Iminosugars as glucosylceramide processing enzymes inhibitors: design, synthesis and evaluation

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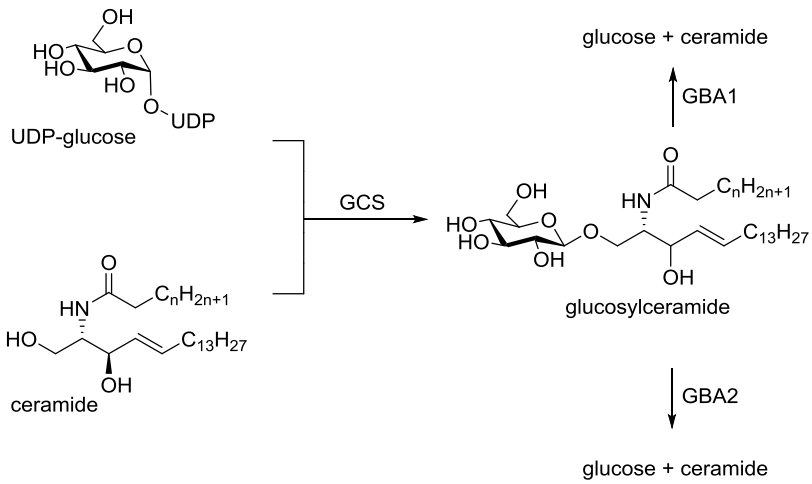
4 Discovery of *N*-alkyl Deoxynojirimycin Derivatives as Potential GBA2 Inhibitors

Introduction

GBA2 (EC3.2.1.45, GH116) is a membrane-bound, non-lysosomal retaining β-glucosidase. GBA2 was first described by Matern *et al*. who annotated the enzyme as a bile acid active glycosidase,[1] but is now widely known to partake in the degradation of glucosylceramide (GlcCer).[2] GBA2 is associated with a number of physiological and pathological processes, such as neuronal development, lysosomal storage diseases (LSD), tumorigenicity and inflammatory diseases.[3]

GlcCer is synthesized on the outer endoplasmic reticulum leaflet by glucosylceramide synthase (GCS) from UDP-glucose and ceramide (Figure 1), and degraded in lysosomes by lysosomal glucocerebrosidase (GBA1).[4] In Gaucher disease and Niemann-Pick type C disease (caused by genetic deficiency of GBA1 and acid sphingomyelinase, respectively), GlcCer accumulates in lysosomes, from where it spills over into the cytoplasm where it is degraded by GBA2. This degradation leads to an increase of ceramide concentration in the cytoplasm, which may be responsible for several symptoms observed in patients suffering from Gaucher and Niemann-Pick type C.[5] Mistry *et al*. reported[6] that genetic deletion of the GBA2 gene can relieve clinical symptoms in Gaucher diseased mice, which indicates that GBA2 is a potential target for Gaucher disease treatment. This finding is consistent with the hypothesis that compensatory GBA2 overexpression in Gaucher disease has deleterious effects.[7]

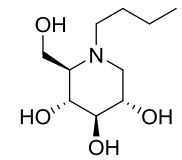
Figure 1*: Glucosylceramide metabolism*



Although GBA2 has been identified to be present in various tissues,[8] its expression and activity appears most abundant in the central nervous system.[9] This indicates that GBA2 may play a role in neuronal development. Relevant evidence to support this observation was shown by Martin *et al.* who demonstrated that the loss of GBA2 function is responsible for motor neuron defects in hereditary spastic paraplegia.[10] Also, mutations in the gene encoding for GBA2 were found in patients suffering from cerebella ataxia, spastic paraplegia, thin corpus callosum and cognitive impairment.[11] These findings underscore the potential correlation between GBA2 and neurodegenerative diseases. GBA2 activity has been connected with tumor biology as well. Inducibly overexpressed GBA2 leads to a decreased anchorage-independent human melanoma cell growth, and thus to the decrease of *in vivo* melanoma tumor growth.[12] In addition, GBA2 activity has also been associated with inflammatory responses. Mistry *et al*. reported that GBA2-deficient mice produce significantly lower amounts of several pro-

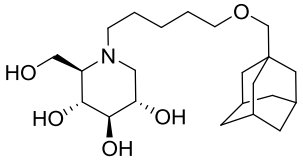
inflammatory cytokines, which indicates that GBA2 may be a relevant target for drugs aiming for reducing inflammation.[6] For all these reasons, the identification of inhibitors selective for GBA2 is a relevant research objective.

***Figure 2**: Structure and IC_{50} values of the lead compounds.*

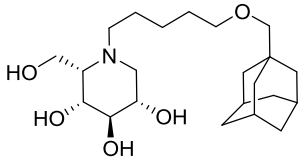


1, Zavesca

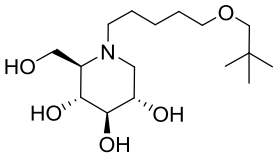
IC_{50} GCS 50 μM
IC_{50} GBA1 520 μM
IC_{50} GBA2 0.3 μM



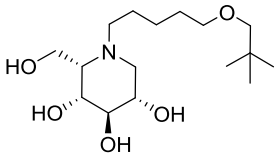
2, MZ-21 IC_{50} GCS 200 nM
IC_{50} GBA1 0.1 μM
IC_{50} GBA2 2 nM



3, MZ-31 IC_{50} GCS 100 nM
IC_{50} GBA1 30 μM
IC_{50} GBA2 1 nM



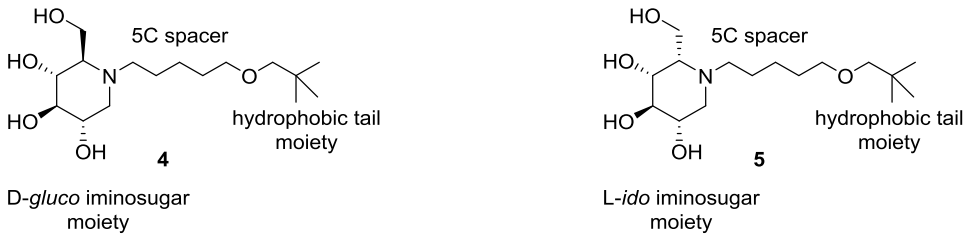
4 , DNJ-NEO IC_{50} GCS 5 μM
IC_{50} GBA1 6 μM
IC_{50} GBA2 5 nM



5, L-*ido* NEO IC_{50} GCS 1.6 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 10 nM

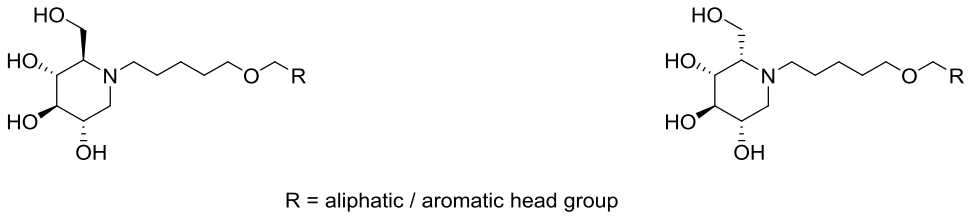
N-alkyl-deoxynojirimycin derivatives are potent GBA2 inhibitors that however display inhibitory activity against the other GlcCer-metabolizing enzymes, GCS and GBA1, as well (Figure 2). *N*-Butyl-deoxynojirimycin (*N*-butyl-DNJ, Zavesca, **1**), a moderately potent GCS inhibitor that at lower concentrations also blocks GBA2 activity, is in clinical use for the treatment of non-neuronopathic Gaucher patients. Inspired by the clinical success of *N*-butyl-DNJ (**1**), a large number of *N*-alkyl-DNJ derivatives have appeared in the literature and that vary in the nature of the *N*-alkyl group, in the configuration of the polyhydroxylated piperidine or a combination thereof.[13-15] Amongst these compounds, *N*-adamantanemethyloxypentyl-DNJ (**2**, MZ-21) and its L-*ido*-configured isoster (**3**, MZ-31) were identified as very potent GCS inhibitors (much more than the clinical compound, Zavesca **1**) that also strongly inhibit GBA2 and to a lesser extend GBA1. In the context of the studies that led to the identification of MZ-21 **2** and MZ-31 **3**, it was observed that *N*-neopentyloxypentyl-DNJ **4** and *N*-neopentyloxypentyl-L-*ido*-DNJ **5**, compounds with comparatively (in relation to **2** and **3**) smaller *N*-alkyl substituents, are potent GBA2 inhibitors with comparatively less activity against GCS and GBA1. Compared with MZ-21 ($IC_{50\,GCS}$ / $IC_{50\,GBA2}$ = 235), compound **4** has a much better GBA2 selectivity ($IC_{50\,GCS}$ / $IC_{50\,GBA2}$ = 1020). Compounds **4** and **5** are nanomolar GBA2 inhibitors while inhibiting GCS and GBA1 only in the micromole range, if at all.

Figure 3: *Structure of the lead N-neopentyloxypentyl-DNJ derivatives* ***4*** *(D-glucose configuration) and* ***5*** *(L-idose configuration)*



Taking compounds **4** and **5** as lead structures and with the aim to investigate whether GBA2 selective inhibitors could be designed, a series D-*gluco* and L-*ido*-DNJ derivatives bearing a variety of aliphatic and aromatic *N*-alkyl substituents (Figure 4) were prepared and evaluated on their potency and selectivity (as compared to GCS and GBA1) as GBA2 inhibitors.

Figure 4*: D-Gluco and L-ido-DNJ derivatives subject of the here presented studies*



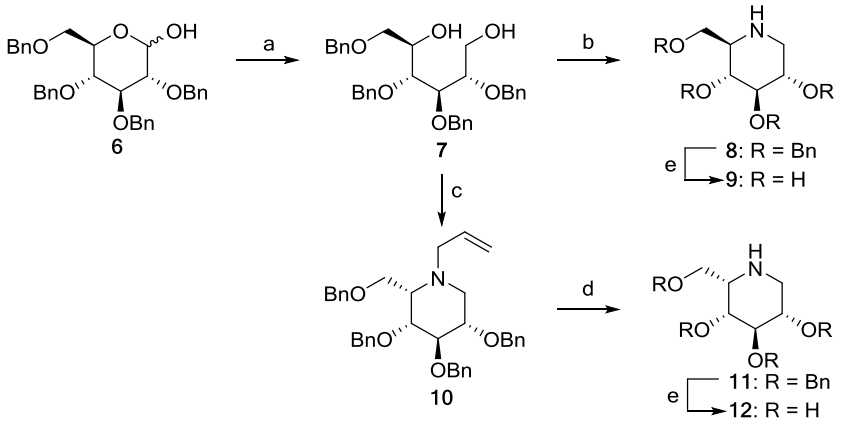
Results and discussion

The synthesis of DNJ (**9**) was accomplished following the established procedure with as key step a double reductive amination of a glucose-derived 5-keto-aldehyde (scheme 1).[16] In the first step, the commercially available 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**6**) was reduced to give partially protected glucitol **7**. Swern oxidation of both the primary and secondary alcohol in **7** followed by double reductive amination gave 2,3,4,6-tetra-*O*-benzyl-DNJ (**8**). Catalytic hydrogenation gave DNJ (**9**) in good yield and sufficient quantities for further elaboration.

Treatment of glucitol **7** with excess methanesulfonyl chloride followed by treatment with allyl amine gave, with inversion of configuration at the carbon bearing the secondary alcohol, fully protected L-*ido*-DNJ **10** in good overall yield. The allyl protecting group in **10** was removed by potassium *tert*-butoxide induced isomerization and subsequent acid-catalysed hydrolysis of

the obtained enamine to give **11** in excellent yield. Compound **11** was globally deprotected (H_2, Pd/C) to give L-*ido*-DNJ **12** for ensuing *N*-alkylation.

Scheme 1: *Synthesis of 1-deoxynojirimycin and L-ido-1-deoxynojirimycin*

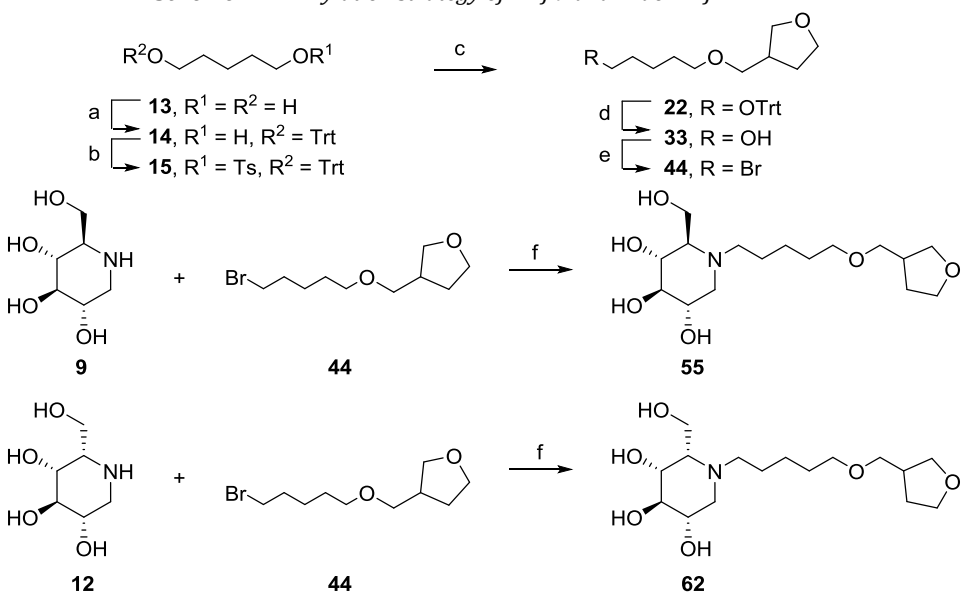


Reagents and conditions: [**a**] $LiAlH_4$, THF; [**b**] 1) $(COCl)_2$, DMSO, DCM; 2) $HCOONH_4$, Na_2SO_4, $NaBH_3CN$, MeOH, 12% 2 steps; [**c**] MsCl, pyridine, allyl amine, reflux, 78% 2 steps; [**d**] *t*BuOK, DMSO, HCl, 92%; [**e**] Pd/C, H_2, 82% (**9**), 76% (**12**).

The synthesis of appropriately functionalized alkylating agents for preparation of the target compounds was accomplished following established procedures. As an example, the synthesis of tetrahydrofuran-3-ylmethyloxypentyl bromide and its use in the *N*-alkylation of DNJ **9** and L-*ido*-DNJ **12** is depicted in Scheme 2. Thus, 1,5-pentanediol (**13**) was treated with one equivalent of trityl chloride (TrtCl) and base, after which the remaining primary alcohol in **14** was transformed into the sulfonate after reacting with *p*-toluenesulfonyl chloride (*p*-TsCl). The tosylate in the thus produced compound **15** was substituted by tetrahydrofuran-3-ylmethyl alcohol, yielding ether **22**. The trityl group in **22** was removed and the resulting alcohol **33** subjected to Appel bromination (treatment with triphenylphosphine and tetrabromomethane) to give bromide **44**. In a similar fashion, all compounds listed in Figure 5 were prepared. Finally, treatment of DNJ **9** with **44** and diisopropyl ethylamine in DMF gave *N*-alkyl-DNJ derivative **55**, and in a similar vein L-*ido*-DNJ derivative **62** was prepared (see experimental for details on the alkyl bromide syntheses and ensuing *N*-alkylation of DNJ **9** and L-*ido*-DNJ **12**).

In a similar way, and in yields varying from 10% up to 88%, *N*-alkyl-DNJ derivatives **4**, **49** - **59** and *N*-alkyl-L-*ido*-DNJ **5**, **60** - **65** were synthesized (Figure 6).

Scheme 2: *N-Alkylation strategy of DNJ* ***9*** *and L-ido-DNJ* ***12***



Reagents and conditions: [**a**] TrtCl, TEA, EtOAc, 85 °C, 3h, 99%; [**b**] *p*-TsCl, TEA, DMAP, DCM, 0 °C to r.t., 2h, 70%; [**c**] 1) THF-3-ylmethanol, NaH, DMF, r.t., 90 min; 2) **15**, 75 °C, 1h, 56%; [**d**] $BF_3{\cdot}OEt_2$, toluene/MeOH (1:1), 1.5h, 72%; [**e**] 1) PPh_3, DCM, r.t., 0 °C; 2) CBr_4, Ar, 2h, 91%; [**f**] DMF, K_2CO_3, 80 °C, 88% (**55**), 30% (**62**).

