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Broadening the reaction scope of unprotected aldoses via their corresponding nitrones: 1,3-dipolar cycloadditions with alkenes

Gatien Messire,^a Fabien Massicot,^a Laura Pascual,^a Emmanuel Riguet,^a Jean-Luc Vasse^a and Jean-Bernard Behr^{*a}

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Condensation reactions of unprotected tetroses and pentoses with hydroxylamines afforded nitrones, which were easily converted to densely functionalized isoxazolidines in the presence of electron-poor alkenes. The 1,3-dipolar cycloaddition occurred with good facial discrimination of the chiral nitrone but under rather low endo/exo control. Stereochemistry of isomers was ascertained by chemical correlation with known derivatives from the literature. Microwave activation appeared as the most efficient reaction mode, affording the expected adducts within several minutes whereas hours were needed under standard heating. Alternatively, the transformation proved also possible under high pressure conditions by using a hand pump system, avoiding any energy source. Although water could not be used as solvent, leading to hydrolysis of the nitrone substrate, a large variety of organic solvents proved efficient. The method has potential use in the preparation of non-ionic carbohydrate-based amphiphiles.

Introduction

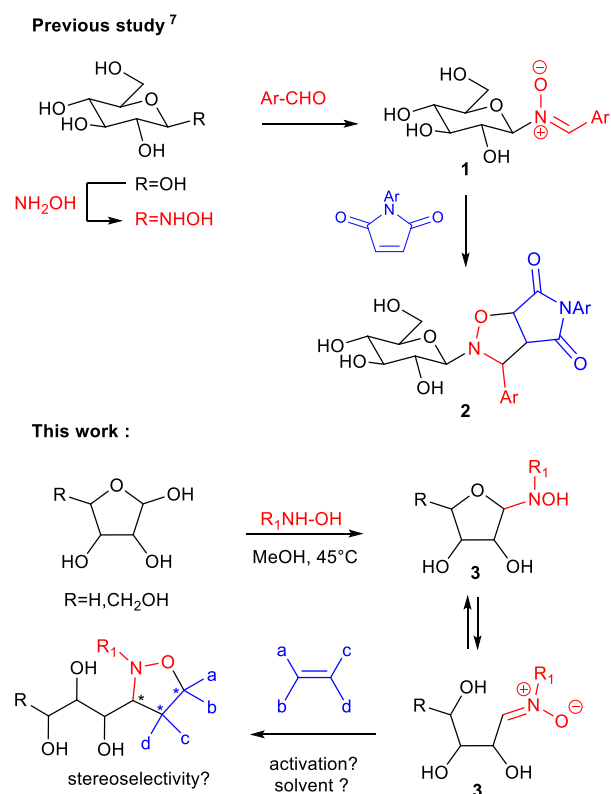
One of the most challenging aims in carbohydrate chemistry is the direct transformation of *unprotected* sugars into more value-added material via economically competitive and environmentally friendly C-C bond forming processes.¹ A number of reactions have been uncovered, which generally exploit the particular and versatile reactivity of the hemiacetal function of unprotected carbohydrates. Some classics are the well-known Kiliani-Fischer, Fischer-Sowden or Wittig reactions engaging a nitrile, a nitroalkyl or a phosphonium ylide nucleophile, respectively.² More recently, the discovery of indium-mediated allylation of unprotected carbohydrates or carbohydrate-derived imines opened new perspectives for their possible valorisation.³ Nitrones are also suitable electrophiles for In-mediated alkylations,⁴ but the alternate reactivity of carbohydrate-derived nitrones in 1,3-dipolar cycloadditions with alkenes or alkynes offers further ways of functionalization.⁵ However, only few studies report the synthesis of unprotected glyconitrones and their addition to unsaturated co-reactants. Actually, several reactions have been described over the years in which the two reactive species (nitrone/alkene) are both part from the same sugar moiety and react in a propitious intramolecular fashion to

afford polycyclic frameworks.⁶ To our knowledge only glucose has been used as an unprotected glycosidic scaffold in the reaction of nitrones with exogenous alkenes. In these studies, D-glucose oxime derived nitrones **1** (Scheme 1) were reacted with N-aryl maleimides or styrene derivatives to give isoxazolidines **2** (Scheme 1).⁷ It is worth mentioning that in these cases, the nitrone function is positioned out of the carbohydrate structure giving rise to hydrolysable *N*-glycosidic isoxazolidines.

Regioisomeric nitrones, in which the C=N bond is supported by the anomeric carbon, might be easily obtained by condensation of an aldose with a hydroxylamine RNH-OH. Such nitrones, although in their protected form, have been used as substrates for the synthesis of biologically relevant Δ^4 -isoxazolines or isoxazolidines via 1,3-dipolar cycloaddition reactions.⁸ Conversely, their unprotected counterparts (*ie* compound **3**, Scheme 1) have been scarcely prepared⁹ and there exist no report of their possible use in 1,3-dipolar cycloadditions with exogeneous alkenes. The present study relies on the straightforward preparation of glyconitrones such as **3** from fully unprotected tetroses and pentoses and their reaction with alkenes in 1,3-dipolar cycloaddition reactions (Scheme 1). The scope of the process has been evaluated, regarding the solvent, the activation mode, the stereoselectivity and the possible dipolarophiles.

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Electronic Supplementary Information (ESI) available: copies of ¹H- and ¹³C-NMR spectra of compounds **4a-e**, **5a-c**, **6a**, **7a**, **10**, **10'**, **10''**, **11-29**; procedure for hydrogenation of **10,10',10''**; procedure for glycosidase inhibition assays.



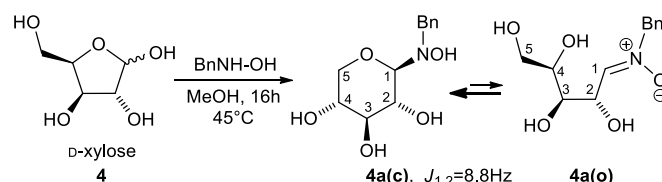
Scheme 1 General strategy for the direct functionalization of aldoses.

Results and discussion

Synthesis of nitrones from aldoses

To explore the feasibility of the considered transformations, we used D-xylose as the starting aldose. D-Xylose is notably found in hemicelluloses, the second most abundant polysaccharide in nature and a by-product of agroindustries that needs to be valorized.¹⁰ Whereas transformation of hemicellulose extracts to simple chemicals (furfural, pentane) has been extensively studied,¹¹ the development of complementary strategies to produce more elaborated products (biobased surfactants for instance) in few steps and with high yields is a sector that remains challenging.¹² Thus, D-xylose appeared as a good model to investigate the formation and stability of nitrones and their reactivity with a range of alkenes in 1,3-dipolar cycloadditions.

According to a reported procedure for the synthesis of related glycosylamines,^{3c} D-xylose was mixed together with benzyloxyamine in methanol at 45° C. Within a few minutes the reaction mixture became homogeneous and TLC showed the formation of a less polar and highly UV-absorbing spot, corresponding to glyconitrone **4a** (Scheme 2).



Scheme 2 Preparation of model nitron **4**.

After 16 hours xylose was totally consumed and **4a** was isolated after evaporation of the volatiles. Nitron **4a** proved stable on silica gel and was purified by chromatography (ethyl acetate/MeOH, 92.5/7.5 v/v as eluent). Although mutarotation might occur with nitrones of general structure **3**, NMR-analysis demonstrated that **4a** adopted mainly a closed form **4a(c)**, the open nitron congener **4a(o)** representing less than 2% under the considered conditions (CD₃OD as the solvent, 20 °C, NMR analysis just after solution preparation). Little evolution was observed even after one week (with only a small increase to 10% of **4a(o)**), which proved the anomeric and the structural stability of the formed compound. Interestingly, in aqueous solution the open form increased to 45% with the nitron proved stable at room temperature for a week, with insignificant hydrolysis to xylose. Finally, in DMSO-d₆, **4a(c)** was the only observable form, with no evolution in time, even after one week. NMR estimation of the equilibrium was based on characteristic signals of the two main forms **4a(o)** (H-1 at 7.4 ppm, CH₂Ph at 5.0 ppm, C-1 at 146 ppm) and **4a(c)** (H-1 at 3.9, ppm, CH₂Ph at 4.1 ppm, C-1 at 93 ppm), as shown in Figure 1.

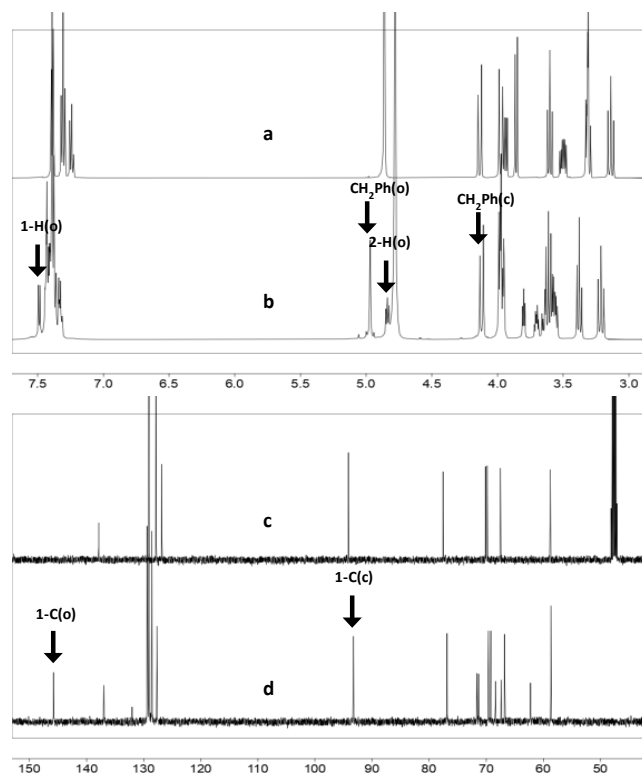
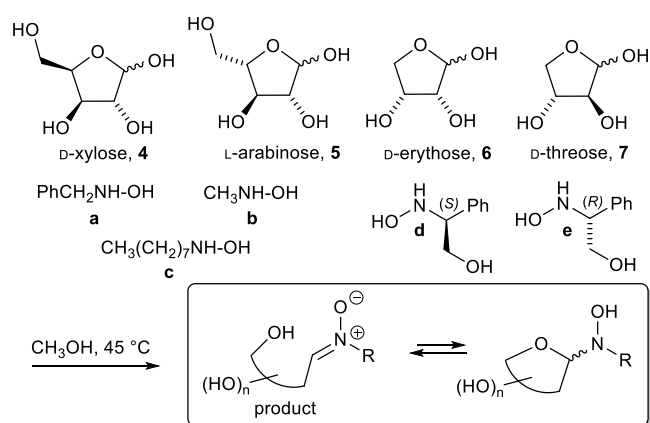


Figure 1 ¹H and ¹³C NMR of nitron **4a**, in CD₃OD (a,c) or D₂O (b,d), showing the equilibrium between the open (o) and closed (c) forms.

Using the same simple procedure, we were able to prepare a series of sugar-nitrones by varying either the aldose (L-arabinose, D-threose, D-erythrose) or the hydroxylamine, giving rise to a representing pool of tetrose or pentose-based nitrones with variable characteristics regarding the substituent at nitrogen. Their structures are given in Table 1, as well as the yield of formation and the ratio of open/closed forms. As observed by NMR (CD₃OD), anomeric composition of each nitron was clearly related to the nature of the carbohydrate and of the hydroxylamine used. Whereas N-benzylxyloside **4a** appeared almost exclusively as a 6-membered β-anomer, the related nitrones **4d-e** showed a clear inclination for the open form.

Table 1 Starting material for the synthesis of new glyconitrones **4a-e,5a-c,6a,7a**^a



sugar	RNHOH	product	yield ^b	open/closed ^c
4	a	4a	87%	0/100 ^d
4	b	4b	60%	50/50 ^d
4	c	4c	96%	35/65 ^d
4	d	4d	83% ^g	55/45 ^d
4	e	4e	88% ^g	55/45 ^d
5	a	5a	91%	27/73 ^e
5	b	5b	82%	61/39 ^f
5	c	5c	72%	72/28 ^e
6	a	6a	71%	88/12
7	a	7a	68%	83/17

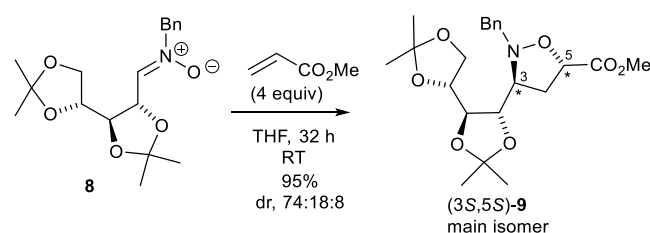
^a Reactions were performed in MeOH with 1.2 equiv. of hydroxylamine vs aldose. ^b Isolated yield (recrystallization or chromatography on silica gel). ^c ratios were determined by ¹H-NMR analysis of the pure nitron in CD₃OD. ^d the closed form is mainly the β-N-pyranoside. ^e the closed form is mainly a furanoside. ^f the closed form is a ca 1:1 mixture of furanoside and pyranoside. ^g 2.1 equiv of hydroxylamine were used to reach complete conversion.

In the case of arabinoside **5a**, the C-4 epimer of xylonitron **4a**, the nitron exists mainly as a furanoside in CD₃OD, as deduced from the significant deshielding of C-1 (δ_c 100 ppm) and a noticeable correlation between H-1 and C-4 in ¹H-¹³C HMBC experiments (no correlation between H-1 and C-5). Interestingly, the mutarotatory

equilibrium was shifted towards the open form with nitrones **6a** and **7a** derived from tetroses, presenting more than 80% of the nitron in its dipolar state.

Model reactions with nitron **4a**

The addition of alkenes to *protected* glyconitrones has been largely studied over the past years.^{8b} For instance, 2,3;4,5-di-*O*-isopropylidene-D-xylonitron **8** was shown to react smoothly with methyl acrylate at room temperature to afford a mixture of three diastereoisomers in 74:18:8 ratio and excellent 95% yield.¹³ The products originate from competing approaches controlled by steric and electronic interactions. As often observed with glyconitrones the reaction is completely regioselective, with exclusive formation of the sterically favoured 5-substituted isoxazolidine **9**.

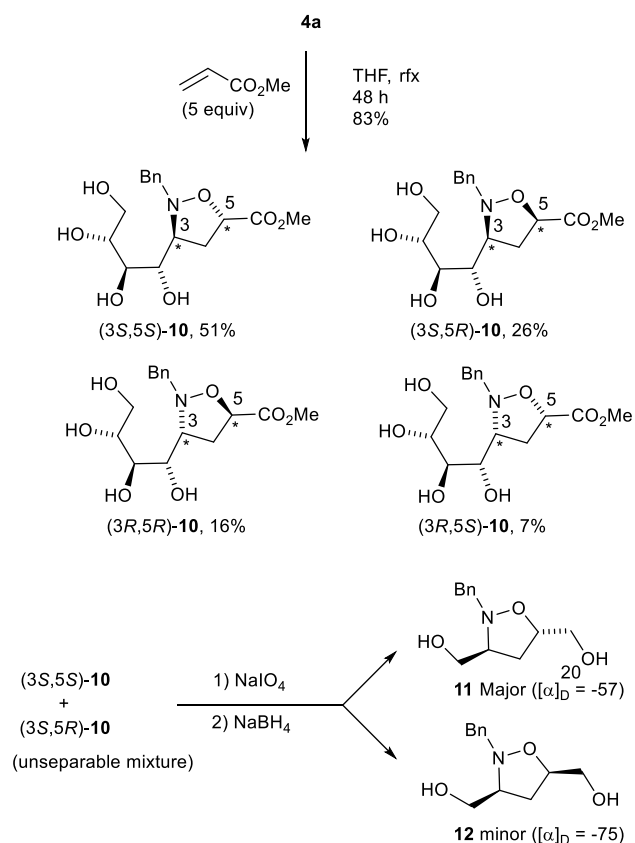


Scheme 3 Known reaction of protected D-xylonitron **8** with methyl acrylate.¹³

The structure of major adduct (3*S*,5*S*)-**9** was ascertained by X-ray diffraction studies, as well as that of its (3*S*,5*R*) epimer, which was formed in 18% ratio.¹³ Both products arise from the approach of methyl acrylate from the sterically less hindered *Si* face of nitron **8**. This result is in agreement with other studies showing that protected α-alkoxy nitrones give preferentially C-1'/C-3 *anti* adducts.¹⁴ In addition, the C-3/C-5 *trans* relative configuration of major isomer (3*S*,5*S*)-**9** results from an *endo* approach of the olefin, the *exo* orientation giving the *cis* (5*R*) epimer.

