Convenient Synthesis of Nucleosides of 2-Deoxy-2-nitro-D-galactose and *N*-Acetyl-D-galactosamine

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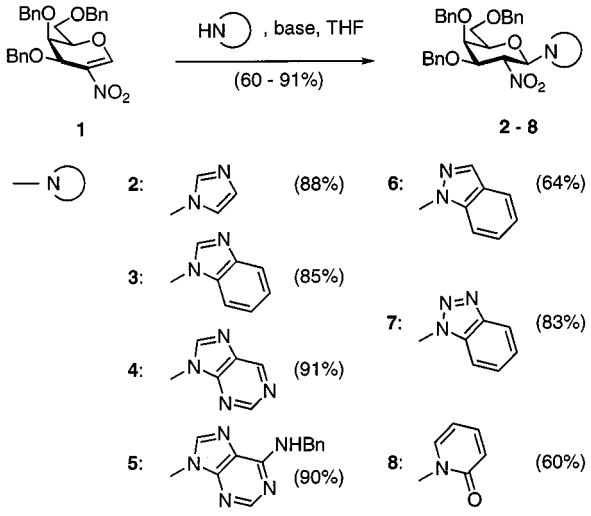
A new method for the construction of nucleosides of 2-deoxy-2-nitro-D-galactose and of *N*-acetyl-D-galactosamine based on addition reactions to 3,4,6-tri-*O*-benzyl-2-nitro-D-galactal (**1**) is presented. The reaction of imidazole, benzimidazole, purine, N^6-benzyladenine, indazole, benzotriazole, and pyridone with **1** under base activation afforded the corresponding β-glycosides with a high degree of stereo- and regioselectivity. Reduction of the 2-deoxy-2-nitro-nucleosides **3** and **4** gave, after *N*-acetylation, the corresponding 2-acetamido-2-deoxy-nucleosides **9** and **10**. Complete deprotection of **9** was achieved with H_2 in the presence of $Pd(OH)_2/C$ and THF as solvent.

Introduction

Nucleosides of 2-nitrogen-substituted pyranoses especially galactopyranoses have not been well studied, and only few syntheses for this class of compounds are reported in literature.[1−4] The preparation of purine and pyrimidine nucleosides of *N*-acetyl-D-galactosamine succeeded with haloses and trifluoroacetyl protection for the amino function at C-2; however, rather harsh conditions are needed for coupling (fusion method), and chloromercurated or silylated bases are required.[2,3] Yields as well as stereoselectivities in the formation of purine nucleosides remained unsatisfactory.[2] Recently, we have introduced the concept of Michael-type addition to 3,4,6-tri-*O*-benzyl-2-nitro-D-galactal (**1**) as a powerful tool in the synthesis of *O*-glycosides of galactosamine.[5,6] Here, a versatile and efficient approach to the synthesis of nucleosides of 2-deoxy-2-nitro-D-galactose and of *N*-acetyl-D-galactosamine is presented, thus widening the scope of the strategy of addition reactions to 2-nitro-D-galactal to the formation of *N*-glycosides.



Scheme 1. Nucleoside formation by Michael addition reactions

Results and Discussion

In a test case we treated our previously established glycosyl donor 3,4,6-tri-*O*-benzyl-2-nitro-D-galactal (**1**)[5,6] with imidazole as nucleophile (Scheme 1). In THF as solvent, glycoside formation was complete within 6 h at room temperature, and we observed the exclusive formation of the corresponding *N*-(3,4,6-tri-*O*-benzyl-2-deoxy-2-nitro-β-D-galactopyranosyl)imidazole (**2**), which was isolated in 88% yield. We then moved to other heterocyclic nitrogen nucleophiles to generalize the methodology. Among the nucleobases studied were benzimidazole, purine, *N*-benzyladenine, indazole, benzotriazole, and pyridone (Scheme 1).

