123. Glycosylphosphonates of 2-Amino-2-deoxy-aldoses. Synthesis of a Phosphonate Analogue of Lipid X[1])

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Dedicated to Prof. Dr. *Vlado Prelog*

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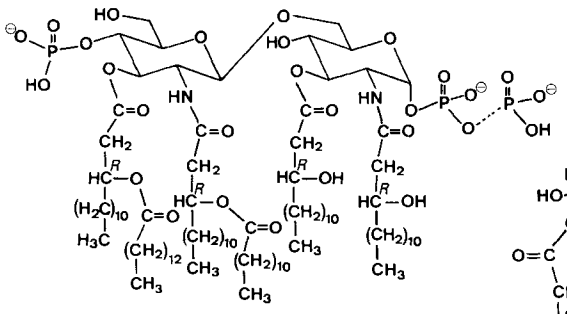
A preparation of glycosylphosphonates (**27, 28, 36, 38,** and **39**) from 2-azido-2-deoxy-glycoses (**26, 35,** and **37**) and the synthesis of the non-isosteric phosphonate analogue **3a** of lipid X (**2**) are described. The 2-azido group was introduced by azidonitration. Treatment of the 1-*O*-acetyl-2-azido-2-deoxy-β-D-galactopyranose **22** with 1.5–3 equiv. of $P(OMe)_3$ and 1.2–2.5 equiv. of $TfOSiMe_3$ gave mainly recovered starting material. In $P(OMe)_3$ as the solvent, the dimethyl phosphoramidate **24** was obtained by way of a *Staudinger* reaction, even in the presence of $TfOSiMe_3$. Treatment of the benzylated α-D-*galacto*-trichloroacetimidate **26,** however, with $P(OMe)_3$ and $TfOSiMe_3$ gave a 1:1 mixture of the α- and β-D-*galacto*-phosphonates **27** and **28**, while the acetylated α-D-*gluco*-imidate **35** led to the α-D-*gluco*-configurated phosphonate **36**. The stereoselectivity of the phosphonate formation is related to the relative ease of formation of oxonium-ion intermediates from **26** and **35**. Starting from the phosphonate **36**, deacetylation, benzylidenation, reduction of the azido group, acylation with (*R*)-3-(benzyloxy)tetradecanoic acid and deprotection yielded the desired compound **3a** which was crystallized in the presence of 2 equiv. of (aminomethylidyne)trimethanol (*Tris*). The structure of the phosphonates was deduced from their ^1H-, ^{13}C-, and ^{31}P-NMR spectra.

Introduction. – Lipid A is the lipophilic moiety of the lipopolysaccharides which form the outer layer of the outer membrane of gram-negative bacteria. It is responsible for most of the endotoxic properties of such bacteria [1]. Lipid A is essentially a β-1′,6-linked D-glucosamine disaccharide carrying phosphate residues at C(1) and C(4′) and



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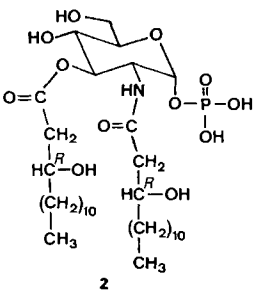

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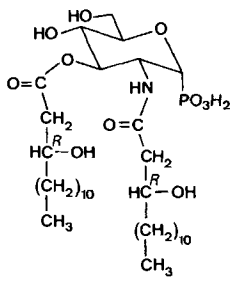


3a

[1]) Presented in part by *K. B.* at the Carbohydrate Group Spring Meeting of the Royal Society of Chemistry in Cambridge, 29th March–1st April, 1987.

several *N*- and *O*-bound long-chain acyl groups [2]. This is illustrated by the structure of lipid A (**1**) of *E. coli* [3]. Lipid X (**2**), a monosaccharide isolated from *E. coli* mutants, is a biosynthetic precursor of **1** corresponding to the reducing end. The glycosidation of lipid X with UDP-2,3-diacyl-D-glucosamine is catalyzed by the enzyme disaccharide-1-phosphate-synthase [4]. The function of the phosphate group at C(1) in the endotoxic reactions of lipid A is not clear. The phosphate group might be important only because of its influence on the solubility of lipid A, but it might also fulfil a more specific role. It is unknown if the phosphate group is split off *in vivo*. Some of these questions could possibly be answered with the help of nonhydrolyzable phosphonate analogues.

The choice of the phosphonate is based upon a comparison of its steric and polar properties with those of the corresponding phosphate. In isosteric phosphonate analogues, a methylene group or a substituted methylene group replaces the alkoxy O-atom of the parent phosphate, whereas in non-isosteric phosphonate analogues the P-atom is directly bound to the alkyl residue. The polar properties of phosphonates are usually discussed in terms of their pK_a values. Phosphonates which are not appropriately substituted by acceptor groups are less acidic than phosphates [5–8].

The polar properties of glycosylphosphonates (= α-alkoxyphosphonates) should be similar to those of the corresponding glycosylphosphates. The synthesis of such non-isosteric but *bona fide* isopolar glycosylphosphonate analogues has recently been described by *Meuwly* and *Vasella* [9]. Treatment of benzylated 1-*O*-acetyl-glycoses with trialkyl phosphite in the presence of trimethylsilyl trifluoromethanesulfonate ($TfOSiMe_3$) yielded mainly 1,2-*cis*-configurated dialkyl phosphonates. The almost exclusive formation of 1,2-*cis*-configurated phosphonates has been explained by postulating an equilibrium between the anomeric phosphonium-salt intermediates and a stabilization of the *cis*-configurated salts through formation of a pentacoordinated species by participation of the neighbouring benzyloxy group. To check this rationalization, the influence of a non-participating group at C(2) should be examined. Moreover, the application of this method to the synthesis of glycosylphosphonates of 2-amino-2-deoxy-sugars is desirable considering the importance of amino sugars and their phosphates. For these reasons, we decided to synthesize the non-isosteric glycosylphosphonate analogue **3a** of lipid X.

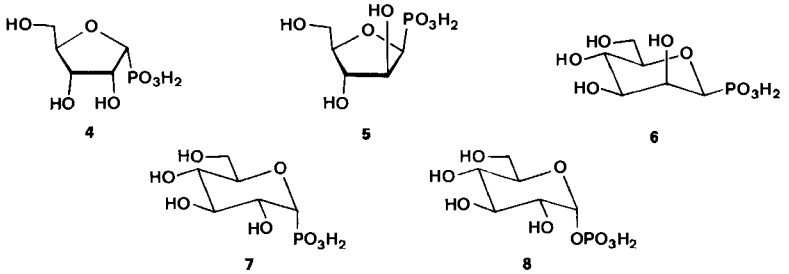
The assumption of the isopolar character of such non-isosteric glycosylphosphonate analogues was checked on the basis of their pK_a' values[2]). The pK_a' values of the glycosylphosphonates **4**–**7** [9] are collected in *Table 1*. Comparison of the $pK_a'(2)$ value of

Table 1. *pK_a' Values of Glycosylphosphonic Acids* **4**–**7**[a]) *and of* α-D-*Glucose-1-phosphate* (**8**)

Compound	$pK_a'(1)$	$pK_a'(2)$
4	2.72	6.50
5	2.63	6.10
6	2.60	6.12
7	2.77	6.38
8	–	6.22 [10]

[a]) These pK_a' values were determined by titration of aqueous solutions of the glycosylphosphonic acids with 0.1N NaOH.

[2]) K_a' describes the apparent acidity constant measured on the basis of concentrations (no activity correction).



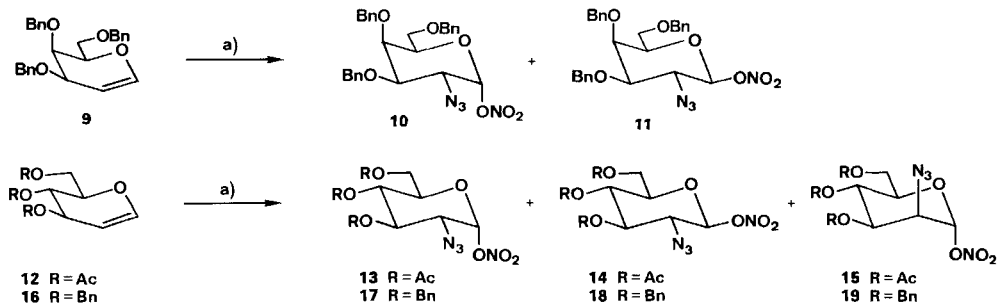
(α-D-glucopyranosyl)phosphonic acid (**7**) with the reported value of α-D-glucose-1-phosphate (**8**) [10] confirms their almost isopolar character (see *Table 1*).

In the following we report the preparation of the starting materials by azidonitration, the preparation of dimethyl (2-azido-2-deoxy-glycopyranosyl)phosphonates, and the synthesis of the desired phosphonic acid **3a.**

Results and Discussion. – 1. *Azidonitration.* For the synthesis of the desired phosphonic acid **3a**, the azido group appeared to be the most appropriate non-participating N-containing functional group at C(2). It is easily introduced by azidonitration of the corresponding glycal [11] and easily transformed into an amino and hence into an acylamino group. Since the azidonitration of galactals is more diastereoselective than the one of glucals [11], the phosphonate synthesis was first examined using galactose derivatives.

The azidonitrations of the tri-*O*-benzyl-D-galactal **9** [12], of the tri-*O*-acetyl-D-glucal **12** [13], and of the tri-*O*-benzyl-D-glucal **16** [14] *(Scheme 1)* followed established procedures. From **9** we obtained 48–51% of the α-D-anomer **10** which crystallized from Et_2O/hexane at −20° and 6–8% of the β-D-anomer **11**[3]). Azidonitration of **12** yielded 16–19% of the α-D-*gluco*-azide **13**, 25–28% of the β-D-*gluco*-azide **14**, and 26–29% of the α-D-*manno*-azide **15**[3]). These diastereoisomers were only partially separated by medium pressure liquid chromatography. Pure samples of **13** and of **15** were obtained by fractional crystallization. The β-D-anomer **14** did not crystallize. Azidonitration of the

Scheme 1



a) NaN_3, $Ce(NH_4)_2(NO_3)_6$, MeCN, −20°.

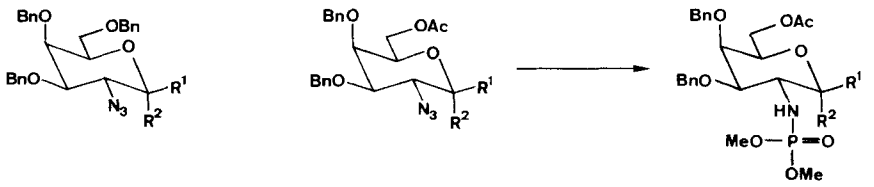
[3]) These ratios were determined from the integrals of the H–C(1) signals in the ^{1}H-NMR spectrum of the mixture of the diastereoisomers.

tri-*O*-benzyl-D-glucal **16** yielded 33% of the α-D-*gluco*-azide **17**, 13% of the β-D-*gluco*-azide **18**, and 13% of the α-D-*manno*-azide **19**[3]).

Thus, in the products of the azidonitration carrying an equatorial 2-azido group, the configuration at C(1) seems to depend on the nature of the protecting groups at C(3), C(4), and C(6). Taking into account the results of the azidonitration of 3,4,6-tri-*O*-acetyl-D-galactal described by *Lemieux* and *Ratcliffe* [11], it appears that 1,2-*trans*-configurated products (equatorial ONO_2 group at C(1)) are preferentially formed from acetylated glycals and 1,2-*cis*-configurated compounds (axial ONO_2 group at C(1)) from benzylated glycals.

2. *Phosphonoylation.* Treatment of the 1:1 mixture of the anomeric 1-*O*-acetyl-2-azido-2-deoxy-D-galactopyranoses **20** and **21**, obtained from **10** and **11** [11], with 1.5–3 equiv. of $P(OMe)_3$ and 1.2–2.5 equiv. of $TfOSiMe_3$ (*cf.* [9]) gave mainly recovered starting material besides several decomposition products. In $P(OMe)_3$ as the solvent, the acetate **22**[4]) gave the dimethyl phosphoramidate **24** (95%), even in the presence of $TfOSiMe_3$ *(Scheme 2)*. The reaction occurred without anomerization.