Based on these results from the literature, we treated D-xylonitron **4a** (a mere unprotected copy of **8**) under the conditions described above. However, very low conversion was observed after 48 h using either THF or DMF as solvent and **4a** was recovered almost unchanged (Table 2). Interestingly, when the reaction was attempted in refluxing THF in the presence of 5 mol. equiv. of methyl acrylate (Scheme 4) complete disappearance of the starting material occurred in 48 h, with concomitant formation of isoxazolidine isomers **10**, detectable as a unique less polar spot on TLC (dichloromethane/methanol, 9:1, v:v). NMR analysis of the crude mixture¹⁵ revealed the presence of four diastereoisomers **10** in the ratio 51:26:16:7, which were isolated as a mixture in 83% overall yield. The reaction proved remarkably clean since no by-product formed, possibly arising from hydrolysis of **4a** or from transesterification of **10**. Separation of all isomers in a stereochemically pure form proved difficult, however, a fraction containing the two major compounds could be isolated. The configurations of these latter might be assigned according to the general rules addressed above, *ie* the *anti-trans* isomer (3*S*,5*S*)-**10** overriding the *anti-cis* (3*S*,5*R*)-**10**. This prediction was ascertained by chemical correlation with their known protected analogues

(3*S*,5*S*)-**9** and (3*S*,5*R*)-**9** (Scheme 3), which were prepared by us using the method from the literature (5 steps from D-xylose).¹³ The two major diastereoisomers, the absolute configuration of which are established, were separated and subjected to acidic treatment for deprotection. NMR data of the samples thus obtained were superimposable with those of our products (3*S*,5*S*)-**10** and (3*S*,5*R*)-**10** respectively, confirming the assigned structures. The relative configuration of (3*S*,5*S*)-**10** and (3*S*,5*R*)-**10** was also affirmed by subsequent treatment with NaIO₄ and NaBH₄, affording an easily separable mixture of known *trans* and *cis* bis-hydroxymethyl-isoxazolidines **11** and **12** (Scheme 4). NMR data were superimposable with those described in the literature for these two epimers.¹⁶ The configurations of the two minor isomers were confirmed analogously. To this purpose, a mixture of (3*R*,5*R*)-**10**/(3*R*,5*S*)-**10** was subjected to NaIO₄ oxidation followed by reduction with NaBH₄. As expected, *trans* and *cis* bis-hydroxymethyl isoxazolidines *ent*-**11** and *ent*-**12** were obtained, which showed comparable NMR data but opposite optical rotations, when compared to **11** and **12**. Hence, their (3*R*) configuration originates from less favourable *Re*-sided approach of the dipolarophile and the *cis/trans* relative configuration of the substituents in the isoxazolidine ring comes from the same level of *endo/exo* repartition.



Scheme 4 Reaction of unprotected D-xylonitrone **4a** with methyl acrylate. Chemical correlation to ascertain the configuration of minor adducts.

The scope of solvents and of activation methods was analysed in a next series of experiments to uncover the most efficient and sustainable synthetic protocols.¹⁷ Glyconitrone **4a** is only soluble in polar solvents such as methanol, DMF or water. Nevertheless, the reaction proved possible in almost all tested solvents (Table 2).

Good yields were obtained in DMF (93%), ethylene glycol (74%) or toluene (69%) when the reaction was conducted at 80 °C for 16 h. MeOH, EtOH, or acetonitrile proved also possible, but with prolonged reaction times with the alcohols due to reaction temperature below 80 °C. In water, hydrolysis of **4a** was kinetically favoured over reaction with methyl acrylate and only xylose was isolated after several hours at 80 °C.

Table 2 Scope of solvents and activation mode.^a

solvent	T°	time	yield ^b	diastereoisomeric ratio ^{c,d}			
<i>Standard thermal heating</i>							
THF	20 °C	48 h	– ^e	–	–	–	–
DMF	20 °C	48 h	– ^e	–	–	–	–
THF	66 °C ^f	48 h	83%	51	26	16	7
DMF	80 °C	16 h	93%	48	25	19	8
ethylene glycol	80 °C	16 h	74%	49	27	17	7
toluene	80 °C	16 h	69%	37	34	20	9
MeOH	65 °C ^f	48 h	80%	47	28	13	12
EtOH	78 °C ^f	40 h	75%	52	25	13	10
CH ₃ CN	80 °C	16 h	81%	42	31	17	10
Ph-CF ₃	80 °C	40 h	42%	37	35	19	9
water	80 °C	16 h	– ^g	–	–	–	–
C ₆ H ₁₂	80 °C	16 h	– ^h	–	–	–	–
methyl acrylate	80 °C ^f	30 min	85%	44	31	16	9
<i>Micro-wave irradiationⁱ</i>							
DMF	80 °C ^j	20 min	92%	44	27	18	11
methyl acrylate	50 °C ^j	1 h	81%	44	32	15	9
methyl acrylate	80 °C ^k	10 min	92%	45	31	15	9
– ^l	53 °C ^j	1 h	82% ^m	42	29	18	11
– ^l	80 °C ^k	10 min	89% ⁿ	42	30	17	11
<i>High-pressure conditions^o</i>							
DMF	20 °C	48 h	83%	53	24	14	9
MeOH	20 °C	48 h	80%	48	27	15	10

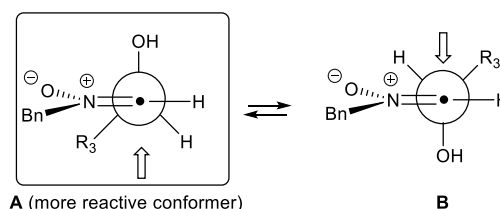
^a Reaction of **4a** with 5 equiv. methyl acrylate; the reaction mixture was heated at indicated T° until complete disappearance of starting nitrone (TLC). ^b Overall isolated yield (chromatography on silica gel). ^c ratios were determined by ¹H-NMR and ¹³C-NMR and confirmed by HPLC in some cases. ^d Given ratio for isomers (3*S*,5*S*):(3*S*,5*R*):(3*R*,5*R*):(3*R*,5*S*) respectively. ^e Only 17% conversion in THF and 13% in DMF after 48h. ^f In refluxing solvent. ^g Hydrolysis of nitrone to xylose. ^h Recovery of starting nitrone. ⁱ Fixed power at 150W, with an air-cooling system. ^j Recorded temperature. ^k fixed temperature in this case. ^l Nitrone **4a** was mixed with 5 equiv of methyl acrylate, no solvent. ^m 92% conversion. ⁿ 97% conversion. ^o A pressure of 10 kbar was applied in the reaction vessel.

Attempts to perform the reaction in cyclohexane proved unsuccessful either, **4a** being recovered unchanged. Insolubility of the nitron in trifluorotoluene might also account for the lower yield (42%) obtained with this solvent. The time of reaction was reduced to only 30 min when methyl acrylate itself was used as the solvent (80°C, 85% isolated yield). In all cases, the diastereoisomeric ratio was determined by analysis of the crude reaction mixture and proved similar to that observed in THF. For each reaction, (3*S*,5*S*)-**10** appears as the major product, originating from *Si*/*endo* preferred approach. However, facial discrimination (*ie* combined 3*S* products vs 3*R* isomers) is significantly lower with unprotected **4a**, culminating at 77:23 in EtOH or THF, than with isopropylidene-protected nitron **8** (92:8). Since better yields were obtained in DMF, it was used as solvent in the next assays. In order to minimize the energy input of the reaction of unprotected glyconitrones, we looked for a possible application of less-demanding energy sources. Microwave (MW) irradiation has emerged as a powerful activation mode to accomplish expeditious chemical transformations in organic chemistry, with reduced reaction times and, sometimes, enhanced selectivity.¹⁸ MW technique also allows for solvent-free reactions, a solution to diminish waste and cost. When nitron **4a** was irradiated at 150 W in DMF (controlled temperature at 80°C by simultaneous air cooling) in the presence of 5 equiv. methyl acrylate, complete conversion occurred in only 20 min (Table 2) affording the mixture of isomers in similar yield and stereoselectivity than standard heating. The presence of DMF as a co-solvent had a significant influence on time and yield (92%) since methyl acrylate alone required 1 h of irradiation under the same conditions, despite the large excess of reagent used in this case, to afford **10** in 81% isolated yield. Obviously, DMF as a polar organic solvent induced stronger absorption of microwaves and consequently increased heating of the medium, with a strong impact on the reaction kinetics. It was possible to overcome the low susceptibility of methyl acrylate to microwaves by increasing temperature in the reaction vessel (no air cooling) and complete conversion occurred in 10 minutes (92% yield). Interestingly, a solvent-free version of the reaction that involved only 5 equivalents of methyl acrylate vs nitron also proved successful, affording **10** in 89% yield without DMF or any other co-solvent.

High pressure technology as a mode of activation has also found applications in organic synthesis, particularly in cycloaddition reactions.¹⁹ These reactions are archetypes of reactions processing a negative activation volume and thus considerable increase in the reaction rate can be expected by applying high pressure.^{19b} A test reaction was effected here in a 1.5 mL reactor containing **4a** and 5 equiv. of methyl acrylate, in DMF or MeOH. The mixture was subjected to 10 kbar, using a hand pump system, which avoids any energy source. Complete conversion required 48 h, affording **10** in 83% yield and the same diastereomeric repartition as above. High pressure plays a fundamental role in this transformation since almost no reaction occurred when **4a** was stirred in a round-bottom flask for 48h at room temperature and under atmospheric pressure (5% conversion only). These experiments showed that high pressure is an economical alternative to produce the expected isoxazolidines from unprotected glyconitron **4a**, although reaction times were longer with respect to standard heating. Conversely, MW-assisted approach abbreviated significantly the reaction time and this activation mode was chosen in further transformations.

Stereochemistry of the reaction

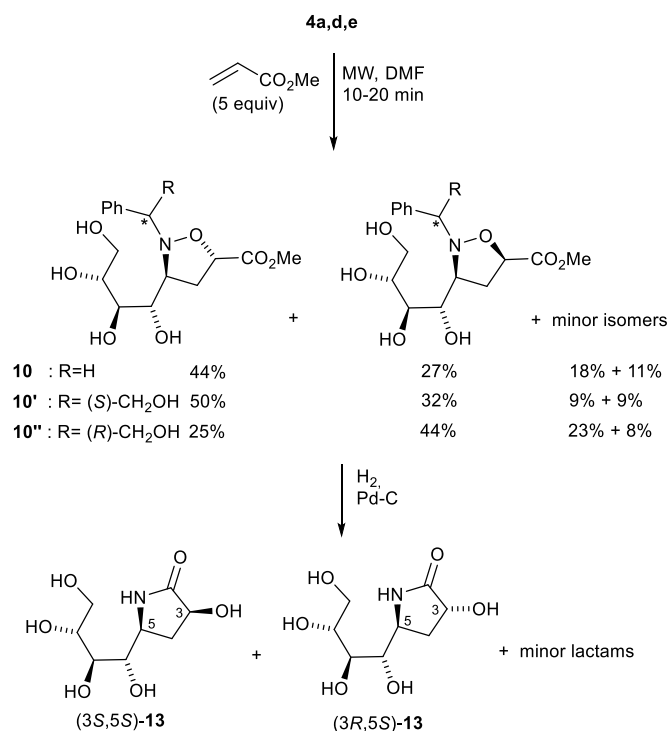
Although the mechanism of nitron-alkene cycloadditions has been extensively outlined,²⁰ the stereochemical outcome is usually difficult to predict and is sensitive to minor structural changes in either component. However, three main features might govern the stereochemical repartition of final compounds: (*Z*)/(*E*)-configuration of the starting nitron, its α -chirality and *endo*/*exo* approach. In their open form, glyconitrones such as **4a** mainly exist as *Z* stereoisomers, characterized by an azomethine proton at δ 6.5-7 ppm in the ¹H-NMR spectrum. The (*E*) isomer (expected deshielded signal at 8.0-8.5 ppm, due to spatial proximity of oxygen) was not observable in the spectra of nitrones **4-6**. Concerning facial selectivity with respect to α -chirality of nitrones, there are precedents in the literature showing good agreement with Felkin-Ahn models.^{21a-c} Accordingly, as initially calculated by Ahn and confirmed by further studies,²² α -alkoxy nitrones in their reactive conformation present the C₂-O bond perpendicularly to the plane of the (*Z*) C=N bond, giving rise to two possible conformers (Scheme 5).



Scheme 5 More reactive conformer of alkoxy nitron **4a** accounting for preferred *Si* face attack of the dipolarophile.

Conformation **A** is expected to be the most reactive because it limits interactions of R₃ (sugar chain) with the dipolarophile as it approaches. This rationale is supported by the fact that bulky protecting groups such as in **8** significantly increase selectivity (scheme 3). With conformer **A**, attack from the less hindered *Si* face accounts for the 3*S* configuration of the major isoxazolidines **10** and the resulting 1',3-*anti* relative configuration.^{21d} Finally, the *endo*/*exo* ratio in 1,3-dipolar cycloadditions of nitrones is not clear-cut since stabilizing secondary orbital overlaps are not essential orienting factors.^{21b} However, in the reaction of protected sugar nitrones an *endo* transition state seems predominant affording 3,5-*trans* isomers. Our results are in agreement with these statements and (3*S*,5*S*)-**10** stems from preferential *endo* orientation of the dipolarophile.

To explore the feasibility of double asymmetric induction,²³ we used nitrones **4d** and **4e**, which feature an additional chiral auxiliary at nitrogen (Scheme 6). Excellent selectivities have been obtained in 1,3-dipolar cycloadditions of nitrones with alkenes by using phenylglycinol as an inductor.²⁴



Scheme 6 Reactions with chiral auxiliary at nitrogen.

Here, only a slight increase in facial selectivity was observed with (*S*)-phenylglycinol (82:18 ratio of combined 3*S* vs 3*R* isomers **10'**). On the other hand, the (*R*)-configured moiety had significant impact on the orientation of the alkene, leading mostly to the (3*S*,5*R*)-**10''** diastereoisomer, as a result of preferential *exo* approach in this case. The absolute configurations of adducts of general structure **10'** and **10''** were assigned after hydrogenolysis into lactams **13** followed by correlation with the same products obtained from **10** (see the Supplementary Information).

Scope of alkenes and nitrones

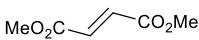
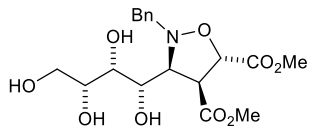
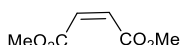
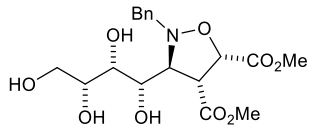

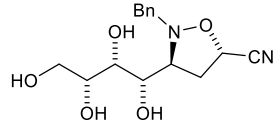
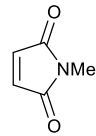
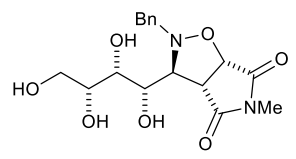
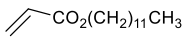
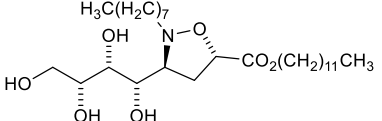
The reaction was applied next to *N*-methyl or *N*-octyl substituted nitrones **4b,c**, as well as analogues derived from *L*-arabinose, *D*-erythrose and *D*-threose **5-7**, using methyl acrylate as the dipolarophile (Table 3, entries 1-7). Reactions were performed in DMF under MW irradiation (150 W, controlled temperature 80°C with air-cooling) for 20 minutes with nitrones **4-5** and 10 minutes with nitrones **6-7**, by using 5 equiv. of alkene. In all cases, the corresponding isoxazolidines were obtained in good yields (55-95%). As discussed above with **4a**, the formed product was composed of four stereoisomers, which were not separable by chromatography on silica gel.

The stereochemical outcome of the cycloaddition was assumed to follow the general rules discussed in the preceding session. The facial approach is guided by steric interactions controlled by hydroxyl at C-2 in the nitron substrate (Scheme 5). Hence, the (2*R*) configuration of xylose, arabinose and erythrose triggers preferential attack from the *Si* face with an alkene in *endo* orientation, affording the major (3*S*,5*S*)-isoxazolidines. In the case of threose-derived nitron **7a**, the opposite configuration at C-2 might drive the major attack from the opposite *Re* face, giving rise to (3*R*,5*R*)-isoxazolidine as the main product. Again, this was assessed by chemical correlation. A sample containing the two major diastereoisomers could be separated during purification of **20** (Table 3, entry 7) and was subjected to the NaIO₄/NaBH₄ protocol as shown in Scheme 4. After purification, the two dihydroxymethyl-isoxazolidines *ent*-**11** and *ent*-**12** were isolated in a pure form showing a positive optical rotation, opposite to that observed for **11-12**, which assessed the configuration shown for **20** in Table 3.²⁵

A range of electron-deficient alkenes were subjected next to cycloaddition with nitron **4a** (Table 3, entries 8-16). The structures of the major compounds are shown in Table 3, assuming the same rules of selectivity as in the preceding examples (*endo Si* approach). Good yields of the expected isoxazolidines were obtained with *tert*-butyl-, benzyl- or dodecyl-acrylate, acrylonitrile, dimethylfumarate and dimethylmaleate in the range 75-93%. The reaction with octadecylacrylate (entry 11) proved much more sluggish and concurrent hydrolysis of the nitron overrode the expected cycloaddition affording **23** in only 25% yield. Four stereoisomers were obtained in almost all cases, showing roughly the same 75:25 level of stereofacial preference. Interestingly, the reaction with *N*-methylmaleimide proved more selective, affording a 67:28:5:0 repartition of isomers (95:5 facial preference) in 82% yield. Finally, the reaction proved as effective with nitron **4c** (entry 16), resulting in the bicatenar amphiphilic structure **29** in 80% yield.