Figure 5*: Yields of the syntheses of the alkylating agents and their precursors*

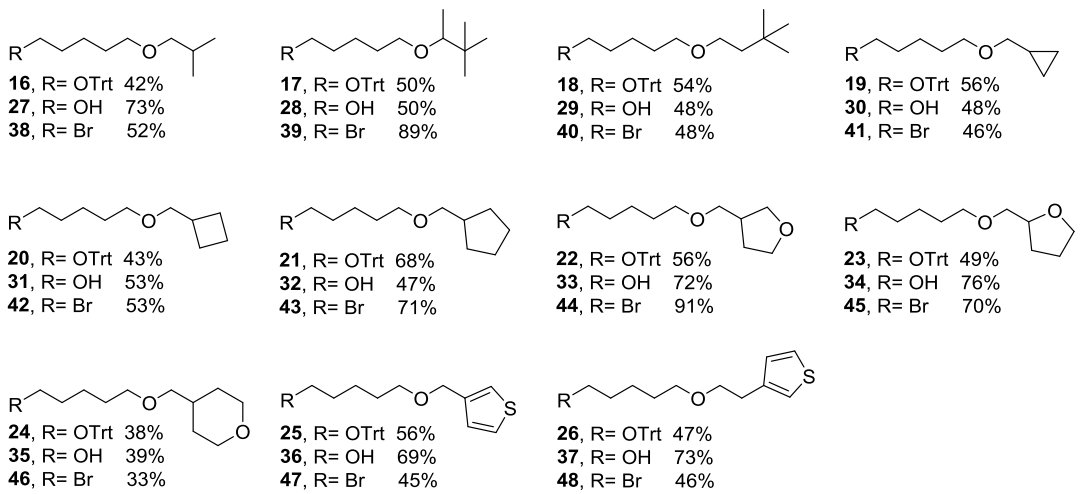
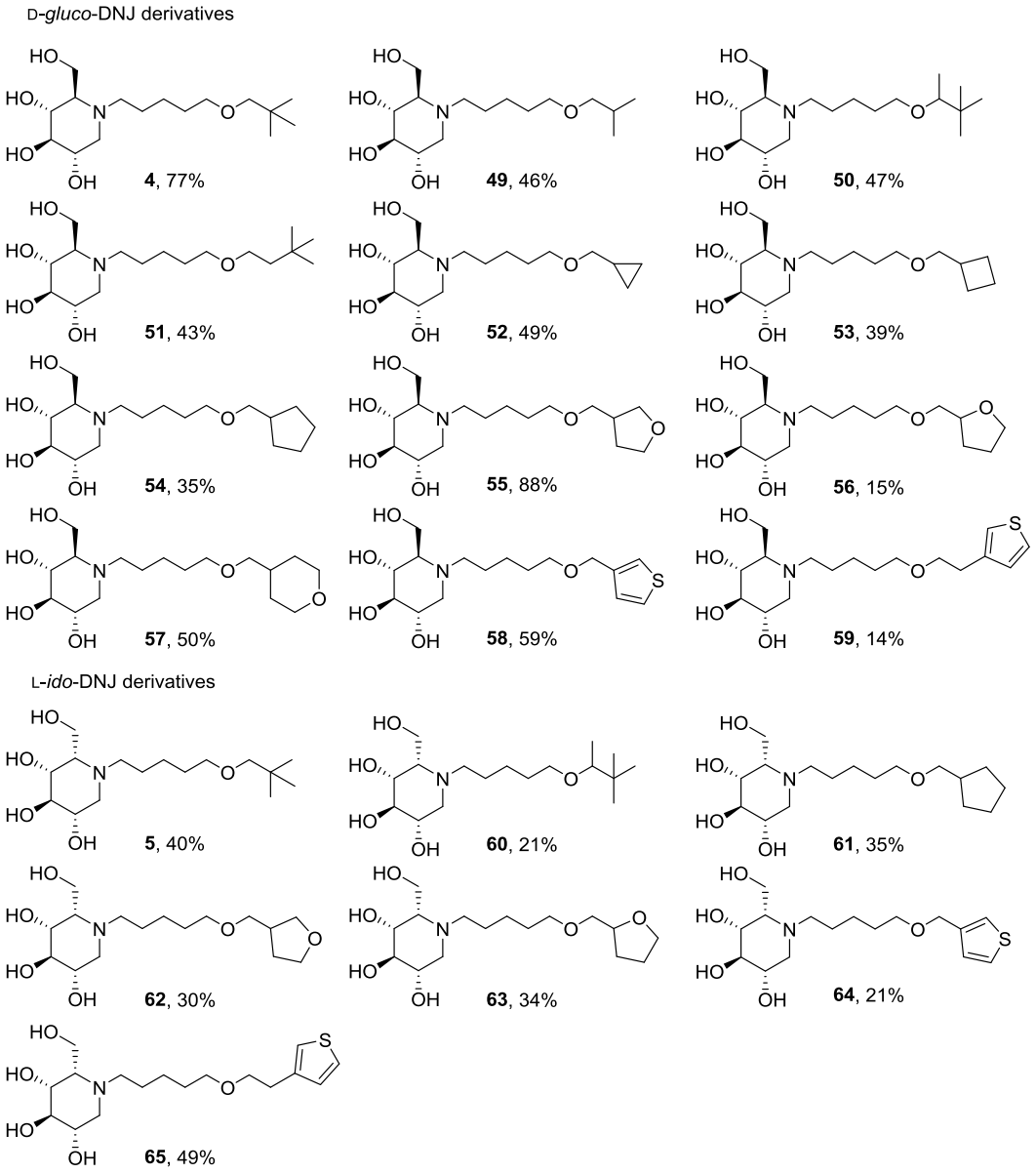


***Figure 6**: Isolated yields of the N-alkylated D-gluco and L-ido iminosugars*



Inhibition activity

Table 1 shows the inhibitory results of lead structure **4** together with *N*-alkyl-DNJ derivatives (**49** - **59**) on the three enzymes involved in glycosylceramide metabolism: GCS, GBA1 and GBA2. From the results on the series of branched alkyl analogues (**49** - **51**), it can be observed that extending the neopentyl group in **4** with one carbon, as in **51**, results in more potent GCS inhibitory activity. The absence (**49**) or presence (**50**) of an additional methyl

moiety gave no significant difference in inhibitory potency towards GCS, compared to **4**. Within the cycloalkyl series (**52** - **54**), the compound with the largest substituent proved to be the most potent GCS inhibitor (inhibitory activity: **54** > **53** > **52**), whereas the tetrahydrofuran- and tetrahydropyran-modified DNJ derivatives **55** - **57** proved to be poor GCS inhibitors. The thiophene containing iminosugars (**58** and **59**) inhibit GCS almost as potently as the literature compound, MZ-21 (**4**). Amongst all the compounds, cyclopentyl-DNJ derivative **54** appeared the most potent GCS inhibitor (IC_{50} = 0.12), whereas compounds **51**, **53**, **58** and **59** are also potent GCS inhibitors with sub-micromolar IC_{50} values. Altogether, these results indicate that a sizeable hydrophobic nonpolar *N*-alkyl group is critical for GCS activity.

***Table 1**: GCS, GBA1 and GBA2 IC_{50} values of the alkylated D-gluco iminosugars*

Compound	*IC_{50} GCS (μM)*	*IC_{50} GBA1 (μM)*	*IC_{50} GBA2 (nM)*
D-*gluco*-DNJ series			
4	5 ± 0.9	6 ± 0.4	5 ± 0.07
49	4 ± 0.1	17 ± 1	7 ± 1
50	6 ± 0.9	3 ± 0.2	4 ± 0.2
51	0.8 ± 0.03	4 ± 0.009	5 ± 0.3
52	7 ± 1	51 ± 2	18 ± 0.2
53	0.6 ± 0.03	12 ± 0.2	9 ± 0.9
54	0.1 ± 0.06	6 ± 0.4	4 ± 0.2
55	>50	156 ± 6	42 ± 5
56	>50	325 ± 14	120 ± 8
57	10 ± 0.7	63 ± 2	35 ± 2
58	0.4 ± 0.06	11 ± 0.2	4 ± 0.6
59	0.4 ± 0.05	6 ± 0.2	2 ± 0.1

With respect to GBA1 inhibitory activity, it was observed that with the exception of compounds **50**, **51**, **54** and **59**, most compounds are less potent than lead compound **4**. This may suggest that a nonpolar hydrophobic moiety of a certain size is essential for GBA1 inhibitory activity. Looking at the nature of the alkyloxy substituent, branched alkyl moieties are favorable with respect to GBA1 inhibitory activity (inhibitory potency: **50** > **4** > **49**). From the cycloalkyl series, it can be concluded that the larger the substituent is, the more potent the compound inhibits GBA1 (inhibitory potency: **54** > **53** > **52**). As was observed for GCS inhibition, the tetrahydrofuranyl/tetrahydropyranyl-DNJ derivatives are poor GBA1 inhibitors (compare, for instance, the GBA1 inhibition values measured for cyclopentanyl-DNJ derivative

54 with those obtained for tetrahydrofuranyl-DNJ derivatives **55** and **56**). Another observed trend is that an extra methylene moiety (**4** versus **51**, **58** versus **59**) is beneficial for GBA1 inhibitory activity. The most potent GBA1 inhibitor of this series finally appeared to be compound **50**.

***Table 2**: GCS, GBA1 and GBA2 IC_{50} values of the alkylated L-ido iminosugars*

Compound	*IC_{50} GCS (μM)*	*IC_{50} GBA1 (μM)*	*IC_{50} GBA2 (nM)*
L-*ido*-DNJ series			
5	3 ± 0.1	>1000	10 ± 0.3
60	5 ± 0.1	196 ± 15	7 ± 0.5
61	0.12 ± 0.005	176 ± 16	3 ± 0.1
62	1 ± 0.2	>1000	25 ± 0.7
63	2.5 ± 0.4	>1000	21 ± 4
64	0.05 ± 0.002	328 ± 26	2 ± 0.3
65	0.12 ± 0.008	205 ± 0.4	11 ± 0.04

Looking at GBA2 inhibitory activity, finally, it can be seen that all *N*-alkyl-DNJ derivatives tested are potent GBA2 inhibitors. Again, compounds **55**, **56**, and **57** featuring a tetrahydrofuranyl/tetrahydropyranyl moiety are the weakest inhibitors of the series. However, GBA2 inhibitory activity is less affected by the presence of an oxygen atom than GBA1 and GCS inhibitory activities. When comparing tetrahydrofuranyl-DNJ **55** with cyclopentyl-DNJ **54**, it can be seen that substituting one of the cyclopentyl carbons (as in **54**) for oxygen (as in **55**) led to a 500-fold decrease in GCS inhibitory activity, a 25-fold decrease in GBA1 inhibitory activity, and a 10-fold decrease in GBA2 inhibitory activity. Thus, while compound **55** is less potent than carbon analogue **54**, it is the more selective GBA2 inhibitor. Amongst the cycloalkyl-DNJ derivatives, compound **54** featuring a cyclopentane moiety appeared to be the most potent GBA2 inhibitor.

In summary on this part, DNJ derivative **55** appears to be the most GBA2 selective compound ($IC_{50\,GCS}$ / $IC_{50\,GBA2}$ = 1176, $IC_{50\,GBA1}$ / $IC_{50\,GBA2}$ = 3682), and while less active it is also more selective than compound **4**, which served as the starting point of the here-presented studies ($IC_{50\,GCS}$ / $IC_{50\,GBA2}$ = 1020, $IC_{50\,GBA1}$ / $IC_{50\,GBA2}$ = 1252). At the same time, all DNJ derivatives follow the general trend that, in case GCS is inhibited, also GBA1 is inhibited with considerable potency. As has been shown before, altering the configuration of the piperidine moiety from D-glucose to L-idose can abolish GBA1 inhibition.

Accordingly, a number of alkyl substituents were selected and the corresponding *N*-alkyl-L-*ido*-DNJ derivatives were prepared (Scheme 2) and evaluated (Table 2) as GCS/GBA1/GBA2 inhibitors. As *N*-alkyl moieties, the most effective substituents from the D-*gluco*-DNJ series in terms of activity and selectivity were selected, leading to compounds **60** – **65**, the inhibitory potency of which was compared with lead L-*ido*-DNJ derivative **5**. All L-*ido* derivatives tested are more potent GCS inhibitors in comparison with their D-*gluco* congeners. This follows the trend witnessed in earlier studies, and the same holds true for GBA1 inhibition (all L-*ido*-DNJ derivatives tested are considerably weaker GBA1 inhibitors compared to the D-*gluco*-DNJ analogues). Finally and importantly, there is not much difference between GBA2 inhibitory potency when going from a D-*gluco*-DNJ derivative to its configurational L-*ido*-DNJ derivative (compare the GBA2 inhibitory potency of **60** with that of **50**; **61** with **54**; **62** with **55**; **63** with **56**; **64** with **58**; and **65** with **59**). Hence all L-*ido*-DNJ derivatives tested are potent GCS/GBA2 inhibitors with a considerable therapeutic window towards GBA1 – the enzyme one would like to avoid targeting when aiming for the development of new and improved substrate reduction therapies for Gaucher patients. Amongst the compounds tested thiophene-DNJ derivative **64** appears to be the most potent analogue and further testing of this compound in relevant biological systems may be considered.

Conclusion

In this Chapter 17 new *N*-alkyl-DNJ derivatives are described, the structures of which are inspired by neopentyl-DNJ derivatives **4** and **5**. From the compounds tested, DNJ derivative **55** may well be the most selective, nanomolar GBA2 inhibitor reported to date. The most potent GBA2 inhibitors in turn appear to be **59** and **64.** These compounds, as well as thiophene-L-*ido*-DNJ derivative **58**, which came out as the most most potent GCS inhibitor, deserves more in-depth studies with respect to their *in situ* and even *in vivo* efficacy to modulate GlcCer metabolism through inhibition of GCS and/or GBA2.

Experimental Section

Enzyme inhibition assays: The potencies (IC_{50} values) of the *N*-alkyl-DNJ derivatives as GCS, GBA1 and GBA2 inhibitors were determined by exposing cells or enzyme preparations to an appropriated range of iminosugar concentrations.

GCS: IC_{50} values for GCS activity were measured using living cells with NBD-ceramide as substrate.[17] Briefly, cells were incubated 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 compound concentrations. The cells were harvested after 2h followed by lipid extraction. The formed C6-NBD-glucosylceramide was quantified using a Molecular Dynamics Typhoon

phosphor imaging device. IC_{50} values were determined from the titration curves. The experiment was performed twice.

GBA1: IC_{50} values for lysosomal GBA1 were measured using 4-methylumbeliferyl-β-D-glucoside as substrate.[18] Briefly, recombinant GBA1 was incubated with increasing compound concentrations for 30 min at 0 °C. Enzyme activity was determined with 3.7 mM 4-methylumbelliferyl-β-D-glucopyranoside in McIlvaine buffer (0.1 M citrate and 0.2 M phosphate buffer), pH 5.2, 0.1% Triton X-100 (v/v) and sodium taurocholate (0.2%, w/v). Assays performed in triplicate were incubated at 37 °C for 30 min and quenched by the addition of glycine/NaOH (0.2 mL, pH 10.6). The amount of liberated 4-methylumbeliferyl was determined with a PerkinElmer Life Sciences LS30 fluorimeter, excitation wavelength 366 nm, emission wavelength 445 nm.

GBA2: IC_{50} values for the non-lysosomal glucocerebrosidase (GBA2) were measured with 4-methylumbeliferyl-β-D-glucoside as substrate.[18] GBA2-rich membrane suspensions were prepared from enzyme-overexpressing HEK cells by sonicating, and the suspension was pre-incubated for 30 min at 37 °C with conduritol-B-epoxide (1 mM, CBE, Sigma) to inhibit the lysosomal glucocerebrosidase (GBA1). The prepared GBA2-rich suspension was then incubated with increasing compound concentrations for another 30 min, and then incubated with 3.7 mM 4-methylumbeliferyl-β-D-glucoside in McIlvaine buffer (0.1 M citrate and 0.2 M phosphate buffer), pH 5.8. Assays were incubated at 37 °C for 1 hour and quenched by the addition of glycine/NaOH (0.2 mL, pH 10.6). The amount of liberated 4-methylumbeliferyl was determined with a PerkinElmer Life Sciences LS30 fluorimeter, excitation wavelength 366 nm, emission wavelength 445 nm. Assays were performed in triplicate.

General compound synthesis, purification and analysis methods: All solvents and reagents were obtained commercially and used as received unless stated otherwise. Reactions were executed at room temperature unless stated otherwise. Moisture sensitive reactions were performed under argon atmosphere. Water was removed from starting compounds by repetitive coevaporation with toluene. Solvents were removed by evaporation under reduced pressure. DCM, DMF, and THF were dried over activated 4Å molecular sieves for at least 12 hours before use. Compounds were visualized during TLC analyses by UV (254 nm), and with the following staining solutions: aqueous solution of $KMnO_4$ (5 g/L) and K_2CO_3 (25 g/L). Visualization of hemiacetals and glycosides was achieved by spraying with a solution of 20% H_2SO_4 in ethanol followed by charring at ≈ 200 °C. Column chromatography purification was performed on silica gel (40-63 μm). ^1H and ^{13}C-APT NMR spectra were recorded on a Bruker AV 400 (400/100 MHz) or Bruker 600 (600/150 MHz) spectrometer in $CDCl_3$, MeOD or D_2O. Chemical shifts are given in ppm (δ) relative to TMS as internal standard (^1H NMR in $CDCl_3$) or the signal of the deuterated solvent.[19] Coupling constants (*J*) are given in Hz. High resolution mass spectra were recorded by direct injection (2 μL of a 2 μM solution in water/acetonitrile/*tert*-butanol 1:1:1 v/v/v) on a mass spectrometer (Thermo Finnigan LTQ Orbitrap) equipped with an electrospray ion source with resolution R = 60000 at m/z 400 (mass range m/z = 150-2000). IR spectra were recorded on a Shimadzu FTIR-8300 and are reported in cm^{-1}. Optical rotation were measured on an automatic polarimeter of sodium D-line, at λ =589 nm. Size-exclusion purifications were performed on an ÄKTA-explorer, column size d = 26 mm, l = 60 mm, mobile phase NH_4HCO_3 (0.15 M) in H_2O, flow 1.5 mL/min. HPLC Purification were performed on a Prep LCMS, Gemini from Phenomenex B.V. (C-18, 110 Å, 5 μm, 19 x 150 mm column).

General procedure A: Substitution of the tosyl group. A dry solution of alcohol (5 mmol) in DMF (15 mL) was charged with NaH (10 mmol) and stirred for 90 min. Then a dry solution of **15** (4.5 mmol) in DMF (15 mL) was added. The reaction mixture was heated to 75 °C for 1 h.

After complete consumption of the starting material (TLC monitored), the mixture was cooled to room temperature, quenched by the addition of water (3 mL) and concentrated. The residue was dissolved in a mixture of TEAA (0.1 M), EtOAc and sat. aq. $NaHCO_3$ (80 mL, 2:3:3) and extracted with EtOAc (3 x 30 mL). The organic phase was dried ($MgSO_4$), filtered and concentrated. Purification by silica gel column chromatography (0 - 10% EtOAc in PE) gave the target compound.

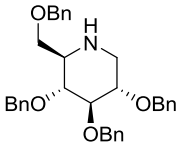
General Procedure B: Deprotection of the trityl-group. To a solution of alkyloxyl-1-trityloxpentane (2.0 mmol) in toluene/MeOH (1:1, 20 mL, 0.1 M) was added $BF_3{\cdot}Et_2O$ (3.0 mmol, 1.5 eq). This mixture was stirred for 1.5 h at r.t. After complete consumption of the starting material (TLC monitored), the mixture was diluted with EtOAc (30 mL) and washed with sat. aq. $NaHCO_3$ (50 mL). The water layer was extracted with EtOAc (3 x 30 mL) and the combined organic layers were dried ($MgSO_4$), filtered, concentrated and the residue purified by silica gel column chromatography (1:9 → 1:4 → 1:1 → 1:0, EtOAc:PE) to give target alcohol chain.

