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Selective Protection/Deprotection in 1-Deoxynojirimycin Scaffold: Regioselective Mono-Benzoylation and Alkylation using TBAB-NaOH Catalytic System

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Abstract

Protecting groups play an important role in the carbohydrate chemistry and considerably influence the reactivity of substrate. A study of the substitution of various protecting groups in 1-deoxynojirimycin was carried out. Substrate *N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol was subjected to alkylation at positions 2- and 3- to obtain di-substituted products and *N*-Cbz group was selectively removed by using NaOH in EtOH/H_2O. Regioselective benzoylation and alkylation of *N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol were conducted under the action of TBAB-NaOH catalytic system. It was found that all protected and mono-protected analogs form simultaneously and their structures were confirmed by spectroscopic means. The results showed that electrophiles play an important role in determining the product distribution.

Keywords: 1-Deoxynojirimycin; protecting groups; regioselectivity; TBAB-NaOH catalytic system

1. Introduction

1-Deoxynojirimycin (1-DNJ) **1** is a naturally occurring polyhydroxylated alkaloid containing an endocyclic nitrogen atom (Figure 1).[1] It is a true structural analogue of pyranosides which is therefore well recognized by glycosidases (enzymes that catalyze the cleavage of glycosidic bonds in oligoscaccharides and glycoconjugates).[2–4] This sugar-shaped alkaloid has been found to be a potent inhibitor of a number of sugar processing enzymes, *e.g.* glycosidases and glycosyltransferases.[5,6] There has been a considerable interest in the synthesis of 1-DNJ analogs because they have demonstrated anti HIV, antiviral, antidiabetic, immunorepressive and anti-cancer properties.[7–14] Besides this, 1-DNJ derivatives which have pharmacophoric groups attached, are potentially bioactive compounds.[15]

Protecting groups play a crucial role in carbohydrate chemistry and glycosylation chemistry due to the presence of multiple functional groups.[16] They not only give protection but also influence the reactivity of substrates (imino-

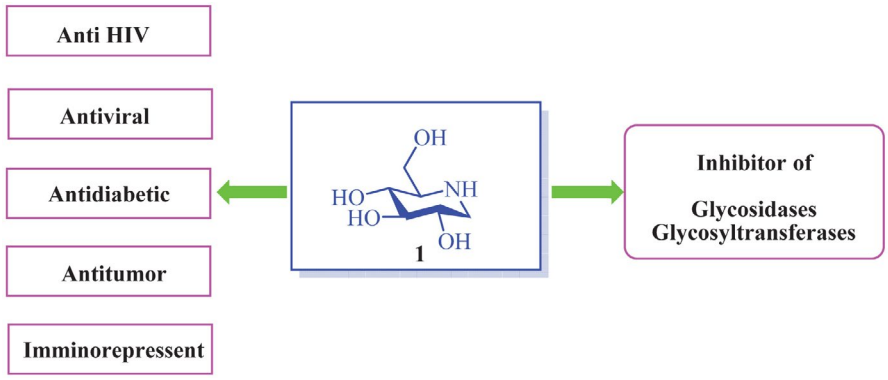


Figure 1. Structure of 1-deoxynojirimycin **1** and a short summary of its properties.

sugar) and their selectivity in glycosylations. It has been observed that benzylidene and isopropylidene groups grafted onto the DNJ scaffold have potential bioactivities towards different sugar-processing enzymes. With the increasing need for biologically active oligosaccharides and glycoconjugates, glycosylation chemistry has been extensively studied.[17] However, few synthetic methods exist for the replacement of hydroxy groups by other groups.[18] Therefore, advanced methods are required for selective protection and deprotection to improve synthetic efficacy.[19]

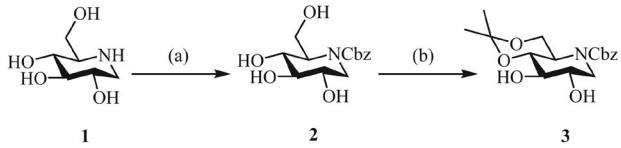
The control of regioselectivity is one of the major tasks and is conventionally accomplished by protecting group chemistry.[20] Therefore, the preparation of selectively protected iminosugars bearing a single free hydroxy group symbolizes a breakthrough in carbohydrate chemistry. Bu_2SnO, an organotin catalyst has previously been used for regioselective mono-alkylation of *N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-benzylidene-D-glucitol at elevated temperature.[18,21] We have used TBAB-NaOH catalytic system for regioselective mono-alkylation and mono-benzoylation of *N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol at room temperature. The choice of this new catalytic system is due to its easey availability and its activity under mild reaction conditions.

Herein, we describe the synthesis of 1-DNJ derivatives, selectively protected at positions 2- or 3- by varying reaction parameters. Partially protected derivatives were subjected to selective removal of the *N*-protecting group (Cbz) by using NaOH as the base. Regioselective benzoylation and alkylation of *N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol was carried out using a TBAB-NaOH catalyst system. We concluded that the electrophilic reagents with different steric and electronic effects have considerable impact on the reactivity of the secondary hydroxy groups which is an important method to evaluate the regioselectivity using TBAB-NaOH catalytic system.

2. Results and Discussion

2. 1. Synthesis of *N*-Benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol

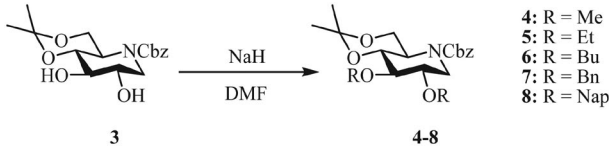
N-Benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol (**3**) was prepared in two steps from 1-deoxynojirimycin (**1**) in 70% overall yield (Scheme 1). The reaction of 1-deoxynojirimycin (**1**) with benzyl chloroformate in saturated aqueous $NaHCO_3$ afforded *N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-D-glucitol (**2**) in 87% yield.[18,22] Crude compound **2** was directly converted into *N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol (**3**) (70%) using 2,2-dimethoxypropane and *p*-TsOH in anhydrous DMF (Scheme 1).



Scheme 1. Synthesis of substrate **3**. Reagents and conditions: (a) *N*-benzyloxycarbonyl chloride, DMF, $NaHCO_3$, rt, 24 h; (b) 2,2-dimethoxypropane, DMF, rt, 24 h.

2. 2. Protection of 2,3-Diol of *N*-Benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-Isopropylidene-D-glucitol and Subsequent Cbz Removal

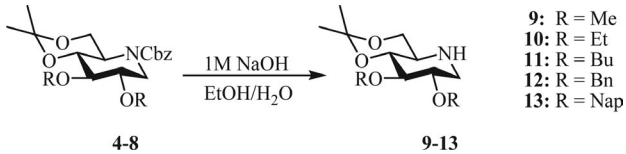
Protection at positions 2- and 3- of compound **3** was carried out using a catalytic amount of NaH as the base in anhydrous DMF with varying alkylating reagents (methyl iodide/ethyl iodide/butyl bromide/benzyl bromide/naphthyl bromide) as shown in Scheme 2.