Table 3 Scope of nitrones and alkenes.^a

entry	nitron	alkene	product	structure ^b	yield ^c	ratio ^{d,e}
1	4b		14		77%	63 : 25 : 7 : 5
2	4c		15		82%	50 : 26 : 17 : 7
3	5a		16		90%	46 : 24 : 22 : 8
4	5b		17		55%	66 : 22 : 7 : 5
5	5c		18		95%	46 : 37 : 9 : 8
6	6a		19		84%	48 : 26 : 20 : 6
7	7a		20		75%	49 : 24 : 19 : 8 ^f
8	4a		21		89%	46 : 26 : 18 : 10
9	4a		22		93%	47 : 26 : 20 : 7
10	4a		23		92%	46 : 26 : 20 : 8
11	4a		24		25%	44 : 27 : 19 : 10

12	4a		25		76%	51 : 22 : 16 : 11
13	4a		26		79%	62 : 19 : 12 : 7
14	4a		27		85%	50 : 30 : 12 : 8
15	4a		28		82%	67 : 28 : 5 : 0
16	4c		29		80%	53 : 21 : 20 : 6

^a all the reactions were performed under MW irradiation (fixed power, 150 W) for 10–20 min in DMF with 5 equiv alkene. ^b Structure of the expected major anti/trans isomer, assuming identical control than that observed for **10**. ^c Isolated yield. ^d Ratios were determined by ¹H-NMR and ¹³C-NMR and confirmed by HPLC when possible. ^e Given ratio for anti/trans, anti/cis, syn/trans, syn/cis isomers respectively. ^f Configurations of isomers were confirmed by chemical correlation.

Thus, the reaction of unprotected glyconitrone with electron-poor alkenes appears as a synthetic tool of general use, affording substituted isoxazolidines in a minimum number of steps by using sustainable synthetic protocols and with excellent atomic balance. Apart from their intrinsic properties, isoxazolidines are easily transformed into lactams (scheme 6). The resemblance of the obtained structure **13** with polyhydroxypyrrrolidine-like iminosugars prompted us to test its tendency to inhibit glycosidases.²⁶ Unfortunately, lactam **13** (as a mixture of four stereoisomers) was inactive at 1 mM against any of the following enzymes: α -glucosidase from rice and from yeast, β -glucosidase from almond, β -glucosidase and α -rhamnosidase from *A. niger*, β -galactosidase from *A. oryzae*. Only a slight inhibition (8%) of α -mannosidase from Jack bean could be detected.

Conclusions

In conclusion, we report here a valuable alternative for the direct transformation of unprotected aldoses into elaborated products. The process consists in primary condensation with an hydroxylamine followed by 1,3-dipolar cycloaddition with an electron-deficient alkene. It was applied to tetroses and pentoses, affording the expected polyhydroxyalkyl-isoxazolidines in good yields and appreciable stereoselectivity. Nevertheless, the strategy allows the formation of amphiphilic compounds in very few steps. The hydrophilicity of the polar

head might be controlled by the choice of the starting aldose. Dual carbon chain tails might be adjusted via the starting hydroxylamine and the alkene, giving rise to carbohydrate-based mono or bi-catenar non-ionic amphiphiles. In addition, reduction of the N-O bond allows further fonctionnalization. Applied to isoxazolidine **10** this transformation gave 3-hydroxy-5-tetrahydroxybutyl-pyrrolidin-2-one **13**, which was tested as glycosidase inhibitor but proved inactive against the panel of tested enzymes.

Experimental SECTION

General methods

Reactants and reagents were purchased from standard suppliers (Sigma-Aldrich, Alfa-Aesar, Fisher Scientific) and were used without further purification. MeOH, DMF, toluene and THF were dried on an Innovative Technology, Inc. Pure Solv MD system; the other solvents were dried according to conventional methods. Reactions were monitored by TLC using Silica gel F254 (0.2 mm) TLC plates, detection being carried out by spraying with an aqueous solution of KMnO₄ (2%) / Na₂CO₃ (4%) or alcoholic solutions of phosphomolybdic acid or *p*-anisaldehyde, followed by heating. Column chromatography purifications were performed over silica gel M 9385 (40–63 μ m) Kieselgel 60. NMR spectra were recorded on Bruker AC 250 (250 MHz for ¹H, 62.5 MHz for ¹³C), 500 (500 MHz

for ^1H , 125 MHz for ^{13}C) or 600 (600 MHz for ^1H , 150 MHz for ^{13}C) spectrometers. Chemical shifts are expressed in parts per million (ppm) and were calibrated to deuterated or residual non-deuterated solvent peaks for ^1H and ^{13}C spectra. Coupling constants are in Hz and splitting pattern abbreviations are: br, broad; s, singlet; d, doublet; t, triplet; m, multiplet. DEPT 1D NMR experiments, COSY, HSQC, and HMBC 2D NMR experiments were used to confirm the NMR peak assignments for all compounds. Optical rotations were determined at 20 °C with a Perkin-Elmer Model 241 polarimeter, usually in methanol. Due to mutarotation, optical rotation of nitrones was time dependent. The given value is the one that was observed 5-10 minutes after sample preparation. High Resolution Mass Spectra (HRMS) were performed on Q-TOF Micro micromass positive ESI (CV = 30 V). Elemental analysis were performed on a Thermo Electron CHNS FlashEA 1112 series apparatus. Melting points (mp) were determined on a Tottoli apparatus and were uncorrected. Microwave reactions were realized in a CEM Corporation-Discover S-Class apparatus using either the "fixed power control" mode with the cooling function activated or the "fixed temperature control" mode; reaction temperatures : measured with a volume-independent, noninvasive infrared temperature control system; reaction agitation: electromagnetic stirring with adjustable speeds. High-pressure reactions were performed in a piston-cylinder device equipped with hand pump with spindle drive type apparatus designed for pressures up to 10 kbar (Nova Swiss SARL, France). Experiments were conducted in 1.5 mL Teflon capsule inserted into the high-pressure vessel filled with white spirit as a transmission medium.

General procedures for the synthesis of sugar-nitrones **4a-e**, **5a-c**, **6a** and **7a**:

General procedure A: To a solution of hydroxylamine **a**, **c**, **d** or **e** (1.6 mmol, 1.2 equiv. (1.46 mmol, 1.1 equiv. for aldoses **6** and **7**) for **a** ; 2.0 mmol, 1.5 equiv. for **c** ; 2.8 mmol, 2.1 equiv. for **d** and **e**) in methanol (5.0 mL) under argon was added aldose **4-7** (1.33 mmol, 1 equiv.). The solution was heated at 45°C and stirred until total consumption of the starting aldose (typically 16 h for pentoses, 2h for tetroses). Methanol was removed under reduced pressure and the residue was purified by recrystallization or using chromatography on silica gel to afford the corresponding glyconitronone **4a**, **4c-e**, **5a**, **5c**, **6a** and **7a**.

General procedure B: To a solution of sodium methoxide (4.0 mmol, 216 mg, 1.2 equiv) in methanol under argon was added *N*-hydroxymethylamine hydrochloride **b** (4.0 mmol, 334 mg, 1.2 equiv.). After 10 min of stirring, aldose **4** or **5** (3.33 mmol, 500 mg, 1 equiv.) was added and the solution was heated at 45°C and stirred until total consumption of the starting aldose. Methanol was removed and the residue was purified using chromatography on silica gel to afford the corresponding glyconitronone **4b** or **5b**.

***N*-Benzyl-1-(hydroxyamino)- β -D-xylopyranose (**4a**):** According to general procedure A, the reaction of D-xylose **4** (6.82 mmol, 1.022 g, 1 equiv.) and *N*-hydroxybenzylamine **a** (8.17 mmol, 1.006 g, 1.2 equiv.) and purification of the resulting residue by chromatography on silica gel (ethyl acetate / methanol 92.5:7.5) afforded **4a** (1.512 g, 5.93 mmol), yield 87%; colourless solid, mp 96°C; $[\alpha]_D^{20}$ -8.4 (c 0.47 in MeOH); ^1H NMR (CD₃OD, 500 MHz) δ 3.15 (1H, dd, J = 10.9, 10.9 Hz, 5- H_aH_b), 3.31 (1H, m, 3-H), 3.51 (1H, ddd, J = 10.5, 9.0, 5.5

Hz, 4-H), 3.61 (1H, dd, J = 9.0, 9.0 Hz, 2-H), 3.87 (1H, d, J = 8.8 Hz, 1-H), 3.94 (1H, dd, J = 11.2, 5.5 Hz, 5- H_aH_b), 3.98 (1H, d, J = 13.3 Hz, CH_aH_bPh), 4.14 (1H, d, J = 13.2 Hz, CH_aH_bPh), 7.24-7.26 (1H, m, Ar-H), 7.30-7.33 (2H, m, 2 x Ar-H), 7.39-7.41 (2H, m, 2 x Ar-H); ^{13}C NMR (CD₃OD, 125 MHz) δ 60.2 (CH₂Ph), 68.9 (C-5), 71.2 (C-4), 71.5 (C-2), 78.9 (C-3), 95.5 (C-1), 128.2 (Ar-C), 129.2 (2 x Ar-C), 130.5 (2 x Ar-C), 139.3 (Ar-C^V); elemental analysis found C, 56.30 ; H, 6.66 ; N, 5.58 Calc. for C₁₂H₁₇NO₅ : C, 56.46 ; H, 6.71 ; N, 5.49%; HRMS (ESI⁺) m/z calcd for C₁₂H₁₇NO₅Na [M + Na]⁺ 278.1004, found 278.1009.

***N*-Methyl-1-(hydroxyamino)-D-xylopyranose (**4b**):** According to general procedure B, the reaction of D-xylose **4** (3.33 mmol, 500 mg, 1 equiv.) and *N*-hydroxymethylamine hydrochloride **b** (4 mmol, 334 mg, 1.2 equiv.) and purification of the resulting residue by chromatography on silica gel (ethyl acetate / methanol 80:20) afforded **4b** (358 mg, 2 mmol) as a yellow oil, yield 60%; $[\alpha]_D^{20}$ -11.3 (c 0.43 in MeOH); ^1H NMR (CD₃OD, 500 MHz) δ 2.70 (0.15H, s, CH₃^(afur)), 2.73 (2.24H, s, CH₃^(β pyr)), 3.18 (0.71H, dd, J = 11.1, 11.1 Hz, 5- H_aH_b ^(β pyr)), 3.31-3.34 (0.67H, m, 3-H^(β pyr)), 3.47-3.51 (1.53H, m, 2-H^(β pyr)), 4-H^(β pyr)), 3.62-3.69 (0.42H, m, 5-H^(open)), 3.71-3.79 (0.91H, m, CH₃^(open) + 4-H^(open) + 5- H_aH_b ^(afur)), 3.80-3.85 (0.97H, m, 3-H^(open) + 5- H_aH_b ^(afur) + 1-H^(β pyr)), 3.93 (0.74H, dd, J = 11.1, 5.5 Hz, 5- H_aH_b ^(β pyr)), 3.99 (0.05H, dd, J = 4.5, 2.7 Hz, 3-H^(afur)), 4.10-4.13 (0.06H, m, 4-H^(afur)), 4.21 (0.05H, dd, J = 2.6, 2.6 Hz, 2-H^(afur)), 4.33 (0.04H, d, J = 2.5 Hz, 1-H^(open)); 4.88-4.90 (0.28H, m, 2-H^(open)), 7.23 (0.18H, d, J = 5.9 Hz, 1-H^(open)); ^{13}C NMR (CD₃OD, 125 MHz) δ 42.7 (CH₃^(β pyr)), 43.8 (CH₃^(afur)), 52.3 (CH₃^(open)), 61.9 (C-5^(afur)), 64.0 (C-5^(open)), 68.8 (C-5^(β pyr)), 69.6 (C-2^(open)), 71.2 (C-4^(β pyr)), 71.6 (C-2^(β pyr)), 73.2 (C-4^(open)), 73.4 (C-3^(open)), 77.5 (C-3^(afur)), 79.0 (C-3^(β pyr)), 79.3 (C-2^(afur)), 82.8 (C-4^(afur)), 96.8 (C-1^(β pyr)), 103.1 (C-1^(afur)), 146.8 (C-1^(open)); HRMS (ESI⁺) m/z calcd for C₆H₁₃NO₅Na [M + Na]⁺ 202.0691, found 202.0695.

***N*-Octyl-1-(hydroxyamino)-D-xylopyranose (**4c**):** According to general procedure A, the reaction of D-xylose **4** (1.33 mmol, 200 mg, 1 equiv.) and *N*-hydroxyoctylamine **c** (2.0 mmol, 290 mg, 1.5 equiv.) and purification of the resulting residue by chromatography on silica gel (ethyl acetate / methanol 95:5) afforded **4c** (354 mg, 1.28 mmol) as a colourless sticky foam, yield 96%; $[\alpha]_D^{20}$ -3.3 (c 0.49 in MeOH); ^1H NMR (CD₃OD, 500 MHz) δ 0.90 (3H, t, J = 7.2 Hz, CH₃), 1.27-1.39 (10H, m, 5 x CH₂^(octyl)), 1.55-1.61 (1.45H, m, CH₂^(octyl- β pyr)), 1.84-1.90 (0.29H, m, CH₂^(octyl-open)), 2.70 (0.73H, ddd, J = 12.6, 8.4, 7.1 Hz, N-CH₂H_bC₇H₁₅^(β pyr)), 3.02 (0.72H, ddd, J = 12.6, 8.1, 5.9 Hz, N-CH₂H_bC₇H₁₅^(β pyr)), 3.16 (0.76H, dd, J = 10.9, 10.9 Hz, 5- H_aH_b ^(β pyr)), 3.34 (0.80H, dd, J = 9.1, 9.1 Hz, 3-H^(β pyr)), 3.48 (0.80H, ddd, J = 10.6, 8.9, 5.5 Hz, 4-H^(β pyr)), 3.55 (0.71H, dd, J = 8.9, 8.9 Hz, 2-H^(β pyr)), 3.61-3.68 (0.42H, m, 2 x 5-H^(open)), 3.70-3.74 (0.20H, m, 4-H^(open)), 3.79-3.85 (1.22H, m, 3-H^(open) + N-CH₂C₇H₁₅^(open) + 1-H^(β pyr)), 3.90 (0.79H, dd, J = 11.2, 5.4 Hz, 5- H_aH_b ^(β pyr)), 4.88-4.90 (0.22H, m, 2-H^(open)), 7.24 (0.17H, d, J = 5.9 Hz, 1-H^(open)); ^{13}C NMR (CD₃OD, 125 MHz) δ 14.4 (CH₃^(open)), 14.4 (CH₃^(β pyr)), 23.7 (CH₂^(octyl-open)), 23.7 (CH₂^(octyl- β pyr)), 27.3 (CH₂^(octyl-open)), 28.3 (CH₂^(octyl- β pyr) + CH₂^(octyl-open)), 28.8 (CH₂^(octyl- β pyr)), 30.2 (CH₂^(octyl-open)), 30.2 (CH₂^(octyl-open)), 30.4 (CH₂^(octyl- β pyr)), 30.7 (CH₂^(octyl- β pyr)), 32.9 (CH₂^(octyl-open)), 33.0 (CH₂^(octyl- β pyr)), 56.2 (N-CH₂C₇H₁₅^(β pyr)), 64.0 (C-5^(open)), 65.9 (N-CH₂C₇H₁₅^(open)), 68.9 (C-5^(β pyr)), 69.6 (C-2^(open)), 71.2 (C-4^(β pyr)), 71.5 (C-2^(β pyr)), 73.3 (C-4^(open)), 73.5 (C-3^(open)), 78.9 (C-3^(β pyr)), 96.5 (C-1^(β pyr)), 145.9 (C-1^(open)); HRMS (ESI⁺) m/z calcd for C₁₃H₂₈NO₅ [M + H]⁺ 278.1967, found 278.1967.

