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Original article

Syntheses and immunomodulatory activity of 3-*O*-[2′-hydroxy-3′-*N*,*N*-disubstituted aminopropan-1′-yl]-α-D-glucofuranoses☆

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Abstract – A number of 3-*O*-[2′-hydroxy-3′-*N*,*N*-aminopropan-1′-yl]-α-D-glucofuranoses were synthesised by regioselective oxirane ring opening in compound **2** with different secondary amines followed by selective deacetalisation. All the compounds were tested for their immunomodulatory potential in vitro; seven of them expressed significant immunostimulant activity. © 2001 Éditions scientifiques et médicales Elsevier SAS

immunomodulation / glucofuranoses / allofuranoses

1. Introduction

The intricate modulatory interactions between various components of the immune system are of paramount importance in providing protection against pathogens and resulting pathogenic condition [1]. Consequently major efforts were devoted to develop drugs that can modulate the immune system in a beneficial manner.

A large number of compounds with diverse chemical structure and molecular weight are reported to be effective immunomodulators [2]. In most of the infectious diseases, the immune system is down regulated and the body is prone to many opportunistic infections; the HIV infection (AIDS) being the glaring example of such a case. Therefore, the need to develop nontoxic and site-specific immunomodulators is greatly felt. Low molecular weight sugar derivatives with aminoalkyl appendages are known as potent immunomodulators [3, 4]. One such compound, therafectin (**1**), a candidate drug for the treatment of rheumatoid arthritis, and its analogues are known to be associated with antifungal [5], antiparasitic [6], antiviral [7, 8] and various other biological activities [9, 10]. In continuation of our work on aminoalkyl derivatives of sugars we have synthesised β-hydroxy aminopropyl ether derivatives of 1,2-*O*-isoproylidene-α-D-glucofuranoses and evaluated them for their immunomodulatory activities. Introduction of β-hydroxy functionality in the side chain increases the water solubility and at the same time provides one more binding site in the molecule.

2. Chemistry

The syntheses of compounds starts with diacetone-α-D-glucose (**1a**) [11] which on reaction with racemic epichlorohydrin in organic or aq. medium at room temperature in the presence of tetrabutyl ammonium-bromide gave the corresponding 3-*O*-[2′(*R*/*S*)-3′-epoxypropan-1′-yl] derivative (**2**) in quantitative yield. The compound **2** on regioselective oxirane ring opening with secondary amines, viz. dimethyl-, diethyl-, di-isopropylamines, pyrrolidine, piperidine, *N*,*N*-dicy-

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clohexyl amine, 1-methyl piperazine, morpholine and 1-[2-pyridyl] piperazine in refluxing methanol gave the corresponding products (**3**–**11**) as a 1:1 diastereoisomeric mixture in moderate to good yield. The characteristic H-1 and H-2 in **3** appeared as doublets at 5.90 and 4.56, respectively, besides other usual signals. Compounds **3**–**11** on selective deacetalisation of 5,6-*O*-isopropylidene with aq. HCl (3%) at room temperature afforded the corresponding (2′*R*/*S*)-1,2-*O*-isopropylidene-3-*O*-[2′-hydroxy-3′-(*N*-amino-propan-1′-yl]-α-D-glucofuranose derivatives (**12**–**20**) as a (1:1) diastereoisomeric mixture in good yield (*figure 1*). The structures of all the compounds were determined on the basis of spectroscopic data and elemental analysis. The allofuranose analogue of compound **20** was prepared by reaction of diacetone-α-D-allofuranose (**21**) [12] with racemic epichlorohydrin to give the intermediate (2′*R*/*S*)-*O*-[2′,3′-epoxypropan-1′-yl]-α-D-allofuranose (**22**), which on oxirane ring opening with pyridyl piperazine gave compound **23**, the latter on selective deacetalisation with aq. HCl furnished the corresponding allofuranose derivative (**24**) (*figure 2*).

The syntheses of pure diastereoisomers of compound **20** were carried out by reacting alcohol **1a** with (*S*-) and (*R*-)-epichlorohydrins separately to afford the corresponding compounds 3-*O*-[(2′*S*), 3′-epoxypropan-1′-yl]-and 3-*O*-[(2′*R*), 3′-epoxypropan-1′-yl]-α-D-glucofuranose derivatives **25** and **26**, respectively, in good yield (*figure 3*). The latter on

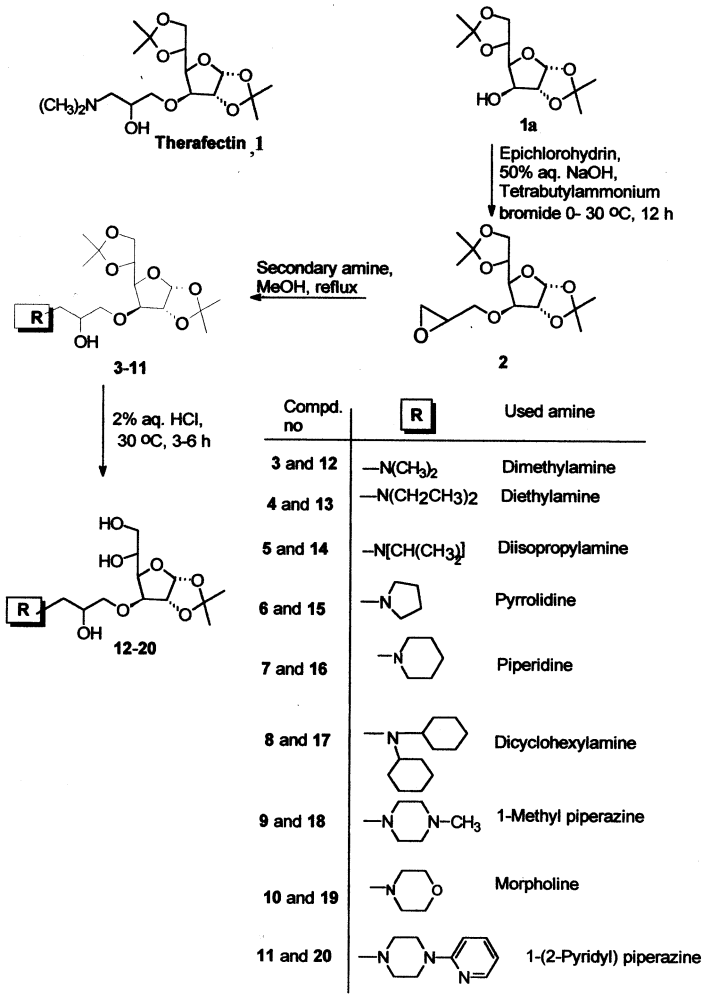

Figure 1. Syntheses of 3-*O*-[2′-hydroxy-*N*,*N*-disubstituted aminopropan-1′-yl]-α-D-glucofuranoses.

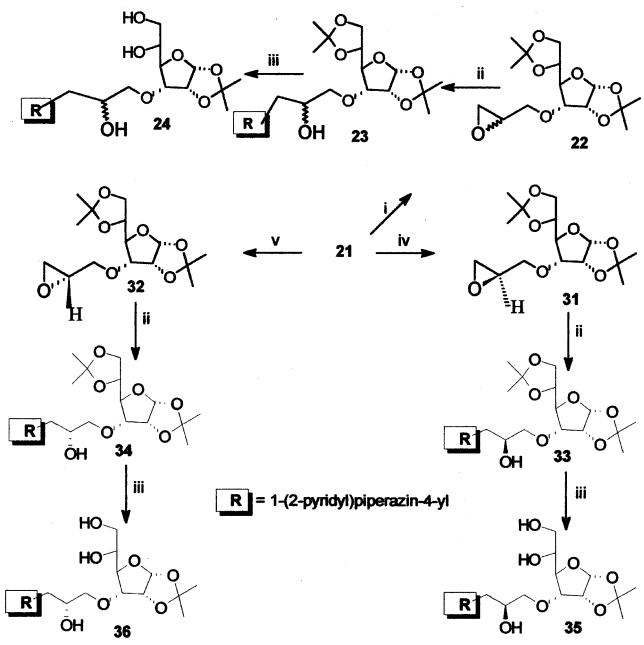

Figure 2. Reagents and conditions: (i) racemic epichlorohydrin, 50% aq. NaOH, tetrabutyl ammonium bromide 0–30°C, 12 h; (ii) 1-(2-pyridyl) piperazine, methanol, reflux; (iii) 3% aq. HC, 30°C, 6 h; and (iv) (*S*)-epichlorohydrin, 50% aq. NaOH, tetrabutyl ammonium bromide 30°C, 6 h (*R*)-epichlorohydrin, 50% aq. NaOH, tetrabutyl ammonium bromide.

