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# *N*-Substituted (β-D-galactopyranosylmethyl)amines, and *C*-β-D-galactopyranosylformamides, and related compounds*

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ABSTRACT

A series of *N*-substituted (β-D-galactopyranosylmethyl)amines, a series of *N*-substituted *C*-β-D-galactopyranosylformamides, and other *C*-β-D-galactopyranosyl compounds have been synthesized and characterized. Most were prepared from β-D-galactopyranosyl cyanide via *C*-β-D-galactopyranosylformic acid.

## INTRODUCTION

In an effort to produce stable, reversible inhibitors of the neutral β-galactosidase of *E. coli* lacZ, a series of *C*-galactosyl compounds was designed, prepared, and characterized. Both *N*-substituted (β-D-galactopyranosylmethyl)amines and *C*-β-D-galactopyranosylformamides[§] were made to (*a*) study the effect, on binding and inhibition, of variation in the $pK_a$ of the inhibitor resulting from variation in the *N*-substituent, and (*b*) study the separate contribution of the hydrophobic aglycon on inhibitor binding. *C*-β-D-Galactopyranosyl compounds with $sp^2$ and $sp^1$ hybridization at C-1′ were also synthesized to determine the effect on binding of such hybridization (as compared to $sp^3$ hybridization at C-1′)*. The inhibition studies are being reported separately.

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§In this paper, a nomenclature convention recommended by the principal author (J.N.B.) has been used. In it the *C*-glycosyl part of the subject compounds has been named as an intact moiety. According to another completely proper convention that may be, and often is, used, these compounds would be named as derivatives of higher-carbon sugars. Compound **2**, for example, would be 3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptonamide, and **12** would be named as an amino-anhydro-deoxyheptitol. The "glycosyl" convention is recommended for present purposes because higher-carbon sugar names are not easily applied to compounds having large or complex nonglycosyl portions, or even to compounds such as **17–19**.

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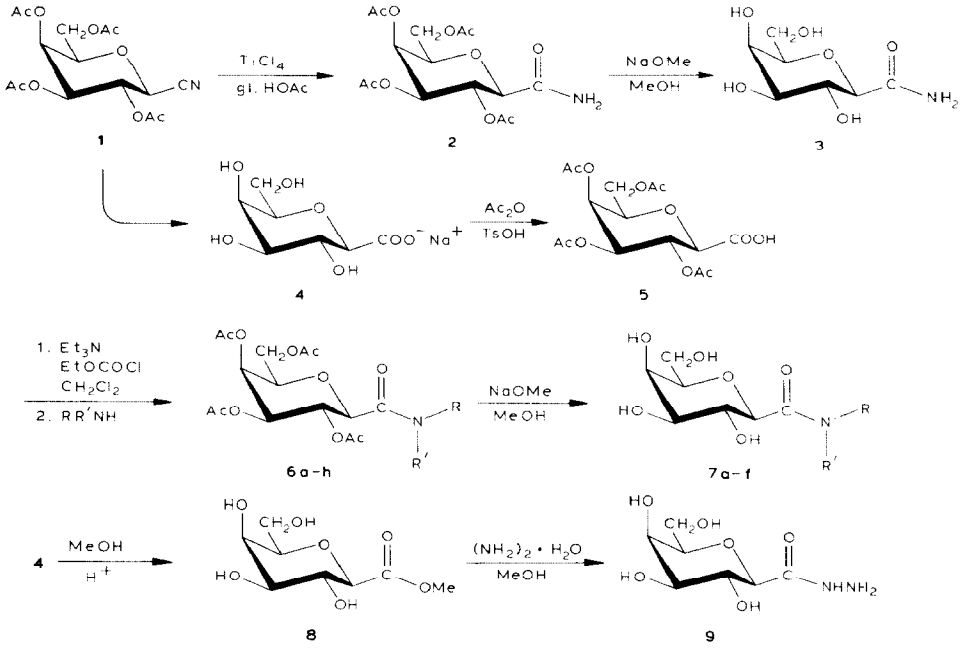
RESULTS AND DISCUSSION

Compound **2** was prepared in an 80% yield by treating readily available 2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranosyl cyanide[1] (**1**) with glacial acetic acid in the presence of titanium tetrachloride. It had been synthesized previously by treating **1** with glacial acetic acid and hydrogen bromide[2]. Compound **2** was *O*-deacetylated to give the unprotected amide (**3**). The structure of **3** was confirmed by elemental analysis (Table I) and $^{13}$C-n.m.r. (Table II). The $^{13}$C-n.m.r. data showed remarkable similarity to those of previously characterized **4**, which show chemical shifts for C-1, C-3, and C-5 significantly downfield from those of the *α*-D anomer[2]. Additional confirmation of the *β*-D-configuration of compound **3** is provided by the fact that it is a competitive inhibitor ($K_i$ = 9.8 mM) of *E. coli* lacZ *β*-galactosidase[3].

Compound **4** was acetylated with acetic anhydride, using *p*-toluenesulfonic acid as a catalyst[2], to give **5**, which was precursor to the *N*-substituted *C*-*β*-D-galactopyranosyl-formamides (**7a–h**) and -methylamines (**11a–h**).

Per-*O*-acetylated, *N*-substituted *C*-*β*-D-galactopyranosylformamides (**6a–h**) were prepared in good yields by converting the acid **5** into a mixed anhydride and reacting the




*Here, C-1′ refers to the carbon atom of the nonsugar portion joined to C-1 of the glycosyl ring, *i.e.*, the first exocyclic carbon atom of the *C*-glycosyl compounds.

TABLE I

Elemental analysis data

| *Compound* | *Attached group*[a] | *Composition (%)* | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | *C* | | *H* | | *N* | | *Cl,F* | |
| | | *Calc.* | *Found* | *Calc.* | *Found* | *Calc.* | *Found* | *Calc.* | *Found* |
| **3** | $-CONH_2$ | 40.58 | 40.62 | 6.28 | 6.45 | 6.76 | 6.69 | | |
| **6a** | $-CONHPh$ | 55.87 | 55.70 | 5.58 | 5.63 | 3.10 | 3.05 | | |
| **7a** | $-CONHPh$ | 51.77 | 51.84 | 6.36 | 6.58 | 4.64 | 4.91 | | |
| **11a** | $-CH_2NHPh$ | 57.98 | 58.09 | 7.11 | 7.16 | 5.20 | 5.12 | | |
| **7b** | $-CONH(p\text{-}NO_2Ph)$ | 47.56 | 48.31 | 4.88 | 5.15 | 8.24 | 7.74 | | |
| **6c** | $-CONHCH_2Ph$ | 56.77 | 56.77 | 5.85 | 5.89 | 3.00 | 2.93 | | |
| **7c** | $-CONHCH_2Ph$ | 56.56 | 56.55 | 6.44 | 6.55 | 4.71 | 4.62 | | |
| **11c** | $-CH_2NHCH_2Ph\cdot HCl\cdot H_2O$ | 49.77 | 50.25 | 7.17 | 7.89 | 4.15 | 4.12 | (Cl) 10.52 | 9.69 |
| **6d** | $-CONHCyh$ | 55.14 | 55.28 | 6.83 | 6.99 | 3.06 | 3.08 | | |
| **7d** | $-CONHCyh$ | 53.97 | 53.88 | 8.01 | 8.39 | 4.84 | 4.62 | | |
| **11d** | $-CH_2NHCyh\cdot HCl\cdot 0.5\ H_2O$ | 48.67 | 48.83 | 8.48 | 8.37 | 4.37 | 4.29 | (Cl) 11.05 | 10.53 |
| **6e** | $-CONHHxy$ | 54.89 | 54.88 | 7.24 | 7.36 | 3.05 | 2.89 | | |
| **7e** | $-CONHHxy\cdot 0.5\ H_2O$ | 52.00 | 52.09 | 8.74 | 9.49 | 4.67 | 4.77 | | |
| **6f** | $-COMor$ | 51.23 | 51.19 | 6.11 | 6.21 | 3.11 | 2.98 | | |
| **7f** | $-COMor\cdot C_3H_8O$ | 49.85 | 48.87 | 8.07 | 8.28 | 4.15 | 4.13 | | |
| **11f** | $-CH_2Mor\cdot 0.5\ H_2O$ | 48.53 | 48.31 | 8.15 | 8.71 | 5.15 | 5.11 | | |
| **11g** | $-CH_2NHCH_2CH_2OCH_3$ (syrup) | 47.81 | 45.75 | 8.37 | 8.36 | 5.58 | 4.84 | | |
| **11h** | $-CH_2NHCH_2CF_3$ | 39.27 | 39.28 | 5.82 | 6.16 | 5.09 | 5.03 | (F) 20.73 | 20.90 |
| **8** | $-COOCH_3$ | 43.24 | 43.05 | 6.35 | 6.51 | | | | |
| **9** | $-CONHNH_2$ | 37.81 | 37.78 | 6.30 | 6.46 | 12.60 | 12.32 | | |
| **14a** | $-CH_2NHCOCH_3$ | 45.92 | 46.05 | 7.23 | 7.93 | 5.95 | 5.32 | | |
| **14b** | $-CH_2NHCOPh$ | 56.55 | 56.27 | 6.73 | 6.44 | 4.71 | 4.58 | | |
| **15** | $-CN$ | 44.41 | 43.81 | 5.82 | 5.84 | 7.40 | 7.31 | | |
| **18** | $-CH_2CH=CH_2$ | 52.90 | 52.68 | 7.84 | 8.12 | | | | |
| **19** | $-CH_2CH_2CH_3$ | 52.39 | 51.85 | 8.73 | 9.04 | | | | |