***N*-((S)-2'-hydroxy-1'-phenylethyl)-1-(hydroxyamino)-D-xylopyranose (**4d**):** According to general procedure A, the reaction of D-xylose **4** (1.67 mmol, 250 mg, 1 equiv.) and (S)-2-(hydroxyamino)-2-phenylethanol **d** (3.9 mmol, 600 mg) and

purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 8:2) afforded **4d** (396 mg) as a colourless hygroscopic solid, yield 83%; [α]_D²⁰ +26.3 (c 0.48 in MeOH); ¹H NMR (CD₃OD, 500 MHz) δ 3.16 (0.38H, dd, *J* = 10.9, 10.9 Hz, 5-*H*_oH_b^(β pyr)), 3.37 (0.42H, dd, *J* = 9.2, 9.2 Hz, 3-*H*^(β pyr)), 3.48 (0.41H, ddd, *J* = 10.6, 8.9, 5.4 Hz, 4-*H*^(β pyr)), 3.55-3.70 (2.56H, m, 4-*H*^(open) + 2 x 5-*H*^(open) + 2-*H*^(β pyr) + 2'-*H*_oH_b^(β pyr)), 3.73-3.74 (0.53H, m, 3-*H*^(open)), 3.80-3.89 (1.67H, m, 5-*H*_aH_b^(β pyr) + 2'-*H*_aH_b^(β pyr) + 2'-*H*_oH_b^(open)), 4.23-4.26 (0.77H, m, 1-*H*^(β pyr), 1'-*H*^(β pyr)), 4.43 (0.54H, dd, *J* = 11.8, 9.4 Hz, 2'-*H*_aH_b^(open)), 4.92 (0.57H, dd, *J* = 5.7, 5.7 Hz, 2-*H*^(open)), 5.12 (0.52H, dd, *J* = 9.4, 4.0 Hz, 1'-*H*^(open)), 7.22-7.44 (4.63 H, m, 4 x Ar-H, 1-*H*^(open)), 7.51-7.53 (1H, m, Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 62.5 (C-2'^(open)), 63.9 (C-5'^(open)), 65.0 (C-2'^(β pyr)), 68.6 (C-5'^(β pyr)), 69.7 (C-2'^(open)), 71.1 (C-1'^(β pyr)), 71.2 (C-4'^(β pyr)), 71.4 (C-2'^(β pyr)), 73.3 (C-4'^(open)), 73.6 (C-3'^(open)), 79.1 (C-3'^(β pyr)), 80.6 (C-1'^(open)), 93.9 (C-1'^(β pyr)), 128.1, 128.7, 129.0, 129.1, 129.4, 129.5, 129.7 and 130.1 (10 x Ar-C), 135.8 (Ar-C'^(open)), 141.9 (Ar-C'^(β pyr)), 145.6 (C-1'^(open)); HRMS (ESI⁺) *m/z* calcd for C₁₃H₂₀NO₆ [M + H]⁺ 286.1291, found 286.1291.

N-((R)-2'-hydroxy-1'-phenylethyl)-1-(hydroxyamino)-D-

xylopyranose (4e): According to general procedure A, the reaction of D-xylose **4** (2.33 mmol, 350 mg) and (R)-2-(hydroxyamino)-2-phenylethanol **e** (4.87 mmol, 746 mg) and purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 8:2) afforded **4e** (582 mg) as a colourless solid, yield 88%; mp 63°C; [α]_D²⁰ -24.9 (c 0.43 in MeOH); ¹H NMR (CD₃OD, 600 MHz) δ 2.60 (0.60H, dd, *J* = 10.9, 10.9 Hz, 5-*H*_oH_b^(β pyr)), 3.01 (0.60H, dd, *J* = 9.1, 9.1 Hz, 3-*H*^(β pyr)), 3.33-3.37 (1.25H, m, 1-*H*^(β pyr), 4-*H*^(β pyr)), 3.56-3.60 (1.29H, m, 2 x 5-*H*^(open) + 2-*H*^(β pyr)), 3.72-3.76 (1.60H, m, 4-*H*^(open) + 5-*H*_aH_b^(β pyr) + 3-*H*^(open) + 2'-*H*_oH_b^(open)), 3.90 (0.65H, dd, *J* = 11.0, 6.6 Hz, 2'-*H*_oH_b^(β pyr)), 3.99 (0.72H, dd, *J* = 11.0, 4.0 Hz, 2'-*H*_aH_b^(β pyr)), 4.13 (0.66H, dd, *J* = 6.5, 4.1 Hz, 1'-*H*^(β pyr)), 4.40 (0.29H, dd, *J* = 11.5, 9.9 Hz, 2'-*H*_aH_b^(open)), 4.82-4.84 (0.33H, m, 2-*H*^(open)), 5.06 (0.28H, dd, *J* = 9.8, 3.8 Hz, 1'-*H*^(open)), 7.22-7.34 (4.80H, m, 4 x Ar-H^(β pyr) + 5 x Ar-H^(open)), 7.39 (0.38H, d, *J* = 6.0 Hz, 1-*H*^(open)), 7.46-7.48 (0.45H, m, Ar-H^(β pyr)); ¹³C NMR (CD₃OD, 150 MHz) δ 62.6 (C-2'^(open)), 64.0 (C-5'^(open)), 65.9 (C-2'^(β pyr)), 68.6 (C-5'^(β pyr)), 69.8 (C-2'^(β pyr)), 70.0 (C-1'^(β pyr)), 71.1 (C-4'^(β pyr)), 71.1 (C-2'^(β pyr)), 73.1 (C-4'^(open)), 73.9 (C-3'^(open)), 78.8 (C-3'^(β pyr)), 80.5 (C-1'^(open)), 92.5 (C-1'^(β pyr)), 128.6, 128.9, 129.0, 129.2, 129.3, 129.5, 129.7, 130.2 and 130.2 (10 x Ar-C), 135.6 (Ar-C'^(open)), 140.1 (Ar-C'^(β pyr)), 145.8 (C-1'^(open)); HRMS (ESI⁺) *m/z* calcd for C₁₃H₂₀NO₆ [M + H]⁺ 286.1291, found 286.1290.

N-Benzyl-1-(hydroxyamino)-L-arabinofuranose (5a): According to general procedure A, the reaction of L-arabinose **5** (3.41 mmol, 511 mg, 1 equiv.) and *N*-hydroxybenzylamine **a** (5.11 mmol, 629 mg, 1.5 equiv.) and purification of the resulting residue by chromatography on silica gel (ethyl acetate / methanol 92.5:7.5) afforded **5a** (787 mg, 3.09 mmol) as a colorless solid, yield 53%; F_{dec.} = 139°C; [α]_D²⁰ +36.2 (c 0.77 in DMSO) - optical specific rotation evolves towards a negative value due to mutarotation and reaches an equilibrium within 24 hours to reach [α]_D²⁰ -46.6 (c 0.77 in DMSO); ¹H NMR (CD₃OD, 500 MHz) δ 3.59-3.65 (1H, m, 5-*H*_oH_b^(β fur) + 5-*H*_oH_b^(open)), 3.68-3.84 (1.62H, m, 5-*H*_aH_b^(β fur) + 5-*H*_aH_b^(open) + 3-*H*^(open) + 4-*H*^(open)), 3.90 (0.72H, d, *J* = 13.4 Hz, CH₂H_bPh^(β fur)), 3.92-3.94 (0.74H, m, 3-*H*^(β fur)), 3.97-4.00 (0.75H, m, 4-*H*^(β fur)), 4.11 (0.75H, d, *J* = 13.4 Hz, CH₂H_bPh^(β fur)), 4.36 (0.67H, dd, *J* = 6.2, 5.0 Hz, 2-*H*^(β fur)), 4.49 (0.67H, d, *J* = 5.0 Hz, 1-*H*^(β fur)), 4.97 (0.50H, m, CH₂Ph^(open)), 5.02 (0.26H, dd, *J* = 5.8, 2.3 Hz, 2-*H*^(open)), 7.21-7.25 (0.77H, m, Ar-H), 7.29-7.32 (1.52H, m, Ar-H), 7.34 (0.28H, d, *J* = 5.8 Hz, 1-*H*^(open)), 7.38-7.43 (2.23H, m, Ar-H), 7.45-7.48 (0.52H, m, Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 60.6 (CH₂Ph^(β fur)), 62.9 (C-5'^(β fur)), 64.7 (C-5'^(open)), 68.2 (C-2'^(open)), 69.7

(CH₂Ph^(open)), 72.7, 72.8 (C-4'^(open) + C-3'^(open)), 77.5 (C-3'^(β fur)), 79.6 (C-2'^(β fur)), 85.1 (C-4'^(β fur)), 100.0 (C-1'^(β fur)), 128.1, 128.2, 129.1, 129.2, 129.9, 130.0, 130.3, 130.4 and 130.5 (10 x Ar-C), 134.3 (Ar-C'^(open)), 139.3 (Ar-C'^(β fur)), 146.7 (C-1'^(open)); elemental analyses found C, 56.24; H, 6.81; N, 5.41. Calc. for C₁₂H₁₇NO₅: C, 56.46; H, 6.71; N, 5.49%; HRMS (ESI⁺) *m/z* calcd for C₁₂H₁₈NO₅ [M + H]⁺ 256.1185, found 256.1188.

N-Methyl-1-(hydroxyamino)-L-arabinopyranose (5b): According to general procedure B, the reaction of L-arabinose **5** (3.33 mmol, 500 mg, 1 equiv.) and *N*-hydroxymethylamine hydrochloride **b** (4.0 mmol, 334 mg, 1.2 equiv.) and purification of the resulting residue by chromatography on silica gel (ethyl acetate / methanol 80:20) afforded **5b** (489 mg, 2.73 mmol) as a yellow oil, yield 82%; [α]_D²⁰ +3.2 (c 0.50 in MeOH); ¹H NMR (CD₃OD, 500 MHz) δ 2.70 (0.94H, s, CH₃^(fur)), 2.75 (1.05H, s, CH₃^(pyr)), 3.53-3.56 (0.38H, m, 3-*H*^(pyr)), 3.57-3.62 (0.76H, m, 5-*H*_oH_b^(pyr) + 5-*H*_oH_b^(fur)), 3.66 (0.34H, dd, *J* = 11.2, 5.6 Hz, 5-*H*_oH_b^(open)), 3.73 (0.90H, s, CH₃^(open)), 3.74-3.83 (2.39H, m, 5-*H*_aH_b^(fur) + 5-*H*_aH_b^(open) + 3-*H*^(open) + 4-*H*^(open) + 1-*H*^(pyr) + 2-*H*^(pyr) + 4-*H*^(pyr)), 3.91-3.93 (0.57H, m, 3-*H*^(fur) + 4-*H*^(fur)), 3.96 (0.45H, dd, *J* = 12.6, 2.1 Hz, 5-*H*_aH_b^(pyr)), 4.26 (0.32H, dd, *J* = 6.2, 4.9 Hz, 2-*H*^(fur)), 4.32 (0.32H, d, *J* = 4.9 Hz, 1-*H*^(fur)), 5.03 (0.30H, m, 2-*H*^(open)), 7.25 (0.28H, dd, *J* = 5.80, 1.0 Hz, 1-*H*^(open)); ¹³C NMR (CD₃OD, 125 MHz) δ 42.7 (CH₃^(pyr)), 43.5 (CH₃^(fur)), 52.4 (CH₃^(open)), 62.8 (C-5'^(fur)), 64.7 (C-5'^(open)), 68.3 (C-2'^(open)), 69.3 (C-2'^(pyr)), 69.4 (C-5'^(pyr)), 70.5 (C-4'^(open)), 72.6 (C-3'^(open) + C-4'^(open)), 75.4 (C-3'^(pyr)), 77.6 (C-3'^(fur)), 79.5 (C-2'^(fur)), 84.9 (C-4'^(fur)), 96.9 (C-1'^(pyr)), 101.3 (C-1'^(fur)), 147.3 (C-1'^(open)); HRMS (ESI⁺) *m/z* calcd for C₆H₁₃NO₅Na [M + Na]⁺ 202.0691, found 202.0690.

N-Octyl-1-(hydroxyamino)-L-arabinofuranose (5c): According to general procedure A, the reaction of L-arabinose **5** (1.33 mmol, 200 mg, 1 equiv.) and *N*-hydroxyoctylamine **c** (2.0 mmol, 290 mg, 1.5 equiv.) and purification of the resulting residue by chromatography on silica gel (ethyl acetate / methanol 95:5) afforded **5c** (266 mg, 0.96 mmol) as a colourless sticky foam, yield 72%; mp 130°C; [α]_D²⁰ +24.8 (c 0.45 in MeOH); ¹H NMR (CD₃OD, 500 MHz) δ 0.90 (3H, t, *J* = 6.9 Hz, CH₃), 1.29-1.42 (10H, m, 5 x CH₂^(octyl)), 1.58-1.64 (0.66H, m, CH₂^(octyl)), 1.86-1.92 (1.34H, m, CH₂^(octyl)), 2.64-2.75 (0.34H, m, N-CH₂H_bC₇H₁₅^(fur) + N-CH₂H_bC₇H₁₅^(pyr)), 2.95-3.06 (0.34H, m, N-CH₂H_bC₇H₁₅^(fur) + N-CH₂H_bC₇H₁₅^(pyr)), 3.52-3.62 (0.37H, m, 5-*H*_oH_b^(fur) + 5-*H*_oH_b^(pyr) + 3-*H*^(pyr)), 3.66 (0.69H, dd, *J* = 11.2, 5.5 Hz, 5-*H*_oH_b^(open)), 3.72-3.87 (3.73H, m, 1-*H*^(pyr) + 4-*H*^(pyr) + 2-*H*^(pyr) + 3-*H*^(open) + 4-*H*^(open) + N-CH₂C₇H₁₅^(open) + 5-*H*_aH_b^(open) + 5-*H*_aH_b^(fur)), 3.91-3.94 (0.56H, m, 4-*H*^(fur) + 3-*H*^(fur) + 5-*H*_aH_b^(pyr)), 4.31 (0.24H, m, 2-*H*^(fur)), 4.39 (0.24H, d, *J* = 5.0 Hz, 1-*H*^(fur)), 5.04 (0.65H, dd, *J* = 5.8, 2.3 Hz, 2-*H*^(open)), 7.25 (0.66H, d, *J* = 5.8 Hz, 1-*H*^(open)); ¹³C NMR (CD₃OD, 125 MHz) δ 14.4 (CH₃), 23.7, 23.7, 27.3, 28.3, 28.4, 28.5, 28.7, 30.2, 30.5, 30.7, 32.9 and 33.0 (CH₂^(octyl)), 56.0 (N-CH₂C₇H₁₅^(pyr)), 56.5 (N-CH₂C₇H₁₅^(fur)), 62.9 (C-5'^(fur)), 64.8 (C-5'^(open)), 65.9 (N-CH₂C₇H₁₅^(open)), 68.2 (C-2'^(open)), 69.2 (C-2'^(pyr)), 69.4 (C-5'^(pyr)), 70.6 (C-4'^(pyr)), 72.8 (C-3'^(open)), 72.9 (C-4'^(open)), 75.4 (C-3'^(pyr)), 77.5 (C-3'^(fur)), 79.4 (C-2'^(fur)), 85.0 (C-4'^(fur)), 96.6 (C-1'^(pyr)), 100.7 (C-1'^(fur)), 146.4 (C-1'^(open)); HRMS (ESI⁺) *m/z* calcd for C₁₃H₂₈NO₅ [M + H]⁺ 278.1967, found 278.1970.

N-Benzyl-1-(hydroxyamino)- α -D-erythrose (6a): According to general procedure A, the reaction of D-erythrose **6** (3.58 mmol, 430 mg, 1 equiv.) and *N*-hydroxybenzylamine **a** (3.94 mmol, 485 mg, 1.1 equiv.) and the purification of the resulting residue by chromatography on silica gel (dichloromethane / methanol 90:10) afforded **6a** (575 mg, 2.56 mmol) as an orange/yellow solid, yield 71%; mp 75°C; ¹H NMR (CD₃OD, 500 MHz) δ 3.57-3.65 (1.66H, m, 4-

H^(open), 3.82 (0.16H, dd, $J = 9.2, 3.5$ Hz, 4- $H_{\alpha}H_{\beta}$ ^(α -closed)), 3.84-3.89 (0.85H, m, H-3^(open)), 3.93 (0.18H, d, $J = 13.2$ Hz, $CH_{\alpha}H_{\beta}Ph$ ^(α -closed)), 4.06 (0.15H, d, $J = 13.2$ Hz, $CH_{\alpha}H_{\beta}Ph$ ^(α -closed)), 4.14 (0.16H, dd, $J = 9.2, 4.6$ Hz, 4- $H_{\alpha}H_{\beta}$ ^(α -closed)), 4.26-4.29 (0.13H, m, H-3^(α -closed)), 4.32-4.35 (0.16H, m, H-2^(α -closed)), 4.57 (0.12H, d, $J = 4.3$ Hz, H-1^(α -closed)), 4.85 (0.93H, dd, $J = 5.7, 5.7$ Hz, H-2^(open)), 4.97 (0.85H, d, $J = 13.5$ Hz, $CH_{\alpha}H_{\beta}Ph$ ^(open)), 5.01 (0.81H, d, $J = 13.5$ Hz, $CH_{\alpha}H_{\beta}Ph$ ^(open)), 7.23-7.33 (0.57H, m, Ar-H), 7.36 (0.85H, d, $J = 6.2$ Hz, H-1^(open)), 7.38-7.44 (2.79H, m, Ar-H), 7.48-7.50 (1.63H, m, Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 60.9 (CH₂Ph^(α -closed)), 63.8 (C-4^(open)), 68.8 (C-2^(open)), 69.8 (CH₂Ph^(open)), 72.3 (C-3^(α -closed)), 74.2 (C-4^(α -closed)), 74.4 (C-3^(open)), 74.7 (C-2^(α -closed)), 100.5 (C-1^(α -closed)), 128.1, 129.2, 129.8, 130.0, 130.3, 130.5 (6 x Ar-C), 134.4 (Ar-C^{(V(open))}), 139.2 (Ar-C^{(V(α -closed))}), 145.5 (C-1^(open)); elemental analyses found C, 57.62; H, 6.56; N, 6.34 Calc. for C₁₁H₁₅NO₄, 0.2 H₂O : C, 57.79; H, 6.70; N, 6.12%; HRMS (ESI⁺) m/z calcd for C₁₁H₁₅NO₄Na [M + Na]⁺ 248.0899, found 248.0892.

