Preparation of an Advanced Intermediate for the Synthesis of Stable Analogues of Guanofosfocin

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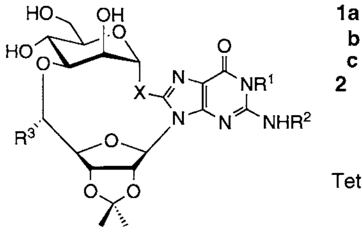
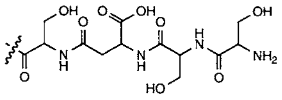
The synthesis of *C*-mannosyl-guanosine **23**, an advanced intermediate for the preparation of stable analogues of guanofosfocin, is described. This convergent approach features an improved *Traube*-type synthesis of a 8-substituted guanine, followed by ribosylation. NMR Studies show that the *C*-mannopyranosyl moiety of **23** adopts a distorted $^1C_4$ conformation while the nucleoside is predominantly *syn*-oriented.

Introduction. – The guanofosfocins (**1**) are chitin synthase inhibitors and represent a promising new lead in the search for antifungal antibiotics. Chitin synthases are responsible for the assembly of chitin, the main skeletal component of the fungal cell wall, from uridine 5′-diphosphatidyl *N*-acetylglucosamine (UDP-GlcNAc), and the guanofosfocins strongly inhibit all isoforms of chitin synthase (Chs), which were tested [1] including Chs1–3 from *S. cerevisiae*[1]. The guanofosfocins were isolated in 1996 by *Nippon Roche* [1][4], guanofosfocins A and B originating from *Streptomyces* sp. AB2570 and guanofosfocin C from *Trichoderma* sp. FD3572. The structure of these cyclic nucleotide analogues was determined by a combination of NMR spectroscopy and degradation studies, purification and structural elucidation of **1a**–**1c** being considerably hampered by their sensitivity to hydrolysis and to O_2. Indeed, the guanofosfocins suffer a number of major drawbacks, which limit their usefulness as therapeutic agents. They are highly susceptible to hydrolysis[2], attributable to the



1a X = O, R^1 = Me, R^2 = H, R^3 = *O*-pyrophosphate
b X = O, R^1 = R^2 = H, R^3 = *O*-pyrophosphate
c X = O, R^1 = H, R^2 = tetrapeptide, R^3 = *O*-pyrophosphate
2 X = CH_2, R^1 = R^2 = H, R^3 = O

Tetrapeptide =



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[1] This broad spectrum of activity is particularly appealing. At least three isoforms of Chs have been found in the more common species of fungi such as *Saccharomyces cerevisiae* and *Candida albicans*. Each of the isoforms assumes a specific role in the production of chitin and its incorporation in the fungal cell wall [2]. However, gene-disruption studies have shown that some species are still viable when only one isozyme is deleted, and that a lethal effect could only be achieved when more than one of the enzyme sub-types are repressed [3].

[2] According to [1], guanofosfocins undergo complete decomposition in aqueous solution at ambient temperature within one day.

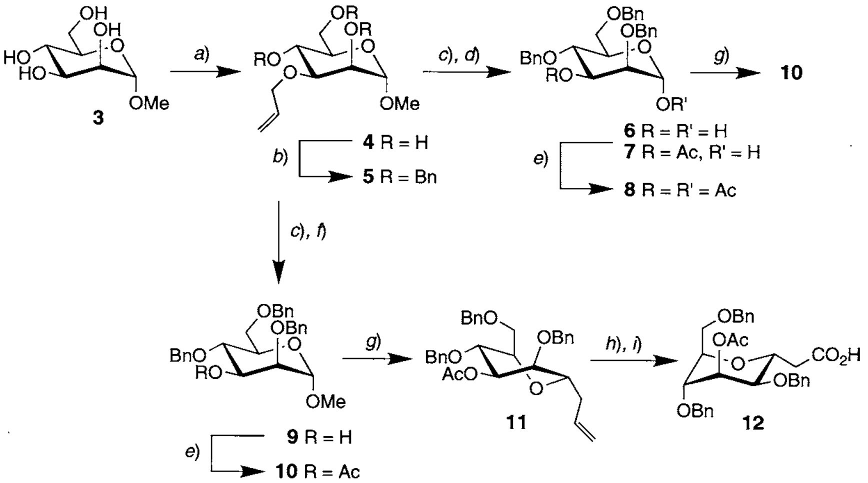
strained eleven-membered ring in conjunction with the labile acetal groups, and they do not show any inhibitory activity against whole cells, presumably because the pyrophosphate group hinders their transport across the fungal cell wall. Nevertheless, the guanofosfocins remain highly interesting as lead compounds to design modified derivatives or analogues.

To date, no synthesis of guanofosfocin itself or its analogues has been published. Among the small number of known synthetic studies on the construction of the molecular skeleton [5][6], none have addressed the problem of overcoming the instability of the guanofosfocins. Their susceptibility to hydrolysis is no surprise, considering the structural elements represented by the pyrophosphorylated hemiacetal and the *O*-(alkoxy)alkylated isourea (*O*-mannosylated 8-hydroxyguanidine). The concept of replacing *O*- by *C*-glycosides to confer superior stability with minimal steric impact has been well explored in synthesis [7], and we identified the carba-analogue **2** as an intermediate target.

Our initial approaches to the synthesis of guanofosfocin analogues relied on using commercially available guanosine as a starting material. However, incorporation of the CH_2 group linking the mannose and guanine moieties with the correct configuration proceeded in unsatisfactory yield. As a consequence, we turned our attention to a synthetic route where the purine ring is elaborated after a stereoselective *C*-glycosylation of mannose. Stereoselective *N*(9)-ribosylation of the 8-substituted guanine would complete the synthesis of the nucleoside portion of the target molecule and allow a variety of ring-closing tactics to be deployed for the completion of the carba-guanofosfocin skeleton. We planned first to study a macrolactonisation approach to this skeleton, and report on the synthesis of the hydroxy acid **23** (*cf.* *Scheme 4*).

Results and Discussion. – The stereocontrolled synthesis of α-D-*C*-glycosides is well documented [7], and *Kishi*'s *Lewis* acid-mediated *C*-allylation provides an efficient and reliable access to a range of α-*C*-glycosides [8]. Following the route outlined in *Scheme 1*, we thus prepared the α-*C*-mannoside **12** in 22% overall yield from methyl α-D-mannoside (**3**). To allow for the formation of a linkage to C(5′) of the guanosine moiety in the latter stages of the synthesis, it was necessary to protect mannose so as to selectively liberate the C(3)–OH group. For this, **3** was regioselectively *O*-allylated to give **4** in a yield of 48% *via* the 2,3-di-*O*-stannylene acetal. Standard benzylation of the remaining OH groups afforded **5**. The subsequent steps required that the 3-*O*-allyl group be removed before the *C*-allylation was carried out. Initially, this was achieved by isomerisation of the allyloxy to a prop-2-enyloxy group, followed by acid-catalysed hydrolysis and acetylation, to give **8** in yields of 30–60%. Consistently satisfactory yields could not, however, be obtained by this method due to the formation of side products. While the diacetate **8** was efficiently transformed into the desired *C*-glycoside **10** in 66% yield, we decided to optimise the route by selectively removing the 3-*O*-allyl group of **5** and then carrying out the *C*-glycosylation on the methyl glycoside **10**. Despite a longer reaction time, we isolated **11** in a yield of 59% upon treating **9** with allyl(trimethyl)silane and TMSOTf, this sequence turning out to be more reliable. Analysis of the ^{1}H-NMR spectrum of **11** revealed that a conformational change of the pyranose ring from $^4C_1$ to an equilibrium between $^4C_1$ and $^1C_4$ conformers occurred upon replacing the anomeric MeO and AcO substituents with an allyl group. The value of *ca.* 2 Hz for *J*(1,2) in **10**, typical for a vicinal equatorial/axial arrangement, rises to 4.2 Hz in **11**, and the *J*(3,4) value drops from more than 9 Hz in **9** and **10** to 7.6 Hz in **11**. The synthesis of **12** was completed by ozonolysis of **11**, followed by reductive workup to furnish the aldehyde, which was immediately oxidised with $NaClO_2$ to give the carboxylic acid **12** in 80% yield. The value of $J(1,2) = 8.3$ Hz in **12** shows that the preferred conformation is still close to $^1C_4$, an indication of the increased steric demand of the carboxymethyl group, as compared to the allyl group.

Scheme 1



a) Bu_2SnO, MeOH, reflux, then AllBr, Bu_4NI, PhMe, 70°; 48%. *b*) NaH, BnBr, Bu_4NI, THF; 90%. *c*) *t*-BuOK, dioxane, 100°. *d*) 1M H_2SO_4, AcOH, 100°; 40% of **9**, 53% of **6** and **7**. *e*) Ac_2O, pyridine, 4-(dimethylamino)pyridine (DMAP), CH_2Cl_2; 44% of **8** from **6** and **7**, 95% of **10** from **9**. *f*) 0.2M HCl, acetone, 70–75°. *g*) AllTMS, TMSOTf, MeCN, 0° → 23°; 66% from **8**, 59% from **10**. *h*) O_3, CH_2Cl_2, −78° → 23°, then Me_2S. *i*) $NaClO_2$, 2-methylbut-2-ene, NaH_2PO_4, *t*-BuOH; 93% from **11**.

To build up the purine ring around the carboxy group of **12**, we decided to apply a *Traube* synthesis according to the methodology described by *Pfleiderer* and co-workers [9]. The known pyrimidine **13** [10] was prepared in two steps from commercially available 6-chloropyrimidine-2,4-diamine and regioselectively acylated with an activated derivative of **12** (*Scheme 2*). The gradual disappearance and then reappearance of the blue colour of **13** during acylation at low temperature is indicative of an initial *O*-acylation to **14**, followed by an acyl transfer in agreement with earlier observations by *Pfleiderer* and co-workers[3]). Two procedures for the N^4-acylation of **13** were investigated. The first involved treatment with a mixed anhydride, prepared *in situ* from **12** by treatment with isobutyl chloroformate, and *N*-methylmorpholine. This procedure did not prove satisfactory due to moderate and variable yields. However, the reaction of **13** in the presence of pyridine with the acid chloride derived from **12** gave consistently higher yields of the amide **15** than the mixed anhydride and became the method of choice.

