New ureas containing glycosyl and diphenylphosphinyl scaffolds: synthesis and the first attempts to use them in asymmetric synthesis

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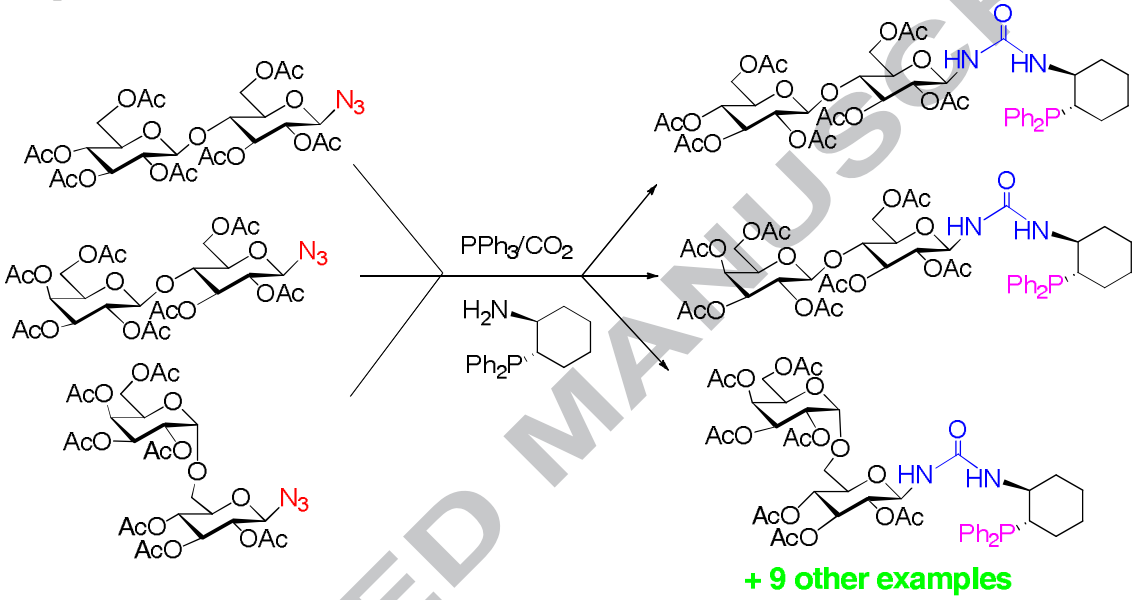
Graphical Abstract:



Abstract:
Chiral ureas containing glycosyl and diphenylphosphinyl scaffolds were found to be an effective organocatalyst. They were synthesised in high yields by a one-pot tandem Staudinger/aza-Wittig coupling reaction. The first attemps of using them in asymmetric synthesis are presented. Yields of the Morita-Baylis-Hillman reaction were moderate with an enantiomeric excess of up to 80 %.

Keywords: saccharides, organocatalysts, chiral ligands, urea

1. Introduction

Saccharides, as naturally occurring compounds with defined stereogenic centre, are useful building blocks for many interesting structures.[1] Carbohydrates, which are inexpensive and readily available natural materials, have only recently also been employed as chiral backbones of organocatalysts. Examples of effective catalysts with a thiourea bridge which are often combined with saccharides, can be found in the literature.[2,9] Much less examples of application of urea saccharide organocatalyst in asymmetric synthesis can be found in the chemical reports.[3] Another significant feature of saccharides is their hydrophilicity which enables to perform enantioselective syntheses in aqueous media.

A wide range of saccharide combinations with chiral phosphines that incorporate a urea bridge is presented in this paper which describes the derivatives able to act both as organocatalysts or chiral ligands in metal complexs. Derivative **L1** is an effective chiral ligand in the stereoselective synthesis of vinyl-tetrahydrofurans.[4] The positive results of this reaction encouraged us to obtain a larger group of this type of compounds and to study them also as organocatalysts. The saccharide derivatives that include a chiral phosphine moiety were tested as organocatalysts in the Morita-Baylis-Hillman and aza-Henry reaction. There are known examples of effective thiourea sugar derivatives acting as organocatalysts in such type of reactions[1c,d,2f,11d], but there are no reports describing the use of saccharides urea derivatives.

Enantioselective synthesis remains a challenge in organic chemistry due to the great importance of single stereoisomers in biologicall processes and also in many industrial sectors such as pharmaceutical and food chemistry. The activity of such optically pure compounds strongly depends on their absolute configuration. Chemical yields and stereoselectivity of the asymmetric reaction are related with the choice of the appropriate chiral ligand/catalyst in such transformation. Organophosphane derivatives constitute an important class of compounds using as chiral catalysts in asymmetric synthesis. [5,6]

Enantioselective reactions with organocatalysts have come into prominence.[7] The chiral organic molecules sometimes various complex structure, can interact in the transition state with substrates resulting in asymmetric induction leading to the desired products in an enantioselective process. Nevertheless, it is very important to exclude even trace amounts of metal deriving from organocatalysts before the application of desired chiral products in the industry (especially pharmaceutical one).

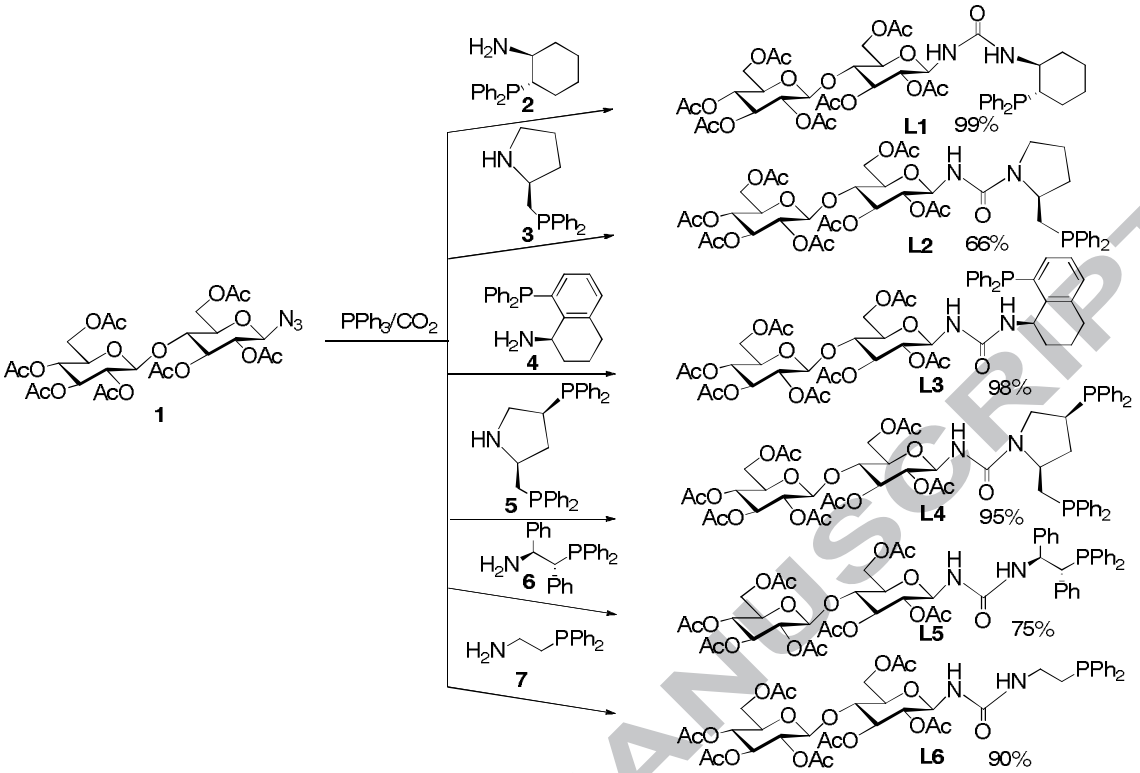
The Morita-Baylis-Hillman (MBH) reaction is used to the C-C bond formation[8-10] and is known as a powerful tool for the construction of densely functionalized alcohols. It is well established that the MBH reaction efficiently covers simple starting materials into highly functionalized product which are versatile synthetic intermediates in organic synthesis. The asymmetric version of this reaction has attracted much attention in recent years.

