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4"-O-Alkylated α-Galactosylceramide Analogues as *i*NKT-Cell Antigens: Synthetic, Biological, and Structural Studies

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Invariant natural killer T-cells (*i*NKT) are a glycolipid-responsive subset of T-lymphocytes that fulfill a pivotal role in the immune system. The archetypical synthetic glycolipid, α-galactosylceramide (α-GalCer), whose molecular framework is inspired by a group of amphiphilic natural products, remains the most studied antigen for *i*NKT-cells. Nonetheless, the potential of α-GalCer as an immunostimulating agent is compromised by the fact that this glycolipid elicits simultaneous secretion of Th1- and Th2-cytokines. This has incited medicinal chemistry efforts to identify analogues that are able to perturb the Th1/Th2 balance. In this work, we present the synthesis of an extensive set of 4"-O-alkylated α-GalCer analogues, which were evaluated in vivo for their cytokine induction. We have found that conversion of the 4"-OH group to ether moieties decreases the immunogenic potential in mice relative to α-GalCer. Yet, the benzyl-modified glycolipids are able to produce a distinct pro-inflammatory immune response. The crystal structures suggest an extra hydrophobic interaction between the benzyl moiety and the α2-helix of CD1d.

Introduction

A screening of lipophilic extracts from the marine sponge *Agelas mauritianus* by the Pharmaceutical Research Laboratories at Kirin Brewery in the early 1990s led to the discovery of the agelasphins, a group of structurally related amphiphilic natural products belonging to the cerebroside family.[1] Structural refinement of agelasphin 9b (AGL-9b; **1**, Figure 1) resulted in the synthesis of α-galactosylceramide (α-GalCer or KRN7000; **2**), a glycolipid that displayed promising antitumor activity in a murine B16 melanoma model.[2] α-GalCer is composed of a D-galactopyranosyl unit, connected to a lipophilic ceramide tail via an α-glycosidic bond. This ceramide, in turn, consists of D-*ribo*-phytosphingosine, which is N-acylated with hexacosanoic (cerotic) acid. The α-anomeric configuration is noteworthy, as the β-configuration is a characteristic feature of most mammalian glycolipids.[3]

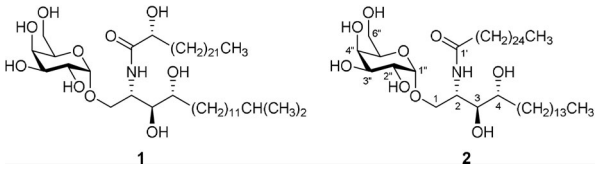

Figure 1. Structures of agelasphin 9b (**1**) and α-galactosylceramide (**2**).

The mode of action of α-GalCer relies on a high-affinity binding event with CD1d, a major histocompatibility complex (MHC) class I-like non-polymorphic glycoprotein associated with the membrane of antigen presenting cells (APCs). This binary α-GalCer-CD1d complex is presented to the semi-invariant αβ T-cell receptor (TCR) of invariant natural killer T-cells (*i*NKT), a distinct population of CD1d-restricted T-lymphocytes, to form a ternary complex.[4] The crystal structures of α-GalCer bound to both mouse (mCD1d) and human CD1d (hCD1d) were published in 2005, revealing that the two lipophilic chains of the ceramide are accommodated in two discrete hydrophobic pockets (A′ and F′) of a narrow binding groove flanked by two α-helices (α1 and α2), which settle on top of a β-sheet containing six β-strands. The phytosphingosine chain is buried in the F′-pocket, whereas the acyl chain is entrenched in the A′-pocket, adopting a helical anti-clockwise conformation.[5,6] The galactose ring protrudes from the CD1d binding groove and is stabilized by a hydrogen bond network. Both the 2"- and 3"-OH are bound to Asp153 (α2-helix of mCD1d). The 3- and 4-OH of the phytosphingosine chain engage in a hydrogen bond with Asp80 (α1-helix of mCD1d) and Thr156 (α2-helix) reaches out to the glycosidic oxygen and the NH moiety of the amide.

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The crystal structure of the trimolecular hCD1d–glycolipid–hTCR complex was published in 2007.[7] The TCR, a heterodimeric receptor consisting of an invariant α- and a slightly variable β-chain, docks onto the α-helices of CD1d in a parallel manner, with the α-chain hovering above the CD1d binding cleft and the β-chain sitting offset to the C-terminal end of the α1-helix. The binding footprint between the TCR and the CD1d–glycolipid complex is conserved between humans and mice, and independent from the paired β-chain and the glycolipid antigen presented by CD1d.[8] The main interactions between the TCR and the binary CD1d–glycolipid complex arise through the α-chain, in particular the CDR1α- and CDR3α-loops. With respect to the human TCR, the 2"-, 3"- and 4"-OH of the galactose unit form a hydrogen bond with Gly96 (CDR3α) and Ser30 and Phe29 (CDR1α) respectively. The 3-OH of the phytosphingosine interacts with Arg95 (CDR3α). As for the murine TCR, the 3"- and 4"-OH engage in a hydrogen bond with Asn30 (CDR1α). The other interactions are conserved between the human and murine structures.

Upon formation of the trimolecular complex, the *i*NKT-cell is stimulated to secrete massive amounts of pro-inflammatory T-helper 1 (Th1) cytokines, such as interferon-γ (IFN-γ) and tumor necrosis factor alpha (TNF-α), and anti-inflammatory Th2-cytokines, such as interleukin-4 (IL-4) and interleukin-10 (IL-10).[9,10] These cytokines act as small-protein modulators of the immune system through autocrine, paracrine and endocrine cell signaling. However, as both cytokine types antagonize each other, a polarization of the Th1/Th2 balance is highly desired from a pathological and therapeutic point of view. It has been shown that structural alteration of α-GalCer may shift this Th1/Th2 balance, and thus, a lot of research has been focusing on the synthesis and biological assessment of analogues that are able to skew the cytokine response profile toward either Th1 or Th2.[11] Modifications that establish more intimate interactions with CD1d and the TCR, thereby stabilizing the trimolecular complex, tend to drive the cytokine polarization toward Th1,[12] due to the fact that prolonged stimulation of the TCR augments the IFN-γ production by the *i*NKT-cells as compared with IL-4 production.[13] Promising Th1-polarizers could be used as vaccine adjuvants, to combat cancer (immuno-oncology), or as antibacterial and antiviral agents, and thus target a broad spectrum of diseases that have an immunopathological foundation.

Because the galactose unit contacts both the TCR and CD1d, modifications of the OH groups on the pyranose ring directly influence the binding affinity and thus the stability of the resulting complex. Over the years, quite a few galactose-modified analogues have been synthesized and tested for their activity in vitro and in vivo, the minority of them producing a therapeutically attractive cytokine response profile. However, those analogues have yielded a lot of valuable information concerning the importance of the galactose OH groups. The 2"-OH turns out to be crucial for the antigenicity of α-GalCer: methylation significantly decreases C57Bl/6 murine splenocyte proliferation,[14] while fluorine substitution at C2" leads to an inactive analogue.[15] The C2"-epimer, α-mannosylceramide (α-ManCer), triggers only low levels of cytokine release when presented by CD1d.[16] The introduction of a sulfate group on the 3"-OH yields a compound that is equally active as α-GalCer.[17]

Because the 6"-OH group is solvent exposed, forming no direct contacts with either CD1d or the TCR, structural variations at this position have been extensively explored.[18–25] This has led to the discovery of selected analogues with a distinctly improved Th1-polarized antigenic profile (Figure 2), including the 1-naphthylurea (NU-α-GalCer, **3**),[26,27] the *O*-methylated (RCAI-61, **4**),[28] the 4-pyridinylcarbamate (PyrC-α-GalCer, **5**)[29] and other carbamate derivatives.[30]

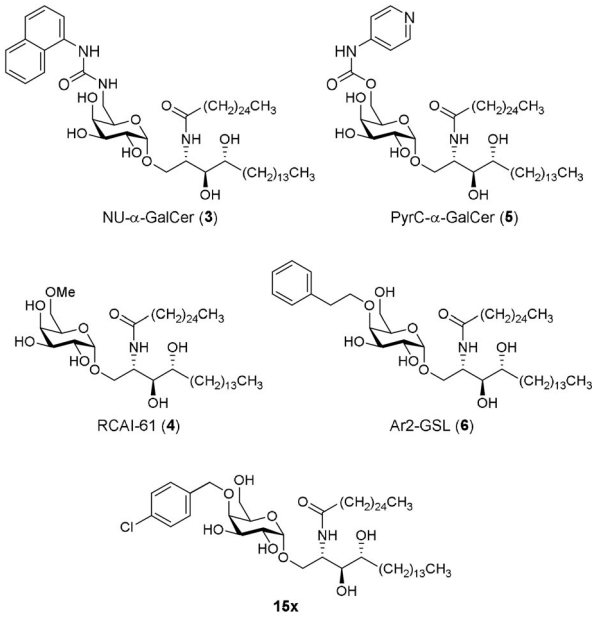


Figure 2. Previously reported sugar-modified α-GalCer analogues with an improved antigenic profile.

The 4"-OH is a H-bond donor to the carboxamide side chain of Asn30α (mTCR-CDR1α-loop) and the backbone carbonyl group of Phe29α (hTCR-CDR1α-loop). Its importance for *i*NKT-cell activation has been less profoundly studied, but severe disturbance of the hydrogen bond through either its removal (4"-deoxy-α-GalCer)[31] or inversion of its configuration (α-glucosylceramide or α-GlcCer),[4] results in poorly immunostimulating compounds. However, Wu et al. have found that certain α-GluCer analogues with a terminal aromatic ring in the acyl chain are more potent NKT-stimulators in humans and act as an effective adjuvant for a carbohydrate vaccine in mice.[32] Zhang and co-workers have reported a small set of phenyl-containing 4"-analogues that are able to stimulate murine NKT-hybridomas and cytokine release by mouse splenocytes.[33] Particularly, the phenylethyl ether derivative (Ar2-GSL, **6**) excites the murine immune system in a Th1-polarizing manner. However, to explain the observed polarization, the researchers used an in silico model with a human instead of a mouse TCR. Given the relative homology between the structure of the mTCR and the hTCR,[34] this is a legitimate action. Yet, in this particular case, the correlation between this model and the observed cytokine profiles is doubtful because of a crucial differ-

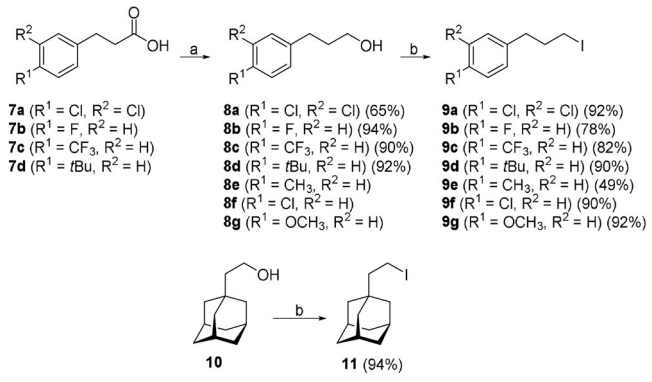
ence in amino acid composition of the TCR's α-chain. The Vα24Vβ11 hTCR contains an aromatic residue, Phe51α, which is predicted to undergo a π–π stacking interaction with Ar2-GSL, consequently stabilizing the trimolecular complex. In the Vα14Vβ8.2 mTCR, the residue at this position is a non-aromatic aspartic acid (Asp51α), which is not able to establish such an interaction. Hence, more in-depth molecular biology research is required.

Through the synthesis of a structurally diverse set of 4"-modified α-GalCer analogues, we have recently demonstrated that incorporation of a *p*-chlorobenzyl group yields a promising Th1-biasing lead structure in mice.[35] To more thoroughly investigate the potential of 4"-O-alkylated α-GalCer analogues to stimulate *i*NKT-cells in a Th1-dependent manner, we synthesized an extensive panel of α-GalCer analogues mainly containing aromatic modifications with various substituents and varying linker lengths, along with a smaller set of aliphatic and cycloaliphatic derivatives. These compounds were tested for their ability to stimulate cytokine release in mice. Using surface plasmon resonance (SPR), we also determined the real-time binding kinetics of the Vα14Vβ8.2 mTCR toward the different mCD1d–glycolipid complexes. A selected set of eight analogues was co-crystallized with mCD1d and the Vα14Vβ8.2 mTCR to elucidate the crystal structures of the ternary complexes, thereby shedding more light on the structural basis of murine *i*NKT-cell activation.

Results and Discussion

Chemistry

In our previous report,[35] we disclosed a useful precursor (**12**) for the efficient synthesis of 4"-O-modified α-GalCer analogues, which constituted an ideal starting point for the synthesis of the 4"-ether derivatives. A Williamson ether synthesis between **12** and the appropriate alkyl halides (bromide or iodide) delivered compounds **13a**–**w** (Table 1). The non-commercially available iodides (phenylpropyl derivatives **9a**-**g** and adamantane derivative **11**) were synthesized from the corresponding alcohols **8a**–**g** by an Appel reaction with I_2 (Scheme 1). Some of the alcohols were accessed from the corresponding carboxylic acids (**7a**–**d**) through a BH_3-mediated reduction.



Scheme 1. Synthesis of the alkyl halides: a) BH_3·THF, THF, 0 °C; b) I_2, PPh_3, imidazole, CH_2Cl_2, 0 °C.

The azides were reduced using hydrogen sulfide in a 1:1 pyridine/water mixture, as Staudinger conditions with trimethylphosphine in THF did not yield satisfactory results. The resulting amines were coupled with *N*-succinimidyl hexacosanoate (NSHC) under basic conditions to deliver the corresponding amides **14a**–**w**. Overall deprotection was achieved by HCl-mediated cleavage of the *p*-methoxybenzyl (PMB) ethers, furnishing the 4"-alkylated analogues **15a**–**w**. The low yields for the deprotection may be attributed to the low solubility of the deprotected compounds in 1,4-dioxane and related solvents. Attempts to deprotect the phenylethyl ether failed due to concomitant cleavage of this ether under the acidic conditions, and this analogue was eventually left out of the series since it had been previously reported.

In vivo studies

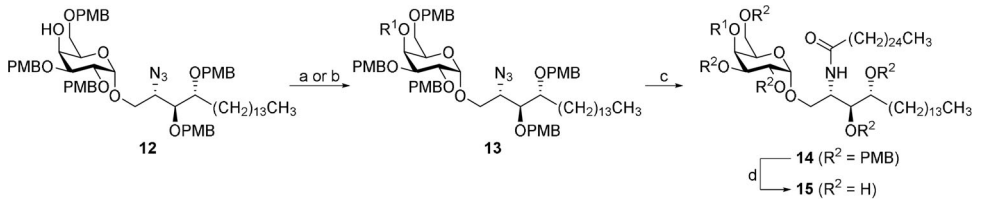
To assess the activity of the 4"-alkylated α-GalCer analogues in vivo, we intraperitoneally injected male C57BL/6 mice with 5 μg of each glycolipid ($\pm 2.0\times10^{-4}$ g kg^{-1}). The blood serum levels of IFN-γ and IL-4 were quantified by ELISA, 16 h and 4 h after injection, respectively, and compared with those elicited by α-GalCer (Figure 3). In general, none of the analogues is able to produce the same cytokine levels as α-GalCer. Increasing the linker length between 4"-O and the phenyl group (**15a**–**e**) significantly decreases the antigenicity, with the phenyl-*n*-hexyl analogue (**15e**) being only marginally active. Probably, docking of the TCR onto the CD1d–glycolipid complex is hampered by the longer chain derivatives, which are solvent exposed, consequently jeopardizing formation of a stable ternary complex. An alternative explanation could be the low solubility of the glycolipids, resulting in lower CD1d-loading and less TCR activation.

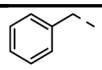
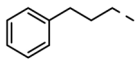
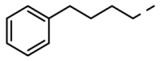
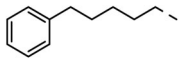
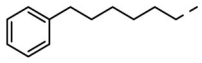
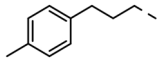
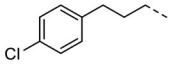
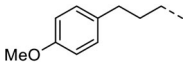
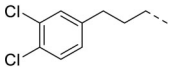
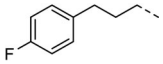
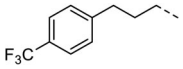
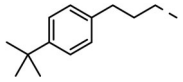
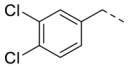
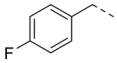
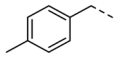
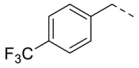
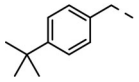
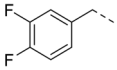
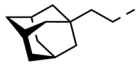
The benzyl series (**15m**–**r**) is able to skew the Th-bias toward a pro-inflammatory Th1 profile. This tendency is still present, albeit much less pronounced, in the phenylpropyl series (**15f**–**l**). This is also apparent from Figure 4, showing a plot of the IFN-γ/IL-4-ratios for each glycolipid; the higher the ratio, the stronger the Th1-polarizing behavior. The influence of the substituents on the aromatic core seems to be negligible, giving only slight differences in cytokine release.

Among the cycloaliphatic ethers, the cyclopropyl methyl (**15s**) and cyclobutyl methyl (**15t**) analogues are strongly Th1-polarizing, whereas the adamantyl derivative (**15u**) has a limited immunogenic potency. In accordance with the known 4"-*O*-methylether analogue, the 4"-*O*-*n*-propyl (**15v**) and 4"-*O*-allyl (**15w**) derivatives are weakly Th1-polarizing.

Additionally, we performed an in vivo kinetic experiment in which the cytokine release at different points in time (2, 4, 8, 16, 20 and 24 h after intraperitoneal injection) was assessed (Figure 5). With regard to IL-4 secretion, a peak is reached at 4 h after injection, whereas the IFN-γ secretion shows a gradual increases in concentration toward the 16 h or the 24 h checkpoint. The data clearly show a Th1-dependent immune

Table 1. Synthesis of 4″-alkylated α-GalCer analogues.[a]



Compound suffix	R^1	Yield [%] 12→13	13→14	14→15
a		95	72	24
b		75	81	28
c		84	80	25
d		89	74	34
e		94	71	29
f		93	72	33
g		86	78	34
h		94	81	21
i		57	55	28
j		68	59	7
k		84	68	28
l		91	63	22
m		93	68	29
n		94	78	23
o		92	63	18
p		94	88	21
q		98	74	20
r		92	60	34
s		91	84	15
t		62	81	23
u		68	65	31
v		76	91	13
w		91	75	22

[a] Reagents and conditions: a) R^1-Br, NaH, TBAI, DMF, RT; b) R^1-I, NaH, DMF, RT; c) 1. H_2S, pyridine, H_2O, RT, 2. NSHC, Et_3N, THF, 70 °C; d) HCl (4 M in 1,4-dioxane), 1,4-dioxane, anisole, RT.

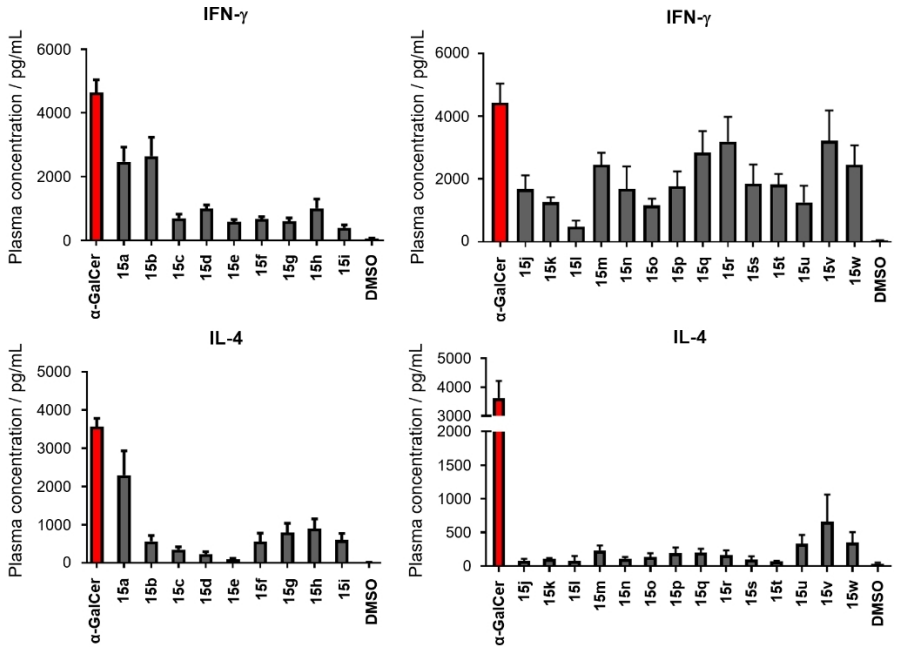


Figure 3. In vivo stimulation of IFN-γ and IL-4 secretion in male C57BL/6 mice after intraperitoneal injection with 5 μg of each glycolipid. Results are means ± SEM ($n = 8$).

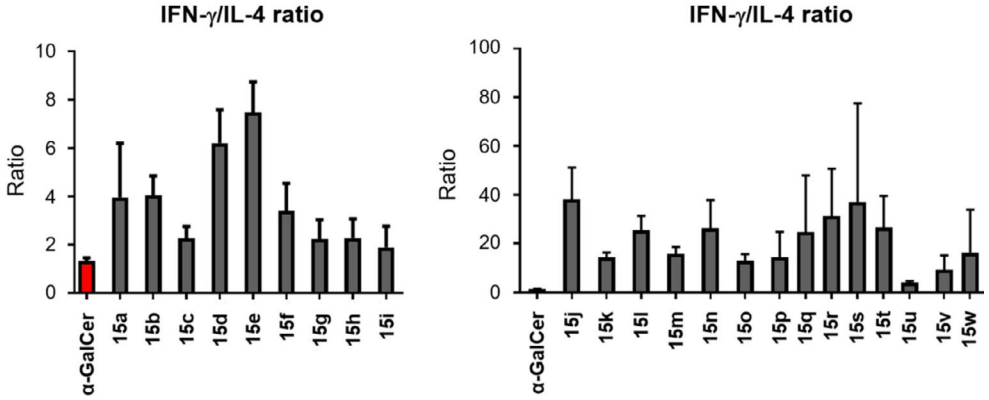


Figure 4. Plotted IFN-γ/IL-4-ratios for each glycolipid. Results are means ± SEM ($n = 8$).

response upon stimulation with the benzyl-modified analogues (**15a**–**q**) and the cyclopropyl methyl derivative (**15s**).

Kinetic data

We determined the real-time binding characteristics of the refolded Vα14Vβ8.2 mTCR toward the different glycolipids bound to mCD1d using surface plasmon resonance (SPR). To this end, TCR with increasing concentrations (ranging from 25 to 400 nM) was sequentially passed over the immobilized mCD1d–glycolipid complex, with a 3 min association and a final 10 min dissociation, using the single-cycle function of the Biacore T200. The calculated equilibrium binding constant (K_D) of α-GalCer, 13.6 nM, is in agreement with data previously reported in literature.[36] Generally, the glycolipids lead to a TCR-binding affinity that is similar to or lower than that of α-GalCer (Table 2). In particular, a decreased association rate (k_a) can be noticed. However, some of the analogues, such as *p*-methylbenzyl derivative **15o** ($K_D = 14.1$ nM; $k_d = 2.94 \times 10^{-3}$ s^{-1}), *p*-(trifluoromethyl)benzyl derivative **15p** ($K_D = 13.3$ nM; $k_d = 3.06 \times 10^{-3}$ s^{-1}) and *p*-(*tert*-butyl)benzyl derivative **15q** ($K_D = 7.1$ nM; $k_d = 1.94 \times 10^{-3}$ s^{-1}), can compensate for this by a much slower dissociation rate (k_d), suggesting that these modifications assist in binding the TCR. This is also evident from the corresponding sensorgrams (Figure 6).

Although no clear trend is discernable by increasing the linker length, there is a noticeable discrepancy between the benzyl analogue (**15a**) and those with a longer linker (**15b**–**e**), especially with respect to the dissociation rate. This indicates that binding of the TCR toward the mCD1d–**15a** complex is more efficient, likely owing to the lower steric hindrance exerted by the benzyl substituent. The discrepancy is also clear in

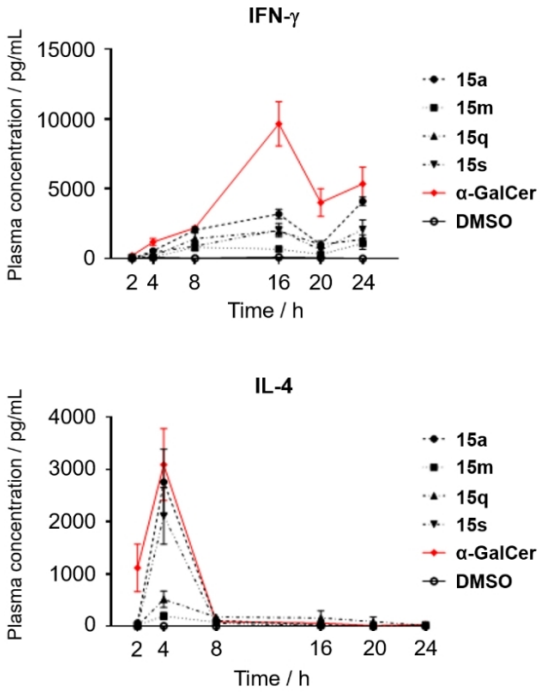


Figure 5. Time-dependent pattern of cytokine release (IFN-γ and IL-4) in mouse serum after intraperitoneal injection of glycolipids. Results are means ± SEM ($n = 8$).

the substituted phenylpropyl (**15f–l**) versus benzyl (**15m–r** and the previously reported *p*-chlorobenzyl analogue **15x**, shown in Figure 2) series, the latter members having an equilibrium binding constant similar to α-GalCer, while the former prove to be weaker binding ligands.

