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An efficient and highly diastereoselective synthesis of *C*-glycosylated 1,3-oxazolidines from *N*-methyl-D-glucamine

R. Fernando Martínez [a,*], Martín Ávalos [a], Reyes Babiano [a], Pedro Cintas [a], José L. Jiménez [a], Mark E. Light [b], Juan C. Palacios [a], Esther M.S. Pérez [a]

[a] Departamento de Química Orgánica e Inorgánica, QUOREX Research Group, Universidad de Extremadura, E-06071 Badajoz, Spain
[b] Department of Chemistry, University of Southampton, Highfield, Southampton SO17 1BJ, UK

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ABSTRACT

A one-pot procedure for preparing chiral 1,3-oxazolidines derived from *N*-methyl-D-glucamine and aryl aldehydes is described. It has been carried out by using readily available reagents and operationally simple conditions allowing the preparation of the acyclic C-nucleoside analogs in high yields. The structure of these derivatives has been fully characterized by NMR correlations and single-crystal X-ray diffraction. Some reactions also provide access to the corresponding tetrahydro-1,3-oxazines by an alternative ring closure. Mechanistic considerations account for the observed steric course.

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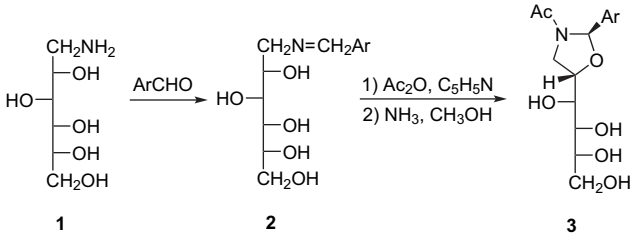
1. Introduction

C-Nucleoside analogs in which an open-chain sugar is linked to a heterocyclic moiety through a carbon–carbon bond represent attractive structures in view of the biological and therapeutic activities exhibited by naturally occurring C-nucleosides and their synthetic surrogates.[1]

Recently, we have shown that imines derived from sugar aminopolyols, such as D-glucamine (**1**), can be converted into inherently chiral *N*-acyloxazolidines (**3**) under acylating conditions, a process occurring through the intermediacy of a transient iminium ion (Scheme 1).[2] Both chiral oxazolidines and oxazolidinones have proved to be versatile auxiliaries in asymmetric induction.[3]

In general, imines like RCH=NCH$_2$CHOH–R[1] are stable enough and do not cyclize in solution; however, N-substitution leads to an iminium species that further evolves to the corresponding 1,3-oxazolidine. This strategy has in fact become the usual synthesis of such saturated heterocycles.[4] Since some 1-alkylamino-1-deoxyalditols are commercially available, such as *N*-methyl, *N*-ethyl, and *N*-(2-hydroxyethyl)-D-glucamine, and *N*-methyl-D-galactamine, we were stimulated to further explore the preparation of new and robust chiral 1,3-oxazolidines derived from aromatic aldehydes.

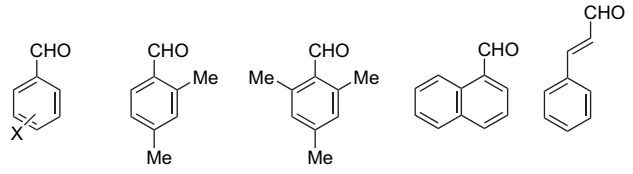


Scheme 1.

2. Results and discussion

2.1. Synthesis of *N*-methyl-1,3-oxazolidines

Herein, we report the condensation of *N*-methyl-D-glucamine (**4**) with different monosubstituted benzaldehydes (**5a**–**5j**, **5m**, **5o**, **5q**) and polysubstituted benzaldehydes (**5k**, **5l**), as well as 1-naphthaldehyde (**5n**) and cinnamaldehyde (**5p**). Two protocols were developed; the first (method A) involves the reaction of **4** with the corresponding aldehyde in water plus a small amount of methanol to ensure homogenization, which causes the rapid separation of the adduct, either spontaneously or after solvent evaporation. In method B, a mixture of **4** and the aldehyde derivative is refluxed in benzene with azeotropic water removal (Dean–Stark). The resulting adducts are filtered from the hot benzene solution to avoid crystallization of the remaining aldehyde.



5a-5j, 5m, 5o, 5q **5k** **5l** **5n** **5p**

* Corresponding author.
E-mail address: rmarvaz@unex.es (R.F. Martínez).

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Table 1
Isolated yields (%) in the condensation of **4** and aldehydes

Entry	Aldehyde	X	Product	Yield (%) **A**[a]/**B**[b]
1	**5a**	4-NO_2	**6a**	80/93
2	**5b**	3-MeO	**6b**	79/92
3	**5c**	3-Br	**6c**	76/95
4	**5d**	4-Cl	**6d**	70/97
5	**5e**	H	**6e**	57/97
6	**5f**	2-Me	**6f**	18/96
7	**5g**	3-Me	**6g**	60/91
8	**5h**	4-Me	**6h**	79/90
9	**5i**	4-Et	**6i**	41/98
10	**5j**	4-MeO	**6j**	76/84
11	**5k**		**6k**	31/85
12	**5n**		**7**+**8**	98[c]/97[c]
13	**5o**	2-OH	**9**+**10**+**11**	61[c]/95[c]
14	**5p**		**12**+**13**+**14**	47[c]/100[c]
15	**5q**	4-CHO	**15**	51/57(87[d])

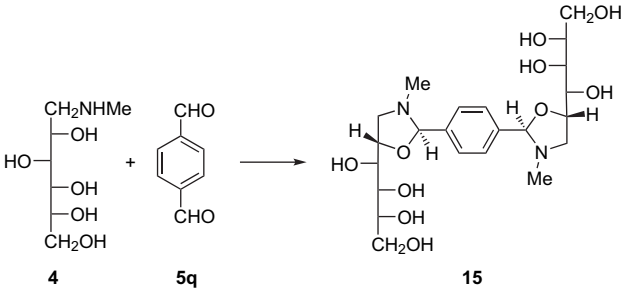
[a] In water.
[b] In benzene at reflux.
[c] Combined yield.
[d] Combined yield of **15**–**17**.

As shown in Table 1, the latter protocol does usually produce higher yields, substantially improved in a few cases with respect to the aqueous variation, for which yields range from low, presumably due to steric effects in the case of *o*-substituted aldehydes **5f** and **5k** (entries 6 and 11), to good, especially with electron-withdrawing groups (entries 1–4). No product could be obtained, either by method A or by method B, starting from 2,4,6-trimethylbenzaldehyde (**5l**) and 4-dimethylaminobenzaldehyde (**5m**). The absence of reactivity in **5m** may be attributed to the strong donor effect of the dimethylamino group that decreases the electrophilic character of the carbonyl group. This argument has equally been invoked to account for the inertness of **5m** in the benzoin condensation.[5]

When these reactions were conducted with aldehydes **5a**–**5k**, the sole products were the corresponding *trans*-oxazolidines **6a**–**6k** (Scheme 2), in which the new chiral center possesses *R* configuration. With 1-naphthaldehyde (**5n**), its condensation with **4** led, in both methods A and B, to a mixture of *trans*- and *cis*-oxazolidines (**7** and **8**, respectively). Both methods also gave **7**/**8** in a ratio of ~75:25 that increased up to 81:19 after crystallization from ethanol. Further recrystallizations, however, did not alter that proportion nor did they facilitate stereoisomer separation.

With *o*-salicylaldehyde (**5o**) these methodologies gave rise to a mixture of three products, which were identified as oxazolidines **9** (trans-configured) and **10** (cis), and the tetrahydro-1,3-oxazine **11** in an approximate proportion of 40:35:25, respectively, as determined by ^{1}H NMR integration. Similar results were obtained with cinnamaldehyde (**5p**) affording a mixture of such five- and six-membered heterocycles in 52:32:16 ratio (for **12**/**13**/**14**, respectively). In both cases, those proportions are identical by both synthetic methods (A and B) and remain essentially unchanged after successive crystallizations from ethanol. Separation of the individual isomers could not be achieved.

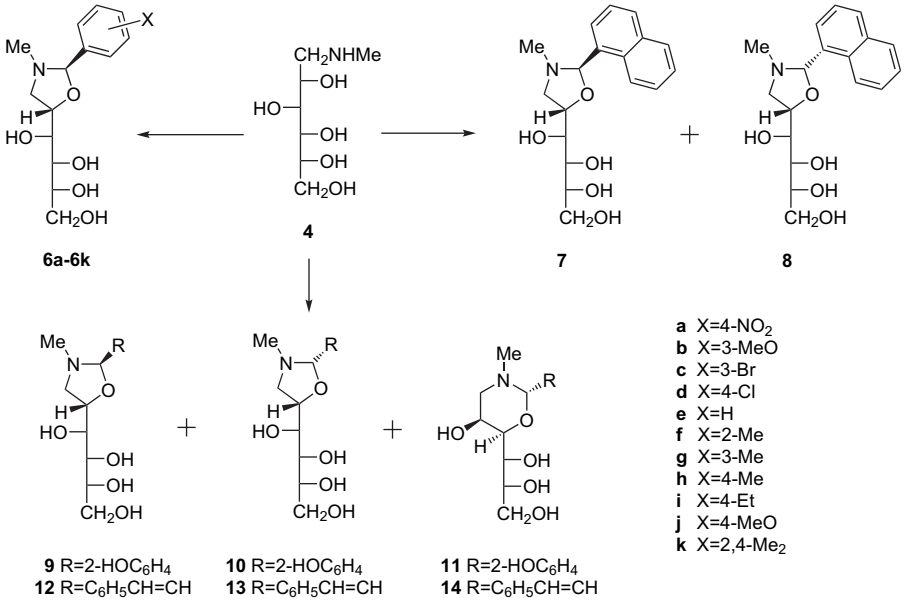
The bifunctional aldehyde **5q** reacted with 2 equiv of **4** in aqueous medium with complete stereoselectivity as only compound **15** could be isolated. This substance contains two oxazolidine rings, both having the same configuration at the newly created chiral centers (2*R*,2′*R*) (vide infra) (Scheme 3).



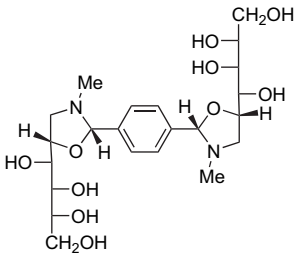
4 **5q** **15**

Scheme 3.