In all these cases, addition of a second base with reduced nucleophilicity was required to obtain a good rate of reaction and high yields. A combination of 1.2 equiv. of *N*-methylimidazole and catalytic amounts of DBU proved to be very efficient. All reactions proceeded smoothly at room temperature and completed within 6−48 h. Uniformly, in all cases studied β-glycosides were isolated in good to excellent yields varying between 60% for the pyridone glycoside **8** and 91% for the purine glycoside **4**. Thus, under the conditions favoring β-glycoside formation with *O*-nucleophiles,[5] with nitrogen heterocycles as *N*-nucleophiles, the β-glycosides were obtained exclusively. This is presumably due to kinetically favored β-side addition to the $^5H_4$ conformer of **1**.[5] The β-selectivity could be also due to hydrogen bond interaction of the *N*-nucleophiles with O-4 of the sterically favored $^4H_5$ conformer of **1**.[5,7] The anomeric diastereocontrol is particularly worth mentioning because it adds further value to this convenient *N*-glycoside bond formation.

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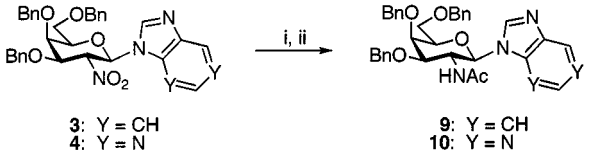
In the glycosylation of purine, the protected adenine derivative, indazole, benzotriazole, and pyridone, more than one regioisomer can form, for at least two or more nucleophilic centers are present in the heterocyclic base. In all cases, only one single considerable product was observed and characterized. The regiochemical outcome for all reactions is shown in Scheme 1. The purine heterocycles formed N-9 nucleosides **4** and **5**; benzotriazole and indazole were glycosylated at N-1, leading to nucleosides **6** and **7**. Nucleophilic attack of the pyridone occurred via the nitrogen atom, leading to glycoside **8**. Hence, in all experiments, a remarkable degree of stereo- as well as regioselectivity was observed.

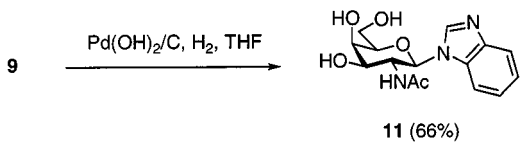
The regiochemical outcome of glycosylation was unequivocally determined using the three-bond ^{1}H-^{13}C spin-spin long-range coupling between the anomeric proton of the carbohydrate moiety and the α-carbon atoms of the heterocycle next to the glycosylation site. In the purine nucleoside **4**, for instance, C-4, C-5, and C-8 were first assigned by means of their ^{1}H-^{13}C long-range coupling to either 2-H, 6-H, and 8-H (C-4) or 8-H only (C-5), or a lack thereof (C-8). The anomeric proton in glycoside **4** shows a ^{1}H-^{13}C long-range coupling to C-4 and C-8 proving attachment of the glycosyl residue at N-9. Structures **5** and **7** were determined the same way; structure **6** was ascertained by a NOE experiment.

In order to show that this route is suitable for the synthesis of 2-amino-2-deoxynucleosides, the benzimidazole nucleoside **3** and the purine nucleoside **4** were exemplarily reduced to the corresponding amines, which were isolated after *N*-acetylation (Scheme 2).



Scheme 2. Reduction of 2-nitro nucleosides to 2-amino nucleosides; reagents: i) Raney nickel T4 (Pt), H_2, EtOH; ii) Ac_2O, pyridine

For the hydrogenation reaction we used platinized Raney nickel T4,[8] a catalyst, which had proven to work very efficiently in a related problem.[6] After reduction with the system Raney nickel T4 (Pt)/H_2 in ethanol as solvent, and subsequent *N*-acetylation, the 2-acetamido nucleosides **9** and **10** were obtained in 54% and 51% yield, respectively. The benzyl protection remains intact during the reduction of the nitro group. Complete deprotection is possible using H_2/Pearlman's catalyst in THF, as shown for the deprotection of **9** to give **11** in 66% yield (Scheme 3).



Scheme 3. Deprotection of a 2-acetamido nucleoside

Conclusion

In conclusion, a new and versatile approach to the synthesis of nucleosides of 2-deoxy-2-nitro-D-galactose and *N*-acetyl-D-galactosamine was established. The high degree of stereo- and regioselectivity, the use of unmodified heterocyclic bases in nucleoside synthesis, as well as the convenient experimental conditions underline the efficiency of this approach.