Among the aliphatic modifications, only the cyclobutyl methyl derivative (**15t**) shows a relatively low TCR affinity (K_D = 137.8 nM). This behavior is evident from the corresponding sensorgram (Figure 6), showing a very fast ($k_d = 3.62 \times 10^{-2}$ s^{-1}) and complete dissociation in between the individual association steps.

Protein crystallography

We were able to determine the crystal structures of the ternary complexes of six benzyl ether modified glycolipids, **15a**, **15m**, **15o**, **15p**, **15q** and **15x** (Figure 7), with mCD1d and the refolded Vα14Vβ8.2 mTCR. Furthermore, the cyclopropyl methyl (**15s**) and allyl (**15w**) derivatives were also successfully co-crystallized. The structures of **15a** and **15p** each contain two ternary complexes in the asymmetric unit, crystallizing in the monoclinic crystal system (space group C121), while the other structures each contained one ternary complex, crystallizing in the higher symmetrical orthorhombic crystal system (space group $C222_1$). All of the structures displayed well-defined electron density for the glycolipids, which allowed unambiguous fitting of the ligands within mCD1d (Figure 8).

Unfortunately, attempts to obtain crystals from complexes with the phenylpropyl glycolipids failed, presumably because of insufficient loading of the glycolipids onto mCD1d.

Each of the ternary complexes adopts a similar structural assembly, with the TCR docking onto the mCD1d–glycolipid complex in a parallel manner, directly above the F′-pocket of mCD1d (Figure 7). As observed for α-GalCer, the acyl chain of the 4″-modified analogues is bound in the A′-pocket through a distinct anti-clockwise orientation, and the phytosphingosine chain is imbedded in the F′-pocket. The similar binding affini-

Table 2. Kinetic data of TCR binding to mCD1d–glycolipid complexes, as measured by SPR.

Glycolipid	K_D (k_d/k_a) [nM]	k_a [M^{-1}s^{-1}]	k_d [s^{-1}]	R_{max} (RU)	Chi^2 (RU^2)
α-GalCer	13.6	1.00×10^6	1.36×10^{-2}	12.0	9.5
15a	18.5	2.31×10^5	4.28×10^{-3}	100.4	1.37
15b	107.1	2.93×10^5	3.13×10^{-2}	30.1	65.8
15c	80.4	1.23×10^5	9.89×10^{-3}	42.1	11.7
15d	138.3	1.19×10^5	1.64×10^{-2}	31.5	23.4
15e	65.7	2.91×10^5	1.91×10^{-2}	31.2	39.0
15f	39.2	3.18×10^5	1.25×10^{-2}	54.2	26.6
15g	45.9	3.04×10^5	1.39×10^{-2}	50.7	28.5
15h	93.9	1.12×10^5	1.05×10^{-2}	97.2	20.5
15i	109.2	9.53×10^4	1.04×10^{-2}	63.3	17.5
15j	36.9	2.14×10^5	7.88×10^{-3}	149.1	5.9
15k	47.9	2.56×10^5	1.22×10^{-2}	70.3	23.4
15l	60.6	2.86×10^5	1.73×10^{-2}	37.2	25.8
15m	14.3	2.26×10^5	3.22×10^{-3}	50.3	0.39
15n	22.0	2.24×10^5	4.94×10^{-3}	98.7	1.7
15o	14.1	2.08×10^5	2.94×10^{-3}	101.7	0.71
15p	13.3	2.30×10^5	3.06×10^{-3}	140.8	1.39
15q	7.1	2.71×10^5	1.94×10^{-3}	58.3	0.22
15r	22.0	2.20×10^5	4.85×10^{-3}	122.3	2.13
15s	51.5	2.53×10^5	1.31×10^{-2}	203.2	27.7
15t	137.8	2.63×10^5	3.62×10^{-2}	152.5	50.8
15u	38.5	2.40×10^5	9.23×10^{-3}	71.9	8.5
15v	45.2	3.23×10^5	1.46×10^{-2}	163.9	33.4
15w	19.1	2.24×10^5	4.30×10^{-3}	178.5	2.5
15x	16.0	2.31×10^5	3.68×10^{-3}	62.7	0.63

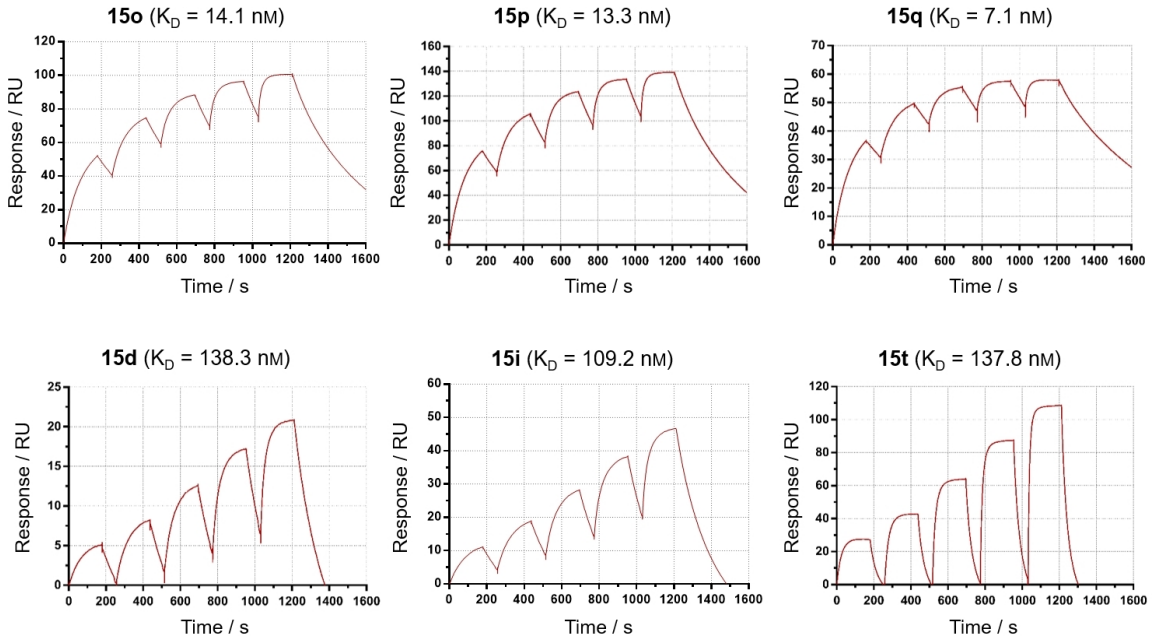


Figure 6. SPR sensorgrams, measured from single-cycle TCR kinetics by kinetic titration with five increasing concentrations of Vα14Vβ8.2 mTCR (25, 50, 100, 200 and 400 nM). Top row: glycolipids inducing highest TCR affinity. Bottom row: glycolipids showing lowest TCR affinity.

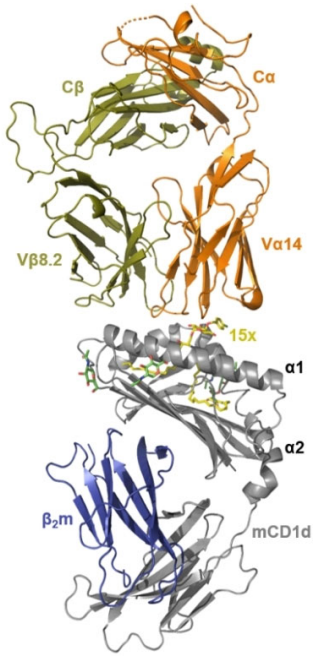


Figure 7. Overview of the ternary complex with **15x**, with indication of the constituent chains.

ties of α-GalCer and the benzyl-modified analogues (K_D = 7–22 nM) are consistent with the closely correlating superposition of the galactose unit and other components of the TCR docking site in the crystal structures (Figure 9). These aspects highlight the vastly conservative interaction pattern exhibited by TCR-mediated recognition of the binary mCD1d–glycolipid complex.[37]

The hydrogen bond interactions observed between α-GalCer and mCD1d and the TCR are all conserved for the 4″-O-alkylated analogues (Figures 10A, C). Due to conversion of the alcohol to an ether, the hydrogen bond with Asn31 (CDR1α) is disrupted, which is evident from the larger intermolecular distance between the 4″-O and the amino acid residue: 3.2 Å for α-GalCer versus 4.0 Å for **15a**, which is too far to form a hydrogen bond.

Interestingly, the phenyl ring of all benzyl-modified analogues adopts a similar orientation (Figure 11), in parallel with the α2-helix of mCD1d, suggesting an additional van der Waals interaction between the phenyl ring and Gly155 (Figures 10B, D). We assume that the disappearance of the hydrogen bond with 4″-O is partly compensated by this hydrophobic interaction, as the TCR binding affinity is only slightly lower than that of α-GalCer, whereas 4″-deoxy-α-GalCer was shown to have a 10-fold decreased binding affinity.[38] This destabilization event is however not evident from the TCR dissociation rate, which, for all benzyl-type modifications, is lower than α-GalCer. For comparison, in hCD1d the 4″-OH contributes less to hTCR binding, as lack of the interaction decreases the hTCR binding affinity by only twofold.[39]

As for the crystal structures of the cyclopropyl methyl (**15s**) and allyl (**15w**) analogues, no extra hydrophobic interactions are observed with the ether modifications (Figure 12). Both the cyclopropyl and allyl groups are more solvent-exposed than their phenyl counterparts, but do not seem to hamper TCR recruitment, due to their relatively small size.

Conclusions

In conclusion, based on a late-stage diversification strategy we synthesized an extensive panel of 4″-O-alkylated α-GalCer ana-

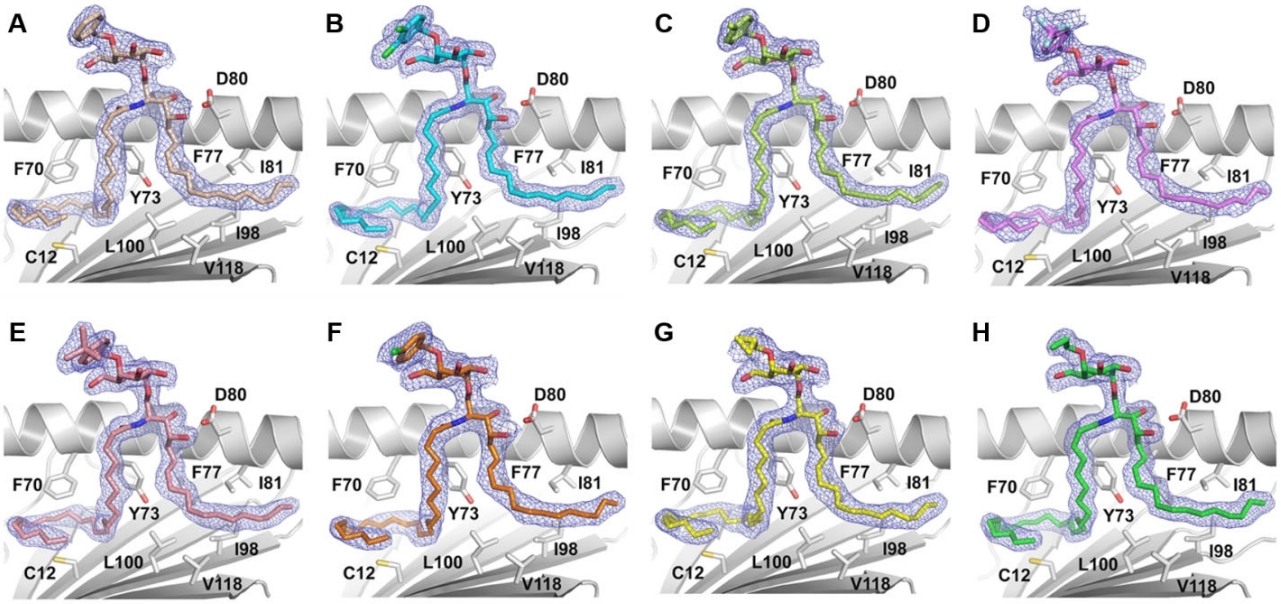


Figure 8. Stereo view of electron density for the different mCD1d-bound glycolipids. The $2F_o-F_c$ electron density map is contoured at 1σ and shown in a blue mesh around the glycolipids: A) **15a**, B) **15m**, C) **15o**, D) **15p**, E) **15q**, F) **15x**, G) **15s**, H) **15w**. The relevant amino acid residues of CD1d are indicated as a reference.

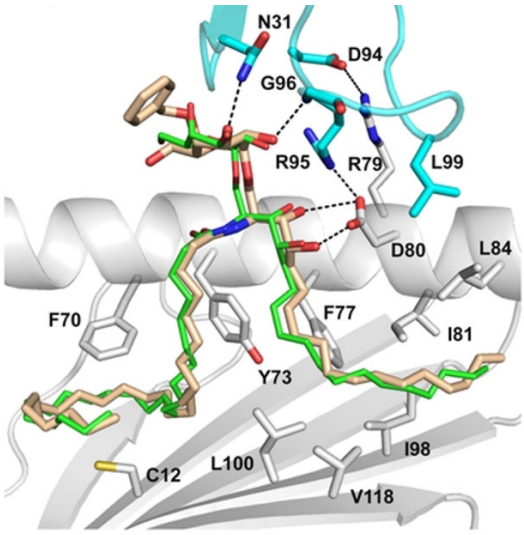


Figure 9. Superposition of mCD1d–TCR-bound glycolipid **15a** with mCD1d–TCR-bound α-GalCer (PDB ID: 3HE6), highlighting the conserved binding mode. The carbon atoms of glycolipid **15a** are shown in brick red, and α-GalCer in green. The hydrogen bond contacts are indicated as dashed lines.

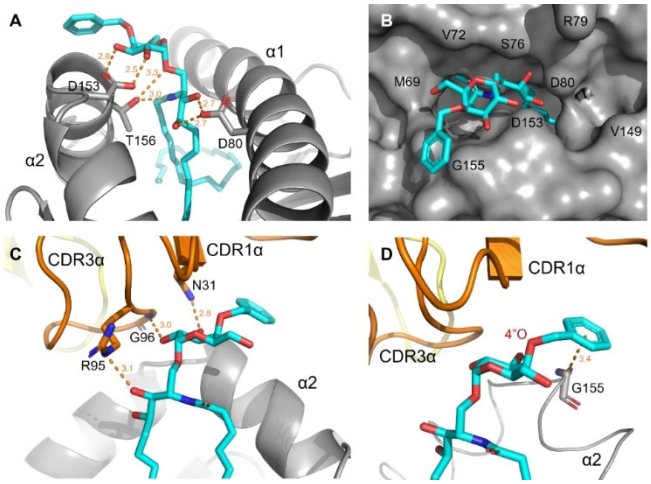


Figure 10. A) Main hydrogen bond contacts between **15a** (blue) and mCD1d (grey). B) Glycolipid ligand presentation shown from top view with the molecular surface of mCD1d in grey and ligand as blue sticks. C) Main hydrogen bond contacts between **15a** (blue) and the Vα14-chain of the mTCR (orange). D) van der Waals interaction between the phenyl ring and G155 of the α2-helix of mCD1d.

logues bearing several aromatic and (cyclo)aliphatic moieties. The in vivo stimulation of murine *i*NKT-cells by the benzyl-type modifications as well as the small cycloaliphatic derivatives showed a clear pro-inflammatory response, despite the fact that their overall antigenicity was lower relative to α-GalCer.

To gain insight into the molecular recognition, the crystal structures of selected complexes with mCD1d and the mTCR was elucidated. Whilst having a similar binding conformation as that of α-GalCer, the benzyl-type modifications showed an additional weak van der Waals interaction between the phenyl ring and Gly155 of mCD1d, thereby slightly compensating the weakening of the hydrogen bond to the 4"-O atom. Nonetheless, the Th1-polarizing ability of these modifications may be valuable for potential applications in immuno-oncology and vaccinations, and should inspire further research on promising galactose-modified analogues of α-GalCer.

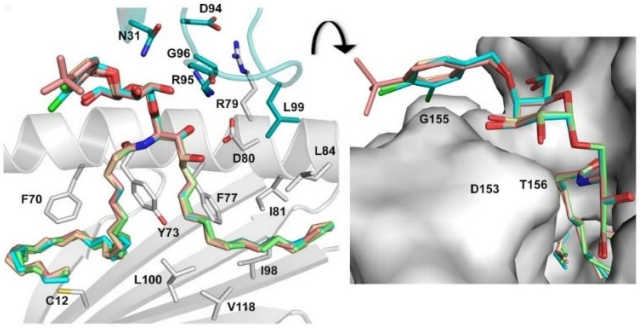


Figure 11. Superposition of mCD1d–TCR-bound glycolipids **15a** (pale brown), **15m** (cyan), **15o** (lemon green), and **15q** (brick red), representing a similar mode of binding for all four benzyl-type glycolipids. The relevant amino acid residues from mCD1d and the TCR α-chain that shape the glycolipid binding pocket are represented as grey and cyan sticks, respectively.

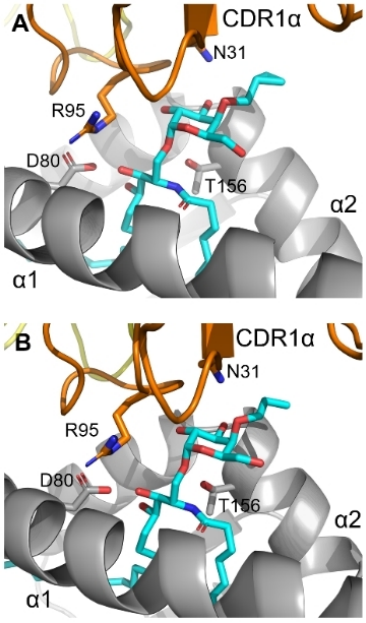


Figure 12. A) Binding conformation of **15s** (blue) at the mCD1d–TCR interface. B) Binding conformation of **15w** (blue) at the mCD1d–TCR interface.

Experimental Section

Chemistry

General experimental information. All reactions were performed in flame-dried round-bottomed flasks sealed with rubber septa. Reactions were magnetically stirred using Teflon-coated stir bars. Where appropriate, reactions were carried out in dry solvents and under an inert atmosphere of argon. Anhydrous solvents were purchased from commercial sources in septum-sealed bottles and kept under an argon atmosphere. Dropwise addition of reagents or solutions was carried out using a syringe pump. Yields refer to chromatographically and spectroscopically (^{1}H NMR) pure homogeneous materials. Reagents were purchased at the highest commercial quality and used without additional purification. Hydrogen sulfide was purchased from Alpha Gaz in a gas cylinder (14 bar), that was fitted with a slow-release valve to safely fill balloons. *CAUTION: hydrogen sulfide is an extremely flammable, corrosive, toxic and malodorous gas, which should only be handled by experienced chemists in a well-ventilated area!* Petroleum ether for flash column chromatography was distilled prior to use. α-GalCer (**2**) was synthesized according to a literature procedure.[40] Reactions were monitored by thin layer chromatography (TLC), carried out on precoated Macherey–Nagel® SIL G/UV$_{254}$ plates using ultraviolet light (254 nm wavelength) as visualizing agent and either *p*-anisaldehyde, potassium permanganate or ceric ammonium molybdate (CAM) as staining agents. Flash column chromatography was performed manually using Grace Davisil® silica gel (40–60 μm particle size) or automatically using a Grace Reveleris X2 purification system with disposable silica gel flash cartridges. NMR spectra were recorded on a Varian Mercury-300 spectrometer or a Bruker Avance II 500 spectrometer and were calibrated using residual undeuterated solvent as an internal reference ($CDCl_3$: ^{1}H NMR: $\delta = 7.26$ ppm, ^{13}C NMR: $\delta = 77.16$ ppm; [D_5]pyridine: ^{1}H NMR: $\delta = 8.74$ ppm, ^{13}C NMR: $\delta = 150.35$ ppm; CD_3OD: ^{1}H NMR: $\delta = 3.31$ ppm, ^{13}C NMR: $\delta = 49.86$ ppm). Chemical shifts are expressed in parts per million (ppm) and coupling constants are given in Hertz (Hz). The following abbreviations or combinations thereof were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintuplet, m = multiplet, b = broad signal or band. High-resolution mass spectra (HRMS) were recorded on a Waters LCT Premier XE TOF equipped with an electrospray ionization (ESI-MS) interface and a modular Lockspray TM interface. Samples were infused in a MeCN/water (1:1) + 0.1% *v/v* formic acid mixture at a rate of 100 μL min^{-1}. Purity of the final compounds was ascertained by quantitative NMR or LC–MS analysis; all glycolipids were found to be ≥95% pure. LC–MS analyses were carried out on a Waters Alliance 2695 XE separation module by using a Phenomenex Kinetex 5 μm EVO C18 column and a triple gradient system (0.1% *v/v* TFA in water, 0.05% *v/v* TFA in methanol and 0.1% *v/v* formic acid in 2-propanol), coupled to a Waters 2996 Photodiode Array Detector. Optical rotations of the final compounds were recorded on a PerkinElmer 241 polarimeter, using a sodium-vapor lamp (D-line; λ = 589.3 nm). Samples were either dissolved in pyridine (Sigma–Aldrich, reagent grade) or methanol (Sigma–Aldrich, HPLC grade).

General procedure A: carboxylic acid reduction. To a cooled (0 °C) solution of the carboxylic acid (1 mmol) in dry THF (2.5 mL mmol^{-1}) was added BH_3·THF (3 mL, 1 M in THF, 3 equiv) in a dropwise fashion. The reaction mixture was allowed to warm to RT and stirred for 1 h. The mixture was quenched with water (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over anhydrous magnesium sulfate and concentrated in vacuo. The crude residue was purified by flash chromatography (petroleum ether → petroleum ether/EtOAc 70:30).

General procedure B: iodination. To a cooled (0 °C) solution of the alcohol (1 mmol) in CH_2Cl_2 (2 mL mmol^{-1}) were added imidazole (1.3 mmol, 1.3 equiv), triphenylphosphine (1.3 mmol, 1.3 equiv) and iodine crystals (1.3 mmol, 1.3 equiv). The resulting yellow suspension was allowed to warm to RT and stirred for 1 h. The mixture was quenched with 2 M aqueous sodium thiosulfate (3 mL), diluted with water (15 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated in vacuo. The crude residue was purified by flash chromatography (petroleum ether).

General procedure C1: alkylation of precursor 12 with alkyl iodides. To a cooled (0 °C) solution of **12** (1 mmol) in DMF (10 mL mmol^{-1}) were added the alkyl iodide (5 mmol, 5 equiv) and sodium hydride (6 mmol, 60 w% dispersion in mineral oil, 6 equiv). The reaction mixture was allowed to warm to RT and stirred for 17 h. The mixture was quenched with MeOH (3 mL), diluted with saturated aqueous sodium bicarbonate (15 mL) and extracted with

CH_2Cl_2 (3×10 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated in vacuo. The crude residue was purified by flash chromatography (petroleum ether → petroleum ether/EtOAc 70:30).

General procedure C2: alkylation of precursor 12 with alkyl bromides. To a cooled (0 °C) solution of **12** (1 mmol) in DMF (10 mL mmol^{-1}) were added the alkyl bromide (5 mmol, 5 equiv), TBAI (0.1 mmol, 0.1 equiv) and sodium hydride (6 mmol, 60 w% dispersion in mineral oil, 6 equiv). The reaction mixture was allowed to warm to RT and stirred for 17 h. The mixture was quenched with MeOH (3 mL), diluted with saturated aqueous sodium bicarbonate (15 mL) and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated in vacuo. The crude residue was purified by flash chromatography (petroleum ether→petroleum ether/EtOAc 70:30).

General procedure D: azide reduction and amide formation. The azide (1 mmol) was dissolved in pyridine (15 mL) and water (15 mL). Hydrogen sulfide was bubbled through the mixture for 2 h, using a balloon. The flask was then carefully sealed and the resulting yellow emulsion was stirred for 2 days, during which a color change to (dark) orange can be observed. The volatiles were evaporated and the crude product was co-evaporated with toluene (5×20 mL) to remove traces of water. The crude amine from the previous step was taken up in THF (25 mL) and Et_3N (2.5 mL), and NSHC (3 mmol, 3 equiv) was added. The mixture was heated at 70 °C for 24 h. Removal of the volatiles yielded a crude product that was purified by flash chromatography (petroleum ether→petroleum ether/EtOAc 70:30).