However, the same condensation conducted in refluxing benzene provided a mixture of **15**, its 2*S*,2′*S* diastereomer (**16**), and the isomeric bis-tetrahydro-1,3-oxazine **17** in an approximate proportion of 66:22:12, respectively, from which pure **15** could be isolated by crystallization from ethanol.



Scheme 2.



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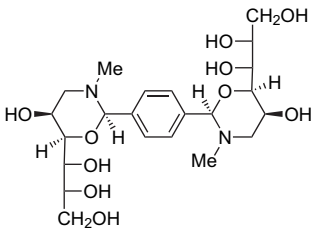

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2.2. Structural determination

Structural elucidation of the above substances can easily be inferred from spectroscopic and analytical data. With the sole exception of IR bands at 3500–3100 cm^{-1} (OH groups), no significant absorptions are observed beyond 1600 cm^{-1}, in agreement with the saturated character of the heterocycles. Tables 2 and 3 also collect ^{1}H and ^{13}C NMR chemical shifts of the heterocyclic moiety. The proton resonances at ~4.5 to 5.5 ppm and the ^{13}C shift at ~97 ppm are consistent with the typical values encountered for the H-2 and C-2 signals of the oxazolidine ring.[6–8] Sugar carbons resonated at around ~71 ppm, another feature usually typical of acyclic polyhydroxyalkyl chains.[9,10]

Moreover, the mass spectrum of compound **6k** showed fragmentations similar to those found in other polyhydroxylalkyl heterocycles such as Het^{+}, $Het–CH{=}OH^{+}$, and $Het–CHOHCH{=}OH^{+}$, which evidence the presence of the *N*-methyl-oxazolidine moiety (Fig. 1S and Chart 1 in Supplementary data).

Table 2
Selected chemical shifts (δ, ppm) of the heterocyclic protons of chiral oxazolidines[a]

Product	H-2	H-5	H-4a	H-4b	$\Delta\delta_{H\text{-}4}$[c]	Config.[d]
6a	4.75	4.32	3.35	2.42	0.93	*R*
6e	4.56	4.28	3.33	2.37	0.96	*R*
6h	4.51	4.25	3.34	2.34	1.00	*R*
6j	4.48	4.24	3.30	2.31	0.99	*R*
7	5.21	4.37	3.29	2.54	0.75	*R*
8	5.48	4.28	3.14	2.85	0.29	*S*
15	4.56	4.26	3.32	2.35	0.97	*R*
16	4.70	4.18	3.08	2.67	0.41	*S*
18[b]	4.77	4.38	2.48	2.50	0.98	*R*
19[b]	4.71	4.24	3.24	2.76	0.48	*S*

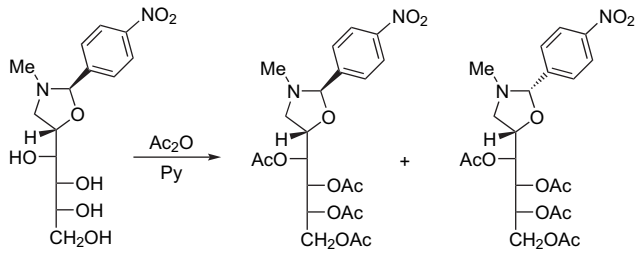
[a] At 400 MHz, in DMSO-d_6.
[b] In $CDCl_3$.
[c] $\Delta\delta_{H\text{-}4}=\delta_{H\text{-}4a}-\delta_{H\text{-}4b}$.
[d] Stereochemistry at C-2.

Table 3
Selected ^{13}C chemical shifts (δ, ppm) of chiral oxazolidines[a]

Product	Heterocycle				Polyhydroxyalkyl chain			
	C-2	C-4	C-5	N–Me	C-1′	C-2′	C-3′	C-4′
6a	96.0	57.0	79.8	37.7	71.4	71.3	71.3	63.6
6e	97.6	57.2	79.1	37.5	71.4	71.4	71.3	63.7
6j	97.2	57.0	78.7	37.4	71.3	71.3	71.2	63.6
7	96.9	57.4	78.4	38.0	71.4	71.3	71.3	63.7
8	96.1	53.6	77.8	39.4	71.4	71.2	71.2	63.6
9	95.8	56.5	79.3	37.5	71.6	71.6	71.5	68.8
10	96.9	55.2	77.8	38.0	71.8	71.7	71.6	63.9
12	97.4	57.1	78.9	38.0	71.6	71.6	71.6	63.9
13	98.1	55.4	77.8	38.8	71.5	71.3	71.2	64.0
15	97.5	57.3	79.3	37.7	71.6	71.5	71.5	63.8
16	98.3	55.8	77.9	38.6	71.6	71.5	71.5	64.0
18[b]	96.7	57.2	76.0	37.6	70.2	68.7	68.1	61.7
19[b]	98.0	56.4	75.4	38.1	70.9	69.2	68.0	61.7

[a] At 100 MHz, in DMSO-d_6.
[b] In $CDCl_3$.

A further proof supporting the heterocyclic nature of these condensation products could be obtained through an acetylated derivative of **6a**, prepared by conventional room-temperature reaction with acetic anhydride and pyridine. NMR analysis of the crude mixture revealed the formation of approximately equal amounts of **18** and **19**; the latter could be isolated by evaporating to dryness and treating the resulting oil with diethyl ether (Scheme 4).



6a **18** **19**

Scheme 4.

The structure of **19** was in addition confirmed by X-ray diffraction analysis as suitable crystals were grown from ethanol solutions (Fig. 1).[11] NMR data of **19** (Tables 2 and 3) fully agree with those of **6a–6k**, **7–10**, **12**, **13**, **15**, **16** and **18**, thereby confirming the presence of the oxazolidine core in these substances.

Crude mixtures resulting from the condensation of **4** with aldehydes **5o–5q** were analyzed by NMR analysis and evidenced the presence of three isomeric substances having similar chemical shifts and splitting patterns (Fig. 2S in Supplementary data). The structure of tetrahydro-1,3-oxazine (attributed to minor products) is based on spectroscopic data; proton and carbon resonances (Tables 4 and 5) are close to those of the above oxazolidines and were assigned by two-dimensional correlations.

2.3. Geometric isomerization of 1,3-oxazolidines

At this stage, it is worth pointing out that acetylation of **6a** does lead to not only the expected oxazolidine **18** but also **19**. Furthermore, NMR monitoring of a $CDCl_3$ solution of **19** revealed a slow

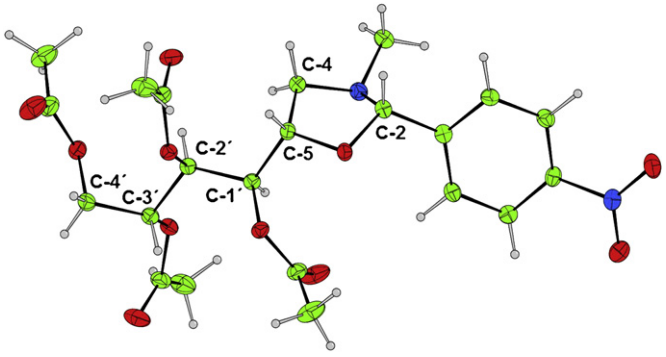


Figure 1. ORTEP diagram for the *N*-methyl oxazolidine **19**. Thermal ellipsoids were drawn at 35% probability level.

Table 4
Chemical shifts (δ, ppm) of the heterocyclic protons in *N*-Methyl-tetrahydro-1,3-oxazines[a]

Product	H-2	H-4a	H-4b	H-5	OH-5	H-6	NCH_3
11	4.63	3.04	2.56	3.82	5.22	4.21	2.00
14	4.26	2.93	2.60	3.70	4.96	4.13	2.21
17	4.59	3.00	2.68	3.74	5.00	4.26	2.09

[a] At 400 MHz recorded in DMSO-d_6.

Table 5
Selected ^{13}C resonances (δ, ppm) of *N*-Methyl-tetrahydro-1,3-oxazines[a]

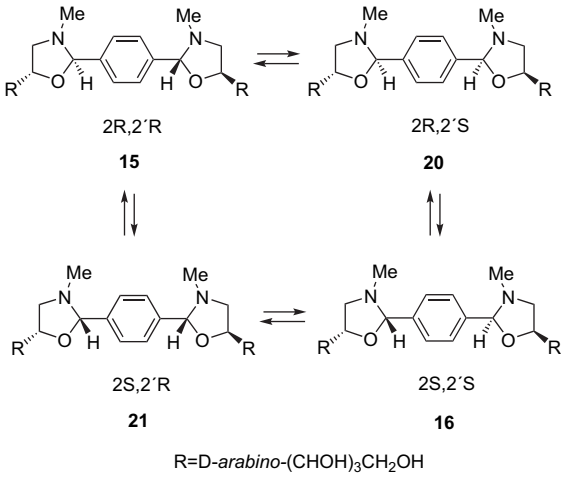
Product	Heterocycle				Polyhydroxyalkyl chain			
	C-2	C-4	C-5	C-6	N–Me	C-1′	C-2′	C-3′
11	94.7	59.9	73.7	77.7	39.8	70.9	66.1	63.1
14	94.8	60.4	74.0	77.6	39.8	70.9	66.9	63.2
17	95.7	60.7	74.0	78.3	39.7	70.9	66.8	63.1

[a] At 100 MHz in DMSO-d_6.

and gradual transformation of this substance into a mixture of **18** and **19** (Fig. 2). Since both derivatives are present in nearly equal amounts after equilibration, their stability should be similar. This isomerization should be occurring via acid catalysis. When acid impurities present in $CDCl_3$ are removed (by passing it through an alumina column), such isomerization slows down. Thus, only 25% and 38% of **18** is formed after 24 and 48 h, respectively (Fig. 3S in Supplementary data). In contrast, this conversion was not detected at all in DMSO-d_6 (a solvent lacking acid character) after 6 days. This behavior points to an easy isomerization between oxazolidines, despite Baldwin rules disfavor a 5-*endo-trig* cyclization relative to the 6-*endo-trig* one,[12,13] which would afford the corresponding oxazines. Nevertheless, David and co-workers have demonstrated that 5-*endo-trig* cyclizations of imines and iminium ions leading either to oxazolidines or to oxazines proceeds quickly.[14]