Scheme 2



20 R^1 = H, R^2 = OAc
21 R^1 = OAc, R^2 = H

22 R^1 = OAc, R^2 = H
23 R^1 = H, R^2 = OAc

24 R^1 = OAc, R^2 = H

The IR spectrum of **24** shows a weak NH absorption at 3410 cm^{-1}. In the ^{1}H-NMR spectrum, the 2 characteristic *d* of the $(MeO)_2P(O)$ group are observed at 3.65 and 3.66 ppm (^3J(H,P) = 11.2 Hz). The signal of HN occurs as a *t* at 2.66 ppm (^3J(NH,H–C(2)) = ^2J(NH,P) = 8.5 Hz). In the ^{13}C-NMR spectrum, the signal of the 2 MeO occurs at 53.25 ppm (^2J(C,P) = 4.7 Hz). The values of ^3J(C(1), P) and ^3J(C(3),P) are 2.3 and 4.1 Hz, respectively. The value of the ^{31}P-NMR chemical shift of 10.72 ppm is in the range described for the dimethyl alkylphosphoramidates in [15].

These results indicate that a better leaving group at C(1) might be required. According to known procedures [12], the mixture of the anomeric nitrates **10** and **11** was transformed *via* **25** into the trichloroacetimidate **26** *(Scheme 3)*. Treatment of the crude imidate **26** with 2.5 equiv. of $P(OMe)_3$ and 1.7 equiv. of $TfOSiMe_3$ in dry CH_2Cl_2[5]) gave the dimethyl phosphonates **27** and **28** in a 1:1 ratio[6]) (each in 32% yield from **25**) together with a mixture of the trichloroacetamides **29** and **30** (9.5% from **25**). Reduction of the azido group of **27** and **28** with $NaBH_4$ and $NiCl_2 \cdot 6H_2O$ followed by acetylation with Ac_2O [16] gave the *N*-acetyl derivatives **31** (70%) and **32** (78%), which were hydrogenolyzed to **33** (89%) and **34** (91%), respectively[7]).

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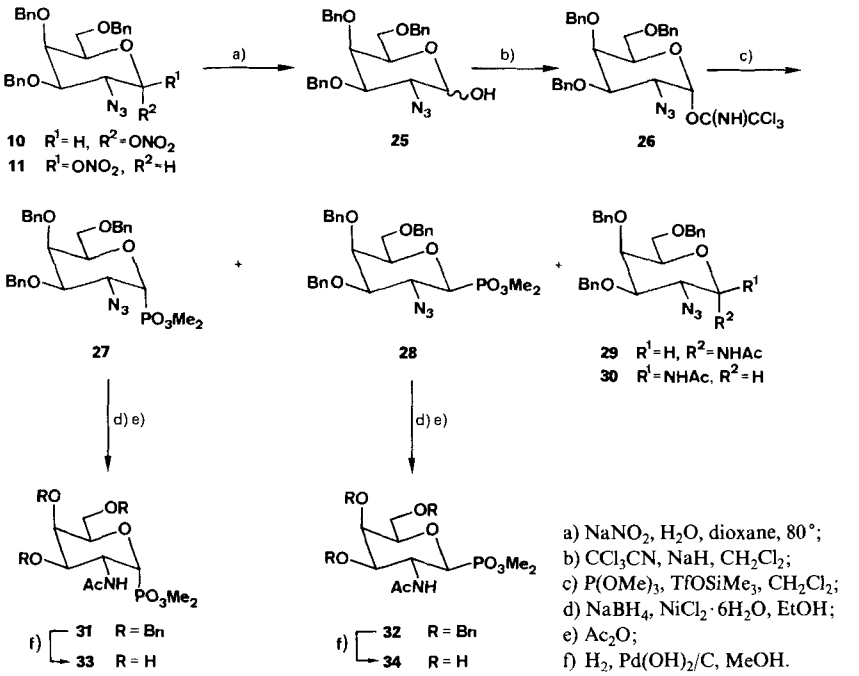
[4]) Compound **22** was obtained together with **23** from the acetolysis of the mixture of the anomers **20** and **21**; they were used besides **20** and **21** in preliminary experiments for the phosphonate synthesis.

[5]) Distilled over P_2O_5. These conditions are crucial, at least in the reaction of **35**.

[6]) The 1:1 ratio was also obtained using purified α-D-trichloroacetimidate **26**.

[7]) Catalytic transfer hydrogenolysis [17] worked only for batches up to *ca.* 100 mg.

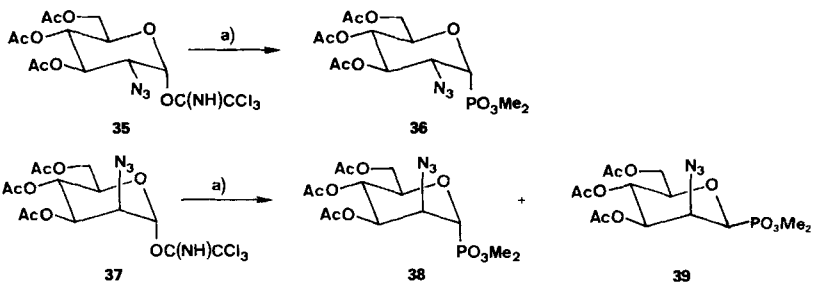
Scheme 3



Treatment of the acetylated α-D-*gluco*-configurated trichloroacetimidate **35** with $P(OMe)_3$ and $TfOSiMe_3$ in dry CH_2Cl_2[5]) gave the α-D-*gluco*-configurated dimethyl phosphonate **36** (76%; *Scheme 4*). The corresponding β-D-anomer was not found; main by-products were the corresponding trichloroacetamides and the 2-(dimethoxyphosphoryl)amino derivative.

The structures of the dimethyl phosphonates **27, 28,** and **36** were mainly deduced from their spectra. The IR spectra show the presence of the azido group (strong absorption at 2110 cm^{-1}). In the ^{1}H-NMR spectra, the $(MeO)_2P(O)$ group gives rise to 2 typical *d* at 3.41–3.56 ppm ($^3J(H,P)$ = 10.2–11 Hz, 6H). In the ^{13}C-NMR spectra, the Me signals of the $(MeO)_2P(O)$ group *(qd)* occur at 52.9–53.82 ppm with $^2J(C,P)$ = 6.3–7 Hz. The presence of a dialkoxyphosphoryl group is confirmed by the ^{31}P-NMR spectra with signals at 21.04–23.15 ppm.

Scheme 4



The anomeric configuration is evident from the ^{1}H- and ^{13}C-NMR spectra[8]). In the ^{1}H-NMR spectra, the signals of H–C(1) of **27** and **36** are found at 4.20 ppm ($3J(1,2) = 6.7$ Hz) and 3.97 ppm ($^3J(1,2) = 7.1$ Hz), respectively, while the corresponding signal of **28** occurs at a higher field and has a larger coupling constant (3.42 ppm, $^3J(1,2) = 10.2$ Hz); this indicates the α-D-configuration for **27** and **36** and the β-D-configuration of **28** [9]. The values of ^3J(H–C(2),P) are *ca.* 32 Hz for the α-D-anomers **27** and **36** (*trans*-diaxial orientation) and *ca.* 10 Hz for the β-D-anomer **28** (synclinal orientation) [9]. In agreement with these assignments, the signals of H–C(3) and H–C(5) of the α-D-anomer **27** occur at lower fields than those of the β-D-anomer **28** (deshielding effect of the $(MeO)_2P(O)$ group; $\delta\Delta$ = 1.49 ppm for H–C(3) and $\delta\Delta > 1.32$ ppm for H–C(5)) [9].

In the ^{13}C-NMR spectra, the C(1) signals of **27, 28,** and **36** are found at 70.4, 74.71, and 70.96 ppm, respectively, the signal of the α-D-anomer **27** occurring at a higher field than the one of the corresponding β-D-anomer **28** ($\delta\Delta$ = 4.31 ppm) [9]. The values of ^1J(C(1),P) agree with the proposed anomeric configurations, being larger for the β-D-anomer **28** (172.8 Hz) than for the α-D-anomers **27** (*ca.* 160 Hz) and **36** (155.9 Hz) [9]. Relatively large values of ^3J(C(3),P) and ^3J(C(5),P) (16 and 16.3 Hz) are found for the β-D-anomer **28**, due to the antiperiplanar orientation of the P-atom and the C(3)- and C(5)-atoms, respectively [18]; the corresponding values for the α-D-anomers **27** and **36** are much smaller (3.4 and 1.5 Hz, 0 and 1.5 Hz, respectively). In agreement with the proposed configurations, the signals of C(3) and C(5) of the α-D-anomer **27** are found at a higher field than the corresponding signals of the β-D-anomer **28** (*gauche*-γ-effect; $\delta\Delta$ = 3.56 and 4.6 ppm, respectively) [19].

Since the trichloroacetimidates **26** and **35** were submitted to the same reaction conditions, the high diastereoselectivity in the formation of **36** must be a consequence of the different protecting groups and/or of the different configuration at C(4). It is known that benzylated compounds are more reactive than the corresponding acetylated derivatives in processes occurring *via* oxonium-ion intermediates [20] and that *galacto*-configurated compounds tend to be more reactive in glycosidation reactions than the corresponding *gluco*-configurated compounds. The stereoselectivity of the syntheses of α-D-glycosides decreases with increasing reactivity of the glycosyl halides [21]. A rationalization of the diastereoselectivities of the phosphonoylations must consider the following factors: *a)* Formation and equilibration of intermediate triflates [20] [22] [23]. As in the case of the halides [20], the β-D-triflates should react faster than their anomers to give the α-D-phosphonium-ion intermediates, and the difference in reactivity of the anomeric triflates would be smaller in the more reactive benzylated derivatives. *b)* Equilibration of the phosphonium-salt intermediates (*via* oxonium ions) [9]. In the absence of neighbouring-group participation and under thermodynamic control, the reverse anomeric effect [24] should favour the β-D-anomer. One expects that the benzylated phosphonium-salt intermediates equilibrate faster than the corresponding acetates and that the velocity of the dealkylation depends only weakly on the nature of the protecting groups.

Reaction *via* equilibrating triflates followed by a relatively rapid dealkylation of slowly equilibrating phosphonium salts would favour the formation of α-D-anomers. This situation is expected for acetylated products, where the formation of oxonium-ion intermediates is disfavoured. In the case of benzylated products, the difference in reactivity of the triflates (if formed) is expected to be smaller, while equilibration of the phosphonium-ion intermediates should be faster; hence higher proportions of β-D-anomers are expected.

In keeping with this, the *manno*-imidate **37** reacted under the conditions used for **26** and **35** to give mainly the α-D-configurated dimethyl phosphonate **38** besides **39** (58%; **38/39** = 6:1; preliminary experiments, *Scheme 4*).

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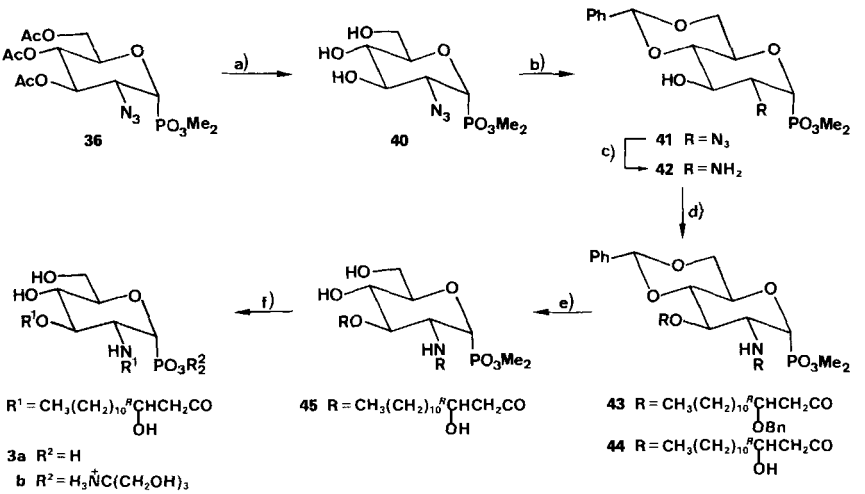
[8]) For a detailed discussion, see [9] and lit. cit. therein.

3. *Synthesis of the Phosphonate Analogue* **3** *of Lipid X (Scheme 5).* The imidates **35** and **37** were prepared according to [12] and separated by flash chromatography. The low overall yield of the desired **35** (21% form **12**) is mainly due to the low stereoselectivity of the azidonitration which gave only 45% of the *gluco*-configurated nitrates **13** and **14**. Treatment of **35** with $P(OMe)_3$ and $TfOSiMe_3$ yielded 76% of the dimethyl phosphonate **36** (see above) which was deacetylated with NaOMe in MeOH to give the crystalline **40** (90%; *Scheme 5*). Benzylidenation of **40** with $ZnCl_2$ in benzaldehyde yielded 92% of **41.**

Scheme 5



a) NaOMe, MeOH; b) $ZnCl_2$, PhCHO; c) $NaBH_4$, $NiCl_2 \cdot 6H_2O$, EtOH; d) ROH, DCC, $(Me_2N)Py$, CH_2Cl_2; e) H_2, $Pd(OH)_2/C$, MeOH; f) Me_3SiBr, CH_2Cl_2.

