Tetrahedron Vol. 47, No. 32, pp 6113-6126, 1991
Printed in Great Britain

0040-4020/91 $3.00+.00

C-GLYCOSIDE SYNTHESES II: HENRY CONDENSATIONS OF 4,6-O-ALKYLIDENE PYRANOSES WITH A 1,3-PROTON TRANSFER CATALYST- A ROUTE TO BLOCKED AMINOMETHYL-C-GLYCOSIDES[1].

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(*Received in USA 2 April* 1991)

ABSTRACT

In the presence of a novel 1,3-proton transfer catalyst (2-hydroxypyridine (2-HP)/ 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)/ molecular sieves), 4,6-*O*-benzylidene-D-glucopyranose (1), 4,6-*O*-isopropylidene-D-mannose (12), and 4,6-*O*-isopropylidene-D-glucose (16) undergo Henry condensations with nitromethane in THF to give acetal protected nitromethyl C-glycopyranosides (2, 13, and 17, respectively), which were characterized as their O-acetyl derivatives (5, 15, and 18, respectively). The Henry product from 4,6-*O*-benzylidene-Dglucopyranose could be reduced, with retention of the 4,6-*O*-benzylidene protecting group, by a specially prepared form of elemental iron in aqueous tetrahydrofuran under CO_2 to aminomethyl-C-glycopyranoside (16), characterized as N-acetyl, peracetyl, and N-Cbz derivatives (7, 8, 9, 10), and converted with diazonium salt to a triazene derivative (11). Nitroalkenes are only mechanistic intermediates in our condensations with nitromethane, but they undergo Michael additions with a second mole of nitromethane to give novel 5,7-*O*-alkylidene-1,2-deoxy-1 nitro-2-nitromethyl-D-heptitols (3 and 14) as side-products.

INTRODUCTION

C-glycosides are important as potential enzyme-inhibitors[2] and as chiral synthons, suitable for the synthesis of many natural products[3]. Specifically, C-glycopyranosyl nitromethanes may be reduced to aminomethyl-C-glycosides that could be widely elaborated at the amino function.

Unprotected C-glycopyranosyl nitromethanes (2,6-anhydro-1-deoxy-1-nitroheptitols)[4-7] and C-glycofuranosyl nitromethanes (2,5-anhydro-1-deoxy-1-nitrohexitols)[8,9] were obtained by Henry condensations of hexoses and pentoses, respectively with nitromethane. The strongly basic conditions of these syntheses cause decomposition of the sugar and formation of methazonic acid[10] from the nitromethane. Reaction products are often obtained in low yields.

For 4,6-*O*-acetalated hexoses, only one Henry condensation leading to a cyclic C-glycoside has so far been reported. In the presence of methoxide, the Henry condensation of nitromethane with 4,6-*O*-benzylidene glucopyranose (1) gave 2,6-anhydro-5,7-*O*-benzylidene-1-deoxy-1-nitro-D-glycero-D-guloheptitol (2) and the acyclic 5,7-*O*-benzylidene-1-deoxy-1-nitro-D-glycero-D-guloheptitol (4) in low yields (5% and 21%, respectively)[11]. The acyclic reaction product was de-*O*-benzylidenated and was reduced with Raney nickel to give the corresponding amino-sugar. The cyclic product was not reduced to the β-aminomethyl-C-glucoside[11]. Such reductions have since been carried out[9,12] but not on 4,6-*O*-acetalated C-glycosyl nitromethanes.

Low yield makes the procedure of Sowden and Fischer[11] useless for the production of

large amounts of cpd. 2 as a starting material. Direct syntheses of similar compounds with other pyranose configurations are even less promising, since other 4,6-*O*-benzylidene pyranoses are not easily accessible in good yield. Up to this day, cpd. 2 had remained the only member of its class.

However, we were very interested in syntheses with 4,6-*O*-acetalated sugars for several reasons: (a) The hydrophobic character of the protected glycosyl moiety may improve work up procedures. (b) When the acetal moiety is preserved in the reduction of the nitro group to the amino group, selective sulfonylations[13] and inversions on the pyranose ring are possible, that will allow syntheses of configurationally altered C-glycosyl amino methanes. We have considerable experience in this methodology[14]. (c) Finally, acetal blocking groups may be removed under very mild conditions. The Henry condensation with 4,6-trans-*O*-acetalated pyranoses is probably quite different from that of free sugars: Conformational restraints within the protected glycosyl moiety can be expected to retard ring opening to the aldehyde form[15], which must be present for the condensation with nitromethyl anion.

On this basis, we planned enhancement of the slow, and therefore probably, rate determining ring opening to the aldehyde form with 2-HP as a 1,3-proton transfer catalyst[16]. Such ring opening is postulated to operate in the anomerization of 2,3,4,6-tetra-*O*-methyl glucose with 2-HP in an aprotic solvent[16]. The optimal basicity for the Henry condensation was empirically achieved by addition of DBU. Molecular sieves, in a good, anhydrous solvent (THF) for cpd. 1, were added to remove water produced in the reaction.

DISCUSSION

The acid catalyzed reaction of the very DMF soluble β-D-glucose with benzaldehyde dimethylacetal, similar to published procedures[17,18], gave rapid and convenient formation of the 4,6-*O*-benzylidene compound[19], and minimized the formation of cis 1,2-*O*-benzylidenated side products, such as 1,2:3,5-di-*O*-benzylidene-α-D-glucofuranose and 1,2:4,6-di-*O*-benzylidene-α-D-glucopyranose[20-22]. Crystallizations, from water, and then from dioxane\ether, gave very pure cpd. 1, free of D-glucose.

In our hands, the literature procedures for 4,6-*O*-isopropylidene-D-mannopyranose (12)[23a], and 4,6-*O*-isopropylidene-D-glucopyranose (16)[23b] gave impure material that needed to be purified as shown in the experimental.

With unprotected sugars under strongly basic conditions in previous Henry condensations, the intermediate nitroalkenes sometimes were cyclized to the nitromethyl C-glycosides *in situ*[7,8], but in other cases, a separate cyclization step had to be carried out[4-6].

1,3 proton transfers, important in establishment of ring-chain equilibria, must also operate in β-elimination and β-addition (recyclization, in our case) under neutral conditions. A generalization of the action of a 1,3 proton transfer catalyst can be made as follows: (1) The catalyst is itself a 1,3 proton transfer system, with an sp_2 carbon in

the 2-position, so that proton transfer can occur in one bimolecular step with protons of catalyst and substrate in optimal H-bonding (bond angle=180°). at the elongated sides of the hexagonal activated complex; (2) The two catalyst tautomers, convertible by 1,3 proton transfer, have similar stabilities; (3) In the pH range of the synthesis, the catalyst system and the substrate each have single acidic protons, not two such protons, or none.