The aza-Henry reaction is a highly valuable C-C bond forming process. The resulting nitroamine adduct can be either reduced producing 1,2 diamines or oxidized affording α-amino acids. They have remarkable structural units, which we can find in biologically active compounds or natural products. These moieties can be used as valuable building block, chiral auxiliaries, and metal ligands.[11]

2. Results and discussion

2.1. Synthesis organocatalysts

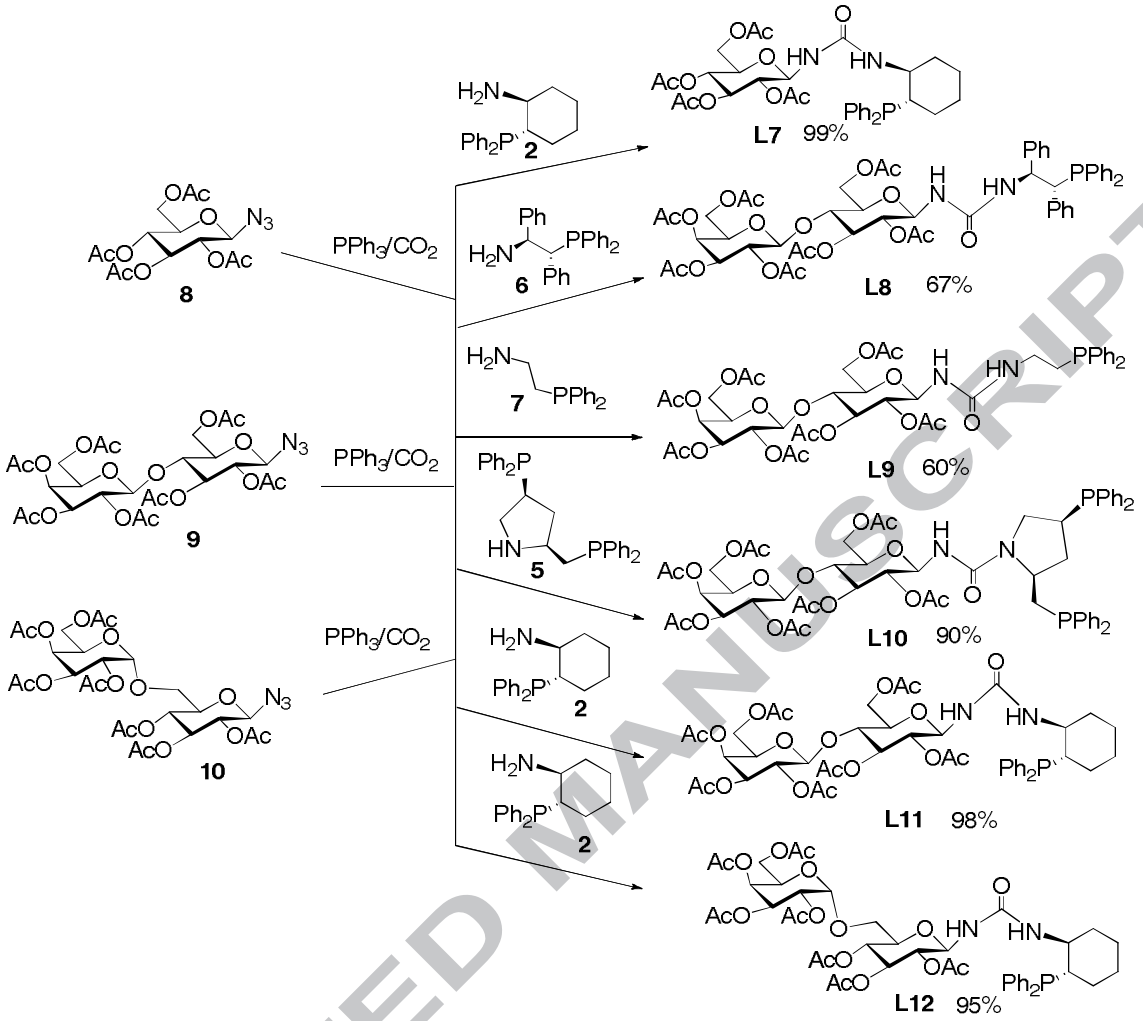
The synthetic route for the preparation of the chiral, sterically congested, bifunctional urea-phosphine organocatalysts is straightforward (Scheme 1). Bifunctional ureas **L1-6** were synthesised in high yields by coupling of the corresponding azido-cellobiose **1**[12a] with chiral amines **2-6** and achiral amine **7** in the presence of PPh_3 and CO_2.[13] All the amine derivatives are commercial products.



Scheme 1

The highest yield, 99%, was obtained for ligand **L1** while the lowest yield of 66% was achieved for ligand **L2** with unit proline **3**. The simple and efficient synthesis of urea derivatives which is carried out under mild conditions, could be an attractive method for the preparation of this type of sugar organocatalists.

Next the aza-Wittig reaction of other mono- and disaccharides was investigated (Scheme 2).



Scheme 2

Organocatalyst **L7** was obtained in a high 99% yield from azido-glucose **8**[12b] and the aminocyclohexane **2**. The yields of ligands **L8-12** from azido-lactose **9**[12a] and azido-melibiose**10**[12a] were also satisfactory (60 to 98%).

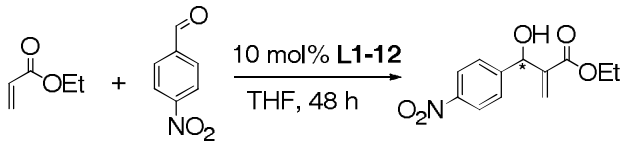
The spectroscopic data of organocatalysts **L1-12** (IR, NMR and elemental analysis) are in full accordance with the proposed structures.

2.2 Application of the organocatalysts L1-12 in asymmetric synthesis

2.2.1 Morita-Baylis-Hillman reaction

Initially, we chose the reaction of ethyl acrylate with *p*-nitrobenzaldehyde as a model transformation in which organocatalysts **L1-12** were evaluated. The reaction was performed for 48 hours in THF using 10 mol% of the organocatalysts.The results are summarised in Table 1.

Table 1. Screening of the catalysts in the Morita-Baylis-Hillman reaction of ethyl acrylate and *p*-nitrobenzaldehyde.



Entry	Catalysts	Yield (%)[a]	ee (%)[b]
1	**L1**	30	58
2	**L6**	28	4
3	**L7**	33	61
4	**L9**	21	2
5	**L11**	60	80
6	**L12**	36	72

[a] Yield refers to isolated pure product after column chromatography.
[b] Enantioselectivity was measured by HPLC on a Chiralpak OD-H column (25 cm x 4.6 mm); flow rate =1 ml min^{-1}; hexane/*i*-propanol (95/5), t_R (major) = 17.14 min and t_R (minor) = 18.30 min.

The best result was obtained in the presence of **L11** as the organocatalyst at room temperature (Table 1, entry 5). Under the same conditions **L12** gave a product with a lower yield and a slightly lower enantioselectivity (Table 1**,** entry 6). Only a trace quantity of the product was observed in the presence of **L3, L5** and **L8**. The lowest enantioselectivity was observed for **L6** and **L9** bearing an achiral amine moiety (Table1, entry 2, 4). Ligands bearing tertiary nitrogen atom (**L2, L4, L10**) in the urea subunit were completely nonreactive. Table 1 reveals that the stereogenic centre which is located on the amine moiety exerts a crucial influence on both the stereochemistry and yield of the reaction. These results also showed that the distance between the phosphine (base) and the urea bridge had an effect on both the enantioselectivity and yield. In the nonpolar solvent such as toluene using the best disaccharide organocatalysts **L1**, **L11** and **L12** observed only traces of product MBH reaction.
Proposed transition state of this asymmetric MBH reaction is illustrated in Figure 1.

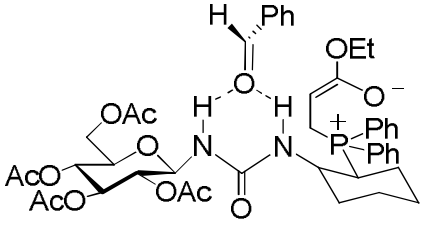
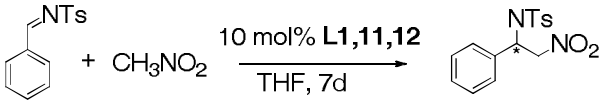


Figure 1

The urea hydrogens forms a hydrogen-bond with the aldehyde carbonyl group, and the alkoxy enolate was formed *via* an phosphinoyl attack on an activated carbonyl group from *si*-face and give *R*-product.

