* 410 (14%) (MNa^+); ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 7.5−7.2 (m, 10H), 5.54 (s, 1H), 4.97 (d, 1H, *J* = 7.9 Hz), 4.88 (d, 1H, *J* = 11.7 Hz), 4.61 (d, 1H, *J* = 11.7 Hz), 4.55 (dd, 1H, *J* = 7.9, 10.0 Hz), 4.4 (m, 2H), 3.81 (t, 1H, *J* = 10.1 Hz), 3.55 (m, 2H), 2.78 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 136.4, 135.5, 129.6, 128.6, 128.5, 128.4, 127.9, 126.2, 102.3, 98.8, 90.1, 80.3, 71.6, 71.2, 68.2, 66.4; EI-HR calcd for $C_{20}H_{21}NO_7$ 387.1318, found 387.1316. Anal. Calcd for $C_{20}H_{21}NO_7$: C, 62.01; H, 5.46; N, 3.62. Found: C, 61.93; H, 5.42; N, 3.56.

Benzyl 4,6-*O*-benzylidene-2-deoxy-2-nitro-α-D-glucopyranoside (15): yield 75%; mp 180−182 °C; $[\alpha]_D$ +148.2 (*c* 0.5, $CHCl_3$); IR (KBr) 1560 cm^{-1}; MS (CI) *m*/*z* 388 (3%) (MH^+); MS (FAB) *m*/*z* 410 (8%) (MNa^+); ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 7.6−7.2 (m, 10H), 5.54 (s, 1H), 5.40 (d, 1H, *J* = 4.2 Hz), 4.82 (t, 1H, *J* = 9.6 Hz), 4.63 (2d, 2H, *J* = 11.2 Hz)), 4.53 (dd, 1H, *J* = 4.1, 9.5 Hz), 4.23 (dd, 1H, *J* = 4.8, 10.0 Hz), 3.96 (td, 1H, *J* = 4.8, 9.8 Hz), 3.73 (t, 1H, *J* =10.1 Hz), 3.59 (t, 1H, *J* = 9.5 Hz), 2.85 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 136.6, 135.6, 129.4, 128.6, 128.4, 127.9, 126.2, 102.2, 95.6, 87.1, 80.2, 70.4, 68.5, 66.8, 62.6. Anal. Calcd for $C_{20}H_{21}NO_7$: C, 62.01; H, 5.46; N, 3.62. Found: C, 61.75; H, 5.53; N, 3.45.

Dodecyl 4,6-*O*-benzylidene-2-deoxy-2-nitro-*β*-D-allopyranoside (16): yield 84%; mp 47−49 °C; $[\alpha]_D$ −30.3 (*c* 0.7, $CHCl_3$); IR (KBr) 1551 cm^{-1}; MS (FAB) *m*/*z* 488 (100%) (MNa^+); ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 7.6−7.3 (m, 5H), 5.60 (s, 1H), 5.34 (d, 1H, *J* = 8.3 Hz), 4.78 (bs, 1H), 4.40 (m, 2H), 4.05 (td, 1H, *J* = 4.9, 9.5 Hz), 3.85−3.65 (m, 4H), 2.52 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 136.5, 129.5, 128.4, 126.1, 102.0, 97.2, 85.1, 78.0, 71.3, 68.7, 68.3, 62.9, 31.9, 29.6, 29.5, 29.3, 25.8, 22.7, 14.1. Anal. Calcd for $C_{25}H_{39}NO_7$: C, 64.49; H, 8.44; N, 3.01. Found: C, 64.61; H, 8.15; N, 2.94.

Benzyl 4,6-*O*-benzylidene-2-deoxy-2-nitro-*β*-D-allopyranoside (17): yield 75%; mp 165−167 °C; $[\alpha]_D$ −66.3 (*c* 0.8, $CHCl_3$); IR (KBr) 1560 cm^{-1}; MS (CI) *m*/*z* 388 (3%) (MH^+); MS (FAB) *m*/*z* 410 (70%) (MNa^+); ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 7.5−7.2 (m, 10H), 5.60 (s, 1H), 5.49 (d, 1H, *J* = 8.3 Hz), 4.92 (d, 1H, *J* = 11.0 Hz), 4.79 (t, 1H, *J* = 2.7 Hz), 4.72 (d, 1H, *J* = 11.0 Hz), 4.45 (m, 2H), 4.06 (td, 1H, *J* = 4.9, 9.8 Hz), 3.79 (t, 1H, *J* = 10.3 Hz), 3.64 (dd, 1H, *J* = 2.4, 9.4 Hz), 2.62 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 136.4, 136.1, 129.5, 128.5, 128.3, 126.1, 102.0, 96.6, 84.9, 77.9, 72.6, 68.7, 68.3, 62.9; EI-HR calcd for $C_{20}H_{21}NO_7$ 387.1318, found 387.1322. Anal. Calcd for $C_{20}H_{21}NO_7$: C, 62.01; H, 5.46; N, 3.62. Found: C, 61.82; H, 5.34; N, 3.39.

Cyclohexyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-nitro-*β*-D-glucopyranoside (18): yield 88%; mp 153−155 °C; $[\alpha]_D$ −10.3 (*c* 0.5, $CHCl_3$); IR (KBr) 1551 cm^{-1}; MS (CI) *m*/*z* 470 (5%) (MH^+); MS (FAB) *m*/*z* 492 (95%) (MNa^+); ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 7.6−7.1 (m, 10H), 5.60 (s, 1H), 4.96 (d, 1H, *J* = 8.0 Hz), 4.84 (d, 1H, *J* = 11.3 Hz), 4.62 (d, 1H, *J* = 11.3 Hz), 4.51 (dd, 1H, *J* = 8.0, 10.0 Hz), 4.36 (dd, 1H, *J* = 4.8, 10.4 Hz), 4.28 (dd, 1H, *J* = 9.1, 10.0 Hz), 3.81 (t, 1H, *J* = 10.2 Hz), 3.73 (t, 1H, *J* = 9.1 Hz), 3.6 (m, 1H), 3.53 (td, 1H, *J* = 4.8, 9.7 Hz), 1.9−1.1 (10H); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 136.9, 136.8, 129.2, 128.4, 128.3, 128.1, 126.0, 101.6, 98.6, 90.2, 81.3, 78.3, 77.1, 74.6, 68.4, 66.4, 33.1, 30.9, 25.3, 23.7, 23.4; EI-HR calcd for $C_{26}H_{31}NO_7$ 469.2101, found 469.2106. Anal. Calcd for $C_{26}H_{31}NO_7$: C, 66.51; H, 6.65; N, 2.98. Found: C, 66.60; H, 6.48; N, 2.89.

Phenyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-nitro-*β*-D-glucopyranoside (19): yield 80%; mp 192−194 °C; $[\alpha]_D$ −11.9 (*c* 0.7, $CHCl_3$); MS (CI) *m*/*z* 464 (1%) (MH^+); MS (FAB) *m*/*z* 486 (35%) (MNa^+); ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 7.6−6.9 (m, 15H), 5.62 (s, 1H), 5.45 (d, 1H, *J* = 8.2 Hz), 4.88 (d, 1H, *J* = 11.3 Hz), 4.82 (dd, 1H, *J* = 8.2, 10.1 Hz), 4.66 (d, 1H, *J* = 11.3 Hz), 4.4 (m, 2H), 3.85 (t, 1H, *J* = 10.1 Hz), 3.82 (t, 1H, *J* = 9.2 Hz), 3.65 (td, 1H, *J* = 4.6, 9.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 156.1, 136.8, 136.7, 129.7, 129.3, 128.5, 128.4, 128.2, 126.0. 124.2, 117.5, 101.7, 99.1, 89.6, 81.1, 77.0, 74.9, 68.3, 66.7. Anal. Calcd for $C_{26}H_{25}NO_7$: C, 67.38; H, 5.44; N, 3.02. Found: C, 67.17; H, 5.49; N, 2.86.

Benzyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-nitro-*β*-D-allopyranoside (20): yield 68%; mp 122−124 °C; $[\alpha]_D$ −48.5 (*c* 0.8, CH_2Cl_2); MS (FAB) *m*/*z* 500 (100%) (MNa^+); ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 7.6−7.2 (m, 15H), 5.54 (s, 1H), 5.50 (d, 1H, *J* = 8.3 Hz), 4.90 (2d, 2H, *J* = 11.1 Hz), 4.73 (d, 1H, *J* = 11.1 Hz), 4.69 (dd, 1H, *J* = 2.3, 3.1 Hz), 4.55 (d, 1H, *J* = 11.1 Hz), 4.4 (m, 2H), 4.15 (td, 1H, *J* = 5.1, 9.8 Hz), 3.78 (t, 1H, *J* = 10.2 Hz), 3.72 (dd, 1H, *J* = 2.3 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 136.9, 136.3, 129.3, 128.4, 128.3, 128.2, 128.1, 128.0, 126.1, 102.3, 97.0, 84.8, 79.3, 75.1, 75.1, 72.7, 68.8, 63.3. Anal. Calcd for $C_{27}H_{27}NO_7$: C, 67.91; H, 5.70; N, 2.93. Found: C, 67.71; H, 5.64; N, 2.84.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-nitro-*β*-D-glucopyranose (22). When the starting material was **21**, the organic phase was washed successively with 0.1 M aqueous Na_2CO_3 and water, then dried (Na_2SO_4), and concentrated to give a crude product (essentially **22**): yield 85%; MS (FAB) *m*/*z* 400 (37%) (MNa^+); ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 6.04 (d, 1H, *J* = 8.6 Hz), 5.72 (dd, 1H, *J* = 9.2, 10.5 Hz), 5.07 (dd, 1H, *J* = 9.3, 10.0 Hz), 4.67 (dd, 1H, *J* = 8.5, 10.5 Hz), 4.27 (dd, 1H, *J* = 4.4, 12.6 Hz), 4.07 (dd, *J* = 2.2, 12.6 Hz), 3.94 (ddd, *J* = 2.2, 4.3, 10.1 Hz), 2.07, 2.02, 1.99, 1.98 (4s, 12H); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 170.3, 169.4, 169.1, 167.9, 90.7, 85.7, 72.8, 71.1, 67.2, 60.9, 20.5, 20.4, 20.3, 20.2. When the crude product was chromatographed on silica gel, the decomposition of **22** occurred.

Benzyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-methyl-2-nitro-*β*-D-glucopyranoside (23). To a solution of **14** (1 mmol) in THF (2 mL) were added, successively, freshly powdered potassium hydroxide (0.1 g, 1.8 mmol), 18-crown-6 (11 mg, 0.04 mmol), and methyl iodide (1.1 mmol). The mixture was stirred at room temperature, and the reaction was monitored by TLC; at the end of the reaction the mixture was diluted with CH_2Cl_2 and washed several times with water. Evaporation of the organic phase gave the pure alkylated product. The product obtained was purified by flash chromatography on silica gel: yield 68%; mp 120−122 °C; $[\alpha]_D$ −144.6 (*c* 0.4, CH_2Cl_2); MS (CI) *m*/*z* 402 (5%) (MH^+), MS (FAB) *m*/*z* 424 (75%) (MNa^+); ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 7.6−7.2 (m, 10H), 5.56 (s, 1H), 4.93 (d, 1H, *J* = 8.1 Hz), 4.86 (d, 1H, *J* = 11.7 Hz), 4.62 (d, 1H, *J* = 11.7 Hz), 4.51 (dd, 1H, *J* = 8.1, 10.0 Hz), 4.38 (dd, 1H, *J* = 4.7, 10.5 Hz), 4.07 (dd, 1H, *J* = 9.1, 10.0 Hz), 3.82 (t, 1H, *J* = 10.2 Hz), 3.66 (t, *J* = 9.2 Hz), 3.52 (s, 3H), 3.5 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 136.7, 136.6, 129.2, 128.6, 128.3, 127.9, 126.0, 101.5, 98.9, 89.7, 81.2, 79.5, 71.5, 68.3, 66.5, 61.1. EI-HR calcd for $C_{21}H_{23}NO_7$ 401.1475, found 401.1468. Anal. Calcd for $C_{21}H_{23}NO_7$: C, 62.84; H, 5.78; N, 3.49. Found: C, 62.66; H, 5.71; N, 3.38.

Acetylation of 2-Nitrosugar Compounds (12 and 14). Compounds **12** and **14** (1 mmol) were acetylated in the usual way with acetic anhydride/pyridine (1:1) (4 mL). The reaction mixture was kept overnight at room temperature and then poured into ice water. The solid obtained was isolated by filtration and recrystallized from ethanol−water.

Cyclohexyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-2-nitro-*β*-D-glucopyranoside (24): yield 90%; mp 144−146 °C; $[\alpha]_D$ −45.9 (*c* 0.6, $CHCl_3$); MS (CI) *m*/*z* 422 (4%) (MH^+); MS (FAB) *m*/*z* 444 (100%) (MNa^+); ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 7.5−7.3 (m, 5H), 5.79 (dd, 1H, *J* = 9.5, 10.2 Hz), 5.49 (s, 1H), 5.11 (d, 1H, *J* = 8.0 Hz), 4.55 (dd, 1H, *J* = 8.0, 10.3 Hz), 4.37 (dd, 1H, *J*= 4.1, 10.4 Hz), 3.8 (t, 1H, *J* = 10.0 Hz), 3.6 (m, 3H), 2.06 (s, 3H), 1.9−1.1 (10H); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 169.0, 136.5, 129.3, 128.3, 126.1, 101.8, 98.6, 88.7, 78.6, 78.1, 70.4, 68.3, 66.5, 33.1, 30.9, 25.3, 23.7, 23.4, 20.5. Anal. Calcd for $C_{21}H_{27}NO_8$: C, 59.91; H, 6.46; N, 3.33. Found: C, 59.65; H, 6.35; N, 3.32.

Benzyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-2-nitro-*β*-D-glucopyranoside (25): yield 86%; mp 169−171 °C; $[\alpha]_D$ −89.4 (*c* 0.5, $CHCl_3$); MS (FAB) *m*/*z* 452 (100%) (MNa^+); ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 7.5−7.2 (m, 10H), 5.77 (dd, 1H, *J* = 9.3, 10.2 Hz), 5.50 (s, 1H), 5.07 (d, 1H, *J* = 8.1 Hz), 4.90 (d, 1H, *J* = 11.5 Hz), 4.63 (d, 1H, *J* = 11.5 Hz), 4.60 (dd, 1H, *J* = 8.2, 10.3 Hz), 4.39 (dd, 1H, *J*= 4.3, 10.4 Hz), 3.7 (m, 3H), 2.05 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 169.0, 136.4, 135.4, 129.3, 128.6, 128.5, 128.3, 128.0, 126.1, 101.8, 98.9, 88.3, 78.1, 71.9, 70.2, 68.2, 66.6, 20.4. Anal. Calcd for $C_{22}H_{23}NO_8$: C, 61.53; H, 5.40; N, 3.26. Found: C, 61.27; H, 5.34; N, 3.19.

Reaction of 3-*O*-Acetyl-2-nitrosugar Compounds (24 and 25) with Sodium Hydrogencarbonate. Compounds **24** and **25** (1 mmol) and dry sodium hydrogencarbonate (500 mg) in distilled benzene (25 mL) were heated for 24 h under reflux, with stirring. Ethanol (some drops) was added, the reaction mixture was cooled and filtered, and the filtrate was evaporated to give a solid residue. Crystallization from ethanol afforded the desired product.

Cyclohexyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-ethyl-2-nitro-*β*-D-glucopyranoside (26): yield 85%; mp 143−145 °C; $[\alpha]_D$ −57.1 (*c* 0.9, $CHCl_3$); MS (CI) *m*/*z* 408 (5%) (MH^+); MS (FAB) *m*/*z* 430 (100%) (MNa^+); ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 7.5−7.3 (m, 5H), 5.55 (s, 1H), 4.99 (d, 1H, *J* = 8.1 Hz), 4.45 (dd, 1H, *J* = 8.1, 10.1 Hz), 4.33 (dd, 1H, *J* = 4.7, 10.4 Hz), 4.14 (dd, 1H, *J* = 8.8, 10.1 Hz), 3.8 (m, 2H), 3.6 (m, 4H), 2.0−1.2 (10H), 1.12 (t, 3H, *J* = 7 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 136.8, 129.1, 128.3, 125.9, 101.4, 98.6, 90.5, 81.1, 78.2, 78.0, 68.7, 68.3, 66.5, 33.1, 30.9, 25.3, 23.7, 23.4, 15.3; EI-HR calcd for $C_{21}H_{29}NO_7$ 407.1944, found 407.1955. Anal. Calcd for $C_{21}H_{29}NO_7$: C, 61.90; H, 7.17; N, 3.44. Found: C, 61.83; H, 6.96; N, 3.39.

Benzyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-ethyl-2-nitro-*β*-D-glucopyranoside (27): yield 80%; mp 110−112 °C; $[\alpha]_D$ −127.7 (*c* 0.3, CH_2Cl_2); MS (CI) *m*/*z* 416 (7%) (MH^+); MS (FAB) *m*/*z* 438 (100%) (MNa^+); ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 7.5−7.2 (m, 10H), 5.56 (s, 1H), 4.93 (d, 1H, *J* = 8.2 Hz), 4.87 (d, 1H, *J* = 11.8 Hz), 4.60 (d, 1H, *J* = 11.8 Hz), 4.51 (dd, 1H, *J* = 8.1, 10.0 Hz), 4.37 (dd, 1H, *J* = 4.7, 10.4 Hz), 4.13 (dd, 1H, *J* = 8.9, 10.0 Hz), 3.85 (m, 2H), 3.55 (m, 3H), 1.10 (t, 3H, *J* = 7 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 136.8, 135.6, 129.2, 128.6, 128.3, 127.9, 125.9, 101.5, 98.9, 90.0, 81.1, 77.9, 71.4, 68.8, 68.3, 66.0, 15.2. Anal. Calcd for $C_{22}H_{25}NO_7$: C, 63.61; H, 6.07; N, 3.37. Found: C, 63.87; H, 5.82; N, 3.29.

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Supporting Information Available: ^{1}H and ^{13}C NMR for compounds **2**, **3**, **6**−**20**, and **22**−**27**, COSY for compounds **11** and **12**, CHCORR for compound **11**, IR for compounds **12**, **16** and **18**, and MS/FAB for **22** (68 pages). This material is contained in libraries on microfiche, inmediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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