JOC*Note*

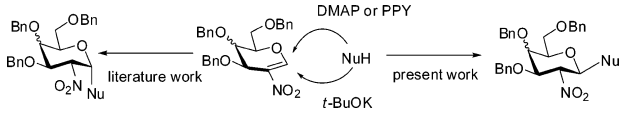
An Efficient Route toward 2-Amino-β-D-galacto- and -glucopyranosides via Stereoselective Michael-Type Addition of 2-Nitroglycals

Weihua Xue, Jiansong Sun,* and Biao Yu*

State Key Laboratory of Bioorganic and Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, China

byu@mail.sioc.ac.cn

Received March 25, 2009



Under the catalysis of DMAP or PPY in CH_2Cl_2, the Michael-type addition of nucleophiles to 2-nitrogalactal or 2-nitroglucal leads in excellent yields and stereoselectivity to the corresponding β-galacto- or -glucopyranosides, which are ready precursors to the biologically significant β-D-galactosamine and -glucosamine units.

2-Amino-2-deoxy-glycosides exist as integral structural components in polysaccharides and glycoconjugates, such as glycolipids, glycoproteins, proteoglycans, and antibiotics, and are associated with a wide range of biological processes,[1] whereas 2-amino-2-deoxy-D-gluco- and -galactopyranosides are the most common units, which occur in either α- or β-glycosidic linkage. Synthesis of these important linkages has become a topic of special challenge in carbohydrate chemistry since the very early years.[2,3] The synthetic obstacles include the following: (1) Although 2-amino- and 2-acetamido-2-deoxy-D-glucose are largely available starting materials, 2-amino-2-deoxy-D-galactose is not. (2) The use of 2-acetamido-derivatives in the synthesis is highly problematic, due to the oxazoline formation, *O*-glycosylation of the amide moiety,[4] and the usually poor solubility. Thus, a special protecting group or a latent group has to be employed for the 2-amino-group in the synthesis.[3] (3) Construction of the 1,2-*trans*-β-D-glycosides can be secured by the participation of the 2-*N*-protecting group (or the nitrogen itself);[5] nevertheless, synthesis of the 1,2-*cis*-α-D-glycosides shall preclude this anchimeric involvement of the 2-amino-function.[2b] Considering these problems together, an attractive solution is to employ 2-nitroglycals as key precursors;[6] the 2-nitroglucal and galactal derivatives can be prepared readily from glucose and galactose. Although these 2-nitroglycals were introduced by Lemieux et al. in 1968,[7] the full utility of these derivatives in the synthesis of 2-amino-2-deoxy-glycosides has only been explored recently by Schmidt and co-workers.[6] In general, Michael-type addition of nucleophiles to 2-nitroglucals and 2-nitrogalactals can be high yielding and stereoselective, leading to the 2-amino-2-deoxy-D-gluco or -galactopyranosides (but not the manno- or talosides); and the α/β selectivity is highly dependent on the addition partners, the base used, and the reaction conditions. The nitro group can later be reduced into the amino group with Raney nickel in satisfactory yields.[6]

Remarkably, addition of *O*-nucleophiles to 2-nitrogalactals in the presence of a strong base, such as *t*-BuOK, mostly provides the corresponding 2-deoxy-2-nitro-α-D-galactopyranosides in satisfactory yields and high stereoselectivity.[6] Thus, Schmidt and co-workers have been able to synthesize the core structures of the mucin-type glycoprotein which contain *N*-acetylaminogalactose α-linked to the hydroxyl group of L-serine and L-threonine.[8] In the presence of weak bases or with 2-nitroglucals as Michael acceptors, the addition reaction turns out to be β selective; however, the yield and α/β selectivity are often unsatisfactory.[9,10] Thus, the 2-amino-β-*O*-glycosides are synthesized from 2-nitroglycals via conformational stereocontrol[9b] or via an indirect sequence, i.e., addition with thiophenol and subsequent use of the resulting 2-nitro thioglycosides as glycosylation donors to couple with alcohols.[11] Here we report that highly β-selective addition of nucleophiles onto 2-nitroglycals can be achieved simply with 4-dimethylaminopyridine (DMAP) or 4-(1-pyrrolidino)pyridine (PPY) as a base and CH_2Cl_2 as solvent.