The azide **41** was reduced with $NaBH_4$ and $NiCl_2 \cdot 6H_2O$ to the amine **42** which was acylated with 2.1 equiv. of *(R)*-3-(benzyloxy)tetradecanoic acid[9]) in the presence of 2.1 equiv. of dicyclohexylcarbodiimide (DCC) and 0.1 equiv. of 4-(dimethylamino)pyridine to give **43** (80% from **41**). The benzylidene and the benzyl groups of **43** were removed by hydrogenolysis (2½–3 h, $Pd(OH)_2/C$ in MeOH, 4 bar; 94%). Prolonged hydrogenolysis gave many decomposition products. Hydrogenolysis in the presence of Pd/C led to selective removal of the benzyl groups and to the formation of the benzylidene-diol **44** (40%). Transesterification of the methyl ester **45** with bromotrimethylsilane followed by hydrolysis gave the phosphonic acid **3a**. Crystallization of crude **3a** with 2 equiv. of (aminomethylidyne)trimethanol *(Tris)* yielded the pure bis*(Tris)* salt **3b**[10]).

The following spectroscopic data are relevant for the structure determination of **3a/b**. The presence of the phosphono group is shown by the ^{31}P-NMR signal at 19.41 ppm of **3a**. In the ^{1}H-NMR spectrum of **3b**, the α-D-configuration is confirmed by the values of the coupling constants $^3J(1,2)$ (= 6.8 Hz) and $^3J(H–C(2),P)$ (= 26.7 Hz). The value of $^3J(H–C(2),P)$ is only slightly smaller than the one found for the α-D-dimethyl phosphonates **36** and **40**–**45** (31.6–34.5 Hz). In the ^{13}C-NMR spectrum of **3a**, the value of $^1J(C(1),P)$ (= 155 Hz)

[9]) We thank Dr. *H. Braunschweiger, Sandoz,* Muttenz, for a generous gift of the enantiomerically pure (*R*)-3-(benzyloxy)tetradecanoic acid.

[10]) We thank Dr. *I. Macher, Sandoz* Forschungsinstitut, Wien, for suggesting this method [25].

is typical for α-D-configurated phosphonates, as is the fact that no coupling between the P-atom and C(3) or C(5) is found. The IR spectrum of **3b** shows the presence of the carbonyl absorptions of the ester and amide functions (1730, 1630, and 1550 cm^{-1}) besides strong OH bands. In the ^{1}H-NMR spectrum, the *t* of the terminal CH_3 groups occurs at 0.91 ppm (J = 6.8 Hz). The 18 methylene groups $CH_2(5')$ to $CH_2(13')$ and $CH_2(5'')$ to $CH_2(13'')$[11]) give rise to a broad *s* at 1.4–1.5 ppm. The signal of $CH_2(4')$ and $CH_2(4'')$ is a broad *s* at 1.31 ppm. The $CH_2(2')$ and $CH_2(2'')$ groups give rise to 2 *ABX* systems at 2.26–2.52 ppm. The signals of H–C(3') and H–C(3'') occur as *m* at 3.5–4.0 ppm. In the ^{13}C-NMR spectrum, the presence of the 2 acyl chains is shown by the *s* of the ester and amide CO groups at 173.90 and 174.50 ppm, respectively, by the *t* of the CH_2 groups at 23.7–45.1 ppm, and by the *q* of the 2 terminal CH_3 groups at 14.44 ppm. C(3') and C(3'') give rise to 2 *d* at 68–70 ppm. The fact that only one signal is found for C(3') and C(3''), respectively, shows that the product is homogeneous.

Table 2. *Calculated and Experimental Values of Coupling Constants*

Compound	Calculated values [Hz]				Experimental values [Hz]			
	J(1,2)	J(2,3)	J(3,4)	J(4,5)	J(1,2)	J(2,3)	J(3,4)	J(4,5)
27	3.3	9.9	2.9	2.9	6.7	10.2	2.6	a)
28	10.5	9.9	2.9	2.9	10.2	9.8	2.7	a)
31	3.3	9.9	2.9	2.9	6.6	10.3	a)	a)
32	10.5	9.9	2.9	2.9	9.5	10	a)	a)
36	3.3	9.9	9.2	9.2	7.1	10.1	9.7	9.0
45	3.3	9.9	9.2	9.2	7.4	10.6	9.3	a)
3b	3.3	9.9	9.2	9.2	6.8	10.3	9.2	9.2

a) This value cannot be determined from the ^{1}H-NMR spectrum.

The ring conformations of **27, 28, 31, 32, 36, 45,** and **3b** have been examined qualitatively on the basis of the vicinal H,H'-coupling constants[12]) and the vicinal H–C(2),P-coupling constant [27–29]: In *Table 2,* the experimental values of the H,H'-coupling constants of the phosphonates **27, 28, 31, 32, 36, 45,** and **3b** are compared to the calculated values assuming ideal chair conformation. The experimental and calculated values for $^3J(2,3)$, $^3J(3,4)$, and $^3J(4,5)$ of all phosphonates correspond well to each other, as do the $^3J(1,2)$ values of the β-D-anomers **28** and **32.** However, the $^3J(1,2)$ values for the α-D-anomers in the *galacto-* and *gluco-*series (**27, 31, 36, 45,** and **3b**) are sensibly larger than the calculated ones. Apparently, the $(RO)_2P(O)$ groups of these α-D-anomers are diverted from their axial position towards a pseudo-equatorial orientation, while the molecule remains as far as possible in a chair conformation. This observation is confirmed by the ^3J(H–C(2),P) values for the *galacto-* and *gluco-*configurated α-D-anomers (26.7–34.1 Hz), which are slightly smaller than the expected values for a dihedral angle of 180° [27].

We thank the *Sandoz* Forschungsinstitut, Vienna, for generous support.

11) The acyl chains are numbered with primed and doubly primed locants.

12) Using the modified *Karplus* equation of *Durette* and *Horton* [26] $^3J(H,H') = (7.8-1.0\cos\Phi+5.6\cos2\Phi)$ *f*; Φ = dihedral angle; $f = 1-0.1\ \Delta X$; $\Delta X = \Sigma(X_R i - X_H)$; X = *Pauling* electronegativity of the substituents on the $R^1R^2HC-CH'R^3R^4$ fragment. Instead of the group electronegativity for R^i, only the electronegativity of the atom of R^i directly bound to the H–C–C–H' fragment was considered.

Experimental Part

General. See [30]. After workup, processing of the org. layer as usual implies drying ($MgSO_4$) and evaporation of the solvent under vacuum at or below 40°. Qualitative TLC: 0.25 mm precoated silica-gel plates (*Merck*, Kieselgel *60* F_{254}) with the solvent systems indicated. Flash chromatography: silica gel *Merck 60* (0.040–0.063 mm). Medium pressure liquid chromatography (MPLC): silica gel *Merck 60* (0.015–0.040 mm). ^{1}H-, ^{13}C-, and ^{31}P-NMR spectra: chemical shifts in ppm relative to TMS as internal standard (^{1}H- and ^{13}C-NMR) or relative to H_3PO_4 as external standard (^{31}P-NMR). FC: flash chromatography.

General Procedure for the Azidonitration. Finely ground NaN_3 and cerium(IV) ammonium nitrate ($Ce(NH_4)_2(NO_3)_6$) were dried over silica gel under high vacuum (h. v.) for 48 h. MeCN was distilled over P_2O_5 (1%) and – immediately before use –over anh. K_2CO_3 (5%). Under N_2, NaN_3 (*ca.* 1.5 equiv.) and $Ce(NH_4)_2(NO_3)_6$ (*ca.* 3 equiv.) were added to a soln. of the glycal in dry MeCN at −20°. The suspension was vigorously stirred at −20°, until the starting material had disappeared (TLC). The mixture was diluted with CH_2Cl_2 and extracted with ice-cold H_2O. The org. layer was processed as usual.

*2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-α- and -β-*D*-galactopyranosyl Nitrate* (**10** and **11**, resp.). Azidonitration of 2.50 g (6.0 mmol) of **9** [31] [32] in 36 ml of MeCN with 577 mg (8.88 mmol) of NaN_3 and 11.62 g (21.2 mmol) of $Ce(NH_4)_2(NO_3)_6$ for 4½ h yielded, after FC (hexane/AcOEt 7:3), 1.76 g (56%) of **10/11**, ratio 85–90: 10–15 by ^{1}H-NMR (H–C(1))[13]. The α-D-anomer **10** was crystallized from Et_2O/hexane at −20°.

Data of **10**: R_f (hexane/Et_2O 2:1) 0.36. M.p. 64–65°. $[\alpha]_D^{25} = +87.8°$ (*c* = 1.13, $CHCl_3$). IR: 3090*w*, 3060*w*, 3040*w*, 3000*w*, 2920*w*, 2870*w*, 2115*s*, 1660*s*, 1495*w*, 1450*w*, 1365*w*, 1350*w*, 1315*w*, 1280*s*, 1140*m*, 1125*m*, 1100*m*, 1045*m*, 1025*m*, 980*w*, 945*w*, 910*w*, 820*s*, 695*m*, 660*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.34–7.16 (*m*, 15 arom. H); 6.18 (*d*, *J* = 4.2, H–C(1)); 4.80, 4.45 (*AB*, *J* = 11.1, PhCH_2); 4.68, 4.64 (*AB*, *J* = 11.4, PhCH_2); 4.40, 4.34 (*AB*, *J* = 11.7, PhCH_2); 4.20 (*dd*, *J* = 4.2, 10.8, H–C(2)); 4.02–3.97 (*m*, H–C(4), H–C(5)); 3.78 (*dd*, *J* = 10.8, 2.6, H–C(3)); 3.54 (*dd*, *J* = 7.8, 9.1, H_A–C(6)); 3.45 (*dd*, *J* = 5.4, 9.1, H_B–C(6)). ^{13}C-NMR (50 MHz, $CDCl_3$): 137.89 (*s*); 137.49 (*s*); 137.03 (*s*); 128.6–127.6 (*m*); 98.08 (*d*); 77.54 (*d*); 75.03 (*t*); 73.59 (*t*); 72.60 (*d*); 72.48 (*d*); 72.35 (*t*); 67.70 (*t*); 57.96 (*d*). Anal. calc. for $C_{27}H_{28}N_4O_7$ (520.55): C 62.30, H 5.42, N 10.76; found: C 62.50, H 5.61, N 10.52.

*3,4,6-Tri-*O*-acetyl-2-azido-2-deoxy-α- and -β-*D*-glucopyranosyl Nitrate* (**13** and **14**, resp.) *and 3,4,6-Tri-*O*-acetyl-2-azido-2-deoxy-α-*D*-mannopyranosyl Nitrate* (**15**). Azidonitration of 15 g (0.055 mol) of **12** [33] in 320 ml of MeCN with 5.5 g (0.085 mol) of NaN_3 and 100 g (0.182 mol) of $Ce(NH_4)_2(NO_3)_6$ for 7 h gave, after MPLC (hexane/CH_2Cl_2/AcOEt 2:1:1), 15.14 g (73%) of **13/14/15** (by ^{1}H-NMR: **13**, 18.8%; **14**, 25.9%; **15**, 28.3%). Pure **13** and **15** were obtained by fractional crystallization, after MPLC, of the fractions enriched with **13** and **15**, respectively.

Data of **13**: R_f (hexane/CH_2Cl_2/AcOEt 2:1:1) 0.25. M.p. 137–138°. $[\alpha]_D^{25} = +142.7°$ (*c* = 0.93, $CHCl_3$). IR: 3020*w*, 2960*w*, 2940*w*, 2920*w*, 2110*s*, 1750*s*, 1670*s*, 1450*w*, 1425*w*, 1380*m* (sh), 1365*s*, 1280*s*, 1140*m*, 1120*m*, 1080*m*, 1050*m*, 1030*m*, 970*w*, 955*w*, 940*w*, 895*w*, 810*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 6.33 (*d*, *J* = 4.2, H–C(1)); 5.40 (*dd*, *J* = 10.7, 9.4, H–C(3)); 5.13 (*t*, *J* = 9.4, H–C(4)); 4.33 (*dd*, *J* = 3.9, 12.4, H_A–C(6)); 4.3–4.1 (*m*, H–C(5)); 4.08 (*dd*, *J* = 2.0, 12.4, H_B–C(6)); 3.86 (*dd*, *J* = 4.2, 10.7, H–C(2)); 2.11 (*s*, CH_3CO); 2.09 (*s*, CH_3CO); 2.06 (*s*, CH_3CO). ^{13}C-NMR (50 MHz, $CDCl_3$): 170.33 (*s*); 169.62 (*s*); 169.46 (*s*); 96.26 (*d*); 70.48 (*d*); 70.34 (*d*); 67.43 (*d*); 61.02 (*t*); 59.35 (*d*); 20.56 (*q*); 20.52 (*q*); 20.45 (*q*). Anal. calc. for $C_{12}H_{16}N_4O_{10}$ (376.28): C 38.30, H 4.29, N 14.89; found: C 38.39, H 4.43, N 15.14.

