

ortho-Carborane-Modified *N*-Substituted Deoxynojirimycins

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N-alkyl-deoxynojirimycins (DNMs) are an important class of glycoprocessing enzyme inhibitors. Our work on DNMs focuses on identifying potent and selective inhibitors of the human enzymes, glucosylceramide synthase (GCS), lysosomal glucosylceramidase (GBA) and neutral glucosylceramidase (GBA2). We have previously reported on *N*-alkylated DNM

derivatives bearing various hydrophobic head groups (aliphatic, aromatic, branched, cyclic). In this study we report effective procedures for the synthesis of *ortho*-carborane-modified DNMs and establish the inhibitory potency of six new DNM derivatives **3–8** against GCS, GBA and GBA2.

Introduction

Deoxynojirimycin (DNM) derivatives bearing alkyl substituents at the piperidine nitrogen constitute an important class of inhibitors of glycoprocessing enzymes.^[1] *N*-Hydroxyethyl-DNM (Miglitol), a broad-spectrum intestinal glycosidase inhibitor, is in clinical use as an antidiabetic agent for the treatment of type 2 diabetes.^[2] The glucosylceramide synthase (GCS) inhibitor, *N*-butyl-DNM (Zavesca), is used to treat the lysosomal storage disorder, Gaucher disease.^[3]

Besides these clinically approved drugs, numerous studies, conducted by several research groups worldwide describe the design, synthesis and evaluation of DNM derivatives varying in configuration and bearing a variety of predominantly hydrophobic and bulky *N*-substitutions as glycosidase/glycosyl transferase inhibitors.^[4] Our early forays in this area of research involved the evaluation of adamantane-containing *N*-alkyl-DNM **1** (AMP-DNM, Figure 1) as glucosylceramide synthase inhibitor.^[5] We found that AMP-DNM **1** outperforms the clinical drug, *N*-butyl-DNM, in that **1** is the more potent GCS inhibitor. Compound **1**, however, also displays broad-spectrum activity against human lysosomal glucosylceramidase (GBA – the enzyme deficient in Gaucher patients), human neutral glucosylceramidase (GBA2) as well as intestinal glycosidases. In a subsequent study, we found that *ido*-AMP-DNM

2, the C5-epimer of AMP-DNM **1** (glucopyranose numbering), inhibits GCS slightly more potently, is somewhat less active against GBA (though an equally effective GBA2 inhibitor) and has little to no intestinal glycosidase inhibitory activity relative to **1**.^[6] At this time, GCS was identified as a potential target for the treatment of type 2 diabetes^[7] and we proposed AMP-DNM **1** as a lead for type 2 diabetes therapy development based on its dual activity as a GCS inhibitor and inhibitor of intestinal glycosidases (the main target of the aforementioned antidiabetic agent, Miglitol).^[8] *L*-*ido*-AMP-DNM **2**, in turn and based on its more selective inhibition of enzymes involved in glucosylceramide metabolism (GCS, GBA2), was viewed as a promising lead for new therapies aimed at lysosomal storage disorders.^[9]

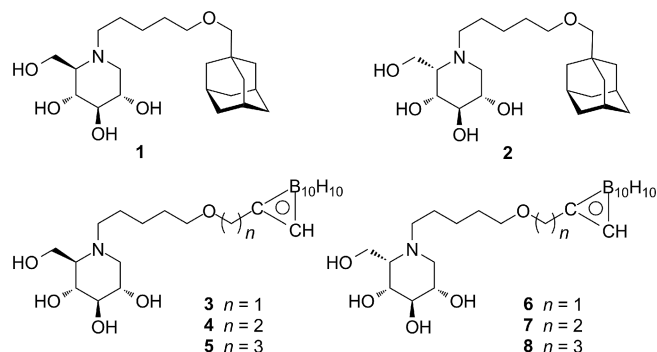


Figure 1. Lead structures AMP-DNM **1** and *ido*-AMP-DNM **2** and *ortho*-carborane-substituted analogues **3–8** subject of the here-presented studies.

Based on the above considerations we recently carried out studies in which we varied the hydrophobic moiety, attached to the DNM and *L*-*ido*-DNM core through a pentyloxy spacer, and assessed inhibitory potency of the resulting focused library against GCS, GBA and GBA2.^[10]

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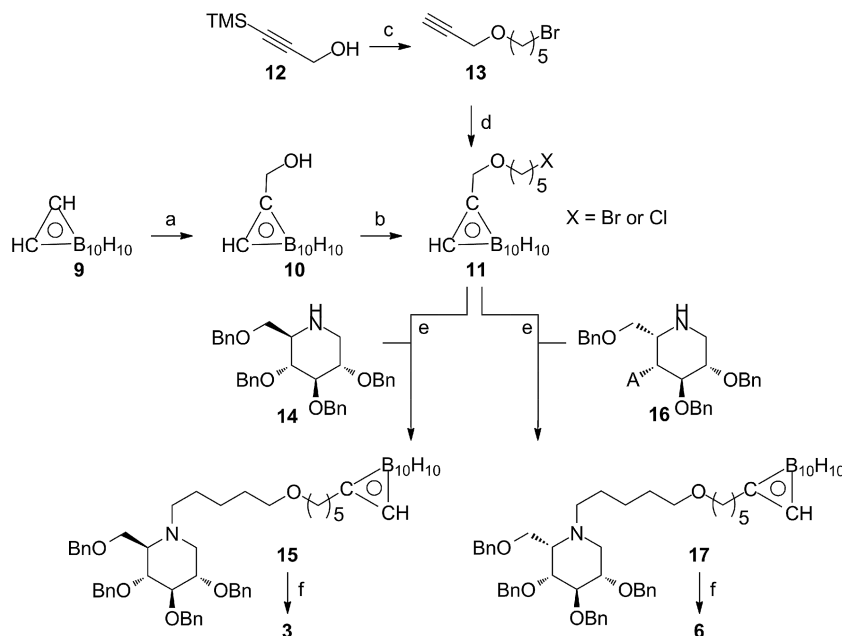
Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/ejoc.201500364>.

From these series, in which both aliphatic and aromatic functionalities varying in size and structure were included, we found that compounds bearing (substituted) biphenyls are considerably more potent inhibitors of both GCS and GBA2. Selectivity profiles appeared otherwise unchanged, with the DNM series being broad-spectrum inhibitors against both glucosylceramide metabolism enzymes and intestinal enzymes, and the *L-ido*-congeners selective for the former. One hydrophobic moiety not included in these studies is the *ortho*-carborane, and our attention was drawn to this moiety specifically because of literature precedence in which carboranes are used as isosteres both for phenyl and adamantyl substituents.^[11] This invited the question of whether *ortho*-carborane – considered a highly stable pharmacophore less prone to catabolic degradation than phenyl/adamantyl – appended to DNM or *L-ido*-DNM, would lead to effective GCS/GBA/GBA2 inhibitors. And, if so, would the inhibitory profile resemble those of AMP-DNM **1** and *L-ido*-AMP-DNM **2** or those of the more potent biphenyl-substituted derivatives. With the aim of answering this question, and in general, to arrive at synthetic strategies that enable the introduction of *ortho*-carborane moieties into glycosidase inhibitors, we set out to synthesize and evaluate *ortho*-carborane-DNM derivatives **3–5** and the corresponding *L-ido*-analogues **6–8**, all featuring the pentyloxy moiety as in parent compounds **1** and **2** and varying in the number of carbons ($n = 1, 2, 3$) separating the linker and the *ortho*-carborane. The results of these studies pertaining to both compound synthesis and inhibition potency of compounds **3–8** against the glucosylceramide processing enzymes, GCS, GBA and GBA2, are presented here.

Results and Discussion

The synthesis of *ortho*-carborane-modified *N*-alkyl-DNM **3** and *N*-alkyl-*ido*-DNM **6** – the structurally closest analogues of lead structures **1** and **2**, respectively – is depicted in Scheme 1. In a first attempt to generate bromide **11** as the DNM/*ido*-DNM alkylating agent, *ortho*-carborane **9** was treated with formaldehyde and tetrabutylammonium fluoride.^[12] The resulting hydroxymethylated *ortho*-carborane **10** was obtained in good yield, but subsequent *O*-alkylation (**10** to **11**) proved troublesome, possibly due to the relative acidity of the remaining carborane-CH in **10**; low yields were obtained when using stoichiometric NaH and double alkylation at the –OH and –CH positions was observed upon increasing the amount of base. We therefore turned our attention to an alternative route.

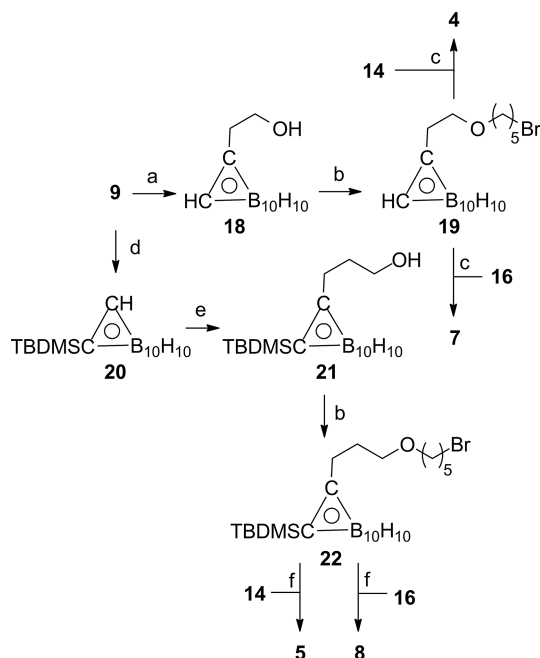
This alternative route is based on literature precedence demonstrating that modified *ortho*-carboranes can be obtained by reacting decaborane with an appropriately modified, terminal alkyne, under the agency of the ionic liquid, 1-butyl-3-methylimidazolium chloride (BmimCl) as the activating agent.^[13] Propargyl ether **13** was therefore prepared by alkylation of TMS-propargyl alcohol **12** with 1,5-di-bromopentane, using sodium hydride as the base, and tetrabutylammonium iodide (TBAI) as a catalyst. Reaction of **13** and decaborane in toluene at elevated temperature and in the presence of BmimCl afforded target *ortho*-carborane **11** in good yield, but as a mixture of the expected bromide and the corresponding chloride. This mixture – resulting from nucleophilic substitution of the bromide by chloride anion present in the reaction mixture – was used without



Scheme 1. Reagents and conditions: (a) TBAF, formaldehyde (37% v/v in H₂O), THF (86%); (b) 1,5-dibromopentane, NaH, TBAI, THF, 0 °C to reflux (9%); (c) NaH, 1,5-dibromopentane, TBAI, THF, 0 °C to room temp. (58%); (d) decaborane, BmimCl, toluene, 80 °C to 105 °C (62%); (e) **14** or **16**, K₂CO₃, CH₃CN, reflux (**15**: 59%, **17**: 78%); (f) H₂ (4 bar), Pd/C, 0.01 M HCl (aq), EtOH (**3**: 13%, **6**: 19%).

further purification in the next step. At this stage we attempted to *N*-alkylate unprotected DNM (DNM, DMF, **11**, 90 °C).^[14] However, this approach proved abortive due to degradation of the *ortho*-carborane. Reaction of **11** with 2,3,4,6-tetra-*O*-benzyl-DNM **14** in refluxing acetonitrile with potassium carbonate as the base proceeded slowly, but over the course of 4 d protected carborane-DNM derivative **15** was obtained in 59% yield.^[15] Palladium-catalyzed hydrogenolysis of the benzyl ethers in **15** followed by reversed phase HPLC purification afforded target **3** in poor yield but as a completely homogenous substance. In a similar fashion, and with comparable efficiency, but involving benzyl-protected *ido*-DNM derivative **16**, the C5 epimer **6** (with respect to **3**) was obtained.

