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Modular Furanoside Pseudodipeptides and Thioamides, Readily Available Ligand Libraries for Metal-Catalyzed Transfer Hydrogenation Reactions: Scope and Limitations

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Abstract: Two new highly modular carbohydrate-based, pseudodipeptide and thioamide ligand libraries have been synthesized for the rhodium- and ruthenium-catalyzed asymmetric transfer hydrogenation (ATH) of prochiral ketones. These series of ligands can be prepared efficiently from easily accessible D-xylose and D-glucose. The ligand libraries contain two main ligand structures (pseudodipeptide and thioamide) that have been designed by making systematic modifications to one of the most successful ligand families developed for the ATH. As well as studying the effect of these two ligand structures on the catalytic performance, we also evaluated the effect of modifying several of the ligand parameters. We found that the effectiveness of the ligands at transferring the chiral information in the product can be tuned by correctly choosing the ligand components (ligand structure and ligand parameters). Excellent enantioselectivities (*ee*s up to 99%) were therefore obtained in both enantiomers of the alcohol products using a wide range of substrates.

Keywords: asymmetric catalysis; carbohydrates; ketones; rhodium; ruthenium; transfer hydrogenation

Introduction

Fine chemicals and natural product chemistry rely on enantiomerically pure compounds. The discovery of synthetic routes for preparing these compounds is one of the most persistently pursued goals in chemistry. Asymmetric catalysis is one of the most attractive approaches, because it can provide very high reactivity and selectivity, and is environmentally friendly.[1] In this respect, the enantioselective reduction of prochiral ketones has acquired greater importance, since the resulting enantioenriched secondary alcohols are key intermediates for the preparation of a large number of biologically active compounds.[2] Asymmetric transfer hydrogenation (ATH) has proven to be an efficient, mild and versatile method for this particular transformation, in which the use of molecular hydrogen or highly reactive hydride reagents can be avoided.[3] Nowadays, most transfer hydrogenations are performed using transition metal complexes, mainly based on ruthenium, rhodium or iridium.[3] Recently, the use of iron-based catalysts has also shown interesting results, but their scope is still low compared to that of the Ru catalysts.[4] In the mid 1990s, Noyori and co-workers found that ruthenium η^6-arene complexes in combination with vicinal amino alcohol or diamine ligands served as efficient catalysts for the reduction of ketones and ketimines, respectively, under ATH conditions.[5] Since then, many types of chiral ligands have been developed, some of which have been successfully applied in selective transfer hydrogenation.[6] In this context, Adolfsson's group reported that amino acid-derived pseudodipeptides **1**[6i,7] and thioamides **2**[6j,8] (Figure 1) in combination with Ru or Rh half-sandwich complexes are excellent catalysts for the ATH of aryl alkyl ketones. These ligands are based on the combination of different *N*-Boc-protected α-amino acids and β-amino alcohols (for type **1**) or on thioamides (for type **2**), respectively. Both showed the advantage of possessing a modular ligand building block: the amino acid part.

Despite all these important contributions, ligands based on simple starting materials and that have high modularity still need to be further explored. For this purpose, carbohydrates are particularly advantageous thanks to their low price and easy modular construc-

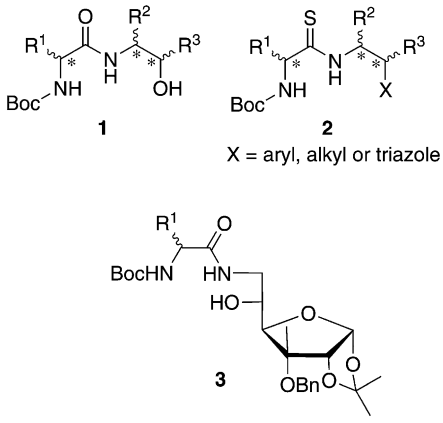


Figure 1. General structure of pseudodipeptide ligands **1**, thioamide ligands **2** and sugar-based pseudodipeptide ligands **3**.

tions.[9] Although they have been successfully used in other enantioselective reactions, they have only very recently shown their huge potential as a source of highly effective chiral ligands in this process.[10,11] In this context and based on previous successful ligands **1**, we have recently reported new pseudodipeptide ligands **3** (Figure 1) in which the β-amino alcohol part is replaced by a readily available sugar β-amino alcohol moiety. These new carbohydrate-based pseudodipeptide ligands **3** were the first successful sugar-based ligands applied in the Ru-catalyzed asymmetric transfer hydrogenation of several ketones.[10] Despite this success, the use of other carbohydrate-based pseudodipeptide ligands or carbohydrate-based thioamides has yet to be reported. Therefore, a systematic study of the possibilities offered by carbohydrate-based pseudodipeptides and thioamides as new ligands for ATH reactions was persued. To this end, in this paper we prepared and evaluated two new carbohydrate-based libraries of 36 potential pseudodipeptides and 36 potential thioamide ligands (Figure 2 and Figure 3). The first set (ligands **L1**–**L4a**–**i**) is based on the previous sugar-based pseudodipeptide ligands **3**, in which a 1,3-amino alcohol sugar core was used instead of a classical 1,2-amino alcohol motif (Figure 2).

In the second set (carbohydrate-thioamide **L5**–**L8a**–**i** ligands), the peptide bond in the previous ligands **L1**–**L4a**–**i** was converted to a thioamide group (Figure 3). As well as being prepared from commercially available D-glucose or D-xylose, both ligand li-

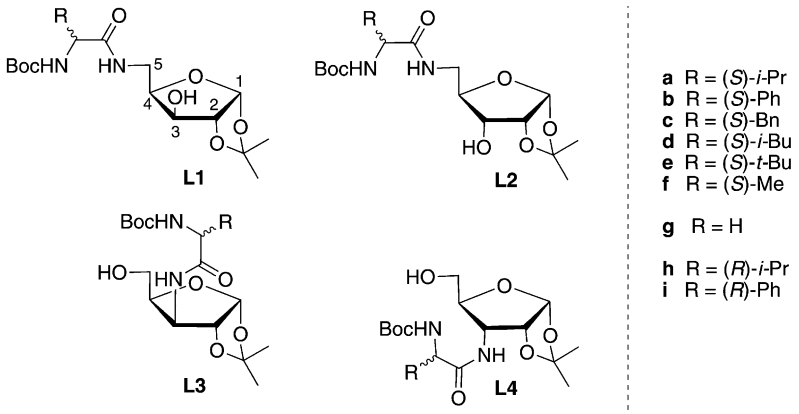


Figure 2. Furanoside pseudodipeptide ligand library **L1**–**L4a**–**i**.