Data of **14**: ^{1}H-NMR (200 MHz, $CDCl_3$)[14]): 5.63 (*d*, *J* = 8.9, H–C(1)); 5.19 (*t*, *J* = 9.6, 1 H); 5.05 (*t*, *J* = 9.5, 1 H); 4.4–3.8 (*m*, H–C(5), H_A–(6), H_B–C(6)); 3.70 (*dd*, *J* = 8.9, 9.7, H–C(2)); 2.13–2.03 (3*s*, 3 CH_3CO).

Data of **15**: R_f (hexane/CH_2Cl_2/AcOEt 2:1:1) 0.29. M.p. 85–86°. $[\alpha]_D^{25} = +100.2°$ (*c* = 1.12, $CHCl_3$). IR: 3020*w*, 2960*w*, 2110*s*, 1750*s*, 1670*s*, 1455*w*, 1430*w*, 1370*s*, 1350*w*, 1270*s*, 1155*s*, 1090*m*, 1065*m*, 1045*m*, 1010*w*, 960*m*, 915*w*, 820*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 6.21 (*d*, *J* = 1.9, H–C(1)); 5.42 (*t*, *J* = 9.6, H–C(4)); 5.26 (*dd*, *J* = 3.8, 9.6, H–C(3)); 4.29 (*dd*, *J* = 5.1, 12.8, H_A–C(6)); 4.20 (*dd*, *J* = 1.9, 3.8, H–C(2)); 4.11 (*dd*, *J* = 2.3, 12.8, H_B–C(6)); 4.2–4.0 (*m*, H–C(5)); 2.13 (*s*, CH_3CO); 2.11 (*s*, CH_3CO); 2.08 (*s*, CH_3CO). ^{13}C-NMR (50 MHz, $CDCl_3$): 170.50 (*s*); 169.73 (*s*); 169.25 (*s*); 97.07 (*d*); 71.18 (*d*); 70.36 (*d*); 64.83 (*d*); 61.39 (*t*); 58.77 (*d*); 20.60 (*q*); 20.52 (*q*); 20.37 (*q*). Anal. calc. for $C_{12}H_{16}N_4O_{10}$ (376.28): C 38.30, H 4.29, N 14.89; found: C 38.48, H 4.19, N 14.88.

*2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-α- and -β-*D*-glucopyranosyl Nitrate* (**17** and **18**, resp.) *and 2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-*D*-mannopyranosyl Nitrate* (**19**). Azidonitration of 2 g (4.8 mmol) of **16** [32] [33] in 26 ml of

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[13]) ^{1}H-NMR (200 MHz, $CDCl_3$) of **10**: 6.24 (*d*, *J* = 4.2, H–C(1)); of **11**: 5.44 (*d*, *J* = 8.9, H–C(1)).

[14]) Determined from the spectrum of **13/14**.

MeCN with 495 mg (7.7 mmol) of NaN_3 and 8.40 g (19.6 mmol) of $Ce(NH_4)_2(NO_3)_6$ yielded, after FC (hexane/AcOEt 7:3), 59% of **17/18/19** (by ^{1}H-NMR: **17**, 33%; **18**, 13%; **19**, 13%).

1-O-Acetyl-2-azido-3,4,6-tri-O-benzyl-2-deoxy-α- and β-D-galactopyranose (**20** and **21**, resp.). According to [11], a mixture of 263 mg (0.51 mmol) of **10/11** and of 83.7 mg (1.02 mmol) of anh. NaOAc in 1.2 ml of AcOH was stirred at 100° for 2 h. The mixture was diluted with 6 ml of CH_2Cl_2 and extracted with 5 ml of ice-cold H_2O, 2.5 ml of sat. aq. $NaHCO_3$ soln. (2 ×), and 4 ml of H_2O. The org. layer was processed as usual. FC (hexane/AcOEt 4:1) gave 213.6 mg (84%) of **20/21** in a 1:1 ratio[15]). Each anomer was crystallized from Et_2O/hexane. IR of **20/21**: 3080*w*, 3060*w*, 3030*w*, 3000*m*, 2950*m*, 2920*m*, 2870*m*, 2115*s*, 1760*s*, 1635*w*, 1495*w*, 1450*m*, 1370*m*, 1360*m*, 1345*m*, 1280*m*, 1260*m*, 1120*s*, 1095*s*, 1050*s*, 1030*m*, 1010*m*, 990*m*, 930*m*, 910*w*, 880*w*, 690*m*.

Data of **20**: R_f (hexane/AcOEt 4:1) 0.25. M.p. 88° ([32]: 88–90°). ^{1}H-NMR (200 MHz, $CDCl_3$): 7.45–7.19 (*m*, 15 arom. H); 6.24 (*d*, *J* = 3.5, H–C(1)); 4.90, 4.55 (*AB*, *J* = 11.4, PhCH_2); 4.78, 4.71 (*AB*, *J* = 11.3, PhCH_2); 4.49, 4.41 (*AB*, *J* = 11.7, PhCH_2); 4.10 (*dd*, *J* = 3.5, 10.6, H–C(2)); 4.03–3.96 (*m*, H–C(5)); 3.91 (*dd*, *J* = 10.6, 2.6, H–C(3)); 3.63 (*dd*, *J* = 7.9, 9.0, H_A–C(6)); 3.53 (*dd*, *J* = 5.6, 9.0, H_B–C(6)); 2.13 (*s*, CH_3CO).

Data of **21**: R_f (hexane/AcOEt 4:1) 0.21. M.p. 72° ([32]: 71°). ^{1}H-NMR (200 MHz, $CDCl_3$): 7.41–7.24 (*m*, 15 arom. H); 5.41 (*d*, *J* = 8.5, H–C(1)); 4.90, 4.59 (*AB*, *J* = 11.3, PhCH_2); 4.73, 4.66 (*AB*, *J* = 11.6, PhCH_2); 4.47, 4.40 (*AB*, *J* = 11.7, PhCH_2); 4.01–3.91 (*m*, H–C(2), H–C(4)); 3.67 (*dd*, *J* = 6.7, 9.9, H_A–C(6)); 3.72–3.56 (*m*, H–C(5), H_B–C(6)); 3.44 (*dd*, *J* = 10.3, 2.8, H–C(3)); 2.15 (*s*, CH_3CO).

1,6-Di-O-acetyl-2-azido-3,4-di-O-benzyl-2-deoxy-β- and -α-D-galactopyranose (**22** and **23**, resp.). A mixture of 1.62 g (3.1 mmol) of **10/11** and 516 mg (6.29 mmol) of anh. NaOAc in 7.5 ml of AcOH wa stirred at 100° for 2 h. After workup as described above for **20/21**, 0.5 ml of conc. H_2SO_4 were added at 0° to the crude **20/21** in 25 ml of Ac_2O. After stirring at r.t. for 1 h, the mixture was diluted with 100 ml of Et_2O and extracted with ice-cold H_2O, sat. aq. Na_2CO_3 soln. (2 ×), and again with H_2O. The org. layer was processed as usual. FC (hexane/AcOEt 7:3) gave 882 mg (60% from **10/11**) of the mixture of the anomers **22** and **23** in a 8:92 ratio[15]). IR of **22/23**: 3090*w*, 3060*w*, 3030*w*, 3000*w*, 2940*w*, 2900*w*, 2880*w*, 2115*s*, 1740*s*, 1490*w*, 1450*m*, 1370*m*, 1310*w*, 1280*m*, 1150*m*, 1105*s*, 1080*s*, 1055*s*, 1030*m*, 1005*m*, 980*w*, 915*w*, 880*w*, 860*w*, 690*w*.

Data of **22**: ^{1}H-NMR (200 MHz, $CDCl_3$): 7.45–7.20 (*m*, 10 arom. H); 5.41 (*d*, *J* = 8.5, H–C(1)); 4.94, 4.61 (*AB*, *J* = 11.6, PhCH_2); 4.76 (*s*, PhCH_2); 4.16 (*dd*, *J* = 6,8, 11.4, H_A–C(6)); 4.07 (*dd*, *J* = 5.7, 11.4, H_B–C(6)); 3.98 (*dd*, *J* = 8.5, 10.3, H–C(2)); 3.80 (*dd*, *J* = 2.7, ≤ 1, H–C(4)); 3.64 (*m*, *J* = 6.8, 5.7, ≤ 1, H–C(5)); 3.45 (*dd*, *J* = 10.3, 2.7, H–C(3)); 2.16 (*s*, CH_3CO); 1.97 (*s*, CH_3CO). ^{13}C-NMR (50 MHz, $CDCl_3$): 170.42 (*s*); 168.97 (*s*); 137.61 (*s*); 137.15 (*s*); 128.7–127.9 (*m*); 92.95 (*d*); 80.88 (*d*); 74.54 (*t*); 73.35 (*d*); 73.01 (*t*); 71.60 (*d*); 62.71 (*t*); 61.86 (*d*); 20.93 (*q*); 20.71 (*q*).

Data of **23**: ^{1}H-NMR (200 MHz, $CDCl_3$): 7.48–7.26 (*m*, 10 arom. H); 6.26 (*d*, *J* = 3.7, H–C(1)); 4.93, 4.57 (*AB*, *J* = 11.3, PhCH_2); 4.79 (*s*, PhCH_2); 4.16 (*dd*, *J* = 7.1, 11.0, H_A–C(6)); 4.12 (*dd*, *J* = 3.6, 10.5, H–C(2)); 4.08 (*dd*, *J* = 5.6, 10.9, H_B–C(6)); 4.02–3.94 (*m*, H–C(4), H–C(5)); 3.90 (*dd*, *J* = 10.3, 2.4, H–C(3)); 2.13 (*s*, CH_3CO); 1.99 (*s*, CH_3CO). ^{13}C-NMR (50 MHz, $CDCl_3$): 170.41 (*s*); 168.78 (*s*); 137.62 (*s*); 137.18 (*s*); 128.6–127.5 (*m*); 90.97 (*d*); 77.74 (*d*); 74.69 (*t*); 72.55 (*t*); 72.51 (*d*); 70.80 (*d*); 62.78 (*t*); 58.94 (*d*); 20.91 (*q*); 20.70 (*q*).

1,6-Di-O-acetyl-3,4-di-O-benzyl-2-deoxy-2-[(dimethoxyphosphoryl)amino]-β-D-galactopyranose (**24**). A soln. of 100 mg (0.21 mmol) of **22** in 300 µl (315.6 mg, 2.54 mmol) of $P(OMe)_3$ was stirred under Ar at r.t. for 10 min. After standing for 1.5 h at r.t., the mixture was evaporated *i.v.* FC (AcOEt) of the residue (dissolved in CH_2Cl_2) gave 112 mg (95%) of **24** which crystallized from CH_2Cl_2/hexane. R_f (AcOEt) 0.20. M.p. 194–195° (dec.). $[\alpha]_D^{25}$ = +16.5° (*c* = 1.03, $CHCl_3$). IR: 3410*w*, 3090*w*, 3070*w*, 3030*w*, 3000*m*, 2960*w*, 2930*w*, 2860*w*, 1750*s*, 1495*w*, 1455*m*, 1435*w*, 1370*m*, 1140*m*, 1110*s*, 1080*s*, 1055*s*, 950*w*, 840*m*, 695*w*. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.43–7.27 (*m*, 10 arom. H); 5.52 (*d*, *J* = 8.2, H–C(1)); 4.93, 4.62 (*AB*, *J* = 11.6, PhCH_2); 4.82, 4.66 (*AB*, *J* = 11.5, PhCH_2); 4.18 (*dd*, *J* = 6.8, 11.3, H_A–C(6)); 4.11 (*dd*, *J* = 5.6, 11.3, H_B–C(6)); 3.88–3.87 (*m*, H–C(4)); 3.72–3.55 (*m*, H–C(2), H–C(5)); 3.66 (*d*, *J*(H,P) = 11.2, $POCH_3$); 3.65 (*d*, *J*(H,P) = 11.2, $POCH_3$); 3.49 (*dd*, *J* = 10.4, 2.5, H–C(3)); 2.66 (*t*, *J*(NH,P) = *J*(NH,2) = 8.5, NH); 2.13 (*s*, CH_3CO); 1.99 (*s*, CH_3CO). ^{13}C-NMR (50 MHz, $CDCl_3$): 170.44 (*s*); 169.54 (*s*); 137.82 (*s*); 137.27 (*s*); 128.53–127.66 (*m*); 93.95 (*dd*, *J*(C,P) = 2.3, C(1)); 80.88 (*dd*, *J*(C,P) = 4.1, C(3)); 74.30 (*t*); 73.10 (*d*); 72.48 (*t*); 71.33 (*d*); 62.93 (*t*); 53.30 (*d*); 53.25 (*qd*, *J*(C,P) = 4.7, 2 $POCH_3$); 20.93 (*q*); 20.70 (*q*). ^{31}P-NMR (80 MHz, $CDCl_3$): +10.72. Anal. calc. for $C_{26}H_{34}NO_{10}P$ (551.54): C 56.62, H 6.21, N 2.54, P 5.62; found: C 56.40, H 6.40, N 2.37, P 5.41.