Scheme 2. Synthesis of 2,3-disubstituted/protected derivatives **4**–**8** of **3**. Reagents and conditions: NaH, DMF, different alkylating reagents (methyl iodide/ethyl iodide/butyl bromide/benzyl bromide/naphthyl bromide), rt, 6 h.

All reactions were conducted at room temperature and the protected products **4**–**8** were obtained in good yields (67–95%, see Table 1).

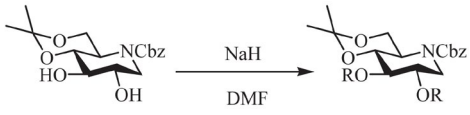
Next, we selectively removed the Cbz protecting group from protected iminosugar derivatives to obtain free NH group. Compound **4** was chosen as the model target for Cbz removal and was subjected to different bases (*i.e.* K_2CO_3, NaOH and I_2) in varying solvents (*i.e.* EtOH, MeOH, DCM). After exploring different conditions with varying bases and solvents, NaOH in EtOH/H_2O mixture gave the optimum yield of **9** (Scheme 3).



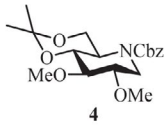
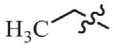
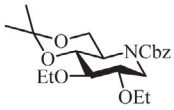
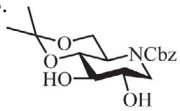
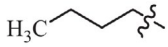
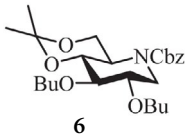
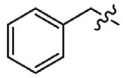
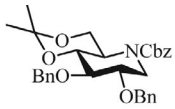
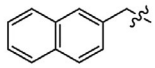
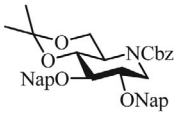
Scheme 3. Cbz deprotection of **4**–**8.** Reagents and conditions: 1 M NaOH, EtOH/H_2O, 80 °C, 6–12 h.

Deprotection of compounds **4**–**8** underwent smoothly under this generalized optimum deprotection conditions at refluxing temperature (6–12 hours) and afforded **9**–**13** in good yields: 73–83% (Table 2).

Table 1: 2,3-diol protection of **3** with different alkylating reagents.

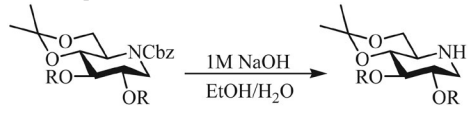


3 **4-8**

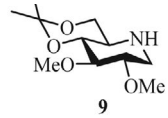
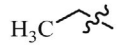
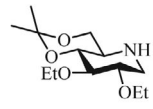
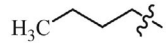
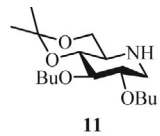
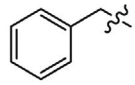
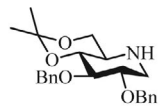
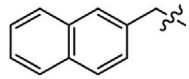
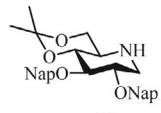
Entry	Substrate[a]	R	Product	Yield[b] (%)
1.			 **4**	87
2.			 **5**	77
3.			 **6**	67
4.			 **7**	81
5.			 **8**	95

[a] Conditions: Substrate (0.296 mmol), alkylating reagent (4 eq), NaH (5 eq), DMF (5 mL), 0–25 °C, 6 h; [b] isolated yield.

Table 2: Cbz deprotection of 4–8.



4-8 **9-13**

Entry	Substrate[a]	R	Product	Yield[b] (%)
1.	4		 **9**	80
2.	5		 **10**	77
3.	6		 **11**	74
4.	7		 **12**	83
5.	8		 **13**	73

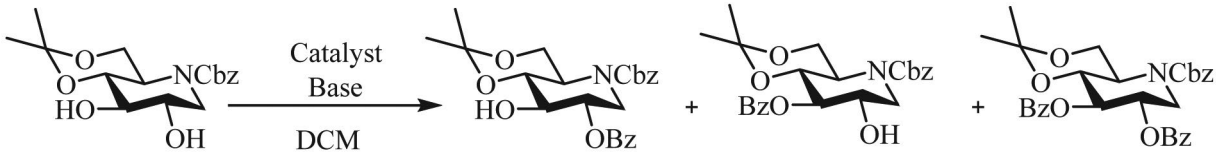
[a] Conditions: Substrate (100 mg), EtOH/H_2O 1:1 (10 mL), NaOH (1 M), 80 °C, 6–12 h; [b] isolated yield.

2. 3. Regioselective Mono-esterification and Alkylation of *N*-Benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol

2. 3. 1. Benzoylation as the Model Reaction

Selective mono-protection in azasugars/iminosugars scaffold is challenging and demanding. The position of free hydroxy groups in iminosugars has a pronounced effect on enzyme binding. For example, Chery *et al.*[14] demonstrated the importance of free 2-OH group for enzyme binding for HIV-protease inhibition. It was observed that 4,6-*O*-benzylidene protected iminosugars along with selective mono-pivolylation at positions 2- or 3- gave promising results when compared to the original drug. The selective mono-esterification and alkylation is very crucial and Bu_2SnO have previously been used for this purpose. However, due to toxicity of this catalyst, there is a need for other mild and less toxic reagents.

For mono protection we have chosen benzoyl chloride as the model electrophile. Compound **3** was reacted



3 **14a** **14b** **14c**

Scheme 4. Probing optimizing conditions for mono-esterification.

with benzoyl chloride in the presence of the catalyst-base mixture in DCM. Effect of different combinations of the catalyst (*i.e.* DMAP, TBAB) and the base (*i.e.* TEA, K_2CO_3, NaOH, KI) were observed on product formation (Scheme 4, Table 3).

Compound **3** was converted into 2-benzoylated (**14a**, 45%) and 2,3-di-benzoylated product (**14c**, 20%) completely within two hours upon treatment with DMAP-TEA combination (entry 1, Table 3). Reaction underwent incompletely when TBAB was used as the catalyst in the presence of K_2CO_3. Even after 48 hours 30% of the starting material was recovered but this combination improved the yield of **14a** upto 55% (entry 2, Table 3). Surprisingly, when the base was switched to NaOH, the reaction time was efficiently reduced to 4 hours and gave **14a** in 70% yield with no recovered starting material (entry 3, Table 3). After experiencing the good results from TBAB-NaOH combination, we switched the catalyst to DMAP and noted the effects. However DMAP-NaOH (entry 4, Table 3) did not prove to be specific for mono esterification and gave 2-benzoylated (**14a**, 46%), 3-benzoylated (**14b**, 7%) and 2,3-dibenzoylated (**14c**, 12.36%) products. This reaction condition gave **14a** with improved yield as compared to DMAP-TEA system (entry 1), but prolonged reaction time was a drawback. The combination of DMAP-KI did not give satisfactory results and only traces of **14a** and **14b** were observed (entry 5, Table 3). After probing optimized conditions for esterification, it was concluded that C-2 position is more reactive towards mono-benzoylation when TBAB-NaOH combination was used. Here, NaOH acted as a promoter for the reaction.