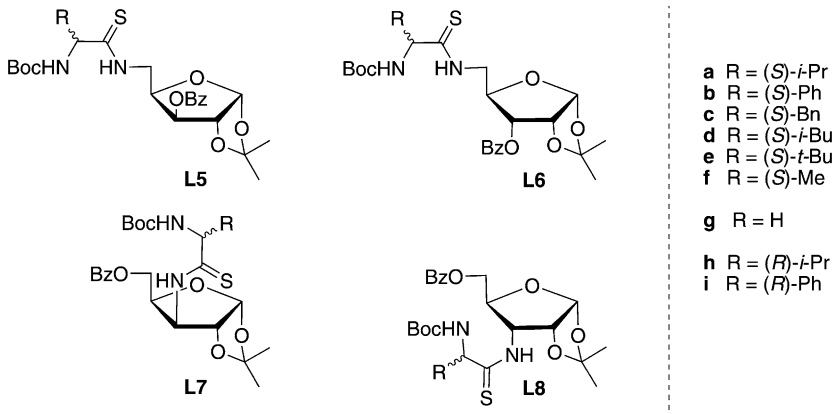


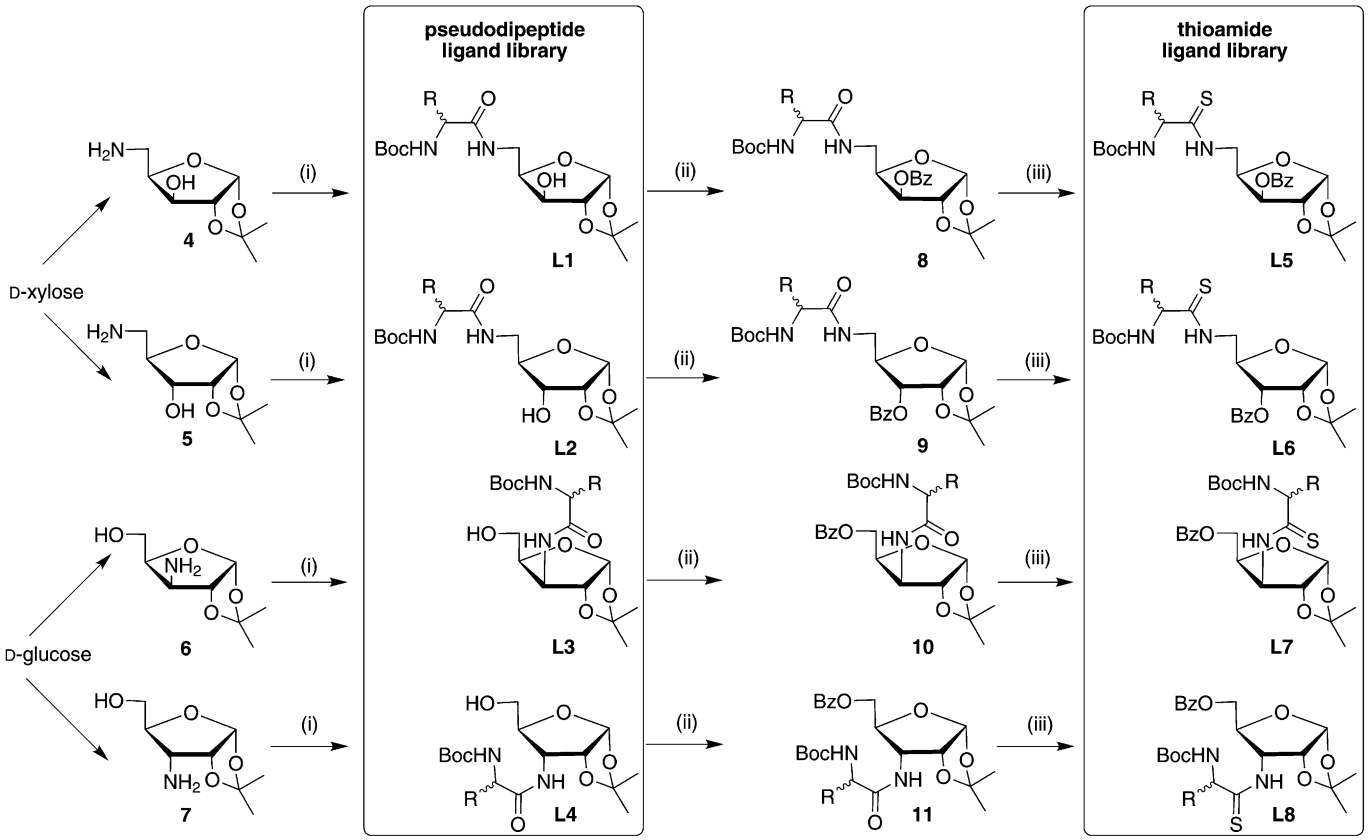
Figure 3. Furanoside-based thioamide ligand library **L5**–**L8a**–**i**.

braries also have the advantage of a flexible ligand scaffold that enables various ligand parameters to be easily tuned so that the catalyst performance can be maximized. With these libraries, then, we investigated the effect of systematically varying the position of the amino acids/thioamide groups at either C-5 (ligands **L1/L2** and **L5/L6**) or C-3 (ligands **L3/L4** and **L7/L8**) of the furanoside backbone, the configuration at C-3 of the furanoside backbone and substituents/configurations (**a–i**) in the amino acid/thioamide moieties. By carefully selecting the ligand components we achieved both enantiomers of the desired alcohols in high enantioselectivities and activities for a wide range of substrates.

