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D-Xylose derived oxazolidin-2-ones as chiral auxiliaries in stereoselective aldol reactions †

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Abstract: Chiral N-acylated oxazolidin-2-one derivatives from D-xylose have been shown to undergo diastereoselective aldol reactions via their lithium imide enolates to afford β-hydroxylated products. Aliphatic substrates and aldehydes were shown to yield 'non-Evans' *syn*-aldols readily interpreted by assuming chelated chair-like transition states. When substrates and aldehydes bearing aromatic groups are used chelated boat- or twist-boat-like transition states seem to become similarly or even more probable so that *anti*- or *syn*-aldols are also formed from *cis*- or *trans*-enolates, respectively. © 1997 Elsevier Science Ltd

The aldol addition is a useful tool for the synthesis of biologically important natural products and considerable attention has been paid to the development of chiral enolate synthons and their practical utility in aldol processes during the last decade.[1] Among them chiral N-acylated oxazolidin-2-ones pioneered by D. A. Evans[2] have been proved to be particularly effective for controlling a broad variety of reactions of attached acyl fragments. Thus the employment of enantiomerically pure cyclic carbamates has become a widely used standard procedure in modern stereoselective organic chemistry, especially in aldol reactions.[3,4]

However, preparative access to chiral auxiliaries is quite difficult because enantiomerically pure amino alcohols are required or, even worse, resolution of the correspondingly prepared racemic oxazolidin-2-ones is necessary. Thus several groups, among them I. Gosney and H. Kunz, prepared some oxazolidin-2-one derivatives from the '*chiral pool*', namely from terpenes[5] and carbohydrates,[6,7] but the onerous formation of the heterocyclic system remains a problem of all of I. Gosney's and H. Kunz' reagents.

Recently we reported two new reagents, 3,5-O-isopropylidene- and 3,5-O-benzylidene-α-D-xylofurano[1,2,d]oxazolidin-2′-one **1** and **2**, readily prepared in multigram-scale by a simple two step synthesis from inexpensive D-xylose. Within the scope of current studies of efficiency of **1** and **2** in stereoselective synthesis we were able to illustrate their practical value as CDA's for the resolution of carboxylic and sulfonic acids[8] and as auxiliaries in diastereoselective C–C-bond[9,10] and halogen–C-bond formation.[10] The success of these reactions encouraged us to investigate extensions to reactions generating more than one stereogenic centre. Therefore, the purpose of this paper is to demonstrate **1** and **2** also to be efficiently employed as cheap chiral auxiliaries in lithium-mediated aldol reactions.[11]

Glyco-oxazolidin-2-ones **1** and **2** were prepared following the potassium cyanate methodology discovered in our laboratory in a joint co-operation with Hungarian colleagues[12] and subsequent protection of the remaining hydroxy groups with acetal protective groups (Figure 1).

To get a number of sterically different constrained N-acyl derivatives of **1** and **2** several acyl chlorides were coupled with **1** and **2** using either the standard n-butyllithium procedure[2] or N,N-dimethylaminopyridine (DMAP) methodology[13] to get stable N-acyl oxazolidin-2-ones **3–8** in yields between 93 and 98% (Figure 2).

† Dedicated to Professor Hans Paulsen on occasion of his 75th birthday.

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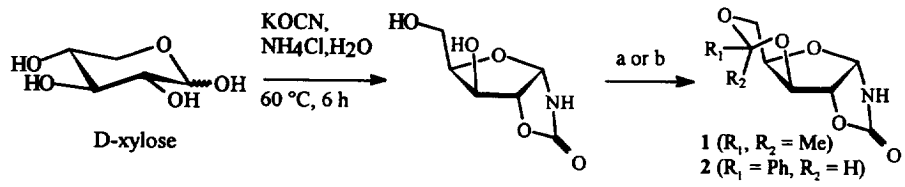
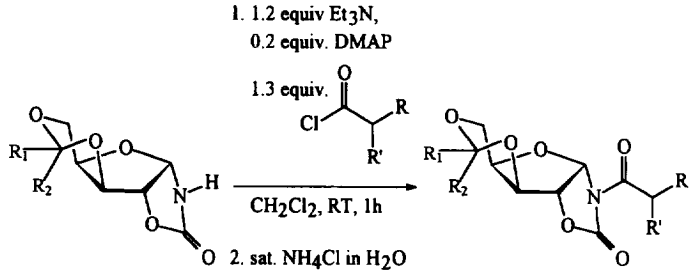


Figure 1. Preparation of 3,5-O-isopropylidene- and 3,5-O-benzylidene-α-D-xylofurano[1,2,d]oxazolidine-2′-one: (a) acetone, conc. H_2SO_4, 1 h, RT, (b) benzaldehyde, anhyd. $ZnCl_2$, 4 h, RT.



	R_1	R_2	R	R'
3	Ph	H	H	H
4	Me	Me	Me	H
5	Me	Me	Et	H
6	Me	Me	Me	Me
7	Me	Me	Ph	H
8	Me	Me	Bn	H

Figure 2. N-Acylation sequence using catalytical amounts of DMAP.

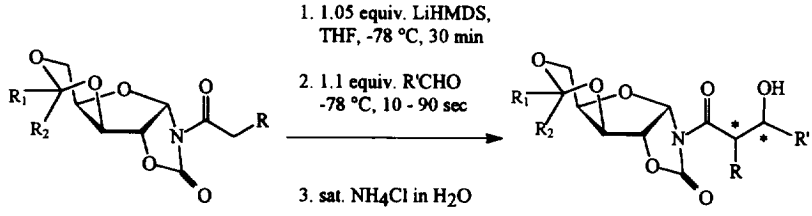


Figure 3. Aldol reaction.

Despite of the poor results other groups[2,14–17] obtained with lithium enolates in stereoselective aldol reactions we first examined lithium-mediated reactions because of the ecological and economical advantages of lithium compared with the commonly used boron enolates.The N-acyl precursors **3–5**, **7**, and **8** were transformed into enolates using a slight excess of lithium bis(trimethylsilyl)amide (LiHMDS) as base. Employing this procedure we were not able to get an enolate from the α-disubstituted N-isobutyryl derivative **6** probably because LiHMDS is a base too weak for achieving enolization.

The enolates of the α-non- or -monosubstituted N-acyl derivatives were allowed to react with a 1.1 fold excess of carbonyl component at −78°C in order to get β-hydroxylated N-acyl compounds as shown in Figure 3. Ketones are not reactive under these conditions (Figure 4).

Analyses of crude reaction mixtures by ^{1}H- and ^{13}C-NMR spectroscopy showed sufficient chemical shift differences to determine the diastereomeric ratios. In all but one case the major diastereomer was readily purified on silica using petroleum ether/ethyl acetate as eluent. As a bonus it should be noticed that the crystalline nature of these compounds also offers the opportunity to attempt purification by fractional crystallisation. The results summarised in Tables 1 and 2 reflect the diastereo- and enantiofacial selection dictated by **1** and **2** for the aldol reactions of aliphatic N-acyl substrates and carbonyl compounds and N-acyl derivatives or aldehydes bearing arylic groups, respectively. In order to arrange the diastereoselectivities more clearly we combined all amounts of the minor diastereomers.

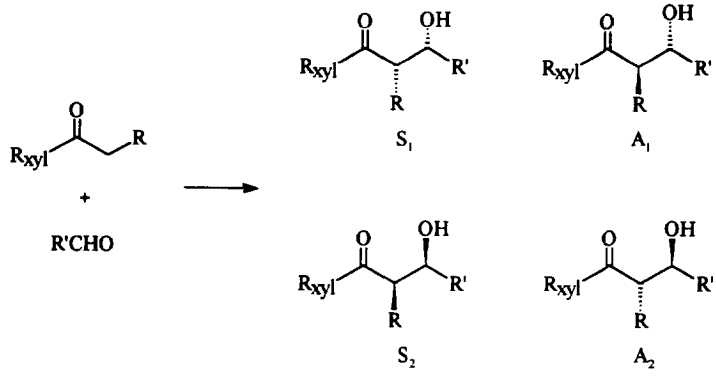


Figure 4. Possible stereoisomeric products obtainable from an aldol reaction.

