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An approach to the generation of simple analogues of the antitumour agent spicamycin †

Stéphane Mons[a,b] **and George W. J. Fleet***[a]

[a] *Dyson Perrins Laboratory, University of Oxford, South Parks Road, Oxford, UK OX1 3QY. E-mail: George.Fleet@chem.ox.ac.uk*

[b] *Institut de Chimie des Substances Naturelles, CNRS, Avenue de la Terrasse, 91198 Gif sur Yvette cedex, France*

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The one-step glycosylation of arylamines in acidic medium is extended to adenine derivatives for the first time, providing a considerable improvement over existing reactions. This method is used to prepare some rhamnospicamycin analogues containing different base moieties. Results suggest that this novel approach will be applicable to a wide range of carbohydrates and arylamines, possibly leading to a combinatorial library of analogues of spicamycin for the better understanding of the modes of action of this antitumour antibiotic family.

1. Introduction

Spicamycin **1** (Fig. 1) is an antitumour antibiotic isolated from cultures of *Streptomyces alanosinicus*,[1] and occurs naturally as a family of compounds which differ only by the nature and length of the fatty chain portion of the molecule. The structure of this nucleoside is quite unusual since the adenine moiety is linked through its N^6 amino group, as evidenced by X-ray crystallographic studies,[2] instead of the common 9-position.

Extensive structure–activity relationship (SAR) studies directed towards the influence of the amino acid and the fatty chain moieties in spicamycin analogues have led to the discovery of two potentially antitumour drugs: SPM VIII **1** (R^1 = dodecanoyl),[3] which proved to be more potent than the commonly used mitomycin C against human gastric cancer SC-9,[4] and KRN5500 **1** (R^1 = (2*E*,4*E*)-tetradecadienoyl). The latter, which is currently in Phase 1 clinical trials in the USA,[5–7] exhibits a potent activity against Colo 205 colon carcinoma xenografts *in vivo*.[8–10] Recent studies suggest that it may be used as an anti-leukemic agent[11,12] and for combination chemotherapy with cisplatin, carboplatin or etoposide against non-small-cell lung cancer.[13] KRN5500 has the ability to potently decrease pain which is resistant to other pain relief methods, such as opioid drugs.[14] Incorporation of KRN5500 into polymeric micelles has been shown to diminish the pulmonary toxicity.[15]

Very little is known about the mechanisms of action of the spicamycin family and its metabolites,[16] SAN **1** (R = H) and SAN-Gly **1** (R^1 = H), but they seem to involve alteration of the glycoprotein expression and modification of the cellular secretion pathway.[17,18] As such, spicamycin would have a completely different mode of action compared to conventional antitumour drugs, which makes its study particularly interesting. No SAR study has been carried out to elucidate the role of the carbohydrate or the nucleoside base moieties in the biological activity, except for the rhamnose analogues we have previously described,[19] and some analogues of septacidin **4**,[20] a natural

† This is one of a number of contributions from the current members of the Dyson Perrins Laboratory to mark the end of almost 90 years of organic chemistry research in that building, as all its current academic staff move across South Parks Road to a new purpose-built laboratory.

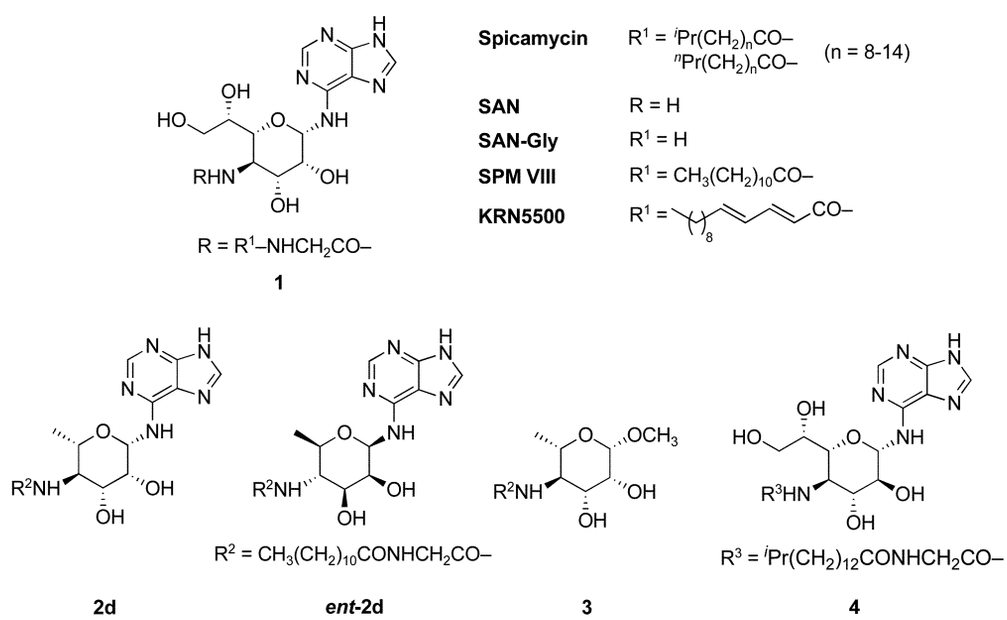

Fig. 1

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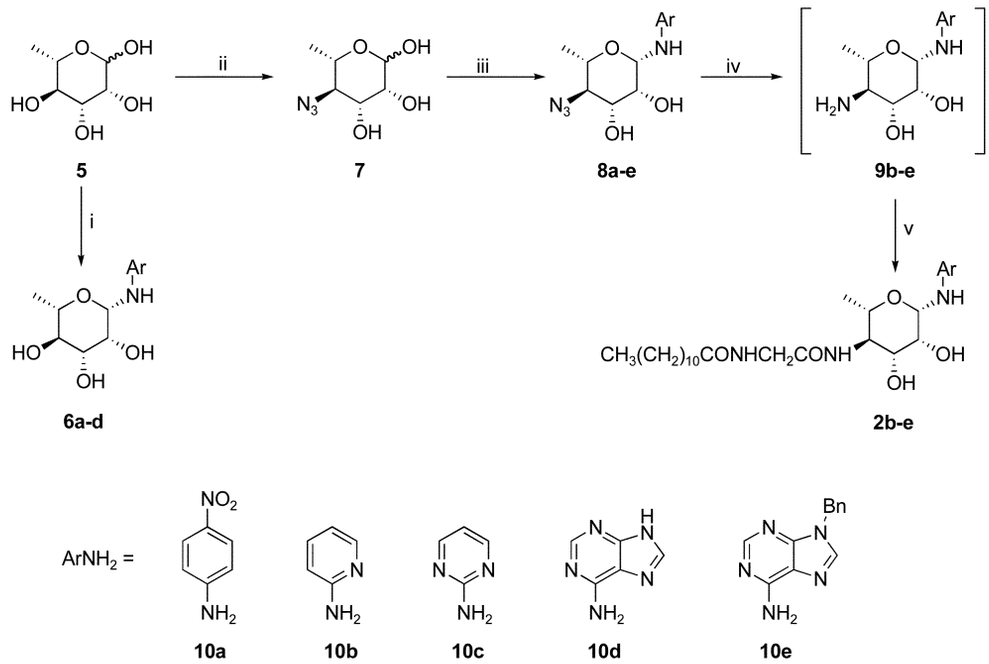

Scheme 1 *Reagents*: (i) $ArNH_2$, MeOH, H_2O, AcOH, reflux, 3 min to 6 days; (ii) see Martín *et al.*,[19] (iii) $ArNH_2$, MeOH, H_2O, AcOH, reflux, 1 h to 2 days; (iv) H_2, Pd/C, MeOH, rt, 40 min; (v) dodecanoylglycine, EDCI, HOBT, DMF, rt, 12 h.

isomer of spicamycin. Our results showed that the structure of **1** can be simplified as in **2d** without significant loss of activity, though the pattern of mannose incorporation in HL60 cells was modified. By contrast, neither the enantiomer of **2d**, *ent*-**2d**, nor the compound **3**, where the adenine moiety was replaced by a methoxy group, were active.