Production of compounds **4** and **5** (one and two-carbon homologues respectively of **3**) as well as compounds **7** and **8** (homologues of **6**) is depicted in Scheme 2. In a two-step procedure *ortho*-carborane **9** was deprotonated (*n*BuLi in THF) and then treated with ethylene oxide to give carborane derivative **18** as the one-carbon homologue of carborane **10**. In contrast to *O*-alkylation of **10**, which proceeded with difficulty necessitating an alternative route, *O*-alkylation of **18** with 1,5-dibromopentane proceeded without complications to give bromide **19**. With this alkylating agent and following the synthesis used to generate **3** and **6**, DNM derivative **4** and *ido*-DNM derivative **7** were prepared with comparable efficiency.



Scheme 2. Reagents and conditions: (a) 1) *n*BuLi, THF; 2) ethylene oxide (2.5–3.3 M), THF (65%); (b) 1,5-dibromopentane, NaH, TBAI, THF, 0 °C to reflux (79% **19**, 65% **22**); (c) 1) **14** or **16**, K₂CO₃, CH₃CN, reflux; 2) H₂ (4 bar), Pd/C, 0.01 M HCl (aq), EtOH (3% **4**, 7% **7**); (d) *n*BuLi, TBDMSCl, toluene/Et₂O, 0 °C to room temp. (87%); (e) 1) *n*BuLi, THF; 2) oxetane, THF (76%); (f) 1) **14** or **16**, K₂CO₃, CH₃CN, reflux; 2) TFA/TBAF, THF, –78 °C to room temp.; 3) H₂ (4 bar), Pd/C, 0.01 M HCl (aq), EtOH (18% **5**, 17% **8**).

The final set of C5-epimeric compounds **5** and **8** was obtained from mono-(*tert*-butyldimethylsilyl)-protected *ortho*-carborane **20**, prepared from carborane **9** using previously reported procedures.^[16] Reaction of **20** with oxetane under basic conditions (deprotonation using a slight excess of *n*BuLi in THF, followed by addition of oxetane) gave hydroxypropyl carborane **21** in good yield and without migration of the TBDMS group from the carborane carbon to the hydroxyl group (a side reaction that occurred when reacting **20** with ethylene oxide, as we found when attempting to synthesize **18** from **20**). Hydroxyl group alkylation of **21** with 1,5-dibromopentane followed by *N*-alkylation of benzylated DNM and *ido*-DNM derivatives **14** and **16**, TBDMS removal, and final catalytic hydrogenation gave target compounds **5** and **8** in relatively good overall yields (relative to **4** and **7**).

The inhibitory potencies of carborane-DNM derivatives **3–8** against GCS, GBA and GBA2 were assessed in comparative studies including lead structures AMP-DNM **1** and AMP-*ido*-DNM **2**.

The overall trends in activity and specificity of the two sets of new carborane compounds (DNM compounds **3–5** vs. *ido*-DNM compounds **6–8**) parallel, to a large extent, those of parent compounds **1** and **2**, respectively (Table 1). Compounds **3–5** are less potent GCS inhibitors relative to AMP-DNM **1** whereas the corresponding *ido*-DNM derivatives **6–8** display GCS inhibitory activities on par with parent compound. Thus, the slightly improved GCS inhibition displayed by *ido*-DNM relative to DNM, and taking into account the otherwise identical structures, appears somewhat more pronounced in the *ortho*-carborane series than in the adamantane series. Importantly, substituting adamantane for *ortho*-carborane did not lead to the marked improvement in GCS inhibition previously observed for 1,4-biphenyl derivatives – especially in the *L-ido*-series.^[10] With respect to GBA, compounds in both the DNM and *ido*-DNM series are somewhat more potent inhibitors than parent compounds **1** and **2**. Conversely, all eight compounds are highly potent GBA2 inhibitors. Within the series of compounds evaluated here one- or two-carbon homologation appears to have little influence on the potency of enzyme inhibitory activity with relation to all three enzymes studies.

Table 1. IC₅₀ values (numbers are micromolar) for compounds **1–8** as inhibitors of GCS, GBA and GBA2. The SD values were always less than 20% in the case of GCS measurements, and always less than 15% in the case of GBA and GBA2 measurements.

	1	2	3	4	5	6	7	8
GCS	0.2	0.1	0.75	0.9	0.5	0.1	0.1	0.08
GBA	0.1	2.0	0.02	0.03	0.03	0.8	0.5	0.5
GBA2	0.002	0.001	0.002	0.001	0.001	0.001	0.002	0.001

Conclusions

In conclusion, we have reported synthetic procedures enabling facile access to deoxynojirimycin derivatives featur-

ing an *ortho*-carborane-modified *N*-alkyl substituent. To the best of our knowledge, the six new DNM derivatives described here constitute the first examples in which carborane moieties – attracting increasing attention from the medicinal chemistry community in recent years as pharmacophores – are combined with iminosugars. Thus, even though the adamantane-for-carborane substitution does not result in improved inhibitors for the glucosylceramide processing enzymes (GCS, GBA and GBA2) studied here, the synthetic routes outlined here enable generation of related compounds. For instance, other configurational DNM analogues or, alternatively, pyrrolidine iminosugars are now accessible. For instance, other configurational DNM analogues or, alternatively, pyrrolidine immunosugars are now accessible, allowing the preparation of focused libraries aimed at different biological targets. From a synthetic point of view, yields are not impressive, especially for the final debenzoylation steps and alkylation of unprotected iminosugars proved abortive. However, we stress that all compounds were obtained with relative ease, in suitable quantities for biological evaluation and in good purity. Our results also highlight effective synthetic strategies for generating *ortho*-carborane-alkyl halides **11**, **19** and **22**, which may find use in the synthesis of carborane-containing bioactive molecules other than those based on iminosugars and aimed at targets other than the glycoprocessing enzymes evaluated here.

Experimental Section

General: All general chemicals (Sigma–Aldrich, Fluka, Acros, Merck) were used as received. *ortho*-Carborane was purchased from Katchem spol. s. r.o. (Czech Republic). All solvents used for reactions were of analytical grade. Tetrahydrofuran, diethyl ether, toluene, DMF and dichloromethane were dried overnight over activated molecular sieves (4 Å). Methanol, acetonitrile and dimethyl sulfoxide were stored over molecular sieves (3 Å). Flash chromatography was performed on silica gel (Screening Devices BV, 40–63 µm, 60 Å). The eluents ethyl acetate, toluene and petroleum ether (40–60 °C boiling point range) were of technical grade and distilled before use. Reactions were monitored by thin layer chromatography (TLC) analysis using Merck aluminum sheets (Silica gel 60, F₂₅₄). Compounds were visualized by UV absorption (254 nm) and spraying for general compounds with an aqueous solution of KMnO₄ (20 g/L) and K₂CO₃ (10 g/L), for carboranes 0.5% PdCl₂ in 10% hydrochloric acid in acetone and for amines ninhydrin (0.75 g/L) and acetic acid (12.5 mL/L) in ethanol, followed by charring at ca. 150 °C. ¹H, ¹³C, COSY, HSQC and ¹¹B NMR spectra were recorded with a Bruker AV-400 (400/100 MHz) or Bruker DMX-600 (600/150 MHz). ¹¹B spectra were recorded with BF₃ etherate as internal standard. Chemical shifts are given in ppm (δ) relative to tetramethylsilane, CDCl₃ or CD₃OD as internal standards. Coupling constants (*J*) are given in Hz. All ¹³C-NMR spectra are proton decoupled APT measurements. LC/MS measurements were conducted using a Thermo Finnigan LCQ Advantage MAX ion-trap mass spectrometer (ESI⁺) coupled to a Surveyor HPLC system (Thermo Finnigan) equipped with a standard C18 (Gemini, 4.6 mmD × 50 mmL, 5 µ particle size, Phenomenex) analytical column and buffers A: H₂O, B: CH₃CN, C: 0.1% aq. TFA. HPLC-MS purifications of final compounds were performed

with an Agilent Technologies 1200 series automated HPLC system with a Quadropole MS 6130, equipped with a C18 semiprep column (Gemini, 250 × 10 mm, 5 µ particle size, Phenomenex). High resolution mass spectra (HRMS) were recorded with a LTQ Orbitrap (Thermo Finnigan) mass spectrometer equipped with an electron spray ion source in positive mode (source voltage 3.5 kV, sheath gas flow 10 mL min⁻¹, capillary temperature 250 °C) with resolution *R* = 60000 at *m/z* 400 (mass range *m/z* = 150–2000) and dioctylphthalate (*m/z* = 391.28428) as a lock mass. Optical rotation measurements were performed with a Propol automatic polarimeter at room temperature. IR spectra were recorded using a Shimadzu FTIR-8300 and absorptions are given in cm⁻¹.