2.2.2. Aza-Henry reaction.
The best disaccharide organocatalysts **L1**, **L11** and **L12** were also tested in the aza-Henry reaction. The results are collected in Table 2.

Table 2. Screening of the catalysts in the aza-Henry reaction of nitromethane and *N*-tosylimine



Entry	Catalyst	Solvent	% yield[a]	%R/S[b]
1	L1	THF	70	50/50
2	L11	THF	45	52/48
3	L12	THF	91	49/51

[a] Yield refers to isolated pure product after column chromatography.
[b] Enantioselectivity was measured by HPLC on a Chiralpak OD-H column (25 cm x 4.6 mm); flow rate =1 ml min^{-1}; hexane/*i*-propanol (80/20), t_R (S) = 16.12 min and t_R (R) = 18.12 min.[15]

In present of the derivative **L1** and **L12** products of aza-Henry reaction were synthesised with high yield but with low enantioselectivity. Organocatalyst **L11** was much less effiecient**.**

3. Conclusions

In conclusion, we have prepared a new chiral bifunctional phosphinoureas derived from saccharides and in high yields using simple procedure. Organocatalysts **L11** and **L12** were efficient for the asymmetric Morita-Baylis-Hillman reaction of an acrylate with an aldehyde. The presence of phosphine (base) in the organocatalysts is necessary for the aza-Henry reaction. Therefore we have motivated to test their efficiency also in this reaction. They were also efficient in the asymmetric aza-Henry reaction but products of this synthesis were obtained in low enantioselectivity. Further refinement of the MBH reaction and other asymmetric reactions are under active investigation also in aqueous media.

4. Experimental

4.1. General comments

All solvents and reagents were purchased from Sigma-Aldrich and used as supplied, without additional purification. NMR spectra were recorded in $CDCl_3$, on Brucer Avance III (600 MHz for ^{1}H NMR, 150 MHz for ^{13}C NMR); coupling constants are reported in Hz. Optical rotation were measured on a Perkin-Elmer 241 MC polarimeter with a sodium lamp at room temperature. Melting points were determined on a DigiMelt apparatus and are uncorrected. Chromatographic purification of the compounds was achieved with 230-400 mesh size silica gel. The reaction were monitored by TLC (Merck TLC Silicagel 60 F_{254}). IR spectra were recorded on a Mattson 1000 ATI Unicam FT-IR spectrometer. The enantiomeric excesses were determined by HPLC (ProStar Varian) employing a Chiralpak OD-H column (25cm x 4.6 mm).

4.2. General procedure for the synthesis of organocatalysts L1-12.

Triphenylphosphine (3.3 mmol) was added to a solution of peracetylazidosaccharide (1.1 mmol) in toluene (8 ml). The resulting solution was stirred at room temperature for 1 h and then flushed with CO_2. Next, the appropriate amine (1 mmol) was added. The mixture was stirred for 24 h under CO_2 bubbling conditions. After evaporation of the solvent, the residue was purified by flash chromatography on silica gel eluting with ethyl EtOAc/hexane or EtOAc/MeOH.

4.2.1. *N*-[(1*S*.2*S*)-2-(diphenylphosphino)cyclohexsyl]-*N*‘-(2,3,6, 2‘,3‘,4‘,6‘-hexa-*O*-acetyl-β-D-cellobiose)urea (**L1**)[7]

4.2.2. *N*-{(*S*)-2-[(Diphenylphosphino)methyl]-pyrrolidyne}-*N*‘-(2,3,6, 2‘,3‘,4‘,6‘-hexa-*O*-acetyl-β-D-cellobiose)urea (**L2**)

Yield %: 66 (614mg) as a white powder (AcOEt/Hexane 9:1, R_f=0.69); Mp: 109-110°C, $[\alpha]_D^{22} = -31.6$ (c 0.5, CH_2Cl_2); Anal. for $C_{45}H_{55}N_2O_{18}P$ (930.32), calc.: C 56.77, H 5.96, N 3.01, found: C 56.81, H 6.03, N 3.06.

IR (KBr, cm^{-1}): 3432, 3054, 1751, 1659 1231, 1040, 744, 699.

NMR ^{1}H(600MHz, $CDCl_3$); 7.54-7.19(m, 10H, Ar) 5.20 (t, 1H, H-3, $J_{3,2}$=9.3, $J_{3,4}$=9.3); 5.07-5.04 (m, 3H, H-3’, H-1, NH); 4.99(t, 1H, H-4’, $J_{4',3'}$=9.6, $J_{4',5'}$=9.6); 4.84(dd, 1H, H-2‘, $J_{2',3'}$=9.3, $J_{2',1'}$=7.6); 4.70(tl, 1H, H-2, $J_{2,1}$=9.3, $J_{2,3}$=9,3); 4.42(d, 1H, H-1’, $J_{1',2'}$=7.6) ; 4.38(dd, 1H, H-6a, $J_{6a,6b}$=12, $J_{6a,5}$=1.6) ; 4.28(dd, 1H, H-6‘a, $J_{6'a,6'b}$=12, $J_{6'a,5'}$=4.7); 4.06(dd, 1H, H-6b, $J_{6b,6a}$=12, $J_{6b,5}$=4.3) ; 3.98(dd, 1H, H-6’b, $J_{6'b,6'a}$=12, $J_{6'b5'}$=2.2), 3,69 (t, 1H, H-4, $J_{4,3}$=9.3, $J_{4,5}$=9.1); 3.63(ddd, 1H, H-5, $J_{5,4}$=9.1, $J_{5,6a}$=1.6, $J_{5,6b}$=4,3); 3.57(ddd, 1H, H-5’, $J_{5',4'}$=9.6, $J_{5'6'a}$=4,7, $J_{5',6'b}$=2,2); 3.19-3,12(m, 2H, H-2“, H-5‘‘$_a$); 2.82-2.74(m, 1H, H-5‘‘$_b$); 2.13-1.87(m, 27H, 7CH_3, Ac, 2H-6“, 2H-4“, 2H-3“)

NMR ^{13}C(150MHz, $CDCl_3$); 170.45-168.98(7CO, Ac) ; 154.34 (CO, Urea); 137.15-128.37 C_{Ar} 100.61 C-1’ ; 80.20 C-1;76.32 C-4; 73.99 C-5; 72.98 C-3‘; 72.29 C-3; 72.01 C-5‘; 71.61 C-2‘; 71.28 C-2; 67.99 C-4; 62.06 C-6; 61.74 C-6’;55.80(d, C-2“ J_{C-P} = 23.8 Hz); 45.62 C-5“; 33.41 (d, C-6‘‘ J_{C-P} = 16.5 Hz); 29.64(d, C-3‘‘, J_{C-P} = 11.8 Hz); 23.72(C-4‘‘); 21.93-20.94(7CH_3, Ac,)

NMR ^{31}P(243MHz, $CDCl_3$) -21.95

4.2.3. *N*-[(*R*)-8-(Diphenylphosphino)-1,2,3,4-tetrahydronaphtalene]-*N*‘-(2,3,6, 2‘,3‘,4‘,6‘-hexa-*O*-acetyl-β-D-cellobiose)urea (**L3**)

Yield %: 98 (972mg) as a white powder (AcOEt/Hexane 9:1, R_f=0.76); Mp: 110-112°C, $[\alpha]_D^{22} = -21.6$ (c 0.5, CH_2Cl_2); Anal. for $C_{49}H_{57}N_2O_{18}P$ (992.32), calc.: C 59.27, H 5.79, N 2.82, found: C 59.02, H 5.73, N 2.81.

IR (KBr, cm^{-1}): 3408, 3069, 3054, 1748, 1652, 1228, 1039, 742, 698.