A general method for preparing 6-(pyranosylamino)purines is still lacking to allow more in-depth SAR study on the carbohydrate and nucleobase parts of spicamycin. A few methods are described and use glycosylamines as the starting material but, because of the poor nucleophilicity of such amines and their propensity to dimerise,[21] it is necessary to use either a very electrophilic aryl chloride and build the adenine heterocycle, as we did earlier,[19,22] or a palladium-mediated coupling with a protected 6-chloropurine.[23] The former method is a multistep procedure and affords low to moderate yields of the expected product, while the latter involves use of expensive catalysts. In the perspective of extending these methods to the preparation of analogues of spicamycin containing bases other than adenine, they are also limited by the availability of the corresponding aryl chlorides. Some solid-state one-step ribosylations of adenine are described but are of little synthetic interest.[24,25]

This paper reports a new route to the preparation of rhamnospicamycin analogues which is much faster than previous procedures and likely broader in scope. This approach is based on a one-step glycosylation of adenine, or other arylamines.

2. Synthesis

Glycosylation of amines using a lactol in neutral or acidic medium is well known. Among the numerous examples available in the literature, the method described by Honeyman attracted our attention regarding the yields obtained, the extremely short reaction time and the high concentrations used, which should make easier large-scale preparations.[26] Also, this reaction requires no protection of the carbohydrate and was successfully applied to a wide variety of sugars, unlike solvent-free methods.[24,25]

The direct glycosylation of *p*-nitroaniline **10a**, 2-aminopyridine **10b**, 2-aminopyrimidine **10c** and adenine **10d** with L-rhamnose afforded the corresponding *N*-aryl-β-L-rhamnopyranosylamines **6a–d** in yields ranging from 15 to 95% in only one synthetic step (Scheme 1, Table 1). Low yield for the adenine derivative **6d** seems to be attributable to a lower stability of the compound which decomposes in the course of the reaction, especially because the poor solubility of adenine in the solvent makes the reaction much longer than others.

Table 1 Reaction times and isolated yields in the preparation of compounds **6a–d** and **8a–e**

Carbohydrate	$ArNH_2$	Product	Reaction time	Yield[a] (%)
5	**10a**	**6a**	3 min	95
5	**10b**	**6b**	3 min	91
5	**10c**	**6c**	4 h	83
5	**10d**	**6d**	6 days	10 [15]
7	**10a**	**8a**	12 h	86
7	**10b**	**8b**	1 h	49 [61]
7	**10c**	**8c**	24 h	69 [83]
7	**10d**	**8d**	2 days[b]	10 [16]
7	**10e**	**8e**	2 days	20 [43]

[a] Yields in square brackets are based on recovered starting material. [b] Reaction was carried out at 100 °C in a sealed tube.

The *p*-nitrophenyl derivative **6a** was unambiguously shown to be a pyranose ring with the β-L-rhamnose configuration, as depicted in Scheme 1. 2D-NMR experiments (COSY, HMQC and HMBC) showed in every case a strong $^3J_{H,H}$ coupling between the NH group and the anomeric proton, which ascertained the site of attachment on the amine moiety. Additional heteronuclear couplings of the NH group with carbons C-2′ on the carbohydrate (strong) and C-1 on the base (weak), and for **6a** and **6b**, between the anomeric proton and the carbon C-1 (strong), were also observed. The assignment of the anomeric configuration was made on the basis that chemical shifts of the carbohydrate protons, except H-1′, and coupling constants all around the ring were almost identical to that of **6a**, which is known to have a β configuration (Table 2).

The synthesis of rhamnospicamycin analogues requires the presence of a primary amino group at position C-4 with the same configuration as in L-rhamnose. The use of an azide as a masked amine seemed to be particularly convenient here since it may be reduced in neutral conditions, either by catalytic hydrogenation or by a Staudinger reaction, accommodating the reactivity of the base fragment. In order to avoid cross-

Table 2 ^{1}H Chemical shifts and coupling constants for the carbohydrate fragment of compounds **6a**–**d**, **8a**–**e** and **2b**–**e**

	Chemical shifts (ppm)						Coupling constants/Hz			
	H-1	H-2	H-3	H-4	H-5	H-6	1–2	2–3	3–4	5–6
2b	5.19	3.92	3.67	3.89	3.54	1.20	1.2	3.2	10.6	6.0
2c	5.38	3.92	3.67	3.89	3.51	1.19	1.0	3.2	10.5	6.2
2d	5.68[a]	4.01	3.73	3.94	3.61	1.21	1.2	3.2	10.5	6.1
2e	5.67[a]	3.98	3.70	3.91	3.59	1.19	1.2	3.2	10.4	6.0
6a	4.87	3.96	3.56	3.47–3.33[b]		1.31	1.0	3.4	9.1	5.8
6b	5.16	3.72	3.54	3.48–3.32[b]		1.28	1.1	3.4	9.1	5.7
6c	5.39	3.92	3.54	3.48–3.32[b]		1.29	1.1	3.4	9.2	5.6
6d	5.72[a]	4.00	3.59	3.52–3.31[b]		1.29	1.2	3.4	9.3	5.8
8a	4.93	3.94	3.70	3.45–3.28[b]		1.36	1.0	3.3	9.7	6.0
8b	5.14	3.90	3.68	3.47–3.34[b]		1.30	1.1	3.3	9.7	6.0
8c	5.36	3.89	3.68	3.38–3.27[b]		1.30	1.2	3.3	9.5	5.8
8d	5.69[a]	3.98	3.74	3.52–3.45[b]		1.32	1.0	3.3	9.7	6.0
8e	5.65[a]	3.97	3.75	3.50–3.30[b]		1.33	1.1	3.3	9.7	5.8

Spectra were recorded in CD_3OD at 400 MHz.[a] Broad singlet. [b] Individual chemical shifts could not be derived from the spectrum.

reactions of the base during the transformation of compounds **6a**–**d** to **8a**–**e**, and to adopt a more convergent approach, we introduced the azido group prior to glycosylation. 4-Azido-4-deoxy-L-rhamnose **7** was prepared in seven steps from L-rhamnose, as described previously,[19] and was used in the glycosylation of amines **10a**–**e** to afford 4-azido-4-deoxy-*N*-aryl-β-L-rhamnosylamines **8a**–**e** in 16–86% yield (Table 1). In particular, we obtained the adenine derivative **8d** that we had not been able to prepare previously using lower concentrations of the reaction medium.[19] In the case of **8a**, a mixture of anomers was sometimes obtained after short reaction time but equilibrated to the thermodynamically more stable β-anomer on prolonged heating. We could otherwise not detect the α anomer for any of the other compounds, though it has been observed with another cyclic acetal.[27]

It is noteworthy that the highest yield reported for the preparation of a 6-spicaminyl-9*H*-purine is less than 24%‡ and requires more than seven steps to achieve the conversion of the lactol into a glycosylamine, the coupling with protected 6-chloropurine and the deprotection.[23] In comparison, we obtained the adenine derivatives **8d** and **8e** in only one step in comparable (16%) or much higher (43%) yield, the difference probably arising from the better solubility of 9-benzyladenine **10e** in the reaction medium; **8e** may then serve as an indirect way to prepare **2d**, with the additional advantage of providing easier purification.