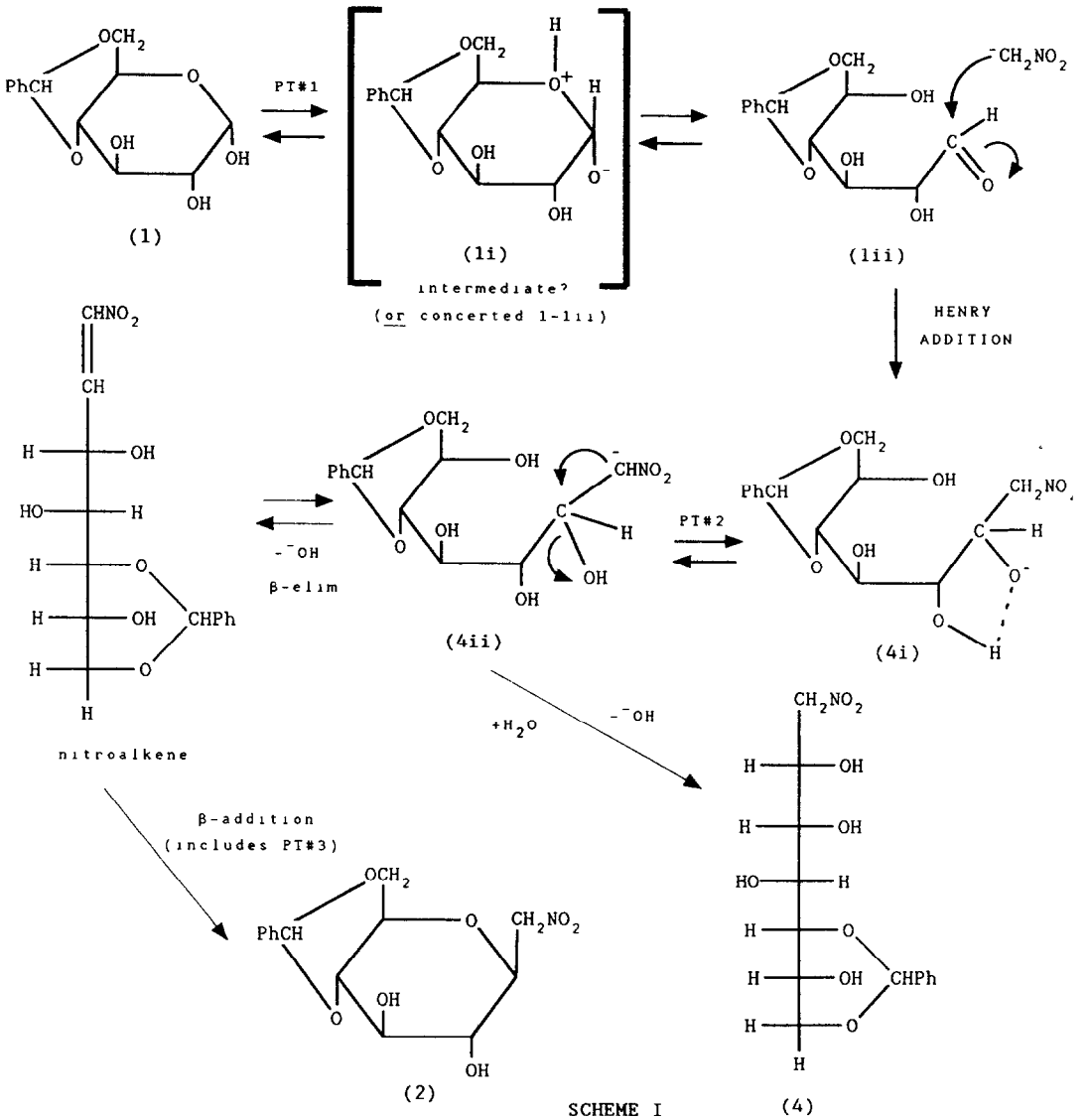
Possible mechanisms of our Henry condensations, for the example of 4,6-*O*-benzylidene-D-glucopyranose (1), under essentially neutral conditions using 2-HP/DBU/molecular sieves, may be discussed via Scheme I (mechanistic intermediates are labeled "i"). Not only the generation of the pyranose aldehyde form (1ii), but also the dehydration of its Henry adduct (4, 4i, 4ii) to the nitroalkene, and the cyclization by β-addition of the C-5 hydroxyl group to give cpd. 2, involve catalyzable 1,3 proton transfers (PT#1-#3). Of these, PT#1, leading to the unstable zwitter ion 1i, is most likely rate determining. Ring opening of 1i to 1ii, with charge collapse, could be expected to be so fast that 1i, energetically close to hypothetical transition states (1 → 1i, or 1 → 1ii, concerted), could be indistinguishable as a mechanistic intermediate. Indeed Swain and Brown[16a] have shown that proton transfer and ring opening are probably concerted, albeit for 2-HP catalyzed ring opening of the conformationally less restricted 2,3,4,6-tetra-*O*-methyl-D-glucose (in contrast, ring opening of a glycosidic alkoxide intermediate[15], under basic conditions, would not involve charge collapse, and would be slow). The nitroalkene intermediate (not among the final products) would accumulate if PT#3 in the β-addition of C-5 hydroxyl would not be catalyzed as well. The proton transfer PT#3, not shown, is similar to a reversal of PT#1, with nitronate anion or the alkene, taking the place of the alkoxide (1i) or the carbonyl (1ii) in the two step or concerted reaction types, respectively.

Nitromethane has a pK_a similar to phenol. Thus, nitromethyl anion is more stable than alkoxide. This could explain that our system so far has failed to catalyze Henry condensations of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose and 2,3:4,6-di-*O*-isopropylidene-D-mannopyranose, compounds that lack the stabilization potential of the 2-hydroxyl proton for the alkoxide in the Henry adduct 4i.

The molecular sieves, of course, favor the dehydrated products nitroalkene and cpd. 2 over cpd. 4. Greatly diminished yields of cpd. 2 resulted from the omission of the sieves, which points to thermodynamic control of our reaction, as does exclusive formation of the β-anomer (2).

For maximal yield, the system needs to be fine tuned to the appropriate basicity by adjusting the 2-HP/DBU ratio. For best yields, 2-HP is typically equal or less compared to DBU, which makes a simple base catalysis improbable. Instructive in this respect is also the yield improvement brought about for the preparation of cpd. 2 by procedure B, in which DBU is added slowly. It is likely, that similar improvements are possible for cpds. 13 and 17. One equivalent of 2-HP and 0.5 equivalents DBU under a nitrogen atmosphere, gave a 39% yield of nitromethyl C-glycoside (2) (69% by procedure B), comparing very favorably with

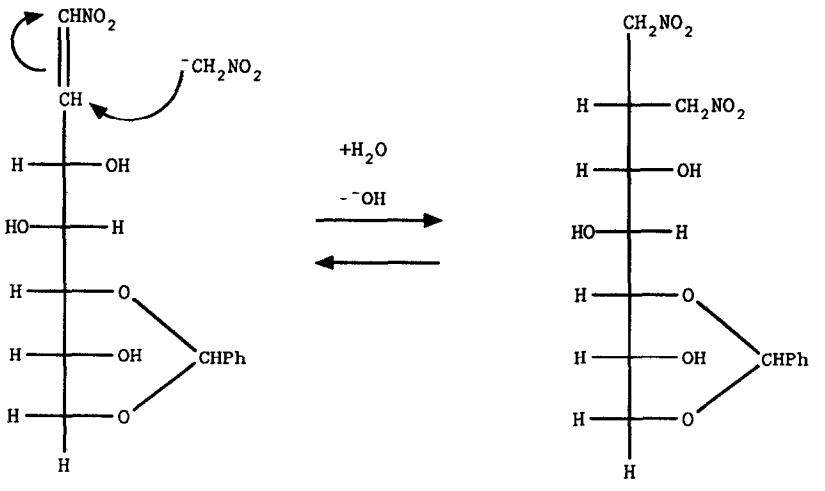
the literature preparation[11] Variations of temperature and of the molar ratios of 2-HP/DBU/cpd. 1 led to varying amounts of condensation products For example, with a 2-HP/DBU/cpd. 1 ratio of 2:1:1 at room temperature, the amount of cyclic nitromethyl C-glycoside (2) was 4% and the amount of acyclic nitromethyl heptitol (4) was 4%. A ratio of 1:2:1 at room temperature gave yields of 8% and 2% of the cyclic (2) and acyclic (4) products, respectively. A ratio of 1:1:1 at -10 °C yielded 7% of the acyclic (4) product whereas no cyclic product (2) was found. An increase of temperature to 70 °C with a ratio of 2·1:1 gave no evidence of products formed.