General Procedure C: Bromination. To a solution of alkyloxyl-1-pentanol (1 mmol) in DCM (100 mL, 0.01 M) was added PPh_3 (0.40 g, 1.5 mmol, 1.5 eq) and cooled to 0 °C. Then CBr_4 (0.5 g, 1.5 mmol, 1.5 eq) was added and the reaction mixture was stirred at 0 °C until TLC analysis monitored the complete consumption of starting compound. After which Celite was added and the volatiles were evaporated. The residue was purified with silica gel column chromatography (0 - 100% toluene in heptane → 2 - 20% EtOAc in toluene) to give the bromide spacer.

General Procedure D: Alkylation of iminosugars. To a mixture of the 1-bromo-5-alkyloxy-pentane (0.3 mmol, 1.5 eq) and di-isopropylethylamine (DiPEA, 0.1 mL, 0.6 mmol, 3 eq) was added a solution of iminosugar (0.03 g, 0.2 mmol) in DMF (1 mL). The mixture was stirred overnight at 70 °C. After cooling to r.t., the mixture was filtered and concentrated. The crude product was purified using HPLC.

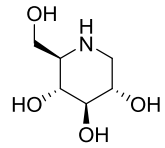
Synthesis of DNJ and L-*ido*-DNJ

2,3,4,6-Tetra-*O*-benzyl-1-deoxynojirimycin (8):



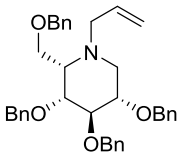
A solution of $(COCl)_2$ (0.70 mL, 8.16 mmol) in dry DCM (5 mL) under argon atmosphere, was cooled to -78 °C. DMSO (0.71 mL, 10.0 mmol) dissolved in dry DCM (5 mL) was added dropwise. After 40 minutes, **7** (1.02 g, 1.88 mmol, co-evaporated with toluene 3 x) in dry DCM (3 mL), was added dropwise to the mixture. The reaction was stirred for 2 hours at -78 °C, after which Et_3N (3.40 mL, 24.4 mmol) was added dropwise. The mixture was gradually warmed to -5 °C after which it was poured into a cooled (0 °C) MeOH solution (50 mL) containing $NaCNBH_3$ (0.50 g, 8.00 mmol), $HCOONH_4$ (2.53 g, 40.1 mmol), and Na_2SO_4 (0.89 g, 6.24 mmol). The mixture was stirred overnight during which the reaction mixture was allowed to warm up to r.t. TLC analysis showed complete consumption of the starting material (1:1, PE:EtOAc, R_F = 0.36). After filtration, the volatiles were evaporated, and the residue was dissolved in EtOAc (70 mL), washed with sat. aq. $NaHCO_3$ (70 mL). The organic layer was dried (Na_2SO_4) filtrated and concentrated. The residue was purified with silica gel column chromatography (2:1 → 1:2, PE:EtOAc) to give the pure product **8** in 12% overall yield (0.114 g, 0.218 mmol). R_F = 0.36 (1:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.13 (m, 20H, H_{Ar} Bn), 5.00 – 4.38 (m, 8H, 4 x CH_2 Bn), 3.66 (dd, *J* = 9.0, 2.5 Hz, 1H, H-6a), 3.58 – 3.44 (m, 3H, H-2, H-3, H-6b), 3.35 (t, *J* = 9.2 Hz, 1H, H-4), 3.23 (dd, *J* = 12.3, 4.9 Hz, 1H, H-1a), 2.71 (ddd, *J* = 9.7, 5.9, 2.6 Hz, 1H, H-5), 2.49 (dd, *J* = 12.2, 10.3 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9 – 138.0 (C_q Bn), 128.4 – 127.6 (CH_{Ar} Bn), 87.3 (C-3), 80.6 (C-2), 80.1 (C-4), 75.7, 75.2, 73.4, 72.8 (4 x CH_2 Bn), 70.2 (C-6), 59.8 (C-5), 48.1 (C-1).

1-Deoxynojirimycin (9):



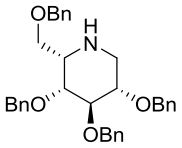
8 (2.00 g, 3.82 mmol) was dissolved in EtOH (120 mL) and pH was adjusted to 2 with HCl solution (1 M). The solution was flushed with argon (3 x), after which two spatula tips of Pd/C (20%) was added. Then the mixture was exposed to H_2 atmosphere (4 bar) for 24 hours. The catalyst was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified on silica gel column chromatography (4:1, EtOAc:MeOH + 1% NH_4OH → 6:4:1, EtOH:H_2O:NH_4OH) to give **9** in 82% yield (511 mg, 3.13 mmol). ^{1}H NMR (400 MHz, MeOD) δ 3.92 (dd, *J* = 10.9, 3.1 Hz, 1H, H-6a), 3.67 (dd, *J* = 10.9, 6.5 Hz, 1H, H-6b), 3.49 (ddd, *J* = 10.6, 8.7, 5.1 Hz, 1H, H-2), 3.28 (t, *J* = 8.1 Hz, 1H, H-3), 3.24 (t, *J* = 9.1 Hz, 1H, H-4), 3.18 (dd, *J* = 12.1, 5.1 Hz, 1H, H-1a), 2.54 (ddd, *J* = 9.4, 6.4, 3.1 Hz, 1H, H-5), 2.52 (dd, *J* = 12.1, 10.7 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 81.5 (C-3), 74.2 (C-4), 73.5 (C-2), 64.0 (C-6), 63.7 (C-5), 51.9 (C-1).

2,3,4,6-Tetra-*O*-benzyl-L-*ido*-*N*-allyl-1-deoxynojimycin (10):



MsCl (4.2 mL, 53.1 mmol) was added dropwise to a cooled mixture (0 °C) of pyridine (90 mL) and **7** (11.5 g, 21.2 mmol). The mixture was stirred for 3 hours at r.t., after which TLC analysis (2:1, PE:EtOAc, R_F = 0.13) showed complete consumption of the starting material. Water (60 mL) was added and the solution was concentrated. The residue was dissolved in EtOAc (130 mL), and successively washed with HCl (100 mL, 1M, 2 x), sat. aq. $NaHCO_3$ (100 mL) and brine (100 mL). The organic layer was dried (Na_2SO_4), filtered and concentrated. The residue was co-evaporated with toluene (3 x). Allylamine (90 mL) was added to dissolve the methanesulfonylated product, and the solution was heated to reflux for 14 hours, until TLC analysis (2:1, PE:EtOAc) showed complete consumption of the starting material. After concentration, the residue was dissolved with EtOAc (110 mL), washed with sat. aq. $NaHCO_3$ (100 mL, 2 x) and brine (100 mL). The organic layer was dried (Na_2SO_4), filtered and concentrated. The residue was purified on silica gel column chromatography (17:3, PE:EtOAc) to give **10** in 78% yield (9.30 g, 16.5 mmol). R_F = 0.76 (2:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.27 (m, 20H, H_{Ar} Bn), 5.77 (ddt, *J* = 16.8, 10.3, 6.3 Hz, 1H, H-2'), 5.12 (dd, *J* = 23.6, 6.2 Hz, 2H, H-3"), 4.90 – 4.46 (m, 8H, 4 x CH_2 Bn), 3.84 (dd, *J* = 10.2, 6.8 Hz, 1H, H-1a'), 3.72 (dd, *J* = 10.2, 2.5 Hz, 1H, H-1b"), 3.69 (dd, *J* = 7.6, 4.2 Hz, 1H, H-4), 3.60 – 3.50 (m, 2H, H-2, H-3), 3.42 (ddd, *J* = 10.1, 5.8, 1.6 Hz, 1H, H-5), 3.37 (dd, *J* = 6.9, 2.0 Hz, 1H, H-6a), 3.18 (dd, *J* = 14.1, 6.9 Hz, 1H. H-6b), 2.92 (dd, *J* = 11.9, 4.9 Hz, 1H, H-1a), 2.53 (dd, *J* = 11.8, 9.8 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 138.8, 138.7, 138.6 (4 x C_q Bn), 136.3 (C-2"), 128.5 – 127.6 (CH_{Ar} Bn), 117.2 (C-3"), 83.1 (C-4), 80.2 (C-3), 78.9 (C-2), 75.5, 73.4, 73.1 72.8 (4 x CH_2 Bn), 64.7 (C-1"), 60.1 (C-5), 58.1 (C-6), 49.1 (C-1).

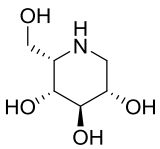
2,3,4,6-Tetra-*O*-benzyl-L-*ido*-1-deoxynojimycin (11):



A mixture of DMSO (35 mL), *t*BuOK (1.00 g, 8.91 mmol) and **10** (9.30 g, 16.5 mmol, co-evaporated with toluene 3 x) was heated to 100 °C and stirred under argon atmosphere. After 1 hour stirring, HCl solution (30 mL, 1M) was added and the heating resource was removed. After 30 minutes, the mixture was poured into a mixture of sat. aq. $NaHCO_3$ (100 mL) and Et_2O (150 mL). The organic layer was separated and the water layer was re-extracted with Et_2O (150 mL, 2 x). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. The residue was purified with silica gel column chromatography (2:1 → 1:2 → 0:1, PE:EtOAc) to give the pure product **11** with a yield of 92% (7.93 g, 15.1 mmol). R_F = 0.13 (1:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.22 (m, 20H, H_{Ar} Bn), 4.68 – 4.49 (m, 8H, 4 x CH_2 Bn), 3.68 (t, *J* = 9.2 Hz, 1H, H-6a), 3.62 (t, *J* = 5.3 Hz, 1H, H-3), 3.55 (dd, *J* = 9.5, 5.2 Hz, 1H, H-6b), 3.45 (td, *J* = 6.6, 4.1 Hz, 1H, H-2), 3.38 (ddd, *J* = 8.7, 5.0, 3.6 Hz, 1H, H-5), 3.01 (dd, *J* = 12.9, 4.1 Hz, 1H, H-1a), 2.86 (dd, J = 12.8, 6.7 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7 – 138.4 (C_q Bn), 128.5 – 127.7 (CH_{Ar}

Bn), 77.3 (C-3), 77.0 (C-2), 74.2 (CH_2 Bn), 73.5 (CH_2 Bn), 72.7 (CH_2 Bn), 72.2 (CH_2 Bn), 67.3 (C-6), 54.7 (C-5), 44.3 (C-1).

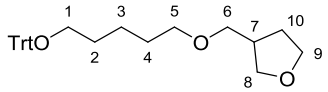
L-*Ido*-1-deoxynojimycin (12):



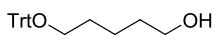
11 (2.30 g, 4.39 mmol) was dissolved in EtOH (150 mL) and pH was adjusted to 2 with HCl solution (1 M). The solution was flushed with argon for 3 times, after which two spatula tips of Pd/C (20%) was added. The suspension was exposed to H_2 atmosphere (4 bar) and shaken for 24 hours. The catalyst was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified with silica gel column chromatography (4:1 EtOAc:MeOH + 1% NH_4OH → 6:4:1, EtOH: H_2O:NH_4OH) to give the **12** in 76% yield (840 mg, 3.32 mmol). ^{1}H NMR (400 MHz, MeOD) δ 3.95 – 3.93 (m, 2H, H-2, H-3), 3.89 (dd, *J* = 5.7, 2.0 Hz, 1H, H-4), 3.85 (dd, *J* = 11.0, 2.1 Hz, 1H, H-6a), 3.81 (dd, *J* = 11.7, 5.1 Hz, 1H, H-6b), 3.47 (ddd, *J* = 8.9, 5.0, 1.9 Hz, 1H, H-5), 3.36 (dd, *J* = 13.2, 2.0 Hz, 1H, H-1a), 3.24 (dd, *J* = 13.2, 1.7 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 69.2 (C-4), 68.4 (C-3), 68.0 (C-2), 60.3 (C-6), 58.2 (C-5), 46.9 (C-1).

Synthesis of the bromide-spacers

***Figure 7**: Proton and carbon NMR numbering of the linker molecules (**16**- **48**)*

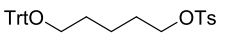


5-Trityloxy-1-pentanol (14):



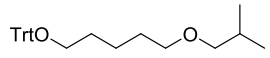
Trityl chloride (55.82 g, 200 mmol), 1,5-pentanediol (100 mL, 954 mmol), EtOAc (500 mL) and TEA (56 mL, 396 mmol) were mixed. The mixture was stirred for 3h at 85 °C. After complete conversion of the starting material (1:1, PE:EtOAc) the mixture was washed successively with HCl (4 x 100 mL, 1M) and sat. aq. $NaHCO_3$ (4 x 100 mL), dried ($MgSO_4$) and concentrated to give compound **22** (68.67 g, 198.20 mmol, 99% yield). R_F = 0.70 (1:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.36 (m, 6H, H_{Ar} Trt), 7.29 – 7.17 (m, 9H, H_{Ar} Trt), 3.57 – 3.55 (m, 2H, H_2-1), 3.07 – 3.05 (m, 2H, H_2-5), 1.65 – 1.63 (m, 2H, H_2-4), 1.55 – 1.35 (m, 4H, H_2-2, H_2-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4 (C_q Trt), 128.6 – 126.8 (CH Trt), 86.3 (C_q Trt), 63.4 (C-1), 62.7 (C-5), 32.5 (C-4), 29.7 (C-2), 22.4 (C-3).

5-(Toluene-4-sulfonyl)-1-trityloxypentane (15):



p-Toluenesulfonyl chloride (8.83 g, 46.3 mmol) was added to a dry and cooled (0 °C) mixture of **14** (10.72 g, 30.94 mmol), TEA (7 mL, 49.5 mmol) and DMAP (0.19 g, 1.56 mmol) in DCM (93 mL). The mixture was stirred for 2h while warming to r.t. The mixture was washed successively with HCl (100 mL, 1M), sat. aq. $NaHCO_3$ (100 mL) and sat. aq. NaCl (100 mL). The organic phase was dried ($MgSO_4$), filtered and concentrated. Purification of the residue with silica gel column chromatography (10 – 16% EtOAc in PE) gave compound **15** (10.9 g, 21.7 mmol, 70%) as a white solid. R_F = 0.78 (25% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, 2H, H_{Ar} Ts), 7.42 (d, 6H, H_{Ar} Trt), 7.24 – 7.19 (m, 10H, H_{Ar} Trt/Ts), 7.16 – 7.13 (m, 3H, H_{Ar} Trt), 3.94 (t, 2H, H-5), 3.00 (t, 2H, H_2-1), 1.94 (s, 3H, CH_3 Ts), 1.54 – 1.49 (m, 4H, H_2-2, H_2-4), 1.35 – 1.33 (m, 2H, H_2-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8 (C_q Ts), 144.5(C_q Trt), 133.3(C_q Ts), 130.0 (CH, Ts), 128.9 – 127.1 (CH Trt), 86.5 (C_q Trt), 70.7 (C-5), 63.2(C-1), 29.4 (C-2), 28.7 (C-4), 22.4 (C-3), 21.7 (CH_3 Ts).

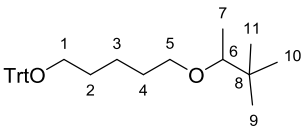
5-(2-Methyl-1-propyloxy)-1-trityloxypentane (16):



Compound **15** (4.60 mmol) was subjected to the general procedure A, using 2-methyl-1-propanol (5.05 mmol) to provide **16** (0.77 g, 1.92

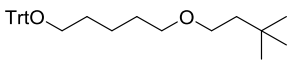
mmol) in a yield of 42%, as thick oil, after silica gel column chromatography purification. R_F = 0.65 (10% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (m, *J* = 8.6, 2.2, 1.6 Hz, 6H, H_{Ar} Trt), 7.32 – 7.14 (m, 9H, H_{Ar} Trt), 3.37 (t, *J* = 6.5 Hz, 2H, H_2-5), 3.14 (d, *J* = 6.8 Hz, 2H, H_2-6), 3.06 (t, *J* = 6.6 Hz, 2H, H_2-1), 1.84 (dp, *J* = 6.7 Hz, 1H, H-7), 1.71 – 1.60 (m, 2H, H_2-2), 1.59 – 1.50 (m, 2H, H_2-4), 1.50 – 1.37 (m, 2H, H_2-3), 0.89 (d, *J* = 6.7 Hz, 6H, 2 x CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6 (C_q Trt), 128.8 (CH Trt), 127.7 (CH Trt), 126.9 (CH Trt), 86,4 (C_q Trt), 77.9 (C-6), 71.0 (C-5), 63.6 (C-1), 30.0 (C-2), 29.7 (C-4), 28.5 (C-7), 23.1 (C-3), 19.5 (2 x CH_3). IR/cm^{-1}: 3061, 2930, 2901, 2866, 1597, 1489, 1448, 1392, 1364, 1176, 1072.

5-(3,3-Dimethyl-2-butoxy)-1-trityloxypentane (17):



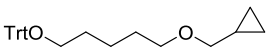
Compound **15** (4.43 mmol) was subjected to the general procedure A, using 3,3-dimethyl-2-butanol (5.06 mmol) to provide **17** (0.95 g, 2.21 mmol) in a 50% yield, as thick oil, after silica gel column chromatography purification. R_F = 0.79 (5% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.36 (m, 6H, H_{Ar} Trt), 7.28 – 7.11 (m, 12H, H_{Ar} Trt), 3.53 (dt, *J* = 9.4, 5.8 Hz, 1H, H-5a), 3.21 (dd, *J* = 9.2, 6.2 Hz, 1H, H-5b), 3.06 (t, *J* = 6.6 Hz, 2H, H_2-1), 2.93 (q, *J* = 6.3 Hz, 1H, H-6), 1.74 – 1.35 (m, 6H, H_2-2, H_2-3, H_2-4), 1.01 (d, *J* = 6.3 Hz, 3H, H_3-7), 0.87 (s, 9H, H_3-9, H_3-10, H_3-11). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7 (C_q Trt), 128.8 (CH Trt), 127.9 (CH Trt), 126.9 (CH Trt), 86.4 (C_q Trt), 83.4 (C-6), 69.8 (C-5), 63.7 (C-1), 35.3 (C-8), 30.3 (C-2), 30.1 (C-4), 26.2 (C-7), 23.3 (C-3), 14.1 (C-9, C-10, C-11). IR/cm^{-1}: 3059, 3022, 2936, 2866, 1597, 1489, 1448, 1389, 1362, 1219, 1090, 1072.