[a]Cyh = cyclohexyl, Hxy = *n*-hexyl, Mor = morpholino

TABLE II

$^{13}$C-n.m.r. spectral data

| *Compound* | *Attached group*[a] | *Solvent* | *Chemical shift (p.p.m.)* | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | *C-1* | *C-2* | *C-3* | *C-4* | *C-5* | *C-6* | *C-1'* | *Remaining carbon atoms* |
| **3** | $-CONH_2$ | $D_2O$ | 79.3 | 69.6 | 74.4 | 69.6 | 79.5 | 62.1 | 175.2 | |
| **4** | $COO^-Na^+$ | $D_2O$ | 79.1 | 69.9 | 74.7 | 69.9 | 80.4 | 62.2 | 177.7 | |
| **7a** | CONHPh | $D_2O$ | 80.2 | 69.6 | 74.4 | 69.6 | 80.3 | 62.1 | 170.7 | 122.5, 126.8, 130.0, 136.9 |
| **11a** | $-CH_2NHPh$ | $D_2O$ | 78.8 | 69.9 | 74.8 | 70.0 | 79.4 | 62.5 | 46.5 | 115.9, 120.2, 130.4, 148.8 |
| **11a·HCl** | $-CH_2NHPh\cdot HCl$ | $D_2O$ | 74.4 | 69.7 | 74.5 | 69.8 | 79.5 | 62.5 | 53.8 | 123.5, 130.1, 131.2, 134.7 |
| **7b** | $-CONH(p\text{-}NO_2Ph)$ | $Me_2SO\text{-}d_6$ | 80.1 | 68.3 | 74.5 | 68.9 | 81.1 | 61.0 | 168.8 | 145.0, 119.3, 142.6, 125.1 |
| **7c** | $CONHCH_2Ph$ | $D_2O$ | 79.4 | 69.7 | 74.4 | 69.7 | 79.6 | 62.1 | 172.2 | 43.6, 128.1, 128.3, 129.5, 138.4 |
| **11c·HCl** | $CH_2NHCH_2Ph\cdot HCl$ | $D_2O$ | 75.5 | 69.6 | 74.4 | 69.8 | 79.5 | 62.5 | 49.2[b] | 52.1[b], 130.1, 130.6, 130.8, 131.3 |
| **7d** | –CONHCyh | $D_2O$ | 79.6 | 69.7 | 74.4 | 69.7 | 80.0 | 62.0 | 171.1 | 25.3, 25.7, 32.7, 49.7 |
| **11d·Hcl** | $-CH_2NHCyh\cdot HCl$ | $D_2O$ | 75.8 | 69.5 | 74.4 | 69.8 | 79.5 | 62.5 | 58.4 | 24.8, 25.3, 29.4, 29.8, 46.6 |
| **7e** | CONHHxy | $D_2O$ | 79.5 | 69.7 | 74.4 | 69.7 | 79.8 | 62.0 | 172.0 | 14.1, 22.7, 26.5, 29.0, 31.5, 40.1 |
| **11e** | $-CH_2NHHxy$ | $D_2O$ | 76.0 | 69.9 | 74.5 | 69.6 | 79.5 | 62.5 | 49.8[b] | 14.1, 22.6, 26.3, 26.5, 31.3, 48.9[b] |
| **7f** | –COMor | $D_2O$ | 75.8 | 69.2 | 74.4 | 69.7 | 79.9 | 61.9 | 169.4 | 24.6[c], 43.6, 47.3, 65.1[c], 67.1 |
| **11f** | $-CH_2Mor$ | $D_2O$ | 76.6 | 69.8 | 74.8 | 70.0 | 79.3 | 62.6 | 60.6 | 54.0, 66.8 |
| **11g** | $-CH_2NHCH_2CH_2OCH_3$ | $D_2O$ | 78.1 | 70.1 | 74.8 | 70.7 | 79.5 | 70.0 | 48.2[b] | 50.5[b], 59.0, 62.6 |
| **11h** | $CH_2NHCH_2CF_3$ | $D_2O$ | 78.3 | 61.6 | 73.9 | 69.1 | 78.5 | 50.0 | 48.3[b] | 48.9[b], 133.8, 128.2, 122.7, 117.2 (quartet for $-CF_3$). |
| **8** | $-COOCH_3$ | $D_2O$ | 79.3 | 69.2 | 74.3 | 69.5 | 79.8 | 61.9 | 172.3 | 53.8($CH_3$) |
| **9** | $CONHNH_2$ | $D_2O$ | 79.0 | 69.4 | 74.3 | 69.6 | 79.7 | 62.0 | 170.9 | |
| **10** | $-CH_2OH$ | $D_2O$ | 80.8 | 68.2 | 74.8 | 70.0 | 79.3 | 62.3 | 62.4 | |
| **12** | $-CH_2NH_2$ | $D_2O$ | 79.5 | 69.9 | 75.1 | 71.2 | 81.6 | 62.5 | 42.8 | |
| | $\alpha\text{-}CH_2NH_2$[d] | $D_2O$ | 77.1 | 69.7 | 70.6 | 68.7 | 72.9 | 61.9 | 35.2 | |
| **14a** | $CH_2NHCOCH_3$ | $D_2O$ | 78.8 | 69.2 | 74.6 | 70.0 | 79.5 | 62.4 | 41.4 | 22.5, 175.3 |
| **14b** | $-CH_2NHCOC_6H_5$ | $D_2O$ | 78.0 | 68.4 | 73.5 | 68.9 | 78.3 | 61.2 | 41.0 | 126.9, 128.4, 133.2, 131.8, 171.1 |
| **15** | CN | $D_2O$ | 67.3 | 69.3 | 73.7 | 69.6 | 80.0 | 61.0 | 117.9 | |
| **18** | $CH_2CH=CH_2$ | $D_2O$ | 71.4 | 68.0 | 69.4 | 68.7 | 74.7 | 60.7 | 28.5 | 134.6, 171.1 |