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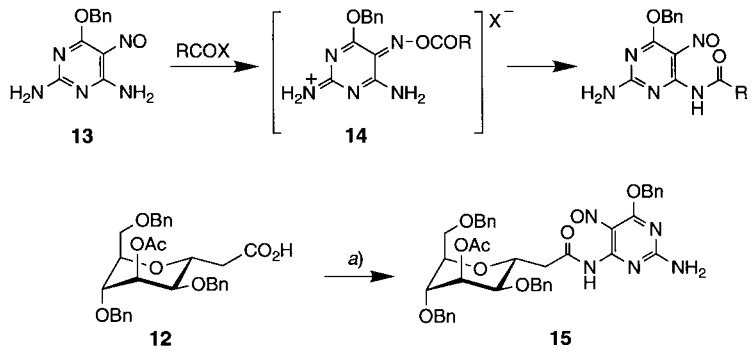
[3]) See [11] for a similar *O*-sulfonylation of an amino(nitroso)pyrimidine followed by a rearrangement.

Scheme 2



a) $(COCl)_2$, cat. DMF, PhH, then **13**, THF, pyridine, – 60° → 23°; 81%.

According to *Pfleiderer*'s procedure, the amino(nitroso)pyrimidine **15** is reduced to the corresponding diamine and then subjected to a condensation so as to close the fused imidazole ring. This condensation was effected by heating or treatment with $SOCl_2$, but it proceeded in yields of only 65 and 48%, respectively. In an effort to improve the efficiency of this step, we reasoned that treatment with a P^{III} reagent should accomplish the direct transformation of the amide **15** into the desired guanine **18**. Upon testing this hypothesis, we found that **15** was indeed converted in high yield into **18** by heating with 2 mol-equiv. of Ph_3P in xylene under reflux (*Scheme 3*). The 8-substituted purine was isolated by column chromatography of the crude, although traces of the phosphine oxide remained. We found that this problem is circumvented by using 1 mol-equiv. of 1,2-bis(triphenylphosphino)ethane due to the precipitation of its bis-oxide from the reaction medium. We have explored the scope of this transformation by using a variety of carboxylic acids, and found this method to be a general and convenient one for the preparation of 8-substituted guanines [12].

Although detailed mechanistic studies have not been carried out, a plausible pathway, which is consistent with our observations, is shown in *Scheme 3*. Nucleophilic addition of a triaryl or trialkylphosphine (*cf.* [12]) to the nitroso group of **15** is expected to lead to the zwitterion **16**, which is converted to the iminophosphorane **17** by a second equiv. of phosphine, either by substitution or by elimination – addition[4]). This should be followed by an aza-*Wittig* process leading to the guanine **18**. This transfomation is analogous to the synthesis of indoles from [*o*-(acylamino)benzyl]triphenylphosphonium salts reported by *Le Corré et al.* [13].

Efficient *N*-glycosylation of the guanine **18** required the protection of the N^2-amino group. Treating **18** with isobutyric anhydride in toluene at reflux led to **19** besides some N^2,N^9-diamide; the diamide was readily converted to the monoamide **19** by warming in MeOH. Ribosylation with 1-*O*-acetyl-2,3,4-tri-*O*-benzoyl-*β*-D-ribofuranose (**20**) provided stereo- and regioselectively the nucleoside **21** in a yield of 76%. The 1,2-*trans* configuration of the ribosyl moiety of **21**, expected as a result of the participation of the

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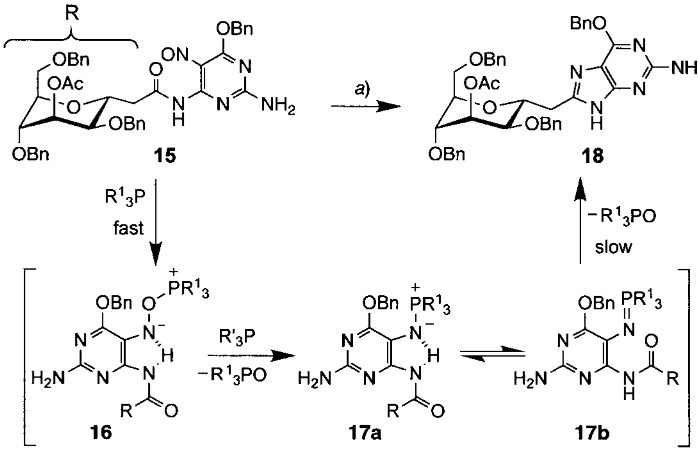
[4]) Although we cannot exclude the involvement of a nitrene, we found no evidence for the formation of this reactive intermediate.

Scheme 3



a) 1,2-Bis(diphenylphosphino)ethane (DPPE), *o*-xylene, 80° → reflux; 90%.

C(2′)−OBz group, is evidenced by $J(1',2') = 1.4$ Hz. The determination of the regioselectivity is less straightforward, considering the absence of the diagnostic data for H−C(8). A comparison of nucleoside derivatives has led to empirical criteria for distinguishing between N^7- and N^9-glycosylated regioisomers. A study of the NMR spectra of 54 8-unsubstituted guanosines has revealed that the value of δ(C(5)) is probably the diagnostically most-useful criterium for this purpose [14]. Although the NMR data of **21** fall within the same range as other N^9-glycosylated guanosines[5], it is not clear how this parameter is affected by *C*(8)-substitution. However, there is not a significant change in the chemical shift of the CH_2 H-atoms of the O^6-Bn group of **19** upon ribosylation to **21** ($\Delta\delta$(H) = 0.12 ppm), nor do the benzylic H-atoms show any NOE upon irradiation of H−C(1′), H−C(2′), or H−C(3′), in keeping with ribosylation at N(9).

Deacylation of **21** with MeONa/MeOH led to the tetrol **22** (73%). Isopropylidenation with 2,2-dimethoxypropane in the presence of TsOH, followed by selective oxidation of the primary OH group [15], furnished the desired acid **23** (*Scheme 4*).

The conformation of **21** depicted in *Scheme 4* is evidenced by the vicinal coupling constants for the CH_2 group at C(1″) (9.3 and 5.3 Hz); it must be assumed that the nucleobase avoids a 1,5 interaction with the O−C(2″) substituent. In agreement with this, H_A, characterised by the smaller coupling constant, resonates at lower field. Rather strong NOEs are observed between H−C(1′) and H_B of **21** and **23** (werk ones with H_A) of the said CH_2 group, evidencing a predominant *syn* conformation. The *S*/*N* equilibrium, as deduced from the $J(1',2')/J(3',4')$ ratio[6]) strongly favours the *N*(3′-*endo*) conformation, in keeping with a low field signal for H−C(3′) (7.05 ppm).

^{1}H-NMR Spectroscopy indicates that the preferred conformation of the pyranose ring of **21**, **22**, and **23** is still $^1C_4$ (*e.g.*, in **23** $J(1'',2'') = 7.6$ Hz) in contrast to an analogous

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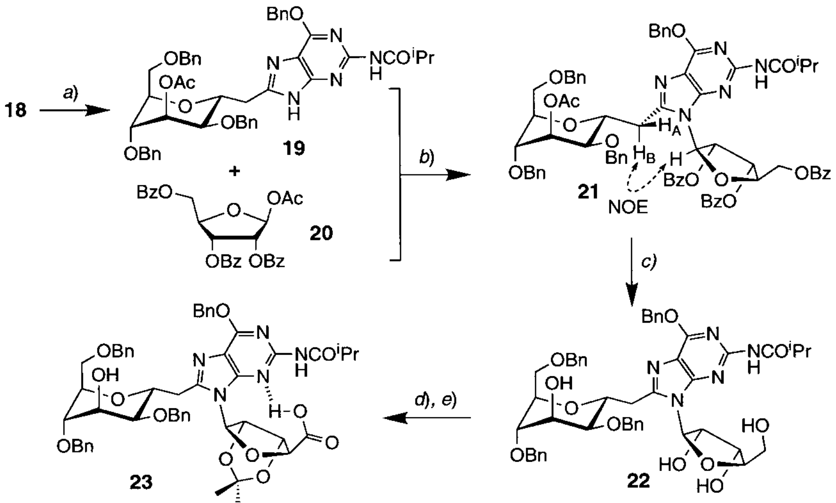
[5] The ranges found are δ(C(5))(N^9): 113.75–123.70 ppm; δ(C(5))(N^7): 104.56–115.09 ppm. Values of δ(C(5)) for **21**, **22**, and **23** are 117.27, 117.91, and 116.70 ppm, respectively.

[6] According to [16], $K_{S/N} \approx J(1',2')/J(3',4')$; for **21**, this ratio corresponds to a value of 0.26.

Scheme 4



a) (i-PrCO$)_2$O, PhMe, reflux; then MeOH, 50°; 80%. *b*) *N*,*O*-Bis(trimethylsilyl)acetamide (BSA), MeCN, 80° → 23°, then **20**, 23° → 65°; 76%. *c*) K_2CO_3, CH_2Cl_2, MeOH, 0° → 23°; 73%. *d*) Cat. TsOH · H_2O, 2,2-dimethoxypropane, acetone, then 10% aq. HCl. *e*) 2,2,6,6-Tetramethylpiperidinooxy (TEMPO), NaOCl, KBr, Bu_4NCl, $NaHCO_3$, CH_2Cl_2/H_2O, 0°; 61%.

mannose–guanosine hybrid prepared by *Sugimura* and *Natsui* [5], in which the $^4C_1$ conformer is preferred ($J(1'',2'') = 2$ Hz), indicating that stereoelectronic effects are more significant than steric demands in these cases. The conformation around C(1'')–CH_2–C(8) of **23** does not significantly differ from that of **21**.

We thank Dr. *B. Bernet* for checking the *Exper. Part*, and *Nippon Roche Research Center*, Kamakura, for generous support.

