Synthesis and Evaluation of Sphingolipid Analogues
Modification of the Hydroxy Group at C(1) of 7-Oxasphingosine, and of the Hydroxy Group at C(1) and the Amide Group of 7-Oxaceramides

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The analogues **7**–**9** of 7-oxaceramide and 7-oxasphingosine were synthesized from the known azidosphingosine **21**. The 1,4-disubstituted 1,2,3-triazole analogues **10**–**16** of ceramides were synthesized by the click reaction of the known azide **24**. None of the analogues **7**–**15** was active as inhibitor of SPHK type 1 and of acid sphingomyelinase, whereas **16** is a weak inhibitor of SPHK1. Triazoles **10**, **11**, and **15** did not inhibit ceramide phosphorylation by CerK, and none of **7**, **8**, and **10**–**15** activated invariant natural killer T (iNKT) cell clones when presented by human CD1d-transfected antigen-presenting cells (APC) or by plate-bound human CD1d [55]. Triazoles **14** and **15** prevent binding of α-galactosylceramide (α-GalCer) to plate-bound human CD1d and subsequent T-cell response to α-GalCer. Only **15** reduced activation by α-GalCer significantly and independently of the cytokine measured.

Introduction. – The ability of sphingolipids and glycosphingolipids to modulate apoptosis [1–7] and immune responses [8–13] is likely to depend on specific receptor interactions with both the polar head group and the lipid tails of the sphingosine and fatty acid moieties. The exploration of these interactions is based on crystal-structure analyses of receptors in complex with the lipids [14][15], and on the synthesis and biological evaluation of analogues [16]. We disclosed the synthesis of a few analogues of sphingosine (Sph; **1**) and ceramide (Cer; **2**; *Fig. 1*) *viz.*, 7-oxasphingosine (**3**), the corresponding ceramide **4**, the thioamide **5**, and the *N*-methyl Cer **6** [17]. 7-Oxasphingosine (**3**) was synthesized to facilitate the incorporation of modified lipid moieties and the exploration of their interaction with receptors. The analogues **5** and **6** were prepared to investigate the H-bond donor and acceptor roles of the amide function in Cer, as thioamide **5** was expected to be a weaker H-bond acceptor than Cer [18], while *N*-methylation lowers the energy difference between the (*E*)- and (*Z*)-isomers [19] and offsets the H-bond-donating properties of the amide moiety.

The apoptosis-inducing properties of the analogues **3**–**6** were compared to those of Sph **1** and Cer **2** using a human neuroblastoma (SK-N-BE) and a murine-promyelocyte-derived (32d) cell line. In both SK-N-BE and 32d cells, 7-oxasphingosine (**3**) exhibited toxicity equal to that of sphingosine, even in the presence of *N*,*N*-dimethylsphingosine. Compounds **4**–**6** do not differ in their effect on the viability of

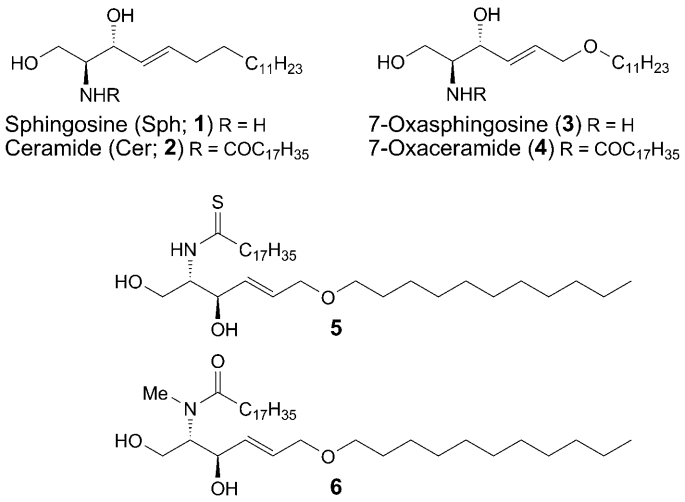


Fig. 1. *Structures of sphingosine* **1**, *ceramide* **2**, *7-oxasphingosine* **3**, *7-oxaceramide* **4**, *the thioamide* **5**, *and the* N-*methylceramide* **6**

cells and in their ability to trigger cell proliferation. However, in the presence of *N*,*N*-dimethylsphingosine (DMS), an inhibitor of sphingosine kinase (SPHK), Cer **2** showed stronger effects than the thio-ceramide **5** in 32d cells, while **5** was efficacious in SK-N-BE cells, where it showed an IC_{50} value of 3 nM, as compared to 100 nM for Cer. The *N*-methylamide **6** behaved similarly to Cer **2** [17]. The data suggest that there is neither a major difference in the degradation of Cer and its 7-oxa- and *N*-methyl analogues to the respective Sph derivatives, nor in the recognition of the resulting Sph and oxasphingosine by SPHK. The greater potency shown by the thio-Cer **5** in SK-N-BE cells devoid of SPHK activity (as the result of DMS treatment) suggests that **5** may have a higher affinity than Cer to death effectors, such as ion channels, protein kinase, and phosphatase, or a decreased capacity to be phosphorylated by either ceramide kinase or SPHK.

We wished to further modify the H-bond-accepting and -donating properties of Cer and Sph, and considered the urea **7**, the sulfonamide **8**, the Sph analogue **9**, and the triazoles **10**–**16** to be of interest (*Fig. 2*).

The urea derivative **7** was expected to be a better H-bond acceptor [20] and a poorer H-bond donor than the corresponding amide, considering that ureas have higher pK_a values (*ca.* 26–27) than amides (*ca.* 20–23) [20][21], while the biological effects of replacing a CH_2 by an NH group remained to be explored. The lower pK_a values of sulfonamides (*ca.* 12) [22] should make **8** a better H-bond donor than the corresponding amide. The sulfonyl group is a poor H-bond acceptor as compared to the C=O group [23], but the change of geometry may be more significant, as the tetrahedral S- and the pyramidal N-atoms of sulfonamides [24] differ significantly from the trigonal geometry of the amide moiety [25].

In the 1-(dimethylamino)-deoxy-7-oxasphingosine (**9**), the C(1)–OH group of Sph is replaced with a basic functionality; the corresponding ammonium salt may act as

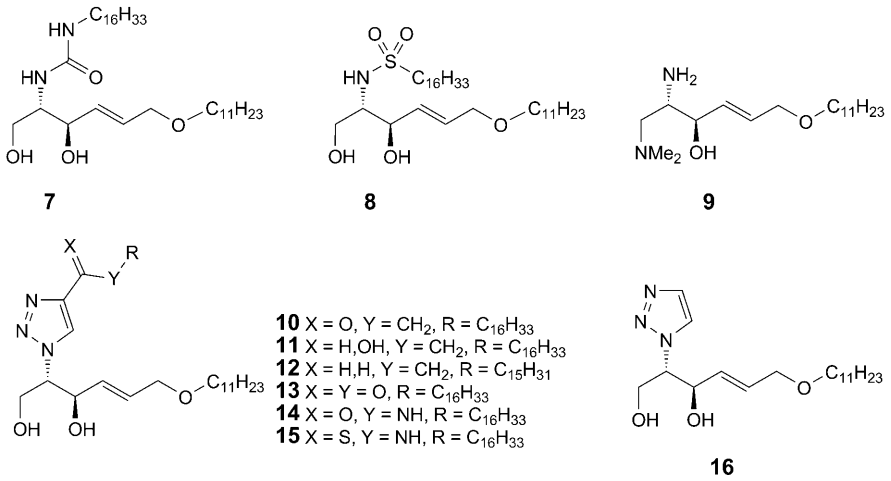


Fig. 2. *Analogues of 7-oxasphingosine and 7-oxaceramide with a modified C(1)–OH, or amide moiety*

a good H-bond donor, but the analogue can no longer be phosphorylated at O–C(1).

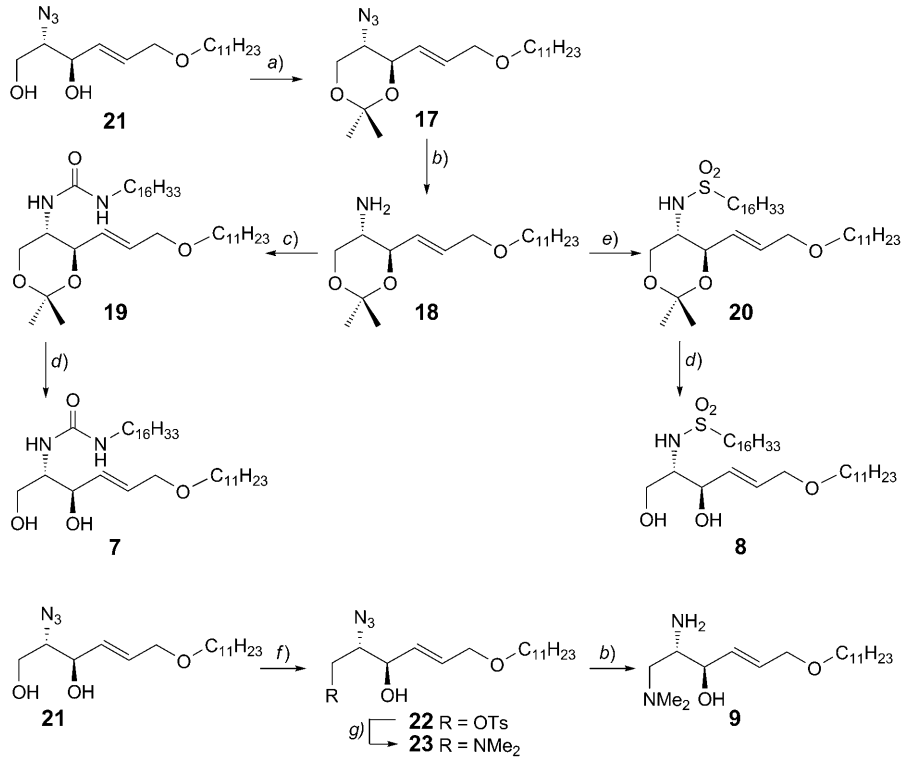
1,2,3-Triazoles are non-hydrolysable bioisosters of amides [26][27], readily obtained by the click reaction [26–32]. They mimic geometric and electronic features of a configurationally biased amide bond, and participate in dipole–dipole interactions [31][33] and H-bonding. They may act as H-bond acceptors and as (weak) donors, depending on their substitution. In 1,4-disubstituted 1,2,3-triazoles, N(2) and N(3) exhibit H-bond accepting properties, whereas the strong dipole moment of triazole causes the polarization of H–C(5) that may act as a week H-bond donor [26–36].

The triazole ring of the envisaged analogues **10**–**16** (*Fig. 2*) orients the acyl chain in a way that prevents a parallel orientation with the alkyl chain of the Sph moiety, and its polar substituents may serve as H-bond acceptors in a position differing from the C=O group of the *C(2)*-acylamino chain. These features are of interest, as the crystal structure of α-GalCer bound to the human and mouse CD1d receptor shows that the two alkyl chains diverge from each other [14], suggesting that the configuration of the amide moiety, besides its H-bond-acceptor and -donor properties, plays an important role in interacting with receptors. The triazoles should be readily available from the known azide intermediate in the synthesis of 7-oxaceramide [17]. After we had completed the synthesis of the triazoles **10**–**16**, *Kim et al.* published a synthesis of related ceramides [37] and *O*-glycosides [38] that stimulated cytokine production, comparable to the one of α-GalCer, and exhibited a stronger Th2 cytokine response.

Biological properties for which we considered testing these analogues comprise T-cell suppression [40], and the interaction with sphingosine and ceramide kinases, and with acid sphingomyelinase [41].

Results and Discussion. – *Synthesis.* The amine **18** (*Scheme 1*) was obtained in high yield by reduction of the protected azido-7-oxasphingosine **17** that had been prepared in 94% yield by isopropylidenation of the derivative **21** [17]. Coupling of **18** with

Scheme 1



a) 2,2-Dimethoxypropane, $TsOH \cdot H_2O$, acetone, 25°; 94%. *b*) $LiAlH_4$, Et_2O, 0°; 97% of **18**; 90% of **9**. *c*) $C_{16}H_{33}NCO$, Et_3N, CH_2Cl_2, 10–25°; 77%. *d*) 60% CF_3CO_2H, THF; 89% for **7**; 94% for **8**. *e*) $C_{16}H_{33}SO_2Cl$, Et_3N, CH_2Cl_2, 0–25°; 89%. *f*) TsCl, Et_3N, 4-(Dimethylamino)pyridine (DMAP), CH_2Cl_2, 10°; 79%. *g*) Me_2NH, THF, 25°; 60%.

hexadecyl isocyanate [42] yielded 77% of the protected urea **19** that was smoothly deprotected by 60% CF_3COOH in THF to give the desired analogue **7** (89%). Condensation of **18** with hexadecyl sulfonyl chloride [43] in the presence of Et_3N yielded 89% of the protected sulfonamide **20** that was de-isopropylidenated to the sulfonamide **8** (94%). The chemical shifts and coupling constants of the analogues **7** and **8** of 7-oxaceramide, and the known Cer **2** and 7-oxaceramide **4** are summarized in *Table 1*.

To obtain the 1-(dimethylamino) deoxy-7-oxasphingosine (**9**), we monotosylated the azido-7-oxasphingosine **21** [17] (*Scheme 1*) in the presence of Et_3N and 4-(dimethylamino)pyridine (DMAP) at 10° to obtain 79% of **22**. Replacing Et_3N by pyridine or by $EtN(i\text{-}Pr)_2$ resulted in a slower reaction, and increasing the temperature above 35° led to tosylation of both OH groups, while addition of a catalytic amount of DMAP increased the rate of tosylation without impairing the selectivity. The expected selective tosylation of the primary OH group is evidenced by the HO–C(3) *doublet* at 2.26 ppm ($J(3,OH) = 4.5$ Hz) and the downfield shift for C(1) from 62.47 (**21**) to 68.58 ppm (**22**). Treating **22** with Me_2NH in THF provided the protected azido-

Table 1. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *for the Ceramide* **2**, *7-Oxaceramide* **4**, *Urea* **7**, *and Sulfonamide* **8** (in $CDCl_3$)

	2[a])	**4**[b])	**7**[c])	**8**
H–C(1)	3.93	3.96–3.88	3.83	3.90
H′–C(1)	3.68	3.74–3.65	3.69	3.71
H–C(2)	3.88	3.96–3.88	3.77	3.49–3.40
H–C(3)	4.31	4.38	4.36	4.44
H–C(4)	5.51	5.79	5.78	5.78
H–C(5)	5.76	5.91	5.89	5.93
CH_2(6)	2.03	3.98	3.97	3.98
NH	6.21	6.33	1.81	5.32
HO–C(3)	2.70	3.26	1.81	3.07
HO–C(1)	2.70	2.97	1.81	2.81
J(1,1′)	11.2	[d])	10.8	11.7
J(1,2)	3.4	[d])	4.2	4.5
J(1′,2)	3.4	[d])	3.0	3.3
J(2,3)	3.6	4.0	3.8	[d])
J(3,4)	6.5	5.3	5.2	5.7
J(4,5)	15.4	15.4	15.6	15.9
J(5,6)	6.8	5.1	5.4	5.1
J(NH,2)	7.3	7.2	–	8.7
J(OH,3)	[d])	[d])	–	–
J(OH,1)	3.6	[d])	–	–
J(OH,1′)	7.5	[d])	–	–

[a]) From [16a,b]. [b]) From [17]. [c]) Three drops of CD_3OD were added. [d]) Not assigned.

dimethylamino derivative **23**, and its reduction with $LiAlH_4$ provided the dimethylamino compound **9** in a yield of 42–43% from **21**.