[a]Cyh = cyclohexyl, Hxy = *n*-hexyl, Mor = morpholino. [b] Assignments uncertain, may be switched. [c] Resonance of 2-propanol. [d] (α-D-galactopyranosylmethyl)-amine for comparison.

product with the appropriate amine. The anomeric configurations of these compounds were confirmed by interpretation of their $^1$H-n.m.r. spectra. They were then reduced with lithium aluminum hydride to give the corresponding *N*-substituted (β-D-galactopyranosylmethyl)amines (**11a–h**), or deacetylated with sodium methoxide in methanol to give unprotected *N*-substituted formamides (**7a–h**). Most of these products were obtained in relatively good yields (~60%), although low yields in the reduction of amides by lithium aluminium hydride have been reported[4]. Possible explanations for the low yields (10–28%) in three cases are the formation of side products and loss of amine on the cation-exchange column. Mass spectral data, obtained by chemical ionization, showed the expected molecular ions. Optical rotations and $^{13}$C-n.m.r. data also confirmed the structures. As may be seen in Table II, C-1 of the pyranosyl ring of the amines (**11a–h**) resonated over a wide range, the chemical shift depending on the charge on the nitrogen atom. For example, the C-1 chemical shifts of **11c**·HCl and **11d**·HCl were 75.5 and 75.8, respectively. However, **11a** ($pK_a$ 4.0) was unprotonated in $D_2O$ and its C-1 signal appeared at 78.8 p.p.m., in contrast to that for the hydrochloride salt at 74.4 p.p.m. The amino group of **11f** was partially protonated in $D_2O$; its C-1 signal was found at 76.6 p.p.m.

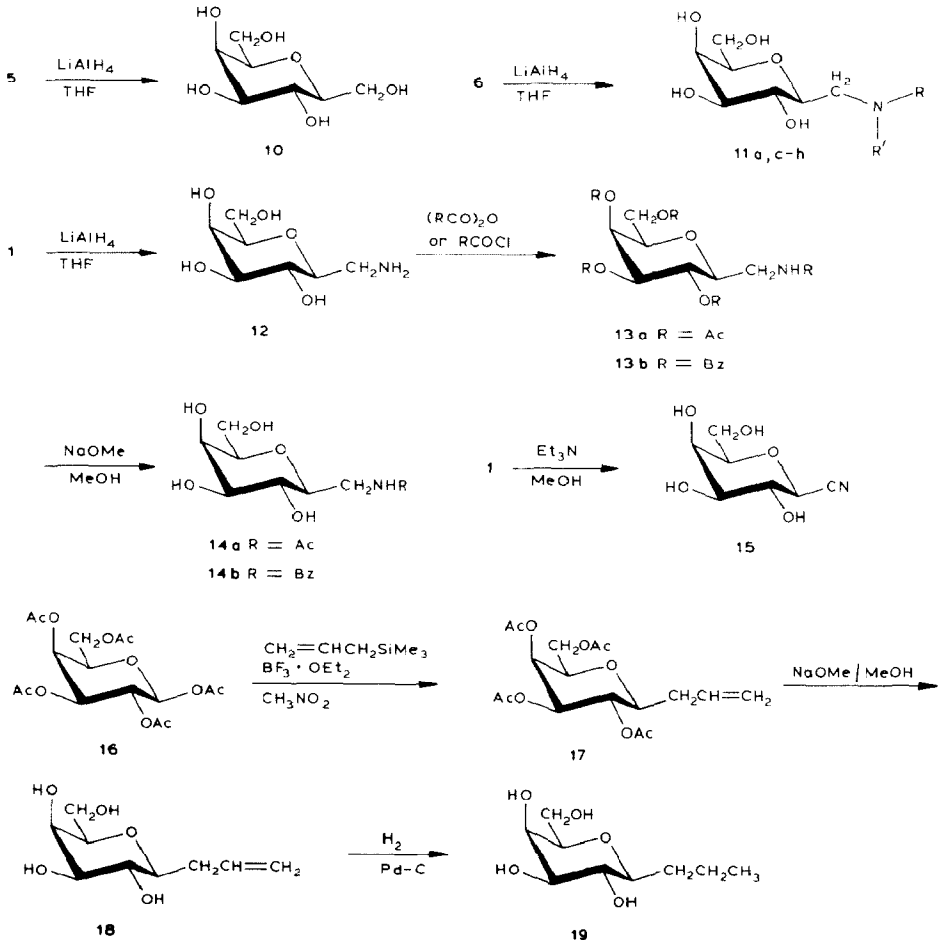
Compound **12** was prepared by concurrent reduction and deacetylation[5] of **1**. The compound was then acetylated to give the crystalline, fully acetylated (β-D-galactopyranosyl)methylamine **13a**, which was O-deacetylated, via transesterification, to **14a**. Likewise, perbenzoylation of **12** gave **13b**, which upon *O*-deacylation via transesterification produced **14b**. Compounds **14a** and **14b** are reversible inhibitors ($K_i$ = 3.3 and 3.8 mM, respectively) of *E. coli* lacZ β-galactosidase[3], which along with the physical data (Tables I–II) indicates preservation of the β-D configuration.

Compound **1** was deacetylated using triethylamine in dry methanol to give the unprotected β-D-galactopyranosyl cyanide (**15**), which was purified by silica-gel and Sephadex LH-20 column chromatography and then crystallized. The low yield (42%) was due to the formation of side products, presumably formed by nucleophilic addition to the carbon atom of the cyano group, which were removed by the purification steps. The structure of **15** was also confirmed by physical measurements and the fact that it has *E. coli* lacZ β-galactosidase-inhibitory activity ($K_i$ = 2.0 mM)[3].

Compound **5** on reduction with lithium aluminum hydride[13] gave **10**. This compound was previously prepared by the deamination of **12** with aqueous nitrous acid[5]. Physical data and the fact that it is a reversible inhibitor of *E. coli* lacZ β-galactosidase ($K_i$ = 10.6 mM)[3] confirmed the β-D configuration.

Esterification of **4** with dry methanol in the presence of a cation-exchange resin (acid form) gave crystalline **8**. Treatment of a solution of **8** in dry methanol with hydrazine monohydrate gave the readily crystallizable hydrazide **9**. The relatively high-field values of δ for C-1 (79.0 and 79.3 p.p.m.) confirms that these are *C*-aldohexopyranosyl compounds, whereas the relatively low-field values of δ for C-3 (74.3 p.p.m.) and C-5 (79.7 and 79.8 p.p.m.) provide strong evidence for assigning an equatorial orientation to the C-1 substituent, *i.e.*, the β-D configuration[6] (for comparison see refs. 7–9).

3-(Tetra-*O*-acetyl-β-D-galactopyranosyl)-1-propene (**17**) was prepared from **16** and allyltrimethylsilane in the presence of boron trifluoride etherate. Deacetylation produced **18**, which was catalytically reduced to 1-β-D-galactopyranosylpropane (**19**). Mass spectra, $^{13}C$-n.m.r., and specific optical rotations confirmed the expected structures.