Experimental Part

General. Solvents were distilled before use: THF and toluene from Na and benzophenone, CH_2Cl_2 and MeCN from CaH_2. Reactions were carried out under an Ar or N_2 atmosphere, 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 $(NH_4)_6Mo_7O_{24}$ · 6 H_2O, 0.4 g of $Ce(SO_4)_2$). Flash chromatography (FC): silica gel *Fluka 60* (0.04–0.063 mm). M.p.: uncorrected. Optical rotations: 1-dm cell at 25°, 589 nm. FT-IR spectra: *ca.* 2% soln. in $CHCl_3$, dispersion in KBr, or as a thin film; absorption in cm^{-1}. ^{1}H- and ^{13}C-NMR spectra: chemical shifts δ in ppm rel. to TMS as external standard, and coupling constants *J* in Hz. MALDI-MS and HR-MALDI-MS: in gentisic acid (=2,5-dihydroxybenzoic acid, DHB) matrix.

*Methyl 3-*O*-Allyl-α-*D*-mannopyranoside* (**4**). A suspension of methyl α-D-mannopyranoside (5.00 g, 25.75 mmol) in dry MeOH (120 ml) at 23° was treated with Bu_2SnO (6.41 g, 25.75 mmol) and heated at reflux until a clear soln. was obtained (*ca.* 2 h), and then for a further 4 h. After allowing the soln. to cool to 23°, the solvent was evaporated, and the residue was dried *in vacuo* (0.1 Torr, 3 h). The resulting off-white powder was suspended in toluene (1200 ml), treated with Bu_4NI (9.51 g, 25.75 mmol) and allyl bromide (21.8 ml, 257.5 mmol) at 23°, and stirred at 67–70° for 48 h. Cooling to 23° and removal of the volatiles gave a brown syrup, which was partitioned between H_2O (100 ml) and AcOEt (200 ml). The aq. phase was extracted with AcOEt until the extracts were colourless (4 × 60 ml), and TLC of the aqueous phase showed it to be free of organotin derivatives. The combined org. phases were washed with H_2O (4 × 15 ml), and the combined aq.

phases were again washed with AcOEt (4 × 15 ml). The aq. phase was then evaporated under reduced pressure (15 mbar, bath temp. 35°) to give the crude product as a clear yellow oil. Purification by FC (silica gel; AcOEt/acetone, 9:1) gave **4** (2.88 g, 48%). Colourless oil. R_f (AcOEt/acetone 5:1) 0.27. $[\alpha]_D^{25} = +56.6$ ($c = 0.99$, MeOH). IR ($CHCl_3$): 3429*m* (br.), 3013*m*, 2933*m*, 1453*w*, 1421*w*, 1351*w*, 1253*w*, 1133*s*, 1104*s*, 1064*s*, 984*s*, 909*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 5.96 (*ddt*, *J* = 17.1, 10.3, 5.9, CH_2=C*H*); 5.32 (*dq*, *J* = 17.1, 1.5, (*Z*) CH*H*=CH); 5.23 (*dq*, *J* = 10.3, 1.3, (*E*) CH*H*=CH); 4.76 (*d*, *J* = 1.3, H–C(1)); 4.19 (*ddt*, *J* = 12.3, 5.9, 1.2), 4.08 (*ddt*, *J* = 12.6, 6.1, 1.3, CH_2=CH–CH_2O); 3.99 (*dd*, *J* = 3.5, 1.5, H–C(2)); 3.98 (*t*, *J* = 9.6, H–C(4)); 3.90 (*dd*, *J* = 12.1, 3.4, H_A–C(6)); 3.82 (*dd*, *J* = 12.1, 2.8, H_B–C(6)); 3.60 (*dd*, *J* = 9.6, 3.4, H–C(3)); 3.56 (*dt*, *J* = 9.6, 3.1, H–C(5)); 3.40 (br. *s*, exchanges with D_2O, 3 OH); 3.36 (*s*, MeO). ^{13}C-NMR ($CDCl_3$, 75 MHz): 134.24 (*d*, CH_2=*C*H); 118.09 (*t*, *C*H_2=CH); 100.69 (*d*, C(1)); 79.16 (*d*, C(3)); 72.13 (*d*, C(5)); 70.75 (*t*, CH_2=CH–*C*H_2O); 67.85 (*d*, C(2)); 64.93 (*d*, C(4)); 61.33 (*t*, C(6)); 54.95 (*q*, MeO). HR-MALDI-MS: 257.0996 (15, $[M + Na]^+$, $C_{10}H_{18}NaO_6^+$; calc. 257.1101). Anal. calc. for $C_{10}H_{18}O_6$ (234.20): C 51.27, H 7.74; found: C 51.24, H 7.54.

*Methyl 3-*O*-Allyl-2,4,6-tri-*O*-benzyl-α-*D*-mannopyranoside* (**5**). NaH (60% in paraffin; 3.54 g, 81.05 mmol) was added portionwise during 5 min to a stirred soln. of **4** (4.22 g, 18.01 mmol) in THF (4.22 ml) at 0°. The mixture was allowed to warm to 23°, stirred for 1.5 h, and re-cooled to 0°. To the resulting grey slurry was added Bu_4NI (0.33 g, 0.90 mmol), followed by BnBr (12.85 ml, 108.03 mmol), dropwise, over 20 min. The mixture was slowly allowed to reach 23°, stirred for 48 h, cooled to 0°, and treated cautiously with EtOH (*ca.* 15 ml). The mixture was poured into H_2O (100 ml) and extracted with AcOEt (3 × 50 ml). The combined extracts were washed with brine (50 ml), dried, and evaporated to give an orange oil. Unreacted BnBr was removed by treating a soln. of the oil in Et_2O (100 ml) with Et_3N (*ca.* 15 ml, 108 mmol) and allowing to stand for 24 h, and removing the precipitate by filtration through a silica pad. Evaporation and FC (silica gel; cyclohexane/AcOEt, 20:1 → 15:1 → 5:1) afforded **5** (8.15 g, 90%). Pale yellow oil. R_f (cyclohexane/AcOEt 7:1) 0.21. $[\alpha]_D^{25} = +34.5$ ($c = 1.09$, $CHCl_3$); [17]: +33.3 ($c = 0.4$, $CHCl_3$). IR ($CHCl_3$): 3067*w*, 3032*w*, 3011*m*, 2916*m*, 2866*m*, 1646*w*, 1603*w*, 1496*w*, 1454*m*, 1362*m*, 1327*w*, 1263*w*, 1106*s*, 1063*s*, 909*s*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.41–7.19 (*m*, 15 arom. H); 5.93 (*ddt*, *J* = 17.1, 10.6, 5.3, CH_2=C*H*); 5.31 (*dq*, *J* = 17.1, 1.9, (*Z*) CH*H*=CH); 5.17 (*dq*, *J* = 10.3, 1.3, (*E*) CH*H*=CH); 4.87 (*d*, *J* = 10.6, PhC*H*); 4.79 (*d*, *J* = 12.4, PhC*H*); 4.77 (*s*, H–C(1)); 4.73 (*d*, *J* = 12.4, PhC*H*); 4.67 (*d*, *J* = 12.1, PhC*H*); 4.55 (*d*, *J* = 12.1, PhC*H*); 4.50 (*d*, *J* = 10.7, PhC*H*); 4.08 (br. *d*, *J* = 5.0, CH_2=CHCH_2O); 3.92 (br. *t*, *J* = 9.0, H–C(4)); 3.80–3.69 (*m*, H–C(2), H–C(3), H–C(5), 2 H–C(6)), 3.32 (*s*, MeO). ^{13}C-NMR ($CDCl_3$, 75 MHz): 138.18, 138.21, 138.13 (3*s*); 134.78 (*d*, CH_2=*C*H); 128.13, 127.79, 127.62, 127.58, 127.39, 127.28 (several *d*); 116.51 (*t*, *C*H_2=CH); 98.88 (*d*, C(1)); 79.79 (*d*, C(3)); 75.02 (*t*, Ph*C*H_2); 74.78, 74.41 (2*d*, C(2), C(4)); 73.29, 72.50 (2*t*, Ph*C*H_2); 71.58 (*d*, C(5)); 70.96 (*t*, CH_2=CH*C*H_2); 69.25 (*t*, C(6)); 54.69 (*q*, MeO). HR-MALDI-MS: 527.2398 (100, $[M + Na]^+$, $C_{31}H_{36}NaO_6^+$; calc. 527.2410).