(1'-Hydroxymethyl)-1,2-dicarba-closo-dodecaborane (10): To a solution of *ortho*-carborane **9** (288 mg, 2.0 mmol, 1 equiv.) in THF (10 mL) was added formaldehyde (37% w/w in water, 164 µL, 2.2 mmol, 1.1 equiv.) at room temp. under an argon atmosphere. Next, TBAF (1.0 M in THF, 6.0 mL, 6.0 mmol, 3 equiv.) was added dropwise affording a pale yellow solution. The reaction was stirred for 2 h after which TLC showed complete conversion of starting material and the mixture was quenched with a satd. aq. NH₄Cl solution (15 mL). Water (15 mL) was added and the aqueous layer was extracted with Et₂O (3 × 30 mL). The combined organic layers were washed with brine (80 mL), dried with MgSO₄, filtered and concentrated under reduced pressure. Silica column chromatography (5% → 30% EtOAc in PE) yielded alcohol **10** as a white powder (297 mg, 1.71 mmol, 86%), m.p. 223 °C. *R*_f = 0.3 (4:1 PE/EtOAc). ¹H NMR (400 MHz, CDCl₃): δ = 4.06 (s, 2 H, CH₂), 3.89 (s, 1 H, BCH), 3.15–1.36 (m, 10 H, BH), 2.47 (s, 1 H, OH) ppm. ¹³C NMR (101 MHz, CDCl₃): δ = 74.95, 65.03, 57.89 ppm. ¹¹B NMR (128 MHz, CDCl₃): δ = -2.87, -5.16, -9.22, -11.84, -13.19 ppm. FT-IR (thin film): ν̄ = 3590, 3385, 3079 (BCH), 2578 (B–H), 1703, 1377, 1262, 1212, 1115, 1044, 1018, 995, 908 cm⁻¹. ESI-HRMS (*m/z*): calculated for [C₃H₁₄B₁₀O + CH₃CN + H]⁺ 216.23861, observed 216.23882.

[1'-(5''-Bromopentyl)methoxy]-1,2-dicarba-closo-dodecaborane (11): Procedure starting from **10**: Alcohol **10** (347 mg, 2.0 mmol, 1 equiv.) was dissolved in dry THF (20 mL) and cooled to 0 °C under an argon atmosphere. NaH (60% dispersion in mineral oil, 88 mg, 2.0 mmol, 1.1 equiv.) was added, and a white suspension was formed. Next, 1,5-dibromopentane (1.36 mL, 10 mmol, 5 equiv.) and TBAI (74 mg, 0.20 mmol, 0.1 equiv.) were added. The mixture was stirred for 5 min at 0 °C and then brought to reflux. After 4.5 h NaH (40 mg, 1.0 mmol, 0.5 equiv.) was added and the reaction was refluxed for 72 h. Another portion of NaH (0.5 equiv.) was added and refluxing was continued overnight. Although the starting material was not completely converted, the reaction was quenched by dropwise addition of a satd. aq. NH₄Cl solution (30 mL). Water (30 mL) was added and the aqueous layer was extracted with CH₂Cl₂ (3 × 70 mL). The combined organic layers were washed with brine (240 mL), dried with MgSO₄, filtered and concentrated under reduced pressure. Silica column chromatography (0% → 32% EtOAc in PE) afforded primary bromide **11** as a pale yellow oil (55 mg, 0.17 mmol, 9%) as well as recovered starting compound **10** (104 mg, 0.60 mmol, 30%). *R*_f = 0.7 (4:1 PE/EtOAc). ¹H NMR (400 MHz, CDCl₃): δ = 3.95 (s, 1 H, BCH), 3.84 (s, 2 H, CH₂O), 3.47 (t, *J* = 6.2 Hz, 2 H, CH₂), 3.41 (t, *J* = 6.7 Hz, 2 H, CH₂), 2.76 (s, 10 H, BH), 1.87 (p, *J* = 14.1, 6.8 Hz, 2 H, CH₂), 1.61–1.54 (m, 2 H, CH₂), 1.53–1.45 (m, 2 H, CH₂) ppm. ¹³C NMR (101 MHz, CDCl₃): δ = 71.87, 71.82, 57.69, 33.66, 32.39, 28.51, 24.71 ppm. ¹¹B NMR (128 MHz, CDCl₃): δ = -3.17, -5.00, -9.21, -11.68, -13.32 ppm. FT-IR (thin film): ν̄ = 3082 (BCH), 2938, 2868, 2584 (BH), 1455, 1364, 1252, 1123, 1067, 1017 cm⁻¹. Procedure starting from **13**: To a solution of **13** (0.80 g, 4.0 mmol) in

a biphasic mixture of 1-butyl-3-methylimidazolium chloride (0.20 g) and toluene (5 mL) was added decaborane (0.18 g, 1.5 mmol) at 80 °C under an argon atmosphere. The reaction was heated to 105 °C for 3 h. The ionic liquid layer was then extracted with toluene and the combined toluene layers were loaded onto a silica column (pentane). The product was purified (0%→7% EtOAc in pentane) resulting in a mixture of the title compound and its chloro-derivative according to NMR analysis (2:1) in 62% yield (289 mg, 0.93 mmol). ¹H NMR (400 MHz, CDCl₃): δ = 3.94 (s, 1 H, BCH), 3.84 (s, 2 H, OCH₂), 3.54 (t, *J* = 6.6 Hz, 0.7 H, CH₂Cl), 3.47 (t, *J* = 6.2 Hz, 2 H, CH₂), 3.41 (t, *J* = 6.7 Hz, 1.5 H, CH₂Br), 3.07–1.34 (m, 10 H, 10 × BH), 1.92–1.83 (m, 1.5 H, CH₂CH₂Br), 1.81–1.74 (m, 0.7 H, CH₂CH₂Cl), 1.62–1.54 (m, 2 H, CH₂), 1.54–1.44 (m, 2 H, CH₂) ppm. ¹³C NMR (101 MHz, CDCl₃): δ = 72.79, 71.87, 71.82, 57.70, 44.91 (CH₂Cl), 33.66, 32.39, 32.26 (CH₂-2,Cl), 28.64 (CH₂-4,Cl), 28.51, 24.70, 23.44 (CH₂-3,Cl) ppm.

1-Bromo-5-(prop-2-yn-1-yloxy)pentane (13): Sodium hydride (60% dispersion in mineral oil, 1.4 g, 35 mmol) was added to a cooled (0 °C) solution of TMS-propargyl alcohol (1 mL, 0.90 g, 7.0 mmol) in dry THF (120 mL) under argon. The reaction was stirred for 5 min before the addition of dibromopentane (19 mL, 140 mmol, 20 equiv.) and tetrabutyl ammonium iodide (200 mg, 0.7 mmol, 0.1 equiv.). The reaction was stirred for 2 h at room temperature and carefully poured onto a cooled mixture of ammonium chloride (sat. aq.)/ice. The product was extracted with DCM (3 ×), the organic layers dried with MgSO₄, filtered, and concentrated in vacuo. Purification by silica column chromatography (1%→5% EtOAc in pentane) gave the product as slightly yellow oil (838 mg, 4.1 mmol, 58%). *R*_f = 0.6 (10:1 PE/EtOAc). ¹H NMR (400 MHz, CDCl₃): δ = 4.13 (d, *J* = 2.3 Hz, 2 H, CH₂), 3.52 (t, *J* = 6.3 Hz, 2 H, CH₂), 3.42 (t, *J* = 6.8 Hz, 2 H, CH₂), 2.45 (d, *J* = 2.3 Hz, 1 H, CH), 1.94–1.84 (m, 2 H, CH₂), 1.67–1.58 (m, 2 H, CH₂), 1.56–1.48 (m, 2 H, CH₂) ppm. ¹³C NMR (101 MHz, CDCl₃): δ = 79.97, 74.32, 69.80, 58.13, 33.79, 32.60, 28.73, 24.91 ppm. ESI-HRMS (*m/z*): calculated for [C₈H₂₃B₁₀BrO + CH₃CN + H]⁺ 366.22533, observed 366.22587.

(2'-Hydroxyethyl)-1,2-dicarba-closo-dodecaborane (18): *ortho*-Carborane **9** (72 mg, 0.50 mmol, 1 equiv.) was dissolved in dry THF (5 mL) and cooled to 0 °C under an argon atmosphere. *n*BuLi (1.6 M in THF, 0.33 mL, 0.53 mmol, 1.05 equiv.) was added dropwise and the reaction was brought to room temp. after 20 min and stirred for 2.5 h. The mixture was again cooled to 0 °C and ethylene oxide (2.5–3.3 M in THF, 0.17 mL, 0.43–0.56 mmol, 0.85–1.1 equiv.) was added, affording a turbid solution. After 10 min at 0 °C, the mixture was stirred for 3 h at room temp. Water (40 mL) was added and extracted with Et₂O (3 × 40 mL). The combined organic layers were washed with brine (100 mL), dried with MgSO₄, filtered, and concentrated in vacuo. Silica column chromatography (10%→40% EtOAc in pentane) yielded alcohol **18** as a white powder (61 mg, 0.32 mmol, 65%). *R*_f = 0.2 (4:1 PE/EtOAc). ¹H NMR (400 MHz, CDCl₃): δ = 3.98 (s, 1 H, C_{carb}H), 3.80 (t, *J* = 5.8 Hz, 2 H, CH₂OH), 3.11–1.45 (m, 10 H, BH), 2.50 (t, *J* = 5.9 Hz, 2 H, CH₂CH₂OH), 1.62 (s, 1 H, OH) ppm. ¹³C NMR (101 MHz, CDCl₃): δ = 73.13, 60.81, 60.52, 39.87 ppm. ¹¹B NMR (128 MHz, CDCl₃): δ = −2.19, −5.48, −9.55, −11.01, −12.13, −12.90 ppm. FT-IR (thin film): $\tilde{\nu}$ = 3601, 3389, 3075 (BCH), 2961, 2934, 2893, 2572 (BH), 1426, 1123, 1076, 1046, 1020, 866 cm^{−1}. ESI-HRMS (*m/z*): calculated for [C₄H₁₆B₁₀O + CH₃CN + H]⁺ 230.25426, observed 230.25446.

[2'-(5''-Bromopentyl)ethoxy]-1,2-dicarba-closo-dodecaborane (19): Alcohol **18** (33 mg, 0.18 mmol, 1 equiv.) was dissolved in dry THF

(2 mL) and cooled to 0 °C under an argon atmosphere. NaH (60% dispersion in mineral oil, 11 mg, 0.26 mmol, 1.5 equiv.) was added forming a white suspension. Next, 1,5-dibromopentane (0.12 mL, 0.90 mmol, 5 equiv.) and TBAI (7 mg, 0.02 mmol, 0.1 equiv.) were added. The mixture was stirred for 5 min at 0 °C and then brought to reflux. After 6 h the mixture was cooled to 0 °C and quenched by dropwise addition of a satd. aq. NH₄Cl solution (5 mL). Water (20 mL) was added and the aqueous layer was extracted with Et₂O (3 × 25 mL). The combined organic layers were washed with brine (75 mL), dried with MgSO₄, filtered and concentrated under reduced pressure. Primary bromide **19** was obtained by silica column chromatography (0%→8% EtOAc in pentane) as colorless oil (48 mg, 0.14 mmol, 79%). *R*_f = 0.7 (4:1 PE/EtOAc). ¹H NMR (400 MHz, CDCl₃): δ = 3.92 (s, 1 H, BCH), 3.49 (t, *J* = 5.6 Hz, 2 H, CH₂), 3.45–3.33 (m, 4 H, 2 × CH₂), 2.94–1.10 (m, 10 H, BH), 2.50 (t, *J* = 5.6 Hz, 2 H, CH₂), 1.87 (p, *J* = 13.8, 6.7 Hz, 2 H, CH₂), 1.64–1.40 (m, 4 H, 2 × CH₂) ppm. ¹³C NMR (101 MHz, CDCl₃): δ = 73.47, 70.89, 68.37, 60.24, 37.68, 33.76, 32.49, 28.81, 24.96 ppm. ¹¹B NMR (128 MHz, CDCl₃): δ = −2.12, −5.51, −9.77, −10.87, −12.10, −12.91 ppm. FT-IR (thin film): $\tilde{\nu}$ = 3074 (BCH), 2936, 2866, 2576 (BH), 1483, 1457, 1429, 1364, 1282, 1249, 1115, 1020 cm^{−1}. ESI-HRMS (*m/z*): calculated for [C₉H₂₅B₁₀BrO + CH₃CN + H]⁺ 380.24098, observed 380.24050.