2. 3. 2. NMR Spectral Analysis of Mono-benzoylated Product

^{1}H NMR spectra of compounds **14a**, **14b** and **14c** were compared with that of compound **3**. Upon comparison of spectrum of compound **3** with **14c** (Figure 2), two peaks, *i.e.* δ = 3.45 ppm and δ = 3.63 ppm (in spectrum of

Table 3: Optimization of conditions for regioselective benzoylation of **3**.

Entry	Catalyst[a]	Solvent	Base	Time (h)	14a[b] (%)	14b[b] (%)	14c[b] (%)	Recovered starting material[c] (%)
1.	DMAP	DCM	TEA	2	45	–	20	–
2.	TBAB	DCM	K_2CO_3	48	55	–	–	30
3.	TBAB	DCM	NaOH	4	70	–	20	–
4.	DMAP	DCM	NaOH	72	46	7	12.36	–
5.	DMAP	DCM	KI	72	traces	traces	–	–

[a] Condition: Catalyst (1.5 eq), base (2 eq), BzCl (1.5 eq), solvent (10 mL), 25 °C, 8–72 h; [b] isolated yield.; [c] recovered starting material.

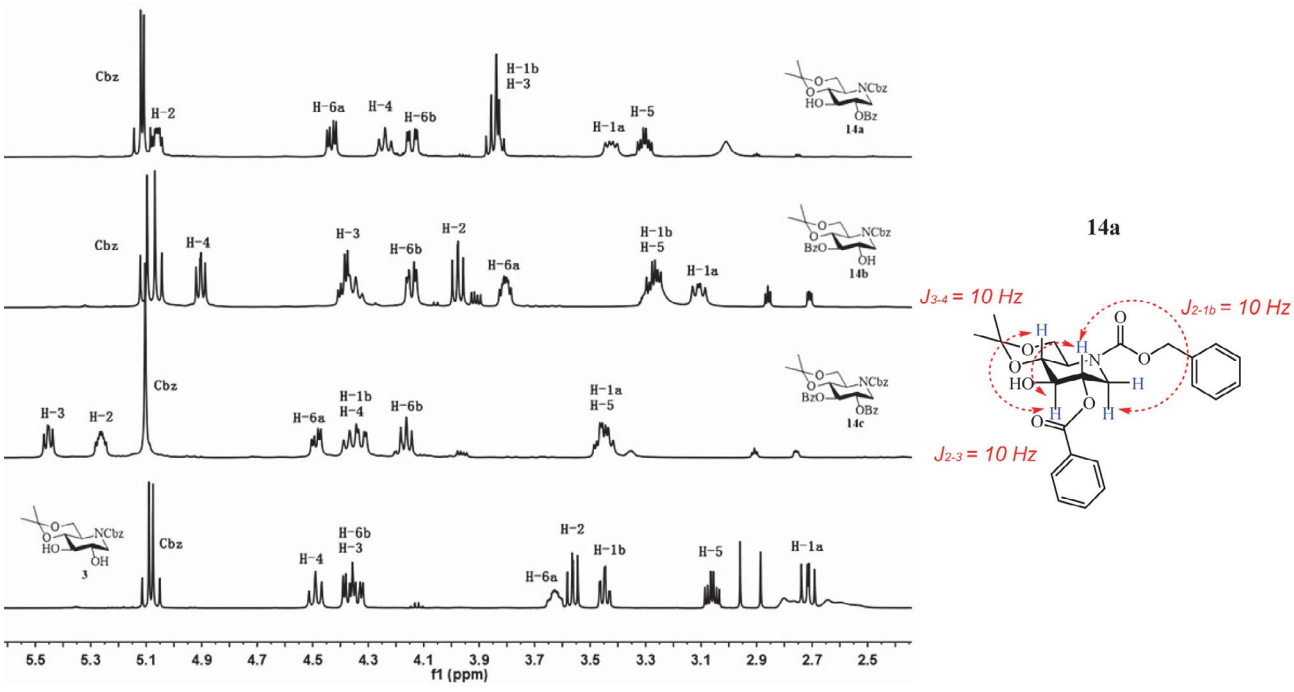


Figure 2. ^{1}H NMR spectra of compounds **3**, **14a**, **14b**, **14c** and corresponding coupling pattern of **14a**.

compound **3**) disappeared and two new peaks appeared at δ = 5.26 ppm and δ = 5.45 ppm in the spectrum of compound **14c**. The chemical shifts of H-2 and H-3 moved towards lower field indicating that both hydroxy groups are protected by benzoyl groups. It was observed that H-3 chemical shift (at δ = 3.45 ppm in the spectrum of **3**) moved towards lower field at δ = 4.45 ppm in the spectrum of compound **14b** indicating that this position is substituted. Similar trend was seen in the spectrum of **14a** where H-2 signal moved to δ = 5.06 ppm from δ = 3.63 ppm (in the spectrum compound **3**) indicating that position 2- is protected. The coupling constants, *i.e.* J_{2-3}, J_{3-4} , J_{2-1b} for compound **14a** were found to be 10 Hz as shown in the Figure 2.

2. 3. 3. Regioselective Alkylation

After probing optimized conditions for mono-esterification, similar conditions were applied for regioselective alkylation by varying electrophiles (*i.e.* benzyl bromide and naphthyl bromide) as shown in Table 4. The reactions proceeded efficiently under these conditions, *i.e.* at 25 °C catalyzed by TBAB-NaOH system. Data summarized in Table 4 clearly indicate the differentiation of reactivity of hydroxy groups towards regioselective alkylation. Both electrophiles gave mono-substituted and di-substituted products in varying ratio. For example, in the case of benzylation (entry 1, Table 4), 2-substituted product **15a** was predominant (70%) as compared to 3-substituted product **15b** (14%). Besides mono-substituted products, fully protected product **7** (10%) was also obtained. However, when more bulky electrophile, *i.e.* naphthyl bromide (entry 2, Table 4) was used, then conversion towards both, mono- and di-substituted products decreased. Decrease in product formation can be explained due to the bulkiness of the electrophile (entry 2) which caused additional steric hindrance.

3. Experimental

3. 1. General

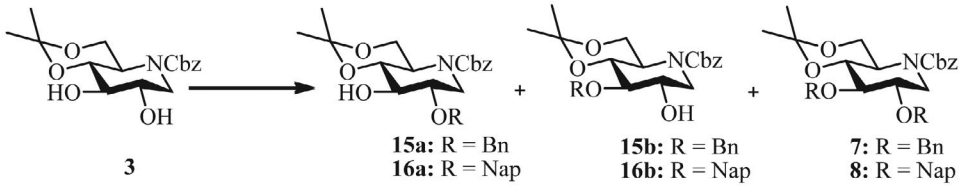
All commercially available chemicals were of analytical grade and were used without further purification. Solvents were dried prior to use according to standard methods. Reactions were performed at ambient temperature unless stated otherwise. Moisture sensitive reactions were carried out under an argon environment. The progression of reactions was monitored by thin layer chromatography (TLC) on silica gel coated plates. Spots were detected under UV-light (254 nm) or visualized via exposure to iodine vapor. Flash chromatography was performed on silica gel (Merk-230 mesh). ^{1}H and ^{13}C NMR were recorded on a Bruker-500 (at 500 or 126 MHz) in $CDCl_3$. Chemical shifts are given in ppm relative to tetramethylsilane as the internal standard (δ_{TMS} = 0 ppm).