N-Benzyl-1-(hydroxyamino)- β -D-threose (7a): According to general procedure A, the reaction of D-threose **7** (2.55 mmol, 306 mg, 1 equiv.) and N-hydroxybenzylamine **a** (2.81 mmol, 345 mg, 1.1 equiv.) and purification of the resulting residue by chromatography on silica gel (dichloromethane / methanol 90:10) afforded **7a** (389 mg, 1.73 mmol) as a yellowish solid, yield 68%; mp 126°C; $[\alpha]_D^{20}$ -36.3 (c 0.40 in MeOH); ν_{max}/cm^{-1} 409, 702, 935, 1031, 1111, 1152, 1455, 1614, 3076, 3288; ¹H NMR (CD₃OD, 500 MHz) δ 3.59 (0.83H, dd, $J = 11.4, 6.0$ Hz, 4- $H_{\alpha}H_{\beta}$ ^(open)), 3.65 (0.87H, dd, $J = 11.4, 5.3$ Hz, 4- $H_{\alpha}H_{\beta}$ ^(open)), 3.85 (0.81, td, $J = 5.6, 3.9$ Hz, 3-H^(open)), 3.87-3.93 (0.34H, m, 4- $H_{\alpha}H_{\beta}$ ^(β -closed) + $CH_{\alpha}H_{\beta}Ph$ ^(β -closed)), 4.04-4.13 (0.50H, m, 3-H^(β -closed) + 4- $H_{\alpha}H_{\beta}$ ^(β -closed) + $CH_{\alpha}H_{\beta}Ph$ ^(β -closed)), 4.30 (0.18H, dd, $J = 3.1, 3.1$ Hz, 2-H^(β -closed)), 4.48 (0.15H, d, $J = 3.2$ Hz, 1-H^(β -closed)), 4.84 (0.94H, dd, $J = 5.9, 3.9$ Hz, 2-H^(open)), 4.96-5.01 (1.66, m, CH₂Ph^(open)), 7.24-7.33 (0.59H, m, Ar-H), 7.35 (0.80H, d, $J = 5.9$ Hz, 1-H^(open)), 7.38-7.44 (2.76H, m, Ar-H), 7.47-7.49 (1.56H, m, Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 60.6 (CH₂Ph^(β -closed)), 63.9 (C-4^(open)), 68.7 (C-2^(open)), 69.7 (CH₂Ph^(open)), 73.7 (C-3^(open)), 74.5 (C-4^(β -closed)), 77.7 (C-3^(β -closed)), 79.7 (C-2^(β -closed)), 101.9 (C-1^(β -closed)), 128.2, 129.2, 129.9, 130.0, 130.3 and 130.5 (6 x Ar-C), 134.3 (Ar-C^{(V(open))}), 139.1 (Ar-C^{(V(β -closed))}), 146.1 (C-1^(open)); elemental analyses found C, 58.46; H, 6.67; N, 6.35 Calc. for C₁₁H₁₅NO₄ : C, 58.66; H, 6.71; N, 6.22%; HRMS (ESI⁺) m/z calcd for C₁₁H₁₅NO₄Na [M + Na]⁺ 248.0899, found 248.0906.

Scope of solvents and activation mode: General procedures for the 1,3 dipolar cycloaddition of methyl acrylate on sugar-nitrone 4a.

Method a - thermal activation: To a solution of sugar-nitrone **4a** (0.50 mmol, 128 mg, 1 equiv.) in the specified solvent (10 mL) at room temperature was added methyl acrylate (2.50 mmol, 215 mg, 5 eq.). The solution was heated to the selected temperature and stirred until total consumption of the starting nitrone (0.5h to 48h, TLC monitoring). The solvent was removed under reduced pressure and the residue was purified using chromatography on silica gel (dichloromethane / methanol 95:5) to afford isoxazolidine **10**, as a mixture of diastereoisomers.

Method b - microwave activation: sugar-nitrone **4a** (0.2 mmol, 51 mg, 1 equiv.), the specified solvent (1.2 mL) and methyl acrylate (1 mmol, 86 mg, 5 equiv.) were placed in a 10 mL vial. The vial was sealed with a Teflon-lined silicon cap and placed into the microwave cavity. Depending on the control mode, the solution was heated in either "fixed power control" mode (fixed power 150W) with the cooling function activated or in "fixed temperature control" mode

(fixed temperature 80 °C) until consumption of the starting nitrone. The solvent was then removed under reduced pressure. The crude was purified using chromatography on silica gel (dichloromethane / methanol 95:5) to afford **10**.

Method c - high pressure activation: sugar-nitrone **4a** (0.17 M, 0.25 mmol, 64 mg, 1 equiv.), solvent (1.4 mL) and methyl acrylate (1.25 mmol, 108 mg, 5 equiv.) were placed in a 1.5 mL Teflon capsule. The capsule was then subjected to 10 kbar using a hand pump system. After 48 hours, the system was returned to atmospheric pressure and the mixture was concentrated under reduced pressure. The residue was purified using chromatography on silica gel (dichloromethane / methanol 95:5) to afford **10**, as a mixture of four isomers.

Additional HPLC chromatography allowed the isolation in a pure state of three isomers **10**, which were fully characterized (see below).

(3S,5S,1'S,2'R,3'R)-3-(1',2',3',4'-tetrahydroxybutyl)-2-benzyl-5-carboxymethylisoxazolidine ((3S,5S)-10): colourless powder; mp 128°C; $[\alpha]_D^{20}$ -53 (c 0.54 in MeOH); ¹H NMR (CD₃OD, 600 MHz) δ 2.62 (1H, ddd, $J = 13.0, 7.6, 7.6$ Hz, 4- $H_{\alpha}H_{\beta}$), 2.85 (1H, ddd, $J = 13.0, 8.6, 2.8$ Hz, 4- $H_{\alpha}H_{\beta}$), 3.51 (1H, dd, $J = 8.2, 2.4$ Hz, 1'-H), 3.54-3.58 (2H, m, 3-H + 4'- $H_{\alpha}H_{\beta}$), 3.62 (1H, dd, $J = 11.3, 4.7$ Hz, 4'- $H_{\alpha}H_{\beta}$), 3.70-3.73 (5H, m, 3'-H + 2'-H + CH₃), 3.89 (1H, d, $J = 13.3$ Hz, $CH_{\alpha}H_{\beta}Ph$), 4.11 (1H, d, $J = 13.3$ Hz, $CH_{\alpha}H_{\beta}Ph$), 4.54 (1H, t, $J = 8.2$ Hz, 5-H), 7.19-7.21 (1H, m, Ar-H), 7.25-7.28 (2H, m, 2 x Ar-H), 7.38-7.39 (2H, m, 2 x Ar-H); ¹³C NMR (CD₃OD, 150 MHz) δ 34.7 (C-4), 52.8 (CH₃), 63.1 (CH₂Ph), 64.1 (C-4'), 68.7 (C-3), 72.0 (C-1'), 72.2 (C-2'), 74.4 (C-3'), 78.0 (C-5), 128.3, 129.1 and 130.6 (5 x Ar-C), 139.0 (Ar-C^(V)), 174.5 (C=O); HRMS (ESI⁺) m/z calcd for C₁₆H₂₄NO₇ [M + H]⁺ 342.1553, found 342.1552.

(3S,5R,1'S,2'R,3'R)-3-(1',2',3',4'-tetrahydroxybutyl)-2-benzyl-5-carboxymethylisoxazolidine ((3S,5R)-10): colourless oil; $[\alpha]_D^{20}$ -40 (c 0.48 in MeOH); ¹H NMR (CD₃OD, 600 MHz) δ 2.58 (1H, ddd, $J = 13.0, 5.8, 3.2$ Hz, 4- $H_{\alpha}H_{\beta}$), 2.78 (1H, ddd, $J = 13.0, 9.8, 7.8$ Hz, 4- $H_{\alpha}H_{\beta}$), 3.49 (1H, ddd, $J = 8.2, 3.2, 3.2$ Hz, 3-H), 3.53-3.57 (2H, m, 1'-H + 4'- $H_{\alpha}H_{\beta}$), 3.61 (1H, dd, $J = 11.3, 4.8$ Hz, 4'- $H_{\alpha}H_{\beta}$), 3.69-3.73 (4H, m, CH₃ + 3'-H), 3.78 (1H, dd, $J = 4.5, 2.3$ Hz, 2'-H), 3.91 (1H, d, $J = 13.7$ Hz, $CH_{\alpha}H_{\beta}Ph$), 3.95 (1H, d, $J = 13.7$ Hz, $CH_{\alpha}H_{\beta}Ph$), 4.78 (1H, dd, $J = 9.8, 5.9$ Hz, 5-H), 7.19-7.22 (1H, m, Ar-H), 7.25-7.28 (2H, m, 2 x Ar-H), 7.35-7.37 (2H, m, 2 x Ar-H); ¹³C NMR (CD₃OD, 150 MHz) δ 35.3 (C-4), 52.8 (CH₃), 61.8 (CH₂Ph), 64.1 (C-4'), 67.9 (C-3), 72.0 (C-2'), 72.9 (C-1'), 74.6 (C-3'), 76.0 (C-5), 128.4, 129.2 and 130.4 (5 x Ar-C), 138.6 (Ar-C^(V)), 173.6 (C=O); HRMS (ESI⁺) m/z calcd for C₁₆H₂₄NO₇ [M + H]⁺ 342.1553, found 342.1554.

(3R,5R,1'S,2'R,3'R)-3-(1',2',3',4'-tetrahydroxybutyl)-2-benzyl-5-carboxymethylisoxazolidine ((3R,5R)-10): colorless oil; $[\alpha]_D^{20}$ +38 (c 1.17 in MeOH); ¹H NMR (CD₃OD, 500 MHz) δ 2.59 (1H, ddd, $J = 12.5, 8.8, 3.4$ Hz, 4- $H_{\alpha}H_{\beta}$), 2.73-2.78 (1H, m, 4- $H_{\alpha}H_{\beta}$), 3.57-3.69 (6H, m, 3-H + 1'-H + 2'-H + 3'-H + 2 x 4'H), 3.79 (3H, s, CH₃), 4.03 (1H, d, $J = 13.2$ Hz, $CH_{\alpha}H_{\beta}Ph$), 4.20 (1H, d, $J = 13.2$ Hz, $CH_{\alpha}H_{\beta}Ph$), 4.64 (1H, dd, $J = 8.8, 7.0$ Hz, 5-H), 7.24-7.28 (1H, m, Ar-H), 7.30-7.34 (2H, m, 2 x Ar-H), 7.42-7.44 (2H, m, 2 x Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 35.6 (C-4), 52.8 (CH₃), 64.0 (CH₂Ph), 64.0 (C-4'), 68.3 (C-3), 72.4 (C-2'), 73.6 (C-1'), 74.5 (C-3'), 78.2 (C-5), 128.4, 129.3 and 130.7 (5 x Ar-C), 138.9 (Ar-C^(V)), 174.5 (C=O); HRMS (ESI⁺) m/z calcd for C₁₆H₂₄NO₇ [M + H]⁺ 342.1553, found 342.1556.

General procedures for the 1,3 dipolar cycloaddition of alkenes with sugar-nitrones: A solution of sugar-nitron (0.2 mmol), DMF (1.2 mL) and alkene (1 mmol, 5 equiv.) were placed in a 10 mL vial. The vial was sealed with a Teflon-lined silicon cap and placed into the microwave cavity. The solution was then heated using a “fixed power control” mode (fixed power 150W) with the cooling function activated, for 20 min. The solvent was removed under reduced pressure. The crude was purified using chromatography on silica gel to afford the corresponding isoxazolidine as an inseparable mixture of diastereoisomers (ratio given in Table 3).

(1'S,2'R,3'R)-3-(1',2',3',4'-tetrahydroxybutyl)-2-((S)-2a-hydroxy-1a-phenylethyl)-5-carboxymethylisoxazolidine (10'): According to general procedure, the reaction of **4d** (0.34 mmol, 97 mg, 1 equiv.) and methyl acrylate (1.7 mmol, 146 mg, 5 equiv.) and purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 92.5:7.5) afforded **10'** (85 mg, 0.23 mmol) as a mixture of 4 diastereoisomers; colourless oil; yield 67%; ¹H NMR (CD₃OD, 500 MHz) δ 2.19 (0.07H, ddd, *J* = 12.9, 5.5, 4.2 Hz, 4-H_aH_b^(3R,5S)), 2.28-2.34 (0.09H, m, 4-H_aH_b^(3R,5S)), 2.43-2.46 (0.35H, m, 2 x 4-H^(3R,5R)), 2.53 (0.39H, ddd, *J* = 12.8, 9.1, 6.3 Hz, 4-H_aH_b^(3S,5S)), 2.61 (0.30H, ddd, *J* = 13.3, 5.3, 1.7 Hz, 4-H_aH_b^(3S,5R)), 2.70 (0.31H, ddd, *J* = 13.2, 10.4, 7.6 Hz, 4-H_aH_b^(3S,5R)), 2.85-2.92 (0.40H, m, 4-H_aH_b^(3S,5S)), 3.32-4.26 (12H, m, CH₃ + 2 x 4'-H + 3'-H + 2'-H + 1'-H + 3-H + 1a-H + 2 x 2a-H), 4.31 (0.10H, dd, *J* = 9.35, 5.55 Hz, 5-H^(3R,5S)), 4.49 (0.22H, dd, *J* = 8.35, 8.35 Hz, 5-H^(3R,5R)), 4.67 (0.41H, dd, *J* = 8.70, 8.70 Hz, 5-H^(3S,5S)), 4.90 (0.32H, m, 5-H^(3S,5R)), 7.25-7.46 (5H, m, 5 x Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 33.4 (C-4^(3S,5S)), 34.1 (C-4^(3S,5R)), 35.1 (C-4^(3R,5R)), 36.1 (C-4^(3R,5S)), 52.6 (CH₃^(3R,5R)), 52.8 (CH₃^(3R,5S)), 52.8 (CH₃^(3S,5R)), 53.0 (CH₃^(3S,5S)), 63.9 (C-4^(3R,5S)), 64.0 (C-4^(3R,5R)), 64.0 (C-4^(3S,5S)), 64.1 (C-4^(3S,5R)), 65.0 (C-2a^(3R,5S)), 65.7 (C-3^(3R,5S)), 65.7 (C-3^(3R,5R)), 65.9 (C-2a^(3S,5R)), 65.9 (C-2a^(3S,5S)), 65.9 (C-3^(3R,5R)), 66.2 (C-2a^(3S,5S)), 66.3 (C-3^(3S,5S)), 71.2 (C-2^(3S,5R)), 71.2 (C-2^(3S,5S)), 71.6 (CH^(3R,5S)), 71.7 (C-1a^(3S,5R)), 71.8 (C-1^(3S,5S)), 71.9 (CH^(3R,5R)), 72.2 (CH^(3R,5R)), 72.6 (C-1^(3S,5R)), 72.7 (CH^(3R,5R)), 73.0 (C-1a^(3S,5S)), 73.5 (CH^(3R,5R)), 74.0 (CH^(3R,5S)), 74.6 (CH^(3R,5R)), 74.7 (CH^(3R,5S)), 75.0 (C-3^(3S,5S)), 75.1 (C-3^(3S,5R)), 76.6 (C-5^(3S,5R)), 76.7 (C-5^(3R,5S)), 77.8 (C-5^(3R,5R)), 78.8 (C-5^(3S,5S)), 128.4, 129.0, 129.1, 129.2, 129.3, 129.7, 129.7, 130.0, 130.1, 130.2 and 130.3 (12 x Ar-C), 139.0, 140.0, 140.3 and 140.3 (4 x Ar-C^(3R,5R)), 173.2, 173.4, 174.0 and 174.9 (4 x C=O); HRMS (ESI⁺) *m/z* calcd for C₁₇H₂₆NO₈ [M + H]⁺ 372.1658, found 372.1662.