2.4. Absolute configuration at C-2 of chiral oxazolidines and oxazines

Although the steric course of imine and iminium cyclization to produce oxazolidines has been previously documented,[4,15] such pathways are not completely applicable to the present case with the sole exception of *N*-acyloxazolidines.[2] However, we were able to establish unequivocally the absolute stereochemistry of the newly generated stereocenter by spectroscopic correlation. The key point of this reasoning is based on the stereochemistry at C-2 of compound **19**, which has been determined to be *S* (Fig. 1). NMR analysis shows that the two protons at C-4 of the oxazolidine ring exhibit very distinctive shifts with a difference $\Delta\delta^{cis}_{H\text{-}4}$=0.48 ppm ($\Delta\delta_{H\text{-}4}=\delta_{H\text{-}4a}-\delta_{H\text{-}4b}$) (Table 2). Such a difference increases to $\Delta\delta^{trans}_{H\text{-}4}$=0.98 ppm for the isomeric structure **18** that does necessarily possesses *R* configuration at C-2. These shift differences and a nearly constant variation ($\Delta\Delta\delta_{H\text{-}4}=\Delta\delta^{trans}_{H\text{-}4}-\Delta\delta^{cis}_{H\text{-}4}$=0.5 ppm) may be employed as diagnostic criteria to denote the stereochemistry, either *R* or *S*, in the rest of the synthesized oxazolidines. Data from Table 2 plus those collected in Section 4 point to 2*R*-configured products in the case of oxazolidines **6a**–**6k** as well as major adducts **7**, **9**, **12**, **15**, and **18**, whereas they are consistent with the opposite 2*S* configuration in **8**, **10**, **13**, **16**, and **19**. Again, these correlations are similar to those found in *N*-acyloxazolidines derived from D-glucamine and corroborate the stereochemistry previously assigned to these substances.[2] Particular attention deserves the stereochemistry in adducts derived from **4** plus terephthaldehyde (**5q**) as four different stereoisomers can be potentially formed as depicted in Scheme 5: (2*R*,2′*R*), (2*R*,2′*S*), (2*S*,2′*R*), and (2*S*,2′*S*).



Scheme 5.

Obviously, the bis-oxazolidines with configurations (2*R*,2′*R*) and (2*S*,2′*S*) possess a C_2 symmetry axis that halves the expected proton and carbon NMR signals; in stark contrast, the derivatives having

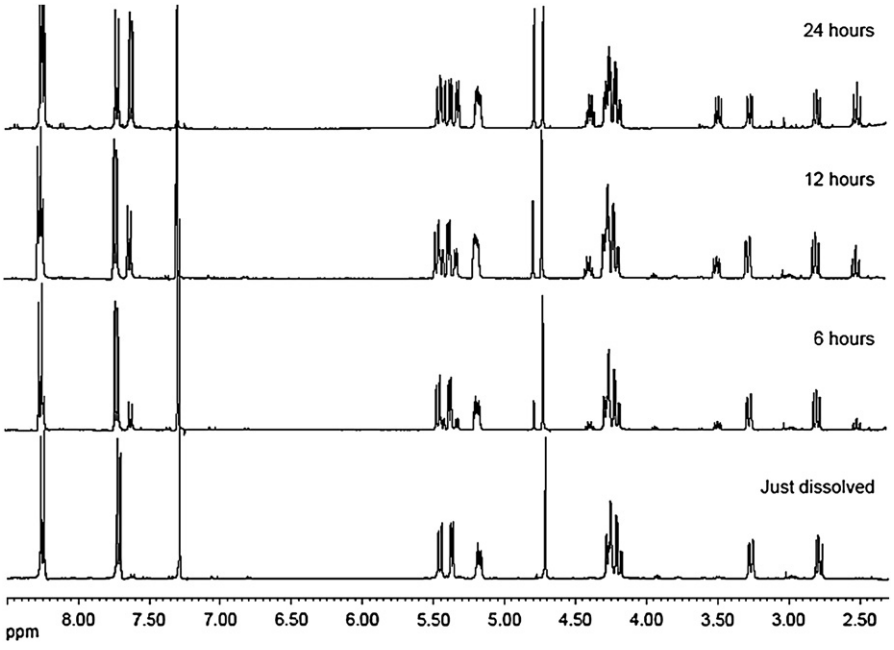


Figure 2. Equilibration of isomers **18** and **19** in $CDCl_3$ solution.

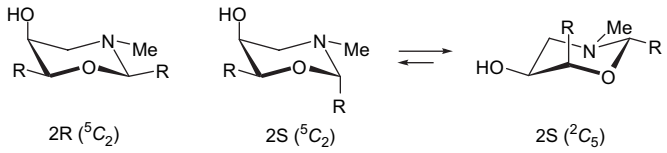


Figure 3. Conformations of tetrahydro-1,3-oxazines.

the (2*R*,2′*S*) and (2*S*,2′*R*) configurations would exhibit duplicated signals. A detailed ^{13}C NMR analysis of the crude sample reveals the existence of three isomers, from which the major ones only show the half of possible signals, thus agreeing with oxazolidines **15** (2*R*,2′*R*) and **16** (2*S*,2′*S*), whose stereochemistries have been assigned through the magnitudes of $\Delta\delta_{H\text{-}4}$ (0.97 ppm and 0.43 ppm, respectively). The minor adduct equally shows a simplified spectrum with the half of signals, a fact ruling out the isomers **20** (2*R*,2′*S*) and **21** (2*S*,2′*R*). Since its ^{13}C resonances are different from those of **15** and **16**, the isomer should be the symmetrical bis(tetrahydro-1,3-oxazine) **17**.

We have tentatively assigned an *R* configuration at C-2 for **11** and **14**, and (2*R*,2′*R*) for **17**, because they lead to the most stable conformation of the tetrahydro-1,3-oxazine: $^5C_2$,[16] which places the bulkiest substituents in equatorial dispositions (Fig. 3). Moreover, this argument is also consistent with the stereochemical outcome that likely follows this transformation (vide infra).

2.5. Stability of *N*-methyl oxazolidines and *N*-methyl-tetrahydro-1,3-oxazines

Calculations in vacuum at the DFT level (B3LYP/6-31G*) of theory,[17] and with a PCM(B3LYP/6-31G*) SCRF model[18] to consider the solvent, have also been carried out using Gaussian 03[19] to asses the relative stability of the different isomeric species. As representative example, Table 6 shows the computed energies for oxazolidines **9** and **10** and their isomeric oxazine **11**. In the gas phase, the oxazine derivative has a larger stability, while compound **9** becomes more stable in DMSO. It is noteworthy that energy differences between **9** and **10** remain constant in both gas phase and after considering solvent effects. Accordingly, the experimental ratio **9**>**10**>**11** (40:35:25, respectively) follows a different trend to thermodynamic stability and reflects that formation of these heterocyclic species should be occurring under kinetic control. This conclusion may be extrapolated to other series such as **12**–**14** and **15**–**17**.

Table 7 shows the calculated energies for the trans- and cis-acetylated oxazolidines **18** and **19**. Such calculations evidence the same stability of both isomers, in the gas phase as well as by considering solvent effects ($CHCl_3$), in agreement with the experimental observations.

Table 6
Calculated relative energies of compounds **9**–**11**[a]

Product	**9**	**10**	**11**
Vacuum[b]	12.17	18.12	0.00
DMSO[c]	0.00	7.29	2.38

[a] In kcal mol^{-1}.
[b] At the B3LYP/6-31G* level.
[c] PCM(B3LYP/6-31G*) SCRF.

Table 7
Calculated relative energies of compounds **18** and **19**[a]

Product	**18**	**19**
Vacuum[b]	0.82	0.00
$CHCl_3$[c]	0.59	0.00

[a] In kcal mol^{-1}.
[b] At the B3LYP/6-31G* level.
[c] PCM(B3LYP/6-31G*) SCRF.

2.6. Mechanistic considerations in the formation of heterocyclic rings

Scheme 6 accounts for the formation of oxazolidines and tetrahydro-1,3-oxazines. The former substances are generated via 5-*endo*-*trig* cyclization of the iminium ion, entropically favored with respect to the alternative 6-*endo*-*trig* that provides the 1,3-oxazine derivative.

This stereochemical result assumes that cyclization of the (*E*)-iminium cation occurs preferentially through the most stable conformation. The first and second chiral centers of *N*-methyl-D-glucamine, having *S* and *R* configurations, respectively, as well as their hydroxyl substituents lie in the *Re* face of the carbon of iminium ion. The subsequent cyclization could then take place on such a face to give a new chiral center with configuration *R* and relative stereochemistry trans between the polyhydroxyl chain at C-5 and the aromatic substituent at C-2.

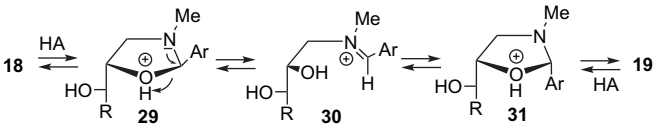
N-Methyl-D-glucamine is not more stable in an extended zig-zag (*P*) conformation (**22**) due to the 1,3-diaxial interaction present between the hydroxyl groups at C-2 and C-4 rather this sugar adopts a $_3G^+$ conformation (**23**) generated by 60° rotation around the C3–C4 bond.[20] A small rotation around the C–N bond converts this initial conformation into a favored disposition (**24**) to reach the transition structure that leads to a *trans*-oxazolidine (2*R*-configured, **26**, path a) by ring closure.

Counterclockwise rotation at an angle of 120° around the C1–C2 bond then generates the $_1G^-{}_3G^+$ conformation (**25**), in which the planar iminium group is placed between the hydroxyl groups of the aforementioned carbon atoms; the first on the *Si* face and the other on the *Re* face. Further cyclization of such hydroxyl groups gives rise to a *cis*-oxazolidine (2*S*-configured, **27**, path b) and a *cis*-tetrahydro-1,3-oxazine (2*R*-configured, **28**, path c), respectively, the former being entropically favored. The $_1G^-{}_3G^+$ conformation (**25**) should be less stable than **24** because the bulkier iminium group bisects the angle between the hydroxyl substituent and the sugar chain, thereby generating two strong *gauche* interactions in addition to a 1,3-diaxial one between the hydroxyl at C-2 and the iminium group. Conversely, only one *gauche* interaction with the hydroxyl group occurs in **24**. As a result, the transition structures leading to **27** and **28**, which arise from **25**, should likewise be less stable than the corresponding ones to **26** generated from the more stable conformation **24**. Overall, this explains why the relative amounts of products in experiments, i.e., **26**>**27**>**28** (kinetic control) contradicts the thermodynamic stability **26**>**28**>**27**.