General procedure E: overall deprotection. To a solution of the *per*-PMB-protected analogue (0.1 mmol) in 1,4-dioxane (1.75 mL) were added sequentially anisole (1 mmol, 10 equiv) and HCl (1.75 mL, 4 M in 1,4-dioxane) at RT. The progress of the reaction was followed through HRMS measurements; the reaction typically finished after stirring at RT for about 6–8 h. The volatiles were carefully removed in vacuo and the crude product was purified by flash chromatography (CH_2Cl_2→CH_2Cl_2/MeOH 90:10).

3-(3,4-Dichlorophenyl)propan-1-ol (8a): Following general procedure A, 3-(3,4-dichlorophenyl)propanoic acid **7a** (2.312 g, 10.55 mmol) afforded **8a** (1.401 g, 65%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33 (d, J = 8.0 Hz, 1H), 7.28 (d, J = 2.1 Hz, 1H), 7.03 (dd, J = 8.0, 2.1 Hz, 1H), 3.66 (t, J = 6.3 Hz, 2H), 2.67 (t, J = 7.8 Hz, 2H), 1.91–1.80 (m, 2H), 1.45 ppm (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.2, 132.3, 130.5, 130.4, 129.9, 128.1, 61.9, 33.9, 31.3 ppm; HRMS (ESI-MS) m/z: calcd for $C_9H_{11}Cl_2O$ $[M+H]^+$ 205.0181, found 205.0185; R_f (petroleum ether/EtOAc 50:50): 0.31.

3-(4-Fluorophenyl)propan-1-ol (8b): Following general procedure A, 3-(4-fluorophenyl)propanoic acid **7b** (0.500 g, 2.973 mmol) afforded **8b** (0.431 g, 94%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.18–7.10 (m, 2H), 7.00–6.91 (m, 2H), 3.64 (t, J = 6.4 Hz, 2H), 2.67 (t, J = 7.7 Hz, 2H), 2.18 (bs, 1H), 1.91–1.80 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.1 (d, J = 243.8 Hz), 137.5 (d, J = 3.5 Hz), 129.8 (d, J = 8.0 Hz), 115.1 (d, J = 20.7 Hz), 62.0, 34.3, 31.3 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ = −117.76 ppm (tt, J = 14.1, 5.1 Hz, 1F); HRMS (ESI-MS) m/z: calcd for $C_9H_{12}FO$ $[M+H]^+$ 155.0867, found 155.0871; R_f (petroleum ether/EtOAc 50:50): 0.32.

3-[4-(Trifluoromethyl)phenyl]propan-1-ol (8c): Following general procedure A, 3-[4-(trifluoromethyl)phenyl]propanoic acid **7c** (0.500 g, 2.290 mmol) afforded **8c** (0.422 g, 90%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.2 Hz, 2H), 3.66 (t, J = 6.4 Hz, 2H), 2.76 (t, J = 7.7 Hz, 2H), 2.11 (bs, 1H), 1.95–1.84 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.1, 128.8, 126.3, 125.4 (q, J = 3.7 Hz), 122.7, 61.9, 33.9, 32.0 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ = −62.35 ppm (s, 3F); HRMS (ESI-MS) m/z: calcd for $C_{10}H_{12}F_3O$ $[M+H]^+$ 205.0835, found 205.0833; R_f (petroleum ether/EtOAc 50:50): 0.30.

3-[4-(*tert*-Butyl)phenyl]propan-1-ol (8d): Following general procedure A, 3-[4-(*tert*-butyl)phenyl]propanoic acid **7d** (0.500 g, 2.424 mmol) afforded **8d** (0.428 g, 92%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.32 (m, 2H), 7.20–7.15 (m, 2H), 3.70 (t, J = 6.5 Hz, 2H), 2.71 (t, J = 7.8 Hz, 2H), 1.98–1.89 (m, 2H), 1.87 (bs, 1H), 1.35 ppm (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.7, 138.8, 128.2, 125.4, 62.4, 34.3, 31.6, 31.5 ppm; HRMS (ESI-MS) m/z: calcd for $C_{13}H_{21}O$ $[M+H]^+$ 193.1587, found 193.1591; R_f (petroleum ether/EtOAc 50:50): 0.36.

1,2-Dichloro-4-(3-iodopropyl)benzene (9a): Following general procedure B, **8a** (1.401 g, 6.83 mmol) afforded **9a** (1.982 g, 92%) as an orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35 (d, J = 8.1 Hz, 1H), 7.29 (d, J = 2.2 Hz, 1H), 7.03 (dd, J = 8.1, 2.2 Hz, 1H), 3.15 (t, J = 6.6 Hz, 2H), 2.69 (t, J = 7.4 Hz, 2H), 2.15–2.04 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.7, 132.5, 130.6, 130.5, 130.3, 128.1, 35.4, 34.4, 5.7 ppm; HRMS (ESI-MS) m/z: calcd for $C_9H_{10}Cl_2I$ $[M+H]^+$ 314.9199, found 314.9195; R_f (petroleum ether/EtOAc 90:10): 0.56.

1-Fluoro-4-(3-iodopropyl)benzene (9b): Following general procedure B, **8b** (0.431 g, 2.795 mmol) afforded **9b** (0.574 g, 78%) as an orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.20–7.13 (m, 2H), 7.03–6.94 (m, 2H), 3.16 (t, J = 7.1 Hz, 2H), 2.72 (t, J = 7.3 Hz, 2H), 2.11 ppm (quint, J = 7.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.5 (d, J = 244.6 Hz), 136.1 (d, J = 3.5 Hz), 130.0 (d, J = 7.1 Hz), 115.4 (d, J = 21.9 Hz), 35.4, 35.0, 6.2 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ = −117.02 ppm (tt, J = 13.9, 4.9 Hz, 1F); HRMS (ESI-MS) m/z: calcd for $C_9H_{11}FI$ $[M+H]^+$ 264.9884, found 264.9886; R_f (petroleum ether/EtOAc 90:10): 0.62.

1-(3-Iodopropyl)-4-(trifluoromethyl)benzene (9c): Following general procedure B, **8c** (0.422 g, 2.070 mmol) afforded **9c** (0.532 g, 82%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.56 (d, J = 8.1 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 3.17 (t, J = 6.8 Hz, 2H), 2.80 (t, J = 7.4 Hz, 2H), 2.14 ppm (quint, J = 7.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.7, 129.0, 128.5, 125.6 (q, J = 3.5 Hz), 122.6, 36.1, 34.6, 5.8 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ = −62.38 ppm (s, 3F); HRMS (ESI-MS) m/z: calcd for $C_{10}H_{11}F_3I$ $[M+H]^+$ 314.9852, found 314.9854; R_f (petroleum ether/EtOAc 90:10): 0.57

1-(*tert*-Butyl)-4-(3-iodopropyl)benzene (9d): Following general procedure B, **8d** (0.428 g, 2.230 mmol) afforded **9d** (0.609 g, 90%) as an orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.36 (m, 2H), 7.23–7.17 (m, 2H), 3.23 (t, J = 6.8 Hz, 2H), 2.76 (t, J = 7.2 Hz, 2H), 2.19 (quint, J = 7.1 Hz, 2H), 1.38 ppm (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.0, 137.4, 128.3, 125.5, 35.8, 35.0, 34.5, 31.5, 6.7 ppm; HRMS (ESI-MS) m/z: calcd for $C_{13}H_{20}I$ $[M+H]^+$ 303.0604, found 303.0601; R_f (petroleum ether/EtOAc 90:10): 0.64.

1-(3-Iodopropyl)-4-methylbenzene (9e): Following general procedure B, 3-(4-methylphenyl)-propan-1-ol **8e** (2.271 g, 15.12 mmol) afforded **9e** (1.932 g, 49%) as an orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.10 (s, 4H), 3.17 (t, J = 6.8 Hz, 2H), 2.70 (t, J = 7.3 Hz, 2H), 2.33 (s, 3H), 2.12 ppm (quint, J = 7.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.4, 135.8, 129.3, 128.6, 35.9, 35.2, 21.2, 6.6 ppm; HRMS (ESI-MS) m/z: calcd for $C_{10}H_{14}I$ $[M+H]^+$ 261.0135, found 261.0136; R_f (petroleum ether/EtOAc 90:10): 0.67.

1-Chloro-4-(3-iodopropyl)benzene (9 f): Following general procedure B, 3-(4-chlorophenyl)-propan-1-ol **8 f** (2.288 g, 13.41 mmol) afforded **9 f** (3.379 g, 90%) as an orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, J = 7.8 Hz, 2H), 7.11 (d, J = 7.8 Hz, 2H), 3.13 (t, J = 6.8 Hz, 2H), 2.69 (t, J = 7.4 Hz, 2H), 2.08 ppm (quint, J = 7.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.9, 132.0, 130.0, 128.7, 35.6, 34.7, 6.1 ppm; HRMS (ESI-MS) m/z: calcd for $C_9H_{11}ClI$ $[M+H]^+$ 280.9588, found 280.9590; R_f (petroleum ether/EtOAc 90:10): 0.61.

1-(3-Iodopropyl)-4-methoxybenzene (9 g): Following general procedure B, 3-(4-methoxyphenyl)-propan-1-ol **9 g** (2.284 g, 13.74 mmol) afforded **9 g** (3.457 g, 92%) as an orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.15–7.09 (m, 2H), 6.87–6.81 (m, 2H), 3.79 (s, 3H), 3.16 (t, J = 6.8 Hz, 2H), 2.68 (t, J = 7.3 Hz, 2H), 2.10 ppm (quint, J = 7.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.2, 132.5, 129.6, 114.0, 55.4, 35.4, 35.2, 6.6 ppm; HRMS (ESI-MS) m/z: calcd for $C_{10}H_{14}IO$ $[M+H]^+$ 277.0084, found 277.0083; R_f (petroleum ether/EtOAc 90:10): 0.51.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-benzyl-α-D-galactopyranosyloxy]-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13 a): Following general procedure C2, intermediate **12** (0.200 g, 0.181 mmol) afforded **13 a** (0.207 g, 95%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.17 (m, 15H), 6.97–6.77 (m, 10H), 4.97 (d, J = 11.4 Hz, 1H), 4.91 (d, J = 3.4 Hz, 1H), 4.79 (d, J = 11.2 Hz, 2H), 4.70 (d, J = 11.2 Hz, 1H), 4.66 (d, J = 11.6 Hz, 1H), 4.63–4.57 (m, 3H), 4.53 (d, J = 11.1 Hz, 1H), 4.43 (d, J = 11.6 Hz, 2H), 4.32 (d, J = 11.2 Hz, 1H), 4.07 (dd, J = 9.8, 3.4 Hz, 1H), 4.04–3.94 (m, 4H), 3.82 (s, 3H), 3.81 (s, 3H), 3.80 (s, 6H), 3.78 (s, 3H), 3.77–3.72 (m, 3H), 3.61 (m, 1H), 3.56–3.43 (m, 2H), 1.79–1.48 (m, 4H), 1.37–1.19 (m, 22H), 0.93 ppm (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3, 159.2, 159.1, 138.9, 131.1, 131.0, 130.6, 130.4, 130.2, 129.7, 129.6, 129.5, 129.4, 129.2, 128.3, 128.3, 127.6, 113.8, 113.7, 98.9, 78.9, 78.7, 78.6, 76.1, 75.3, 74.8, 73.4, 73.2, 73.0, 72.8, 71.7, 69.8, 68.7, 68.6, 62.1, 55.3, 55.2, 32.0, 30.1, 29.9, 29.8, 29.8, 29.5, 25.4, 22.8, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{71}H_{94}NO_{13}$ $[M-N_2+H]^+$ 1168.6720, found 1168.6726; R_f (petroleum ether/EtOAc 70:30): 0.43.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(3-phenylpropyl)-α-D-galactopyranosyloxy]-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)-octadecane (13 b): Following general procedure C1, intermediate **12** (0.200 g, 0.181 mmol) afforded **13 b** (0.166 g, 75%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.13 (m, 15H), 6.93–6.74 (m, 10H), 4.90 (d, J = 3.3 Hz, 1H), 4.77 (d, J = 11.5 Hz, 1H), 4.71 (d, J = 11.3 Hz, 1H), 4.64 (d, J = 11.5 Hz, 1H), 4.63 (d, J = 11.4 Hz, 1H), 4.59 (dd, J = 13.7, 11.2 Hz, 2H), 4.53 (d, J = 11.0 Hz, 1H), 4.46 (d, J = 11.7 Hz, 1H), 4.42 (d, J = 11.5 Hz, 1H), 4.36 (d, J = 11.3 Hz, 1H), 4.06–3.87 (m, 5H), 3.80 (s, 6H), 3.80 (s, 3H), 3.79–3.71 (m, 4H), 3.78 (s, 3H), 3.74 (s, 3H), 3.69–3.57 (m, 2H), 3.55–3.45 (m, 2H), 2.66 (t, J = 7.5 Hz, 2H), 1.55–1.81 (m, 2H), 1.75–1.41 (m, 4H), 1.37–1.21 (m, 22H), 0.91 ppm (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.4, 159.3, 159.1, 142.4, 131.1, 131.0, 130.6, 130.4, 130.2, 129.7, 129.6, 129.5, 129.4, 129.2, 128.6, 128.3, 125.8, 113.9, 113.8, 113.7, 99.0, 79.0, 78.7, 78.5, 75.9, 73.5, 73.3, 73.0, 72.8, 72.6, 71.7, 69.7, 68.6, 68.5, 62.1, 55.3, 55.2, 32.5, 32.0, 31.9, 30.1, 29.9, 29.8, 29.7, 29.5, 25.5, 22.8, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{73}H_{98}NO_{13}$ $[M-N_2+H]^+$ 1196.7033, found 1196.7038; R_f (petroleum ether/EtOAc 70:30): 0.53.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(4-phenylbutyl)-α-D-galactopyranosyloxy]-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13 c): Following general procedure C1, intermediate **12** (0.200 g, 0.181 mmol) afforded **13 c** (0.189 g, 84%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37–7.12 (m, 15H), 6.94–6.74 (m, 10H), 4.88 (d, J = 2.9 Hz, 1H), 4.77 (d, J = 11.5 Hz, 1H), 4.70 (dd, J = 21.1, 11.1 Hz, 2H), 4.62 (d, J = 11.5 Hz, 1H), 4.60 (s, 2H), 4.53 (d, J = 11.0 Hz, 1H), 4.47 (d, J = 11.5 Hz, 1H), 4.43 (d, J = 11.0 Hz, 1H), 4.38 (d, J = 11.5 Hz, 1H), 4.06–3.89 (m, 5H), 3.81 (2 × s, 2×3H), 3.80 (2 × s, 2×3H), 3.79 (m, 1H), 3.76 (s, 3H), 3.75–3.69 (m, 3H), 3.68–3.57 (m, 2H), 3.54–3.44 (m, 2H), 2.62 (t, J = 7.5 Hz, 2H), 1.75–1.48 (m, 8H), 1.37–1.22 (m, 22H), 0.93 ppm (t, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3, 159.2, 159.1, 142.7, 131.1, 131.0, 130.6, 130.4, 130.2, 129.7, 129.6, 129.5, 129.4, 129.2, 128.5, 128.3, 125.7, 113.9, 113.8, 113.7, 99.0, 79.0, 78.7, 78.6, 76.0, 75.8, 73.4, 73.3, 73.2, 73.0, 72.6, 71.7, 69.7, 68.5, 62.1, 55.3, 55.2, 35.7, 32.0, 30.0, 30.0, 29.9, 29.8, 29.5, 28.1, 22.8, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{74}H_{100}NO_{13}$ $[M-N_2+H]^+$ 1210.7189, found 1210.7189; R_f (petroleum ether/EtOAc 70:30): 0.59.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(5-phenylpentyl)-α-D-galactopyranosyloxy]-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13 d): Following general procedure C1, intermediate **12** (0.200 g, 0.181 mmol) afforded **13 d** (0.201 g, 89%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.14 (m, 15H), 6.95–6.76 (m, 10H), 4.91 (d, J = 3.2 Hz, 1H), 4.78 (d, J = 11.6 Hz, 1H), 4.71 (dd, J = 19.6, 11.6 Hz, 2H), 4.64 (d, J = 11.6 Hz, 1H), 4.62 (s, 2H), 4.54 (d, J = 11.1 Hz, 1H), 4.49 (d, J = 11.5 Hz, 1H), 4.44 (d, J = 11.0 Hz, 1H), 4.40 (d, J = 11.3 Hz, 1H), 4.08–3.87 (m, 5H), 3.82 (s, 3H), 3.81 (s, 3H), 3.80 (s, 6H), 3.79 (m, 1H), 3.77 (s, 3H), 3.76–3.73 (m, 3H), 3.70–3.58 (m, 3H), 3.55–3.43 (m, 2H), 2.63 (t, J = 7.8 Hz, 2H), 1.73–1.53 (m, 6H), 1.48–1.20 (m, 26H), 0.94 ppm (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.2, 159.1, 158.9, 142.6, 130.9, 130.4, 130.2, 130.0, 129.5, 129.5, 129.3, 129.2, 129.0, 128.3, 128.1, 125.5, 113.7, 113.6, 113.5, 113.4, 98.8, 78.8, 78.5, 78.4, 76.1, 75.7, 73.3, 73.2, 73.1, 72.9, 72.4, 71.5, 69.6, 68.4, 61.9, 55.1, 55.1, 35.9, 31.9, 31.3, 30.1, 29.9, 29.7, 29.6, 29.6, 29.3, 25.8, 25.3, 22.6, 14.1 ppm; HRMS (ESI-MS) m/z: calcd for $C_{75}H_{102}NO_{13}$ $[M-N_2+H]^+$ 1224.7346, found 1224.7345; R_f (petroleum ether/EtOAc 70:30): 0.41.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(6-phenylhexyl)-α-D-galactopyranosyloxy]-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13 e): Following general procedure C1, intermediate **12** (0.200 g, 0.181 mmol) afforded **13 e** (0.216 g, 94%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.16 (m, 15H), 6.93–6.78 (m, 10H), 4.91 (d, J = 3.2 Hz, 1H), 4.79 (d, J = 11.5 Hz, 1H), 4.71 (dd, J = 18.7, 11.5 Hz, 2H), 4.64 (d, J = 11.5 Hz, 1H), 4.61 (dd, J = 13.7, 11.3 Hz, 2H), 4.54 (d, J = 11.3 Hz, 1H), 4.50 (d, J = 11.6 Hz, 1H), 4.44 (d, J = 11.1 Hz, 1H), 4.41 (d, J = 11.5 Hz, 1H), 4.07–3.87 (m, 5H), 3.82 (s, 3H), 3.81 (s, 3H), 3.80 (2×s, 2×3H), 3.79 (m, 1H), 3.77–3.72 (m, 3H), 3.76 (s, 3H), 3.70–3.59 (m, 2H), 3.55–3.42 (m, 2H), 2.63 (t, J = 7.7 Hz, 2H), 1.73–1.50 (m, 6H), 1.47–1.23 (m, 28H), 0.93 ppm (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3, 159.2, 159.1, 131.1, 130.6, 130.3, 130.2, 129.7, 129.6, 129.5, 129.3, 129.1, 128.4, 128.3, 125.6, 113.8, 113.7, 113.6, 98.7, 78.9, 78.6, 78.5, 76.0, 75.7, 73.5, 73.4, 73.2, 73.0, 72.5, 71.7, 69.7, 68.5, 62.1, 55.2, 55.2, 36.0, 32.0, 31.6, 30.3, 29.9, 29.8, 29.7, 29.4, 29.2, 26.1, 25.4, 22.8, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{76}H_{104}NO_{13}$ $[M-N_2+H]^+$ 1238.7502, found 1238.7493; R_f (petroleum ether/EtOAc 70:30): 0.52.

(2*S*,3*S*,4*R*)-1-{2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-[3-(4-methylphenyl)propyl)-α-D-galactopyranosyloxy}-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13 f): Following general procedure C1, intermediate **12** (0.200 g, 0.181 mmol) afforded **13 f** (0.209 g, 93%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.18 (m, 10H), 7.13–7.05 (m, 4H), 6.92–6.76 (m, 10H), 4.90 (d, J = 3.4 Hz, 1H), 4.77 (d, J = 11.5 Hz, 1H), 4.71 (d, J = 11.4 Hz, 1H), 4.65 (d, J = 11.5 Hz, 1H), 4.64 (d, J = 11.5 Hz, 1H), 4.60 (dd, J = 13.6, 11.0 Hz, 2H), 4.53 (d, J = 11.1 Hz, 1H), 4.46 (d, J = 11.6 Hz, 1H), 4.42 (d, J = 11.1 Hz, 1H), 4.37 (d, J = 11.5 Hz, 1H), 4.07–3.88 (m, 5H), 3.81 (s,

6H), 3.80 (s, 3H), 3.79 (s, 3H), 3.78–3.71 (m, 4H), 3.75 (s, 3H), 3.69–3.57 (m, 2H), 3.55–3.45 (m, 2H), 2.63 (t, J=7.7 Hz, 2H), 2.34 (s, 3H), 1.95–1.81 (m, 2H), 1.71–1.40 (m, 4H), 1.37–1.22 (m, 22H), 0.92 ppm (t, J=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.3, 159.2, 159.1, 142.7, 131.1, 131.0, 130.6, 130.4, 130.2, 129.7, 129.6, 129.5, 129.4, 129.2, 128.5, 128.3, 125.7, 113.9, 113.8, 113.7, 99.0, 79.0, 78.7, 78.6, 75.9, 75.8, 73.4, 73.3, 73.2, 73.0, 72.6, 71.7, 69.7, 68.5, 62.1, 55.3, 55.2, 35.7, 32.0, 30.0, 29.9, 29.8, 29.5, 28.1, 22.8, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{74}H_{100}NO_{13}$ $[M-N_2+H]^+$ 1210.7189, found 1210.7192; R_f (petroleum ether/EtOAc 70:30): 0.57.

(2*S*,3*S*,4*R*)-1-{2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-[3-(4-chlorophenyl)propyl]-α-D-galactopyranosyloxy}-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13g): Following general procedure C1, intermediate **12** (0.200 g, 0.181 mmol) afforded **13g** (0.196 g, 86%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.31–7.16 (m, 12H), 7.11–7.05 (m, 2H), 6.92–6.76 (m, 10H), 4.90 (d, J=3.3 Hz, 1H), 4.76 (d, J=11.7 Hz, 1H), 4.72 (d, J=11.4 Hz, 1H), 4.65 (d, J=11.5 Hz, 1H), 4.63 (d, J=11.5 Hz, 1H), 4.60 (dd, J=13.8, 11.0 Hz, 2H), 4.53 (d, J=11.0 Hz, 1H), 4.47 (d, J=11.5 Hz, 1H), 4.43 (d, J=11.2 Hz, 1H), 4.36 (d, J=11.4 Hz, 1H), 4.06–3.84 (m, 5H), 3.82 (s, 3H), 3.81 (s, 3H), 3.80 (s, 3H), 3.79 (s, 3H), 3.78–3.71 (m, 4H), 3.74 (s, 3H), 3.68–3.57 (m, 2H), 3.53–3.42 (m, 2H), 2.61 (t, J=7.6 Hz, 2H), 1.91–1.46 (m, 4H), 1.42–1.20 (m, 24H), 0.92 ppm (t, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.3, 159.2, 159.1, 142.7, 131.1, 131.0, 130.6, 130.4, 130.2, 129.7, 129.6, 129.5, 129.4, 129.2, 128.5, 128.3, 125.7, 113.9, 113.8, 113.7, 99.0, 79.0, 78.7, 78.6, 75.9, 75.8, 73.4, 73.3, 73.2, 73.0, 72.6, 71.7, 69.7, 68.5, 62.1, 55.3, 55.2, 35.7, 32.0, 30.0, 29.9, 29.8, 29.5, 28.1, 22.8, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{73}H_{97}ClNO_{13}$ $[M-N_2+H]^+$ 1230.6643, found 1230.6650; R_f (petroleum ether/EtOAc 70:30): 0.48.