Experimental Section

General: Solvents were removed under reduced pressure while maintaining the water bath temperature below 40 °C. − Chromatography was done on silica gel for flash chromatography 40 μm (J. T. Baker) at 3 bar pressure. − For thin-layer chromatography TLC plastic sheets, silica gel 60 F_{254}, were used and the compounds visualized by illumination under UV light at 254 nm and by treatment with 5% $(NH_4)_2MoO_4$, 0.1% $Ce(SO_4)_2$ in 10% H_2SO_4 and heating to 160 °C. − Optical rotations were measured at 25 °C with a Perkin−Elmer polarimeter 241/MS using the sodium D line. − NMR: Bruker AC 250 Cryospec, Bruker DR 600, TMS or the solvent residual peak were used as internal standard. $^{3}J_{C,4}$ couplings were observed in gradient-selected heteronuclear multi-bond correlations (HMBC). − MALDI-MS: Kratos Kompact Maldi 1, 2,5-dihydroxybenzoic acid was used as matrix. − FAB-MS: Finnigan MAT 312/AMD 5000, 790 eV, 70 °C. − Yields are calculated based on consumed **1** where its recovery is stated.

***N*-(3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-β-D-galactopyranosyl)-imidazole (2):** Nitrogalactal **1**[5,6] (150 mg, 0.325 mmol) and imidazole (27 mg, 0.390 mmol) in THF (2 mL) were stirred at room temperature for 6 h. The solvent was evaporated and the crude product purified by flash chromatography with toluene/ethyl acetate (1:1) as eluent to yield **2** (152 mg, 88%). − R_f = 0.45 (toluene/ethyl acetate, 1:3); $[\alpha]_D^{25}$ = +19.1 (*c* = 1, $CHCl_3$). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.59−3.62 (m, 2 H, 6a′- and 6b′-H), 3.85 (t, 1 H, ^{3}J = 7.1 Hz, 5′-H), 4.31 (d, 1 H, ^{3}J = 1.9 Hz, 4′-H), 4.20 (dd, 1 H, $^{3}J_{2,3}$ = 10.3 Hz, $^{3}J_{3,4}$ = 2.6 Hz, 3′-H), 4.42−4.83 (m, 6 H, benzyl H), 5.20 (t, 1 H, ^{3}J = 10.0 Hz, 2′-H), 5.57 (d, 1 H, $^{3}J_{1,2}$ = 9.3 Hz, 1′-H), 7.05−7.07 (m, 2 H, im-H), 7.23−7.39 (m, 15 H, arom. H), 7.58 (s, 1 H, im-H). − MS (FAB): calcd. 529 + 1 (H) = 530, 529 + 23 (Na) = 552; found 530 $[M + H]^+$, 552 $[M + Na]^+$.

General Procedure for the Preparation of Nucleosides 3−8: Nitrogalactal **1** (1.0 equiv.) and the nitrogen heterocycle (1.2 equiv.) were dissolved in dry THF (75−150 equiv.). The reaction was activated by addition of *N*-methylimidazole (1.2 equiv.) and a catalytic amount of DBU (0.2−0.3 equiv.) to the stirred solution at room temperature. The reaction mixture was stirred for 6−48 h at that temperature before the solvent was evaporated and the residue purified by flash chromatography to yield products **3−8**.

***N*-(3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-β-D-galactopyranosyl)-benzimidazole (3):** Flash chromatography using toluene/ethyl acetate (4:1) as eluent afforded 85% of pure **3**. − R_f = 0.49 (toluene/ethyl acetate, 1:1); $[\alpha]_D^{25}$ = −1.9 (*c* = 1, $CHCl_3$). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.58−3.71 (m, 2 H, 6a′- and 6b′-H), 3.95 (t, 1 H, ^{3}J = 6.5 Hz, 5′-H), 4.19 (d, 1 H, ^{3}J = 2.2 Hz, 4′-H), 4.29 (dd, 1 H, $^{3}J_{2,3}$ = 10.3 Hz, $^{3}J_{3,4}$ = 2.5 Hz, 3′-H), 4.40−5.02 (m, 6 H, benzyl H), 5.60 (t, 1 H, ^{3}J = 10.0 Hz, 2′-H), 5.90 (d, 1 H, $^{3}J_{1,2}$ = 9.3 Hz, 1′-H), 7.13−7.40 (m, 17 H, arom. H), 7.50 (d, 1 H, ^{3}J = 8.4 Hz, benzim H), 7.77 (d, 1 H, ^{3}J = 8.0 Hz, benzim H), 7.90 (s,