## EXPERIMENTAL

*Materials.* — The following materials were obtained from the sources indicated and used without further treatment: Celite filter aid (Fisher Scientific Co.); molecular sieves type 4A (Davison Chemical); Amberlite IR-120 medium-porosity cation-exchange resin (Mallinckrodt); D-galactose (Sigma Chemical); dichloromethane (Burdick and Jackson Laboratories); mercuric cyanide (99.7%), lithium aluminum hydride, and

titanium tetrachloride (Aldrich Chemical Co.). All other reagents were further purified prior to use. Nitromethane (Aldrich Chemical Co.) was distilled from anhydrous $CaSO_4$ and stored over 4A molecular sieves; tetrahydrofuran (THF) (Fisher Scientific Co.) was dried with $LiAlH_4$, distilled, and stored over 4A molecular sieves. Ethyl chloroformate (Matheson, Coleman and Bell) was distilled and stored over anhydrous $CaCO_3$. Absolute methanol was prepared from commercial methanol by the method of Lund and Bjerrum[19]. The following amines were distilled and stored over sodium hydroxide pellets: aniline, benzylamine, *n*-hexylamine (Matheson Coleman and Bell); morpholine, 4-nitroaniline, 2-methoxyethylamine, 2,2,2-trifluorethylamine (Aldrich Chemical), cyclohexylamine (Eastman Kodak); and triethylamine (Pierce Chemical).

*General methods.* — Melting points were determined with a Thomas–Hoover Uni-melt apparatus and are uncorrected. Optical rotations were determined at 20° with a Perkin–Elmer 241 Polarimeter. N.m.r. spectra ($^1H$ and $^{13}C$) of $D_2O$ solutions were recorded with either a Nicolet NT-200 (200 MHz) FT-NMR or a Varian XL 400 (400 MHz) FT-NMR spectrometer. Tetramethylsilane (TMS) in deuteriochloroform and dioxane (66.5 p.p.m. from TMS) in deuterium oxide were used as internal references for the determination of chemical shifts ($\delta$) in $^1H$- and $^{13}C$-n.m.r., respectively. Mass spectra were obtained from either the Purdue University Campus-wide Mass Spectrometry Center or the Midwest Center for Mass Spectrometry, Department of Chemistry, University of Nebraska, (a National Science Foundation Regional Instrumentation Facility, Grant No. CHE 8211164). Microanalyses were obtained from either the Department of Chemistry, Purdue University or MicAnal, Tucson, AZ.

All evaporations were conducted under reduced pressure at $<40°$.

*Chromatography.* — Silica Gel 60 (230–400 mesh, E. Merck) was used for column chromatography. T.l.c. was conducted on Silica Gel 60-precoated aluminum sheets (E. Merck). Spots on t.l.c. plates were detected by spraying with 15% (v/v) sulfuric acid in 50% (v/v) aqueous ethanol and heating for several minutes at ~ 150°. Amines were also detected by spraying t.l.c. plates with a 1% (w/v) solution of ninhydrin in acetone. The following solvent systems were used for development (v/v): A, 1:1 toluene – diethyl ether; B, 1:1 toluene–acetone; C, 9:2:1 ethyl acetate–2-propanol–water; D, 9:4:2 ethyl acetate–2-propanol–water; E, 3:2:1 ethyl acetate–acetic acid–water; F, 3:2:1 ethyl acetate–pyridine–water; G, 8:2:1 ethyl acetate–acetic acid–water; H, 3:1 petroleum ether–diethyl ether; and I, 3:1 toluene–ethyl acetate.

*General procedure for the synthesis of per-O-acetylated* N-*substituted* C-β-D-*galactopyranosylformamides.* — To a stirred solution of **5** (1.88 g, 5.0 mmol) in dry dichloromethane (20 mL) cooled in an ice–salt bath was added triethylamine (0.70 mL, 5.0 mmol) and ethyl chloroformate (0.48 mL, 5.0 mmol). After 15 min, 5.0 mmol of the amine was added. When the reaction was complete, the reaction mixture was washed with aqueous 0.25M HCl (10 mL), water (10mL), saturated sodium hydrogencarbonate (4°, 10 mL), and water (10 mL) in that order. The solution was then dried with anhydrous $Na_2SO_4$, filtered, and evaporated.

*General procedure for the reduction of* N-*substituted amides to* N-*substituted methylamines.* — The compound to be reduced (a per-*O*-acetylated, *N*-substituted

*C*-β-D-galactopyranosylformamide) (12.0 mmol) was dissolved in dry THF (30 mL) and added dropwise, but rapidly, to a suspension of an excess of $LiAlH_4$ (0.86 g, 22.7 mmol), all operations being done under anhydrous conditions. An additional 10 mL of dry THF was used to wash the last traces of reactant into the reaction mixture, which was then heated to a gentle boil under reflux. Periodically, the reaction mixture was checked for the presence/absence of starting material by t.l.c. (solvent E). When the reaction was complete (~5 h), absolute ethanol was added cautiously until the excess of $LiAlH_4$ was decomposed (no additional evolution of $H_2$ upon further addition of ethanol). Additions were then made of water (40 mL), conc. ammonium hydroxide (60 mL), and Celite (previously washed with water, 5M ammonium hydroxide, and absolute ethanol). After being stirred, the mixture was filtered through a thin layer of Celite (washed as described). Both the flask and the residue on the filter were washed extensively with 5M ammonium hydroxide. The combined filtrate and washings were reduced in volume and passed through a column of Amberlite IR-120 ($H^+$ form, medium porosity) cation-exchange resin; the column was washed extensively with water. Then, resin-bound products were eluted with M $NH_4OH$. Finally, the eluate was evaporated to dryness. The residue was dissolved in methanol (3 × 100 mL), and the solution was filtered and concentrated to a syrup. The syrup was dissolved in a small volume of aqueous 0.1M ammonium hydroxide and applied to a column of Sephadex G-25 (200 × 2 cm), which was eluted with aqueous 0.1M ammonium hydroxide.

*General procedure for* O-*deacetylation.* — Anhydrous methanol was added to the compound to be deacetylated. A catalytic amount of 4.0M methanolic sodium methoxide was then added, and the solution or suspension was stirred. If the product crystallized or precipitated, it was collected by filtration; if not, the reaction was monitored by t.l.c. (solvent A). In the latter case, when deacetylation was complete, the reaction mixture was stirred with Amberlite IR-120 ($H^+$) medium-porosity cation-exchange resin for 0.5 h and filtered, and the filtrate was evaporated to a syrup.

C-*(2,3,4,6-Tetra*-O-*acetyl-β-*D-*galactopyranosyl)formamide* (**2**). — To a stirred suspension of **1** (3.57 g, 10.0 mmol) in glacial acetic acid (10 mL), cooled in an ice bath, were added titanium tetrachloride (2.18 mL, 2.0 mmol) (suspension turns yellow) and water (0.18 mL, 10.0 mmol). After 30 min the ice bath was removed, and the mixture was stirred for 5 h at room temperature. The solution was then poured into stirred ice and water (50 mL) and **2** was obtained by extraction with chloroform (3 × 50 mL). The combined chloroform extracts were washed with cold, saturated, aqueous sodium hydrogencarbonate (n × 50 mL, until the aqueous layer was basic to litmus paper) and water (50 mL). The chloroform layer was dried with anhydrous $Na_2SO_4$ and filtered. The filtrate was evaporated, and **2** was crystallized by dissolution in chloroform (5 mL) and the addition of diethyl ether (20 mL). This gave 3.0 g (8.0 mmol, 80%) of material melting partially at 113–115° and fully at 146–148°; the lit.[2] mentions melting partially at 112–114° and fully at 146–147°.