The 1,4-disubstituted 1,2,3-triazoles **30**–**34** (*cf. Scheme 2*) were obtained in yields of 81–91% as single regioisomers by cycloaddition of the azido derivatives **24** [17] to the alkynes **25**–**29** [26–32] in the presence of $CuSO_4$ and ascorbic acid [32], either in H_2O (for **30**–**32**) or in H_2O/i-PrOH 1:1 (for **33**–**34**) at 55–60°.

The alkynone **25** was obtained in 60% yield by acylation of stearoyl chloride with (trimethylsilyl)acetylene [44][45] in the presence of $AlCl_3$ in CH_2Cl_2. Nonadec-1-yne (**26**) was prepared in 71% yield from octadecanal by a *Corey–Fuchs* reaction [46], whereas the ester **27** was obtained by *Mitsunobu* reaction of hexadecan-1-ol with propargylic acid (90%) [47]. Amide **28** was synthesized by coupling [48] between hexadecanamine and propargylic acid (84%).

The triazoles **30**–**34** were debenzylated by treatment with $AlCl_3$ in the presence of anisole [49] to afford the desired triazole derivatives **10**, **12**–**14**, and **16** (*Scheme 2* and *Table 2*). The structure of these 1,4-disubstituted 1,2,3-triazoles is evidenced by the chemical shift for C(4) and C(5) of the triazolyl unit, resonating at 139.5–151.1 and 126.9–129.7 ppm, respectively[1]).

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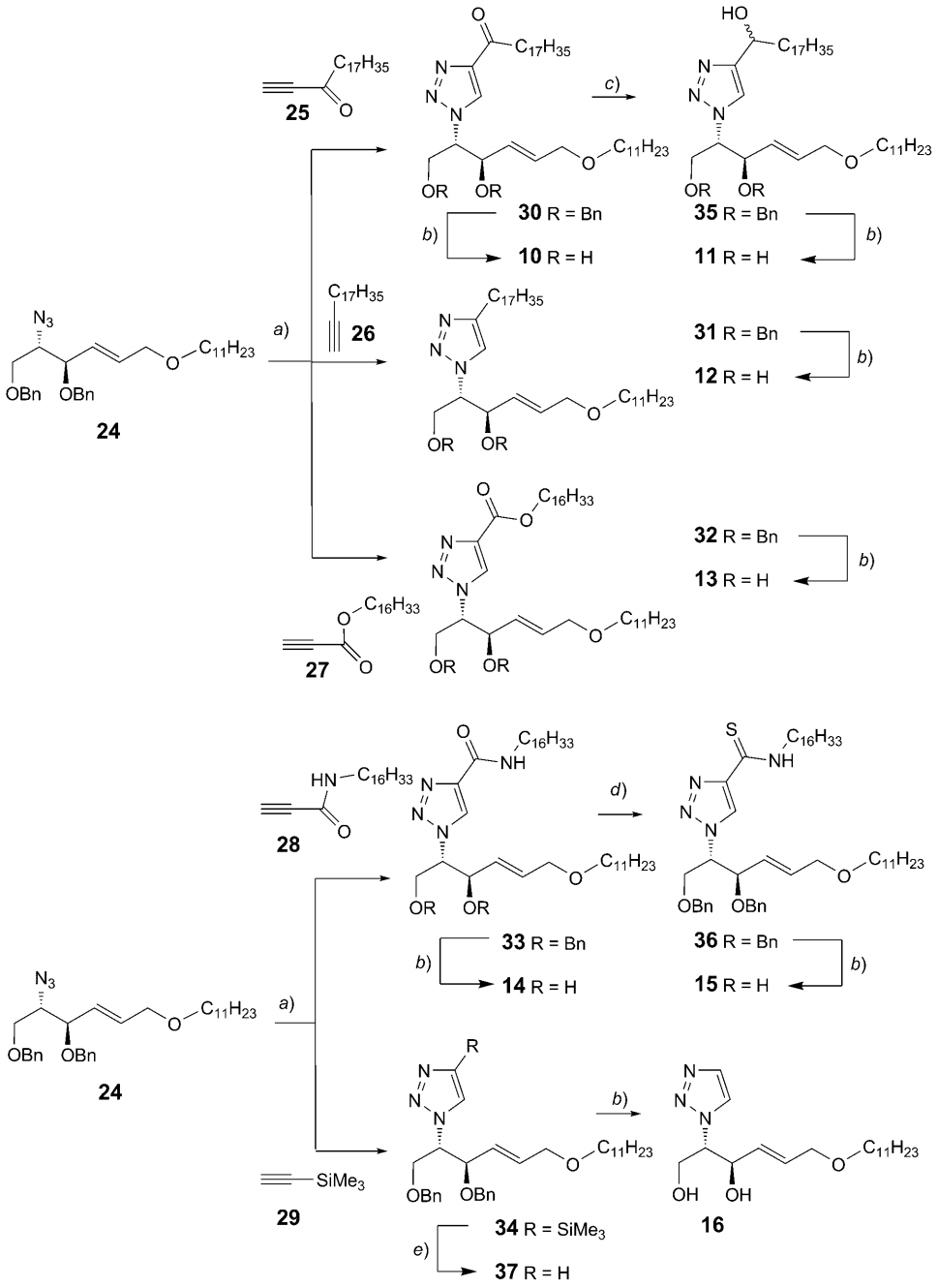
[1]) Typical chemical shifts for C(4) and C(5) of 1,4-disubstituted 1,2,3-triazoles are 143–148 and 117–126 ppm, respectively, differing from those of 1,5-disubstituted 1,2,3-triazoles (131–139 and 130–147 ppm, resp.) [50].

Scheme 2



a) $CuSO_4$, Ascorbic acid, H_2O (H_2O/^{i}PrOH 1:1 for **33**–**34**), 60°; 91% of **30**; 81% of **31**; 84% of **32**; 90% of **33**; 84% of **34**. *b*) $AlCl_3$, Anisole, 1,2-dichloroethane, 25°; 78% of **10**; 71% of **11**; 86% of **12**; 91% of **13**; 89% of **14**; 80% of **15**; 70% of **16**. *c*) $NaBH_4$, THF/H_2O (3:2), 0°–25°, 24 h; 88%. *d*) *Lawesson*'s reagent, toluene, 75°; 84%. *e*) $Bu_4NF \cdot 3\,H_2O$, THF, AcOH, 25°; 97%.

Table 2. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the Ceramide* **2**, *7-Oxaceramide* **4**, *and the 1,2,3-Triazole Analogues* **10**–**16** (in $CDCl_3$)

	2[a])	**4**[b])	**10**	**11**[c])	**12**	**13**	**14**	**15**	**16**
H–C(1)	3.93	3.96–3.88	4.37–4.30	4.30	4.29	4.36	4.35	4.27	4.31
H′–C(1)	3.68	3.74–3.65	4.15–4.08	4.15	4.14–4.06	4.13	4.03	4.08	4.12
H–C(2)	3.88	3.96–3.88	4.67–4.63	4.75	4.46	4.64	4.71–4.65	4.60	4.57
H–C(3)	4.31	4.38	4.75	4.87	4.74	4.79	4.71–4.65	4.69	4.74
H–C(4)	5.51	5.79	5.73	5.71	5.67	5.77	5.71	5.69	5.68
H–C(5)	5.76	5.91	5.88	5.84	5.83	5.92	5.86	5.84	5.83
CH_2(6)	2.03	3.98	3.92	3.91	3.90	3.93	3.91	3.90	3.90
HO–C(3)	2.70	3.26	3.18	[d])	3.88	3.38	4.41	3.35	3.70
HO–C(1)	2.70	2.97	2.91	[d])	3.59	3.19	4.17	3.11	3.44
J(1,1′)	11.2	[d])	[d])	[d])	11.1	11.8	11.4	12.0	12.0
J(1,2)	3.4	[d])	[d])	[d])	5.7	5.2	4.8	5.7	5.4
J(1′,2)	3.4	[d])	[d])	[d])	3.6	2.7	2.4	3.6	3.6
J(2,3)	3.6	4.0	[d])	[d])	[d])	[d])	[d])	[d])	[d])
J(3,4)	6.5	5.3	[d])	[d])	5.7	5.7	5.1	5.6	5.7
J(4,5)	15.4	15.4	15.6	15.6	15.6	15.3	15.3	15.6	15.6
J(5,6)	6.8	5.1	5.1	4.8	5.1	5.4	5.4	5.4	4.8
J(NH,2)	7.3	7.2	–	–	–	–	–	–	–
J(OH,3)	[d])	[d])	[d])	[d])	6.9	[d])	4.8	[d])	4.2
J(OH,1)	3.6	[d])	[d])	[d])	3.0	[d])	4.8	–	–
J(OH,1′)	7.5	[d])	[d])	[d])	3.0	–	6.3	–	6.2

[a]) From [16a,b]. [b]) From [17]. [c]) Not assigned. [d]) NMR Spectrum was recorded at 45°.

The protected 4-acyltriazole **30** was reduced with $NaBH_4$ to the corresponding alcohols **35** (88%) that were debenzylated to the triols **11**. The thioamide **36** was obtained in 84% yield from amide **33** by treatment with *Lawesson*'s reagent, and deprotected to **15** (*Scheme 2*).

Biological Results. – *Phosporylation by Ceramide Kinase* (*CerK*). Compounds **7**–**15** were tested for activity as inhibitors of SPHK type 1 and of acid sphingomyelinase according to established assay methods [51][52]; none of them was found to be active. The monosubstituted triazolyl derivative **16** was found to be a weak inhibitor of SPHK1, inhibiting the enzyme by 62% at 100 μM and by 25% at 10 μM. For compounds **10**, **11**, and **15**, we checked whether they would be accepted as substrate by ceramide kinase [53]; however, no phosphorylation of the compounds was detectable.

T-Cell Suppression. Compounds **7**, **8**, and **10**–**15** did neither show any activatory capacity on iNKT-cell clones when presented by human CD1d-transfected antigen-presenting cells (APC) nor by plate-bound human CD1d (data not shown). None of the compounds proved cytotoxic for APC or iNKT cells at tested doses (up to 20 μg/ml), as assessed by flow cytometry (data not shown).

Lack of stimulatory activity may not exclude the capacity of these compounds to bind to CD1d. This was investigated using a competition assay to evaluate the capacity of the compounds to prevent binding of α-GalCer to CD1d and, thus, to prevent T-cell

activation. Only compound **15** was able to compete, although this competition was only achieved at 15-fold molar excess over α-GalCer (*Fig. 3*,*a* and *b*; data not shown). In additional experiments, we investigated whether **15** was capable of competing with α-GalCer in living cells. In contrast to the strong inhibition seen in the plate-bound assay, **15** was incapable of reducing T-cell activation at all tested doses of α-GalCer.

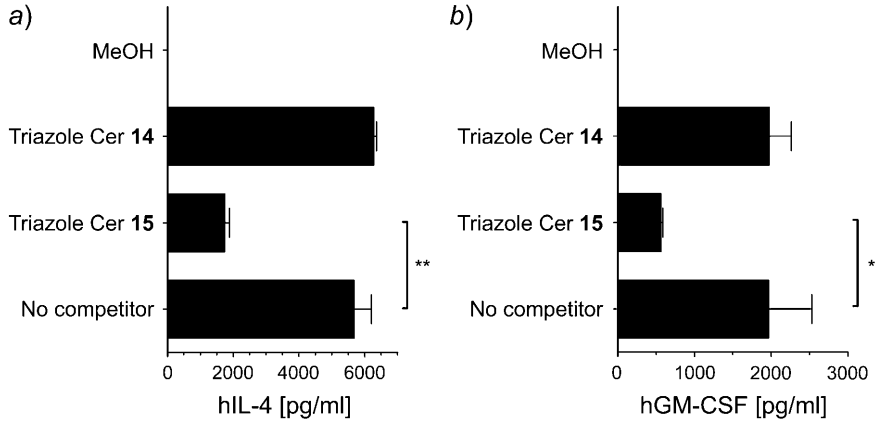


Fig. 3. *Triazoles* **14** *and* **15**: *competition with α-GalCer.* Ceramide analogues **14** and **15** were tested for their capacity to prevent binding of α-GalCer to plate-bound human CD1d and subsequent T-cell response to α-GalCer. Supernatants were taken after 24 h, and released human IL-4 (*a*) and human GM-CSF (*b*) were measured by ELISA and expressed as pg/ml ± SD of duplicates. Only **15** was significantly reducing activation by α-GalCer independently of the cytokine measured (**: $P<0.01$; *: $P<0.05$).

This unexpected discrepancy between plate-bound and living cell competition assays might be explained with the instability of the thioamide moiety of **15** inside living cells. To test the stability of the thioamide **15**, we performed plate-bound assays at pH 4 and 7. At pH 4, an increase in cytokine release as compared to pH 7 was seen, and a partial degradation of **15** was thus assumed (*Fig. 4*,*a* and *b*). In living cells, **15** requires trafficking to lysosomes, where lipid antigens are loaded onto CD1d molecules [54]. Therefore, it is tempting to speculate that the acidic late-endosomal microenvironment affects the stability of **15**.

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Experimental Part

1. *Synthesis. General.* THF was distilled from Na and benzophenone, CH_2Cl_2 from P_2O_5, and MeOH and MeCN from CaH_2. Reactions were carried out under Ar, unless stated otherwise. Qual. TLC: precoated silica-gel plates (*Merck* silica gel *60* F_{254}); detection by heating with 'mostain' (400 ml of 10% H_2SO_4 soln., 20 g of $(NH_4)_6Mo_7O_{24}\cdot 6\,H_2O$, 0.4 g of $Ce(SO_4)_2$). Flash chromatography (FC): silica gel *Fluka 60* (0.04–0.063 mm). Optical rotations: 1-dm cell at 25°, 589 nm. FT-IR Spectra: KBr or *ca.* 2% soln. in $CHCl_3$, $\tilde{\nu}$ in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: chemical shifts δ in ppm rel. to Me_4Si as external standard, and coupling constants J in Hz. HR-MALDI-MS: in gentisic acid (=2,5-dihydroxybenzoic acid, DHB) matrix.

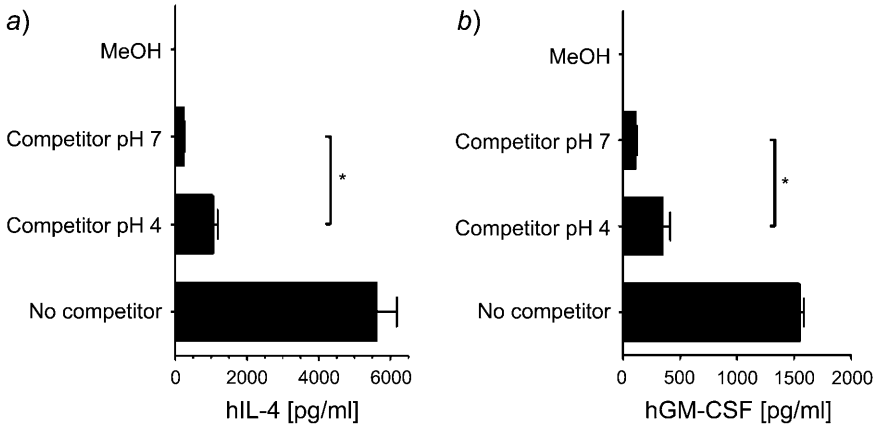

Fig. 4. *Triazole* **15** *is sensitive at low pH.* A competition experiment was performed at pH 4 or 7. Supernatants were taken after 24 h, and released human IL-4 (*a*) and human GM-CSF (*b*) were measured by ELISA, and expressed as pg/ml ± SD of duplicates. At pH 4, triazole **15** shows less competition than at pH 7, independently of the cytokine measured (*: $P < 0.05$).