1 H, benzim H). − MS (FAB): calcd. 579 + 1 (H) = 580, 579 + 23 (Na) = 602; found 580 $[M + H]^+$, 602 $[M + Na]^+$.

9-(3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-β-D-galactopyranosyl)purine (4): Flash chromatography using toluene/ethyl acetate (3:2) as eluent afforded 91% of pure **4** along with 40% of recovered **1**. − R_f = 0.31 (toluene/ethyl acetate, 1:1); $[\alpha]_D^{25}$ = +20.3 (*c* = 2, $CHCl_3$). − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.57−3.62 (m, 2 H, 6a′- and 6b′-H), 3.97 (t, 1 H, ^3J = 6.6 Hz, 5′-H), 4.15 (d, 1 H, ^3J = 2.4 Hz, 4′-H), 4.35 (dd, 1 H, $^3J_{2,3}$ = 10.3 Hz, $^3J_{3,4}$ = 2.6 Hz, 3′-H), 4.40−4.95 (m, 6 H, benzyl H), 5.68 (t, 1 H, ^3J = 10.0 Hz, 2′-H), 6.20 (d, 1 H, $^3J_{1,2}$ = 9.6 Hz, 1′-H), 7.24−7.37 (m, 15 H, arom. H), 8.28, 8.98, 9.14 (3 s, 3 H, purine H). − ^{13}C NMR (150 MHz, $CDCl_3$): δ = 67.5, 71.4, 72.6, 73.6, 75.0, 79.4, 79.9, 85.9, 128 (m), 133.7, 136.0, 137.2, 137.5, 142.6 (C-8), 149.1, 150.9 (C-4), 153.2. − MS (FAB): calcd. 581 + 1 (H) = 582; found 582 $[M + H]^+$. − $C_{32}H_{31}N_5O_6$ (581.6): calcd. C 66.08, H 5.37, N 12.04; found C 66.32, H 5.45, N 11.65.

***N*^{6}-Benzyl 9-(3,4,6-tri-*O*-benzyl-2-deoxy-2-nitro-β-D-galactopyranosyl)adenine (5):** Flash chromatography using toluene/ethyl acetate (3:1) as eluent afforded 90% of pure **5** along with 25% of recovered **1**. − R_f = 0.61 (toluene/ethyl acetate, 1:1); $[\alpha]_D^{25}$ = +2.0 (*c* = 0.5, $CHCl_3$). − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.56 (dd, 1 H, ^2J = 9.2 Hz, ^3J = 5.5 Hz, 6a′-H), 3.60 (dd, 1 H, ^2J = 9.2 Hz, ^3J = 7.8 Hz, 6b′-H), 3.94 (t, 1 H, ^3J = 6.3 Hz, 5′-H), 4.13 (d, 1 H, ^3J = 2.7 Hz, 4′-H), 4.31 (dd, 1 H, $^3J_{2,3}$ = 10.3 Hz, $^3J_{3,4}$ = 2.7 Hz, 3′-H), 4.40−4.90 (m, 8 H, benzyl H), 5.55 (t, 1 H, ^3J = 10.0 Hz, 2′-H), 6.10 (d, 1 H, $^3J_{1,2}$ = 9.7 Hz, 1′-H), 6.70 (br. d, 1 H, NH), 7.19−7.36 (m, 20 H, arom. H), 7.63, 8.87 (2 br. s, 2 H, adenine H). − ^{13}C NMR (150 MHz, $CDCl_3$): δ = 67.4, 71.5, 72.5, 73.6, 75.0, 76.6, 79.5, 79.7, 86.0, 119.2, 128 (m), 136.2, 137.1, 137.2, 137.6, 138.3 (C-8), 148.8 (C-4), 153.8, 154.7. − MS (FAB): calcd. 686 + 1 (H) = 687; found 687 $[M + H]^+$.