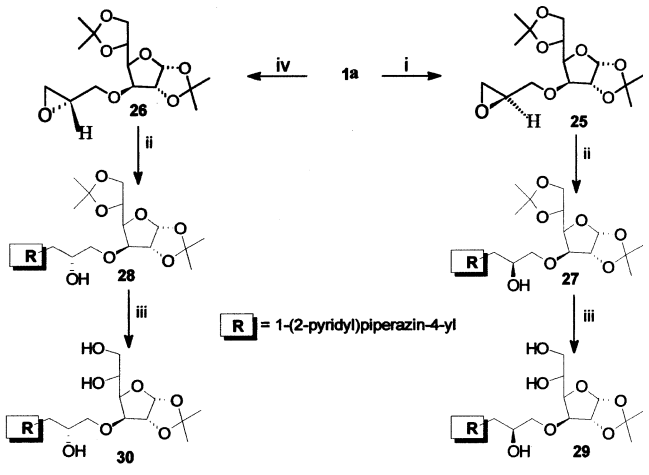

Figure 3. Reagents and conditions: (i) (*S*)-epichlorohydrin, 50% aq. NaOH, tetrabutyl ammonium bromide; (ii) 1-(2-pyridyl) piperazine, methanol, reflux; (iii) 3% aq. HCl 30°C, 6 h; and (iv) (*R*)-epichlorohydrin, 50% aq. NaOH, tetrabutyl ammonium bromide.

oxirane ring opening with 1-(2-pyridyl) piperazine in refluxing methanol gave the corresponding 3-*O*-[(2′*S*)- and (2′*R*)-β-hydroxy-3′-{1-(2-pyridyl) piperazin-4-yl}]-α-D-glucofuranose derivatives **27** and **28**, respectively, in good yield. The above compounds, on selective deacetalisation, gave the desired pure diastereoisomers **29** and **30** in fair yield. The pure diastereoisomers of compound **24** could be obtained by the reaction of allofuranose derivative (**21**) with (*S*)- and (*R*)-epichlorohydrins separately to give the corresponding 3-*O*-[(2′*S*- and 2′*R*)-3′-epoxypropan-1′-yl]-α-D-allofuranose derivatives **31** and **32**, respectively. The latter on oxirane ring opening with 1-(2-pyridyl) piperazine followed by selective deacetalisation of 5,6-acetal in the intermediate compounds **33** and **34** afforded, respectively, the required pure diastereoisomers **35** and **36** in good yield (*figure 2*).

3. Immunomodulatory activity

The immunomodulatory activity was assessed by examining the effect of these compounds on mitogen-induced lymphocyte proliferation (lymphocyte transformation test, LTT) and mixed lymphocyte reaction (MLR). For MLR splenocytes prepared from two genetically different strains of mice (Swiss and Fawn of both sexes, weighing 20–30 g) were co-cultured in a 96-well flat bottom plate in the presence of RPMI-1640 medium containing foetal calf serum (10%), glutamine (2 mM), HEPES (10 mM), streptomycin (100 U mL^{-1}), penicillin (100 μg mL^{-1}) and gentamycin (40 μg mL^{-1}).

The compounds were added to the wells in 50, 10 and 1 μg mL^{-1} final concentrations in a total volume of 200 μL, and three wells were used for each concentration. The plate was placed in a humid CO_2 incubator maintained at 37°C. After 72 h, each well was pulsed with 0.5 μCi of [^{3}H]-thymidine and the plate was returned to the incubator. The cells, after 18 h, were harvested on to glass fibre filters employing a PHD cell harvester (Cambridge). Thymidine incorporated into the DNA was measured by liquid scintillation spectrometry.

For LTT, on the other hand, splenocytes obtained from Swiss mouse only were cultured with or without test compounds exactly as described for MLR. In this case, however, concanavalin-A (con-A) at a subopti-

mal concentration of 0.2 μg mL^{-1} was used as a mitogen.

The results have been expressed as transformation index (TI), which represents the ratio of thymidine incorporation by splenocytes in presence of the compound to that in the control (i.e. no drug).

4. Results and discussion

The results of the various compounds on LTT and MLR are given in *table I*. It is quite clear that compounds other than **3**–**6**, **10**, **15**, **18**, **19** and **24** registered immunomodulatory activity at one or the other concentration. However, taking a stimulation index (SI) of 2.0 as a cut point only seven compounds, i.e. **12**–**14**, **16**, **20**, **29** and **30** qualify the criteria of being good immunostimulants. On careful examination of the result it becomes clear that in general deacetalisation of 5,6-*O*-isopropylidene group yields better immunostimulants. The immune response varies with the nature of the substituted amine in the appended β-hydroxy aminopropyl side chain at the 3-*O*- position of the glucofuranose derivatives. The side chain having one to two carbon flexible aminoalkyl chains offers good immunostimulation (compounds **12**–**14**). However, restricting the flexibility of amine substituent in compound **13** results in the loss of immunostimulatory activity, as is evident from the observation that the compounds having pyrrolidine (**15**) and *N*-methyl piperazine (**19**) as terminal amine substituent virtually produce no immunostimulation. However, release of strain by introducing an extra –CH_2 unit, piperidine (**16**) gave better immunostimulation. The replacement of alkyl amines with an amine having hydrophobic as well as polar character such as 1-(2-pyridylpiperazine (**30**) elicit the best immunostimulant response in the series. Further change in configuration at C-3 from -(gluco) to α-(allo) in compound **20** results in drastic loss of the activity (compound **24**). That the inactivity is not due to the antagonistic effect of individual diastereoisomers has also been ruled out, as even the individual diastereoisomers **35** and **36** did not exhibit any significant immunostimulation. Contrary to the configuration at C-3, the immunomodulatory activity is

Table I. Effect of compounds **3**–**20**, **24**, **29**, **30** **35** and **36** on lymphocyte proliferation (LTT) and mixed lymphocyte reaction (MLR)

Compd. No.	LTT (μg mL^{-1})			MLR (μg mL^{-1})		
	50	10	1	1	50	10
3	ND	1.14 ± 0.26	0.90 ± 0.21	0.83 ± 0.10	1.18 ± 0.24	1.39 ± 0.44
4	ND	1.06 ± 0.14	1.11 ± 0.19	0.85 ± 0.12	1.33 ± 0.21	1.32 ± 0.31
5	ND	1.14 ± 0.31	0.97 ± 0.03	1.94 ± 0.27	1.72 ± 0.32	1.60 ± 0.20
6	1.110 ± 0.31	1.49 ± 0.27	1.00 ± 0.21	0.75 ± 0.19	0.74 ± 0.28	0.80 ± 0.14
7	ND	1.09 ± 0.10	0.82 ± 0.16	1.50 ± 0.21	1.52 ± 0.28	1.58 ± 0.26
8	ND	0.86 ± 0.19	0.83 ± 0.14	1.49 ± 0.20	0.91 ± 0.26	1.32 ± 0.21
9	ND	1.08 ± 0.15	0.97 ± 0.24	1.06 ± 0.15	1.15 ± 0.20	1.53 ± 0.25
10	0.86 ± 0.19	1.01 ± 0.30	1.10 ± 0.28	0.77 ± 0.16	0.86 ± 0.21	0.90 ± 0.23
11	1.91 ± 0.25	1.50 ± 0.20	1.63 ± 0.20	1.61 ± 0.40	1.20 ± 0.10	1.35 ± 0.23
12	1.410 ± 0.26	2.56 ± 0.32	1.73 ± 0.34	2.60 ± 0.15	2.61 ± 0.36	2.13 ± 0.32
13	2.23 ± 0.35	2.43 ± 0.30	2.26 ± 0.65	2.44 ± 0.26	2.58 ± 0.23	1.54 ± 0.33
14	1.66 ± 0.15	2.21 ± 0.35	1.92 ± 0.17	2.39 ± 0.17	3.11 ± 0.34	2.02 ± 0.15
15	1.40 ± 0.32	1.12 ± 0.26	1.14 ± 0.15	0.72 ± 0.18	0.89 ± 0.21	0.78 ± 0.23
16	3.23 ± 0.52	2.41 ± 0.26	1.90 ± 0.17	1.71 ± 0.12	3.13 ± 0.20	1.62 ± 0.18
17	1.33 ± 0.30	1.14 ± 0.31	1.52 ± 0.29	2.51 ± 0.43	1.51 ± 0.27	2.70 ± 0.10
18	1.30 ± 0.39	0.98 ± 0.28	0.90 ± 0.16	0.70 ± 0.27	0.72 ± 0.24	0.78 ± 0.15
19	0.92 ± 0.19	0.90 ± 0.22	1.10 ± 0.25	0.81 ± 0.27	0.78 ± 0.15	0.83 ± 0.18
20	2.63 ± 0.36	2.41 ± 0.32	2.22 ± 0.30	4.34 ± 0.81	3.10 ± 0.20	2.10 ± 0.20
24	0.60 ± 0.36	ND	ND	ND	ND	ND
29	2.50 ± 0.73	2.35 ± 0.30	2.12 ± 0.13	ND	ND	ND
30	2.10 ± 0.23	1.85 ± 0.25	2.10 ± 0.33	ND	ND	ND
35	0.80 ± 0.34	0.85 ± 0.36	0.82 ± 0.32	ND	ND	ND
36	0.60 ± 0.23	0.65 ± 0.25	0.67 ± 0.38	ND	ND	ND
Therafectin	0.47 ± 0.18	0.76 ± 0.23	1.35 ± 0.12	0.68 ± 0.02	0.69 ± 0.01	0.76 ± 0.06