(1'S,2'R,3'R)-3-(1',2',3',4'-tetrahydroxybutyl)-2-((R)-2a-hydroxy-1a-phenylethyl)-5-carboxymethylisoxazolidine (10''): According to general procedure, the reaction of **4e** (0.347 mmol, 99 mg, 1 equiv.) and methyl acrylate (1.74 mmol, 149 mg, 5 equiv.) and purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 92.5:7.5) afforded **10''** (63 mg, 0.170 mmol) as a mixture of 4 diastereoisomers; sticky yellowish solid; yield 49%; ¹H NMR (CD₃OD, 500 MHz) δ 2.30-2.42 (0.72H, m, 4-H), 2.53 (0.39H, ddd, *J* = 13.0, 5.3, 3.3 Hz, 4-H_aH_b^(3S,5S)), 2.60-2.63 (0.45H, m, 4-H), 2.77 (0.31H, ddd, *J* = 12.9, 8.2, 2.2 Hz, 4-H), 3.44-3.83 (8.79H, m, CH₃ + 4'-H + 3'-H + 2'-H + 1'-H + 3-H), 3.91-4.13 (3.24H, m, 2a-H + 1a-H + CH), 4.38 (0.40H, dd, *J* = 9.8, 5.3 Hz, 5-H^(3S,5S)), 4.44 (0.25H, dd, *J* = 8.5, 8.5 Hz, 5-H^(3R,5R)), 4.76 (0.27H, dd, *J* = 8.8, 8.8 Hz, 5-H^(3S,5R)), 4.92 (0.17H, dd, *J* = 10.5, 5.1 Hz, 5-H^(3R,5S)), 7.24-7.44 (5H, m, 5 x Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 34.0 (C-4^(3R,5S)), 34.0 (C-4^(3S,5R)), 34.1 (C-4^(3R,5R)), 35.5 (C-4^(3S,5S)), 52.6 (CH₃^(3S,5R)), 52.7 (CH₃^(3S,5R)), 52.9 (CH₃^(3R,5S)), 53.0 (CH₃^(3R,5R)), 63.9 (C-4^(3R,5S)), 64.0 (C-4^(3R,5R)), 64.1 (C-4^(3S,5R)), 64.2 (C-4^(3S,5S)), 65.2 and 65.3 (2 x CH), 65.3 (C-2a^(3S,5S)),

65.7 (C-2a^(3R,5S)), 65.9 (C-2a^(3S,5R)), 66.0 (C-2a^(3R,5R)), 66.3 and 66.7 (2 x C-3), 71.1 (C-1a), 71.3, 71.6 and 71.8 (3 x CH), 71.9 (C-1a), 71.9 (C-1a), 72.4 (C-1a), 72.8 and 72.9 (2 x CH), 74.5 (C-3^(3R,5R)), 74.7 (C-3^(3R,5S)), 74.7 (C-3^(3S,5S)), 74.8 (C-3^(3S,5R)), 76.5 (C-5^(3S,5S)), 76.8 (C-5^(3R,5S)), 77.3 (C-5^(3R,5R)), 79.3 (C-5^(3S,5R)), 128.4, 128.9, 129.0, 129.1, 129.2, 129.3, 129.7, 129.7, 130.0, 130.1, 130.2 and 130.3 (12 x Ar-C), 139.0, 140.0, 140.3 and 140.3 (4 x Ar-C^(3R,5R)), 173.2, 173.4, 174.0 and 174.9 (4 x C=O); HRMS (ESI⁺) *m/z* calcd for C₁₇H₂₆NO₈ [M + H]⁺ 372.1658, found 372.1659.

(1'S,2'R,3'R)-3-(1',2',3',4'-tetrahydroxybutyl)-2-methyl-5-carboxymethylisoxazolidine (14): According to general procedure, the reaction of **4b** (0.251 mmol, 45 mg, 1 equiv.) and methyl acrylate (1 mmol, 108 mg, 5 equiv.) and purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 92.5:7.5) afforded **14** (51 mg, 0.192 mmol) as a mixture of 4 diastereoisomers; colourless oil; yield 77%; ¹H NMR (CD₃OD, 500 MHz) δ 2.29-2.34 (0.11H, m, 4-H_aH_b^(3R,5S)), 2.51-2.71 (1.08H, m, 4-H), 2.74 (0.73H, s, N-CH₃^(3S,5R)), 2.77 (1.22H, s, N-CH₃^(3S,5S)), 2.81-2.90 (1.73H, m, 4-H + N-CH₃^(3R,5R) + N-CH₃^(3R,5S)), 3.16-3.27 (0.35H, m, 3-H), 3.34-3.38 (0.83H, m, 3-H), 3.58-3.8 (7.92H, m, 1'-H + 2'-H + 3'-H + 4'-H + CH₃), 4.57-4.63 (0.70H, m, 5-H^(3S,5S) + 5-H^(3S,5R)), 4.77 (0.12H, dd, *J* = 9.2, 6.1 Hz, 5-H^(3R,5S)), 4.81 (0.23H, dd, *J* = 9.7, 5.8 Hz, 5-H^(3R,5R)); ¹³C NMR (CD₃OD, 125 MHz) δ 34.4 (C-4^(3S,5S)), 34.9 (C-4^(3S,5R)), 36.0 (C-4^(3R,5S)), 36.1 (C-4^(3R,5R)), 45.0, 46.0, 46.3 and 47.2 (4 x N-CH₃), 52.7, 52.8 and 52.8 (3 x CH₃), 63.9, 63.9 and 64.1 (C-4'), 70.1, 70.3 and 70.9 (C-3), 71.8, 72.2, 72.3, 72.3, 72.5, 73.8, 74.2 (C-1' + C-2'), 74.3, 74.4, 74.6 and 74.7 (4 x C-3'), 75.5 (C-5^(3R,5S)), 75.8 (C-5^(3R,5R)), 77.3 (C-5^(3S,5R)), 77.6 (C-5^(3S,5S)), 173.6, 173.8, 174.2 and 174.4 (4 x C=O); HRMS (ESI⁺) *m/z* calcd for C₁₀H₂₀NO₇ [M + H]⁺ 266.1240, found 266.1239.

(1'S,2'R,3'R)-3-(1',2',3',4'-tetrahydroxybutyl)-2-octyl-5-carboxymethylisoxazolidine (15): According to general procedure, the reaction of **4c** (0.188 mmol, 52 mg, 1 equiv.) and methyl acrylate (0.939 mmol, 81 mg, 5 equiv.) and the purification of the resulting residue by chromatography on silica gel (dichloromethane / methanol 94:6) afforded **15** (56 mg, 0.154 mmol) as a mixture of 4 diastereoisomers; colourless sticky solid; yield 82%; ¹H NMR (CD₃OD, 500 MHz) δ 0.94 (3H, t, *J* = 6.4 Hz, CH₃^(octyl)), 1.30-1.44 (10H, m, 5 x CH₂^(octyl)), 1.60-1.74 (2H, m, CH₂^(octyl)), 2.27-2.32 (0.10H, m, 4-H), 2.53-3.01 (4H, m, 4-H + N-CH₂), 3.40-3.44 (0.36H, m, CH), 3.49-3.82 (4.15H, m, CH + 4'-H), 3.75-3.81 (4.80H, m, CH + CH₃), 4.57-4.65 (0.80H, m, 5-H), 4.72-4.77 (0.36H, m, 5-H); ¹³C NMR (CD₃OD, 125 MHz) δ 14.4 (CH₃^(octyl)), 23.7, 28.3, 28.9, 30.4, 30.6 and 33.0 (CH₂^(octyl)), 34.3 (C-4^(3S,5S)), 35.1 (C-4^(3S,5R)), 35.2 (C-4^(3R,5R)), 35.4 (C-4^(3R,5S)), 52.8 (CH₃), 58.2 and 59.5 (N-CH₂^(octyl)), 63.9, 63.9 and 64.2 (C-4'), 68.5, 69.0, 69.2 and 69.2 (C-3), 71.9, 72.0, 72.1, 72.2, 72.3, 73.0, 73.3, 74.4, 74.6, 74.6 and 74.7 (CH), 75.8, 77.0 and 77.8 (C-5), 173.2, 173.6, 174.5 and 174.6 (C=O); HRMS (ESI⁺) *m/z* calcd for C₁₇H₃₄NO₇ [M + H]⁺ 364.2335, found 364.2334.

(1'S,2'R,3'S)-3-(1',2',3',4'-tetrahydroxybutyl)-2-benzyl-5-carboxymethylisoxazolidine (16): According to general procedure, the reaction of **5a** (0.275 mmol, 70 mg, 1 equiv.) and methyl acrylate (1.37 mmol, 118 mg, 5 equiv.) and purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 95:5) afforded **16** (85 mg, 0.249 mmol) as a mixture of 4 diastereoisomers; yellowish solid; yield 90%; ¹H NMR (CD₃OD, 500 MHz) δ 2.31 (0.09H, ddd, *J* = 12.9, 6.2, 4.8 Hz, 4-H_aH_b^(3R,5S)), 2.53-2.88 (1.46H, m, 4-H), 2.91 (0.42H, ddd, *J* = 12.8, 8.6, 2.8 Hz, 4-H_aH_b^(3S,5S)), 3.42-3.83 (8.94H, m, 3-H + 1'-H + 2'-H + 3'-H + 4'-H +

CH₃), 3.92 (0.45H, d, *J* = 13.4 Hz, CH_oH_bPh^(3S,5S)), 3.97 (0.27H, d, *J* = 13.8 Hz, CH_oH_bPh^(3S,5R)), 4.02 (0.26H, d, *J* = 13.8 Hz, CH_oH_bPh^(3S,5R)), 4.05 (0.12H, d, *J* = 13.7 Hz, CH_oH_bPh^(3R,5S)), 4.08 (0.21H, d, *J* = 13.6 Hz, CH_oH_bPh^(3R,5R)), 4.16 (0.12H, d, *J* = 13.7 Hz, CH_oH_bPh^(3R,5S)), 4.17 (0.39H, d, *J* = 13.4 Hz, CH_oH_bPh^(3S,5S)), 4.21 (0.23H, d, *J* = 13.3 Hz, CH_oH_bPh^(3R,5R)), 4.57-4.65 (0.65H, m, 5-H^(3S,5S) + 5-H^(3S,5R)), 4.76-4.83 (0.45H, m, 5-H^(3R,5R) + 5-H^(3R,5S)), 7.24-7.34 (m, 3H, 3 x Ar-H), 7.39-7.45 (m, 2H, 2 x Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 35.0 (C-4^(3S,5S)), 35.6 (C-4^(3R,5R)), 35.7 (C-4^(3S,5R)), 35.7 (C-4^(3R,5S)), 52.7, 52.7, 52.8 and 52.8 (4 x CH₃), 62.0 (CH₂Ph^(3S,5R)), 63.3 (CH₂Ph^(3S,5S)), 64.9, 65.0 and 65.0 (4 x C-4'), 68.0 (C-3^(3S,5R)), 68.3 (C-3^(3R,5S)), 68.6 (C-3^(3S,5S)), 68.7 (C-3^(3R,5R)), 70.3 (C-1'^(3S,5S)), 71.2 (C-1'^(3S,5R)), 71.3 (C-1'^(3R,5R)), 71.8 (C-1'^(3R,5S)), 72.2, 72.2, 72.5, 72.6, 72.7, 72.8, 73.3 and 73.5 (4 x C-2' and 4 x C-3'), 76.1 (C-5^(3R,5R) and C-5^(3R,5S)), 78.1 (C-5^(3S,5S)), 78.1 (C-5^(3S,5R)), 128.3, 128.3, 128.4, 129.1, 129.2, 129.2, 130.4, 130.5, 130.6 and 130.6 (12 x Ar-C), 138.6, 138.7, 138.9 and 139.1 (4 x Ar-C^{IV}), 173.5, 174.4 and 174.6 (4 x C=O); HRMS (ESI⁺) *m/z* calcd for C₁₆H₂₄NO₇ [M + H]⁺ 342.1553, found 342.1557.

(1'S,2'R,3'S)-3-(1',2',3',4'-tetrahydroxybutyl)-2-methyl-5-carboxymethylisoxazolidine (17): According to general procedure, the reaction of **5b** (0.285 mmol, 51 mg, 1 equiv.) and methyl acrylate (1.42 mmol, 123 mg, 5 equiv.) and purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 92.5:7.5) afforded **17** (42 mg, 0.158 mmol) as a mixture of 4 diastereoisomers; yellowish sticky solid; yield 55%; ¹H NMR (CD₃OD, 500 MHz) δ 2.23-2.28 (0.11H, m, 4-H), 2.45-2.51 (0.21H, m, 4-H), 2.60-2.66 (0.89H, m, 4-H), 2.72 (0.66H, s, N-CH₃^(3S,5R)), 2.75 (1.22H, s, N-CH₃^(3S,5S)), 2.80-2.90 (1.74H, m, 4-H + N-CH₃^(3R,5R) + N-CH₃^(3R,5S)), 3.06-3.21 (0.39H, m, 3-H), 3.22-3.31 (0.59H, m, 3-H), 3.43-3.49 (0.37H, m), 3.62-3.82 (7.74H, m, 1'-H + 2'-H + 3'-H + 4'-H + CH₃), 4.57 (0.66H, dd, *J* = 8.1, 8.1 Hz, 5-H), 4.74 (0.14H, dd, *J* = 8.8, 6.4 Hz, 5-H), 4.78 (0.28H, dd, *J* = 9.4, 5.9 Hz, 5-H); ¹³C NMR (CD₃OD, 125 MHz) δ 34.8 (C-4^(3S,5S)), 35.3 (C-4^(3S,5R)), 36.2 (C-4^(3R,5R)), 36.5 (C-4^(3R,5S)), 45.2, 46.3 and 47.2 (N-CH₃), 52.7, 52.7 and 52.8 (CH₃), 64.9, 64.9, 65.0 and 65.0 (4 x C-4'), 69.9, 70.5, 70.6, 71.0, 71.7, 72.3, 72.4, 72.6, 72.6, 72.7, 73.2 and 73.3 (C-3 + C-5' + C-6' + C-7'), 75.4 (C-5^(3R,5S)), 75.8 (C-5^(3R,5R)), 77.2 (C-5^(3S,5R)), 77.6 (C-5^(3S,5S)), 173.8, 174.1, 174.2 and 174.5 (4 x C=O); HRMS (ESI⁺) *m/z* calcd for C₁₀H₂₀NO₇ [M + H]⁺ 266.1240, found 266.1240.

(1'S,2'R,3'S)-3-(1',2',3',4'-tetrahydroxybutyl)-2-octyl-5-carboxymethylisoxazolidine (18): According to general procedure, the reaction of **5c** (0.278 mmol, 77 mg, 1 equiv.) and methyl acrylate (1.39 mmol, 120 mg, 5 equiv.) and purification of the resulting residue by chromatography on silica gel (dichloromethane / methanol 94:6) afforded **18** (96 mg, 0.264 mmol) as a mixture of 4 diastereoisomers; colourless solid; yield 95%; ¹H NMR (CD₃OD, 500 MHz) δ 0.92 (3H, t, *J* = 6.5 Hz, CH₃^(octyl)), 1.28-1.41 (10H, m, 5 x CH₂^(octyl)), 1.56-1.68 (2H, m, CH₂^(octyl)), 2.25 (0.10H, ddd, *J* = 12.8, 6.4, 4.7 Hz, 4-H_oH_b^(3R,5S)), 2.50 (0.12H, ddd, *J* = 12.7, 9.0, 3.5 Hz, 4-H_oH_b^(3R,5R)), 2.57-3.01 (3.61H, m, 4-H + N-CH₂), 3.34-3.37 (0.35H, m, 3-H), 3.41-3.46 (0.63H, m, 3-H), 3.49-3.82 (8H, m, 1'-H + 2'-H + 3'-H + 4'-H + CH₃), 4.55-4.63 (0.86H, m, 5-H), 4.72-4.75 (0.42H, m, 5-H); ¹³C NMR (CD₃OD, 125 MHz) δ 14.4 (CH₃^(octyl)), 23.7, 28.3, 28.3, 28.8, 28.9, 30.4, 30.6 and 33.0 (CH₂^(octyl)), 34.6 (C-4^(3S,5S)), 35.3 (C-4^(3R,5R)), 35.5 (C-4^(3S,5R)), 35.6 (C-4^(3R,5S)), 52.7 and 52.8 (CH₃), 57.6, 58.5, 59.1 and 59.7 (N-CH₂), 64.9, 64.9, 65.0 et 65.0 (C-4'), 68.6 (C-3^(3S,5R)), 68.9 (C-3^(3S,5S)), 69.3 (C-3^(3R,5R)), 69.4 (C-3^(3R,5S)), 70.1 and 71.1 (C-1'), 72.2, 72.2, 72.5, 72.6, 72.7, 72.7, 73.3 and 73.5 (C-2' + C-3'), 75.8, 77.7 and 77.8 (C-5), 173.2, 173.6 and 174.7 (C=O); HRMS (ESI⁺) *m/z* calcd for C₁₇H₃₄NO₇ [M + H]⁺ 364.2335, found 364.2339.