Table 1. Aldol reactions of aliphatic N-acyl derivatives **4-6** with aliphatic carbonyl components

N-acyl derivative	carbonyl component	diastereomeric ratio[a]	major product	configuration of major product	yield of major product[b]
4 (R = methyl)	acetaldehyde	10 : 1	**9**	*syn*-α[*R*],β[*S*]	37 %
4 (R = methyl)	acrolein	5 : 1	**10**	*syn*-α[*R*],β[*S*]	39 %
4 (R = methyl)	acetone	no reaction	-	-	-
4 (R = methyl)	butyraldehyde	6 : 1	**11**	*syn*-α[*R*],β[*S*][c]	29 %
4 (R = methyl)	iso-butyraldehyde	15 : 1	**12**	*syn*-α[*R*],β[*S*]	39 %
4 (R = methyl)	hexanal	7 : 1	**13**	*syn*-α[*R*],β[*S*][c]	25 %
4 (R = methyl)	octanal	8 : 1	**14**	*syn*-α[*R*],β[*S*][c]	35 %
4 (R = methyl)	cyclohexanone	no reaction	-	-	-
5 (R = ethyl)	acrolein	4 : 1	**15**	*syn*-α[*R*],β[*S*][c]	34 %
5 (R = ethyl)	iso-butyraldehyde	6 : 1	**16**	*syn*-α[*R*],β[*S*][c]	38 %
6 (2 x R = methyl)	iso-butyraldehyde	no reaction	-	-	-

[a] determined by 500 MHz ^{1}H- and 125 MHz ^{13}C-NMR spectroscopy using 1D Win NMR software from *Bruker*, to arrange the data more clearly the minor diastereomers were summed up
[b] after column chromatography
[c] assignment of relative *syn*-configuration was made by analysis of the vicinal coupling constant $^3J_{\alpha,\beta}$, absolute configurations were assigned analogous to the unambiguously identified aldol products **9**, **10**, and **12**

The absolute configurations of **9**, **10**, **12**, **17**, **18**, and **22** were assigned by comparison of the specific rotations of the almost enantiopure β-hydroxy carboxylic acids obtained upon cleavage of the elaborated N-acyl oxazolidin-2-ones with lithium hydroperoxide[18] with literature values. The relative *syn*-configurations of the other aldol products were assigned by determination of the vicinal coupling constants $^3J_{\alpha,\beta}$ with all but one of them being noticeably smaller than 4 Hz, thus strongly indicating *syn*-configurations.[14c] The stereochemical assignment of aldol **20** was made due to its vicinal coupling constant $^3J_{\alpha,\beta}$=7.0 Hz indicating *anti*-configuration.[14c] Due to this agreement with the results of the clearly identified products the absolute configurations were allotted analogous to **9**, **10**, and **12**, **18**, and **22**, respectively.

In all aldol reactions shown in Table 1 the sense of stereochemical induction is readily interpreted by applying the widely accepted Zimmerman–Traxler pericyclic chair-like transition state model.[19]

Table 2. Aldol reactions of N-acyl derivatives or aldehydes bearing arylic groups

N-acyl derivative (R)	aldehyde	diastereomeric ratio[a]	major product	configuration of major product	yield of major product[b]
3 (R = H)	benzaldehyde	2 : 1	17	β[*R*]	26 %
4 (R = Me)	benzaldehyde	5 : 3	18	*syn*-α[*R*],β[*R*]	[c]
4 (R = Me)	cinnamaldehyde	2 : 1	19	*syn*-α[*R*],β[*S*][d]	46 %
5 (R = Et)	benzaldehyde	4 : 3	20	*anti*-α[*R*],β[*S*][d]	26 %
7 (R = Ph)	acetaldehyde	12 : 1	21	*syn*-α[*S*],β[*R*][d]	22 %
8 (R = Bn)	acetaldehyde	15 : 1	22	*syn*-α[*S*],β[*R*]	26 %

[a] determined by 500 MHz ^{1}H- and 125 MHz ^{13}C-NMR spectroscopy using 1D Win NMR software from *Bruker*, to arrange the data more clearly the minor diastereomers were summed up
[b] after column chromatography
[c] major diastereomer was still contamined with minor one(s) after column chromatography
[d] assignment of relative *syn*- / *anti*-configuration was made by analysis of the vicinal coupling constant $^3J_{\alpha,\beta}$, absolute configurations were assigned analogous to the unambiguously identified aldol products **17**, **18**, and **22**

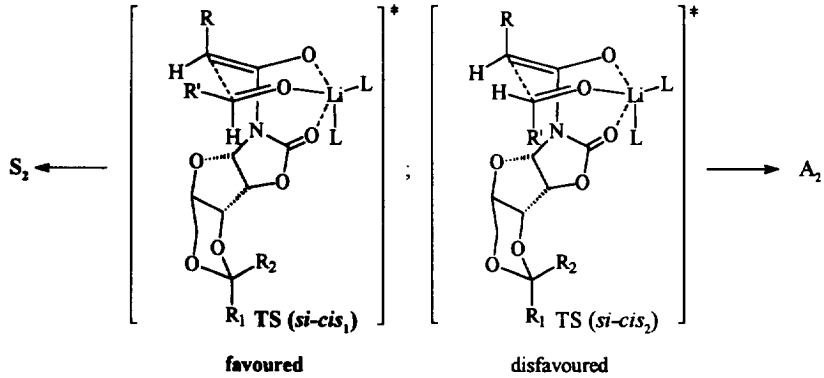


Figure 5. Chair-like transition states.

In accordance with our previous results lithium chelated *cis*-enolates ('*Z*')[20] were obtained from imides with non-arylic acyl moieties upon treatment with LiHMDS. Diastereofacial *si*-face attack is dictated by the protected sugar skeleton 1[*S*],2[*R*] connected to the oxazolidin-2-one ring, assuming coordination to the oxazolidin-2-one carbonyl is still existing in the transition state like generally suggested for lithium enolates.[2,14–17] Thus the enolates react with aldehydes via transition states TS (*si–cis*$_1$) and TS (*si–cis*$_2$) shown in Figure 5 to yield *syn*- and *anti*-configurated products S_2 and A_2, respectively. The 1,3-diaxial interactions between the auxiliary and the aldehyde moiety (R′) predict TS (*si–cis*$_1$) to be favoured and the *syn*-isomer S_2 to be the major product.

However, results of arylic N-acyl precursors or arylic aldehydes cannot be interpreted in this way, or at least not exclusively. Similar results were reported by others explaining them by assuming boat- or twist-boat-like transition states to become similar or even more probable if arylic groups are involved.[2,9,14–17,21] Thus leading to larger amouts of *anti*- and *syn*-configurated aldols A_1 and S_1 from *cis*- and *trans*-enolates, respectively (Figure 6).

Employing this explanation the stereochemical outcomes become apparent. Especially when aromatic aldehydes are used the energetic differences between the chair- and boat- or twist-boat-like transition states are quite small[14–17,21] and so a noticeable decrease in diastereoselectivity is observed compared with the reactions described above.

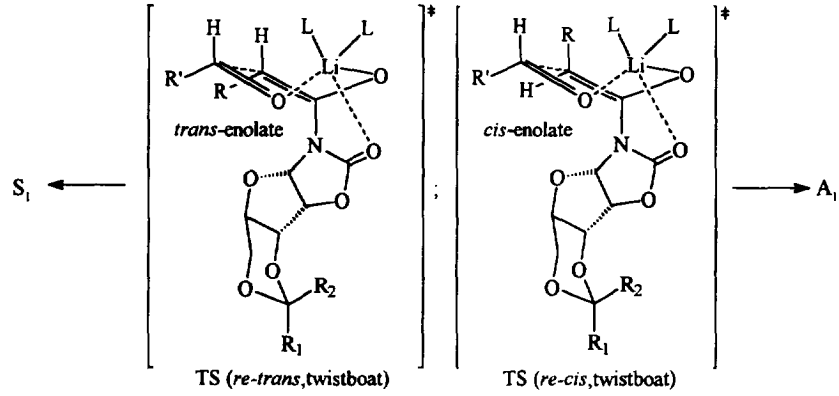


Figure 6. Twist-boat-like transition states.

As already found in our previous investigations *trans*-enolates of imides **7** and **8** seem strongly preferred due to some stereoelectronic interaction between the furanoid oxygen atom and the arylic ring system in the attached acyl moiety. Hence, aldehyde attack proceeds from the less hindered *re*-face to produce *syn*-configurated S_1-aldols via a nearly exclusively formed boat- or twist-boat-like transition state.

In conclusion we have demonstrated that cheap D-xylose based **1** and **2** can be easily employed as chiral auxiliaries in lithium-mediated aldol reactions. Especially aliphatic N-acyl substrates react with aliphatic aldehydes to yield predictable *syn*-aldols with inverse configuration compared to the products obtained by Evans' standard boron-mediated aldol procedure. If arylic groups are involved the stereochemical results have to be explained in a more sophisticated manner. Further studies are in progress to gain access to other aldols employing other counterions with different coordination characteristics to enlarge the glyco-oxazolidin-2-ones' range of application in aldol reactions.

Experimental

General

All reactions were performed in flame-dried glassware with magnetic stirring under nitrogen. Tetrahydrofuran (THF) was distilled from sodium wire and benzophenone, dichloromethane (CH_2Cl_2) from calcium hydride, acetone from phosphorus pentaoxide. n-Butyl lithium was purchased as 1.6 M solution in hexane-fraction and lithium bis(trimethylsilyl)amide as 1 M solution in hexane from *Aldrich*. Acyl chlorides were either commercially available and freshly distilled or prepared from the corresponding carboxylic acids with thionyl chloride. All aldehydes were freshly distilled prior to use. Products were purified, if necessary, by column chromatography on silica gel 60 (0.063–0.2 mm) with petroleum ether/ethyl acetate (7/4 v/v) as eluent. Thin layer chromatography was performed on TC-layers *Silicagel 60 F_{254}* from *Merck*. NMR spectra were recorded in *deutero*-chloroform with tetramethylsilane as internal standard on a *Bruker AM 300* (^{1}H=300.1; ^{13}C=75.8 MHz) or on a *Bruker AMX R 500* instrument (^{1} H=500.1; ^{13}C=125.8 MHz). Mass spectra were taken on a *Finnigan MAT 212* with data system *SS 300* or on a *Finnigan MAT 95* with data system *DEC-Station 5000*. Microanalyses were carried out on a *Carlo Erba 1104* or on a *Fison Instruments EA 1108*. Melting points were measured on a hot-stage microscope *SM-Lux* from *Leitz* and are uncorrected. Specific optical rotations were determined with a *Perkin Elmer Polarimeter 241 MC* or *343*.