independent of the configuration at **C-2′** in the appended side chain as the immunostimulatory effect of pure diastereoisomers (compounds **29** and **30**) is almost equal to that of the diastereoisomeric mixture (**20**). Detailed biological evaluation regarding the possible use of compound **20** in combating fungal infections has been studied and is the subject matter of another communication.

5. Conclusions

To summarise, we have synthesised ether derivatives of 1,2-*O*-isopropylidene-α-D-glucofuranoses having 3-*O*-(β-hydroxy amino alkyl) chain as immunomodulators where the immunostimulant activity is dependent on the configuration of C-3, but independent of the absolute configuration in the side chain.

6. Experimental

6.1. Chemistry

Melting points were determined on a Buchi 510 apparatus and are uncorrected. Elemental analysis for all new compounds were performed on a Carlo Erba Model 1108 elemental analyser and data of C, H, and N are within ±0.4% of calculated values. Thin layer chromatography was used to monitor the reactions. IR spectra were recorded using a Perkin–Elmer 881 spectrophotometer and the values are expressed as ν^{max} cm^{-1}. Mass spectral data were run on JEOL-300 spectrophotometer and ^{1}H-NMR spectra were recorded on a Brucker 200 and 400 MHz spectrophotometer.

6.1.1. General procedure for the preparation of compounds *2*, *22*, *25*, *26*, *31* and *32*

6.1.1.1. (2′*R*/*S*)-1,2,5,6-di-*O*-isopropylidene-3-*O*-[2′,3′-epoxypropan-1′-yl]-α-D-glucofuranose (*2*)

Epichlorohydrine (50 mL, 640 mmol) was magnetically stirred with aq. NaOH (50%, 100 mL) for 0.5 h with tetrabutyl ammonium bromide (5.0 g, 15.5 mmol). To the stirring reaction mixture diacetone glucose (**1a**) (20 g, 76.92 mmol) was slowly added at 0°C and stirring continued at same temperature for 3 h followed by additional 9 h at r.t. The reaction mixture was poured over crushed ice and extracted with EtOAc (3×100 mL), the organic layer was washed with aq. NH_4Cl (10%, 2×20 mL) followed by water (2×20 mL) and dried (Na_2SO_4). Evaporation of the organic solvent under reduced pressure gave a syrup which was purified by column chromatography (SiO_2 60–120 mesh), using $CHCl_3$–MeOH (9:1) as the eluant to afford **2** [13] as colourless oil, yield, 2.03 g, 90%.

6.1.1.2. (2′*R*/*S*)-1,2,5,6-di-*O*-isopropylidene-3-*O*-(2′,3′-epoxypropan-1′-yl)-α-D-allofuranose (*22*)

It was obtained by reaction of (±)epichlorohydrin and allofuranose (**21**) as described in the case of **2** as colourless syrup, yield 80%; $[\alpha]_D$ (−) 42.18 (*c*, 0.014, $CHCl_3$); EIMS; 316 $[M+1]^+$; IR (neat): 2900, 2800 (C–H stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.80$ and 5.78 (two d, $J = 4.5$ Hz, 1H, diastereoisomeric, H-1), 4.76 and 4.68 (two pseudo triplets, $J = 4.5$ Hz, 1H, diastereoisomeric, H-2), 4.38 (m, 1H, H-5), 4.12–4.08 (m, 2H, H-3 and H-4), 4.02 (m, 2H, H-6), 3.90 and 3.52 (each m, each 1H, H-1′A and H-1′B), 3.20 (m, 1H, H-2′), 2.81 and 2.63 (each m, each 1H, H-3′A and H-3′B), 1.57, 1.48, 1.39 and 1.37 (each s, each 3H, 2×C$(CH_3)_2$); Anal. $C_{15}H_{24}O_7$ (C, H, N).

6.1.1.3. (2′*S*)-1,2,5,6-di-*O*-isopropylidene-3-*O*-(2′,3′-epoxypropan-1′-yl)-α-D-glucofuranose (*25*)

Colourless oil, yield 60%; $[\alpha]_D$ (+) 80.2 (*c*, 0.007,$CHCl_3$); FABMS; 317 $[M+1]^+$; IR: 2900, 2800 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = ?5.87$ (d, $J = 4.5$ Hz, 1H, H-1), 4.55 (d, $J = 4.5$ Hz, 1H, H-2), 4.31 (m, 2H, H-3, H-4), 4.00–3.90 (m, 3H, H-6, H-1′), 3.48 (d, $J = 12$ Hz, $J = 8$ Hz, 1H, H-1′), 3.15 (m, 1H, H-2′), 2.82 and 2.62 (two dd, $J = 12$ Hz, $J = 8$ Hz, each 1H, H-3′), 1.59, 1.48, 1.39 and 1.31 (each s, each 3H, 2×C$(CH_3)_2$); Anal. $C_{15}H_{24}O_7$ (C, H).

6.1.1.4. (2′*R*)-1,2,5,6-di-*O*-isopropylidene-3-*O*-(2′,3′-epoxypropan-1′-yl)-α-D-glucofuranose (*26*)

Colourless oil, yield 75%; $[\alpha]_D$ (−) 60.4 (*c*, 0.008,$CHCl_3$); FABMS; 317 $[M+1]^+$; IR: 2928, 2832 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.89$ (d, $J = 4.5$ Hz, 1H, H-1), 4.61 (d, $J = 4.5$ Hz, 1H, H-2), 4.32 (m, 2H, H-3, H-4), 4.00–3.90 (m, 3H, H-6, H-1′), 3.65 (d, $J = 12$ Hz, $J = 8$ Hz, 1H, H-1′), 3.15 (m, 1H, H-2′), 2.82 and 2.65 (two dd, $J = 12$ Hz, $J = 8$ Hz, each 1H, H-3′), 1.51, 1.42, 1.36 and 1.31 (each s, each 3H, 2×C$(CH_3)_2$); Anal. $C_{15}H_{24}O_7$ (C, H).

6.1.1.5. (2′S)-1,2,5,6-di-O-isopropylidene-3-O-(2′,3′-epoxypropan-1′-yl)-α-D-allofuranose ***(31)***

Yield 85%; $[\alpha]_D$ (−) 20.45 (*c*, 0.008,$CHCl_3$); FABMS: 317 $[M+1]^+$; IR: 2989, 2933 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.78$ (d, $J = 4.5$ Hz, 1H, H-1), 4.67 (pseudo-triplet, 1H, H-2), 4.40 (m, 1H, H-4), 4.06–3.98 (m, 4H, H-3, H-5, H-6), 3.57 and 3.47 (two dd, $J = 12$ Hz, $J = 8$ Hz, each 1H, H-1′), 3.20 (m, 1H, H-2′), 2.80 and 2.62 (two dd, $J = 12$ Hz, $J = 8$ Hz, each 1H, H-3′), 1.57, 1.46, 1.37 and 1.35 (each s, each 3H, 2×$C(CH_3)_2$); Anal. $C_{15}H_{24}O_7$ (C, H).

