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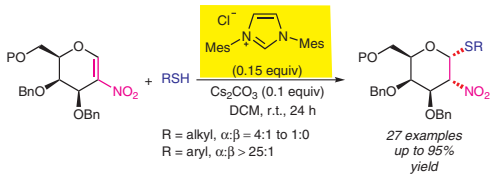
N-Heterocyclic Carbene Catalyzed Stereoselective Synthesis of 2-Nitro-thiogalactosides

Yu-Long Hu ‡
Bo-Bo Gou ‡
Jiao Wang
Ming Zhao
Jia-Lin Liu
Jie Chen*
Ling Zhou*

Key Laboratory of Synthetic and Natural Functional Molecule Chemistry of Ministry of Education, Department of Chemistry & Materials Science, National Demonstration Center for Experimental Chemistry Education, Northwest University, Xi'an 710127, P. R. of China
chmchenj@nwu.edu.cn
zhoul@nwu.edu.cn

‡ These authors contributed equally to this work.



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Abstract A highly selective NHC-catalyzed Michael addition of alkanethiols or thiophenol to 2-nitro-D-galactal compounds for the synthesis of 2-nitro-thiogalactoside derivatives has been developed for the first time. A wide variety of 1,2-*cis*-2-nitro-thiogalactosides can be prepared in good to excellent yields and high to excellent α-selectivities.

Key words N-heterocyclic carbenes, thiols, glycosylation, diastereoselectivity, catalysis

2-Amino-2-deoxyglycosides are ubiquitously distributed in organisms, such as the cells of glycolipid, lipopolysaccharide, glycoprotein, heparin, hyaluronic acid, heparan sulfate, chondroitin sulfate, and numerous aminoglycosidic antibiotics.[1] Many of these play vital roles in biochemistry and biology.[1,2] Besides *O*-glycosides, thioglycosides make up the most abundant family of naturally occurring thiosugars.[3] Thioglycosides are widely used as protecting groups in oligosaccharide synthesis, and the thio function can be activated by using a series of electrophiles to generate glycosylating species.[3,4] Moreover, it is already acknowledged that *S*-glycosides are more stable than *O*-glycosides in the chemical and enzymatic milieu.[5] Consequently, the design and synthesis of specific thioglycosides for potential use as carbohydrate therapeutics has attracted considerable attention. Many remarkable endeavors have been made to develop the thioglycosylation method over the past decades.[4,6–10] However, compared with the well-documented methodologies for the construction of *O*-glycosides, α-selective construction of thioglycosides has met with limited success. Although direct reaction of glycosyl thiols with alkyl halides provides the opportunity to construct thioglycosides in a stereoselective manner, the efficient synthesis of glycosyl thiols is not easy.[7] Therefore, the development of efficient and diastereoselective synthetic methods to synthesize thioglycosides using simple starting materials is highly desirable.

Scheme 1 outlines current procedures for the construction of 2-amino-2-deoxy thioglycoside bonds from thiols. For example, β-selective thioglycoside bond formation can be achieved by S_N2 reaction of halogenoses under basic conditions,[8] because the halogen atom generally adopts the axial position. Similar results could also be obtained under Lewis acid conditions.[9] Very recently, Borbás and co-workers developed a photoinitiated thiol-ene coupling reaction of 2-substituted glycals with thiols to give 1,2-*cis*-α-thioglycosides at –80 °C.[10] Notably, 2-nitroglycals are efficient glycosyl donors for the formation of glycosidic bonds, offering excellent yields and high stereoselectivities.[11] Indeed, reaction of 2-nitrogalactal with thiophenol in the presence of a stoichiometric amount of TlOEt gave the desired β-thioglycoside as the major products.[12] Schmidt and co-workers developed ^{t}BuOK-catalyzed thioglycosylation of 2-nitrogalactals with thiophenol to construct *S*-glycosidic bonds with excellent β-selectivity.[13] Recently, they explored the same reaction with excellent α-selectivity by using TEA as the catalyst and controlling the reaction times.[14] Sun, Yu, and co-workers developed DMAP-catalyzed glycosylation of 2-nitrogalactals with thiophenol to give β-thiogalactopyranoside as the major product.[15] However, all these reactions were performed by using thiophenols; reaction of 2-nitrogalactals with thiols to give (alkylthio)glycosides has remained unknown.

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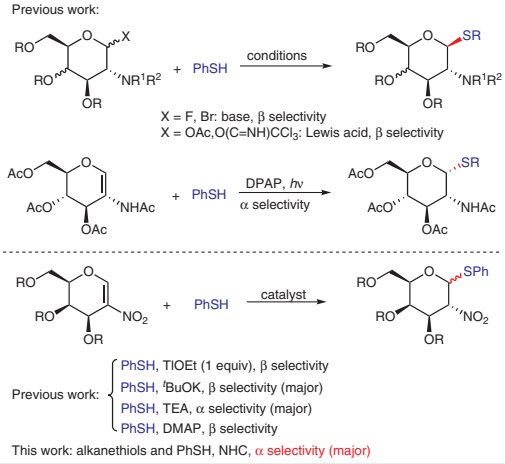
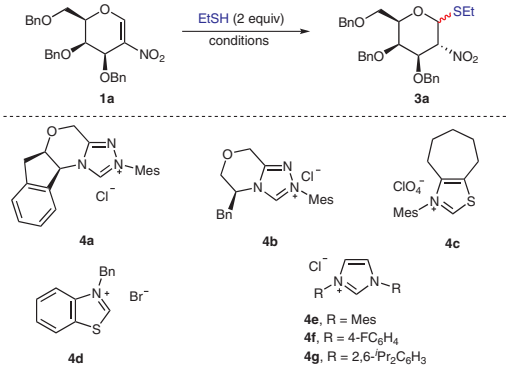


Scheme 1 2-Amino-2-deoxythioglycoside bond formation

In the past decades, N-heterocyclic carbene (NHC) catalyzed reactions have emerged as one of the most powerful strategies to construct complex molecules.[16] Recently, we have developed several unconventional NHC-catalyzed reactions.[17] Among them, NHC-catalyzed glycosylation of 2-nitrogalactals with alcohols and phenol has been developed, and a variety of 1,2-*cis*-2-nitroglycosides can be prepared in good to excellent yields and high to excellent α-selectivities.[18] To continue our research interest in the development and application of NHC-catalyzed reactions and C–S bond construction,[17–19] and to develop a new strategy for the selective construction of *S*-glycosides, herein, we report an efficient and stereoselective NHC-catalyzed Michael addition of thiols and thiophenol to 2-nitrogalactals to give α-thiogalactopyranosides as the major products.

Inspired by Schmidt's thioglycosylation reactions and the hydrogen-bonding activation model of NHC with the sulfhydryl group,[20] we hypothesized that such a bulky NHC–thiol complex would be well suited as a mild promoter for the stereoselective glycosylation of 2-nitroglycals. To test this hypothesis, 2-nitrogalactal (**1a**) and ethanethiol (**2a**) were selected as model substrates. As shown in Table 1, after treatment of 2-nitrogalactal and ethanethiol in a ratio of 1:2 in the presence of triazolium salt **4a** and cesium carbonate in dichloromethane at room temperature for 72 hours, the desired thiogalactopyranoside **3a** was obtained in 55% yield, albeit as a 2:1 α/β anomeric mixture (entry 1). Then various NHC catalysts were screened; the chiral triazolium salt **4b** returned product **3a** in 79% yield and as a 5:1 α/β anomeric mixture after 72 hours (entry 2). Thiazolium salt **4c** gave a further increase in α-selectivity (entry 3). The benzothiazole salt **4d** resulted in 80% yield with moderate stereoselectivity (entry 4). To our delight, when imidazolium salts **4e–g** were utilized as catalysts, the yields were all improved (entries 5–7). More importantly, a 13:1 α/β ratio was obtained when the imidazolium salt **4e** with two bulky 2,4,6-trimethylphenyl substituents was used (entry 5). These results suggest that steric bulk in the aromatic substituent of the NHC plays a crucial role in determining glycosylation stereoselectivity (entry 5 vs entries 6 and 7).