Results and Discussion

Synthesis of Pseudodipeptide L1–L4a–i and Thioamide L5–L8a–i Ligand Libraries

The sequence for synthesizing pseudodipeptide **L1–L4a–i** and thioamide **L5–L8a–i** ligand libraries is illustrated in Scheme 1. These ligand libraries were prepared from the corresponding easily accessible 1,3-amino alcohol sugar derivatives (**4–7**, Scheme 1). Compounds **4–7** were easily made in few steps from the corresponding D-xylose or D-glucose.[12] These compounds (**4–7**) were chosen as intermediates for preparing ligands because the various elements that make it possible to study the position in which the α-amino acid/thioamide is coupled (at either C-5 or C-3) and the configuration of C-3 of the sugar amino alcohol can be easily incorporated. Initially, we synthesized the pseudodipeptide ligand library **L1–L4a–i** by coupling a series of *N*-Boc-protected amino acids with the corresponding amino alcohols **4–7** using isobutyl chloroformate in the presence of *N*-methylmorpholine (Scheme 1, step i).[6i] In this step the desired diversity in the substituents and configuration of the amino acid part was also attained (**a–i**). Then, we synthesized thioamide ligands **L5–L8a–h** from the previously obtained pseudodipeptide ligands **L1–L4a–i** in a two-step procedure. The first step was the benzoylation of the hydroxy group attached at either C-3 (**L1** and **L2**) or C-5 (**L3** and **L4**) of the furanoside backbone (**8–11**, Scheme 1, step ii). The second step is the formation of the desired thioamide ligands **L5–L8a–i** by treating the corresponding benzoyl-protected pseudodipeptide compounds with Lawesson's reagent (Scheme 1, step iii).[6j] It should be pointed out that under the conditions described in this paper Lawesson's reagent was



Scheme 1. Synthesis of pseudodipeptide ligand library **L1–L4a–i** and thioamide ligand library **L5–L8a–i**. *Reaction conditions:* (i) *i*-BuOCOCl/NMM/THF/−15 °C; (ii) BzCl/Py/CH_2Cl_2/0 °C to room temperature; (iii) Lawesson's reagent/THF/60 °C.

unable to produce the desired thioamides when *tert*-butyl groups (**e**) were present in the α-amino acid moiety.

All the ligands were isolated by purification on neutral silica gel (12–87% yield). They were stable at room temperature and characterized by ^{1}H and ^{13}C NMR spectroscopy. The spectral assignments (see Experimental Section) were based on information from ^{1}H-^{1}H and ^{13}C-^{1}H correlation measurements and were as expected for these C_1 ligands.

Asymmetric Transfer Hydrogenation

Asymmetric Transfer Hydrogenation of Acetophenone

In a first set of experiments, we used the Ru- and Rh-catalyzed transfer hydrogenation of acetophenone **S1** to study the potential of both ligand libraries. **S1** was chosen as a model substrate because the reaction was performed with a wide range of ligands, which enabled the efficiency of the various ligand systems to be compared directly.[3–5] In all cases, the catalysts were generated *in situ* from the corresponding ligand and either $[RuCl_2(p\text{-cymene})]_2$ or $[RhCl_2Cp^*]_2$ [pentamethylcyclopentadienylrhodium(III) chloride dimer].

Initially we investigated the pseudo-dipeptide ligand library **L1**–**L4a**–**i**. The results are summarized in Table 1. Activities and enantioselectivities were low for both Ru- and Rh-catalytic systems. Comparing entries 2–4 we can conclude that the catalyst deactivates quickly under the reaction conditions. This behaviour can be explained by the previous mechanistic studies with pseudodipeptide ligands **1**,[7g] which proposed compound **12** as the key species responsible for the catalytic activity (Figure 4). In this compound, pseudodipeptide ligands are coordinated to the metal through all of the ligand functionalities. Therefore, the alcohol functionality and the peptide nitrogen of the ligand coordinate as anions (note that the reaction proceeds under basic conditions) and the carbamate binds in a neutral fashion (Figure 4). Our pseudodipeptide ligand library **L1**–**L4a**–**i** differs from previous successful pseudodipeptide ligands **1** in the fact that 1,3-amino alcohols are used instead of the previously described 1,2-amino alcohols. This change should result in the formation of a reaction intermediate **12** in which the coordination of the alcohol as an alkoxide forms a six-membered chelate, which is less fav-

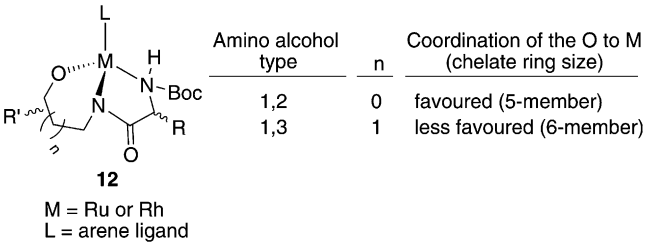
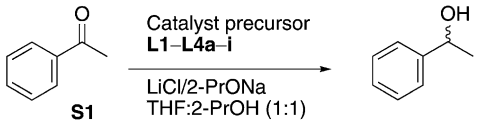


Figure 4. Proposed key reaction intermediate **12** in the ATH of ketones using pseudodipeptide ligands **1** and **L1**–**L4a**–**i**, respectively.