6.1.1.6. (2′R)-1,2,5,6-di-O-isopropylidene-3-O-(2′,3′-epoxypropan-1′-yl)-α-D-allofuranose ***(32)***

Colourless oil, yield 80%; $[\alpha]_D$ (−) 25.14 (*c*, 0.05, $CHCl_3$); EIMS: 315 $[M-1]^+$; FTIR: 2990, 2942 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.79$ (d, $J = 4.5$ Hz, 1H, H-1′), 4.74 (pseudo triplet, 1H, H-2), 4.38 (dd, 1H, H-4), 4.00–4.10 (m, 4H, H-3, H-5 and H-6), 3.94 (dd, $J = 12$ Hz, $J = 8$ Hz, 1H, H-3′A), 2.63 (dd, $J = 12$ Hz, $J = 8$ Hz, 1H, H-3′B), 1.59, 1.46, 1.39 and 1.35 (each s, each 3H, 2×$C(CH_3)_2$); Anal. $C_{15}H_{24}O_7$ (C, H, N).

6.1.2. General procedure for the preparation of compounds ***3***–***11***, ***23***, ***27***, ***28***, ***33*** *and* ***34***

6.1.2.1. (2′R/S)-1,2,5,6-di-O-isopropylidene-3-O-[3′-(N,N-dimethylamino)-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose ***(3)***

A solution of compound **2** (2.83 g, 8.95 mmol) in methanol (20 mL) was refluxed with dimethyl amine hydrochloride (0.73 g, 8.95 mmol) in the presence of $NaHCO_3$ (0.2 g, 2.38 mmol) for 8 h. The excess of solvent was evaporated and residue dissolved in EtOAc (50 mL), filtered. The organic layer was dried (Na_2SO_4) and evaporated under reduced pressure to give an oil which was purified by column chromatography (SiO_2) using $CHCl_3$–MeOH (9:1) as the eluant to give compound **3** (all other compounds of this series were prepared similarly using corresponding amines) as colourless oil yield, 2.03 g, 63%; $[\alpha]_D$ (−) 25.94 (*c*, 0.001.$CHCl_3$); FABMS; *m*/*z*: 362 $[M+1]^+$; IR (neat): 2980, 2940 and 2780 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.90$ (d, $J = 4.5$ Hz, 1H, H-1), 4.58 (d, $J = 4.5$ Hz, 1H, H-2), 4.32 (m, 1H, H-5), 4.15 (m, 2H, H-3 and H-4), 4.00 (m, 2H, H-1′), 3.88 (m, 1H, H-2′), 3.88 and 3.79 (m, 2H, H-6A and H-6B), 3.75, 3.64, and 3.58 (three sets of dd, $J = 12$ Hz, $J = 8$ Hz, 2H, diastereoisomeric H-3′), 2.39 (s, 6H, $N(CH_3)_2$), 1.51, 1.46, 1.38 and 1.32 (each s, each 3H, 2×$(CH_3)_2$); Anal. $C_{17}H_{31}NO_7$ (C, H, N).

6.1.2.2. (2′R/S)-1,2,5,6-di-O-isopropylidene-3-O-[3′-(N,N-diethylamino)-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose ***(4)***

Colourless oil, yield 60%; MS; *m*/*z*: 389 [M], IR (neat): 3000, 2940, 2900 and 2820 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.90$ (d, $J = 4.5$ Hz, 1H, H-1), 4.60 (d, $J = 4.5$ Hz, 1H, H-2), 4.32 (m, 1H, H-4), 4.12 (m, 2H, H-3 and H-5), 4.00 (m, 3H, H-1′ and H-6A), 3.81 (m, 2H, H-2′ and H-6B), 3.65, 3.55 and 3.48 (three sets of dd, $J = 12$ Hz, $J = 7$ Hz, 2H, H-3′), 2.55 (m, 4H, $N(CH_2CH_3)_2$), 1.50, 1.43, 1.36 and 1.32 (each s, each 3H, 2×$(C(CH_3)_2)$, 1.03 (two t merged with each other, $J = 7.5$ Hz, 6H, $N(CH_2CH_3)_2$); Anal. $C_{19}H_{35}NO_7$ (C, H, N).

6.1.2.3. (2′R/S)-1,2,5,6-di-O-isopropylidene-3-O-[3′-(N,N-disopropylamino)-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose ***(5)***

Colourless oil, yield 57%; $[\alpha]_D$ (−) 21.10 (*c*, 0.01, $CHCl_3$); FABMS; *m*/*z*: 419 $[M+2]^+$, 418 $[M+1]^+$; IR (neat): 3500, 2980, 2840, 2800 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.90$ (d, $J = 4.5$ Hz, 1H, H-1), 4.62 (d, $J = 4.5$ Hz, 1H, H-2), 4.35 (m, 1H, H-4), 4.13 (m, 2H, H-3 and H-5), 4.04 and 3.89 (two dd, $J = 12$ Hz, $J = 8$ Hz, 2H, H-1′A and H-1′B), 3.75 and 3.68 (two m, 2H, H-6A and H-6B), 3.56 (m, 1H, H-2′), 3.51 and 3.40 (two dd, $J = 12$ Hz, $J = 7$ Hz, 2H, H-3′), 3.04 (sextet, $J = 7.5$ Hz, 2H, $[-\{CH(CH_3)_2\}_2]$, 2.50 (bs, 1H, OH), 1.51, 4.46, 1.38 and 1.33 (each s, each 3H, 2×$[C(CH_3)_2)]$, 1.08 and 1.01 (two d, $J = 7.5$ Hz, 12H, $[-\{CH(CH_3)_2\}_2]$; Anal. $C_{21}H_{39}NO_7$ (C, H, N).

6.1.2.4. (2′-R/S)-1,2,5,6-di-O-isopropylidene-3-O-[3′-(pyrrolidin-1-yl)-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose ***(6)***

Colourless oil, yield 57%; $[\alpha]_D$ (−) 20.13 (*c*, 0.02, $CHCl_3$); EIMS; *m*/*z*: 387 $[M^+]$; FTIR (neat): 3454 (OH), 3020, 2985, 2935, 2806 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.90$ (d, $J = 4.5$ Hz, 1H, H-1), 4.58 (d, $J = 4.5$ Hz, 1H, H-2), 4.32 (m, 1H, H-4), 4.12 (m, 2H, H-3 and H-5), 4.00 (m, 2H, H-1′), 3.92 (m, 1H, H-2′), 3.82 and 3.67 (two m, 2H, H-6), 3.57 and 3.44 (two dd, $J = 12$ Hz, $J = 7$ Hz, 2H, H-3′), 2.72 (m, 4H, pyrrolidin ring protons), 1.80 (bs, 4H, pyrrolidin ring protons), 1.50, 1.42, 1.38 and 1.32 (each s, each 3H, 2×$C(CH_3)_2$); Anal. $C_{19}H_{33}NO_7$ (C, H, N).

*6.1.2.5. (2′R/S)-1,2,5,6-di-O-isopropylidene-3-O-[3′-(piperidin-1-yl)-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose (**7**)*

Colourless oil, yield 59%; $[\alpha]_D$ (−) 20.12 (*c*, 0.016, $CHCl_3$); FABMS: 402 $[M+1]^+$; IR (neat): 3450 (OH), 3000, 2950, 2800, 2790 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.90$ (d, $J = 4.5$ Hz, 1H, H-1), 4.59 (d, $J = 4.5$ Hz, 1H, H-2), 4.32 (m, 1H, H-4), 4.12 (m, 2H, H-3 and H-5), 3.98 (m, 2H, H-1′), 3.90 (m, 1H, H-2′), 3.75 (m, 2H, H-6), 3.63, 3.57 and 3.48 (three dd, $J = 15$ Hz, $J = 5$ Hz, 2H, H-3′), 2.37 and 2.40 (m, 6H, piperidin ring protons), 1.59 (bs, 4H, piperidin ring protons), 1.51, 1.46, 1.38 and 1.32 (each s, each 3H, 2×–C(CH_3)$_2$); Anal. $C_{20}H_{35}NO_7$ (C, H, N).