Table 1 Optimization of the Reaction Conditions[a]



Entry	Catalyst	Solvent	Time (h)	Yield (%)[b]	Ratio α/β[c]
1	**4a**	DCM	72	55	2:1
2	**4b**	DCM	72	79	5:1
3	**4c**	DCM	48	60	7:1
4	**4d**	DCM	24	80	5:1
5	**4e**	DCM	24	85	13:1
6	**4f**	DCM	24	87	6:1
7	**4g**	DCM	24	82	5:1
8[d]	**4e**	DCM	48	71	3:1
9[e]	**4e**	DCM	36	75	6:1
10[f]	**4e**	DCM	48	80	9:1
11	**4e**	*n*-hexane	48	77	6:1
12	**4e**	CCl_4	48	80	7:1
13	**4e**	MeCN	72	72	3:1
14	**4e**	1,4-dioxane	72	trace	–
15[g]	**4e**	DCM	8	81	8:1
16[h]	**4e**	DCM	72	60	12:1
17[i]	**4e**	DCM	72	trace	–
18[j]	–	DCM	0.5	75	2:1
19	–	DCM	0.5	80	3:1

[a] Reaction conditions: **1a** (0.10 mmol), EtSH (0.20 mmol), catalyst **4** (0.015 mmol, 15 mol%), Cs_2CO_3 (0.010 mmol, 10 mol%), solvent (1.0 mL), r.t., under argon.
[b] Yields of isolated products.
[c] Determined by ^{1}H NMR spectroscopy.
[d] K_2CO_3 as base.
[e] KHMDS as base.
[f] ^{t}BuOK as base.
[g] At 40 °C.
[h] At 0 °C.
[i] At –30 °C.
[j] TEA as base.

Then various bases were evaluated; K_2CO_3, KHMDS, and ^{t}BuOK all provided diminished yields with decreased stereoselectivities (Table 1, entries 8–10). It seems that the bulky cesium ion may also impact the selectivity. Next, we decided to explore the solvent effects by using **4e** as the model catalyst. The reactions proceeded smoothly in nonpolar solvents such as *n*-hexane or CCl_4, giving the desired product in 77–80% yield with clearly decreased α/β ratios (entry 5 vs entries 11 and 12). Notably, a poorer stereoselectivity was observed when the polar solvent acetonitrile was used (α/β 3:1, entry 13). However, no reaction was detected when the polar solvent 1,4-dioxane was used (entry 14). Further optimization of this reaction by varying the temperature allowed us to explore the optimal conditions; higher and lower reaction temperatures all returned lower stereoselectivities (entries 15–17). In addition, when TEA or Cs_2CO_3 was used as base without NHC under the optimal conditions, both returned the desired product quickly, albeit with poor stereoselectivity (entries 18 and 19).

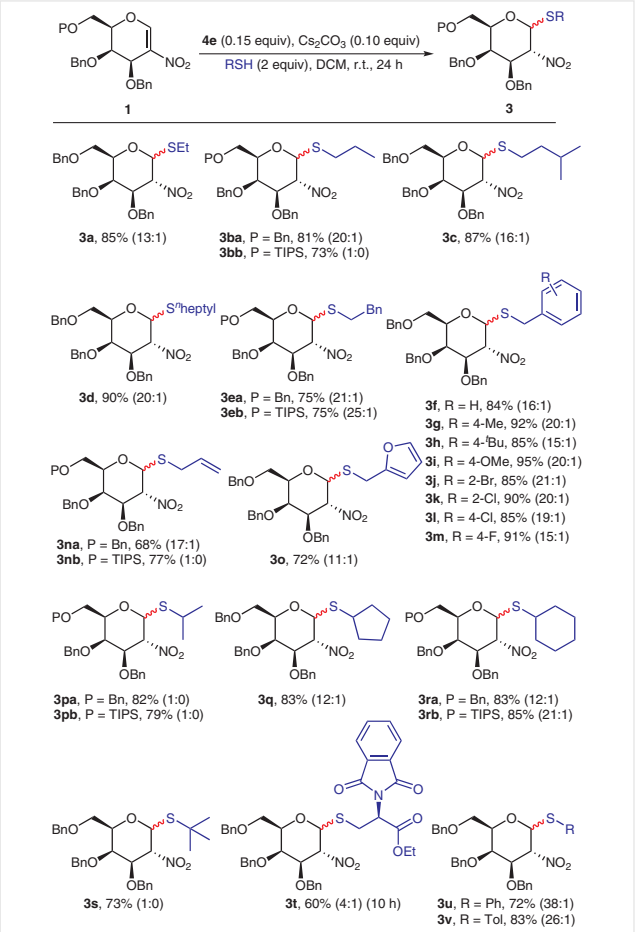
To test the stability of compound **3a**α and the equilibration between **3a**α and **3a**β, compound **3a**α was treated with a series of reaction conditions. As shown in Table 2, after treatment of **3a**α under the optimal conditions in the absence of EtSH for 1 hour, about 5% of starting material **1a** was observed (entry 1). Upon addition of EtSH, **3a**α was retained (entry 2). These results indicate that this Michael addition reaction is reversible. Interestingly, **3a**β was observed after 24 hours under the same reaction conditions or when using more NHC catalyst (entries 3–5). Precatalyst **4e** in the absence of Cs_2CO_3 gave no reaction, while Cs_2CO_3 in the absence of **4e** returned **3a**β as a major product after 24 hours (entries 6–8); this suggests that the base plays a key role in the reversible process.

Table 2 Stability of **3a**α in DCM at Room Temperature[a]

Entry	**4e** (equiv)	Cs_2CO_3 (equiv)	EtSH (equiv)	Time (h)	Products[b]
1	0.15	0.1	0	1	**1a** + **3a**α (1:18)
2	0.15	0.1	2	1	**3a**α
3	0.15	0.1	2	24	**3a**α + **3a**β (15:1)
4	0.75	0.5	2	1	**3a**α + **3a**β (22:1)
5	0.75	0.5	2	24	**3a**α + **3a**β (3:1)
6	0.75	0	2	24	**3a**α
7	0	0.5	2	1	**3a**α + **3a**β (8:1)
8	0	0.5	2	24	**3a**α + **3a**β (1:12)

[a] Reaction conditions: **3a**α (1.0 equiv), **4e**, EtSH, Cs_2CO_3, DCM, r.t., 24 h.
[b] Yields 90–100%; product ratios obtained by ^{1}H NMR spectroscopy.

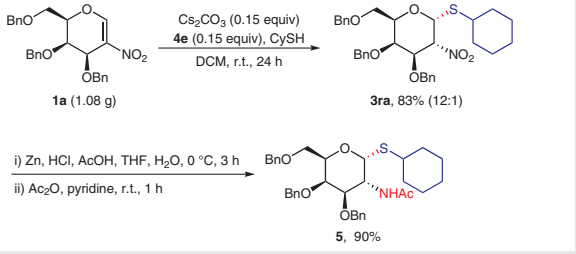
With the optimized conditions in hand, we tested this method on a series of thiols (Scheme 2). The reactions all proceeded smoothly to yield the corresponding *S*-glycosides in good to excellent yields and high to excellent stereoselectivities. Alkanethiols all gave good yields (73–90%) and high to excellent α-stereoselectivities (13:1 to only α; **3a–d**, **3pa–pb**, **3s**). Various benzyl thiols were well tolerated by this method, and the corresponding products were obtained in excellent yields and α-selectivities (**3f–m**). Allyl thiol, furfuryl thiol, cyclopentanethiol, and cyclohexanethiol all gave the corresponding thioglycosides in good yields (68–85%) and high to excellent α-stereoselectivities (11:1 to only α; **3na–o**, **3q–rb**). Notably, the reaction of C-6 silyl-protected galactal with some thiols afforded the desired products with clearly improved α/β ratios (**3bb**, **3eb**, **3nb**, **3rb** vs **3ba**, **3ea**, **3na**, **3ra**), probably for steric reasons. Apart from the simple thiols described above, an L-cysteine derivative were also selected as substrates to test this method. Satisfactorily, the desired **3t** was obtained in moderate yield (60%) with acceptable α-selectivity (α/β 4:1). To further demonstrate the value of this method, weakly nucleophilic



Scheme 2 NHC-catalyzed stereoselective glycosylation of 2-nitrogalactals with thiols and thiophenol. *Reagents and conditions*: **1** (0.10 mmol), RSH (0.20 mmol), **4e** (0.015 mmol), Cs_2CO_3 (0.010 mmol), DCM (1.0 mL), r.t., under argon, 24 h; yields shown are for isolated products; both isomers were separated by flash column chromatography.

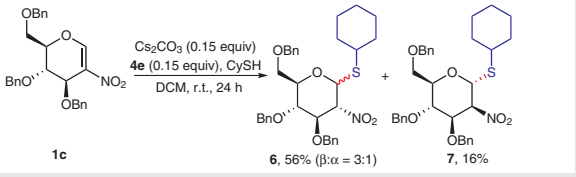
thiophenols were used as glycosylation acceptors, giving the desired products **3u** and **3v** smoothly (**3u**, 72% yield, α/β 38:1; **3v**, 83% yield, α/β 26:1).