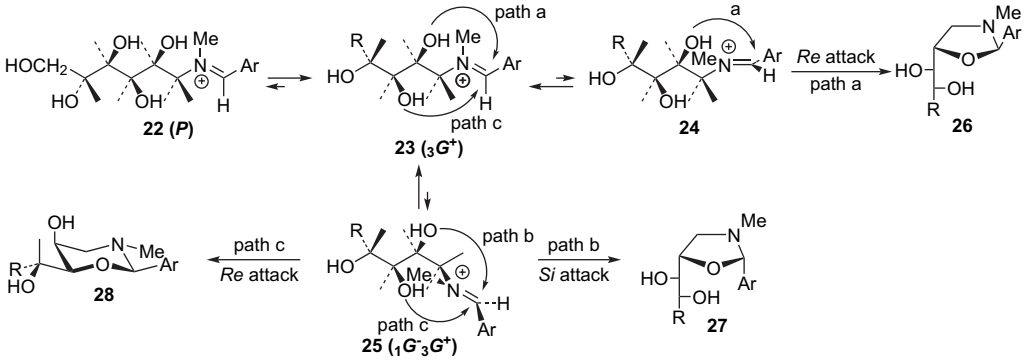
The $_1G^-{}_3G^-$ conformation, generated by clockwise rotation at an angle of 120° around the C1–C2 bond, has a lower energy than that of $_1G^-{}_3G^+$ (**25**); however, such an arrangement puts away the iminium group, thus impeding the ring closure.

Alternative to the cyclization through the *Si* face of (*E*)-iminium cation, cyclization of the C-2 hydroxyl group through the *Re* face of the (*Z*)-iminium cation would give rise to a *cis*-oxazolidine, as well as the corresponding *cis*-oxazine resulting from the cyclization of the hydroxyl group at C-3. However, the latter has not been detected experimentally.

Finally, equilibration between *trans*- and *cis*-oxazolidines (**18** and **19**) should be occurring under acid catalysis, a fact that regenerates the cation intermediate (**30**).



(R=D-*erythro*-CHOAcCHOAcCH$_2$OAc; Ar=4-NO$_2$C$_6$H$_4$)



Scheme 6.

In solvents devoid of such properties (e.g., DMSO), no equilibration takes place.

3. Conclusions

In summary, we have demonstrated a convenient one-pot protocol for the formation of chiral oxazolidines with high or complete stereoselectivity from *N*-methylaminopolyols and aromatic aldehydes bypassing the Schiff base stage. Given the availability of *N*-alkyl-D-glycamines, this methodology should facilitate access to mono- and bis-*C*-glycosylated oxazolidines (and oxazines) as suitable scaffolds.

4. Experimental

4.1. General

Melting points were determined on Gallenkamp and Electrothermal apparatus, and are uncorrected. Optical rotations were measured on a Perkin–Elmer 241 polarimeter. IR spectra were recorded in the range 4000–600 cm^{-1} on FT-IR THERMO spectrophotometer. Solid samples were recorded on KBr (Merck) pellets. ^1H and ^{13}C NMR spectra were recorded on a Bruker 400 AC/PC instrument at 400 and 100 MHz, respectively, or with a Bruker AC 200-E instrument at 200 and 50.3 MHz, respectively, in different solvent systems. Assignments were confirmed by homo- and hetero-nuclear double-resonance and DEPT (distortionless enhancement by polarization transfer). TMS was used as the internal standard (δ=0.00 ppm) and all *J* values are given in hertz. Microanalyses were carried out on a Leco 932 analyser at the *Universidad de Extremadura* (Spain). High resolution mass spectra (chemical ionization) were recorded on an Autospec-Q spectrometer by the *Servicio de Espectrometría de Masas de la Universidad de Sevilla* (Spain).

4.2. Condensation of *N*-methyl-D-glucamine with aldehydes

Method A. To a solution of *N*-methyl-D-glucamine (55.2 mmol) in water (70 mL) was slowly added a solution of the corresponding aldehyde (55.0 mmol) in a few volume of methanol. The mixture was stirred at room temperature, which afforded a precipitate within few minutes. The resulting product was collected by filtration, successively washed with cold water, ethanol, and diethyl ether, and recrystallized from ethanol.

Method B. To a suspension of *N*-methyl-D-glucamine (10.0 mmol) in benzene (15 mL) was added the corresponding aldehyde (15.0 mmol). The mixture was refluxed for 4–5 h with concomitant water removal (Dean–Stark). The product was filtered and washed with cold benzene and recrystallized from ethanol.

*4.2.1. (2R,5S)-3-Methyl-2-(4-nitrophenyl)-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**6a**)*

Method A (80%); method B (93%); mp 160–162 °C; $[\alpha]_D^{22}$ +11 (*c* 0.5, pyridine); ν_{max}/cm^{-1} 3400–3200 (OH), 1605, 1520, 1457 (arom), 1085, 1030 (C–O). ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 8.23 (d, *J* 8.8 Hz, 2H, H-arom), 7.71 (d, *J* 8.8 Hz, 2H, H-arom), 4.75 (s, 1H, H-2), 4.62 (d, *J* 6.4 Hz, 1H, OH), 4.52 (d, *J* 6.0 Hz, 1H, OH), 4.36 (d, *J* 4.0 Hz, 1H, OH), 4.35 (t, $J_{4',OH}$=$J_{4'',OH}$ 3.0 Hz, 1H, OH-4′), 4.32 (dt, $J_{4a,5}$=$J_{5,1'}$ 6.6 Hz, $J_{4b,5}$ 9.2 Hz, 1H, H-5), 3.70 (t, $J_{1',5}$=$J_{1',OH}$ 7.4 Hz, $J_{1',2'}$ 0 Hz, 1H, H-1′), 3.60 (m, $J_{4',OH}$ 3.2 Hz, $J_{3',4'}$ 5.6 Hz, 1H, H-4′), 3.50 (m, 1H, H-3′), 3.42 (dt, $J_{4'',4'}$ 11.2 Hz, $J_{4'',3'}$=$J_{4'',OH}$ 5.6 Hz, 1H, H-4″), 3.35 (dd, $J_{4a,4b}$ 9.4 Hz, $J_{4a,5}$ 5.8 Hz, 1H, H-4a), 3.22 (t, $J_{2',3'}$=$J_{2',OH'}$ 7.8 Hz, 1H, H-2′), 2.42 (t, $J_{4a,4b}$=$J_{4b,5}$ 9.4 Hz, 1H, H-4b), 2.14 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 148.03 (C-arom), 147.24 (C-arom), 129.24 (2C, C-arom), 123.59 (2C, C-arom), 96.02 (C-2), 79.76 (C-5), 71.36, 71.27 (C-1′, C-2′, C-3′), 63.60 (C-4′), 57.05 (C-4), 37.67 (CH_3–N). Anal. Calcd for $C_{14}H_{20}N_2O_7$: C, 51.22; H, 6.14; N, 8.53. Found: C, 51.20; H, 6.35; N, 8.60.

*4.2.2. (2R,5S)-2-(3-Methoxyphenyl)-3-methyl-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**6b**)*

Method A (79%); method B (92%); mp 133–135 °C; $[\alpha]_D^{23}$ +12 (*c* 0.5, pyridine); ν_{max}/cm^{-1} 3500–3100 (OH), 1603 (arom), 1160, 1097, 1031 (C–O). ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 7.29 (t, *J* 7.8 Hz, 1H, H-arom), 7.00 (m, 2H, H-arom), 6.91 (dd, *J* 1.8, 7.8 Hz, 1H, H-arom), 4.58 (d, *J* 6.0 Hz, 1H, OH), 4.54 (s, 1H, H-2), 4.34 (m, 2H, OH), 4.27 (dt, $J_{4a,5}$=$J_{4b,5}$ 8.8 Hz, $J_{5,1'}$ 6.4 Hz, 1H, H-5), 3.69 (s, 3H, OCH_3), 3.68 (t, $J_{1',5}$=$J_{1',OH}$ 6.0 Hz, $J_{1',2'}$ 0 Hz, 1H, H-1′), 3.60 (d, $J_{4',4''}$ 10.0 Hz, 1H, H-4′), 3.50 (m, 1H, H-3′), 3.42 (m, 1H, H-4″), 3.32 (dd, $J_{4a,4b}$ 8.8 Hz, $J_{4a,5}$ 5.6 Hz, 1H, H-4a), 3.21 (t, $J_{2',3'}$ 6.8 Hz, 1H, H-2′), 2.34 (t, $J_{4a,4b}$=$J_{4b,5}$ 9.4 Hz, 1H, H-4b), 2.00 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 159.40, 141.21, 129.38, 120.55, 114.64, 113.31 (C-arom), 97.38 (C-2), 79.10 (C-5), 71.42, 71.36, 71.30 (C-1′, C-2′, C-3′), 63.66 (C-4′), 57.11 (C-4), 55.29 (OCH_3), 37.61 (CH_3). Anal. Calcd for $C_{15}H_{23}NO_6$: C, 57.50; H, 7.40; N, 4.47. Found: C, 57.32; H, 7.65; N, 4.62.