(1'S,2'R)-3-(1',2',3'-trihydroxypropyl)-2-benzyl-5-carboxymethylisoxazolidine (19): According to general procedure, the reaction of **6a** (0.284 mmol, 64 mg, 1 equiv.) and methyl acrylate (1.41 mmol, 121 mg, 5 equiv.) and purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 95:5) afforded **19** (53 mg, 0.17 mmol) as a mixture of 4 diastereoisomers; yellow oil; yield 60%; ¹H NMR (CD₃OD, 500 MHz) δ 2.51 (0.07H, ddd, *J* = 12.7, 6.4, 5.1 Hz, 4-H_oH_b^(3R,5S)), 2.63-2.89 (2H, m, 4-H), 3.41-3.45 (0.25H, m, 3-H^(3S,5R)), 3.47-3.71 (4.64H, m, 3'-H + 2'-CH + 1'-H + 3-H), 3.73-3.80 (3H, m, CH₃), 3.94-4.21 (2H, m, CH₂Ph), 4.60-4.65 (0.66H, m, 5-H^(3S,5S) + 5-H^(3R,5R)), 4.78-4.88 (0.38H, m, 5-H^(3S,5R) + 5-H^(3R,5S)), 7.25-7.36 (3H, m, 3 x Ar-H), 7.40-7.45 (2H, m, 2 x Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 34.0 (C-4^(3S,5S)), 34.2 (C-4^(3S,5R)), 36.4 (C-4^(3R,5S)), 36.5 (C-4^(3R,5R)), 52.7, 52.7, 52.8 and 52.8 (4 x CH₃), 61.6, 62.7, 63.1 and 64.0 (4 x CH₂Ph), 64.3, 64.6 and 64.6 (4 x C-3'), 67.4 (C-3^(3R,5S)), 67.6 (C-3^(3R,5R)), 68.4 (C-3^(3S,5R)), 69.0 (C-3^(3S,5S)), 71.3 (C-1'^(3S,5S)), 71.8 (C-1'^(3S,5R)), 73.7 (C-1'^(3R,5S)), 73.7 (C-1'^(3R,5R)), 74.3 (C-2'^(3R,5S)), 74.4 (C-2'^(3R,5R)), 75.1 (C-2'^(3S,5S)), 75.2 (C-2'^(3S,5R)), 76.1 (C-5^(3S,5R)), 76.1 (C-5^(3R,5S)), 78.1 (C-5^(3S,5S)), 78.4 (C-5^(3R,5R)), 128.3, 128.5, 129.2, 129.2, 129.3, 129.3, 130.4, 130.4 and 130.6 (Ar-C), 138.0, 138.4, 138.6 and 139.0 (4 x Ar-C^{IV}), 173.2, 173.5, 174.3 and 174.4 (4 x C=O); HRMS (ESI⁺) *m/z* calcd for C₁₅H₂₂NO₆ [M + H]⁺ 312.1447, found 312.1445.

(1'R,2'R)-3-(1',2',3'-trihydroxypropyl)-2-benzyl-5-carboxymethylisoxazolidine (20): According to general procedure, the reaction of **7a** (0.318 mmol, 72 mg, 1 equiv.) and methyl acrylate (1.59 mmol, 137 mg, 5 equiv.) and purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 95:5) afforded **20** (74 mg, 0.238 mmol) as a mixture of 4 diastereoisomers; yellowish oil; yield 75%; ¹H NMR (CD₃OD, 500 MHz) δ 2.36 (0.1H, ddd, *J* = 12.9, 5.9, 4.8 Hz, 4-H_oH_b^(3S,5R)), 2.57-2.94 (1.9H, m, 4-H), 3.49-3.67 (4.20H, m, 3'-H + 2'-H + 1'-H + 3-H), 3.75-3.91 (3H, m, CH₃), 3.84-3.87 (0.52H, m, 2'-H^(3S,5R)), 3.90-3.92 (0.26H, m, 2'-H^(3R,5S)), 3.94-4.24 (2H, m, CH₂Ph), 4.59-4.63 (0.47H, m, 5-H^(3R,5R)), 4.64-4.67 (0.19H, m, 5-H^(3S,5S)), 4.80-4.85 (0.40H, m, 5-H^(3R,5S) + 5-H^(3S,5R)), 7.27-7.37 (3H, m, 3 x Ar-H), 7.44-7.47 (2H, m, 2 x Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 34.7 (C-4^(3R,5R)), 35.3 (C-4^(3R,5S)), 35.5 (C-4^(3S,5S)), 35.5 (C-4^(3S,5R)), 52.7 and 52.8 (CH₃), 61.9, 62.5, 63.2 and 63.9 (CH₂Ph), 64.3 (C-3^(3S,5S)), 64.5 (C-3^(3S,5R)), 64.7 (C-3^(3R,5R)), 64.9 (C-3^(3R,5S)), 67.7 (C-3), 68.1 (C-3^(3S,5S)), 68.3 (C-3), 68.3 (C-3^(3R,5R)), 71.1, 72.0, 72.3 and 72.7 (C-1'), 72.9 and 73.2 (C-2'), 76.0 (C-5^(3R,5S)), 76.0 (C-5^(3S,5R)), 78.0 (C-5^(3R,5R)), 78.1 (C-5^(3S,5S)), 128.3, 128.3, 128.4, 129.1, 129.2, 129.3, 130.3, 130.4, 130.5 and 130.6 (Ar-C), 138.5, 138.6, 138.8 and 139.0 (4 x Ar-C^{IV}), 173.2, 173.5, 174.4 and 174.5 (4 x C=O); HRMS (ESI⁺) *m/z* calcd for C₁₅H₂₂NO₆ [M + H]⁺ 312.1447, found 312.1451.

(1'S,2'R,3'R)-3-(1',2',3',4'-tetrahydroxybutyl)-2-benzyl-5-carboxy(tert-butyl)isoxazolidine (21): According to general procedure, the reaction of **4a** (0.212 mmol, 54 mg, 1 equiv.) and *tert*-butylacrylate (1.06 mmol, 136 mg, 5 equiv.) and purification of the resulting residue by chromatography on silica gel (dichloromethane / methanol 95:5) afforded **21** (72 mg, 0.188 mmol) as a mixture of 4 diastereoisomers; sticky yellowish solid; yield 89%; ¹H NMR (CD₃OD, 500 MHz) δ 1.49-1.54 (9H, m, CH₃), 2.30 (0.08H, ddd, *J* = 13.0, 5.8, 4.2 Hz, 4-H_oH_b), 2.54-2.65 (0.87H, m), 2.68-2.74 (0.20H, m), 2.78-2.89 (0.79H, m), 3.51-3.71 (4.47H, m), 3.73-3.81 (1.42H, m), 3.85-3.88 (0.29H, m), 3.93-3.98 (0.95H, m), 4.01-4.08 (0.43H, m), 4.16-4.21 (0.43H, m), 4.22-4.25 (0.20H, m), 4.46-4.49 (0.42H, m), 4.50-4.54 (0.20H, m), 4.66-4.70 (0.34H, m),

7.25-7.35 (3H, m, 3 x Ar-H), 7.42-7.47 (2H, m, 2 x Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 28.2 and 28.2 (CH₃), 34.7 (C-4^(3S,5S)), 35.4 (C-4^(3S,5R)), 35.5 (C-4^(3R,5S)), 35.6 (C-4^(3R,5R)), 61.9, 63.2, 63.9, 64.0, 64.1, 64.1, 67.8, 68.1, 68.3, 68.6, 71.9, 71.9, 72.0, 72.2, 72.3, 73.0, 73.5, 73.8, 74.4, 74.4, 74.6, 74.7, 76.6, 78.8, 79.0, 83.0, 83.0, 83.2 and 83.2 (C), 128.2, 128.3, 128.3, 129.1, 129.2, 129.2, 130.3, 130.4, 130.6 and 130.6 (Ar-C), 138.6, 138.6, 138.9 and 139.0 (4 x Ar-C^{IV}), 172.1, 172.4, 173.1 and 173.2 (4 x C=O); HRMS (ESI⁺) m/z calcd for C₁₉H₃₀NO₇ [M + H]⁺ 384.2022, found 384.2016.

(1'S,2'R,3'R)-3-(1',2',3',4'-tetrahydroxybutyl)-2-benzyl-5-

carboxybenzylisoxazolidine (22): According to general procedure, the reaction of **4a** (0.290 mmol, 74 mg, 1 equiv.) and benzylacrylate (1.45 mmol, 235 mg, 5 equiv.) and purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 95:5) afforded **22** (113 mg, 0.271 mmol) as a mixture of 4 diastereoisomers; colourless oil; yield 93%; ¹H NMR (CD₃OD, 500 MHz) δ 2.36 (0.08H, ddd, *J* = 13.0, 5.6, 4.6 Hz, 4-*H_oH_b*^(3R,5S)), 2.57-2.86 (1.39H, m, 4-H), 2.91 (0.45H, ddd, *J* = 12.9, 8.6, 2.7 Hz, 4-*H_oH_b*^(3S,5S)), 3.48-3.74 (4.59H, m, 3-H + 1'-H + 2'-H + 3'-H + 4'-H), 3.76-3.80 (1.23H, m, 1'-H + 2'-H + 3'-H), 3.83-3.84 (0.27H, m, 1'-H + 2'-H + 3'-H), 3.91 (0.45H, d, *J* = 13.4 Hz, *CH_oH_bPh*^(3S,5S)), 3.98 (0.21H, d, *J* = 13.2 Hz, *CH_oH_bPh*^(3R,5R)), 3.99 (0.46H, s, *CH₂Ph*^(3S,5R)), 4.03 (0.12H, d, *J* = 13.6 Hz, *CH_oH_bPh*^(3R,5S)), 4.11 (0.12H, d, *J* = 13.7 Hz, *CH₂H_bPh*^(3R,5S)), 4.13 (0.42H, d, *J* = 13.4 Hz, *CH₂H_bPh*^(3S,5R)), 4.17 (0.21H, d, *J* = 13.2 Hz, *CH₂H_bPh*^(3R,5R)), 4.57-4.63 (0.51H, m, 5-H^(3S,5S)), 4.68 (0.19H, dd, *J* = 8.6, 7.1 Hz, 5-H^(3R,5R)), 4.81 (0.12H, dd, *J* = 9.5, 5.8 Hz, 5-H^(3R,5S)), 4.84 (0.23H, dd, *J* = 9.7, 5.8 Hz, 5-H^(3S,5R)), 5.15-5.25 (2H, m, O-CH₂Ph), 7.22-7.44 (10H, m, 10 x Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 34.7, 35.2 and 35.5 (4 x C-4), 61.9, 62.6, 63.2 and 63.9 (CH₂Ph), 64.0 and 64.1 (C-4'), 67.9 (O-CH₂Ph), 68.0 (C-3^(3R,5R)), 68.1 (O-CH₂Ph), 68.2 (C-3^(3R,5S)), 68.3 (C-3^(3S,5R)), 68.6 (C-3^(3S,5S)), 72.0, 72.0, 72.2, 72.3, 73.0, 73.5 and 73.9 (C-1' + C-2'), 74.4, 74.6 and 74.6 (C-3'), 76.1 (C-5^(3S,5R) + C-5^(3S,5S)), 78.2 (C-5^(3S,5S)), 78.3 (C-5^(3R,5R)), 128.2, 128.3, 129.1, 129.2, 129.3, 129.3, 129.4, 129.4, 129.6, 129.6, 130.3, 130.4, 130.5 and 130.6 (Ar-C), 137.0, 137.0, 138.5, 138.6, 138.7 and 138.9 (Ar-C^V), 172.6, 172.9 and 173.7 (C=O); HRMS (ESI⁺) m/z calcd for C₂₂H₂₈NO₇ [M + H]⁺ 418.1866, found 418.1865.

(1'S,2'R,3'R)-3-(1',2',3',4'-tetrahydroxybutyl)-2-benzyl-5-

carboxydodecylisoxazolidine (23): According to general procedure, the reaction of **4a** (0.314 mmol, 80 mg, 1 equiv.) and dodecylacrylate (1.57 mmol, 418 mg, 5 equiv.) and purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 95:5) afforded **23** (143 mg, 0.289 mmol) as a mixture of 4 diastereoisomers; sticky yellowish solid; yield 92%; ¹H NMR (CD₃OD, 500 MHz) δ 0.92 (3H, t, *J* = 7 Hz, CH₃), 1.31-1.40 (18H, m, 9 x CH₂^(dodecyl)), 1.64-1.71 (2H, m, CH₂^(dodecyl)), 2.35 (0.1H, ddd, *J* = 13.0, 6.0, 4.4 Hz, 4-*H_oH_b*^(3R,5S)), 2.55-2.85 (1.41H, m, 4-H), 2.91 (0.46H, ddd, *J* = 13.0, 8.5, 2.8 Hz, 4-*H_oH_b*^(3S,5S)), 3.49-3.86 (6H, m, 3-H + 1'-H + 2'-H + 3'-H + 4'-H), 3.95 (0.42H, d, *J* = 13.4 Hz, *CH_oH_bPh*^(3S,5S)), 3.98 (0.26H, d, *J* = 13.6 Hz, *CH_oH_bPh*^(3S,5R)), 4.02 (0.25H, d, *J* = 13.6 Hz, *CH₂H_bPh*^(3S,5R)), 4.04 (0.20H, d, *J* = 13.2 Hz, *CH_oH_bPh*^(3R,5R)), 4.05 (0.14H, d, *J* = 13.6 Hz, *CH_oH_bPh*^(3R,5S)), 4.12 (0.14H, d, *J* = 13.6 Hz, *CH₂H_bPh*^(3R,5S)), 4.14-4.23 (2.60H, m, *CH₂H_bPh*^(3S,5S) + *CH₂H_bPh*^(3R,5R) + O-CH₂^(dodecyl)), 4.58 (0.45H, dd, *J* = 8.2, 8.2 Hz, 5-H^(3S,5S)), 4.63 (0.20H, dd, *J* = 8.8, 7.0 Hz, 5-H^(3R,5R)), 4.79 (0.12H, dd, *J* = 9.4, 5.9 Hz, 5-H^(3R,5S)), 4.81 (0.23H, dd, *J* = 9.7, 5.8 Hz, 5-H^(3S,5R)), 7.24-7.34 (3H, m, 3 x Ar-H), 7.39-7.46 (2H, m, 2 x Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 14.5 (CH₃), 23.7, 26.9, 27.0, 27.0, 29.6, 29.7, 30.3, 30.4, 30.5, 30.6, 30.7, 30.7, 30.7, 30.7, 30.8 and 33.1 (CH₂^(dodecyl)), 34.7 (C-4^(3S,5S)),

35.4 and 35.5 (2 x C-4), 61.9 (CH₂Ph^(3S,5R)), 62.6 (CH₂Ph^(3R,5S)), 63.2 (CH₂Ph^(3S,5S)), 64.0 (C-4'), 64.0 (CH₂Ph^(3R,5R)), 64.1 and 64.2 (2 x C-4'), 66.5 and 66.5 (O-CH₂^(dodecyl)), 68.0 (C-3^(3S,5R)), 68.2 (C-3^(3R,5S)), 68.3 (C-3^(3R,5R)), 68.7 (C-3^(3S,5S)), 72.0, 72.1, 72.2, 72.4, 73.0, 73.5 and 73.9 (C-1' + C-2'), 74.5, 74.7 and 74.7 (C-3'), 76.1 (C-5^(3S,5R)), 76.2 (C-5^(3R,5S)), 78.3 (C-5^(3S,5S)), 78.4 (C-5^(3R,5R)), 128.3, 128.3, 128.4, 128.4, 129.1, 129.2, 129.2, 129.3, 130.4, 130.4, 130.5, 130.6 and 130.7 (Ar-C), 138.6, 138.7, 138.8 and 139.0 (4 x Ar-C^V), 172.9, 173.2, 174.0 and 174.0 (4 x C=O); HRMS (ESI⁺) m/z calcd for C₂₇H₄₅NO₇Na [M + Na]⁺ 518.3094, found 518.3082.

(1'S,2'R,3'R)-3-(1',2',3',4'-tetrahydroxybutyl)-2-benzyl-5-

carboxyoctadecylisoxazolidine (24): According to general procedure, the reaction of **4a** (0.443 mmol, 113 mg, 1 equiv.) and octadecylacrylate (2.22 mmol, 718 mg, 5 equiv.) and purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 95:5) afforded **24** (65 mg, 0.112 mmol) as a mixture of 4 diastereoisomers; yellow powder; yield 25%; ¹H NMR (CD₃OD, 500 MHz) δ 0.92 (t, *J* = 6.6 Hz, 3H, CH₃), 1.26-1.39 (m, 30H, CH₂^(octadecyl)), 1.65-1.70 (2H, m, CH₂^(octadecyl)), 2.32-2.37 (0.08H, m, H-4), 2.53-2.92 (2.09H, m, H-4), 3.52-3.67 (4.39H, m), 3.74-3.84 (1.62H, m), 3.93-4.06 (1.29H, m), 4.15-4.22 (2.78H, m), 4.55-4.64 (0.73H, m, H-5), 4.77-4.82 (0.35H, m, H-5), 7.24-7.33 (3H, m, 3 x Ar-H), 7.41-7.44 (2H, m, 2 x Ar-H); ¹³C NMR (CD₃OD, 150 MHz) δ 14.5 (CH₃), 23.8, 27.0, 27.0, 29.6, 29.7, 30.4, 30.4, 30.5, 30.7, 30.7, 30.7, 30.7, 30.8 and 30.8 (CH₂^(octadecyl)), 33.1 (C-4^(3S,5S)), 34.7 (C-4^(3S,5R)), 35.4 (C-4^(3R,5S)), 35.5 (C-4^(3R,5R)), 61.9, 63.2, 63.9, 64.0, 64.1, 64.1, 66.5, 66.5, 68.0, 68.2, 68.3, 68.7, 72.0, 72.0, 72.2, 72.4, 73.0, 73.5, 73.9, 74.5, 74.5, 74.7, 74.7, 76.1, 78.3, 78.4 (CH + O-CH₂^(octadecyl) + CH₂Ph + C-4'), 128.3, 128.3, 128.4, 128.4, 129.2, 129.2, 129.2, 129.3, 130.4, 130.5, 130.5, 130.6 and 130.7 (Ar-C), 138.6 (Ar-C^{V(3R,5S)}), 138.7 (Ar-C^{V(3S,5R)}), 138.9 (Ar-C^{V(3R,5R)}), 139.0 (Ar-C^{V(3S,5S)}), 173.0, 173.2, 174.0 and 174.1 (4 x C=O); HRMS (ESI⁺) m/z calcd for C₃₃H₅₈NO₇ [M + H]⁺ 580.4213, found 580.4217.