*(*E*)-2-Azido-2,4,5-trideoxy-1,3*-O-*isopropylidene-6*-O-*undecyl*-D-erythro-*hex-4-enitol* (**17**). An ice-cold soln. of **21** (253 mg, 0.77 mmol) in acetone (4 ml) was treated with 2,2-dimethoxypropane (402.3 mg, 3.86 mmol) and $TsOH \cdot H_2O$ (14.7 mg, 0.077 mmol), stirred at r.t. for 2.5 h, and evaporated. A soln. of the residue in Et_2O (100 ml) was washed with H_2O (2 × 50 ml), and the aq. phase was extracted with Et_2O (2 × 50 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 1:9) gave **17** (266 mg, 94%). Colourless oil. R_f (AcOEt/hexane 1:9) 0.33. $[\alpha]_D^{25} = -15.1$ ($c = 2.0$, $CHCl_3$). IR ($CHCl_3$): 3000*w*, 2925*s*, 2856*m*, 2110*s*, 1602*w*, 1465*w*, 1382*w*, 1371*w*, 1304*w*, 1264*m*, 1160*w*, 1101*m*, 1018*m*, 979*w*, 939*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 5.98 (*dtd*, $J = 15.5, 5.3, 0.9$, H–C(5)); 5.75 (*ddt*, $J = 15.6, 6.6, 1.5$, H–C(4)); 4.12 (*dd*, $J = 9.6, 6.3$, H–C(3)); 4.00 (br. *dd*, $J = 5.4, 1.2$, 2 H–C(6)); 3.94 (*dd*, $J \approx 11.6, 5.6$, H–C(1)); 3.66 (*dd*, $J = 11.4, 10.2$, H′–C(1)); 3.42 (*t*, $J = 6.8$, 2 H–C(1′)); 3.30 (*td*, $J = 9.8, 5.5$, H–C(2)); 1.63–1.52 (*m*, 2 H–C(2′)); 1.47, 1.41 (2*s*, Me_2C); 1.36–1.21 (*m*, 16 H); 0.88 (*t*, $J =$ 6.6, Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 132.05 (*d*, C(4)); 128.40 (*d*, C(5)); 98.84 (*s*, *Me*$_2$C); 73.17 (*d*, C(3)); 70.76 (*t*, C(6)); 70.46 (*t*, C(1′)); 62.30 (*t*, C(1)); 58.40 (*d*, C(2)); 31.98, 29.80, 29.68, 29.57, 29.41, 26.24, 22.77 (several *t*); 28.83, 19.16 (2*q*, Me_2C); 14.22 (*q*, Me). HR-ESI-MS: 390.2725 (100, $[M + Na]^+$, $C_{20}H_{37}N_3NaO_3^+$; calc. 390.2727). Anal. calc. for $C_{20}H_{37}N_3O_3$ (367.53): C 65.36, H 10.15, N 11.43; found: C 65.39, H 10.05, N 11.60.

*(*E*)-2-Amino-2,4,5-trideoxy-1,3*-O-*isopropylidene-6*-O-*undecyl*-D-erythro-*hex-4-enitol* (**18**). A stirred suspension of $LiAlH_4$ (54.7 mg, 1.44 mmol) in Et_2O (10 ml) was cooled to 0°, treated dropwise with a soln. of **17** (265 mg, 0.72 mmol) in Et_2O (5 ml), stirred at 0° for 1 h, and treated dropwise with H_2O (0.4 ml), 1N NaOH (0.8 ml), and H_2O (1.2 ml). The suspension was then filtered through *Celite*, and the filtrate was extracted with AcOEt (2 × 100 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated to afford crude **18** (245 mg, 99.5%) that was used without further purification. A pure sample of **18** was obtained by FC (MeOH/CH_2Cl_2 1:19). Colourless oil. R_f (MeOH/CH_2Cl_2 1:19) 0.24. $[\alpha]_D^{25} = -2.3$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3479*w* (br.), 3377*w*, 3000*m*, 2928*s*, 2856*s*, 1666*w*, 1655*w*, 1602*w*, 1463*w*, 1458*w*, 1382*m*, 1373*m*, 1264*m*, 1213*m*, 1158*m*, 1103*m*, 1078*m*, 1016*m*, 975*w*, 941*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 5.91 (br. *dt*, $J \approx 15.6, 5.3$, H–C(5)); 5.68 (*ddt*, $J \approx 15.6, 7.5, 1.4$, H–C(4)); 3.98 (br. *d*, $J = 6.0$, 2 H–C(6)); 3.91 (*dd*, $J = 9.3, 7.5$, H–C(3)); 3.86 (*dd*, $J \approx 11.3, 5.6$, H–C(1)); 3.54 (*dd*, $J = 11.3$, 10.4, H′–C(1)); 3.42 (*t*, $J \approx 6.6$, 2 H–C(1′)); 2.71 (*td*, $J \approx 9.9, 5.2$, H–C(2)); 1.63–1.51 (*m*, 2 H–C(2′)) 1.48, 1.41 (2*s*, Me_2C); 1.42 (br. *s*, NH_2); 1.36–1.20 (*m*, 16 H); 0.87 (*t*, $J \approx 6.7$, Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 131.88 (*d*, C(4)); 129.60 (*d*, C(5)); 98.45 (*s*, Me_2C); 77.38 (*d*, C(3)); 70.89 (*t*, C(6)); 70.58 (*t*,

C(1′)); 65.57 (*t*, C(1)); 49.12 (*d*, C(2)); 32.01, 29.84, 29.74, 29.62, 29.45, 26.29, 22.81 (several *t*); 29.41, 19.23 (2*q*, *Me*$_2$C); 14.26 (*q*, Me). HR-MALDI-MS: 342.3000 (100, $[M+H]^+$, $C_{20}H_{40}NO_3^+$; calc. 342.3003).

*(*E*)-2,4,5-Trideoxy-2-[3-(hexadecyl)ureido]-1,3-*O*-isopropylidene-6-*O*-undecyl-*D*-erythro-hex-4-enitol* (**19**). An ice-cold soln. of **18** (66 mg, 0.193 mmol) in CH_2Cl_2 (2 ml) was treated with ice-cold soln. of hexadecyl isocyanate (56.9 mg, 0.21 mmol), followed by Et_3N (54 µl, 0.39 mmol), stirred for 18 h, and evaporated. A soln. of the residue in CH_2Cl_2 (50 ml) was washed with H_2O (20 ml). The aq. phase was extracted with CH_2Cl_2 (3 × 20 ml). The combined org. phases were dried (Na_2SO_4) and evaporated. FC (AcOEt/hexane 1:4 → 3:7 → 1:1) gave pure **19** (90 mg, 77%). White fluffy powder. R_f (CH_2Cl_2/MeOH 95:5) 0.80. $[\alpha]_D^{25} = +15.7$ ($c = 0.3$, $CHCl_3$). IR (ATR): 3320*w*, 2957*w*, 2918*s*, 2850*s*, 1622*s*, 1575*s*, 1467*m*, 1378*w*, 1370*w*, 1290*w*, 1261*w*, 1243*m*, 1199*m*, 1158*w*, 1108*m*, 1077*m*, 1022*m*, 967*w*, 940*w*, 869*w*, 720*w*, 657*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 5.87 (*dt*, *J* = 15.6, 5.5, H−C(5)); 5.72 (*dd*, *J* = 15.6, 6.5, H−C(4)); 4.52 (*t*, *J* = 5.2, HN−C(1″)); 4.36 (*d*, *J* = 7.2, HN−C(2)); 4.12 (*dd*, *J* = 9.1, 6.5, H−C(3)); 4.00 (*dd*, *J* = 11.0, 4.9, 1 H−C(1)); 3.97–3.89 (*m*, 2 H−C(6)); 3.66 (*dd*, *J* = 10.8, 9.0, 1 H−C(1)); 3.60–3.52 (*m*, H−C(2)); 3.39 (*t*, *J* = 6.7, 2 H−C(1′)); 3.10 (*q*, *J* ≈ 6.7, 2 H−C(1″)); 1.59–1.50 (*m*, 2 H−C(2′)); 1.47–1.38 (*m*, 2 H−C(2″)); 1.47, 1.41 (2*s*, *Me*$_2$C); 1.36–1.16 (*m*, 42 H); 0.87 (*t*, *J* = 6.7, 2 Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 157.26 (*s*, C=O); 131.09 (*d*, C(4)); 129.78 (*d*, C(5)); 98.80 (*s*, Me$_2$*C*); 73.45 (*d*, C(3)); 70.77 (*t*, C(6)); 70.71 (*t*, C(1′)); 63.56 (*t*, C(1)); 49.23 (*d*, C(2)); 40.71 (*t*, C(1″)); 32.03 (2*t*); 30.28, 29.89 (2*t*); 29.82, 29.75, 29.68, 29.48 (several *t*); 28.56, 19.78 (2*q*, *Me*$_2$C); 27.07, 26.32 (2*t*); 14.26 (*q*, Me). HR-MALDI-MS: 631.6369 (100, $[M+Na]^+$, $C_{37}H_{72}N_2NaO_4^+$; calc. 631.5390). Anal. calc. for $C_{37}H_{72}N_2O_4$ (608.9786): C 72.97, H 11.92, N 4.60; found: C 73.01, H 12.06, N 4.55.

*(*E*)-2,4,5-Trideoxy-2-[3-(hexadecyl)ureido]-6-undecyl-*D*-erythro-hex-4-enitol* (**7**). A soln. of **19** (40 mg, 0.066 mmol) in THF (1 ml) was treated with 60% aq. CF_3COOH (2 ml), stirred at 25° for 30 min, and evaporated. A soln. of the residue in CH_2Cl_2/MeOH 95:5 (0.5 ml) was filtered through a short pad of silica gel (*Lichoprep*-NH_2) (CH_2Cl_2/MeOH 97:3) to yield pure **7** (33 mg, 89%). White shiny crystals. M.p. 102.6°. R_f (CH_2Cl_2/MeOH 95:5) 0.14. $[\alpha]_D^{25} = +1.6$ ($c = 0.25$, THF). IR (ATR): 3369*m*, 2925*w*, 2916*s*, 2849*s*, 2795*w*, 1589*s*, 1520*w*, 1464*w*, 1360*w*, 1321*w*, 1261*m*, 1223*w*, 1141*w*, 1100*m*, 1083*m*, 1051*m*, 986*w*, 956*w*, 884*w*, 812*w*, 721*m*, 673*w*. ^{1}H-NMR ($CDCl_3$/CD_3OD (2 drops), 300 MHz): 5.89 (*dt*, *J* = 15.9, 5.4, H−C(5)); 5.78 (br. *dd*, *J* = 15.6, 5.4, irrad. at 4.36 → *d*, *J* = 15.9, H−C(4)); 4.36 (*t*, *J* ≈ 4.2, irrad. at 3.77 → *d*, *J* = 5.2, H−C(3)); 3.97 (*d*, *J* = 5.1, irrad. at 5.89 → *s*, 2 H−C(6)); 3.83 (*dd*, *J* = 10.8, 4.2, 1 H−C(1)); 3.77 (*q*, *J* = 3.8, irrad. at 4.36 → *t*, *J* = 3.6, H−C(2)); 3.69 (*dd*, *J* = 10.8, 3.0, 1 H−C(1)); 3.42 (*t*, *J* = 6.8, 2 H−C(1′)); 3.13 (*t*, *J* = 7.1, 2 H−C(1″)); 1.62–1.52 (*m*, 2 H−C(2′)); 1.52–1.42 (*m*, 2 H−C(2″)); 1.46–1.24 (*m*, 42 H); 0.87 (*t*, *J* ≈ 6.8, 2 Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 158.84 (*s*, C=O); 131.59 (*d*, C(4)); 128.94 (*d*, C(5)); 73.87 (*d*, C(3)); 70.99 (*t*, C(6)); 70.62 (*t*, C(1′)); 62.80 (*t*, C(1)); 55.50 (*d*, C(2)); 40.74 (*t*, C(1″)); 31.98 (2*t*); 30.03–29.41 (several *t*); 26.96, 26.20 (2*t*), 22.76 (2*t*); 14.21 (*q*, 2 He). HR-ESI-MS: 591.5071 (100, $[M + Na]^+$, $C_{34}H_{68}N_2NaO_4^+$; calc. 591.5077). Anal. calc. for $C_{34}H_{68}N_2O_4$ (568.9147): C 71.78, H 12.05, N 4.92; found: C 71.88, H 12.04, N 4.86.

*(*E*)-2,4,5-Trideoxy-2-(hexadecanesulfonamido)-1,3-*O*-isopropylidene-6-*O*-undecyl-*D*-erythro-hex-4-enitol* (**20**). An ice-cold soln. of **18** (50 mg, 0.15 mmol) in CH_2Cl_2 (5 ml) was treated successively with Et_3N (102 µl, 0.732 mmol) and hexadecylsulfonyl chloride (118.9 mg, 0.37 mmol). The mixture was stirred at 25° for 72 h, diluted with CH_2Cl_2 (50 ml), and washed with H_2O (20 ml). The aq. phase was extracted with CH_2Cl_2 (2 × 50 ml). The combined org. phases were washed with brine, dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 1:9 → 1:4) gave pure **20** (82 mg, 89%). White fluffy powder. R_f (CH_2Cl_2/MeOH 95:5) 0.79. IR (ATR): 2954*w*, 2919*s*, 2850*s*, 2795*w*, 1467*w*, 1440*w*, 1351*w*, 1301*w*, 1272*w*, 1219*w*, 1121*s*, 1089*m*, 1062*m*, 1034*m*, 1020*w*, 987*w*, 959*w*, 889*w*, 860*w*, 773*m*, 724*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 5.94 (*dt*, *J* = 15.3, 4.8, H−C(5)); 5.74 (*ddt*, *J* = 15.3, 7.2, 1.2, H−C(4)); 4.37 (*d*, *J* = 8.4, NH); 4.08 (*dd*, *J* = 12.0, 5.8, 1 H−C(1)); 4.03 (*dd*, *J* = 9.9, 7.5, H−C(3)); 3.96 (*dd*, *J* = 5.1, 1.2, 2 H−C(6)); 3.67 (*dd*, *J* = 11.4, 9.6, 1 H−C(1)); 3.41 (*t*, *J* = 6.9, 2 H−C(1′)); 3.26 (*qd*, *J* ≈ 9.6, 5.1, H−C(2)); 3.04–2.88 (*m*, 2 H−C(1″)); 1.80–1.72 (*m*, 2 H−C(2″)); 1.60–1.51 (*m*, 2 H−C(2′)); 1.47, 1.41 (2*s*, Me$_2$C); 1.37–1.19 (*m*, 42 H); 0.87 (*t*, *J* = 6.6, Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 132.69 (*d*, C(4)); 128.19 (*d*, C(5)); 98.89 (*s*, Me$_2$*C*); 73.45 (*d*, C(3)); 71.09 (*t*, C(6)); 70.26 (*t*, C(1′)); 64.39 (*t*, C(1)); 53.83 (*t*, C(1″)); 51.90 (*d*, C(2)); 32.03 (2*t*); 29.88, 29.70, 29.53, 29.48, 29.32 (several *t*); 28.69, 19.48 (2*q*, *Me*$_2$C); 28.43, 26.31, 23.80 (3*t*); 22.82 (2*t*); 14.26 (*q*, Me). HR-ESI-MS: 634.4838 (100, $[M+Na]^+$, $C_{36}H_{69}NNaO_4S^+$; calc. 634.4840).