3,5-O-Isopropylidene-α-D-xylofurano[1,2,d]oxazolidin-2'-one 1

120.0 g (686 mmol) α-D-xylofurano[1,2,d]oxazolidin-2'-one (prepared from D-xylose according to the literature) were suspended in 1.2 l abs. acetone and treated with 30 ml concentrated sulphuric acid at room temperature. Stirring was continued for one hour. After reaction reached completion (TC-

control) the solution was neutralized with saturated aqueous Na_2CO_3-solution. Acetone was removed *in vacuo* and the remaining aqueous phase was exhaustively extracted with dichloromethane. After evaporation of the organic phase the residue was dissolved in acetone and mixed with 100 ml water. Evaporation of acetone and crystallization from water yields a first crop of **1**. The last steps can be repeated several times with step by step concentration of the aqueous phase. Finally 125.50 g (85%) of the acetal protected glyco-oxazolidin-2-one were obtained after high vacuum drying. Mp 112–114°C (dichloromethane/petroleum ether 40/60); $[\alpha]_D^{20}$=+73 (c=1.2, acetone); ^{1}H-NMR (500,1 MHz): δ=5.832 (d,1H,$^3J_{1,2}$=5.1 Hz, H-1), 4.880 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.461 (d,1H, $^3J_{3,4}$=2.5 Hz, H-3), 3.924 (m,1H, $^3J_{4,5}$=2.5 Hz, H-4), 4.157 (dd,1H, $^2J_{5,5'}$=−13.4 Hz, H-5), 4.057 (d,1H, $^3J_{4,5'}$=0 Hz, H-5'), 1.471 (s, 3H, H-7), 1.392 (s, 3H, H-7'), 6.146 (s, 1H, NH); ^{13}C-NMR (125.8 MHz): δ=85.68 (C-1), 84.57 (C-2), 70.48 (C-3), 72.44 (C-4), 59.62 (C-5), 97.99 (C-6), 28.80 (C-7), 18.66 (C-7'), 157.13 (NCOO); M=215.2 g mol^{-1}; MS (CI - iso-butane): m/z=216 (MH^+, 100); Anal. calcd. for $C_9H_{13}O_5N$: C 50.23, H 6.05, N 6.51. Found C 49.94, H 5.87, N 7.06.

3,5-O-Benzylidene-α-D-xylofurano[1,2,d]oxazolidin-2'-one **2**

40.0 g (229 mmol) α-D-xylofurano[1,2,d]oxazolidin-2'-one were stirred together with 150 g (1.096 mol) anhyd. $ZnCl_2$ and 750 ml freshly distilled benzaldehyde at room temperature for four hours. After cooling to 0°C 1 l water was added and the mixture was stirred an additional hour. After standing at 4°C for 15 h a first crop of crystals can be obtained by filtration. The phases were separated and the aqueous phase was extracted three times with ether. The organic phases were combined and the ether evaporated. After adding the five-fold volume of petroleum ether to the benzaldehyde phase the product was filtered. The combined crystalline product fractions are washed repeatedly with water and petroleum ether and finally high vacuum dried to yield 51.25 g (85%) of the desired product. Mp 216–218°C (dichloromethane/petroleum ether 40/60); $[\alpha]_D^{20}$=+39 (c=1, chloroform); ^{1}H-NMR (500,1 MHz): δ=5.899 (d,1H,$^3J_{1,2}$=5.7 Hz, H-1), 5.020 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.619 (d,1H, $^3J_{3,4}$=1.9 Hz, H-3), 4.058 (m,1H, $^3J_{4,5}$=1.9 Hz, H-4), 4.464 (dd,1H, $^2J_{5,5'}$=−13.4 Hz, H-5), 4.236 (d,1H, $^3J_{4,5'}$=0 Hz, H-5'), 5.530 (s, 1H, H-6), 7.49–7.38 (m, 5H, H_{arom}), 6.030 (s, 1H, NH); ^{13}C-NMR (125.8 MHz): δ=86.13 (C-1), 83.74 (C-2), 71.15 (C-3), 78.06 (C-4), 66.17 (C-5), 99.59 (C-6), 136.99–126.00 (C_{arom}), 156.86 (NCOO); M=263.3 g mol^{-1}; MS (CI - iso-butane): m/z=264 (MH^+, 100); Anal. calcd. for $C_{13}H_{13}O_5N$: C 59.31, H 4.94, N 5.32. Found C 60.60, H 4.85, N 5.55.

General procedure for the N-acylation with n-butyl lithium

0.1 mol of the acetal protected glyco-oxazolidin-2-one were dissolved in 250–300 ml abs. THF and cooled to − 78°C. 0.101 mol (64 ml, 1.01 equiv.) n-butyl lithium solution were added over 10–15 min and additionally stirred 15 min before 0.11 mol (1.1 equiv.) of the acyl chloride were added in one portion. The reaction mixture was stirred 25 min at −78°C, then warmed to 0°C and stirred for another 30 min. The mixture was quenched by addition of 80 ml saturated NH_4Cl-solution. The volatiles were removed *in vacuo*.

variation 1: If the product readily crystallised from the aqueous phase it was filtered off, washed with saturated $NaHCO_3$−, saturated NaCl-solution, and petroleum ether 40/60, and dried in high vacuum.

variation 2: If the product did not crystallise it was extracted with dichloromethane. The organic phase was washed with $NaHCO_3$− and saturated NaCl-solution, dried over $MgSO_4$ and evaporated.

If necessary the N-acyl derivative can be recrystallised from dichloromethane/petroleum ether mixtures.

N-Acetyl-3,5-O-benzylidene-α-D-xylofurano[1,2,d]oxazolidin-2'-one **3**

17.6 g (0.067 mol) **2** were allowed to react with 5.26 ml (0.074 mol) acetyl chloride according to the general procedure, variation 2 to yield 18.36 g (93%) of **3**. Mp 136°C (MTBE); $[\alpha]_D^{20}$=+70 (c=1.8, acetone); ^{1}H-NMR (500.1 MHz): δ=6.274 (d,1H,$^3J_{1,2}$=5.1 Hz, H-1), 4.811 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.547 (d,1H, $^3J_{3,4}$=1.9 Hz, H-3), 3.874 (m,1H, $^3J_{4,5}$=0 Hz, H-4), 4.368 (dd,1H, $^2J_{5,5'}$=−13.4

Hz, H-5), 4.049 (d,1H, $^3J_{4,5'}$=1.9 Hz, H-5'), 5.403 (s, 1H, H-6), 7.42–7.32 (m, 5H, H_{arom}), 2.454 (s, 3H, H-2''); ^{13}C-NMR (125.8 MHz): δ=86.22 (C-1), 77.70 (C-2), 71.53 (C-3), 77.13 (C-4), 65.44 (C-5), 99.00 (C-6), 136.84–125.59 (C_{arom}), 151.89 (NCOO), 169.29 (C-1''), 23.29 (C-2''); M=305.3 g mol^{-1}; MS (CI, iso-butane): m/z=306 (MH^+, 100); Anal. calcd. for $C_{15}H_{15}O_6N$: C 59.01, H 4.95, N 4.59. Found C 59.85, H 5.03, N 4.63.

N-Isobutyryl-3,5-O-isopropylidene-α-D-xylofurano[1,2,d]oxazolidin-2'-one **6**

21.5 g (0.1 mol) **1** gave 27.7 g (97%) of the desired N-acyl derivative **6** upon treatment with 11.5 ml (0.11 mol) isobutyryl chloride according to the general n-butyl lithium procedure, variation 1. Mp 150°C (MTBE); $[\alpha]_D^{20}$=+96 (c=1.3, acetone); ^{1}H-NMR (300.1 MHz): δ=6.371 (d,1H,$^3J_{1,2}$=5.0 Hz, H-1), 4.818 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.505 (d,1H, $^3J_{3,4}$=2.8 Hz, H-3), 3.906 (m,1H, $^3J_{4,5}$=2.2 Hz, H-4), 4.119 (m, 2H, H-5, H-5'), 1.472 (s, 3H, H-7), 1.406 (s, 3H, H-7'), 3.659 (m, 1H, $^3J_{2'',3''}$=6.6 Hz, H-2''), 1.219 (d, 3H, H-3''), 1.190 (d, 3H, $^3J_{2'',3'''}$=7.2 Hz, H-3'''); ^{13}C-NMR (75.8 MHz): δ=86.62 (C-1), 81.40 (C-2), 71.43 (C-3), 72.30 (C-4), 59.50 (C-5), 98.06 (C-6), 28.59 (C-7), 18.86 (C-7'), 151.73 (NCOO), 176.91 (C-1''), 32.95 (C-2''), 18.74 (C-3''), 18.63 (C-3'''); M=285.3 g mol^{-1}; MS (CI, iso-butane): m/z=286 (MH^+, 100); Anal. calcd. for $C_{13}H_{19}O_6N$: C 54.73, H 6.71, N 4.91. Found C 54.30, H 6.69, N 4.64.