*4.2.3. (2R,5S)-2-(3-Bromophenyl)-3-methyl-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**6c**)*

Method A (76%); method B (95%); mp 166–168 °C; $[\alpha]_D^{21}$ +7 (*c* 0.5, pyridine); ν_{max}/cm^{-1} 3400–3200 (OH), 1578, 1474 (arom), 1090, 1024 (C–O). ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 7.61 (s, 1H, H-arom), 7.55 (d, *J* 8.0 Hz, 1H, H-arom), 7.43 (d, *J* 8.0 Hz, 1H, H-arom), 7.34 (t, *J* 7.7 Hz, 1H, H-arom), 4.58 (d, *J* 4.4 Hz, 1H, OH), 4.56 (s, 1H, H-2), 4.50 (d, *J* 5.6 Hz, 1H, OH), 4.34 (t, *J* 6.0 Hz, 1H, OH), 4.26 (m, 1H,

H-5), 3.66 (t, $J_{1',5}$=$J_{1',OH}$ 6.8 Hz, $J_{1',2'}$ 0 Hz, 1H, H-1′), 3.58 (m, 1H, H-4′), 3.48 (m, 1H, H-3′), 3.40 (dt, $J_{4'',OH}$=$J_{4'',3'}$ 5.6 Hz, $J_{4'',4'}$ 11.2 Hz, 1H, H-4″), 3.31 (dd, $J_{4a,4b}$ 8.8 Hz, $J_{4a,5}$ 6.0 Hz, 1H, H-4a), 3.20 (t, $J_{2',3'}$=$J_{2',OH}$ 7.8 Hz, 1H, H-2′), 2.35 (t, $J_{4b,4a}$=$J_{4b,5}$ 9.2 Hz, 1H, H-4b), 2.10 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 138.38, 133.18, 129.80, 128.09 (C-arom), 96.30 (C-2), 79.98 (C-5), 71.07, 71.00, 70.93 (C-1′, C-2′, C-3′), 63.33 (C-4′), 56.77 (C-4), 37.30 (CH_3). Anal. Calcd for $C_{14}H_{20}BrNO_5$: C, 46.42; H, 5.57; N, 3.87. Found: C, 46.27; H, 5.88; N, 4.06.

4.2.4. (2R,5S)-2-(4-Chlorophenyl)-3-methyl-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**6d**)

Method A (70%); method B (97%); mp 193–195 °C; $[\alpha]_D^{22}$ +6 (*c* 0.5, pyridine); ν_{max}/cm^{-1} 3400–3200 (OH), 1602, 1492, 1459 (arom), 1088, 1032 (C–O). ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 7.46 (d, *J* 8.8 Hz, 2H, H-arom), 7.43 (d, *J* 8.8 Hz, 2H, H-arom), 4.59 (d, *J* 6.8 Hz, 1H, OH), 4.57 (s, 1H, H-2), 4.51 (d, *J* 5.6 Hz, 1H, OH), 4.35 (t, *J* 5.6 Hz, 1H, OH), 4.34 (d, *J* 7.6 Hz, 1H, OH), 4.26 (m, 1H, H-5), 3.67 (t, $J_{1',5}$=$J_{1',OH}$ 6.8 Hz, $J_{1',2'}$ 0 Hz, 1H, H-1′), 3.59 (m, 1H, H-4′), 3.49 (m, 1H, H-3′), 3.40 (m, 1H, H-4″), 3.32 (m, 1H, H-4A), 3.20 (t, $J_{2',3'}$=$J_{2',OH}$ 7.6 Hz, 1H, H-2′), 2.35 (t, $J_{4b,4a}$=$J_{4b,5}$ 9.2 Hz, 1H, H-4b), 2.12 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 138.89, 133.70, 130.31, 128.61 (C-arom), 96.16 (C-2), 79.11 (C-5), 71.07, 70.95 (C-1′, C-2′, C-3′), 63.32 (C-4′), 56.71 (C-4), 37.30 (CH_3). Anal. Calcd for $C_{14}H_{20}ClNO_5$: C, 52.92; H, 6.34; N, 4.41. Found: C, 53.10; H, 6.35; N, 4.35.

4.2.5. (2R,5S)-3-Methyl-2-phenyl-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**6e**)

Method A (57%); method B (97%); mp 129–131 °C; $[\alpha]_D^{21}$ +12 (*c* 0.5, pyridine); IR (KBr) ν_{max}/cm^{-1} 3400–3100 (OH), 1477, 1457 (arom), 1095, 1024 (C–O). ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 7.44 (m, 2H, H-arom), 7.36 (m, 3H, H-arom), 4.57 (d, *J* 6.4 Hz, 1H, OH), 4.56 (s, 1H, H-2), 4.51 (d, *J* 5.6 Hz, 1H, OH), 4.35 (d, *J* 5.2 Hz, 1H, OH), 4.34 (t, *J* 7.6 Hz, 1H, OH), 4.28 (m, $J_{5,4b}$ 8.8 Hz, $J_{5,1'}$ 6.4 Hz, 1H, H-5), 3.70 (dd, $J_{1',5}$=$J_{1',OH}$ 6.0 Hz, $J_{1',2'}$ 0 Hz, 1H, H-1′), 3.61 (dd, $J_{4',4''}$ 11.0 Hz, $J_{4',3'}$ 2.6 Hz, 1H, H-4′), 3.51 (m, 1H, H-3′), 3.42 (dt, $J_{4'',4'}$ 10.6 Hz, $J_{4'',3'}$=$J_{4'',OH}$ 5.6 Hz, 1H, H-4″), 3.33 (dd, $J_{4a,4b}$ 8.8 Hz, $J_{4a,5}$ 6.0 Hz, 1H, H-4a), 3.24 (t, $J_{2',3'}$=$J_{2',OH}$ 6.8 Hz, 1H, H-2′), 2.37 (t, $J_{4b,4a}$=$J_{4b,5}$ 9.0 Hz, 1H, H-4b), 2.09 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 139.54, 129.05, 128.32, 128.26 (C-arom), 97.57 (C-2), 79.13 (C-5), 71.42, 71.36, 71.30 (C-1′, C-2′, C-3′), 63.69 (C-4′), 57.17 (C-4), 37.55 (CH_3). Anal. Calcd for $C_{14}H_{21}NO_5$: C, 59.35; H, 7.47; N, 4.94. Found: C, 59.02; H, 7.42; N, 5.10.

4.2.6. (2R,5S)-3-Methyl-2-(2-methylphenyl)-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**6f**)

Method A (18%); method B (96%); mp 110–112 °C; $[\alpha]_D^{20}$ +22 (*c* 0.5, pyridine); ν_{max}/cm^{-1} 3400–3200 (OH), 1453 (arom), 1057, 1031 (C–O). ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 7.43 (d, *J* 7.2 Hz, 1H, H-arom), 7.20 (m, 3H, H-arom), 4.81 (s, 1H, H-2), 4.55 (d, *J* 6.4 Hz, 1H, OH), 4.50 (d, *J* 5.2 Hz, 1H, OH), 4.34 (m, 2H, OH), 4.23 (dt, $J_{4a,5}$=$J_{4b,5}$ 8.8 Hz, $J_{5,1'}$ 6.6 Hz, 1H, H-5), 3.68 (t, $J_{1',5}$=$J_{1',OH}$ 6.2 Hz, $J_{1',2'}$ 0 Hz, 1H, H-1′), 3.58 (m, 1H, H-4′), 3.49 (m, 1H, H-3′), 3.40 (dt, $J_{4'',4'}$ 10.0 Hz, $J_{4'',3'}$=$J_{4'',OH}$ 5.0 Hz, 1H, H-4″), 3.31 (m, 1H, H-4a), 3.21 (t, $J_{2',3'}$=$J_{1',2'}$ 7.6 Hz, 1H, H-2′), 2.41 (t, 1H, H-4b), 2.38 (s, 3H, CH_3–arom), 2.08 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 137.08, 136.19, 130.44, 128.24, 128.10, 125.44 (C-arom), 95.21 (C-2), 78.07 (C-5), 71.12, 71.06, 71.00 (C-1′, C-2′, C-3′), 63.34 (C-4′), 56.67 (C-4), 37.15 (CH_3–N), 18.59 (CH_3). Anal. Calcd for $C_{15}H_{23}NO_5 \cdot {}^1/_2\ H_2O$: C, 58.81; H, 7.90; N, 4.57. Found: C, 59.05; H, 8.04; N, 4.89.

4.2.7. (2R,5S)-3-Methyl-2-(3-methylphenyl)-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**6g**)

Method A (60%); method B (91%); mp 165–167 °C; $[\alpha]_D^{21}$ +14 (*c* 0.5, pyridine); ν_{max}/cm^{-1} 3400–3200 (OH), 1479, 1458 (arom), 1035 (C–O). ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 7.22 (m, 3H, H-arom), 7.15 (d, *J* 7.20 Hz, 1H, H-arom), 4.55 (d, *J* 6.8 Hz, 1H, OH), 4.51 (s, 1H, H-2), 4.50 (d, *J* 6.4 Hz, 1H, OH), 4.34 (t, *J* 5.6 Hz, 1H, OH), 4.31 (d, *J* 7.6 Hz, 1H, OH), 4.26 (m, 1H, H-5), 3.67 (t, $J_{1',5}$ 6.8 Hz, $J_{1',OH}$ 6.4 Hz, $J_{1',2'}$ 0 Hz, 1H, H-1′), 3.59 (m, 1H, H-4′), 3.49 (m, 1H, H-3′), 3.40 (dt, $J_{4'',OH}$=$J_{4'',3'}$ 5.6 Hz, $J_{4'',4'}$ 10.9 Hz, 1H, H-4″), 3.32 (dd, $J_{4a,4b}$ 8.9 Hz, $J_{4a,5}$ 5.8 Hz, 1H, H-4a), 3.21 (t, $J_{2',3'}$=$J_{2',OH}$ 7.4 Hz, 1H, H-2′), 2.34 (t, $J_{4b,4a}$=$J_{4b,5}$ 8.8 Hz, 1H, H-4b), 2.31 (s, 3H, CH_3–arom), 2.08 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 139.19, 137.11, 129.33, 128.43, 127.85, 125.13 (C-arom), 97.28 (C-2), 78.75 (C-5), 71.03, 70.97 (C-1′, C-2′, C-3′), 63.34 (C-4′), 56.85 (C-4), 37.27 (CH_3), 20.94 (CH_3–arom). Anal. Calcd for $C_{15}H_{23}NO_5$: C, 60.59; H, 7.80; N, 4.71. Found: C, 60.39; H, 7.68; N, 4.79.