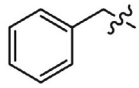
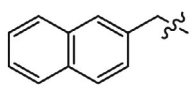
3. 2. Synthesis of *N*-Benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol (3)

To a stirring solution of *N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-D-glucitol (**2**) (7.27 g, 24.45 mmol) in DMF (60 mL) was added catalytic amount of *p*-toluenesulfonic acid monohydrate (PTSA) (140 mg) until pH = 1.5 was obtained. Then, 2,2-dimethoxypropane (2 eq, 6 mL) was added and the reaction mixture was stirred for 24 hours at room temperature until completion. Reaction mixture was quenched with aq. $NaHCO_3$ solution and extractions were made with ethyl acetate EA (100 mL × 3). Combined organic layers were washed with brine (100 mL × 3) and dried over Na_2SO_4. Purification via flash column chromatography using gradient elution (SiO_2, petroleum ether/ethyl acetate 1:1, v/v) gave **3** as a colorless oil (4.68 g, 70%).

Yield: 4.68 g, 70%, colorless oil, R_f = 0.28 (petroleum ether/ethyl acetate 1:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ

Table 4: Regioselective alkylation of **3**.



Entry	Reagent[a] (R)	Catalyst	Base	Solvent	Products	Yield[b] (%) 15a–16a	15b–16b	7,8
1.		TBAB	NaOH	DCM	15a, 15b, 7	70	14	10
2.		TBAB	NaOH	DCM	16a, 16b, 8	38	20	4

[a] Condition: RBr (1.5 eq), catalyst (1.5 eq), base (2 eq), solvent (10 mL), 25 °C, 24 h; [b] isolated yield.

1.41 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 2.71 (dd, *J* = 13.3, 10.7 Hz, 1H, H-1a), 3.06 (td, *J* = 15.0, 10.4, 5.0 Hz, 1H, H-5), 3.45 (dd, *J* = 8.6, 1.8 Hz, 1H, H-3), 3.56 (dd, *J* = 10.0, 8.8 Hz, 1H, H-4), 3.62 (ddd, *J* = 10.8, 5.7, 2.8 Hz, 1H, H-2), 4.26–4.43 (m, 2H, H-1b and H-6b), 4.49 (t, *J* = 11.3 Hz, 1H, H-6a), 5.08 (2d, *J* = 12.2 Hz, 2H, CH_2-Ar), 7.23–7.45 (m, 5H, H-Ar). ^{13}C NMR (126 MHz, $CDCl_3$) δ 18.16 (CH_3), 28.26 (CH_3), 48.43 (C-1), 54.78 (C-6), 60.94 (C-5), 66.57 (CH_2-Ar), 68.56 (C-2), 72.25 (C-3), 75.83 (C-4), 98.20 (CH), 127.15, 127.36, 127.67 (CH-Ar), 134.98 (C-Ar), 153.88 (C=O).

3. 3. General Procedure A: 2,3-Dialkyltaion of *N*-Benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol (3) to obtain 4–8

Sodium hydride NaH (5 eq, 60 mg, 1.48 mmol) was added to the stirring solution of **3** (100 mg, 0.296 mmol) in dry DMF (5 mL) at 0 °C. Alkylating reagent (4 eq, 1.18 mmol), *i.e.* methyl iodide for **4**, ethyl iodide for **5**, butyl bromide for **6**, benzyl bromide for **7** and naphthyl bromide for **8** was added slowly and the reaction mixture was stirred at room temperature for 6 hours. Reaction progression was monitored by TLC and after completion the reaction was quenched by addition of water. The reaction mixture was poured into water and repeatedly extracted with ethyl acetate EA (100 mL × 3). Combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated.

_N_-Benzyloxycarbonyl-2,3-di-_O_-methyl-1,5-dideoxy-1,5-imino-4,6-_O_-isopropylidene-D-glucitol (4)

Yield: 95 mg, 87%, yellow oil, R_f = 0.25 (petroleum ether/ethyl acetate 6:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 3.18 (dd, *J* = 8.4, 4.2 Hz, 1H, H-1a), 3.23-3.30 (m, 2H, H-2 and H-1b), 3.36 (s, 3H, OCH_3), 3.51 (s, 3H, OCH_3), 3.61–3.63 (m, 2H, H-5 and H-3), 3.80 (dd, *J* = 10.7, 8.5 Hz, 1H, H-6a), 4.00 (t, *J* = 10.6 Hz, 1H, H-4), 4.37 (dd, *J* = 11.3, 4.7 Hz, 1H, H-6b), 5.09 (d, *J* = 12.3 Hz, 1H, CH_2-Ar), 5.15 (d, *J* = 12.3 Hz, 1H, CH_2-Ar), 7.25–7.38 (m, 5H, H-Ar). ^{13}C NMR (126 MHz, $CDCl_3$) δ 18.25 (CH_3), 28.21 (CH_3), 42.68 (C-1), 51.61 (C-6), 56.16 (OCH_3), 58.04 (OCH_3), 61.97 (C-5), 66.46 (CH_2-Ar), 71.93 (C-2), 78.34 (C-3), 82.70 (C-4), 98.07 (CH), 127.06, 127.24, 127.62, 127.89 (C-Ar), 135.26 (CH-Ar), 155.15 (C=O).

_N_-Benzyloxycarbonyl-2,3-di-_O_-ethyl-1,5-dideoxy-1,5-imino-4,6-_O_-isopropylidene-D-glucitol (5)

Yield: 90 mg, 77%, yellow oil, R_f = 0.38 (petroleum ether/ethyl acetate 6:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.14 (t, *J* = 7.0 Hz, 3H, CH_3-Ethyl), 1.26 (t, *J* = 7.1 Hz, 3H, CH_3-Ethyl), 1.40 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 3.22–3.27 (m, 1H, H-1a), 3.32–3.34 (m, 2H, H-2 and H-1b), 3.52–3.59 (m, 2H, H-5 and H-3), 3.67–3.70 (m, 1H, H-3), 3.72–3.80 (m, 5H, 2 × CH_2-Ethyl and H-6a), 4.07–4.16 (m, 1H, H-6b), 4.36 (dd, *J* = 11.4, 4.8 Hz, 1H, H-4), 5.07–5.16 (m, 2H, CH_2-Ar), 7.27–7.38 (m, 5H, H-Ar). ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.47 (CH_3-Ethyl), 14.70 (CH_3-Ethyl), 18.28 (CH_3), 28.23 (CH_3), 44.15 (C-1), 52.30 (C-6), 61.90 (C-5), 64.32 (CH_2-Ethyl), 66.22 (CH_2-Ethyl), 72.32 (C-2), 76.81 (C-4), 81.66 (C-3), 97.93 (CH), 127.02, 127.19, 127.59 (C-Ar), 135.33 (CH-Ar), 155.01 (C=O).