*1,3-Di-*O*-acetyl-2,4,6-tri-*O*-benzyl-α-*D*-mannopyranose* (**8**). *t*-BuOK (1.65 g, 14.70 mmol) was added to a soln. of **5** (3.83 g, 7.60 mmol) in 1,4-dioxane (50 ml), and the resulting mixture was heated to 100° and stirred for 20 h. After cooling to 0°, cold H_2O (50 ml) and AcOEt (150 ml) were added, and the mixture was transferred to a separating funnel and extracted. The aq. phase was further extracted with AcOEt (2 × 50 ml). The combined org. extracts were washed with brine (35 ml), dried, and evaporated to afford a yellow oil. ^{1}H-NMR Spectroscopy showed that **5** had been consumed, and that the crude product was sufficiently pure to be used directly in the next step. A soln. of the crude (3.71 g, 7.35 mmol) in glacial AcOH (56 ml) and 1M aq. H_2SO_4 (14 ml) was heated to 100° for 10 h. After cooling to 0°, the pH of the mixture was adjusted to 3–4 by the addition of 10M aq. NaOH (*ca.* 4 ml). AcOH was removed under reduced pressure, and the residue was partitioned between H_2O (50 ml) and AcOEt (100 ml). The aq. phase was extracted with AcOEt (2 × 50 ml). The combined org. layers were washed with sat. aq. $NaHCO_3$ soln. until the washings were basic. Drying, evaporation, and FC (silica gel; cyclohexane/AcOEt, 9:1 → 8:1 → 7:1 → 6:1) gave **9** (1.37 g, 40%), and an inseparable mixture of diol **6** and lactol **7** (53% combined yield). A soln. of 2,4,6-tri-*O*-benzyl-D-mannopyranose and 3-*O*-acetyl-2,4,6-tri-*O*-benzyl-D-mannopyranose (1.85 g, 3.92 mmol) in CH_2Cl_2 (20 ml) was treated with Ac_2O (0.924 ml, 9.80 mmol), pyridine (0.79 ml, 9.8 mmol), and DMAP (5 mg, 0.039 mmol), and stirred at 23° for 17 h. Evaporation, co-evaporation with toluene (2 × 10 ml), and FC (silica gel, cyclohexane/AcOEt 7:1 → 6:1) gave **8** (1.72 g, 44% over two steps). Colourless oil. R_f (cyclohexane/AcOEt 2:1) 0.40. $[\alpha]_D^{25} = +14.0$ ($c = 0.64$, $CHCl_3$). IR ($CHCl_3$): 3067*w*, 3031*m*, 3014*m*, 2927*w*, 2870*w*, 1740*s*, 1454*m*, 1371*m*, 1245*s*, 1097*s*, 1015*s*, 957*s*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 7.38–7.17 (*m*, 15 arom. H); 6.23 (*d*, *J* = 2.2, H–C(1)); 5.22 (*dd*, *J* = 9.6, 3.4, H–C(3)); 4.76 (*d*, *J* = 12.0, PhC*H*); 4.71 (*d*, *J* = 11.6, PhC*H*); 4.67 (*d*, *J* = 10.7, PhC*H*); 4.58 (*d*, *J* = 12.5, PhC*H*); 4.54 (*d*, *J* ≈ 11, PhC*H*); 4.52 (*d*, *J* ≈ 12, PhC*H*); 4.16 (*t*, *J* = 9.6, H–C(4)); 3.93 (*ddd*, *J* = 9.8, 3.9, 1.9, H–C(5)); 3.87 (*dd*, *J* = 3.4, 2.2, H–C(2)); 3.82 (*dd*, *J* = 11.0, 4.0, H_A–C(6)); 3.71 (*dd*, *J* = 11.0, 1.9, H_B–C(6)); 2.10, 1.97 (2*s*, 2 AcO). ^{13}C-NMR ($CDCl_3$, 50 MHz): 170.35, 169.22 (2*s*, 2 C=O); 138.22, 138.11, 137.59 (3*s*); 128.46, 128.43, 128.38, 127.96, 127.80, 127.75, 127.66 (several *d*); 91.41 (*d*, C(1)); 74.80, 73.54, 72.68 (3*t*, 3 Ph*C*H_2); 74.44, 74.10, 73.07, 72.73 (4*d*, C(2), C(3), C(4), C(5)); 68.49 (*t*, C(6)); 20.89, 20.81 (2*q*, 2 Me). HR-MALDI-MS: 557.2146 (100, $[M+Na]^+$, $C_{31}H_{34}NaO_8^+$; calc. 557.2151).

*Methyl 2,4,6-Tri-*O*-benzyl-α-*D*-mannopyranoside* (**9**). *t*-BuOK (3.82 g, 34.0 mmol) was added to a soln. of **4** (8.6 g, 17.02 mmol) in 1,4-dioxane (100 ml), and the resulting mixture was heated to 100° and stirred for 20 h. After cooling to 0°, cold H_2O (120 ml) and AcOEt (150 ml) were added, and the mixture was transferred to a separating funnel and extracted. The aq. phase was further extracted with AcOEt (2 × 100 ml). The combined org. extracts were washed with brine (100 ml), dried, and evaporated to afford a yellow oil. ^{1}H-NMR Spectroscopy showed that **4** had been consumed, and that the crude product was sufficiently pure to be used directly in the next step. A soln. of the crude (8.6 g, 17.0 mmol) in acetone (110 ml) was treated with 0.2M aq. HCl soln. (110 ml). The turbid mixture was heated to 70–75° and stirred vigorously for 7 h, cooled to r.t., and diluted with AcOEt (75 ml). Acetone was removed under reduced pressure (*ca.* 500 mbar, 30° bath temp.). After dilution with AcOEt (150 ml) and separation of the layers, the aq. layer was extracted with AcOEt (2 × 150 ml). The combined org. phases were washed with sat. aq. $NaHCO_3$ soln. (3 × 30 ml) and brine (50 ml), dried, and evaporated to give **9** as a yellow oil. ^{1}H-NMR Spectroscopy showed that this material was sufficiently pure to be used directly in the next step. R_f (cyclohexane/AcOEt 1:1) 0.28. $[\alpha]_D^{25} = +14.5$ ($c = 1.00$, $CHCl_3$); [17]: $+16.9$ ($c = 1.5$, $CHCl_3$). IR (neat): 3546*w* (br.), 3468*m* (br.), 3030*w*, 2908*w*, 1604*w*, 1496*w*, 1453*m*, 1365*w*, 1268*w*, 1208*s*, 1136*m*, 1095*s*, 1060*s*, 1026*m*, 966*m*, 907*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.39–7.22 (*m*, 15 arom. H); 4.86 (*d*, $J = 11.1$, PhC*H*); 4.85 (*d*, $J = 1.8$, H–C(1)); 4.76 (*d*, $J = 12.0$, PhC*H*); 4.69 (*d*, $J = 12.3$, PhC*H*); 4.57 (*d*, $J = 12.0$, PhC*H*); 4.56 (*d*, $J = 12.0$, PhC*H*); 4.53 (*d*, $J = 10.8$, PhC*H*); 3.97 (br. *t*, $J = 9.4$, H–C(4)); 3.83–3.69 (*m*, H–C(2), H–C(3), H–C(5), 2 H–C(6)), 3.36 (*s*, MeO); 2.35 (*d*, $J = 9.9$, HO–C(3)). ^{13}C-NMR ($CDCl_3$, 75 MHz): 138.41, 138.28, 137.67 (3*s*); 128.52, 128.30, 128.28, 127.96, 127.88, 127.72, 127.59, 127.49 (several *d*); 97.83 (*d*, C(1)); 78.27, 77.00 (2*d*, C(2), C(4)); 74.74, 73.37, 72.78, (3*t*, 3 Ph*C*H_2); 71.76, 70.71 (2*d*, C(3), C(5)); 69.13 (*t*, C(6)); 54.79 (*q*, MeO). HR-MALDI-MS: 487.2097 (100, $[M+Na]^+$, $C_{28}H_{32}NaO_6^+$; calc. 487.2097).

*Methyl 3-*O*-Acetyl-2,4,6-tri-*O*-benzyl-α-*D*-mannopyranoside* (**10**). A soln. of **9** (11.20 g, 24.11 mmol) in CH_2Cl_2 (143 ml) was treated with Ac_2O (4.55 ml, 48.22 mmol), DMAP (0.148 g, 1.21 mmol), and pyridine (2.92 ml, 36.17 mmol), stirred for 13 h, diluted with CH_2Cl_2 (100 m), and washed with sat. aq. NH_4Cl soln. (50 ml) and sat. aq. $NaHCO_3$ soln. (100 ml). The aq. phase was extracted with CH_2Cl_2 (3 × 100 ml). Washing of the combined org. phases with brine (50 ml), drying, evaporation, and FC (silica gel; cyclohexane/AcOEt, 9:1) afforded **10** (11.69 g, 95%). Colourless oil. R_f (cyclohexane/AcOEt 1:1) 0.28. $[\alpha]_D^{25} = +8.8$ ($c = 1.00$, $CHCl_3$). IR (neat): 3063*w*, 3030*w*, 2929*w*, 2907*w*, 2866*w*, 1738*m*, 1496*w*, 1453*w*, 1364*m*, 1234*s*, 1096*s*, 1060*s*, 1027*s*, 969*s*, 909*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.40–7.17 (*m*, 15 arom. H); 5.38 (*dd*, $J = 9.3$, 3.3, H–C(3)); 4.80 (*d*, $J = 1.8$, H–C(1)); 4.73 (*d*, $J = 12.0$, PhC*H*); 4.70 (*d*, $J = 12.3$, PhC*H*); 4.67 (*d*, $J = 11.4$, PhC*H*); 4.59 (*d*, $J = 12.3$, PhC*H*); 4.56 (*d*, $J = 12.3$, PhC*H*); 4.52 (*d*, $J = 11.4$, PhC*H*); 4.08 (*t*, $J = 9.3$, H–C(4)); 3.89 (*dd*, $J = 3.3$, 1.8, H–C(2)); 3.85–3.72 (*m*, H–C(5), 2 H–C(6)); 3.36 (*s*, MeO). ^{13}C-NMR ($CDCl_3$, 75 MHz): 170.0 (C=O); 138.03, 137.75 (3*s*); 128.16, 128.13, 127.65, 127.59, 127.41, 127.36 (several *d*); 98.61 (*d*, C(1)); 75.77, 73.79, 73.32, 71.29, (4*d*, C(2), C(3), C(4), C(5)); 74.52, 73.36, 72.47 (3*t*, 3 Ph*C*H_2); 68.84 (*t*, C(6)), 54.82 (*q*, MeO); 21.08 (*q*, Me). HR-MALDI-MS: 529.2203 (60, $[M+Na]^+$, $C_{30}H_{34}NaO_7^+$; calc. 529.2202).