1-(3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-β-D-galactopyranosyl)indazole (6): Flash chromatography using toluene/ethyl acetate (98:2) as eluent afforded 64% of pure **6** along with 29% of recovered **1**. − R_f = 0.45 (toluene/ethyl acetate, 9:1); $[\alpha]_D^{25}$ = +4.6 (*c* = 2, $CHCl_3$). − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.58 (dd, 1 H, ^2J = 9.5 Hz, ^3J = 5.5 Hz, 6a′-H), 3.72 (dd, 1 H, ^2J = 9.5 Hz, ^3J = 7.8 Hz, 6b′-H), 3.93 (t, 1 H, ^3J = 7.8 Hz, 5′-H), 4.19 (d, 1 H, ^3J = 2.7 Hz, 4′-H), 4.31 (dd, 1 H, $^3J_{2,3}$ = 10.5 Hz, $^3J_{3,4}$ = 2.7 Hz, 3′-H), 4.35−4.95 (m, 6 H, benzyl H), 5.92 (t, 1 H, ^3J = 10.0 Hz, 2′-H, NOE with 7-H, no NOE with 3-H), 6.11 (d, 1 H, $^3J_{1,2}$ = 9.3 Hz, 1′-H, NOE with 7-H, no NOE with 3-H), 7.18 (t, 1 H, ^3J = 7.6 Hz, indazole H), 7.23−7.34 (m, 15 H, arom. H), 7.50 (d, 1 H, ^3J = 8.4 Hz, 7-H), 7.69 (d, 1 H, ^3J = 8.0 Hz, indazole H), 8.05 (s, 1 H, 3-H). − ^{13}C NMR (150 MHz, $CDCl_3$): δ = 67.7, 71.3, 72.3, 73.6, 74.8, 76.0, 80.0, 84.9, 85.1, 119.7, 121.3, 121.9, 125.1, 128 (m), 135.9, 136.5, 137.4, 137.8, 139.4. − MS (EI): calcd. 579; found 579 $[M]^+$, 488, 209, 118, 91. − $C_{34}H_{33}N_3O_6$ (579.7): calcd. C 70.45, H 5.74, N 7.25; found C 70.38, H 5.81, N 7.10.

1-(3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-β-D-galactopyranosyl)benzotriazole (7): Flash chromatography using toluene/ethyl acetate (97:3) as eluent afforded 83% of pure **7**. − R_f = 0.47 (toluene/ethyl acetate, 9:1); $[\alpha]_D^{25}$ = −13.5 (*c* = 1, $CHCl_3$). − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.60−3.62 (m, 1 H, 6a′-H), 3.67−3.70 (m, 1 H, 6b′-H), 4.01 (t, 1 H, ^3J = 6.6 Hz, 5′-H), 4.19 (d, 1 H, ^3J = 2.6 Hz, 4′-H), 4.38 (dd, 1 H, $^3J_{2,3}$ = 10.4 Hz, $^3J_{3,4}$ = 2.6 Hz, 3′-H), 4.43 (d, 1 H, ^2J = 11.8, benzyl H), 4.48 (d, 1 H, ^2J = 11.8, benzyl H), 4.58 (d, 1 H, ^2J = 11.5, benzyl H), 4.65 (d, 1 H, ^2J = 11.0, benzyl H), 4.69 (d, 1 H, ^2J = 11.5, benzyl H), 4.99 (d, 1 H, ^2J = 11.0, benzyl H), 5.76 (t, 1 H, ^3J = 10.0 Hz, 2′-H), 6.45 (d, 1 H, $^3J_{1,2}$ = 9.5 Hz, 1′-H), 7.25−7.38 (m, 17 H, arom. H), 7.62, 8.06 (2 d, 2 H, benzotriazole H). − ^{13}C NMR (150 MHz, $CDCl_3$): δ = 67.5, 71.3, 72.6, 73.7, 75.0, 76.4, 79.5, 85.0, 85.3, 110.6, 120.5, 124.7, 128 (m), 131.4 (C-7a), 136.3, 137.3, 137.6, 146.5. − MS (EI): calcd. 580; found 580 $[M]^+$, 489, 308, 264, 197, 91.