C-*β-*D-*Galactopyranosylformamide* (**3**). — A stirred suspension of **2** (0.94 g, 2.5 mmol) in dry methanol (10 mL) was deacetylated by the general procedure (25 μL of NaOMe–MeOH). First, the reaction mixture became homogeneous; then, after 30 min,

**3** crystallized. The mixture was stirred for an additional 2 h, then cooled to 4°. The crystals collected by filtration and washed with cold methanol weighed 0.39 g (1.88 mmol, 75%); m.p. 194–196°. Recrystallization from 100% ethanol gave pure **3** (0.34 g, 1.64 mmol, 87% recovery), m.p. 196–197°, $[\alpha]_D^{20}$ +67.8° (*c* 1.15, $H_2O$), $R_F$ 0.15 (solvent D).

*(β-D-Galactopyranosylmethyl)amine* (**12**). — Compound **1** (14.3 g, 40 mmol) in dry THF (150 mL) was reduced by the general procedure, using 5.7 g (150 mmol) of $LiAlH_4$ in dry THF (250 mL), a reaction time of 5 h, and an addition of 240 mL of conc. ammonium hydroxide before filtration. The residual pale yellow syrup crystallized after several cycles of dissolution in absolute ethanol and evaporation. The solid was extracted with five 200-mL portions of boiling absolute ethanol, and the hot extracts were filtered through Celite. On concentration and cooling to −5°, **12** crystallized. The yield was 5.00 g (25.9 mmol, 65%), m.p. 189–191°. A second crop (0.4 g, 2.2 mmol, 5.4%; m.p. 191–192°) was obtained by evaporating the mother liquor and crystallizing the residue from ethanol. Recrystallization of the first crop from methanol gave pure **12**, yield 4.5 g (23.3 mmol, 90% recovery); homogeneous by t.l.c. (solvent E); m.p. 191–192°; $[\alpha]_D^{20}$ +32.8° (*c* 0.98, water); lit.[5] m.p. 191–192°, $[\alpha]_D$ +30.0° (*c* 1.61, water).

C-*(2,3,4,6-Tetra*-O-*acetyl-β-D-galactopyranosyl)formic acid* (**5**). — The title compound was prepared by a modification of the method of Myers and Lee[2]. To a stirred solution of *p*-toluenesulfonic acid monohydrate (21.2 g, 112 mmol) in acetic anhydride (96 mL, 1.01 mol) cooled in an ice bath, sodium *C*-β-D-galactopyranosylformate[2] (**4**) (25.2 g, 101 mmol) was added portionwise over a period of 1 h. The ice bath was removed, and the mixture was stirred for 24 h at room temperature. The reaction mixture was then poured slowly into vigorously stirred cold (0°) water (500 mL), whereupon **5** crystallized immediately. After being dried *in vacuo* in a desiccator the crystals weighed 24.4 g (64.9 mmol, 64%), m.p. 134–137°. The mother liquor was saturated with NaCl (~4M), and extracted with chloroform (6 × 100 mL). The combined chloroform extracts were dried with anhydrous $Na_2SO_4$, filtered, and concentrated to a small volume. Acetic acid, present in the solution, was removed by azeotropic distillation with toluene under diminished pressure. The residual crystalline **5** was dissolved in chloroform, the solution was filtered, and the filtrate was concentrated to a syrup which on the addition of toluene (100 mL) gave a second crop of crystals (12.5 g, 33.2 mmol, 33%), m.p. 132–136°. The total yield was 36.9 g (97%).

The first crop of **5** was dehydrated by azeotropic distillation with acetone (50 mL) and toluene (50 mL). This treatment was followed by dissolution in 1:1 v/v chloroform–toluene and evaporation (3 ×). Finally, the compound was recrystallized by dissolution in chloroform, evaporation of the solution, and addition of toluene (100 mL) to give 23.0 g (61.1 mmol, 94% recovery) of pure material, m.p. 139–141°, lit.[2] m.p. 137–139°. The second crop was recrystallized by dissolution in chloroform, evaporation of the solution, and addition of diethyl ether (4 mL.mmol$^{-1}$) to yield an additional 12.0 g (31.9 mmol, 96% recovery) of **5**, m.p. 136–137°.

N-*Phenyl*-C-*(2,3,4,6-tetra*-O-*acetyl-β-D-galactopyranosyl)formamide* (**6a**). — Crude **6a** (see general procedure) was crystallized by the addition of diethyl ether (20

mL) to yield 1.86 g (4.11 mmol, 82%), m.p. 151–153°; homogeneous by t.l.c. (solvent A, $R_F$ 0.38). This on recrystallization by dissolution in methylene chloride, evaporation of the solution, and addition of diethyl ether (2 mL.mmol$^{-1}$) gave material (96% recovery) melting at 151.5–153°. A twice recrystallized sample, used for analysis, had m.p. 152–153°; $[\alpha]_D^{20}$ +43.9° (*c* 1.35, $CH_2Cl_2$).

C-*β*-D-*Galactopyranosyl*-N-*phenylformamide* (**7a**). — A stirred suspension of **6a** (0.45 g, 1.0 mmol) in dry methanol (5.0 mL) was deacetylated by the general procedure (10 *μ*L of NaOMe–MeOH). The reaction mixture became homogeneous and **7a** crystallized quickly (~5 min). The mixture was stirred for 30 min, then cooled to 4°, and crystals of **7a** were collected by filtration and washed with cold methanol. The yield was 0.19 g (0.63 mmol, 63%), homogeneous by t.l.c. (solvent C, $R_F$ 0.39); when heated slowly, it melted gradually at 110°. Recrystallization from 100% ethanol gave an analytical sample (recovery 79%) melting at 110°; $[\alpha]_D^{20}$ +2.5° (*c* 0.40, water); m.s.: *m/z* 329 (M + 1) and 346 (M + 18).

N-*(β-D-Galactopyranosylmethyl)aniline* (**11a**). — Compound **11a** crystallized on standing; yield 2.24 g (8.33 mmol, 69%). Recrystallization from ethyl acetate gave 1.94 g (7.2 mmol, 60% of pure **11a**, homogeneous by t.l.c. (solvent E, $R_F$ 0.60); m.p. 152–153.5°, $[\alpha]_D^{20}$ −5.0° (*c* 1.32, water). An additional 0.14 g (4.3%), having m.p. 151–153°, was recovered from the mother liquor.

C-*β*-D-*Galactopyranosyl*-N-*(4-nitrophenyl)formamide* (**7b**). — The general procedure for the synthesis of per-*O*-acetylated *N*-substituted *C*-*β*-D-galactopyranosylformamides was followed with the exception that, after 3.5 h, a second portion of *p*-nitroaniline (0.069 g, 0.5 mmol) was added to the reaction mixture. After 5 h (total), no starting material remained (t.l.c., solvent B), and the reaction mixture was worked up. Crystallization of the syrup from 2-propanol (25 mL) gave *C*-(2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranosyl)-*N*-(4-nitrophenyl)formamide (**6b**), yield 2.0 g (4.1 mmol, 81.1%); m.p. 150–152°.

A stirred suspension of **6b** (2.0 g, 4.0 mmol) in dry methanol (16 mL) was deacetylated by the general procedure (40.3 *μ*L of NaOMe–MeOH). The reaction mixture became homogeneous quickly (5 min), and the product crystallized in 1.5 h. The suspension was stirred for another 1 h, then cooled to 4°. Crystals were collected by filtration and washed with cold methanol, yield 1.1 g (3.7 mmol, 92%); m.p. 206–208°. Recrystallization of 0.50 g (1.5 mmol) from dry methanol gave 0.33 g (1.0 mmol, 67% recovery) of pure crystals, m.p. 208°; $[\alpha]_D^{20}$ +60.9° (*c* 0.70, 2:1 v/v $H_2O$–EtOH); $R_F$ 0.68 (solvent D).