2-Azido-3,4,6-tri-O-benzyl-2-deoxy-D-galactopyranose (**25**). According to [12], 980 mg (1.88 mmol) of **10/11** gave 681 mg (75%) of **25**. IR: 3590*w*, 3080*w*, 3060*w*, 3030*w*, 3000*w*, 2920*w*, 2860*w*, 2110*s*, 1490*w*, 1450*w*, 1400*w*, 1360*w*, 1320*w*, 1260*m*, 1150*m*, 1100*s*, 1080*m*, 1060*s*, 1025*m*, 1000*m*, 950*w*, 910*w*, 870*w*, 690*w*.

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[15]) Determined from the integrals of H–C(1) in the ^{1}H-NMR spectrum of the mixture.

O-(2-Azido-3,4,6-tri-O-benzyl-2-deoxy-α-D-galactopyranosyl) Trichloroacetimidate (**26**). According to [12], a soln. of 4.05 g (8.5 mmol) of **25** in 120 ml of dry CH_2Cl_2 was treated with 8.3 ml (82.4 mmol) of CCl_3CN and 250 mg (10.4 mmol) of NaH at r.t. under N_2. After 4 h, the mixture was filtered through *Celite* and evaporated to give 6.48 g of crude **26** which was directly used for the phosphonate synthesis. A small batch of the crude product was purified by FC (hexane/AcOEt 2:1). R_f (hexane/AcOEt 2:1) 0.51. IR: 3340*w*, 3080*w*, 3060*w*, 3000*w*, 2920*w*, 2870*w*, 2110*s*, 1670*m*, 1490*w*, 1450*w*, 1360*w*, 1350*m*, 1280*m*, 1135*m*, 1125*m*, 1090*m*, 1070*m*, 1025*s*, 965*m*, 930*w*, 885*w*, 865*w*, 840*w*, 690*w*, 660*w*, 640*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.66 (*s*, NH); 7.5–7.2 (*m*, 15 arom. H); 6.39 (*d*, J = 3.4, H–C(1)); 4.92, 4.58 (*AB*, J = 11.2, PhCH_2); 4.80, 4.70 (*AB*, J = 11.3, PhCH_2); 4.49, 4.42 (*AB*, J = 11.7, PhCH_2); 4.19 (*dd*, J = 3.4, 10.7, H–C(2)); 4.2–4.1 (*m*, H–C(4), H–C(5)); 4.04 (*dd*, J = 10.7, 2.6, H–C(3)); 3.67 (*dd*, J = 7.9, 9.1, H_A–C(6)); 3.55 (*dd*, J = 5.4, 9.1, H_B–C(6)).

Dimethyl (2-Azido-3,4,6-tri-O-benzyl-2-deoxy-α- and -β-D-galactopyranosyl)phosphonate (**27** and **28**, resp.) *and N-(2-Azido-3,4,6-tri-O-benzyl-2-deoxy-D-galactopyranosyl)acetamides* (**29** and **30**, resp.). To a mixture of 6.48 g of crude **26**, 26 ml of dry CH_2Cl_2 (distilled over P_2O_5), and 2.43 ml (20.60 mmol) of freshly distilled $P(OMe)_3$ were added under N_2 2.67 ml (14.72 mmol) of $TfOSiMe_3$ at 0° over 10 min. The mixture was stirred for 1 h at r.t., diluted with CH_2Cl_2, and extracted with H_2O. After usual processing of the org. layer, FC (hexane/AcOEt 2:3) gave 1.53 g (31.7%) of **27**, 1.54 g (31.9%) of **28**, and 500 mg (9.5%) of **29/30.**

Data of **27**: R_f (hexane/AcOEt 2:3) 0.36. $[\alpha]_D^{25}$ = +43.7° (c = 1.04,$CHCl_3$). IR: 3080*w*, 3060*w*, 3030*w*, 2990*m*, 2950*m*, 2900*w*, 2860*m*, 2810*w*, 2110*s*, 1490*w*, 1450*m*, 1360*m*, 1330*m*, 1305*m*, 1250*s*, 1110*s* (sh), 1085*s*, 1060–1020*s*, 980*m* (sh), 910*w*, 865*w*, 830*m*, 690*m*. ^{1}H-NMR (400 MHz, C_6D_6): 7.4–7.0 (*m*, 15 arom. H); 4.78, 4.35 (*AB*, J = 11.2, PhCH_2); 4.6–4.5 (*m*, H–C(5)); 4.57 (*dd*, J = 10.2, 2.6, H–C(3)); 4.48, 4.36 (*AB*, J = 11.5, PhCH_2); 4.32, 4.24 (*AB*, J = 11.8, PhCH_2); 4.4–4.2 (*m*, J(2,P) ≈ 32, H–C(2)); 4.20 (*dd*, J = 6.7, J(1,P) = 11.2, H–C(1)); 3.84 (*m*, H–C(4)); 3.75 (*dd*, J = 6.6, 9.7, H_A–C(6)); 3.63 (*dd*, J = 5.9, 9.7, H_B–C(6)); 3.56 (*d*, J(H,P) = 10.7, $POCH_3$); 3.46 (*d*, J(H,P) = 10.8, $POCH_3$). ^{13}C-NMR (50 MHz, $CDCl_3$): 138.00 (*s*); 137.88 (*s*); 137.54 (*s*); 128.4–127.4 (*m*); 77.88 (*dd*, J(C,P) = 1.5); 75.37 (*dd*, J(C,P) = 3.4); 74.24 (*t*); 73.24 (*t*); 73.04 (*d*); 72.63 (*t*); 70.4 (*dd*, J(C,P) = 160, C(1)); 68.29 (*t*); 58.48 (*d*); 53.52 (*qd*, J(C,P) = 6.8, $POCH_3$); 52.9 (*qd*, J(C,P) = 7, $POCH_3$). ^{31}P-NMR (80 MHz, $CDCl_3$): +23.15. Anal. calc. for $C_{29}H_{34}N_3O_7P$ (567.58): C 61.37, H 6.04, N 7.40, P.5.45; found: C 61.65, H 6.38, N 7.20, P 5.20.

Data of **28**: R_f (hexane/AcOEt 2:3) 0.21. IR: 3080*w*, 3060*w*, 3030*w*, 2990*m*, 2950*w*, 2920*w*, 2860*w*, 2850*w*, 2110*s*, 1490*w*, 1450*m*, 1360*m*, 1340*w*, 1250*m*, 1145*m*, 1110*s*, 1090*s*, 1055*s*, 1035*s*, 910*w*, 820*w*, 690*m*. ^{1}H-NMR (400 MHz, C_6D_6): 7.4–7.0 (*m*, 15 arom. H); 4.83, 4.45 (*AB*, J = 11.6, PhCH_2); 4.45 (*q*, J = 10, H–C(2)); 4.35 (*s*, PhCH_2); 4.26, 4.20 (*AB*, J = 11.9, PhCH_2); 3.71 (*m*, H–C(4)); 3.53 (*d*, J(H,P) = 10.2, $POCH_3$); 3.50 (*d*, J(H,P) = 10.4, $POCH_3$); 3.55–3.47 (*m*, H_A–C(6), H_B–C(6)); 3.42 (*t*, J = 10.2, H–C(1)); 3.18 (*m*, H–C(5)); 3.08 (*dd*, J = 9.8, 2.7, H–C(3)). ^{13}C-NMR (50 MHz, $CDCl_3$): 138.34 (*s*); 137.70 (*s*); 137.44 (*s*); 128.9–127.3 (*m*); 82.48 (*dd*, J(C,P) = 16.3); 78.93 (*dd*, J(C,P) = 16.0); 74.71 (*dd*, J(C,P) = 172.8, C(1)); 74.47 (*t*); 73.46 (*t*); 72.32 (*d*); 72.32 (*t*); 68.44 (*t*); 59.19 (*dd*, J(C,P) = 2.7); 53.82 (*qd*, J(C,P) = 6.5, $POCH_3$); 53.38 (*qd*, J(C,P) = 6.3, $POCH_3$). ^{31}P-NMR (80 MHz, $CDCl_3$): +21.04. Anal. calc. for $C_{29}H_{34}N_3O_7P$ (567.58): C 61.37, H 6.04, N 7.40, P 5.45; found: C 61.62, H 6.32, N 7.25, P 5.22.

Data of **29/30**: $[\alpha]_D^{25}$ = +19.9° (c = 0.64, $CHCl_3$). IR: 3410*w*, 3090*w*, 3060*w*, 3000*w*, 2920*w*, 2870*w*, 2120*s*, 1730*s*, 1560*m* (sh), 1500*m*, 1455*m*, 1360*m*, 1350*w*, 1300*w* (sh), 1260*m*, 1250*w* (sh), 1100*s*, 1065*s* (sh), 1030*m*, 1000*m*, 910*w*, 840*m*, 820*m*, 695*m*. ^{13}C-NMR (50 MHz, $CDCl_3$): 161.76 (*s*); 161.60 (*s*); 137.61 (*s*); 137.49 (*s*); 137.16 (*s*); 137.04 (*s*); 136.80 (*s*); 128.86–127.49 (*m*); 91.97 (*s*); 81.52 (*d*); 80.37 (*t*); 80.37 (*d*); 78.28 (*d*); 77.05 (*d*); 75.48 (*d*); 74.99 (*t*); 74.55 (*t*); 73.49 (*t*); 72.40 (*t*); 72.02 (*t*); 71.96 (*d*); 71.59 (*d*); 67.66 (*t*); 67.56 (*t*); 62.48 (*d*); 58.82 (*d*).

Dimethyl (2-Acetamido-3,4,6-tri-O-benzyl-2-deoxy-α-D-galactopyranosyl)phosphonate (**31**). $NaBH_4$ (200 mg) was added at r.t. over 1 h to a soln. of 973 mg (1.71 mmol) of **27** in 72 ml of a soln. of $NiCl_2 \cdot 6H_2O$ and H_3BO_3 in EtOH [16]. The mixture was stirred at r.t. for 14 h, filtered through *Celite*, and 5 ml of Ac_2O were added to the filtrate. This mixture was stirred at r.t. for 19 h, diluted with 300 ml of CH_2Cl_2, and extracted with H_2O, sat. aq. $NaHCO_3$ soln., and H_2O. The org. layer was processed as usual. FC (AcOEt/MeOH 19:1) gave 696 mg (70%) of **31**. R_f (AcOEt/MeOH 10:1) 0.41. $[\alpha]_D^{25}$ = +31.1° (c = 1.07, $CHCl_3$). IR: 3420*m*, 3090*w*, 3060*w*, 3030*w*, 3000*m*, 2960*m*, 2930*m*, 2870*m*, 2860*m*, 1680*s*, 1510*m*, 1500*m*, 1455*m*, 1370*m*, 1310*m*, 1290*m*, 1250*s*, 1095*s*, 1050*s*, 910*m*, 865*w*, 840*m*, 695*m*. ^{1}H-NMR (400 MHz, (D_5)pyridine): 9.08 (*d*, J(2,NH) = 7.3, NH); 7.58–7.21 (*m*, 15 arom. H); 5.36–5.25 (*m*, H–C(2)); 5.20 (*dd*, J(1,P) = 12.0, J = 5.2, H–C(1)); 4.84 (*AB*, J = 11.7, PhCH_2); 4.80 (*AB*, J = 11.7, PhCH_2); 4.62 (*AB*, J = 11.7, PhCH_2); 4.61 (*AB*, J = 12.1, PhCH_2); 4.57 (*AB*, J = 11.9, PhCH_2); 4.51 (*AB*, J = 11.6, PhCH_2); 4.32 (*m*, H–C(4)); 4.19 (*m*, H–C(5)), 4.01 (*t*, J = 5.1, H_A–C(6)); 3.96 (*dd*, J = 10.6, 4.5, H–C(3)); 3.88 (*d*, J = 10.6, $POCH_3$); 3.80 (*t*, J = 5.1, H_B–C(6)); 3.76 (*d*, J = 10.8, $POCH_3$); 2.13 (*s*, CH_3CO). ^{13}C-NMR (50 MHz, $CDCl_3$): 170.43 (*s*); 138.18 (*s*); 138.08 (*s*); 137.72 (*s*); 128.9–127.3 (*m*); 75.69 (*dd*,

J(C,P) = 9.3); 74.16 (*dd*, J(C,P) = 7.2); 73.10 (*t*); 72.58 (*t*); 72.09 (*t*); 72.01 (*d*); 66.30 (*t*); 65.54 (*dd*, J(C,P) = 165.4, C(1)); 54.21 (*qd*, J(C,P) = 6.2, $POCH_3$); 52.61 (*qd*, J(C,P) = 7.4, $POCH_3$); 48.66 (*d*); 23.16 (*q*). ^{31}P-NMR (80 MHz, $CDCl_3$): +23.82. Anal. calc. for $C_{31}H_{38}NO_8P$ (583.62): C 63.80, H 6.56, N 2.40, P 5.30; found: C 63.82, H 6.53, N 2.31, P 5.10.