Table 1. Selected results for the Ru- and Rh-catalyzed asymmetric transfer hydrogenation reaction of **S1** using pseudodipeptide ligands **L1**–**L4a**–**i**.[a]



Entry	Ligand	Catalyst precursor	Temperature [°C]	% Conversion (Time [h])[b]	% *ee*[b]
1	**L1a**	$[RuCl_2(p\text{-cymene})_2]_2$	25	3 (2)	18 (*R*)
2	**L1a**	$[RuCl_2(p\text{-cymene})_2]_2$	50	11 (1)	12 (*R*)
3	**L1a**	$[RuCl_2(p\text{-cymene})_2]_2$	50	13 (3)	12 (*R*)
4	**L1a**	$[RuCl_2(p\text{-cymene})_2]_2$	50	14 (10)	11 (*R*)
5	**L2a**	$[RuCl_2(p\text{-cymene})_2]_2$	25	3 (2)	16 (*S*)
6	**L2a**	$[RuCl_2(p\text{-cymene})_2]_2$	50	3 (1)	14 (*S*)
7	**L3a**	$[RuCl_2(p\text{-cymene})_2]_2$	25	1 (2)	3 (*S*)
8	**L4a**	$[RuCl_2(p\text{-cymene})_2]_2$	25	6 (2)	0
9	**L1b**	$[RuCl_2(p\text{-cymene})_2]_2$	50	12 (1)	11 (*R*)
10	**L1f**	$[RuCl_2(p\text{-cymene})_2]_2$	50	9 (1)	12 (*R*)
11	**L1h**	$[RuCl_2(p\text{-cymene})_2]_2$	50	10 (1)	4 (*S*)
12	**L1a**	$[RhCl_2Cp^*]_2$	25	5 (24)	14 (*R*)
13	**L2a**	$[RhCl_2Cp^*]_2$	25	3 (24)	6 (*S*)

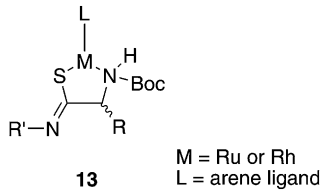
[a] *Reaction conditions:* **S1** (1 equiv., 0.2 M in 2-propanol/THF: 1/1), $[RuCl_2(p\text{-cymene})]_2$ (0.25 mol%) or $[RhCl_2Cp^*]_2$ (0.25 mol%), ligand (0.55 mol%), NaO-*i*-Pr (5 mol%), LiCl (10 mol%) at room temperature.

[b] Conversion and enantiomeric excess was determined by GC (CP Chirasil DEX CB).

oured than when 1,2-amino alcohols are used (which form a more stable five-membered chelate), thus favouring catalyst decomposition after only a few turnovers (Figure 4).[13]

In our efforts to improve catalytic performance and take advantage of our modular ligand systems we went on to develop and screen the thioamide ligand library **L5**–**L8a**–**i**. Recently, thioamide-based ligands **2** (Figure 1) have demonstrated their potential utility in the ATH of several aryl alkyl ketones, affording the desired alcohols in a range of 59–97% *ee*.[6j,8] Our new ligand library **L5**–**L8a**–**i** was designed on the basis of previous mechanistic studies with successful thioamide ligands **2** that showed that this type of ligand coordinates to the metal in a bidentate fashion, through the carbamate nitrogen and the thioamide sulfur atoms, to form a five-membered ring (Figure 5).[8a] In order to obtain the same coordination pattern we developed the thioamide ligands **L5**–**L8a**–**i** in which the hydroxy group is protected to prevent its coordination to the metal in the form of alkoxide. The enantioselectivity, then, is expected to be high.

The results using ligands **L5**–**L8a**–**i** are summarized in Table 2. With ligands **L5**–**L7a**, we first investigated



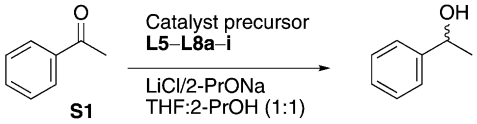
13

Figure 5. Proposed key reaction intermediate **13** in the ATH of ketones using thioamide ligands **2**.

the effect of the catalyst precursor. We found it had an important effect on both the activity and enantioselectivity of the reaction (Table 2, entries 1–8). Results were best therefore with the catalyst precursor $[RhCl_2Cp^*]_2$. The other ligands were then screened using $[RhCl_2Cp^*]_2$ as the optimum source of metal.

We then moved on to investigate the effect of the ligand parameters on the catalytic performance. The results indicate that enantioselectivity is highly affected by the position of the thioamide group at either C-5 or C-3 of the furanoside backbone, the configuration of C-3 and the substituents/configurations in the thioamide moiety.

Table 2. Selected results for the Ru- and Rh-catalyzed asymmetric transfer hydrogenation reaction of **S1** using thioamide ligands **L5**–**L8a**–**i**.[a]



S1

Entry	Ligand	Catalyst precursor	% Conversion (Time [h])[b]	% *ee*[b]
1	**L5a**	$[RuCl_2(p\text{-cymene})_2]_2$	39 (2)	82 (*R*)
2	**L5a**	$[RhCl_2Cp^*_2]_2$	64 (1)	86 (*R*)
3	**L6a**	$[RuCl_2(p\text{-cymene})_2]_2$	24 (2)	80 (*R*)
4	**L6a**	$[RhCl_2Cp^*_2]_2$	59 (1)	92 (*R*)
5	**L7a**	$[RuCl_2(p\text{-cymene})_2]_2$	10 (2)	79 (*R*)
6	**L7a**	$[RhCl_2Cp^*_2]_2$	72 (1)	97 (*R*)
7	**L8a**	$[RuCl_2(p\text{-cymene})_2]_2$	29 (2)	91 (*R*)
8	**L8a**	$[RhCl_2Cp^*_2]_2$	53 (1)	94 (*R*)
9	**L5b**	$[RhCl_2Cp^*_2]_2$	67 (1)	70 (*R*)
10	**L5c**	$[RhCl_2Cp^*_2]_2$	65 (1)	76 (*R*)
11	**L5d**	$[RhCl_2Cp^*_2]_2$	59 (1)	88 (*R*)
12	**L5f**	$[RhCl_2Cp^*_2]_2$	74 (1)	69 (*R*)
13	**L5g**	$[RhCl_2Cp^*_2]_2$	44 (1)	5 (*S*)
14	**L5h**	$[RhCl_2Cp^*_2]_2$	63 (1)	91 (*S*)
15	**L5i**	$[RhCl_2Cp^*_2]_2$	64 (1)	67 (*S*)
16	**L7b**	$[RhCl_2Cp^*_2]_2$	52 (1)	90 (*R*)
17	**L7d**	$[RhCl_2Cp^*_2]_2$	55 (1)	98 (*R*)
18	**L7h**	$[RhCl_2Cp^*_2]_2$	25 (1)	93 (*S*)
19[c]	**L7a**	$[RhCl_2Cp^*_2]_2$	59 (1)	93 (*R*)
20[c]	**L8a**	$[RhCl_2Cp^*_2]_2$	45 (1)	88 (*R*)