4.2.8. (2R,5S)-3-Methyl-2-(4-methylphenyl)-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**6h**)

Method A (79%); method B (90%); mp 170–172 °C; $[\alpha]_D^{21}$ +11 (*c* 0.5, pyridine); ν_{max}/cm^{-1} 3400–3100 (OH), 1457 (arom), 1062, 1029 (C–O). ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 7.31 (d, *J* 7.6 Hz, 2H, H-arom), 7.17 (d, *J* 7.6 Hz, 2H, H-arom), 4.54 (d, *J* 5.2 Hz, 1H, OH), 4.51 (s, 1H, H-2), 4.50 (d, 1H, OH), 4.30 (m, 2H, OH), 4.25 (c, $J_{4a,5}$=$J_{4b,5}$=$J_{5,1'}$ 7.2 Hz, 1H, H-5), 3.67 (t, $J_{1',5}$=$J_{1',OH}$ 6.4 Hz, $J_{1',2'}$ 0 Hz, 1H, H-1′), 3.59 (dd, $J_{4',4''}$ 10.0 Hz, $J_{4',3'}$ 5.0 Hz, 1H, H-4′), 3.49 (m, 1H, H-3′), 3.41 (dt, $J_{4'',4'}$ 10.8 Hz, $J_{4'',3'}$=$J_{4'',OH}$ 5.6 Hz, 1H, H-4″), 3.34 (dd, $J_{4a,4b}$ 8.4 Hz, $J_{4a,5}$ 6.4 Hz, 1H, H-4a), 3.21 (t, $J_{2',3'}$ ≈ $J_{1',2'}$ 7.6 Hz, 1H, H-2′), 2.34 (t, $J_{4a,4b}$=$J_{4b,5}$ 9.6 Hz, 1H, H-4b), 2.06 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 138.18 (C-arom), 136.51 (C-arom), 128.80 (2C, C-arom), 128.17 (2C, C-arom), 97.38 (C-2), 78.91 (C-5), 71.33, 71.27, 71.21 (C-1′, C-2′, C-3′), 63.60 (C-4′), 57.11 (C-4), 37.46 (CH_3–N), 21.08 (CH_3). Anal. Calcd for $C_{15}H_{23}NO_5$: C, 60.59; H, 7.80; N, 4.71. Found: C, 60.33; H, 7.64; N, 4.84.

4.2.9. (2R,5S)-2-(4-Ethylphenyl)-3-methyl-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**6i**)

Method A (41%); method B (98%); mp 133–135 °C; $[\alpha]_D^{20}$ +8 (*c* 0.5, pyridine); ν_{max}/cm^{-1} 3400–3200 (OH), 1490, 1454 (arom), 1093, 1033 (C–O). ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 7.33 (d, *J* 7.6 Hz, 2H, H-arom), 7.20 (d, *J* 8.0 Hz, 2H, H-arom), 4.55 (d, *J* 6.4 Hz, 1H, OH), 4.52 (s, 1H, H-2), 4.51 (d, *J* 6.0 Hz, 1H, OH), 4.36 (t, *J* 5.6 Hz, 1H, OH), 4.32 (d, *J* 7.2 Hz, 1H, OH), 4.25 (m, 1H, H-5), 3.67 (t, $J_{1',5}$=$J_{1',OH}$ 6.4 Hz, $J_{1',2'}$ 0 Hz, 1H, H-1′), 3.59 (m, 1H, H-4′), 3.49 (m, 1H, H-3′), 3.40 (m, 1H, H-4″), 3.32 (dd, $J_{4a,4b}$ 8.8 Hz, $J_{4a,5}$ 6.0 Hz, 1H, H-4a), 3.21 (t, $J_{2',3'}$=$J_{2',OH}$ 7.6 Hz, 1H, H-2′), 2.60 (c, *J* 7.6 Hz, 2H, CH_2–Ar), 2.34 (t, $J_{4b,4a}$=$J_{4b,5}$ 9.2 Hz, 1H, H-4b), 2.08 (s, 3H, CH_3), 1,18 (t, *J* 7.6 Hz, 3H, CH_3–Ar). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 144.81, 137.00, 128.47, 127.89 (C-arom), 97.66 (C-2), 79.14 (C-5), 71.59, 71.54, 71.46 (C-1′, C-2′, C-3′), 63.85 (C-4′), 57.36 (C-4), 37.77 (CH_3), 28.44 (CH_2–Ar), 16.08 (CH_3–Ar). Anal. Calcd for $C_{16}H_{25}NO_5$: C, 61.72; H, 8.09; N, 4.50. Found: C, 61.55; H, 8.20; N, 4.46.

4.2.10. (2R,5S)-2-(4-Methoxyphenyl)-3-methyl-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**6j**)

Method A (76%); method B (84%); mp 170–172 °C; $[\alpha]_D^{22}$ +11 (*c* 0.5, pyridine); ν_{max}/cm^{-1} 3400–3100 (OH), 2960 (OCH_3), 1613, 1515 (arom), 1097, 1032 (C–O). ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 7.34 (t, *J* 8.4 Hz, 1H, H-arom), 6.91 (d, *J* 8.4 Hz, 2H, H-arom), 4.54 (d, *J* 6.4 Hz, 1H, OH), 4.48 (s, 1H, H-2), 4.33 (m, 2H, OH), 4.29 (d, *J* 7.6 Hz, 1H, OH), 4.24 (m, $J_{4a,5}$=$J_{4b,5}$ 8.7 Hz, 1H, H-5), 3.75 (s, 3H, OCH_3), 3.65 (t, $J_{1',5}$=$J_{1',OH}$ 6.8 Hz, $J_{1',2'}$ 0 Hz, 1H, H-1′), 3.58 (m, $J_{4',4''}$ 10.3 Hz, $J_{4',OH}$ 5.4 Hz, $J_{4',3'}$ 3.6 Hz, 1H, H-4′), 3.47 (m, 1H, H-3′), 3.38 (dt, $J_{4'',OH}$=$J_{4'',3'}$ 5.2 Hz, $J_{4'',4'}$ 11.2 Hz, 1H, H-4″), 3.30 (dd, $J_{4a,4b}$ 8.8 Hz, $J_{4a,5}$ 6.0 Hz, 1H, H-4a), 3.20 (t, $J_{2',3'}$=$J_{2',OH}$ 7.4 Hz, 1H, H-2′), 2.31 (t, $J_{4a,4b}$=$J_{4b,5}$ 9.0 Hz, 1H, H-4b), 2.06 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 159.83, 131.35, 129.47, 113.61 (C-arom), 97.20 (C-2), 78.73 (C-5), 71.33, 71.27, 71.18 (C-1′, C-2′, C-3′), 63.60 (C-4′), 57.05 (C-4), 55.29 (OCH_3), 37.40 (CH_3). Anal. Calcd for $C_{15}H_{23}NO_6 \cdot {}^1/_2\ H_2O$: C, 55.89; H, 7.50; N, 4.35. Found: C, 55.97; H, 7.38; N, 4.47.

*4.2.11. (2R,5S)-2-(2,4-Dimethylphenyl)-3-methyl-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**6k**)*

Method A (31%); method B (85%); mp 148–150 °C; $[\alpha]_D^{20}$ +14 (*c* 0.5, pyridine); ν_{max}/cm^{-1} 3500–3100 (OH), 1600 (arom), 1161.64, 1082.3, 1031.39 (C–O). ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 7.31 (d, *J* 7.6 Hz, 1H, H-arom), 6.99 (d, *J* 7.6 Hz, 1H, H-arom), 6.98 (s, 1H, H-arom), 4.76 (s, 1H, H-2), 4.55 (m, 2H, OH), 4.34 (m, 2H, OH), 4.22 (m, 1H, H-5), 3.68 (m, 1H, H-1′), 3.60 (m, 1H, H-4′), 3.48 (m, 1H, H-3′), 3.40 (m, 1H, H-4″), 3.33 (m, 1H, H-4a), 3.21 (t, $J_{2',3'}$=$J_{2',OH}$ 7.6 Hz, 1H, H-2′), 2.37 (t, $J_{4b,4a}$=$J_{4b,5}$ 9.4 Hz, 1H, H-4b), 2.34 (s, 3H, CH_3–arom), 2.25 (s, 3H, CH_3–arom), 2.05 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 137.60, 137.14, 133.50, 131.32, 128.53, 126.26 (C-arom), 95.53 (C-2), 78.25 (C-5), 71.39, 71.33, 71.27 (C-1′, C-2′, C-3′), 63.63 (C-4′), 57.26 (C-4), 37.73 (CH_3), 20.93, 18.80 (CH_3–arom). HRMS-CI ($C_{16}H_{26}NO_5[M+H]^+$) calcd: 312.181098; found: 312.181732.

*4.2.12. (2R,5S)-3-Methyl-2-(1-naphthyl)-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**7**) and (2S,5S)-3-methyl-2-(1-naphthyl)-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**8**)*

Method A (98); method B (97%); ratio 75:25 (**7**/**8**); mp 154–157 °C; $[\alpha]_D^{21}$ +9 (*c* 0.5, pyridine); ν_{max}/cm^{-1} 3400–3100 (OH), 1589, 1506, 1452 (arom), 1070, 1028 (C–O). Anal. Calcd for $C_{18}H_{23}NO_5$: C, 64.85; H, 6.95; N, 4.20. Found: C, 64.62; H, 7.15; N, 4.21.

*4.2.12.1. Spectroscopic data for compound **7**.* ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 8.49 (d, *J* 7.6 Hz, 1H, H-arom), 7.93 (m, 2H, H-arom), 7.67 (d, *J* 7.2 Hz, 1H, H-arom), 7.51 (m, 3H, H-arom), 5.21 (s, 1H, H-2), 4.55 (d, *J* 4.4 Hz, 1H, OH), 4.50 (d, *J* 6.0 Hz, 1H, OH), 4.37 (m, 2H, OH), 4.37 (m, 1H, H-5), 3.78 (t, $J_{1',OH}$=$J_{1',5}$ 6.4 Hz, $J_{1',2'}$ 0 Hz, 1H, H-1′), 3.61 (m, 1H, H-4′), 3.53 (m, 1H, H-3′), 3.42 (m, 1H, H-4″), 3.40 (m, 1H, H-2′), 3.29 (t, $J_{4a,4b}$=$J_{4a,5}$ 7.2 Hz, 1H, H-4a), 2.54 (t, $J_{4a,4b}$=$J_{4b,5}$ 9.2 Hz, 1H, H-4b), 2.10 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 134.04, 131.73, 129.68, 128.74, 126.86, 126.13, 125.52, 125.45 (C-arom), 96.90 (C-2), 78.37 (C-5), 71.39, 71.33 (C-1′, C-2′, C-3′), 63.75 (C-4′), 57.38 (C-4), 38.03 (CH_3–N).