*Dimethyl (2-Acetamido-3,4,6-tri-O-benzyl-2-deoxy-β-*D*-galactopyranosyl)phosphonate* (**32**). Similar to the reaction of **27**, 600 mg (1.06 mmol) of **28** gave, after FC (AcOEt/MeOH 9:1), 481 mg (78%) of **32**. R_f (AcOEt/MeOH 9:1) 0.30. $[\alpha]_D^{25}$ = +32.1° (*c* = 1.07, $CHCl_3$). IR: 3450*m*, 3090*w*, 3060*w*, 3030*w*, 3000*s*, 2980*s*, 2930*m*, 2870*s*, 1680*s*, 1510*m*, 1495*m*, 1455*m*, 1380*m*, 1370*m*, 1350*m*, 1280*m*, 1240*s*, 1150*m*, 1110*s*, 1060*s*, 1040*s*, 1030*s*, 915 *w*, 820*m*, 695*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.37–7.22 (*m*, 15 arom. H); 5.86 (*d*, J(2,NH) = 7.6, NH); 4.90, 4.56 (*AB*, J = 11.5, PhCH_2); 4.67, 4.53 (*AB*, J = 11.6, PhCH_2); 4.46 (*dd*, J(1,P) = 10.8, J = 8.9, H–C(1)), 4.36 (*dd*, J = 10.3, 2.6, H–C(3)); 4.0–3.9 (*m*, 2H); 3.78 (*d*, J(H,P) = 10.4, $POCH_3$); 3.73 (*d*, J(H,P) = 10.7, $POCH_3$); 3.8–3.5 (*m*, 3H); 1.90 (*s*, CH_3CO). ^{13}C-NMR (50 MHz, $CDCl_3$): 171.32 (*s*); 138.62 (*s*); 138.16 (*s*); 137.86 (*s*); 128.6–127.3 (*m*); 79.06 (*dd*, J(C,P) = 16.2); 78.46 (*dd*, J(C,P) = 16.9); 74.52 (*t*); 73.38 (*t*); 73.38 (*d*); 72.37 (*t*); 72.31 (*dd*, J(C,P) = 169.4, C(1)); 68.81 (*t*); 54.31 (*qd*, J(C,P) = 6.6, $POCH_3$); 53.02 (*qd*, J(C,P) = 7.0, $POCH_3$); 50.47 (*d*); 23.63 (*q*, CH_3). ^{31}P-NMR (80 MHz, $CDCl_3$): +21.91. Anal. calc. for $C_{31}H_{38}NO_8P$ (583.62): C 63.80, H 6.56, N 2.40, P 5.30; found: C 63.65, H 6.74, N 2.25, P 5.21.

*Dimethyl (2-Acetamido-2-deoxy-α-*D*-galactopyranosyl)phosphonate* (**33**). A) *By Catalytic Transfer Hydrogenolysis* [17]. A soln. of 100 mg (0.17 mmol) of **31** in 9 ml of MeOH and 1 ml of HCOOH was added to a suspension of 690 mg of 10% Pd/C in 10 ml of MeOH. The mixture was stirred at r.t. for 5 h. FC (AcOEt/MeOH 2:1) afforded 50.4 mg (94%) of **33**.

B) *By Catalytic Hydrogenolysis*. Hydrogenolysis of 100 mg (0.17 mmol) of **31** in 12 ml of MeOH over 70 mg of 10% $Pd(OH)_2$/C under H_2 (4 bar) at r.t. for 2 h gave, after FC (AcOEt/MeOH 1:1), 48 mg (89%) of **33**. R_f (AcOEt/MeOH 2:1) 0.17[16]). M.p. 205–206°. $[\alpha]_D^{25}$ = +127.6° (*c* = 1.02, MeOH). IR (KBr): 3410*s*, 3300*s*, 3240*s*, 3080*m*, 3010*w*, 2980*w*, 2960*m*, 2940*w*, 2900*m*, 2870*m*, 1645*s*, 1570*s*, 1455*m* (sh), 1435*m*, 1385*m*, 1365*m*, 1320*m*, 1290*w*, 1270*m*, 1235*s*, 1230*s*, 1195*m*, 1180*m*, 1160*m*, 1140*m*, 1120*s*, 1105*s*, 1080*s*, 1055*s*, 1045*s*, 1035*s* (sh), 1020*s*, 925*w*, 880*m*, 830*m*, 810*s*, 790*m*, 770*m*, 710*m*, 665*m*, 640*m*, 610*m*. ^{1}H-NMR (200 MHz, CD_3OD): 4.71 (*dd*, J(1,P) = 11.0, J = 6.6, H–C(1)); 4.35 (*ddd*, J(2,P) = 31.7, J = 6.6, 10.3, H–C(2)); 4.2–4.0 (*m*, 2H); 4.0–3.6 (*m*, 2H); 3.85 (*d*, J(H,P) = 10.7, $POCH_3$); 3.75 (*d*, J(H,P) = 10.8, $POCH_3$); 3.32–3.29 (*m*, H–C(4)); 1.98 (*s*, CH_3CO): ^{13}C-NMR (50 MHz, D_2O): 175.64 (*s*); 77.41 (*dd*, J(C,P) = 1.6); 69.57 (*dd*, J(C,P) = 153.3, C(1)); 68.05 (*d*); 67.49 (*d*); 61.53 (*t*); 54.40 (*qd*, J(C,P) = 7.4, $POCH_3$); 53.54 (*qd*, J(C,P) = 7.6, $POCH_3$); 48.23 (*dd*, J(C,P) = 1.6); 22.03 (*q*). ^{31}P-NMR (80 MHz, D_2O): +26.54. Anal. calc. for $C_{10}H_{20}NO_8P$ (313.25): C 38.34, H 6.44, N 4.47, P 9.89; found: C 38.31, H 6.60, N 4.40, P 9.72.

*Dimethyl (2-Acetamido-2-deoxy-β-*D*-galactopyranosyl)phosphonate* (**34**). Hydrogenolysis of 100 mg of **32** under H_2 (4 bar) as described for **33** *(B)* afforded, after FC (AcOEt/MeOH 1:1), 49 mg (91%) of **34**. R_f (AcOEt/MeOH 2:1) 0.11[16]). $[\alpha]_D^{25}$ = +24.3° (*c* = 1.04, MeOH). ^{1}H-NMR (200 MHz, CD_3OD): 4.24 (*q*, $J \approx 10$, H–C(2)); 3.88 (*dd*, J(1,P) = 10.9, J = 9.5, H–C(1)); 3.82 (*dd*, J(H,P) = 10.7, $POCH_3$); 3.80 (*d*, J(H,P) = 10.7, $POCH_3$); 3.9–3.6 (*m*, 3H); 3.54–3.48 (*m*, 1H); 3.33–3.29 (*m*, H–C(4)); 1.96 (*s*, CH_3CO). ^{13}C-NMR (50 MHz, D_2O): 174.46 (*s*); 81.25 (*dd*, J(C,P) = 15.6); 72.14 (*dd*, J(C,P) = 17.1); 72.67 (*dd*, J(C,P) = 172.2, C(1)); 68.47 (*d*); 61.62 (*t*); 54.54 (*qd*, J(C,P) = 6.7, $POCH_3$); 54.31 (*qd*, J(C,P) = 7.3, $POCH_3$); 47.8 (*d*); 22.50 (*q*). ^{31}P-NMR (80 MHz, D_2O): +23.98. Anal. calc. for $C_{10}H_{20}NO_8P$ (313.25): C 38.34, H 6.44, N 4.47, P 9.89; found: C 38.53, H 6.71, N 4.65, P 9.79.

*O-(3,4,6-Tri-O-acetyl-2-azido-2-deoxy-α-*D*-glucopyranosyl) Trichloroacetimidate* (**35**), *O-(3,4,6-Tri-O-acetyl-2-azido-2-deoxy-α-*D*-mannopyranosyl) Trichloroacetimidate* (**37**). Azidonitration of 29.5 g (0.108 mol) of **12** in 630 ml of MeCN with 10.8 g (0.166 mol) of NaN_3 and 196.4 g (0.358 mol) of $Ce(NH_4)_2(NO_3)_6$ over 7 h afforded 41.14 g of crude **13–15**. To a soln. of 22.45 g of **13–15** in 135 ml of dioxane were added 28.0 g (0.406 mol) of $NaNO_2$ in 30 ml of H_2O [12]. After stirring at 80° for 10 h, ice was added and the mixture extracted with CH_2Cl_2. After the usual processing of the org. layer, 22.42 g of crude product were obtained. According to [12], a mixture of 22.42 g of this crude product, 280 ml of dry CH_2Cl_2, 14 ml of CCl_3CN, and 840 mg (35 mmol) of NaH was stirred under N_2 at r.t. for 4 h. After filtration through *Celite*, evaporation, and FC (hexane/AcOEt 3:1), 5.00 g (17.8% from **12**) of **35**, 4.20 g (14.9%) of **37**, and 1.68 g (6.0%) of **35/37** were obtained. The imidate **35** was crystallized from Et_2O/hexane.

Data of **35**: R_f (hexane/AcOEt 1:1) 0.49. M.p. 130° ([12]: 130°). IR: 3350*w*, 3030*w*, 2960*w*, 2920*w*, 2850*w*, 2110*s*, 1750*s*, 1675*m*, 1370*m*, 1280*m*, 1255*s*, 1140*m*, 1095*s*, 1085*s*, 1050*s*, 1020*s*, 970*m*, 920*w*, 910*w*, 860*w*, 640*w*. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.84 (*s*, NH); 6.49 (*d*, J = 3.5, H–C(1)); 5.53 (*dd*, J = 10.3, 9.5, H–C(3)); 5.16 (*dd*,

[16]) Detection by dipping the plate into 10% ethanolic phosphomolybdic acid and heating to *ca.* 200°.

J = 9.3, 10.0, H–C(4)); 4.29 (*dd*, J = 4.0, 12.0, H_A–C(6)); 4.3–4.1 (*m*, H–C(5)); 4.10 (*dd*, J = 2.0, 12.1, H_B–C(6)); 3.78 (*dd*, J = 3.6, 10.5, H–C(2)); 2.12 (*s*, CH_3CO); 2.06 (*s*, 2 CH_3CO).

Data of **37**: R_f (hexane/AcOEt 1:1) 0.53. IR: 3350*w*, 3030*w*, 2960*w*, 2920*w*, 2110*s*, 1750*s*, 1675*m*, 1430*w*, 1370*s*, 1330*m*, 1150*m*, 1070*s* (sh), 1060*s*, 1040*s*, 1010*m*, 975*s*, 960*m*, 940*m*, 835*m*, 640*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.78 (*s*, NH); 6.30 (*d*, J = 1.8, H–C(1)); 5.5–5.4 (*m*, H–C(3), H–C(4)); 4.3–4.1 (*m*, H–C(2), H–C(5), H_A–C(6), H_B–C(6)); 2.12 (*s*, CH_3CO); 2.10 (*s*, CH_3CO); 2.07 (*s*, CH_3CO).