*3-*O*-Acetyl-2,4,6-tri-*O*-benzyl-1-deoxy-1-(prop-2-enyl)-α-*D*-mannopyranose* (**11**). a) *From Diacetate* **8**. A soln. of **8** (0.925 g, 1.73 mmol) in MeCN (5 ml) was cooled to 0°, and treated with allyl(trimethyl)silane (0.55 ml, 3.45 mmol) and, dropwise, with TMSOTf (0.16 ml, 0.88 mmol). The resulting soln. was stirred at 0° for 3 h, after which it had become pale yellow, then it was allowed to warm to 23° and stirred for a further 5.5 h. The orange mixture was diluted with CH_2Cl_2 (20 ml) and washed with sat. aq. $NaHCO_3$ soln. (10 ml) The aq. layer was extracted with CH_2Cl_2 (3 × 5 ml). The combined org. extracts were washed with brine (10 ml), dried, and concentrated to give an orange oil. FC (silica gel; cyclohexane/AcOEt 7:1 → 6:1) afforded **11** (0.59 g, 66%). Colourless syrup.

b) *From Monoacetate* **10**. A soln. of **10** (5.13 g, 10.14 mmol) in MeCN (40 ml) was cooled to 0° and treated with allyl(trimethyl)silane (4.85 ml, 30.42 mmol) and, dropwise, with TMSOTf (1.47 ml, 8.10 mmol). The resulting pale yellow soln. was stirred at 0° for 2 h, then allowed to warm to 23° over a period of 2 h, and stirred for a further 20 h at this temp. TLC revealed the presence of some unreacted starting material. The orange mixture was diluted with CH_2Cl_2 (175 ml) and washed with sat. aq. $NaHCO_3$ soln. (90 ml). The aq. layer was extracted with CH_2Cl_2 (3 × 50 ml). The combined org. extracts were washed with brine (50 ml), dried, and evaporated to give an orange oil. FC (silica gel, loaded with CH_2Cl_2; cyclohexane/AcOEt, 12:1) afforded **11** (3.12 g, 59%). Colourless syrup. R_f (cyclohexane/AcOEt 3:1) 0.43. $[\alpha]_D^{25} = -6.6$ ($c = 1.00$, $CHCl_3$). IR ($CHCl_3$): 3064*w*, 3030*w*, 2906*w*, 2865*w*, 1738*m*, 1641*w*, 1605*w*, 1496*w*, 1454*w*, 1366*m*, 1232*s*, 1089*s*, 1074*s*, 1027*s*, 997*s*, 912*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.23–7.38 (*m*, 15 arom. H); 5.83 (*ddt*, $J = 17.1$, 10.2, 6.9, CH_2=C*H*CH_2); 5.29 (*dd*, $J = 7.2$, 3.3, H–C(3)); 5.18–5.09 (*m*, C*H*$_2$=CHCH_2); 4.66 (*d*, $J = 11.1$, PhC*H*); 4.65 (*d*, $J = 12.3$, PhC*H*);

4.59 (*d*, *J* = 12.3, PhC*H*); 4.57 (*d*, *J* = 10.5, PhC*H*); 4.55 (*d*, *J* = 12.9, PhC*H*); 4.54 (*d*, *J* = 12.0, PhC*H*); 4.03 (*ddd*, *J* = 7.6, 6.2, 4.2, H–C(1)); 3.94 (*t*, *J* = 7.2, H–C(4)); 3.84 (*td*, *J* = 6.9, 3.3, H–C(5)); 3.77 (*dd*, *J* = 10.4, 6.0, H–C(6)); 3.76 (*dd*, *J* = 4.2, 3.3, H–C(2)); 3.69 (*dd*, *J* = 10.4, 3.6, H–C(6)); 2.52–2.36 (*m*, CH_2=CHC*H*$_2$); 2.00 (*s*, AcO). ^{13}C-NMR ($CDCl_3$, 75 MHz): 170.08 (*s*, C=O); 138.02, 137.83, 137.66 (3*s*); 133.77 (*d*, CH_2=*C*HCH_2); 128.22, 128.16, 127.88, 127.63, 127.59, 127.41 (several *d*); 117.48 (*t*, *C*H$_2$=CHCH_2); 75.16, 74.01, 73.32, 72.78, 71.40 (5*d*, C(1), C(2), C(3), C(4), C(5)); 74.01, 73.32, 71.66 (3*t*, 3 Ph*C*H$_2$); 68.74 (*t*, C(6)); 34.41 (*t*, CH_2=CH*C*H$_2$); 21.09 (*q*, Me). HR-MALDI-MS: 539.2397 (100, $[M + Na]^+$, $C_{32}H_{36}NaO_6^+$; calc. 539.2410). Anal. calc. for $C_{32}H_{36}O_6$ (516.58): C 74.40, H 7.02; found: C 74.36, H 7.23.

*(3-*O*-Acetyl-2,4,6-tri-*O*-benzyl-α-*D*-mannopyranosyl)acetic Acid* (**12**). A stream of O_3 was bubbled through a cooled (– 78°) soln. of **11** (1.92 g, 3.72 mmol) in CH_2Cl_2 (65 ml) until a permanent blue colour was observed (*ca.* 20 min). The soln. was then purged of O_3 by flushing with O_2 and treated at – 78° with Me_2S (4.10 ml, 55.8 mmol) before being allowed to warm to 23°, and stirred overnight. After evaporation, a soln. of the resulting turbid yellow oil in *t*-BuOH (62 ml) at 23° was treated with 2-methylbut-2-ene (15.8 ml, 149 mmol) and then, dropwise, with a soln. of $NaClO_2$ (3.36 g, 37.15 mmol) and NaH_2PO_4 (3.48 g, 22.31 mmol) in H_2O (50 ml), causing the transient appearance of a yellow colour. After stirring for 20 h at 23°, the turbid soln. was evaporated. A soln. of the residue in AcOEt (50 ml) was washed with sat. aq. NH_4Cl soln. (30 ml). The aq. layer was extracted with AcOEt (3 × 50 ml), after which none of the product could be detected in the aq. phase by TLC. The combined org. phases were dried and evaporated. FC (silica gel; cyclohexane/AcOEt/HCO_2H 2 : 1 : 0.01) afforded **12** (1.84 g, 93%). Colourless syrup. R_f (cyclohexane/AcOEt/AcOH 1 : 1 : 0.01) 0.29. $[\alpha]_D^{25} = +2.4$ ($c = 0.88$, $CHCl_3$). IR ($CHCl_3$): 3541*w*, 3500–2500*w* (br.), 3066*w*, 3007*m*, 1737*s*, 1602*w*, 1496*w*, 1454*m*, 1370*m*, 1093*s*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.37–7.23 (*m*, 15 arom. H); 5.36 (*dd*, *J* = 5.6, 3.1, H–C(3)); 4.63 (*d*, *J* = 11.8, PhC*H*); 4.58 (*d*, *J* = 11.8, PhC*H*); 4.56 (*d*, *J* = 12.1, PhC*H*); 4.54 (*s*, PhC*H*$_2$), 4.48 (*d*, *J* = 11.5, PhC*H*); 4.33 (*ddd*, *J* = 8.8, 7.3, 4.4, H–C(1)); 3.98 (*ddd*, *J* = 6.2, 5.3, 4.3, H–C(5)); 3.80 (*dd*, *J* = 5.6, 4.3, H–C(4)); 3.77 (*dd*, *J* = 10.3, 6.2, H–C(6)); 3.71 (*dd*, *J* = 7.2, 3.1, H–C(2)); 3.66 (*dd*, *J* = 10.3, 5.3, H–C(6)); 2.76 (*dd*, *J* = 16.1, 4.4, CH_A–C(1)); 2.59 (*dd*, *J* = 16.1, 8.7, CH_B–C(1)); 1.97 (*s*, AcO). ^{13}C-NMR ($CDCl_3$, 75 MHz): 175.51 (*s*, *C*OOH); 170.19 (*s*, Me*C*O); 138.04, 137.78, 137.44 (3*s*); 128.53, 128.46, 128.25, 128.06, 127.95, 127.86, 127.78 (several *d*); 75.00, 74.23, 74.07, 68.54, 68.07 (5*d*, C(1), C(2), C(3), C(4), C(5)); 73.36, 72.90, 71.40 (3*t*, 3 Ph*C*H$_2$); 67.82 (*t*, C(6)); 30.07 (*t*, CH_2–C(1)); 20.80 (*q*, Me). HR-MALDI-MS: 557.2141 (100, $[M + Na]^+$, $C_{31}H_{34}NaO_8^+$; calc. 557.2151). Anal. calc. for $C_{31}H_{34}O_8$ (534.55): C 69.65, H 6.50; found: C 69.65, H 6.41.

6-(Benzyloxy)-5-nitrosopyrimidine-2,4-diamine (**13**). Na Metal (5.47 g, 238.7 mmol) was added in small pieces, with stirring, to BnOH (150 ml) at 60°. After the addition was complete, the yellow soln. was heated to 80° for 3.5 h, after which all Na had been consumed. The mixture was then treated portionwise during 5 min with 6-chloropyrimidine-2,4-diamine (28.45 g, 196.8 mmol) and heated to 150° for 5 h to give a turbid orange soln., and allowed to cool to r.t. BnOH was removed by distillation under reduced pressure (55–65°/0.5 Torr). A soln. of the yellow residue in CH_2Cl_2 (700 ml) was washed with H_2O (2 × 200 ml). The combined aq. layers were extracted with CH_2Cl_2 (2 × 90 ml), the combined org. phases were divided into two equal portions, and each was washed with brine (2 × 150 ml), dried, recombined, and evaporated to give a cream-coloured solid. Residual solvent was removed by drying at 0.5 Torr. Two recrystallisations in toluene afforded off-white crystals of 6-(benzyloxy)pyrimidine-2,4-diamine (23.8 g, 56%). R_f (CH_2Cl_2/MeOH/Et_3N 20 : 1 : 0.1) 0.14. M.p. 105–106° ([10]: 108–109°). IR (KBr): 3447*s*, 3390*s*, 3345*s*, 3190*m*, 3063*m*, 3035*w*, 2952*w*, 2937*w*, 2883*w*, 1957*w*, 1880*w*, 1633*s*, 1613*s*, 1583*s*, 1498*m*, 1450*s*, 1423*s*, 1356*s*, 1289*w*, 1202*s*, 1077*w*, 1020*s*, 954*w*, 908*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.41–7.30 (*m*, 5 arom. H); 5.31 (*s*, H–C(5)); 5.27 (*s*, PhC*H*$_2$); 4.77, 4.55 (2*s*, exchange with D_2O, 2 NH_2). ^{13}C-NMR ($CDCl_3$, 75 MHz): 171.03, 165.43 (2*s*, C(2), C(6)); 162.68 (*s*, C(4)); 136.91 (*s*); 128.37 (2*d*); 127.78 (3*d*); 78.49 (*d*, C(5)); 67.36 (*t*, Ph*C*H$_2$). EI-MS: 216 (40, M^+), 110 (65, $[M - BnO + H]^+$), 69 (100, $[M - HN{=}CHNH_2]^+$). Anal. calc. for $C_{11}H_{12}N_4O$ (216.24): C 61.10, H 5.59, N 25.91; found: C 61.28, H 5.64, N 25.83.