1-(tert-Butyldimethylsilyl)-1,2-dicarba-closo-dodecaborane (20):^[16] To a solution of *ortho*-carborane **9** (2.88 g, 20.0 mmol, 1 equiv.) in dry toluene and Et₂O (18 mL, 2:1, v/v) was added *n*BuLi (2.5 M in hexane, 8.4 mL, 21.0 mmol, 1.05 equiv.) at 0 °C under an argon atmosphere. The solution immediately became turbid and was stirred for 2 h while gradually warming to room temp. The mixture was cooled again to 0 °C and TBDMSCl (3.32 g, 22.0 mmol, 1.1 equiv.) in a 3 mL solution of toluene and Et₂O (2:1, v/v) was added with a syringe and stirred overnight at room temp. After addition of water (50 mL), the aqueous layer was extracted with Et₂O (3 × 50 mL). The combined organic layers were dried with MgSO₄, filtered, and concentrated in vacuo. Flash column chromatography (0%→30% EtOAc in PE) afforded **20** as a colorless oil, which solidified to a white powder upon standing (4.48 g, 17.3 mmol, 87%). *R*_f = 0.8 (19:1 pentane/EtOAc). ¹H NMR (400 MHz, CDCl₃): δ = 3.44 (s, 1 H, CHB), 3.24–1.38 (m, 10 H, 10 × BH), 1.02 (s, 9 H, 3 × CH₃), 0.23 (s, 6 H, 2 × CH₃) ppm. ¹³C NMR (101 MHz, CDCl₃): δ = 66.16, 60.39, 27.11, 19.45, −4.42 ppm. ¹¹B NMR (128 MHz, CDCl₃): δ = 0.18, −1.88, −7.10, −10.81, −12.34, −13.32 ppm. FT-IR (thin film): $\tilde{\nu}$ = 3080 (BCH), 2976, 2961, 2937, 2863, 2611, 2589, 2566 (BH), 1468, 1364, 1265, 1256, 1072, 1030, 1003, 872 cm^{−1}. ESI-HRMS (*m/z*): calculated for [C₈H₂₆B₁₀Si + CH₃CN + H]⁺ 300.31452; observed 300.31492.

1-(tert-Butyldimethylsilyl)-2-(3'-hydroxypropyl)-1,2-dicarba-closo-dodecaborane (21): Compound **20** (2.59 g, 10.0 mmol) was dissolved in dry THF (50 mL) and *n*BuLi (1.6 M in hexane, 6.88 mL, 11.0 mmol, 1.1 equiv.) was added slowly, upon which the reaction mixture changed from colorless to bright orange/red. After stirring for 1 h, trimethylene oxide (1.30 mL, 20.0 mmol, 2 equiv.) was added and the mixture was stirred overnight at room temperature under an argon atmosphere. Subsequently, *n*BuLi (1.6 M in hexane, 1.56 mL, 2.5 mmol, 0.25 equiv.) and trimethylene oxide (0.33 mL, 5.0 mmol, 0.5 equiv.) were added and the mixture was stirred for 3 h. The mixture was diluted with diethyl ether and washed with water (1 × 40 mL). After the layers were separated, the aqueous layer was extracted with diethyl ether (2 × 30 mL) and the combined organic layers were dried (MgSO₄), filtered and concentrated under reduced pressure. Flash silica column chromatography (5%→25% EtOAc in PE) afforded alcohol **21** as a white powder (3.08 g, 8.6 mmol, 86%). *R*_f = 0.3 (4:1 PE/EtOAc). ¹H NMR

(400 MHz, CDCl₃): δ = 3.61 (t, J = 5.9 Hz, 2 H, CH₂), 3.09–1.58 (m, 10 H, 10 $\times$ BH), 2.39–2.30 (m, 2 H, CH₂), 1.81–1.72 (m, 2 H, CH₂), 1.51 (s, 1 H, OH), 1.06 (s, 9 H, 3 $\times$ CH₃), 0.33 (s, 6 H, 2 $\times$ CH₃) ppm. ¹³C NMR (101 MHz, CDCl₃): δ = 81.40, 76.58, 61.71, 34.74, 33.08, 27.72, 20.48, –2.35 ppm. ¹¹B NMR (128 MHz, CDCl₃): δ = 0.09, –4.06, –7.43, –10.42 ppm. FT-IR (thin film): $\tilde{\nu}$ = 3560, 3323, 2936, 2569, 1466, 1258, 1057, 838 cm^{–1}. ESI-HRMS (m/z): calculated for [C₁₁H₃₂B₁₀OSi + CH₃CN + H]⁺ 358.35639; observed 358.35701.

1-(tert-Butyldimethylsilyl)-2-[3'-(5''-bromopentyl)propoxy]-1,2-dicarba-closo-dodecaborane (22): Alcohol **21** (317 mg, 1.0 mmol, 1 equiv.) was dissolved in dry THF (10 mL) and cooled to 0 °C under an argon atmosphere. NaH (60% dispersion in mineral oil, 200 mg, 5.0 mmol, 5 equiv.) was added forming a white suspension. Next, 1,5-dibromopentane (2.72 mL, 20 mmol, 20 equiv.) and TBAI (37 mg, 0.10 mmol, 0.1 equiv.) were added. The mixture was stirred for 5 min at 0 °C and then heated to reflux. After 1.5 h of stirring TLC showed complete conversion of starting material and the mixture was cooled to 0 °C and quenched by dropwise addition of a satd. aq. NH₄Cl solution (20 mL). Water (20 mL) was added and the aqueous layer was extracted with CH₂Cl₂ (2 $\times$ 40 mL). The combined organic layers were washed with brine (80 mL), dried with MgSO₄, filtered and concentrated under reduced pressure. Purification by silica column chromatography (50% $\rightarrow$ 0% PE in toluene) yielded primary bromide **22** as a colorless oil (304 mg, 0.65 mmol, 65%). R_f = 0.9 (4:1 PE/EtOAc). ¹H NMR (400 MHz, CDCl₃): δ = 3.47–3.27 (m, 6 H, 3 $\times$ CH₂), 3.06–1.39 (m, 10 H, BH), 2.37–2.27 (m, 2 H, CH₂), 1.86 (p, J = 14.0, 6.8 Hz, 2 H, CH₂), 1.76 (m, 2 H, CH₂), 1.61–1.43 (m, 4 H, 2 $\times$ CH₂), 1.06 (s, 9 H, 3 $\times$ CH₃), 0.33 (s, 6 H, 2 $\times$ CH₃) ppm. ¹³C NMR (101 MHz, CDCl₃): δ = 81.55, 76.53, 70.83, 69.51, 35.20, 33.76, 32.69, 30.56, 29.01, 27.75, 25.05, 20.46, –2.39 ppm. ¹¹B NMR (128 MHz, CDCl₃): δ = 0.12, –4.04, –7.40, –10.32 ppm. FT-IR (thin film): $\tilde{\nu}$ = 2936, 2862, 2568 (BH), 1473, 1365, 1256, 1116, 1067 cm^{–1}. ESI-HRMS (m/z): calculated for [C₁₆H₄₁B₁₀BrOSi + CH₃CN + H]⁺ 508.34310, observed 508.34328.

General Procedure A – N-Alkylation with 2,3,4,6-Tetra-O-benzyl-1-D-glucio-deoxyojirimycin or 2,3,4,6-Tetra-O-benzyl-L-ido-1-deoxyojirimycin: To a solution of the carborane compound (1.1 equiv.) in dry CH₃CN (0.1 M) at room temperature under an argon atmosphere was added the corresponding DNM derivative (1 equiv., syntheses as described previously^[6]) and K₂CO₃ (4 equiv.). The mixture was brought to reflux and stirred until TLC showed complete conversion (typically after 3–7 d). Work-up involved the addition of water (30 mL) and extraction of the aqueous layer with EtOAc (3 $\times$ 30 mL). The combined organic layers were washed with brine (1 $\times$ 90 mL), dried with MgSO₄, filtered, and concentrated in vacuo. Purification by silica flash column chromatography (5% $\rightarrow$ 40% EtOAc in pentane) afforded the N-alkylated DNM compounds as colorless oils.

General Procedure B – Pd/C Catalyzed Hydrogenolysis: In a Parr shaker flask the N-alkylated DNM derivative was dissolved in EtOH (0.01 M) and acidified with 1 M aq. HCl to pH $\approx$ 2. The flask was evacuated and back-filled with argon. A catalytic amount of Pd/C (10% on activated carbon) was added and the flask was brought under vacuum and ventilated with hydrogen gas (3 $\times$). The flask was filled with 4 bar of hydrogen gas and mechanically agitated in a Parr apparatus for 24 h. The reaction was filtered over a Whatman glass microfiber filter, which was washed with EtOH. The solvents were removed by co-evaporation with toluene (3 $\times$) under reduced pressure. HPLC-MS purification afforded the title compounds as the corresponding TFA salt.