[a] *Reaction conditions:* **S1** (1 equiv., 0.2 M in 2-propanol/THF: 1/1), $[RuCl_2(p\text{-cymene})]_2$ (0.25 mol%) or $[RhCl_2Cp^*]_2$ (0.25 mol%), ligand (0.55 mol%), NaO-*i*-Pr (5 mol%), LiCl (10 mol%) at room temperature.
[b] Conversion and enantiomeric excess was determined by GC (CP Chirasil DEX CB).
[c] No LiCl was added.

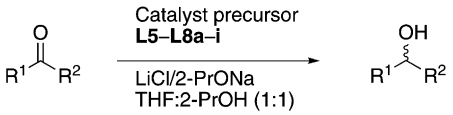
Interestingly, we found a cooperative effect between the position of the thioamide group and the configuration of carbon atom C-3 of the furanoside backbone (Table 2, entries 2, 4, 6 and 8). The results indicate that the matched combination is achieved with ligands **L7**, which have the thioamide moiety attached to C-3 and an *S* configuration of carbon atom C-3 (entry 6).

We next studied the effect of the substituents and configuration of the thioamide moiety with ligands **L5a–i**. Systematic variation of the electronic and steric properties of thioamide substituents indicated that enantioselectivities were mainly controlled by the steric properties of these substituents and were higher when more sterically demanding substituents were present (i.e., *i*-Bu ≈ *i*-Pr > Bn > Ph ≈ Me). Little effect of the thioamide substituents on activity was observed. In addition, the presence of a chiral thioamide substituent is crucial if levels of enantioselectivity are to be high (Table 2, entries 2, 9–12 *vs.* 13). We also found that the sense of enantioselectivity is governed by the absolute configuration of the substituent in the thioamide moiety (Table 2, entries 2 *vs.* 14 and 6 *vs.* 18). Both enantiomers of the reduction products can therefore be accessed in high enantioselectivity simply by changing the absolute configuration of the thioamide substituent.

The best results were therefore obtained with ligands **L7a** and **L7d** (Table 2, entries 6 and 17, *ee*s up to 98%). Interestingly, catalytic systems Rh-**L7a** and Rh-**L7b** provided higher enantioselectivities than those obtained using previously described Rh-**2** catalysts (*ee*s up to 96%).[8c]

Finally, we also evaluated the efficiency of these catalysts without the addition of LiCl (entries 19 and 20). The results are in line with the decrease in activity and enantioselectivity previously observed using thioamide ligands **2**, which, as expected, agrees with a similar coordination mode and mechanism for the asymmetric transfer hydrogenation reaction. The higher *ee*s obtained using our sugar-based ligands (see also results in Table 3, *vide infra*) are therefore most

Table 3. Selected results for the Rh-catalyzed asymmetric transfer hydrogenation reaction of several aryl-alkyl ketones using thioamide ligands **L5**–**L8a**–**i**.[a]



Entry	Substrate	R^1	R^2	Ligand	% Conversion (Time [h])[b]	% *ee*[b]
1	**S1**	C_6H_5	Me	**L7a**	85 (3)	97 (*R*)
2	**S1**	C_6H_5	Me	**L7d**	72 (3)	98 (*R*)
3	**S2**	4-Me-C_6H_4	Me	**L7a**	68 (3)	98 (*R*)
4	**S2**	4-Me-C_6H_4	Me	**L7d**	60 (3)	98 (*R*)
5	**S2**	4-Me-C_6H_4	Me	**L7h**	49 (3)	94 (*S*)
6	**S3**	4-Br-C_6H_4	Me	**L7a**	94 (2)	97 (*R*)
7	**S3**	4-Br-C_6H_4	Me	**L7d**	78 (2)	97 (*R*)
8	**S4**	4-F-C_6H_4	Me	**L7a**	95 (2)	97 (*R*)
9	**S4**	4-F-C_6H_4	Me	**L7d**	85 (2)	98 (*R*)
10	**S5**	4-CF_3-C_6H_4	Me	**L7a**	90 (1)	96 (*R*)
11	**S5**	4-CF_3-C_6H_4	Me	**L7d**	91 (2)	97 (*R*)
12	**S5**	4-CF_3-C_6H_4	Me	**L7h**	88 (3)	95 (*S*)
13	**S6**	1-naphthyl	Me	**L7a**	87 (3)	99 (*R*)
14	**S6**	1-naphthyl	Me	**L7d**	65 (3)	99 (*R*)
15	**S6**	1-naphthyl	Me	**L7h**	59 (3)	97 (*S*)
16	**S7**	3-MeO-C_6H_4	Me	**L7a**	87 (24)	95 (*R*)
17	**S7**	3-MeO-C_6H_4	Me	**L7d**	69 (24)	95 (*R*)
18	**S7**	3-MeO-C_6H_4	Me	**L7h**	54 (24)	93 (*S*)
19	**S8**	2-MeO-C_6H_4	Me	**L7a**	18 (24)	37 (*S*)
20	**S8**	2-MeO-C_6H_4	Me	**L7d**	12 (24)	34 (*S*)
21	**S9**	C_6H_5	Et	**L7a**	76 (24)	96 (*R*)
22	**S9**	C_6H_5	Et	**L7d**	71 (24)	97 (*R*)
23	**S10**	C_6H_5	*i*-Pr	**L7a**	68 (24)	98 (*R*)
24	**S10**	C_6H_5	*i*-Pr	**L7d**	67 (24)	98 (*R*)
25	**S11**	4-MeO-C_6H_4-CH_2CH_2	Me	**L7a**	15 (24)	41 (*R*)