N-*Benzyl*-C-*(2,3,4,6-tetra*-O-*acetyl-β*-D-*galactopyranosyl)formamide* (**6c**). — Compound **6c** (see general procedure) crystallized upon addition of 3:1 v/v diethyl ether–petroleum ether (20 mL). The yield was 1.89 g (4.06 mmol, 81%), m.p. 116.5–118.5°; t.l.c. with solvent A ($R_F$ 0.27) revealed the presence of a contaminant ($R_F$ 0.44). Recrystallization by dissolution in methylene chloride, evaporation of the solution, and addition of 3:1 v/v diethyl ether–petroleum ether (2 mL.mmol$^{-1}$ gave **6c** (recovery 96%) melting at 117–118.5°; homogeneous by t.l.c. (solvent A). A twice recrystallized sample used for analysis had m.p. 117.5–118.5°; $[\alpha]_D^{20}$ +6.15° (*c* 1.16, $CH_2Cl_2$).

N-*Benzyl*-C-β-D-*galactopyranosylformamide* (**7c**). — A stirred suspension of **6c** (0.46 g, 1.0 mmol) in dry methanol (5.0 mL) was deacetylated by the general procedure (10 μL of NaOMe–MeOH). The reaction mixture became homogeneous quickly, and **7c** crystallized (~5 min). The suspension was stirred for 30 min, then cooled to 4°, and crystals of **7c** were collected by filtration and washed with cold methanol. The yield was 0.28 g (0.952 mmol, 95%), m.p. 226.5–227.2°; homogeneous by t.l.c. (solvent C, $R_F$ 0.35). Recrystallization from 100% ethanol gave an analytical sample having m.p. 226.5–227.5°; $[\alpha]_D^{20}$ +42° (*c* 0.28, water).

N-*Benzyl*-(β-D-*galactopyranosylmethyl*)*amine* (**11c**) *hydrochloride*. — Compound **11c** (syrup, 1.0 g), from **6c** by the general procedure for reduction, was dissolved in aqueous 0.25M HCl, and the solvent was evaporated off. Excess HCl was removed by evacuation, and the product was crystallized by dissolution in 100% ethanol (10 mL) and addition of diethyl ether (20 mL). The yield of **11c**·HCl was 0.96 g (3.0 mmol, 50%), homogeneous by t.l.c. (solvent E, $R_F$ 0.40); m.p.: decomp. at 80°; $[\alpha]_D^{20}$ +8.7° (*c* 1.43, $H_2O$).

N-*Cyclohexyl*-C-(*2,3,4,6,-tetra*-O-*acetyl*-β-D-*galactopyranosyl*)*formamide* (**6d**). — Compound **6d** (see general procedure) was dissolved in dichloromethane (5 mL) and crystallized by the addition of diethyl ether (15 mL) and petroleum ether (25 mL). The yield was 1.55 g (3.39 mmol, 68%), m.p. 139.5–141°; homogeneous by t.l.c. (solvent A, $R_F$ 0.30). A twice recrystallized sample, used for analysis, had m.p. 140–141°; $[\alpha]_D^{20}$ +19° (*c* 1.66, $CH_2Cl_2$).

N-*Cyclohexyl*-C-β-D-*galactopyranosylformamide* (**7d**). — A stirred suspension of **6d** (0.46 g, 1.0 mmol) in dry methanol (5.0 mL) was deacetylated by the general procedure (10 μL of NaOMe–MeOH). The reaction mixture became homogeneous quickly, and **7d** crystallized (~5 min). The mixture was stirred for 30 min, then cooled to 4°. Crystals were collected by filtration, washed with cold methanol, and dried to yield 0.27 g (0.93 mmol, 93%); m.p. 228–229.5°; homogeneous by t.l.c. (solvent C, $R_F$ 0.34). Recrystallization from 100% ethanol gave an analytical sample (recovery 93%) having m.p. 228.5–229.5°; $[\alpha]_D^{20}$ +45° (*c* 0.48, water).

N-*Cyclohexyl*-(β-D-*galactopyranosylmethyl*)*amine* (**11d**) *hydrochloride*. — Compound **11d** (syrup, 0.23 g), from **6d** by the general procedure for reduction, was dissolved in aqueous 0.25M HCl (4.0 mL), and the solvent was evaporated off. Excess HCl was removed by evacuation, and the product was crystallized by dissolution in 2-propanol (2.0 mL) and addition of diethyl ether (6.0 mL). The yield of **11d**·HCl was 0.42 g (1.34 mmol, 11%); homogeneous by t.l.c. (solvent E, $R_F$ 0.42); m.p. 143–145°; $[\alpha]_D^{20}$ +14° (*c* 1.00, water).

N-*Hexyl*-C-(*2,3,4,6-tetra*-O-*acetyl*-β-D-*galactopyranosyl*)*formamide* (**6e**). — Compound **6e** (see general procedure) crystallized upon addition of 1:1 v/v diethyl ether–petroleum ether (20 mL). The yield was 1.78 g (3.88 mmol, 77%), m.p. 99.5–101°; homogeneous by t.l.c. (solvent A, $R_F$ 0.33). When this material was recrystallized by dissolution in dichloromethane, evaporation of the solution, and addition of 1:1 v/v diethyl ether–petroleum ether (2 mL.mmol$^{-1}$). The recovery was 92%, m.p. 100–101°. Twice recrystallized product, used for analysis, had m.p. 100–101°; $[\alpha]_D^{20}$ +28° (*c* 1.13, $CH_2Cl_2$).

C-*β*-D-*Galactopyranosyl*-N-*hexylformamide* (**7e**). — A stirred suspension of **6e** (0.46 g, 1.0 mmol) in dry methanol (5.0 mL) was deacetylated by the general procedure (10 μL of NaOMe–MeOH). The syrupy product, dissolved in boiling 2-propanol (3 mL) and allowed to crystallize, yielded 0.28 g (0.96 mmol, 96%) of **7e**, m.p. 136–137°; homogeneous by t.l.c. (solvent C, $R_F$ 0.52). The twice recrystallized compound, used for analysis, had m.p. 136–137°; $[\alpha]_D^{20}$ +45° (*c* 1.00, water).

N-*Hexyl-(β-*D-*galactopyranosylmethyl)amine* (**11e**). — The syrup obtained by reduction of **6d** did not crystallize, but was homogeneous by t.l.c. (solvent E, $R_F$ 0.53). The yield was 2.0 g (7.2 mmol, 60%), $[\alpha]_D^{20}$ +14° (*c* 1.46, water).

N,N-*(Oxydiethylene)*-C-*(2,3,4,6-tetra-*O*-acetyl-β-*D-*galactopyranosyl)formamide* (**6f**). — Compound **6f** (see general procedure) crystallized upon dissolution in chloroform (5 mL) and addition of diethyl ether (20 mL). The yield was 1.7 g (3.8 mmol, 76%), m.p. 124.8–126.5°; homogeneous by t.l.c. (solvent A, $R_F$ 0.52). When this material was recrystallized by dissolution in chloroform (0.5 mL.mmol$^{-1}$) and addition of diethyl ether (4 mL.mmol$^{-1}$) the recovery was 96%, m.p. 125.5–126.5°. Twice recrystallized **6f**, used for analysis, had m.p. 125.5–126.5°; $[\alpha]_D$ +24° (*c* 0.8, $CH_2Cl_2$).