SCHEME I

Flash chromatography of the product mixture in the mother liquor of the cyclic nitromethyl C-glycoside led to the isolation of the acyclic addition products. 5,7-*O*-Benzylidene-1-deoxy-1-nitro-D-glycero-D-guloheptitol (4), formed by the Henry addition of nitromethane, was found in only 3.3% yield but in purer form than in the literature[11] (Scheme I).

5,7-*O*-Benzylidene-1,2-dideoxy-1-nitro-2-nitromethyl-D-glucoheptitol (3), presumably formed by the Michael addition of another mole of nitromethane to the unsaturated intermediate in the cyclization mechanism (Scheme II), was found in 6.3% yield.



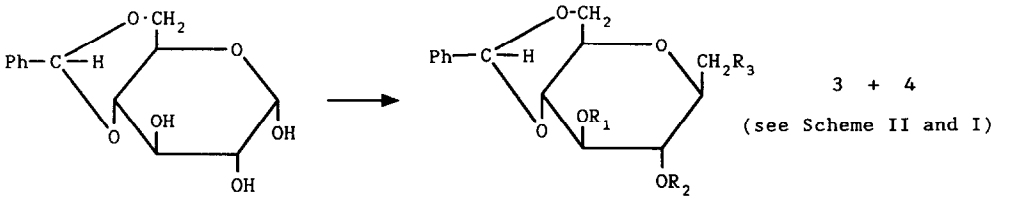
nitroalkene
(see Scheme I)

SCHEME II

(3)

Compound 2 was elaborated and derivatized as shown in Scheme III. Acetylation of the cyclic nitromethyl C-glycoside with acetic anhydride, 4-dimethylaminopyridine (DMAP), and triethylamine gave the diacetate (5). Conventional acetylation with acetic anhydride and pyridine catalyst gave lower yields. DMAP has been shown to be a superior catalyst in similar acylations[24].

The reduction of nitro-compounds to amines has been accomplished by a variety of reaction conditions including catalytic hydrogenation with conventional metal catalysts, Fe^0/HCl, $LiAlH_4$, and others[25]. Catalytic hydrogenations with homogeneous catalysts have been used for the selective reduction to various oximes and amines[26]. Nitro sugars have been reduced by catalytic hydrogenation with platinum, palladium-on-carbon, and Raney nickel under slightly acidic conditions[27].



(2) R_1=R_2=H; R_3=NO_2

(5) R_1=R_2=Ac; R_3=NO_2

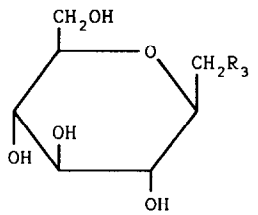
(6) R_1=R_2=H; R_3=NH_2

(7) R_1=R_2=H; R_3=NHAc

(8) R_1=R_2=Ac, R_3=NHAc

(9) R_1=R_2=H,
R_3=$NHCO_2CH_2C_6H_5$

(11) R_1=R_2=H,
R_3=NH-N_2Ar-*p*-NO_2



(10) R_3=$NHCO_2CH_2C_6H_5$

SCHEME III

Reduction of the benzylidenated nitromethyl C-glycoside (2) to the corresponding aminomethyl C-glycoside (6) by these methods was precluded since the benzylic position of the benzylidene group is sensitive to reduction with H_2/catalyst and also to solvolysis with acid However, we could reduce compound 2 by elemental Fe° in water and THF under a CO_2 atmosphere to the amine in good yield under very mild, neutral conditions. Reduction of $FeSO_4$ with $KHCO_3$/$NaBH_4$ gave elemental Fe° with a much larger and more active surface area than that on filings or powder The reducing species is presumably soluble $Fe(HCO_3)_2$, which is oxidized to $Fe(OH)_3$ This, in turn, can be reduced again by Fe° to $Fe(HCO_3)_2$, allowing the reduction of the nitro group to proceed in the dissolved state Replacement of the CO_2 atmosphere by N_2 led to a complex reaction mixture, presumably by incomplete reaction A CO_2 atmosphere as a reaction auxiliary has been used before by one of us[28]

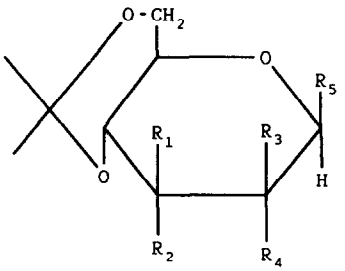
Acetylation of the 1-aminomethyl-4,6-*O*-benzylidene-1-deoxy-β-D-glucopyranose (6) with acetic anhydride/pyridine in methanol or with acetic anhydride/DMAP/triethylamine gave the 1-acetamidomethyl C-glycoside (7) or the 1-acetamidomethyl-2,3-diacetyl C-glycoside (8), respectively (Scheme III)

Benzyl chloroformate, with the aminomethyl C-glycoside (6) in the presence of $NaHCO_3$, gave 4,6-*O*-benzylidene-1-(benzyloxycarbonyl)aminomethyl-1-deoxy-β-D-glucopyranose (9), which was de-*O*-benzylidenated to 1-(benzyloxycarbonyl)-aminomethyl-1-deoxy-β-D-glucopyranose (10) Removal of the benzyloxycarbonyl group by hydrogenation would give the salt

free unprotected aminomethyl C-glycoside which could be used for the syntheses of enzyme inhibitors or potentially active C-glycosyl compounds through the formation of heterocyclic ring systems at the amino group.

Glycosyl methyl triazenes are known to be enzyme inhibitors[29] and are of biochemical interest[30] Previous methods of preparation gave very poor yields of the triazene in solution, and assays of triazene concentration had to be made due to the instability of the triazene[29b-c] Aminomethyl C-glycosides can be converted to triazenes through coupling with diazonium salts[31] We were able to prepare a stable, crystalline triazene (11) in good yield by the coupling of *p*-nitrobenzene diazonium hexafluorophosphate to the 4,6-*O*-benzylidenated aminomethyl C-glycoside (6) (Scheme III) The crystalline triazene appears to decompose somewhat during recrystallization and elemental analysis, and gave slightly lower analytical values for nitrogen The use of different diazonium salts could improve the stability of the triazene[32] and will be investigated.

Similar nitromethane condensations with 4,6-*O*-isopropylidene-α-D-mannopyranose (12) and 4,6-*O*-isopropylidene-α-D-glucopyranose (16) also gave cyclic products (Scheme IV).



(12) R_1=R_3=R_5=OH, R_2=R_4=H

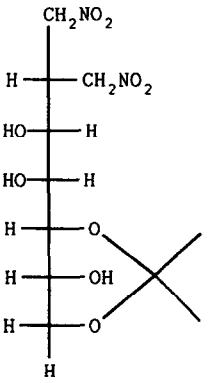
(13) R_1=R_3=OH, R_2=R_4=H, R_5=CH_2NO_2

(15) R_1=R_3=OAc, R_2=R_4=H; R_5=CH_2NO_2

(16) R_1=R_4=R_5=OH; R_2=R_3=H

(17) R_1=R_4=OH; R_2=R_3=H, R_5=CH_2NO_2

(18) R_1=R_4=OAc, R_2=R_3=H, R_5=CH_2NO_2



(14)

SCHEME IV

Nitromethane was condensed with 4,6-*O*-isopropylidene-α-D-mannose with a 2-HP/DBU/cpd 12 ratio of 2.1.1 and gave 1-deoxy-4,6-*O*-isopropylidene-1-nitromethyl-β-D-mannopyranose (13), and 1-deoxy-4,6-*O*-isopropylidene-1,1-di(nitromethyl)-D-mannitol (14). The nitromethane condensation of 4,6-*O*-isopropylidene-α-D-glucose with a 2-HP/DBU/cpd. 16 ratio of 1.1 1 gave 1-deoxy-4,6-*O*-isopropylidene-1-nitromethyl-β-D-glucopyranose (17) Acetylation of 13 and 17 with DMAP and triethylamine gave the corresponding diacetates, 15 and 18, which were used to confirm the cyclic structures by NMR analysis. The cyclic structure of 2, 13, 17, and their derivatives, with their thermodynamically favored β-configuration[33], was further proven by NMR analysis, including comprehensive decoupling experiments.