[a] *Reaction conditions:* ketone (1 equiv., 0.2 M in 2-propanol/THF: 1/1), $[RhCl_2Cp^*]_2$ (0.25 mol%), ligand (0.55 mol%), NaO-*i*-Pr (5 mol%), LiCl (10 mol%) at room temperature.

[b] Conversion and enantiomeric excess was determined by GC (CP Chirasil DEX CB).

likely due to interactions between the ligand and the Cp* of the starting complex when the Rh hydride is formed, and/or delivered to the substrate.

Asymmetric Transfer Hydrogenation of Different Aryl Alkyl Ketones

To further study the potential of these readily available ligands, we evaluated them in the ATH of other ketones **S2**–**S10**. The results are summarized in Table 3. In general, the trends were the same as for the ATH of **S1**. Results were best with ligands **L7a** and **L7d**. Again, both enantiomers of the secondary alcohol product were accessible in high enantioselectivities (*ee*s up to 99%, that is, Table 3, entries 3–5 and 10–15). We found that activities were best when electron-withdrawing groups at the *para* position were present (entries 6–12 *vs.* 3–5). However, enantioselectivity was hardly affected by the presence of electron-withdrawing or electron-donating groups at the *para* position of the phenyl group (entries 1–12). This behaviour contrasts with the electronic effect on enantioselectivity observed for previous thioamide ligands.[6j,8] Therefore, several *para*-substituted aryl ketones, including those containing 2-naphthyl groups, can be efficiently reduced using Rh-**L7a** and Rh-**L7d** catalytic systems (*ee*s ranging from 97% to 99%). The catalytic performance (activity and enantioselectivity) of the reaction was influenced by steric factors on the aryl substituent. Although enantioselectivity was hardly affected by the presence of *meta*-substituents in the phenyl group (entries 16 and 17), both activity and enantioselectivity decreased considerably when *ortho*-substituted aryl ketones were used (entries 19 and 20). On the other hand, enantioselectivities are not affected by the steric bulk of the alkyl substituent (entries 1 and 2 *vs.* 21–24). In line with previous results using thioamide ligands **2** the reduction of alkyl alkyl ketones proceeds with low conversions and enantioselectivities (entry 25).

In summary, the modular ligand design (position of the thioamide group, configuration at C-3 of the furanoside backbone and the substituents/configurations of the thioamide moieties) has been shown to be highly successful, both in finding highly selective ligands for almost each substrate, and identifying three general ligands **L7a**, **L7d** and **L7h** with good performance over the entire range of substrates (*ee*s up to 99%). It should be pointed out that these catalysts are also very tolerant to the electronic nature of the aryl ring and to the steric bulk of the alkyl group. Interestingly, when these latter results are compared with the enantioselectivities obtained with their corresponding non-sugar-based thioamide ligands **2**,[14] we can conclude that introducing a sugar amino alcohol moiety is advantageous. These results are among the best that have been reported.[3]

Conclusions

Two new highly modular carbohydrate-based, pseudodipeptide and thioamide ligand libraries have been synthesized for the Rh- and Ru-catalyzed asymmetric transfer hydrogenation of several ketones. Both ligand libraries have the advantage that they can be efficiently prepared from commercial α-amino acids, D-xylose and D-glucose, inexpensive natural chiral feedstocks. These ligand libraries contain two main ligand structures (pseudodipeptides and thioamides) that have been designed by systematically modifying one of the most successful ligand families developed for this process. As well as studying the effect of these two ligand structures on the catalytic performance, we also evaluated the effect of modifying several ligand parameters (the position of the amino acids/thioamide groups at either C-5 or C-3 of the furanoside backbone, the configuration at C-3 of the furanoside backbone and substituents/configurations in the amino acids/thioamide moieties). By carefully selecting the ligand components, we have developed the first carbohydrate-based thioamide ligand library that provides high enantioselectivity in a broad range of aryl alkyl ketones (*ee*s up to 99%). It should be noted that both enantiomers of alcohol products can be obtained with high enantioselectivities by simply changing the absolute configuration of the thioamide substituent. This finding represents an improvement to the previous successfully pseudodipeptide ligands **3**. In contrast to previous successful thioamides, enantioselectivity is hardly affected by the presence of electron-withdrawing or electron-donating groups, therefore, a range of *para*- and *meta*-substituted aryl alkyl ketones were efficiently reduced. We have therefore demonstrated that the introduction of a furanoside amino sugar moiety into the ligand design is advantageous and it efficiently transfers the chiral information to the products (*ee*s ranging from 95% to 99% in the reduction of a range of *para*- and *meta*-substituted aryl alkyl ketones). These results, which are among the best that have been reported for this process, open up a new class of readily available ligands for the highly enantioselective ATH.

Experimental Section

General Considerations

All reactions were carried out using standard Schlenk techniques under an argon atmosphere. Solvents were purified and dried by standard procedures. Sugar amino alcohols **4**–**7**

were prepared as previously described.[12] ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded using a 400 MHz spectrometer. Chemical shifts are relative to that of $SiMe_4$ (^{1}H and ^{13}C) as internal standard. ^{1}H and ^{13}C assignments were made on the basis of ^{1}H-^{1}H gCOSY and ^{1}H-^{13}C gHSQC.