General procedure for the N-acylation with N,N-dimethyl aminopyridine

A solution of 0.1 mol **1** or **2** in 350 ml abs. dichloromethane was treated with 1.2 equiv. (16.6 ml, 0.12 mol) triethylamine and a catalytical amount of DMAP (2.44g, 0.02 mol, 0.2 equiv.). At room temperature 0.13 mol (1.3 equiv.) acyl chloride (advantageously freshly prepared or distilled) were added in one portion. The solution was stirred until reaction reached completion (TC-control). The mixture was quenched with 100 ml saturated NH_4Cl-solution and the volatiles evaporated. The aqueous phase is extracted four times with dichloromethane. After washing with saturated $NaHCO_3$– and sat. NaCl-solution, drying over $MgSO_4$, evaporation of the organic solvent, and high vacuum drying the n-acylated product was obtained in good purity.

N-Propionyl-3,5-O-isopropylidene-α-D-xylofurano[1,2,d]oxazolidin-2'-one **4**

33.75 g (0.157 mol) **1** were treated with 17.8 ml (0.204 mol) propionyl chloride according general DMAP procedure to yield 40.0 g (94%) of **4**. Mp 142°C (THF); $[\alpha]_D^{20}$=+124 (c=1.65, acetone); ^{1}H-NMR (500.1 MHz): δ=6.348 (d,1H,$^3J_{1,2}$=5.1 Hz, H-1), 4.796 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.476 (d,1H, $^3J_{3,4}$=2.6 Hz, H-3), 3.882 (m,1H, $^3J_{4,5}$=1.9 Hz, H-4), 4.089 (m, 2H, H-5, H-5'), 1.443 (s, 3H, H-7), 1.373 (s, 3H, H-7'), 2.887 (q, 2H, $^3J_{2'',3''}$=7.6 Hz, H-2''), 1.156 (t, 3H, H-3''); ^{13}C-NMR (125.8 MHz): δ=86.27 (C-1), 81.58 (C-2), 71.41 (C-3), 72.19 (C-4), 59.42 (C-5), 98.04 (C-6), 28.58 (C-7), 18.79 (C-7'), 152.13 (NCOO), 173.42 (C-1''), 29.29 (C-2''), 7.87 (C-3''); M=271.3 g mol^{-1}; MS (CI, iso-butane): m/z=272 (MH^+, 100); Anal. calcd. for $C_{12}H_{17}O_6N$: C 53.13, H 6.32, N 5.16. Found C 53.04, H 6.35, N 5.07.

N-Butyryl-3,5-O-isopropylidene-α-D-xylofurano[1,2,d]oxazolidin-2'-one **5**

13.55 g (0.063 mol) **1** gave 18.00 g (98%) **5** upon treatment with 8.55 ml (0.082 mol) butyryl chloride according to the DMAP procedure. Mp 88°C (CH_2Cl_2/petroleum ether); $[\alpha]_D^{20}$=+126 (c=0.95, acetone); ^{1}H-NMR (500.1 MHz): δ=6.241 (d,1H,$^3J_{1,2}$=5.1 Hz, H-1), 4.727 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.409 (d,1H, $^3J_{3,4}$=2.5 Hz, H-3), 3.806 (m,1H, $^3J_{4,5}$=2.5 Hz, H-4), 4.028 (dd, 1H, $^2J_{5,5'}$=–14.0 Hz, H-5), 3.972 (d, 1H, $^3J_{4,5'}$=0 Hz, H-5'), 1.367 (s, 3H, H-7), 1.275 (s, 3H, H-7'), 2.744 (t, 2H, $^3J_{2'',3''}$=7.6 Hz, H-2''), 1.584 (m, 2H, $^3J_{3'',4''}$=7.6 Hz, H-3'') 0.879 (t, 3H, H-4''); ^{13}C-NMR (125.8 MHz): δ=86.03 (C-1), 81.30 (C-2), 71.12 (C-3), 71.90 (C-4), 59.14 (C-5), 97.72 (C-6), 28.37 (C-7), 18.54 (C-7'), 151.89 (NCOO), 172.24 (C-1''), 37.14 (C-2''), 17.05 (C-3''), 13.28 (C-4''); M=285.3 g mol^{-1}; MS (CI, iso-butane): m/z=286 (MH^+, 100), 571 (MMH^+, 20); Anal. calcd. for $C_{13}H_{19}O_6N$: C 54.73, H 6.71, N 4.91. Found C 54.77, H 6.81, N 4.84.

N-(2''-Phenyl-acetyl)-3,5-O-isopropylidene-α-D-xylofurano[1,2,d]oxazolidin-2'-one **7**

When 2.15 g (0.01 mol) **1** were treated with 1.7 ml (0.013 mol) phenyl acetyl chloride 3.2 g (93%) **7** were obtained following the general DMAP procedure. Mp 113°C (acetone); $[\alpha]_D^{20}$=+119 (c=1, acetone); ^{1}H-NMR (500.1 MHz): δ=6.275 (d,1H,$^3J_{1,2}$=5.1 Hz, H-1), 4.737 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.442 (d,1H, $^3J_{3,4}$=2.6 Hz, H-3), 3.749 (m,1H, $^3J_{4,5}$=1.9 Hz, H-4), 4.007 (m, 2H, H-5, H-5'), 1.399 (s, 3H, H-7), 1.344 (s, 3H, H-7'), 4.242 (d, 1H, $^2J_{2'',2'''}$=−15.9 Hz, H-2''), 4.162 (d, 1H, H-2'''), 7.28–7.22 (m, 5H, H_{arom}); ^{13}C-NMR (125.8 MHz): δ=86.19 (C-1), 81.34 (C-2), 71.10 (C-3), 71.84 (C-4), 59.07 (C-5), 97.73 (C-6), 28.38 (C-7), 18.53 (C-7'), 151.83 (NCOO), 170.25 (C-1''), 41.34 (C-2''), 132.75–126.96 (C_{arom}); M=333.3 g mol^{-1}; MS (CI, iso-butane): m/z=334 (MH^+, 100); Anal. calcd. for $C_{17}H_{19}O_6N$: C 61.25, H 5.75, N 4.20. Found C 61.72, H 5.77, N 4.28.

N-(3''-Phenyl-propionyl-3,5-O-isopropylidene-α-D-xylofurano[1,2,d]oxazolidin-2'-one **8**

Following general DMAP procedure 2.15 g (0.01 mol) **1** were N-acylated with 1.94 ml (0.013 mol) 3-phenyl propionyl chloride to yield 3.4 g (97%) **8**. Mp 150°C (THF); $[\alpha]_D^{20}$=+93 (c=0.8, acetone); ^{1}H-NMR (500.1 MHz): δ=6.343 (d,1H,$^3J_{1,2}$=5.7, Hz, H-1), 4.783 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.447 (d,1H, $^3J_{3,4}$=1.9 Hz, H-3), 3.848 (m,1H, $^3J_{4,5}$=1.9 Hz, H-4), 4.089 (m, 2H, H-5, H-5'), 1.488 (s, 3H, H-7), 1.386 (s, 3H, H-7'), 2.995 (t, 2H, $^3J_{2'',3''}$=7.6 Hz, H-2''), 3.217 (t, 2H, H-3''), 7.27–7.20 (m, 5H, H_{arom}); ^{13}C-NMR (125.8 MHz): δ=86.28 (C-1), 81.61 (C-2), 71.45 (C-3), 72.16 (C-4), 59.41 (C-5), 98.06 (C-6), 28.59 (C-7), 18.81 (C-7'), 152.03 (NCOO), 171.88 (C-1''), 30.00 (C-2''), 37.31 (C-3''), 140.21–126.26 (C_{arom}); M=347.4 g mol^{-1}; MS (CI, iso-butane): m/z=348 (MH^+, 100); Anal. calcd. for $C_{18}H_{21}O_6N$: C 62.24, H 6.09, N 4.03. Found C 62.55, H 6.12, N 3.89.

General procedure for the lithium-mediated aldol reactions

5.5 ml (5.5 mmol) 1 M LiHMDS-solution are cooled to −78°C. 5 mmol of a N-acyl derivative in 15–20 ml abs. THF were added dropwise with stirring and stirring was continued for 30 min after complete addition at −78°C. After addition of 1.1 equiv. of a freshly distilled aldehyde the mixture was allowed to react for 10–90 sec before the solution was quenched with 20 ml of saturated aqueous NH_4Cl-solution. Phases were separated. The aqueous phase was again extracted with dichloromethane. Combined organic phases were washed with sat. NaCl-solution and dried over $MgSO_4$. The crude reaction mixture was obtained by evaporation of the solvent. The NMR spectra recorded from this mixture revealed the diastereomeric ratio of the aldol reaction. The major product was separated by column chromatography.