_N_-Benzyloxycarbonyl-2,3-di-_O_-butyl-1,5-dideoxy-1,5-imino-4,6-_O_-isopropylidene-D-glucitol (6)

Yield: 90 mg, 67%, colorless oil, R_f = 0.23 (petroleum ether/ethyl acetate10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.90 (t, *J* = 10.4 Hz, 3H, CH_3-Butyl), 0.92 (t, *J* = 11.4 Hz, 3H, CH_3-Butyl), 1.33–1.39 (m, 4H, 2 × CH_2-Butyl), 1.39 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.49–1.53 (m, 4H, 2 × CH_2-Butyl), 3.19–3.27 (m, 2H, CH_2-Butyl), 3.28–3.39 (m, 2H, CH_2-Butyl), 3.44–3.54 (m, 2H, H-1a and H-1b), 3.62 (dt, *J* = 14.8, 9.5, 6.5 Hz, 1H, H-5), 3.65–3.73 (m, 2H, H-3 and H-2), 3.77 (dd, *J* = 10.6, 8.5 Hz, 1H, H-6a), 4.08 (t, *J* = 10.6 Hz, 1H, H-6b), 4.37 (dd, *J* = 11.4, 4.7 Hz, 1H, H-4), 5.05–5.20 (m, 2H, CH_2-Ar), 7.23–7.44 (m, 5H, H-Ar). ^{13}C NMR (126 MHz, $CDCl_3$) δ 12.80 (CH_3-Butyl), 12.88 (CH_3-Butyl), 18.26 (2 × CH_2-Butyl), 28.20 (CH_3), 28.21 (CH_3), 31.03 (CH_2-Butyl), 31.20 (CH_2-Butyl), 44.03 (C-1), 52.19 (C-6), 61.98 (C-5), 66.34 (CH_2-Ar), 68.66 (CH_2-Butyl), 70.56 (CH_2-Butyl), 72.37 (C-2), 77.05 (C-4), 81.58 (C-3), 97.91 (C-H), 127.02, 127.19, 127.59 (C-Ar), 135.32 (CH-Ar), 155.03 (C=O).

_N_-Benzyloxycarbonyl-2,3-di-_O_-benzyl-1,5-dideoxy-1,5-imino-4,6-_O_-isopropylidene-D-glucitol (7)

Yield: 125 mg, 81%, white solid, mp: 40 °C, R_f = 0.11 (petroleum ether/ethyl acetate 3:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.44 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 3.31 (td, *J* = 14.8, 10.5, 4.8 Hz, 1H, H-1a), 3.42–3.60 (m, 3H, H-1b, H-2 and H-5), 3.70–3.81 (m, 1H, H-3), 3.92 (dd, *J* = 10.7, 8.0 Hz, 1H, H-6a), 4.12 (t, *J* = 10.6 Hz, 1H, H-4), 4.40 (dd, *J* = 11.4, 4.7 Hz, 1H, H-6b), 4.53–4.60 (m, 2H, CH_2-Ar), 4.70 (d, *J* = 11.6 Hz, 1H, CH_2-Ar), 4.79 (d, *J* = 11.6 Hz, 1H, CH_2-Ar), 5.07–5.14 (m, 2H, CH_2-Ar), 7.24–7.41 (m, 15H, H-Ar). ^{13}C NMR (126 MHz, $CDCl_3$) δ 18.35 (CH_3), 28.28 (CH_3), 43.93 (C-1), 52.19 (C-6), 61.98 (C-5), 66.45 (CH_2-Ar), 70.58 (CH_2-Ar), 72.65 (CH_2-Ar), 72.84 (C-3), 75.02 (C-2), 81.44 (C-4), 98.02 (CH), 126.69, 126.90, 127.08, 127.26, 127.36, 127.45, 127.64 (C-Ar), 135.24 (CH-Ar), 137.03 (CH-Ar), 137.66 (CH-Ar), 155.05 (C=O).

_N_-Benzyloxycarbonyl-2,3-di-_O_-naphthyl-1,5-dideoxy-1,5-imino-4,6-_O_-isopropylidene-D-glucitol (8)

Yield: 175 mg, 95%, colorless oil, R_f = 0.31 (petroleum ether/ethyl acetate 6:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.56 (s, 3H, CH_3), 1.62 (s, 3H, CH_3), 3.43 (td, *J* = 14.8, 10.4, 4.7 Hz, 1H, H-1a), 3.62 (m, 1H, H-1b), 3.71–3.73 (m, 2H, H-2 and H-5), 3.90 (d, *J* = 13.3 Hz, 1H, H-3), 4.06 (dd, *J* = 10.4, 8.0 Hz, 1H, H-6a), 4.24 (t, *J* = 10.7 Hz, 1H, H-6b), 4.51 (dd, *J* = 11.4, 4.6 Hz, 1H, H-4), 4.76 (d, *J* = 11.8 Hz, 1H, CH_2-

Naph), 4.84 (d, *J* = 12.0 Hz, 1H, CH_2-Naph), 4.95 (d, *J* = 11.9 Hz, 1H, CH_2-Naph), 5.05 (d, *J* = 11.9 Hz, 1H, CH_2-Naph), 5.13 (d, *J* = 12.3 Hz, 1H, CH_2-Ar), 5.21 (d, *J* = 12.3 Hz, 1H, CH_2-Ar), 7.38–7.40 (m, 5H, H-Ar), 7.51–7.56 (m, 6H, H-Naph), 7.72–8.00 (m, 8H, H-Naph). ^{13}C NMR (126 MHz, $CDCl_3$) δ 18.44 (CH_3), 28.39 (CH_3), 44.00 (C-1), 52.30 (C-6), 62.04 (C-5), 66.49 (CH_2-Ar), 70.69 (CH_2-Naph), 72.70 (CH_2-Naph), 72.90 (C-2), 81.50 (C-4), 89.63 (C-3) 98.13 (CH), 124.75, 124.92, 125.08, 125.21, 125.58, 126.04, 126.79, 127.02, 127.10, 127.28, 127.66 (C-Ar and C-Naph), 132.10 (2 × C-Naph), 132.39 (2 × C-Naph), 134.52 (CH-Naph), 135.18 (CH-Naph), 135.28 (CH-Ar), 155.09 (C=O).

3. 4. General Procedure B: Removal of *N*-Protecting Group (Cbz) to Obtain 9–13

Substrates **4**–**8** (100 mg) were dissolved in 1:1 ethanol/water (10 mL) and NaOH (1 M) was added. The reaction mixture was stirred at 80 °C for 6–12 hours. After completion of the reaction as indicated by TLC, the solvents were removed *in vacuo* and extractions were made with ethyl acetate EA (100 mL × 3). Combined organic layers were dried over Na_2SO_4, filtered and concentrated.

2,3-Di-*O*-methyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol (9)

Yield: 51 mg, 80%, yellow oil, R_f = 0.16 (petroleum ether/ethyl acetate 1:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.97 (s, 1H, NH), 2.40–2.50 (m, 2H, H-1a and H-1b), 2.53 (td, *J* = 14.7, 10.1, 4.8 Hz, 1H, H-5), 3.10 (t, *J* = 8.7 Hz, 1H, H-2), 3.17 (dd, *J* = 9.9, 5.1 Hz, 1H, H-3), 3.29 (dd, *J* = 11.8, 5.1 Hz, 1H, H-6a), 3.44 (s, 3H, OCH_3), 3.55 (s, 3H, OCH_3), 3.62 (m, 1H, H-4), 3.79 (dd, *J* = 10.8, 4.7 Hz, 1H, H-6b). ^{13}C NMR (126 MHz, $CDCl_3$) δ 18.16 (CH_3), 28.42 (CH_3), 47.23 (C-1), 53.63 (OCH_3), 57.61 (OCH_3), 59.49 (C-6), 62.33 (C-5), 74.63 (C-2), 79.82 (C-3), 83.77 (C-4), 98.09 (CH).