NMR ^{1}H(600MHz, $CDCl_3$); 7.44-7.11(m, 13 H, Ar,); 5.60-5.52(m, 1H, H-1“); 5.17-5.11 (m, 3H, H-1, H-3, H-3‘);5.09(t, 1H, H-4’, $J_{4',3'}$=9.6, $J_{4',5'}$=9.6); 4.94(dd, 1H, H-2‘, $J_{2',3'}$=9.1, $J_{2',1'}$=7.9); 4.61-4.52(m, 2H, NH, H-2); 4.50(d, 1H, H-1’, $J_{1',2'}$=7.9) ; 4.45(d, 1H, H-6a, $J_{6a,6b}$=12) ; 4.39(dd, 1H, H-6‘a, $J_{6'a,6'b}$=12, $J_{6'a,5'}$=4.2); 4.26-4.18(m, 1H, NH); 4.13(dd, 1H, H-6b, $J_{6b,6a}$=12, $J_{6b,5}$=4.0) ; 4.10(dd, 1H, H-6’b, $J_{6'b,6'a}$=12); 3.70-3.69(m, 2H, H-4, H-5‘); 3,50-3.40 (m, 1H, H-5); 3.87-3,76(m, 2H, 2H-4‘‘); 2.33-2.26(m, 1H, H-2“a); 2.10- 2.00(7s, 21H, 7CH_3, Ac); 1.84-1.63(m, 3H, H-2‘‘$_b$, 2H-3“)

NMR ^{13}C(150MHz, $CDCl_3$); 171.03-169.00(7CO, Ac) ; 154.35 (CO, Urea); 140.16-127.64 C_{Ar}; 100.72 C-1’ ; 80.05 C-1; 76.47 C-4; 73.83 C-5; 72.94 C-3; 72.34 C-3‘; 71.97 C-5‘, 71.61 C-2‘; 70.82 C-2; 67.94 C-4‘; 62.16 C-6; 61.66 C-6’; 47.20(d C-1‘‘ $J_{C,P}$ = 21.5); 30.05 C-4“; 29.37 C2“; 20.01-20.47 (7CH_3, Ac); 17.63 C3“

NMR ^{31}P(243MHz, $CDCl_3$) -18.06

4.2.4. *N*-[(2*S*,4*S*)-(-)-4-Diphenylphosphino-2-(diphenylphosphinomethyl)pyrrolidyne]-*N*‘-(2,3,6, 2‘,3‘,4‘,6‘-hexa-*O*-acetyl-β-D-cellobiose)urea (**L4**)

Yield %: 95 (1059mg) as a white powder (AcOEt/MeOH 6:1, R_f=0.64); Mp: 98-100°C, $[\alpha]_D^{22} = -16.0$ (c 0.1, CH_2Cl_2); Anal. for $C_{56}H_{64}N_2O_{18}P_2$ (1114.36), calc.: C 60.32, H 5.79, N 2.51, found: C 60.42, H 6.05, N 2.45.

IR (KBr, cm^{-1}): 3432, 3054, 1751, 1655 1231, 1039, 744, 698.

NMR ^{1}H(600MHz, $CDCl_3$); 7.50-726(m, 20H, Ar) 5.18 (t, 1H, H-3, $J_{3,2}$=9.3, $J_{3,4}$=9.3); 5.07-5.04 (m, 3H, H-3’, H-1, NH); 4.98(t, 1H, H-4’, $J_{4',3'}$=9.6, $J_{4',5'}$=9.6); 4.84(t, 1H, H-2‘,

$J_{2',3'}$=9.3, $J_{2',1'}$=7.9); 4.67(t, 1H, H-2, $J_{2,1}$=9.3, $J_{2,3}$=9,3); 4.42(d, 1H, H-1', $J_{1',2'}$=7.9) ; 4.37(dl, 1H, H-6a, $J_{6a,6b}$=12) ; 4.27(dd, 1H, H-6'a, $J_{6'a,6'b}$=12, $J_{6'a,5'}$=4.7); 4.06(dd, 1H, H-6b, $J_{6b,6a}$=12, $J_{6b,5}$=3.9) ; 3.97(dd, 1H, H-6'b, $J_{6'b,6'a}$=12, $J_{6'b5'}$=1,9), 3,93-3.81(m, 1H, H-2''), 3,67 (t, 1H, H-4, $J_{4,3}$=9.7, $J_{4,5}$=9.1); 3.62(ddd, 1H, H-5, $J_{5,4}$=9,7, $J_{5,6b}$=4,1); 3.57(ddd, 1H, H-5', $J_{5',4'}$=9.6, $J_{5'6'a}$=4,5, $J_{5',6'b}$=2,4); 3.45-3,35(m, 1H, H-5''a); 3.11(dd, 1H, H-5''$_b$, $J_{4"b,4"a}$ = 19.0, $J_{4"b,3"}$ = 9.7); 3.10-3.00(m, 1H, H-6"$_a$); 2.77-2.70(m, 1H, H-4''); 2.20-2.11(m, 1H, H-3''a); 2.12-1.97(m, 22H, H-6''b, 7CH_3, Ac); 1.74-1.63(m, 1H, H-3''b)

NMR ^{13}C(150MHz, $CDCl_3$); 171.54-168.98(7CO, Ac) ; 154.15 (CO, Urea); 137.15-128.37 C_{Ar} 100.59 C-1' ; 80.28 C-1; 76.23 C-4; 74.03 C-5; 72.97 C-3'; 72.27 C-3; 72.00 C-5'; 71.60 C-2'; 71.28 C-2; 67.98 C-4'; 62.04 C-6; 61.73 C-6'; 56.69 (dd, C-2'' J_{C-P} = 19.12, 10.7 Hz); 50.07(d, C-5'', J_{C-P} = 28.7 Hz); 37.14(dd, C-3'',J_{C-P} = 19.7, 8.9 Hz); 35.37(d, C-4'',J_{C-P} = 9.5 Hz);34.68(d, C-6'', J_{C-P}=13.3 Hz); 21.93-20.94(7CH_3, Ac)

NMR ^{31}P(243MHz, $CDCl_3$) -8.71, -22.65

4.2.5. *N*-[(1*S*,2*S*)-2-(Diphenylphosphino)-1,2-diphenylethyl]-*N*'-(2,3,6,2',3',4',6'-hexa-*O*-acetyl-β-D-cellobiose)urea (**L5**)

Yield %: 75 (782mg) as a white powder (AcOEt/Hexane 9:1, R_f=0.48), Mp: 141-142˚C, $[\alpha]_D^{22} = +8.0$ (c 0.7, CH_2Cl_2); Anal. for $C_{53}H_{59}N_2O_{18}P$ (1042.35), calc.: C 61.03, H 5.70, N 2.69, found: C 61.24, H 5.81, N 2.46.

IR (KBr, cm^{-1}): 3385, 3061, 3031, 1755, 1696, 1232, 1039, 720, 700.

NMR ^{1}H(600MHz, $CDCl_3$); 7.44-6.93(m, 22H, Ar, 2NH); 5.41(dl, 1H, H-1'', $J_{1",2"}$=6.1Hz); 5.28 (t, 1H, H-3, $J_{3,2}$=9.3, $J_{3,4}$=9.3); 5.13 (t, 1H, H-3', $J_{3',2'}$=9.3, $J_{3',4'}$=9.3); 5.06(t, 1H, H-4', $J_{4',3'}$=9.3, $J_{4',5'}$=9.6);5.03(t, 1H, H-1, $J_{1,2}$=8.3, $J_{1,NH}$=9.3); 4.99-4.92(m, 1H, H-2); 4.91(t, 1H, H-2', $J_{2',3'}$=9.3, $J_{2',1'}$=7.9); 4.61-4.52(m, 1H, H-6a); 4.52(d, 1H, H-1', $J_{1',2'}$=7.9) ; 4.36(dd, 1H, H-6'a, $J_{6'a,6'b}$=12, $J_{6'a,5'}$=4.3); 4.14 (dd, 1H, H-6b, $J_{6b,6a}$=12, $J_{6b,5}$=3.7) ; 4.07(dd, 1H, H-6'b, $J_{6'b,6'a}$=12, $J_{6'b5'}$=1,3), 3,94(dd, 1H, H-2''$J_{1",P}$=9.0, $J_{1",2"}$=6.1 Hz), 3,83 (t, 1H, H-4, $J_{4,3}$=9.3, $J_{4,5}$=8.5); 3.77-3.70(m, 1H, H-5); 3.66(ddd, 1H, H-5', $J_{5',4'}$=9.6, $J_{5'6'a}$=4,5, $J_{5',6'b}$=1,8); 2.21-1.97(7s, 21H, 7CH_3, Ac);

NMR ^{13}C(150MHz, $CDCl_3$); 171.54-168.98(7CO, Ac) ; 154.15 (CO, Urea); 131.22-126.40 C_{Ar} 100.72 C-1' ; 80.14 C-1;76.31 C-4; 73.97 C-5; 73.03 C-3'; 72.70 C-3; 72.02 C-5'; 71.61 C-2'; 71.00 C-2; 67.91 C-4; 61.94 C-6; 61.67 C-6'; 58.95 (d, C-1'' J_{C-P} = 10.7 Hz); 51.90 C-2"; 20.94-20.51(7CH_3, Ac)

NMR ^{31}P(243MHz, $CDCl_3$) +35.55

4.2.6. *N*-[2-(Diphenylphosphino)ethyl]-*N*'-(2,3,6,2',3',4',6'-hexa-*O*-acetyl-β-D-cellobiose)urea (**L6**)

Yield %: 90 (801mg) as a white powder (AcOEt/Hexane 9:1, R_f=0.71); Mp: 118-121˚C, $[\alpha]_D^{22} = -16.0$ (c 0.2, CH_2Cl_2); Anal. for $C_{41}H_{51}N_2O_{18}P$ (890.21), calc.: C 55.28, H 5.77, N 3.14, found: C 55.39, H 5.73, N 2.99.