Anal. calc. for $C_{36}H_{69}NO_4S$ (612.01): C 70.65, H 11.36, N 2.29, S 5.24; found: C 70.61, H 11.34, N 2.35, S 5.13.

*(*E*)-2,4,5-Trideoxy-2-(hexadecanesulfonamido)-6-*O*-undecyl-*D*-erythro-hex-4-enitol* (**8**). A soln. of **20** (31.7 mg, 0.05 mmol) in THF (1 ml) was treated with 60% aq. CF_3COOH (2 ml), stirred at 25° for 30 min, and evaporated. A soln. of the residue in AcOEt (20 ml) was washed with brine. The aq. phase was extracted with AcOEt (2 × 10 ml), and the combined org. phases were dried (Na_2SO_4), and evaporated. The crude was filtered through a short pad of silica gel (AcOEt/hexane 1:1) to yield pure **8** (28 mg, 94%). Colourless crystals. M.p. 69.7°. R_f (CH_2Cl_2/MeOH 95:5) 0.14. R_f (CH_2Cl_2/MeOH 9:1) 0.50. $[\alpha]_D^{25} = +2.3$ ($c = 0.15$, $CHCl_3$). IR (ATR): 3465*w*, 3276*w*, 2953*w*, 2918*s*, 2848*s*, 2795*w*, 1465*w*, 1441*w*, 1350*w*, 1303*w*, 1271*w*, 1219*w*, 1121*s*, 1089*m*, 1062*m*, 1034*m*, 1020*w*, 987*w*, 959*w*, 889*w*, 865*w*, 773*m*, 723*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 5.93 (*dt*, $J = 15.9, 5.4$, H–C(5)); 5.78 (br. *dd*, $J = 15.9, 5.7$, H–C(4)); 5.32 (*d*, $J = 8.7$, exchange with D_2O, NH); 4.44 (br. *s*, H–C(3)); 3.98 (*d*, $J = 5.1$, 2 H–C(6)); 3.90 (*dd*, $J = 11.7, 4.5$, 1 H–C(1)); 3.71 (*dd*, $J = 11.1, 3.3$, 1 H–C(1)); 3.49–3.40 (*m*, H–C(2)); 3.43 (*t*, $J = 6.6$, 2 H–C(1′)); 3.10–3.04 (*m*, 2 H–C(1″)); 3.07 (br. *s*, exchange with D_2O, OH); 2.81 (br. *s*, exchange with D_2O, OH); 1.87–1.77 (*m*, 2 H–C(2″)); 1.62–1.53 (*m*, 2 H–C(2′)); 1.44–1.25 (*m*, 42 H); 0.87 (*t*, $J \approx 6.8$, 2 Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 130.59 (*d*, C(4)); 130.10 (*d*, C(5)); 74.28 (*d*, C(3)); 71.21 (*t*, C(6)); 70.54 (*t*, C(1′)); 62.64 (*t*, C(1)); 58.34 (*d*, C(2)); 54.02 (*t*, C(1″)); 32.10 (2*t*); 29.88–29.74 (several *t*); 29.55 (2*t*); 29.35, 28.51 (2*t*); 26.34, 23.85 (2*t*), 22.87 (2*t*); 14.30 (*q*, 2 Me). HR-MALDI-MS: 612.4632 (100, $[M + Na]^+$, $C_{33}H_{67}NNaO_5S^+$; calc. 612.4638). Anal. calc. for $C_{33}H_{67}NO_5S$ (589.9538): C 67.18, H 11.45, N 2.37; found: C 67.16, H 11.55, N 2.42.

*(*E*)-2-Azido-2,4,5-trideoxy-1-*O*-[(4-methylphenyl)sulfonyl]-6-*O*-undecyl-*D*-erythro-hex-4-enitol* (**22**). A soln. of **21** (200.5 mg, 0.61 mmol) in CH_2Cl_2 (5 ml) was treated with TsCl (128.4 mg, 0.67 mmol), followed by Et_3N (0.17 ml, 1.23 mmol) and DMAP (7.5 mg, 0.061 mmol), stirred at 10° for 30 min, diluted with Et_2O (50 ml), and washed with H_2O (50 ml). The aq. phase was extracted with Et_2O (3 × 50 ml). The combined org. phases were washed with brine, dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 1:9 → 1:4) gave pure **22** (233 mg, 79%). Colourless oil. IR ($CHCl_3$): 3329*w* (br.), 2923*s*, 2853*s*, 2098*s*, 1465*w*, 1375*m*, 1266*m*, 1180*w*, 1168*m*, 1110*m*, 1096*w*, 1070*m*, 1064*m*, 1012*m*, 972*m*, 852*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.80 (*d*, $J = 8.4$, 2 arom. H); 7.36 (*d*, $J = 8.5$, 2 arom. H); 5.87 (*dtd*, $J = 15.6, 5.1, 0.7$, H–C(5)); 5.71 (*ddt*, $J = 15.6, 6.5, 1.3$, H–C(4)); 4.22 (*dd*, $J = 10.6, 3.8$, 1 H–C(1), H–C(3)); 4.09 (*dd*, $J = 10.6, 7.4$, 1 H–C(1)); 3.95 (*d*, $J = 5.1$, 2 H–C(6)); 3.64 (*ddd*, $J = 7.3, 5.6, 3.7$, H–C(2)); 3.40 (*t*, $J = 6.7$, 2 H–C(1′)); 2.45 (*s*, *Me*); 2.27 (*d*, $J = 4.3$, OH); 1.57 (*quint.*, $J = 6.9$, 2 H–C(2′)); 1.34–1.23 (*m*, 16 H); 0.87 (*t*, $J = 6.7$, Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 145.13, 132.33 (2*s*); 131.70 (*d*, C(4)); 129.86 (2*d*); 128.89 (*d*, C(5)); 127.88 (2*d*); 71.49 (*d*, C(3)); 70.81 (*t*, C(6)); 70.08 (*t*, C(1′)); 68.58 (*t*, C(1)); 63.93 (*d*, C(2)); 31.78 (*t*); 29.59–29.23 (several *t*); 26.04, 22.58 (2*t*), 21.58 (*q*, Me); 14.01 (*q*, Me). HR-MALDI-MS: 504.2502 (100, $[M + Na]^+$, $C_{24}H_{39}N_3NaO_5S^+$; calc. 504.2508).

*(*E*)-2-Azido-1,2,4,5-tetradeoxy-1-(dimethylamino)-6-*O*-undecyl-*D*-erythro-hex-4-enitol* (**23**). A mixture of **22** (190 mg, 0.39 mmol) and Me_2NH (40% in H_2O, 2 ml) was stirred at 80° for 15 h, cooled to 25°, diluted with H_2O (5 ml), and extracted with AcOEt (3 × 50 ml). The combined org. phases were washed with brine, dried (Na_2SO_4), and evaporated. The residue was filtered through a short pad of silica gel (AcOEt) to afford pure **23** (83 mg, 60%). Colourless oil. IR ($CHCl_3$): 3329*w* (br.), 3140*w* (br.), 2923*s*, 2852*s*, 2803*w*, 2099*s*, 1465*w*, 1365*w*, 1266*m*, 1108*s*, 1041*m*, 1012*m*, 972*m*, 832*w*, 721*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 5.95 (*dt*, $J = 15.9, 5.3$, H–C(5)); 5.78 (*dd*, $J = 15.5, 6.2$, H–C(4)); 4.19 (*t*, $J \approx 6.8$, H–C(3)); 4.01 (*d*, $J = 5.4$, 2 H–C(6)); 3.43 (*t*, $J = 6.7$, 2 H–C(1′)); 3.37 (*td*, $J = 7.6, 5.8$, H–C(2)); 2.68–2.55 (*m*, 2 H–C(1)); 2.32 (*s*, Me_2N); 1.58 (*quint.*, $J = 6.9$, 2 H–C(2′)); 1.35–1.23 (*m*, 16 H); 0.88 (*t*, $J = 6.6$, Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 131.70 (*d*, C(4)); 130.29 (*d*, C(5)); 76.25 (*d*, C(3)); 70.65, 70.60 (2*t*, C(6), C(1′)); 62.32 (*t*, C(1)); 61.13 (*d*, C(2)); 46.02 (*q*, Me_2N); 32.02 (*t*); 29.88–29.46 (several *t*); 26.30, 22.82 (2*t*), 14.27 (*q*, Me). HR-MALDI-MS: 355.3062 (100, $[M + H]^+$, $C_{19}H_{39}N_4O_2^+$; calc. 355.3073). Anal. calc. for $C_{19}H_{38}N_4O_2$ (354.53): C 64.37, H 10.80, N 15.80; found: C 64.62, H 10.85, 15.96.

*(*E*)-2-Amino-1,2,4,5-tetradeoxy-1-(dimethylamino)-6-*O*-undecyl-*D*-erythro-hex-4-enitol* (**9**). A suspension of $LiAlH_4$ (14.4 mg, 0.38 mmol) in Et_2O (5 ml) was treated with a soln. of **23** (66 mg, 0.19 mmol) in Et_2O (5 ml) and stirred at 0° for 1 h. The mixture was treated dropwise with H_2O (0.1 ml), 1M NaOH (0.2 ml), and H_2O (0.3 ml). The suspension was filtered through *Celite*, washing with AcOEt. After evaporation of the combined filtrate and washings, a soln. of the residue in AcOEt (20 ml) was washed

with H_2O (5 ml). The aq. phase was extracted with AcOEt (3×30 ml). The combined org. phases were washed with brine, dried (Na_2SO_4), and evaporated. FC (CH_2Cl_2/MeOH/Et_3N 95:5:1) afforded pure **9** (56 mg, 90%). Colourless oil. IR ($CHCl_3$): 3330*w* (br.), 3148*w* (br.), 2923*s*, 2852*s*, 2802*w*, 1465*w*, 1365*w*, 1266*m*, 1108*s*, 1041*m*, 1012*m*, 972*m*, 832*w*, 721*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 5.86 (*dt*, $J=15.3$, 5.4, H–C(5)); 5.67 (br. *dd*, $J=15.3$, 6.3, H–C(4)); 4.13 (*t*, $J=6.4$, H–C(3)); 4.13 (br. *s*, exchange with D_2O, NH_2, OH); 3.96 (*d*, $J=5.7$, 2 H–C(6)); 3.38 (*t*, $J=6.6$, 2 H–C(1′)); 2.96 (*q*, $J\approx6.9$, H–C(2)); 2.53 (*dd*, $J=12.6$, 6.6, 1 H–C(1)); 2.43 (*dd*, $J=12.9$, 7.5, 1 H–C(1)); 2.28 (*s*, Me_2N); 1.54 (*quint.*, $J=6.9$, 2 H–C(2′)); 1.31–1.23 (*m*, 16 H); 0.84 (*t*, $J=6.6$, Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 131.41 (*d*, C(4)); 130.00 (*d*, C(5)); 76.37 (*d*, C(3)); 70.62 (*t*, C(6), C(1′)); 62.80 (*t*, C(1)); 51.53 (*d*, C(2)); 45.72 (*q*, Me_2N); 31.95 (*t*); 29.80–29.38 (several *t*); 26.23, 22.74 (2*t*), 14.20 (*q*, Me). HR-MALDI-MS: 329.3162 (100, $[M+H]^+$, $C_{19}H_{41}N_2O_2^+$; calc. 329.3168). Anal. calc. for $C_{19}H_{40}N_2O_2 \cdot 0.75\,H_2O$ (342.04): C 66.72, H 12.23, N 8.19; found: C 66.56, H 12.04, N 8.31.

Icos-1-yn-3-one (**25**). A 50-ml two-necked flask was charged with $AlCl_3$ (490 mg, 3.675 mmol) in CH_2Cl_2 (5 ml), cooled to $-15°$ and treated with (trimethylsilyl)acetylene (0.59 ml, 4.2 mmol). The resulting reddish yellow mixture was treated with a (slow addition) ice-cooled soln. of stearoyl chloride (1.06 g, 3.5 mmol) in CH_2Cl_2 (5 ml), stirred at $-15°$ for 2 h (TLC (Et_2O/hexane 1:25, visualized with $KMnO_4$) showed complete conversion of stearoyl chloride). The reaction was quenched with slow addition of ice-cold 10% aq. HCl (3 ml), and the mixture was diluted with H_2O (20 ml) and extracted with Et_2O (3×150 ml). The combined org. phase was washed with sat. aq. $NaHCO_4$ and brine, dried (Na_2SO_4), and evaporated. FC (Et_2O/hexane 1:25) yielded pure **25** (60%). Colourless powder. M.p. 38–39°. R_f (Et_2O/hexane 1:25) 0.17. IR ($CHCl_3$): 3299*m*, 3028*w*, 2927*s*, 2855*s*, 2097*m*, 1681*s*, 1466*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 3.20 (*s*, H–C(1)); 2.58 (*t*, $J=7.5$, 2 H–C(1′)); 1.67 (*quint.*, $J=7.5$, 2 H–C(2′)); 1.24–1.17 (*m*, 28 H); 0.88 (*t*, $J=6.3$, Me). ^{13}C-NMR ($CDCl_3$, 300 MHz): 187.81 (*s*, C=O); 81.65 (*s*, C(2)); 78.40 (*d*, C(1); 45.65 (*d*, C(1′)); 32.11 (*t*, C(2′)); 29.87–29.07 (several *t*); 23.95, 22.88 (2*t*); 14.30 (*q*, Me). HR-EI-MS: 292.2746 (M^+), 291.2686 ($[M-H]^+$), 263.2375 ($[M-C_2H_5]^+$), 249.2215 ($[M-C_3H_7]^+$), 235.2056 ($[M-C_4H_9]^+$), 221.1894 ($[M-C_5H_{11}]^+$), 207.1751 ($[M-C_6H_{13}]^+$), 179.1444 ($[M-C_7H_{15}]^+$), 165.1295 ($[M-C_8H_{17}]^+$), 151.1147 ($[M-C_9H_{19}]^+$).

Nonadec-1-yne (**26**). Compound **26** was prepared according to the *Corey–Fuchs* method from octadecanal (stearaldehyde), which, in turn, was prepared by pyridinium chlorochromate-mediated oxidation of the commercially available octadecan-1-ol according to the procedure reported in [37][48]. A mixture of PPh_3 (391 mg, 1.49 mmol) and CBr_4 (247 mg, 0.745 mmol) in CH_2Cl_2 (2 ml) was cooled to 0°, treated with octadecanal (100 mg, 0.373 mmol) in one lot, and stirred at 0° for 0.5 h and at 25° for 0.5 h. The mixture was diluted with hexane, and the supernatant was filtered through *Celite*. The solid was dissolved in CH_2Cl_2, reprecipitated by the addition of hexane, and filtered. The process was repeated until the 1,1-dibromononadec-1-ene was completely washed out. The combined filtrates were evaporated to afford the crude 1,1-dibromoundec-1-ene, which was dissolved in dry THF (3 ml) under N_2 and cooled to $-78°$. The soln. was treated dropwise with 1.6M BuLi in hexane (0.93 ml, 1.49 mmol), stirred for 1 h, warmed to 25°, stirred for 4 h, treated dropwise with H_2O, and extracted with hexane. Evaporation and FC (hexane) gave pure **26** (75 mg, 76%) as a white solid, whose spectral and physical data were identical to those reported in [37]. M.p. 36–37°. R_f (hexane) 0.47. IR (ATR): 3287*w*, 2953*w*, 2915*s*, 2848*s*, 2113*w*, 1472*m*, 1462*m*, 1278*w*, 729*w*, 719*m*, 684*m*, 666*m*, 652*m*, 628*s*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 2.18 (*td*, $J=6.9$, 3.0, 2 H–C(3)); 1.94 (*t*, $J=2.4$, H–C(1)); 1.55–1.26 (*m*, 30 H); 0.88 (*t*, $J=6.6$, Me). ^{13}C-NMR ($CDCl_3$, 300 MHz): 84.83 (*s*, C(2)); 68.05 (*s*, C(1)); 32.04 (*t*); 29.80 (several *t*); 29.63 (*t*); 29.48 (*t*); 29.24 (*t*); 28.89 (*t*); 28.61 (*t*); 22.83 (*t*); 18.54 (*t*); 14.27 (*q*, Me).