To test the synthetic practicability of this stereoselective glycosylation method, a scaled-up experiment was carried out under the optimal reaction conditions, and **3ra** was obtained in comparable yield and selectivity (Scheme 3; 83% yield, α/β 12:1). To further demonstrate the synthetic practicability of the newly developed methodology, synthesis of mycothiol analogue **5** was carried out. Reduction of the nitro group of α-thioglycoside **3ra** by using Zn/HCl in a mixture of AcOH/THF/H_2O, followed by N-acetylation with acetic anhydride in pyridine, furnished the target **5** in 90% yield over two steps (Scheme 3).[21]



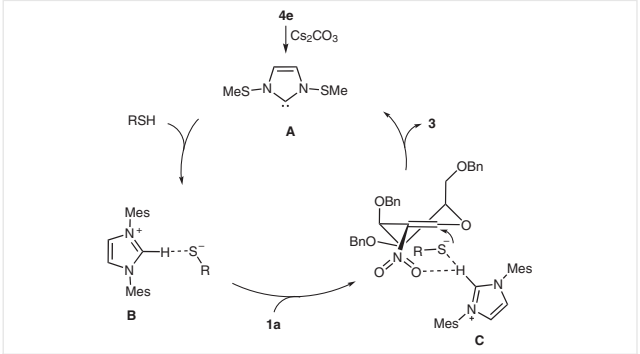
Scheme 3 Gram-scale preparation of **3ra** and synthesis of compound **5**

2-Nitroglucal was also examined under the optimal reaction conditions. Not surprisingly, the desired thioglycoside **6** was obtained with β-selectivity as the major product, together with the minor product **7** (Scheme 4). These results are accordance with our previously proposed mechanism,[18] that the C-4 stereocenter is also responsible for the stereocontrol in this glycosylation reaction.



Scheme 4 Reaction of 2-nitroglucal with cyclohexanethiol

Based on the literature and our previous work, a plausible mechanism is proposed (Scheme 5). The deprotonation of imidazolium salt **4e** by Cs_2CO_3 leads to carbene **A**, which is also recognized as a carbon-centered Brønsted base. Subsequently, **A** interacts with the sulfhydryl group via hydrogen bonding to give an NHC–HSR complex **B**, which facilitates the Michael addition of the sulfhydryl group to the 2-nitrogalactal from the sterically favored side. Finally, an α-anomer bearing a C-2 carbanion intermediate was generated stereoselectively, together with **4e**. Then protonation of the C-2 carbanion intermediate with **4e** at the β-side leads to the 1,2-*cis*-glycoside product and regenerates the NHC organocatalyst.



Scheme 5 Proposed mechanism

In summary, we have described the first NHC-catalyzed direct and stereoselective thioglycosylation of 2-nitrogalactals to afford α-*S*-linked-2-amino-2-deoxygalactosides in good to excellent yields and high selectivities under simple and practicable conditions. The method is widely applicable to a range of nucleophilic acceptors, covering various alkanethiols and thiophenols. Furthermore, we have demonstrated the applicability of the catalytic method in the synthesis of mycothiol analogues. This NHC-catalyzed system has the potential to be a valuable platform for a wide range of broadly useful stereocontrolled syntheses of glycopeptides, 2-amino sugars, and other bioactive natural or non-natural products. Further investigations aiming at a better understanding of the mechanism and extending the scope as well as application of this glycosylation reaction are underway.

All reactions that required anhydrous conditions were carried by standard procedures under argon atmosphere. Commercially available reagents were used as received. The solvents were dried by distillation over the appropriate drying reagents. IR spectra were recorded on a TENSOR 27FT-IR spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a Varian (400 MHz) spectrometer. Chemical shifts (δ) are reported in ppm relative to TMS (δ = 0.00) for the ^1H NMR and chloroform (δ = 77.0) for the ^{13}C NMR measurements. High resolution mass spectra were obtained on an UltiMate 3000 spectrometer. Enantiomeric excesses were determined by HPLC analysis on Dionex UltiMate 3000 HPLC units, including the following instruments: pump, LPG-3400SD; detector, VWD-3100; column, Daicel Chiralpak IA, IB, IC, or ID. Optical rotations were recorded on a Jasco DIP-1000 polarimeter. Reactions were followed by TLC (0.254 mm silica gel 60-F plates). Visualization was accomplished with UV light. Flash chromatography separations were performed on 200–300 mesh silica gel.

NHC-Catalyzed Stereoselective Glycosylation of 2-Nitrogalactal; General Procedure

A suspension of Cs_2CO_3 (3.3 mg, 0.010 mmol), **4e** (5.1 mg, 0.015 mmol), and tri-*O*-benzyl-2-nitrogalactal (**1a**; 46 mg, 0.10 mmol, 1.0 equiv) in anhydrous DCM (1.0 mL, 0.01 M) was stirred in a Schlenk flask under an argon atmosphere at room temperature for 0.5 h. To the mixture was added the appropriate RSH (0.20 mmol, 2.0 equiv) in one portion. The reaction mixture was stirred until the consumption

of **1a**, as monitored by TLC. Upon completion of the reaction, the solvent was removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, *n*-hexane/EtOAc) to yield the corresponding product **3**.

Ethyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3aα, 3aβ)

Yield: **3a**α: 41 mg (79%) and **3a**β: 3 mg (6%); clear oils.

3aα

$[\alpha]_D^{24}$ +12.9 (*c* 2.0, $CHCl_3$).

IR (KBr): 2922, 2360, 1552, 1357, 1062, 739 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.19 (m, 15 H), 5.73 (d, *J* = 6.0 Hz, 1 H), 5.28 (dd, *J* = 10.8, 6.0 Hz, 1 H), 4.84 (d, *J* = 11.1 Hz, 1 H), 4.71 (s, 2 H), 4.51–4.41 (m, 3 H), 4.40–4.35 (m, 1 H), 4.29 (dd, *J* = 10.8, 2.5 Hz, 1 H), 4.03–3.99 (m, 1 H), 3.62–3.50 (m, 2 H), 2.67–2.50 (m, 2 H), 1.24 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.87, 137.67, 137.09, 128.51, 128.44, 128.34, 128.18, 128.13, 127.85, 127.76, 84.35, 81.50, 75.93, 75.18, 73.50, 73.38, 73.11, 69.93, 68.24, 25.16, 14.53.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{29}H_{33}NO_6SNa$: 546.1921; found: 546.1922.

***n*-Propyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3baα, 3baβ)**

Yield: **3ba**α: 41 mg (77%) and **3ba**β: 2 mg (4%); clear oils.

3baα

$[\alpha]_D^{24}$ +8.8 (*c* 0.5, $CHCl_3$).

IR (KBr): 2938, 1907, 1554, 1099, 734, 688 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.21 (m, 15 H), 5.71 (d, J = 6.0 Hz, 1 H), 5.28 (dd, *J* = 10.8, 6.0 Hz, 1 H), 4.84 (d, *J* = 11.1 Hz, 1 H), 4.75–4.69 (m, 2 H), 4.47 (dd, *J* = 11.4, 5.9 Hz, 2 H), 4.42 (d, *J* = 11.7 Hz, 1 H), 4.37 (t, *J* = 6.5 Hz, 1 H), 4.29 (dd, *J* = 10.9, 2.9 Hz, 1 H), 4.01 (d, *J* = 2.5 Hz, 1 H), 3.60–3.52 (m, 2 H), 2.63–2.47 (m, 2 H), 1.65–1.57 (m, 2 H), 0.93 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.88, 137.69, 137.11, 128.51, 128.43, 128.34, 128.19, 128.12, 127.84, 127.73, 84.39, 81.90, 75.90, 75.17, 73.48, 73.40, 73.12, 69.95, 68.28, 33.15, 22.68, 13.29.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{30}H_{35}NO_6SNa$: 560.2077; found: 560.2071.

***n*-Propyl 3,4-Di-*O*-benzyl-2-deoxy-2-nitro-6-*O*-triisopropylsilyl-8-D-galactopyranoside (3bb)**

Yield: 44 mg (73%); clear oil.

3bbα

$[\alpha]_D^{22}$ +9.7 (*c* 1.0, $CHCl_3$).