*4.2.12.2. Spectroscopic data for compound **8**.* ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 8.39 (d, *J* 8.0 Hz, 1H, H-arom), 7.93 (m, 2H, H-arom), 7.78 (d, *J* 7.2 Hz, 1H, H-arom), 7.51 (m, 3H, H-arom), 5.48 (s, 1H, H-2), 4.46 (d, *J* 7.0 Hz, 1H, OH), 4.40 (m, 2H, OH), 4.36 (d, *J* 3.6 Hz, 1H, OH), 4.28 (q, $J_{4a,5}$=$J_{4b,5}$=$J_{5,1'}$ 6.8 Hz, 1H, H-5), 3.78 (m, 1H, H-1′), 3.61 (m, 1H, H-4′), 3.53 (m, 1H, H-3′), 3.42 (m, 1H, H-4″), 3.40 (m, 1H, H-2′), 3.14 (dd, $J_{4a,4b}$ 10.0 Hz, $J_{4a,5}$ 5.6 Hz, 1H, H-4A), 2.85 (t, $J_{4a,4b}$=$J_{4b,5}$ 8.8 Hz, 1H, H-4b), 2.27 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 134.53, 133.88, 131.90, 129.33, 126.31, 125.67, 125.60, 125.00 (C-arom), 96.11 (C-2), 77.85 (C-5), 71.45, 71.18 (C-1′, C-2′, C-3′), 63.60 (C-4′), 53.59 (C-4), 39.36 (CH_3–N).

*4.2.13. (2R,5S)-3-Methyl-2-(2-hydroxyphenyl)-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**9**), (2S,5S)-3-methyl-2-(2-hydroxyphenyl)-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**10**), and (2R,5R)-5-hydroxy-3-methyl-2-(2-hydroxyphenyl)-5-(D-erythro-1,2,3-trihydroxypropyl)tetrahydro-1,3-oxazine (**11**)*

Method A (61%); method B (95%); ratio 40:35:25 (**9**/**10**/**11**).

*4.2.13.1. Spectroscopic data for compound **9**.* ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 10.71 (br s, 1H, OH-arom), 7.20 (m, 1H, H-arom), 6.76 (m, 3H, H-arom), 4.85 (s, 1H, H-2), 4.21 (m, 1H, H-5), 3.67 (m, 1H, H-1′), 3.60 (m, 1H, H-4′), 3.56 (m, 1H, 3′), 3.48 (m, 1H, H-4″), 3.39 (dd, $J_{4a,4b}$ 9.2 Hz, $J_{4a,5}$ 6.4 Hz, 1H, H-4a), 3.36 (d, $J_{2',3'}$ 6.4 Hz, 1H, H-2′), 2.40 (t, $J_{4a,4b}$=$J_{4b,5}$ 9.2 Hz, 1H, H-4b), 2.20 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 157.82–116.03 (C-arom), 95.77 (C-2), 79.32 (C-5), 71.59, 71.56, 71.46 (C-1′, C-2′, C-3′), 63.83 (C-4′), 56.49 (C-4), 37.51 (CH_3).

*4.2.13.2. Spectroscopic data for compound **10**†.* ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 7.20 (m, 1H, H-arom), 6.76 (m, 3H, H-arom), 4.87 (s, 1H, H-2), 4.21 (m, 1H, H-5), 3.67 (m, 1H, H-1′), 3.60 (m, 1H, H-4′), 3.56 (m, 1H, 3′), 3.48 (m, 1H, H-4″), 3.36 (d, $J_{2',3'}$ 6.4 Hz, 1H, H-2′), 3.14 (dd, $J_{4a,4b}$ 7.6 Hz, $J_{4a,5}$ 4.4 Hz, 1H, H-4a), 2.69 (t, $J_{4a,4b}$=$J_{4b,5}$ 8.8 Hz, 1H, H-4b), 2.22 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 157.74–116.03 (C-arom), 96.89 (C-2), 77.81 (C-5), 71.76, 71.65, 71.62 (C-1′, C-2′, C-3′), 63.90 (C-4′), 55.21 (C-4), 37.99 (CH_3).

*4.2.13.3. Spectroscopic data for compound **11**†.* ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 7.57 (d, *J* 7.6 Hz, 1H, H-arom), 7.41 (d, *J* 8.4 Hz, 1H, H-arom), 6.84 (d, *J* 8.4 Hz, 1H, H-arom), 5.22 (br s, 1H, OH-5), 4.63 (s, 1H, H-2), 4.21 (m, 1H, H-6), 3.82 (m, 1H, H-5), 3.67–3.04 (m, 4H, H-1′, H-2′, H-3′, H-3″), 3.04 (dd, $J_{4a,4b}$ 12.4 Hz, $J_{4a,5}$ 2.4 Hz, 1H, H-4a), 2.56 (d, $J_{4a,4b}$ 12.4 Hz, 1H, H-4b), 2.00 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 156.84–116.03 (C-arom), 94.71 (C-2), 77.66 (C-6), 73.71 (C-5), 70.88, 66.10 (C-1′, C-2′), 63.08 (C-3′), 59.90 (C-4), 39.87 (CH_3).

*4.2.14. (2R,5S)-3-Methyl-2-styryl-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**12**), (2S,5S)-3-methyl-2-styryl-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**13**), and (2R,5R)-5-hydroxy-3-methyl-2-styryl-5-(D-erythro-1,2,3-trihydroxypropyl)tetrahydro-1,3-oxazine (**14**)*

Method A (47%); method B (100%); ratio 52:32:16 (**12**/**13**/**14**).

*4.2.14.1. Spectroscopic data for compound **12**.* ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 7.49 (t, *J* 7.2 Hz, 1H, H-arom), 7.48 (d, *J* 8.0 Hz, 1H, H-arom), 7.36 (t, *J* 7.2 Hz, 2H, H-arom), 7.29 (d, *J* 7.2 Hz, 1H, H-arom), 6.70 (d, *J* 16.0 Hz, 1H, Ar–C*H*=CH–), 6.13 (dd, *J* 16.0, 6.4 Hz, 1H, Ar–CH=C*H*), 4.55 (d, *J* 6.4 Hz, 1H, OH), 4.49 (d, *J* 5.6 Hz, 1H, OH), 4.45 (m, 1H, OH), 4.35 (m, 1H, OH), 4.21 (d, $J_{2,CH}$ 7.2 Hz, H-2), 4.13 (m, 1H, H-5), 3.64 (t, $J_{1',OH}$=$J_{1',5}$ 5.6 Hz, $J_{1',2'}$ 0 Hz, 1H, H-1′), 3.59 (m, 1H, H-4′), 3.48 (m, 1H, H-3′), 3.40 (dt, $J_{4'',OH}$=$J_{4'',3'}$ 5.2 Hz, $J_{4'',4'}$ 10.8 Hz, 1H, H-4″), 3.23 (dd, $J_{4a,4b}$ 9.0 Hz, $J_{4a,5}$ 6.1 Hz, 1H, H-4a), 3.19 (t, $J_{2',3'}$=$J_{2',OH}$ 8.0 Hz, 1H, H-2′), 2.28 (t, $J_{4a,4b}$=$J_{4b,5}$ 9.6 Hz, 1H, H-4b), 2.21 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 136.34–127.11 (C-arom), 97.43 (C-2), 78.91 (C-5), 71.59 (C-1′, C-2′, C-3′), 63.88 (C-4′), 57.11 (C-4), 37.99 (CH_3).

*4.2.14.2. Spectroscopic data for compound **13**.* ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 7.49 (t, *J* 7.2 Hz, 1H, H-arom), 7.48 (d, *J* 8.0 Hz, 1H, H-arom), 7.36 (t, *J* 7.2 Hz, 2H, H-arom), 7.27 (d, *J* 7.2 Hz, 1H, H-arom), 6.71 (d, *J* 16.0 Hz, 1H, Ar–C*H*=CH–), 6.14 (dd, *J* 16.0, 6.0 Hz, 1H, Ar–CH=C*H*), 4.55 (d, *J* 6.4 Hz, 1H, OH), 4.49 (d, *J* 5.6 Hz, 1H, OH), 4.45 (m, 1H, OH), 4.35 (m, 1H, OH), 4.30 (d, $J_{2,CH}$ 7.2 Hz, 1H, H-2), 4.13 (m, 1H, H-5), 3.70 (t, $J_{1',OH}$=$J_{1',5}$ 6.4 Hz, $J_{1',2'}$ 0 Hz, 1H, H-1′), 3.59 (m, 1H, H-4′), 3.48 (m, 1H, H-3′), 3.40 (dt, $J_{4'',OH}$=$J_{4'',3'}$ 5.2 Hz, $J_{4'',4'}$ 10.8 Hz, 1H, H-4″), 3.19 (t, $J_{2',3'}$=$J_{2',OH}$ 8.0 Hz, 1H, H-2′), 3.07 (dd, $J_{4a,4b}$ 9.8 Hz, $J_{4a,5}$ 4.4 Hz, 1H, H-4a), 2.60 (t, $J_{4a,4b}$=$J_{4b,5}$ 8.4 Hz, 1H, H-4b), 2.26 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 136.34–127.11 (C-arom), 98.09 (C-2), 77.76 (C-5), 71.50, 71.35, 71.24 (C-1′, C-2′, C-3′), 64.03 (C-4′), 55.41 (C-4), 38.77 (CH_3).

*4.2.14.3. Spectroscopic data for compound **14**.* ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 7.51–7.27 (m, 5H, H-arom), 6.74 (d, *J* 16.0 Hz, 1H, Ar–C*H*=CH–), 6.25 (dd, *J* 16.0, 6.0 Hz, 1H, Ar–CH=C*H*), 4.96 (d, *J* 4.8 Hz, 1H, OH-5), 4.70 (d, *J* 4.8 Hz, 1H, OH), 4.26 (d, $J_{2,CH}$ 6.4 Hz, 1H, H-2), 4.13 (m, 1H, H-6), 3.70 (m, 1H, H-5), 3.71–3.05 (m, 4H, H-1′, H-2′, H-3′, H-3″), 2.93 (dd, $J_{4a,4b}$ 13.2 Hz, $J_{4a,5}$ 2.0 Hz, 1H, H-4a), 2.60 (m, 1H, H-4b), 2.21 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 136.34–127.11 (C-arom), 94.83 (C-2), 77.62 (C-6), 74.00 (C-5), 70.86, 66.92 (C-1′, C-2′), 63.23 (C-3′), 60.36 (C-4), 39.77 (CH_3).

† ^{1}H NMR data refer to the sample exchanged with D_2O.