N-(syn-2''[R],3''[S]-3''-Hydroxy-2''-methyl-butyryl)-3,5-O-isopropylidene-α-D-xylofurano[1,2, d]oxazolidin-2'-one **9**

Aldol reaction of 3 mmol (0.81 g) **4** with 3.3 mmol (0.18 ml) acetaldehyde afforded 0.35 g (37%) **9** after column chromatography as the major product. Mp 149°C (CH_2Cl_2, petroleum ether); $[\alpha]_D^{20}$=+138.6 (c=0.75, acetone); ^{1}H-NMR (500.1 MHz): δ=6.377 (d,1H,$^3J_{1,2}$=5.7 Hz, H-1), 4.817 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.493 (d,1H, $^3J_{3,4}$=2.5 Hz, H-3), 3.894 (m,1H, H-4), 4.104 (m, 2H, H-5, H-5'), 1.454 (s, 3H, H-7), 1.388 (s, 3H, H-7'), 3.652 (dq, 1H, $^3J_{2'',3''}$ ($^3J_{\alpha,\beta}$)=3.2 Hz, H-2''), 4.160 (dq, 1H, $^3J_{3'',4''}$=6.4 Hz, H-3''), 1.189 (d, 3H, H-4''), 1.230 (d, 3H, $^3J_{2'',Me}$=7.0 Hz, C-2''-CH_3), 2.655 (s, 1H, OH); ^{13}C-NMR (125–8 MHz): δ=86.37 (C-1), 81.52 (C-2), 71.55 (C-3), 72.20 (C-4), 59.42 (C-5), 98.08 (C-6), 28.54 (C-7), 18.82 (C-7'), 151.85 (NCOO), 176.2 (C-1''), 43.48 (C-2''), 67.47 (C-3''), 10.28 (C-4''), 10.28 (C-2''-CH_3); M=315.3 g mol^{-1}; MS (CI, iso-butane): m/z=317 (MH_2^+, 100), 299 (MH_2^+, 20); Anal. calcd. for $C_{14}H_{21}O_7N$: C 53.33, H 6.71, N 4.44. Found C 53.36, H 6.54, N 4.43.

N-(syn-2''[R],3''[S]-3''-Hydroxy-2''-methyl-pent-4''-enoyl)-3,5-O-isopropylidene-α-D-xylofurano[1,2,d]oxazolidin-2'-one ***10***

In the way described above imide **4** (3 mmol) and 3.3 mmol (0.22 ml) acrolein gave 0.38 g (39%) aldol **10**. Mp 135°C (CH_2Cl_2, petroleum ether); $[\alpha]_D^{20}$=+113.3 (c=0.52, acetone); ^{1}H-NMR (500.1 MHz): δ=6.364 (d,1H,$^3J_{1,2}$=5.1 Hz, H-1), 4.822 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.494 (d,1H, $^3J_{3,4}$=2.5 Hz, H-3), 3.909 (m,1H, H-4), 4.099 (m, 2H, H-5, H-5'), 1.456 (s, 3H, H-7), 1.389 (s, 3H, H-7'), 3.804 (dq, 1H, $^3J_{2'',3''}$ ($^3J_{\alpha,\beta}$)=3.2 Hz, H-2''), 4.533 (dd, 1H, $^3J_{3'',4''}$=7.0 Hz, H-3''), 5.825 (ddd, 1H, $^3J_{4'',5t''}$=17.2 Hz, H-4''), 5.345 (dd, 1H, $^2J_{5t'',5c''}$=1.3 Hz, H-5t''), 5.212 (dd, 1H, $^3J_{4'',5c''}$=10.8 Hz, H-5c''), 1.182 (d, 3H, $^3J_{2'',Me}$=7.0 Hz, C-2''–CH_3), 2.718 (s, 1H, OH); ^{13}C-NMR (125.8 MHz): δ=86.55 (C-1), 81.53 (C-2), 71.53 (C-3), 72.40 (C-4), 59.42 (C-5), 98.12 (C-6), 28.58 (C-7), 18.85 (C-7'), 151.83 (NCOO), 176.08 (C-1''), 42.72 (C-2''), 72.21 (C-3''), 136.89 (C-4''), 116.48 (C-5''), 10.56 (C-2''–CH_3); M=327.3 g mol^{-1}; MS (CI, iso-butane): m/z=328 (MH^+, 24), 310 (MH^+–H_2O, 100); Anal. calcd. for $C_{15}H_{21}O_7N$: C 55.04, H 6.47, N 4.28. Found C 54.84, H 6.44, N 3.53.

N-(syn-2''[R],3''[S]-3''-Hydroxy-2''-methyl-hexanoyl)-3,5-O-isopropylidene-α-D-xylofurano[1,2,d]oxazolidin-2'-one ***11***

The lithium enolate of **4** (3 mmol) was reacted with butyraldehyde (3.3 mmol, 0.30 ml) as described above to obtain 0.30 g (29%) **11** as the major product. Mp 123°C (dichloromethane/petroleum ether); $[\alpha]_D^{20}$=+136.9 (c=1.26, acetone); ^{1}H-NMR (500.1 MHz): δ=6.372 (d,1H,$^3J_{1,2}$=5.7 Hz, H-1), 4.817 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.491 (d,1H, $^3J_{3,4}$=2.5 Hz, H-3), 3.893 (m,1H, H-4), 4.102 (m, 2H, H-5, H-5'), 1.452 (s, 3H, H-7), 1.386 (s, 3H, H-7'), 3.657 (q, 2H, $^3J_{2'',3''}$ ($^3J_{\alpha,\beta}$)=2.6 Hz, H-2''), 3.955 (dt, 1H, $^3J_{3'',4''}$=3.8 Hz, H-3''), 1.509 (m, 2H, $^3J_{4'',5''}$=6.4 Hz, H-4''), 1.350 (m, 2H, $^3J_{5'',6''}$=7.0 Hz, H-5''), 0.918 (t, 3H, H-6''), 1.216 (d, 3H, $^3J_{2'',Me}$=6.4 Hz, C-2''–CH_3), 2.621 (s, 1H, OH); ^{13}C-NMR (125.8 MHz): δ=86.39 (C-1), 81.52 (C-2), 71.56 (C-3), 72.21 (C-4), 59.42 (C-5), 98.09 (C-6), 28.55 (C-7), 18.83 (C-7'), 151.73 (NCOO), 176.84 (C-1''), 42.45 (C-2''), 70.91 (C-3''), 35.90 (C-4''), 19.14 (C-5''), 13.92 (C-6''), 10.03 (C-2''–CH_3); M=343.4 g mol^{-1}; MS (CI, iso-butane): m/z=345 (MH_2^+, 100), 327 (MH_2^+–H_2O, 20); Anal. calcd. for $C_{16}H_{25}O_7N$: C 55.97, H 7.34, N 4.08. Found C 56.24, H 7.25, N 4.10.

N-(syn-2''[R],3''[S]-2'',4''-Dimethyl-3''-hydroxy-pentanoyl)-3,5-O-isopropylidene-α-D-xylofurano[1,2,d]oxazolidin-2'-one ***12***

The general aldol procedure was followed using 3 mmol (0.81 g) **4** and 3.3 mmol (0.30 ml) isobutyraldehyde to yield 0.40 g (39%) of **12** as the major product. Mp 135°C (dichloromethane/petroleum ether); $[\alpha]_D^{20}$=+119.7 (c=0.60, acetone); ^{1}H-NMR (500.1 MHz): δ=6.393 (d,1H,$^3J_{1,2}$=5.5 Hz, H-1), 4.843 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.522 (d,1H, $^3J_{3,4}$=2.2 Hz, H-3), 3.923 (m,1H, H-4), 4.129 (m, 2H, H-5, H-5'), 1.477 (s, 3H, H-7), 1.411 (s, 3H, H-7'), 3.874 (dq, 2H, $^3J_{2'',3''}$ ($^3J_{\alpha,\beta}$)=2.6 Hz, H-2''), 3.530 (dt, 1H, $^3J_{3'',4''}$=7.0 Hz, H-3''), 1.695 (m, 1H, $^3J_{4'',5'''}$=6.4 Hz, H-4''), 1.013 (d, 3H, $^3J_{4'',5''}$=6.4 Hz, H-5''), 0.881 (d, 3H, H-5'''), 1.202 (d, 3H, $^3J_{2'',Me}$=7.2 Hz, C-2''–CH_3), 2.645 (s, 1H, OH); ^{13}C-NMR (125.8 MHz): δ=86.45 (C-1), 81.55 (C-2), 71.61 (C-3), 72.22 (C-4), 59.45 (C-5), 98.10 (C-6), 28.57 (C-7), 18.85 (C-7'), 151.58 (NCOO), 177.17 (C-1''), 40.13 (C-2''), 76.33 (C-3''), 30.83 (C-4''), 19.31 (C-5''), 18.80 (C-5'''), 9.55 (C-2''–CH_3); M=343.4 g mol^{-1}; MS (CI, iso-butane): m/z=345 (MH_2^+, 54), 327 (**4**H_2^+–H_2O, 100); Anal. calcd. for $C_{16}H_{25}O_7N$: C 55.97, H 7.34, N 4.08. Found C 56.51, H 7.28, N 4.05.