(2*S*,3*S*,4*R*)-1-{2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-[3-(4-methoxyphenyl)propyl]-α-D-galactopyranosyloxy}-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13h): Following general procedure C1, intermediate **12** (0.200 g, 0.181 mmol) afforded **13h** (0.229 g, 94%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.32–7.18 (m, 10H), 7.13–7.06 (m, 2H), 6.92–6.76 (m, 12H), 4.90 (d, J=3.4 Hz, 1H), 4.77 (d, J=11.6 Hz, 1H), 4.72 (d, J=11.4 Hz, 1H), 4.65 (d, J=11.5 Hz, 1H), 4.64 (d, J=11.3 Hz, 1H), 4.60 (dd, J=13.5, 11.0 Hz, 2H), 4.53 (d, J=11.1 Hz, 1H), 4.47 (d, J=11.5 Hz, 1H), 4.42 (d, J=11.4 Hz, 1H), 4.36 (d, J=11.3 Hz, 1H), 4.06–3.87 (m, 5H), 3.81 (2×s, 2×3H), 3.80 (s, 3H), 3.80–3.71 (m, 4H), 3.79 (s, 6H), 3.74 (s, 3H), 3.69–3.57 (m, 2H), 3.56–3.44 (m, 2H), 2.61 (t, J=7.6 Hz, 2H), 1.95–1.79 (m, 2H), 1.71–1.21 (m, 26H), 0.92 ppm (t, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.3, 159.2, 159.1, 142.7, 131.1, 131.0, 130.6, 130.4, 130.2, 129.7, 129.6, 129.5, 129.4, 129.2, 128.5, 128.3, 125.7, 113.9, 113.8, 113.7, 99.0, 79.0, 78.7, 78.5, 75.8, 75.7, 73.4, 73.3, 73.2, 73.0, 72.6, 71.7, 69.7, 68.5, 62.1, 55.3, 55.2, 35.7, 32.0, 30.0, 29.9, 29.8, 29.5, 28.1, 22.8, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{74}H_{100}NO_{14}$ $[M-N_2+H]^+$ 1226.7138, found 1226.7146; R_f (petroleum ether/EtOAc 70:30): 0.46.

(2*S*,3*S*,4*R*)-1-{2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-[3-(3,4-dichlorophenyl)propyl]-α-D-galactopyranosyloxy}-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13i): Following general procedure C1, intermediate **12** (0.200 g, 0.181 mmol) afforded **13i** (0.134 g, 57%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.33–7.15 (m, 12H), 7.00–6.73 (m, 11H), 4.88 (d, J=3.1 Hz, 1H), 4.75 (d, J=11.4 Hz, 1H), 4.71 (d, J=11.1 Hz, 1H), 4.64 (d, J=11.6 Hz, 1H), 4.61 (d, J=11.6 Hz, 1H), 4.59 (dd, J=14.2, 11.1 Hz, 2H), 4.52 (d, J=11.1 Hz, 1H), 4.46 (d, J=11.3 Hz, 1H), 4.41 (d, J=11.1 Hz, 1H), 4.35 (d, J=11.5 Hz, 1H), 4.06–3.82 (m, 5H), 3.80 (s, 6H), 3.79 (s, 3H), 3.78 (s, 3H), 3.77–3.69 (m, 4H), 3.72 (s, 3H), 3.65–3.53 (m, 2H), 3.50–3.40 (m, 2H), 2.57 (t, J=7.6 Hz, 2H), 1.87–1.46 (m, 4H), 1.40–1.18 (m, 24H), 0.90 ppm (t, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.3, 159.2, 159.1, 142.7, 132.1, 130.9, 130.8, 130.6, 130.5, 130.3, 130.2, 130.1, 129.7, 129.6, 129.5, 129.4, 129.2, 128.1, 113.9, 113.8, 113.7, 113.7, 98.9, 78.9, 78.7, 78.4, 75.9, 75.8, 73.4, 73.2, 72.9, 72.7, 72.1, 71.7, 69.6, 68.6, 68.3, 62.1, 55.3, 55.2, 32.0, 31.6, 30.1, 29.9, 29.8, 29.7, 29.4, 25.4, 22.8, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{73}H_{96}Cl_2NO_{13}$ $[M-N_2+H]^+$ 1264.6253, found 1264.6249; R_f (petroleum ether/EtOAc 70:30): 0.42.

(2*S*,3*S*,4*R*)-1-{2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-[3-(4-fluorophenyl)propyl]-α-D-galactopyranosyloxy}-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13j): Following general procedure C1, intermediate **12** (0.200 g, 0.181 mmol) afforded **13j** (0.154 g, 68%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.32–7.19 (m, 10H), 7.14–7.07 (m, 2H), 6.97–6.76 (m, 12H), 4.91 (d, J=3.3 Hz, 1H), 4.77 (d, J=11.5 Hz, 1H), 4.73 (d, J=11.4 Hz, 1H), 4.65 (d, J=11.7 Hz, 1H), 4.64 (d, J=11.4 Hz, 1H), 4.61 (dd, J=13.5, 11.0 Hz, 2H), 4.54 (d, J=11.2 Hz, 1H), 4.48 (d, J=11.4 Hz, 1H), 4.43 (d, J=11.2 Hz, 1H), 4.37 (d, J=11.4 Hz, 1H), 4.07–3.85 (m, 5H), 3.81 (s, 6H), 3.80 (s, 3H), 3.80–3.70 (m, 4H), 3.79 (s, 3H), 3.74 (s, 3H), 3.69–3.57 (m, 2H), 3.54–3.44 (m, 2H), 2.62 (t, J=7.6 Hz, 2H), 1.92–1.77 (m, 2H), 1.74–1.48 (m, 2H), 1.42–1.21 (m, 24H), 0.92 ppm (t, J=6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=161.1 (d, J=243.0 Hz), 159.4, 159.3, 159.1, 137.9 (d, J=3.4 Hz), 131.0 (d, J=4.5 Hz), 130.6, 130.4, 130.1, 129.9, 129.8, 129.7, 129.6, 129.5, 129.4, 129.2, 115.0 (d, J=21.8 Hz), 113.9, 113.8, 113.7, 99.0, 79.0, 78.7, 78.5, 75.8, 73.4, 73.2, 72.9, 72.7, 72.4, 71.7, 69.7, 68.6, 68.4, 62.1, 55.3, 55.2, 32.1, 32.0, 31.6, 30.1, 29.9, 29.8, 29.7, 29.5, 25.5, 22.8, 14.2 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ=−117.97 ppm (tt, J=9.2, 4.8 Hz, 1F); HRMS (ESI-MS) m/z: calcd for $C_{73}H_{97}FNO_{13}$ $[M-N_2+H]^+$ 1214.6938, found 1214.6936; R_f (petroleum ether/EtOAc 70:30): 0.54.

(2*S*,3*S*,4*R*)-1-{2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-[3-(4-trifluoromethylphenyl)propyl]-α-D-galactopyranosyloxy}-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13k): Following general procedure C1, intermediate **12** (0.200 g, 0.181 mmol) afforded **13k** (0.196 g, 84%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.48 (d, J=8.1 Hz, 2H), 7.34–7.20 (m, 12H), 6.94–6.77 (m, 10H), 4.93 (d, J=3.1 Hz, 1H), 4.78 (d, J=11.6 Hz, 1H), 4.75 (d, J=11.0 Hz, 1H), 4.68 (d, J=11.2 Hz, 1H), 4.65 (d, J=11.6 Hz, 1H), 4.62 (dd, J=13.7, 11.3 Hz, 2H), 4.56 (d, J=11.3 Hz, 1H), 4.50 (d, J=11.7 Hz, 1H), 4.45 (d, J=11.3 Hz, 1H), 4.38 (d, J=11.3 Hz, 1H), 4.09–3.86 (m, 5H), 3.82–3.73 (m, 4H), 3.81 (s, 9H), 3.79 (s, 3H), 3.73 (s, 3H), 3.69–3.59 (m, 2H), 3.56–3.46 (m, 2H), 2.71 (t, J=7.6 Hz, 2H), 1.95–1.77 (m, 2H), 1.74–1.23 (m, 26H), 0.93 ppm (t, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.4, 159.3, 159.2, 159.1, 146.5, 131.0, 130.9, 130.6, 130.3, 130.1, 129.7, 129.6, 129.5, 129.4, 129.2, 128.9, 125.2 (q, J=3.5 Hz), 113.8, 113.7, 98.9, 78.9, 78.7, 78.5, 75.9, 75.8, 73.4, 73.2, 72.9, 72.8, 72.2, 71.7, 69.6, 68.6, 68.3, 62.1, 55.3, 55.2, 55.1, 32.3, 32.0, 31.7, 30.1, 29.9, 29.8, 29.7, 29.5, 25.4, 22.8, 14.2 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ=−62.16 ppm (s, 3F); HRMS (ESI-MS) m/z: calcd for $C_{74}H_{97}F_3NO_{13}$ $[M-N_2+H]^+$ 1264.6907, found 1264.6910; R_f (petroleum ether/EtOAc 70:30): 0.47.

(2*S*,3*S*,4*R*)-1-{2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-[3-(4-*tert*-butylphenyl)propyl]-α-D-galactopyranosyloxy}-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13l): Following general procedure C1, intermediate **12** (0.200 g, 0.181 mmol) afforded **13l** (0.211 g, 91%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.36–7.11 (m, 14H), 6.97–6.77 (m, 10H), 4.93 (d, J=3.3 Hz, 1H), 4.81 (d, J=11.6 Hz, 1H), 4.75 (d, J=11.3 Hz, 1H), 4.68 (d, J=11.3 Hz, 2H), 4.63 (dd, J=13.0, 11.5 Hz, 2H), 4.56 (d, J=11.2 Hz, 1H), 4.49 (d, J=11.0 Hz, 1H), 4.45 (d, J=10.9 Hz, 1H), 4.40 (d, J=11.3 Hz, 1H), 4.09–3.91 (m, 5H), 3.83–3.74 (m, 4H), 3.82 (s, 9H), 3.80 (s, 3H), 3.76 (s, 3H), 3.73–3.61 (m, 2H), 3.59–3.50 (m, 2H), 2.67 (t, J=7.6 Hz,

2H), 1.99–1.85 (m, 2H), 1.77–1.50 (m, 2H), 1.38–1.26 (m, 24H), 1.36 (s, 9H), 0.95 ppm (t, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 159.3, 159.2, 159.1, 148.4, 139.2, 131.1, 131.0, 130.6, 130.4, 130.1, 129.7, 129.6, 129.5, 129.4, 129.2, 128.2, 125.2, 113.8, 113.7, 113.6, 99.0, 78.9, 78.6, 78.5, 75.8, 75.7, 73.4, 73.2, 73.0, 72.8, 72.6, 71.7, 69.7, 68.5, 62.1, 55.3, 55.2, 55.1, 34.4, 32.0, 31.9, 31.5, 30.0, 29.9, 29.8, 29.7, 29.5, 29.4, 25.4, 22.8, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{77}H_{106}NO_{13}$ $[M-N_2+H]^+$ 1252.7659, found 1252.7661; R_f (petroleum ether/EtOAc 70:30): 0.71.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(3,4-dichlorobenzyl)-α-D-galactopyranosyloxy]-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13 m): Following general procedure C2, intermediate **12** (0.200 g, 0.181 mmol) afforded **13 m** (0.212 g, 93%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.46–7.04 (m, 13H), 6.92–6.78 (m, 10H), 4.88 (d, J=2.4 Hz, 1H), 4.82 (d, J=11.5 Hz, 1H), 4.78 (d, J=10.9 Hz, 1H), 4.75 (d, J=11.6 Hz, 1H), 4.65 (d, J=11.5 Hz, 1H), 4.64 (d, J=11.5 Hz, 1H), 4.62 (d, J=11.1 Hz, 1H), 4.60 (s, 2H), 4.53 (d, J=11.2 Hz, 1H), 4.47 (d, J=10.9 Hz, 1H), 4.46 (d, J=11.7 Hz, 1H), 4.32 (d, J=11.6 Hz, 1H), 4.05–3.93 (m, 4H), 3.90 (bs, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.79 (s, 6H), 3.77 (s, 3H), 3.76–3.70 (m, 3H), 3.64–3.51 (m, 2H), 3.45 (dd, J=9.0, 5.7 Hz, 1H), 1.79–1.47 (m, 2H), 1.43–1.20 (m, 24H), 0.91 ppm (t, J=6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.4, 159.3, 159.2, 159.1, 139.3, 132.2, 131.3, 130.9, 130.8, 130.6, 130.5, 130.3, 130.2, 129.9, 129.8, 129.7, 129.6, 129.5, 129.2, 128.7, 127.2, 126.0, 113.8, 113.7, 98.9, 78.9, 78.7, 78.4, 75.9, 73.4, 73.2, 73.0, 72.9, 71.7, 69.4, 68.7, 68.1, 63.7, 62.1, 55.3, 55.2, 32.0, 30.1, 29.9, 29.8, 29.7, 29.5, 29.4, 25.4, 22.8, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{71}H_{92}Cl_2NO_{13}$ $[M-N_2+H]^+$ 1236.5940, found 1236.5941; R_f (petroleum ether/EtOAc 70:30): 0.57.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(4-fluorobenzyl)-α-D-galactopyranosyloxy]-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13 n): Following general procedure C2, intermediate **12** (0.200 g, 0.181 mmol) afforded **13 n** (0.207 g, 94%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.35–7.18 (m, 12H), 6.98 (d, J=8.7 Hz, 2H), 6.92–6.78 (m, 10H), 4.91 (d, J=2.5 Hz, 1H), 4.89 (d, J=10.6 Hz, 1H), 4.79 (d, J=11.2 Hz, 1H), 4.77 (d, J=11.4 Hz, 1H), 4.67 (d, J=11.4 Hz, 1H), 4.66 (d, J=11.6 Hz, 1H), 4.61 (dd, J=13.5, 11.2 Hz, 2H), 4.53 (d, J=11.2 Hz, 1H), 4.51 (d, J=11.2 Hz, 1H), 4.46 (d, J=11.6 Hz, 1H), 4.43 (d, J=11.2 Hz, 1H), 4.33 (d, J=11.6 Hz, 1H), 4.08–3.95 (m, 4H), 3.93 (bs, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.80 (s, 6H), 3.78–3.72 (m, 3H), 3.77 (s, 3H), 3.65–3.58 (m, 1H), 3.57–3.42 (m, 2H), 1.73–1.48 (m, 2H), 1.45–1.18 (m, 24H), 0.92 ppm (t, J=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=162.2 (d, J=246.0 Hz), 159.3, 159.2, 159.1, 134.6 (d, J=3.4 Hz), 131.0, 130.9, 130.6, 130.3, 130.1, 130.0 (d, J=8.1 Hz), 129.7, 129.6, 129.5, 129.4, 129.2, 115.0 (d, J=22.0 Hz), 113.8, 113.7, 98.8, 78.9, 78.7, 78.6, 76.0, 75.3, 74.1, 73.4, 73.2, 72.9, 71.7, 69.6, 68.6, 68.5, 62.1, 55.3, 55.2, 55.1, 32.0, 30.0, 29.9, 29.8, 29.7, 29.4, 25.4, 22.8, 14.2 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ=−115.00 ppm (tt, J=9.6, 4.9 Hz, 1F); HRMS (ESI-MS) m/z: calcd for $C_{71}H_{93}FNO_{13}$ $[M-N_2+H]^+$ 1186.6625, found 1186.6622; R_f (petroleum ether/EtOAc 70:30): 0.43.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(4-methylbenzyl)-α-D-galactopyranosyloxy]-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13 o): Following general procedure C2, intermediate **12** (0.200 g, 0.181 mmol) afforded **13 o** (0.201 g, 92%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.38–7.08 (m, 14H), 6.95–6.77 (m, 10H), 4.92 (d, J=11.5 Hz, 1H), 4.91 (d, J=3.0 Hz, 1H), 4.78 (d, J=11.5 Hz, 2H), 4.69 (d, J=11.2 Hz, 1H), 4.66 (d, J=11.5 Hz, 1H), 4.60 (dd, J=13.0, 11.4 Hz, 2H), 4.56 (d, J=11.0 Hz, 1H), 4.53 (d, J=10.7 Hz, 1H), 4.42 (d, J=11.7 Hz, 2H), 4.32 (d, J=11.4 Hz, 1H), 4.11–3.91 (m, 5H), 3.82 (s, 3H), 3.81 (s, 3H), 3.80 (s, 6H), 3.77 (s, 3H), 3.76–3.71 (m, 3H), 3.64–3.56 (m, 1H), 3.54–3.43 (m, 2H), 2.36 (s, 3H), 1.73–1.44 (m, 2H), 1.44–1.18 (m, 24H), 0.93 ppm (t, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.3, 159.2, 159.1, 137.2, 135.8, 131.1, 131.0, 130.6, 130.4, 130.2, 129.7, 129.6, 129.5, 129.4, 129.2, 128.9, 128.5, 113.8, 113.7, 98.9, 78.9, 78.8, 78.6, 76.1, 74.8, 74.6, 73.4, 73.1, 73.0, 72.8, 71.7, 69.8, 68.8, 68.5, 62.1, 55.3, 55.2, 32.0, 30.0, 29.9, 29.8, 29.7, 29.6, 29.5, 25.4, 22.8, 21.3, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{72}H_{96}NO_{13}$ $[M-N_2+H]^+$ 1182.6876, found 1182.6877; R_f (petroleum ether/EtOAc 70:30): 0.45.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(4-trifluoromethylbenzyl)-α-D-galactopyranosyloxy]-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13 p): Following general procedure C2, intermediate **12** (0.200 g, 0.181 mmol) afforded **13 p** (0.216 g, 94%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.54 (d, J=8.4 Hz, 2H), 7.37 (d, J=8.4 Hz, 2H), 7.32–7.17 (m, 10H), 6.93–6.77 (m, 10H), 4.96 (d, J=12.1 Hz, 1H), 4.91 (d, J=2.8 Hz, 1H), 4.79 (d, J=11.1 Hz, 1H), 4.75 (d, J=11.3 Hz, 1H), 4.66 (d, J=11.5 Hz, 2H), 4.61 (dd, J=13.9, 11.1 Hz, 2H), 4.57 (d, J=12.1 Hz, 1H), 4.53 (d, J=11.0 Hz, 1H), 4.47 (d, J=11.3 Hz, 1H), 4.44 (d, J=11.0 Hz, 1H), 4.32 (d, J=11.5 Hz, 1H), 4.07–3.96 (m, 4H), 3.94 (bs, 1H), 3.80 (s, 6H), 3.79 (s, 3H), 3.78 (s, 3H), 3.77 (s, 3H), 3.76–3.71 (m, 3H), 3.65–3.54 (m, 2H), 3.47 (dd, J=8.9, 5.6 Hz, 1H), 1.75–1.47 (m, 2H), 1.42–1.18 (m, 24H), 0.92 ppm (t, J=6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 159.4, 159.3, 159.2, 159.1, 143.0, 131.0, 130.8, 130.6, 130.3, 130.0, 129.7, 129.6, 129.5, 129.4, 129.2, 128.0, 125.1 (q, J=3.8 Hz), 113.8, 113.7, 98.9, 78.9, 78.8, 78.5, 76.0, 75.9, 74.0, 73.5, 73.2, 73.0, 72.8, 71.7, 69.5, 68.7, 68.2, 62.1, 55.3, 55.2, 32.0, 30.1, 29.9, 29.8, 29.7, 29.5, 25.4, 22.8, 14.2 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ= −62.35 ppm (s, 3F); HRMS (ESI-MS) m/z: calcd for $C_{72}H_{93}F_3NO_{13}$ $[M-N_2+H]^+$ 1236.6594, found 1236.6593; R_f (petroleum ether/EtOAc 70:30): 0.48.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(4-*tert*-butylbenzyl)-α-D-galactopyranosyloxy]-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13 q): Following general procedure C2, intermediate **12** (0.200 g, 0.181 mmol) afforded **13 q** (0.222 g, 98%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.44–7.18 (m, 14H), 6.94–6.79 (m, 10H), 4.95 (d, J=11.2 Hz, 1H), 4.91 (d, J=3.4 Hz, 1H), 4.79 (d, J=11.6 Hz, 2H), 4.70 (d, J=11.2 Hz, 1H), 4.67 (d, J=11.4 Hz, 1H), 4.61 (dd, J=12.9, 11.4 Hz, 2H), 4.57 (d, J=11.2 Hz, 1H), 4.53 (d, J=10.4 Hz, 1H), 4.43 (d, J=11.3 Hz, 1H), 4.41 (d, J=11.4 Hz, 1H), 4.33 (d, J=11.4 Hz, 1H), 4.11–3.92 (m, 5H), 3.81 (2 × s, 2×3H), 3.80 (s, 6H), 3.77 (s, 3H), 3.76–3.70 (m, 3H), 3.65–3.57 (m, 1H), 3.56–3.45 (m, 2H), 1.74–1.48 (m, 2H), 1.42–1.21 (m, 24H), 1.35 (s, 9H), 0.93 ppm (t, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 159.3, 159.2, 159.1, 150.5, 135.8, 131.1, 131.0, 130.6, 130.3, 160.2, 129.7, 129.6, 129.5, 129.4, 129.2, 128.2, 125.1, 113.8, 113.7, 98.9, 78.9, 78.7, 78.6, 76.0, 74.9, 74.5, 73.4, 73.1, 72.9, 72.7, 71.6, 69.8, 68.8, 68.5, 62.1, 55.2, 55.2, 34.5, 32.0, 31.4, 30.0, 29.9, 29.8, 29.7, 29.4, 25.4, 22.8, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{75}H_{102}NO_{13}$ $[M-N_2+H]^+$ 1224.7346, found 1224.7349; R_f (petroleum ether/EtOAc 70:30): 0.52.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(3,4-difluorobenzyl)-α-D-galactopyranosyloxy]-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13 r): Following general procedure C2, intermediate **12** (0.200 g, 0.181 mmol) afforded **13 r** (0.205 g, 92%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.34–7.17 (m, 10H), 7.11 (ddd, J=11.0, 7.9, 2.1 Hz, 1H), 7.03 (dd, J=10.3, 8.2 Hz, 1H), 6.96–6.78 (m, 11H), 4.88 (d, J=2.5 Hz, 1H), 4.81 (t, J=10.9 Hz, 2H), 4.76 (d, J=11.4 Hz, 1H), 4.66 (d, J=11.6 Hz, 1H), 4.65 (d, J=11.4 Hz, 1H), 4.60 (dd, J=14.0, 11.1 Hz, 2H), 4.53 (d, J=11.1 Hz, 1H), 4.47 (d, J=11.4 Hz, 1H), 4.44 (d, J=10.9 Hz, 1H), 4.43 (d, J=