Determination of the structure and anomeric configuration of **8a**–**e** was achieved as above from 2D-NMR experiments and comparison of the proton chemical shifts and coupling constants in the carbohydrate fragment with those of **6a**. The slight increase in the average $^{3}J_{3'-4'}$ and $^{3}J_{5'-6'}$, when compared to data for compounds **6a**–**d**, must account for the minor conformational changes accompanying the replacement of the hydroxyl at C-4 by an azido group in **8a**–**e** (Table 2). Azides **8b**–**e** were reduced by catalytic hydrogenation using palladium on charcoal in methanol to give the corresponding amines **9b**–**e** which were used, without isolation, for the peptide coupling with dodecanoylglycine in DMF. Rhamnospicamycin analogues **2b**, **2c**, **2d** and **2e** were obtained in 72, 71, 60 and 89% yield, respectively, over two steps. Analyses for **2d** showed that this compound was identical to the L-(+)-rhamnospicamycin obtained previously in our laboratory by building the adenine moiety.[19] Homo- and hetero-nuclear correlations and comparison of the chemical shifts and coupling constants in **2b**, **2c** and **2e** with data for **2d** unambiguously proved the structure and β-configuration of these analogues (Table 2). Retrospectively, it also provided another evidence for the structure of the precursor azides **8b**–**e**.

‡ From ref. 23. This calculation excludes the protection steps and anomeric acetylation, whose yields could not be derived from description of the synthesis.

3. Summary

One-step glycosylation of adenine derivatives was achieved on the N^6-amino group, following the general acid-catalysed reaction of lactols with arylamines. The yields for adenine derivatives and other aromatic amines are at least comparable to those provided by existing methods, and usually much better, with the advantage of considerably decreasing the number of synthetic steps as no protection is required. Also, this method does not require the availability of aromatic chlorides nor the use of expensive catalysts. Because this glycosylation is quite broad in scope, it may be anticipated that a large variety of analogues containing different carbohydrate and base moieties can be rapidly synthesised for the study of the mechanisms of action of the spicamycin family. Preliminary results in our laboratory show that adenine reacts with D-glucose in the conditions mentioned in the present paper to afford the corresponding 6-(β-D-glucosylamino)-9*H*-purine in 25% yield, based on recovered starting material, where solvent-free reaction fails.[24,25] This new approach allowed the preparation of several dodecanoyl-L-(+)-rhamnospicamycin analogues.

4. Experimental

Proton nuclear magnetic resonance spectra (δ_H) were recorded on a Bruker DPX 400 (400 MHz) or Bruker AMX 500 (500 MHz) spectrometer, and were calibrated according to the chemical shift of residual protons in the deuterated solvent. ^{13}C Nuclear magnetic resonance spectra (δ_C) were recorded on a Bruker DPX 400 (100 MHz) or Bruker AMX 500 (125 MHz) spectrometer and were calibrated using the chemical shift of the deuterated solvent. All the compounds were subjected to ^{1}H,^{1}H-COSY, ^{1}H,^{13}C-HMQC and ^{1}H,^{13}C-HMBC experiments to ascertain assignments. Chemical shifts are quoted in ppm on the δ-scale. The following abbreviations are used to denote multiplicities: s, singlet; d, doublet; dd, double-doublet; ddd, double-double-doublet; t, triplet; q, quartet; dq, double-quartet; quint, quintuplet; m, multiplet; br, broad; app, apparent. Second order spin systems are described using standard nomenclature. Infra-red spectra were recorded on a Perkin-Elmer 1750 FT IR spectrophotometer and peaks are given in cm^{-1}. Mass spectra were recorded on a VG platform (atmospheric pressure chemical ionisation [APCI] in a solvent mixture

MeOH/H_2O/MeCN, positive or negative ionisation as stated) or a VG 20–250 spectrometer (chemical ionisation [CI NH_3] as stated). Optical rotations were measured on a Perkin-Elmer 241 polarimeter with a path length of 1 dm. Concentrations (*c*) are given in g/100 ml. Microanalyses were performed in duplicate by the microanalysis service of the Inorganic Chemistry Laboratory (Oxford). Melting points (mp) were measured on a Leica Galen III apparatus and are uncorrected. Thin layer chromatography (TLC) was carried out on aluminium sheets coated with $60F_{254}$ silica from Merck, and plates were developed using a spray of vanillin (8 g l^{-1}) in 95% ethanol containing 1% (v/v) sulfuric acid, and subsequent heating. Flash chromatography was carried out using Sorbsil C60 40/60 silica. Solvents and commercially available reagents were dried and purified before use according to standard procedures.