IR (KBr): 2923, 2376, 1556, 1114, 734, 688 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.26 (m, 10 H), 5.71 (d, *J* = 6.0 Hz, 1 H), 5.28 (dd, *J* = 10.8, 6.0 Hz, 1 H), 4.85 (d, *J* = 11.1 Hz, 1 H), 4.77 (d, *J* = 10.8 Hz, 1 H), 4.72 (d, *J* = 10.9 Hz, 1 H), 4.53 (d, *J* = 11.1 Hz, 1 H), 4.33 (dd, *J* = 10.8, 2.7 Hz, 1 H), 4.20 (t, *J* = 6.5 Hz, 1 H), 3.97 (d, *J* = 2.3 Hz, 1 H), 3.73 (d, *J* = 6.5 Hz, 2 H), 2.64–2.48 (m, 2 H), 1.65–1.56 (m, 2 H), 1.10–1.03 (m, 21 H), 0.95 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.98, 137.16, 128.53, 128.31, 128.30, 128.16, 128.12, 127.79, 84.50, 81.68, 75.92, 75.18, 73.38, 73.24, 71.78, 61.74, 32.91, 22.68, 17.94, 13.29, 11.76.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{32}H_{49}NO_6SSiNa$: 626.2942; found: 626.2930.

3-Methylbutyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3cα, 3cβ)

Yield: **3c**α: 47 mg (83%) and **3c**β: 3 mg (4%); clear oils.

3cα

$[\alpha]_D^{22}$ +12.5 (*c* 1.0, $CHCl_3$).

IR (KBr): 2953, 1570, 1373, 1068, 734, 673 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.18 (m, 15 H), 5.71 (d, *J* = 5.8 Hz, 1 H), 5.28 (dd, *J* = 10.4, 6.3 Hz, 1 H), 4.84 (d, *J* = 11.1 Hz, 1 H), 4.75–4.67 (m, 2 H), 4.52–4.34 (m, 4 H), 4.29 (d, *J* = 10.8 Hz, 1 H), 4.00 (s, 1 H), 3.62–3.49 (m, 2 H), 2.66–2.49 (m, 2 H), 1.69–1.54 (m, 1 H), 1.49–1.40 (m, 2 H), 0.85 (dd, *J* = 6.3, 3.7 Hz, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.78, 137.57, 136.97, 128.48, 128.40, 128.31, 128.15, 128.12, 128.09, 127.83, 127.73, 84.30, 81.68, 75.84, 75.11, 73.43, 73.24, 73.04, 69.87, 68.18, 37.98, 29.03, 27.17, 22.18, 22.03.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{32}H_{39}NO_6SNa$: 588.2390; found: 588.2385.

1-Heptyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3dα, 3dβ)

Yield: **3d**α: 51 mg (86%) and **3d**β: 3 mg (4%); clear oils.

3dα

$[\alpha]_D^{22}$ +8.2 (*c* 1.0, $CHCl_3$).

IR (KBr): 2938, 1601, 1053, 795, 689 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.22 (m, 15 H), 5.71 (d, *J* = 6.0 Hz, 1 H), 5.28 (dd, *J* = 10.8, 6.0 Hz, 1 H), 4.84 (d, *J* = 11.1 Hz, 1 H), 4.75–4.68 (m, 2 H), 4.47 (dd, *J* = 11.4, 5.3 Hz, 2 H), 4.43 (s, 1 H), 4.38 (dd, *J* = 11.5, 4.9 Hz, 1 H), 4.29 (dd, *J* = 10.9, 2.9 Hz, 1 H), 4.01 (d, *J* = 2.5 Hz, 1 H), 3.61–3.51 (m, 2 H), 2.64–2.49 (m, 2 H), 1.60–1.51 (m, 2 H), 1.32–1.19 (m, 8 H), 0.87 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.79, 137.59, 137.03, 128.49, 128.41, 128.32, 128.16, 128.13, 128.09, 127.83, 127.73, 84.31, 81.78, 75.84, 75.12, 73.44, 73.23, 73.05, 69.84, 68.19, 31.61, 31.06, 29.21, 28.72, 28.61, 22.54, 14.07.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{34}H_{43}NO_6SNa$: 616.2703; found: 616.2714.

2-Phenylethyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3eaα, 3eaβ)

Yield: **3ea**α: 42 mg (71%) and **3ea**β: 2 mg (4%); clear oils.

3eaα

$[\alpha]_D^{21}$ +5.8 (*c* 3.0, $CHCl_3$).

IR (KBr): 3014, 1540, 1114, 1084, 750, 689 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.24 (m, 15 H), 7.24–7.19 (m, 3 H), 7.14 (d, *J* = 7.1 Hz, 2 H), 5.71 (d, *J* = 6.0 Hz, 1 H), 5.27 (dd, *J* = 10.9, 6.0 Hz, 1 H), 4.84 (d, *J* = 11.2 Hz, 1 H), 4.71 (s, 2 H), 4.48 (d, *J* = 3.1 Hz, 1

H), 4.45 (d, *J* = 2.5 Hz, 1 H), 4.40 (d, *J* = 11.7 Hz, 1 H), 4.34 (t, *J* = 6.4 Hz, 1 H), 4.28 (dd, *J* = 10.9, 2.7 Hz, 1 H), 4.00 (d, *J* = 2.1 Hz, 1 H), 3.59–3.49 (m, 2 H), 2.90–2.75 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.78, 137.78, 137.58, 137.03, 128.51, 128.47, 128.44, 128.35, 128.17, 128.13, 127.88, 127.87, 127.78, 126.48, 84.29, 81.84, 75.85, 75.17, 73.52, 73.29, 73.11, 70.03, 68.28, 35.92, 32.31.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{35}H_{37}NO_6SNa$: 622.2234; found: 622.2238.

2-Phenylethyl 3,4-Di-*O*-benzyl-2-deoxy-2-nitro-6-*O*-triisopropylsilyl-8-D-galactopyranoside (3eb*α*, 3eb*β*)

Yield: **3eb**α: 49 mg (72%) and **3eb**β: 2 mg (3%); clear oils.

3eb*α*

$[\alpha]_D^{21}$ +7.7 (*c* 1.0, $CHCl_3$).

IR (KBr): 3021, 1531, 1099, 1003, 738, 682 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.26 (m, 12 H), 7.24–7.12 (m, 3 H), 5.68 (d, *J* = 6.0 Hz, 1 H), 5.27 (dd, *J* = 10.3, 5.4 Hz, 1 H), 4.84 (d, *J* = 11.1 Hz, 1 H), 4.75 (d, *J* = 10.8 Hz, 1 H), 4.70 (d, *J* = 10.8 Hz, 1 H), 4.52 (d, *J* = 11.1 Hz, 1 H), 4.30 (dd, *J* = 10.9, 2.9 Hz, 1 H), 4.18 (t, *J* = 6.5 Hz, 1 H), 3.96 (d, *J* = 2.5 Hz, 1 H), 3.73 (d, *J* = 6.6 Hz, 2 H), 2.90–2.75 (m, 4 H), 1.05–1.00 (m, 21 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.71, 137.91, 137.10, 128.54, 128.49, 128.43, 128.33, 128.30, 128.19, 128.15, 127.83, 126.48, 84.42, 81.67, 75.88, 75.19, 73.29, 73.24, 71.89, 61.73, 36.01, 32.05, 17.94, 11.74.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{37}H_{51}NO_6SSiNa$: 688.3099; found: 688.3105.

Benzyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3f*α*, 3f*β*)

Yield: **3f**α: 46 mg (79%) and **3f**β: 3 mg (5%); clear oils.

3f*α*

$[\alpha]_D^{24}$ +46.4 (*c* 1.0, $CHCl_3$).

IR (KBr): 2920, 1551, 1463, 1335, 1267, 752 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.15 (m, 20 H), 5.54 (d, *J* = 6.0 Hz, 1 H), 5.23 (dd, *J* = 10.8, 6.0 Hz, 1 H), 4.82 (d, *J* = 11.2 Hz, 1 H), 4.68 (s, 2 H), 4.49–4.38 (m, 3 H), 4.38–4.23 (m, 2 H), 3.99 (d, *J* = 2.3 Hz, 1 H), 3.81–3.67 (m, 2 H), 3.62–3.49 (m, 1 H), 3.44–3.34 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.78, 137.67, 137.02, 136.54, 128.99, 128.52, 128.49, 128.45, 128.32, 128.15, 128.11, 127.86, 127.78, 127.32, 84.16, 80.13, 76.15, 75.12, 73.51, 73.32, 73.09, 70.09, 68.29, 34.30.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{35}NO_6SNa$: 608.2077; found: 608.2073.

4-Methylbenzyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3g*α*, 3g*β*)

Yield: **3g**α: 52 mg (87%) and **3g**β: 3 mg (5%); clear oils.