CONCLUSION

Our weakly basic 1,3-proton transfer catalyst on molecular sieves catalyzes aldol type condensations of nitromethyl anion with hemiacetals. Under favorable conformational conditions, recyclization to nitromethyl-C-glycopyranosides occurs by a β-elimination/addition sequence. Also obtained were products of Michael addition of a second mole of nitromethane to the unsaturated intermediates resulting from β-elimination The selective reduction of nitro groups with retention of benzylidene acetal blocking groups is possible with an especially active form of elemental Fe^{0} in aqueous organic (THF) solvent under CO_2

Experimental Procedures

Infrared spectra were recorded with a Perkin-Elmer spectrophotometer Model 283 from potassium bromide pellets. Melting points are uncorrected and were determined on a Thomas-Hoover melting point apparatus, Model 6404H. Optical rotations were measured at the sodium D line with an O C. Rudolph and Sons polarimeter, Model 956, in chloroform (c=1) unless otherwise specified All compounds synthesized were homogeneous by thin layer chromatography analysis, on plates coated with 0 25 mm of silica gel GF from Analtech, Inc Plates were developed with system A: methylcyclohexane/tetrahydrofuran (4·1); system B dichloromethane/dioxane (3·1); system C: dichloromethane/ethyl acetate/diethyl ether (3 1 1), or system D: chloroform/methanol (9:1). Suitable compounds were visualized under UV light, and all by spraying the plates with 10% sulfuric acid in methanol, and by heating them for up to 20 min at 150 °C C-glycosidic compounds charred noticeably slower than normal carbohydrate derivatives. For flash chromatography, 40 μm silica gel was used Column sizes were 5 cm ID X 45 cm (200g SiO_2) or 1.9 cm ID X 45 cm (30g SiO_2). ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini 300 FTNMR spectrophotometer with deuterated chloroform as solvent, and with 1% tetramethylsilane as internal standard, unless otherwise specified Assignments were made by homonuclear decoupling 2D experiments (COSY) and heteronuclear shift correlation 2D experiments (HETCOR) Elemental analyses were done by Beller Microanalytisches Laboratorium, Gottingen, West Germany.

4,6-*O*-Benzylidene-α-D-glucopyranose (1)

β-D-Glucose (72 0 g, 0 4 mol) was dissolved in ≈ 2 min in DMF (90 °C, 100 ml) The solution was quickly cooled in an ice bath and was magnetically stirred, while cold (-20 °C) benzaldehyde dimethylacetal (67 5 ml, 0.45 mol) was added When the mixture reached ≈ 40 °C (≈ 4 min), a solution of *p*-toluenesulfonic acid monohydrate (0 5 g, 2 6 mmol) in DMF (3 ml) was added The mixture was stirred under vacuum (≈ 2 torr) in order to distill methanol (along with some benzaldehyde dimethylacetal and DMF, ≈ 40 ml) into a cold trap (≈ -50 °C) After 8 h, the mixture, then at 17 °C, was neutralized with $NaHCO_3$ (0 5 g, 6 mmol), and was concentrated *in vacuo* Traces of DMF were removed by codistillation with xylene from the residual oil, which was stirred at 90 °C with toluene (200 ml) and H_2O

(200 ml) In this way, emulsions were avoided. The phases cleared immediately and were separated. The H_2O phase was quickly cooled, was treated with charcoal, was filtered, and was concentrated *in vacuo*. Water (100 ml) was added and the mixture was cooled (≈ 5 °C) overnight The resulting crystalline mass was filtered and was washed with minimal ice water to give **1** 36 g; mp 182-184 °C. The mother liquor, after several days at 0 °C, afforded additional **1**: 10 5 g, mp 182-184 °C. Recrystallization from hot dioxane/ ether gave pure **1**· 45 g (42%); mp 186-187 °C, $[\alpha]_D^{20}$ + 14° → + 4 4° (ethanol, final, 72 h); TLC system C: R_f 0 31, Lit[19b] mp 186-187 °C, $[\alpha]_D^{20}$ + 4° (ethanol)

2,6-Anhydro-5,7-O-benzylidene-1-deoxy-1-nitro-D-glycero-D-guloheptitol (2)

Procedure A: 1,8-Diazabicyclo[5 4.0]undec-7-ene (DBU; 4.2 ml, 28 mmol) was added to a solution of **1** (15 0 g, 55 9 mmol), 2-hydroxy pyridine (2.66 g, 28 mmol), nitromethane (100 ml), THF (100 ml), and molecular sieves (3 A, 35 g) The mixture was stirred under N_2 (7 days) at room temperature, was filtered and was concentrated *in vacuo* . A solution of the residual oil in ethyl acetate (100 ml) was extracted with cold (≈ 5 °C) citric acid (10%; 2 X 100 ml), cold (≈ 5 °C) satd $NaHCO_3$ (3 X 100 ml), and H_2O (100 ml), was dried (Na_2SO_4) and was concentrated *in vacuo* Addition of THF to the residual syrup and cooling (5 °C),produced a crystalline mass, which was filtered off and was washed with a minimal amount of diisopropyl ether to give **2** 4 0 g The mother liquor was cooled (5 °C) overnight and afforded another crop of **2** 0 8 g, Total yield of **2** including material from the chromatographic purification of **3** 6 7 g (39%), mp 213-214 °C, $[\alpha]_D^{20}$ -42 6° (methanol); Lit[11] mp 211-212 °C, $[\alpha]_D^{31}$ -35 4° (methanol), TLC system C R_f 0 70, IR 3420, 3480 (OH), 1385, 1560 (NO_2), 690, 760 (C_6H_5) cm^{-1}, ^1H NMR (DMSO-d_6) 4 06 (t, $J_{a,a}$=9 3 Hz, H^1), 3 20 (q, H^2), 3 50 (q, H^3), 3 44 (m, H^4), 3 62 (t, H^5), 3 47, 4 17 (dd, dd, two-H^6), 4 60, 4 95 (dd, dd, CH_2NO_2), 5 60 (s, CH-Ph), 7 40 (m, C_6H_5), 5 48, 5 66 (br, br, two-OH), ^{13}C NMR (DMSO-d_6) 77 54 (C^1), 71 56 (C^2), 70 15 (C^3), 80 81 (C^4), 73 90 (C^5), 67 87 (C^6), 77 67 (CH_2NO_2), 101 0 (CH-Ph), 126 7, 128 4, 129 2 (Ph), Anal Calcd for $C_{14}H_{17}O_7N$ (311 29) C, 54.02, H, 5 51, N, 4 50 Found C, 54 16, H, 5.68, N, 4 41

Procedure B. A solution of DBU (4 0 ml, 26 7 mmol) and THF (20 ml) was slowly dropped (3-4 h) into a solution of **1** (10 0 g, 37 2 mmol), 2-hydroxy pyridine (1 80 g, 18 9 mmol), nitromethane (6 ml, 110 8 mmol), THF (25 ml), and molecular sieves (3 A, 8 g), stirred under N_2 at room temperature After 12 h and after 24 h, CH_3NO_2 (3 ml) was added After 72 h, the mixture was filtered and was concentrated *in vacuo* The residual oil in ethyl acetate (100 ml) was washed as in procedure A Addition of cold THF to the residue from the evaporation of the ethyl acetate phase gave **2** 5.0 g (mp 213-214 °C). Diethyl ether (20 ml) was added to the mother liquor which was cooled (5 °C) overnight, giving crude **2** 4 0 g (mp 190-195 °C), Recystallization from THF gave pure **2** 3 0 g Total yield of **2** 8 0 g (69%), mp 213-214 °C, Physical properties identical to compound 2 from procedure A. Side products were not isolated