4.1 2-[4′-Deoxy-4′-(dodecanoylglycyl)amino-β-L-rhamnopyranosylamino)pyridine 2b

Azide **8b** (20 mg, 0.075 mmol) was dissolved in 5 ml methanol and 1 ml water. 10 mg 10% palladium on charcoal was added and the mixture was stirred at room temperature under an atmosphere of hydrogen. After 40 min, TLC showed no starting material. Reaction mixture was filtered through Celite and evaporated to dryness. The residue was dissolved in 1.5 ml dry DMF with *N*-hydroxybenzotriazole monohydrate (HOBT) (17 mg, 0.111 mmol), dodecanoylglycine (21 mg, 0.082 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (29 mg, 0.151 mmol). The mixture was stirred overnight and evaporated *in vacuo*. The residue was purified by flash chromatography on silica (CH_2Cl_2/MeOH 9 : 1 to 8 : 2) then a preparative TLC (CH_2Cl_2/MeOH 3 : 1) to afford the title compound (26 mg, 72%) as a white solid. R_f 0.15 (CH_2Cl_2/MeOH 9 : 1); mp (MeOH) 182–184 °C; $[\alpha]_D^{22}$ +39.2 (*c* = 0.475, pyridine); δ_H (pyridine d_5, 400 MHz) 8.78 (d, 1H, *J* = 9.8 Hz, CONHCH$_2$CON*H*), 8.69 (t, 1H, *J* = 5.4 Hz, CON*H*CH$_2$-CONH), 8.06 (dd, 1H, *J* = 1.9, 5.1 Hz, H-5), 7.20 (ddd, 1H, *J* = 1.9, 7.1, 8.4 Hz, H-3), 7.05 (d, 1H, *J* = 9.9 Hz, NH-pyridyl), 6.61 (d, 1H, *J* = 8.4 Hz, H-2), 6.40 (ddd, 1H, *J* = 0.7, 5.1, 7.1 Hz, H-4), 5.61 (d, 1H, *J* = 9.9 Hz, H-1′), 4.63 (app. q, 1H, *J* = 9.8 Hz, H-4′), 4.26 (d, 1H, *J* = 3.2 Hz, H-2′), 4.22 (ABX, 1H, *J* = 5.6, 16.1 Hz, CONHC*H*$_2$CONH), 4.12 (ABX, 1H, *J* = 5.4, 16.1 Hz, CONHC*H*$_2$CONH), 4.08 (dd, 1H, *J* = 3.2, 9.8 Hz, H-3′), 3.71 (qd, 1H, *J* = 6.1, 9.8 Hz, H-5′), 2.18 (t, 2H, *J* = 7.5 Hz, CH$_2$C*H*$_2$CONH), 1.56 (app quint, 2H, *J* = 7.5 Hz, C*H*$_2$CH$_2$CONH), 1.29 (d, 3H, *J* = 6.1 Hz, H-6′), 1.14–0.92 (m, 16H, CH_2 fatty chain), 0.66–0.61 (m, 3H, CH_3 fatty chain); δ_C (pyridine d_5, 100 MHz) 174.1 (*C*ONHCH$_2$CONH), 171.3 (CONHCH$_2$*C*ONH), 158.7 (C-1), 148.8 (C-5), 137.9 (C-3), 114.5 (C-4), 109.4 (C-2), 81.1 (C-1′), 74.0 (C-3′), 73.7 (C-5′), 72.4 (C-2′), 55.0 (C-4′), 44.2 (CONH*C*H$_2$CONH), 36.7 (CH$_2$-*C*H$_2$CONH), 32.4, 30.20, 30.16, 30.10, 30.04, 29.97 (6s, CH_2 fatty chain), 26.5 (*C*H$_2$CH$_2$CONH), 23.3 (CH_2 fatty chain), 19.2 (C-6′), 14.6 (CH_3 fatty chain); IR (KBr) 3421 (free ν_{OH}), 3309 (br, ν_{NH}, ν_{OH}), 2923, 2851, 1651, 1639 (ν_{CO} amide), 1606, 1575, 1524, 1445, 1398, 1323, 1264, 1194, 1155, 1087, 1064, 1015, 971, 770; *m/z* (APCI+) 137 [2-aminopyridine + Ac]$^+$ (100%), 479 [M + H]$^+$ (31%); *m/z* (APCI−) 297 (100%), 477 [M − H]$^-$ (66%); HRMS (CI NH_3) *m/z* 479.3227 [M + H]$^+$ (calcd. for $C_{25}H_{43}N_4O_5$ *m/z* 479.3233).

4.2 2-[4′-Deoxy-4′-(dodecanoylglycyl)amino-β-L-rhamnopyranosylamino)pyrimidine 2c

Following the same procedure as described above for **2b**, the title compound was obtained in 71% yield (29 mg, 0.060 mmol) as a white solid starting from **8c** (22.5 mg, 0.085 mmol). R_f 0.10 (CH_2Cl_2/MeOH 9 : 1); mp (MeOH) 187–189 °C; $[\alpha]_D^{24}$ +24.7 (*c* = 0.15, pyridine); δ_H (pyridine d_5, 400 MHz) 8.79 (d, 1H, *J* = 9.8 Hz, CONHCH$_2$CON*H*), 8.69 (t, 1H, *J* = 5.4 Hz, CON*H*CH$_2$CONH), 8.16 (d, 2H, *J* = 4.8 Hz, H-3), 7.57 (d, 1H, *J* = 9.9 Hz, N*H*-pyrimidine), 6.31 (t, 1H, *J* = 4.8 Hz, H-4), 5.77 (dd, 1H, *J* = 1.0, 9.9 Hz, H-1′), 4.64 (app. q, 1H, *J* = 9.8 Hz, H-4′), 4.27 (dd, 1H, *J* = 1.0, 3.2 Hz, H-2′), 4.22 (*A*BX, 1H, *J* = 5.6, 16.2 Hz, NHC*H*$_2$CO), 4.12 (A*B*X, 1H, *J* = 5.4, 16.2 Hz, NHC*H*$_2$CO), 4.09 (dd, 1H, *J* = 3.2, 9.8 Hz, H-3′), 3.72 (qd, 1H, *J* = 6.0, 9.8 Hz, H-5′), 2.40 (t, 2H, *J* = 7.5 Hz, CH$_2$C*H*$_2$CO), 1.56 (app quint, 2H, *J* = 7.5 Hz, C*H*$_2$CH$_2$CO), 1.29 (d, 3H, *J* = 6.0 Hz, H-6′), 1.13–0.94 (m, 16H, CH_2 fatty chain), 0.67–0.61 (m, 3H, CH_3 fatty chain); δ_C (pyridine d_5, 100 MHz) 174.2 (*C*ONHCH$_2$CONH), 171.4 (CONHCH$_2$*C*ONH), 162.8 (C-1), 158.9 (br s, C-3), 112.7 (C-4), 81.0 (C-1′), 74.01, 73.95 (C-3′, C-5′), 72.3 (C-2′), 54.9 (C-4′), 44.2 (CONH*C*H$_2$CONH), 36.8 (CH$_2$*C*H$_2$CONH), 32.48, 30.27, 30.23, 30.17, 30.11, 30.04 (6s, CH_2 fatty chain), 26.5 (*C*H$_2$CH$_2$CONH), 23.3 (CH_2 fatty chain), 19.2 (C-6′), 14.7 (CH_3 fatty chain); IR (KBr) 3430 (free ν_{OH}), 3410, 3305 (br, bonded ν_{OH}), 2922, 2850, 1657, 1639, 1594, 1576, 1539, 1525, 1457, 1261, 1190, 1093, 1064, 1015, 976, 893, 800, 627; *m/z* (APCI+) 138 [2-aminopyrimidine + Ac]$^+$ (100%), 480 [M + H]$^+$ (97%); *m/z* (APCI−) 514 : 516 [M + Cl]$^-$ (3 : 1, 100%); HRMS (CI NH_3) *m/z* 480.3183 [M + H]$^+$ (calcd. for $C_{24}H_{42}N_5O_5$ *m/z* 480.3186).