3g*α*

$[\alpha]_D^{20}$ +13.2 (*c* 1.0, $CHCl_3$).

IR (KBr): 3044, 1585, 1220, 764, 673 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.18 (m, 15 H), 7.13 (d, *J* = 7.9 Hz, 2 H), 7.06 (d, *J* = 8.0 Hz, 2 H), 5.52 (d, *J* = 6.0 Hz, 1 H), 5.22 (dd, *J* = 10.8, 6.0 Hz, 1 H), 4.82 (d, *J* = 11.2 Hz, 1 H), 4.68 (s, 2 H), 4.49–4.40 (m, 3 H), 4.36 (t, *J* = 6.4 Hz, 1 H), 4.31 (dd, *J* = 10.9, 2.7 Hz, 1 H), 3.99 (d, *J* = 2.4 Hz, 1 H), 3.74 (d, *J* = 13.2 Hz, 1 H), 3.64 (d, *J* = 13.2 Hz, 1 H), 3.58–3.51 (m, 1 H), 3.44 (dd, *J* = 9.2, 6.1 Hz, 1 H), 2.30 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.70, 137.61, 136.97, 136.95, 133.25, 129.19, 128.89, 128.48, 128.44, 128.31, 128.17, 128.13, 128.09, 127.85, 127.75, 84.08, 79.86, 76.12, 75.07, 73.47, 73.17, 73.02, 69.94, 68.27, 33.85, 21.08.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{35}H_{37}NO_6SNa$: 622.2234; found: 622.2241.

4- *tert*-Butylbenzyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3h*α*, 3h*β*)

Yield: **3h**α: 51 mg (80%) and **3h**β: 3 mg (5%); clear oils.

3h*α*

$[\alpha]_D^{22}$ +14.9 (*c* 2.0, $CHCl_3$).

IR (KBr): 2953, 1554, 1129, 765, 704 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.24 (m, 15 H), 7.21–7.16 (m, 4 H), 5.55 (d, *J* = 5.8 Hz, 1 H), 5.23 (dd, *J* = 10.6, 6.0 Hz, 1 H), 4.82 (d, *J* = 11.2 Hz, 1 H), 4.68 (s, 2 H), 4.50–4.30 (m, 5 H), 3.98 (s, 1 H), 3.75 (d, *J* = 13.3 Hz, 1 H), 3.66 (d, *J* = 13.2 Hz, 1 H), 3.58–3.46 (m, 2 H), 1.29 (s, 9 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 150.22, 137.72, 137.61, 136.95, 133.23, 128.67, 128.49, 128.45, 128.32, 128.17, 128.15, 128.11, 127.86, 127.76, 84.11, 79.90, 76.13, 75.08, 73.49, 73.21, 73.05, 69.94, 68.34, 34.44, 33.76, 31.26.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{38}H_{43}NO_6SNa$: 664.2703; found: 664.2698.

4-Methoxybenzyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3i*α*, 3i*β*)

Yield: **3i**α: 56 mg (90%) and **3i**β: 3 mg (5%); clear oils.

3i*α*

$[\alpha]_D^{25}$ +23.4 (*c* 2.0, $CHCl_3$).

IR (KBr): 2922, 1560, 1460, 1375, 752 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.13 (m, 17 H), 6.79 (d, *J* = 8.5 Hz, 2 H), 5.52 (d, *J* = 6.0 Hz, 1 H), 5.22 (dd, *J* = 10.8, 6.0 Hz, 1 H), 4.82 (d, *J* = 11.2 Hz, 1 H), 4.68 (s, 2 H), 4.50–4.39 (m, 3 H), 4.37 (t, *J* = 6.4 Hz, 1 H), 4.35–4.24 (m, 1 H), 4.07–3.92 (m, 1 H), 3.79–3.77 (m, 3 H), 3.73–3.62 (m, 2 H), 3.58–3.44 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.80, 137.76, 137.67, 137.01, 130.16, 128.49, 128.45, 128.32, 128.27, 128.17, 128.14, 128.10, 127.86, 127.76, 113.91, 84.13, 79.89, 76.18, 75.10, 73.51, 73.31, 73.07, 70.06, 68.40, 55.21, 33.63.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{35}H_{37}NO_7SNa$: 638.2183; found: 638.2179.

2-Bromobenzyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3j*α*, 3j*β*)

Yield: **3j**α: 54 mg (81%) and **3j**β: 3 mg (4%); clear oils.

3j*α*

$[\alpha]_D^{25}$ +12.6 (*c* 2.0, $CHCl_3$).

IR (KBr): 3075, 1555, 1113, 734, 673 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.50 (d, *J* = 7.9 Hz, 1 H), 7.38–7.25 (m, 15 H), 7.23–7.15 (m, 2 H), 7.07 (t, *J* = 7.6 Hz, 1 H), 5.66 (d, *J* = 5.9 Hz, 1 H), 5.26 (dd, *J* = 10.9, 5.9 Hz, 1 H), 4.82 (d, *J* = 11.2 Hz, 1 H), 4.68 (s, 2 H), 4.46 (d, *J* = 11.2 Hz, 1 H), 4.42 (s, 2 H), 4.36 (t, *J* = 6.4 Hz, 1 H), 4.30 (dd, *J* = 10.9, 1.7 Hz, 1 H), 4.01 (s, 1 H), 3.89 (d, *J* = 13.3 Hz, 1 H), 3.84 (d, *J* = 13.3 Hz, 1 H), 3.54 (t, *J* = 8.2 Hz, 1 H), 3.38 (dd, *J* = 8.8, 6.0 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.70, 137.57, 136.92, 136.04, 133.08, 130.99, 129.00, 128.48, 128.44, 128.32, 128.21, 128.12, 128.10, 127.87, 127.80, 127.39, 124.47, 84.08, 80.55, 75.98, 75.14, 73.45, 73.09, 73.03, 69.94, 67.92, 34.86.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{34}BrNO_6SNa$: 686.1182; found: 686.1180.

2-Chlorobenzyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3kα, 3kβ)

Yield: **3k**α: 53 mg (86%) and **3k**β: 3 mg (4%); clear oils.

3kα

$[\alpha]_D^{22}$ +15.4 (*c* 1.0, $CHCl_3$).

IR (KBr): 3029, 1570, 1220, 1114, 779, 673 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.26 (m, 15 H), 7.23–7.19 (m, 2 H), 7.18–7.10 (m, 2 H), 5.65 (d, *J* = 5.9 Hz, 1 H), 5.26 (dd, *J* = 11.3, 5.4 Hz, 1 H), 4.82 (d, *J* = 11.2 Hz, 1 H), 4.67 (s, 2 H), 4.46 (d, *J* = 11.1 Hz, 1 H), 4.41 (d, *J* = 12.7 Hz, 2 H), 4.35 (t, *J* = 6.5 Hz, 1 H), 4.30 (dd, *J* = 10.9, 1.3 Hz, 1 H), 4.01 (s, 1 H), 3.88 (d, *J* = 13.3 Hz, 1 H), 3.84 (d, *J* = 13.5 Hz, 1 H), 3.54 (t, *J* = 8.2 Hz, 1 H), 3.38 (dd, *J* = 8.7, 6.1 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.70, 137.58, 136.92, 134.41, 134.05, 130.95, 129.77, 128.80, 128.48, 128.43, 128.32, 128.20, 128.13, 128.10, 127.87, 127.86, 127.78, 126.74, 84.09, 80.52, 75.98, 75.14, 73.45, 73.10, 73.03, 69.91, 67.95, 32.09.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{34}ClNO_6SNa$: 642.1688; found: 642.1701.

4-Chlorobenzyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3lα, 3lβ)

Yield: **3l**α: 50 mg (81%) and **3l**β: 3 mg (4%); clear oils.

3lα

$[\alpha]_D^{25}$ +19.2 (*c* 2.0, $CHCl_3$).

IR (KBr): 2922, 1554, 1498, 1361, 1097, 742 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.16 (m, 19 H), 5.51 (d, *J* = 5.9 Hz, 1 H), 5.23 (dd, *J* = 10.6, 6.0 Hz, 1 H), 4.82 (d, *J* = 11.2 Hz, 1 H), 4.68 (s, 2 H), 4.52–4.36 (m, 3 H), 4.30 (d, *J* = 7.3 Hz, 2 H), 3.98 (s, 1 H), 3.75–3.62 (m, 2 H), 3.53–3.38 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.71, 137.61, 136.96, 135.17, 133.14, 130.36, 128.69, 128.52, 128.48, 128.35, 128.18, 128.15, 127.92, 127.80, 84.08, 80.03, 76.12, 75.13, 73.56, 73.26, 73.13, 70.22, 68.37, 33.56.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{34}ClNO_6SNa$: 642.1688; found: 642.1677.