2,3-Di-*O*-ethyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol (10)

Yield: 51 mg, 77%, yellow oil, R_f = 0.44 (petroleum ether/ethyl acetate 1:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.16 (t, *J* = 6.2 Hz, 6H, 2 × CH_3-Ethyl), 1.37 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.97 (s, 1H, NH), 2.47–2.49 (m, 2H, H-5 and H-1a), 2.85 (s, 1H, H-1b), 3.15–3.21 (m, 3H, H-2, H-3 and H-6a), 3.40 (t, *J* = 9.0 Hz, 1H, H-4), 3.58–3.80 (m, 5H, 2 × CH_2-Ethyl and H-6b). ^{13}C NMR (126 MHz, $CDCl_3$) δ 12.88 (CH_3-Ethyl), 18.16 (CH_3-Ethyl), 28.46 (CH_3), 28.69 (CH_3), 48.16 (C-1), 53.81 (C-6), 62.67 (C-5), 70.22 (CH_2-Ethyl), 71.65 (CH_2-Ethyl), 75.02 (C-2), 78.79 (C-4), 82.72 (C-3), 97.94 (CH).

2,3-Di-*O*-butyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol (11)

Yield: 52 mg, 74%, yellow oil, R_f = 0.37 (petroleum ether/ethyl acetate 1:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.4 Hz, 6H, 2 × CH_3-Butyl), 1.37 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.46–1.55 (m, 8H, 4 × CH_2-Butyl), 1.98 (s, 1H, NH), 2.40–2.55 (m, 2H, H-5 and H-1a), 3.15 (d, *J* = 8.7 Hz, 1H, H-1b), 3.16–3.29 (m, 2H, H-2 and H-3), 3.39 (t, *J* = 9.2 Hz, 1H, H-6a), 3.52–3.69 (m, 4H, 2 × CH_2-Butyl), 3.70–3.81 (m, 2H, H-6b and H-4). ^{13}C NMR (126 MHz, $CDCl_3$) δ 12.88 (2 × CH_3-Butyl), 18.16 (2 × CH_2-Butyl), 28.46 (CH_3), 28.69 (CH_3), 29.18 (CH_2-Butyl), 30.43 (CH_2-Butyl), 48.16 (C-1), 53.81 (C-6), 62.67 (C-5), 70.22 (CH_2-Butyl), 71.65 (CH_2-Butyl), 75.02 (C-2), 78.79 (C-4), 82.72 (C-3), 97.94 (CH).

2,3-Di-*O*-benzyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol (12)

Yield: 62 mg, 83%, colorless oil, R_f = 0.11 (petroleum ether/ethyl acetate 3:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.52 (s, 3H, CH_3), 1.56 (s, 3H, CH_3), 2.07 (s, 1H, NH), 2.61–2.67 (m, 2H, H-1a and H-5), 3.30 (dd, *J* = 12.0, 4.6 Hz, 1H, H-1b), 3.52–3.64 (m, 3H, H-2, H-3 and H-6a), 3.67 (t, *J* = 10.7 Hz, 1H, H-4), 3.89 (dd, *J* = 10.9, 4.9 Hz, 1H, H-6b), 4.74 (d, *J* = 11.7 Hz, 1H, CH_2-Ar), 4.84 (d, *J* = 11.7 Hz, 1H, CH_2-Ar), 4.87 (d, *J* = 11.4 Hz, 1H, CH_2-Ar), 4.98 (d, *J* = 11.4 Hz, 1H, CH_2-Ar), 7.30–7.51 (m, 10H, H-Ar). ^{13}C NMR (126 MHz, $CDCl_3$) δ 18.32 (CH_3), 28.59 (CH_3), 48.28 (C-1), 53.78 (C-6), 62.73 (C-5), 72.38 (CH_2-Ar), 74.00 (CH_2-Ar), 75.52 (C-2), 78.30 (C-4), 82.94 (C-3), 98.07 (CH), 126.50, 126.71, 126.84, 127.01, 127.29, 127.44 (C-Ar), 137.67 (CH-Ar), 138.27 (CH-Ar).

2,3-Di-*O*-naphthyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol (13)

Yield: 55 mg, 73%, colorless oil, R_f = 0.2 (petroleum ether/ethyl acetate 1:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (s, 3H, CH_3), 1.54 (s, 3H, CH_3), 2.18 (s, 1H, NH), 2.63 (m, 2H, H-1a and H-5), 3.28 (m, 1H, H-1b), 3.62–3.70 (m, 4H, H-2, H-3, H-6a and H-4), 3.86 (d, *J* = 6.3 Hz, 1H, H-6b), 4.88 (d, *J* = 11.9 Hz, 1H, CH_2-Naph), 4.96 (d, *J* = 11.9 Hz, 1H, CH_2-Naph), 5.02 (d, *J* = 11.7 Hz, 1H, CH_2-Naph), 5.12 (d, *J* = 11.7 Hz, 1H, CH_2-Naph), 7.45–7.51 (m, 5H, H-Naph), 7.58 (d, *J* = 8.4 Hz, 1H, H-Naph), 7.74–7.90 (m, 8H, H-Naph). ^{13}C NMR (126 MHz, $CDCl_3$) δ 18.37 (CH_3), 28.64 (CH_3), 48.20 (C-1), 53.70 (C-6), 62.66 (C-5), 72.43 (CH_2-Naph), 74.04 (CH_2-Naph), 74.09 (C-2), 78.27 (C-4), 82.87 (C-3), 98.14 (CH), 124.75, 124.96, 125.13, 125.32, 125.54, 125.58, 126.75, 126.99, 127.22 (C-Naph), 132.06 (2 × C-Naph), 132.35 (C-Naph), 132.42 (C-Naph), 135.13 (CH-Naph), 135.84 (CH-Naph).

3. 5. General Procedure C: Regioselctive Mono-Benzoylation and Alkylation to Obtain 14a–16a and 14b–16b

To a suspension of *N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol (**3**) (100 mg, 0.296 mmol) in methylene chloride (DCM) (10 mL), tetrabutylammonium bromide (TBAB) (1.5 eq, 143.13 mg,

0.44 mmol) was added. Sodium hydroxide solution (2 eq, 23.68 mg, 0.59 mmol) 0.5 mL was added to the reaction, followed by the addition of benzoyl chloride (for compounds **14a** and **14b**)/alkylating reagent *i.e.* benzyl bromide for compounds **15a** and **15b** and naphthyl bromide for compounds **16a** and **16b** (1.5 eq, 0.44 mmol). Reaction mixture was stirred at room temperature for 8–24 hours. Upon completion, the reaction mixture was filtered and washed with water (100 mL × 3) and brine (100 mL × 3). Organic layer was dried over Na_2SO_4, filtered and concentrated.