IR (KBr, cm^{-1}): 3412, 3058, 3031, 1755, 1686, 1232, 1039, 723, 697.

NMR ^{1}H(600MHz, $CDCl_3$); 7.68-7.31(m, 10H, Ar); 5.24 (t, 1H, H-3, $J_{3,2}$=9.6, $J_{3,4}$=9.6); 5.16(d, 1H, NH, $J_{NH,1}$=9.0Hz), 5.13 (t, 1H, H-3', $J_{3',2'}$=9.6, $J_{3',4'}$=9.6); 5.06(t, 1H, H-4', $J_{4',3'}$=9.6, $J_{4',5'}$=9.6); 5.02(t, 1H, H-1, $J_{1,2}$=9.0, $J_{1,NH}$=9.6); 4.91(dd, 1H, H-2', $J_{2',3'}$=9.6, $J_{2',1'}$=7.8); 4.84(tl, 1H, NH, $J_{NH,1''a,b}$=5.4 Hz); 4.78(t, 1H, H-2, $J_{2,1}$=9.6, $J_{2,3}$=9,6); 4.49(d, 1H, H-1', $J_{1',2'}$=7.8) ; 4.44(dd, 1H, H-6a, $J_{6a,6b}$=12.3, $J_{6a,5}$=1.8 Hz); 4.35(dd, 1H, H-6'a, $J_{6'a,6'b}$=12.3, $J_{6'a,5'}$=4.3 Hz); 4.13(dd, 1H, H-6b, $J_{6b,6a}$=12.3, $J_{6b,5}$=5.7) ; 4.03(dd, 1H, H-6'b, $J_{6'b,6'a}$=12, $J_{6'b5'}$=2,3); 3,75 (t, 1H, H-4, $J_{4,3}$=9.6, $J_{4,5}$=9.0); 3.67(ddd, 1H, H-5, , $J_{5,4}$=9.0, $J_{5,6a}$=1,8, $J_{5,6b}$=5.7); 3.64(ddd, 1H, H-5', $J_{5',4'}$=9.6, $J_{5'6'a}$=4.3, $J_{5',6'b}$=1,8); 3.32-3,25(m, 2H, 2H-1''); 2.25(t, 2H, 2H-2'', J=7.3); 2.08- 1.97(7s, 21H, 7CH_3, Ac);

NMR ^{13}**C**(150MHz, $CDCl_3$); 171.54-168.98(7CO, Ac) ; 154.15 (CO, Urea); 131.75-128.49 C_{Ar} 100.67 C-1', 80.21 C-1;76.34 C-4; 74.13 C-5; 72.97 C-3'; 72.47 C-3; 71.96 C-5'; 71.58 C-2'; 70.87 C-2; 67.89 C-4; 62.05 C-6; 61.63 C-6'; 37.60. (d, C-1'' J_{C-P} = 19.6 Hz); 21.06(d, C-2'', J_{C-P} =5.4 Hz); 21.04-20.52($7CH_3$, Ac)
NMR ^{31}**P**(243MHz, $CDCl_3$) -22.19

4.2.7. *N*-[(1*S*.2*S*)-2-(diphenylphosphino)cyclohexsyl]-*N*'-(2,3,4,6-tetra-*O*-acetyl-β-D-glucose)urea (**L7**)
Yield %: 99 (650mg) as a white powder (AcOEt/Hexane 9:1, R_f=0.80); Mp: 91-93°C, $[\alpha]_D^{22} = +41.3$ (c 0.3, CH_2Cl_2); Anal. for $C_{33}H_{41}N_2O_{10}P$ (656.25), calc.: C 60.36, H 6.29, N 4.27, found: C 60.41, H 6.48, N 4.39.
IR (KBr, cm^{-1}): 3404, 3071, 3054, 1752, 1655, 1230, 1038, 744, 699.
NMR ^{1}**H**(600MHz, $CDCl_3$); 7.49-7.34(m, 10H, Ar); 5.33 (t, 1H, H-3, $J_{3,2}$=9.3, $J_{3,4}$=9.6); 5.25(t, 1H, H-1, $J_{1,NH}$=9.3, $J_{1,2}$=9.1), 5.16 (t, 1H, H-3, $J_{3,2}$=9.3, $J_{3,4}$=9.6); 5.09(t, 1H, H-4, $J_{4',3'}$=9.6, $J_{4',5'}$=9.8); 5.02(dl,1H, NH, $J_{NH,1}$=9.3); 4.89(t, 1H, H-2, $J_{2,3}$=9.3, $J_{2,1}$=9.1); 4.71-4.59(m, 1H, NH); 4.33(dl, 1H, H-6a, $J_{6a,6b}$=12) ; 4.11(dl, 1H, H-6b, $J_{6a,6b}$=12); 3.83(dl, 1H, H-5, $J_{5,4}$=9.8); 3.58-3,49(m, 1H, H-1''); 2.24-2.14(m, 2H, H-2'',H-6''a); 2.08- 1.92(7s, 21H, $7CH_3$, Ac); 1.84-1.68(m, 3H, H-4''a, H-5"a, H-3"a); 1.35-1.21(m, 3H, H-3"b, H-4"b, H-6"b); 1.03-0.93(m, 1H, H-5"b)
NMR ^{13}**C**(150MHz, $CDCl_3$); 171.06-169.69(4CO, Ac) ; 155.09 (CO, Urea); 134.59-128.22 C_{Ar}, 80.117 C-1; 73.21 C-5, 73.02 C-4; 70.64 C-2; 68.35 C-4; 61.85 C-6; 61.63; 51.20(d, C-1'',J_{C-P} =13.7 Hz) 41.10 (d, C-2'' J_{C-P} = 16. Hz); 34.30 (C-6''); 27.38 (C-5''); 25.45 (C-4''); 24.41(C-3''); 20.80-20.58($4CH_3$, Ac)
NMR ^{31}**P**(243MHz, $CDCl_3$) -8.74