Schmidt et al. found that addition of methanol to 3,4,6-tri-*O*-benzyl-2-nitro-D-galactal (**1a**) in the presence of NaOMe in THF at room temperature gave methyl 3,4,6-tri-*O*-benzyl-2-nitro-α-D-galactopyranoside (**3**$\boldsymbol{\alpha}$) as the major product in 82% yield, while the β-anomer **3**$\boldsymbol{\beta}$ was isolated in 10% yield (entry 1, Table 1). When Et_3N was used as a base, the α/β selectivity of the reaction was reversed, leading to the β-anomer predominantly in 80% yield, and the α-anomer was isolated in 10% yield (entry 2).[9a] We found that DMAP (1.0 equiv), a weaker base (pK_a 9.70) than Et_3N (pK_a 10.65), was better to promote the β selective addition of methanol to galactal **1a**. In fact, no α-anomer was detected (entry 3); and the yield of the β-galactoside **3**$\boldsymbol{\beta}$ could be raised to 97% when the reaction was

(1) (a) Schauer, R. *Adv. Carbohydr. Chem. Biochem.* **1982**, *40*, 131. (b) Hakomori, S. *Annu. Rev. Immunol.* **1984**, *2*, 103. (c) Dwek, R. A. *Chem. Rev.* **1996**, *96*, 683. (d) Zachara, N. E.; Hart, G. W. *Chem. Rev.* **2002**, *102*, 431.

(2) (a) Röhle, G.; Wulff, G. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 157. (b) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155.

(3) (a) Banoub, J.; Boullanger, P.; Lafont, D. *Chem. Rev.* **1992**, *92*, 1167. (b) Debenham, J.; Rodebaugh, R.; Fraser-Reid, B. *Liebigs Ann.* **1997**, 791. (c) Bongat, A. F. G.; Demchenko, A. V. *Carbohydr. Res.* **2007**, *342*, 374.

(4) Liao, L.; Auzanneau, F.-I. *J. Org. Chem.* **2005**, *70*, 6265.

(5) (a) Yang, Y.; Yu, B. *Tetrahedron Lett.* **2007**, *48*, 4557. (b) Chen, J.; Yu, B. *Tetrahedron Lett.* **2008**, *49*, 1682.

(6) (a) Reddy, B. G.; Schmidt, R. R. *Nat. Protoc.* **2008**, *3*, 114. (b) Schmidt, R. R.; Vankar, Y. D. *Acc. Chem. Res.* **2008**, *41*, 1059.

(7) Lemieux, R. U.; Nagabhushan, T. L.; O'Neill, I. K. *Can. J. Chem.* **1968**, *46*, 413.

(8) (a) Winterfeld, G. A.; Schmidt, R. R. *Angew. Chem., Int. Ed.* **2001**, *40*, 2654. (b) Winterfeld, G. A.; Khodair, A. I.; Schmidt, R. R. *Eur. J. Org. Chem.* **2003**, 1009.

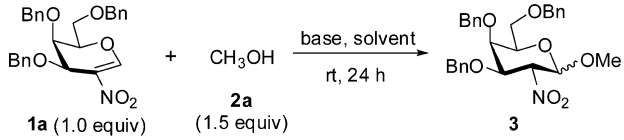
(9) (a) Das, J.; Schmidt, R. R. *Eur. J. Org. Chem.* **1998**, 1609. (b) Geiger, J.; Reddy, B. G.; Winterfeld, G. A.; Weber, R.; Przybylski, M.; Schmidt, R. R. *J. Org. Chem.* **2007**, *72*, 4367.

(10) Holzapfel, C. W.; Marais, C. F.; van Dyk, M. S. *Synth. Commun.* **1988**, *18*, 97.

(11) Barroca, N.; Schmidt, R. R. *Org. Lett.* **2004**, *6*, 1551.