4.3 6-[4′-Deoxy-4′-(dodecanoylglycyl)amino-β-L-rhamnopyranosylamino)-9*H*-purine 2d

Following the same procedure as described above for **2b**, the title compound was obtained in 60% yield (47 mg, 0.090 mmol) as a white solid starting from **8d** (41 mg, 0.147 mmol). The hydrogenation step was carried out in 12 ml methanol and 2 ml water. Analyses were fully consistent with data previously reported.[19,22]

4.4 9-Benzyl-6-[4′-deoxy-4′-(dodecanoylglycyl)amino-β-L-rhamnopyranosylamino)-9*H*-purine 2e

Following the same procedure as described above for **2b**, the title compound was obtained in 89% yield (27 mg, 0.044 mmol) as a white solid starting from **8e** (20 mg, 0.050 mmol). The hydrogenation step was carried out in 8 ml methanol and 2 ml water and the product was purified by crystallisation in methanol. R_f 0.10 (CH_2Cl_2/MeOH 9 : 1); mp (MeOH) 214–216 °C (dec.); $[\alpha]_D^{24}$ +10.3 (*c* = 0.29, pyridine); δ_H (pyridine d_5, 400 MHz) 8.83 (d, 1H, *J* = 9.3 Hz, CONHCH$_2$CON*H*), 8.71 (app t, 1H, *J* = 5.6 Hz, CON*H*CH$_2$CONH), 8.52 (s, 1H, H-2), 8.08 (s, 1H, H-8), 7.85 (d, 1H, *J* = 7.8 Hz, NH-purine), 7.21–7.02 (m, 5H, Ph), 6.10 (d, 1H, *J* = 7.8 Hz, H-1′), 5.21 (s, 2H, C*H*$_2$Ph), 4.70 (app q, 1H, *J* = 9.3 Hz, H-4′), 4.37 (br s, 1H, H-2′), 4.24 (*A*BX, 1H, *J* = 5.6, 16.1 Hz, NHC*H*$_2$CO), 4.19–4.11 (m, 2H, NHC*H*$_2$CO, H-3′), 3.80 (br s, 1H, H-5′), 2.19 (t, 2H, *J* = 7.5 Hz, CH$_2$C*H*$_2$CONH), 1.57 (app quint, 2H, *J* = 7.5 Hz, C*H*$_2$CH$_2$-CONH), 1.33 (d, 3H, *J* = 5.7 Hz, H-6′), 1.18–0.91 (m, 16H, CH_2 fatty chain), 0.67–0.61 (m, 3H, CH_3 fatty chain); δ_C (pyridine d_5, 100 MHz) 174.6 (*C*ONHCH$_2$CONH), 171.9 (CONH-CH$_2$*C*ONH), 155.2 (br s, C-6), 154.1 (C-2), 151.4 (C-4), 142.4 (br s, C-8), 138.1 (Ph C-1), 130.0 (Ph C-2 or C-3), 129.2 (Ph C-4), 129.0 (Ph C-2 or C-3), 121.5 (br s, C-5), 80.0 (br s, C-1′), 74.7 (C-5′), 74.3 (C-3′), 72.6 (C-2′), 55.3 (C-4′), 47.9 (*C*H$_2$Ph), 44.7 (NH*C*H$_2$CO), 37.3 (CH$_2$*C*H$_2$CONH), 33.0, 30.75, 30.71, 30.64, 30.58, 30.51, 30.43 (7s, CH_2 fatty chain), 27.0 (*C*H$_2$CH$_2$-CONH), 23.8 (CH_2 fatty chain), 19.7 (C-6′), 15.1 (CH_3 fatty chain); IR (KBr) 3392, 3310 (br, ν_{OH}, ν_{NH}), 2924, 2852, 1647, 1624 (ν_{CO} amide), 1588, 1534, 1483, 1458, 1408, 1337, 1292, 1230, 1130, 1091, 1067, 1022, 970, 862, 798, 731, 697, 647; *m/z* (APCI+) 268 [9-benzyladenine + Ac + H]$^+$ (100%), 610 [M + H]$^+$ (9%); *m/z* (APCI−) 255 [dodecanoylglycinamide]$^-$ (33%), 297 (100%), 608 [M − H]$^-$ (37%); HRMS (CI NH_3) *m/z* 610.3690 [M + H]$^+$ (calcd. for $C_{32}H_{48}N_7O_5$ *m/z* 610.3717).

4.5 1-Nitro-4-(β-L-rhamnopyranosylamino)benzene hydrate 6a

L-Rhamnose monohydrate (2.052 g, 11.26 mmol) and *p*-nitroaniline (1.954 g, 14.15 mmol) were suspended in a mixture of

MeOH/H_2O/AcOH 8 : 1 : 4 (6.5 ml). The suspension was heated to reflux for 3 min and allowed to cool to room temperature. Filtration and washing of the solid with absolute ethanol, then ether, afforded the title compound **6a** (3.183 g, 95%) as a bright yellow powder which can be used without purification (microanalysis found C 48.75%, H 5.66%, N 9.30%; $C_{12}H_{16}N_2O_6 \cdot {}^3/_4H_2O$ requires C 48.40%, H 5.92%, N 9.41%). Recrystallisation from methanol/water afforded an analytically pure sample. R_f 0.75 (AcOEt/MeOH 3 : 1); mp (MeOH/H_2O) 214–216 °C (dec.) {lit. 232 °C[28] (MeOH) 208 °C[29]}; $[a]_D^{22}$ +304 (c = 1, pyridine) {lit.[28] +319 in pyridine}; δ_H (DMSO d_6, 400 MHz) 8.01 ($AA'XX'$, 2H, J = 0.3, 2.5, 9.6 Hz, H-3), 7.29 (d, 1H, J = 8.4 Hz, NH), 6.89 ($AA'XX'$, 2H, J = 0.3, 2.5, 9.6 Hz, H-2), 4.97 (d, 1H, J = 5.2 Hz, OH-2′), 4.83–4.80 (m, 3H, H-1′, OH-3′, OH-4′), 3.77–3.74 (m, 1H, H-2′), 3.42–3.35 (m, 1H, H-3′), 3.32–3.25 (m, 1H, H-5′), 3.22–3.15 (m, 1H, H-4′), 1.13 (d, 3H, J = 6.0 Hz, H-6′); δ_C (DMSO d_6, 100 MHz) 153.1 (C-1), 137.3 (C-4), 125.8 (C-3), 112.7 (C-2), 80.6 (C-1′), 73.8 (C-3′), 72.8, 71.8 (C-4′, C-5′), 70.7 (C-2′), 18.0 (C-6′); IR (film) 3325 (br, ν_{OH}, ν_{NH}), 1601, 1535, 1503, 1342, 1274, 1082, 1001, 834, 790, 752; m/z (APCI+) 138 [aniline]$^+$ (33%), 148 [rhamnosyl + H]$^+$ (100%), 284 [M]$^+$ (10%); m/z (APCI−) 179 [aniline + MeCN]$^-$ (100%), 283 [M − H]$^-$ (23%); Microanalysis found C 48.48%, H 5.70%, N 9.40% ($C_{12}H_{16}N_2O_6 \cdot {}^3/_4H_2O$ requires C 48.40%, H 5.92%, N 9.41%).