*6.1.2.6. (2′R/S)-1,2,5,6-di-O-isopropylidene-3-O-[3′-(N,N-dicyclohexylamino)-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose (**8**)*

Colourless oil, yield 30%; $[\alpha]_D$ (−) 20.57 (*c*, 0.06, $CHCl_3$); EIMS; *m*/*z*: 497 $[M]^+$; IR (neat): 3500, 3000, 2950, 2850; ^{1}H-NMR ($CDCl_3$): $\delta = 5.89$ (d, $J = 4.5$ Hz, 1H, H-1), 4.61 (d, $J = 4.5$ Hz, 1H, H-2), 4.32 (m, 1H, H-4), 4.15 (m, 2H, H-3 and H-5), 3.95 and 3.86 (two dd, $J = 12$ Hz, $J = 8$ Hz, 2H, H-1′), 3.65 and 3.61 (two dd, $J = 10$ Hz, $J = 5$ Hz, 2H, H-6), 2.68 and 2.50 (two dd, $J = 12$ Hz, $J = 7$ Hz, 2H, H-3′), 2.35 (bs, 1H, –OH), 2.22 (m, 2H, cyclohexylprotons), 1.75 (m, 8H, cyclohexyl protons), 1.60 (m, 4H, cyclohexyl protons), 1.50, 1.42, 1.35 and 1.31 (each s, each 3H, 2×–C(CH_3)$_2$), 1.15 (m, 8H, cyclohexyl ring protons); Anal. $C_{27}H_{47}NO_7$ (C, H, N).

*6.1.2.7. (2′R/S)-1,2,5,6-di-O-isopropylidene-3-O-[3′-(4-methylpiperazin-1-yl)-2-hydroxy-propan-1′-yl]-α-D-glucofuranose (**9**)*

Colourless oil, yield 60%; $[\alpha]_D$ (−) 17.89 (*c*, 0.016, $CHCl_3$); FABMS; *m*/*z*: 417 $[M+1]^+$; IR (neat): 3500, 3000, 2980, 2960, 2800; ^{1}H-NMR ($CDCl_3$): $\delta = 5.89$ (d, $J = 4.5$ Hz, 1H, H-1), 4.58 (d, $J = 4.5$ Hz, 1H, H-2), 4.31 (m, 1H, H-4), 4.12 (m, 2H, H-3 and H-5), 4.00 (m, 2H, H-1′), 3.90 (m, 1H, H-2′), 3.78 and 3.65 (two dd, $J = 14$ Hz, $J = 8$ Hz, 2H, H-6), 3.58 and 3.42 (each dd, $J = 12$ Hz, $J = 7$ Hz, each 1H, H-3′A and H-3′B), 2.48 (m, 8H, piperazinyl protons), 2.30 (s, 3H, N–CH_3), 1.50, 1.43, 1.38 and 1.32 (each s, each 3H, 2×–C(CH_3)$_2$); Anal. $C_{17}H_{32}NO_7$ (C, H, N).

*6.1.2.8. (2′R/S)-1,2,5,6-di-O-isopropylidene-3-O-[3′-(morpholin-4-yl)-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose (**10**)*

Colourless oil, yield 80%; $[\alpha]_D$ (−) 21.16 (*c*, 0.018, $CHCl_3$); EIMS; *m*/*z*: 403 $[M]^+$; IR (neat): 3452 (OH), 3018, 2933, 2868, 2819 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.90$ (d, $J = 4.5$ Hz, 1H, H-1), 4.60 (d, $J = 4.5$ Hz, 1H, H-2), 4.32 (m, 2H, H-3 and H-4), 4.15 (m, 5H, H-5 and morpholin ring protons), 4.02 (m, 3H, H-2′ and H-6), 3.65 (m, 2H, H-3′), 2.51 (m, 4H, morpholin ring protons), 1.50, 1.42, 1.35 and 1.30 (each s, each 3H, 2×–C(CH_3)$_2$); Anal. $C_{19}H_{33}NO_8$ (C, H, N).

*6.1.2.9. (2′R/S)-1,2,5,6-di-O-isopropylidene-3-O-[3′-{1-(2-pyridyl)-piperazin-4-yl}-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose (**11**)*

Colourless oil, yield 60%; $[\alpha]_D$ (−) 13.55 (*c*, 0.017, $CHCl_3$); FABMS; *m*/*z*: 480 $[M^+ + 1]$; IR (neat): 3400 (OH), 3000, 2940, 2900, 2840 (CH stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 8.20$ (d, $J = 5$ Hz, 1H, pyridyl protons), 7.48 (dd, $J = 8$ Hz, $J = 1.5$ Hz, 1H, pyridyl protons), 6.63 (m, 2H, pyridyl protons), 5.90 (d, $J = 4.5$ Hz, 1H, H-1), 4.60 (d, $J = 4.5$ Hz, 1H, H-2), 4.33 (m, 1H, H-4), 4.12 (m, 2H, H-3 and H-5), 4.00 (two dd, $J = 12$ Hz, $J = 8$ Hz, each 1H, H-1′), 3.85 (m, 1H, H-2′), 3.72 and 3.61 (each dd, $J = 12$ Hz, $J = 5$ Hz, each 1H, H-6A and H-6B), 3.46 (two dd, $J = 12$ Hz, $J = 7$ Hz, 2H, H-3′), 2.70 (m, 2H, piperazinyl ring protons), 2.62, 2.38 (m, 6H, piperazinyl ring protons), 1.50, 1.43, 1.38 and 1.30 (each s, each 3H, 2×–C(CH_3)$_2$); Anal. $C_{24}H_{37}N_3O_7$ (C, H, N).

*6.1.2.10. (2′R/S)-1,2,5,6-di-O-isopropylidene-3-O-[3′-{1-(2-pyridyl)-piperazin-4-yl}-2′-hydroxy-propan-1′-yl]-α-D-allofuranose (**23**)*

Colourless oil, yield 66%; $[\alpha]_D$ (−) 14.12 (*c*, 0.018, $CHCl_3$); FABMS; *m*/*z*: 480 $[M^+ + 1]$; FTIR: 3427, 2931, 2895, 2831 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 8.20$ (d, $J = 8$ Hz, 1H, pyridyl proton), 7.48 (dd, $J = 8$ Hz, $J = 4$ Hz, 1H, pyridyl proton), 6.66 (m, 2H, pyridyl proton), 5.80 (d, $J = 4.5$ Hz, 1H, H-1), 4.69 (pseudo triplet, $J = 4.5$ Hz, 1H, H-2), 4.39 (m, 1H, H-4), 4.12 (m, 2H, H-3 and H-5), 4.06 and 4.00 (each dd, $J = 12$ Hz, $J = 8$ Hz, each 1H, H-1′A and H-1′B), 3.86 (m, 1H, H-2′), 3.58 (m, 4H, H-3′ and H-6), 2.72 (m, 2H, piperazin ring protons), 2.60 (m, 6H, piperazin ring protons), 1.59, 1.49, 1.38 and 1.35 (each s, each 3H, 2×C(CH_3)$_2$); Anal. $C_{24}H_{37}N_3O_7$ (C, H, N).

*6.1.2.11. (2′S)-1,2,5,6-di-O-isopropylidene-3-O-[3′-{1-(2-pyridyl)-piperazin-4-yl}-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose (**27**)*

Colourless oil, yield 60%; $[\alpha]_D$ (−) 14.16 (*c*, 0.005, $CHCl_3$); FABMS; *m*/*z*: 479 $[M+1]^+$; FTIR: 3450 (–OH), 2980, 2900, 2880 (CH_3 and CH_2 stretching); ^{1}H-NMR

($CDCl_3$): $\delta = 8.20$ (d, $J = 5$ Hz, 1H, pyridyl proton), 7.80 (dd, $J = 8$ Hz, $J = 1.5$ Hz, 1H, pyridyl proton), 6.65 (m, 2H, pyridyl proton), 5.90 (d, $J = 4.5$ Hz, 1H, H-1′), 4.58 (d, $J = 4.5$ Hz, 1H, H-2), 4.32 (m, 1H, H-4), 4.12 (m, 2H, H-3, H-5), 4.02 (two dd, $J = 12$ Hz, $J = 8$ Hz, 2H, H-1′), 3.85 (dd, $J = 14$ Hz, $J = 3.5$ Hz, 1H, H-2′), 3.60–3.42 (m, 4H, H-3′, H-6), 3.00 (m, 2H, piperazinyl protons), 2.70, 2.55, 2.40 (each m, each 2H, piperazinyl ring proton), 1.50, 1.43, 1.38, 1.32 (each s, each 3H, $2\times C(CH_3)_2$); Anal. $C_{24}H_{37}N_3O_7$ (C, H, N).