Hexadecyl Prop-2-ynoate (**27**). A mixture of diethyl azodicarboxylate (DEAD) (736.5 mg, 4.229 mmol) and prop-2-ynoic acid (0.26 ml, 4.229 mmol) in THF (10 ml) was treated dropwise at 0° with a mixture of hexadecan-1-ol (512.6 mg, 2.114 mmol) and PPh_3 (1.109 g, 4.229 mmol) in THF (10 ml), stirred for 1.5 h, and evaporated under reduced pressure to give a colourless residue, which was filtered through a short pad of silica gel using Et_2O/hexane 1:9 as eluent to afford pure **27** (560 mg, 90%). Colourless gum. R_f (Et_2O/hexane 1:9) 0.54. ^{1}H-NMR ($CDCl_3$, 300 MHz): 4.19 (*t*, $J=6.7$, 2 H–C(1′)); 2.87 (*s*, H–C(1)); 1.67 (*quint.*, $J=7.2$, 2 H–C(2′)); 1.38–1.21 (*m*, 26 H); 0.88 (*t*, $J=6.7$, Me). ^{13}C-NMR ($CDCl_3$, 300 MHz): 152.70 (*s*, C=O); 74.82 (*s*, C(2)); 74.39 (*d*, C(1); 66.55 (*d*, C(1′)); 32.04 (*t*, C(2′)); 29.86–29.28 (several *t*); 28.42 (*t*); 25.86 (*t*); 22.82 (*t*); 14.27 (*q*, Me).

N-*Hexadecylprop-2-ynamide* (**28**). A mixture of prop-2-ynoic acid (0.1 ml, 1.62 mmol) and *N*,*N*′-dicyclohexylcarbodiimide (DCC; 401.17 mg, 1.944 mmol) in CH_2Cl_2 (10 ml) was treated dropwise over 10 min, at 0°, with a soln. of hexadecylamine (391.2 mg, 1.62 mmol) in CH_2Cl_2 (5 ml), and stirred for 1 h. The mixture was allowed to warm to 25° and stirred for 1.5 h. The mixture was filtered through a sintered funnel (No. 3) to remove the precipitated dicyclohexylurea, and the filtrate was evaporated. FC (silica gel; AcOEt/hexane 1:9→1:4) afforded pure **28** (400 mg, 84%). Colourless solid. R_f (AcOEt/hexane 1:1) 0.42. ^{1}H-NMR ($CDCl_3$, 300 MHz): 5.92 (*s*, NH); 3.29 (*td*, *J* = 7.1, 6.1, 2 H–C(1′)); 2.76 (*s*, H–C(1)); 1.52 (*quint.*, *J* = 7.1, 2 H–C(2′)); 1.31–1.25 (*m*, 26 H); 0.87 (*t*, *J* = 6.7, Me). ^{13}C-NMR ($CDCl_3$, 300 MHz): 151.97 (*s*, C=O); 77.34 (*s*, C(2)); 72.77 (*d*, C(1); 39.84 (*d*, C(1′)); 31.84 (*t*); 30.46 (*t*); 29.58–29.10 (several *t*); 26.71, 26.37 (2*t*), 14.02 (*q*, Me). HR-EI: 293.2701 (M^+), 292.2635 ($[M-H]^+$), 264.2323 ($[M-C_2H_5]^+$), 250.2167 ($[M-C_3H_7]^+$), 236.2012 ($[M-C_4H_9]^+$), 222.1856 ($[M-C_5H_{11}]^+$), 96.0453 ($[M-C_{14}H_{29}+H]^+$), 83.0365 ($[M-C_{15}H_{31}+H]^+$).

*(*E*)-1,3-Di*-O-*benzyl-2,4,5-trideoxy-2-(4-octadecanoyl-1*H*-1,2,3-triazol-1-yl)-6*-O-*undecyl*-D-erythro-*hex-4-enitol* (**30**). A mixture of **24** (151 mg, 0.297 mmol) and **25** (130.5 mg, 0.446 mmol) was treated with a soln. of $CuSO_4$ (0.7 mg, 0.0045 mmol) in H_2O (0.5 ml) and ascorbic acid (10.5 mg, 0.06 mmol) in H_2O (0.5 ml). The mixture was heated to 60°, stirred for 20 h, allowed to cool to r.t., diluted with H_2O (5 ml), and extracted with Et_2O (2 × 30 ml). The org. phases were washed with brine, dried (Na_2SO_4), and evaporated. FC (silica gel; Et_2O/hexane 1:4) yielded pure **30** (216 mg, 91%). White solid. M.p. 53.7°. R_f (Et_2O/hexane 3:7) 0.20. $[\alpha]_D^{25} = -58.0$ (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): 3160*w*, 3030*w*, 3008*w*, 2927*s*, 2855*s*, 1684*m*, 1602*w*, 1529*w*, 1496*w*, 1467*w*, 1455*w*, 1365*w*, 1107*m*, 1027*w*, 974*w*, 911*w*, 836*w*, 781*s*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.17 (*s*, C=CHN); 7.35–7.17 (*m*, 10 arom. H); 5.71 (*dt*, *J* = 15.6, 5.1, H–C(5)); 5.49 (br. *dd*, *J* = 15.6, 8.1, H–C(4)); 4.87 (*dt*, *J* = 15.3, 8.7, 5.7, H–C(2)); 4.59 (*d*, *J* = 11.7, PhC*H*); 4.49 (*d*, *J* = 11.7, PhC*H*); 4.44 (*d*, *J* = 11.7, PhC*H*); 4.29 (*d*, *J* = 12.0, PhC*H*); 4.29 (*t*, *J* ≈ 7.4, H–C(3)); 4.09 (br. *dd*, *J* = 10.5, 6.9, 1 H–C(1)); 3.91 (br. *dd*, *J* = 10.2, 3.6, 1 H–C(1)); 3.86 (br. *d*, *J* = 5.4, 2 H–C(6)); 3.35–3.21 (*AB*, 2 H–C(1′)); 3.09 (br. *t*, *J* = 7.5, 2 H–C(2″)); 1.80–1.69 (*m*, 2 H–C(2′)); 1.43–1.58 (*m*, 2 H–C(3″)); 1.40–1.20 (*m*, 44 H); 0.88 (*t*, *J* ≈ 6.8, 2 Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 195.7 (*s*, *C*=O); 147.79 (*s*, *C*=CHN); 137.42, 137.34 (2*s*); 134.57 (*d*, C(4)); 128.66 (4*d*); 128.16 (2*d*); 128.07 (2*d*); 127.91 (2*d*); 127.06 (*d*, C=*C*HN); 126.17 (*d*, C(5)); 78.28 (*d*, C(3)); 73.62, 71.0 (2*t*, 2 Ph*C*H$_2$); 70.75, 70.16 (2*t*, C(6), C(1′)); 67.58 (*t*, C(1)); 64.74 (*d*, C(2)); 38.80 (*t*); 32.11 (2*t*); 29.89–29.54 (several *t*); 26.38, 24.17 (2*t*); 22.88 (2*t*); 14.31 (*q*, 2 Me). HR-MALDI-MS: 800.6286 (100, $[M+H]^+$, $C_{51}H_{82}N_3O_4^+$; calc. 800.6305). Anal. calc. for $C_{51}H_{81}N_3O_4$ (800.2065): C 76.55, H 10.20, N 5.25; found: C 76.31, H 10.43, N 5.14.

*(*E*)-2,4,5-Trideoxy-2-(4-octadecanoyl-1*H*-1,2,3-triazol-1-yl)-6*-O-*undecyl*-D-erythro-*hex-4-enitol* **(10)**. A soln. of **30** (50 mg, 0.062 mmol) in $ClCH_2CH_2Cl$ (1 ml) was treated with anisole (0.08 ml, 0.75 mmol) and $AlCl_3$ (75 mg, 0.56 mmol), stirred at 25° for 24 h, treated with 1M HCl (0.5 ml), diluted with H_2O, and extracted with AcOEt (3 × 25 ml). The combined org. layers were washed with sat. aq. $NaHCO_3$ soln. and brine, dried (Na_2SO_4), and evaporated. FC (silica gel; AcOEt/hexane 1:1) gave pure **10** (30 mg, 78%). White solid. M.p. 80°. R_f (AcOEt/hexane 1:1) 0.28. $[\alpha]_D^{25} = +3.0$ (*c* = 0.25, $CHCl_3$). IR ($CHCl_3$): 3284*w* (br.), 2954*m*, 2920*s*, 2849*s*, 1688*m*, 1530*w*, 1468*m*, 1403*w*, 1366*w*, 1333*w*, 1251*w*, 1183*w*, 1118*m*, 1104*m*, 1081*m*, 1045*m*, 1015*m*, 973*m*, 778*w*, 720*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.38 (*s*, C=CHN); 5.88 (*dtd*, *J* = 15.6, 5.1, 0.9, H–C(5)); 5.73 (br. *ddt*, *J* = 15.5, 5.8, 1.25, H–C(4)); 4.75 (br. *q*, *J* ≈ 4.6, H–C(3)); 4.67–4.63 (*m*, H–C(2)); 4.37–4.30 (*m*, 1 H–C(1)); 4.15–4.08 (*m*, 1 H–C(1)); 3.92 (*d*, *J* = 5.1, 2 H–C(6)); 3.36 (*t*, *J* = 6.3, 2 H–C(1′)); 3.18 (*d*, *J* = 4.5, HO–C(3)); 3.08 (*t*, *J* = 7.5, 2 H–C(2″)); 2.91 (*t*, *J* = 5.7, HO–C(1)); 1.77–1.67 (*m*, 2 H–C(2′)); 1.58–1.50 (*m*, 2 H–C(3″)); 1.38–1.25 (*m*, 44 H); 0.86 (*t*, *J* ≈ 6.8, 2 Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 195.49 (*s*, *C*=O); 147.20 (*s*, *C*=CHN); 131.10 (*d*, C(4)); 129.12 (*d*, C=*C*HN); 126.52 (*d*, C(5)); 72.45 (*d*, C(3)); 70.95, 70.08 (2*t*, C(6), C(1′)); 65.99 (*d*, C(2)); 61.24 (*t*, C(1)); 39.69 (*t*); 31.99 (2*t*); 29.78–29.43 (several *t*); 26.21, 24.01 (2*t*); 22.77 (2*t*); 14.22 (*q*, 2 Me). HR-MALDI-MS: 620.5350 (100, $[M+H]^+$, $C_{37}H_{70}N_3O_4^+$; calc. 620.5366). Anal. calc. for $C_{37}H_{69}N_3O_4$ (619.9615): C 71.68, H 11.22, N 6.78; found: C 71.79, H 11.26 , N 6.69.

*(*E*)-1,3-Di*-O-*benzyl-2,4,5-trideoxy-2-[4-(1-hydroxyoctadecyl)-1*H*-1,2,3-triazol-1-yl]-6*-O-*undecyl*-D-erythro-*hex-4-enitol* (**35**). A soln. of **30** (100 mg, 0.125 mmol) in THF/H_2O 3:2 (1.5 ml) was cooled to 0°, treated with $NaBH_4$ (4.8 mg, 0.125 mmol), stirred for 30 min, then warmed to r.t., and stirred for 24 h. The mixture was neutralized with 1M HCl, diluted with H_2O, and extracted with AcOEt (2 × 50 ml). The combined org. layers were washed with sat. aq. $NaHCO_3$ soln. and brine, dried (Na_2SO_4), and

evaporated. FC (silica gel; Et_2O/hexane 8:2) gave pure **35** (88 mg, 88%). White solid. M.p. 64.2°. R_f (Et_2O/hexane 4:1) 0.46. $[\alpha]_D^{25} = -10.1$ ($c = 1.1$, $CHCl_3$) IR ($CHCl_3$): 3609*w*, 3432*w* (br.), 2927*s*, 2855*s*, 1496*w*, 1465*m*, 1455*m*, 1365*w*, 1099*m*, 1048*m*, 1028*m*, 972*w*, 783*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.57 (*s*, C=CHN); 7.36–7.19 (*m*, 10 arom. H); 5.66 (*dt*, *J* = 15.6, 5.1, H–C(5)); 5.48 (br. *dd*, *J* = 15.6, 8.1, H–C(4)); 4.87–4.79 (*m*, H–C(2), H–C(1″)); 4.60 (*d*, *J* = 11.7, PhC*H*); 4.50 (*d*, *J* = 11.7, PhC*H*); 4.45 (*d*, *J* = 11.7, PhC*H*); 4.30 (*d*, *J* = 11.7, PhC*H*); 4.28 (*t*, *J* ≈ 8.0, H–C(3)); 4.09 (br. *dd*, *J* = 10.5, 6.9, 1 H–C(1)); 3.91 (br. *dd*, *J* = 10.2, 3.6, 1 H–C(1)); 3.86 (br. *d*, *J* = 5.4, 2 H–C(6)); 3.35–3.24 (*AB*, 2 H–C(1′)); 2.26 (br. *s*, OH); 1.80–1.69 (*m*, 2 H–C(2′)); 1.43–1.58 (*m*, 2 H–C(2″)); 1.40–1.20 (*m*, 44 H); 0.88 (*t*, *J* ≈ 6.8, 2 Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 151.13 (*s*, *C*=CHN); 137.43 (*d*, C(4)); 137.36 (2*s*); 133.65, 128.35 (4*d*); 127.73 (4*d*); 127.58 (2*d*); 127.34 (*d*, C=*C*HN); 120.86 (*d*, C(5)); 78.37 (*d*, C(3)); 73.24, 70.72 (2*t*, 2 Ph*C*H$_2$); 70.59, 70.04 (2*t*, C(6), C(1′)); 67.71 (*t*, C(1)); 67.05 (*d*, C(2″)); 64.08 (*d*, C(2)); 37.23 (*t*); 31.82 (2*t*); 29.61–29.27 (several *t*); 26.08, 25.40 (2*t*); 22.59 (2*t*); 14.03 (*q*, 2 Me). HR-MALDI-MS: 824.6262 (100, $[M + Na]^+$, $C_{51}H_{83}N_3NaO_4^+$; calc. 824.6281). Anal. calc. for $C_{51}H_{83}N_3O_4$ (802.2224): C 76.36, H 10.43, N 5.24; found: C 76.39, H 10.49, N 5.28.