4.6 2-(β-L-Rhamnopyranosylamino)pyridine 6b

L-Rhamnose monohydrate (1.498 g, 8.22 mmol) and 2-aminopyridine (868 mg, 9.22 mmol) were suspended in a mixture of MeOH/H_2O/AcOH 8 : 1 : 4 (4 ml). The suspension was heated to reflux for 3 min during which solution occurred. A hard gel formed on cooling which was ground in a mortar and washed with absolute ethanol. Recrystallisation from a mixture of acetonitrile/ethanol 1 : 2 afforded the title compound (792 mg, 40%) as white needles. Evaporation of the filtrates and purification of the residue by column chromatography (CH_2Cl_2/MeOH 95 : 5 to 70 : 30) gave an additional amount of **6b** (1.009 g, 51%) as a white solid with a total yield of 91%. R_f 0.30 (CH_2Cl_2/MeOH 85 : 15); mp (EtOH) 201–203 °C (dec.); $[a]_D^{22}$ +132 (c = 1, pyridine); δ_H (DMSO d_6, 400 MHz) 8.01 (dd, 1H, J = 2.0, 5.0 Hz, H-5), 7.44 (ddd, 1H, J = 2.0, 6.8, 8.4 Hz, H-3), 6.67 (dd, 1H, J = 0.4, 8.4 Hz, H-2), 6.60 (ddd, 1H, J = 0.4, 5.0, 6.8 Hz, H-4), 6.39 (d, 1H, J = 8.8 Hz, NH), 5.19 (d, 1H, J = 8.8 Hz, H-1′), 4.93 (d, 1H, J = 4.8 Hz, OH-2′), 4.74 (d, 1H, J = 5.2 Hz, OH-4′), 4.71 (d, 1H, J = 5.6 Hz, OH-3′), 3.71–3.67 (m, 1H, H-2′), 3.39–3.30 (m, 1H, H-3′), 3.22–3.11 (m, 2H, H-4′, H-5′), 1.10 (d, 3H, J = 5.6 Hz, H-6′); δ_C (DMSO d_6, 100 MHz) 157.2 (C-1), 147.5 (C-5), 137.2 (C-3), 113.5 (C-4), 108.6 (C-2), 79.2 (C-1′), 74.2 (C-3′), 72.8, 72.0 (C-4′, C-5′), 71.2 (C-2′), 18.1 (C-6′); IR (KBr) 3398, 3150 (br, ν_{OH}, ν_{NH}), 2974, 2911, 1608, 1572, 1522, 1459, 1445, 1362, 1322, 1284, 1261, 1138, 1086, 1074, 1005, 971, 899, 770, 668; m/z (APCI+) 222 [M − H_2O]$^+$ (30%), 240 [M]$^+$ (100%), 241 [M + H]$^+$ (82%); m/z (APCI−) 135 [2-aminopyridine + MeCN]$^-$ (100%), 239 [M − H]$^-$ (12%); Microanalysis found C 54.92%, H 6.76%, N 11.71% ($C_{11}H_{16}N_2O_4$ requires C 54.99%, H 6.71%, N 11.66%).

4.7 2-(β-L-Rhamnopyranosylamino)pyrimidine 6c

L-Rhamnose monohydrate (1.016 g, 5.577 mmol) and 2-aminopyrimidine (599 mg, 6.30 mmol) were suspended in a mixture of MeOH/H_2O/AcOH 8 : 1 : 4 (3.25 ml). The suspension was heated to reflux for 3.5 hours during which solution occurred. A hard gel formed on cooling which was dissolved in 200 ml hot absolute ethanol and left overnight at 6 °C. The gel was ground in a mortar, filtered and dried *in vacuo* to afford the title compound (1.112 g, 83%) as an amorphous colourless solid. ^{1}H NMR showed no impurity. R_f 0.25 (CH_2Cl_2/MeOH 85 : 15); mp (EtOH) 194–196 °C; $[a]_D^{23}$ +79.1 (c = 1.05, pyridine); δ_H (DMSO d_6, 400 MHz) 8.37 (d, 2H, J = 4.7 Hz, H-3), 6.75 (t, 1H, J = 4.7 Hz, H-4), 6.55 (d, 1H, J = 9.8 Hz, NH), 5.25 (d, 1H, J = 9.8 Hz, H-1′), 5.09 (s, 1H, OH-2′), 4.79 (s, 1H, OH-4′), 4.76 (s, 1H, OH-3′), 3.72 (s, 1H, H-2′), 3.40–3.32 (m, 1H, H-3′), 3.20–3.10 (m, 2H, H-4′, H-5′), 1.11 (d, 3H, J = 5.2 Hz, H-6′); δ_C (DMSO d_6, 125 MHz, 80 °C) 162.0 (C-1), 159.0 (C-3), 113.0 (C-4), 80.2 (C-1′), 75.1 (C-3′), 74.0 (C-5′), 73.0 (C-4′), 71.9 (C-2′), 18.8 (C-6′); IR (KBr) 3446 (br, ν_{OH}, ν_{NH}), 3272 (br, ν_{OH}, ν_{NH}), 2987, 2906, 1588, 1574, 1521, 1456, 1419, 1362, 1320, 1256, 1225, 1190, 1083, 1062, 1020, 967, 906, 858, 804, 789, 700, 652, 630, 525; m/z (APCI+) 137 [2-aminopyrimidine + MeCN + H]$^+$ (100%), 206 [M − $2H_2O$ + H]$^+$ (47%), 224 [M − H_2O + H]$^+$ (40%), 242 [M + H]$^+$ (29%); m/z (APCI−) 136 [2-aminopyrimidine + MeCN]$^-$ (100%), 240 [M − H]$^-$ (82%); HRMS (CI NH_3) m/z 242.1129 [M + H]$^+$ (calcd. for $C_{10}H_{16}N_3O_4$ m/z 242.1141).

4.8 6-(β-L-Rhamnopyranosylamino)-9*H*-purine 6d

L-Rhamnose monohydrate (1.044 g, 5.73 mmol) and adenine (1.262 g, 9.34 mmol) were suspended in a mixture of MeOH/H_2O/AcOH 10 : 0.6 : 4 (14 ml). The suspension was heated to reflux for 6 days, then evaporated to dryness. Purification by repeated flash chromatography on silica (AcOEt/MeOH 1 : 0 to 1 : 1) afforded L-rhamnose (295 mg, 1.80 mmol) and the title compound (161 mg, 15% based on recovered starting material) as a white powder. A sample was recrystallised from isopropanol for analytical purposes. R_f 0.15 (AcOEt/MeOH 3 : 1); mp (iPrOH) 178–180 °C; $[a]_D^{23}$ +45.3 (c = 0.258, pyridine); δ_H (DMSO d_6, 500 MHz, 80 °C) 8.28 (s, 1H, H-2), 8.13 (s, 1H, H-8), 6.86 (d, 1H, J = 8.5 Hz, C6-NH), 5.72 (d, 1H, J = 8.5 Hz, H-1′), 3.83 (d, 1H, J = 3.0 Hz, H-2′), 3.46 (dd, 1H, J = 3.0, 9.5 Hz, H-3′), 3.32–3.21 (m, 2H, H-4′, H-5′), 1.16 (d, 3H, J = 6.0 Hz, H-6′); δ_C (DMSO d_6, 125 MHz, 80 °C) 153.4, 153.3 (C-4, C-6), 152.9 (C-2), 141.5 (C-8), 118.7 (C-5), 79.3 (C-1′), 75.1 (C-3′), 74.1 (C-5′), 72.9 (C-4′), 71.8 (C-2′), 18.8 (C-6′); IR (KBr) 3368 (br, ν_{OH}, ν_{NH}), 2989, 2921, 2852, 1617 (br), 1521, 1457, 1401, 1327, 1244, 1146, 1082, 1062, 1013, 969, 945, 900, 797, 758, 694, 640, 621; m/z (APCI+) 136 [adenine + H]$^+$ (39%), 178 (100%), 282 [M + H]$^+$ (87%); m/z (APCI−) 134 [adenyl]$^-$ (23%), 176 [adenine + MeCN]$^-$ (100%), 280 [M − H]$^-$ (16%); HRMS (CI NH_3) m/z found 282.1206 [M + H]$^+$ (calcd. for $C_{11}H_{16}N_5O_4$ m/z 282.1202).