***N*-(3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-β-D-galactopyranosyl)-pyridone (8):** Flash chromatography using toluene/ethyl acetate (9:1) as eluent afforded 60% of pure **8** along with 42% of recovered **1**. − R_f = 0.23 (toluene/ethyl acetate, 3:1); $[\alpha]_D^{25}$ = +65.0 (*c* = 1, $CHCl_3$). − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.56−3.63 (m, 2 H, 6a′- and 6b′-H), 3.92 (t, 1 H, ^3J = 6.8 Hz, 5′-H), 4.10 (d, 1 H, ^3J = 2.4 Hz, 4′-H), 4.37 (dd, 1 H, $^3J_{2,3}$ = 10.3 Hz, $^3J_{3,4}$ = 2.6 Hz, 3′-H), 4.41−4.85 (m, 6 H, benzyl H), 5.05 (t, 1 H, ^3J = 10.0 Hz, 2′-H), 6.21 (t, 1 H, ^3J = 6.8 Hz, pyridone H), 6.46 (d, 1 H, ^3J = 9.3 Hz, pyridone H), 6.53 (d, 1 H, $^3J_{1,2}$ = 9.5 Hz, 1′-H), 7.24−7.36 (m, 17 H, arom. H). − ^{13}C NMR (150 MHz, $CDCl_3$): δ = 67.4, 71.8, 72.8, 73.5, 75.0, 76.3, 78.9, 79.3, 86.5, 106.9, 120.9, 128 (m), 132.0, 137.0 (t), 139.9, 161.3. − MS (FAB): calcd. 556 + 1 (H) = 557; found 557 $[M + H]^+$.

***N*-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-galactopyranosyl)-benzimidazole (9):** Compound **3** (100 mg, 0.173 mmol) was dissolved in EtOH (5 mL) and transferred to a hydrogenation vessel. Platinized Raney nickel T4 catalyst was freshly prepared as described in the literature[8] and the material obtained from 2 g of Raney nickel/aluminum alloy was suspended in EtOH (15 mL). From a homogenous suspension of this catalyst 5 mL was added to the reaction vessel and the suspension shaken under H_2 at room temperature for 12 h. The catalyst was filtered off and all volatiles were removed. The residue was dissolved in pyridine/acetic anhydride (2:1, 5 mL) and stirred for 3 h. Removal of the volatiles and flash chromatography (toluene/acetone, 3:1→3:2) gave **9** (56 mg, 54%). − R_f = 0.24 (toluene/acetone, 1:1); $[\alpha]_D^{25}$ = −6.85 (*c* = 2, $CHCl_3$). − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.73 (s, 3 H, NHCOC*H*$_3$), 3.62−3.69 (m, 2 H, 6a′- and 6b′-H), 4.01 (t, 1 H, ^3J = 6.3 Hz, 5′-H), 4.13 (s, 1 H, 4′-H), 4.33 (br. d, 1 H, $^3J_{2,3}$ = 10.1 Hz, 3′-H), 4.45 (d, 1 H, ^2J = 11.9, benzyl H), 4.50 (d, 1 H, ^2J = 11.9, benzyl H), 4.57 (br. d, 1 H, ^3J = 9.8, 2′-H), 4.63 (d, 1 H, ^2J = 11.0, benzyl H), 4.64 (d, 1 H, ^2J = 11.7, benzyl H), 4.75 (d, 1 H, ^2J = 11.7, benzyl H), 5.03 (d, 1 H, ^2J = 11.0, benzyl H), 6.33 (d, 1 H, $^3J_{1,2}$ = 9.5 Hz, 1′-H), 6.75 (br. s, 1 H, NH), 7.22−7.36 (m, 17 H, arom. H), 7.74, 7.86 (2 d, 2 H, ^3J = 8.1 Hz, benzim H), 8.90 (br. s, 1 H, benzim H). − ^{13}C NMR (150 MHz, $CDCl_3$): δ = 23.2, 68.3, 72.6, 73.5, 74.8, 76.1, 78.5, 128 (m), 137.6, 137.8, 138.4, 171.4. − MS (FAB): calcd. 591 + 23 (Na) = 614; found 614 $[M + Na]^+$. − $C_{36}H_{37}N_3O_5 \cdot 0.5\ H_2O$ (600.7): calcd. C 71.98, H 6.38, N 6.99; found C 71.93, H 6.24, N 6.72.