A suspension of 6-(benzyloxy)pyrimidine-2,4-diamine (23.8 g, 110.1 mmol) in AcOH/H_2O 3 : 7 (208 ml) was heated to 80° until a pale yellow soln. was obtained (30 min). A soln. of $NaNO_2$ (15.11 g, 219.0 mmol) in H_2O (30 ml) was added dropwise until the evolution of NO_2 was observed. A purple solid formed during the addition. The slurry was cooled to 23°, and the solids were removed by suction filtration, and washing successively with cold H_2O and Et_2O. Drying of the solid *in vacuo* (0.1 Torr) afforded **13** (25.02 g, 93%). Violet crystals. R_f (CH_2Cl_2/MeOH/Et_3N 20 : 1 : 0.1) 0.23. M.p. 210–204° (dec., [10]: 205–212° (dec.)). IR (KBr): 3480*s*, 3301*s*, 3175*s*, 2962*m*, 1620*s*, 1574*s*, 1498*s*, 1476*s*, 1458*m*, 1420*s*, 1376*s*, 1347*s*, 1319*m*, 1250*s*, 1131*s*, 1083*m*, 1058*m*, 995*m*, 927*m*, 912*w*. ^{1}H-NMR ((D_6)DMSO, 300 MHz): 9.99, 7.97 (2*d*, *J* = 2.7, NH_2); 7.83, 7.77 (2*s*, NH_2); 7.48–7.29 (*m*, 5 arom. H); 5.51 (*s*, PhC*H*$_2$). ^{13}C-NMR ((D_6)DMSO, 75 MHz): 170.20, 163.09 (2*s*, C(2), C(6)); 150.63 (*s*, C(4)); 139.34 (*s*); 135.93 (*s*, C(5)); 128.27 (2*d*); 128.24 (2*d*); 127.97 (*d*); 67.79 (*t*, Ph*C*H$_2$). Anal. calc. for $C_{11}H_{12}N_4O$ (245.24): C 53.95, H 4.32, N 28.62; found: C 53.87, H 4.52, N 28.56.

*2-(3-*O*-Acetyl-2,4,6-tri-*O*-benzyl-α-*D*-mannopyranosyl)-*N*-[2-amino-6-(benzyloxy)-5-nitrosopyrimidin-4-yl]acetamide* (**15**). A soln. of **12** (1.86 g, 3.47 mmol) in benzene (125 ml) was treated with oxalyl chloride (1.17 ml, 13.83 mmol) and DMF (2 drops). Gentle effervescence was observed when the pale yellow soln. was stirred at 25° for 3 h. The volatiles were removed *in vacuo* to give the crude acid chloride ($\tilde{\nu}$ 1797 cm^{-1}) as an orange oil. A soln. of the crude material in THF (20 ml) was added dropwise over 30 min to a cooled (–60°) soln. of **13** (0.774 g, 3.15 mmol) in THF (220 ml) and pyridine (0.28 ml, 3.46 mmol). Upon addition of the acid chloride, the blue soln. gradually became emerald green and then pale orange. Upon increasing the temp. to –50°, the colour reverted to green becoming more intense at –45° and blue-green at –35°. The mixture was warmed to 23°, diluted with AcOEt (50 ml) and filtered through *Celite*. Evaporation of the filtrate gave the crude product as a blue oil. FC (silica gel; cyclohexane/AcOEt, 4 : 1 → 2 : 1) afforded **15** (2.16 g, 81%). Blue foam. R_f (CH_2Cl_2/MeOH 30 : 1) 0.30. $[\alpha]_D^{25} \approx +45$ ($c = 0.99$, $CHCl_3$). IR (neat): 3412*m*, 3007*m*, 1734*m*, 1620*s*, 1599*s*, 1537*s*, 1471*s*, 1349*s*, 1089*s*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 12.27 (*s*, exchanges with D_2O, N*H*CO); 7.55 – 7.23 (*m*, 20 arom. H); 6.48, 5.64 (br. *s*, exchanges with D_2O, NH_2); 5.66 (*s*, PhCH_2); 5.42 (*dd*, $J = 5.5$, 3.0, H–C(3)); 4.62 (*d*, $J = 11.5$, PhC*H*); 4.58 (*d*, $J = 11.5$, 2 PhC*H*); 4.50 – 4.43 (*m*, 3 PhC*H*, H–C(1)); 4.08 (br. *q*, $J \approx 5.3$, H–C(5)); 3.85 (*t*, $J = 5.6$, H–C(4)); 3.76 (*dd*, $J = 10.0$, 6.0, H_A–C(6)); 3.76 (*dd*, $J = 9.9$, 3.0, H–C(2)); 3.71 (*dd*, $J = 10.0$, 5.3, H_B–C(6)); 3.09 (*dd*, $J = 15.1$, 5.3, CH_A–C(1)); 2.97 (*dd*, $J = 15.1$, 7.5, CH_B–C(1)); 1.96 (*s*, AcO). ^{13}C-NMR ($CDCl_3$, 75 MHz, assignments based on HSQC and COSY): 170.53, 169.77, 163.56 (3*s*, Me*C*O, NH*C*O, C(2′), C(6′)); 144.5 (br. *s*, C(4′)); 138.56, 137.62, 137.36, 137.02 (4*s*); 135.06 (C(5′)); 128.40, 128.28, 128.25, 128.15, 128.03, 127.80, 127.72, 127.63, 127.47 (several *d*); 74.66 (*d*, C(2)); 74.08 (*d*, C(4)); 74.04 (*d*, C(5)); 73.11, 72.87, 71.39, 69.30 (4*t*, 4 Ph$C\mathrm{H}_2$); 68.64 (*d*, C(3)); 68.29 (*d*, C(1)); 67.95 (*t*, C(6)); 41.06 (*t*, $C\mathrm{H}_2$–C(1)); 21.00 (*q*, Me). HR-MALDI-MS: 784.2960 (100, $[M + Na]^+$, $C_{42}H_{43}N_5NaO_9^+$; calc. 784.2958).

*8-[(3-*O*-Acetyl-2,4,6-tri-*O*-benzyl-α-*D*-mannopyranosyl)methyl]-*O^6*-benzylguanine* (**18**). A soln. of **15** (0.978 g, 1.28 mmol) in *o*-xylene (40 ml) was treated with 1,2-bis(diphenylphosphino)ethane (0.561 g, 1.41 mmol) and then heated to 80° for 30 min. A colour change from blue to green was observed during the 15 – 20 min following the addition of the phosphine accompanied by the development of turbidity. The mixture was heated to reflux for 2 h during which time it became yellow and then allowed to cool to r.t. overnight. The precipitated phosphine oxide was removed by filtration through *Celite*, rinsing with toluene until the washings were colourless. Evaporation of the combined filtrates and FC (silica gel; AcOEt) afforded **18** (0.840 g, 90%). Pale yellow foam. R_f (CH_2Cl_2/MeOH 20 : 1) 0.23. $[\alpha]_D^{25} = +3.4$ ($c = 0.14$, $CHCl_3$). IR (neat): 3363*w*, 3007*m*, 1740*s*, 1625*s*, 1590*s*, 1466*m*, 1454*m*, 1411*m*, 1089*s*, 909*m*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 12.45 (br. *s*, exchanges with D_2O, H–N(9)); 7.50 – 7.15 (*m*, 20 arom. H); 5.56 (*d*, $J = 12.3$, PhC*H*); 5.53 (*d*, $J = 12.3$, PhC*H*); 5.51 (*t*, $J \approx 3.6$, H–C(3′)); 5.02 (br. *s*, exchanges with D_2O, NH_2); 4.64 (*d*, $J = 11.6$, PhC*H*); 4.63 (*d*, $J = 10.9$, PhC*H*); 4.60 (*d*, $J = 13.0$, PhC*H*); 4.53 (*d*, $J = 12.1$, PhC*H*); 4.44 (*d*, $J = 11.4$, PhC*H*); 4.42 (*d*, $J = 12.1$, PhC*H*); 4.21 (*ddd*, $J =$ 8.1, 5.4, 2.7, H–C(5′)); 4.16 (br. *dt*, $J = 9.6$, 2.3, H–C(1′)); 3.69 (*dd*, $J = 10.0$, 8.1, H–C(6′)); 3.68 (*dd*, $J = 8.7$, 3.2, H–C(2′)); 3.65 (*dd*, $J = 3.9$, 2.8, H–C(4′)); 3.55 (*dd*, $J = 10.2$, 5.4, H′–C(6′)); 3.45 (*dd*, $J = 15.0$, 2.2, H_AC–C(8)); 2.90 (*dd*, $J = 15.0$, 10.5, H_BC–C(8)); 1.93 (*s*, Me). ^{13}C-NMR ($CDCl_3$, 125 MHz, assignments based on HSQC and COSY): 169.78 (*s*, C=O); 160.14, 158.60 (2*s*, C(2), C(6)); 155.57 (*s*, C(4)); 148.39 (*s*, C(8)); 137.43, 137.35, 137.21, 136.63 (4*s*); 128.59, 128.46, 128.39, 128.37, 128.27, 128.21, 128.09, 127.92, 127.86, 127.83, 127.80, 127.74 (several *d*); 114.81 (*s*, C(5)); 74.52 (*d*, C(4′)); 74.47 (*d*, C(5′)); 74.19 (*d*, C(2′)); 73.21, 72.38, 71.35 (3*t*, 3 Ph$C\mathrm{H}_2$); 69.48 (*d*, C(1′)); 67.72 (*t*, Ph$C\mathrm{H}_2$); 66.94 (*d*, C(3′)); 66.75 (*t*, C(6)); 31.56 (*t*, $C\mathrm{H}_2$–C(8)); 20.84 (*q*, Me). HR-MALDI-MS: 730.3237 (100, $[M + H]^+$, $C_{42}H_{44}N_5O_7^+$; calc. 730.3241). Anal. calc. for $C_{42}H_{43}N_5O_7$ (799.93): C 69.07, H 6.17, N 8.76; found: C 68.97, H 6.14, N 9.56.