*Dimethyl (3,4,6-Tri-*O*-acetyl-2-azido-2-deoxy-α-*D*-glucopyranosyl)phosphonate* (**36**). A soln. of 1.20 g (2.52 mmol) of **35** in 36 ml of dry CH_2Cl_2 at 0° under N_2 was treated first with 600 µl (5.08 mmol) of $P(OMe)_3$ and then, within 5 min, with 550 µl (3.03 mmol) of $TfOSiMe_3$. The mixture was stirred under N_2 at r.t. for 1 h, diluted with 50 ml of CH_2Cl_2, and extracted with a sat. aq. soln. of $NaHCO_3$ and of NaCl. The org. layer was processed as usual. FC of the residue (hexane/AcOEt 1:3) yielded 820 mg (76%) of **36** which crystallized from Et_2O. R_f (hexane/AcOEt 1:3) 0.20. M.p. 74–75°. $[\alpha]_D^{25}$ = +52.8° (*c* = 1.06, $CHCl_3$). IR: 3030*w*, 3000*w*, 2960*w*, 2920*w*, 2860*w*, 2110*s*, 1750*s*, 1450*w*, 1370*m*, 1330*w*, 1100*m*, 1045*s*, 965*w*, 910*w*, 890*w*, 835*m*. ^{1}H-NMR (200 MHz, C_6D_6): 6.12 (*dd*, J = 10.1, 9.6 H–C(3)); 5.11 (*dd*, J = 9.9, 9.0, H–C(4)); 4.6–4.4 (*m*, H–C(5)); 4.27 (*dd*, J = 4.9, 12.4, H_A–C(6)); 4.09 (*dd*, J = 2.3, 12.4, H_B–C(6)); 3.97 (*dd*, J(1,P) = 11.9, J = 7.1, H–C(1)); 3.45 (*d*, J(H,P) = 10.7, $POCH_3$); 3.41 (*d*, J(H,P) = 11.0, $POCH_3$); 3.30 (*ddd*, J(2,P) = 31.6, J = 7.1, 10.1, H–C(2)); 1.75 (*s*, CH_3CO); 1.72 (*s*, CH_3CO); 1.64 (*s*, CH_3CO). ^{13}C-NMR (50 MHz, $CDCl_3$): 170.37 (*s*); 169.79 (*s*); 169.52 (*s*); 73.19 (*dd*, J(C,P) = 1.5); 71.67 (*d*); 70.96 (*dd*, J(C,P) = 155.9, C(1)); 68.11 (*d*); 61.93 (*t*); 59.32 (*dd*, J(C,P) = 2.3); 53.52 (*dd*, J(C,P) = 6.9, $POCH_3$); 53.24 (*dd*, J(C,P) = 6.7, $POCH_3$); 20.67 (*q*); 20.60 (*q*); 20.57 (*q*). ^{31}P-NMR (80 MHz, $CDCl_3$): +21.64. Anal. calc. for $C_{14}H_{22}N_3O_{10}P$ (423.32): C 39.72, H 5.24, N 9.92, P 7.31; found: C 39.44, H 5.21, N 9.85, P 7.42.

*Dimethyl (3,4,6-Tri-*O*-acetyl-2-azido-2-deoxy-α- and -β-*D*-mannopyranosyl)phosphonate* (**38** and **39**, resp.). Treatment of 1.05 g (2.2 mmol) of **37** in 30 ml of CH_2Cl_2 with 500 µl (4.24 mmol) of $P(OMe)_3$ and 460 µl (2.54 mmol) of $TfOSiMe_3$ as described for **36** gave, after FC (AcOEt), 468.1 mg (50.1%) of **38** and 78.9 mg (8.4%) of **39**.

Data of **38**: IR: 3030*w* (sh), 3000*w*, 2960*w*, 2850*w*, 2110*s*, 1745*s*, 1450*w*, 1370*m*, 1330*w*, 1270*m* (sh), 1240*m*, 1120*m*, 1050*s*, 980*w*, 955*w*, 915*w*, 835*w*. ^{1}H-NMR (200 MHz, $CDCl_3$): 5.58 (*dd*, J = 3.6, 9.3, H–C(3)); 5.31 (*t*, J = 9.1, H–C(4)); 4.46–4.36 (*m*, H–C(5)); 4.36–4.22 (*m*, H–C(2), H_A–C(6), H_B–C(6)); 4.10 (*dd*, J(1,P) = 12.3, J = 2.5, H–C(1)); 3.91 (*d*, J = 10.7, $POCH_3$); 3.87 (*d*, J = 10.8, $POCH_3$); 2.12 (*s*, CH_3CO); 2.09 (*s*, CH_3CO); 2.07 (*s*, CH_3CO).

Data of **39**: IR: 3030*w* (sh), 3000*m*, 2960*m*, 2860*w*, 2110*s*, 1750*s*, 1450*m*, 1430*w*, 1370*s*, 1145*m*, 1110*s*, 1050*s*, 975*w*, 960*w*, 915*w*, 900*w*, 860*m*, 830*w*. ^{1}H-NMR (200 MHz, $CDCl_3$): 5.36 (*t*, J = 9.9, H–C(4)); 5.08 (*dd*, J = 3.8, 9.9, H–C(3)); 4.32–4.30 (*m*, 1H); 4.23 (*dd*, J = 5.1, 13, H_A–C(6)); 4.15 (*dd*, J = 3.2, 13, H_B–C(6)); 3.97 (*d*, J(1,P) = 15.7, J = 1.5, H–C(1)); 3.89 (*d*, J(H,P) = 10.8, $POCH_3$); 3.85 (*d*, J(H,P) = 10.8, $POCH_3$); 3.61 (*ddd*, J = 9.9, 4.8, 2.8, H–C(5)); 2.13 (*s*, CH_3CO); 2.08 (*s*, CH_3CO); 2.06 (*s*, CH_3CO).

*Dimethyl (2-Azido-2-deoxy-α-*D*-glucopyranosyl)phosphonate* (**40**). A mixture of 0.3 ml of 0.4M NaOMe in MeOH and 1.15 g (2.7 mmol) of **36** in 20 ml of dry MeOH was stirred at r.t. for 1 h and then neutralized with 2N HCl at 0°. FC (AcOEt/MeOH 9:1) gave 730 mg (90%) of **40** which crystallized from AcOEt. R_f (AcOEt/MeOH 9:1) 0.20. M.p. 125°. $[\alpha]_D^{25}$ = +69.7° (*c* = 1.01, $CHCl_3$). IR (KBr): 3520*s*, 3340*s*, 2960*w*, 2940*w*, 2900*w*, 2850*w*, 2110*s*, 1480*w*, 1450*m*, 1420*w*, 1390*w*, 1360*m*, 1340*m*, 1305*m*, 1270*m*, 1240*s*, 1210*w*, 1180*w*, 1125*m*, 1100*s*, 1060*s*, 1040*s*, 1020*s*, 955*m*, 850*m*, 835*m*, 785*m*, 755*w*, 710*m*, 680*m*, 640*w*. ^{1}H-NMR (400 MHz, CD_3OD): 4.53 (*dd*, J(1,P) = 11.2, J = 7.2, H–C(1)); 4.04 (*t*, J = 9.4, H–C(3)); 3.85 (*d*, J(H,P) = 10.8, $POCH_3$); 3.82 (*d*, J(H,P) = 10.9, $POCH_3$); 3.9–3.8 (*m*, H_A–C(6)); 3.79 (*ddd*, J(2,P) = 34.5, J = 7.3, 10.0, H–C(2)); 3.71–3.68 (*m*, H–C(5)); 3.63 (*dd*, J = 5.4, 12.0, H_B–C(6)); 3.33–3.28 (*m*, H–C(4)). ^{13}C-NMR (50 MHz, CD_3OD): 79.73 (*dd*, J(C,P) = 1.5); 74.47 (*d*); 72.66 (*dd*, J(C,P) = 153.3, C(1)); 71.66 (*d*); 63.45 (*dd*, J(C,P) = 3.3); 62.77 (*t*); 54.32 (*qd*, J(C,P) = 7.2, $POCH_3$); 53.49 (*qd*, J(C,P) = 7.4, $POCH_3$). ^{31}P-NMR (80 MHz, CD_3OD): +25.30. Anal. calc. for $C_8H_{16}N_3O_7P$ (297.21): C 32.33, H 5.43, N 14.14, P 10.42; found: C 32.57, H 5.31, N 13.91, P 10.20.

*Dimethyl (2-Azido-4,6-*O*-benzylidene-2-deoxy-α-*D*-glucopyranosyl)phosphonate* (**41**). To a mixture of 615 mg (2.07 mmol) of **40** (powdered and dried over P_2O_5) and 300 mg of freshly melted $ZnCl_2$ were added 12 ml of benzaldehyde. The mixture was vigorously stirred for 3 h and then evaporated. FC (200 ml of each hexane/AcOEt 1:1, 2:3, and 1:2) gave 733 mg (92%) of **41**. R_f (hexane/AcOEt 1:2) 0.28. $[\alpha]_D^{25}$ = +18.1° (*c* = 1.05, $CHCl_3$). IR: 3590*w*, 3350*w* (br.), 2990*w*, 2950*w*, 2850*w*, 2110*s*, 1450*w*, 1380*w*, 1315*w*, 1250*s*, 1105*s*, 1080*m*, 1050*s*, 1030*s*, 975*m*, 920*w*, 830*m*, 690*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.48–7.42 (*m*, 2 arom. H); 7.36–7.33 (*m*, 3 arom. H); 5.50 (*s*, PhC*H*); 4.48 (*t*, J = 9.4, H–C(3)); 4.37 (*dd*, J(1,P) = 11.9, J = 7.4, H–C(1)); 4.27 (*dd*, J = 5.0, 10.4, H_{eq}–C(6)); 4.03–3.97 (*m*, H–C(5)); 3.93 (*ddd*, J(2,P) = 33.8, J = 7.4, 9.6, H–C(2)); 3.83 (*d*, J(H,P) = 10.8, $POCH_3$); 3.82 (*d*, J(H,P) = 10.7, $POCH_3$); 3.62 (*t*, J = 10.2, H_{ax}–C(6)); 3.48 (*t*, J = 9.4, H–C(4)). ^{13}C-NMR (50 MHz, $CDCl_3$): 136.86 (*s*); 133.3–126.3 (*m*); 102.15 (*d*); 81.45 (*d*); 72.50 (*dd*, J(C,P) = 155.6, C(1)); 70.50 (*d*); 68.59 (*t*); 67.92

(*d*); 61.80 (*dd*, *J*(C,P) = 2.6); 53.33 (*qd*, *J*(C,P) = 7.1, $POCH_3$); 53.12 (*qd*, *J*(C,P) = 6.9, $POCH_3$). ^{31}P-NMR (80 MHz, $CDCl_3$): +23.07. Anal. calc. for $C_{15}H_{20}N_3O_7P$ (385.32): C 46.76, H 5.23, N 10.90, P 8.04; found: C 46.67, H 5.17, N 11.15, P 7.95.

*Dimethyl (2-Amino-4,6-*O*-benzylidene-2-deoxy-α-*D*-glucopyranosyl)phosphonate* (**42**). Within 1 h, 90 mg of $NaBH_4$ were added at r.t. to 300 mg (0.78 mmol) of **41** in 40 ml of $NiCl_2 \cdot 6H_2O$ and H_3BO_3 in EtOH [16]. After stirring for 20 h at r.t., the mixture was filtered through *Celite* and evaporated. The residue was diluted with 200 ml of CH_2Cl_2 and washed with H_2O. After the usual processing of the org. layer, 226 mg (80%) of **42** were obtained as a white foam which was directly used for the acylation step. R_f (AcOEt/MeOH 4:1) 0.18[17]. IR ($CHCl_3$): 3600*w*, 3400*w* (br.), 3000*m*, 2960*w*, 2920*w*, 2870*w*, 2850*w*, 1450*w*, 1380*w*, 1310*w*, 1290*w*, 1240*m*, 1120*s*, 1085*s*, 1050*s*, 1030*s*, 910*w*, 830*m*, 695*w*, 655*w*.