C-*β*-D-*Galactopyranosyl*-N,N-*(oxydiethylene)formamide* (**7f**). — A stirred suspension of twice recrystallized **6f** (3.56 g, 8.0 mmol) in dry methanol (50 mL) was deacetylated by the general procedure (50 μL of NaOMe–MeOH). When the syrupy product was dissolved in 2-propanol (16 mL) and cooled to −20° crystals of **7f**·2-propanol (mol ratio 1:1) were deposited. These were collected by filtration at 4° and stored in a desiccator at −20°. The yield of product homogeneous by t.l.c. (solvent C, $R_f$ 0.14) was 2.24 g (6.6 mmol, 83%). When slowly heated, **7f** melted at 45–54°; $[\alpha]_D^{20}$ +26° (*c* 1.22, water).

N-*(β-*D-*Galactopyranosylmethyl)morpholine* (**11f**). — The syrup (3.25 g), obtained by reduction of **6f**, crystallized on standing; m.p. 94–99°. After recrystallization from ethyl acetate the yield of **11f** was 2.59 g (82%), m.p. 96.5–99°; homogeneous by t.l.c. (solvent E, $R_F$ 0.23). The twice recrystallized compound, used for analysis, had m.p. 97.5–99°; $[\alpha]_D^{20}$ −1.21° (*c* 1.175, water).

N-*(2-Methoxyethyl)(β-*D-*galactopyranosylmethyl)amine* (**11g**). — Compound **5** was converted into *N*-(2-methoxyethyl)-*C*-(2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranosyl)formamide (**6g**). After 1.5 h, no starting material remained (t.l.c., solvent B). The syrupy product did not crystallize.

Intermediate **6g** (2.1 g, 4.8 mmol) in dry THF (70 mL) was reduced by the general procedure, using 1.5 g (40 mmol) of $LiAlH_4$ in dry THF (20 mL), a reaction time of 14 h, and addition of 50 mL of conc. ammonium hydroxide before filtration. The resulting residue was dissolved in methanol (4 × 50 mL), and the solution was filtered. The combined filtrate and washings were concentrated to a syrup. The syrup, which did not crystallize, was dissolved in water and lyophilized to give 0.14 g (5.6 mmol, 11%) of **11g** as a dry powder, m.p. 45–50°; $[\alpha]_D^{20}$ +14.4° (*c* 1.46, $H_2O$); $R_F$ 0.16 (solvent E); m.s.: *m/z* 252 (M + 1).

N-*(2,2,2-Trifluoroethyl)(β-*D-*galactopyranosylmethyl)amine* (**11h**). — To a stirred solution of **5** (1.88 g, 5.0 mmol) in dry dichloromethane (20 mL), cooled in an

ice–salt bath, was added triethylamine (0.70 mL, 5.0 mmol) and ethyl chloroformate (0.48 mL, 5.0 mmol). After 15 min, a solution of 2,2,2-trifluoroethylamine hydrochloride (0.74 g, 6.8 mmol) and triethylamine (0.70 mL, 5.0 mmol) was added. At 4 h a check by t.l.c. (solvent G) showed the absence of starting material. After 5 h, the reaction mixture was worked up as described in the general procedure. The resulting syrupy *C*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-*N*-(2,2,2-trifluoroethyl)formamide (**6h**) (2.2 g, 4.8 mmol) in dry THF (70 mL) was reduced by the general procedure, using 1.5 g (40 mmol) of $LiAlH_4$ in dry THF (20 mL), a reaction time of 7 h, and addition of 50 mL of conc. ammonium hydroxide before filtration. The residue after evaporation was extracted with methanol (4 × 50 mL), and the solution was filtered. The insoluble material was washed with methanol, and the combined filtrate and washings were concentrated to a syrup. The syrup, which did not crystallize, was dissolved in water and lyophilized to give 0.39 g (1.4 mmol, 28%) of **11h** as a dry powder, yield m.p. 125–126°; $[\alpha]_D^{20}$ +13.8° (*c* 1.45, $H_2O$); $R_F$ 0.33 (solvent E); m.s.: *m/z* 276 (M + 1) and 293 (M + 18).

N-*Acetyl-(β-D-galactopyranosylmethyl)amine* (**14a**). — To prechilled (0°, ice bath) and stirred pyridine (12.0 mL), **12** (1.93 g, 10.0 mmol) and acetic anhydride (12.0 mL, 127.2 mmol) were added sequentially. After 0.5 h, the ice bath was removed, and the mixture was stirred for 24 h at room temperature. The solution was checked for absence of starting material by t.l.c. (solvent B), then chilled to ~4° in an ice bath; water (10 mL) was added, and stirring was continued for 1 h at room temperature. The reaction mixture was concentrated to a syrup, which was dehydrated by azeotropic distillation with toluene (4 × 50 mL). The white, solid residue was dissolved in chloroform (10 mL) and an equal volume of diethyl ether (10 mL) was added to the solution, which was then filtered. The filtrate was evaporated to a syrup which on crystallization by dissolution in hot absolute ethanol (3 mL) and adding diethyl ether (20 mL) furnished 3.2 g (7.8 mmol, 78%) of *N*-acetyl-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosylmethyl)amine (**13a**), m.p. 154–155°. A second crop of crystals showing m.p. 154–155° was obtained from the mother liquor by repeating the crystallization procedure. The total yield of **13a** was 3.4 g (83%).

Methanolic sodium methoxide (37.5 μL, 0.15 mmol) was added to a stirred suspension of **13a** (3.03 g, 7.50 mmol) in dry methanol (30 mL). Stirring was continued at r.t. for 16 h, at which time no starting material remained. The reaction mixture was worked up in the usual way giving syrupy **14a**. An ethyl acetate solution deposited hygroscopic crystals that were collected and dried *in vacuo* in a desiccator, first at 4° then at room temperature, to furnish 1.6 g (6.8 mmol, 91%), m.p. 88° (foaming at 80°). Recrystallization from ethyl acetate gave 1.35 g (5.74 mmol, 84.4% recovery) of pure compound, m.p. 90° (foaming at 81°); $[\alpha]_D^{20}$ +29° (*c* 1.92, $H_2O$); $R_F$ 0.36 (solvent E).

N-*Benzoyl-(β-D-galactopyranosylmethyl)amine* (**14b**). — To a prechilled (0°, ice bath) and stirred solution of pyridine (7.58 mL, 93.8 mmol) and dry chloroform (20 mL) were added sequentially **12** (1.93 g, 10.0 mmol) and benzoyl chloride (7.25 mL, 62.5 mmol). The reaction mixture was stirred for 1 h at 0°, kept in an ice bath for 1 h, and stirred again, first overnight at 4°, then 5 h at room temperature. Water (15 mL) was added to the reaction mixture to destroy the excess benzoyl chloride and the solution

was checked for absence of starting material by t.l.c. (solvent B). The product was extracted with chloroform (150 mL) from a cold (4°) solution. The chloroform extract was washed with cold 2M sulfuric acid (2 × 50 mL), cold water (50 mL), cold, saturated aqueous sodium hydrogencarbonate (2 × 50 mL), and again with cold water (50 mL). The chloroform layer was dried with anhydrous $Na_2SO_4$, filtered, and evaporated to a syrup, which was triturated with diethyl ether (3 × 50 mL), leaving 4.76 g (6.67 mmol, 66.7%) of *N*-benzoyl-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosylmethyl)amine (**13b**), which did not crystallize.

To a stirred suspension of **13b** (4.76 g; 6.67 mmol) in dry methanol (27 mL) was added methanolic sodium methoxide (267 μL, 1.07 mmol). Stirring was continued for 66 h at room temperature, at which time no starting material remained. The reaction mixture was worked up in the usual way. The syrupy **14b** crystallized from dry methanol (20 mL), yielding 0.98 g (3.3 mmol, 50%), m.p. 170–172°. A second crop of crystals, m.p. 169–171°, was obtained by evaporating the mother liquor and crystallizing the residue from methanol. The total yield was 1.58 g (5.3 mmol, 80%). Recrystallization of 0.8 g from 2-propanol (15 mL) gave an analytical sample weighing 0.70 g (2.4 mmol, 89% recovery), m.p. 172–173°; $[\alpha]_D^{20}$ +1.12° (*c* 11.7, $H_2O$); $R_F$ 0.44 (solvent D).