4-Fluorobenzyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3mα, 3mβ)

Yield: **3m**α: 51 mg (85%) and **3m**β: 3 mg (6%); clear oils.

3mα

$[\alpha]_D^{24}$ +21.7 (*c* 2.0, $CHCl_3$).

IR (KBr): 2922, 2360, 1552, 1388, 1267, 1064, 748 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.16 (m, 17 H), 6.94 (t, *J* = 8.4 Hz, 2 H), 5.50 (d, *J* = 5.7 Hz, 1 H), 5.23 (dd, *J* = 10.1, 6.2 Hz, 1 H), 4.82 (d, *J* = 11.2 Hz, 1 H), 4.69 (s, 2 H), 4.50–4.39 (m, 3 H), 4.37–4.27 (m, 2 H), 3.99 (s, 1 H), 3.76–3.65 (m, 2 H), 3.57–3.40 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 162.00 (d, *J* = 246.1 Hz), 137.67 (d, *J* = 10.1 Hz), 136.98, 132.24 (d, *J* = 2.9 Hz), 130.62 (d, *J* = 8.1 Hz), 128.52, 128.48, 128.36, 128.19, 128.16, 127.91, 127.80, 115.42 (d, *J* = 21.5 Hz), 84.10, 79.95, 76.15, 75.13, 73.56, 73.29, 73.13, 70.22, 68.42, 33.45.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{34}FNO_6SNa$: 626.1983; found: 626.1976.

Allyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3naα, 3naβ)

Yield: **3na**α: 34 mg (64%) and **3na**β: 2 mg (4%); clear oils.

3naα

$[\alpha]_D^{24}$ +7.5 (*c* 0.5, $CHCl_3$).

IR (KBr): 2920, 1625, 1458, 1373, 1066, 734 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.47–7.29 (m, 15 H), 5.84–5.76 (m, 1 H), 5.73 (d, *J* = 6.0 Hz, 1 H), 5.70 (dd, *J* = 10.8, 6.0 Hz, 1 H), 5.21 (d, *J* = 3.2 Hz, 1 H), 5.18 (s, 1 H), 4.91 (d, *J* = 11.2 Hz, 1 H), 4.78 (s, 2 H), 4.57–4.52 (m, 3 H), 4.43 (t, *J* = 6.4 Hz, 1 H), 4.38 (dd, *J* = 10.8, 2.8 Hz, 1 H), 4.09 (d, *J* = 2.0 Hz, 1 H), 3.71–3.57 (m, 2 H), 3.32–3.22 (m, 1 H), 3.21–3.14 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.77, 137.62, 137.01, 132.24, 128.47, 128.41, 128.30, 128.12, 128.08, 127.83, 127.72, 118.62, 84.14, 79.76, 76.14, 75.11, 73.46, 73.27, 73.04, 70.10, 68.27, 32.73.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{33}NO_6SNa$: 558.1921; found: 558.1913.

Allyl 3,4-Di-*O*-benzyl-2-deoxy-2-nitro-6-*O*-triisopropylsilyl-8-D-galactopyranoside (3nb)

Yield: **3nb**: 46 mg (77%); clear oil.

3nbα

$[\alpha]_D^{22}$ +8.5 (*c* 1.0, $CHCl_3$).

IR (KBr): 2968, 2847, 1549, 1068, 734, 659 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.25 (m, 10 H), 5.75–5.69 (m, 1 H), 5.65 (d, *J* = 6.1 Hz, 1 H), 5.30 (dd, *J* = 10.6, 6.3 Hz, 1 H), 5.14 (s, 1 H), 5.11 (d, *J* = 4.6 Hz, 1 H), 4.84 (d, *J* = 11.1 Hz, 1 H), 4.75 (d, *J* = 10.8 Hz, 1 H), 4.71 (d, *J* = 10.8 Hz, 1 H), 4.52 (d, *J* = 11.2 Hz, 1 H), 4.33 (dd, *J* = 10.9, 2.9 Hz, 1 H), 4.18 (t, *J* = 6.5 Hz, 1 H), 3.96 (d, *J* = 2.5 Hz, 1 H), 3.77–3.67 (m, 2 H), 3.23 (dd, *J* = 13.7, 8.9 Hz, 1 H), 3.10 (dd, *J* = 13.7, 5.5 Hz, 1 H), 1.08–0.98 (m, 21 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.91, 137.10, 132.30, 128.54, 128.33, 128.29, 128.17, 127.83, 118.60, 84.30, 79.65, 76.24, 75.13, 73.31, 73.24, 72.05, 61.97, 32.48, 17.95, 11.77.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{32}H_{47}NO_6SSiNa$: 624.2786; found: 624.2770.

2-Furylmethyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3oα, 3oβ)

Yield: **3o**α: 38 mg (66%) and **3o**β: 3 mg (6%); clear oils.

3oα

$[\alpha]_D^{24}$ +20.4 (*c* 2.0, $CHCl_3$).

IR (KBr): 2922, 1553, 1458, 1349, 1064, 744 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.26 (m, 16 H), 6.36–6.32 (m, 1 H), 6.23 (d, *J* = 2.4 Hz, 1 H), 5.78 (d, *J* = 6.0 Hz, 1 H), 5.36 (dd, *J* = 10.8, 6.0 Hz, 1 H), 4.91 (d, *J* = 11.2 Hz, 1 H), 4.77 (s, 2 H), 4.56–4.50 (m, 3 H), 4.40–4.36 (m, 2 H), 4.09 (s, 1 H), 3.92 (d, *J* = 14.8 Hz, 1 H), 3.76 (d, *J* = 14.8 Hz, 1 H), 3.70–3.55 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.73, 142.51, 137.78, 137.64, 136.99, 128.50, 128.44, 128.33, 128.14, 127.86, 127.78, 110.43, 108.29, 84.12, 80.53, 76.09, 75.14, 73.49, 73.25, 73.08, 70.19, 68.18, 26.42.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{32}H_{33}NO_7SNa$: 598.1870; found: 598.1861.

Isopropyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-α-D-galactopyranoside (3pa)

Yield: 44 mg (82%); clear oil; $[\alpha]_D^{24}$ +14.1 (*c* 0.5, $CHCl_3$).

IR (KBr): 2922, 1625, 1560, 1381, 1062, 739, 582 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.20 (m, 15 H), 5.78 (d, *J* = 6.1 Hz, 1 H), 5.27 (dd, *J* = 10.9, 6.1 Hz, 1 H), 4.84 (d, *J* = 11.1 Hz, 1 H), 4.78–4.67 (m, 2 H), 4.47–4.36 (m, 4 H), 4.26 (dd, *J* = 10.9, 3.0 Hz, 1 H), 4.00 (d, *J* = 2.3 Hz, 1 H), 3.62–3.51 (m, 2 H), 3.08–2.97 (m, 1 H), 1.28–1.26 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.92, 137.71, 137.15, 128.51, 128.44, 128.34, 128.21, 127.84, 127.73, 84.33, 80.95, 75.97, 75.21, 73.49, 73.45, 73.13, 69.97, 68.20, 35.80, 23.64, 23.23.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{30}H_{35}NO_6SNa$: 560.2077; found: 560.2078.

Isopropyl 3,4-Di-*O*-benzyl-2-deoxy-2-nitro-6-*O*-triisopropylsilyl-8-D-galactopyranoside (3pb)

Yield: 48 mg (79%); clear oil; $[\alpha]_D^{21}$ +10.2 (*c* 1.0, $CHCl_3$).

IR (KBr): 2893, 1554, 1448, 1053, 734, 688 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.26 (m, 10 H), 5.79 (d, *J* = 6.1 Hz, 1 H), 5.28 (dd, *J* = 10.9, 6.0 Hz, 1 H), 4.84 (d, *J* = 11.1 Hz, 1 H), 4.76 (d, *J* = 10.9 Hz, 1 H), 4.71 (d, *J* = 10.9 Hz, 1 H), 4.52 (d, *J* = 11.1 Hz, 1 H), 4.29 (dd, *J* = 10.9, 3.0 Hz, 1 H), 4.20 (d, *J* = 6.6 Hz, 1 H), 3.96 (d, *J* = 2.5 Hz, 1 H), 3.72 (d, *J* = 6.6 Hz, 2 H), 3.08–3.01 (m, 1 H), 1.26 (d, *J* = 6.8 Hz, 6 H), 1.09–1.03 (m, 21 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.03, 137.22, 128.53, 128.32, 128.16, 128.13, 127.79, 84.44, 80.59, 76.02, 75.21, 73.46, 73.26, 71.84, 61.73, 35.36, 23.54, 23.20, 17.94, 11.79.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{32}H_{49}NO_6SSiNa$: 626.2942; found: 626.2955.

Cyclopentyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3qα, 3qβ)

Yield: **3q**α: 47 mg (77%) and **3q**β: 4 mg (6%); clear oils.

3qα

$[\alpha]_D^{22}$ +9.0 (*c* 2.0, $CHCl_3$).

IR (KBr): 2938, 1601, 1387, 1159, 779, 673 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.19 (m, 15 H), 5.75 (d, *J* = 6.0 Hz, 1 H), 5.27 (dd, *J* = 10.8, 6.0 Hz, 1 H), 4.84 (d, *J* = 11.1 Hz, 1 H), 4.75–4.67 (m, 2 H), 4.50–4.37 (m, 4 H), 4.26 (dd, *J* = 10.8, 2.5 Hz, 1 H), 4.00 (d, *J* = 1.5 Hz, 1 H), 3.62–3.52 (m, 2 H), 3.18–3.10 (m, 1 H), 2.05–1.91 (m, 2 H), 1.73–1.64 (m, 2 H), 1.58–1.45 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.83, 137.63, 137.05, 128.49, 128.40, 128.31, 128.18, 128.11, 128.08, 127.82, 127.70, 75.86, 75.14, 73.42, 73.30, 73.04, 69.92, 68.13, 43.84, 33.79, 33.47, 24.63, 24.25.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{32}H_{37}NO_6SNa$: 586.2234; found: 586.2242.

Cyclohexyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3raα, 3raβ)

Yield: **3ra**α: 44 mg (77%) and **3ra**β: 3 mg (6%); clear oils.

3raα

$[\alpha]_D^{24}$ +38.2 (*c* 1.0, $CHCl_3$).

IR (KBr): 2920, 1536, 1438, 1381, 1269, 754 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.06 (m, 15 H), 5.80 (d, *J* = 6.1 Hz, 1 H), 5.26 (dd, *J* = 10.9, 6.0 Hz, 1 H), 4.84 (d, *J* = 11.2 Hz, 1 H), 4.79–4.88 (m, 2 H), 4.47–4.39 (m, 4 H), 4.26 (dd, *J* = 10.9, 3.0 Hz, 1 H), 3.99 (d, *J* = 2.3 Hz, 1 H), 3.61–3.52 (m, 2 H), 2.85–2.70 (m, 1 H), 1.97–1.87 (m, 2 H), 1.75–1.65 (m, 2 H), 1.41–1.16 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.93, 137.72, 137.16, 128.51, 128.42, 128.33, 128.20, 128.09, 127.81, 127.70, 84.36, 80.90, 75.94, 75.17, 73.49, 73.44, 73.13, 69.95, 68.28, 44.15, 33.85, 33.23, 25.85, 25.69, 25.55.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{33}H_{39}NO_6SNa$: 600.2390; found: 600.2379.

Cyclohexyl 3,4-Di-*O*-benzyl-2-deoxy-2-nitro-6-*O*-triisopropylsilyl-8-D-galactopyranoside (3rbα, 3rbβ)

Yield: **3rb**α: 52 mg (82%) and **3rb**β: 3 mg (3%); clear oils.

3rbα

$[\alpha]_D^{21}$ +12.4 (*c* 1.0, $CHCl_3$).

IR (KBr): 2968, 1554, 1266, 1053, 749, 673 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.24 (m, 10 H), 5.79 (d, *J* = 6.0 Hz, 1 H), 5.26 (dd, *J* = 10.9, 6.0 Hz, 1 H), 4.83 (d, *J* = 11.1 Hz, 1 H), 4.76 (d, *J* = 10.9 Hz, 1 H), 4.71 (d, *J* = 10.9 Hz, 1 H), 4.52 (d, *J* = 11.1 Hz, 1 H), 4.28 (dd, *J* = 10.9, 2.9 Hz, 1 H), 4.22 (t, *J* = 6.5 Hz, 1 H), 3.95 (d, *J* = 2.6 Hz, 1 H), 3.73 (d, *J* = 6.7 Hz, 2 H), 2.90–2.75 (m, 1 H), 1.91 (t, *J* = 13.4 Hz, 2 H), 1.76–1.65 (m, 2 H), 1.54 (s, 1 H), 1.39–1.24 (m, 5 H), 1.07–1.02 (m, 21 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.03, 137.22, 128.52, 128.30, 128.13, 128.10, 127.76, 84.44, 80.68, 75.94, 75.21, 73.47, 73.24, 71.79, 61.69, 43.76, 33.80, 33.21, 25.81, 25.59, 25.55, 17.95, 17.93, 11.76.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{35}H_{53}NO_6SSiNa$: 666.3265; found: 666.3271.

***tert*-Butyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3s)**

Yield: 40 mg (73%); clear oil.

3sα

$[\alpha]_D^{21}$ +13.0 (*c* 0.5, $CHCl_3$).

IR (KBr): 1968, 1615, 1570, 1296, 722, 618 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.18 (m, 15 H), 5.87 (d, *J* = 6.3 Hz, 1 H), 5.27 (dd, *J* = 10.9, 6.3 Hz, 1 H), 4.84 (d, *J* = 11.1 Hz, 1 H), 4.75 (d, *J* = 10.6 Hz, 1 H), 4.71 (d, *J* = 10.6 Hz, 1 H), 4.46 (dd, *J* = 11.3, 3.1 Hz, 2 H), 4.40 (dd, *J* = 12.5, 4.9 Hz, 2 H), 4.19 (dd, *J* = 10.9, 3.0 Hz, 1 H), 4.02 (d, *J* = 2.5 Hz, 1 H), 3.68–3.58 (m, 1 H), 3.50 (dd, *J* = 9.1, 5.6 Hz, 1 H), 1.32 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.95, 137.68, 137.17, 128.48, 128.41, 128.30, 128.21, 128.10, 128.06, 127.82, 127.74, 84.24, 79.90, 75.94, 75.24, 73.48, 73.38, 73.06, 69.84, 67.96, 44.64, 31.14.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{37}NO_6SNa$: 574.2234; found: 574.2225.

Ethyl (2*S*)-3-({(3*R*,4*R*,5*R*,6*R*)-4,5-Bis(benzyloxy)-6-[(benzyloxy)methyl]-3-nitrotetrahydro-2*H*-pyran-2-yl}thio)-2-(1,3-dioxoisoindolin-2-yl)propanoate (3tα, 3tβ)

Yield: **3t**α: 32.5 mg (44%) and **3t**β: 8.5 mg (11%); clear oils.

3tα

$[\alpha]_D^{28}$ +44.6 (*c* 1.0, $CHCl_3$).

IR (KBr): 2922, 1714, 1387, 1227, 1218, 1091, 771 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88–7.81 (m, 2 H), 7.77–7.69 (m, 2 H), 7.39–7.25 (m, 13 H), 7.24–7.17 (m, 2 H), 5.83 (d, *J* = 5.9 Hz, 1 H), 5.26 (dd, *J* = 10.9, 5.9 Hz, 1 H), 4.98 (dd, *J* = 11.1, 5.1 Hz, 1 H), 4.81 (d, *J* = 11.1 Hz, 1 H), 4.64 (s, 2 H), 4.50–4.38 (m, 3 H), 4.27–4.14 (m, 4 H), 3.98 (d, *J* = 2.4 Hz, 1 H), 3.58–3.43 (m, 3 H), 3.36 (dd, *J* = 14.3, 11.2 Hz, 1 H), 1.20 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.71, 167.33, 137.83, 137.68, 136.98, 134.28, 131.64, 128.48, 128.47, 128.33, 128.12, 128.10, 128.04, 127.86, 127.83, 127.76, 123.72, 83.96, 79.94, 75.78, 75.16, 73.51, 73.15, 73.04, 70.21, 67.83, 62.33, 50.32, 29.10, 14.03.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{40}H_{40}N_2O_{10}SNa$: 763.2296; found: 763.2283.

3tβ

$[\alpha]_D^{28}$ +16.2 (*c* 0.5, $CHCl_3$).