11.1 Hz, 1H), 4.33 (d, J=11.6 Hz, 1H), 4.06–3.93 (m, 4H), 3.90 (bs, 1H), 3.81 (2 × s, 2×3H), 3.80 (s, 6H), 3.77 (s, 3H), 3.76–3.70 (m, 3H), 3.64–3.51 (m, 2H), 3.44 (dd, J=9.0, 5.8 Hz, 1H), 1.74–1.46 (m, 2H), 1.39–1.20 (m, 24H), 0.91 ppm (t, J=6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.4, 159.3, 159.2, 159.1, 150.0 (dd, J=247.9, 12.9 Hz), 149.7 (dd, J=246.6, 12.6 Hz), 136.0, 130.9, 130.8, 130.6, 130.3, 129.9, 129.7, 129.6, 129.5, 129.2, 123.8 (dd, J=6.9, 3.4 Hz), 117.0 (d, J=17.2 Hz), 116.8 (d, J=17.3 Hz), 113.8, 98.8, 78.9, 78.7, 78.5, 75.9, 75.8, 73.6, 73.4, 73.2, 73.0, 72.9, 71.7, 69.4, 68.7, 68.1, 62.1, 55.3, 55.2, 32.0, 30.0, 29.9, 29.8, 29.7, 29.5, 25.4, 22.8, 14.2 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ=−138.24 (tt, J=12.1, 8.4 Hz, 1F), −139.89 ppm (ttd, J=21.7, 13.9, 3.8 Hz, 1F); HRMS (ESI-MS) m/z: calcd for $C_{71}H_{92}F_2NO_{13}$ $[M-N_2+H]^+$ 1204.6531, found 1204.6534; R_f (petroleum ether/EtOAc 70:30): 0.48.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-cyclopropylmethyl-α-D-galactopyranosyloxy]-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13s): Following general procedure C2, intermediate **12** (0.200 g, 0.181 mmol) afforded **13s** (0.191 g, 91%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.32–7.18 (m, 10H), 6.91–6.77 (m, 10H), 4.90 (d, J=3.5 Hz, 1H), 4.75 (d, J=11.4 Hz, 1H), 4.72 (d, J=11.3 Hz, 1H), 4.68 (d, J=11.1 Hz, 1H), 4.63 (d, J=11.6 Hz, 1H), 4.59 (dd, J=13.3, 11.3 Hz, 2H), 4.52 (d, J=11.1 Hz, 1H), 4.48 (d, J=11.1 Hz, 1H), 4.41 (d, J=11.1 Hz, 1H), 4.39 (d, J=11.4 Hz, 1H), 4.05–3.87 (m, 4H), 3.81 (m, 1H), 3.80 (s, 12H), 3.76 (s, 3H), 3.75–3.66 (m, 5H), 3.59 (m, 1H), 3.51 (dd, J=8.9, 5.6 Hz, 1H), 3.33 (dd, J=10.0, 6.9 Hz, 1H), 1.72–1.45 (m, 2H), 1.43–1.17 (m, 24H), 1.06 (m, 1H), 0.91 (t, J=6.7 Hz, 3H), 0.55–0.41 (m, 2H), 0.27–0.06 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.3, 159.2, 159.1, 131.1, 130.6, 130.4, 130.2, 129.7, 129.6, 129.5, 129.4, 129.1, 113.8, 113.7, 98.9, 78.9, 78.7, 78.6, 77.9, 76.1, 75.2, 73.4, 73.2, 73.0, 72.6, 71.7, 69.8, 68.6, 68.5, 62.1, 55.3, 55.2, 32.0, 30.1, 29.9, 29.8, 29.7, 29.5, 25.4, 22.8, 14.2, 11.2, 3.4, 2.9 ppm; HRMS (ESI-MS) m/z: calcd for $C_{68}H_{94}NO_{13}$ $[M-N_2+H]^+$ 1132.6720, found 1132.6716; R_f (petroleum ether/EtOAc 70:30): 0.48.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-cyclobutylmethyl-α-D-galactopyranosyloxy]-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)-octadecane (13t): Following general procedure C2, intermediate **12** (0.200 g, 0.181 mmol) afforded **13t** (0.132 g, 62%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.36–7.21 (m, 10H), 6.93–6.84 (m, 8H), 6.81 (d, J=8.6 Hz, 2H), 4.89 (d, J=3.2 Hz, 1H), 4.76 (d, J=11.6 Hz, 1H), 4.73 (d, J=11.2 Hz, 1H), 4.68 (d, J=11.4 Hz, 1H), 4.63 (d, J=11.6 Hz, 1H), 4.60 (dd, J=13.7, 11.1 Hz, 2H), 4.53 (d, J=11.4 Hz, 1H), 4.49 (d, J=11.5 Hz, 1H), 4.42 (d, J=11.1 Hz, 1H), 4.40 (d, J=11.2 Hz, 1H), 4.06–3.88 (m, 5H), 3.81 (s, 12H), 3.78 (m, 1H), 3.77 (s, 3H), 3.76–3.69 (m, 3H), 3.68–3.56 (m, 2H), 3.53–3.40 (m, 2H), 2.56 (septet, J=7.2 Hz, 1H), 2.14–1.96 (m, 2H), 1.95–1.47 (m, 6H), 1.39–1.20 (m, 24H), 0.92 ppm (t, J=6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.3, 159.2, 159.1, 131.1, 131.0, 130.6, 130.4, 130.3, 129.7, 129.6, 129.5, 129.4, 129.1, 113.9, 113.8, 113.7, 99.0, 79.0, 78.7, 78.6, 77.9, 75.8, 75.4, 73.4, 73.2, 73.0, 72.5, 71.7, 69.9, 68.6, 62.1, 55.3, 55.2, 35.4, 32.0, 30.1, 29.9, 29.8, 29.7, 29.5, 25.5, 25.2, 24.9, 22.8, 18.7, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{69}H_{96}NO_{13}$ $[M-N_2+H]^+$ 1146.6876, found 1146.6880; R_f (petroleum ether/EtOAc 70:30): 0.55.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(2-adamantylethyl)-α-D-galactopyranosyloxy]-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)-octadecane (13u): Following general procedure C1, intermediate **12** (0.200 g, 0.181 mmol) afforded **13u** (0.156 g, 68%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.35–7.19 (m, 10H), 6.92–6.76 (m, 10H), 4.86 (d, J=3.1 Hz, 1H), 4.77 (d, J=11.3 Hz, 1H), 4.73 (d, J=11.3 Hz, 1H), 4.64 (d, J=11.2 Hz, 1H), 4.61 (d, J=11.6 Hz, 1H), 4.58 (dd, J=14.0, 11.5 Hz, 2H), 4.52 (d, J=10.8 Hz, 1H), 4.48 (d, J=10.6 Hz, 1H), 4.41 (d, J=11.0 Hz, 1H), 4.40 (d, J=11.4 Hz, 1H), 4.04–3.87 (m, 5H), 3.80 (2×s, 2×6H), 3.78–3.68 (m, 4H), 3.76 (s, 3H), 3.67–3.55 (m, 2H), 3.54–3.45 (m, 2H), 1.92 (bs, 3H), 1.76–1.57 (m, 8H), 1.48 (bs, 6H), 1.40–1.21 (m, 26H), 0.91 ppm (t, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.3, 159.2, 159.1, 131.1, 130.6, 130.4, 130.3, 129.7, 129.6, 129.5, 129.4, 129.2, 113.9, 113.8, 113.7, 99.0, 79.0, 78.6, 78.5, 76.1, 75.6, 73.4, 73.3, 73.1, 72.6, 71.7, 69.7, 69.4, 68.7, 68.5, 62.1, 55.3, 55.2, 44.1, 42.8, 37.2, 32.0, 31.7, 30.1, 29.9, 29.8, 29.7, 29.5, 28.8, 28.7, 25.5, 22.8, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{76}H_{106}NO_{13}$ $[M-N_2+H]^+$ 1240.7659, found 1240.7658; R_f (petroleum ether/EtOAc 70:30): 0.54.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-propyl-α-D-galactopyranosyloxy]-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13v): Following general procedure C1, intermediate **12** (0.200 g, 0.181 mmol) afforded **13v** (0.158 g, 76%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.38–7.22 (m, 10H), 6.95–6.78 (m, 10H), 4.92 (d, J=3.2 Hz, 1H), 4.80 (d, J=11.6 Hz, 1H), 4.76 (d, J=11.6 Hz, 1H), 4.70 (d, J=11.2 Hz, 1H), 4.66 (d, J=11.7 Hz, 1H), 4.62 (dd, J=13.0, 11.3 Hz, 2H), 4.55 (d, J=11.0 Hz, 1H), 4.51 (d, J=11.1 Hz, 1H), 4.45 (d, J=11.1 Hz, 1H), 4.43 (d, J=11.3 Hz, 1H), 4.08–3.86 (m, 5H), 3.82 (s, 12H), 3.80 (m, 1H), 3.78 (s, 3H), 3.77–3.73 (m, 3H), 3.72–3.60 (m, 2H), 3.58–3.41 (m, 2H), 1.75–1.50 (m, 4H), 1.44–1.22 (m, 24H), 0.95 ppm (t, J=7.3 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.3, 159.2, 159.0, 131.1, 130.6, 130.3, 130.2, 129.7, 129.6, 129.5, 129.4, 129.1, 113.8, 113.7, 113.6, 98.9, 78.9, 78.6, 78.5, 77.6, 77.2, 76.8, 76.0, 75.6, 75.2, 73.4, 73.2, 73.0, 72.4, 71.6, 69.7, 68.5, 62.1, 55.2, 55.1, 32.0, 30.0, 29.8, 29.7, 29.4, 25.4, 23.5, 22.7, 14.2, 10.7 ppm; HRMS (ESI-MS) m/z: calcd for $C_{67}H_{94}NO_{13}$ $[M-N_2+H]^+$ 1120.6720, found 1120.6725; R_f (petroleum ether/EtOAc 70:30): 0.52.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-allyl-α-D-galactopyranosyloxy]-2-azido-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (13w): Following general procedure C2, intermediate **12** (0.200 g, 0.181 mmol) afforded **13w** (0.189 g, 91%) as a light-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.32–7.15 (m, 10H), 6.89–6.73 (m, 10H), 5.88 (ddt, J=17.3, 10.4, 5.8 Hz, 1H), 5.19 (dq, J=17.2, 1.4 Hz, 1H), 5.11 (dq, J=10.2, 1.2 Hz, 1H), 4.86 (d, J=3.2 Hz, 1H), 4.73 (d, J=11.4 Hz, 1H), 4.70 (d, J=11.6 Hz, 1H), 4.63 (d, J=10.9 Hz, 1H), 4.59 (d, J=11.3 Hz, 1H), 4.55 (dd, J=12.8, 11.3 Hz, 2H), 4.48 (d, J=11.2 Hz, 1H), 4.44 (d, J=11.4 Hz, 1H), 4.38 (d, J=11.2 Hz, 1H), 4.37 (d, J=11.3 Hz, 1H), 4.06 (dd, J=12.7, 6.3 Hz, 1H), 4.01–3.86 (m, 4H), 3.82 (bs, 1H), 3.75 (s, 12H), 3.73–3.66 (m, 4H), 3.72 (s, 3H), 3.65–3.53 (m, 2H), 3.52–3.43 (m, 1H), 1.70–1.44 (m, 2H), 1.40–1.14 (m, 24H), 0.88 ppm (t, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.3, 159.2, 159.1, 135.5, 131.0, 130.9, 130.5, 130.3, 130.1, 129.6, 129.5, 129.4, 129.3, 129.2, 116.9, 113.8, 113.7, 113.6, 98.8, 78.8, 78.6, 78.4, 76.2, 75.0, 74.1, 73.4, 73.2, 73.0, 72.6, 71.6, 69.6, 68.6, 68.5, 62.1, 55.2, 55.1, 32.0, 30.0, 29.8, 29.7, 29.4, 25.4, 22.7, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{67}H_{92}NO_{13}$ $[M-N_2+H]^+$ 1118.6563, found 1118.6565; R_f (petroleum ether/EtOAc 70:30): 0.37.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-benzyl-α-D-galactopyranosyloxy]-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14a): Following general procedure D, **13a** (0.207 g, 0.173 mmol) afforded **14a** (0.194 g, 72%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.34–7.12 (m, 15H), 6.89–6.76 (m, 10H), 6.15 (d, J=8.6 Hz, 1H), 4.92 (d, J=11.3 Hz, 1H), 4.83 (d, J=3.5 Hz, 1H), 4.70 (dd, J=22.6, 11.5 Hz, 4H), 4.60 (d, J=11.7 Hz, 1H), 4.55 (d, J=11.3 Hz, 1H), 4.53 (d, J=11.1 Hz, 1H), 4.46 (d, J=10.4 Hz, 1H), 4.43 (d, J=10.6 Hz, 1H), 4.35 (d, J=11.3 Hz, 1H), 4.31 (d, J=11.5 Hz, 1H), 4.15 (m, 1H), 4.03 (dd, J=10.8, 4.2 Hz, 2H), 3.96–3.81 (m, 4H), 3.79 (s, 3H), 3.78 (s, 6H), 3.76 (s, 3H), 3.75 (s, 3H), 3.73–3.71 (m, 1H), 3.52–3.37 (m, 3H), 1.96 (m, 4H), 1.68–1.41

(m, 5H), 1.37–1.17 (m, 65H), 0.89 ppm (t, J=6.5 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=173.0, 159.4, 159.3, 159.2, 138.7, 131.0, 130.9, 130.8, 130.7, 129.8, 129.7, 129.6, 129.2, 128.4, 128.3, 127.7, 113.9, 113.9, 99.9, 79.9, 78.8, 78.4, 76.4, 75.1, 74.8, 73.4, 73.3, 73.2, 72.7, 71.4, 70.1, 69.7, 69.1, 55.3, 55.3, 50.4, 36.8, 32.1, 30.0, 29.9, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 26.2, 25.8, 24.9, 22.8, 14.3 ppm; HRMS (ESI-MS) m/z: calcd for $C_{97}H_{146}NO_{14}$ $[M+H]^+$ 1549.0738, found 1549.0737; R_f (petroleum ether/EtOAc 70:30): 0.48.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(3-phenylpropyl)-α-D-galactopyranosyloxy]-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14b): Following general procedure D, **13b** (0.166 g, 0.136 mmol) afforded **14b** (0.175 g, 81%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.32–7.12 (m, 15H), 6.91–6.72 (m, 10H), 6.12 (d, J=8.5 Hz, 1H), 4.84 (d, J=3.6 Hz, 1H), 4.74 (d, J=11.3 Hz, 1H), 4.71 (d, J=11.2 Hz, 1H), 4.65 (dd, J=15.8, 11.0 Hz, 2H), 4.59 (d, J=11.3 Hz, 1H), 4.54 (d, J=11.1 Hz, 1H), 4.48 (d, J=11.6 Hz, 1H), 4.47 (d, J=11.0 Hz, 1H), 4.37 (d, J=11.1 Hz, 2H), 4.17 (m, 1H), 4.05–3.88 (m, 4H), 3.87–3.80 (m, 2H), 3.79 (s, 6H), 3.77 (s, 3H), 3.76 (s, 3H), 3.76–3.73 (m, 2H), 3.72 (s, 3H), 3.63–3.43 (m, 4H), 2.64 (t, J=7.6 Hz, 2H), 2.04–1.80 (m, 6H), 1.71–1.40 (m, 8H), 1.35–1.17 (m, 62H), 0.90 ppm (t, J=6.8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=172.9, 159.5, 159.3, 159.2, 159.1, 142.3, 131.0, 130.9, 130.8, 130.7, 129.8, 129.7, 129.6, 129.6, 129.2, 128.6, 128.4, 125.8, 113.9, 113.8, 99.8, 79.8, 78.6, 78.4, 76.2, 75.9, 73.4, 73.3, 72.8, 72.5, 71.4, 70.1, 69.5, 68.8, 55.3, 55.3, 50.4, 36.8, 32.5, 32.1, 32.0, 30.0, 29.9, 29.8, 29.8, 29.7, 29.6, 29.5, 26.2, 25.8, 22.8, 14.3 ppm; HRMS (ESI-MS) m/z: calcd for $C_{99}H_{149}NO_{14}$ $[M+H]^+$ 1577.1051, found 1577.1057; R_f (petroleum ether/EtOAc 70:30): 0.38.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(4-phenylbutyl)-α-D-galactopyranosyloxy]-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14c): Following general procedure D, **13c** (0.189 g, 0.153 mmol) afforded **14c** (0.196 g, 80%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.35–7.08 (m, 15H), 6.91–6.71 (m, 10H), 6.12 (d, J=8.5 Hz, 1H), 4.81 (d, J=3.3 Hz, 1H), 4.73 (d, J=11.5 Hz, 1H), 4.70 (d, J=10.8 Hz, 1H), 4.67 (dd, J=15.1, 11.3 Hz, 2H), 4.56 (d, J=11.3 Hz, 1H), 4.54 (d, J=11.2 Hz, 1H), 4.48 (d, J=11.5 Hz, 1H), 4.47 (d, J=11.0 Hz, 1H), 4.36 (d, J=11.2 Hz, 2H), 4.17 (m, 1H), 4.03–3.88 (m, 4H), 3.87–3.80 (m, 2H), 3.79 (s, 3H), 3.78 (s, 6H), 3.77 (s, 3H), 3.76–3.72 (m, 2H), 3.74 (s, 3H), 3.62–3.40 (m, 4H), 2.60 (t, J=7.4 Hz, 2H), 1.97 (m, 3H), 1.73–1.43 (m, 11H), 1.38–1.17 (m, 64H), 0.90 ppm (t, J=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=172.9, 159.4, 159.3, 159.2, 159.1, 142.7, 131.0, 130.9, 130.9, 130.8, 129.9, 129.7, 129.6, 129.5, 129.1, 128.5, 128.3, 125.8, 113.9, 113.8, 99.8, 79.9, 78.7, 78.4, 76.2, 75.8, 73.4, 73.3, 72.5, 71.4, 70.1, 69.5, 68.8, 55.3, 55.2, 50.4, 36.8, 35.8, 32.1, 30.0, 29.9, 29.8, 29.7, 29.6, 29.5, 28.1, 26.2, 25.8, 22.8, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{100}H_{152}NO_{14}$ $[M+H]^+$ 1591.1207, found 1591.1221; R_f (petroleum ether/EtOAc 70:30): 0.39.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(5-phenylpentyl)-α-D-galactopyranosyloxy]-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14d): Following general procedure D, **13d** (0.201 g, 0.160 mmol) afforded **14d** (0.190 g, 74%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.33–7.11 (m, 15H), 6.91–6.73 (m, 10H), 6.10 (d, J=8.6 Hz, 1H), 4.83 (d, J=3.6 Hz, 1H), 4.73 (d, J=11.3 Hz, 1H), 4.70 (d, J=10.9 Hz, 1H), 4.66 (dd, J=13.4, 11.5 Hz, 2H), 4.56 (d, J=11.4 Hz, 1H), 4.53 (d, J=11.3 Hz, 1H), 4.49 (d, J=11.7 Hz, 1H), 4.46 (d, J=11.0 Hz, 1H), 4.37 (d, J=11.5 Hz, 1H), 4.36 (d, J=11.2 Hz, 1H), 4.16 (m, 1H), 4.04–3.80 (m, 6H), 3.79 (s, 3H), 3.78 (s, 3H), 3.77 (s, 6H), 3.76–3.70 (m, 2H), 3.74 (s, 3H), 3.62–3.37 (m, 4H), 2.59 (t, J=7.6 Hz, 2H), 1.96 (m, 3H), 1.69–1.46 (m, 9H), 1.39–1.17 (m, 68H), 0.90 ppm (t, J=6.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=172.9, 159.4, 159.3, 159.2, 159.1, 142.8, 131.0, 130.9, 130.8, 130.0, 129.9, 129.7, 129.6, 129.5, 129.1, 128.5, 128.4, 125.7, 113.9, 113.8, 99.8, 79.9, 78.7, 78.4, 76.4, 75.8, 73.6, 73.4, 73.3, 72.4, 71.4, 70.1, 68.9, 55.4, 55.3, 50.4, 36.8, 36.1, 32.1, 31.5, 30.2, 30.0, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 26.2, 26.0, 25.8, 22.8, 14.3 ppm; HRMS (ESI-MS) m/z: calcd for $C_{101}H_{154}NO_{14}$ $[M+H]^+$ 1605.1364, found 1605.1362; R_f (petroleum ether/EtOAc 70:30): 0.45.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(6-phenylhexyl)-α-D-galactopyranosyloxy]-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14e): Following general procedure D, **13e** (0.216 g, 0.171 mmol) afforded **14e** (0.197 g, 71%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.35–7.12 (m, 15H), 6.92–6.72 (m, 10H), 6.14 (d, J=8.5 Hz, 1H), 4.83 (d, J=3.4 Hz, 1H), 4.73 (t, J=10.4 Hz, 2H), 4.67 (s, 2H), 4.58 (d, J=11.1 Hz, 1H), 4.54 (d, J=11.1 Hz, 1H), 4.48 (t, J=10.4 Hz, 2H), 4.39 (d, J=11.2 Hz, 1H), 4.36 (d, J=11.1 Hz, 1H), 4.17 (m, 1H), 4.04–3.82 (m, 6H), 3.79 (s, 3H), 3.77 (s, 9H), 3.76–3.71 (m, 2H), 3.73 (s, 3H), 3.64–3.37 (m, 4H), 2.60 (t, J=7.8 Hz, 2H), 1.97 (m, 2H), 1.70–1.40 (m, 10H), 1.38–1.19 (m, 70H), 0.91 ppm (t, J=6.4 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=172.9, 159.4, 159.3, 159.2, 159.1, 142.8, 130.9, 130.8, 130.7, 129.8, 129.7, 129.6, 129.5, 129.1, 128.4, 128.3, 125.7, 113.9, 113.8, 99.8, 79.8, 78.3, 76.3, 75.7, 73.5, 73.3, 73.2, 72.4, 71.3, 70.1, 68.8, 55.3, 55.2, 50.3, 36.7, 36.0, 32.0, 31.6, 30.3, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 29.2, 26.1, 26.0, 25.8, 22.7, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{102}H_{156}NO_{14}$ $[M+H]^+$ 1619.1520, found 1619.1513; R_f (petroleum ether/EtOAc 70:30): 0.40.

(2*S*,3*S*,4*R*)-1-{2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-[3-(4-methylphenyl)propyl]-α-D-galactopyranosyloxy}-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14f): Following general procedure D, **13f** (0.209 g, 0.169 mmol) afforded **14f** (0.193 g, 72%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.32–7.15 (m, 10H), 7.07 (s, 4H), 6.90–6.75 (m, 10H), 6.14 (d, J=8.6 Hz, 1H), 4.85 (d, J=3.6 Hz, 1H), 4.76 (d, J=11.1 Hz, 1H), 4.73 (d, J=11.3 Hz, 1H), 4.67 (dd, J=15.6, 11.3 Hz, 2H), 4.61 (d, J=11.3 Hz, 1H), 4.56 (d, J=11.3 Hz, 1H), 4.50 (d, J=11.4 Hz, 1H), 4.49 (d, J=11.0 Hz, 1H), 4.39 (d, J=11.7 Hz, 1H), 4.38 (d, J=11.7 Hz, 1H), 4.18 (m, 1H), 4.06–3.90 (m, 4H), 3.89–3.80 (m, 2H), 3.80 (s, 6H), 3.78 (s, 6H), 3.77–3.73 (m, 2H), 3.74 (s, 3H), 3.65–3.43 (m, 4H), 2.62 (t, J=7.7 Hz, 2H), 2.33 (s, 3H), 2.07–1.81 (m, 4H), 1.71–1.42 (m, 6H), 1.37–1.20 (m, 66H), 0.91 ppm (t, J=6.8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=172.8, 159.4, 159.3, 159.2, 159.2, 139.1, 135.1, 130.9, 130.8, 130.7, 129.8, 129.7, 129.6, 129.5, 129.4, 129.1, 129.0, 128.4, 113.9, 113.8, 99.8, 79.8, 78.6, 78.4, 76.1, 75.8, 73.3, 73.2, 72.8, 72.4, 71.3, 70.1, 69.5, 68.8, 55.3, 55.2, 50.3, 36.8, 32.0, 30.0, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 26.1, 25.8, 22.8, 21.1, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{100}H_{152}NO_{14}$ $[M+H]^+$ 1591.1207, found 1591.1210; R_f (petroleum ether/EtOAc 70:30): 0.39.

(2*S*,3*S*,4*R*)-1-{2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-[3-(4-chlorophenyl)propyl]-α-D-galactopyranosyloxy}-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14g): Following general procedure D, **13g** (0.196 g, 0.156 mmol) afforded **14g** (0.196 g, 78%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.31–7.14 (m, 12H), 7.10–7.02 (m, 2H), 6.90–6.72 (m, 10H), 6.10 (d, J=8.4 Hz, 1H), 4.84 (d, J=3.6 Hz, 1H), 4.74 (d, J=11.3 Hz, 1H), 4.71 (d, J=10.9 Hz, 1H), 4.65 (dd, J=19.6, 11.3 Hz, 2H), 4.60 (d, J=11.5 Hz, 1H), 4.55 (d, J=11.3 Hz, 1H), 4.49 (d, J=11.5 Hz, 1H), 4.47 (d, J=11.2 Hz, 1H), 4.38 (d, J=11.3 Hz, 1H), 4.36 (d, J=11.5 Hz, 1H), 4.19 (m, 1H), 4.05–3.89 (m, 3H), 3.88–3.81 (m, 3H), 3.80 (s, 3H), 3.79 (s, 3H), 3.78–3.73 (m, 2H), 3.77 (s, 6H), 3.72 (s, 3H), 3.62–3.39 (m, 4H), 2.59 (t, J=7.6 Hz, 2H), 2.06–1.74 (m, 4H), 1.72–1.39 (m, 6H), 1.36–1.17 (m, 66H), 0.89 ppm (t, J=6.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=172.9, 159.5, 159.3, 159.2, 140.7, 131.4, 130.9, 130.8, 130.7, 129.9, 129.8, 129.7, 129.6, 129.5, 129.2, 128.4, 113.9, 113.8, 99.7, 79.8, 78.6, 78.5,

76.1, 75.9, 73.4, 73.2, 72.6, 72.4, 71.4, 69.9, 69.3, 68.7, 55.3, 55.2, 50.4, 36.8, 32.1, 31.8, 31.7, 30.0, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 26.2, 25.8, 22.8, 14.2 ppm; HRMS (ESI-MS) *m/z*: calcd for $C_{99}H_{149}ClNO_{14}$ $[M+H]^+$ 1611.0661, found 1611.0656; R_f (petroleum ether/EtOAc 70:30): 0.30.

(2*S*,3*S*,4*R*)-1-{2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-[3-(4-methoxyphenyl)propyl]-α-D-galactopyranosyloxy}-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14h); Following general procedure D, **13h** (0.229 g, 0.183 mmol) afforded **14h** (0.237 g, 81%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.15 (m, 10H), 7.11–7.03 (m, 2H), 6.90–6.73 (m, 12H), 6.15 (d, *J* = 8.3 Hz, 1H), 4.85 (d, *J* = 3.4 Hz, 1H), 4.75 (d, *J* = 11.2 Hz, 1H), 4.72 (d, *J* = 10.9 Hz, 1H), 4.66 (dd, *J* = 14.7, 11.0 Hz, 2H), 4.60 (d, *J* = 11.5 Hz, 1H), 4.55 (d, *J* = 11.3 Hz, 1H), 4.49 (d, *J* = 11.5 Hz, 1H), 4.48 (d, *J* = 11.0 Hz, 1H), 4.38 (d, *J* = 11.3 Hz, 2H), 4.18 (m, 1H), 4.05–3.80 (m, 6H), 3.79 (s, 6H), 3.78–3.73 (m, 2H), 3.77 (s, 3H), 3.77 (s, 6H), 3.73 (s, 3H), 3.65–3.42 (m, 4H), 2.59 (t, *J* = 7.6 Hz, 2H), 2.06–1.76 (m, 4H), 1.72–1.40 (m, 6H), 1.37–1.17 (m, 66H), 0.90 ppm (t, *J* = 6.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 159.4, 159.3, 159.2, 159.1, 157.7, 134.2, 130.9, 130.8, 130.7, 129.8, 129.7, 129.6, 129.5, 129.4, 129.3, 129.1, 113.9, 113.8, 113.7, 99.7, 79.8, 78.6, 78.3, 76.1, 75.8, 73.3, 73.2, 72.7, 72.4, 71.3, 70.0, 68.8, 55.2, 55.2, 50.3, 36.7, 32.1, 32.0, 31.5, 29.9, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 26.1, 25.8, 22.8, 14.2 ppm; HRMS (ESI-MS) *m/z*: calcd for $C_{100}H_{152}NO_{15}$ $[M+H]^+$ 1607.1156, found 1607.1153; R_f (petroleum ether/EtOAc 70:30): 0.35.