5,7-O-Benzylidene-1,2-dideoxy-1-nitro-2-nitromethyl-D-glucoheptitol (3)

The mother liquor from **2** (procedure A) was subjected to flash chromatography (5 cm ID X 45 cm) with CH_2Cl_2/ethyl acetate/ether (8 1 1) as the elutent Fractions of 100-125 ml were collected and were concentrated *in vacuo* Fractions 10-20 gave 1 9 g **2** Fractions 27-32 gave crystals that were recrystallized from THF/diisopropyl ether to give **3**. 1.3 g (6 3%), mp 126-127 °C, $[\alpha]_D^{20}$ -38 5° (methanol); TLC system C R_f 0 59; IR 3400, 3500 (OH), 1390, 1550 (NO_2), 695, 740 (C_6H_5) cm^{-1}, ^1H NMR (DMSO-d_6) 3 21 (sx, J=6.8 Hz, H^1), 3 73 (t, H^2) 3 55 (t, H^3), 3 62 (q, H^4), 3 82 (q, H^5), 4 16, 5 17 (dd, t, two-H^6), 4 68, 4 80 (dd, dd, two overlapping-CH_2NO_2), 5 52 (s, CH-Ph), 7 40 (m, C_6H_5), ^{13}C NMR (DMSO-d_6) 38 81 (C^1), 70.22 (C^2), 81 05 (C^3), 60 34 (C^4), 69 18 (C^5), 71 22 (C^6), 74.57 75 31 (two-CH_2NO_2), 100 2 (CH-Ph), 126 5, 128 3, 128 9 (Ph); Anal Calcd for $C_{15}H_{20}O_9N_2$ (372 33) C, 48.39; H, 5.42, N, 7 52 Found C, 48 43, H, 5 29; N, 7 46

5,7-O-Benzylidene-1-deoxy-1-nitro-D-glycero-D-guloheptitol (4)

Fractions 38-42 of the preceding chromatographic purification gave crystals that were recrystallized from THF/diisopropyl ether to give **4**: 0 6 g (3.3%), mp 165-166 °C; $[\alpha]_D^{20}$ -39 9° (methanol), $[\alpha]_D^{20}$ -68 5° (H_2O), Lit[11] mp 160-162 °C, $[\alpha]_D^{28}$ -42 5° (H_2O), TLC

system C: R_f 0.46; IR 3300, 3515 (OH), 1370, 1550 (NO_2), 690, 745 (C_6H_5) cm^{-1}; ^1H NMR (DMSO-d_6) 4.27 (sx, J=7.3 Hz, H^1), 3.63 (t, H^2), 3.97 (m, H^3), 3.69 (q, H^4), 3.76 (seven lines, H^5), 3.55, 4.20 (t, dd, two-H^6), 4.40, 4.75 (dd, dd, CH_2NO_2), 5.54 (s, CH-Ph), 7.42 (m, C_6H_5); ^{13}C NMR (DMSO-d_6) 69.51 (C^1), 73.70 (C^2), 67.44 (C^3), 83.26 (C^4), 60.79 (C^5), 71.21 (C^6), 80.26 (CH_2NO_2), 100.2 (CH-Ph), 126.6, 128.3, 129.0 (Ph); Anal. Calcd for $C_{14}H_{19}O_8N$ (329.31): C, 51.06; H, 5.82; N, 4.26. Found: C, 51.27; H, 5.86; N, 4.25.

3,4-di-O-acetyl-2,6-anhydro-5,7-O-benzylidene-1-deoxy-1-nitro-D-glycero-D-guloheptitol (5)

Acetic anhydride (0.14 ml, 1.4 mmol) was added slowly to a cooled (≈0 °C), stirred mixture of **2** (0.15 g, 0.5 mmol), 4-dimethyl aminopyridine (DMAP, 0.02 g, 0.2 mmol), and triethylamine (0.25 ml, 1.8 mmol) in THF (3 ml). The mixture was allowed to warm to room temperature after 1 h. After 15 h, the mixture was concentrated *in vacuo*. The solution of the residual oil in CH_2Cl_2 (15 ml) was extracted with citric acid (10%, 10 ml), with satd. $NaHCO_3$ (2 X 10 ml), and with H_2O (10 ml). The organic phase was dried (Na_2SO_4) and was concentrated *in vacuo*. Addition of ethanol, cooling (-20 °C) overnight, and filtration afforded **5**: 0.12 g (61%); mp 191-192 °C; $[\alpha]_D^{20}$ -80.9°; Lit[11] mp 192-193 °C, $[\alpha]_D^{23}$ -60 °; TLC system A: R_f 0.28; IR 1375, 1560 (NO_2), 1750 (C=O), 700, 750 (C_6H_5) cm^{-1}; ^1H NMR 3.64 (q, $J_{a,a}$=9.0 Hz, H^1), 4.33 (t, H^2), 4.93 (q, H^3), 5.35 (t, H^4), 3.53 (q, H^5), 3.69, 4.30 (dd, dd, two-H^6), 4.37, 4.47 (dd, dd, CH_2NO_2) 5.47 (s, CH-Ph), 7.38 (m, C_6H_5) 2.03, 2.06 (s, two-Ac); ^{13}C NMR 78.66 (C^1), 75.37 (C^2), 70.38 (C^3), 72.80 (C^4), 71.14 (C^5), 68.61 (C^6), 76.33 (CH_2NO_2), 102.1 (CH-Ph), 126.7, 128.8, 129.8 (Ph), 20.76, 20.87 (two-Ac); Anal. Calcd for $C_{18}H_{21}O_9N$ (395.36): C, 54.68; H, 5.35; N, 3.54. Found: C, 55.23; H, 5.65; N, 3.61.

1-Amino-2,6-anhydro-5,7-O-benzylidene-1-deoxy-D-glycero-D-guloheptitol (6)

A solution of potassium bicarbonate (1.0 M, 3.8 ml, 3.8 mmol) was added to a solution of $FeSO_4$ (0.5 M, 19.8 ml, 9.9 mmol). When the evolution of CO_2 ceased, $NaBH_4$ (0.64 g, 16.9 mmol) was slowly added with stirring to give elemental Fe° that was centrifuged, was washed several times with H_2O, and was added with H_2O (18 ml) to a solution of **2** (1.0 g, 3.2 mmol) in THF (25 ml). The mixture was stirred under CO_2 (92 h), was filtered with the aid of celite (15 g), and was concentrated *in vacuo*. The crystalline mass was dissolved in methanol and was poured on a cation exchange column (3 g: Bio-Rex 70; carboxylic cation exchange resin; 200-400 mesh; 10.2 meq/dry g (H); activated by washing with 10% HCl followed by H_2O until the effluent was neutral). The column was washed with methanol/H_2O (1:1; 100 ml). The compound was eluted with 10% aq Et_3N (150 ml). The effluent was concentrated *in vacuo*. The addition of a minimal amount of methanol, cooling (-10 °C) overnight, and filtration gave **6**: 0.49 g (54%); mp 234-235 °C; $[\alpha]_D^{20}$ -41.7° (MeOH); TLC system $CHCl_3$/MeOH (1·1): R_f 0.31; IR 3300, 3420 (OH), 1600 (NH), 695, 750 (C_6H_5) cm^{-1}; ^1H NMR (DMSO-d_6) 3.19 (t, $J_{a,a}$=7.5 Hz, H^1), 3.22 (t, H^2), 3.34 (m, H^3), 3.40 (q, H^4), 3.37 (q, H^5), 3.65, 4.20 (t, dd, two-H^6), 2.61, 2.87 (dd, dd, CH_2NH_2), 5.28 (br, NH_2) 5.58 (s, CH-Ph), 7.41 (m, C_6H_5); ^{13}C NMR (DMSO-d_6) 72.67 (C^1), 81.85 (C^2), 70.27 (C^3), 74.34 (C^4), 81.39 (C^5), 68.30 (C^6), 43.46 (CH_2NH_2), 101.0 (CH-Ph), 126.7, 128.4, 129.2 (Ph); Anal. Calcd for $C_{14}H_{19}O_5N$ (281.31): C, 59.78; H, 6.81; N, 4.98. Found: C, 59.77; H, 6.86; N, 4.90.