*8-[(3-*O*-Acetyl-2,4,6-tri-*O*-benzyl-α-*D*-mannopyranosyl)methyl]-*O^6*-benzyl-*N^2*-(2-methylpropanoyl)guanine* (**19**). A soln. of **18** (1.659 g, 2.274 mmol) in toluene (35 ml) was treated with isobutyric anhydride (1.89 ml, 11.37 mmol) and heated to reflux for 24 h. Two products were observed by TLC, assumed to be N^2-acylated (more polar) and N^2,N^9-diacylated (less polar) derivatives. After cooling and evaporation, a soln. of the yellow oily residue in MeOH (68 ml) was heated to 50° for 4 h, when TLC showed the conversion of the less polar product into the more polar one. Evaporation and FC (silica gel; cyclohexane/acetone 3 : 1) afforded **19** (1.456 g, 80%). Colourless foam. R_f (cyclohexane/acetone 1 : 1) 0.49. $[\alpha]_D^{25} = -5.2$ ($c = 0.98$, $CHCl_3$). IR (neat): 3215*w*, 3148*w*, 3063*w*, 3030*w*, 2969*w*, 2933*w*, 2871*w*, 1743*m*, 1668*m*, 1600*s*, 1531*w*, 1509*w*, 1497*w*, 1454*m*, 1372*s*, 1349*s*, 1302*w*, 1231*s*, 1144*m*, 1093*s*, 1027*m*, 987*m*, 909*m*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 11.70 (br. *s*, H–N(9)); 9.02 (br. *s*, HN–C(2)); 7.49 – 7.21 (*m*, 20 arom. H); 5.59 (*s*, PhCH_2); 5.43 (*t*, $J = 3.5$, H–C(3′)); 4.63 (*d*, $J = 11.8$, PhC*H*); 4.62 (*d*, $J = 12.4$, PhC*H*); 4.58 (*d*, $J = 11.4$, PhC*H*); 4.56 (*d*, $J = 14.3$, 2 PhC*H*); 4.45 (*d*, $J = 11.5$, PhC*H*); 4.23 (br. *t*, $J = 7.6$, H–C(1′)); 4.19 – 4.16 (*m*, H–C(5′)); 3.77 – 3.72 (*m*, H–C(2′), H–C(6′)); 3.64 (br. *s*, H–C(4′)); 3.70 – 3.35 (br. *s*, Me_2C*H*); 3.50 (*dd*, $J = 10.1$, 4.3, H–C(6′)); 3.38 (*dd*, $J = 15.7$, 2.6, HC–C(8)); 3.11 (*dd*, $J = 15.7$, 10.5, HC–C(8)); 1.95 (*s*, AcO); 1.20, 1.19 (2*d*, $J = 5.3$, Me_2CH). ^{13}C-NMR ($CDCl_3$, 125 MHz, assignments based on HSQC and COSY): 169.89 (*s*, C=O); 159.47, 154.71 (2*s*, C(2), C(6)); 151.34 (*s*, C(4)); 151.07 (*s*, C(8)); 137.44, 137.28, 137.18, 136.12 (4*s*); 129.71, 129.40, 129.10, 128.48, 128.44, 128.18, 128.07, 127.96, 127.85, 127.78, 127.52, (several *d*); 117.17 (*s*, C(5)); 74.39 (*d*, C(4′)); 74.30 (*d*, C(2′)); 73.79 (*d*, C(5′)); 73.24, 72.58, 71.41 (3*t*, 3 Ph*C*H_2); 69.33 (*d*, C(1′)); 68.48 (*t*, Ph*C*H_2); 67.86 (*d*, C(3′)); 67.17 (*t*, C(6′)); 34.29 (*d*, Me_2*C*H); 31.58 (*t*, *C*H_2–C(8)); 20.84 (*q*, *Me*C=O); 19.29 (*q*, *Me*$_2$CH). HR-MALDI-MS: 822.3464 (45, $[M+Na]^+$, $C_{46}H_{49}N_5NaO_8^+$; calc. 822.3479).

*8-[(3-*O*-Acetyl-2,4,6-tri-*O*-benzyl-α-*D*-mannopyranosyl)methyl]-2′,3′,5′-tri-*O*-benzoyl-*O^6*-benzyl-*N^2*-(2-methylpropanoyl)guanosine* (**21**). A soln. of **19** (1.402 g, 1.752 mmol) in MeCN (17 ml) was treated with *N,O*-bis(trimethylsilyl)acetamide (0.86 ml, 3.505 mmol), heated to 80° for 25 min, cooled to 23°, treated with a soln. of *1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-*D*-ribofuranose* (**20**) (0.972 mg, 1.927 mmol) in MeCN (3 ml), followed by TMSOTf (0.41 ml, 2.277 mmol), stirred at 23° for 1 h, and heated to 65° for 1.5 h. The orange soln. was allowed to cool to 23°, diluted with CH_2Cl_2 (200 ml), and washed with 50% sat. aq. $NaHCO_3$ soln. The aq. layer was extracted with CH_2Cl_2 (2 × 100 ml). The combined org. extracts were dried and evaporated. FC (silica gel; cyclohexane/AcOEt, 3:1) afforded **21** (1.663 g, 76%). Colourless foam. R_f (cyclohexane/acetone 2:1) 0.40. $[\alpha]_D^{25} = +7.6$ ($c = 1.03$, $CHCl_3$). IR (neat): 3353*w*, 3063*w*, 3032*m*, 2955*w*, 2925*w*, 2870*w*, 1724*s*, 1602*m*, 1496*w*, 1452*m*, 1422*m*, 1371*m*, 1314*m*, 1266*s*, 1232*s*, 1178*m*, 1094*s*, 1070*m*, 1026*m*, 907*w*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 8.36 (br. *s*, exchanges with D_2O, NH); 8.00 (*dd*, *J* = 8.4, 1.3, 2 arom. H); 7.91 (*dd*, *J* = 8.4, 1.2, 2 arom. H); 7.73 (*dd*, *J* = 8.4, 1.3, 2 arom. H); 7.61 (*dd*, *J* = 7.4, 1.6, 2 arom. H); 7.55 (*dt*, *J* = 7.5, 1.3, 1 arom. H); 7.51 (*dt*, *J* = 7.5, 1.3, 1 arom. H); 7.42–7.11 (*m*, 23 arom. H); 7.05 (*dd*, *J* = 8.6, 5.3, H–C(3′)); 7.00 (*dd*, *J* = 6.5, 2.1, 2 arom. H); 6.69 (*dd*, *J* = 5.3, 1.3, H–C(2′)); 6.50 (*d*, *J* = 1.4, H–C(1′)); 5.71 (*d*, *J* = 12.1, PhC*H*); 5.63 (*d*, *J* = 12.1, PhC*H*); 5.41 (*t*, *J* = 3.7, H–C(3″)); 4.79–4.71 (*m*, H–C(4′), H_A–C(5′)); 4.58 (*d*, *J* = 11.7, PhC*H*); 4.59–4.53 (*m*, H_B–C(5′)); 4.41 (*d*, *J* = 11.7, PhC*H*); 4.37 (*s*, PhC*H*$_2$); 4.28 (*td*, *J* = 9.6, 8.8, 5.3, H–C(1″)); 4.22 (*s*, PhC*H*$_2$); 3.84 (*td*, *J* = 6.3, 2.9, H–C(5″)); 3.73 (*dd*, *J* = 8.2, 3.1, H–C(2″)); 3.59 (*dd*, *J* = 4.5, 3.0, H–C(4″)); 3.53–3.43 (*m*, H_AC–C(8), 2 H–C(6″)); 3.02 (*dd*, *J* = 14.8, 9.3, H_BC–C(8)); 3.00–2.86 (*br. s*, Me_2C*H*); 1.88 (*s*, MeCO); 1.30, 1.28 (2*d*, *J* = 6.9, *Me*$_2$CH). NOEs: irrad. at 6.50 → 1% (H–C(2′)), 0.5% (H–C(4′) and H_AC–C(8)), 2% (H_BC–C(8)). ^{13}C-NMR ($CDCl_3$, 125 MHz): 175.01 (*s*, NH*C*O); 169.85, 166.12, 165.41, 164.99, (4*s*, 4 C=O); 160.04 (*s*, C(6)); 152.71, 151.90, 151.42 (3*s*, C(2), C(4), C(8)); 137.97, 137.61, 137.58, 136.17 (4*s*); 133.52–127.28 (several *d*); 117.27 (*s*, C(5)); 87.49 (*d*, C(1′)); 78.54 (*d*, C(4′)); 74.47 (*d*, C(5″)); 74.37 (*d*, C(2″)); 74.33 (*d*, C(2′)); 74.10 (*d*, C(4″)); 70.84 (*d*, C(3′)); 70.62 (*d*, C(1″)); 73.04, 72.06, 71.08, 68.85 (4*t*, 4 Ph*C*H_2); 67.49 (*t*, C(6″)); 67.40 (*d*, C(3″)); 62.53 (*t*, C(5′)); 36.28 (*d*, Me_2*C*H); 30.32 (*C*H_2–C(1)); 20.88 (*q*, *Me*CO); 19.31, 19.27 (2*q*, *Me*$_2$CH). HR-MALDI-MS: 1266.4667 (90, $[M+Na]^+$, $C_{72}H_{69}N_5NaO_{15}^+$; calc. 1266.4688).