(2*S*,3*S*,4*R*)-1-{2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-[3-(3,4-dichlorophenyl)propyl]-α-D-galactopyranosyloxy}-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14i): Following general procedure D, **13i** (0.134 g, 0.104 mmol) afforded **14i** (0.094 g, 55%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30–7.14 (m, 12H), 6.98–6.71 (m, 11H), 6.07 (d, *J* = 8.3 Hz, 1H), 4.83 (d, *J* = 3.4 Hz, 1H), 4.73 (d, *J* = 11.5 Hz, 1H), 4.70 (d, *J* = 10.9 Hz, 1H), 4.62 (dd, *J* = 14.8, 11.5 Hz, 2H), 4.61 (d, *J* = 11.2 Hz, 1H), 4.54 (d, *J* = 11.5 Hz, 1H), 4.48 (dd, *J* = 10.8, 8.8 Hz, 2H), 4.37 (d, *J* = 11.2 Hz, 1H), 4.35 (d, *J* = 11.5 Hz, 1H), 4.18 (m, 1H), 4.02–3.89 (m, 3H), 3.87–3.80 (m, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 3.77–3.70 (m, 2H), 3.77 (s, 6H), 3.72 (s, 3H), 3.61–3.38 (m, 4H), 2.56 (t, *J* = 7.5 Hz, 2H), 2.06–1.89 (m, 2H), 1.86–1.72 (m, 2H), 1.68–1.39 (m, 6H), 1.36–1.17 (m, 66H), 0.89 ppm (t, *J* = 6.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 159.3, 159.2, 142.6, 130.9, 130.9, 130.8, 130.7, 130.5, 130.2, 129.8, 129.7, 129.6, 129.5, 129.2, 128.1, 113.9, 113.8, 79.8, 78.5, 76.1, 75.9, 73.4, 73.3, 73.2, 72.6, 72.2, 71.4, 69.9, 68.6, 55.3, 55.3, 50.4, 36.8, 32.1, 31.6, 30.0, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 25.8, 22.8, 14.3 ppm; HRMS (ESI-MS) *m/z*: calcd for $C_{99}H_{148}Cl_2NO_{14}$ $[M+H]^+$ 1645.0271, found 1645.0277; R_f (petroleum ether/EtOAc 70:30): 0.36.

(2*S*,3*S*,4*R*)-1-{2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-[3-(4-fluorophenyl)propyl]-α-D-galactopyranosyloxy}-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14j): Following general procedure D, **13j** (0.154 g, 0.124 mmol) afforded **14j** (0.116 g, 59%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30–7.14 (m, 10H), 7.11–7.02 (m, 2H), 6.94–6.72 (m, 12H), 6.08 (d, *J* = 8.5 Hz, 1H), 4.83 (d, *J* = 3.6 Hz, 1H), 4.73 (d, *J* = 11.4 Hz, 1H), 4.70 (d, *J* = 10.9 Hz, 1H), 4.64 (dd, *J* = 18.7, 11.1 Hz, 2H), 4.59 (d, *J* = 11.4 Hz, 1H), 4.54 (d, *J* = 11.2 Hz, 1H), 4.48 (d, *J* = 11.5 Hz, 1H), 4.46 (d, *J* = 11.0 Hz, 1H), 4.37 (d, *J* = 11.1 Hz, 1H), 4.36 (d, *J* = 11.6 Hz, 1H), 4.18 (m, 1H), 4.03–3.81 (m, 6H), 3.79 (s, 3H), 3.78 (s, 3H), 3.77 (s, 6H), 3.77–3.70 (m, 2H), 3.72 (s, 3H), 3.63–3.38 (m, 4H), 2.59 (t, *J* = 7.6 Hz, 2H), 2.04–1.89 (m, 2H), 1.88–1.74 (m, 2H), 1.69–1.37 (m, 6H), 1.35–1.15 (m, 66H), 0.89 ppm (t, *J* = 6.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 161.1 (d, *J* = 242.5 Hz), 159.5, 159.3, 159.2, 137.8 (d, *J* = 2.9 Hz), 131.0, 130.9 (d, *J* = 5.7 Hz), 130.7, 129.9, 129.8, 129.7, 129.6, 129.5, 129.2, 115.0 (d, *J* = 20.8 Hz), 113.9, 113.8, 99.7, 79.8, 78.6, 78.5, 76.1, 75.9, 73.4, 73.2, 72.6, 71.4, 70.0, 69.4, 68.7, 55.3, 55.2, 50.4, 36.8, 32.1, 31.6, 30.0, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 26.2, 25.8, 22.8, 14.3 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ = −117.94 ppm (tt, *J* = 8.4, 5.9 Hz, 1F); HRMS (ESI-MS) *m/z*: calcd for $C_{99}H_{149}FNO_{14}$ $[M+H]^+$ 1595.0957, found 1595.0963; R_f (petroleum ether/EtOAc 70:30): 0.36.

(2*S*,3*S*,4*R*)-1-{2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-[3-(4-trifluoromethylphenyl)propyl]-α-D-galactopyranosyloxy}-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14k): Following general procedure D, **13k** (0.154 g, 0.124 mmol) afforded **14k** (0.170 g, 68%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 7.8 Hz, 2H), 7.31–7.13 (m, 12H), 6.91–6.70 (m, 10H), 6.08 (d, *J* = 8.4 Hz, 1H), 4.84 (d, *J* = 3.3 Hz, 1H), 4.73 (d, *J* = 11.6 Hz, 1H), 4.70 (d, *J* = 11.7 Hz, 1H), 4.69 (d, *J* = 11.5 Hz, 1H), 4.61 (d, *J* = 11.2 Hz, 1H), 4.60 (d, *J* = 11.6 Hz, 1H), 4.54 (d, *J* = 11.5 Hz, 1H), 4.50 (d, *J* = 11.5 Hz, 1H), 4.47 (d, *J* = 10.7 Hz, 1H), 4.38 (d, *J* = 11.2 Hz, 1H), 4.36 (d, *J* = 11.5 Hz, 1H), 4.20 (m, 1H), 4.03–3.82 (m, 6H), 3.79–3.73 (m, 2H), 3.78 (s, 6H), 3.77 (s, 3H), 3.76 (s, 3H), 3.70 (s, 3H), 3.63–3.40 (m, 4H), 2.66 (t, *J* = 7.5 Hz, 2H), 2.05–1.90 (m, 2H), 1.89–1.75 (m, 2H), 1.71–1.40 (m, 6H), 1.36–1.14 (m, 66H), 0.89 ppm (t, *J* = 6.4 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 159.5, 159.3, 159.2, 146.5, 130.9, 130.8, 130.7, 130.6, 129.8, 129.7, 129.6, 129.5, 129.2, 128.9, 125.2 (q, *J* = 3.5 Hz), 113.9, 113.8, 99.7, 79.8, 78.6, 78.5, 76.1, 75.9, 73.4, 73.3, 73.1, 72.7, 72.3, 71.4, 69.9, 69.3, 68.6, 55.3, 55.2, 50.4, 36.8, 32.3, 32.0, 31.7, 30.0, 29.9, 29.8, 29.6, 29.5, 29.4, 26.1, 25.8, 22.8, 14.2 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ = −62.24 ppm (s, 3F); HRMS (ESI-MS) *m/z*: calcd for $C_{100}H_{149}F_3NO_{14}$ $[M+H]^+$ 1645.0925, found 1645.0928; R_f (petroleum ether/EtOAc 70:30): 0.39.

(2*S*,3*S*,4*R*)-1-{2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-[3-(4-*tert*-butylphenyl)propyl]-α-D-galactopyranosyloxy}-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14l): Following general procedure D, **13l** (0.211 g, 0.165 mmol) afforded **14l** (0.169 g, 63%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.22 (m, 10H), 7.15 (dd, *J* = 25.4, 8.3 Hz, 4H), 6.92–6.74 (m, 10H), 6.12 (d, *J* = 8.8 Hz, 1H), 4.85 (d, *J* = 3.5 Hz, 1H), 4.75 (d, *J* = 10.9 Hz, 1H), 4.72 (d, *J* = 10.5 Hz, 1H), 4.66 (dd, *J* = 15.2, 10.9 Hz, 2H), 4.60 (d, *J* = 11.4 Hz, 1H), 4.55 (d, *J* = 11.1 Hz, 1H), 4.49 (d, *J* = 11.5 Hz, 1H), 4.48 (d, *J* = 10.8 Hz, 1H), 4.38 (d, *J* = 11.1 Hz, 2H), 4.18 (m, 1H), 4.06–3.83 (m, 6H), 3.80 (s, 6H), 3.78 (s, 3H), 3.77 (s, 3H), 3.76–3.71 (m, 2H), 3.73 (s, 3H), 3.65–3.44 (m, 4H), 2.63 (t, *J* = 7.8 Hz, 2H), 2.06–1.80 (m, 4H), 1.73–1.41 (m, 6H), 1.37–1.20 (m, 66H), 1.32 (s, 9H), 0.90 ppm (t, *J* = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 159.4, 159.3, 159.2, 159.1, 148.6, 139.2, 131.0, 130.9, 130.8, 130.7, 129.8, 129.7, 129.6, 129.5, 129.1, 128.2, 125.2, 113.9, 113.8, 99.8, 79.8, 78.7, 78.4, 76.2, 75.9, 73.4, 73.3, 72.9, 72.5, 71.4, 70.1, 69.5, 68.9, 55.3, 55.2, 50.4, 36.8, 34.4, 32.1, 31.9, 31.8, 31.5, 30.0, 29.9, 29.8, 29.7, 29.6, 29.5, 26.2, 25.8, 22.8, 14.2 ppm; HRMS (ESI-MS) *m/z*: calcd for $C_{103}H_{158}NO_{14}$ $[M+H]^+$ 1633.1677, found 1633.1672; R_f (petroleum ether/EtOAc 70:30): 0.38.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(3,4-dichlorobenzyl)-α-D-galactopyranosyloxy]-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14m): Following general procedure D, **13m** (0.212 g, 0.168 mmol) afforded **14m** (0.186 g, 68%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 1.9 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.29–7.22 (m, 8H), 7.17 (d, *J* = 8.6 Hz, 2H), 7.04 (dd, *J* = 8.2, 1.8 Hz, 1H), 6.90–6.76 (m, 10H), 6.05 (d, *J* = 8.6 Hz, 1H), 4.82 (d, *J* = 3.5 Hz, 1H), 4.79 (d, *J* = 11.5 Hz, 1H), 4.75 (d, *J* = 11.4 Hz, 1H), 4.73 (d, *J* = 11.3 Hz, 1H), 4.70 (d, *J* = 11.0 Hz, 1H), 4.62 (d, *J* = 11.3 Hz, 1H), 4.60 (d, *J* = 11.4 Hz, 1H), 4.54 (d, *J* = 11.2 Hz, 1H), 4.49 (d, *J* = 11.4 Hz, 1H), 4.47 (d, *J* = 11.2 Hz, 1H), 4.44 (d, *J* = 11.6 Hz, 1H), 4.39 (d, *J* = 11.3 Hz, 1H), 4.33 (d, *J* = 11.6 Hz, 1H), 4.20

(m, 1H), 4.02–3.83 (m, 6H), 3.80 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 3.77 (s, 3H), 3.76 (m, 1H), 3.75 (s, 3H), 3.53–3.42 (m, 3H), 2.05–1.87 (m, 2H), 1.73–1.39 (m, 6H), 1.37–1.16 (m, 66H), 0.90 ppm (t, J= 6.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 159.5, 159.4, 159.3, 139.1, 132.3, 131.4, 130.9, 130.7, 130.6, 130.2, 129.9, 129.7, 129.6, 129.5, 129.1, 127.3, 113.9, 113.8, 113.7, 99.6, 79.7, 78.6, 78.5, 76.3, 75.8, 73.4, 73.3, 73.2, 73.1, 73.0, 71.4, 69.7, 69.4, 68.4, 55.3, 50.4, 36.8, 32.0, 30.0, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 26.1, 25.8, 22.8, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{97}H_{144}Cl_2NO_{14}$ $[M+H]^+$ 1616.9958, found 1616.9953; R_f (petroleum ether/EtOAc 70:30): 0.39.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(4-fluorobenzyl)-α-D-galactopyranosyloxy]-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14n): Following general procedure D, **13n** (0.207 g, 0.170 mmol) afforded **14n** (0.207 g, 78%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.11 (m, 12H), 6.94 (t, J= 8.7 Hz, 2H), 6.84 (dt, J= 8.9, 2.6 Hz, 8H), 6.78 (d, J= 8.7 Hz, 2H), 6.13 (d, J= 8.6 Hz, 1H), 4.84 (d, J= 11.8 Hz, 1H), 4.82 (d, J= 2.5 Hz, 1H), 4.73 (d, J= 11.2 Hz, 1H), 4.72 (t, J= 11.4 Hz, 2H), 4.64 (d, J= 11.4 Hz, 1H), 4.59 (d, J= 11.4 Hz, 1H), 4.53 (d, J= 11.4 Hz, 1H), 4.50 (d, J= 10.9 Hz, 1H), 4.49 (d, J= 11.2 Hz, 1H), 4.46 (d, J= 11.6 Hz, 1H), 4.36 (d, J= 11.4 Hz, 1H), 4.31 (d, J= 11.6 Hz, 1H), 4.17 (m, 1H), 4.05–3.81 (m, 6H), 3.78 (s, 3H), 3.77 (s, 6H), 3.75 (s, 3H), 3.74 (s, 3H), 3.72 (m, 1H), 3.52–3.35 (m, 3H), 2.04–1.87 (m, 2H), 1.71–1.38 (m, 6H), 1.31–1.20 (m, 66H), 0.89 ppm (t, J= 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 162.3 (d, J= 246.9 Hz), 159.4, 159.3, 159.2, 134.5 (d, J= 2.3 Hz), 130.9, 130.8, 130.6, 130.0 (d, J= 8.1 Hz), 129.7, 129.6, 129.5, 129.1, 115.1 (d, J= 20.7 Hz), 113.9, 113.8, 99.7, 79.8, 78.6, 78.4, 76.3, 75.2, 74.0, 73.3, 73.1, 72.8, 71.3, 69.9, 69.6, 68.8, 55.2, 50.3, 36.8, 32.0, 30.0, 29.8, 29.7, 29.6, 29.8, 29.4, 26.1, 25.8, 22.8, 14.2 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ = −114.80 ppm (tt, J= 8.4, 6.0 Hz, 1F); HRMS (ESI-MS) m/z: calcd for $C_{97}H_{145}FNO_{14}$ $[M+H]^+$ 1567.0644, found 1567.0648; R_f (petroleum ether/EtOAc 70:30): 0.38.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(4-methylbenzyl)-α-D-galactopyranosyloxy]-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14o): Following general procedure D, **13o** (0.201 g, 0.166 mmol) afforded **14o** (0.163 g, 63%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.20 (m, 8H), 7.19–7.06 (m, 6H), 6.89–6.75 (m, 10H), 6.18 (d, J= 8.5 Hz, 1H), 4.87 (d, J= 11.5 Hz, 1H), 4.82 (d, J= 3.6 Hz, 1H), 4.74 (d, J= 11.2 Hz, 1H), 4.72 (d, J= 11.2 Hz, 1H), 4.70 (d, J= 11.0 Hz, 1H), 4.66 (d, J= 11.5 Hz, 1H), 4.59 (d, J= 11.3 Hz, 1H), 4.54 (d, J= 11.5 Hz, 1H), 4.53 (d, J= 11.3 Hz, 1H), 4.46 (d, J= 11.0 Hz, 1H), 4.42 (d, J= 11.7 Hz, 1H), 4.34 (d, J= 11.3 Hz, 1H), 4.30 (d, J= 11.7 Hz, 1H), 4.14 (m, 1H), 4.08–3.98 (m, 2H), 3.95–3.81 (m, 4H), 3.78 (s, 3H), 3.78 (s, 6H), 3.75 (s, 3H), 3.74 (s, 3H), 3.73–3.68 (m, 1H), 3.52–3.43 (m, 2H), 3.38 (dd, J= 9.0, 6.2 Hz, 1H), 2.33 (s, 3H), 2.04–1.88 (m, 2H), 1.71–1.39 (m, 6H), 1.36–1.16 (m, 66H), 0.89 ppm (t, J= 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 159.4, 159.3, 159.2, 137.4, 135.6, 130.9, 130.7, 129.8, 129.7, 129.6, 129.5, 129.1, 129.0, 128.5, 113.9, 113.8, 99.9, 79.9, 78.8, 78.3, 76.4, 74.6, 74.5, 73.4, 73.3, 73.2, 72.7, 71.3, 70.2, 69.8, 69.2, 55.3, 50.4, 36.8, 32.0, 30.0, 29.8, 29.7, 29.6, 29.5, 29.4, 26.2, 25.8, 22.8, 21.3, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{98}H_{148}NO_{14}$ $[M+H]^+$ 1563.0894, found 1563.0899; R_f (petroleum ether/EtOAc 70:30): 0.37.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(4-trifluoromethylbenzyl)-α-D-galactopyranosyloxy]-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14p): Following general procedure D, **13p** (0.216 g, 0.171 mmol) afforded **14p** (0.189 g, 88%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.51 (d, J= 8.3 Hz, 2H), 7.32 (d, J= 8.3 Hz, 2H), 7.28–7.20 (m, 8H), 7.16 (d, J= 8.5 Hz, 2H), 6.88–6.74 (m, 10H), 6.07 (d, J= 8.5 Hz, 1H), 4.91 (d, J= 12.2 Hz, 1H), 4.83 (d, J= 3.5 Hz, 1H), 4.73 (d, J= 11.5 Hz, 1H), 4.70 (d, J= 11.3 Hz, 1H), 4.69 (d, J= 11.5 Hz, 1H), 4.61 (t, J= 11.0 Hz, 2H), 4.55 (d, J= 11.8 Hz, 1H), 4.53 (d, J= 11.2 Hz, 1H), 4.47 (d, J= 11.6 Hz, 1H), 4.46 (d, J= 11.0 Hz, 1H), 4.37 (d, J= 11.3 Hz, 1H), 4.31 (d, J= 11.6 Hz, 1H), 4.19 (m, 1H), 4.02–3.91 (m, 3H), 3.88 (s, 1H), 3.87–3.79 (m, 2H), 3.79–3.74 (m, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 3.76 (s, 3H), 3.75 (s, 3H), 3.74 (s, 3H), 3.51–3.44 (m, 3H), 2.03–1.88 (m, 2H), 1.70–1.38 (m, 6H), 1.35–1.15 (m, 66H), 0.88 ppm (t, J= 6.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 159.5, 159.4, 159.3, 142.9, 130.9, 130.8, 160.5, 129.7, 129.6, 129.1, 128.0, 125.2 (q, J= 3.4 Hz), 113.9, 113.8, 99.6, 79.7, 78.6, 78.5, 76.2, 75.9, 74.0, 73.3, 73.2, 73.1, 72.8, 71.4, 69.7, 69.3, 68.5, 55.3, 55.2, 50.4, 36.8, 32.0, 30.0, 29.9, 29.8, 29.6, 29.5, 29.4, 26.1, 25.8, 22.8, 14.2 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ = −62.42 ppm (s, 3F); HRMS (ESI-MS) m/z: calcd for $C_{98}H_{145}F_3NO_{14}$ $[M+H]^+$ 1617.0612, found 1617.0616; R_f (petroleum ether/EtOAc 70:30): 0.34.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(4-*tert*-butylbenzyl)-α-D-galactopyranosyloxy]-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14q): Following general procedure D, **13q** (0.222 g, 0.177 mmol) afforded **14q** (0.211 g, 74%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.16 (m, 14H), 6.94–6.78 (m, 10H), 6.24 (d, J= 8.7 Hz, 1H), 4.94 (d, J= 11.2 Hz, 1H), 4.85 (d, J= 3.5 Hz, 1H), 4.76 (t, J= 11.2 Hz, 2H), 4.73 (dd, J= 17.8, 11.4 Hz, 2H), 4.63 (d, J= 11.2 Hz, 1H), 4.58 (d, J= 11.4 Hz, 1H), 4.56 (d, J= 11.2 Hz, 1H), 4.49 (d, J= 11.2 Hz, 1H), 4.44 (d, J= 11.6 Hz, 1H), 4.37 (d, J= 11.4 Hz, 1H), 4.34 (d, J= 11.4 Hz, 1H), 4.18 (m, 1H), 4.12–4.01 (m, 2H), 3.99–3.85 (m, 4H), 3.81 (s, 3H), 3.80 (s, 6H), 3.78 (s, 3H), 3.77 (s, 3H), 3.79–3.71 (m, 1H), 3.58–3.41 (m, 3H), 2.07–1.91 (m, 2H), 1.76–1.41 (m, 6H), 1.39–1.19 (m, 66H), 1.35 (s, 9H), 0.92 ppm (t, J= 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 159.4, 159.3, 159.2, 150.7, 135.6, 130.9, 130.8, 130.7, 129.8, 129.7, 129.6, 129.5, 129.1, 128.3, 125.2, 113.9, 113.8, 99.8, 79.8, 78.8, 78.1, 76.3, 74.7, 74.5, 73.4, 73.3, 73.2, 72.6, 71.3, 70.1, 69.7, 69.1, 55.3, 55.2, 50.3, 36.7, 34.6, 32.0, 31.4, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 26.2, 25.8, 22.8, 14.2 ppm; HRMS (ESI-MS) m/z: calcd for $C_{101}H_{154}NO_{14}$ $[M+H]^+$ 1605.1364, found 1605.1370; R_f (petroleum ether/EtOAc 70:30): 0.40.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-(3,4-difluorobenzyl)-α-D-galactopyranosyloxy]-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14r): Following general procedure D, **13r** (0.205 g, 0.166 mmol) afforded **14r** (0.157 g, 60%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.3–7.23 (m, 8H), 7.18 (d, J= 8.7 Hz, 2H), 7.09 (ddd, J= 11.4, 7.9, 2.0 Hz, 1H), 7.03 (dd, J= 10.4, 8.1 Hz, 1H), 6.95–6.77 (m, 11H), 6.11 (d, J= 8.5 Hz, 1H), 4.83 (d, J= 3.4 Hz, 1H), 4.81 (d, J= 11.5 Hz, 1H), 4.76 (d, J= 12.0 Hz, 1H), 4.74 (d, J= 11.3 Hz, 1H), 4.72 (d, J= 11.4 Hz, 1H), 4.64 (d, J= 10.3 Hz, 1H), 4.61 (d, J= 10.1 Hz, 1H), 4.56 (d, J= 11.3 Hz, 1H), 4.50 (d, J= 11.5 Hz, 1H), 4.48 (d, J= 10.5 Hz, 1H), 4.45 (d, J= 11.3 Hz, 1H), 4.39 (d, J= 11.3 Hz, 1H), 4.34 (d, J= 11.5 Hz, 1H), 4.20 (m, 1H), 4.05–3.92 (m, 3H), 3.91–3.82 (m, 3H), 3.81 (s, 3H), 3.80 (s, 6H), 3.79–3.75 (m, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.54–3.40 (m, 3H), 2.03–1.90 (m, 2H), 1.72–1.40 (m, 6H), 1.38–1.15 (m, 66H), 0.90 ppm (t, J= 6.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 159.5, 159.4, 159.2, 150.1 (dd, J= 247.5, 12.5 Hz), 149.7 (dd, J= 247.9, 12.9 Hz), 135.8, 130.9, 130.7, 130.5, 129.7, 129.6, 129.5, 129.1, 123.9 (dd, J= 5.7, 3.4 Hz), 117.0 (d, J= 17.2 Hz), 116.9 (d, J= 17.3 Hz), 113.9, 113.8, 99.6, 79.7, 78.6, 78.4, 76.2, 75.6, 73.6, 73.3, 73.2, 73.1, 72.9, 71.4, 69.7, 69.5, 68.5, 55.3, 55.2, 50.3, 36.8, 32.0, 30.0, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 26.1, 25.8, 22.8, 14.2 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ = −138.06 (tt, J= 12.7, 7.8 Hz, 1F), −139.64 ppm (ttd, J= 21.2, 13.7, 3.8 Hz, 1F); HRMS