N-(syn-2''[R],3''[S]-3''-Hydroxy-2''-methyl-octanoyl)-3,5-O-isopropylidene-α-D-xylofurano[1,2,d]oxazolidin-2'-one ***13***

This isomer was obtained as the major compound (0.28 g, 25%) from the aldol reaction of 3 mmol (0.81 g) **4** with 0.40 ml (3.3 mmol) hexanal according to the general procedure. Mp 108°C (dichloromethane/petroleum ether); $[\alpha]_D^{20}$=+114.9 (c=1.27, acetone); ^{1}H-NMR (500.1 MHz): δ (d,1H,$^3J_{1,2}$=5.1 Hz, H-1), 4.808 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.482 (d,1H, $^3J_{3,4}$=1.9 Hz, H-3), 3.883

(m,1H, H-4), 4.090 (m, 2H, H-5, H-5′), 1.442 (s, 3H, H-7), 1.373 (s, 3H, H-7′), 3.647 (q, 2H, $^3J_{2'',3''}$ ($^3J_{\alpha,\beta}$)=2.5 Hz, H-2″), 3.916 (m, 1H, H-3″), 1.85–1.26 (m, 8H, H-4″–H-7″), 0.860 (t, 3H, $^3J_{7'',8''}$=7.0 Hz, H-6″), 1.198 (d, 3H, $^3J_{2'',Me}$=7.0 Hz, C-2″–*C*H$_3$), 2.660 (s, 1H, OH); ^{13}C-NMR (125.8 MHz): δ=86.40 (C-1), 81.50 (C-2), 71.20 (C-3), 72.18 (C-4), 59.41 (C-5), 98.07 (C-6), 28.54 (C-7), 18.81 (C-7′), 151.75 (NCOO), 176.76 (C-1″), 42.54 (C-2″), 71.53 (C-3″), 33.75 (C-4″), 31.66 (C-5″), 25.59 (C-6″), 22.51 (C-7″), 13.96 (C-8″), 9.99 (C-2″–*C*H$_3$); M=371.4 g mol^{-1}; MS (CI, iso-butane): m/z=373 (MH_2^+, 100), 355 ($MH_2^+-H_2O$, 48); Anal. calcd. for $C_{18}H_{29}O_7N$: C 58.21, H 7.87, N 3.77. Found C 58.40, H 7.79, N 3.99.

*N-(*syn*-2″[R],3″[S]-3″-Hydroxy-2″-methyl-decanoyl)-3,5-O-isopropylidene-α-*D*-xylofurano[1,2, d]oxazolidin-2′-one* ***14***

This isomer was obtained as the major compound (0.42 g, 35%) from the aldol reaction of 3 mmol (0.81 g) **4** with 0.52 ml (3.3 mmol) octanal according to the general procedure. Mp 108°C (dichloromethane/petroleum ether); $[\alpha]_D^{20}$=+110.3 (c=2.08, acetone); ^{1}H-NMR (500.1 MHz): δ=6.372 (d,1H, $^3J_{1,2}$=5.7 Hz, H-1), 4.816 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.491 (d,1H, $^3J_{3,4}$=2.5 Hz, H-3), 3.893 (m,1H, H-4), 4.103 (m, 2H, H-5, H-5′), 1.453 (s, 3H, H-7), 1.387 (s, 3H, H-7′), 3.658 (q, 2H, $^3J_{2'',3''}$ ($^3J_{\alpha,\beta}$)=2.5 Hz, H-2″), 3.938 (m, 1H, H-3″), 1.53–1.25 (m, 8H, H-4″–H-9″), 0.862 (t, 3H, $^3J_{9'',10''}$=7.0 Hz, H-6″), 1.214 (d, 3H, $^3J_{2'',Me}$=7.0 Hz, C-2″–*C*H$_3$), 2.630 (s, 1H, OH); ^{13}C-NMR (125.8 MHz): δ=86.42 (C-1), 81.55 (C-2), 71.59 (C-3), 72.24 (C-4), 59.45 (C-5), 98.11 (C-6), 28.58 (C-7), 18.86 (C-7′), 151.76 (NCOO), 176.87 (C -1″), 42.56 (C-2″), 71.23 (C-3″), 33.81 (C-4″), 31.80 (C-5″), 29.48 (C-6″), 29.20 (C-7″), 25.98 (C-8″), 22.62 (C-9″), 14.06 (C-10″), 10.04 (C-2″–*C*H$_3$); M=399.5 g mol^{-1}; MS (CI, iso-butane): m/z=401 (MH_2^+, 100), 383 ($MH_2^+-H_2O$, 86); Anal. calcd. for $C_{20}H_{33}O_7N$: C 60.13, H 8.33, N 3.51. Found C 60.48, H 8.20, N 3.64.

*N-(*syn*-2″[R],3″[S]-2″-Ethyl-3″-hydroxy-pent-4″-enoyl)-3,5-O-isopropylidene-α-*D*-xylofurano[1, 2,d]oxazolidin-2′-one* ***15***

In the way described above imide **5** (3 mmol, 0.86 g) and 3.3 mmol (0.22 ml) acrolein gave 0.35 g (34%) aldol **15**. Mp 105°C (CH_2Cl_2, petroleum ether); $[\alpha]_D^{20}$=+98.5 (c=0.55, acetone); ^{1}H-NMR (500.1 MHz): δ=6.393 (d,1H, $^3J_{1,2}$=5.1 Hz, H-1), 4.804 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.480 (d,1H, $^3J_{3,4}$=2.5 Hz, H-3), 3.887 (m,1H, $^3J_{4,5}$=1.9 Hz, H-4), 4.103 (dd, 1H, $^2J_{5,5'}$=−13.4 Hz,H-5), 4.070 (dd, 1H, $^3J_{4,5'}$=1.9 Hz, H-5′), 1.450 (s, 3H, H-7), 1.381 (s, 3H, H-7′), 3.922 (m, 1H, $^3J_{2'',3''}$ ($^3J_{\alpha,\beta}$)=4.5 Hz, $^3J_{2'',Et}$=9.5 Hz, H-2″), 4.411 (dd, 1H, $^3J_{3'',4''}$=6.4 Hz, H-3″), 5.870 (ddd, 1H, $^3J_{4'',5t''}$=17.2 Hz, H-4″), 5.182 (dd, 1H, $^2J_{5t'',5c''}$=1.3 Hz, H-5t″), 5.299 (dd, 1H, $^3J_{4'',5c''}$=10.8 Hz, H-5c″), 1.796 (m, 1H, $^3J_{Et}$=7.6 Hz, C-2″–*C*H$_2$), 1.626 (m, 1H, $^3J_{2'',Et'}$=4.5 Hz, C-2″–*C*H$_2$′), 0.899 (dd, 3H, $^3J_{Et'}$=7.6 Hz, -CH$_2$–*C*H$_3$), 2.392 (s, 1H, OH); ^{13}C-NMR (125.8 MHz): δ=86.56 (C-1), 81.31 (C-2), 71.33 (C-3), 72.32 (C-4), 59.40 (C-5), 98.09 (C-6), 28.59 (C-7), 18.84 (C-7′), 152.29 (NCOO), 174.36 (C-1″), 49.83 (C-2″), 73.51 (C-3″), 137.07 (C-4″), 116.76 (C-5″), 20.29 (C-2″–*C*H$_2$), 11.90 (-CH$_2$–*C*H$_3$); M=341.4 g mol^{-1}; MS (CI, iso-butane): m/z=341 (MH^+, 22), 324 (MH^+-H_2O, 100); Anal. calcd. for $C_{16}H_{23}O_7N$: C 56.30, H 6.79, N 4.10. Found C 55.57, H 6.73, N 3.42.