10.1021/jo900609s CCC: $40.75
Published on Web 05/19/2009

TABLE 1. Michael-Type Addition of Methanol to 3,4,6-Tri-*O*-benzyl-2-nitro-D-galactal (1a)



entry	base (equiv)	solvent	yield,[a] %	α/β
1[9a]	NaOMe (0.2)	THF	92	8:1
2[9a]	NEt_3 (>10)	THF	90	1:8
3	DMAP (1.0)	THF	91	0:1[b]
4	DMAP (1.0)	CH_2Cl_2	97	0:1
5	DMAP (0.5)	CH_2Cl_2	93	0:1
6	DMAP (0.15)	CH_2Cl_2	90	0:1
7	DMAP (0.03)	CH_2Cl_2	20	0:1
8	DMAP (0.15)	THF	39	1:5[b]
9	DMAP (0.15)	toluene	78	0:1
10	DMAP (0.15)	CH_3CN	41	0:1

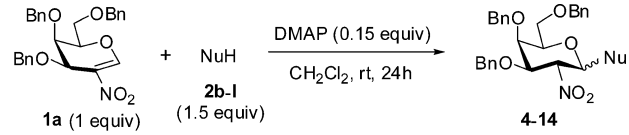
[a] Isolated yield. [b] Determined by HPLC.

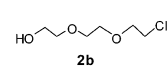
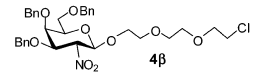
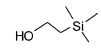
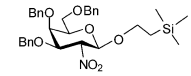
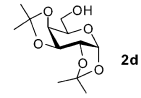
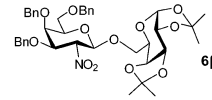
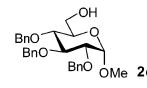
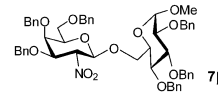
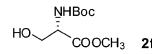
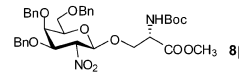
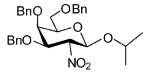
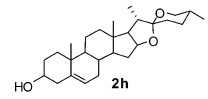
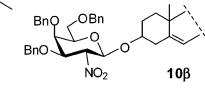
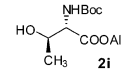
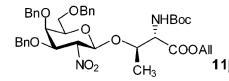
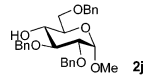
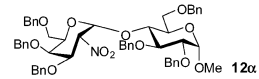
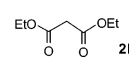
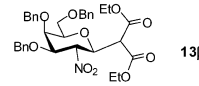
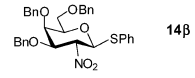
performed in CH_2Cl_2 (entry 4). The addition proceeded slower when a catalytic amount of DMAP (down to 0.15 equiv) was used, while the β-adduct **3*β*** was still isolated as the sole product in 90% yield within 24 h (entries 5 and 6). However, further reducing the amount of DMAP to 0.03 equiv made the reaction hardly proceed (entry 7). THF, toluene, and acetonitrile were then tested as the reaction solvent when 0.15 equiv of DMAP was used as the base (entries 8−10). The reaction became much more sluggish than in CH_2Cl_2 and provided the β-galactoside **3*β*** in 39%, 78%, and 41% yield, respectively. Moreover, the stereoselectivity of the reaction in THF was compromised (α/β = 1:5).

With DMAP (0.15 equiv) as base and CH_2Cl_2 as solvent, we then examined the generality of this β-selective addition of 2-nitrogalactal (**1a**) with nucleophiles (Table 2). A panel of alcohols (**2b**−**j**) were selected as nucleophiles, including the functionalized primary alcohols **2b** and **2c**, the primary sugar alcohols **2d** and **2e**, the serine and threonine derivatives **2f** and **2i**, the secondary 2-propanol **2g** and steroidal **2h**, and the highly hindered glucose 4-ol **2j**. All the addition reactions, except with **2j**, provided the corresponding β-galactosides (**4*β***−**10*β***) in high yields (82−96%) and satisfactory stereoselectivity (α/β > 6.5:1; entries 1−8). Among them, the addition with achiral alcohols **2c** and **2g** and the L-serine and -threonine derivatives **2f** and **2i** afforded the β-galactosides exclusively. Addition with methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside **2j** was an exception, leading to the α-galactoside **12α** as the sole product in 69% yield (entry 9). The substantially lower yield might be attributed to the highly steric demanding property of the 4-OH of **2j**, and the "double stereodifferentiation" of the coupling partners (**1a** and **2j**) preclude formation of the β-product.[12] Diethyl malonate (**2k**) and thiophenol (**2*l***) as *C*- and *S*-nucleophiles,[11,13] respectively, were also examined to react with 2-nitrogalactal (**1a**) under the present conditions (entries 10 and 11), and the corresponding β-*C*- and *S*-galactosides **13*β*** and **14*β*** were isolated as the sole products in excellent yields (88% and 93%, respectively).