4.2.8. *N*-[(1*S*,2*S*)-2-(Diphenylphosphino)-1,2-diphenylethyl]-*N*'-(2,3,6,2',3',4',6'-hexa-*O*-acetyl-β-D-lactose)urea (**L8**)
Yield %: 67 (698mg) as a white powder (AcOEt/Hexane 9:1, R_f=0.49); Mp: 92-94°C, $[\alpha]_D^{22} = +16.0$ (c 0.1, CH_2Cl_2); Anal. for $C_{53}H_{59}N_2O_{18}P$ (1042.35), calc.: C 61.03, H 5.70, N 2.69, found: C 60.75, H 5.74, N 2.73.
IR (KBr, cm^{-1}): 3385, 3061, 3031, 1755, 1696, 1232, 1039, 720, 700.
NMR ^{1}**H**(600MHz, $CDCl_3$); 7.69-6.97(m, 22H, Ar, 2NH); 5.45(dl, 1H, H-1'', $J_{1',2'}$=9.1Hz); 5.37(d, 1H, H-4', $J_{4',3'}$ =3.3 Hz); 5.31 (t, 1H, H-3, $J_{3,2}$=8.5, $J_{3,4}$=9.3); 5.12 (dd, 1H, H-2', $J_{2',1'}$=8.0, $J_{2',3'}$=2.4); 5.06(t, 1H, H-1, $J_{1,2}$=9.3, $J_{1,NH}$=9.3);4.98-4.96(m, 2H, H-2,H-3'); 4.61-4.53(m, 1H, H-6a); 4.51(d, 1H, H-1', $J_{1',2'}$=7.9); 4.19-4.11(m, 3H, H-6b, 2H-6'); 4.00(dd, 1H, H-2''$J_{1'',P}$=9.1, $J_{1'',2''}$=5.9 Hz), 3.89 (t, 1H, H-5', $J_{5'4'}$= 7.0, $J_{5'6'}$= 7.1 Hz); 3,83 (t, 1H, H-4, $J_{4,3}$=9.3, $J_{4,5}$=8.5); 3.77-3.70(m, 1H, H-5); 2.21- 1.97(7s, 21H, $7CH_3$, Ac);
NMR ^{13}**C**(150MHz, $CDCl_3$); 170.37-168.97(7CO, Ac) ; 155.92 (CO, Urea); 140.76-126.45 C_{Ar}; 100.97 C-1' ; 80.12 C-1; 76.31 C-5'; 73.97 C-5; 73.00 C-3; 71.08 C-3'; 72.02 C-5';69.50 C-2; 99.13 C-2'; 66.76 C-4; 62.07 C-6; 60.96 C-6'; 58.91 C-1''; 52.08 C-2"; 20.94-20.51($7CH_3$, Ac)
NMR ^{31}**P**(243MHz, $CDCl_3$) +34.49
4.2.9. *N*-[2-(Diphenylphosphino)ethyl]-*N*'-(2,3,6,2',3',4',6'-hexa-*O*-acetyl-β-D-lactose)urea (**L9**)
Yield %: 60 (534mg) as a white powder (AcOEt/Hexane 9:1, R_f=0.71); Mp: 114-116°C, $[\alpha]_D^{22} = -6.4$ (c 0.5, CH_2Cl_2); Anal. for $C_{41}H_{51}N_2O_{18}P$ (890.21), calc.: C 55.28, H 5.77, N 3.14, found: C 55.19, H 5.83, N 3.16.
IR (KBr, cm^{-1}): 3409, 3056, 1751, 1684, 1232, 1048.

NMR ^{1}H(600MHz, $CDCl_3$); 7.44-7.33(m, 10H, Ar); 5.37(d, 1H, H-4‘, $J_{4',3'}$ =3,4); 5.29 (t, 1H, H-3, $J_{3,2}$=9.3, $J_{3,4}$=9.3); 5.18(d,1H, NH, $J_{NH,1}$=9.1); 5.12 (dd, 1H, H-2‘, $J_{2',3'}$=10.3, $J_{2',1'}$=7.9); 5.06(t, 1H, H-1, $J_{1,2}$=9.3, $J_{1,NH}$=9.1);4.97(dd, 1H, H-3‘, $J_{3',2'}$=10.3, $J_{3',4'}$ =3.4); 4.88(dd, 1H, NH, $J_{NH,1"a}$ = 5.4, $J_{NH,1"b}$ = 5.5); 4.82(dd, 1H, H-2, $J_{2,3}$=9.3, $J_{2,1}$=9.3); 4.49(d, 1H, H-1’, $J_{1',2'}$=7.9); 4,45(dd, 1H, H-6a, $J_{6a,6b}$ =12, $J_{6a,5}$ =1.6); 4.19-4.14(m, 2H, H-6b, H-6‘a); 4.09(dd, 1H, H-6’b, $J_{6'b,6b}$ =12, $J_{6'b,5'}$ =7.5); 3.88 (t,1H, H-5‘, $J_{5'6'a'}$= 6.6, $J_{5'6'b}$ = 7.5); 3,82(t, 1H, H-4, $J_{4,3}$=9.3, $J_{4,5}$=9.7); 3.71(ddd, 1H, H-5, $J_{5,4}$=9.7, $J_{5,6a}$=1,6, $J_{5,6b}$=4,8); 3.37-3.27(m,2H, 2H-1“); 2.28(t, 2H, 2H-2“, $J_{2",1"}$ = 7.3); 2.18- 1.98(7s, 21H, $7CH_3$, Ac);
NMR ^{13}C(150MHz, $CDCl_3$); 171.25-168.96(7CO, Ac) ; 155.96 (CO, Urea); 137.68-128.57 C_{Ar}; 100.96 C-1’ ; 80.23 C-1; 76.09 C-4; 74.16 C-5; 72.70 C-3; 71.05 C-3‘; 70.98 C-2;70.71 C-5‘; 69.08 C-2‘; 66.65 C-4‘; 62.13 C-6; 60.78 C-6’; 37.68 (d, C-1‘‘;$J_{C,P}$ = 21), 29.55 (d, C-2‘‘;$J_{C,P}$ = 13.2) 20.86-20.47($7CH_3$, Ac)
NMR ^{31}P(243MHz, $CDCl_3$) -21.6

4.2.10. *N*-[(2*S*,4*S*)-(-)-4-Diphenylphosphino-2-(diphenylphosphinomethyl)pyrrolidyne]-*N*‘-(2,3,6, 2‘,3‘,4‘,6‘-hexa-*O*-acetyl-β-D-lactose)urea (**L10**)
Yield %: 90 (1003mg) as a white powder (AcOEt/MeOH 6:1, R_f=0.69); Mp: 124-126˚C, $[\alpha]_D^{22} = -25.8$ (c 0.85, $CHCl_3$); Anal. for $C_{56}H_{64}N_2O_{18}P_2$ (1114.36), calc.: C 60.32, H 5.79, N 2.51, found: C 60.35, H 6.03, N 2.45.
IR (KBr, cm^{-1}): 3432, 3054, 1751, 1655 1231, 1039, 744, 698.
NMR ^{1}H(600MHz, $CDCl_3$); 7.64-7.18(m, 20H, Ar), 5.29(dd, 1H, H-4‘, J=3,3, 0,7 Hz); 5.21 (t, 1H, H-3, $J_{3,2}$=9.3, $J_{3,4}$=9.3); 5.08(t, 1H, H-1, $J_{1,2}$=8.9, $J_{1,NH}$=9.2); 5.04 (dd, 1H, H-2‘, $J_{2',3'}$=10.3, $J_{2',1'}$=7.9); 5.02(d, 1H, NH, $J_{NH,1}$ = 9.2); 4.88(dd, 1H, H-3‘, $J_{3',2'}$=10.3, $J_{3',4'}$ =3.4); 4.68(dd, 1H, H-2, $J_{2,3}$=9.3, $J_{2,1}$=8.9); 4.39(d, 1H, H-1’, $J_{1',2'}$=7.9); 4,35(dd, 1H, H-6a, $J_{6a,6b}$ =12, $J_{6a,5}$ =1.6); 4.08-4.04(m, 2H, H-6b, H-6‘a); 4.01(dd, 1H, H-6’b, $J_{6'b,6b}$ =12,0 $J_{6'b,5'}$ =7.2); 3.92-3.81(m, 1H, H-2“); 3.78 (t,1H, H-5‘, $J_{5'6'a'}$= 6.6, $J_{5'6'b}$ = 7.2); 3,79(t, 1H, H-4, $J_{4,3}$=9.3, $J_{4,5}$=9.7); 3.64(ddd, 1H, H-5, $J_{5,4}$=9.7, $J_{5,6a}$=1,6, $J_{5,6b}$=4,8); 3.55-3,48(m, 1H, H-5‘‘a); 3.13(dd, 1H, H-5‘‘b, $J_{4"b,4"a}$ = 19.0, $J_{4"b,3"}$ = 9.8); 3.10-3.03(m, 1H, H-6“a); 2.77-2.72(m, 1H, H-4‘‘); 2.20-2.14(m, 1H, H-3‘‘a); 2.18- 1.97(m, 22H, H-6‘‘b, $7CH_3$, Ac); 1.76-1.70(m, 1H, H-3‘‘b)
NMR ^{13}C(150MHz, $CDCl_3$); 171.51-168.98(7CO, Ac) ; 154.15 (CO, Urea); 137.15-128.37 C_{Ar} 100.88 C-1’ ; 80.24 C-1;75.99 C-4; 74.05 C-5; 72.52 C-3; 71.37 C-2; 71.07 C-3‘ 70.78 C-5‘; 69.08 C-2‘; 66.72 C-4‘; 62.04 C-6; 60.97 C-6’; 56.67 (dd, C-2‘‘ J_{C-P} = 22.0, 5.6 Hz); 50.07(d, C-5‘‘, J_{C-P} = 28.5 Hz); 37.10(dd, C-3‘‘,J_{C-P} = 16.7, 8.0 Hz); 35.44(d, C-4‘‘,J_{C-P} = 14.0 Hz); 34.68(d, C-6‘‘, JC-P=18.8 Hz); 20.86-20.47($7CH_3$, Ac)
NMR ^{31}P(243MHz, $CDCl_3$) -7.93, -21.87