2,3,4,6-Tetra-O-benzyl-N-{5'-[1'-(1''',2'''-dicarba-closo-dodecaboranyl)methoxy]pentyl}-D-glucio-1-deoxyojirimycin (15): Compound **11** (63 mg, 0.20 mmol, 1.2 equiv.) was treated with 2,3,4,6-tetra-O-benzyl-D-glucio-1-deoxyojirimycin **14** (87 mg, 0.17 mmol, 1 equiv.) according to general procedure A, providing **15** (75 mg, 0.10 mmol, 59%). R_f = 0.6 (2:1 pentane/EtOAc). ¹H NMR (400 MHz, CDCl₃): δ = 7.38–7.21 (m, 18 H, CH_{Ar}), 7.18–7.08 (m, 2 H, CH_{Ar}), 4.95 (d, J = 11.1 Hz, 1 H, CH₂-H), 4.88 (d, J = 10.8 Hz, 1 H, CH₂-H), 4.81 (d, J = 11.1 Hz, 1 H, CH₂-H), 4.70 (d, J = 11.6 Hz, 1 H, CH₂-H), 4.65 (d, J = 11.6 Hz, 1 H, CH₂-H), 4.48 (d, J = 12.2 Hz, 1 H, CH₂-H), 4.45 (d, J = 12.2 Hz, 1 H, CH₂-H), 4.42 (d, J = 11.1 Hz, 1 H, CH₂-H), 3.90 (s, 1 H, BCH), 3.80 (s, 2 H, CH₂), 3.69–3.61 (m, 2 H, CH, CH₂-H), 3.61–3.50 (m, 2 H, CH, CH₂-H), 3.50–3.42 (t, J = 9.0 Hz, 1 H, CH), 3.38 (t, J = 6.4 Hz, 2 H, CH₂), 3.07 (dd, J = 11.1, 4.8 Hz, 1 H, CH₂-H), 2.97–1.54 (m, 10 H, BH), 2.72–2.62 (m, 1 H, CH₂-H), 2.60–2.50 (m, 1 H, CH₂-H), 2.30 (d, J = 9.5 Hz, 1 H, CH), 2.21 (t, J = 10.8 Hz, 1 H, CH₂-H), 1.48 (p, J = 7.0 Hz, 2 H, CH₂), 1.43–1.30 (m, 2 H, CH₂), 1.24–1.08 (m, 2 H, CH₂) ppm. ¹³C NMR (101 MHz, CDCl₃): δ = 139.09, 138.63, 137.90, 128.49, 128.48, 128.45, 128.43, 127.97, 127.92, 127.75, 127.67, 127.56, 87.46, 78.69, 78.62, 75.43, 75.31, 73.55, 72.90, 72.10, 71.84, 65.63, 63.93, 57.67, 54.58, 52.25, 29.23, 23.97, 23.61 ppm. ¹¹B NMR (128 MHz, CDCl₃): δ = –3.10, –4.96, –9.17, –11.67, –13.23 ppm. [α]_D²⁰ = +4.6 (c = 1.3, CH₂Cl₂). FT-IR (thin film): $\tilde{\nu}$ = 3085 (BCH), 3063, 3030, 2934, 2864, 2585 (BH), 1496, 1454, 1361, 1207, 1172, 1092, 1072, 1028, 910 cm^{–1}. ESI-HRMS (m/z): calculated for [C₄₂H₅₉B₁₀NO₅ + H]⁺ 767.54637, observed 767.54556.

2,3,4,6-Tetra-O-benzyl-N-{5'-[1'-(1''',2'''-dicarba-closo-dodecaboranyl)methoxy]pentyl}-L-ido-1-deoxyojirimycin (17): Compound **11** (55 mg, 0.17 mmol, 1.1 equiv.) was treated with 2,3,4,6-tetra-O-benzyl-L-ido-1-deoxyojirimycin **16** (81 mg, 0.15 mmol, 1 equiv.) according to general procedure A, affording title compound **17** (86 mg, 0.11 mmol, 75%). R_f = 0.9 (1:1 pentane/EtOAc). ¹H NMR (400 MHz, CDCl₃): δ = 7.44–7.14 (m, 20 H, CH_{Ar}), 4.85 (d, J = 10.9 Hz, 1 H, CH₂-H), 4.79 (d, J = 10.9 Hz, 1 H, CH₂-H), 4.71 (d, J = 11.6 Hz, 1 H, CH₂-H), 4.68–4.60 (m, 3 H, CH₂-H, CH₂), 4.52 (d, J = 12.2 Hz, 1 H, CH₂-H), 4.48 (d, J = 12.2 Hz, 1 H, CH₂-H), 3.91 (s, 1 H, BCH), 3.86–3.75 (m, 3 H, CH₂-H, CH₂), 3.75–3.68 (m, 1 H, CH₂-H), 3.65 (dd, J = 9.0, 5.8 Hz, 1 H, CH), 3.60–3.45 (m, 2 H, 2 $\times$ CH), 3.44–3.30 (m, 3 H, CH₂, CH), 3.04–1.56 (m, 10 H, BH), 2.85 (dd, J = 11.7, 5.1 Hz, 1 H, CH₂-H), 2.75–2.65 (m, 1 H, CH₂-H), 2.57–2.48 (m, 2 H, CH₂-H, CH₂-H), 1.50 (p, J = 14.2, 6.7 Hz, 2 H, CH₂), 1.46–1.35 (m, 2 H, CH₂), 1.31–1.19 (m, 2 H, CH₂) ppm. ¹³C NMR (101 MHz, CDCl₃): δ = 139.17, 138.74, 138.67, 138.61, 128.47, 128.42, 128.37, 128.05, 127.86, 127.72, 127.64, 127.59, 127.54, 83.14, 80.34, 78.92, 75.48, 73.37, 73.14, 72.86, 72.81, 72.20, 71.78, 64.50, 59.85, 57.67, 54.63, 49.97, 29.20, 27.68, 23.73 ppm. ¹¹B NMR (128 MHz, CDCl₃): δ = –3.14, –4.98, –9.18, –11.67, –13.25 ppm. [α]_D²⁰ = –19.3 (c = 1.4, CH₂Cl₂). FT-IR (thin film): $\tilde{\nu}$ = 3085 (BCH), 3062, 3030, 2932, 2862, 2585, 1496, 1453, 1363, 1206, 1091, 1071, 1028, 910 cm^{–1}. ESI-HRMS (m/z): calculated for [C₄₂H₅₉B₁₀NO₅ + H]⁺ 767.54562, observed 767.54556.

N-{5'-[1'-(1''',2'''-Dicarba-closo-dodecaboranyl)methoxy]pentyl}-D-glucio-1-deoxyojirimycin TFA Salt (3): Compound **15** (75 mg, 0.10 mmol) was treated according to general procedure B. HPLC-MS purification (A: 0.1% TFA in H₂O; B: linear gradient 36% $\rightarrow$ 42% CH₃CN in 12 min; flow: 5 mL/min) followed by lyophilisation provided the TFA salt of iminosugar **3** as a colorless oil (6.9 mg, 13.3 μ mol, 13%). ¹H NMR (600 MHz, MeOD): δ = 4.52 (s, 1 H, BCH), 4.12 (d, J = 12.5 Hz, 1 H, CH₂-H), 3.92 (s, 2 H, CH₂), 3.90 (d, J = 12.8 Hz, 1 H, CH₂-H), 3.68 (td, J = 10.8, 4.9 Hz,

1 H, CH), 3.59 (t, $J = 9.8$ Hz, 1 H, CH), 3.53 (t, $J = 6.2$ Hz, 2 H, CH₂), 3.44 (dd, $J = 12.0, 4.8$ Hz, 1 H, CH₂-H), 3.41–3.33 (m, 2 H, CH, CH₂-H), 3.20 (td, $J = 12.5, 4.8$ Hz, 1 H, CH₂-H), 3.03 (d, $J = 9.9$ Hz, 1 H, CH), 2.98 (t, $J = 11.7$ Hz, 1 H, CH₂-H), 2.80–1.57 (m, 10 H, BH), 1.84–1.78 (m, 1 H, CH₂-H), 1.77–1.71 (m, 1 H, CH₂-H), 1.66 (p, $J = 6.9$ Hz, 2 H, CH₂), 1.46 (dq, $J = 14.3, 7.3$ Hz, 2 H, CH₂) ppm. ¹³C NMR (151 MHz, MeOD): $\delta = 162.42$ (CF₃CO₂H), 77.80, 74.83, 72.84, 72.11, 68.40, 67.44, 67.01, 60.66, 54.52, 54.48, 53.84, 29.53, 23.95, 23.50 ppm. ¹¹B NMR (128 MHz, MeOD): $\delta = -3.24, -5.21, -9.61, -11.72, -13.26$ ppm. $[a]_D^{20} = -3.1$ ($c = 0.13$, MeOH). FT-IR (thin film): $\tilde{\nu} = 3333, 2940, 2866, 2587, 2322, 1672, 1435, 1362, 1204, 1187, 1132, 1032$ cm⁻¹. ESI-HRMS (m/z): calculated for [C₁₄H₃₅B₁₀NO₅ + H]⁺ 406.35986, observed 406.35918.

***N*-{5'-[1''-(1''',2'''-Dicarba-closo-dodecaboranyl)methoxy]pentyl}-L-ido-1-deoxynojirimycin TFA Salt (6):** Compound **17** (86 mg, 0.11 mmol) was subjected to general procedure B. HPLC-MS purification (A: 0.1% TFA in H₂O; B: linear gradient 36→42% CH₃CN in 12 min; flow: 5 mL/min) followed by lyophilization provided the TFA salt of iminosugar **6** as a colorless oil (11.0 mg, 21.2 μ mol, 19%). ¹H NMR (600 MHz, MeOD): $\delta = 4.52$ (s, 1 H, BCH), 4.08–3.94 (m, 4 H, CH₂, 2 $\times$ CH), 3.92 (s, 2 H, CH₂), 3.90–3.84 (m, 1 H, CH), 3.56–3.47 (m, 4 H, CH₂, CH₂-H, CH), 3.40–3.27 (m, 3 H, CH₂-H, CH₂), 2.72–1.61 (m, 10 H, BH), 1.91–1.83 (m, 1 H, CH₂-H), 1.79–1.70 (m, 1 H, CH₂-H), 1.66 (p, $J = 6.3$ Hz, 2 H, CH₂), 1.45 (p, $J = 7.5, 7.0$ Hz, 2 H, CH₂) ppm. ¹³C NMR (151 MHz, MeOD): $\delta = 162.94, 162.70, 162.47, 162.25$ (4 $\times$ CF₃CO₂H), 75.21, 73.20, 72.55, 72.40, 68.96, 68.02, 63.83, 61.48, 61.00, 55.04, 54.47, 29.91, 24.37, 23.23 ppm. ¹¹B NMR (128 MHz, MeOD): $\delta = -3.26, -5.24, -9.66, -11.71, -13.29$ ppm. $[a]_D^{20} = +9.1$ ($c = 0.22$, MeOH). FT-IR (thin film): $\tilde{\nu} = 3351, 2950, 2928, 2871, 2588, 1672, 1433, 1362, 1202, 1132, 1071$ cm⁻¹. ESI-HRMS (m/z): calculated for [C₁₄H₃₅B₁₀NO₅ + H]⁺ 406.35986, observed 406.35907.