Compared to the Michael-type addition with 2-nitrogalactals, addition with 2-nitroglucals suffers with moderate yield and poor

TABLE 2. DMAP-Catalyzed Michael-Type Addition of Nucleophiles to 3,4,6-Tri-*O*-benzyl-2-nitro-D-galactal (1a)



Entry	Nucleophiles	Products	Yield (%)	β/α
1	 **2b**	 **4β**	91	8:1
2	 **2c**	 **5β**	95	1:0
3	 **2d**	 **6β**	89	6.5:1
4	 **2e**	 **7β**	87	13:1
5	 **2f**	 **8β**	91	1:0
6	 **2g**	 **9β**	92	1:0
7	 **2h**	 **10β**	96	10:1
8	 **2i**	 **11β**	82	1:0
9	 **2j**	 **12α**	69	0:1
10	 **2k**	 **13β**	88	1:0
11	PhSH **2l**	 **14β**	93	1:0

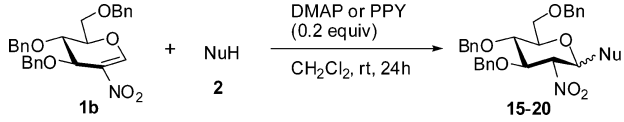
α/β selectivity. Under the catalysis of DMAP (0.2 equiv) in CH_2Cl_2, the addition of methanol to 3,4,6-tri-*O*-benzyl-2-nitro-D-glucal (**1b**)[11] proceeded smoothly, providing the expected methyl β-glucoside **15*β*** predominantly in 85% yield, with the α-anomer being isolated in 9% yield (entry 1, Table 3). However, under similar conditions, the addition of 2-(trimethylsilyl)ethanol (**2c**) with glucal **1b** became sluggish; the corresponding β-glucoside **16*β*** was isolated as the sole product but in only 50% yield (entry 2). With the primary sugar alcohols **2d** and **2e**, respectively, as nucleophiles, the addition reaction hardly proceeded, providing the β-glucoside **17*β*** and **18*β*** in only ∼20% yield (entries 4 and 6). Interestingly, replacement of DMAP with 4-(1-pyrrolidino)pyridine (PPY)[14] as the base improved substantially the above addition reactions; the expected β-adducts **16*β***, **17*β***, and **18*β*** were furnished in 95%, 71%, and 77% yield, respectively, without detection of the α-anomers (entries 3, 5, and 7). Under the catalysis of PPY, the addition of 2-propanol **2g** and thiophenol **2*l***, respectively, with 2-nitro-

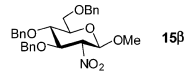
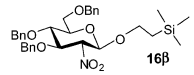
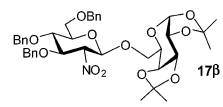
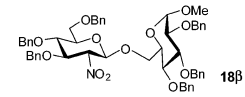
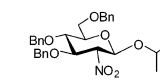
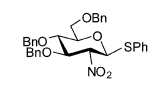
(12) Spijker, N. M.; van Boeckel, C. A. A. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 180.

(13) Pachamuthu, K.; Gupta, A.; Das, J.; Schmidt, R. R.; Vankar, Y. D. *Eur. J. Org. Chem.* **2002**, 1479.

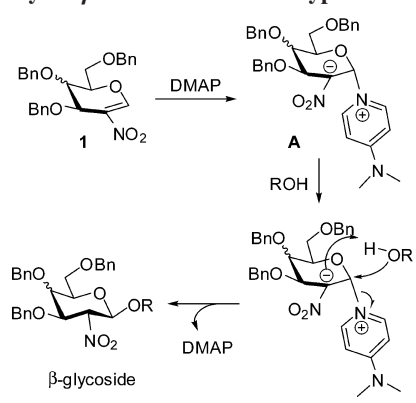
(14) Scriven, E. F. V. *Chem. Soc. Rev.* **1983**, *12*, 129.