4.2.11. *N*-[(1*S*.2*S*)-2-(diphenylphosphino)cyclohexsyl]-*N*‘-(2,3,6, 2‘,3‘,4‘,6‘-hexa-*O*-acetyl-β-D-lactose)urea(**L11**)
Yield %: 67 (698mg) as a white powder (AcOEt/Hexane 9:1, R_f=0.49); Mp: 146-147˚C, $[\alpha]_D^{22} = +31.2$ (c 0.5, CH_2Cl_2); Anal. for $C_{45}H_{57}N_2O_{18}P$ (944.33), calc.: C 57.20.03, H 6.08, N 2.96, found: C 57.05, H 6.03, N 2.93.
IR (KBr, cm^{-1}): 3385, 3061, 3031, 1755, 1696, 1232, 1039, 720, 700.
NMR ^{1}H(600MHz, $CDCl_3$); 7.60-7.29(m, 10H, Ar); 5.37(d, 1H, H-4‘, $J_{4',3'}$ = 3.0 Hz); 5.31 (t, 1H, H-3, $J_{3,2}$=9.4, $J_{3,4}$=9.3); 5.23-5.16(m, 1H, H-1); 5.12 (dd, 1H, H-2‘, $J_{2',3'}$=10.4, $J_{2',1'}$=7.9; 5.07-4.94(m, 1H, NH); 4.97 (dd, 1H, $J_{3',2'}$= 10.4, $J_{3',4'}$= 3.0); 4.82(t, 1H, $J_{2,3}$=9.4, $J_{2,1}$=9.3); 4.49(d, 1H, H-1’, $J_{1',2'}$=7.9); 4.44 (dl, 1H, $J_{6a,6b}$=11.0, H-6a); 4.20-4.12(m, 2H, 2H-6‘); 4.09(dd, 1H, $J_{6b,6a}$=11.0); 3.88(t,1H, $J_{5'6'a}$= 7.0, $J_{5'6'b}$=6.8, H-5‘); 3,81 (t, 1H, , $J_{4,3}$=9.4, $J_{4,5}$=9.6, H-4); 3.77-3.70(m, 1H, H-5); 3.58-3,49(m, 1H, H-1‘‘); 2.29-2.11(m, 2H, H-2‘‘,H-

6‘‘a); 2.18- 1.98(7s, 21H, 7CH_3, Ac); 1.84-1.61(m, 3H, H-4‘‘a, H-5“a, H-3“a); 1.36-1.19(m, 3H, H-3“b, H-5“b, H-6“b); 1.05-0.95(m, 1H, H-4“b)
NMR ^{13}C(150MHz, $CDCl_3$); 171.20-168.96(7CO, Ac) ; 155.12 (CO, Urea); 134.61-128.35 C_{Ar}; 100.91 C-1’ ; 80.06 C-1; 76.11 C-4; 74.17 C-5; 72.79 C-3; 71.07 C-3‘; 71.07 C-2; 70.71 C-5‘;69.09 C-2‘; 66.68 C-4‘; 62.16 C-6; 60.83 C-6’; 51.10(d, C-1‘‘,J_{C-P} =13.2 Hz) 41.10 (d, C-2‘‘ J_{C-P} = 15.8 Hz); 34.25 (C-6‘‘); 27.23 (C-4‘‘); 25.46 (C-3‘‘); 24.42(C-5‘‘); 21.00-20.47(7CH_3, Ac)
NMR ^{31}P(243MHz, $CDCl_3$) -8.61

4.2.12. *N*-[(1*S*.2*S*)-2-(diphenylphosphino)cyclohexsyl]-*N*‘-(2,3,4, 2‘,3‘,4‘,6‘-hexa-*O*-acetyl-β-D-melibiose)urea(**L12**)
Yield %: 95 (897mg) as a white powder (AcOEt/CH_2Cl_2 3:2, R_f=0.76); Mp: 182-184˚C, $[\alpha]_D^{22} = +90.4$ (c 0.5, CH_2Cl_2); Anal. for $C_{45}H_{57}N_2O_{18}P$ (944.33), calc.: C 57.20.03, H 6.08, N 2.96, found: C 56.98, H 5.93, N 2.87.
IR (KBr, cm^{-1}): 3409, 3072, 3056, 1755, 1697, 1225, 1048, 721, 700.
^{1}H NMR (600 MHz, $CDCl_3$): 7.51-7.29(m, 10 H, Ar); 5,45 (d, 1H ,$J_{3'-4'}$=$J_{4'-5'}$=3,7, H4’); 5,34 (dd, 1H, $J_{3'4'}$=3,7 , $J_{2'-3'}$= 10,9, H3’) , 5,31 (d, 1H, $J_{1'-2'}$=3,7, H1’); 5,30 (t, 1H, J_{2-3}= J_{3-4} =9,6, H3); 5,21 (t, 1H, J_{NH-1}=9,7, J_{1-2}=9,6, H1); 5,09 (t, 1H, J_{4-5}=9,6 , J_{3-4} =9,6, H4); 5,05 (dd, 1H, $J_{1'-2'}$=3,7, $J_{2'-3'}$=10,9, H2’); 4.98 (d,1H, J_{NH-1}= 9.7, NH); 4,78 (t, 1H, J_{2-3}=J_{1-2}=9,6, H2), 4.69 (d,1H, $_{JNH-1"}$= 8.2, NH); 4,22 (t, 1H, $J_{4'-5'}$= 3,6, $J_{5'6'}$=6,8, H5’), 4,12 (d, 1H, $J_{6'a-6'b}$ = 12.0, H6’a); 4,06 (dd, 1H, $J_{6'b-6'a}$ = 12.0, $J_{6'b-5'}$= 6.8, H6’b) 3,77 (ddd, 1H, $J_{5,4}$=9.6, $J_{5,6a}$=2,4, $J_{5,6b}$=3,8, H5); 3,74 (dd, 1H , J_{5-6b}= 2,4, J_{6a-6b}=12,0 , H6a); 3,67 (dd, 1H, J_{5-6b}=3.8 , J= 12.0, H6b); 3.58-3,49(m, 1H, H-1‘‘); 2.24-2.11(m, 2H, H-2‘‘,H-6‘‘a); 2.08- 1.92(7s, 21H, 7CH_3, Ac); 1.84-1.68(m, 3H, H-4‘‘a, H-5“a, H-3“a); 1.36-1.21(m, 3H, H-3“b, H-5“b, H-6“b); 1.03-0.93(m, 1H, H-4“b)
^{13}C NMR (500 MHz, $CDCl_3$): 170.88-169.39 (C=O);, 155.28 (C=O_{urea}); 137.07-128.14 (Ar); 96.07 C-1’; 79.87 C-1; 74.13 C-5; 73.23 C-3; 70. 57 C-2; 68.95 C-4; 68.38 C-2’; 68.16 C-4‘; 67.44 C-3’; 66.32 C5’; 65.15 C-6; 60.36 C-6’; 51.18(d, C-1‘‘,J_{C-P} =26.2 Hz) 41.10 (d, C-2‘‘ J_{C-P} = 15.8 Hz); 34.33 (C-6‘‘); 27.40 (C-4‘‘); 25.48 (C-3‘‘); 24.41(C-5‘‘); 20.99-20.56(7CH_3, Ac)
NMR ^{31}P(243MHz, $CDCl_3$) -8.60

4.3. Typical procedure for the asymmetric Morita-Baylis-Hillman reaction

To a solution of the appropriate urea (0.01 mmol) in THF (1.0 ml) was added the acrylate (0.5 mmol) at room temperature. After stirring for 15 min as this temperature, the aldehyde (0.1 mmol) was added. The resulting mixture was stirred for 48 h. After removing the solvent under reduced pressure, the residue was purified by column chromatography to afford the desired product, and the *ee* value was determined by HPLC analysis using a chiral column.