***N*-{5'-[2''-(1''',2'''-Dicarba-closo-dodecaboranyl)ethoxy]pentyl}-D-gluco-1-deoxynojirimycin TFA Salt (4):** Compound **19** (61 mg, 0.18 mmol, 1.1 equiv.) was treated with 2,3,4,6-tetra-*O*-benzyl-D-gluco-1-deoxynojirimycin **14** (86 mg, 0.16 mmol, 1 equiv.) according to general procedure A yielding benzyl-protected **4** (85 mg, 0.11 mmol, 68%). $R_f = 0.9$ (1:1 pentane/EtOAc). ¹H NMR (400 MHz, CDCl₃): $\delta = 7.41$ –7.18 (m, 18 H, CH_{Ar}), 7.18–7.02 (m, 2 H, CH_{Ar}), 4.96 (d, $J = 11.1$ Hz, 1 H, CH₂-H), 4.87 (d, $J = 10.8$ Hz, 1 H, CH₂-H), 4.81 (d, $J = 11.1$ Hz, 1 H, CH₂-H), 4.69 (d, $J = 11.6$ Hz, 1 H, CH₂-H), 4.65 (d, $J = 11.6$ Hz, 1 H, CH₂-H), 4.47 (s, 2 H, CH₂), 4.40 (d, $J = 10.8$ Hz, 1 H, CH₂-H), 3.88 (s, 1 H, BCH), 3.70–3.61 (m, 2 H, CH, CH₂-H), 3.61–3.50 (m, 2 H, CH, CH₂-H), 3.50–3.41 (m, 3 H, CH, CH₂), 3.31 (t, $J = 6.4$ Hz, 2 H, CH₂), 3.08 (dd, $J = 11.1, 4.8$ Hz, 1 H, CH₂-H), 2.98–1.54 (m, 10 H, BH), 2.73–2.63 (m, 1 H, CH₂-H), 2.62–2.52 (m, 1 H, CH₂-H), 2.47 (t, $J = 5.7$ Hz, 2 H, CH₂), 2.30 (d, $J = 9.5$ Hz, 1 H, CH), 2.23 (t, $J = 10.8$ Hz, 1 H, CH₂-H), 1.48 (p, $J = 14.3, 7.1$ Hz, 2 H, CH₂), 1.43–1.31 (m, 2 H, CH₂), 1.24–1.13 (m, 2 H, CH₂) ppm. ¹³C NMR (101 MHz, CDCl₃): $\delta = 139.08, 138.62, 137.90, 128.51, 128.48, 128.46, 128.43, 128.42, 127.96, 127.91, 127.74, 127.65, 127.55, 87.46, 78.67, 78.62, 75.43, 75.29, 73.53, 73.45, 72.88, 71.06, 68.31, 65.54, 63.84, 60.22, 54.57, 52.33, 37.62, 29.52, 24.18, 23.54$ ppm. ¹¹B NMR (128 MHz, CDCl₃): $\delta = -2.07, -5.47, -9.72, -10.86, -12.13, -12.87$ ppm. $[a]_D^{20} = +4.8$ ($c = 1.2$, CH₂Cl₂). FT-IR (thin film): $\tilde{\nu} = 3086$ (BCH), 3063, 3030, 2933, 2863, 2804, 2581 (BH), 1722, 1496, 1454, 1361, 1315, 1274, 1207, 1091, 1028 cm⁻¹. ESI-HRMS (m/z): calculated for [C₄₃H₆₁B₁₀NO₅ + H]⁺ 781.56208, observed 781.56143. Benzylated **4** (85 mg, 0.11 mmol) was treated ac-

cording to general procedure B. HPLC-MS purification (A: 0.1% TFA in H₂O; B: linear gradient 36→42% CH₃CN in 12 min; flow: 5 mL/min) followed by lyophilization provided the TFA salt of iminosugar **4** as a colorless oil (2.2 mg, 4.2 μ mol, 4%). ¹H NMR (600 MHz, MeOD): $\delta = 4.48$ (s, 1 H, BCH), 4.12 (d, $J = 12.4$ Hz, 1 H, CH₂-H), 3.90 (d, $J = 10.5$ Hz, 1 H, CH₂-H), 3.67 (td, $J = 10.8, 4.8$ Hz, 1 H, CH), 3.59 (t, $J = 9.7$ Hz, 1 H, CH), 3.52 (t, $J = 5.9$ Hz, 2 H, CH₂), 3.47–3.41 (m, 3 H, CH₂-H, CH₂), 3.39–3.33 (m, 2 H, CH, CH₂-H), 3.23–3.15 (m, 1 H, CH₂-H), 3.03 (d, $J = 9.2$ Hz, 1 H, CH), 3.01–2.94 (m, 1 H, CH₂-H), 2.78–1.59 (m, 10 H, BH), 2.54 (t, $J = 5.9$ Hz, 2 H, CH₂), 1.86–1.78 (m, 1 H, CH₂-H), 1.74 (d, $J = 5.9$ Hz, 1 H, CH₂-H), 1.64 (p, $J = 6.9$ Hz, 2 H, CH₂), 1.47 (dq, $J = 14.1, 7.7$ Hz, 2 H, CH₂) ppm. ¹³C NMR (151 MHz, MeOD): $\delta = 162.94$ (CF₃CO₂H), 78.18, 75.15, 71.36, 69.46, 68.81, 67.85, 67.39, 63.06, 54.93, 54.27, 38.59, 30.14, 24.49, 23.91 ppm. ¹¹B NMR (128 MHz, MeOD): $\delta = -2.69, -5.83, -9.82, -11.20, -11.88, -13.07$ ppm. $[a]_D^{20} = -4.6$ ($c = 0.04$, MeOH). FT-IR (thin film): $\tilde{\nu} = 3348, 2938, 2870, 2588$ (BH), 1674, 1436, 1204, 1133, 1032 cm⁻¹. ESI-HRMS (m/z): calculated for [C₁₅H₃₇B₁₀NO₅ + H]⁺ 420.37556, observed 420.37515.

***N*-{5'-[2''-(1''',2'''-Dicarba-closo-dodecaboranyl)ethoxy]pentyl}-L-ido-1-deoxynojirimycin TFA Salt (7):** Compound **19** (65 mg, 0.19 mmol, 1.2 equiv.) was treated with 2,3,4,6-tetra-*O*-benzyl-1-L-ido-deoxynojirimycin **16** (86 mg, 0.16 mmol, 1 equiv.) according to general procedure A affording benzylated **7** as a colorless oil (78 mg, 0.10 mmol, 63%). $R_f = 0.9$ (1:1 EtOAc/pentane). ¹H NMR (400 MHz, CDCl₃): $\delta = 7.39$ –7.23 (m, 20 H, CH_{Ar}), 4.85 (d, $J = 10.9$ Hz, 1 H, CH₂-H), 4.79 (d, $J = 10.9$ Hz, 1 H, CH₂-H), 4.71 (d, $J = 11.6$ Hz, 1 H, CH₂-H), 4.68–4.60 (m, 3 H, CH₂-H, CH₂), 4.52 (d, $J = 12.2$ Hz, 1 H, CH₂-H), 4.48 (d, $J = 12.2$ Hz, 1 H, CH₂-H), 3.89 (s, 1 H, BCH), 3.81 (dd, $J = 10.1, 6.6$ Hz, 1 H, CH₂-H), 3.71 (dd, $J = 10.1, 2.3$ Hz, 1 H, CH₂-H), 3.66 (dd, $J = 9.3, 5.7$ Hz, 1 H, CH), 3.59–3.48 (m, 2 H, 2 $\times$ CH), 3.45 (t, $J = 5.7$ Hz, 2 H, CH₂), 3.39–3.28 (m, 3 H, CH, CH₂), 3.10–1.55 (m, 10 H, BH), 2.85 (dd, $J = 11.9, 5.3$ Hz, 1 H, CH₂-H), 2.74–2.66 (m, 1 H, CH₂-H), 2.57–2.48 (m, 2 H, 2 $\times$ CH₂-H), 2.46 (t, $J = 5.7$ Hz, 2 H, CH₂), 1.50 (p, $J = 14.6, 6.6$ Hz, 2 H, CH₂), 1.46–1.37 (m, 2 H, CH₂), 1.26 (p, $J = 7.3$ Hz, 2 H, CH₂) ppm. ¹³C NMR (101 MHz, CDCl₃): $\delta = 139.19, 138.75, 138.69, 138.63, 128.48, 128.43, 128.41, 128.38, 128.06, 127.87, 127.85, 127.72, 127.64, 127.56, 127.54, 83.16, 80.37, 78.96, 75.49, 73.50, 73.36, 73.14, 72.78, 71.21, 68.28, 64.49, 60.21, 59.85, 54.69, 49.95, 37.61, 29.50, 27.77, 23.95$ ppm. ¹¹B NMR (128 MHz, CDCl₃): $\delta = -2.07, -5.46, -9.73, -10.82, -12.13, -12.84$ ppm. $[a]_D^{20} = -18.9$ ($c = 1.0$, CH₂Cl₂). FT-IR (neat): $\tilde{\nu} = 3086$ (BCH), 3063, 3030, 2933, 2862, 2582 (BH), 1496, 1453, 1363, 1091, 1028, 909 cm⁻¹. ESI-HRMS (m/z): calculated for [C₄₃H₆₁B₁₀NO₅ + H]⁺ 781.56208, observed 781.56147. Benzylated **7** (78 mg, 0.10 mmol) was subjected to general procedure B. HPLC-MS purification (A: 0.1% TFA in H₂O; B: linear gradient 36→42% CH₃CN in 12 min; flow: 5 mL/min) followed by lyophilization provided the TFA salt of iminosugar **7** as a colorless oil (6.0 mg, 11.3 μ mol, 11%). ¹H NMR (600 MHz, MeOD): $\delta = 4.47$ (s, 1 H, BCH), 4.06–3.91 (m, 4 H, CH₂, 2 $\times$ CH), 3.90–3.83 (m, 1 H, CH), 3.55–3.47 (m, 4 H, CH₂, CH₂-H, CH), 3.43 (t, $J = 6.2$ Hz, 2 H, CH₂), 3.38–3.26 (m, 3 H, CH₂, CH₂-H), 2.81–1.55 (m, 10 H, BH), 2.53 (t, $J = 5.9$ Hz, 2 H, CH₂), 1.91–1.82 (m, 1 H, CH₂-H), 1.79–1.70 (m, 1 H, CH₂-H), 1.64 (p, $J = 6.5$ Hz, 2 H, CH₂), 1.46 (p, $J = 7.3, 6.6$ Hz, 2 H, CH₂) ppm. ¹³C NMR (151 MHz, MeOD): $\delta = 162.77$ (CF₃CO₂H), 75.16, 72.38, 71.39, 69.44, 68.96, 68.02, 63.83, 63.03, 61.44, 55.09, 54.49, 38.59, 30.15, 24.50, 23.24 ppm. ¹¹B NMR (128 MHz, MeOD): $\delta = -2.69, -5.83, -9.85, -11.21, -11.92, -13.10$ ppm. $[a]_D^{20} = +9.9$ ($c = 0.12$, MeOH). FT-IR (thin film): $\tilde{\nu} = 3337, 3078$ (BC-H), 2941, 2869, 2586 (B-H), 1674, 1433, 1203,

1133, 1070 cm⁻¹. ESI-HRMS (*m/z*): calculated for [C₁₅H₃₇B₁₀NO₅ + H]⁺ 420.37556, observed 420.37511.