4.9 1-(4′-Deoxy-4′-azido-β-L-rhamnopyranosylamino)-4-nitrobenzene 8a

4-Azido-4-deoxy-L-rhamnose[19] **7** (298 mg, 1.58 mmol) and *p*-nitroaniline (322 mg, 2.33 mmol) were dissolved in a mixture of MeOH/H_2O/AcOH 8 : 1 : 4 (1 ml). The solution was heated to reflux for 12 hours. The reaction mixture was evaporated to dryness and purified by flash chromatography on silica (hexane/AcOEt 1 : 1) to afford the title compound (421 mg, 86%) as a bright yellow solid. A sample was recrystallised from isopropanol for analytical purposes. R_f 0.25 (hexane/AcOEt 1 : 1); mp (iPrOH) 191–192 °C (dec.); $[a]_D^{22}$ +246 (c = 1, pyridine); δ_H (DMSO d_6, 400 MHz) 8.01 ($AA'XX'$, 2H, J = 0.3, 2.5, 9.6 Hz, H-3), 7.33 (d, 1H, J = 8.8 Hz, NH), 6.90 ($AA'XX'$, 2H, J = 0.3, 2.5, 9.6 Hz, H-2), 5.51 (d, 1H, J = 6.6 Hz, OH-3′), 5.27 (d, 1H, 5.7 Hz, OH-2′), 4.91 (d, 1H, J = 8.8 Hz, H-1′), 3.77 (dd, 1H, J = 3.2, 5.7 Hz, H-2′), 3.65 (ddd, 1H, J = 3.2, 6.6, 9.8 Hz, H-3′), 3.42–3.33 (m, 1H, H-5′), 3.28 (app t, J = 9.8 Hz, H-4′), 1.17 (d, 3H, J = 6.0 Hz, H-6′); δ_C (DMSO d_6, 100 MHz) 153.7 (C-1), 138.4 (C-4), 126.6 (C-3), 113.6 (C-2), 81.3 (C-1′), 73.7 (C-3′), 71.4 (C-2′), 71.1 (C-5′), 65.7 (C-4′), 19.4 (C-6′); IR (film) 3332 (br, ν_{OH}, ν_{NH}), 2912, 2465, 2114 (N_3), 1604, 1534, 1502, 1489, 1348, 1330, 1298, 1277, 1182, 1115, 1057, 1002, 912, 832, 785, 751; m/z (APCI+) 139 [*p*-nitroaniline + H]$^+$ (100%), 310 [M + H]$^+$ (42%); m/z (APCI−) 137 [*p*-nitroaniline − H]$^-$ (23%), 179 [*p*-nitroaniline + MeCN]$^-$ (100%), 308 [M − H]$^-$ (38%); HRMS (CI NH_3 −ve) m/z found 308.0995 [M − H]$^-$ (calcd. for $C_{12}H_{15}N_5O_5$ m/z 308.0995).

4.10 2-(4′-Deoxy-4′-azido-β-L-rhamnopyranosylamino)-pyridine 8b

Following the same procedure as for **8a** with **7** (303 mg, 1.60 mmol) and 2-aminopyridine (239 mg, 2.54 mmol) the title compound was obtained (208 mg, 61% based on recovered starting material) as a white solid along with 61 mg (0.32 mmol) of the starting carbohydrate after flash chromatography on silica (AcOEt). A sample was recrystallised from isopropanol for analytical purposes. R_f 0.30 (AcOEt); mp (iPrOH) 178–180 °C; $[\alpha]_D^{22}$ +60.8 (c = 1.01, pyridine); δ_H (DMSO d_6, 500 MHz, 80 °C) 8.01 (ddd, 1H, J = 0.5, 1.5, 6.0 Hz, H-5), 7.46 (ddd, 1H, J = 1.5, 7.5, 8.5 Hz, H-3), 6.70 (ddd, 1H, J = 0.5, 1.0, 8.5 Hz, H-2), 6.62 (ddd, 1H, J = 1.0, 6.0, 7.5 Hz, H-4), 6.25 (d, 1H, J = 9.5 Hz, NH), 5.22 (dd, 1H, J = 1.0, 9.5 Hz, H-1′), 5.05 (d, 1H, J = 6.5 Hz, OH-3′), 4.94 (d, 1H, J = 5.0 Hz, OH-2′), 3.79–3.77 (m, 1H, H-2′), 3.66 (ddd, 1H, J = 3.0, 6.5, 9.5 Hz, H-3′), 3.32–3.23 (m, 2H, H-4′, H-5′), 1.19 (d, 3H, J = 6.0 Hz, H-6′); δ_C (DMSO d_6, 100 MHz) 157.1 (C-1), 147.5 (C-5), 137.3 (C-3), 113.7 (C-4), 108.8 (C-2), 79.1 (C-1′), 73.1 (C-3′), 0.7 (C-2′), 70.6 (C-5′), 65.1 (C-4′), 18.6 (C-6′); IR (KBr) 3476 (br, ν_{OH}, ν_{NH}), 2418, 3081, 2940, 2907, 2875, 2715, 2126 ($\nu_{N=N=N}$), 1610, 1574, 1516, 1444, 1386, 1317, 1301, 1279, 1226, 1196, 1159, 1100, 1083, 1066, 1014, 968, 911, 878, 845, 774, 739, 646, 620, 593, 555, 510; m/z (APCI+) 137 (100%), 266 [M + H]$^+$ (48%); m/z (APCI−) 135 [2-aminopyridine + MeCN]$^-$ (100%), 264 [M − H]$^-$ (67%); HRMS (CI NH_3) m/z 266.1254 [M + H]$^+$ (calcd. for $C_{11}H_{16}N_5O_3$ m/z 266.1253).