*Dimethyl {4,6-*O*-Benzylidene-3-*O*-[(*R*)-3-(benzyloxy)tetradecanoyl]-2-[(*R*)-3-(benzyloxy)tetradecanoylamino]-2-deoxy-α-*D*-glucopyranosyl}phosphonate* (**43**). To a mixture of 600 mg (1.67 mmol) of **42**, 1.177 g (3.52 mmol) of (*R*)-3-(benzyloxy)tetradecanoic acid and 27 mg (0.22 mmol) of 4-(dimethylamino)pyridine in 20 ml of dry CH_2Cl_2 at −15° (ice/NaCl) were added 726 mg (3.52 mmol) of dicyclohexylcarbodiimide. The mixture was allowed to warm up to 0° (cooling with ice/H_2O) and was stirred for 4 h, filtered through *Celite*, and evaporated. A soln. of the residue in toluene/AcOEt 3:1 was again filtered through *Celite* and purified by FC (150 ml of toluene/AcOEt 3:1, then toluene/AcOEt 2:1) to give 1.33 g (80%) of **43**. $[\alpha]_D^{25}$ = +29.3° (*c* = 1.03, $CHCl_3$). IR ($CHCl_3$): 3400*w*, 3320*w*, 3080*w*, 3060*w*, 3020*w*, 2990*m*, 2920*s*, 2850*s*, 1735*m*, 1670*m*, 1350*m*, 1305*m*, 1250*m*, 1175*m*, 1125*m*, 1085*s*, 1045*s*, 1025*s*, 965*w*, 910*w*, 830*m*, 690*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.4–7.2 (*m*, 15 arom. H); 6.76 (*d*, *J*(NH,2) = 7.7, NH); 5.72 (*t*, *J* = 9.9, H–C(3)); 5.46 (*s*, PhC*H*); 4.67 (*dd*, *J*(1,P) = 9.9, *J* = 7.3, H–C(1)); 4.65–4.48 (*m*, H–C(2)); 4.57, 4.52 (*AB*, *J* = 11.7, PhCH_2); 4.48, 4.37 (*AB*, *J* = 11.6, PhCH_2); 4.32 (*dd*, *J* = 4.9, 10.4, H_{eq}–C(6)); 4.05–3.95 (*m*, H–C(5)); 3.85–3.77 (*m*, 2 H); 3.75 (*d*, *J*(H,P) = 10.7, $POCH_3$); 3.69 (*t*, *J* = 10.2, H_{ax}–C(6)); 3.68 (*t*, *J* = 9.4, H–C(4)); 3.62 (*d*, *J*(H,P) = 10.9, $POCH_3$); 2.65 (*dd*, *J* = 15.1, 6.3, 1 H); 2.43 (*dd*, *J* = 15.1, 5.9, 1 H); 2.37 (*d*, *J* = 5.6, 2 H); 1.57–1.39 (*m*, 4 H); 1.30–1.19 (*m*, 36 H); 0.88 (*dd*, *J* = 6.1, 6.9, 2 CH_3). ^{13}C-NMR (50 MHz, $CDCl_3$): 171.88 (*s*); 171.74 (*s*); 138.49 (*s*); 138.38 (*s*); 136.72 (*s*); 129.0–126.1 (*m*); 101.54 (*d*); 79.14 (*d*); 75.66 (*d*); 75.38 (*d*); 71.49 (*dd*, *J*(C,P) = 151.1, C(1)); 71.13 (*t*); 69.74 (*d*); 68.63 (*t*); 68.43 (*d*); 53.44 (*dd*, *J*(C,P) = 7.0, $POCH_3$); 52.55 (*dd*, *J*(C,P) = 7.4, $POCH_3$); 50.67 (*dd*, *J*(C,P) = 1.7); 41.07 (*t*); 39.61 (*t*); 34.49 (*t*); 33.76 (*t*); 31.88 (*t*); 29.61 (*t*); 29.32 (*t*); 25.32 (*t*); 25.12 (*t*); 22.65 (*t*); 14.09 (*q*). ^{31}P-NMR (80 MHz, $CDCl_3$): +24.34. Anal. calc. for $C_{57}H_{86}NO_{11}P$ (992.29): C 69.00, H 8.74, N 1.41, P 3.12; found: C 68.70, H 9.00, N 1.48, P 2.99.

Hydrogenolysis of **43**. A) Hydrogenolysis of 110 mg (0.11 mmol) of **43** in 11 ml of MeOH in the presence of 100 mg of 10% Pd(OH)$_2$/C under H_2 (4 bar) at r.t. for 3 h gave, after FC ($CHCl_3$/MeOH 20:1, then 10:1), 54 mg (94%) of *dimethyl {2-deoxy-3-*O*-[(*R*)-3-hydroxytetradecanoyl]-2-[(*R*)-3-hydroxytetradecanoylamino]-α-*D*-glucopyranosyl}phosphonate* (**45**) which was crystallized from hot CH_2Cl_2. R_f (AcOEt/MeOH 9:1) 0.28. M.p. 130–131°. $[\alpha]_D^{25}$ = +28.5° (*c* = 0.54, $CHCl_3$). IR: 3590*w*, 3350*m*, 2995*w*, 2950*m*, 2920*s*, 2850*s*, 1730*m*, 1660*m*, 1540*w*, 1520*w*, 1505*w*, 1460*w*, 1300*w*, 1255*m*, 1170*m*, 1100*m*, 1050*s*, 835*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.19 (*d*, *J*(NH,2) = 7.5, NH); 5.61 (*dd*, *J* = 10.5, 9.3, H–C(3)); 4.75 (*dd*, *J*(1,P) = 10.7, *J* = 7.4, H–C(1)); 4.72–4.65 (*m*, 1 H); 4.46 (*ddt*, *J*(2,P) = 34.1, *J* = 7.4, 10.8, H–C(2)); 4.24–4.15 (br. *s*, H); 4.0–3.5 (*m*, 8 H); 3.87 (*d*, *J*(H,P) = 10.7, $POCH_3$); 3.73 (*d*, *J*(H,P) = 10.9, $POCH_3$); 2.57 (*dd*, *J* = 14.1, 2.6, 1 H); 2.44 (*dd*, *J* = 14.6, 2.4, 1 H); 2.40 (*dd*, *J* = 14.0, 10.0, 1 H); 2.23 (*dd*, *J* = 14.6, 8.7, 1 H); 1.5–1.4 (*m*, 4 H); 1.26 (br. *s*, 36 H); 0.88 (*t*, *J* = 6.8, 2 CH_3). ^{13}C-NMR (50 MHz, $CDCl_3$): 173.12 (*s*); 173.00 (*s*); 77.44 (*d*); 73.67 (*d*); 70.11 (*dd*, *J*(C,P) = 152.4, C(1)); 69.69 (*d*); 68.80 (*d*); 68.31 (*d*); 62.41 (*t*); 54.05 (*qd*, *J*(C,P) = 7.0, $POCH_3$); 52.80 (*qd*, *J*(C,P) = 7.2, $POCH_3$); 49.91 (*d*); 43.45 (*t*); 43.18 (*t*); 37.47 (*t*); 36.76 (*t*); 31.91 (*t*); 29.67 (*t*); 29.36 (*t*); 25.76 (*t*); 25.63 (*t*); 22.67 (*t*); 14.09 (*q*). ^{31}P-NMR (80 MHz, $CDCl_3$): +24.35. Anal. calc. for $C_{36}H_{70}NO_{11}P$ (723.93): C 59.73, H 9.75, N 1.93, P 4.28; found: C 59.44, H 9.82, N 1.68, P 4.02.

B) Hydrogenolysis of 193 mg (0.23 mmol) of **43** in 7 ml of MeOH in the presence of 120 mg of 10% Pd/C under H_2 (4 bar) at r.t. for 2½ h gave, after FC ($CHCl_3$/MeOH 10:1), 63.7 mg (40%) of *dimethyl {4,6-*O*-benzylidene-2-deoxy-3-*O*-[(*R*)-3-hydroxytetradecanoyl]-2-[(*R*)-3-hydroxytetradecanoylamino]-α-*D*-glucopyranosyl}phosphonate* (**44**). ^{1}H-NMR (200 MHz, $CDCl_3$): 7.48–7.27 (*m*, 5 arom. H); 6.71 (*d*, *J*(NH,2) = 7.4, NH); 5.63 (*t*, *J* ≈ 10, H–C(3)); 5.53 (*s*, PhC*H*); 4.84 (*dd*, *J*(1,P) = 10.4, *J* = 7.6, H–C(1)); 4.65–4.48 (*ddt*, *J*(2,P) = 34, *J* = 10, 7.5, H–C(2)); 4.36–4.28 (*m*, 2 H); 3.98–3.66 (*m*, 4 H); 3.91 (*d*, *J*(H,P) = 10.8, $POCH_3$); 3.82 (*d*, *J*(H,P) = 10.9, $POCH_3$); 2.56 (*dd*, *J* = 15.7, 3.7, 1 H); 2.47 (*dd*, *J* = 15.7, 7.3, 1 H); 2.35 (*dd*, *J* = 14.1, 2.0, 1 H); 2.17 (*dd*, *J* = 14.1, 9.5, 1 H); 1.55–1.34 (*m*, 4 H); 1.25 (br. *s*, 36 H); 0.88 (*t*, *J* = 6.8, 2 CH_3).

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[17]) Detection by spraying the plate with a ninhydrine soln. (400 mg of ninhydrine in 100 ml of a soln. of 290 ml of 2-butanol, 100 ml of H_2O, and 10 ml of AcOH) followed by short heating to *ca.* 200°.

{2-Deoxy-3-O-[(R)-3-hydroxytetradecanoyl]-2-[(R)-3-hydroxytetradecanoylamino]-α-D-glucopyranosyl} phosphonic Acid (**3a**) *and its Bis{[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]ammonium} Salt* **3b.** Under N_2, 70 µl (0.54 mmol) of bromotrimethylsilane were added dropwise within 10 min to a soln. of 100 mg (0.14 mmol) of **45** in 10 ml of dry CH_2Cl_2 at 0°. After 5 h, the mixture was diluted with MeOH and evaporated. Addition of H_2O led to precipitation of the acid. After lyophilization of this suspension, 90 mg of **3a** were obtained. Crystallization of the crude **3a** from EtOH with 2 equiv. of *Tris* gave pure **3b.** R_f($CHCl_3$/MeOH/H_2O/NH_3[18]) 20:15:2:1) 0.35. pK_a'(1) 3.1 (MeOH), 2.9 ($CH_3OCH_2CH_2OH$); pK_a'(2) 8.3 (MeOH), 8.4 ($CH_3OCH_2CH_2OH$)[19]). IR (KBr) of **3b**: 3700–3100*s*, 2920*s*, 2850*s*, 1730*m*, 1630*s*, 1550*s*, 1470*m*, 1460*m*, 1400*m*, 1380*m*, 1295*m*, 1260*m*, 1200*m*, 1170*m*, 1130*m*, 1100*s*, 1050*s*, 1030*s*, 930*m*, 870*w*, 750*w*, 720*w*, 630*m*. ^{1}H-NMR (400 MHz, CD_3OD) of **3b**: 5.67 (*dd*, *J* = 10.3, 8.8, H–C(3)); 4.29 (*ddd*, *J*(2,P) = 26.7, *J* = 6.8, 10.4, H–C(2)); 4.20–4.14 (*m*, H–C(5)); 4.13 (*dd*, *J*(1,P) = 11.3, *J* = 6.8, H–C(1)); 4.00–3.97 (*m*, 1 H); 3.94–3.91 (*m*, 1 H); 3.87 (*dd*, *J* = 11.8, 2.0, H_A–C(6)); 3.47 (*t*, *J* = 9.2, H–C(4)); 2.52 (*dd*, *J* = 15.2, 5.0, 1 H); 2.45 (*dd*, *J* = 15.2, 7.9, 1 H); 2.33 (*dd*, *J* = 14.2, 4.0, 1 H); 2.26 (*dd*, *J* = 14.3, 8.7, 1 H); 1.5–1.4 (*m*, 36 H); 1.31 (br. *s*, 4 H); 0.91 (*t*, *J* = 6.8, 2 CH_3). ^{13}C-NMR (50 MHz, CD_3OD) of **3a**: 174.50 (*s*); 173.90 (*s*); 78.40 (*d*); 74.70 (*d*); 72.65 (*dd*, *J*(C,P) = 155, C(1)); 69.69 (*d*); 69.58 (*d*); 69.34 (*d*); 62.76 (*t*); 51.71 (*d*); 45.06 (*t*); 43.49 (*t*); 38.19 (*t*); 33.04 (*t*); 30.75 (*t*); 30.45 (*t*); 26.68 (*t*); 23.70 (*t*); 14.44 (*q*). ^{31}P-NMR (80 MHz, CD_3OD) of **3a**: +19.41. FAB-MS (thioglycerol matrix) of **3b**[20]): 718 (70, free acid +Na), 696 (20, free acid, 470 (2).

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[18]) 25% aq. soln. of NH_3.

[19]) For the pK_a' determination, the acid **3a** was obtained by passing a MeOH soln. of crystalline **3b** through *Dowex 50W X 4 (Fluka)*. Titration (in MeOH and in 2-methoxyethanol) with 0.1N NaOH gave poor results, the pK_a' values were obtained by back titration with 0.1N HCl. Partial precipitation in basic medium was observed.

[20]) We thank Prof. Dr. *J. Seibl* and his coworkers, ETH Zürich, for this spectrum.

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