5-(3,3-Dimethyl-1-butoxy)-1-trityloxypentane (18):



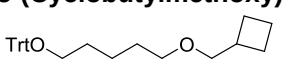
Compound **15** (4.41 mmol) was subjected to the general procedure A, using 3,3-dimethyl-1-butanol (5.07 mmol) to provide **18** (1.02 g, 2.36 mmol) in a 54% yield, as thick oil, after silica gel column chromatography purification. R_F = 0.67 (5% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (dt, *J* = 8.3, 2.2 Hz, 6H, H_{Ar} Trt), 7.25 – 7.16 (m, 6H, H_{Ar} Trt), 7.16 – 7.10 (m, 3H, H_{Ar} Trt), 3.41 (t, *J* = 7.4 Hz, 2H, H_2-5), 3.34 (t, *J* = 6.4 Hz, 2H, H_2-6), 3.06 (td, *J* = 6.9, 3.0 Hz, 2H, H_2-1), 1.63 (p, *J* = 6.8 Hz, 2H, H_2-2), 1.52 (m, 4H, H_2-4, H_2-7), 1.48 - 1.38 (m, 2H, H_2-3), 0.90 (s, 9H, H_3-9, H_3-10, H_3-11). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5 (C_q Trt), 128.7 (C_{Ar} Trt), 127.7 (CH Trt), 126.8 (CH Trt), 86.3 (C_q Trt), 70.8 (C-6), 68.1 (C-5), 63.5 (C-1), 43.0 (C-7), 29.8 (C-2), 29.7 (C-9,10,11), 29.6 (C-4), 29.6 (C-8), 23.1 (C-3). IR/cm^{-1}: 3057, 3022, 2936, 2864, 1597, 1489, 1448, 1364, 1219, 1111, 1072.

5-(Cyclopropylmethoxy)-1-trityloxypentane (19):



Compound **15** (4.41 mmol) was subjected to the general procedure A, using cyclopropylmethanol (5.02 mmol) to provide **19** (0.10 g, 2.49 mmol) in a 56% yield, as thick oil, after silica gel column chromatography purification. R_F = 0.63 (10% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.41 (m, 6H, Trt), 7.28 - 7.19 (m, 6H, H_{Ar} Trt), 7.20 – 7.13 (m, 3H, H_{Ar} Trt), 3.38 (t, *J* = 6.6 Hz, 2H, H_2-5), 3.20 (d, *J* = 6.9 Hz, 2H, H_2-6), 3.06 (t, *J* = 6.6 Hz, 2H, H_2-1), 1.65 (p, *J* = 6.8 Hz, 2H, H_2-2), 1.51 – 1.59 (m, 2H, H_2-4), 1.47 – 1.38 (m, 2H, H_2-3), 1.08 – 0.97 (m, 1H, H-7), 0.52 – 0.45 (m, 2H, H_2-8), 0.16 (dt, *J* = 6.0, 4.5 Hz, 2H, H_2-9). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6 (C_q Trt), 128.8 (CH Trt), 127.8 (CH Trt), 126.9 (CH Trt), 86.4 (C_q Trt), 75.7 (C-7), 70.7 (C-5), 63.7 (C-1), 30.1 (C-2), 29.8 (C-4), 23.1 (C-3), 10.8 (C-7), 3.2 (C-8, C-9). IR/cm^{-1}: 3082, 3057, 3022, 2933, 2862, 1732, 1597, 1489, 1448, 1382, 1219, 1087, 1074.

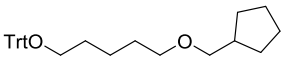
5-(Cyclobutylmethoxy)-1-trityloxypentane (20):



Compound **15** (4.40 mmol) was subjected to the general procedure A, using cyclobutylmethanol (5.01 mmol) to provide **20** (0.79 g, 1.91 mmol) in a 43% yield, as thick oil, after silica gel column chromatography purification. R_F = 0.74 (10% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.43 (m, 6H, H_{Ar} Trt) 7.22 – 7.17 (m, 6H,

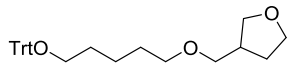
H_{Ar} Trt), 7.14 – 7.10 (m, 3H, H_{Ar} Trt), 3.37 – 3.32 (m, 4H, H_2-5, H_2-6), 3.07 (t, 2H, H_2-1), 2.56 – 2.49 (m, 1H, C-7), 2.04 – 1.97 (m, 2H, H_2-10), 1.86 – 1.79 (m, 2H, H_2-8), 1.75 – 1.40 (m, 8H, H_2-9. H_2-2, H_2-4, H_2-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6 (C_q Trt), 128.9 (CH Trt), 127.9 (CH Trt), 127.0 (CH Trt), 86.5 (C_q Trt), 75.6 (C-6), 71.1 (C-5), 63.7 (C-1), 35.4 (C-7), 29.9 (C-2), 29.8 (C-4), 25.4 (C-8, C-10), 23.2 (C-3), 18.9 (C-9). IR/cm^{-1}: 3084, 3059, 2934, 2862, 1597, 1489, 1448, 1363, 1219, 1111, 1072.

5-(Cyclopentylmethoxy)-1-trityloxypentane (21):



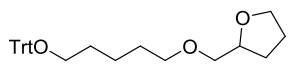
Compound **15** (4.43 mmol) was subjected to the general procedure A, using cyclopentylmethanol (5.09 mmol) to provide **21** (1.29 g, 3.02 mmol) in a 68% yield, as thick oil, after silica gel column chromatography purification. R_F = 0.77 (10% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (m, 6H, H_{Ar} Trt), 7.18 – 7.06 (m, 9H, H_{Ar} Trt), 3.39 – 3.29 (m, 2H, H_2-5), 3.21 (dd, *J* = 7.0, 1.0 Hz, 2H, H_2-6), 3.05 (dt, *J* = 11.1, 6.5 Hz, 2H, H_2-1), 2.10 (q, *J* = 7.4 Hz, 1H, H_2-7), 1.74 – 1.57 (m, 4H, H_2-8, H_2-11), 1.57 – 1.36 (m, 8H, H_2-2, H_2-3, H_2-4, H_2-9), 1.31 – 1.17 (m, 2H, H_2-10). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4 – 125.6 (CH Trt), 75.2 (C-6), 70.6 (C-5), 63.3 (C-1), 38.4 (C-7), 29.4 – 28.7 (C-8, C-9, C-10, C-11), 25.3, 25.1 (C-2, C-4), 22.8 (C-3). IR/cm^{-1}: 3084, 3057, 3022, 2939, 2864, 1597, 1489, 1448, 1367, 1176, 1072.

5-(*R*/*S*-Tetrahydrofuran-3-ylmethoxy)-1-trityloxypentane (22):



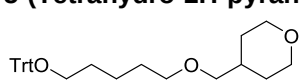
Compound **15** (4.61 mmol) was subjected to the general procedure A, using *R/S* tetrahydrofuran-3-ylmethanol (4.96 mmol) to provide **22** (1.11 g, 2.58 mmol) in a 56% yield, as an oil, after silica gel column chromatography purification. R_F = 0.40 (15% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.40 (m, 6H, H_{Ar} Trt), 7.21 (dd, *J* = 8.5, 6.8 Hz, 6H, H_{Ar} Trt), 7.16 – 7.10 (m, 3H, H_{Ar} Trt), 3.75 (ddd, *J* = 12.1, 8.3, 6.2 Hz, 2H, H-8a, H-9a), 3.68 - 3.55 (m, 1H, H-8b), 3.53 (dd, *J* = 8.7, 5.4 Hz, 1H, H-9b), 3.40 – 3.18 (m, 4H, H_2-5, H_2-9), 3.07 (t, *J* = 6.5 Hz, 2H, H_2-1), 2.49 – 2.35 (m, 1H, H-7), 1.87 (ddt, *J* = 13.9, 8.1, 4.0 Hz, 1H, H-10a), 1.62 (p, *J* = 6.8 Hz, 2H, H_2-2), 1.51 (m, 3H, H_2-4, H-10b), 1.46 – 1.37 (m, 2H, H_2-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6 (C_q Trt), 128.8 (CH Trt), 127.0 (CH Trt), 86.4 (C_q Trt), 73.0 (C-8), 71.1 (C-5), 71.1 (C-9), 67.8 (C-7), 39.4 (C-1), 30.0 (C-10), 29.6 (C-2), 29.2 (C-4), 23.1 (C-3). IR/cm^{-1}: 3445, 2934, 2866, 2347, 1716, 1489, 1448, 1339, 1163, 1074.

5-(*R*/*S*-Tetrahydrofuran-1-ylmethoxy)-1-trityloxypentane (23):



Compound **15** (5.03 mmol) was subjected to the general procedure A, using *R/S* tetrahydrofuran-1-ylmethanol (5.73 mmol) to provide **23** (1.06 g, 2.46 mmol) in a yield of 49%, as an oil, after silica gel column chromatography purification. R_F = 0.52 (15% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.37 (m, 6H, H_{Ar} Trt), 7.32 – 7.23 (m, 6H, H_{Ar} Trt), 7.23 – 7.16 (m, 3H, H_{Ar} Trt), 4.02 (tt, *J* = 7.3, 5.3 Hz, 1H, H-7), 3.85 (ddd, *J* = 8.2, 6.9, 6.1 Hz, 1H, H-10a), 3.73 (ddd, *J* = 8.2, 7.2, 6.3 Hz, 1H, H-10b), 3.53 – 3.37 (m, 4H, H_2-5, H_2-6), 3.05 (t, *J* = 6.6 Hz, 2H, H_2-1), 1.96 – 1.77 (m, 3H, H_2-2, H-9a), 1.69 – 1.60 (m, 2H, H_2-2), 1.60 – 1.52 (m, 3H, H_2-4, H-9b), 1.47 – 1.37 (m, 2H, H_2-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5 (C_q Trt), 128.7 (CH Trt), 127.7 (CH Trt), 126.9 (CH Trt), 86.3 (C_q Trt), 77.9 (C-7), 73.6 (C-6), 71.6 (C-5), 68.4(C-10), 63.6 (C-1), 30.0 (C-9), 29.6 (C-4), 28.2 (C-8), 25.7 (C-2), 22.9 (C-3). IR/cm^{-1}: 3084, 3055, 3022, 2934, 2862, 1597, 1489, 1448, 1373, 1219, 1111, 1074.

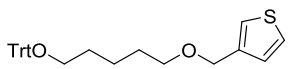
5-(Tetrahydro-2H-pyran-4-ylmethoxy)-1-trityloxypentane (24):



Compound **15** (4.68 mmol) was subjected to the general procedure A, using tetrahydro-2H-pyran-4-ylmethanol (4.34 mmol) to provide **24** (0.79 g, 1.78 mmol) in a yield of 38%, as an oil, after silica gel column chromatography purification. R_F = 0.48 (15% EtOAc in PE). ^{1}H NMR (400 MHz,

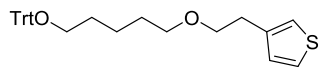
$CDCl_3$) δ 7.48 – 7.35 (m, 6H, H_{Ar} Trt), 7.32 – 7.21 (m, 6H, H_{Ar} Trt), 7.25 – 7.13 (m, 3H, H_{Ar} Trt), 3.99 – 3.89 (m, 2H, H_2-10), 3.42 – 3.30 (m, 4H, H_2-5, H_2-9), 3.21 (d, *J* = 6.6 Hz, 2H, H_2-1), 3.06 (t, *J* = 6.5 Hz, 2H, H_2-6), 1.88 – 1.74 (m, 1H, H-7), 1.70 – 1.57 (m, 4H, H_2-2, H_2-8), 1.57 – 1.47 (m, 2H, H_2-4), 1.47 – 1.38 (m, 2H, H_2-3), 1.35 – 1.25 (m, 2H, H_2-11). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5 (C_q Trt), 128.7 (CH Trt), 127.7 (CH Trt), 126.9 (CH Trt), 86.4 (C_q Trt), 75.9 (C-6), 71.1 (C-1), 67.7 (C-9, C-10), 63.5 (C-5), 35.5 (C-7), 30.1 (C-8, C-11), 29.9 (C-2), 29.6 (C-4), 23.0 (C-3). IR/cm^{-1}: 3085, 3056, 3023, 2932, 2849, 1558, 1506, 1506, 1489, 1227, 1163, 1097.

5-(Thiophen-3-methoxy)-1-trityloxypentane (25):



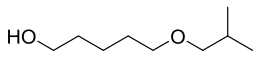
Compound **15** (4.56 mmol) was subjected to the general procedure A, using 3-thiophenmethanol (4.57 mmol) to provide **25** (0.73 g, 2.13 mmol) in a 56% yield, as thick oil, after silica gel column chromatography purification. R_F = 0.79 (15% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.38 (m, 6H, H_{Ar} Trt), 7.28 – 7.20 (m, 6H, H_{Ar} Trt), 7.20 - 7.14 (m, 3H, H_{Ar} Trt), 7.12 (dq, *J* = 3.0, 1.0 Hz, 1H, H thio), 7.04 (dd, *J* = 4.9, 1.3 Hz, 1H, H thio), 7.02 (dd, *J* = 4.9, 1.3 Hz, 1H, H thio), 4.44 (d, *J* = 0.8 Hz, 2H, H_2-6), 3.40 (t, *J* = 6.5 Hz, 2H, H_2-5), 3.05 (t, *J* = 6.6 Hz, 2H, H_2-1), 1.70 – 1.49 (m, 4H, H_2-2, H_2-4), 1.51 – 1.36 (m, 2H, H_2-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6 (C_q Trt), , 128.9 (CH Trt), 127.9 (CH Trt), 127.4 (CH thio), 127.0 (C_q Trt), 126.0 (CH thio), 122.6 (CH thio), 114.7 (C_q Thio), 86.5 (C_q Trt), 70.4 (C-5), 68.3 (C-6), 63.7 (C-1), 30.0 (C-2), 29.8 (C-4), 23.1 (C-3). IR/cm^{-1}: 3501, 3088, 3059, 3024, 2938, 2864, 2316, 1734, 1448, 1364, 1242, 1068, 1034.

5-(Thiophen-3-ethoxy)-1-trityloxypentane (26):



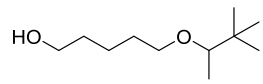
Compound **15** (4.56 mmol) was subjected to the general procedure A, using 3-thiophenethanol (4.57 mmol) to provide **26** (0.97 g, 1.65 mmol) in a 47% yield, as an oil, after silica gel column chromatography purification. R_F = 0.70 (10% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.40 (m, 6H, H_{Ar} Trt), 7.30 – 7.24 (m, 6H, H_{Ar} Trt), 7.22 – 7.19 (m, 3H, H_{Ar} Trt), 7.18 – 7.16 (m, 1H, H-thio), 6.97 (dq, *J* = 3.0, 1.0 Hz, 1H, H thio), 6.94 (dd, *J* = 4.9, 1.3 Hz, 1H, H thio), 3.59 (t, *J* = 7.0 Hz, 2H, H_2-2), 3.41 (t, *J* = 6.5 Hz, 2H, H_2-5), 3.05 (t, *J* = 6.6 Hz, 2H, H_2-1), 2.92 – 2.84 (m, 2H, H_2-1), 1.64 (p, *J* = 6.8 Hz, 2H, H_2-2), 1.55 (dq, *J* = 8.7, 6.5 Hz, 2H, H_2-4), 1.47 – 1.36 (m, 2H, H_2-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5 (C_q Trt), 128.8 (CH Trt), 128.0 (CH thio), 127.8 (CH Trt), 126.9 (CH Trt), 125.2 (CH thio), 121.1 (CH thio), 114.6 (C_q thio), 86.4 (C_q Trt), 71.1 (C-2), 71.0 (C-5), 63.6 (C-1), 30.8 (C-1), 29.9 (C-2), 29.6 (C-4), 23.0 (C-3). IR/cm^{-1}: 3524, 3086, 3057, 2934, 2862, 1738, 1717, 1489, 1447, 1387, 1364, 1242, 1159, 1113, 1069, 1034.

5-(2-Methyl-1-propyloxy)-1-pentanol (27):



Compound **16** (3.56 mmol) was subjected to the general procedure B to provide **27** (0.33 g, 2.07 mmol) in a yield of 73%, as an oil, after silica gel column chromatography purification. R_F = 0.24 (20% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.49 (t, *J* = 6.6 Hz, 2H, H_2-1), 3.31 (t, *J* = 6.5 Hz, 2H, H_2-5), 3.07 (d, *J* = 6.8 Hz, 2H, H_2-6), 1.78 – 1.72 (m, 1H, H-7), 1.53 – 1.43 (m, 4H, H_2-2, H_2-4), 1.37 – 1.27 (m, 2H, H_2-3), 0.81 (s, 3H, H_3-8), 0.79 (s, 3H, H_3-9). ^{13}C NMR (100 MHz, $CDCl_3$) δ 77.8 (C-6), 70.8 (C-5), 62.1 (C-1), 32.3 (C-2), 29.3 (C-4), 28.2 (C-7), 22.3 (C-3), 19.3 (C-8, C-9). IR/cm^{-1}: 3335, 2934, 2859, 1470, 1383, 1366, 1115, 1055, 1007.

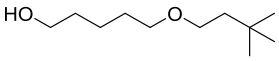
5-(3,3-Dimethyl-2-butoxy)-1-pentanol (28):



Compound **17**(2.21 mmol) was subjected to the general procedure B to provide **28** (0.2089 g, 1.11 mmol) in a 50% yield, as an oil, after silica gel column chromatography purification. R_F = 0.32 (20% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.64 (t, *J* = 6.6 Hz, 2H, H_2-1), 3.57 (dt, *J* = 9.2, 6.1 Hz, 1H, H-5a), 3.26 (dt, *J* = 9.2, 6.6 Hz, 1H, H-5b), 2.95 (q, *J* = 6.3 Hz, 1H, H-6), 1.64 – 1.51 (m, 4H, H_2-2, H_2-4), 1.50 – 1.36 (m, 2H, H_2-3), 1.03 (d, *J* = 6.3 Hz, 3H, H_3-7), 0.87 (s, 9H, H_3-9, H_3-10, H_3-11). ^{13}C

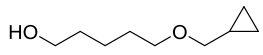
NMR (100 MHz, $CDCl_3$) δ 83.4 (C-6), 69.8 (C-5), 62.8 (C-1), 35.1 (C-8), 32.5 (C-2), 29.8 (C-4), 26.0 (C-9, C-10, C-11), 22.5 (C-3), 14.0 (C-7). IR/cm^{-1}: 3296, 2938, 2866, 1474, 1456, 1388, 1371, 1339, 1209, 1099, 1057.