*N-(*syn*-2″[R],3″[S]-2″-Ethyl-3″-hydroxy-4″-methyl-pentanoyl)-3,5-O-isopropylidene-α-*D*-xylofurano[1,2,d]oxazolidin-2′-one* ***16***

The general aldol procedure was followed using 3 mmol (0.86 g) **5** and 3.3 mmol (0.30 ml) isobutyraldehyde to yield 0.41 g (38%) of **16** as the major product. Mp syrupy; $[\alpha]_D^{20}$=+96.4 (c=0.66, acetone); ^{1}H-NMR (500.1 MHz): δ=6.380 (d,1H, $^3J_{1,2}$=5.1 Hz, H-1), 4.795 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.485 (d,1H, $^3J_{3,4}$=1.9 Hz, H-3), 3.862 (m,1H, $^3J_{4,5}$=1.9 Hz, H-4), 4.098 (dd, 1H, $^2J_{5,5'}$=−13.4 Hz, H-5), 4.067 (d, 1H, $^3J_{4,5'}$=0 Hz, H-5′), 1.439 (s, 3H, H-7), 1.369 (s, 3H, H-7′), 3.979 (m, 2H, $^3J_{2'',3''}$ ($^3J_{\alpha,\beta}$)=3.8 Hz, H-2″), 3.508 (dd, 1H, $^3J_{3'',4''}$=7.0 Hz, H-3″), 1.708 (m, 1H, $^3J_{4'',5'''}$=7.0 Hz, H-4″), 0.958 (d, 3H, $^3J_{4'',5''}$=6.4 Hz, H-5″), 0.901 (d, 3H, H-5‴), 1.848 (m, 1H, $^3J_{2'',Et}$=9.5

Hz, C-2''–CH_2), 1.727 (m, 1H, $^3J_{2'',Et'}$=4.5 Hz, $^3J_{Et'}$=7.6 Hz, C-2''–CH_2'), 0.923 (dd, 3H, $^3J_{Et}$=7.6 Hz,-CH_2–CH_3), 2.382 (s, 1H, OH); ^{13}C-NMR (125.8 MHz): δ=86.56 (C-1), 81.27 (C-2), 71.45 (C-3), 72.28 (C-4), 59.44 (C-5), 98.07 (C-6), 28.55 (C-7), 18.85 (C-7'), 151.86 (NCOO), 176.33 (C-1''), 46.63 (C-2''), 76.70 (C-3''), 31.29 (C-4''), 19.61 (C-5''), 19.20 (C-5'''), 18.47 (C-2''–CH_2), 11.56 (-CH_2–CH_3); M=357.4 g mol^{-1}; MS (CI, iso-butane): m/z=358 (MH^+, 100), 340 (MH^+-H_2O, 28); Anal. calcd. for $C_{17}H_{27}O_7N$: C 57.13, H 7.61, N 3.92. Found C 55.13, H 7.55, N 2.75.

*N-(3''[R]-3''-Hydroxy-3''-phenyl-propionyl)-3,5-O-benzylidene-α-*D*-xylofurano[1,2,d]oxazolidin-2'-one* ***17***

The general aldol procedure was followed using 0.92 g (3 mmol) **3** and 0.34 ml (3.3 mmol) benzaldehyde to yield 0.32 g (26%) of **17** as the major product. Mp 182°C (dichloromethane/petroleum ether); $[\alpha]_D^{20}$=+47.2 (c=0.61, acetone); ^{1}H-NMR (500.1 MHz): δ=6.457 (d,1H,$^3J_{1,2}$=5.7 Hz, H-1), 4.944 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.658 (d,1H, $^3J_{3,4}$=1.9 Hz, H-3), 4.003 (m,1H, $^3J_{4,5}$=0 Hz, H-4), 4.519 (d, 1H, $^2J_{5,5'}$=−13.4, H-5), 4.181 (dd, 1H, $^3J_{4,5'}$=1.9 Hz, H-5'), 5.516 (s, 1H, H-6), 7.47–7.37 (m, 10H, H_{arom}), 3.413 (dd, 1H, $^3J_{2'',3''}$=9.5 Hz, $^2J_{2'',2'''}$=−17.8, H-2''), 3.294 (dd, 1H, $^3J_{2''',3''}$=3.2 Hz, H-2'''), 5.249 (dd, 1H, H-3''), 3.120 (s, 1H, OH); ^{13}C-NMR (125.8 MHz): δ=86.62 (C-1), 80.96 (C-2), 72.00 (C-3), 77.58 (C-4), 65.89 (C-5), 99.71 (C-6), 151.86 (NCOO), 171.80 (C-1''), 44.76 (C-2''), 69.84 (C-3''), 142.13–125.81 (C_{arom}); M=411.4 g mol^{-1}; MS (CI, iso-butane): m/z=394 (MH^+-H_2O, 44), 107 (benzaldehyde−H^+, 100); Anal. calcd. for $C_{22}H_{21}O_7N$: C 64.23, H 5.14, N 3.40. Found C 63.62, H 5.15, N 2.76.

*N-(*syn*-2''[R],3''[R]-3''-Hydroxy-2''-methyl-3''-phenyl-propionyl)-3,5-O-isopropylidene-α-*D*-xylofurano[1,2,d]oxazolidin-2'-one* ***18***

Aldol reaction of 0.81 g (3 mmol) **4** with 0.34 ml (3.3 mmol) benzaldehyde was followed the general procedure to give an inseparable mixture of diastereomers with **18** as the major diastereomer. ^{1}H-NMR (500.1 MHz): δ=6.211 (d,1H,$^3J_{1,2}$=5.1 Hz, H-1), 4.676 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.453 (d,1H, $^3J_{3,4}$=2.5 Hz, H-3), 3.858 (m,1H, H-4), 4.080 (m, 2H, H-5, H-5'), 1.436 (s, 3H, H-7), 1.375 (s, 3H, H-7'), 3.983 (dq, 1H, $^3J_{2'',3''}$ ($^3J_{\alpha,\beta}$)=3.8 Hz, H-2''), 5.064 (d, 1H, H-3''), 1.184 (d, 3H, $^3J_{2'',Me}$=7.0 Hz, C-2''–CH_3), 2.934 (s, 1H, OH), 7.36–7.25 (m, 5H, H_{arom}); ^{13}C-NMR (125.8 MHz): δ=86.50 (C-1), 81.56 (C-2), 71.61 (C-3), 72.12 (C-4), 59.44 (C-5), 98.10 (C-6), 28.59 (C-7), 18.84 (C-7'), 151.63 (NCOO), 175.84 (C-1''), 45.01 (C-2''), 73.57 (C-3''), 10.69 (C-2''–CH_3), 141.21–126.08 (C_{arom}); M=377.4 g mol^{-1}; MS (CI, iso-butane): m/z=360 (MH_2^+, 100); Anal. calcd. for $C_{19}H_{23}O_7N$: C 60.47, H 6.14, N 3.73. Found C 60.46, H 6.43, N 2.61.

*N-(*syn*-2''[R],3''[S]-3''-Hydroxy-2''-methyl-5''-phenyl-pent-4''-enoyl)-3,5-O-isopropylidene-α-*D*-xylofurano[1,2,d]oxazolidin-2'-one* ***19***

As described above lithium mediated aldol reaction of 0.42 ml (3.3 mmol) *trans*-cinnamaldehyde with 3 mmol (0.81 g) **4** gave 0.56 g (46%) of **19** as the major product. Mp 114°C (dichlo romethane / petroleum ether); $[\alpha]_D^{20}$=+105.7 (c=1.63, acetone); ^{1}H-NMR (500.1 MHz): δ=6.378 (d,1H,$^3J_{1,2}$=5.5 Hz, H-1), 4.785 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.503 (d,1H, $^3J_{3,4}$=2.8 Hz, H-3), 3.911 (m,1H, H-4), 4.121 (m, 2H, H-5, H-5'), 1.470 (s, 3H, H-7), 1.406 (s, 3H, H-7'), 3.896 (dq, 1H, $^3J_{2'',3''}$ ($^3J_{\alpha,\beta}$)<2 Hz, H-2''), 4.670 (d, 1H, $^3J_{3'',4''}$=6.1 Hz, H-3''), 6.215 (dd, 1H, $^3J_{4'',5''}$=16.0 Hz, H-4''), 6.672 (d, 1H, H-5''), 7.40–7.26 (m, 5H, H_{arom}), 1.289 (d, 3H, $^3J_{2'',Me}$=7.0 Hz, C-2''–CH_3), 2.771 (s, 1H, OH); ^{13}C-NMR (125.8 MHz): δ=86.45 (C-1), 81.57 (C-2), 71.58 (C-3), 72.55 (C-4), 59.43 (C-5), 98.10 (C-6), 28.57 (C-7), 18.84 (C-7'), 151.85 (NCOO), 175.79 (C-1''), 43.34 (C-2''), 72.18 (C-3''), 131.77 (C-4''), 127.79 (C-5''), 11.12 (C-2''–CH_3), 136.45–126.52 (C_{arom}); M=403.4 g mol^{-1}; MS (CI, iso-butane): m/z=405 (MH_2^+, 4), 387 ($MH_2^+-H_2O$, 54), 133 (cinnamaldehyde−H^+, 100); Anal. calcd. for $C_{21}H_{25}O_7N$: C 62.52, H 6.25, N 3.47. Found C 59.13, H 5.81, N 3.20.