TABLE 3. DMAP or PPY-Catalyzed Michael-Type Addition of Nucleophiles to 3,4,6-Tri-*O*-benzyl-2-nitro-D-glucal (1b)



Entry	Nucleophiles	Base	Products	Yield (%)	β/α
1	**2a**	DMAP	 **15β**	94	9:1
2	**2c**	DMAP	 **16β**	50	1:0
3	**2c**	PPY		95	1:0
4	**2d**	DMAP	 **17β**	17	1:0
5	**2d**	PPY		71	1:0
6	**2e**	DMAP	 **18β**	23	1:0
7	**2e**	PPY		77	1:0
8	**2g**	PPY	 **19β**	92	1:0
9	**2j**	PPY	No Reaction	-	-
10	**2l**	PPY	 **20β**	88	1:0

SCHEME 1. A Plausible Mechanism for the DMAP-Catalyzed *β*-Selective Michael-Type Addition



glucal **1b** also led to the *β*-glucosides in excellent yields (92% and 88%) with complete stereoselectivity (entries 8 and 10). However, addition of more sterically demanding acceptors with 2-nitroglucal **1b** hardly took place; for example, no reaction happened with glucose 4-ol **2j** as a nucleophile under the present conditions (entry 9).

A plausible mechanism, as shown in Scheme 1, was put forward to explain the present *β*-selective addition reaction of 2-nitroglycals. DMAP acted as a nucleophile, in analogy to its role in the Morita−Baylis−Hillman reaction,[15] to attack the anomeric C1 of the Michael acceptor 2-nitroglycal. Approaching DMAP from the α side of the glycal, which adopts the $^4H_5$ conformation, was favored, due to stereoelectronic effects.[16] Thus, the α-glycosyl pyridinium species A was formed.[17] S_N2-type substitution of a nucleophile from the *β* side of the α-pyridinium A and protonation of the axial C2 anion led to the corresponding *β*-galactoside or -glucoside product. Comparing the reaction of galactose and glucose series, the *β* orientation of the 4-*O*-substitution in the galactose derivatives is more advantageous than the α orientation in the glucose counterparts for the formation of the α-pyridinium species A. Thus, the addition of 2-nitrogalactals is easier than that of the 2-nitroglucals. And PPY, which is more nucleophilic than DMAP,[14] is better to undergo addition with the 2-nitroglycal to form the α-pyridinium species A, thus it is a better catalyst for the reaction.

In summary, under the catalysis of DMAP or PPY in CH_2Cl_2, the Michael-type addition of nucleophiles to 2-nitro-galactal or -glucals leads to the corresponding *β*-galacto- or -glucopyranosides in high yields and stereoselectivity. This protocol provides an efficient and expeditious approach to the synthesis of 2-amino-2-deoxy-*β*-D-galacto- and -glucopyranosides, which are integral units in many important oligosaccharides, polysaccharides, and glycoconjugates. Improvement in the addition of 2-nitroglucals with sterically demanding nucleophiles and the mechanistic study of this addition reaction are currently underway, and the results will be reported in due course.

Experimental Section

Typical Procedure for the Michael Addition with 3,4,6-Tri-*O*-benzyl-2-nitro-D-galactal (1a). *N*-Boc-L-serine methyl ester **2f** (33 mg, 0.15 mmol) was added to a mixture of 2-nitro-D-galactal **1a** (46 mg, 0.1 mmol) and DMAP (2 mg) in CH_2Cl_2 (1 mL) in the presence of 4 Å MS. After the mixture was stirred at room temperature for 24 h, 4 Å MS was removed by filtration. The filtrate was concentrated at reduced pressure. The residue was purified by silica gel column chromatography to provide *O*-(3,4,6-tri-*O*-benzyl-2-deoxy-2-nitro-*β*-D-galactopyranosyl)-*N*-Boc-L-serine methyl ester (**8**) as a colorless syrup (60 mg, 91%).