5-(3,3-Dimethyl-1-butoxy)-1-pentanol (29):



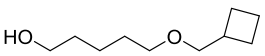
Compound **18** (2.36 mmol) was subjected to the general procedure B to provide **29** (0.2142 g, 1.14 mmol) in a yield of 48%, as an oil, after silica gel column chromatography purification. R_F = 0.22 (20% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.63 (t, *J* = 6.5 Hz, 2H, H_2-1), 3.51 – 3.36 (m, 4H, H_2-5, H_2-2), 1.60 (dq, *J* = 14.6, 6.6 Hz, 4H, H_2-2, H_2-4), 1.54 – 1.49 (m, 2H, H_2-1), 1.48 – 1.37 (m, 2H, H_2-3), 0.92 (s, 9H, H_3-9, H_3-10, H_3-11). ^{13}C NMR (100 MHz, $CDCl_3$) δ 70.9 (C-6), 68.2 (C-5), 62.6 (C-1), 42.9 (C-1), 32.4 (C-2), 29.7 (C-9, C-10, C-11), 29.6 (C-8), 29.5 (C-4), 22.5 (C-3). IR/cm^{-1}: 3345, 2938, 2864, 1472, 1364, 1244, 1194, 1113, 1055.

5-(Cyclopropylmethoxy)-1-pentanol (30):



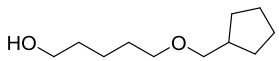
Compound **19** (2.49 mmol) was subjected to the general procedure B to provide **30** (0.19 g, 1.19 mmol) in a yield of 48%, as an oil, after silica gel column chromatography purification. R_F = 0.27 (30% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.63 (t, *J* = 6.5 Hz, 2H, H_2-1), 3.45 (t, *J* = 6.6 Hz, 2H, H_2-5), 3.25 (d, *J* = 6.9 Hz, 2H, H_2-6), 1.61 (m, 4H, H_2-2, H_2-4), 1.49 – 1.36 (m, 2H, H_2-3), 1.12 – 0.98 (m, 1H, H-7), 0.59 – 0.47 (m, 4H, H_2-8, H_2-9). ^{13}C NMR (100 MHz, $CDCl_3$) δ 75.6 (C-6), 70.6 (C-5), 62.5 (C-1) 32.4 (C-2), 29.4 (C-4), 22.4 (C-3), 10.6 (C-7), 3.0 (C-8, C-9). IR/cm^{-1}: 3348, 2934, 2858, 1456, 1382, 1339, 1107, 1051.

5-(Cyclobutylmethoxy)-1-pentanol (31):



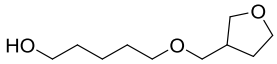
Compound **20** (1.91 mmol) was subjected to the general procedure B to provide **31** (0.18 g, 1.02 mmol) in a yield of 53%, as an oil, after silica gel column chromatography purification. R_F = 0.41 (30% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (t, *J* = 6.6 Hz, 2H, H_2-1), 3.42 (t, *J* = 6.5 Hz, 2H, H_2-5), 3.27 (d, *J* = 7.2 Hz, 2H, H_2-6), 2.17 – 2.13 (m, 1H, H-7), 1.81 – 1.68 (m, 1H, H-8a), 1.64 – 1.50 (m, 7H, H_2-2, H_2-4, H_2-10, H-8b), 1.47 – 1.37 (m, 2H, H_2-3), 1.26 – 1.15 (m, 2H, H_2-9). ^{13}C NMR (100 MHz, $CDCl_3$) δ 75.6 (C-6), 70.9 (C-5), 62.4 (C-1), 39.3 (C-7), 32.4 (C-2), 29.6 (C-8, C-10), 29.3 (C-4), 25.4 (C-9), 22.4 (C-3). IR/cm^{-1}: 3360, 2933, 2858, 1456, 1364, 1113, 1057.

5-(Cyclopentylmethoxy)-1-pentanol (32):



Compound **21** (3.02 mmol) was subjected to the general procedure B to provide **32** (0.27 g, 1.43 mmol) in a yield of 47%, as an oil, after silica gel column chromatography purification. R_F = 0.45 (30% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.63 (t, *J* = 6.5 Hz, 2H, H_2-1), 3.45 – 3.37 (m, 4H, H_2-5, H_2-6), 2.56 (p, *J* = 7.5 Hz, 1H, H-7), 2.11 – 2.00 (m, 2H, H_2-8), 1.97 – 1.79 (m, 2H, H_2-11), 1.77 – 1.65 (m, 2H, H_2-9), 1.64 – 1.54 (m, 4H, H_2-2, H_2-4), 1.46 – 1.37 (m, 2H, H_2-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 75.7 (C-6), 70.9 (C-5), 62.6 (C-1), 35.1 (C-7), 32.4 (C-2), 29.7 (C-8, C-11)29.3 (C-4), 25.2 (C-9, C-10), 22.4 (C-3). IR/cm^{-1}: 3333, 2939, 2862, 1456, 1373, 1361, 1115, 1057.

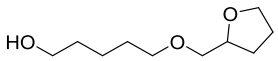
5-(*R*/*S*-Tetrahydrofuran-3-ylmethoxy)-1-pentanol (33):



Compound **22** (3.56 mmol) was subjected to the general procedure B to provide **33** (0.48 g, 2.56 mmol) in a yield of 72%, as an oil, after silica gel column chromatography purification. R_F = 0.33 (1:2, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88 – 3.78 (m, 2H, H-8a,H-9a), 3.72 (dt, *J* = 8.4, 7.2 Hz, 1H, H-8b), 3.65 – 3.52 (m, 3H, H_2-1, H-9b), 3.47 – 3.27 (m, 4H, H_2-5, H_2-6), 2.58 – 2.45 (m, 1H, H-7), 2.06 – 1.94 (m, 1H, H-10a), 1.66 – 1.51 (m, 5H, H_2-2, H_2-4, H-10b), 1.47 – 1.35 (m, 2H, H_2-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 72.8 (C-6), 71.0 (C-5), 70.9 (C-8), 67.6 (C-9), 62.3 (C-1), 39.1 (C-7),

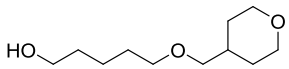
32.4 (C-2), 29.3 (C-4), 29.0 (C-10), 22.4 (C-3). IR/cm^{-1}: 3385, 2934, 2858, 1456, 1375, 1211, 1113, 1072, 1056.

5-(*R*/*S*-Tetrahydrofuran-1-ylmethoxy)-1-pentanol (34):



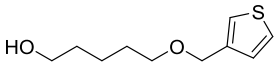
Compound **23** (2.46 mmol) was subjected to the general procedure B to provide **34** (0.35 g, 1.86 mmol) in a yield of 76%, as an oil, after silica gel column chromatography purification. R_F = 0.28 (1:2, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.04 (ddd, *J* = 12.4, 6.9, 5.2 Hz, 1H, H-7), 3.87 (dt, *J* = 8.3, 6.6 Hz, 1H, H-10a), 3.81 – 3.71 (m, 1H, H-10b), 3.61 (t, *J* = 6.5 Hz, 2H, H_2-1), 3.48 (td, *J* = 6.6, 2.2 Hz, 2H, H_2-5), 3.44 – 3.39 (m, 2H, H_2-6), 2.02 – 1.79 (m, 3H, H_2-9, H-8a), 1.66 – 1.54 (m, 5H, H_2-2, H_2-4, H-8b), 1.48 – 1.36 (m, 2H, H_2-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 77.8 (C-7), 73.4 (C-6), 71.4 (C-5), 68.2 (C-10), 62.3 (C-1), 32.4 (C-2), 29.3 (C-4), 28.0 (C-9), 25.5 (C-8), 22.3 (C-3). IR/cm^{-1}: 3410, 2934, 2858, 1645, 1454, 1375, 1109, 1072, 1055.

5-(Tetrahydro-2H-pyran-4-ylmethoxy)-1-pentanol (35):



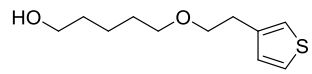
Compound **24** (1.78 mmol) was subjected to the general procedure B to provide **35** (0.14 g, 0.697 mmol) in a yield of 39%, as an oil, after silica gel column chromatography purification. R_F = 0.31 (1:2, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.96 (m, 2H, H-9a, 10a), 3.60 (t, *J* = 6.6 Hz, 2H, H_2-1), 3.45 – 3.34 (m, 4H, H_2-5, H-9b, H-10b), 3.25 (d, *J* = 6.6 Hz, 2H, H_2-6), 1.83 (t, *J* = 3.4 Hz, 1H, H-7), 1.70 – 1.51 (m, 6H, H_2-2,H_2-4, H-8a, H-11a), 1.46 – 1.36 (m, 2H, H_2-3), 1.36 – 1.21 (m, 2H, H-8b, H-11b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 75.9 (C-6), 71.0 (C-5), 67.6 (C-9, C-10), 62.3 (C-1), 35.3 (C-7), 32.4 (C-2), 29.9 (C-8, C-11), 29.3 (C-4), 22.4 (C-3). IR/cm^{-1}: 3445, 2931, 2851, 1437, 1364, 1236, 1117, 1092, 1012.

5-(Thiophen-3-methoxy)-1-pentanol (36):



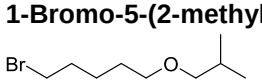
Compound **25** (2.13 mmol) was subjected to the general procedure B to provide **36** (0.23 g, 1.15 mmol) in a yield of 69%, as an oil, after silica gel column chromatography purification. R_F = 0.27 (30% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 4.9, 3.0 Hz, 1H, H thio), 7.19 (ddt, *J* = 2.1, 1.5, 0.9 Hz, 1H, H thio), 7.06 (dd, *J* = 4.9, 1.3 Hz, 1H, H thio), 4.49 (s, 2H, H_2-6), 3.57 (t, *J* = 6.6 Hz, 2H, H_2-1), 3.46 (t, *J* = 6.5 Hz, 2H, H_2-5), 1.66 – 1.57 (m, 2H, H_2-4), 1.57 – 1.50 (m, 2H, H_2-2), 1.45 – 1.36 (m, 2H, H_2-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.6 (C_q thio), 127.3 (CH thio), 125.9 (CH thio), 122.7 (CH thio), 70.2 (C-5), 68.1 (C-6), 62.4 (C-1), 32.4 (C-2), 29.4 (C-4), 22.4 (C-3).

5-(Thiophen-3-ethoxy)-1-pentanol (37):



Compound **26** (1.65 mmol) was subjected to the general procedure B to provide **37** (0.3318 g, 1.55 mmol) in a 73% yield, as an oil, after silica gel column chromatography purification. R_F = 0.30 (30% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (dd, *J* = 4.9, 3.0 Hz, 1H, H thio), 7.01 (dq, *J* = 3.0, 1.0 Hz, 1H, H thio), 6.97 (dd, *J* = 4.9, 1.3 Hz, 1H, H thio), 3.62 (m,4H, H_2-6, H_2-7), 3.45 (t, *J* = 6.5 Hz, 2H, H_2-5), 2.90 (td, *J* = 7.0, 0.8 Hz, 2H, H_2-1), 1.65 – 1.52 (m, 4H, H_2-2, H_2-4), 1.45 – 1.35 (m, 2H, H_2-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.28 (C_q thio), 128.5 (CH thio), 125.2 (CH thio), 121.1 (CH thio), 71.0 (C-7), 70.9 (C-5), 62.6 (C-6), 32.4 (C-4), 30.7 (C-1), 29.4 (C-2), 22.4 (C-3). IR/cm^{-1}: 3360, 2934, 2860, 1456, 1418, 1348, 1250, 1225, 1155, 1094, 1053.

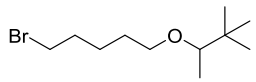
1-Bromo-5-(2-methyl-1-propyloxy)pentane (38):



Alcohol **27** (2.07 mmol) was subjected to the general procedure C to provide **38** (0.24 g, 1.08 mmol) in a yield of 52% after silica gel column chromatography purification. R_F = 0.71 (100% toluene) ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.41 (t, *J* = 6.9 Hz, 2H, H_2-5). 3.40 (t, *J* = 6.3 Hz, 2H, H_2-1), 3.16 (d, *J* = 6.7 Hz, 2H, H_2-6), 1.90 – 1.85 (m, 3H, H_2-2, H-7), 1.65 – 1.56 (m, 2H, H_2-4), 1.56 – 1.47 (m, 2H, H_2-3), 0.92 (s, 3H, H_3-8), 0.89(s, 3H, H_3-

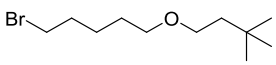
9). ^{13}C NMR (100 MHz, $CDCl_3$) δ 77.9 (C-6), 70.6 (C-5), 33.7 (C-1), 32.6 (C-2), 28.9 (C-4), 28.4 (C-7), 25.0 (C-3), 19.4 (C-8, C-9). IR/cm^{-1}: 2940, 2863, 1473, 1363, 1332, 1100.

1-Bromo-5-(3,3-dimethyl-2-butoxy)pentane (39):



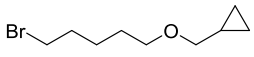
Alcohol **28** (1.11 mmol) was subjected to the general procedure C to provide **39** (0.25 g, 0.99 mmol) in a yield of 89% after silica gel column chromatography purification. R_F = 0.71 (1:1, PE:toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.56 (dt, *J* = 9.5, 5.8 Hz, 1H, H-5a), 3.41 (t, *J* = 6.9 Hz, 2H, H_2-1), 3.24 (dt, *J* = 9.5, 6.1 Hz, 1H, H-5b), 2.94 (q, *J* = 6.3 Hz, 1H, H-6), 1.88 (p, *J* = 7.0 Hz, 2H, H_2-2), 1.64 – 1.44 (m, 4H, H_2-3, H_2-4), 1.03 (d, *J* = 6.3 Hz, 3H, H_3-7), 0.87 (s, 9H, H_3-9, H_3-10, H_3-11). ^{13}C NMR (100 MHz, $CDCl_3$) δ 83.3 (C-6), 69.3 (C-5), 35.1 (C-8), 33.8 (C-1), 32.7 (C-2), 29.3 (C-4), 26.0 (C-9, C-10, C-11), 25.1 (C-3), 13.9 (C-7). IR/cm^{-1}: 2938, 2866, 1477, 1369, 1335, 1099.

1-Bromo-5-(3,3-dimethyl-1-butoxy)pentane (40):



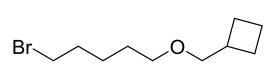
Alcohol **29** (1.14 mmol) was subjected to the general procedure C to provide **40** (0.14 g, 0.54 mmol) in a yield of 48% after silica gel column chromatography purification. R_F = 0.71 (100% toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.50 – 3.38 (m, 6H, H_2-1, H_2-5, H_2-6), 1.96 – 1.84 (m, 2H, H_2-7), 1.67 – 1.56 (m, 2H, H_2-2), 1.59 – 1.40 (m, 4H, H_2-3, H_2-4), 0.93 (s, 9H, H_3-9, H_3-10, H_3-11). ^{13}C NMR (100 MHz, $CDCl_3$) δ 70.6 (C-6), 68.2 (C-5), 43.0 (C-7), 33.7 (C-1), 32.7 (C-2), 29.8 (C-9, C-10, C-11), 29.6 (C-8), 29.0 (C-4), 25.0 (C-3). IR/cm^{-1}: 2951, 2862, 1734, 1486, 1364, 1111.

1-Bromo-5-(cyclopropylmethoxy)pentane (41):



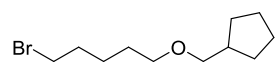
Alcohol **30** (1.19 mmol) was subjected to the general procedure C to provide **41** (0.12 g, 0.54 mmol) in a yield of 46% after silica gel column chromatography purification. R_F = 0.52 (100% toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.44 (t, *J* = 6.4 Hz, 2H, H_2-5), 3.42 (t, *J* = 6.8 Hz, 2H, H_2-1), 3.25 (d, *J* = 6.9 Hz, 2H, H_2-6), 1.89 (dt, *J* = 14.8, 7.0 Hz, 2H, H_2-2), 1.67 – 1.56 (m, 2H, H_2-4), 1.58 – 1.47 (m, 2H, H_2-3), 1.13 – 0.98 (m, 1H, H-7), 0.58 – 0.49 (m, 2H, H_2-8), 0.20 (dt, *J* = 6.1, 4.5 Hz, 2H, H_2-9). ^{13}C NMR (100 MHz, $CDCl_3$) δ 75.6 (C-6), 70.3 (C-5), 33.8 (C-1), 32.6 (C-2), 28.9 (C-4), 24.9 (C-3), 10.6 (C-7), 3.0 (C-8, C-9). IR/cm^{-1}: 2934, 2857, 1732, 1456, 1381, 1337, 1250, 1107, 1016.

1-Bromo-5-(cyclobutylmethoxy)pentane (42):



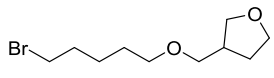
Alcohol **31** (1.02 mmol) was subjected to the general procedure C to provide **42** (0.1276 g, 0.54 mmol) in a yield of 53% after silica gel column chromatography purification. R_F = 0.67 (100% toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.41, (t, *J* = 6.7 Hz, 2H, H_2-5), 3.41 (t, *J* = 6.9 Hz, 2H, H_2-1), 3.38 (d, *J* = 6.8 Hz, 2H, H_2-6), 2.60 – 2.54 (m, 1H, H-7), 2.14 – 2.01 (m, 2H, H_2-8), 1.97 – 1.81 (m, 4H, H_2-2, H_2-10), 1.80 – 1.67 (m, 2H, H_2-9), 1.66 – 1.56 (m, 2H, H_2-4), 1.56 – 1.45 (m, 2H, H_2-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 75.6 (C-6), 70.7 (C-5), 35.2 (C-7), 33.8 (C-1), 32.6 (C-2), 28.9 (C-4), 25.2 (C-8, C-10), 24.9 (C-3), 18.6 (C-9). IR/cm^{-1}: 2932, 2855, 1732, 1456, 1364, 1246, 1111.