O^6-Benzyl-*N^2*-(2-methylpropanoyl)-8-[(2,4,6-tri-*O*-benzyl-α-*D*-mannopyranosyl)methyl]guanosine* (**22**). A soln. of **22** (1.663 g, 1.337 mmol) in CH_2Cl_2/MeOH 1:1 (30 ml) was cooled to 0°, treated with K_2CO_3 (0.240 g, 1.737 mmol), and stirred for 80 min at 0° and for 2 h at r.t. The pH of the soln. was adjusted to 6–7 by the addition of glacial AcOH. Evaporation, co-evaporation with toluene, and FC (silica gel; cyclohexane/acetone/NH_4OH 2:1:0.01 → 1:1:0.01) afforded **22** (868 mg, 73%). Colourless solid. R_f (cyclohexane/acetone 1:1) 0.43. $[\alpha]_D^{25} = -10.9$ ($c = 0.25$, $CHCl_3$). IR (neat): 3343*w* (br.), 3062*w*, 3030*m*, 2927*m*, 2925*w*, 2872*w*, 1699*w*, 1614*s*, 1592*m*, 1497*m*, 1454*s*, 1427*s*, 1393*m*, 1355*m*, 1234*s*, 1192*m*, 1092*s*, 1071*s*, 1028*m*, 907*w*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.76 (br. *s*, NH); 7.58–7.56 (*m*, 2 arom. H); 7.37–7.26 (*m*, 13 arom. H); 7.13 (*tt*, *J* = 7.3, 1.3, 1 arom. H); 7.07 (*tt*, *J* = 7.5, 1.4, 2 arom. H); 6.85 (*d*, *J* = 6.9, 2 arom. H); 5.98 (*d*, *J* = 6.5, H–C(1′)); 5.68 (*d*, *J* = 12.1, PhC*H*); 5.63 (*d*, *J* = 12.1, PhC*H*); 4.95 (br. *d*, *J* = 9.0, HO–C(5′)); 4.91 (br. *s*, HO–C(2′)); 4.62 (br. *t*, *J* ≈ 5.9, H–C(2′)); 4.61–4.53 (*m*, 2 PhC*H*$_2$); 4.50 (*dd*, *J* = 5.6, 2.2, H–C(3′); 4.31 (*d*, *J* = 11.3, PhC*H*); 4.25 (*td*, *J* ≈ 8.9, 2.6, H–C(1″)); 4.15 (*q*, *J* = 2.2, H–C(4′)); 4.09 (*d*, *J* = 11.3, PhC*H*); 4.11–4.06 (*m*, H–C(3″), H–C(5″)); 3.90 (*t*, *J* = 10.6, H–C(6″)); 3.85 (br. *d*, *J* = 12.6, H–C(5′)); 3.73 (br. *t*, *J* ≈ 10.3, H–C(5′)); 3.68 (*dd*, *J* = 8.3, 3.0, H–C(2″)); 3.52 (*dd*, *J* = 4.3, 2.5, H–C(4″)); 3.47 (*dd*, *J* = 14.4, 3.2, CH_A–C(8)); 3.36 (*dd*, *J* = 10.7, 3.1, H–C(6″)); 3.14 (br. *s*, HO–C(3′)); 2.95 (*dd*, *J* = 14.4, 9.5, CH_B–C(8)); 2.83 (*sept.*, *J* = 6.7, Me_2C*H*); 2.50 (br. *s*, HO–C(3″)); 1.31, 1.30 (2*d*, *J* = 6.9, *Me*$_2$CH). ^{13}C-NMR ($CDCl_3$, 125 MHz, assignments based on HSQC and COSY): 178.08 (*s*, C=O); 160.10 (s, C(6)); 152.62, 152.56, 150.61 (3*s*, C(2), C(4), C(8)); 137.66, 137.04, 136.76, 135.86 (4*s*); 128.88–127.44 (several *d*); 117.91 (*s*, C(5)); 89.74 (*d*, C(1′)); 86.45 (*d*, C(4′)); 76.10 (*d*, C(2″)); 75.82 (*d*, C(4″)); 74.26 (*d*, C(5″)); 72.45 (*d*, C(2′)); 71.69 (*d*, C(3′)); 73.49, 72.43, 71.51, 69.00 (4*t*, 4 Ph*C*H_2); 68.74 (*d*, C(1″)); 67.63 (*t*, C(6″)); 66.78 (*d*, C(3″)); 63.02 (*t*, C(5′)); 36.47 (*d*, Me_2*C*H); 30.61 (*t*, *C*H_2–C(8)); 19.44, 19.33 (2*q*, *Me*$_2$CH). HR-MALDI-MS: 912.3780 (90, $[M+Na]^+$, $C_{49}H_{55}N_5NaO_{11}^+$; calc. 912.3796).

*1-{*O^6*-Benzyl-*N^2*-(2-methylpropanoyl)-8-[(2,4,6-tri-*O*-benzyl-α-*D*-mannopyranosyl)methyl]guanin-9-yl}-2,3-*O*-isopropylidene-β-*D*-ribofuranosyluronic Acid* (**23**). A soln. of **22** (0.100 g, 0.112 mmol) and TsOH · H_2O (0.005 g, 0.028 mmol) in acetone (5 ml) was treated with 2,2-dimethoxypropane (0.011 ml, 1.798 mmol), stirred for 7 h, neutralised (pH 7–8) by the addition of 1M NH_4OH soln. in acetone/H_2O (3:7), and filtered, and the solids were washed with acetone. Evaporation of the solvent left a residue containing **23** and *ca.* 20% of its 3″-*O*-(2-methoxypropyl) derivative. It was redissolved in CH_2Cl_2, treated with 10% aq. HCl (10 ml), and the mixture was stirred vigorously for 10 min. The org. layer was separated, washed with sat. aq. $NaHCO_3$ soln. (5 ml) and brine (5 ml), dried, filtered, and concentrated to a volume of *ca.* 1 ml. This soln. was treated with a 0.05M soln. of TEMPO in CH_2Cl_2 (0.022 ml, 1.12 μmol), sat. aq. $NaHCO_3$ soln. (0.3 ml), 0.1M aq. KBr (0.11 ml, 1.12 μmol), and 0.5M Bu_4NCl soln. in CH_2Cl_2 (0.11 ml, 5.6 μmol). The vigorously stirred mixture was cooled to 0° and treated dropwise with a mixture of 12% aq. NaOCl soln. (0.48 ml), sat. aq. $NaHCO_3$ soln. (0.1 ml), and brine (0.2 ml) during 45 min, and stirred for 1.5 h. After acidification with 4M HCl (pH 2–3), the product was extracted with CH_2Cl_2 (4 × 20 ml). The combined extracts were washed with brine, dried, and evaporated. FC (silica gel; CH_2Cl_2/MeOH/AcOH 35:1:0.1) gave **23** (65 mg, 61%). Colourless oil. R_f (CH_2Cl_2/MeOH 9:1) 0.39. $[\alpha]_D^{25} = +4.7$ ($c = 0.30$, $CHCl_3$). IR (neat): 3442*w*, 3358*w*, 2928*w*, 2872*w*, 1717*m*, 1607*s*, 1498*w*, 1454*m*, 1426*m*, 1399*m*, 1356*m*, 1215*m*, 1157*m*, 1064*s*, 1027*m*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 9.33 (br. *s*, exchanges with D_2O, NH); 7.62–7.12, 6.97–6.95 (2*m*, 20 arom. H); 6.35 (*s*, H–C(1′)); 5.85 (br. *d*, $J \approx 5$, H–C(3′)); 5.56 (*d*, $J = 12.2$, PhC*H*); 5.52 (*d*, $J = 12.2$, PhC*H*); 5.37 (br. *d*, $J = 5.4$, H–C(2′)); 4.76 (*s*, H–C(4′)); 4.61 (*d*, $J = 11.8$, PhC*H*); 4.59 (*d*, $J = 11.4$, PhC*H*); 4.57 (*d*, $J = 11.7$, PhC*H*); 4.53 (*d*, $J = 11.6$, PhC*H*); 4.28 (*d*, $J = 11.8$ PhC*H*); 4.21–4.30 (*m*, H–C(1″)); 4.17–4.12 (*m*, PhC*H*, H–C(3″)); 4.09 (br. *dd*, $J = 6.9$, 3.4, H–C(5″)); 3.74 (*dd*, $J = 10.7$, 7.4, H–C(6″)); 3.71 (*dd*, $J = 7.6$, 2.8, H–C(2″)); 3.65 (*dd*, $J = 4.6$, 3.1, H–C(4″)); 3.50 (*dd*, $J = 11.0$, 3.9, H–C(6″)); 3.41 (*dd*, $J = 14.6$, 3.9, HC–C(8)); 3.10–3.34 (br. *s*, Me_2CH); 2.99 (*dd*, $J = 14.5$, 9.3, HC–C(8)); 1.55, 1.39 (2*s*, Me_2C); 1.17, 1.16 (2*d*, $J = 6.8$, *Me*$_2$CH). NOEs: irrad. at 6.35 → 0.5% (H–C(4′) and H_AC–C(8)), 2% (H_BC–C(8)). ^{13}C-NMR ($CDCl_3$, 125 MHz, assignments based on HSQC and COSY): 178 (br. *s*, CO_2H); 174.01 (*s*, NH*C*O); 159.57 (C(6)); 153.53, 151.90, 150.56 (3*s*, C(2), C(4), C(8)); 137.93, 137.91, 137.28, 135.89 (4*s*); 128.61–127.12, (several *d*); 116.70 (*s*, C(5)); 112.92 (Me_2*C*); 91.14 (*d*, C(1′)); 87.32 (*d*, C(4′)); 84.50 (*d*, C(3′)); 84.23 (*d*, C(2′)); 76.03 (*d*, C(2″)); 73.94 (*d*, C(4″)); 72.96 (*d*, C(5″)); 73.19, 71.83, 71.35, 69.43 (4*t*, 4 Ph*C*H_2); 69.04 (*d*, C(1″)); 68.04 (*t*, C(6″)); 67.24 (*d*, C(3″)); 34.59 (*d*, Me_2*C*H); 30.41 (*t*, *C*H_2–C(8)); 26.50, 24.67 (2*q*, *Me*$_2$C); 19.29, 18.91 (2*q*, *Me*$_2$CH). HR-MALDI-MS: 944.4063 (15, $[M+H]^+$, $C_{52}H_{58}N_5NaO_{12}^+$; calc. 944.4082).

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