6.1.2.12. (2′R)-1,2,5,6-di-O-isopropylidene-3-O-[3′-{1-(2-pyridyl)-piperazin-4-yl}-2′-hydroxy-propan-1′-yl-α-D-glucofuranose ***(28)***

Colourless oil, yield 60%; $[\alpha]_D$ (−) 12.18 (*c*, 0.06, $CHCl_3$); FABMS; *m*/*z*: 480 $[M+1]^+$; FTIR: 3450 (–OH), 2985, 2935, 2885 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 8.20$ (d, $J = 4.5$ Hz, 1H, pyridyl proton), 7.80 (dd, $J = 8$ Hz, $J = 1.5$ Hz, 1H, pyridyl proton), 6.62 (m, 2H, pyridyl proton), 5.90 (d, $J = 4.5$ Hz, 1H, H-1′), 4.58 (d, $J = 4.5$ Hz, 1H, H-2), 4.32 (m, 1H, H-4), 4.12 (m, 2H, H-3, H-5), 4.00 (two dd, $J = 12$ Hz, $J = 8$ Hz, 2H, H-1′), 3.67 (m, 1H, H-2′), 3.60–3.45 (m, 4H, H-3′, H-6), 3.00 (m, 2H, piperazinyl protons), 2.75–2.40 (m, 6H, piperazinyl ring proton), 1.50,1.45, 1.38, 1.32 (each s, each 3H, $2\times C(CH_3)_2$); Anal. $C_{24}H_{37}N_3O_7$ (C, H, N).

6.1.2.13. (2′S)-1,2,5,6-di-O-isopropylidene-3-O-[3′-{1-(2-pyridyl)-piperazin-4-yl}-2′-hydroxy-propan-1′-yl]-α-D-allofuranose ***(33)***

Colourless oil, yield 60%; $[\alpha]_D$ (−) 14.61 (*c*, 0.004, $CHCl_3$); FABMS; *m*/*z*: 479 $[M+1]^+$; FTIR: 3390 (–OH), 3025, 2935, 2850 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 8.20$ (d, $J = 5$ Hz, 1H, pyridyl proton), 7.50 (dd, $J = 8$ Hz, $J = 5$ Hz, 1H, pyridyl proton), 6.66 (dd, $J = 5$ Hz, $J = 1.5$ Hz, 2H, pyridyl proton), 5.79 (d, $J = 4.5$ Hz, 1H, H-1′), 4.69 (pseudo triplet, $J = 4.5$ Hz, 1H, H-2), 4.37 (m, 1H, H-4), 4.07–3.98 (m, 4H, H-3, H-5, H-1′), 3.75 (m, 2H, H-6), 3.64 and 3.52 (each dd, $J = 12$ Hz, $J = 8$ Hz, each 1H, H-3′), 3.00–2.89 (m, 5H, piperazinyl ring proton), 2.75, 2.65 (two m, 3H, piperazinyl ring proton), 1.58, 1.48, 1.37, 1.34 (each s, each 3H, $2\times C(CH_3)_2$); Anal. $C_{21}H_{33}N_3O_7$ (C, H, N).

6.1.2.14. (2′R)-1,2,5,6-di-O-isopropylidene-3-O-[3′-{1-(2-pyridyl-piperazin-4-yl}-2′-hydroxy-propan-1′-yl]-α-D-allofuranose ***(34)***

Colourless oil, yield 60%; $[\alpha]_D$ (−) 14.61 (*c*, 0.04, $CHCl_3$); FABMS; 479 $[M]^+$; FTIR: 3363 (–OH), 3020, 2987, 2937 and 2844 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 8.20$ (d, $J = 5$ Hz, 1H, pyridyl proton), 7.50 (dd, $J = 8$ Hz, $J = 4$ Hz, 1H, pyridyl proton), 6.66 (m, 2H, pyridyl proton), 5.79 (d, $J = 4.5$ Hz, 1H, H-1′), 4.69 (pseudo triplet, 1H, H-2), 4.37 (m, 1H, H-4), 4.07 (m, 3H, H-3, H-5 and H-1′A), 3.98 (m, 1H, H-1′B), 3.93 (m, 1H, H-2′), 3.75 (m, 2H, H-6), 3.64 (dd, $J = 12$ Hz, $J = 8$ Hz, 1H, H-3′A), 3.52 (dd, $J = 12$ Hz, $J = 8$ Hz, 1H, H-3′B), 2.90 (m, 5H, piperazinyl proton), 2.75 and 2.65 (two m, 3H, piperazinyl proton), 1.58, 1.48, 1.37, 1.34 (each s, each 3H, $2\times C(CH_3)_2$); Anal. $C_{24}H_{37}N_3O_7$ (C, H, N).

6.1.3. General Procedure for the preparation of compounds ***12–20***, ***24***, ***29***, ***30***, ***35***, ***36***

6.1.3.1. (2′R/S)-1,2-O-isopropylidene-3-O-[3′-(N,N-dimethylamino)-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose ***(12)***

The compound **4** (2.7 g, 7.47 mmol) was magnetically stirred with aq. HCl (3%, 12 mL, pH 1–2) at r.t. (35°C) for 3 h. Reaction mixture neutralised with solid $NaHCO_3$ till the pH is 7. It was filtered, solvent evaporated under reduced pressure to give a residual mass, which was extracted with chloroform (3×50 mL). Organic layer dried (Na_2SO_4) and evaporated under reduced pressure to give a syrup, which was purified by column (SiO_2) chromatography using $CHCl_3$–MeOH (95:5) as the eluant to give the desired compound **22** as colourless oil (all other compounds of this series were prepared similarly from the corresponding intermediates). Yield 75%; $[\alpha]_D$ (−) 39.40 (*c*, 0.012, $CHCl_3$); FABMS; *m*/*z*: 321 $[M]^+$; IR (neat): 3400 (OH), 2990, 2940, 2860, 2800 (C–H stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.96$ (d, $J = 4.5$ Hz, 1H, H-1), 4.54 (d, $J = 4.5$ Hz, 1H, H-2), 4.15 (m, 1H, H-4), 4.10 (m, 2H, H-3, OH), 4.00 (m, 2H, H-1′), 3.87 (m, 3H, H-5 and H-6), 3.78 (m, 1H, H-2′), 3.56 and 3.52 (two dd, $J = 8$ Hz, $J = 5$ Hz, 2H, H-3′), 2.30 (s, 6H, $N(CH_3)_2$), 1.51, 1.33 (each s, each 3H, $-C(CH_3)_2$); Anal. $C_{24}H_{27}NO_7$ (C, H, N).

6.1.3.2. (2′R/S)-1,2-O-isopropylidene-3-O-[3′-(N,N-diethylamino)-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose ***(13)***

Colourless oil, yield 89%; $[\alpha]_D$ (−) 29.86 (*c*, 0.016, $CHCl_3$); EIMS; 349 $[M]^+$; IR (neat): 3400 (OH), 3000, 2940, 2900, 2840 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.94$ (d, $J = 4.5$ Hz, 1H, H-1), 4.55 (d, $J = 4.5$ Hz, 1H, H-2), 4.19 (m, 1H, H-4), 4.12 (m, 1H, H-3), 4.05 and 3.99 (two dd, $J = 12$ Hz, $J = 4$ Hz, 2H,

H-1′), 3.85 (m, 3H, H-5 and H-6), 3.76 (m, 1H, H-2′), 3.68, 3.60, 3.52 (three dd, $J = 12$ Hz, $J = 8$ Hz, 2H, H-3′), 3.30 (bs, 1H, OH), 2.65 (m, 4H, N–(CH_2–CH_3)$_2$], 2.4 and 2.28 (bs, OH), 1.50 and 1.42 (each s, each 3H, $C(CH_3)_2$), 1.10 and 1.07 (each t, $J = 7.5$ Hz, each 3H, N–CH_2 (CH_3)$_2$); Anal. $C_{16}H_{31}NO_7$ (C, H, N).