Typical Procedure for the Preparation of Pseudodipeptide Ligands L1–L4a–i

To a cooled solution (−15 °C) of the desired N-Boc-protected amino acid (1 mmol) in THF (2 mL), *N*-methylmorpholine (NMM, 1.15 mmol, 126 μL) and isobutyl chloroformate (1.15 mmol, 150 μL) were slowly added. After 45 min, a solution of the desired amino alcohol (1 mmol, 189.2 mg), previously azeotropically dried with toluene, in THF (2 mL) was added and the resulting mixture was stirred at room temperature for 2 h. The crude mixture was purified by flash chromatography to produce the corresponding ligands as white solids.

L1a: Yield: 315 mg (81%); ^{1}H NMR ($CDCl_3$): δ = 0.91 (d, 3H, CH_3, *i*-Pr, $^3J_{H,H}$ = 7.2 Hz), 0.94 (d, 3H, CH_3, *i*-Pr, $^3J_{H,H}$ = 7.2 Hz), 1.29 (s, 3H, CH_3), 1.43 (s, 9H, CH_3, *t*-Bu), 1.46 (s, 3H, CH_3), 2.13 (m, 1H, CH, *i*-Pr), 3.24 (m, 1H, H-5), 3.81 (m, 1H, H-5′), 3.87 (m, 1H, CH), 3.95 (d, 1H, H-3, $^3J_{3,4}$ = 2.4 Hz), 4.03 (m, 1H, H-4), 4.56 (d, 1H, H-2, $^3J_{2,1}$ = 3.6 Hz), 4.99 (m, 1H, NH), 5.89 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 6.72 (m, 1H, NH); ^{13}C NMR ($CDCl_3$): δ = 19.3 (CH_3, *i*-Pr), 26.0 (CH_3), 26.8 (CH_3), 28.3 (CH_3, *t*-Bu), 30.3 (CH, *i*-Pr), 37.1 (C-5), 60.2 (CH), 73.7 (C-3), 78.7 (C, *t*-Bu), 79.8 (C-4), 84.7 (C-2), 104.8 (C-1), 111.5 (CMe_2), 151.2 (CO), 174.1 (CO); anal. calcd. (%) for $C_{18}H_{32}N_2O_7$: C 55.65, H 8.30, N 7.21; found: C 55.69, H 8.34, N 7.18.

L1b: Yield: 334 mg (79%); ^{1}H NMR ($CDCl_3$): δ = 1.26 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.40 (s, 9H, CH_3, *t*-Bu), 3.22 (m, 1H, H-5), 3.78 (m, 2H, H-5' and H-3), 3.92 (m, 1H, H-4), 4.48 (d, 1H, H-2, $^3J_{2,1}$ = 3.6 Hz), 5.23 (m, 1H, CH), 5.70 (m, 1H, NH), 5.82 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 7.00 (m, 1H, NH), 7.34 (m, 5H, CH=); ^{13}C NMR ($CDCl_3$): δ = 26.3 (CH_3), 26.9 (CH_3), 28.5 (CH_3, *t*-Bu), 37.5 (C-5), 58.7 (CH), 74.0 (C-3), 79.8 (C-4), 80.8 (C, *t*-Bu), 84.9 (C-2), 104.9 (C-1), 111.7 (CMe_2), 127.2 (CH=), 128.9 (CH=), 129.3 (CH=), 137.3 (C), 155.4 (CO), 172.9 (CO); anal. calcd (%) for $C_{21}H_{30}N_2O_7$: C 59.70, H 7.16, N 6.63; found: C 59.74, H 7.18, N 6.59.

L1c: Yield: 375 mg (86%); ^{1}H NMR ($CDCl_3$): δ = 1.28 (s, 3H, CH_3), 1.38 (s, 9H, CH_3, *t*-Bu), 1.42 (s, 3H, CH_3), 3.02 (m, 2H, CH_2, Bn), 3.13 (m, 1H, H-5), 3.70 (m, 1H, H-5′), 3.95 (m, 2H, H-3 and H-4), 4.32 (m, 1H, CH), 4.55 (d, 1H, H-2, $^3J_{2,1}$ = 3.6 Hz), 5.16 (m, 1H, NH), 5.82 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 6.69 (m, 1H, NH), 7.1–7.3 (m, 5H, CH=); ^{13}C NMR ($CDCl_3$): δ = 26.0 (CH_3), 26.7 (CH_3), 28.3 (CH_3, *t*-Bu), 37.2 (C-5), 38.3 (CH_2), 55.9 (CH), 73.7 (C-3), 79.6 (C-4), 80.6 (C, *t*-Bu), 84.8 (C-2), 104.8 (C-1), 111.5 (CMe_2), 127.1 (CH=), 128.7 (CH=), 129.2 (CH=), 136.2 (C), 155.5 (CO), 173.6 (CO); anal. calcd. (%) for $C_{22}H_{32}N_2O_7$: C 60.54, H 7.39, N 6.42; found: C 60.52, H 7.37, N 6.47.

L1d: Yield: 350 mg (87%); ^{1}H NMR ($CDCl_3$): δ = 0.92 (m, 6H, CH_3, *i*-Bu), 1.29 (s, 3H, CH_3), 1.42 (s, 9H, CH_3, *t*-Bu), 1.45 (s, 3H, CH_3), 1.47 (m, 1H, CH_2, *i*-Bu), 1.64 (m, 2H, CH and CH_2, *i*-Bu), 3.22 (m, 1H, H-5), 3.78 (m, 1H, H-5′), 3.94 (d, 1H, H-3, $^3J_{3,4}$ = 2.4 Hz), 4.01 (m, 1H, H-4), 4.05 (m, 1H, CH), 4.56 (d, 1H, H-2, $^3J_{2,1}$ = 3.6 Hz), 4.92 (m, 1H, NH), 5.89 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 6.86 (m, 1H, NH); ^{13}C NMR ($CDCl_3$): δ = 21.9 (CH_3, *i*-Bu), 22.8 (CH_3, *i*-Bu), 24.7 (CH_2, *i*-Bu), 26.0 (CH_3), 26.8 (CH_3), 28.3 (CH_3, *t*-Bu), 37.0 (C-5), 40.5 (CH, *i*-Bu), 53.1 (CH), 75.6 (C-3), 79.8 (C-4), 80.3 (C, *t*-Bu), 84.7 (C-2), 104.8 (C-1), 111.5 (CMe_2), 155.8 (CO), 175.0 (CO); anal. calcd. (%) for $C_{19}H_{34}N_2O_7$: C 56.70, H 8.51, N 6.96; found: C 56.69, H 8.53, N 6.94.