*β-D-Galactopyranosyl cyanide* (**15**). — Triethylamine (3.4 mL; 25 mmol) was added to a stirred suspension of **1** (1.79 g, 5.0 mmol) in dry methanol (20 mL). Stirring was continued for 6 h at room temperature, at which time no starting material remained (t.l.c., solvent D). Following evaporation, the resulting syrupy product (0.90 g) was purified by chromatography on a silica gel column (60 g, 3 cm dia.), using solvent D. The compound was further purified on a 2.0 x 190-cm column of Sephadex LH-20 equilibrated and eluted with 95% ethanol. Concentration of the eluate gave nearly pure **15**, which crystallized upon dissolution in 2-propanol (20 mL), evaporation of the resulting solution to about 10 mL, and holding at –5° for 24 h. The weight of crystals was 0.25 g (1.32 mmol, 26%), m.p. 114–116°. Evaporation of the mother liquor and crystallization of the residue (2-propanol, 4 mL) gave a second crop, m.p. 114–116°, making the total yield 0.40 g (42%). Recrystallization of **15** (0.25 g, 1.3 mmol) from 2-propanol (3 mL) gave an analytical sample weighing 0.19 g (1.0 mmol, 77% recovery), m.p. 115–116°; $[\alpha]_D^{20}$ +68.2° (*c* 0.88, $H_2O$); $R_F$ 0.59 (solvent D).

*2,6-Anhydro-*D-glycero-L-manno-*heptitol (β-D-galactopyranosylmethanol)* (**10**). — Compound **5** (3.76 g, 10 mmol) in dry THF (90 mL) was reduced according to the general procedure, using 3.13 g (82 mmol) of $LiAlH_4$ in dry THF (40 mL), a reaction time of 12 h, and careful addition of 60 mL of conc. ammonium hydroxide before filtration. The residual syrup was dissolved in 100% ethanol (3 × 100 mL), and the solution was filtered and reconcentrated to a syrup. A solution of this syrup in 100% ethanol (30 mL) held at –5° for 24 h gave crystalline **10** weighing 1.31 g (5.0 mmol, 50%), m.p. 119–121°; lit.[1] m.p. 118–120°. To remove colored impurities a solution of the crystals in hot 95% ethanol was treated with activated charcoal (35 mg) for about 10 min, then filtered, and the filtrate was evaporated to a syrup. Crystallization from 95% ethanol (10 mL) gave pure **10** in a yield of 1.07 g (4.1 mmol, 82% recovery), m.p. 121–122°; $[\alpha]_D^{20}$ +29.0° (*c*1.92, $H_2O$); lit[1] m.p. 121–122°, $[\alpha]_D^{25}$ +32.6° (*c* 1.32, $H_2O$).

*Methyl 2,6-anhydro*-D-glycero-L-manno-*heptonate* (**8**). — To a stirred solution of **4** (4.96 g; 20.0 mmol) in dry methanol (200 mL) was added Amberlite IR-120 ($H^+$) cation-exchange resin (16 g, 74 mequiv.), and stirring was continued for 19 h. At this time no starting material remained (t.l.c.; solvent D). The resin was then removed by filtration and washed five times with 20-mL portions of methanol. The filtrate and washings were evaporated to a syrup, which was dissolved in hot ethyl acetate (500 mL). Crystals of **8**, obtained by holding the solution at −5°, were collected by filtration and dried (vacuum pump) in a cold room at 4°, giving a first crop of 2.7 g (12 mmol, 61%), m.p. 118–120°. A second crop, m.p. 117–119°, was obtained from the mother liquor, bringing the total yield to 3.2 g (72%). Recrystallization of 1.5 g from ethyl acetate (500 mL) gave an analytical sample weighing 1.30 g (5.9 mmol 87% recovery), m.p. 121–123°; $[\alpha]_D^{20}$ −32° (*c* 0.12, $H_2O$); $R_F$ 0.39 (solvent D).

*2,6-Anhydro*-D-glycero-D-manno-*heptonohydrazide* (**9**). — To a stirred solution of **8** (1.20 g, 5.0 mmol) in dry methanol (50 mL) at room temperature hydrazine monohydrate (2.4 mL, 50 mmol) was added slowly. The product began to crystallize from the solution after 3 min, but stirring was continued for 3 h. Then, the solution was held at 4° for 24 h, and crystalline **10** was collected in a yield of 1.19 g (5.0 mmol, 99%), m.p. 217–218°. Recrystallization of 0.50 g from hot water (2 mL) and 2-propanol (15 mL) gave an analytical sample weighing 0.48 g (2.0 mmol, 96% recovery), m.p. 218–219°; $[\alpha]_D^{20}$ +57.1° (*c* 1.02, $H_2O$); $R_F$ 0.35 (solvent F).

*3-(2,3,4,6-Tetra*-O-*acetyl-β-D-galactopyranosyl)-1-propene* (**17**). — Boron trifluoride etherate (3.66 mL, 30.0 mmol) was added to a stirred solution of β-D-galactopyranose pentaacetate[10,11] (**16**; 3.9 g, 10.0 mmol) and allyltrimethylsilane (2.28 g, 20 mmol) in dry nitromethane (40 mL). The reaction mixture was stirred at room temperature for 27 h, at which time no starting material remained (t.l.c., solvent H). After evaporation of the solvent, the product was extracted from the residual syrup with chloroform (100 mL). The chloroform solution was washed with cold water (3 × 25 mL), cold saturated sodium hydrogencarbonate (50 mL), and cold water (50 mL), in that order. The chloroform extract was then dried with anhydrous sodium sulfate, filtered, and evaporated to a syrup. This was purified by chromatography on a Silica Gel 60 column (190 g, 3-cm dia.), using solvent H. The syrupy **17** obtained by evaporation of the eluate, which did not crystallize, weighed 2.13 g (5.46 mmol, 55%).

*3-β-D-Galactopyranosyl-1-propene* (**18**). — To a stirred suspension of **17** (2.13 g, 5.46 mmol) in dry methanol (20 mL) at r.t. was added NaOMe–MeOH (50 μL, 0.2 mmol), and stirring was continued. After 4 h, when no starting material remained (t.l.c., solvents D and I), the reaction mixture was worked up in the usual way. The resulting syrup was dissolved in boiling ethyl acetate (75 mL). After filtration and cooling of the resulting solution, **18** crystallized in a yield of 0.93 g (4.6 mmol, 83%), m.p. 118–122°. Two recrystallizations from ethyl acetate (60 mL each time) gave an analytical sample weighing 0.77 g (3.8 mmol, 83% recovery), m.p. 120–122°; $[\alpha]_D^{20}$ +1.9° (*c* 1.08, $H_2O$); $R_F$ 0.49 (solvent D); m.s.: *m/z* 205 (M + 1) and 222 (M + 18).

*1-β-D-Galactopyranosylpropane* (**19**). — Compound **18** (0.24 g, 1.2 mmol) was dissolved in 95% ethanol and hydrogenated over Pd–C. Following filtration and

evaporation, **19** crystallized from ethyl acetate. The yield was 0.16 g (0.78 mmol, 66%), m.p. 120–122°; $[\alpha]_D^{20}$ +1.3° (*c* 0.8, $H_2O$); $R_F$ 0.49 (solvent D); m.s.: *m/z* 207 (M + 1) and 224 (M + 18).

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