6.1.3.3. (2′R/S)-1,2-O-isopropylidene-3-O-[3′-(N,N-diisopropylamino)-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose ***(14)***

Colourless oil, yield 70%; $[\alpha]_D$ (−) 29.81 (*c*, 0.011, $CHCl_3$); FABMS; *m*/*z*: 378 $[M+1]^+$; IR (neat): 3400 (OH), 2990, 2860, 2800 (C–H stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.94$ (d, $J = 4.5$ Hz, 1H, H-1), 4.55 (d, $J = 4.5$ Hz, 1H, H-2), 4.13 (m, 2H, H-3 and H-4), 4.05 and 3.96 (m, 2H, H-1′), 3.89 and 3.76 (m, 3H, H-5 and H-6), 3.67 (m, 3H, H-2′, H-3′), 3.29 (bs, 1H, –OH), 2.60 (bs, 1H, OH), 2.48 (sextet, $J = 7.5$ Hz, 2H, N–{C*H*–$(CH_3)_2$}$_2$), 2.25 (bs, 1H, –OH), 1.49 and 1.32 (each s, each 3H, $C(CH_3)_2$), 0.80 and 0.78 (each d, each 6H, $J = 7.5$ Hz, 2×N–[CH(CH_3)$_2$]; Anal. $C_{18}H_{35}NO_7$ (C, H, N).

6.1.3.4. (2′R/S)-1,2-O-isopropylidene-3-O-[3′(-pyrrolidin-1-yl)-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose ***(15)***

Colourless oil, yield 80%; $[\alpha]_D$ (−) 23.02 (*c*, 0.016, $CHCl_3$); FABMS; *m*/*z*: 348 $[M+1]^+$; IR (neat): 3400 (OH), 3000, 2950, 2850, 2800 (C–H stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.91$ (d, $J = 4.5$ Hz, 1H, H-1), 4.54 (d, $J = 4.5$ Hz, 1H, H-2), 4.14 (m, 2H, H-3 and H-4), 4.00 (m, 1H, H-2′), 3.92 (m, 3H, H-3 and H-5), 3.66 (m, 2H, H-6), 3.36 and 2.85 (each dd, $J = 12$ Hz, $J = 4.5$ Hz, each 1H, H-3′A and H-3′B), 2.68 (m, 4H, pyrolidin ring protons), 2.49 (m, 4H, pyrrolidin ring protons), 1.49 and 1.32 (each s, each 3H, $C(CH_3)_2$); Anal. $C_{16}H_{29}NO_7$ (C, H, N).

6.1.3.5. (2′R/S)-1,2-O-isopropylidene-3-O-[3′-(piperidin-1-yl)-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose ***(16)***

Colourless oil, yield 70%; $[\alpha]_D$ (−) 26.23 (*c*, 0.016, $CHCl_3$); FABMS; *m*/*z*: 362 $[M+1]^+$; IR (neat): 3400 (OH), 3000, 2950, 2850, 2800 (C–H stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.91$ (d, $J = 4.5$ Hz, 1H, H-1), 4.54 (d, $J = 4.5$ Hz, 1H, H-2), 4.14 (m, 2H, H-3 and H-4), 3.90 (m, 4H, H-5, H-1′ and H-2′), 3.68 (m, 2H, H-6), 3.30 (bs, –OH), 2.60, 2.30, 2.21 (m, 6H, piperidin ring protons), 1.57 (m, 4H, piperidin ring protons), 1.49 and 1.32 (each s, each 3H, $C(CH_3)_2$), 1.48 (m, 2H, piperidin ring protons); Anal. $C_{17}H_{31}NO_7$ (C, H, N).

6.1.3.6. (2′R/S)-1,2-O-isopropylidene-3-O-[3′-(N,N-dicyclohexylamino)-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose ***(17)***

Colourless oil, yield 57%; $[\alpha]_D$ (−) 31.14 (*c*, 0.028, $CHCl_3$); EIMS; *m*/*z*: 457 $[M^+ + 1]$; IR (neat): 3400 (OH), 2940, 2850 (C–H stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.97$ (d, $J = 4.5$ Hz, 1H, H-1), 4.57 (d, $J = 4.5$ Hz, 1H, H-2), 4.34 (m, 2H, H-4), 4.18 (m, 2H, H-3 and H-5), 3.96 and 3.85 (each dd, $J = 12$ Hz, $J = 4.5$ Hz, each 1H, H-1′A and H-1′B), 3.68 (m, 1H, H-2′), 3.54 and 3.46 (m, 2H, H-6), 3.22 (bs, –OH), 2.79 and 2.62 (each dd, $J = 11$ Hz, $J = 4.5$ Hz, each 1H, H-3′A and H-3′B), 2.42 (m, 2H, cyclohexyl proton), 2.18 (bs, OH), 1.78 and 1.60 (two m, 6H and 4H cyclohexyl protons), 1.50 and 1.32 (each s, each 3H, –$C(CH_3)_2$), 1.25 (m, 10H, cyclohexyl protons); Anal. $C_{24}H_{43}NO_7$ (C, H, N).

6.1.3.7. (2′R/S)-1,2-O-isopropylidene-3-O-[3′-(4-methyl-piperazin-1-yl)-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose ***(18)***

Colourless oil, yield 89%; $[\alpha]_D$ (−) 24.26 (*c*, 0.08, $CHCl_3$); FABMS; 377 $[M^+ + 1]$; IR (neat): 3400 (OH), 2990, 2920, 2800 (C–H stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.94$ (d, $J = 4.5$ Hz, 1H, H-1), 4.53 (d, $J = 4.5$ Hz, 1H, H-2), 4.35 (m, 1H, H-5), 4.14 (m, 2H, H-3 and H-5), 4.15 (dd, $J = 12$ Hz, $J = 5$ Hz, 2H, H-1′), 3.89 (m, 1H, H-2′), 3.68 (m, 2H, H-6), 3.48 and 3.56 (each dd, $J = 15$ Hz, $J = 7$ Hz, each 1H, H-3′A and H-3′B), 3.30 (bs, OH), 2.54 (m, 8H, piperazin ring protons), 2.30 (s, 3H, N–CH_3), 1.50 and 1.32 (each s, each 3H, –$C(CH_3)_2$); Anal. $C_{17}H_{32}N_2O_7$ (C, H, N).

6.1.3.8. (2′R/S)-1,2-O-isopropylidene-3-O-[3′-(morpholin-4-yl)-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose ***(19)***

Colourless oil, yield 80%; $[\alpha]_D$ (−) 26.28 (*c*, 0.014, $CHCl_3$); FABMS; *m*/*z*: 364 $[M+1]^+$; IR (neat): 3420 (OH), 2980, 2920, 2800 (C–H stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 5.94$ (d, $J = 4.5$ Hz, 1H, H-1), 4.54 (d, $J = 4.5$ Hz, 1H, H-2), 4.15 (m, 2H, H-3 and H-4), 4.02 (m, 3H, H-5 and H-1′), 3.90 (m, 3H, H-6 and H-2′), 3.75 (m, 6H, H-3′ and morpholin ring protons), 2.64 and 2.42 (m, 4H, morpholin ringl protons), 1.52, 1.32 (each s, each 3H, $C(CH_3)_2$); Anal. $C_{16}H_{29}NO_8$ (C, H, N).