Typical Procedure for the Michael Addition with 3,4,6-Tri-*O*-benzyl-2-nitro-D-glucal (1b). Methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **2e** (93 mg, 0.2 mmol) was added to a mixture of 2-nitro-D-glucal **1b** (46 mg, 0.1 mmol) and PPY (3 mg) in CH_2Cl_2 (1 mL) in the presence of 4 Å MS. After the solution was stirred at room temperature for 24 h, 4 Å MS was removed by filtration. The filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography to provide methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4,6-tri-*O*-benzyl-2-deoxy-2-nitro-*β*-D-glucopyranosyl)-α-D-glucopyranoside (**18*β***) as a colorless syrup (71 mg, 77%).

[2-(2-Chloroethoxyl)ethoxy]ethyl 3,4,6-tri-*O*-benzyl-2- deoxy-2-nitro-*β*-D-galactopyranoside (4*β*): $[\alpha]^{20}_D$ +12.7 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 7.38−7.23 (m, 15H), 4.88−4.84 (m, 3H), 4.63−4.45 (m, 5H), 4.08−3.88 (m, 3H), 3.76−3.56 (m,14H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 137.8, 137.5, 136.6, 128.6, 128.5, 128.3, 128.2, 128.0, 127.9, 127.8 (2C), 100.2, 87.5, 79.4, 74.8, 73.7, 73.6, 72.3, 71.4, 71.3, 70.7, 70.5, 70.2, 69.0, 68.0, 42.8, 29.7; HRMS (ESI) calcd for $C_{33}H_{40}ClNO_9Na$ $[M + Na]^+$ 652.2347, found 652.2296.

***O*-(3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-*β*-D-galactopyranosyl)-*N*-Boc-L-serine methyl ester (8*β*):** $[\alpha]^{20}_D$ +116.7 (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 7.38−7.22 (m, 15H), 5.25 (d, *J* = 7.8 Hz, 1H,), 4.87 (d, *J* = 11.1 Hz, 1H), 4.83 (d, *J* = 9.3 Hz, 1H), 4.73 (d, *J* = 7.8 Hz, 1H), 4.62 (AB, 2H), 4.50−4.44 (m, 3H), 4.40−4.37 (m, 1H), 4.22 (dd, *J* = 2.7, 10.2 Hz, 1H), 4.05−3.99

(15) (a) Shi, M.; Li, C.; Jiang, J. *Chem. Commun.* **2001**, 833. (b) Porzelle, A.; Williams, C. M.; Schwartz, B. D.; Gentle, I. R. *Synlett* **2005**, 2923.

(16) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: Oxford, UK, 1983; pp 29−40.

(17) (a) Lemieux, R. U.; Hendriks, K. B.; Stick, R. V.; James, K. *J. Am. Chem. Soc.* **1975**, *97*, 4056. (b) Zhu, J.; Bennet, A. J. *J. Am. Chem. Soc.* **1998**, *120*, 3887.

(m, 2H), 3.79 (dd, J = 3.6, 10.5 Hz, 1H), 3.71 (s, 3H), 3.63−3.57 (m, 3H), 1.44 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 137.8, 137.5, 136.5, 128.6 (2C), 128.4, 128.3, 128.2, 128.0 (2C), 127.9, 100.4, 86.9, 80.1, 79.3, 77.24, 74.9, 74.0, 73.6, 72.4, 71.4, 69.5, 67.7, 53.7, 52.6, 28.3; HRMS (ESI) calcd for $C_{36}H_{44}N_2O_{11}Na$ [M + Na]$^+$ 703.2819, found 703.2860.

Diosgenyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-nitro-α-D-galactopyranoside (10α): $[\alpha]^{25}_D$ +34.2 (*c* 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.21 (m, 15H), 5.42 (d, J = 4.3 Hz, 1H), 5.27 (d, J = 4.1 Hz, 1H), 4.98 (dd, J = 4.3, 10.6 Hz, 1H), 4.85 (d, J = 11.2 Hz, 1H), 4.78 (AB, J = 10.8 Hz, 2H), 4.50−4.38 (m, 5H), 4.12 (t, J = 6.5 Hz, 1H), 4.01 (d, J = 2.6 Hz, 1H), 3.57−3.55 (m, 2H), 3.48−3.37 (m, 3H), 2.30 (d, J = 7.8 Hz, 2H), 2.00−1.95 (m, 2H), 1.88−0.78 (m, 35H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.4, 138.1, 137.8, 137.5, 128.5 (2C), 128.3, 128.2, 128.1, 128.0, 127.8, 121.9, 109.3, 95.1, 84.7, 80.8, 78.7, 75.1, 73.6, 73.4, 73.1, 69.7, 68.5, 66.9, 62.1, 56.5, 50.0, 41.6, 40.3, 39.8, 39.7, 36.8, 32.1, 31.9, 31.4, 30.3, 29.7, 28.8, 27.3, 20.8, 19.4, 17.1, 16.3, 14.5; HRMS (ESI) calcd for $C_{54}H_{70}NO_9$ [M + H]$^+$ 876.5030, found 876.5037.

Diosgenyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-nitro-β-D-galactopyranoside (10β): $[\alpha]^{25}_D$ −40.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.23 (m, 15H), 5.30−5.28 (m, 1H), 4.86−4.82 (m, 3H), 4.61 (d, J = 12.7 Hz, 1H), 4.56 (d, J = 11.4 Hz, 1H), 4.47 (d, J = 11.3 Hz, 3H), 4.42 (dd, J = 7.4, 15.3 Hz, 1H), 4.05 (dd, J = 2.2, 9.6 Hz, 1H), 3.98 (d, J = 2.5 Hz, 1H), 3.65−3.58 (m, 3H), 3.50−3.45 (m, 2H), 3.39 (t, J = 10.9 Hz, 1H), 2.04−0.77 (m, 37H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.1, 137.9, 137.7, 136.6, 128.5 (2C), 128.3 (2C), 128.2, 127.9 (2C), 127.8, 121.8, 109.3, 98.7, 87.8, 80.8, 79.6, 79.3, 74.7, 73.8, 73.6, 72.2, 71.4, 68.1, 66.8, 62.1, 56.5, 50.1, 41.6, 40.2, 39.8, 38.0, 37.1, 36.8, 32.1, 31.8, 31.4, 30.3, 29.3, 28.8, 20.8, 19.3, 17.1, 16.2, 14.5; HRMS (ESI) calcd for $C_{54}H_{69}NO_9Na$ [M + Na]$^+$ 898.4861, found 898.4873.

***O*-(3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-β-D-galactopyranosyl)-*N*-Boc-L-threonine allyl ester (11β):** $[\alpha]^{25}_D$ +19.9 (*c* 0.5, $CDCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.22 (m, 15H), 5.85−5.75 (m, 1H), 5.25−5.07 (m, 3H), 4.87 (d, J = 11.4 Hz, 1H), 4.78−4.69 (m, 2H), 4.63 (d, J = 11.7 Hz, 1H), 4.54 (d, J = 7.5 Hz, 3H), 4.46−4.44 (m, 3H), 4.37−4.35 (m, 1H), 4.28 (d, J = 9.6 Hz, 1H), 4.00 (d, J = 6.6 Hz, 1H), 3.61−3.50 (m, 3H), 1.46 (s, 9H), 1.13 (d, J = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 156.1, 137.8, 137.5, 136.5, 131.7, 128.5 (2C), 128.3, 128.2, 128.1, 128.0, 127.9, 127.8 (2C), 118.3, 98.3, 87.3, 80.0, 79.2, 75.1, 74.9, 73.6, 72.2, 71.4, 67.4, 65.9, 58.1, 28.3, 16.4; HRMS (ESI) calcd for $C_{39}H_{48}N_2O_{11}$ [M + Na]$^+$ 743.3167, found 743.3155.