1-Bromo-5-(cyclopentylmethoxy)pentane (43):



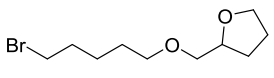
Alcohol **32** (1.43 mmol) was subjected to the general procedure C to provide **43** (0.25 g, 1.01 mmol) in a yield of 71% after silica gel column chromatography purification. R_F = 0.71 (100% toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.43 (dd, *J* = 6.7, 6.0 Hz, 2H, H_2-5), 3.43 (t, *J* = 6.8 Hz, 1H, H_2-1), 3.27 (d, *J* = 7.1 Hz, 2H, H_2-6), 2.17 – 2.11 (m, 1H, H-7), 1.89 (dt, *J* = 14.1, 7.0 Hz, 2H, H_2-2), 1.79 – 1.66 (m, 2H, H_2-8), 1.64 – 1.45 (m, 8H, H_2-3, H_2-4, H_2-11, H_2-9), 1.29 – 1.16 (m, 2H, H_2-10). ^{13}C NMR (100 MHz, $CDCl_3$) δ 75.6 (C-6), 70.6 (C-5), 39.5 (C-7), 33.8 (C-1), 32.6 (C-2), 29.6 (C-8, C-11), 28.9 (C-4), 25.4 (C-9, C-10), 25.0 (C-3). IR/cm^{-1}: 2940, 2857, 1734, 1452, 1366, 1250, 1111.

1-Bromo-5-(*R*/*S*-tetrahydrofuran-3-ylmethoxy)pentane (44):



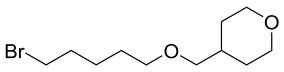
Alcohol **33** (1.86 mmol) was subjected to the general procedure C to provide **44** (0.58 g, 2.32 mmol) in a yield of 91% after silica gel column chromatography purification. R_F = 0.33 (5% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.87 – 3.78 (m, 2H, H-8a, H-9a), 3.78 – 3.66 (m, 1H, H-8b), 3.56 (dd, *J* = 8.7, 5.4 Hz, 1H, H-9b), 3.46 – 3.25 (m, 6H, H_2-1, H_2-5, H_2-6), 2.54 – 2.48 (m, 1H, H-7), 2.06 – 1.94 (m, 1H, H-10a), 1.92 – 1.83 (m, 2H, H_2-2), 1.65 – 1.54 (m, 3H, H_2-4, H-10b), 1.54 – 1.45 (m, 2H, H_2-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 73.0 (C-6), 71.0 (C-9), 70.8 (C-5), 67.7 (C-8), 39.2 (C-7), 33.7 (C-1), 32.6 (C-2), 29.1 (C-10), 28.8 (C-4), 24.9 (C-3). IR/cm^{-1}: 2934, 2857, 1486, 1111, 1076.

1-Bromo-5-(*R*/*S*-tetrahydrofuran-1-ylmethoxy)pentane (45):



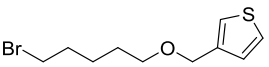
Alcohol **34** (1.86 mmol) was subjected to the general procedure C to provide **45** (0.33 g, 1.30 mmol) in a yield of 70% after silica gel column chromatography purification. R_F = 0.33 (5% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.04 (m, 1H, H-7), 3.88 (m, 1H, H-10a), 3.75 (m, 1H, H-10b), 3.49 (m, 2H, H_2-5), 3.47-3.39 (m, 4H, H_2-1, H_2-6), 1.99 – 1.83 (m, 5H, H_2-2. H-8a , H_2-9), 1.66-1.62 (m, 3H, H-8b, H_2-4), 1.61-1.53 (m, 2H, H_2-3). ^{13}C NMR (400 MHz, $CDCl_3$) δ 77.9 (C-7), 73.6 (C-6), 71.2 (C-5), 68.3 (C-10), 33.8 (C-1), 32.6 (C-2), 28.8 (C-4), 28.1 (C-8), 25.6 (C-9), 24.9 (C-3). IR/cm^{-1}: 2938, 2860, 1456, 1437, 1117, 1070.

1-Bromo-5-(tetrahydro-2H-pyran-4-ylmethoxy)pentane (46):



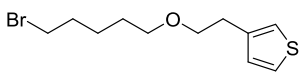
Alcohol **35** (0.31 mmol) was subjected to the general procedure C to provide **46** (0.061 g, 0.23 mmol) in a 33% yield after silica gel column chromatography purification. R_F = 0.35 (5% EtOAc in PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.00 – 3.94 (m, 2H, H-9a, H-10a), 3.45 – 3.35 (m, 6H, H_2-1, H_2-5, H-9b, H-10b), 3.25 (d, *J* = 6.6 Hz, 2H, H_2-6), 1.93 – 1.77 (m, 3H, H_2-2, H-7), 1.68 – 1.55 (m, 4H, H_2-4, H-8a, H-11a), 1.55 – 1.46 (m, 2H, H_2-3), 1.42 – 1.19 (m, 2H, H-8b, H-11b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 76.0 (C-6), 70.8 (C-5), 67.8 (C-9, C-10), 35.5 (C-7), 33.8 (C-1), 32.6 (C-2), 30.0 (C-8, C-11), 28.9 (C-4), 24.9 (C-3). IR/cm^{-1}: 2924, 2845, 1734, 1384, 1115, 1092.

1-Bromo-5-(thiophen-3-methoxy)pentane (47):



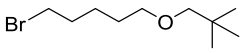
Alcohol **36** (1.15 mmol) was subjected to the general procedure C to provide **47** (0.19 g, 0.74 mmol) in a yield of 45% after silica gel column chromatography purification. R_F = 0.67 (100% toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 5.0, 3.0 Hz, 1H, H thio), 7.23 (dd, *J* = 2.9, 1.2 Hz, 1H, H thio), 7.10 (dd, *J* = 5.0, 1.2 Hz, 1H, H thio), 4.56 – 4.51 (s, 2H, H_2-6), 3.50 (t, *J* = 6.3 Hz, 2H, H_2-5), 3.44 (t, *J* = 6.8 Hz, 2H, H_2-1), 1.90 (p, *J* = 7.0 Hz, 2H, H_2-2), 1.72 – 1.59 (m, 2H, H_2-4), 1.62 – 1.48 (m, 2H, H_2-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.7 (C_q thio), 127.3 (CH thio), 126.0 (CH thio), 122.6 (CH thio), 70.0 (C-6), 68.2 (C-5), 33.8 (C-1), 32.6 (C-2), 28.9 (C-4), 25.0 (C-3). IR/cm^{-1}: 3000, 2934, 2857, 1732, 1153, 1096.

1-Bromo-5-(thiophen-3-ethoxy)pentane (48):



Alcohol **37** (1.55 mmol) was subjected to the general procedure C to provide **48** (0.28 g, 0.99 mmol) in a yield of 46% after silica gel column chromatography purification. R_F = 0.67 (100% toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.21 (m, 1H, H thio), 7.02 – 6.98 (m, 1H, H thio), 6.97 (dd, *J* = 4.9, 1.3 Hz, 1H, H thio), 3.62 (t, *J* = 7.0 Hz, 2H, H_2-6), 3.44 (t, *J* = 6.3 Hz, 2H, H_2-5), 3.39 (t, *J* = 6.8 Hz, 2H, H_2-1), 2.90 (td, *J* = 7.0, 0.8 Hz, 2H, H_2-7), 1.92 – 1.79 (m, 2H, H_2-2), 1.64 – 1.54 (m, 2H, H_2-4), 1.53 – 1.44 (m, 2H, H_2-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.4 (C_q thio), 128.5 (CH thio), 125.2 (CH thio), 121.1 (CH thio), 71.1 (C-6), 70.6 (C-5), 33.9 (C-1), 32.6 (C-2), 30.8 (C-7), 28.9 (C-4), 25.0 (C-3). IR/cm^{-1}: 3102, 2934, 2857, 1734, 1109.

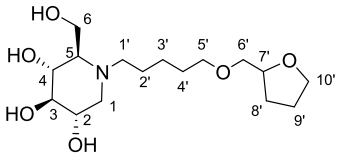
1-Bromo-5-(2,2-dimethyl-1-propoxy) pentane (66):



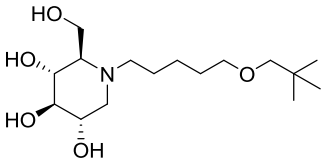
68 (2.72 g, 11.46 mmol) was synthesized from corresponding alcohol (2.70 g, 15.49 mmol) according to the general procedure C in a yield of 74%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.42 (t, *J* = 6.8 Hz, 2H, H_2-1), 3.41 (t, *J* = 6.2 Hz, 2H, H_2-5), 3.04 (s, 2H, H_2-6), 1.91 – 1.87 (m, 2H, H_2-2), 1.67 – 1.42 (m, 4H, H_2-4, H_2-3), 0.90 (s, 9H, H_3-8, H_3-9, H_3-10). ^{13}C NMR (100 MHz, $CDCl_3$) δ 81.6 (C-6), 71.3 (C-5), 34.1 (C-1), 32.8 (C-2), 28.9 (C-5), 26.9 (C-8, C-9, C-10), 25.1 (C-3). IR/cm^{-1}: 2941, 2863, 1473, 1363, 1331, 1102.

Synthesis of the alkylated iminosugars

***Figure 8**: Proton and carbon NMR numbering of iminosugars (**4**, **5**, **49** - **65**)*

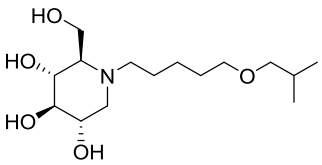


***N*-[5-(3,3-Dimethyl-1-propyloxy)pentyl]-1-deoxynojirimycin (4):**



Bromide **66** (0.30 mmol) was subjected to the general procedure D with 1-deoxynojirimycin (0.20 mmol) to provide **4** (30 mg, 0.094 mmol, yield 77%). ^{1}H NMR (400 MHz, MeOD) δ 4.01 (dd, *J* = 12.3, 2.0 Hz, 1H, H-6a), 3.89 (dd, *J* = 12.3, 3.0 Hz, 1H, H-6b), 3.62 (ddd, *J* = 10.8, 9.2, 4.9 Hz, 1H, H-2), 3.52 (t, *J* = 9.6 Hz, 1H, H-4), 3.44 (t, *J* = 6.2 Hz, 2H, H_2-5'), 3.32 – 3.24 (m, 2H, H-3, H-1a), 3.17 (td, *J* = 12.1, 11.5, 5.5 Hz, 1H, H-1'a), 3.08 (s, 2H, H_2-6'), 3.00 (td, *J* = 12.7, 12.0, 5.4 Hz, 1H, H-1'b), 2.78 – 2.70 (m, 1H, H-1b), 2.72 (t, *J* = 11.4 Hz, 1H, H-5), 1.69 – 1.65 (m, 4H, H_2-2', H_2-4'), 1.44 (ddd, *J* = 17.2, 9.0, 5.9 Hz, 2H, H_2-3'), 0.91 (s, 9H, H_3-8', H_3-9', H_3-10'). ^{13}C NMR (100 MHz, $CDCl_3$) δ 82.5 (C-6'), 79.0 (C-3), 72.1 (C-5'), 69.9 (C-4), 68.8 (C-2), 67.4 (C-5), 56.5 (C-6), 55.7 (C-1), 54.0 (C-1'), 32.9 (C-7'), 30.4 (C-4'), 27.1 (C-8', C-9', C-10'), 24.8 (C-3'), 24.4 (C-2'). IR/cm^{-1}: 3284, 2347, 2326, 1018. HRMS: found 320.2431 $[C_{16}H_{33}NO_5+H]^+$, calculated for $[C_{16}H_{33}NO_5+H]^+$ 320.2432.

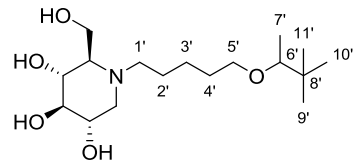
***N*-[5-(2-Methyl-1-propyloxy)pentyl]-1-deoxynojirimycin (49):**



Bromide **38** (0.30 mmol) was subjected to the general procedure D with 1-deoxynojirimycin (0.20 mmol) to provide **49** (28 mg, 0.092 mmol, yield 46%). ^{1}H NMR (400 MHz, MeOD) δ 4.07 (d, *J* = 12.4 Hz, 1H, H-6a), 3.93 (dd, *J* = 12.5, 2.9 Hz, 1H, H-6b), 3.67 (td, *J* = 10.1, 4.5 Hz, 1H, H-2), 3.58 (t, *J* = 9.6 Hz, 1H, H-4), 3.47 (t, *J* = 6.3 Hz, 2H, H_2-5'), 3.43 – 3.24 (m, 3H, H-1a, H-3, H-1'a), 3.22 (d, *J* = 6.6 Hz, 2H, H_2-6'), 3.10 (br s, 1H, H-1'b), 2.92 – 2.74 (m, 2H, H-5, H-1b), 1.89 – 1.81 (m, 1H, H-7'), 1.80 – 1.72 (m, 2H, H_2-2'), 1.71 – 1.62 (m, 2H, H_2-4'), 1.54 – 1.41 (m, 2H, H_2-3'), 0.93 (d, *J* = 6.7 Hz, 6H, H_3-8', H_3-9'). ^{13}C NMR (100 MHz, MeOD) δ 77.6 (C-6'), 77.2 (C-3), 70.2 (C-5'), 68.1 (C-4), 67.0 (C-2), 66.1 (C-5), 55.5 (C-6), 54.0 (C-1), 52.6 (C-1'), 28.9 (C-4'), 28.2 (C-7'), 23.3 (C-3'), 22.9 (C-2'), 18.3 (C-8', C-9'). $[\alpha]^{20}_D$ = -7.17 (c = 0.56, MeOH). IR/cm^{-1}: 3333, 2871, 1670, 1432, 1383, 1201, 1131, 1031. HRMS: found 306.22757 $[C_{15}H_{31}NO_5+H]^+$, calculated for $[C_{15}H_{31}NO_5+H]^+$ 306.22750.

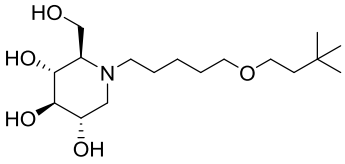
***N*-[5-(3,3-Dimethyl-2-butoxy)pentyl]-1-deoxynojirimycin (50):**

Bromide **39** (0.32 mmol) was subjected to the general procedure D with 1-deoxynojirimycin (0.20 mmol) to provide **50** (31 mg, 0.094 mmol, yield 47%). ^{1}H NMR (400 MHz, MeOD) δ 4.14 (d, *J* = 12.4 Hz, 1H, H-6a), 3.93 (dd, *J* = 12.6, 2.7 Hz, 1H, H-6b), 3.72 (td, *J* = 10.4, 4.9 Hz, 1H, H-2),



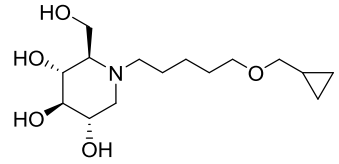
3.68 – 3.58 (m, 3H, H-3, H-4, H-5'a), 3.48 (dd, *J* = 12.0, 4.9 Hz, 1H, H-1a), 3.43 – 3.35 (m, 3H, H-1'a, H-3, H-5'b), 3.22 (td, *J* = 12.2, 5.1 Hz, 1H, H-1'b), 3.07 (br d, *J* = 9.8 Hz, 1H, H-5), 3.03 (d, *J* = 6.3 Hz, 1H, H-6'), 3.01 (dd, *J* = 12.5, 10.9 Hz, 1H, H-1b), 1.81 (dt, *J* = 11.1, 5.7 Hz, 2H, H_2-2'), 1.65 (dt, *J* = 8.8, 5.8 Hz, 2H, H_2-4'), 1.57 – 1.44 (m, 2H, H_2-3'), 1.07 (d, *J* = 6.3 Hz, 3H, H_3-7'), 0.90 (s, 9H, H_3-9', H_3-10', H_3-11'). ^{13}C NMR (100 MHz, MeOD) δ 83.3 (C-6'), 76.7 (C-3), 68.9 (C-5'), 67.4 (C-4), 66.4 (C-2), 66.0 (C-5), 53.5 (C-6), 53.5 (C-1), 52.9 (C-1'), 34.6 (C-8'), 29.3 (C-4'), 25.0 (C-9', C-10', C-11'), 23.2 (C-3'), 22.6 (C-2'), 12.8 (C-7'). $[\alpha]^{20}_D$ = -6.94 (c = 0.63, MeOH). IR/cm^{-1}: 3330, 2956, 2875, 1672, 1439, 1203, 1134, 1029. HRMS: found 334.25885 $[C_{17}H_{35}NO_5+H]^+$, calculated for $[C_{17}H_{35}NO_5+H]^+$ 334.25880.

N-[5-(3,3-Dimethyl-1-butoxy)pentyl]-1-deoxynojirimycin (51):



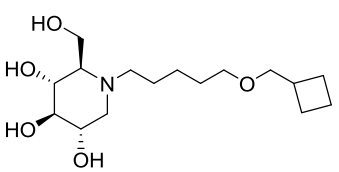
Bromide **40** (0.299 mmol) was subjected to the general procedure D with 1-deoxynojirimycin (0.20 mmol) to provide **51** (28 mg, 0.085 mmol, yield 43%). ^{1}H NMR (400 MHz, MeOD) δ 4.12 (d, *J* = 12.5 Hz, 1H, H-6a), 3.93 (dd, *J* = 12.3, 2.8 Hz, 1H, H-6b), 3.71 (td, *J* = 10.4, 10.0, 4.4 Hz, 1H, H-2), 3.62 (t, *J* = 9.7 Hz, 1H, H-4), 3.50 (t, *J* = 7.3 Hz, 2H, H_2-6'), 3.50 (dd, *J* = 9.0, 1.5 Hz, 1H, H-1a), 3.46 (t, *J* = 6.3 Hz, 2H, H_2-5'), 3.43 – 3.36 (m, 2H, H-3, H-1'a), 3.22 (td, *J* = 12.1, 5.2 Hz, 1H, H-1b), 3.07 (br d, *J* = 10.3 Hz, 1H, H-5), 3.00 (t, *J* = 11.7 Hz, 1H, H-1b), 1.90 – 1.71 (m, 2H, H_2-2'), 1.65 (ddd, *J* = 13.7, 7.5, 6.0 Hz, 2H, H_2-4'), 1.51 (t, *J* = 7.4 Hz, 2H, H_2-7'), 1.53 – 1.43 (m, 2H, H_2-3'), 0.94 (s, 9H, H_3-9', H_3-10', H_3-11'). ^{13}C NMR (100 MHz, MeOD) δ 76.7 (C-3), 70.0 (C-5'), 67.9 (C-6'), 67.4 (C-4), 66.4 (C-2), 66.0 (C-5), 53.4 (C-6), 53.3 (C-1), 52.9 (C-1'), 42.6 (C-7'), 29.7 (C-4), 28.7 (C-9', C-10', C-11'), 25.8 (C-3), 25.0 (C-2), 22.6 (C-8'). $[\alpha]^{20}_D$ = +0.56 (c = 0.57, MeOH). IR/cm^{-1}: 3343, 2954, 2870, 1673, 1433, 1203, 1134. HRMS: found 334.25886 $[C_{17}H_{35}NO_5+H]^+$, calculated for $[C_{17}H_{35}NO_5+H]^+$ 334.25880.