9-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-galactopyranosyl)-purine (10): Compound **7** (313 mg, 0.538 mmol) was treated as described for the preparation of **9** to give **10** (162 mg, 51%) after flash chromatographic purification with toluene/acetone (2:3→1:2). − R_f = 0.31 (toluene/acetone, 1:2); $[\alpha]_D^{25}$ = +20.71 (*c* = 2, $CHCl_3$). − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.57 (s, 3 H, NHCOC*H*$_3$), 3.61−3.64 (m, 2 H, 6a′- and 6b′-H), 3.95 (t, 1 H, ^3J = 6.5 Hz, 5′-H), 3.99 (dd, 1 H, $^3J_{2,3}$ = 10.6, $^3J_{3,4}$ = 2.6 Hz, 3′-H), 4.12 (d, 1 H, $^3J_{3,4}$ = 2.9 Hz, 4′-H), 4.43 (d, 1 H, ^2J = 11.8, benzyl H), 4.47 (d, 1 H, ^2J = 11.8, benzyl H), 4.52 (d, 1 H, ^2J = 12.0, benzyl H), 4.66 (d, 1 H, ^2J = 11.4, benzyl H), 4.77 (d, 1 H, ^2J = 12.0, benzyl H), 4.81 (dd, 1 H, $^3J_{1,2}$ = 8.3, $^3J_{2,3}$ = 10.2, 2′-H), 4.98 (d, 1 H, ^2J = 11.4, benzyl H), 5.77 (br. s, 1 H, NH), 5.94 (d, 1 H, $^3J_{1,2}$ = 9.8 Hz, 1′-H), 7.26−7.39 (m, 15 H, arom. H), 8.52, 9.04, 9.10 (3 s, 3 H, purine H). − ^{13}C NMR (150 MHz, $CDCl_3$): δ = 22.9, 51.9, 68.3, 71.7, 71.9, 73.6, 74.8, 76.6, 78.6, 81.9, 128 (m), 133.7, 137.4, 137.5,

138.1, 146.0, 151.0, 152.1, 170.7. − MS (MALDI-TOF): calcd. 593.3 + 23.0 (Na) = 616.3; found 616.7 $[M + Na]^+$. − $C_{34}H_{35}N_5O_5 \cdot 0.5\ H_2O$ (602.9): calcd. C 67.76, H 6.02, N 11.62; found C 68.10, H 6.13, N 11.39.

***N*-(2-Acetamido-2-deoxy-β-D-galactopyranosyl)benzimidazole (11):** Compound **9** (30 mg, 0.051 mmol) was dissolved in dry THF (2 mL) and stirred together with $Pd(OH)_2/C$ (20% Pd, 30 mg) under H_2 for 4 d. The catalyst was filtered off and washed carefully with MeOH. The filtrate was concentrated and purified by flash chromatography (chloroform/methanol, 2:1) to give **11** (11 mg, 66%). − R_f = 0.58 (chloroform/methanol, 1:1); $[\alpha]_D^{25} = +3.56$ (c = 0.5, $CHCl_3$). − ^{1}H NMR (600 MHz, CD_3OD): δ = 1.65 (s, 3 H, NHCOC*H*$_3$), 3.77−3.85 (m, 3 H, 5′-, 6a′- and 6b′-H), 3.91 (dd, 1 H, $^3J_{2,3}$ = 10.5 Hz, $^3J_{3,4}$ = 3.1 Hz, 3′-H), 4.03 (d, 1 H, $^3J_{4,3}$ = 3.2 Hz, 4′-H), 4.60 (t, 1 H, $^3J_{2,1}$ = 10.1 Hz, $^3J_{2,3}$ = 10.1 Hz, 2′-H), 5.64 (d, 1 H, $^3J_{1,2}$ = 9.7 Hz, 1′-H), 7.25−7.32 (m, 2 H, benzim H), 7.63, 7.71 (2 d, 2 H, ^3J = 8.0 Hz, benzim H), 8.33 (s, 1 H, benzim H). − ^{13}C NMR (150 MHz, CD_3OD): δ = 22.5, 30.7, 53.4, 62.6, 69.8, 72.9, 79.8, 85.2, 97.2, 112.6, 120.1, 123.9, 124.5, 143.3, 173.7. − MS (FAB): calcd. 321 + 1 (H) = 322, 321 + 23 (Na) = 344; found 322 $[M + H]^+$, 344 $[M + Na]^+$.

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