*4.2.15. 1,4-Bis[(2R,5S)-3-methyl-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidin-2-yl]benzene (**15**), 1,4-bis[(2S,5S)-3-methyl-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidin-2-yl]benzene (**16**), and 1,4-bis[(2R,5R)-5-hydroxy-3-methyl-5-(D-erythro-1,2,3-trihydroxypropyl)tetrahydro-1,3-oxazin-2-yl]benzene (**17**)*

Only compound **15** could be obtained using method A in 51% yield. Method B, however, affords a mixture of **15**–**17** (66:22:12) in 87% yield. Recrystallization of this crude mixture from ethanol gave rise to pure **15** (57% global yield).

*4.2.15.1. Data for compound **15**.* Method A (51%); method B (57%); mp 128–130 °C; $[\alpha]_D^{23}$ +10 (*c* 0.5, pyridine); ν_{max}/cm^{-1} 3400–3200 (OH), 1632, 1463 (arom), 1073, 1025 (C–O). ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 7.42 (s, 2H, H-arom), 4.57 (d, *J* 6.4 Hz, 1H, OH), 4.56 (s, 1H, H-2), 4.50 (d, *J* 6.0 Hz, 1H, OH), 4.35 (t, *J* 6.2 Hz, 1H, OH), 4.32 (d, *J* 7.6 Hz, 1H, OH), 4.26 (m, 1H, H-5), 3.67 (t, $J_{1',5}=J_{1',OH}$ 6.4 Hz, $J_{1',2'}$ 0 Hz, 1H, H-1′), 3.58 (m, $J_{4',4''}$ 8.8 Hz, $J_{4',OH}$ 5.4 Hz, $J_{4',3'}$ 3.4 Hz, 1H, H-4′), 3.48 (m, $J_{3',2'}$ 8.4 Hz, $J_{3',OH}$ 5.4 Hz, $J_{3',4'}$ 3.0 Hz, 1H, H-3′), 3.38 (dt, $J_{4'',OH}=J_{4'',3'}$ 6.8 Hz, 1H, H-4″), 3.32 (dd, $J_{4a,4b}$ 8.8 Hz, $J_{4a,5}$ 6.4 Hz, 1H, H-4a), 3.20 (t, $J_{2',3'}=J_{2',OH}$ 7.6 Hz, 1H, H-2′), 2.35 (t, $J_{4b,4a}=J_{4b,5}$ 9.2 Hz, 1H, H-4b), 2.10 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 139.79 (2C, arom), 127.64 (4C, C-arom), 96.95 (C-2), 78.78 (C-5), 71.05, 71.02, 70.96 (C-1′, C-2′, C-3′), 63.32 (C-4′), 56.81 (C-4), 37.24 (CH_3). Anal. Calcd for $C_{22}H_{36}N_2O_{10}\cdot{}^1/_2\ H_2O$: C, 52.17; H, 7.30; N, 5.79. Found: C, 52.36; H, 7.18; N, 5.67.

*4.2.15.2. Spectroscopy data for compound **16**.* ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 7.36 (s, 4H, H-arom), 4.70 (s, 1H, H-2), 4.18 (dt, $J_{4a,5}$ 4.4 Hz, $J_{4b,5}=J_{5,1'}$ 7.6 Hz, 1H, H-5), 3.66 (t, $J_{1',5}=J_{1',OH}$ 6.4 Hz, $J_{1',2'}$ 0 Hz, 1H, H-1′), 3.66–3.30 (m, 3H, H-3′, H-4′, H-4″), 3.20 (t, $J_{2',3'}=J_{2',OH}$ 7.6 Hz, 1H, H-2′), 3.08 (dd, $J_{4a,4b}$ 9.2 Hz, $J_{4a,5}$ 4.0 Hz, 1H, H-4a), 2.65 (t, $J_{4b,4a}=J_{4b,5}$ 8.0 Hz, 1H, H-4b), 2.16 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 139.77 (2C, arom), 128.41 (4C, C-arom), 98.26 (C-2), 77.88 (C-5), 71.05, 71.02, 70.96 (C-1′, C-2′, C-3′), 64.01 (C-4′), 55.77 (C-4), 38.57 (CH_3).

*4.2.15.3. Spectroscopy data for compound **17**.* ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 7.47 (d, *J* 6.8 Hz, 2H, H-arom), 7.42 (d, *J* 6.8 Hz, 2H, H-arom), 5.00 (d, *J* 4.8 Hz, 1H, OH-5), 4.59 (s, 1H, H-2), 4.26 (m, 1H, H-6), 3.74 (m, 1H, H-5), 3.67–3.30 (m, 4H, H-1′, H-2′, H-3′, H-3″), 3.00 (d, $J_{4a,4b}$ 11.2 Hz, 1H, H-4a), 2.68 (d, $J_{4b,4a}$ 11.2 Hz, 1H, H-4b), 2.09 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ 128.01 (4C, arom), 127.94 (2C, arom), 95.75 (C-2), 78.34 (C-6), 73.94 (C-5), 70.93, 66.76 (C-1′, C-2′), 63.13 (C-3′), 60.68 (C-4), 39.70 (CH_3).

*4.2.16. (2R,5S)-3-Methyl-2-(4-nitrophenyl)-5-(1,2,3,4-tetra-O-acetyl-D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**18**) and (2S,5S)-3-methyl-2-(4-nitrophenyl)-5-(1,2,3,4-tetra-O-acetyl-D-arabino-1,2,3,4-tetrahydroxybutyl)oxazolidine (**19**)*

To a suspension of the oxazolidine **6a** (5.0 mmol) in pyridine (6.7 mL) was added acetic anhydride (6.5 mL). The mixture was kept at room temperature overnight and then evaporated. The resulting crude mixture consisted of **18** and **19** (1:1 ratio), from which the latter could be isolated by crystallization from diethyl ether (32%).

*4.2.16.1. Data for compound **19**.* It was recrystallized from ethanol. Mp 119–120 °C; $[\alpha]_D^{22}$ +23 (*c* 0.5, chloroform); ν_{max}/cm^{-1} 1746 (C=O), 1605, 1529, 1462 (arom), 1247, 1230 (C–O–C, ester), 1078, 1043 (C–O). ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.22 (d, *J* 8.8 Hz, 2H, H-arom), 7.69 (d, *J* 8.4 Hz, 2H, H-arom), 5.43 (dd, $J_{2',1'}$ 2.0 Hz, $J_{2',3'}$ 9.0 Hz, 1H, H-2′), 5.34 (dd, $J_{1',2'}$ 2.0 Hz, $J_{1',5}$ 6.4 Hz, 1H, H-1′), 5.16 (ddd, $J_{3',2'}$ 9.0 Hz, $J_{3',4''}$ 4.2 Hz, $J_{3',4'}$ 2.6 Hz, 1H, H-3′), 4.69 (s, 1H, H-2), 4.24 (m, 1H, H-5), 4.23 (m, 1H, H-4′), 4.17 (dd, $J_{4'',4'}$ 12.8 Hz, $J_{4'',3}$ 4.4 Hz, 1H, H-4″), 3.24 (dd, $J_{4a,4b}$ 10.4 Hz, $J_{4a,5}$ 3.2 Hz, 1H, H-4a), 2.76 (dd, $J_{4b,4a}$ 10.4 Hz, $J_{4b,5}$ 8.0 Hz, 1H, H-4b), 2.23 (s, 3H, CH_3), 2.02, 2.04, 2.06, 2.09 (s, 12H, CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 170.60, 170.35, 170.06, 169.90 (C=O), 148.48, 145.59, 129.04, 123.42 (C-arom), 98.04 (C-2), 75.43 (C-5), 70.91, 69.16, 68.01 (C-1′, C-2′, C-3′), 61.73 (C-4′), 56.43 (C-4), 38.12 (CH_3), 20.93, 20.82, 20.74 (CH_3CO). Anal. Calcd for $C_{22}H_{28}N_2O_{11}$: C, 53.22; H, 5.68; N, 5.64. Found: C, 52.82; H, 5.88; N, 5.76.

*4.2.16.2. Spectroscopic data for compound **18**.* This substance could not be isolated, although its characterization was carried out by NMR analysis of the crude mixture: ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.24 (d, *J* 8.4 Hz, 2H, H-arom), 7.62 (d, *J* 8.8 Hz, 2H, H-arom), 5.41 (dd, $J_{2',1'}$ 2.2 Hz, $J_{2',3'}$ 9.0 Hz, 1H, H-2′), 5.32 (dd, $J_{1',2'}$ 2.4 Hz, $J_{1',5}$ 6.0 Hz, 1H, H-1′), 5.17 (m, 1H, H-3′), 4.77 (s, 1H, H-2), 4.38 (dt, $J_{5,4a}=J_{5,1'}$ 6.4 Hz, $J_{5,4b}$ 8.8 Hz, 1H, H-5), 4.26 (m, 1H, H-4′), 4.18 (dd, $J_{4'',4'}$ 12.8 Hz, $J_{4'',3}$ 4.4 Hz, 1H, H-4″), 3.48 (dd, $J_{4a,4b}$ 9.6 Hz, $J_{4a,5}$ 6.0 Hz, 1H, H-4a), 2.50 (t, $J_{4b,4a}=J_{4b,5}$ 9.2 Hz, 1H, H-4b), 2.26 (s, 3H, CH_3), 2.14, 2.12, 2.08, 2.08 (s, 12H, CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 170.57, 170.49, 169.97, 169.85 (C=O), 148.50, 145.45, 128.78, 123.56 (C-arom), 96.69 (C-2), 76.05 (C-5), 70.23, 68.69, 68.11 (C-1′, C-2′, C-3′), 61.73 (C-4′), 57.17 (C-4), 37.64 (CH_3), 20.89, 20.85, 20.78 (CH_3CO).

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Supplementary data

Copies of ^1H and ^{13}C NMR spectra for all new compounds; Figures 1S, 2S, and 3S, and Chart 1; Cartesian coordinates of compounds **9**–**11**, **18**, and **19**. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.04.082.

References and notes

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11. Crystallized from ethanol. $C_{22}H_{28}N_2O_{11}$, M=496.46, orthorhombic, space group $P2_12_12_1$, a=7.44300(10) Å, b=15.7931(2) Å, c=20.6396(3) Å, V=2426.15(6) Å^3, Z=4, F(000)=1048, absorption coefficient 0.110 mm^{-1}, D_c=1.359 Mg m^{-3}, θ range (3.03−27.48°). Crystal data for compound **19** have been deposited with the Cambridge Crystallographic Data Centre (CCDC-665884) and can be obtained, upon request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.
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