(ESI-MS) *m/z*: calcd for $C_{97}H_{144}F_2NO_{14}$ $[M+H]^+$ 1585.0549, found 1585.0553; R_f (petroleum ether/EtOAc 70:30): 0.44.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-cyclopropylmethyl-α-D-galactopyranosyloxy]-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14 s): Following general procedure D, **13 s** (0.191 g, 0.165 mmol) afforded **14 s** (0.209 g, 84%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29–7.13 (m, 10H), 6.88–6.72 (m, 10H), 6.14 (d, *J* = 8.6 Hz, 1H), 4.83 (d, *J* = 3.5 Hz, 1H), 4.71 (d, *J* = 11.4 Hz, 1H), 4.69 (d, *J* = 11.0 Hz, 1H), 4.64 (dd, *J* = 16.9, 11.4 Hz, 2H), 4.56 (d, *J* = 11.1 Hz, 1H), 4.49 (d, *J* = 11.0 Hz, 2H), 4.45 (d, *J* = 11.0 Hz, 1H), 4.37 (d, *J* = 11.4 Hz, 1H), 4.34 (d, *J* = 11.2 Hz, 1H), 4.15 (m, 1H), 4.05–3.88 (m, 3H), 3.86–3.79 (m, 2H), 3.77 (s, 9H), 3.76–3.58 (m, 4H), 3.75 (s, 3H), 3.73 (s, 3H), 3.53 (dd, *J* = 8.9, 6.3 Hz, 1H), 3.46 (m, 1H), 3.29 (dd, *J* = 10.0, 6.9 Hz, 1H), 2.03–1.86 (m, 2H), 1.71–1.38 (m, 6H), 1.35–1.14 (m, 66H), 1.02 (m, 1H), 0.88 (t, *J* = 6.6 Hz, 6H), 0.50–0.39 (m, 2H), 0.21–0.05 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.8, 159.4, 159.3, 159.2, 159.1, 130.9, 130.8, 130.7, 129.8, 129.7, 129.6, 129.5, 129.1, 113.9, 113.8, 99.8, 79.9, 78.6, 78.3, 78.0, 76.3, 75.2, 73.4, 73.2, 72.4, 71.3, 70.1, 69.6, 68.9, 55.3, 50.3, 36.8, 32.0, 30.0, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 26.2, 25.8, 22.8, 14.2, 11.2, 3.4, 2.9 ppm; HRMS (ESI-MS) *m/z*: calcd for $C_{94}H_{146}NO_{14}$ $[M+H]^+$ 1513.0738, found 1513.0734; R_f (petroleum ether/EtOAc 70:30): 0.33.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-cyclobutylmethyl-α-D-galactopyranosyloxy]-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14 t): Following general procedure D, **13 t** (0.132 g, 0.112 mmol) afforded **14 t** (0.138 g, 81%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.19 (m, 10H), 6.92–6.82 (m, 8H), 6.79 (d, *J* = 8.6 Hz, 2H), 6.18 (d, *J* = 8.7 Hz, 1H), 4.83 (d, *J* = 3.6 Hz, 1H), 4.74 (d, *J* = 11.3 Hz, 1H), 4.72 (d, *J* = 11.1 Hz, 1H), 4.69 (s, 2H), 4.59 (d, *J* = 11.0 Hz, 1H), 4.55 (d, *J* = 10.8 Hz, 1H), 4.52 (d, *J* = 11.0 Hz, 1H), 4.45 (d, *J* = 10.2 Hz, 1H), 4.41 (d, *J* = 10.7 Hz, 1H), 4.38 (d, *J* = 10.5 Hz, 1H), 4.17 (m, 1H), 4.07–3.84 (m, 6H), 3.80 (s, 9H), 3.78 (s, 3H), 3.76 (s, 3H), 3.75–3.69 (m, 2H), 3.65–3.47 (m, 3H), 3.43 (dd, *J* = 9.1, 6.9 Hz, 1H), 2.55 (septet, *J* = 7.2 Hz, 1H), 2.12–1.93 (m, 4H), 1.92–1.44 (m, 10H), 1.39–1.17 (m, 66H), 0.91 ppm (t, *J* = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 159.4, 159.3, 159.2, 159.1, 131.0, 130.9, 130.7, 129.9, 129.7, 129.6, 129.5, 129.1, 113.9, 113.8, 99.8, 79.8, 78.7, 78.3, 77.9, 76.1, 75.5, 73.4, 73.2, 72.3, 71.3, 70.2, 69.5, 68.9, 55.3, 55.2, 50.3, 36.8, 35.4, 32.0, 30.0, 29.8, 29.7, 29.6, 29.5, 29.4, 29.2, 26.2, 25.8, 25.2, 24.9, 22.8, 18.7, 14.2 ppm; HRMS (ESI-MS) *m/z*: calcd for $C_{95}H_{148}NO_{14}$ $[M+H]^+$ 1527.0894, found 1527.0889; R_f (petroleum ether/EtOAc 70:30): 0.45.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(p-methoxybenzyl)-4-*O*-(2-adamantylethyl)-α-D-galactopyranosyloxy]-2-hexacosanoylamino-3,4-di-*O*-(p-methoxybenzyl)octadecane (14 u): Following general procedure D, **13 u** (0.156 g, 0.123 mmol) afforded **14 u** (0.129 g, 65%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.17 (m, 10H), 6.89–6.73 (m, 10H), 6.15 (d, *J* = 8.6 Hz, 1H), 4.80 (d, *J* = 3.6 Hz, 1H), 4.74 (d, *J* = 11.5 Hz, 2H), 4.70 (d, *J* = 11.2 Hz, 1H), 4.63 (d, *J* = 11.1 Hz, 1H), 4.56 (d, *J* = 11.2 Hz, 1H), 4.53 (d, *J* = 10.5 Hz, 1H), 4.49 (d, *J* = 10.6 Hz, 1H), 4.45 (d, *J* = 11.2 Hz, 1H), 4.39 (d, *J* = 11.7 Hz, 1H), 4.35 (d, *J* = 11.3 Hz, 1H), 4.15 (s, 1H), 4.03–3.81 (m, 6H), 3.79 (9H), 3.77 (s, 3H), 3.74 (s, 3H), 3.74–3.70 (m, 2H), 3.62–3.42 (m, 4H), 2.03–1.90 (m, 2H), 1.91 (bs, 3H), 1.74–1.55 (m, 8H), 1.54–1.36 (m, 4H), 1.46 (bs, 6H), 1.34–1.18 (m, 68H), 0.89 ppm (t, *J* = 6.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 159.4, 159.3, 159.2, 131.0, 130.9, 130.8, 129.9, 129.7, 129.6, 129.5, 129.2, 113.9, 113.8, 113.7, 99.8, 79.8, 78.7, 78.3, 76.4, 75.6, 73.4, 72.4, 71.3, 70.0, 69.4, 69.3, 68.9, 55.3, 55.2, 50.4, 44.1, 42.8, 37.2, 36.8, 32.1, 31.8, 30.0, 29.9, 29.8, 29.7, 29.6, 29.5, 28.8, 26.2, 25.8, 22.8, 14.2 ppm; HRMS (ESI-MS) *m/z*: calcd for $C_{102}H_{158}NO_{14}$ $[M+H]^+$ 1621.1677, found 1621.1675; R_f (petroleum ether/EtOAc 70:30): 0.49.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-propyl-α-D-galactopyranosyloxy]-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14 v): Following general procedure D, **13 v** (0.158 g, 0.138 mmol) afforded **14 v** (0.188 g, 91%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31–7.17 (m, 10H), 6.89–6.73 (m, 10H), 6.14 (d, *J* = 8.6 Hz, 1H), 4.82 (d, *J* = 3.6 Hz, 1H), 4.73 (d, *J* = 11.3 Hz, 1H), 4.69 (d, *J* = 10.8 Hz, 1H), 4.66 (s, 2H), 4.56 (d, *J* = 11.3 Hz, 1H), 4.53 (d, *J* = 10.9 Hz, 1H), 4.47 (t, *J* = 11.2 Hz, 2H), 4.38 (d, *J* = 10.7 Hz, 1H), 4.35 (d, *J* = 10.6 Hz, 1H), 4.15 (m, 1H), 4.02–3.88 (m, 3H), 3.87–3.81 (m, 3H), 3.77 (s, 9H), 3.77–3.70 (m, 2H), 3.76 (s, 3H), 3.73 (s, 3H), 3.63–3.50 (m, 2H), 3.49–3.43 (m, 1H), 6.84 (dt, *J* = 9.0, 6.8 Hz, 1H), 2.05–1.87 (m, 2H), 1.69–1.39 (m, 8H), 1.35–1.14 (m, 66H), 0.88 ppm (t, *J* = 7.0 Hz, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 159.4, 159.3, 159.2, 159.1, 130.9, 130.8, 129.9, 129.7, 129.6, 129.5, 129.1, 113.9, 113.8, 99.8, 79.8, 78.6, 78.3, 76.2, 75.7, 75.3, 73.4, 73.3, 72.3, 71.3, 70.1, 69.4, 68.8, 55.3, 55.2, 50.3, 36.8, 32.0, 30.0, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 26.2, 25.8, 23.5, 22.8, 14.2, 10.8 ppm; HRMS (ESI-MS) *m/z*: calcd for $C_{93}H_{146}NO_{14}$ $[M+H]^+$ 1501.0738, found 1501.0742; R_f (petroleum ether/EtOAc 70:30): 0.42.

(2*S*,3*S*,4*R*)-1-[2,3,6-Tri-*O*-(*p*-methoxybenzyl)-4-*O*-allyl-α-D-galactopyranosyloxy]-2-hexacosanoylamino-3,4-di-*O*-(*p*-methoxybenzyl)octadecane (14 w): Following general procedure D, **13 w** (0.189 g, 0.165 mmol) afforded **14 w** (0.185 g, 75%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.20 (m, 10H), 6.91–6.77 (m, 10H), 6.15 (d, *J* = 8.7 Hz, 1H), 5.90 (ddt, *J* = 17.0, 10.3, 6.0 Hz, 1H), 5.23 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.15 (dq, *J* = 10.4, 1.4 Hz, 1H), 4.85 (d, *J* = 3.6 Hz, 1H), 4.74 (t, *J* = 11.3 Hz, 2H), 4.69 (dd, *J* = 14.1, 11.4 Hz, 2H), 4.59 (d, *J* = 11.3 Hz, 1H), 4.55 (d, *J* = 11.2 Hz, 1H), 4.50 (t, *J* = 10.3 Hz, 2H), 4.42 (d, *J* = 11.5 Hz, 1H), 4.38 (d, *J* = 11.4 Hz, 1H), 4.19 (m, 1H), 4.13–3.91 (m, 4H), 3.89–3.82 (m, 3H), 3.80 (s, 9H), 3.78 (s, 3H), 3.76 (s, 3H), 3.75–3.71 (m, 2H), 3.65–3.46 (m, 3H), 2.06–1.88 (m, 2H), 1.74–1.42 (m, 6H), 1.40–1.19 (m, 66H), 0.91 ppm (t, *J* = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.8, 159.4, 159.3, 159.2, 135.4, 130.9, 130.8, 130.7, 129.8, 129.7, 129.6, 129.5, 129.1, 117.1, 113.9, 113.8, 99.7, 79.7, 78.4, 78.3, 76.4, 74.8, 74.1, 73.3, 73.2, 72.5, 71.3, 69.9, 69.4, 68.8, 55.2, 55.1, 50.3, 36.7, 32.0, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 26.1, 25.8, 22.8, 14.2 ppm; HRMS (ESI-MS) *m/z*: calcd for $C_{93}H_{144}NO_{14}$ $[M+H]^+$ 1499.0581, found 1499.0583; R_f (petroleum ether/EtOAc 70:30): 0.36.

(2*S*,3*S*,4*R*)-1-(4-*O*-Benzyl-α-D-galactopyranosyloxy)-2-hexacosanoylaminooctadecane-3,4-diol (15 a): Following general procedure E, **14 a** (0.194 g, 0.125 mmol) afforded **15 a** (0.029 g, 24%) as a white solid. ^{1}H NMR (500 MHz, [D_5]pyridine): δ = 8.12 (s, 1H), 7.62–7.52 (m, 2H), 7.35–7.19 (m, 3H), 5.91 (bs, 5H), 5.55–5.32 (m, 4H), 5.07–4.77 (m, 2H), 4.67–4.41 (m, 4H), 4.40–4.10 (m, 4H), 2.60–2.39 (m, 2H), 2.34–2.09 (m, 1H), 1.95–1.15 (m, 71H), 0.98–0.88 ppm (m, 6H); HRMS (ESI-MS) *m/z*: calcd for $C_{57}H_{106}NO_9$ $[M+H]^+$ 948.7862, found 948.7864; R_f (CH_2Cl_2/MeOH 90:10): 0.13. $[\alpha]_D^{21}$ = +47.3 (*c* = 0.23 in pyridine).

(2*S*,3*S*,4*R*)-1-[4-*O*-(3-Phenylpropyl)-α-D-galactopyranosyloxy]-2-hexacosanoylaminooctadecane-3,4-diol (15 b): Following general procedure E, **14 b** (0.175 g, 0.111 mmol) afforded **15 b** (0.030 g, 28%) as a white solid. ^{1}H NMR (500 MHz, [D_5]pyridine): δ = 8.12 (s, 1H), 7.61–7.51 (m, 2H), 7.33–7.18 (m, 3H), 5.92 (bs, 5H), 5.50–5.33 (m, 4H), 5.09–4.79 (m, 2H), 4.66–4.43 (m, 4H), 4.40–4.10 (m, 4H), 2.61–2.41 (m, 2H), 2.33–2.09 (m, 1H), 2.05–1.12 (m, 75H), 0.99–0.89 ppm (m, 6H); HRMS (ESI-MS) *m/z*: calcd for $C_{59}H_{110}NO_9$ [*M*+

H]$^+$ 976.8175, found 976.8175; R_f (CH_2Cl_2/MeOH 90:10): 0.13. $[\alpha]_D^{21} = +52.1$ ($c = 0.19$ in pyridine).

(2*S*,3*S*,4*R*)-1-[4-*O*-(4-Phenylbutyl)-α-D-galactopyranosyloxy]-2-hexacosanoylaminooctadecane-3,4-diol (15c): Following general procedure E, **14c** (0.196 g, 0.123 mmol) afforded **15c** (0.03 g, 25%) as a white solid. ^{1}H NMR (500 MHz, [D$_5$]pyridine): $\delta = 8.10$ (m, 1H), 7.63–7.56 (m, 1H), 7.34–7.17 (m, 4H), 6.23 (bs, 5H), 5.55–5.33 (m, 2H), 4.95–4.75 (m, 1H), 4.65–4.44 (m, 4H), 4.39–4.10 (m, 6H), 4.00–3.83 (m, 1H), 2.68–2.40 (m, 4H), 1.94–1.13 (m, 76H), 0.98–0.87 ppm (m, 6H); HRMS (ESI-MS) *m/z*: calcd for $C_{60}H_{112}NO_9$ $[M+H]^+$ 990.8332, found 990.8334; R_f (CH_2Cl_2/MeOH 90:10): 0.12. $[\alpha]_D^{21} = +49.1$ ($c = 0.20$ in pyridine).

(2*S*,3*S*,4*R*)-1-[4-*O*-(5-Phenylpentyl)-α-D-galactopyranosyloxy]-2-hexacosanoylaminooctadecane-3,4-diol (15d): Following general procedure E, **14d** (0.190 g, 0.118 mmol) afforded **15d** (0.041 g, 34%) as a white solid. ^{1}H NMR (500 MHz, [D$_5$]pyridine): $\delta = 7.38$–7.30 (m, 5H), 5.59–5.38 (m, 2H), 5.22 (bs, 5H), 4.92–4.80 (m, 1H), 4.65–4.50 (m, 3H), 4.40–4.16 (m, 6H), 3.94–3.78 (m, 2H), 2.63–2.42 (m, 4H), 1.95–1.16 (m, 78H), 0.98–0.89 ppm (m, 6H) (NH not observed); HRMS (ESI-MS) *m/z*: calcd for $C_{61}H_{114}NO_9$ $[M+H]^+$ 1004.8488, found 1004.8486; R_f (CH_2Cl_2/MeOH 90:10): 0.09. $[\alpha]_D^{21} = +53.1$ ($c = 0.24$ in pyridine).

(2*S*,3*S*,4*R*)-1-[4-*O*-(6-Phenylhexyl)-α-D-galactopyranosyloxy]-2-hexacosanoylaminooctadecane-3,4-diol (15e): Following general procedure E, **14e** (0.197 g, 0.122 mmol) afforded **15e** (0.036 g, 29%) as a white solid. ^{1}H NMR (500 MHz, [D$_5$]pyridine): $\delta = 7.40$–7.30 (m, 5H), 5.53–5.36 (m, 2H), 5.39 (bs, 5H), 4.92–4.79 (m, 1H), 4.64–4.45 (m, 3H), 4.39–4.17 (m, 6H), 3.97–3.73 (m, 2H), 2.66–2.40 (m, 4H), 1.96–1.13 (m, 80H), 0.99–0.87 ppm (m, 6H) (NH not observed); HRMS (ESI-MS) *m/z*: calcd for $C_{62}H_{116}NO_9$ $[M+H]^+$ 1018.8645, found 1018.8648; R_f (CH_2Cl_2/MeOH 90:10): 0.16. $[\alpha]_D^{21} = +48.9$ ($c = 0.20$ in pyridine).

(2*S*,3*S*,4*R*)-1-{4-*O*-[3-(4-Methylphenyl)propyl]-α-D-galactopyranosyloxy}-2-hexacosanoylaminooctadecane-3,4-diol (15f): Following general procedure E, **14f** (0.193 g, 0.121 mmol) afforded **15f** (0.040 g, 33%) as a white solid. ^{1}H NMR (500 MHz, [D$_5$]pyridine): $\delta = 7.17$–7.04 (m, 4H), 5.53–5.37 (m, 2H), 5.36 (bs, 5H), 4.91–4.79 (m, 1H), 4.66–4.48 (m, 3H), 4.40–4.18 (m, 6H), 4.00–3.79 (m, 2H), 2.86–2.70 (m, 2H), 2.58–2.45 (m, 2H), 2.24 (s, 3H), 2.08–1.95 (m, 2H), 1.96–1.13 (m, 72H), 0.98–0.88 ppm (m, 6H) (NH not observed); HRMS (ESI-MS) *m/z*: calcd for $C_{60}H_{112}NO_9$ $[M+H]^+$ 990.8332, found 990.8332; R_f (CH_2Cl_2/MeOH 90:10): 0.14. $[\alpha]_D^{21} = +47.8$ ($c = 0.23$ in pyridine).

(2*S*,3*S*,4*R*)-1-{4-*O*-[3-(4-Chlorophenyl)propyl]-α-D-galactopyranosyloxy}-2-hexacosanoylaminooctadecane-3,4-diol (15g): Following general procedure E, **14g** (0.196 g, 0.122 mmol) afforded **15g** (0.042 g, 34%) as a white solid. ^{1}H NMR (500 MHz, [D$_5$]pyridine): $\delta = 7.33$–7.26 (m, 2H), 7.19–7.13 (m, 2H), 5.54–5.39 (m, 2H), 5.51 (bs, 5H), 4.93–4.80 (m, 1H), 4.66–4.48 (m, 3H), 4.40–4.17 (m, 6H), 3.97–3.77 (m, 2H), 2.80–2.67 (m, 2H), 2.59–2.44 (m, 2H), 2.07–1.15 (m, 74H), 0.98–0.89 ppm (m, 6H) (NH not observed); HRMS (ESI-MS) *m/z*: calcd for $C_{59}H_{109}ClNO_9$ $[M+H]^+$ 1010.7785, found 1010.7784; R_f (CH_2Cl_2/MeOH 90:10): 0.12. $[\alpha]_D^{21} = +42.1$ ($c = 0.18$ in pyridine).

(2*S*,3*S*,4*R*)-1-{4-*O*-[3-(4-Methoxyphenyl)propyl]-α-D-galactopyranosyloxy}-2-hexacosanoylaminooctadecane-3,4-diol (15h): Following general procedure E, **14h** (0.237 g, 0.147 mmol) afforded **15h** (0.031 g, 21%) as a white solid. ^{1}H NMR (500 MHz, [D$_5$]pyridine): $\delta = 8.12$ (d, $J = 8.5$ Hz, 1H), 7.22–7.17 (m, 2H), 6.96–6.91 (m, 2H), 5.85 (bs, 4H), 5.56–5.47 (m, 1H), 5.41 (d, $J = 2.9$ Hz, 1H), 4.92 (d, $J = 7.8$ Hz, 1H × 0.5), 4.84 (d, $J = 8.5$ Hz, 1H × 0.5), 4.67–4.42 (m, 4H), 4.39–4.21 (m, 5H), 4.20–4.14 (m, 1H), 4.02–3.86 (m, 2H), 3.70 (s, 3H), 2.85–2.70 (m, 2H), 2.61–2.40 (m, 2H), 2.09–1.97 (m, 2H), 1.95–1.68 (m, 4H), 1.65–1.16 (m, 68H), 0.98–0.90 ppm (m, 6H); HRMS (ESI-MS) *m/z*: calcd for $C_{60}H_{112}NO_{10}$ $[M+H]^+$ 1006.8281, found 1006.8279; R_f (CH_2Cl_2/MeOH 90:10): 0.18. $[\alpha]_D^{21} = +46.6$ ($c = 0.24$ in pyridine).

(2*S*,3*S*,4*R*)-1-{4-*O*-[3-(3,4-Dichlorophenyl)propyl]-α-D-galactopyranosyloxy}-2-hexacosanoylaminooctadecane-3,4-diol (15i): Following general procedure E, **14i** (0.094 g, 0.057 mmol) afforded **15i** (0.017 g, 28%) as a white solid. ^{1}H NMR (500 MHz, [D$_5$]pyridine): $\delta = 8.10$ (d, $J = 8.5$ Hz, 1H), 7.43–7.33 (m, 2H), 7.10–7.02 (m, 1H), 5.56–5.42 (m, 1H), 5.49 (bs, 5H), 4.93–4.82 (m, 1H), 4.69–4.48 (m, 3H), 4.46–4.16 (m, 7H), 3.98–3.84 (m, 2H), 2.85–2.64 (m, 2H), 2.59–2.41 (m, 2H), 2.01–1.70 (m, 6H), 1.62–1.23 (m, 68H), 0.98–0.88 ppm (m, 6H); HRMS (ESI-MS) *m/z*: calcd for $C_{59}H_{108}Cl_2NO_9$ $[M+H]^+$ 1044.7396, found 1044.7394; R_f (CH_2Cl_2/MeOH 90:10): 0.07. $[\alpha]_D^{21} = +46.2$ ($c = 0.22$ in pyridine).

(2*S*,3*S*,4*R*)-1-{4-*O*-[3-(4-Fluorophenyl)propyl]-α-D-galactopyranosyloxy}-2-hexacosanoylaminooctadecane-3,4-diol (15j): Following general procedure E, **14j** (0.116 g, 0.0727 mmol) afforded **15j** (0.005 g, 7%) as a white solid. ^{1}H NMR (300 MHz, [D$_5$]pyridine): $\delta = 8.07$ (d, $J = 8.5$ Hz, 1H), 7.21–7.15 (m, 2H), 7.08–6.99 (m, 2H), 4.97–4.67 (m, 13H), 4.65–4.50 (m, 1H), 4.36–4.19 (m, 4H), 3.97–3.82 (m, 1H), 2.84–2.68 (m, 2H), 2.44 (t, $J = 7.5$ Hz, 2H), 2.09–1.92 (m, 2H), 1.88–1.74 (m, 1H), 1.53–1.25 (m, 71H), 0.93 ppm (t, $J = 6.6$ Hz, 6H); ^{19}F NMR (282 MHz, [D$_5$]pyridine): $\delta = -118.19$ ppm (m, 1F); HRMS (ESI-MS) *m/z*: calcd for $C_{59}H_{109}FNO_9$ $[M+H]^+$ 994.8081, found 994.8080; R_f (CH_2Cl_2/MeOH 90:10): 0.22. $[\alpha]_D^{21} = +56.4$ ($c = 0.13$ in pyridine).

(2*S*,3*S*,4*R*)-1-{4-*O*-[3-(4-Trifluoromethylphenyl)propyl]-α-D-galactopyranosyloxy}-2-hexacosanoylaminooctadecane-3,4-diol (15k): Following general procedure E, **14k** (0.170 g, 0.103 mmol) afforded **15k** (0.030 g, 28%) as a white solid. ^{1}H NMR (300 MHz, [D$_5$]pyridine): $\delta = 7.58$ (d, $J = 8.1$ Hz, 2H), 7.35 (d, $J = 7.9$ Hz, 2H), 6.05 (bs, 7H), 5.60–5.38 (m, 1H), 4.69–4.42 (m, 3H), 4.41–4.13 (m, 6H), 4.02–3.84 (m, 2H), 2.94–2.72 (m, 2H), 2.64–2.42 (m, 2H), 2.10–1.70 (m, 6H), 1.61–1.20 (m, 68H), 0.99–0.90 ppm (m, 6H) (NH not observed); ^{19}F NMR (282 MHz, [D$_5$]pyridine): $\delta = -61.68$ ppm (s, 3F); HRMS (ESI-MS) *m/z*: calcd for $C_{60}H_{109}F_3NO_9$ $[M+H]^+$ 1044.8049, found 1044.8043; R_f (CH_2Cl_2/MeOH 90:10): 0.20. $[\alpha]_D^{21} = +43.8$ ($c = 0.25$ in pyridine).