1-Acetamido-2,6-anhydro-5,7-O-benzylidene-1-deoxy-D-glycero-D-guloheptitol (7)

Acetic anhydride (0.14 ml, 1 5 mmol) was added dropwise to a magnetically stirred solution of **6** (0 28 g, 1.0 mmol) in methanol (10 ml). After 1 h, acetic anhydride (0.14 ml, 1.5 mmol) and pyridine (0.14 ml, 1.7 mmol) were added and the mixture was stirred for another 1 h. Pyridine (0.14 ml, 1 7 mmol) was added to the mixture and the mixture was concentrated *in vacuo*. Addition of methanol and filtration afforded **7**: 0.32 g (99%); mp 202-203 °C; $[\alpha]_D^{20}$ -37.9° (methanol); TLC system $CHCl_3$/MeOH (1:1): R_f 0.60; IR 3300, 3480 (OH), 1560 (NH), 1635 (C=O), 695, 760 (C_6H_5) cm^{-1}; ^1H NMR (DMSO-d_6) 3.42 (q, $J_{a,a}$=8.0 Hz, H^1), 3 37 (t, H^2), 3.35 (t, H^3), 3.03 (q, H^4), 3.30 (q, H^5), 3.62, 4.21 (dd, dd, two-H^6), 3.09, 3.57 (dd, dd, CH_2NHAc), 7.95 (br, NHAc), 5.60 (s, CH-Ph), 7.42 (m, C_6H_5), 1.88 (s, Ac), 5.27, 5.31 (d, d, two-OH); ^{13}C NMR (DMSO-d_6) 81.26 (C^1), 70.36 (C^2), 79.65 (C^3),

73.95 (C^4), 72.55 (C^5), 68.23 (C^6), 40.62 (CH_2NHAc), 101.0 (CH-Ph), 126.7, 128.4, 129.2 (Ph), 22.53 (Ac); Anal. Calcd for $C_{16}H_{21}O_6N$ (323.35): C, 59.43; H, 6.55; N, 4.33. Found: C, 59.20; H, 6.46; N, 4.27.

1-Acetamido-2,6-anhydro-3,4-di-O-acetyl-5,7-O-benzylidene-1-deoxy-D-glycero-D-guloheptitol (8)

Acetic anhydride (0.37 ml, 4.0 mmol) was added slowly to a cooled (≈0 °C), magnetically stirred mixture of 6 (0.28 g, 1.0 mmol), dimethyl aminopyridine (DMAP, 0.02 g, 0.2 mmol), and triethylamine (0.84 ml, 6.0 mmol) in THF (3 ml). The mixture was allowed to warm to room temperature after 1 h. After 17 h, pyridine (1.5 ml, 18 mmol) and acetic anhydride (0.3 ml, 3.2 mmol) were added to the mixture. After 22 h, methanol (3 ml) was added, and the mixture was concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (15 ml) and was extracted with citric acid (10%; 2 X 10 ml), with satd. $NaHCO_3$ (3 X 10 ml), and with H_2O (10 ml). The organic phase was dried (Na_2SO_4) and was concentrated *in vacuo*. Addition of pet. ether gave 8: 0.25 g (62%); mp 174-175 °C; $[\alpha]_D^{20}$ -156.5°; TLC system C: R_f 0.47; IR 3380 (NH), 1750 (C=O), 770, 600 (C_6H_5) cm^{-1}; ^1H NMR 3.67 (q, $J_{a,a}$=9.5 Hz, H^1), 3.53 (q, H^2), 5.29 (t, H^3), 4.90 (t, H^4), 3.62 (m, H^5), 4.33, 5.10 (dd, dd, two-H^6), 3.25, 3.63 (dd, dd, CH_2NHAc), 5.73 (br, NHAc), 5.46 (s, CH-Ph), 7.38 (m, C_6H_5), 1.96, 2.00, 2.05 (s, three-Ac); ^{13}C NMR 79.13 (C^1), 71.18 (C^2), 73.21 (C^3), 70.27 (C^4), 77.81 (C^5), 68.91 (C^6), 39.90 (CH_2NHAc), 102.0 (CH-Ph), 126.7, 128.9, 129.7 (Ph), 20.88, 20.95, 23.70 (three-Ac); Anal. Calcd for $C_{20}H_{25}O_8N$ (407.42): C, 58.96; H, 6.19; N, 3.44. Found: C, 58.62; H, 6.25; N, 3.36.

2,6-Anhydro-5,7-O-benzylidene-1-benzyloxycarboxamido-1-deoxy-D-glycero-D-guloheptitol (9)

A mixture of benzyl chloroformate (50% in toluene, 1.43 ml, 42 mmol) cpd. 6 (1.0 g, 36 mmol), $NaHCO_3$ (0.40 g, 48 mmol), THF (25 ml), and H_2O (10 ml) was stirred for 18 h and was concentrated *in vacuo*. Ether (25 ml) and satd. $NaHCO_3$ (25 ml) were added and the mixture was stirred until neutral (0.5 h). Filtration of the two phase mixture, followed by washing with H_2O and ether afforded crude 9. Recrystallization from CH_2Cl_2/pet ether gave pure 9: 1.45 g (98%); mp 185-186 °C; $[\alpha]_D^{20}$ -7.90°; TLC system D: R_f 0.70; IR 3300, 3495 (OH), 1690 (C=O), 1525 (NH), 690, 750 (C_6H_5) cm^{-1}; ^1H NMR (DMSO-d_6) 3.41 (t, $J_{a,a}$=9.6 Hz, H^1), 3.35 (t, H^2), 3.38 (q, H^3), 3.08 (q, H^4), 3.31 (t, H^5), 3.60, 4.19 (t, dd, two-H^6), 3.02, 3.57 (dd, dd, CH_2NH-), 5.59 (s, CH-Ph), 5.05 (s, C=$OCH_2C_6H_5$), 7.38 (m, C_6H_5), 7.23 (br, CH_2NH-), 7.38 (m, C=$OCH_2C_6H_5$), 5.28, 5.32 (d, d, two-OH); ^{13}C NMR (DMSO-d_6) 74.12 (C^1), 79.50 (C^2), 81.19 (C^3), 72.73 (C^4), 70.23 (C^5), 68.21 (C^6), 42.56 (CH_2NH-), 101.0 (CH-Ph), 126.7, 128.4, 129.2 (Ph), 65.44 (C=$OCH_2C_6H_5$) 128.2, 128.4, 128.7 (C=$OCH_2C_6H_5$); Anal. Calcd for $C_{22}H_{25}O_7N$ (415.44): C, 63.61; H, 6.07; N, 3.37. Found: C, 63.75; H, 6.20; N, 3.33.