*(*E*)-2,4,5-Trideoxy-2-[5-(1-hydroxyoctadecyl)-1*H*-1,2,3-triazol-1-yl]-6-*O*-undecyl-*D*-erythro-hex-4-enitol* (**11**). A soln. of **35** (47 mg, 0.059 mmol) in $ClCH_2CH_2Cl$ (1 ml) was treated with anisole (76 µl, 0.703 mmol) and $AlCl_3$ (70.3 mg, 0.53 mmol), stirred at 25° for 5 h, treated with 1M HCl (0.5 ml), diluted with H_2O, and extracted with AcOEt (3 × 25 ml). The combined org. layers were washed with 2% aq. NaOH soln., H_2O, and brine, dried (Na_2SO_4), and evaporated. FC (silica gel; AcOEt/hexane 1:1) gave pure **11** (26 mg, 71%). White powder which, at r.t., was insoluble in solvents other than THF. Compound **11** dissolves partially in $CHCl_3$ when heated to 45°. ^{1}H-NMR Measurements in (D_8)THF were not useful, as many signals were overlapping with the THF signals. M.p. 95–99.5°. R_f (AcOEt) 0.40. IR (ATR): 3275 (br.), 3135*w*, 3119*w*, 2955*w*, 2916*s*, 2849*s*, 2795*w*, 1470*m*, 1364*w*, 1328*w*, 1261*w*, 1220*w*, 1117*m*, 1104*m*, 1087*m*, 1030*m*, 998*w*, 974*w*, 962*w*, 842*w*, 808*w*, 718*w*, 703*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz, 45°): 7.69 (*s*, C=CHN); 5.84 (*dt*, *J* = 15.6, 5.1, H–C(5)); 5.71 (*dd*, *J* = 15.6, 8.1, H–C(4)); 4.87 (*m*, H–C(3)); 4.75 (*m*, H–C(2)); 4.52–4.48 (*m*, H–C(1″)); 4.30 (*m*, 1 H–C(1)); 4.15 (*m*, 1 H–C(1)); 3.91 (*dd*, *J* = 4.8, 0.9, 2 H–C(6)); 3.65 (*d*, *J* = 0.9, 1 H); 3.47–3.43 (*m*, 2 H–C(1′)); 3.39 (*t*, *J* = 6.3); 1.85–1.48 (*m*, 2 H–C(2′), 2 H–C(2″)); 1.30–1.26 (*m*, 44 H); 0.89 (*t*, *J* ≈ ≈ 6.6, 2 Me). HR-MALDI-MS: 644.5325 (100, $[M + Na]^+$, $C_{37}H_{71}N_3NaO_4^+$; calc. 644.5342). Anal. calc. for $C_{37}H_{71}N_3O_4 \cdot 0.5\ H_2O$: C 70.43, H 11.50, N 6.66; found: C 70.26, H 11.13, N 6.37.

*(*E*)-1,3-Di-O-benzyl-2,4,5-trideoxy-2-(4-heptadecyl-1*H*-1,2,3-triazol-1-yl)-6-O-undecyl-D*-erythro-hex-4-enitol (**31**). A mixture of **24** (53 mg, 0.104 mmol) and **26** (41.5 mg, 0.157 mmol) was treated with a soln. of $CuSO_4$ (0.25 mg, 0.0016 mmol) in H_2O (0.3 ml) and ascorbic acid (4.0 mg, 0.021 mmol) in H_2O (0.5 ml), heated to 55°, stirred for 48 h, allowed to cool to r.t., diluted with H_2O (2 ml), and extracted with Et_2O (2 × 15 ml). The org. phases were washed with brine, dried (Na_2SO_4), and evaporated. FC (silica gel; Et_2O/hexane 1:1) yielded pure **31** (65 mg, 81%). White amorphous solid. R_f (Et_2O/hexane 1:1) 0.37. $[\alpha]_D^{25} = -11.3$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3026*w*, 2927*s*, 2855*s*, 1496*w*, 1467*w*, 1455*m*, 1365*w*, 1100*m*, 1049*w*, 1028*w*, 973*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.38 (*s*, C=CHN); 7.35–7.27 (*m*, 6 arom. H); 7.25–7.18 (*m*, 4 arom. H); 5.67 (*dt*, *J* = 15.6, 5.4, H–C(5)); 5.48 (br. *dd*, *J* = 15.9, 8.1, H–C(4)); 4.79 (*td*, *J* ≈ 6.6, 3.9, H–C(2)); 4.56 (*d*, *J* = 11.7, PhC*H*); 4.49 (*d*, *J* = 12.3, PhC*H*); 4.44 (*d*, *J* = 12.3, PhC*H*); 4.31 (*d*, *J* = 11.4, PhC*H*); 4.31 (*t*, *J* = 8.1, H–C(3)); 4.09 (br. *dd*, *J* = 10.2, 6.3, 1 H–C(1)); 3.93 (br. *dd*, *J* = 9.9, 3.6, 1 H–C(1)); 3.85 (br. *d*, *J* = 5.4, 2 H–C(6)); 3.34–3.22 (*AB*, 2 H–C(1′)); 2.68 (br. *t*, *J* = 15.6, 2 H–C(1″)); 1.68–1.58 (*m*, 2 H–C(2′)); 1.55–1.48 (*m*, 2 H–C(2″)); 1.26 (*m*, 44 H); 0.88 (*t*, *J* ≈ 6.7, 2 Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 147.91 (*s*, *C*=CHN); 137.55, 137.47 (2*s*); 133.58 (*d*, C(4)); 128.34 (4*d*); 127.70 (4*d*); 127.58 (2*d*); 127.48 (*d*, C=*C*HN); 121.05 (*d*, C(5)); 78.56 (*d*, C(3)); 73.33, 70.83 (2*t*, 2 Ph*C*H$_2$); 70.51, 70.18 (2*t*, C(6), C(1′)); 68.07 (*t*, C(1)); 64.05 (*d*, C(2)); 32.04 (2*t*); 29.84–29.42 (several *t*); 26.33, 25.85 (2*t*), 22.83 (2*t*); 14.28 (*q*, 2 Me). HR-MALDI-MS: 772.6336 (100, $[M+H]^+$, $C_{50}H_{82}N_3O_3^+$; calc. 772.6356). Anal. calc. for $C_{50}H_{81}N_3O_3$ (772.1964): C 77.77, H 10.57, N 5.44; found: C 77.51, H 10.45, N 5.41.

*(*E*)-2,4,5-Trideoxy-2-(4-heptadecyl-1*H*-1,2,3-triazol-1-yl)-6-O-undecyl-D*-erythro-hex-4-enitol (**12**). A soln. of **31** (53 mg, 0.063 mmol) in CH_2Cl_2 (1 ml) was treated with anisole (89.7 µl, 0.826 mmol) and $AlCl_3$ (82.4 mg, 0.618 mmol), stirred at 25° for 24 h, and treated with 1M HCl (0.5 ml), diluted with H_2O (3 ml), and extracted with AcOEt (2 × 20 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (silica gel; AcOEt/hexane 1:9 → 1:1) afforded pure **12** (33 mg, 86%).

White solid. M.p. 69.8°. R_f (AcOEt/hexane 1:1) 0.17. $[\alpha]_D^{25} = +8.0$ ($c = 0.3$, $CHCl_3$). IR ($CHCl_3$): 3397*w* (br.), 3017*m*, 2927*s*, 2855*s*, 1466*m*, 1366*w*, 1110*m*, 974*w*, 767*s*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.51 (*s*, C=CHN); 5.83 ((*dtd*, *J* = 15.6, 5.1, 0.9, H–C(5)); 5.67 (br. *dd*, *J* = 15.6, 5.7, H–C(4)); 4.74 (br. *dd*, *J* = 9.9, 5.1, H–C(3)); 4.46 (*dtd*, *J* = 11.1, 5.7, 3.6, H–C(2)); 4.29 (*td*, *J* = 12.0, 5.7, 1 H–C(1)); 4.14–4.06 (*m*, 1 H–C(1)); 3.90 (*d*, *J* = 4.8, 2 H–C(6)); 3.88 (*d*, *J* ≈ 6.9, HO–C(3)); 3.59 (*t*, *J* = 3.0, HO–C(1)); 3.35 (*t*, *J* = 6.6, 2 H–C(1′)); 2.64 (*t*, *J* = 7.8, 2 H–C(1″)); 1.67–1.49 (*m*, 2 H–C(2′), 2 H–C(2″)); 1.39–1.22 (*m*, 44 H); 0.87 (*t*, *J* ≈ 6.8, 2 Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 147.72 (*s*, *C*=CHN); 130.43 (*d*, C(4)); 129.72 (*d*, C=*C*HN); 121.75 (*d*, C(5)); 72.44 (*d*, C(3)); 70.86, 70.29 (2*t*, C(6), C(1′)); 65.85 (*d*, C(2)); 61.63 (*t*, C(1)); 32.03 (*t*); 29.83–29.48 (several *t*); 26.28 (*t*); 25.71 (*t*); 22.82 (2*t*); 14.26 (*q*, 2 Me). HR-MALDI-MS: 592.5403 (100, $[M+H]^+$, $C_{36}H_{70}N_3O_3^+$; calc. 592.5417). Anal. calc. for $C_{36}H_{69}N_3O_3$ (591.9514): C 73.04, H 11.75, N 7.10; found: C 73.00, H 11.64, N 6.97.

*(*E*)-1,3-Di*-O-*benzyl-2,4,5-trideoxy-2-[4-(hexadecyloxycarbonyl)-1*H*-1,2,3-triazol-1-yl]-6*-O-*undecyl*-D-erythro-*hex-4-enitol* (**32**). A mixture of **24** (50 mg, 0.098 mmol) and **27** (145 mg, 0.49 mmol) was treated with a soln. of $CuSO_4$ (0.3 mg, 0.0019 mmol) in H_2O (0.5 ml) and ascorbic acid (3.5 mg, 0.02 mmol) in H_2O (0.5 ml). The mixture was stirred at 60° for 36 h, allowed to cool to 25°, diluted with H_2O (2 ml), and extracted with AcOEt (2 × 25 ml). The combined org. layers were washed with $NaHCO_3$ soln. and brine, dried (Na_2SO_4), and evaporated. FC (silica gel; Et_2O/hexane 1:9 → 3:7) to yield pure **32** (66 mg, 84%). White solid. M.p. 46.2°. R_f (Et_2O/hexane) 0.34. $[\alpha]_D^{25} = -7.0$ ($c = 0.235$, $CHCl_3$). IR (ATR): 2922*w*, 2852*s*, 1741*w*, 1720*w*, 1542*m*, 1496*w*, 1454*w*, 1390*w*, 1366*w*, 1219*m*, 1196*w*, 1105*w*, 1036*w*, 974*w*, 772*s*, 735*w*, 697*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.18 (*s*, C=CHN); 7.35–7.28 (*m*, 6 arom. H); 7.22–7.17 (*m*, 4 arom. H); 5.71 (*dt*, *J* = 15.6, 5.1, H–C(5)); 5.49 (br. *dd*, *J* = 15.6, 8.1, H–C(4)); 4.88 (*td*, *J* ≈ 6.6, 3.3, H–C(2)); 4.69 (*d*, *J* = 11.7, PhC*H*); 4.50 (*d*, *J* = 12.0, PhC*H*); 4.44 (*d*, *J* = 12.0, PhC*H*); 4.37–4.27 (*m*, PhC*H*, H–C(3), 2 H–C(1″)); 4.11 (*dd*, *J* = 10.2, 6.3, 1 H–C(1)); 3.92 (*dd*, *J* = 10.2, 3.3, 1 H–C(1)); 3.86 (br. *d*, *J* = 4.8, 2 H–C(6)); 3.35–3.22 (*AB*, 2 H–C(1′)); 1.83–1.73 (*m*, 2 H–C(2″)); 1.58–1.48 (*m*, 2 H–C(2′)); 1.39–1.21 (*m*, 42 H); 0.88 (*t*, *J* ≈ 6.5, 2 Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 160.86 (*s*, *C*=O); 139.78 (*s*, *C*=CHN); 137.17 (*d*, C(4)); 137.08 (2*s*); 134.35, 128.40 (5*d*); 127.87 (2*d*); 127.79 (*d*, C=*C*HN); 127.63 (2*d*); 126.72 (*d*, C(5)); 78.05 (*d*, C(3)); 73.33 (*t*, Ph*C*H$_2$); 70.75 (*t*, C(6)); 70.49 (*t*, Ph*C*H$_2$); 69.87 (*t*, C(1′)); 67.32 (*t*, C(1)); 65.25 (*t*, C(1″)); 64.49 (*d*, C(2)); 31.82 (2*t*); 29.60–29.26 (several *t*); 28.59 (*t*); 26.08, 25.81 (2*t*), 22.56 (2*t*); 14.03 (2*q*, 2 Me). HR-MALDI-MS: 802.6078 (100, $[M+H]^+$, $C_{50}H_{80}N_3O_5^+$; calc. 802.6098). Anal. calc. for $C_{50}H_{97}N_3O_5$ (802.1794): C 74.86, H 9.93, N 5.24; found: C 74.86, H 10.00, N 5.04.

*(*E*)-2,4,5-trideoxy-2-[4-(hexadecyloxycarbonyl)-1*H*-1,2,3-triazol-1-yl]-6*-O-*undecyl*-D-erythro-*hex-4-enitol* (**13**). A soln. of **32** (46 mg, 0.057 mmol) in CH_2Cl_2 (2 ml) was treated with anisole (75 µl, 0.694 mmol) and $AlCl_3$ (76.5 mg, 0.573 mmol), stirred at r.t. for 24 h, treated dropwise with 1M HCl (0.1 ml), diluted with H_2O (3 ml), and extracted with AcOEt (2 × 20 ml). The combined org. layers were washed with $NaHCO_3$ soln. and brine, dried (Na_2SO_4), and evaporated. FC (silica gel; AcOEt/hexane 3:7 → 1:1) afforded pure **13** (32.3 mg, 91%). White solid. M.p. 66.5°. R_f (AcOEt/hexane 1:1) 0.18. $[\alpha]_D^{25} = +6.2$ ($c = 0.59$, $CHCl_3$). IR ($CHCl_3$): 3600*w*, 3396 (br.), 2928*s*, 2855*m*, 1721*w*, 1543*w*, 1466*w*, 1398*w*, 1363*w*, 1255*w*, 1162*w*, 1106*w*, 1042*w*, 973*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.40 (*s*, C=CHN); 5.92 (*dtd*, *J* = 15.6, 5.4, 0.9, H–C(5)); 5.77 (br. *dd*, *J* = 15.3, 5.7, H–C(4)); 4.79 (*t*, *J* ≈ 5.1, H–C(3)); 4.64 (*td*, *J* = 5.1, 3.3, H–C(2)); 4.36 (*dd*, *J* = 11.8, 5.2, 1 H–C(1)); 4.32 (*t*, *J* = 6.9, 2 H–C(1″)); 4.13 (*dd*, *J* = 12.0, 2.7, 1 H–C(1)); 3.93 (*d*, *J* = 5.1, 2 H–C(6)); 3.51–3.43 (br. *s*, HO–C(3)); 3.38 (*t*, *J* = 6.6, 2 H–C(1′)); 3.19 (br. *s*, HO–C(1)); 1.81–1.71 (*m*, 2 H–C(2″)); 1.60–1.50 (*m*, 2 H–C(2′)); 1.42–1.25 (*m*, 42 H); 0.87 (*t*, *J* ≈ 6.6, 2 Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 160.69 (*s*, *C*=O); 139.50 (*s*, *C*=CHN); 131.16 (*d*, C(4)); 129.00 (*d*, C=*C*HN); 128.39 (*d*, C(5)); 72.55 (*d*, C(3)); 70.85, 70.00 (2*t*, C(6), C(1′)); 65.83 (*d*, C(2)); 65.45 (*t*, C(1″)); 61.19 (*t*, C(1)); 31.81 (*t*, C(2′)); 29.59–29.52 (several *t*); 29.44 (2*t*); 29.25, 29.20 (2*t*); 28.54 (*t*); 26.04 (*t*); 25.78 (*t*); 22.59 (2*t*); 14.01 (*q*, 2 Me). HR-MALDI-MS: 622.5143 (100, $[M+H]^+$, $C_{36}H_{68}N_3O_5^+$; calc. 622.5159). Anal. calc. for $C_{36}H_{67}N_3O_5$ (621.36143): C 69.52, H 10.86, N 6.76; found: C 69.69, H 10.87, N 6.64.