_N_-Benzyloxycarbonyl-2-_O_-benzoyl-1,5-dideoxy-1,5-imino-4,6-_O_-isopropylidene-D-glucitol (14a)

Yield: 99 mg, 70%, colorless oil, R_f = 0.26 (petroleum ether/ethyl acetate 3:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.45 (s, 3H, CH_3), 1.54 (s, 3H, CH_3), 3.30 (td, *J* = 14.8, 10.1, 4.8 Hz, 1H, H-5), 3.42 (dd, *J* = 13.7, 7.5 Hz, 1H, H-1b), 3.74–3.93 (m, 2H, H-1a and H-3), 4.14 (dd, *J* = 13.9, 4.0 Hz, 1H, H-6b), 4.24 (t, *J* = 10.9 Hz, 1H, H-4), 4.43 (dd, *J* = 11.5, 4.8 Hz, 1H, H-6a), 5.04–5.07 (m, 1H, H-2), 5.08–5.14 (m, 2H, CH_2-Ar), 7.20–7.36 (m, 5H, H-Ar), 7.42–7.45 (m, 2H, H-Bz), 7.58 (dd, *J* = 10.6, 4.3 Hz, 1H, H-Bz), 7.99–8.00 (m, 2H, H-Bz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 18.23 (CH_3), 28.21 (CH_3), 44.22 (C-1), 52.79 (C-6), 61.39 (C-5), 66.64 (CH_2-Ar), 71.94 (C-3), 72.59 (C-2), 73.48 (C-4), 98.56 (CH), 127.07, 127.29, 127.52, 127.64, 128.48, 128.83 (C-Ar and C-Bz), 132.45 (CH-Bz), 135.00 (CH-Ar), 154.56 (C=O-Ar), 164.95 (C=O-Bz).

_N_-Benzyloxycarbonyl-3-_O_-benzoyl-1,5-dideoxy-1,5-imino-4,6-_O_-isopropylidene-D-glucitol (14b)

Yield: (see Table 3) 10 mg, 7%, colorless oil, R_f = 0.36 (petroleum ether/ethyl acetate 3:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.33 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 3.11 (dd, *J* = 14.5, 9.9 Hz, 1H, H-1a), 3.21–3.33 (m, 2H, H-5 and H-1b), 3.77–3.84 (m, 1H, H-6a), 3.98 (t, *J* = 10.3 Hz, 1H, H-2), 4.11–4.18 (m, 1H, H-6b), 4.32–4.42 (m, 1H, H-3), 4.90 (dd, *J* = 9.0, 7.2 Hz, 1H, H-4), 5.06 (d, *J* = 12.2 Hz, 1H, CH_2-Ar), 5.11 (d, *J* = 12.2 Hz, 1H, CH_2-Ar), 7.29–7.33 (m, 5H, H-Ar), 7.40–7.44 (m, 2H, H-Bz), 7.54–7.57 (m, 1H, H-Bz), 7.99–8.00 (m, 2H, H-Bz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 28.15 (CH_3), 28.78 (CH_3), 47.81 (C-1), 53.95 (C-6), 61.39 (C-5), 66.64 (CH_2-Ar), 69.14 (C-2), 69.75 (C-4), 78.78 (C-3), 98.27 (CH), 124.72, 127.18, 127.36, 127.53, 127.68, 128.95, 132.52 (C-Ar and C-Bz), 135.03 (CH-Bz and CH-Ar), 135.42 (CH-Ar), 154.23 (C=O-Ar), 166.78 (C=O-Bz).

_N_-Benzyloxycarbonyl-2,3-di-_O_-benzoyl-1,5-dideoxy-1,5-imino-4,6-_O_-isopropylidene-D-glucitol (14c)

Yield: (see Table 3) 20 mg, 12.36%, white solid, mp: 125 °C, R_f = 0.7 (petroleum ether/ethyl acetate 3:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 3.41–3.45 (m, 2H, H-5 and H-1a), 4.10 (t, *J* = 10 Hz, 1H, H-4), 4.28–4.41 (m, 2H, H-1b and H-6b), 4.48 (dd, *J* = 10, 5 Hz, 1H, H-6a), 5.10 (s, 2H, CH_2-Ar), 5.26 (dt, *J* = 15, 10, 5 Hz, 1H, H-2), 5.45 (dd, *J* = 10, 5 Hz, 1H, H-3), 7.25–7.35 (m, 5H, H-Ar), 7.39–7.43 (m, 4H, H-Bz), 7.53–7.56 (m, 2H, H-Bz), 7.96–8.01 (m, 4H, H-Bz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 18.12 (CH_3), 28.09 (CH_3), 44.96 (C-1), 53.62 (C-6), 61.46 (C-5), 66.71 (CH_2-Ar), 70.04 (C-2 and C-3), 73.76 (C-4), 98.44 (CH), 127.07, 127.42, 127.50, 127.64, 128.80 (C-Ar and C-Bz), 132.19 (2 × CH-Bz), 132.41 (2 × C-Bz), 134.93 (CH-Ar), 154.41 (C=O-Ar), 164.34 (C=O-Bz), 164.67 (C=O-Bz).

_N_-Benzyloxycarbonyl-2-_O_-benzyl-1,5-dideoxy-1,5-imino-4,6-_O_-isopropylidene-D-glucitol (15a)

Yield: 88.63 mg, 70%, colorless oil, R_f = 0.19 (petroleum ether/ethyl acetate 3:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 2.90 (dd, *J* = 9.4, 4.0 Hz, 1H, H-1a), 3.10 (dd, *J* = 9.6, 3.8 Hz, 1H, H-2), 3.39–3.41 (m, 1H, H-1b), 3.70–3.54 (m, 2H, H-5 and H-6a), 4.15 (dd, *J* = 13.6, 4.5 Hz, 1H, H-6b), 4.26–4.39 (m, 2H, H-3 and H-4), 4.64 (s, 2H, CH_2-Ar), 5.04–5.06 (m, 2H, CH_2-Ar), 7.25–7.35 (m, 10H, H-Ar). ^{13}C NMR (126 MHz, $CDCl_3$) δ 28.28 (CH_3), 28.48 (CH_3), 45.61 (C-1), 53.82 (C-6), 61.20 (C-5), 66.52 (CH_2-Ar), 71.20 (C-3), 72.26 (CH_2-Ar), 75.15 (C-2), 79.00 (C-4), 98.29 (CH), 124.72, 126.72, 126.84, 126.93, 127.14, 127.35, 127.55, 127.68 (C-Ar), 135.14 (CH-Ar), 136.97 (CH-Ar), 154.15 (C=O-Ar).