Diethyl (3,4,6-tri-*O*-benzyl-2-deoxy-2-nitro-β-D-galactopyranosyl)malonate (13β): $[\alpha]^{25}_D$ +26.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.23 (m, 15H), 5.24 (t, J = 10.1 Hz, 1H), 4.84 (d, J = 11.2 Hz, 1H), 4.65 (d, J = 11.3 Hz, 1H), 4.52−4.38 (m, 5H), 4.19− 4.10 (m, 5H), 4.05 (d, J = 2.1 Hz, 1H), 3.73 (t, J = 6.7 Hz, 1H), 3.57−3.55 (m, 3H), 1.24 (t, J = 7.2 Hz, 3H), 1.13 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 165.3, 138.0, 137.7, 136.7, 128.5 (2C), 128.3, 128.2, 128.0, 127.9, 127.7, 85.6, 80.2, 77.5, 74.9, 74.8, 73.5, 72.5, 72.1, 67.8, 62.0, 61.9, 53.8, 13.9, 13.8; HRMS (ESI) calcd for $C_{34}H_{39}NO_{10}Na$ [M + Na]$^+$ 644.2489, found 644.2472.

Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-nitro-β-D-glucopyranoside (15β): $[\alpha]^{25}_D$ +13.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.16 (m, 15 H), 4.80−4.49 (m, 8H), 4.28 (t, J = 9.3 Hz, 1H), 3.76−3.70 (m, 3H), 3.58 (dt, J = 3.0, 9.9 Hz, 1H), 3.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.7, 137.4, 136.9, 128.5, 128.4 (2C), 128.1, 128.0 (2C), 127.8 (3C), 127.6, 100.7, 89.6, 81.3, 77.5, 75.4, 75.2, 75.1, 73.5, 67.9, 57.3; HRMS (ESI) calcd for $C_{28}H_{31}NO_7Na$ [M + Na]$^+$ 516.2013, found 516.1999.

(2-Trimethylsilyl)ethyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-nitro-β-D-glucopyranoside (16β): $[\alpha]^{25}_D$ +2.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33−7.17 (m, 15H), 4.81−4.49 (m, 8H), 4.28 (t, J = 9.6 Hz, 1H), 4.04−3.96 (m, 1H), 3.77−3.69 (m, 3H), 3.59−3.50 (m, 2H), 0.97−0.86 (m, 2H), 0.01 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.7, 137.4, 136.9, 128.5, 128.4 (2C), 128.1 (2C), 128.0, 127.9, 127.8 (2C), 127.7 (2C), 99.4, 89.8, 81.4, 77.6, 75.4, 75.2, 75.1, 73.5, 68.0, 67.8, 17.7, −1.5; HRMS (ESI) calcd for $C_{32}H_{41}NO_7SiNa$ [M + Na]$^+$ 602.2551, found 602.2544.

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4,6-tri-*O*-benzyl-2-deoxy-2-nitro-β-D-glucopyranosyl)-α-D-glucopyranoside (18β): $[\alpha]^{25}_D$ +10.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.16 (m, 30H), 4.99 (d, J = 10.8 Hz, 1H), 4.89−4.72 (m, 6 H), 4.66−4.48 (m, 7H), 4.42 (d, J = 11.1 Hz, 1H), 4.28 (dd, J = 9.3, 9.9 Hz, 1H), 4.11 (d, J = 10.5 Hz, 1H), 4.00 (t, J = 9.0, 1H), 3.76−3.64 (m, 5H), 3.57−3.50 (m, 2H), 3.45 (t, J = 9.6 Hz, 1H), 3.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.6, 138.2, 138.1, 137.8, 137.4, 136.8, 128.5, 128.4 (4C), 128.1 (2C), 128.0 (3C), 127.9, 127.8, 127.7 (2C), 127.6 (3C), 100.0, 98.1, 89.4, 82.0, 81.4, 79.6, 77.4 (2C), 75.8, 75.5, 75.4, 75.1, 74.8, 73.4 (2C), 69.4, 68.7, 68.1, 55.2; HRMS (ESI) calcd for $C_{55}H_{59}NO_{12}Na$ [M + Na]$^+$ 948.4019, found 948.4024.

Acknowledgment. This work is supported by the National Natural Science Foundation of China (20621062 and 90713003), the Chinese Academy of Sciences (KJCX2-YW-H08), and the Committee of Science and Technology of Shanghai (07DZ22001).

Supporting Information Available: ^{1}H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO900609S