*(*E*)-1,3-Di*-O-*benzyl-2,4,5-trideoxy-2-{4-[(hexadecylamino)carbonyl]-1*H*-1,2,3-triazol-1-yl}-6*-O-*undecyl*-D-erythro-*hex-4-enitol* (**33**). A mixture of **24** (85 mg, 0.167 mmol) and **28** (49.1 mg, 0.167 mmol) in i-PrOH (2 ml) was treated with a soln. of $CuSO_4$ (0.4 mg, 0.0025 mmol) in H_2O (0.5 ml) and ascorbic acid (6.0 mg, 0.33 mmol) in H_2O (0.5 ml), and stirred at 60° for 24 h. The mixture was allowed to cool to r.t. and extracted with AcOEt (2 × 50 ml). The combined org. layers were washed with brine, dried

(Na_2SO_4), and evaporated. FC (silica gel; Et_2O/hexane 3:7) yielded pure **33** (134 mg, 100%). White solid. M.p. 93.5°. R_f (Et_2O/hexane 1:1) 0.23. $[\alpha]_D^{25} = -8.3$ ($c = 2.3$, $CHCl_3$). IR ($CHCl_3$): 3621*m*, 3419*w*, 3013*m*, 2974*s*, 2928*s*, 2856*s*, 1663*m*, 1576*m*, 1508*w*, 1454*m*, 1391*w*, 1368*w*, 1240*m*, 1046*s*, 974*w*, 877*m*, 668*w*, 570*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.19 (*s*, C=CHN); 7.35–7.18 (*m*, 10 arom. H); 5.70 (*dt*, $J = 15.6$, 5.4, H–C(5)); 5.48 (*ddt*, $J = 15.9$, 8.1, 1.2, H–C(4)); 4.85 (*td*, $J \approx 6.9$, 3.6, H–C(2)); 4.59 (*d*, $J = 11.7$, PhC*H*); 4.50 (*d*, $J = 12.0$, PhC*H*); 4.44 (*d*, $J = 12.0$, PhC*H*); 4.30 (*d*, $J = 11.7$, PhC*H*); 4.29 (*t*, $J = 7.5$, H–C(3)); 4.08 (*dd*, $J = 10.2$, 6.6, 1 H–C(1)); 3.90 (*dd*, $J = 10.2$, 3.6, 1 H–C(1)); 3.85 (*dt*, $J = 5.4$, 1.5, 2 H–C(6)); 3.47–3.40 (*m*, 2 H–C(1″)); 3.32–3.20 (*AB*, 2 H–C(1′)); 1.66–1.48 (*m*, 2 H–C(2′), 2 H–C(2″)); 1.40–1.20 (*m*, 42 H); 0.88 (*t*, $J \approx 6.3$, 2 Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 159.92 (*s*, *C*=O); 143.05 (*s*, *C*=CHN); 137.17, 137.09 (2*s*); 134.28 (*d*, C(4)); 128.40 (4*d*); 127.81 (4*d*); 127.64 (2*d*); 126.90 (*d*, C=*C*HN); 125.56 (*d*, C(5)); 78.08 (*d*, C(3)); 73.49 (*t*, Ph*C*H$_2$); 70.84 (*t*, C(6)); 70.53 (*t*, Ph*C*H$_2$); 70.03 (*t*, C(1′)); 67.57 (*t*, C(1)); 64.68 (*d*, C(2)); 31.26 (*t*, C(1″)); 32.04 (2*t*); 29.82–29.47 (several *t*); 27.12, 26.31 (2*t*); 22.83 (2*t*), 14.03 (2*q*, 2 Me). HR-MALDI-MS: 801.6235 (100, $[M+H]^+$, $C_{50}H_{81}N_4O_4^+$; calc. 801.6258). Anal. calc. for $C_{50}H_{80}N_4O_4$ (801.1946): C 74.96, H 10.06, N 6.99; found: C 74.89, H 10.08, N 6.98.

*(*E*)-2,4,5-Trideoxy-2-{4-[(hexadecylamino)carbonyl]-1*H*-1,2,3-triazol-1-yl}-6-*O*-undecyl-*D*-erythro-hex-4-enitol* (**14**). A soln. of **33** (65 mg, 0.081 mmol) in CH_2Cl_2 (3 ml) was treated with anisole (133 µl, 1.217 mmol) and $AlCl_3$ (129.8 mg, 0.974 mmol), and stirred at r.t. for 24 h. The mixture was cooled to 0°, treated dropwise with 10% HCl (0.5 ml), diluted with H_2O (3 ml), and extracted with AcOEt (5 × 20 ml). The combined org. layers were dried (Na_2SO_4) and evaporated. FC (silica gel; AcOEt/hexane 1:1 → AcOEt) afforded pure **14** (45 mg, 89%). White solid. M.p. 95°. R_f (AcOEt) 0.43. $[\alpha]_D^{25} = +10.1$ ($c = 0.65$, $CHCl_3$). IR ($CHCl_3$): 3691*w*, 3415*w*, 2928*s*, 2855*m*, 1661*w*, 1577*w*, 1509*w*, 1466*w*, 1368*w*, 1213*w*, 1107*w*, 1048*w*, 970*w*, 757*s*, 670*w*, 438*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.55 (*s*, C=C*H*N); 7.28 (*t*, $J = 5.7$, NH); 5.86 (*dt*, $J = 15.3$, 5.1, H–C(5)); 5.71 (br. *dd*, $J = 15.6$, 5.1, H–C(4)); 4.71–4.65 (*m*, H–C(2), H–C(3)); 4.41 (*d*, $J = 4.8$, HO–C(3)); 4.35 (*dt*, $J = 12.0$, 4.8, 1 H–C(1)); 4.17 (*dd*, $J = 6.3$, 4.8, HO–C(1)); 4.03 (*ddd*, $J = 11.4$, 6.0, 2.4, 1 H–C(1)); 3.91 (*d*, $J = 5.4$, 2 H–C(6)); 3.42–3.32 (*m*, 2 H–C(1′), 2 H–C(1″)); 1.64–1.49 (*m*, 2 H–C(2′), 2 H–C(2″)); 1.38–1.21 (*m*, 42 H); 0.87 (*t*, $J \approx 6.8$, 2 Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 160.70 (*s*, *C*=O); 142.31 (*s*, *C*=CHN); 130.60 (*d*, C(4)); 129.57 (*d*, C=*C*HN); 126.24 (*d*, C(5)); 72.19 (*d*, C(3)); 70.68, 70.13 (2*t*, C(6), C(1′)); 66.02 (*d*, C(2)); 60.93 (*t*, C(1)); 39.28 (*t*, C(1″)); 31.82 (2*t*); 29.60–29.25 (several *t*); 26.86, 26.04 (2*t*); 22.59 (2*t*); 14.01 (*q*, 2 Me). HR-MALDI-MS: 643.5122 (100, $[M + Na]^+$, $C_{36}H_{68}N_4NaO_4^+$; calc. 643.5138). Anal. calc. for $C_{36}H_{68}N_4O_4$ (620.9495): C 69.63, H 11.04, N 9.02; found: C 69.53, H 11.04 , N 9.02.

*(*E*)-1,3-Di-*O*-benzyl-2,4,5-trideoxy-2-{4-[(hexadecylamino)thiocarbonyl]-1*H*-1,2,3-triazol-1-yl}-6-*O*-undecyl-*D*-erythro-hex-4-enitol* (**36**). A mixture of **33** (83.7 mg, 0.1045 mmol) and *Lawesson*'s reagent (29.6 mg, 0.073 mmol) in toluene (2 ml) was stirred for 2 h at 75° and then evaporated. The residue after FC (silica gel; Et_2O/hexane 1:4) gave pure **36** (79 mg, 93%). Pale yellow crystals. M.p. 39.9°. R_f (Et_2O/hexane 1:1) 0.50. $[\alpha]_D^{25} = -3.1$ ($c = 0.45$, $CHCl_3$). IR ($CHCl_3$): 3610*w*, 3448 (br.), 3361*w*, 3164*w*, 3016*m*, 2928*s*, 2856*m*, 2401*w*, 1562*w*, 1512*w*, 1455*w*, 1405*w*, 1366*w*, 1221*w*, 1101*w*, 1045*w*, 972*w*, 731*w*, 668*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.89 (*t*, $J \approx 5.6$, NH); 8.37 (*s*, C=CHN); 7.36–7.19 (*m*, 10 arom. H); 5.73 (*dt*, $J = 15.6$, 5.4, H–C(5)); 5.50 (*ddt*, $J = 15.3$, 8.1, 1.2, H–C(4)); 4.82 (*td*, $J = 6.9$, 3.9, H–C(2)); 4.59 (*d*, $J = 11.4$, PhC*H*); 4.50 (*d*, $J = 12.3$, PhC*H*); 4.45 (*d*, $J = 12.0$, PhC*H*); 4.30 (*d*, $J = 11.4$, PhC*H*); 4.28 (*t*, $J = 8.1$, H–C(3)); 4.07 (*dd*, $J = 10.2$, 6.6, 1 H–C(1)); 3.90 (*dd*, $J = 10.5$, 3.9, 1 H–C(1)); 3.88 (*d*, $J = 3.0$, 2 H–C(6)); 3.87–3.79 (*m*, 2 H–C(1″)); 3.34–3.22 (*AB*, 2 H–C(1′)); 1.81–1.71 (*m*, 2 H–C(2″)); 1.57–1.48 (*m*, 2 H–C(2′)); 1.46–1.20 (*m*, 42 H); 0.88 (*t*, $J \approx 6.3$, 2 Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 184.28 (*s*, *C*=S); 147.87 (*s*, *C*=CHN); 137.09 (2*s*); 134.27 (*d*, C(4)); 128.41 (5*d*); 127.91 (2*d*); 127.84 (2*d*); 127.68 (*d*, C=*C*HN); 126.84 (*d*, C(5)); 77.95 (*d*, C(3)); 73.32 (*t*, Ph*C*H$_2$); 70.75 (*t*, C(6)); 70.42 (*t*, Ph*C*H$_2$); 69.91 (*t*, C(1′)); 67.33 (*t*, C(1)); 64.68 (*d*, C(2)); 44.88 (*t*, C(1″)); 31.82 (2*t*); 29.60–29.46 (several *t*); 29.26, 28.13 (2*t*); 26.99, 26.01 (2*t*); 22.59 (2*t*), 14.03 (*q*, 2 Me). HR-MALDI-MS: 817.6009 (100, $[M+H]^+$, $C_{50}H_{81}N_4O_3S^+$; calc. 817.6029). Anal. calc. for $C_{50}H_{80}N_4O_3S$ (817.2602): C 73.48, H 9.87, N 6.86; found: C 73.49, H 9.61, N 6.82.

*(*E*)-2,4,5-Trideoxy-2-{4-[(hexadecylamino)thiocarbonyl]-1*H*-1,2,3-triazol-1-yl}-6-*O*-undecyl-*D*-erythro-hex-4-enitol* (**15**). A soln. of **36** (70 mg, 0.0857 mmol) in CH_2Cl_2 (6 ml) was treated with anisole (75 µl, 0.685 mmol) and $AlCl_3$ (114.2 mg, 0.857 mmol), and stirred at r.t. for 11 h. The mixture was cooled to 0°, treated dropwise with 10% HCl (1.1 ml), and extracted with AcOEt (5 × 30 ml). The combined org.

layers were dried (Na_2SO_4) and evaporated. FC (silica gel; AcOEt/hexane 1:4→1:3) gave pure **15** (43.7 mg, 80%) as pale yellow amorphous solid, which solidified after keeping at −20° for 2 d. M.p. 45.4°. R_f (AcOEt/hexane 1:4) 0.35. $[\alpha]_D^{25} = +8.9$ ($c = 0.65$, $CHCl_3$). IR ($CHCl_3$): 3609*w*, 3362*w*, 3164*w*, 3015*w*, 2928*s*, 2856*m*, 1562*w*, 1511*w*, 1456*w*, 1406*w*, 1368*w*, 1306*w*, 1217*w*, 1111*w*, 1077*w*, 1045*w*, 973*w*, 748*s*, 668. ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.93 (*t*, $J = 5.7$, NH); 8.48 (*s*, C=C*H*N); 5.84 (*dtd*, $J = 15.6$, 5.4, 0.9, H−C(5)); 5.69 (br. *dd*, $J = 15.6$, 6.0, H−C(4)); 4.69 (*t*, $J \approx 5.6$, H−C(3)); 4.60 (*td*, $J = 5.7$, 3.6, H−C(2)); 4.27 (*dd*, $J = 12.3$, 6.0, 1 H−C(1)); 4.08 (*dd*, $J = 12.0$, 3.9, 1 H−C(1)); 3.90 (*d*, $J = 5.4$, 2 H−C(6)); 3.80 (*dd*, $J = 13.2$, 7.2, 2 H−C(1″)); 3.35 (*t*, $J = 6.6$, 2 H−C(1′), HO−C(3)); 3.11 (br. *s*, HO−C(1)); 1.79–1.69 (*m*, 2 H−C(2″)); 1.58–1.48 (*m*, 2 H−C(2′)); 1.42–1.25 (*m*, 42 H); 0.87 (*t*, $J \approx 6.6$, 2 Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 183.88 (*s*, *C*=S); 147.72 (*s*, *C*=CHN); 131.21 (*d*, C(4)); 129.28 (*d*, C=*C*HN); 128.27 (*d*, C(5)); 72.32 (*d*, C(3)); 70.99, 70.14 (2*t*, C(6), C(1′)); 66.30 (*d*, C(2)); 61.26 (*t*, C(1)); 45.21 (*t*, C(1″)); 32.03 (2*t*); 29.81–29.77 (several *t*); 29.65 (2*t*); 29.47 (2*t*); 28.28, 27.17(2*t*); 26.24 (*t*); 22.82 (2*t*); 14.27 (*q*, 2 Me). HR-MALDI-MS: 659.4892 (100, $[M + Na]^+$, $C_{36}H_{68}N_4NaO_3S^+$; calc. 659.4910). Anal. calc. for $C_{36}H_{68}N_4O_3S$ (637.0151): C 67.88, H 10.76, N 8.80; found: C 67.66, H 10.63, N 8.60.