IR (KBr): 2960, 2358, 1714, 1259, 1022, 773 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.85 (m, 2 H), 7.79–7.73 (m, 2 H), 7.38–7.26 (m, 13 H), 7.20 (dd, *J* = 7.1, 2.4 Hz, 2 H), 5.76 (d, *J* = 6.0 Hz, 1 H), 5.22 (dd, *J* = 10.9, 6.0 Hz, 1 H), 5.02 (dd, *J* = 11.1, 4.4 Hz, 1 H), 4.80 (d, *J* = 11.1 Hz, 1 H), 4.64 (s, 2 H), 4.55 (d, *J* = 11.8 Hz, 1 H), 4.47 (dd, *J* = 11.5, 4.5 Hz, 2 H), 4.43–4.38 (m, 1 H), 4.23–4.08 (m, 3 H), 4.03 (d, *J* = 2.3 Hz, 1 H), 3.70–3.54 (m, 3 H), 3.41 (dd, *J* = 14.4, 4.4 Hz, 1 H), 1.19 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.52, 167.50, 137.85, 137.83, 137.00, 134.32, 131.69, 128.47, 128.43, 128.34, 128.12, 128.07, 127.85, 127.81, 127.77, 123.72, 84.26, 83.73, 75.74, 75.19, 73.60, 73.11, 72.99, 70.23, 67.98, 62.32, 53.06, 31.25, 14.01.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{40}H_{40}N_2O_{10}SNa$: 763.2296; found: 763.2289.

Phenyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3uα, 3uβ)

Yield: **3u**α: 40 mg (70%) and **3u**β: 1 mg (2%); white solids.

3uα

$[\alpha]_D^{24}$ +142 (*c* 1.0, $CHCl_3$).

IR (KBr): 2920, 2360, 1542, 1458, 1357, 1056, 744 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.22 (m, 20 H), 5.89 (d, *J* = 5.9 Hz, 1 H), 5.36 (dd, *J* = 10.9, 5.9 Hz, 1 H), 4.88 (d, *J* = 11.2 Hz, 1 H), 4.84–4.75 (m, 2 H), 4.58 (t, *J* = 6.4 Hz, 1 H), 4.55–4.42 (m, 3 H), 4.37 (dd, *J* = 10.9, 2.6 Hz, 1 H), 4.09 (d, *J* = 2.0 Hz, 1 H), 3.67–3.56 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.81, 137.67, 137.03, 132.90, 132.15, 129.12, 128.55, 128.44, 128.35, 128.30, 128.21, 128.18, 128.07, 127.86, 127.85, 127.77, 85.63, 84.47, 75.83, 75.18, 73.50, 73.42, 73.18, 70.60, 68.35.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{33}H_{33}NO_6SNa$: 594.1921; found: 594.1917.

***p*-Tolyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-nitro-1-thio-D-galactopyranoside (3vα, 3vβ)** [14]

Yield: **3v**α: 46 mg (80%) and **3v**β: 1.8 mg (3%); white solids.

3vα

$[\alpha]_D^{24}$ +148 (*c* 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.39–7.23 (m, 17 H), 7.06 (d, *J* = 8.0 Hz, 2 H), 5.96 (d, *J* = 5.9 Hz, 1 H), 5.24 (dd, *J* = 11.1, 5.9 Hz, 1 H), 4.88 (d, *J* = 11.1 Hz, 1 H), 4.76 (d, *J* = 11.2 Hz, 1 H), 4.64 (d, *J* = 11.1 Hz, 1 H), 4.60–4.43 (m, 5 H), 4.34 (d, *J* = 2.5 Hz, 1 H), 3.65 (dd, *J* = 10.1, 5.1 Hz, 1 H), 3.58 (dd, *J* = 10.1, 7.0 Hz, 1 H), 2.25 (s, 3 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 138.27, 138.14, 138.10, 137.55, 132.98, 129.89, 128.40, 128.30, 128.25, 128.03, 127.89, 127.86, 127.67, 127.57, 84.65, 84.44, 75.15, 74.43, 73.44, 72.41, 71.65, 70.72, 68.80, 20.70.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{35}NO_6SNa$: 608.2077; found: 608.2072.

Cyclohexyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-acetamido-8-α-D-galactopyranoside (5)

Yield: 158 mg (90%); white solid; mp 211–213 °C; $[\alpha]_D^{29}$ +11.4 (*c* 1.0, $CHCl_3$).

IR (KBr): 2953, 1646, 1554, 1039, 719, 612 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.93 (d, *J* = 7.8 Hz, 1 H), 7.39–7.22 (m, 15 H), 5.46 (d, *J* = 5.3 Hz, 1 H), 4.73 (dd, *J* = 11.2, 2.3 Hz, 2 H), 4.59 (d, *J* = 11.1 Hz, 1 H), 4.52–4.43 (m, 3 H), 4.43–4.36 (m, 1 H), 4.26 (t, *J* = 6.0 Hz, 1 H), 4.08 (s, 1 H), 3.67 (dd, *J* = 11.4, 2.5 Hz, 1 H), 3.61 (dd, *J* = 9.9, 5.4 Hz, 1 H), 3.55 (dd, *J* = 9.8, 6.9 Hz, 1 H), 2.75 (td, *J* = 9.7, 3.4 Hz, 1 H), 1.89 (d, *J* = 11.8 Hz, 2 H), 1.83 (s, 3 H), 1.67–1.57 (m, 2 H), 1.30–1.15 (m, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 169.54, 138.73, 138.54, 138.30, 128.21, 128.20, 128.16, 127.84, 127.57, 127.48, 127.43, 127.40, 82.80, 76.74, 74.01, 73.47, 72.21, 71.16, 69.89, 69.14, 49.25, 42.22, 33.66, 33.36, 25.45, 25.32, 25.21.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{35}H_{43}NO_5SNa$: 612.2754; found: 612.2747.

Cyclohexyl 3, 4, 6-tri-O-benzyl-2-deoxy-2-nitro-1-thio-D-glucopyranoside (6α, 6β); Cyclohexyl 3, 4, 6-tri-O-benzyl-2-deoxy-2-nitro-1-thio-α-D-mannopyranoside (7α)

Yield: **6**α: 8 mg (14%), **6**β: 24 mg (42%) and **7**α: 9 mg (16%); clear oils.

6β

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.27 (m, 11 H), 7.25–7.17 (m, 4 H), 4.91–4.71 (m, 3 H), 4.68–4.45 (m, 5 H), 4.42–4.22 (m, 1 H), 3.91–3.65 (m, 3 H), 3.64–3.56 (m, 1 H), 2.99–2.89 (m, 1 H), 1.98 (d, *J* = 8.2 Hz, 2 H), 1.73 (d, *J* = 4.9 Hz, 2 H), 1.58 (s, 1 H), 1.48–1.16 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.86, 137.47, 136.88, 128.48, 128.45, 128.36, 128.09, 127.99, 127.84, 127.67, 127.65, 89.64, 82.86, 81.25, 79.47, 75.53, 75.13, 73.42, 68.39, 44.12, 33.96, 33.77, 25.88, 25.75, 25.46.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{33}H_{39}NO_6SNa$: 600.2390; found: 600.2380.

7α

$[\alpha]_D^{29}$ +54.4 (*c* 1.0, $CHCl_3$).

IR (KBr): 2953, 1646, 1554, 1039, 719, 612 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.26 (m, 13 H), 7.18 (dd, *J* = 7.2, 2.0 Hz, 2 H), 5.77 (s, 1 H), 5.00 (dd, *J* = 4.9, 1.2 Hz, 1 H), 4.80 (d, *J* = 10.9 Hz, 1 H), 4.75–4.62 (m, 3 H), 4.50 (dd, *J* = 11.4, 7.6 Hz, 2 H), 4.38–4.29 (m, 1 H), 4.28–4.18 (m, 1 H), 4.06 (dd, *J* = 8.6, 4.9 Hz, 1 H), 3.81 (dd, *J* = 11.0, 5.0 Hz, 1 H), 3.70 (dd, *J* = 10.9, 1.8 Hz, 1 H), 2.93–2.79 (m, 1 H), 1.96 (dd, *J* = 28.4, 13.4 Hz, 2 H), 1.69 (d, *J* = 10.8 Hz, 2 H), 1.56 (s, 1 H), 1.47–1.14 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.11, 137.92, 136.84, 128.59, 128.38, 128.30, 128.23, 128.16, 127.97, 127.81, 127.64, 127.54, 86.98, 79.49, 77.37, 75.11, 74.06, 73.29, 73.03, 72.03, 68.74, 44.52, 33.52, 33.40, 25.90, 25.71, 25.52, 22.63.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{33}H_{39}NO_6SNa$: 600.2390; found: 600.2386.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1690099.

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