4.11 2-(4′-Azido-4′-deoxy-β-L-rhamnopyranosylamino)-pyrimidine 8c

4-Azido-4-deoxy-L-rhamnose[19] **7** (297 mg, 1.57 mmol) and 2-aminopyrimidine (234 mg, 2.46 mmol) were dissolved in a mixture of MeOH/H_2O/AcOH 9.8 : 0.2 : 4 (1 ml). The solution was heated at reflux for 24 hours. The reaction mixture was evaporated to dryness and purified by flash chromatography on silica (hexane/AcOEt 1 : 1 to 0 : 1) to afford the title compound (287 mg, 83% based on recovered starting material) as a white solid along with 50.5 mg (0.27 mmol) of the starting lactol. A sample was recrystallised from methanol for analytical purposes. R_f 0.50 (AcOEt); mp (MeOH) 162 °C; $[\alpha]_D^{24}$ +14.2 (c = 1.165, pyridine); δ_H (DMSO d_6, 500 MHz) 8.38 (d, 2H, J = 5.0 Hz, H-3), 6.77 (t, 1H, J = 5.0 Hz, H-4), 6.60 (d, 1H, J = 9.5 Hz, NH), 5.40 (d, 1H, J = 7.0 Hz, OH-3′), 5.36 (d, 1H, J = 5.5 Hz, OH-2′), 5.30 (dd, 1H, J = 1.0, 9.5 Hz, H-1′), 3.76–3.73 (m, 1H, H-2′), 3.66 (ddd, 1H, J = 3.5, 7.0, 10.0 Hz, H-3′), 3.28–3.19 (m, 2H, H-4′, H-5′), 1.15 (d, 3H, J = 5.5 Hz, H-6′); δ_C (DMSO d_6, 100 MHz) 160.8 (C-1), 158.3 (C-3), 112.4 (C-4), 79.0 (C-1′), 72.8 (C-3′), 70.8 (C-2′), 70.4 (C-5′), 64.9 (C-4′), 18.6 (C-6′); IR (KBr) 3419 (free ν_{OH}), 3346 (br, ν_{OH}, ν_{NH}), 3206 (br, ν_{OH}, ν_{NH}), 2908, 2877, 2115 ($\nu_{N=N=N}$), 1673, 1595, 1573, 1516, 1450, 1390, 1363, 1337, 1280, 1250, 1192, 1148, 1090, 1079, 1063, 1015, 969, 906, 857, 803, 790, 722, 609, 564; m/z (APCI+) 138 [2-aminopyridyl + Ac + H]$^+$ (100%), 267 [M + H]$^+$ (61%); m/z (APCI−) 136 [2-aminopyridyl + Ac − H]$^-$ (100%), 265 [M − H]$^-$ (100%); HRMS (CI NH_3) m/z 267.1199 [M + H]$^+$ (calcd. for $C_{10}H_{15}N_6O_3$ m/z 267.1206).

4.12 6-(4′-Deoxy-4′-azido-β-L-rhamnopyranosylamino)-9*H*-purine 8d

4-Azido-4-deoxy-L-rhamnose[19] **7** (295 mg, 1.56 mmol) and adenine (420 mg, 3.11 mmol) were suspended in a mixture of MeOH/H_2O/AcOH 8 : 1 : 4 (1 ml) in a pressure tube. The solution was heated to 120 °C for 2 hours then 100 °C for 46 hours. The reaction mixture was filtered and the solid washed with methanol. Filtrate was evaporated to dryness and purified by flash chromatography on silica (AcOEt/MeOH 1 : 0 to 8 : 2) to afford the title compound (50 mg, 16% based on recovered starting material) as a white solid along with 97 mg (0.51 mmol) of the starting lactol. ^{1}H NMR showed the presence of 5% of adenine as a contaminant. R_f 0.30 (AcOEt/MeOH 3 : 1); mp (EtOH) 262–263 °C (dec.); δ_H (DMSO d_6, 500 MHz, 80 °C) 8.29 (s, 1H, H-2), 8.15 (s, 1H, H-8), 6.92 (d, 1H, J = 8.5 Hz, C6-NH), 5.73 (d, 1H, J = 8.5 Hz, H-1′), 3.85 (dd, 1H, J = 1.0, 3.5 Hz, H-2′), 3.72 (dd, 1H, J = 3.5, 9.5 Hz, H-3′), 3.38–3.27 (m, 2H, H-4′, H-5′), 1.20 (d, 3H, J = 6.0 Hz, H-6′); δ_C (DMSO d_6, 125 MHz, 80 °C) 153.3, 153.2 (C-4, C-6), 152.9 (C-2), 141.5 (C-8), 118.6 (C-5), 79.4 (brs, C-1′), 73.7 (C-3′), 72.0 (C-5′), 71.3 (C-2′), 66.0 (C-4′), 19.3 (C-6′); m/z (APCI+) 178 [adenyl + Ac + H]$^+$ (100%), 307 [M + H]$^+$ (47%); m/z (APCI−) 176 [adenyl + Ac − H]$^-$ (100%), 305 [M − H]$^-$ (38%); HRMS (CI NH_3) m/z 307.1259 [M + H]$^+$ (calcd. for $C_{11}H_{15}N_8O_3$ m/z 307.1267).

4.13 9-Benzyl-6-(4′-deoxy-4′-azido-β-L-rhamnopyranosylamino)-9*H*-purine 8e

Following the same procedure as for **8a** with **7** (304 mg, 1.61 mmol) and 9-benzyladenine **10e** (500 mg, 2.22 mmol) the title compound was obtained (125 mg, 43% based on recovered starting material) as a white solid along with 167 mg (0.88 mmol) of the starting carbohydrate after flash chromatography on silica (AcOEt/MeOH 100 : 0 to 93 : 7). A sample was recrystallised from ethanol for analytical purposes. R_f 0.55 (AcOEt/MeOH 9 : 1); mp (EtOH) 225–226 °C; $[\alpha]_D^{22}$ +8.02 (c = 1.035, pyridine); δ_H (DMSO d_6, 500 MHz, 80 °C) 8.35 (s, 1H, H-8), 8.30 (s, 1H, H-2), 7.36–7.27 (m, 5H, Ph), 6.91 (d, 1H, J = 9.5 Hz, NH), 5.75 (brd, 1H, J = 9.5 Hz, H-1′), 5.43 (s, 2H, CH_2Ph), 5.31 (d, 1H, J = 4.5 Hz, OH-2′), 5.15 (d, 1H, J = 7.0 Hz, OH-3′), 3.88–3.86 (m, 1H, H-2′), 3.73 (ddd, 1H, J = 3.0, 7.0, 9.5 Hz, H-3′), 3.39–3.28 (m, 2H, H-4′, H-5′), 1.20 (d, 3H, J = 6.0 Hz, H-6′); δ_C (DMSO d_6, 125 MHz, 80 °C) 154.2 (C-6), 153.2 (C-2), 151.1 (C-4), 142.9 (C-8), 137.7 (Ph C-1), 129.5 (Ph C-2 or C-3), 128.6 (Ph C-4), 128.4 (Ph C-2 or C-3), 120.2 (C-5), 79.4 (C-1′), 73.7 (C-3′), 72.0 (C-5′), 71.3 (C-2′), 66.0 (C-4′), 47.3 (CH_2Ph), 19.3 (C-6′); IR (KBr) 3430, 3320 (br, ν_{OH}, ν_{NH}), 2993, 2900, 2109 ($\nu_{N=N=N}$), 1616, 1588, 1480, 1456, 1432, 1407, 1350, 1287, 1268, 1229, 1128, 1077, 1017, 963, 908, 866, 798, 732, 695, 644, 554, 512; m/z (APCI+) 226 [9-benzyladenine + H]$^+$ (58%), 268 [9-benzyladenine + Ac + H]$^+$ (100%), 397 [M + H]$^+$ (49%); m/z (APCI−) 266 [9-benzyladenine + Ac − H]$^-$ (100%), 395 [M − H]$^-$ (6%); HRMS (CI NH_3) m/z 397.1740 [M + H]$^+$ (calcd. for $C_{18}H_{20}N_8O_3$ m/z 397.1737).

4.14 Benzyladenine 10e

This compound was prepared according to a literature procedure.[30] In our hands however, the ratio of 3-/9-isomer was never better than 2 : 1 and only 14% of 9-benzyladenine **10e** could be crystallized as fine white needles. Analyses were consistent with data from the literature.[30,31]

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