2,6-Anhydro-1-benzyloxycarboxamido-1-deoxy-D-glycero-D-guloheptitol (10)

Water (1 ml) was added dropwise to a solution of 9 (0.10 g, 0.24 mmol) in 90% acetic acid (1.0 ml) stirred at 90 °C for 0.5 h. The mixture was concentrated *in vacuo* to give a syrup from which acetic acid was removed by codistillation with H_2O (3 X 15 ml) *in vacuo*. The solution of the residual syrup in H_2O (15 ml) was extracted with ether (4 X 15 ml) and was concentrated *in vacuo*. The resultant syrup was seeded, and was digested with ether. Filtration with ether gave 10: 0.08 g (100%); mp 114-115 °C; $[\alpha]_D^{20}$ -17.9 ° (methanol); TLC system D: R_f 0.32; IR 3350 (OH), 1750 (C=O), 1530 (NH), 690, 735 (C_6H_5) cm^{-1}; ^1H NMR (DMSO-d_6) 2.95 (q, $J_{a,a}$=9.2 Hz, H^1), 3.09 (q, H^2), 3.14 (t, H^3), 3.60 (q, H^4), 2.88 (t, H^5), 3.64 (dd, two-H^6), 2.86, 3.60 (dd, dd, CH_2NH-), 5.05 (s, C=$OCH_2C_6H_5$), 4.47 (br, CH_2NH-), 7.38 (m, C=$OCH_2C_6H_5$), 3.38 (br, five-OH); ^{13}C NMR (DMSO-d_6) 70.71 (C^1), 80.67 (C^2), 78.02 (C^3), 78.55 (C^4), 71.99 (C^5), 62.08 (C^6), 42.78 (CH_2NH-), 65.48 (C=$OCH_2C_6H_5$), 128.2, 128.3, 128.7 (C=$OCH_2C_6H_5$); Anal. Calcd for $C_{15}H_{21}O_7N$ (327.33): C, 55.04; H, 6.47; N, 4.28. Found: C, 54.65; H, 6.60; N, 4.09.

2,6-Anhydro-1-deoxy-1-(*p*-nitrophenyl)triazeno-D-glycero-D-guloheptitol (11)

A solution of *p*-nitrobenzene diazonium hexafluorophosphate (0.54 g, 1.83 mmol) in DMF (10 ml) was slowly added to a cooled (-10 °C), stirred mixture of **6** (0.5 g, 1.78 mmol), Na_2CO_3 (2.5 g, 23.6 mmol) and DMF (10 ml). The mixture was stirred (0.5 h), was allowed to come to room temperature (0.5 h), and was distributed between ether (25 ml) and satd $NaHCO_3$ (3 X 25 ml). The ether layer was dried (Na_2SO_4) and was concentrated *in vacuo*. The residual syrup was dissolved in THF. Addition of pet ether and cooling (-15 °C) overnight gave **11**: 0.45 g (58%); mp 121-122 °C; $[\alpha]_D^{20}$ + 12.8° (methanol); TLC system D: R_f 0.81; IR 3240, 3360 (OH), 1600 (N=N), 685, 695, 745, 760 (2 C_6H_5); ^1H NMR (DMSO-d_6) 3.47 (q, $J_{a,a}$=10.2, H^1), 3.79 (t, H^2), 3.38 (q, H^3), 3.42 (t, H^4), 3.28 (six lines, H^5), 4.16 (dd, two-H^6), 1.77 (dd, CH_2NHN_2-), 5.58 (s, CH-Ph), 7.40 (m, C_6H_5), 7.30, 8.20 (two-d, N_2-Ar-*p*-NO_2), 6.74 (br, NH-N_2-), 5.39, 5.50 (d, d, two-OH); ^{13}C NMR (DMSO-d_6) 74.38 (C^1), 79.12 (C^2), 81.21 (C^3), 70.28 (C^4), 72.50 (C^5), 68.13 (C^6), 67.25 (CH_2NHN_2-), 101.0 (CH-Ph), 126.7, 128.4, 129.2 (Ph), 121.0, 126.3, 138.3 ($CH_2NHN_2C_6H_4NO_2$); Anal. Calcd for $C_{20}H_{22}O_7N_4$ (430.42): C, 55.81; H, 5.15; N, 13.02. Found: C, 55.19; H, 5.53; N, 11.42 (note: probable decomposition in transport to Germany for analysis).

4,6-O-Isopropylidene-α-D-mannopyranose (12)

The literature procedure[23a] was applied to D-mannose (43.2 g, 0.24 mol) to give crude **12** (26 g). Crude cpd. **12** (10 g) was then dissolved in hot THF (100 ml). The THF solution was allowed to cool on a flash chromatography column (prepared with THF) for 2 h. Fractions of 100-125 ml were eluted with THF. Fractions 8-12 gave a mixture (3 g) of mannose and **12** that was saved to be rechromatographed. Fractions 4-7 gave a syrup that was crystallized upon the addition of ethyl acetate to give pure **12**: 7 g. This procedure was repeated twice to give a total of pure **12**: 21 g (40%); mp 156-157 °C; $[\alpha]_D^{20}$ +0.5° (initial) → -13.6° (final, 48 h, H_2O); TLC system B: R_f 0.30; Lit[23a] for α-anomer: mp 156-157 °C; $[\alpha]_D^{20}$ -1° (initial) → -24° (final, 48 h; c=1, H_2O).

2,6-Anhydro-1-deoxy-5,7-O-isopropylidene-1-nitro-D-glycero-D-galactoheptitol (13)

DBU (5.1 ml, 34 mmol) was added to a solution of **12** (15.0 g, 68.1 mmol), 2-hydroxy pyridine (6.5 g, 68 mmol), nitromethane (6.8 ml), THF (75 ml), and molecular sieves (3 A, 19 g) and was magnetically stirred under N_2 (4 days). The mixture was filtered and was concentrated *in vacuo*. The residue was subjected to flash chromatography (200 g SiO_2, 5 cm ID X 45 cm) with THF as the solvent. Fractions of 100-125 ml were collected. Fractions 2-4 gave crystals that were recrystallized from THF/diisopropyl ether to give **13**: 8.9 g (50%); mp 204-205 °C; $[\alpha]_D^{20}$ -43.6° (methanol); TLC system B: R_f 0.65; IR 3400 (OH), 3000, 2930 (CH), 1550, 1370 (NO_2) cm^{-1}; ^1H NMR (DMSO-d_6) 4.25 (q, $J_{a,e}$=3.5 Hz, H^1), 3.75 (t, H^2), 3.55 (q, H^3), 3.62 (t, H^4), 3.18 (six lines, H^5), 3.68, 3.73 (dd, dd, two-H^6), 4.52, 4.84 (dd, dd, CH_2NO_2), 1.31, 1.43 (s, two-CH_3), 3.40 (br, two-OH); ^{13}C NMR (DMSO-d_6) 75.83 (C^1), 70.79 (C^2), 70.68 (C^3), 69.86 (C^4), 71.81 (C^5), 61.43 (C^6), 77.59 (CH_2NO_2), 99.29 ($C(CH_3)_2$), 19.18, 29.17 (two-CH_3); Anal. Calcd for $C_{10}H_{17}O_7N$ (263.25): C, 45.63; H, 6.51; N, 5.32; Found: C, 45.44; H, 6.55; N, 5.54.