N-[5-(Cyclopropylmethoxy)pentyl]-1-deoxynojirimycin (52):



Bromide **41** (0.30 mmol) was subjected to the general procedure D with 1-deoxynojirimycin (0.20 mmol) to provide **52** (30 mg, 0.097 mmol, yield 49%). ^{1}H NMR (400 MHz, MeOD) δ 4.13 (d, *J* = 12.6 Hz, 1H, H-6a), 3.94 (dd, *J* = 12.7, 3.1 Hz, 1H, H-6b), 3.73 (td, *J* = 10.3, 4.7 Hz, 1H, H-2), 3.64 (t, *J* = 9.8 Hz, 1H, H-4), 3.52 (t, *J* = 6.3 Hz, 2H, H_2-5'), 3.51 – 3.46 (m, 1H, H-1a), 3.40 (t, *J* = 9.2 Hz, 1H, H-3), 3.40 – 3.36 (m, 1H, H-1'a), 3.30 (d, *J* = 6.9 Hz, 2H, H_2-6'), 3.23 (td, *J* = 12.3, 5.3 Hz, 1H, H-1'b), 3.08 (br d, *J* = 10.1 Hz, 1H, H-5), 3.01 (t, *J* = 11.7 Hz, 1H, H-1b), 1.91 – 1.73 (m, 2H, H_2-2'), 1.72 – 1.63 (m, 2H, H_2-4'), 1.55 – 1.45 (m, 2H, H_2-3'), 1.10 – 1.00 (m, 1H, H-7'), 0.57 – 0.51 (m, 2H, H_2-8'), 0.22 (dt, *J* = 6.1, 4.4 Hz, 2H, H_2-9'). ^{13}C NMR (100 MHz, MeOD) δ 76.7 (C-3), 75.3 (C-6'), 69.8 (C-5'), 67.4 (C-4), 66.4 (C-2), 66.0 (C-5), 53.6 (C-6), 53.4 (C-1), 52.9 (C-1'), 28.7 (C-4'), 23.1 (C-3'), 22.5 (C-2'), 10.0 (C-7'), 2.1 (C-8', C-9'). $[\alpha]^{20}_D$ = -6.08 (c = 0.59, MeOH). IR/cm^{-1}: 3346, 2866, 1672, 1430, 1202, 1134, 1032. HRMS: found 304.21194 $[C_{15}H_{29}NO_5+H]^+$, calculated for $[C_{15}H_{29}NO_5+H]^+$ 304.21185.

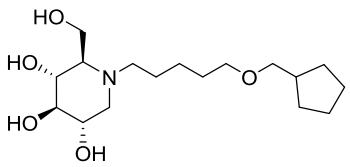
N-[5-(Cyclobutylmethoxy)pentyl]-1-deoxynojirimycin (53):



Bromide **42** (0.31 mmol) was subjected to the general procedure D with 1-deoxynojirimycin (0.20 mmol) to provide **53** (25 mg, 0.079 mmol, yield 39%). ^{1}H NMR (400 MHz, MeOD) δ 4.14 (d, *J* = 12.5 Hz, 1H, H-6a), 3.93 (dd, *J* = 12.7, 3.1 Hz, 1H, H-6b), 3.71 (td, *J* = 10.7, 10.2, 4.7 Hz, 1H, H-2), 3.63 (t, *J* = 9.8 Hz, 1H, H-4), 3.49 (t, *J* = 6.2 Hz, 2H, H_2-5'), 3.48 (dd, *J* = 11.8, 5.2 Hz, 1H, H-1a), 3.43 (d, *J* = 6.8 Hz, 2H, H_2-6'), 3.43 – 3.36 (m, 1H, H-1'a), 3.39 (t, *J* = 9.4 Hz, 1H, H-3),

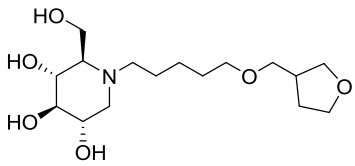
3.22 (td, *J* = 12.3, 5.3 Hz, 1H, H-1'b), 3.06 (br d, *J* = 11.2 Hz, 1H, H-5), 3.01 (t, *J* = 11.7 Hz, 1H, H-1b), 2.63 – 2.53 (m, 1H, H-7'), 2.14 – 2.03 (m, 2H, H_2-8'), 2.03 – 1.91 (m, 2H, H_2-10'), 1.91 – 1.72 (m, 4H, H_2-2', H_2-9'), 1.67 (ddd, *J* = 13.7, 7.5, 5.9 Hz, 2H, H_2-4'), 1.51 – 1.47 (m, 2H, H_2-3'). ^{13}C NMR (100 MHz, MeOD) δ 76.7 (C-3), 75.2 (C-6'), 70.2 (C-5'), 67.4 (C-4), 66.4 (C-2), 66.0 (C-5), 53.5 (C-6), 53.4 (C-1), 52.9 (C-1'), 35.1 (C-7'), 28.7 (C-4'), 24.6 (C-8', C-9'), 23.1 (C-3'), 22.5 (C-2'), 18.0 (C-10'). $[\alpha]^{20}_D$ = -6.02 (c = 0.50, MeOH). IR/cm^{-1}: 3341, 2938, 2865, 1673, 1431, 1202, 1135, 1031. HRMS: found 318.22761 $[C_{16}H_{31}NO_5+H]^+$, calculated for $[C_{16}H_{31}NO_5+H]^+$ 318.22750.

N-[5-(Cyclopentylmethoxy)pentyl]-1-deoxynojirimycin (54):



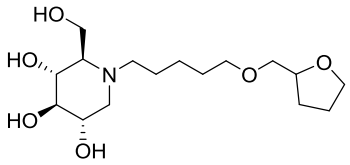
Bromide **43** (0.30 mmol) was subjected to the general procedure D with 1-deoxynojirimycin (0.20 mmol) to provide **54** (23 mg, 0.069 mmol, yield 35%). ^{1}H NMR (400 MHz, MeOD) δ 4.13 (d, *J* = 12.5 Hz, 1H, H-6a), 3.93 (dd, *J* = 12.6, 3.1 Hz, 1H, H-6b), 3.72 (dt, *J* = 14.7, 4.6 Hz, 1H, H-2), 3.63 (t, *J* = 9.7 Hz, 1H, H-4), 3.52 – 3.44 (m, 1H, H-1a), 3.49 (t, *J* = 6.2 Hz, 2H, H_2-5'), 3.43 – 3.35 (m, 2H, H-3, H-1'a), 3.33 (d, *J* = 7.1 Hz, 2H, H_2-6'), 3.22 (td, *J* = 12.3, 5.3 Hz, 1H, H-1'b), 3.07 (d, *J* = 9.5 Hz, 1H, H-5), 3.00 (t, *J* = 11.7 Hz, 1H, H-1b), 2.21 – 2.12 (m, 1H, H-7'), 1.88 – 1.71 (m, 4H, H_2-2', H_2-8'), 1.71 – 1.54 (m, 6H, H_2-9', H_2-10', H_2-4'), 1.51 – 1.48 (m, 2H, H_2-3'), 1.35 – 1.22 (m, 2H, H_2-11'). ^{13}C NMR (100 MHz, MeOD) δ 76.7 (C-3), 75.3 (C-6'), 70.1 (C-5'), 67.4 (C-4), 66.4 (C-2), 66.0 (C-5), 53.5 (C-6), 53.5 (C-1), 52.8 (C-1'), 39.3 (C-7'), 29.2 (C-8', C-11'), 28.7 (C-9', C-10'), 25.0 (C-4'), 23.1 (C-3'), 22.7 (C-2'). $[\alpha]^{20}_D$ = -4.76 (c = 0.46, MeOH). IR/cm^{-1}: 3346, 2950, 2867, 1673, 1433, 1203, 1133, 1032. HRMS: found 332.24323 $[C_{17}H_{33}NO_5+H]^+$, calculated for $[C_{17}H_{33}NO_5+H]^+$ 332.24315.

N-[5-(*R*/*S*-Tetrahydrofuran-3-ylmethoxy)pentyl]-1-deoxynojirimycin (55):



Bromide **44** (0.29 mmol) was subjected to the general procedure D with 1-deoxynojirimycin (0.20 mmol) to provide **55** (58.5 mg, 0.17 mmol, yield 88%). ^{1}H NMR (400 MHz, MeOD) δ 4.14 (d, *J* = 12.6 Hz, 1H, H-6a), 3.93 (dd, *J* = 12.4, 3.0 Hz, 1H, H-6b), 3.85 (dd, *J* = 8.3, 5.5 Hz, 1H, H-9'a), 3.83 (dd, *J* = 8.7, 7.2 Hz, 1H, H-10'a), 3.78 – 3.69 (m, 2H, H-9'b, H-2), 3.63 (t, *J* = 9.8 Hz, 1H, H-4), 3.58 (dd, *J* = 8.6, 5.5 Hz, 2H, H_2-10'b), 3.52 – 3.47 (m,1H, H-1a), 3.50 (td, *J* = 6.3, 1.7 Hz, 2H, H_2-5'), 3.44 (dd, *J* = 9.2, 6.3 Hz, 1H, H-6'a), 3.43 – 3.35 (m, 3H, H-1'a, H-3, H-6'b), 3.20 – 3.18 (m, 1H, H-1'b), 3.07 (br d, *J* = 9.9 Hz, 1H, H-5), 3.01 (t, *J* = 11.7 Hz, 1H, H-1b), 2.59 – 2.48 (m, 1H, H-7'), 2.02 – 1.98 (m, 1H, H-8'a), 1.91 – 1.72 (m, 2H, H_2-2'), 1.72 – 1.60 (m, 3H, H-8'b, H_2-4'), 1.53 – 1.47 (m, 2H, H_2-3'). ^{13}C NMR (100 MHz, MeOD) δ 76.7 (C-3), 72.5 (C-6'), 70.5 (C-10'), 70.3 (C-5'), 67.4 (C-4), 67.3 (C-9'), 66.4 (C-2), 66.0 (C-5), 53.5 (C-6), 53.5 (C-1), 52.9 (C-1'), 39.0 (C-7'), 28.7 (C-4'), 28.5 (C-8'), 23.1 (C-3'), 22.5 (C-2'). IR/cm^{-1}: 3346, 2970, 2942, 1738, 1070, 1430, 1366, 1199, 1132, 898. $[\alpha]^{20}_D$ = -1.89 (c = 1.17, MeOH). HRMS: found 334.22282 $[C_{16}H_{31}NO_6+H]^+$, calculated for $[C_{16}H_{31}NO_6+H]^+$ 334.22241.

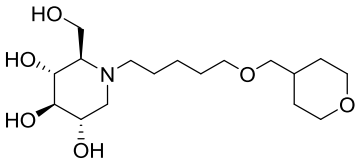
N-[5-(*R*/*S*-Tetrahydrofuran-1-ylmethoxy)pentyl]-1-deoxynojirimycin (56):



Bromide **45** (0.29 mmol) was subjected to the general procedure D with 1-deoxynojirimycin (0.20 mmol) to provide 5**6** (10 mg, 0.030 mmol, yield 15%). ^{1}H NMR (600 MHz, MeOD) δ 4.12 (d, *J* = 11.5 Hz, 1H, H-6a), 4.07 – 4.01 (m, 1H, H-7'), 3.91 (dd, *J* = 12.5, 3.2 Hz, 1H, H-6b), 3.85 (dt, *J* = 8.2, 6.7 Hz, 1H, H-10'a), 3.76 (td, *J* = 7.7, 6.1 Hz, 1H, H-10'b), 3.69 – 3.67 (m, 1H, H-2), 3.60 (dd, *J* = 12.7, 6.6 Hz, 1H, H-4), 3.51 (td, *J* = 6.2, 3.8 Hz, 1H, H-5'), 3.47 – 3.34 (m, 5H, H_2-6', H-1a, H-1'a, H-3), 3.20 (td, *J* = 12.4, 5.0 Hz, 1H, H-1b), 3.04 (d, *J* = 9.9 Hz, 1H, H-5), 2.99 (t, *J* = 11.7 Hz, 1H, H-1'b), 2.01 – 1.95 (m, 1H, H-8'a), 1.94 – 1.87 (m, 1H, H-9'), 1.87 – 1.71 (m, 2H,

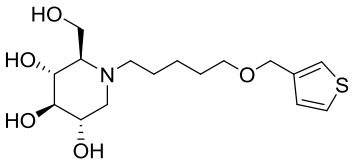
H_2-2'), 1.66 (tt, *J* = 7.5, 5.9 Hz, 2H, H_2-4'), 1.63 – 1.57 (m, 1H, H-8'b), 1.54 – 1.43 (m, 2H, H_2-3'). ^{13}C NMR (150 MHz, MeOD) δ 79.4 (C-7'), 78.2 (C-3), 74.6 (C-6'), 72.0 (C-5'), 69.2 (C-10'), 68.8 (C-5), 67.8 (C-4), 67.4 (C-2), 54.9 (C-1), 54.8 (C-6), 54.3 (C-1'), 29.9 (C-4'), 28.9 (C-8'), 26.6 (C-9'), 24.5 (C-3'), 23.9 (C-2'). IR/cm^{-1}: 3367, 2964, 2902, 1674, 1396, 1066. $[\alpha]^{20}_D$ = -9.8 (c = 0.20, MeOH). HRMS: found 334.22266 $[C_{16}H_{31}NO_6+H]^+$, calculated for $[C_{16}H_{31}NO_6+H]^+$ 334.22241.

N-[5-(Tetrahydro-2H-pyran-4-ylmethoxy)pentyl]-1-deoxynojirimycin (57):



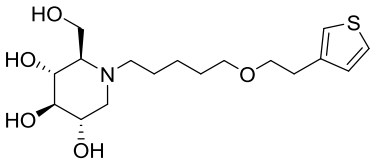
Bromide **46** (0.29 mmol) was subjected to the general procedure D with 1-deoxynojirimycin (0.20 mmol) to provide **57** (35 mg, 0.10 mmol, yield 50%). ^{1}H NMR (400 MHz, MeOD) δ 4.14 (d, *J* = 12.5 Hz, 1H, H-6a), 3.92 (dd, *J* = 11.8, 2.6 Hz, 1H, H-6b), 3.99 – 3.94 (m, 2H, H-9'a, H-10'a), 3.70 (ddd, *J* = 11.2, 9.3, 4.9 Hz, 1H, H-2), 3.62 (dd, *J* = 10.4, 9.2 Hz, 1H, H-4), 3.49 (t, *J* = 6.2 Hz, 2H, H_2-5'), 3.48 – 3.35 (m, 5H, H-9'b, H-10'b, H-1a, H-1'a, H-3), 3.31 (d, *J* = 6.4 Hz, 2H, H_2-6'), 3.23 (dd, *J* = 12.1, 5.3 Hz, 1H, H-1'b), 3.06 (dd, *J* = 10.3, 2.7 Hz, 1H, H-5), 3.01(t, *J* = 11.7 Hz, 1H, H-1b), 1.92 – 1.84 (m, 1H, H-7'), 1.84 – 1.72 (m, 2H, H_2-2'), 1.72 – 1.62 (m, 4H, H_2-4', H-8'a, H-11'a), 1.57 – 1.45 (m, 2H, H_2-3'), 1.34 – 1.32 (m, 2H, H-8'b, H-11'b). ^{13}C NMR (100 MHz, MeOD) δ 76.8 (C-3), 75.5 (C-6'), 70.2 (C-5'), 67.3 (C-9', C-10'), 67.3 (C-4), 66.4 (C-2), 66.0 (C-5), 53.5 (C-6), 53.4 (C-1), 52.8 (C-1'), 35.2 (C-7'), 29.6 (C-8', C-11'), 28.7 (C-4'), 23.1 (C-3'), 22.5 (C-2'). $[\alpha]^{20}_D$ = -4.01 (c = 0.70, MeOH). IR/cm^{-1}: 3333, 2923, 2859, 1671, 1433, 1387, 1200, 1136, 1088, 1032. HRMS: found 348.23809 $[C_{17}H_{33}NO_6+H]^+$, calculated for $[C_{17}H_{33}NO_6+H]^+$ 348.23806.

N-[5-(Thiophen-3-methoxy)pentyl]-1-deoxynojirimycin (58):



Bromide **47** (0.29 mmol) was subjected to the general procedure D with 1-deoxynojirimycin (0.20 mmol) to provide **58** (41 mg, 0.12 mmol, yield 59%). ^{1}H NMR (400 MHz, MeOD) δ 7.41 (dd, *J* = 5.0, 3.0 Hz, 1H, H thio), 7.34 – 7.31 (m, 1H, H thio), 7.10 (dd, *J* = 5.0, 1.2 Hz, 1H, H thio), 4.54 (s, 2H, H_2-6'), 4.12 (d, *J* = 12.2 Hz, 1H, H-6a), 3.92 (dd, *J* = 12.7, 3.1 Hz, 1H, H-6b), 3.71 (td, *J* = 10.1, 4.5 Hz, 1H, H-2), 3.62 (t, *J* = 9.8 Hz, 1H, H-4), 3.54 (t, *J* = 6.2 Hz, 2H, H_2-5'), 3.46 (dd, *J* = 12.1, 4.8 Hz, 1H, H-1a), 3.43 – 3.36 (m, 2H, H-1'a, H-3), 3.21 (td, *J* = 12.3, 5.2 Hz, 1H, H-1'b), 3.11 – 3.02 (m, 1H, H-5), 2.99 (t, *J* = 11.7 Hz, 1H, H-1b), 1.89 – 1.74 (m, 2H, H_2-2'), 1.69 (ddd, *J* = 13.6, 7.5, 6.0 Hz, 2H, H_2-4'), 1.53 – 1.45 (m, 2H, H_2-3'). ^{13}C NMR (100 MHz, MeOD) δ 139.5, 127.1, 125.6, 122.6 (C-thio), 76.7 (C-3), 69.3 (C-5'), 67.6 (C-6'), 67.4 (C-4), 66.4 (C-2), 66.0 (C-5), 53.5 (C-6), 53.5 (C-1), 52.9 (C-1'), 28.6 (C-4'), 23.1 (C-3'), 22.5 (C-2'). $[\alpha]^{20}_D$ = -3.16 (c = 0.82, MeOH). IR/cm^{-1}: 3346, 2963, 2867, 1672, 1429, 1366, 1202, 1133, 1032. HRMS: found 346.16843 $[C_{16}H_{27}NO_5S+H]^+$, calculated for $[C_{16}H_{27}NO_5S+H]^+$ 346.16837.