***N*-{5'-[3'-(1''',2'''-Dicarba-closo-dodecaboranyl)propoxy]pentyl}-D-gluc-1-deoxynojirimycin TFA Salt (5):** Compound **22** (143 mg, 0.31 mmol, 1.5 equiv.) was treated with 2,3,4,6-tetra-*O*-benzyl-D-gluc-1-deoxynojirimycin **14** (107 mg, 0.20 mmol, 1 equiv.) according to general procedure A. Flash column chromatography (100% PE → 30% EtOAc in PE) afforded protected iminosugar as a colorless oil (142 mg, 0.16 mmol, 78%), as well as starting material **22** (34 mg, 0.07 mmol). *R*_f = 0.5 (4:1 pentane/EtOAc). ¹H NMR (400 MHz, CDCl₃): δ = 7.43–7.19 (m, 18 H, CH_{Ar}), 7.18–7.06 (m, 2 H, CH_{Ar}), 4.95 (d, *J* = 11.1 Hz, 1 H, CH₂-H), 4.87 (d, *J* = 10.8 Hz, 1 H, CH₂-H), 4.81 (d, *J* = 11.1 Hz, 1 H, CH₂-H), 4.69 (d, *J* = 11.6 Hz, 1 H, CH₂-H), 4.64 (d, *J* = 11.6 Hz, 1 H, CH₂-H), 4.46 (s, 2 H, CH₂), 4.40 (d, *J* = 10.8 Hz, 1 H, CH₂-H), 3.69–3.59 (m, 2 H, CH, CH₂-H), 3.60–3.50 (m, 2 H, CH, CH₂-H), 3.50–3.41 (m, 1 H, CH), 3.32 (m, 4 H, 2 × CH₂), 3.17–1.63 (m, 10 H, BH), 3.07 (dd, *J* = 11.1, 4.8 Hz, 1 H, CH₂-H), 2.73–2.62 (m, 1 H, CH₂-H), 2.62–2.52 (m, 1 H, CH₂-H), 2.35–2.27 (m, 3 H, CH₂, CH), 2.23 (t, *J* = 10.8 Hz, 1 H, CH₂-H), 1.82–1.70 (m, 2 H, CH₂), 1.47 (p, *J* = 7.1 Hz, 2 H, CH₂), 1.43–1.30 (m, 2 H, CH₂), 1.27–1.12 (m, 2 H, CH₂), 1.05 (s, 9 H, 3 × CH₃), 0.31 (s, 6 H, 2 × CH₃) ppm. ¹³C NMR (101 MHz, CDCl₃): δ = 139.08, 138.64, 137.89, 128.47, 128.41, 127.94, 127.88, 127.73, 127.63, 127.54, 87.47, 81.49, 78.69, 78.64, 76.49, 75.41, 75.27, 73.55, 72.87, 71.03, 69.44, 65.53, 63.81, 54.61, 52.41, 35.15, 30.52, 29.73, 27.75, 24.23, 23.59, 20.43, –2.41 ppm. ¹¹B NMR (128 MHz, CDCl₃): δ = 0.19, –3.97, –7.35, –10.25 ppm. [*α*]_D²⁰ = +3.5 (*c* = 1.2, CH₂Cl₂). FT-IR (thin film): $\tilde{\nu}$ = 3089, 3063, 3031, 2934, 2862, 2801, 2573 (B–H), 1454, 1362, 1265, 1208, 1173, 1091, 1071, 1028 cm⁻¹. ESI-HRMS (*m/z*): calculated for [C₅₀H₇₇B₁₀NO₅Si + H]⁺ 909.66474, observed 909.66473. Protected iminosugar (140 mg, 0.15 mmol, 1 equiv.) was dissolved in dry THF (1 mL) under an argon atmosphere and cooled to –78 °C. TFA (11.1 μL, 0.15 mmol, 1 equiv.) and TBAF (1 M in THF, 0.18 mL, 0.18 mmol, 1.2 equiv.) were added. The mixture was stirred at –78 °C for 15 min, then for 1.5 h at room temp. until TLC showed complete conversion of the starting material. Water (20 mL) was added and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (1 × 60 mL), dried with MgSO₄, filtered, and concentrated in vacuo. Flash column chromatography (10% → 40% EtOAc in PE) yielded benzylated iminosugar as a pale yellow oil (107 mg, 0.13 mmol, 90%). *R*_f = 0.4 (4:1 pentane/EtOAc). ¹H NMR (400 MHz, CDCl₃): δ = 7.36–7.20 (m, 18 H, CH_{Ar}), 7.17–7.09 (m, 2 H, CH_{Ar}), 4.95 (d, *J* = 11.1 Hz, 1 H, CH₂-H), 4.87 (d, *J* = 10.9 Hz, 1 H, CH₂-H), 4.81 (d, *J* = 11.1 Hz, 1 H, CH₂-H), 4.69 (d, *J* = 11.6 Hz, 1 H, CH₂-H), 4.64 (d, *J* = 11.6 Hz, 1 H, CH₂-H), 4.46 (s, 2 H, CH₂), 4.41 (d, *J* = 10.9 Hz, 1 H, CH₂-H), 3.70–3.61 (m, 2 H, CH, CH₂-H), 3.61–3.51 (m, 3 H, BCH, CH, CH₂-H), 3.50–3.41 (t, *J* = 9.0 Hz, 1 H, CH), 3.37–3.27 (m, 4 H, 2 × CH₂), 3.08 (dd, *J* = 11.1, 4.8 Hz, 1 H, CH₂-H), 2.94–1.54 (m, 10 H, 10 × BH), 2.73–2.63 (m, 1 H, CH₂-H), 2.61–2.51 (m, 1 H, CH₂-H), 2.33–2.26 (m, 3 H, CH₂, CH), 2.22 (t, *J* = 10.8 Hz, 1 H, CH₂-H), 1.76–1.67 (m, 2 H, CH₂), 1.49 (p, *J* = 7.3, 6.9 Hz, 2 H, CH₂), 1.45–1.31 (m, 2 H, CH₂), 1.28–1.14 (m, 2 H, CH₂) ppm. ¹³C NMR (101 MHz, CDCl₃): δ = 139.11, 138.66, 137.95, 128.47, 128.43, 128.42, 127.96, 127.91, 127.74, 127.64, 127.54, 87.49, 78.72, 78.66, 75.41, 75.29, 75.22, 73.54, 72.89, 71.10, 69.21, 65.65, 63.92, 61.43, 54.60, 52.38, 35.36, 29.60, 29.58, 24.24, 23.70 ppm. ¹¹B NMR (128 MHz, CDCl₃): δ = –2.30, –5.79, –9.29, –11.47, –12.05, –13.03 ppm. [*α*]_D²⁰ = +5.1 (*c* = 1.1, CH₂Cl₂). FT-IR (thin film): $\tilde{\nu}$ = 3088, 3061, 3030, 2933, 2861, 2801, 2583 (B–H), 1496, 1453, 1360, 1310, 1207, 1172, 1091, 1072, 1027, 909 cm⁻¹. ESI-HRMS (*m/z*): calculated for [C₄₄H₆₃B₁₀NO₅ + H]⁺ 795.57779, observed

795.57710. The benzylated iminosugar (107 mg, 0.13 mmol) was treated according to general procedure B. HPLC-MS purification (A: 0.1% TFA in H₂O; B: linear gradient 37% → 43% CH₃CN in 12 min; flow: 5 mL/min) followed by lyophilisation provided the TFA salt of iminosugar **5** as a white powder (17.8 mg, 32.5 μmol, 25%). ¹H NMR (600 MHz, MeOD): δ = 4.53 (s, 1 H, BCH), 4.12 (d, *J* = 12.5 Hz, 1 H, CH₂-H), 3.90 (d, *J* = 10.9 Hz, 1 H, CH₂-H), 3.68 (td, *J* = 10.7, 4.9 Hz, 1 H, CH), 3.60 (t, *J* = 9.8 Hz, 1 H, CH), 3.48–3.41 (m, 3 H, CH₂-H, CH₂), 3.41–3.33 (m, 4 H, CH₂, CH₂-H, CH), 3.19 (td, *J* = 12.4, 4.7 Hz, 1 H, CH₂-H), 3.04 (d, *J* = 9.9 Hz, 1 H, CH), 2.98 (t, *J* = 11.7 Hz, 1 H, CH₂-H), 2.77–1.55 (m, 10 H, BH), 2.38–2.32 (m, 2 H, CH₂), 1.85–1.77 (m, 1 H, CH₂-H), 1.77–1.69 (m, 3 H, CH₂-H, CH₂), 1.63 (p, *J* = 6.9 Hz, 2 H, CH₂), 1.45 (dq, *J* = 14.5, 7.2 Hz, 2 H, CH₂) ppm. ¹³C NMR (151 MHz, MeOD): δ = 162.86, 162.63, 162.40, 162.16, 120.88, 118.94, 117.02, 115.07 (8 × CF₃CO₂H), 78.13, 77.01, 71.46, 70.33, 68.77, 67.80, 67.44, 63.76, 54.87, 54.28, 35.86, 30.66, 30.12, 24.44, 23.93 ppm. ¹¹B NMR (128 MHz, MeOD): δ = –2.90, –6.14, –9.67, –11.72, –13.09 ppm. [*α*]_D²⁰ = –2.8 (*c* = 0.36, MeOH). FT-IR (thin film): $\tilde{\nu}$ = 3333, 3065, 2936, 2865, 2592 (B–H), 1671, 1456, 1375, 1203, 1132, 1032 cm⁻¹. ESI-HRMS (*m/z*): calculated for [C₁₆H₃₉B₁₀NO₅ + H]⁺ 434.39125, observed 434.39056.