N-(anti-2''[R],3''[S]-2''-Ethyl-3''-hydroxy-3''-phenyl-propionyl)-3,5-O-isopropylidene-α-D-xylofurano[1,2,d]oxazolidin-2'-one ***20***

Aldol reaction of 0.86 g (3 mmol) **5** with 0.34 ml (3.3 mmol) benzaldehyde was followed the general procedure to give **20** as the major diastereomer (0.31 g, 26%). Mp 151°C (dichloromethane / petroleum ether); $[\alpha]_D^{20}$=+30.8 (c=1.49, acetone); ^{1}H-NMR (500.1 MHz): δ=6.335 (d,1H,$^3J_{1,2}$=5.7 Hz, H-1), 4.740 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.366 (d,1H, $^3J_{3,4}$=2.5 Hz, H-3), 3.389 (m,1H, H-4), 3.998 (m, 2H, H-5, H-5'), 1.421 (s, 3H, H-7), 1.364 (s, 3H, H-7'), 4.295 (m, 1H, $^3J_{2'',3''}$ ($^3J_{\alpha,\beta}$)=7.0 Hz, H-2''), 4.857 (d, 1H, H-3''), 1.798 (m, 1H, C-2''–CH_2), 1.505 (m, 1H, $^3J_{Et'}$=7.0 Hz, C-2''–CH_2'), 0.886 (dd, 3H, $^3J_{Et}$=7.0 Hz,-CH_2–CH_3), 2.944 (s, 1H, OH), 7.36–7.25 (m, 5H, H_{arom}); ^{13}C-NMR (125.8 MHz): δ=86.25 (C-1), 81.01 (C-2), 70.77 (C-3), 72.34 (C-4), 59.27 (C-5), 98.01 (C-6), 28.56 (C-7), 18.77 (C-7'), 151.89 (NCOO), 175.91 (C-1''), 50.94 (C-2''), 75.63 (C-3''), 22.78 (C-2''–CH_2), 11.45 (-CH_2–CH_3), 142.10–126.36 (C_{arom}); M=391.4 g mol^{-1}; MS (CI, iso-butane): m/z=375 (MH^+-H_2O, 100); Anal. calcd. for $C_{20}H_{25}O_7N$: C 61.37, H 6.44, N 3.58. Found C 61.38, H 6.30, N 3.56.

N-(syn-2''[S],3''[R]-3''-Hydroxy-2''-phenyl-butyryl)-3,5-O-isopropylidene-α-D-xylofurano[1,2,d]oxazolidin-2'-one ***21***

Lithium mediated aldol reaction of 3 mmol **7** (1.00 g) with 0.18 ml (3.3 mmol) acetaldehyde afforded 0.25 g (22%) **21**. Mp 142°C (dichloromethane/petroleum ether); $[\alpha]_D^{20}$=+118.8 (c=0.58, acetone); ^{1}H-NMR (500.1 MHz): δ=5.798 (d,1H,$^3J_{1,2}$=5.7 Hz, H-1), 4.628 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.396 (d,1H, $^3J_{3,4}$=2.5 Hz, H-3), 3.740 (m,1H, $^3J_{4,5}$=2.5 Hz, H-4), 4.104 (dd, 1H, $^2J_{5,5'}$=−13.4 Hz, H-5), 4.008 (d, 1H, $^3J_{4,5'}$=0 Hz, H-5'), 1.451 (s, 3H, H-7), 1.385 (s, 3H, H-7'), 3.600 (d, 1H, $^3J_{2'',3''}$ ($^3J_{\alpha,\beta}$)<2 Hz, H-2''), 6.412 (dq, 1H, $^3J_{3'',4''}$=6.4 Hz, H-3''), 1.574 (d, 3H, H-4''), 7.32–7.25 (m, 5H, H_{arom}), 3.600 (s, 1H, OH); ^{13}C-NMR (125.8 MHz): δ=86.18 (C-1), 82.28 (C-2), 70.52 (C-3), 72.28 (C-4), 59.57 (C-5), 98.02 (C-6), 28.84 (C-7), 18.65 (C-7'), 154.85 (NCOO), 169.58 (C-1''), 41.30 (C-2''), 76.15 (C-3''), 19.94 (C-4''), 133.49–127.28 (C_{arom}); M=377.4 g mol^{-1}; MS (CI, iso-butane): m/z=243 (MH^+ − 1-phenyl-propan-2-ol, 100); Anal. calcd. for $C_{19}H_{23}O_7N$: C 60.47, H 6.14, N 3.71. Found C 60.45, H 5.77, N 3.69.

N-(syn-2''[S],3''[R]-2''-Benzyl-3''-hydroxy-butyryl)-3,5-O-isopropylidene-α-D-xylofurano[1,2,d]oxazolidin-2'-one ***22***

Lithium mediated aldol reaction of 3 mmol **8** (1.04 g) with 0.18 ml (3.3 mmol) acetaldehyde afforded 0.30 g (26%) **22**. Mp 150°C (dichloromethane/petroleum ether); $[\alpha]_D^{20}$=+30.4 (c=0.54, acetone); ^{1}H-NMR (500.1 MHz): δ=6.256 (d,1H,$^3J_{1,2}$=5.7 Hz, H-1), 4.651 (d,1H, $^3J_{2,3}$=0 Hz, H-2), 4.244 (d,1H, $^3J_{3,4}$=2.5 Hz, H-3), 2.935 (m,1H, $^3J_{4,5}$=1.9 Hz, H-4), 3.927 (dd, 1H, $^2J_{5,5'}$=−14.0 Hz, H-5), 3.887 (d, 1H, $^3J_{4,5'}$=0 Hz, H-5'), 1.384 (s, 3H, H-7), 1.335 (s, 3H, H-7'), 4.339 (ddd, 1H, $^3J_{2'',3''}$ ($^3J_{\alpha,\beta}$)=6.4 Hz, $^3J_{2'',Bn}$=4.5 Hz, H-2''), 4.149 (m, 1H, $^3J_{3'',4''}$=6.4 Hz, H-3''), 1.284 (d, 3H, H-4''), 3.039 (dd, 1H, $^2J_{Bn,Bn'}$=−13.4 Hz, H_{Bn}), 3.020 (dd, 1H, $^3J_{2'',Bn'}$=6.4 Hz, H'_{Bn}), 7.21–7.13 (m, 5H, H_{arom}), 2.558 (s, 1H, OH); ^{13}C-NMR (125.8 MHz): δ=86.06 (C-1), 80.90 (C-2), 70.41 (C-3), 72.23 (C-4), 59.16 (C-5), 97.99 (C-6), 28.57 (C-7), 18.74 (C-7'), 152.04 (NCOO), 174.85 (C-1''), 50.58 (C-2''), 68.45 (C-3''), 19.85 (C-4''), 34.44 (C_{Bn}), 138.40–126.11 (C_{arom}); M=391.4 g mol^{-1}; MS (CI, iso-butane): m/z=392 (MH^+, 100), 374 (MH^+-H_2O, 16); Anal. calcd. for $C_{20}H_{25}O_7N$: C 61.53, H 6.20, N 3.59. Found C 61.79, H 6.38, N 3.60.

General procedure for the cleavage of the elaborated N-acyl derivatives with lithium hydroperoxide

One equivalent of the elaborated N-acyl derivative was dissolved in a 3:1 mixture of THF/H_2O at 0°C and treated stepwise with four equiv. 30% aqueous hydrogen peroxide and two equiv. LiOH*H_2O. After complete hydrolysis (TC-control) excess peroxide was destroyed by treatment with 1,5 N aqueous Na_2SO_3-solution. The solution's pH-factor was set to 9–10 using sat. aqueous $NaHCO_3$-solution. Following removal of THF *in vacuo* the aqueous residue was exhaustively extracted with CH_2Cl_2 to

Table 3. Specific optical rotations of the β-hydroxy carboxylic acids[22–27]

β-hydroxy carboxylic acid	aldol product	$[\alpha]^{20}_{D,exp}$	$[\alpha]^{20}_{D,Lit}$
syn-2[*R*],3[*S*]-3-hydroxy-2-methyl-butanoic acid	**9**	+ 7.0 (c = 0.45, H_2O)	+ 7.5 (c = 10, H_2O)[22]
syn-2[*R*],3[*S*]-3-hydroxy-2-methyl-pent-4-enoic acid	**10**	- 1.9 (c = 0.3, CH_2Cl_2)	- 2.01 (c = 0.2, CH_2Cl_2)[23]
syn-2[*R*],3[*S*]-2,4-dimethyl-3-hydroxy-pentanoic acid	**12**	+ 9.7 (c = 0.3, CH_2Cl_2)	+ 9.1 (c = 0.3, CH_2Cl_2)[24]
3[*R*]-3-hydroxy-3-phenyl-propionic acid	**17**	+ 13.7 (c = 0.3, CH_2Cl_2)	+ 14.9 (c = 0.3, CH_2Cl_2)[25]
syn-2[*R*],3[*R*]-3-hydroxy-2-methyl-3-phenyl-propionic acid	**18**[a]	+ 14.1 (c = 0.3, CH_2Cl_2)	- 26.4 (c = 0.3, CH_2Cl_2)[26] (2[*S*],3[*S*]-enantiomer)
syn-2[*S*],3[*R*]-2- benzyl-3-hydroxy-butanoic acid	**19**	- 61.5 (c = 0.3, CH_2Cl_2)	- 63.5 (c = 0.3, CH_2Cl_2)[27]

[a] major aldol product **18** was still contamined with minor one(s) when cleaved following the general procedure

return the auxiliary upon evaporation of the organic solvent. The aqueous phase was acidified with 2 N aqueous HCl and extracted repeatedly with ethyl acetate to afford the pure β-hydroxy carboxylic acid after cautious removal of the solvent.

The following specific rotations were determined for the carboxylic acids obtained upon cleavage of **9**, **10**, **12**, **17**, **18**, and **22**, respectively (Table 3).

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