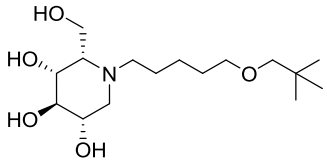
N-[5-(Thiophen-3-ethoxy)pentyl]-1-deoxynojirimycin (59):



Bromide **48** (0.29 mmol) was subjected to the general procedure D with 1-deoxynojirimycin (0.20 mmol) to provide **59** (10 mg, 0.028 mmol, yield 14%). ^{1}H NMR (400 MHz, MeOD) δ 7.33 (dd, *J* = 5.0, 2.9 Hz, 1H, H thio), 7.11 (dd, *J* = 3.0, 1.1 Hz, 1H, H thio), 7.02 (dd, *J* = 4.9, 1.3 Hz, 1H, H thio), 4.12 (d, *J* = 12.5 Hz, 1H, H-6a), 3.92 (d, *J* = 12.3 Hz, 1H, H-6b), 3.74 – 3.70 (m, 1H, H-2), 3.68 (t, *J* = 6.7 Hz, 2H, H_2-6'), 3.62 (t, *J* = 9.7 Hz, 1H, H-4), 3.52 (t, *J* = 6.2 Hz, 2H, H_2-5'), 3.45 (dd, *J* = 12.1, 4.8 Hz, 1H, H-1a), 3.42 – 3.34 (m, 2H, H-3, H-1'a), 3.23 – 3.13 (m, 1H, H-1'b), 3.06 – 3.00 (m, 1H, H-5), 2.97 (t, *J* = 11.7 Hz, 1H, H-1b), 2.91 (dd, *J* = 7.1, 6.3 Hz, 2H, H_2-7'), 1.86 – 1.70 (m, 2H, H_2-2'), 1.70 – 1.62 (m, 2H, H_2-4'), 1.52 – 1.40 (m, 2H, H_2-3'). ^{13}C NMR (100 MHz, MeOD) δ 139.3, 128.1, 124.7, 120.7 (C thio), 76.8 (C-3), 70.8 (C-6'), 69.9 (C-5'), 67.5 (C-4), 66.4 (C-2), 66.0 (C-5), 53.4 (C-1), 53.0 (C-1'), 30.2 (C-7'), 28.7 (C-4'), 24.0 (C-3'),

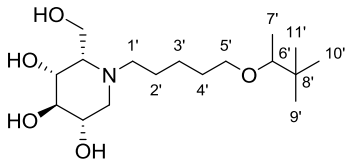
23.1 (C-2'). $[\alpha]^{20}_D$ = -9.09 (c = 0.20, MeOH). IR/cm^{-1}: 3358, 3018, 2943, 2870, 1736, 1677, 1439, 1366, 1205, 1134, 1031. HRMS: found 360.18495 $[C_{17}H_{29}NO_5S+H]^+$, calculated for $[C_{17}H_{29}NO_5S+H]^+$ 360.18392.

_N_-[5-(3,3-Dimethyl-1-propyloxy)pentyl]-1-L-_ido_-1-deoxynojirimycin (5):



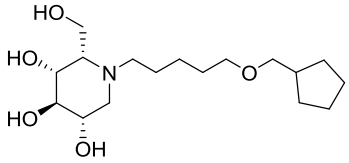
Bromide **66** (0.30 mmol) was subjected to the general procedure D with L-*ido*-1-deoxynojirimycin (0.20 mmol) to provide **5** (16 mg, 0.049 mmol, yield 40%). ^{1}H NMR (400 MHz, MeOD) δ 4.05 (br s, 1H, H-3), 4.03 – 3.94 (m, 3H, H_2-6, H-2), 3.71 – 3.64 (m, 1H, H-4), 3.56 (t, *J* = 7.0 Hz, 1H, H-5), 3.43 (t, *J* = 6.3 Hz, 1H, H-2), 3.27 – 3.18 (m, 2H, H-5'), 3.07 (s, 2H, H_2-6'), 3.10 – 2.87 (m, 4H, H_2-1, H_2-1'), 1.82 – 1.53 (m, 4H, H_2-2', H_2-4'), 1.51 – 1.37 (m, 2H, H_2-3'), 0.90 (s, 9H, H_3-8', H_3-9', H_3-10'). ^{13}C NMR (100 MHz, MeOD) δ 82.4 (C-6'), 72.4 (C-3), 72.3 (C-5'), 70.3 (C-4), 64.0 (C-2), 55.8 (C-6), 55.3 (C-1'), 53.3 (C-1), 32.9 (C-7'), 30.4 (C-4'), 26.7 (C-8', C-9', C-10'), 24.8 (C-2'), 13.3 (C-3'). IR/cm^{-1}: 3369, 2935, 2860, 1066. HRMS: found 320.2431 $[C_{16}H_{33}NO_5+H]^+$, calculated for $[C_{16}H_{33}NO_5+H]^+$ 320.2432.

_N_-[5-(3,3-Dimethyl-2-butoxy)pentyl]-L-_ido_-1-deoxynojirimycin (60):



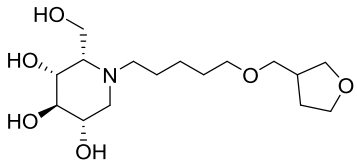
Bromide **39** (0.32 mmol) was subjected to the general procedure D with L-*ido*-1-deoxynojirimycin (0.20 mmol) to provide **60** (14 mg, 0.042 mmol, yield 21%). ^{1}H NMR (400 MHz, MeOD) δ 4.05 (br s, 1H, H-3), 4.03 – 3.95 (m, 3H, H_2-6, H-2), 3.93 – 3.86 (m, 1H, H-4), 3.64 (ddd, *J* = 8.9, 7.6, 4.7 Hz, 1H, H-5'a), 3.58 – 3.47 (m, 2H, H-1a, H-5), 3.41 – 3.30 (m, 4H, H-1a, H_2-1', H-5'b), 3.04 (q, *J* = 6.3 Hz, 1H, H-6'), 1.95 – 1.72 (m, 2H, H_2-2'), 1.66 (dt, *J* = 12.9, 6.2 Hz, 2H, H_2-4'), 1.56 – 1.44 (m, 2H, H_2-3'), 1.08 (d, *J* = 6.4 Hz, 3H, H_3-7'), 0.91 (s, 9H, H_3-9', H_3-10', H_3-11'). ^{13}C NMR (100 MHz, MeOD) δ 83.3 (C-6'), 70.9 (C-3), 68.9 (C-5'), 67.5 (C-2), 66.6 (C-4), 62.4 (C-5), 60.0 (C-6), 53.7 (C-1'), 53.0 (C-1), 34.6 (C-8'), 29.4 (C-4'), 25.0 (C-9', C-10', C-11'), 23.3 (C-3'), 22.0 (C-2'), 12.8 (C-7'). IR/cm^{-1}: 3372, 2972, 1673, 1393, 1203, 1139, 1066. $[\alpha]^{20}_D$ = +1.44 (c = 0.28, MeOH). HRMS: found 334.25937 $[C_{17}H_{35}NO_5+H]^+$, calculated for $[C_{17}H_{35}NO_5+H]^+$ 334.25880.

_N_-[5-(Cyclopentylmethoxy)pentyl]-L-_ido_-1-deoxynojirimycin (61):



Bromide **43** (0.30 mmol) was subjected to the general procedure D with L-*ido*-1-deoxynojirimycin (0.20 mmol) to provide **61** (23 mg, 0.069 mmol, yield 35%). ^{1}H NMR (400 MHz, MeOD) δ 4.05 (br s, 1H, H-3), 4.03 – 3.94 (m, 3H, H_2-6, H-2), 3.90 (br s, 1H, H-4), 3.60 – 3.51 (m, 2H, H-1a, H-5), 3.49 (t, *J* = 6.3 Hz, 2H, H_2-5'), 3.40 – 3.33 (m, 5H, H-1b, H_2-1', H_2-6'), 2.17 (dt, *J* = 14.9, 7.6 Hz, 1H, H-7'), 1.96 – 1.72 (m, 4H, H_2-2', H-8'a, H-11'a), 1.71 – 1.54 (m, 6H, H_2-9', H_2-10', H_2-4'), 1.48 (p, *J* = 7.7 Hz, 2H, H_2-3'), 1.34 – 1.25 (m, 2H, H_2-11'). ^{13}C NMR (100 MHz, MeOD) δ 75.3 (C-6'), 70.9 (C-3), 70.2 (C-5'), 67.5 (C-2), 66.6 (C-4), 62.4 (C-5), 60.0 (C-6), 53.6 (C-1'), 53.0 (C-1), 39.3 (C-7'), 29.2 (C-8', C-11'), 28.7 (C-9', C-10'), 25.0 (C-4'), 23.1 (C-3'), 21.9 (C-2'). IR/cm^{-1}: 3374, 2953, 2873, 1678, 1440, 1205, 1136, 1072. $[\alpha]^{20}_D$ = +4.33 (c = 0.46, MeOH). HRMS: found 332.24355 $[C_{17}H_{33}NO_5+H]^+$, calculated for $[C_{17}H_{33}NO_5+H]^+$ 332.24315.

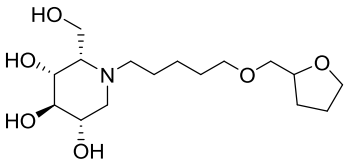
_N_-[5-(_R_/_S_-Tetrahydrofuran-3-ylmethoxy)pentyl]-L-_ido_-1-deoxynojirimycin (62):



Bromide **44** (0.29 mmol) was subjected to the general procedure D with L-*ido*-1-deoxynojirimycin (0.20 mmol) to provide **62** (20 mg, 0.060 mmol, yield 30%). ^{1}H NMR (400 MHz, MeOD) δ 4.08 – 3.95 (m, 4H, H_2-6, H-3, H-2), 3.90 (t, *J* = 3.0 Hz, 1H, H-4), 3.88 – 3.80 (m, 2H. H-9'a, H-10'a), 3.77 – 3.70

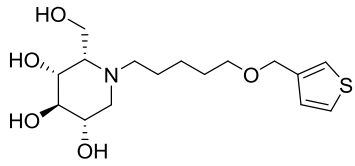
(m, 1H, H-9'b), 3.58 (dd, *J* = 8.6, 5.5 Hz, 1H, H-10'b), 3.56 – 3.52 (m, 2H, H-5, H-1a), 3.50 (td, *J* = 6.3, 1.8 Hz, 2H, H_2-5'), 3.44 (dd, *J* = 9.3, 6.2 Hz, 1H, H-6'), 3.41 – 3.32 (m, 4H, H-1b, H_2-1', H-6'b), 2.59 – 2.49 (m, 1H, H-7'), 2.09 – 1.99 (m, 2H, H_2-8'), 1.97 – 1.72 (m, 2H, H_2-2'), 1.71 – 1.60 (m, 2H, H_2-4'), 1.48 (p, *J* = 7.6 Hz, 2H, H_2-3'). ^{13}C NMR (100 MHz, MeOD) δ 72.5 (C-6'), 70.9 (C-3), 70.5 (C-10'), 70.3 (C-5'), 67.5 (C-2), 67.3 (C-9'), 66.7 (C-4), 62.4 (C-5), 60.0 (C-6), 53.7 (C-1'), 53.0 (C-1), 39.0 (C-7'), 28.7 (C-4'), 28.5 (C-8'), 23.1 (C-3'), 21.9 (C-2'). IR/cm^{-1}: 3355, 2971, 1674, 1201, 1132, 1066. $[\alpha]^{20}_D$ = +10.50 (c = 0.40, MeOH). HRMS: found 334.22299 $[C_{16}H_{31}NO_6+H]^+$, calculated for $[C_{16}H_{31}NO_6+H]^+$ 334.22241.

N-[5-(*R*/*S*-Tetrahydrofuran-1-ylmethoxy)pentyl]-L-*ido*-1-deoxynojirimycin (63):



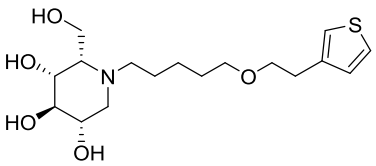
Bromide **45** (0.29 mmol) was subjected to the general procedure D with L-*ido*-1-deoxynojirimycin (0.20 mmol) to provide **63** (23 mg, 0.069 mmol, yield 34%). ^{1}H NMR (400 MHz, MeOD) δ 4.12 – 3.94 (m, 5H, H-3, H-7', H-2, H_2-6), 3.93 – 3.83 (m, 2H, H-4, H-10'a), 3.82 – 3.74 (m, 1H, H-10'b), 3.58 – 3.48 (m, 5H, H-1a, H-5, H_2-5', H-6'a), 3.48 – 3.29 (m, 3H, H-1b, H_2-1'), 2.08 – 1.85 (m, 4H, H-8'a, H_2-9', H-2'a), 1.85 – 1.73 (m, 1H, H-2'b), 1.70 – 1.59 (m, 3H, H_2-4', H-8'b), 1.50 (q, *J* = 7.5 Hz, 2H, H_2-3'). ^{13}C NMR (100 MHz, MeOD) δ 78.0 (C-3), 73.1 (C-6'), 70.9 (C-7'), 70.6 (C-5'), 67.8(C-10'), 67.6 (C-2), 66.7 (C-4), 62.4 (C-5), 59.9 (C-6), 53.7 (C-1'), 53.0 (C-1), 28.6 (C-4'), 27.5 (C-8'), 25.2 (C-9'), 23.1 (C-3'), 21.8 (C-2'). IR/cm^{-1}: 3346, 2871, 1673, 1432, 1200, 1132, 1071. $[\alpha]^{20}_D$ = +12.5 (c = 0.46, MeOH). HRMS: found 334.22280 $[C_{16}H_{31}NO_6+H]^+$, calculated for $[C_{16}H_{31}NO_6+H]^+$ 334.22241.

N-[5-(Thiophen-3-methoxy)pentyl]-L-*ido*-1-deoxynojirimycin (64):



Bromide **47** (0.29 mmol) was subjected to the general procedure D with L-*ido*-1-deoxynojirimycin (0.20 mmol) to provide **64** (14 mg, 0.042 mmol, yield 21%). ^{1}H NMR (400 MHz, MeOD) δ 4.54 (d, *J* = 0.7 Hz, 2H, H_2-6'), 4.04 (br s, 1H, H-3), 4.01 – 3.93 (m, 3H, H_2-6, H-2), 3.89 (t, *J* = 3.7 Hz, 1H, H-4), 3.54 (t, *J* = 6.2 Hz, 2H, H_2-5'), 3.55 – 3.44 (m, 2H, H-1a, H-5), 3.39 – 3.28 (m, 3H, H-1b, H_2-1'), 1.98 – 1.72 (m, 2H, H_2-2'), 1.69 (dt, *J* = 8.3, 6.3 Hz, 2H, H_2-4'), 1.50 (q, *J* = 7.6 Hz, 2H, H_2-3'). ^{13}C NMR (100 MHz, MeOD) δ 139.5(C_q thio), 127.1 , 125.6, 122.6 (CH thio), 70.9 (C-3), 69.3 (C-5'), 67.6 (C-6'), 67.5 (C-2), 66.6 (C-4), 62.4 (C-5), 60.0 (C-6), 53.6 (C-1'), 53.0 (C-1), 28.7 (C-4), 23.1 (C-2), 21.8 (C-3). IR/cm^{-1}: 3346, 2970, 1673, 1409, 1201, 1133, 1066. $[\alpha]^{20}_D$ = +8.28 (c = 0.29, MeOH). HRMS: found 346.16823 $[C_{16}H_{27}NO_5S$ +H]$^+$, calculated for $[C_{16}H_{27}NO_5S+H]^+$ 346.16827.

N-[5-(Thiophen-3-ethoxy)pentyl]-L-*ido*-1-deoxynojirimycin (65):



Bromide **48** (0.29 mmol) was subjected to the general procedure D with L-*ido*-1-deoxynojirimycin (0.20 mmol) to provide **65** (36 mg, 0.099 mmol, yield 49%). ^{1}H NMR (400 MHz, MeOD) δ 7.33 (dd, *J* = 4.9, 3.0 Hz, 2H, H thio), 7.14 – 7.09 (m, 1H, H thio), 7.02 (dd, *J* = 4.9, 1.3 Hz, 1H, H thio), 4.05 (br s, 1H, H-3), 4.01 – 3.95 (m, 3H, H-2, H_2-6), 3.90 (t, *J* = 3.7 Hz, 1H, H-4), 3.68 (t, *J* = 6.7 Hz, 2H, H_2-6'), 3.56 – 3.47 (m, 2H, H-1a, H-5), 3.52 (t, *J* = 6.2 Hz, 2H, H_2-5'), 3.38 – 3.28 (m, 3H, H-1b, H_2-1'), 2.94 – 2.88 (m, 2H, H_2-7'), 1.93 – 1.70 (m, 2H, H_2-2'), 1.70 – 1.64 (m, 2H, H_2-4'), 1.53 – 1.37 (m, 2H, H_2-3'). ^{13}C NMR (100 MHz, MeOD) δ 139.3 (C_q thio), 128.1, 124.7, 120.7 (CH thio), 70.9 (C-3), 70.8 (C-6'), 70.0 (C-5'), 67.5 (C-2), 66.6 (C-4), 62.4 (C-5), 60.0 (C-6), 53.7 (C-1'), 53.0 (C-1), 30.2 (C-7'), 28.7 (C-4'), 23.1 (C-3'), 21.8 (C-2'). IR/cm^{-1}: 3355, 2971, 1674, 1394, 1202, 1066. $[\alpha]^{20}_D$ = +2.52 (c = 0.71, MeOH). HRMS: found 360.18397 $[C_{17}H_{29}NO_5S$ +H]$^+$, calculated for $[C_{17}H_{29}NO_5S+H]^+$ 360.18392.

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