4.3.1. Ethyl 2-[hydroksy-(4-nitro-phenyl)-methyl]-acrylate [14]
^{1}H NMR (600 MHz, $CDCl_3$):8.20(d, 2H, J=8.8 Hz, Ar); 7.57(d, 2H, J=8.8 Hz, Ar); 6.39(s, 1H); 5.84(s, 1H); 5.63(d, 1H, J=6.5 Hz); 4.20(q, 2H, J=7.1Hz); 3.31(d, 1H, J=6.1Hz); 1.27(t, 3H, J=7.1 Hz)

4.4. Typical procedure for the asymmetric aza-Henry reaction.

To a solution of the appropriate urea (0.01 mmol) in THF (1.0 ml) was added the N-tosyl imine (0.1 mmol) and nitromethane (1.0 mmol) at room temperature. The resulting mixture was stirred for 7 days. After removing the solvent under reduced pressure, the residue was

purified by column chromatography to afford the desired product, and the *ee* value was determined by HPLC analysis using a chiral column.

4.4.1. 2-Nitro-1-phenyl-*N*-tosylethanamine[15]
^{1}H NMR (600 MHz, $CDCl_3$):7.65 (d, 2H, J=8.3 Hz, Ar); 7.27-7.23 (m, 5H, Ar); 7.10-7.08 (m, 2H, Ar); 5.29(d, 1H, J=8.2Hz, NH); 4.98(q, 1H); 4.84(dd, 1H, J=6.4, 13.2 Hz); 4.68(dd, 1H, J=6.4, 12.2 Hz); 2.41(s, 3H, CH_3)

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References

[1] (a) Dieguez, M., Pamies, O., Ruiz, A., Diaz, Y., Castillon, S., Claver, C. *Coord. Chem. Rev.* **2004**, *248*, 2165-2192; (b) Gao, P., Wang, Ch., Wu, Y., Zhou, Z., Tang, Ch. *Eur. J. Org. Chem.* **2008**, 4563-4566; (c) Weihong, Y., Feng, S., Xin, Z., Kui, Y., Xinyan, W. *Chin. J. Chem.* **2012**, *30*, 2652-2656; (d) Lu, A., Hu, K., Wang, Y., Song, H., Zhou, Z., Fang, J., Tang, Ch. *J. Org. Chem.*, **2012**, *77*, 6208-6214; (e) Taha, T. A., Richards, M. R., Lowary, T. L. *Chem. Rev.* **2013**, *113,* 1851-1876
[2] (a) Liu, K., Kui, H.-F., Nie, J., Dong, K.-Y., Li, X.-J., Ma, J.-A. *Org. Lett.* **2007**, *9*, 923-925; (b) Pu, H., Li, P., Peng, F., Li, X., Zhang, H., Shao, Z. *Eur. J. Org. Chem.* **2009**, 4622-4626; (c) Gu, Q., Guo, X-T., Wu, X-Y., *Tetrahedron,* **2009**, *65*, 5265-527; (d) Wang, Y., Yang, H., Yu, J., Miao, Z., Chen, R. *Adv. Synth. Catal*, **2009,** *351*, 3057-3062; (e) Chen, J.-R., Cao, Y.-J., Zou, Y.-Q., Tan, F., Fu, L., Zhu, X.-Y., Xiao, W.-J., *Org. Biomol. Chem.,* **2010,** *8*, 1275-1279; (f) Ma, H., Liu, K., Zhang, F.G., Zhu, Ch.L., Nie, J., Ma, J.A. J. Org. Chem., **2010**, *75*, 1402-1409; (g) Nie, J., Li, X.-J., Zheng, D.-H., Zhang, F.-G., Cui, S., Ma, J.-A. *J. Fluorine Chem.,* **2011,** *132,* 468-473; (h) Heravi, M. M., Asadi, S. *Tetrahedron Asymmetry*, **2012**, *23*, 1431-1465; (i) Tsakos, M., Kokotos, Ch.G. *Tetrahedron,* **2013**, *69*, 10199-10222
[3] (a) Becker, C., Hoben, C., Kunz, H. *Adv. Synt. Catal.* **2007**, *349*, 417-424; (b) Puglisi, A., Benaglia, M., Raimondi, L., Lay, L., Poletti, L. *Org. Biomol. Chem.* **2011**, *9*, 3295-3302
[4] Olszewska, B., Szulc, I., Kryczka, B., Kubiak, A., Porwański, S., Zawisza, A. *Tetrahedron: Asymmetry*, **2013**, *24*, 214-216.
[5] Allen, D. W. *Organophosphorus Chem*. **2006**, *35*, 1-91.
[6] Fernandez-Perez, H., Etayo, P., Panossian, A., Vidal-Ferran, A. *Chem. Rev*. **2011**, *111,* 2119-2176.
[7] Pellissier, H. *Tetrahedron*, **2007**, *63*, 9267-9331.
[8] Morita, K., Suzuki, Z., Hirose, H. *Bull. Chem. Soc. Jpn*. **1968**, *41*, 2815.
[9] Baylis, A. B., Hillman, M. E. D. *Patent* 2155113, **1972**.
[10] Wei, Y., Shi, M. *Chem. Rev*. **2013**, *113,* 6659-6690.
[11] (a) Okino, T., Nakamura, S., Furukawa, T., Takemoto, Y. *Org*. Lett. **2004**, *6*, 625; (b) Robak, M.A.T., Trincado, M., Ellman, J. A. *J. Am. Chem. Soc*. **2007**, *129*, 15110-15111; (c) Imashiro, R., Uehara, H., Barbas III, C.F. *Org. Lett*. **2010**, *12*, 5250-5253; (d) Wang, Ch., Zhou, Z., Tang, Ch. *Org. Lett*. **2008**, *10*, 1707-1710; (e) Xie, J., Yoshida, K., Takasu, K., Takemoto, Y., *Tetrahedron Lett*. **2008**, *49*, 6910–6913; (f) Hu, K., Wang, Ch., Ma, X., Wang, Y., Zhou, Z., Tang, Ch. *Tetrahedron: Asymmetry*, **2009**, *20*, 2178-2184; (g) Takada, K., Nagasawa, K., *Adv. Synth. Catal.* **2009***, 351*, 345-347; (h) Han, B., Huang, B., Xu, Z. R., Dong, Xp. *Chinese Chemical Letters*, **2011**, *22*, 923-926; (i) Jia, Z.-X., Luo, Y.-C., Xu, P.-F. *Org. Lett.* **2011***, 13*, 832-835; (j) Parra, A., Alfaro, R., Marzo, L., Moreno-Carrasco, A.,

Ruano J. L. G., Alemán, *J. Chem. Commun.* **2012**, *48*, 9759-9761; (k) Wang, H. Y., Chai, Z., Zhao, G. *Tetrahedron,* **2013**, *69*, 5104-5111; (l) Cao, D., Chai, Z., Zhang, J., Ye Z., Xiao H., Wang H., Chen J., Wu X.G. *Chem. Commun.* **2013**, *49*, 5972-5974

[12] (a) Petö, C., Batta, G., Györgydeák, Z., Sztarisckai, F. *Liebigs Ann. Chem*. **1991**, 505-507; (b) Deras, I. L., Takegawa, K., Kondo, A., Kato, I., Lee, Y. C. *Bioorg. Med. Chem. Lett*. **1998**, *8*, 1763-1766.

[13] (a) Kovacs, J., Pinter, I., Toth, G., Gyorgydeak, Z., Zoll, P. *Carbohydr. Res*. **1993**, *239*, 95-106; (b) Sallas, F., Kovacs, J., Pinter, I., Jicsinszky, L., Marsura, A. *Tetrahedron Lett*., **1996**, *37*, 4011-4014; (c) Porwanski, S., Marsura, A. *Eur. J. Org. Chem*. **2009**, 2047-2050; (d) Porwanski, S., Dumarcay-Charbonnier, F., Menuel, S., Joly, J-P., Bulach, W., Marsura, A. *Tetrahedron,* **2009**, *65*, 4196-5203; (e) Dumarcay-Charbonnier, F., Marsura, A. *Chem. Commun.,,* **2012**, *48*, 732-734; (f) Pintal, M., Kryczka, B., Marsura, A., Porwanski, S. *Carbohydr. Res*. **2014**, *386*, 18-22.

[14] Yuan, K., Song, H.-L., Hu, Y., Wu, X.-Y. *Tetrahedron,* **2009**, *65*, 8185-8190

[15] Zhou, H., Peng, D., Qin, B., Hou, Z., Liu, X., Feng, X. *J. Org. Chem*., **2007**, *72*, 10302-10304