1,2-Dideoxy-5,7-O-isopropylidene-1-nitro-2-nitromethyl-D-mannoheptitol (14)

Fractions 6-7 of the preceding chromatographic purification gave crystals that were recrystallized from THF/pet. ether to give **14**: 0.85 g (4%); mp 163-164 °C; $[\alpha]_D^{20}$ -22.9°; TLC system B: R_f 0.50; IR 3550, 3450 (OH), 3000, 2960 (CH), 1560, 1380 (NO_2) cm^{-1} ; ^1H NMR (DMSO-d_6) 3.35 (q, J=7.5 Hz, H^1), 3.71 (q, H^2), 3.65 (q, H^3), 3.50 (t, H^4), 3.62 (m, H^5), 3.75 (dd, H^6), 4.57, 4.75, 4.80, 4.85 (four overlapping dd, 16 lines, two-CH_2NO_2), 1.28, 1.39 (s, two-CH_3), 4.55, 4.60, 5.40 (d, d, d, three-OH); ^{13}C NMR (DMSO-d_6) 38.47 (C^1), 68.38 (C^2), 68.46 (C^3), 72.41 (C^4), 61.03 (C^5), 64.58 (C^6), 73.79, 76.06 (two-CH_2NO_2), 98.10 ($C(CH_3)_2$), 19.24, 28.26 (two-CH_3); Anal. Calcd for $C_{11}H_{20}N_2$ (324.33): C, 40.74; H, 6.22; N, 8.64; Found: C, 41.10; H, 6.24; N, 8.75.

3,4-Di-O-acetyl-2,6-anhydro-1-deoxy-5,7-O-isopropylidene-1-nitro-D-glycero-D-galactoheptitol (15)

DMAP (0.15 g, 1.2 mmol) and triethylamine (0.64 ml, 4.6 mmol) were added to a cooled (-10 °C), magnetically stirred mixture of 13 (0.5 g, 1.9 mmol) and acetic anhydride (0.56 ml, 5.9 mmol) in THF (3 ml). After 21 h, methanol (3 ml) was added to the mixture and the mixture was concentrated *in vacuo*. The addition of ethanol (3 ml), concentration *in vacuo*, and filtration with minimal ethanol present afforded 15: 0.26 g (62%); mp 178-179 °C; $[\alpha]_D^{20}$ -92.6°; TLC system A: R_f 0.47; IR 2950, 2995 (CH), 1375, 1560 (NO_2), 1750 (C=O), cm^{-1}; ^1H NMR 4.53 (q, $J_{a,e}$=2.7 Hz, H^1), 5.48 (q, H^2), 5.02 (q, H^3), 4.00 (t, H^4), 3.43 (six lines, H^5) 3.79, 3.91 (t, dd, two-H^6), 4.34, 4.44 (dd, dd, CH_2NO_2), 1.38, 1.57 (s, two-CH_3), 2.03, 2.20 (two-Ac); ^{13}C NMR 75.13 (C^1), 69.77 (C^2), 72.19 (C^3), 69.16 (C^4), 73.88 (C^5), 62.66 (C^6), 76.60 (CH_2NO_2), 101.2 ($C(CH_3)_2$), 20.24, 30.01 (two-CH_3), 21.64, 21.78 (two-Ac), 171.0, 171.2 (two-C=O); Anal. Calcd for $C_{14}H_{21}O_9N$ (347.32): C, 48.41; H, 6.10; N, 4.03. Found: C, 48.46; H, 6.03; N, 3.90.

4,6-O-Isopropylidene-α-D-glucopyranose (16)

Crude cpd. 16, prepared[23b] from D-glucose (43.2 g, 0.24 mol), was purified in the manner described for cpd. 12 to give 16: 21 g (40 %); mp 180-181 °C; $[\alpha]_D^{20}$ +3.5° (initial) → -7.0° (final, 48 h, H_2O); TLC system B: R_f 0.19; Lit[23b] for α\β mixture: mp 169.5-170.5 °C; $[\alpha]_D^{27}$ +24° (initial) → -7.3° (final, 48 h, H_2O, c=2.1).

2,6-Anhydro-1-deoxy-5,7-O-isopropylidene-1-nitro-D-glycero-D-guloheptitol (17)

DBU (1.5 ml, 10 mmol) was added to a solution of 16 (2.2 g, 10 mmol), 2-hydroxy pyridine (0.95 g, 10 mmol), nitromethane (1.0 ml), THF (11 ml), and molecular sieves (3 A, 3 g) and was magnetically stirred under N_2 (5 days). The mixture was filtered and was concentrated *in vacuo*. The residue was subjected to flash chromatography (30 g SiO_2, 1 cm ID X 45 cm) with THF as the solvent. Fractions of 50-60 ml were collected. Fractions 2-4 gave crystals that were recrystallized from THF/diisopropyl ether to give 17: 1.0 g (38%); mp 158-159 °C; $[\alpha]_D^{20}$ -27.6° (methanol); TLC system B: R_f 0.65; IR 3380 (OH), 2995, 2905 (CH), 1550, 1375 (NO_2) cm^{-1}; ^1H NMR (DMSO-d_6) 3.95 (t, $J_{a,a}$=9.6 Hz, H^1), 3.03 (q, H^2), 3.36 (t, H^3), 3.32 (q, H^4), 3.28 (six lines, H^5), 3.59, 3.75 (dd, t, two-H^6), 4.52, 4.91 (dd, dd, CH_2NO_2), 1.31, 1.43 (s, two-CH_3), 5.30, 5.58 (d, d, two-OH); ^{13}C NMR (DMSO-d_6) 77.57 (C^1), 71.66 (C^2), 77.43 (C^3), 74.23 (C^4), 71.15 (C^5), 61.44 (C^6), 77.74 (CH_2NO_2), 99.08 ($C(CH_3)_2$), 19.09, 29.04 (two-CH_3); Anal. Calcd for $C_{10}H_{17}O_7N$ (263.25): C, 45.63; H, 6.26; N, 5.32; Found: C, 45.35; H, 6.49; N, 5.34.

3,4-Di-O-acetyl-2,6-anhydro-1-deoxy-5,7-O-isopropylidene-1-nitro-D-glycero-D-guloheptitol (18)

The method described for 15 was applied to the acetylation of 17 to give 18: 0.20 g (48%); mp 162-163 °C; $[\alpha]_D^{20}$ -49.2°; TLC system A: R_f 0.39 ; IR 2950,3000 (CH), 1375, 1560 (NO_2), 1745 (C=O) cm^{-1}; ^1H NMR 4.34 (q, $J_{a,a}$=9.2 Hz, H^1), 5.20 (t, H^2), 4.90 (t, H^3), 3.71 (t, H^4), 3.43 (six lines, H^5) 3.68, 3.94 (dd, dd, two-H^6), 4.30, 4.47 (dd, dd, CH_2NO_2), 1.38, 1.46 (s, two-CH_3), 2.06, 2.07 (two-Ac); ^{13}C NMR 74.90 (C^1), 70.17 (C^2), 72.92 (C^3), 71.20 (C^4), 71.85 (C^5), 61.73 (C^6), 76.05 (CH_2NO_2), 99.93 ($C(CH_3)_2$), 18.99, 28.85 (two-CH_3), 20.62, 20.78 (two-Ac), 170.0, 170.1 (two-C=O); Anal. Calcd for $C_{14}H_{21}O_9N$ (347.32): C, 48.41; H, 6.10; N, 4.03. Found: C, 48.42; H, 6.10; N, 3.72.

ACKNOWLEDGMENTS

This work has been supported by an AREA grant (#1R15 GM38595-01 to P.H. Gross) from NIH. K.N. Drew would like to like to thank ARCS (Achievement Rewards for College Scientists) and UOP for their financial support. This work was taken in part from the doctoral thesis of K.N. Drew, University of the Pacific, 1991. We thank Dr. M.J. Minch for valuable discussions, Xiaojing Wang for his work on procedure B in the preparation of compound 2, and Dr. Jim Shoolery at Varian Associates for the NMR spectra. This work was presented (CARB#28) at the 200th ACS National Meeting in Washington, D.C. (1990).

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