_N_-Benzyloxycarbonyl-3-_O_-benzyl-1,5-dideoxy-1,5-imino-4,6-_O_-isopropylidene-D-glucitol (15b)

Yield: 18.1 mg, 14%, colorless oil, R_f = 0.33 (petroleum ether/ethyl acetate 3:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.47 (s, 3H, CH_3), 1.58 (s, 3H, CH_3), 2.62–2.79 (m, 1H, H-1a), 3.09 (ddd, *J* = 20.9, 12.9, 7.7 Hz, 1H, H-5), 3.30 (t, *J* = 8.3 Hz, 1H, H-1b), 3.56–3.59 (m, 1H, H-6a), 3.79 (dd, *J* = 10.1, 8.6 Hz, 1H, H-2), 4.24 (dd, *J* = 13.4, 4.9 Hz, 1H, H-6b), 4.34 (dd, *J* = 11.9, 4.9 Hz, 1H, H-3), 4.48 (t, *J* = 11.3 Hz, 1H, H-4), 4.65 (d, *J* = 11.6 Hz, 1H, CH_2-Ar), 4.92 (d, *J* = 11.6 Hz, 1H, CH_2-Ar), 5.04–5.06 (m, 2H, CH_2-Ar), 7.24–7.33 (m, 11H, H-Ar). ^{13}C NMR (126 MHz, $CDCl_3$) δ 28.42 (CH_3), 28.77 (CH_3), 48.13(C-1), 54.97 (C-6), 61.23 (C-5), 66.47 (CH_2-Ar), 78.27(C-2), 73.25 (CH_2-Ar), 73.56 (C-4), 83.52 (C-3), 97.75 (CH), 124.71, 126.83, 126.90, 126.93, 127.10, 127.31, 127.57, 127.65 (C-Ar), 135.10 (CH-Ar), 137.68 (CH-Ar), 153.99 (C=O-Ar).

_N_-Benzyloxycarbonyl-2-_O_-naphthyl-1,5-dideoxy-1,5-imino-4,6-_O_-isopropylidene-D-glucitol (16a)

Yield: 54 mg, 38%, colorless oil, R_f = 0.14 (petroleum ether/ethyl acetate 3:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 2.96 (d, *J* = 4 Hz, 1H, H-1a), 3.12 (dd, *J* = 15.0, 10.0 Hz, 1H, H-3), 3.47 (ddd, *J* = 9.1, 6.6, 4.6 Hz, 1H, H-1b), 3.58–3.73 (m, 2H, H-5 and H-6a), 4.15 (dd, *J* = 13.6, 4.3 Hz, 1H, H-2), 4.29–4.33 (m, 2H, H-6b and H-4), 4.81 (s, 2H, CH_2-Naph), 4.99 (d, *J* = 12.2 Hz, 1H, CH_2-Ar), 5.06 (d, *J* = 12.2 Hz, 1H, CH_2-Ar),

7.21–7.32 (m, 5H, H-Ar), 7.44–7.46 (m, 3H, H-Naph), 7.69–7.86 (m, 4H, H-Naph). ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.40 (CH_3), 28.32 (CH_3), 49.26 (C-1), 53.84 (C-6), 61.24 (C-5), 66.48 (CH_2-Naph), 67.80 (C-3), 71.34 (CH_2-Naph), 72.34 (C-2), 75.91 (C-4), 98.33 (CH), 125.09, 126.06, 127.00, 127.01, 127.03, 127.12, 127.22, 127.34, 127.41, 127.68, 127.93, 132.34 (C-Naph and C-Ar), 133.82 (C-Ar), 134.48 (C-Ar), 135.18 (C-Naph), 135.36 (C-Naph), 142.71 (CH-Naph), 145.50 (CH-Ar), 154.15 (C=O-Ar).

_N_-Benzyloxycarbonyl-3-_O_-naphthyl-1,5-dideoxy-1,5-imino-4,6-_O_-isopropylidene-D-glucitol (16b)

Yield: 25 mg, 20%, colorless oil, R_f = 0.26 (petroleum ether/ethyl acetate 3:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.44 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 2.78 (dd, *J* = 10.3, 5.0 Hz, 1H, H-2), 3.12 (td, *J* = 14.8, 10.4, 4.9 Hz, 1H, H-1a), 3.37 (t, *J* = 8.2 Hz, 1H, H-1b), 3.63 (ddd, *J* = 10.2, 8.1, 4.9 Hz, 1H, H-5), 3.70 (q, *J* = 7.0 Hz, 1H, H-6a), 3.85 (dd, *J* = 10.0, 8.7 Hz, 1H, H-3), 4.24 (dd, *J* = 13.4, 4.8 Hz, 1H, H-6b), 4.50 (t, *J* = 11.4 Hz, 1H, H-4), 4.84 (d, *J* = 11.8 Hz, 1H, CH_2-Naph), 5.03–5.10 (m, 3H, CH_2-Naph and CH_2-Ar), 7.20–7.38 (m, 5H, H-Ar), 7.43–7.56 (m, 3H, H-Naph), 7.78–7.82 (m, 4H, H-Naph). ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.38 (CH_3), 26.71 (CH_3), 48.14 (C-1), 54.90 (C-6), 61.28 (C-5), 66.51 (CH_2-Ar), 68.36 (C-2), 73.28 (CH_2-Naph), 73.60 (C-4), 83.48 (C-3), 97.81 (CH), 125.04, 125.26, 125.84, 126.05, 126.74, 126.81, 126.96, 127.13, 127.20, 127.33, 127.68 (C-Naph and C-Ar), 129.97 (C-Naph), 132.11 (C-Naph), 132.38 (CH-Naph), 135.10 (CH-Ar), 154.05 (C=O-Ar).

4. Conclusion

To summarize the results, we have demonstrated experiments directed towards selective removal of *N*-protecting group using NaOH as the base. Optimum reaction conditions were probed for regioselective benzoylation of *N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-isopropylidene-D-glucitol. TBAB-NaOH catalytic system gave regioselective mono-alkylated products majorly at the position 2. All newly synthesized compounds were well characterized by spectroscopic means. It was concluded that TBAB-NaOH catalytic system may be considered as an attractive alternative for the regioselective protection of 1-deoxynojirimycin, particularly protection reactions at 2- and 3-hydroxy groups of *N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-benzylidene-D-glucitol.

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Povzetek

Zaščitne skupine igrajo pomembno vlogo v kemiji ogljikovih hidratov, saj bistveno vplivajo na reaktivnost substratov. Izvedli smo študijo substitucije različnih zaščitnih skupin v 1-deoksinodžirimicinu. Substrat, *N*-benziloksikarbonil-1,5-dideoksi-1,5-imino-4,6-*O*-izopropiliden-D-glucitol smo podvrgli alkiliranju na položajih 2- in 3- in tako pripravili disubstituirane produkte iz katerih smo z uporabo NaOH v EtOH/H_2O selektivno odstranili *N*-Cbz zaščitno skupino. Regioselektivno benzoiliranje in alkiliranje *N*-benziloksikarbonil-1,5-dideoksi-1,5-imino-4,6-*O*-izopropiliden-D-glucitola smo izvedli z uporabo katalitskega sistema TBAB-NaOH. Ugotovili smo, da vsi zaščiteni in mono-zaščiteni analogi nastajajo hkrati; njihove strukture smo potrdili s spektroskopskimi metodami. Rezultati kažejo, da igra elektrofilnost pomembno vlogo pri določanju razmerij med različnimi produkti, ki nastanejo.