(2*S*,3*S*,4*R*)-1-{4-*O*-[3-(4-*tert*-Butylphenyl)propyl]-α-D-galactopyranosyloxy}-2-hexacosanoylaminooctadecane-3,4-diol (15l): Following general procedure E, **14l** (0.169 g, 0.103 mmol) afforded **15l** (0.023 g, 22%) as a white solid. ^{1}H NMR (300 MHz, CD_3OD): $\delta = 7.41$–7.27 (m, 4H), 4.98–4.86 (m, 2H), 4.85 (d, $J = 3.5$ Hz, 1H), 4.65 (bs, 5H), 4.12 (dd, $J = 10.7$, 2.7 Hz, 1H), 3.98–3.74 (m, 7H), 3.73–3.51 (m, 4H), 3.45 (dt, $J = 9.5$, 2.6 Hz, 1H), 2.39 (t, $J = 7.3$ Hz, 2H), 1.71–1.19 (m, 83H), 0.90 ppm (t, $J = 6.7$ Hz, 6H); HRMS (ESI-MS) *m/z*: calcd for $C_{63}H_{118}NO_9$ $[M+H]^+$ 1032.8801, found 1032.8811; R_f (CH_2Cl_2/MeOH 90:10): 0.19. $[\alpha]_D^{21} = +45.1$ ($c = 0.21$ in methanol).

(2*S*,3*S*,4*R*)-1-[4-*O*-(3,4-Dichlorobenzyl)-α-D-galactopyranosyloxy]-2-hexacosanoylaminooctadecane-3,4-diol (15m): Following general procedure E, **14m** (0.186 g, 0.115 mmol) afforded **15m** (0.034 g, 29%) as a white solid. ^{1}H NMR (300 MHz, CD_3OD): $\delta = 7.57$ (d, $J = 1.9$ Hz, 1H), 7.46 (d, $J = 8.2$ Hz, 1H), 7.30 (dd, $J = 8.2$, 1.9 Hz, 1H), 4.99–4.88 (m, 2H), 4.86 (d, $J = 3.5$ Hz, 1H), 4.65 (bs, 5H), 4.13 (dd, $J = 10.9$, 2.8 Hz, 1H), 3.98–3.77 (m, 5H), 3.75–3.52 (m, 4H), 3.46 (dt, $J = 9.6$, 2.7 Hz, 1H), 2.39 (t, $J = 7.3$ Hz, 2H), 1.72–1.21 (m, 72H), 0.90 ppm (t, $J = 6.6$ Hz, 6H); HRMS (ESI-MS) *m/z*: calcd for

$C_{57}H_{104}Cl_2NO_9$ $[M+H]^+$ 1016.7083, found 1016.7082; R_f (CH_2Cl_2/MeOH 90:10): 0.14. $[\alpha]_D^{21} = +42.3$ ($c = 0.26$ in methanol).

(2*S*,3*S*,4*R*)-1-[4-*O*-(4-Fluorobenzyl)-α-D-galactopyranosyloxy]-2-hexacosanoylaminooctadecane-3,4-diol (15n): Following general procedure E, **14n** (0.207 g, 0.132 mmol) afforded **15n** (0.029 g, 23%) as a white solid. ^{1}H NMR (300 MHz, CD_3OD): $\delta = 7.45–7.36$ (m, 2H), 7.09–6.99 (m, 2H), 4.99–4.86 (m, 2H), 4.85 (d, $J = 3.3$ Hz, 1H), 4.66 (bs, 5H), 4.11 (dd, $J = 10.8$, 2.9 Hz, 1H), 3.94–3.76 (m, 5H), 3.73–3.50 (m, 4H), 3.41 (dt, $J = 9.4$, 2.8 Hz, 1H), 2.39 (t, $J = 7.4$ Hz, 2H), 1.72–1.21 (m, 72H), 0.90 ppm (t, $J = 6.7$ Hz, 6H); ^{19}F NMR (282 MHz, CD_3OD): $\delta = -117.26$ ppm (tt, $J = 8.4$, 4.7 Hz, 1F); HRMS (ESI-MS) *m/z*: calcd for $C_{57}H_{105}FNO_9$ $[M+H]^+$ 966.7768, found 966.7773; R_f (CH_2Cl_2/MeOH 90:10): 0.11. $[\alpha]_D^{21} = +41.4$ ($c = 0.25$ in methanol).

(2*S*,3*S*,4*R*)-1-[4-*O*-(4-Methylbenzyl)-α-D-galactopyranosyloxy]-2-hexacosanoylaminooctadecane-3,4-diol (15o): Following general procedure E, **14o** (0.163 g, 0.104 mmol) afforded **15o** (0.018 g, 18%) as a white solid. ^{1}H NMR (300 MHz, CD_3OD): $\delta = 7.31–7.21$ (m, 2H), 7.18–7.10 (m, 2H), 4.98–4.80 (m, 3H), 4.65 (bs, 5H), 4.12 (dd, $J = 11.0$, 2.9 Hz, 1H), 3.92–3.74 (m, 5H), 3.71–3.47 (m, 5H), 2.39 (t, $J = 7.5$ Hz, 2H), 2.32 (s, 3H), 1.71–1.19 (m, 72H), 0.90 ppm (t, $J = 6.7$ Hz, 6H); HRMS (ESI-MS) *m/z*: calcd for $C_{58}H_{108}NO_9$ $[M+H]^+$ 962.8019, found 962.8010; R_f (CH_2Cl_2/MeOH 90:10): 0.11. $[\alpha]_D^{21} = +41.0$ ($c = 0.18$ in methanol).

(2*S*,3*S*,4*R*)-1-[4-*O*-(4-Trifluoromethylbenzyl)-α-D-galactopyranosyloxy]-2-hexacosanoylaminooctadecane-3,4-diol (15p): Following general procedure E, **14p** (0.189 g, 0.117 mmol) afforded **15p** (0.025 g, 21%) as a white solid. ^{1}H NMR (300 MHz, CD_3OD): $\delta = 7.65–7.53$ (m, 4H), 5.09–4.91 (m, 2H), 4.86 (d, $J = 3.4$ Hz, 1H), 4.65 (bs, 5H), 4.12 (dd, $J = 10.9$, 2.6 Hz, 1H), 3.99–3.79 (m, 5H), 3.76–3.51 (m, 4H), 3.46–3.38 (m, 1H), 2.39 (t, $J = 7.4$ Hz, 2H), 1.73–1.18 (m, 72H), 0.90 ppm (t, $J = 6.6$ Hz, 6H); ^{19}F NMR (282 MHz, CD_3OD): $\delta = -64.01$ ppm (s, 3F); HRMS (ESI-MS) *m/z*: calcd for $C_{58}H_{105}F_3NO_9$ $[M+H]^+$ 1016.7736, found 1016.7739; R_f (CH_2Cl_2/MeOH 90:10): 0.17. $[\alpha]_D^{21} = +43.7$ ($c = 0.22$ in methanol).

(2*S*,3*S*,4*R*)-1-[4-*O*-(4-*tert*-Butylbenzyl)-α-D-galactopyranosyloxy]-2-hexacosanoylaminooctadecane-3,4-diol (15q): Following general procedure E, **14q** (0.211 g, 0.131 mmol) afforded **15q** (0.027 g, 20%) as a white solid. ^{1}H NMR (300 MHz, CD_3OD): $\delta = 7.41–7.27$ (m, 4H), 4.98–4.86 (m, 2H), 4.85 (d, $J = 3.5$ Hz, 1H), 4.65 (bs, 5H), 4.12 (dd, $J = 10.7$, 2.7 Hz, 1H), 3.98–3.74 (m, 5H), 3.73–3.51 (m, 4H), 3.45 (dt, $J = 9.5$, 2.6 Hz, 1H), 2.39 (t, $J = 7.3$ Hz, 2H), 1.71–1.19 (m, 81H), 0.90 ppm (t, $J = 6.7$ Hz, 6H); HRMS (ESI-MS) *m/z*: calcd for $C_{61}H_{114}NO_9$ $[M+H]^+$ 1004.8488, found 1004.8490; R_f (CH_2Cl_2/MeOH 90:10): 0.24. $[\alpha]_D^{21} = +44.2$ ($c = 0.22$ in methanol).

(2*S*,3*S*,4*R*)-1-[4-*O*-(3,4-Difluorobenzyl)-α-D-galactopyranosyloxy]-2-hexacosanoylaminooctadecane-3,4-diol (15r): Following general procedure E, **14r** (0.157 g, 0.0990 mmol) afforded **15r** (0.033 g, 34%) as a white solid. ^{1}H NMR (300 MHz, CD_3OD): $\delta = 7.38–7.27$ (m, 1H), 7.25–7.12 (m, 2H), 4.99–4.87 (m, 2H), 4.8 (d, $J = 3.5$ Hz, 1H), 4.65 (bs, 5H), 4.13 (dd, $J = 10.7$, 2.5 Hz, 1H), 3.98–3.76 (m, 5H), 3.72–3.52 (m, 4H), 3.45 (dt, $J = 9.6$, 2.7 Hz, 1H), 2.39 (t, $J = 7.2$ Hz, 2H), 1.73–1.19 (m, 72H), 0.90 ppm (t, $J = 6.8$ Hz, 6H); ^{19}F NMR (282 MHz, CD_3OD): $\delta = -141.09$ (m, 1F), -142.72 ppm (m, 1F); HRMS (ESI-MS) *m/z*: calcd for $C_{57}H_{104}F_2NO_9$ $[M+H]^+$ 984.7674, found 984.7670; R_f (CH_2Cl_2/MeOH 90:10): 0.14. $[\alpha]_D^{21} = +41.4$ ($c = 0.27$ in methanol).

(2*S*,3*S*,4*R*)-1-(4-*O*-Cyclopropylmethyl-α-D-galactopyranosyloxy)-2-hexacosanoylaminooctadecane-3,4-diol (15s): Following general procedure E, **14s** (0.209 g, 0.138 mmol) afforded **15s** (0.019 g, 15%) as a white solid. ^{1}H NMR (300 MHz, CD_3OD): $\delta = 4.99–4.82$ (m, 2H), 4.65 (bs, 5H), 4.12 (dd, $J = 10.7$, 2.8 Hz, 1H), 3.93–3.64 (m, 7H), 3.61–3.49 (m, 2H), 3.47–3.37 (m, 2H), 2.39 (t, $J = 7.2$ Hz, 2H), 1.72–1.22 (m, 72H), 1.10 (m, 1H), 0.90 (t, $J = 6.6$ Hz, 6H), 0.54–0.45 (m, 2H), 0.26–0.18 ppm (m, 2H); HRMS (ESI-MS) *m/z*: calcd for $C_{54}H_{106}NO_9$ $[M+H]^+$ 912.7862, found 912.7857; R_f (CH_2Cl_2/MeOH 90:10): 0.09. $[\alpha]_D^{21} = +33.1$ ($c = 0.24$ in methanol).

(2*S*,3*S*,4*R*)-1-(4-*O*-Cyclobutylmethyl-α-D-galactopyranosyloxy)-2-hexacosanoylaminooctadecane-3,4-diol (15t): Following general procedure E, **14t** (0.138 g, 0.0900 mmol) afforded **15t** (0.019 g, 23%) as a white solid. ^{1}H NMR (300 MHz, CD_3OD): $\delta = 4.99–4.81$ (m, 2H), 4.65 (bs, 5H), 4.12 (dd, $J = 10.6$, 2.7 Hz, 1H), 3.92–3.77 (m, 4H), 3.75–3.62 (m, 4H), 3.59–3.46 (m, 3H), 2.66–2.52 (m, 2H), 2.39 (t, $J = 7.2$ Hz, 2H), 2.13–1.99 (m, 2H), 1.94–1.73 (m, 3H), 1.69–1.20 (m, 72H), 0.90 ppm (t, $J = 6.7$ Hz, 6H); HRMS (ESI-MS) *m/z*: calcd for $C_{55}H_{108}NO_9$ $[M+H]^+$ 926.8019, found 926.8016; R_f (CH_2Cl_2/MeOH 90:10): 0.17. $[\alpha]_D^{21} = +31.7$ ($c = 0.23$ in methanol).

(2*S*,3*S*,4*R*)-1-[4-*O*-(2-Adamantylethyl)-α-D-galactopyranosyloxy]-2-hexacosanoylaminooctadecane-3,4-diol (15u): Following general procedure E, **14u** (0.129 g, 0.0795 mmol) afforded **15u** (0.025 g, 31%) as a white solid. ^{1}H NMR (300 MHz, CD_3OD): $\delta = 4.95$ (td, $J = 8.5$, 3.2 Hz, 1H), 4.83 (d, $J = 3.6$ Hz, 1H), 4.65 (bs, 5H), 4.11 (dd, $J = 10.8$, 2.9 Hz, 1H), 3.96–3.49 (m, 12H), 3.41 (dt, $J = 9.4$, 2.8 Hz, 1H), 2.39 (t, $J = 7.3$ Hz, 2H), 1.93 (bs, 3H), 1.79–1.64 (m, 8H), 1.59–1.54 (m, 4H), 1.44–1.23 (m, 72H), 0.90 ppm (t, $J = 6.7$ Hz, 6H); HRMS (ESI-MS) *m/z*: calcd for $C_{62}H_{118}NO_9$ $[M+H]^+$ 1020.8801, found 1020.8806; R_f (CH_2Cl_2/MeOH 90:10): 0.18. $[\alpha]_D^{21} = +37.1$ ($c = 0.19$ in methanol).

(2*S*,3*S*,4*R*)-1-(4-*O*-propyl-α-D-Galactopyranosyloxy)-2-hexacosanoylaminooctadecane-3,4-diol (15v): Following general procedure E, **14v** (0.188 g, 0.125 mmol) afforded **15v** (0.015 g, 13%) as a white solid. ^{1}H NMR (300 MHz, CD_3OD): $\delta = 4.95$ (td, $J = 8.0$, 2.8 Hz, 1H), 4.84 (d, $J = 3.5$ Hz, 1H), 4.65 (bs, 5H), 4.12 (dd, $J = 10.6$, 2.6 Hz, 1H), 3.92–3.47 (m, 12H), 3.41 (dt, $J = 9.2$, 2.2 Hz, 1H), 2.39 (t, $J = 7.1$ Hz, 2H), 1.72–1.51 (m, 4H), 1.44–1.18 (m, 68H), 0.98–0.84 ppm (m, 9H); HRMS (ESI-MS) *m/z*: calcd for $C_{53}H_{106}NO_9$ $[M+H]^+$ 900.7862, found 900.7859; R_f (CH_2Cl_2/MeOH 90:10): 0.06. $[\alpha]_D^{21} = +34.8$ ($c = 0.22$ in methanol).

(2*S*,3*S*,4*R*)-1-(4-*O*-allyl-α-D-Galactopyranosyloxy)-2-hexacosanoylaminooctadecane-3,4-diol (15w): Following general procedure E, **14w** (0.185 g, 0.123 mmol) afforded **15w** (0.024 g, 22%) as a white solid. ^{1}H NMR (300 MHz, CD_3OD): $\delta = 6.04–5.88$ (m, 1H), 5.32–5.20 (m, 1H), 5.17–5.08 (m, 1H), 4.94 (td, $J = 8.5$, 3.1 Hz, 1H), 4.85 (d, $J = 3.5$ Hz, 1H), 4.65 (bs, 5H), 4.40–4.29 (m, 1H), 4.22–4.05 (m, 2H), 3.93–3.62 (m, 7H), 3.61–3.42 (m, 2H), 2.39 (t, $J = 7.2$ Hz, 2H), 1.72–1.20 (m, 72H), 0.90 ppm (t, $J = 6.7$ Hz, 6H); HRMS (ESI-MS) *m/z*: calcd for $C_{53}H_{104}NO_9$ $[M+H]^+$ 898.7706, found 898.7703; R_f (CH_2Cl_2/MeOH 90:10): 0.19. $[\alpha]_D^{21} = +32.3$ ($c = 0.23$ in methanol).

Bioassays

In vivo mice experiments. Each glycolipid was dissolved in DMSO (Sigma–Aldrich) at 1 mg mL^{-1}, put in a hot bath (80 °C) for 20 min and then sonicated for another 20 min at 80 °C. Next, each glycolipid was batched out in vials (11 μL per vial). Before the in vivo experiment, each vial was provided with 1089 μL of PBS. The vials were put in a hot bath (80 °C) for 20 min and then sonicated for another 20 min at 80 °C. Next, 500 μL (5 μg of each glycolipid; 2.0×10^{-4} g kg^{-1}) of the solutions were injected intraperitoneally into male C57BL/6 mice (purchased from Harlan, each weighing 25 ± 1 g). Each glycolipid was injected in eight mice, with 5 min in be-

tween each injection, to correct for delays that might occur during blood collection.

After 4 h (IL-4) or 16 h (IFN-γ), blood was collected from the mice through retro-orbital blood collection using a microhematocrit blood tube. The serum was separated and stored at −20 °C for ELISA. ELISA was performed following a protocol that was previously reported.[27] Briefly, purified and biotinylated anti-mouse IFN-γ and IL-4 antibodies were obtained from eBiosciences and the ELISA assay was performed according to manufacturer's instructions, using 0.1 M bicarbonate ($NaHCO_3/Na_2CO_3$; pH 9.5) as coating buffer and 0.1% casein as blocking agent. Serum IL-4 and IFN-γ concentrations were calculated by means of standard curves obtained for each cytokine.

All animal experiments were approved by the local Ethics Committee of Laboratory Animal Welfare of Ghent University (reference ECD15/75). Mice used for the experiments were between 5 and 12 weeks old.

Protein expression (mCD1 d): Soluble mCD1d-β2m heterodimeric protein was expressed in sf9-cells and purified as previously reported.[36]

Protein expression (Vα14- and Vβ8.2-chain): Vα14- and Vβ8.2-chain were expressed separately in *E. coli* by co-transfection with the p^{ET}22b and p^{ET}30a plasmids, respectively. The isolated inclusion bodies were dissolved in 50 mM Tris·HCl, 5 mM EDTA, 2 mM DTT, and 6 M guanidine-HCl, pH 7.0, and stored at −80 °C.

Vα14Vβ8.2-mTCR refolding. The mTCR was refolded according to a literature protocol, with minor adaptations.[36] 32 mg of Vα14-chain and 48 mg of Vβ8.2-chain (both reduced) were thawed, mixed, and pulsed with 1 mM DTT. After incubation at 22 °C for 5 min, the mixture was added dropwise to 0.8 L of refolding buffer (50 mM Tris·HCl, 400 mM l-arginine, 5 M urea, 2 mM EDTA, 5 mM reduced glutathione, 0.5 mM oxidized glutathione, 0.2 mM PMSF, pH 8.0) under permanent slow stirring at 4 °C. After 16 h, another 32 mg of Vα14-chain and 32 mg of Vβ8.2-chain (both reduced) were thawed, mixed, pulsed with 1 mM DTT and added to the solution in a dropwise fashion. Stirring was continued for an additional 8 h. The refolding mixture was then dialyzed using 12 000–14 000 MWCO dialysis tubing (Fisherbrand, Fisher), against 18 L of dialysis buffer A (50 mM Tris·HCl, 100 mM urea, pH 8.0) for 24 h, followed by two other dialyses against fresh dialysis buffer B (10 mM Tris·HCl, pH 8.0), each for 24 h.

The dialysis tubing was emptied in a large vessel and DEAE Sepharose™ Fast Flow beads (GE Healthcare, 6 mL of resin slurry containing 45–165 μm spherical beads, washed twice with 15 mL of 10 mM Tris·HCl, pH 8.0) were added to the dialyzed refolding mix and stirred for 3 h at 4 °C. The DEAE beads were collected on a glass Econo-column (Bio-Rad) and washed with 20 mL of 10 mM Tris·HCl, pH 8.0. The refolded TCR was eluted with 100 mM NaCl in 10 mM Tris·HCl, pH 8.0 (2×5 mL), diluted 5-fold with 10 mM Tris·HCl, pH 8.0, and injected into a MonoQ 5/50 GL ion-exchange column (GE Healthcare). The TCR was eluted using a linear gradient (5–30% NaCl over 35 mL). TCR-containing fractions were pooled and the protein concentration was determined using a DU 730 UV/Vis spectrophotometer (Beckman Coulter).

Surface plasmon resonance (SPR) studies. Glycolipids were dissolved in DMSO at 80 °C at a concentration of 3 mg mL^{-1}. mCD1d was incubated overnight at RT with a 24-molar excess of each glycolipid and 0.01 mM tyloxapol. SPR studies were performed at 25 °C on a Biacore T200 (Biacore) instrument running on a HBS buffer (10 mM HEPES pH 7.5, 150 mM NaCl, 3 mM EDTA, 0.05% *v/v* Tween-20). About 800–1000 RU of biotinylated mCD1d, preloaded at room temperature with the glycolipids, were immobilized on a streptavidin-coupled sensor CAP chip (Biacore). Equilibrium affinity was determined by injecting increasing concentrations of Vα14Vβ8.2-mTCR (25, 50, 100, 200 and 400 nM in HBS buffer) at 30 μL min^{-1}. The TCR was injected for a 3-min association and a final 10-min dissociation using the single-cycle kinetic option. Data were processed by means of the BIAevaluation software (version 4.1, Biacore).

Synthesis and purification of mCD1 d–glycolipid–TCR complexes. Glycolipids were dissolved in DMSO at 80 °C at a concentration of 3 mg mL^{-1}. mCD1d (1 mg, 0.66 mg mL^{-1}) was combined with 24-molar excess of glycolipid (150 μL, 3 mg mL^{-1}) and 350 μL HBS buffer (10 mM HEPES pH 7.5, 150 mM NaCl). Following overnight incubation at 22 °C, 0.2 mg of refolded Vα14Vβ8.2-TCR was added and the solution was incubated for 1 h at RT. The complex solution was transferred to a 30 000 MWCO filter tube (Sartorius AG) and concentrated at 4 °C (3800×*g*) to a final volume of ±500 μL. The resulting suspension was transferred to a vial and centrifuged at 4 °C (25 000×*g*) for 10 min. The supernatant was purified using a Superdex S200 10/300 GL size-exclusion column (GE Healthcare), equilibrated in HBS buffer (10 mM HEPES pH 7.5, 150 mM NaCl). The fractions containing the mCD1d–glycolipid–TCR complex were pooled and concentrated at 4 °C to a final volume of 25–40 μL. The concentration of the ternary complex was determined using a DU 730 UV/Vis spectrophotometer (Beckman Coulter).

Crystallography

Crystallization of mCD1 d–glycolipid–TCR complexes. Crystals were grown at 22.3 °C by sitting drop vapor diffusion, while mixing 0.5–1 μL of ternary complex solution with 0.5–1 μL of precipitate. All CD1d–glycolipid–TCR complexes were crystallized in conditions contained within the PEG/Ion-screen (Hampton Research) and needed no further optimization. **15 a** and **15 o** were crystallized in 0.2 M ammonium tartrate dibasic, 20% PEG 4000 (PEG/Ion 1, D2); **15 m**, **15 p**, **15 q**, **15 s**, **15 w** and **15 x** were crystallized in 0.1 M sodium malonate pH 4.0, 12% PEG 3350 (PEG/Ion 1, E1). Single crystals were harvested using a CryoLoop (Hampton Research) and flash cooled with liquid nitrogen (−196 °C) in the same precipitate mixture containing 20% *v/v* glycerol. Samples were stored and shipped in liquid nitrogen.

Protein XRD data collection and refinement. Diffraction data were collected at the Stanford Synchrotron Radiation Laboratory (SSRL), beamline 9-2. All structures were initially refined with REFMAC5. Electron density and difference density maps, all σA-weighted, were inspected and the models were further refined using CCP4i and Coot.

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Conflict of interest

The authors declare no conflict of interest.

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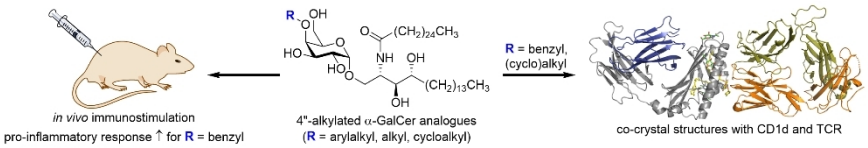

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4"-O-Alkylated α-Galactosylceramide Analogues as *i*NKT-Cell Antigens: Synthetic, Biological, and Structural Studies

Pro-inflammatory cytokine polarization: Introducing (aryl)alkyl groups at the 4"-position of the semi-synthetic glycolipid α-GalCer retains immunostimulating capacity in mice. Introduction of benzyl-type modifications induces a pro-inflammatory cytokine profile, which may eventually lead to therapeutically useful compounds for the treatment of cancer and autoimmune diseases, or as vaccine adjuvants.