(1'S,2'R,3'R)-3-(1',2',3',4'-tetrahydroxybutyl)-2-benzyl-(trans)-4,5-

(dicarboxymethyl)isoxazolidine (25): According to general procedure, the reaction of **4a** (0.471 mmol, 120 mg, 1 equiv.) and dimethylfumarate (2.35 mmol, 339 mg, 5 equiv.) and purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 95:5) afforded **25** (142 mg, 0.356 mmol) as a mixture of 4 diastereoisomers; yellow oil; yield 76%; ¹H NMR (CD₃OD, 500 MHz) δ 3.43-3.72 (4H, m, 4'-H + CH), 3.74-3.80 (4H, m, CH₃ + 4-H^(3S,5S) + CH), 3.81 (1.79H, s, CH₃), 3.82 (1.11H, s, CH₃), 3.86 (0.32H, s, CH₃), 3.89-3.91 (0.19H, m, CH), 3.95-4.01 (0.79H, m, 4-H^(3S,5R) + CH + *CH_oH_bPh*), 4.05 (0.5H, d, *J* = 13.8 Hz, *CH_oH_bPh*), 4.07-4.16 (1.30H, m, *CH₂Ph* + 4-H^(3R,5R)), 4.21 (0.29H, d, *J* = 12.9 Hz, *CH₂H_bPh*), 4.34-4.37 (0.29H, m, CH), 4.43 (0.11H, dd, *J* = 7.9, 1.6 Hz, 4-H^(3R,5S)), 4.64 (0.17H, d, *J* = 4.0 Hz, 5-H^(3R,5R)), 4.80-4.83, (0.17H, m, CH), 5.11 (0.48H, d, *J* = 6.0 Hz, 5-H^(3S,5S)), 5.15 (0.20H, d, *J* = 5.6 Hz, 5-H^(3S,5R)), 7.24-7.37 (3H, m, 3 x Ar-H), 7.40-7.42 (2H, m, 2 x Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 53.1, 53.2, 53.3 and 53.4 (CH₃), 54.7 (C-4^(3R,5R)), 54.9 (C-4^(3S,5R)), 55.0 (C-4^(3S,5S)), 55.5 (C-4^(3R,5S)), 61.5 and 62.2 (CH₂Ph), 64.0, 64.1 and 64.2 (C-4'), 64.9 (CH₂Ph), 68.7, 71.2, 71.7, 71.9, 72.3, 72.6, 72.9, 73.1, 73.3, 73.3, 74.4 and 74.5 (CH), 79.3, 79.6, 79.7 and 80.9 (C-5), 82.9 (CH), 128.4, 128.5, 128.7, 128.9, 129.2, 129.3, 129.4, 129.5, 130.2, 130.4, and 130.4 (Ar-C), 137.3, 138.1, 138.1 and 138.4 (4 x Ar-C^V), 171.1, 171.5, 171.8, 172.4, 174.0, 174.2, 177.3 and 177.6 (8 x C=O); HRMS (ESI⁺) m/z calcd for C₁₈H₂₆NO₉ [M + H]⁺ 400.1608, found 400.1594.

(1'S,2'R,3'R)-3-(1',2',3',4'-tetrahydroxybutyl)-2-benzyl-(cis)-4,5-

(dicarboxymethyl)isoxazolidine (26): According to general procedure, the reaction of **4a** (0.561 mmol, 143 mg, 1 equiv.) and dimethylmaleate (2.80 mmol, 404 mg, 5 equiv.) and purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 95:5) afforded **26** (176 mg, 0.441 mmol) as a mixture of 4 diastereoisomers; colourless oil; yield 79%; ¹H NMR (CD₃OD, 500 MHz) δ 3.51-3.81 (12H, m, 4'-H + 3'-H + 2'-H + 1'-H + 3-H + 2 x CH₃), 3.94-3.99 (0.32H, m, 4-H^(3S,5R) + 4-H^(3R,5R)), 4.01-4.08 (0.80H, m, CH₂Ph^(3R,5R), 4-H^(3S,5S)), 4.10-4.15 (0.32H, m, CH₂Ph^(3R,5S) + 4-H^(3R,5S)), 4.19 (0.69H, d, *J* = 13.9 Hz, CH_oH_bPh^(3S,5S)), 4.25 (0.16H, d, *J* = 13.4 Hz, CH_oH_bPh^(3S,5R)), 4.27 (0.63H, d, *J* = 13.8 Hz, CH_aH_bPh^(3S,5S)), 4.32 (0.20H, d, *J* = 13.4 Hz, CH_aH_bPh^(3S,5R)), 4.77 (0.64H, d, *J* = 8.4 Hz, 5-H^(3S,5S)), 4.82-4.84 (0.16H, m, 5-H^(3S,5R)), 5.09 (0.08H, d, *J* = 8.2 Hz, 5-H^(3R,5S)), 5.12 (0.09H, d, *J* = 6.0 Hz, 5-H^(3R,5R)), 7.25-7.38 (3H, m, 3 x Ar-H), 7.40-7.46 (2H, m, 2 x Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 52.8 (CH₃^(3S,5S)), 52.9 and 52.9 (CH₃), 52.9 (CH₃^(3S,5S)), 53.0 (CH₃^(3S,5R)), 53.1, 53.2 and 53.3 (CH₃), 53.6 (C-4^(3S,5S)), 53.9 (C-4^(3R,5S)), 54.7 (C-4^(3S,5R)), 55.0 (C-4^(3R,5R)), 61.5 (CH₂Ph^(3R,5R)), 62.2 (CH₂Ph^(3R,5S)), 62.7 (CH₂Ph^(3S,5S)), 63.5 (CH₂Ph^(3S,5R)), 64.0 (C-4^(3S,5R)), 64.1 (C-4^(3S,5S)), 64.1 (C-4^(3R,5R)), 64.6 (C-4^(3R,5S)), 71.7, 71.9, 71.9, 72.1, 72.2, 72.2, 72.6, 72.8, 73.1, 73.1, 73.3, 73.4, 74.3, 74.4 and 74.5 (C-3' + C-2' + C-1' + C-3), 78.3 (C-5^(3R,5S)), 79.3 (C-5^(3R,5R)), 79.5 (C-5^(3S,5S)), 79.9 (C-5^(3S,5R)), 128.3, 128.3, 128.4, 128.5, 129.1, 129.2, 129.2, 129.5, 130.2, 130.4, 130.5 and 130.6 (Ar-C), 137.4 (Ar-C^{V(3R,5S)}), 138.4 (Ar-C^{V(3R,5R)}), 138.9 (Ar-C^{V(3S,5S)}), 138.9 (Ar-C^{V(3S,5R)}), 170.0 (C=O^(3R,5S)), 171.2 (C=O^(3S,5S)), 171.5 (C=O^(3S,5R)), 171.8 (C=O^(3R,5R)), 173.2 (C=O^(3S,5S)), 173.4 (C=O^(3S,5R)), 174.0 (C=O^(3R,5S)), 174.2 (C=O^(3R,5R)); HRMS (ESI⁺) *m/z* calcd for C₁₈H₂₆NO₉ [M + H]⁺ 400.1608, found 400.1599.

(1'S,2'R,3'R)-3-(1',2',3',4'-tetrahydroxybutyl)-2-benzyl-5-

cyanoisoxazolidine (27): According to general procedure, the reaction of **4a** (0.263 mmol, 67 mg, 1 equiv.) and acrylonitrile (1.31 mmol, 70 mg, 5 equiv.) and purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 95:5) afforded **27** (69 mg, 0.224 mmol) as a mixture of 4 diastereoisomers; colourless oil; yield 85%; ¹H NMR (CD₃OD, 500 MHz) δ 2.43-2.48 (0.1H, m, 4-H), 2.73-2.97 (1.54H, m, 4-H), 2.99-3.04 (0.29H, m, 4-H), 3.39-3.43 (0.50H, m, 3-H), 3.49 (0.29H, dd, *J* = 8.2, 2.1 Hz, CH), 3.58-3.71 (2.50H, m, 4'-H + CH), 3.74-3.81 (2.67H, m, CH + 3-H), 3.92 (0.49H, d, *J* = 14.2 Hz, CH_oH_bPh^(3S,5S)), 3.93 (0.10H, d, *J* = 14.3 Hz, CH_oH_bPh^(3R,5S)), 4.05 (0.29H, d, *J* = 13.5 Hz, CH_oH_bPh^(3S,5R)), 4.10 (0.63H, m, CH_aH_bPh^(3S,5S) + CH_oH_bPh^(3R,5R)), 4.26 (0.29H, d, *J* = 13.7 Hz, CH_aH_bPh^(3S,5R)), 4.29 (0.15H, d, *J* = 13.4 Hz, CH_aH_bPh^(3R,5R)), 4.38 (0.10H, d, *J* = 14.2 Hz, CH_aH_bPh^(3R,5S)), 4.89-4.95 (0.47H, m, 5-H^(3R,5R) + 5-H^(3S,5R)), 5.01 (0.11H, dd, *J* = 9.2, 4.4 Hz, 5-H^(3R,5S)), 5.04 (0.46H, dd, *J* = 8.6, 4.8 Hz, 5-H^(3S,5S)), 7.26-7.36 (3H, m, 3 x Ar-H), 7.40-7.47 (2H, m, 2 x Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 36.6 (C-4^(3S,5S)), 36.8 (C-4^(3S,5R)), 37.3 (C-4^(3R,5R)), 38.2 (C-4^(3R,5S)), 61.6, 62.7 and 63.6 (CH₂Ph), 64.0, 64.1 and 64.1 (C-4'), 65.0, 65.3, 65.7 and 66.0 (C-5), 67.9, 68.4, 68.7 and 68.8 (C-3), 72.0, 72.2, 72.2, 72.2, 72.3, 72.5, 72.7, 73.6, 74.3, 74.4, 74.4, 74.5 and 74.5 (CH), 120.0, 120.0, 121.3 and 121.4 (CN), 128.2, 128.4, 128.5, 128.6, 129.2, 129.2, 129.3, 129.4, 130.1, 130.2, 130.4 and 130.6 (Ar-C), 138.2, 138.3, 138.3 and 138.6 (Ar-C^V); HRMS (ESI⁺) *m/z* calcd for C₁₅H₂₀N₂O₅Na [M + Na]⁺ 331.1270, found 331.1271.

(1'S,2'R,3'R)-3-(1',2',3',4'-tetrahydroxybutyl)-2-benzyl-5-methyl-dihydro-2H-pyrrolo[3a,7a-d]isoxazole-4,6(3H,5H)-dione (28):

According to general procedure, the reaction of **4a** (0.247 mmol, 63 mg, 1 equiv.) and *N*-methylmaleimide (1.24 mmol, 137 mg, 5 eq.)

and purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 95:5) afforded **28** (74 mg, 0.202 mmol) as a mixture of 3 diastereoisomers; colorless oil; yield 82%; ¹H NMR (CD₃OD, 500 MHz) δ 3.02 (1.76H, s, CH₃), 3.03 (0.93H, s, CH₃), 3.60-3.64 (2.36H, m, 4'-H + CH), 3.67 (0.46H, d, *J* = 4.5 Hz, 4'-H), 3.69 (0.22H, d, *J* = 4.7 Hz, 4'-H), 3.71-3.73 (0.31H, m, CH), 3.77-3.86 (3.57H, m, CH_oH_bPh + CH), 3.92 (0.72H, d, *J* = 13.4 Hz, CH_aH_bPh), 3.96 (0.35H, d, *J* = 13.1 Hz, CH_aH_bPh), 4.01 (0.28H, dd, *J* = 7.6, 2 Hz, 3a-H^(3S,5R)), 4.18 (0.67H, dd, *J* = 7.7, 1.9 Hz, 3a-H^(3S,5S)), 4.85 (0.79H, d, *J* = 7.8 Hz, 7a-H^(3S,5S)), 4.90 (0.43H, d, *J* = 7.7 Hz, 7a-H^(3S,5R)), 4.94 (0.07H, d, *J* = 7.7 Hz, 7a-H^(3R,5R)), 7.24-7.33 (5H, m, 5 x Ar-H); ¹³C NMR (CD₃OD, 125 MHz) δ 25.5 (CH₃), 51.7 (C-3a^(3R,5R)), 52.6 (C-3a^(3S,5S)), 53.6 (C-3a^(3S,5R)), 63.2, 64.0 (CH₂Ph), 64.1 (C-4^(3S,5R)), 64.2 (C-4^(3S,5S)), 64.4 (C-4^(3R,5R)), 69.6, 70.6, 71.4, 71.7, 71.9, 72.0, 72.9, 73.2, 73.4, 74.4 and 74.4 (CH), 77.9 (C-7a^(3R,5R)), 79.5 (C-7a^(3S,5S)), 80.2 (C-7a^(3S,5R)), 128.3, 128.6, 128.8, 129.2, 129.3, 129.4, 129.6, 130.2, 130.4 and 130.5 (Ar-C), 137.8 and 138.0 (Ar-C^V), 177.1, 177.1, 178.7 and 179.1 (4 x C=O); HRMS (ESI⁺) *m/z* calcd for C₁₇H₂₃N₂O₇ [M + H]⁺ 367.1505, found 367.1490.

(1'S,2'R,3'R)-3-(1',2',3',4'-tetrahydroxybutyl)-2-octyl-5-

carboxydodecylisoxazolidine (29): According to general procedure, the reaction of **4c** (0.191 mmol, 53 mg, 1 equiv.) and dodecylacrylate (0.957 mmol, 230 mg, 5 equiv.) and purification of the resulting residue by chromatography on silica gel (CH₂Cl₂ / methanol 95:5) afforded **29** (80 mg, 0.155 mmol) as a mixture of 4 diastereoisomers; colourless sticky solid; yield 81%; ¹H NMR (CD₃OD, 500 MHz) δ 0.87-0.98 (6.00H, m, CH₃), 1.25-1.44 (28.07H, m, CH₂^(dodecyl + octyl)), 1.55-1.72 (3.98H, m, CH₂^(dodecyl + octyl)), 2.28 (0.08H, ddd, *J* = 13.1, 6.5, 4.5 Hz, 4-H_oH_b^(3R,5S)), 2.49-3.01 (3.98H, m, 4-H + N-CH₂^(octyl)), 3.36-3.43 (0.29H, m, 3-H^(3S,5R) + 3-H^(3R,5S)), 3.47-3.55 (1.25H, m, 3-H^(3S,5S) + 3-H^(3R,5R) + 1'-H^(3S,5S)), 3.55-3.74 (2.86H, m, 1'-H^(3R,5R) + 1'-H^(3R,5S) + 2'-H^(3S,5R) + 2'-H^(3R,5R) + 2'-H^(3R,5S) + 4'-H), 3.74-3.84 (1.77H, m, + 1'-H^(3S,5R) + 2'-H^(3S,5S) + 3'-H), 4.12-4.24 (2.03H, m, O-CH₂^(dodecyl)), 4.56 (0.53H, dd, *J* = 8.2, 8.2 Hz, 5-H^(3S,5S)), 4.60 (0.22H, dd, *J* = 9.1, 6.9 Hz, 5-H^(3S,5R)), 4.68-4.74 (0.28H, m, 5-H^(3R,5R) + 5-H^(3R,5S)); ¹³C NMR (CD₃OD, 125 MHz) δ 14.5 and 14.5 (CH₃), 23.7, 23.8, 27.0, 27.0, 28.3, 28.3, 28.4, 29.0, 29.0, 29.7, 29.7, 30.4, 30.4, 30.4, 30.5, 30.7, 30.7, 30.7, 30.8, 30.8, 33.0, 33.1 and 33.1 (CH₂^(dodecyl + octyl)), 34.3 (C-4^(3S,5S)), 35.1 (C-4^(3R,5R)), 35.2 (C-4^(3S,5R)), 35.5 (C-4^(3R,5S)), 58.2 and 59.6 (N-CH₂^(octyl)), 63.9, 64.0 (C-4'), 64.2 (C-4^(3S,5S)), 66.5 and 66.5 (O-CH₂^(dodecyl)), 68.5 (C-3^(3S,5R)), 69.0 (C-3^(3S,5S)), 69.2 (C-3^(3R,5S)), 69.2 (C-3^(3R,5R)), 71.9 (C-1'^(3S,5R)), 72.1 (C-1'^(3S,5S)), 72.2 (C-2'^(3S,5S)), 72.2 (C-2'^(3S,5R)), 73.1 (C-1'^(3R,5R)), 73.3 (C-2'^(3R,5R)), 74.5 (C-3'^(3S,5S)), 74.6 (C-3'^(3R,5R)), 74.7 (C-3'^(3S,5R)), 74.8 (C-3'^(3R,5S)), 75.9 (C-5^(3R,5R)), 75.9 (C-5^(3R,5S)), 78.0 (C-5^(3S,5S)), 78.1 (C-5^(3S,5R)), 172.9, 173.3, 174.1 and 174.2 (4 x C=O); HRMS (ESI⁺) *m/z* calcd for C₂₈H₅₆NO₇ [M + H]⁺ 518.4057, found 518.4055.

Conflicts of interest

"There are no conflicts to declare".

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