***N*-{5'-[3'-(1''',2'''-Dicarba-closo-dodecaboranyl)propoxy]pentyl}-L-ido-1-deoxynojirimycin TFA Salt (8):** Compound **22** (112 mg, 0.24 mmol, 1.2 equiv.) was treated with 2,3,4,6-tetra-*O*-benzyl-L-ido-deoxynojirimycin **16** (104 mg, 0.20 mmol, 1 equiv.) according to general procedure A. Flash column chromatography (100% PE → 30% EtOAc in PE) afforded protected iminosugar as a colorless oil (108 mg, 0.12 mmol, 59%) as well as the TBDMS deprotected product (27 mg, 0.03 mmol, 17%). *R*_f = 0.7 (4:1 pentane/EtOAc). ¹H NMR (400 MHz, CDCl₃): δ = 7.60–6.98 (m, 20 H, CH_{Ar}), 4.84 (d, *J* = 11.0 Hz, 1 H, CH₂-H), 4.79 (d, *J* = 11.0 Hz, 1 H, CH₂-H), 4.71 (d, *J* = 11.6 Hz, 1 H, CH₂-H), 4.68–4.58 (m, 3 H, CH₂, CH₂-H), 4.52 (d, *J* = 12.2 Hz, 1 H, CH₂-H), 4.48 (d, *J* = 12.2 Hz, 1 H, CH₂-H), 3.81 (dd, *J* = 10.1, 6.5 Hz, 1 H, CH₂-H), 3.71 (dd, *J* = 10.1, 2.3 Hz, 1 H, CH₂-H), 3.65 (dd, *J* = 9.0, 5.8 Hz, 1 H, CH), 3.58–3.45 (m, 2 H, 2 × CH), 3.39–3.26 (m, 5 H, CH, 2 × CH₂), 3.11–1.57 (m, 10 H, BH), 2.85 (dd, *J* = 11.8, 5.1 Hz, 1 H, CH₂-H), 2.74–2.65 (m, 1 H, CH₂-H), 2.57–2.47 (m, 2 H, 2 × CH₂-H), 2.35–2.27 (m, 2 H, CH₂), 1.81–1.71 (m, 2 H, CH₂), 1.50 (p, *J* = 14.5, 6.7 Hz, 2 H, CH₂), 1.45–1.36 (m, 2 H, CH₂), 1.26 (p, *J* = 7.4 Hz, 2 H, CH₂), 1.04 (s, 9 H, 3 × CH₃), 0.31 (s, 6 H, 2 × CH₃) ppm. ¹³C NMR (101 MHz, CDCl₃): δ = 139.22, 138.79, 138.72, 138.66, 128.47, 128.42, 128.41, 128.36, 128.06, 127.85, 127.70, 127.63, 127.56, 127.52, 83.18, 81.56, 80.40, 78.99, 76.54, 75.46, 73.37, 73.13, 72.81, 71.16, 69.42, 64.56, 59.90, 54.75, 50.01, 35.19, 30.56, 29.70, 27.90, 27.76, 23.93, 20.44, –2.40 ppm. ¹¹B NMR (128 MHz, CDCl₃): δ = 0.18, –4.00, –7.36, –10.27 ppm. [*α*]_D²⁰ = –17.3 (*c* = 1.8, CH₂Cl₂). ESI-HRMS (*m/z*): calculated for [C₅₀H₇₇B₁₀NO₅Si + H]⁺ 909.66474, observed 909.66459. Fully protected iminosugar (0.15 mmol) containing some TBDMS-deprotected product (0.03 mmol) was dissolved in dry THF (1 mL) under an argon atmosphere and cooled to –78 °C. TFA (10.8 μL, 0.15 mmol, 1 equiv.) and TBAF (1 M in THF, 0.17 mL, 0.17 mmol, 1.2 equiv.) were added. The mixture was stirred at –78 °C for 15 min, then for 1 h at room temp. until TLC showed complete conversion of the starting material. Water (30 mL) was added and extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine (1 × 90 mL), dried with MgSO₄, filtered and concentrated under reduced pressure. Flash column chromatography (10% → 40% EtOAc in PE) yielded the benzylated iminosugar as pale yellow oil (103 mg, 0.13 mmol, 89%). *R*_f = 0.5 (4:1 pentane/EtOAc). ¹H NMR (400 MHz, CDCl₃): δ = 7.44–7.11

(m, 20 H, CH_{AT}), 4.85 (d, *J* = 11.0 Hz, 1 H, CH₂-H), 4.79 (d, *J* = 11.0 Hz, 1 H, CH₂-H), 4.71 (d, *J* = 11.5 Hz, 1 H, CH₂-H), 4.68–4.58 (m, 3 H, CH₂-H, CH₂), 4.52 (d, *J* = 12.2 Hz, 1 H, CH₂-H), 4.48 (d, *J* = 12.2 Hz, 1 H, CH₂-H), 3.81 (dd, *J* = 10.1, 6.6 Hz, 1 H, CH₂-H), 3.71 (dd, *J* = 10.1, 2.4 Hz, 1 H, CH₂-H), 3.65 (dd, *J* = 9.2, 5.8 Hz, 1 H, CH), 3.59–3.44 (m, 3 H, BCH, 2 × CH), 3.38–3.28 (m, 5 H, CH, 2 × CH₂), 3.08–1.58 (m, 10 H, BH), 2.86 (dd, *J* = 11.8, 5.3 Hz, 1 H, CH₂-H), 2.76–2.65 (m, 1 H, CH₂-H), 2.57–2.48 (m, 2 H, 2 × CH₂-H), 2.33–2.24 (m, 2 H, CH₂), 1.76–1.66 (m, 2 H, CH₂), 1.51 (p, *J* = 14.5, 6.8 Hz, 2 H, CH₂), 1.47–1.38 (m, 2 H, CH₂), 1.26 (p, *J* = 7.3 Hz, 2 H, CH₂) ppm. ¹³C NMR (101 MHz, CDCl₃): δ = 139.20, 138.77, 138.71, 138.66, 128.49, 128.44, 128.42, 128.38, 128.08, 127.86, 127.72, 127.65, 127.57, 127.53, 83.18, 80.38, 78.97, 75.50, 73.36, 73.14, 72.80, 71.20, 69.18, 64.54, 61.43, 59.87, 54.70, 49.95, 35.36, 29.59, 29.58, 27.83, 23.90 ppm. ¹¹B NMR (128 MHz, CDCl₃): δ = –2.36, –5.85, –9.33, –11.51, –12.12, –13.09 ppm. [α]_D²⁰ = –19.4 (*c* = 1.7, CH₂Cl₂). FT-IR (thin film): ν̄ = 3086, 3060, 3030, 2932, 2860, 2581 (B–H), 1496, 1453, 1362, 1309, 1250, 1207, 1090, 1069, 1026, 910 cm^{–1}. ESI-HRMS (*m/z*): calculated for [C₄₄H₆₃B₁₀NO₅ + H]⁺ 795.57779, observed 795.57722. Benzylated iminosugar (107 mg, 0.13 mmol) was treated according to general procedure B. HPLC-MS purification (A: 0.1% TFA in H₂O; B: linear gradient 37% → 44% CH₃CN in 12 min; flow: 5 mL/min) followed by lyophilisation provided the TFA salt of iminosugar **8** as a white powder (17.97 mg, 32.82 μmol, 25%). ¹H NMR (600 MHz, MeOD): δ = 4.54 (s, 1 H, BCH), 4.06–3.92 (m, 4 H, 2 × CH, CH₂), 3.91–3.84 (m, 1 H, CH), 3.56–3.46 (m, 2 H, CH, CH₂-H), 3.43 (t, *J* = 6.3 Hz, 2 H, CH₂), 3.39 (t, *J* = 6.0 Hz, 2 H, CH₂), 3.38–3.31 (m, 3 H, CH₂-H, CH₂), 2.78–1.58 (m, 10 H, BH), 2.38–2.33 (m, 2 H, CH₂), 1.90–1.80 (m, 1 H, CH₂-H), 1.77–1.69 (m, 3 H, CH₂-H, CH₂), 1.63 (p, *J* = 6.4 Hz, 2 H, CH₂), 1.44 (p, *J* = 7.5 Hz, 2 H, CH₂) ppm. ¹³C NMR (151 MHz, MeOD): δ = 162.69 (CF₃CO₂H), 77.02, 72.35, 71.48, 70.31, 68.94, 68.02, 63.83, 63.76, 61.41, 55.06, 54.43, 35.87, 30.66, 30.14, 24.46, 23.28 ppm. ¹¹B NMR (128 MHz, MeOD): δ = –2.92, –6.17, –9.68, –11.75, –13.12 ppm. [α]_D²⁰ = +10.0 (*c* = 0.36, MeOH). FT-IR (thin film): ν̄ = 3348, 3065, 2934, 2870, 2592 (B–H), 1673, 1435, 1202, 1133, 1072 cm^{–1}. ESI-HRMS (*m/z*): calculated for [C₁₆H₃₉B₁₀NO₅ + H]⁺ 434.39125, observed 434.39052.

Biology: The inhibitory potencies (IC₅₀ values) of **1–8** for various enzyme activities were determined by exposing cells or enzyme preparations to an appropriate range of iminosugar concentrations. IC₅₀ values for GCS activity were measured using living cells with NBD-ceramide as substrate.^[17] Briefly, cells were incubated in 1 mL of medium with 50 nmol C6-NBD-ceramide {6-[*N*-methyl-*N*-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)aminododecanoyl]sphingosine} in the presence of increasing concentrations of compounds **1–8**. The cells were harvested after 2 h followed by lipid extraction, and separation by thin-layer chromatography. Formed C6-NBD-glucosyl-ceramide was quantified using a Molecular Dynamics Typhoon phosphorimaging device. IC₅₀ values were determined from the titration curves. The experiment was repeated three times. IC₅₀ values for lysosomal GBA were measured using 4-methylumbelliferyl β-D-glucoside as substrate.^[18] Briefly, recombinant glucocerebrosidase was incubated with increasing amounts of compounds **1–8**. Enzyme activity was determined with 3.7 mM 4-methylumbelliferyl β-glucoside (4-MU-β-glucoside) in McIlvaine buffer (0.1 M citrate and 0.2 M phosphate buffer), pH 5.2, 0.1% Triton X100 (v/v) and 0.2% (W/v) sodium taurocholate. Assays, performed in triplicate, were incubated at 37 °C and stopped by the addition of glycine/NaOH (pH 10.6). The amount of liberated 4-MU was determined with a PerkinElmer Life Sciences LS30 fluorometer. IC₅₀ values for the nonlysosomal glucocerebrosidase (GBA2) were measured with

the same substrate as earlier described.^[19] Briefly, GBA2 rich membrane suspensions were prepared from Gaucher disease spleen and incubated with 3.7 mM 4-MU-β-glucoside in McIlvaine buffer (0.1 M citrate and 0.2 M phosphate buffer), pH 5.8, with or without pre-incubation for 30 min at 4 °C with 1 mM CBE (Sigma) to inhibit the lysosomal glucocerebrosidase, GBA. Assays were incubated at 37 °C and stopped by the addition of glycine/NaOH (pH 10.6). The amount of liberated 4-MU was determined with a Perkin-Elmer Life Sciences LS30 fluorometer. Assays were performed in triplicate.

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