*(*E*)-1,3-Di*-O-*benzyl-2,4,5-trideoxy-2-[4-(trimethylsilyl)-1*H*-1,2,3-triazol-1-yl]-6-*O-*undecyl*-D-erythro-*hex-4-enitol* (**34**). A mixture of **24** (86 mg, 0.17 mmol) and **29** (1.2 ml, 8.47 mmol) in H_2O/i-PrOH 1:2 (0.5 ml) was treated with a soln. of $CuSO_4$ (0.5 mg, 0.0032 mmol) in H_2O (0.25 ml) and ascorbic acid (9 mg, 0.051 mmol) in H_2O (0.25 ml), and stirred at 55° for 2 d. The mixture was allowed to cool to 25°, diluted with H_2O (5 ml), and extracted with AcOEt (2 × 50 ml). The org. phases were dried (Na_2SO_4) and evaporated. The residue was filtered through a short pad of silica gel (first using AcOEt/hexane 1:9 as eluent to separate the unreacted **24** (30 mg) and then using AcOEt/hexane 1:4). The fractions that contain **34** were concentrated to yield pure **34** (50 mg, 75%, based on recovery of **24**), which was taken to the next step without further purification. Colourless oil. R_f (AcOEt/hexane 1:4) 0.22. IR ($CHCl_3$): 3692*w*, 3068*w*, 3031*w*, 3010*w*, 2958*m*, 2928*s*, 2856*s*, 1603*w*, 1495*w*, 1484*w*, 1455*w*, 1364*w*, 1258*w*, 1171*w*, 1102*s*, 1028*w*, 1002*w*, 974*w*, 845*s*, 701*w*, 432*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.63 (*s*, C=CHN); 7.35–7.17 (*m*, 10 arom. H); 5.69 (*dt*, $J = 15.3$, 5.1, H−C(5)); 5.50 (*ddt*, $J = 15.6$, 8.1, 1.2, H−C(4)); 4.90 (*td*, $J \approx 6.9$, 4.2, H−C(2)); 4.60 (*d*, $J = 11.7$, PhC*H*); 4.49 (*d*, $J = 12.0$, PhC*H*); 4.44 (*d*, $J = 12.0$, PhC*H*); 4.32 (*t*, $J = 8.7$, H−C(3)); 4.30 (*d*, $J = 11.7$, PhC*H*); 4.10 (*dd*, $J = 10.2$, 6.9, 1 H−C(1)); 3.96 (*dd*, $J = 10.2$, 4.2, 1 H−C(1)); 3.85 (*dd*, $J = 5.7$, 1.2, 2 H−C(6)); 3.32–3.24 (*AB*, 2 H−C(1′)); 1.58–1.49 (*m*, 2 H−C(2′)); 1.34–1.21 (*m*, 16 H); 0.88 (*t*, $J \approx 6.8$, Me); 0.31 (*s*, Me_3Si). ^{13}C-NMR ($CDCl_3$, 75 MHz): 145.75 (*s*, *C*=CHN); 137.57, 137.48 (2*s*); 133.51 (*d*, C(4)); 129.46 (*d*, C=*C*HN); 128.31 (4*d*); 127.67 (2*d*); 127.57 (4*d*); 127.36 (*d*, C(5)); 78.63 (*d*, C(3)); 73.15 (*t*, Ph*C*H$_2$); 70.70 (*t*, C(6)); 70.40 (*t*, Ph*C*H$_2$); 70.04 (*t*, C(1′)); 67.91 (*t*, C(1)); 63.52 (*d*, C(2)); 31.81 (*t*); 29.62–29.52 (several *t*); 29.44, 26.33 (2*t*), 26.11, 22.59 (2*t*); 14.03 (*q*, Me); −1.16 (*q*, 3 Me). HR-MALDI-MS: 606.4075 (100, $[M+Na]^+$, $C_{36}H_{56}N_3O_3Si^+$; calc. 606.4091).

*(*E*)-1,3-Di*-O-*benzyl-2,4,5-trideoxy-2-(1*H*-1,2,3-triazol-1-yl)-6-*O-*undecyl*-D-erythro-*hex-4-enitol* (**37**). A soln. of **34** (46.5 mg, 0.077 mmol) in THF (2 ml) was treated with $Bu_4NF \cdot 3\,H_2O$ (48.3 mg, 0.153 mmol) and AcOH (10 µl), and stirred at 25° for 36 h. The mixture was diluted with AcOEt (50 ml) and washed with H_2O (5 ml). The aq. layer was separated and extracted with AcOEt (2 × 25 ml). The combined org. layers were washed with sat. aq. $NaHCO_3$ soln. and brine, dried (Na_2SO_4), and evaporated. The residue was filtered through a short pad of silica gel using AcOEt/hexane 1:1 as eluent to get crude **37** (39.5 mg, 97%), which was used directly without further purification. Colourless oil. R_f (AcOEt/hexane 3:7) 0.29. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.69 (*d*, $J = 0.9$, *H*C=CHNC(2)); 7.65 (*d*, $J = 0.9$, HC=C*H*NC(2)); 7.36–7.27 (*m*, 6 arom. H); 7.25–7.18 (*m*, 4 arom. H); 5.68 (*dt*, $J = 15.6$, 5.1, H−C(5)); 5.48 (*ddt*, $J = 15.6$, 7.8, 1.2, H−C(4)); 4.88 (*td*, $J \approx 6.6$, 3.9, H−C(2)); 4.61 (*d*, $J = 12.0$, PhC*H*); 4.50 (*d*, $J = 12.0$, PhC*H*); 4.45 (*d*, $J = 12.0$, PhC*H*); 4.34 (*t*, $J \approx 7.7$, H−C(3)); 4.32 (*d*, $J = 11.4$, PhC*H*); 4.13 (*dd*, $J = 10.2$, 6.3, 1 H−C(1)); 3.95 (*dd*, $J = 10.2$, 3.6, 1 H−C(1)); 3.85 (*dt*, $J = 5.1$, 1.8, 2 H−C(6)); 3.33–3.21 (*AB*, 2 H−C(1′)); 1.58–1.48 (*m*, 2 H−C(2′)); 1.33–1.26 (*m*, 16 H); 0.88 (*t*, $J \approx 6.8$, Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 137.48, 137.37 (2*s*); 133.88 (*d*, H*C*=CHNC); 133.37 (*d*, HC=*C*HNC); 128.37 (4*d*); 127.76 (2*d*); 127.70 (2*d*); 127.58 (2*d*); 127.24 (*d*, C(4)); 123.94 (*d*, C(5)); 78.46 (*d*, C(3)); 73.39 (*t*, Ph*C*H$_2$); 70.82 (*t*, C(6)); 70.51 (*t*, Ph*C*H$_2$); 70.12 (*t*, C(1′)); 68.01 (*t*, C(1)); 64.11 (*d*, C(2)); 32.03 (*t*, C(2′)); 29.82 (2*t*); 29.75 (2*t*); 29.65, 29.46 (2*t*); 26.31, 22.83 (2*t*); 14.29 (*q*, Me). HR-MALDI-MS: 534.3681 (100, $[M+H]^+$, $C_{33}H_{48}N_3O_3^+$; calc. 534.3696).

*(*E*)-2,4,5-Trideoxy-2-(1*H*-1,2,3-triazol-1-yl)-6-*O*-undecyl-*D*-erythro-hex-4-enitol* (**16**). A soln. of **37** (39 mg, 0.073 mmol) in CH_2Cl_2 (3 ml) was treated with anisole (63.7 mg, 0.59 mmol) and $AlCl_3$ (97.4 mg, 0.731 mmol), and stirred at 25° for 24 h. The mixture was cooled to 0° and treated dropwise with 1M HCl (0.4 ml). The mixture was diluted with AcOEt (50 ml). The aq. layer was separated and extracted with AcOEt (2 × 25 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (silica gel; AcOEt/hexane 1:1 → AcOEt) gave pure **16** (18 mg, 70%). Colourless oil that solidified upon standing at 5°. M.p. 47.6°. R_f (AcOEt) 0.25. $[\alpha]_D^{25} = +12.0$ ($c = 0.45$, $CHCl_3$). IR ($CHCl_3$): 3609*w*, 3409 (br.), 3014*w*, 2929*s*, 2856*m*, 2397*w*, 1456*w*, 1413*w*, 1366*w*, 1278*w*, 1113*w*, 1073*m*, 973*w*, 750*m*, 669*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.82 (*d*, $J = 0.9$, *H*C=CHNC(2)); 7.64 (*d*, $J = 0.9$, HC=C*H*NC(1)); 5.83 ((*dtd*, $J = 15.6$, 5.1, 0.9, H–C(5)); 5.68 (*ddt*, $J = 15.6$, 5.7, 1.2, H–C(4)); 4.74 (br. *dd*, $J = 10.2$, 5.1, H–C(3)); 4.57 (*td*, $J = 5.4$, 3.6, H–C(2)); 4.31 (*td*, $J = 12.0$, 5.7, 1 H–C(1)); 4.12 (*ddd*, $J = 12.3$, 6.0, 3.6, 1 H–C(1)); 3.90 (*d*, $J = 4.8$, 2 H–C(6)); 3.70 (*d*, $J = 4.2$, HO–C(3)); 3.44 (*t*, $J \approx 6.2$, HO–C(1)); 3.35 (*t*, $J = 6.9$, 2 H–C(1′)); 1.58–1.49 (*m*, 2 H–C(2′)); 1.32–1.26 (*m*, 16 H); 0.87 (*t*, $J \approx 6.8$, 2 Me). ^{13}C-NMR ($CDCl_3$, 75 MHz): 133.16 (*d*, H*C*=CHNC(2)); 130.74 (*d*, HC=*C*HNC(2)); 129.50 (*d*, C(4)); 124.59 (*d*, C(5)); 72.47 (*d*, C(3)); 70.90, 70.21 (2*t*, C(6), C(1′)); 65.92 (*d*, C(2)); 61.60 (*t*, C(1)); 32.02 (*t*, C(2′)); 29.74 (4*t*); 26.62, 29.46 (2*t*); 26.25, 22.81 (2*t*); 14.27 (*q*, Me). HR-MALDI-MS: 354.2746 (100, $[M+H]^+$, $C_{19}H_{36}N_3O_3^+$; calc. 354.2757). Anal. calc. for $C_{36}H_{69}N_3O_3$ (353.4995): C 64.56, H 9.98, N 11.89; found: C 64.31, H 10.27, N 11.64.

2. *Biological Tests. Materials and Methods. T-Cell Clones and APC.* Human CD1d-restricted iNKT-cell clones were derived and cultivated as described in [55]. Human CD1d-transfected C1R or THP1 cells were used as APC in the experiments.

Abbreviations. α-GalCer, α-galactosylceramide; APC, antigen-presenting cells; BSA, bovine serum albumin; FACS, fluorescence-activated cell sorting; FCS, fetal calf serum; IEF, isoelectric focusing; iNKT cells, invariant natural killer T cells; PBMC, peripheral blood mononuclear cells; PBS, phosphate-buffered saline; TCR, T-cell receptor.

Cytotoxicity Assay. Sonicated compounds were incubated overnight with T cells or APC at 37°. Cells were labelled with 5 μg/ml propidium iodide (*Sigma-Aldrich*, St. Louis, Missouri, USA) or 7-aminoactinomycin D (*Invitrogen*, Carlsbad, California, USA), and cell death was assessed by flow cytometry on a *CYAN*™ ADP (*Beckman Coulter*, Fullerton, California, USA) cytometer.

Antigen Presentation Assay. Human CD1d transfectants ($2.5 \cdot 10^4$/well) in RPMI-1640 medium containing 10% FCS were incubated during the assay at 37° with sonicated compounds at the indicated concentrations. T Cells ($7.5 \cdot 10^4$/well) were added after indicated time periods. Supernatants were harvested after 24 h, and released cytokines were measured by ELISA.

Antigen Competition Assay. Human CD1d transfectants ($2.5 \cdot 10^4$/well) in RPMI-1640 medium containing 10% FCS were incubated during the assay at 37° with sonicated antigen at the indicated concentrations. Compounds were given 4.5 h before α-GalCer. T Cells ($7.5 \cdot 10^4$/well) were added 0.5 h after α-GalCer. Supernatants were harvested after 24 h, and released cytokines were measured by ELISA.

Plate-Bound Human CD1d Activation Assay. MaxiSorp™ ELISA plates (*Nunc*, Roskilde, Denmark) were coated overnight at r.t. with 10 μg/ml BIR1.4 (anti-BirA, generated in our laboratory) monoclonal antibody (mAb). IEF-Purified soluble recombinant human CD1d (established in our laboratory with a BirA tag) was incubated overnight at r.t. on washed BIR1.4-coated plates at pre-titrated batch-dependent concentrations (twofold molar excess). Sonicated compounds were added after washing to plate-bound human CD1d overnight at r.t. T Cells ($1.5 \cdot 10^5$/well) were plated in RPMI-1640 medium containing 5% HS and 100 U/ml human IL-2 after extensive washing. Supernatants were harvested after 24 h incubation at 37°, and released cytokines were measured by ELISA.

Plate-Bound Human CD1d Competition Assay. MaxiSorp™ ELISA plates were coated overnight at r.t. with 10 μg/ml BIR1.4 mAb. IEF-Purified soluble recombinant human CD1d was incubated overnight at r.t. on washed BIR1.4-coated plates at pre-titrated batch-dependent concentrations (twofold molar excess). Sonicated compounds were added after washing and given 4.5 h in advance of α-GalCer to plate-bound human CD1d before overnight competition at r.t. T Cells ($1.5 \cdot 10^5$/well) were plated in RPMI-1640 medium containing 5% HS and 100 U/ml human IL-2 after extensive washing. Supernatants were harvested after 24 h incubation at 37°, and released cytokines were measured by ELISA.

ELISA. MaxiSorp™ ELISA plates were coated overnight at 4° with 1 μg/ml 8D4-8 (anti-human IL-4; BD, Franklin Lakes, New Jersey, USA) mAb, with 1 μg/ml MAb1 (anti-human TNF-α; BD) mAb, with 2 μg/ml 6804 (anti-human GM-CSF, R&D, Minneapolis, Minneapolis, USA) mAb, or with 3 μg/ml HB-8700 (anti-human IFN-γ, ATCC) mAb diluted in PBS.

Coated wells were blocked with 0.05% *Tween-20* and 10 mg/ml BSA in PBS (PBST/BSA) and then incubated with the supernatants of the antigen presentation assays.

1 μg/ml MP4-25D2 (anti-human IL-4 biotin labelled; BD) mAb, 0.5 μg/ml MAb11 (anti-human TNF-α biotin labelled, BD) mAb, 1 μg/ml 3209 (anti-human GM-CSF biotin labelled, R&D) mAb, or 0.72 μg/ml γ69 [56] (anti-human IFN-γ biotin labeled, provided by *G. Garotta*) mAb with 0.3 μg/ml streptavidin-HRP (*Zymed*, *Invitrogen*), and *o*-Phenylenediamine dihydrochloride (*Sigma*, according to the manufacturer's instructions) as substrate were used to detect human IL-4, human TNF-α, or human IFN-γ, resp.

The O.D.s of the developed ELISA were read in a *SpectraMax® 190* spectrophotometer at 490 nm (*Molecular Devices*, Sunnyvale, California, USA), then converted to concentrations and expressed as mean pg/ml ± SD of duplicates or triplicates using the SoftMax Pro 5 program by comparison to standards of human IL-4 (produced in our laboratory), recombinant human TNF-α (Immunokontact, *AMS Biotechnology*, Switzerland), human GM-CSF (produced in our laboratory), and recombinant human IFN-γ (*BenderMedSystems*, Vienna, Austria).

Data and Statistical Analysis. Data are at least of two independent experiments and expressed as mean ± standard deviation (SD). Single data points were compared using two-tailed *Student*'s test. Results in figures are flagged with a single asterisk (*) when the P value is less than 0.05, with two asterisks (**) when the P value is less than 0.01.

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