6.1.3.9. (2′R/S)-1,2-O-isopropylidene-3-O-[3′-(1-(2-pyridyl)-piperazin-4-yl)-2′-hydroxy-propan-1′-yl]-α-D-glucofuranose ***(20)***

Colourless oil, yield 75%; $[\alpha]_D$ (−) 22.12 (*c*, 0.014, $CHCl_3$); FABMS: *m*/*z*: 440 $[M+1]^+$; IR (neat): 3400 (OH), 3000, 2980, 2800 (C–H stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 8.20$ (dd, $J = 8$ Hz, $J = 1.5$ Hz, 1H, pyridyl protons), 7.50 (dd, $J = 8$ Hz, $J = 1.5$ Hz, 1H, pyridyl protons), 6.63 (m, 2H, pyridyl protons), 5.93 (d, $J = 4.5$ Hz, 1H, H-1), 4.59 (d, $J = 4.5$ Hz, 1H, H-2), 4.15 (m, 2H, H-3 and H-4), 4.00 (m, 2H, H-1), 3.89 (m, 1H, H-2′), 3.70 (m, 3H, H-5 and H-6), 3.58 (m, 4H, H-3′ and piperazin ring protons), 2.67 (bs, OH), 2.55 and 2.38 (each m, each 2H, piperazin ring protons), 1.50 and 1.32 (each s, each 3H, –C$(CH_3)_2$); Anal. $C_{21}H_{33}N_3O_7$ (C, H, N).

6.1.3.10. (2′R/S)-1,2-O-isopropylidene-3-O-[3′-{1-(2-pyridyl)-piperazin-4-yl}-2′-hydroxy-propan-1′-yl]-α-D-allofuranose ***(24)***

Colourless oil, yield 60%; $[\alpha]_D$ (−) 21.26 (*c*, 0.02, $CHCl_3$); EIMS; 439 $[M^+]$; FTIR: 3388 (OH), 2989, 2933, 2893 and 2835 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 8.20$ (d, $J = 8$ Hz, 1H, pyridyl proton), 7.50 (dd, $J = 8$ Hz, $J = 4$ Hz, 1H, pyridyl proton), 6.66 (m, 2H, pyridyl proton), 5.80 (d, $J = 4.5$ Hz, 1H, H-1), 4.68 (pseudo triplet, $J = 4.5$ Hz, 1H, H-2), 4.38 (m, 1H, H-4), 4.25 (m, 2H, H-3 and H-5), 4.10 and 3.97 (m, 2H, H-1′), 3.72 (m, 1H, H-2′), 3.62 (m, 4H, H-3′ and H-6), 2.82 and 2.70 (each m, 6H, piperazin ring proton), 2.50 (m, 2H, piperazin ring proton), 1.60 and 1.35 (each s, each 3H, $2\times C(CH_3)_2$); Anal. Found: C, 57.92; H, 7.51; N, 9.53. Calc. for $C_{21}H_{33}N_3O_7$: C, 57.40; H, 7.51; N, 9.56%.

6.1.3.11. (2′S)-1,2-O-isopropylidene-3-O-[3′-[{1-(2-pyridyl)-piperazin-4-yl}]-2′-hydroxy-propan-1′-yl-α-D-glucofuranose ***(29)***

Colourless oil, yield 75%; $[\alpha]_D$ (−) 19.21 (*c*, 0.004, $CHCl_3$); FABMS; *m*/*z*: 440 $[M+1]^+$; FTIR: 3384 (–OH), 2935, 2900 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 8.20$ (d, $J = 4.5$ Hz, 1H, pyridyl proton), 7.50 (dd, $J = 10$ Hz, $J = 1.5$ Hz, 1H, pyridyl proton), 6.67 (m, 2H, pyridyl proton), 5.94 (d, $J = 4.5$ Hz, 1H, H-1′), 4.55 (d, $J = 4.5$ Hz, 1H, H-2), 4.15 (m, 1H,H-4), 4.03 (m, 2H, H-3, H-5), 3.89, 3.74 (two dd, $J = 12$ Hz, $J = 1.5$ Hz, 2H, H-1′), 3.68 (m, 1H, H-2′), 2.80 (m, 2H, piperazin ring protons), 2.58, 2.40 (m, 6H, piperazin ring proton), 1.48, 1.32 (each s, each 3H, C$(CH_3)_2$); Anal. $C_{21}H_{33}N_3O_7$ (C, H, N).

6.1.3.12. (2′R)-1,2-di-O-isopropylidene-3-O-[3′-[{1-(2-pyridyl)-piperazin-4-yl}]-2′-hydroxy-propan-1′-yl-α-D-glucofuranose ***(30)***

Colourless oil, yield 75%; $[\alpha]_D$ (−) 20.12 (*c*, 0.016, $CHCl_3$); FABMS; *m*/*z*: 440 $[M+1]^+$; FTIR: 3392 (–OH), 3016, 2848 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 8.20$ (d, $J = 5$ Hz, 1H, pyridyl proton), 7.50 (dd, $J = 8$ Hz, $J = 1.5$ Hz, 1H, pyridyl proton), 6.80 (m, 2H, pyridyl proton), 5.94 (d, $J = 4.5$ Hz, 1H, H-1), 4.56 (d, $J = 4.5$ Hz, 1H, H-2), 4.18 (m, 1H, H-4), 4.12 (dd, $J = 12$ Hz, $J = 4$ Hz, 1H, H-3), 4.05–3.99 (m, 3H, H-5, H-1′), 3.90 (two dd, $J = 12$ Hz, $J = 4.5$ Hz, 1H, H-2′), 3.85 (dd, $J = 14$ Hz, $J = 3.5$ Hz, 1H, H-2′), 3.72–3.64 (m, 4H, H-3′, H-6), 2.89–2.84 (m, 2H, piperazin ring protons), 2.79–2.62 (m, 6H, piperazin ring protons), 1.50, 1.34 (each s, each 3H, C$(CH_3)_2$); Anal. $C_{21}H_{33}N_3O_7$ (C, H, N).

6.1.3.13. (2′S)-1,2-O-isopropylidene-3-O-[3′-{1-(2-pyridyl)-piperazin-4-yl}-2′-hydroxy-propan-1′-yl-α-D-allofuranose ***(35)***

Colourless oil, yield 60%; $[\alpha]_D$ (−) 19.22 (*c*, 0.041, $CHCl_3$); FABMS; *m*/*z*: 440 $[M+1]^+$; FTIR: 3396 (–OH), 3020, 2925, 2850 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 8.20$ (d, $J = 4.5$ Hz, 1H, pyridyl proton), 7.50 (dd, $J = 8$ Hz, $J = 4.5$ Hz, 1H, pyridyl proton), 6.65 (dd, $J = 5$ Hz, $J = 1.5$ Hz, 2H, pyridyl proton), 5.80 (d, $J = 4.5$ Hz, 1H, H-1′), 4.69 (pseudo triplet, $J = 4.5$ Hz, 1H, H-2), 4.14 (m, 1H, H-4), 3.98 (m, 3H, H-3, H-5 and H-1′A), 3.74 (m, 4H, H-1′B, H-2′ and H-6), 3.60 and 3.55 (m, 2H, H-3′), 2.96, 2.83 and 2.63 (m, 8H, piperazin ring protons), 1.59, 1.36 (each s, each 3H, $2\times C(CH_3)_2$); Anal. $C_{21}H_{33}N_3O_7$ (C, H, N).

6.1.3.14. (2′R)-1,2-O-isopropylidene-3-O-[3′-{1-(2-pyridyl)-piperazin-4-yl}-2′-hydroxy-propan-1′-yl]-α-D-allofuranose ***(36)***

Colourless oil, yield 58%; $[\alpha]_D$ (−) 15.41 (*c*, 0.018, $CHCl_3$); FABMS; 440 $[M+1]^+$; FTIR: 3310 (–OH), 3010, 2945, 2889 and 2831 (CH_3 and CH_2 stretching); ^{1}H-NMR ($CDCl_3$): $\delta = 8.20$ (d, $J = 5$ Hz, 1H, pyridyl proton), 7.46 (dd, $J = 8$ Hz, $J = 4$ Hz, 1H, pyridyl proton), 6.60 (m, 2H, pyridyl proton), 5.80 (d, $J = 4.5$ Hz, 1H, H-1′), 4.67 (pseudo triplet, 1H, H-2), 4.32 (m, 1H, H-4), 4.08–4.00 (m, 4H, H-3, H-5 and H-1′A), 3.87 (m, 1H, H-2′), 3.60–3.42 (m, 4H, H-3′, H-6), 2.78, 2.64 and 2.45 (three m, 8H, piperazin ring protons), 1.48, 1.32 (each s, each 3H, $2\times C(CH_3)_2$)); Anal. $C_{24}H_{37}N_3O_7$ (C, H, N).

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