L1e: Yield: 306 mg (76%); ^{1}H NMR ($CDCl_3$): δ = 0.92 (s, 9H, CH_3, *t*-Bu), 1.24 (s, 3H, CH_3), 1.38 (s, 9H, CH_3, *t*-Bu), 1.40 (s, 3H, CH_3), 3.21 (m, 1H, H-5), 3.69 (m, 1H, H-5′), 3.82 (m, 1H, CH), 3.94 (d, 1H, H-3, $^3J_{3,4}$ = 2.0 Hz), 4.02 (m, 1H, H-4), 4.51 (d, 1H, H-2, $^3J_{2,1}$ = 3.6 Hz), 5.30 (m, 1H, NH), 5.84 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 7.03 (m, 1H, NH); ^{13}C NMR ($CDCl_3$): δ = 26.0 (CH_3), 26.7 (CH_3, *t*-Bu), 26.8 (CH_3), 28.3 (CH_3, *t*-Bu), 34.5 (C, *t*-Bu), 37.1 (C-5), 62.2 (CH), 73.7 (C-3), 79.7 (C-4), 80.1 (C, *t*-Bu), 84.8 (C-2), 104.7 (C-1), 111.5 (CMe_2), 155.9 (CO), 173.3 (CO); anal. calcd. (%) for $C_{19}H_{34}N_2O_7$: C 56.70, H 8.51, N 6.96; found: C 56.67, H 8.52, N 6.95.

L1f: Yield: 249 mg (69%); ^{1}H NMR ($CDCl_3$): δ = 1.24 (s, 3H, CH_3), 1.29 (d, 3H, CH_3, $^3J_{H,H}$ = 7.2 Hz), 1.38 (s, 9H, CH_3, *t*-Bu), 1.40 (s, 3H, CH_3), 3.18 (m, 1H, H-5), 3.74 (m, 1H, H-5′), 3.90 (d, 1H, H-3, $^3J_{3,4}$ = 2.4 Hz), 3.96 (m, 1H, H-4), 4.09 (m, 1H, CH), 4.51 (d, 1H, H-2, $^3J_{2,1}$ = 3.6 Hz), 5.00 (m, 1H, NH), 5.84 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 6.91 (m, 1H, NH); ^{13}C NMR ($CDCl_3$): δ = 17.9 (CH_3), 26.0 (CH_3), 26.7 (CH_3), 28.3 (CH_3, *t*-Bu), 37.0 (C-5), 50.1 (CH), 73.7 (C-3), 79.8 (C-4), 80.2 (C, *t*-Bu), 84.7 (C-2), 104.8 (C-1), 111.5 (CMe_2), 155.6 (CO), 175.0 (CO); anal. calcd. (%) for $C_{16}H_{28}N_2O_7$: C 53.32, H 7.83, N 7.77; found: C 53.34, H 7.85, N 7.74.

L1g: Yield: 250 mg (75%); ^{1}H NMR ($CDCl_3$): δ = 1.28 (s, 3H, CH_3), 1.42 (s, 9H, CH_3, *t*-Bu), 1.44 (s, 3H, CH_3), 3.27 (m, 1H, H-5), 3.75 (m, 3H, H-5′, CH_2), 4.05 (d, 1H, H-3, $^3J_{3,4}$ = 2.4 Hz), 4.05 (m, 1H, H-4), 4.54 (d, 1H, H-2, $^3J_{2,1}$ = 3.6 Hz), 5.43 (m, 1H, NH), 5.88 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 7.07 (m, 1H, NH); ^{13}C NMR ($CDCl_3$): δ = 26.0 (CH_3), 26.7 (CH_3), 28.2 (CH_3, *t*-Bu), 37.3 (C-5), 44.1 (CH_2), 73.9 (C-3), 79.6 (C-4), 80.6 (C, *t*-Bu), 84.8 (C-2), 104.7 (C-1), 111.5 (CMe_2), 156.2 (CO), 171.7 (CO); anal. calcd. (%) for $C_{15}H_{26}N_2O_7$: C 52.01, H 7.57, N 8.09; found: C 52.06, H 7.56, N 8.07.

L1h: Yield: 307 mg (79%); ^{1}H NMR ($CDCl_3$): δ = 0.90 (d, 3H, CH_3, *i*-Pr, $^3J_{H,H}$ = 7.2 Hz), 0.93 (d, 3H, CH_3, *i*-Pr, $^3J_{H,H}$ = 7.2 Hz), 1.28 (s, 3H, CH_3), 1.41 (s, 9H, CH_3, *t*-Bu), 1.44 (s, 3H, CH_3), 2.03 (m, 1H, CH, *i*-Pr), 3.20 (m, 1H, H-5), 3.78 (m, 1H, H-5′), 3.95 (m, 1H, CH), 3.98 (d, 1H, H-3, $^3J_{3,4}$ = 2.4 Hz), 4.02 (m, 1H, H-4), 4.55 (d, 1H, H-2, $^3J_{2,1}$ = 4.0 Hz), 5.23 (m, 1H, NH), 5.87 (d, 1H, H-1, $^3J_{1,2}$ = 4.0 Hz), 7.21 (m, 1H, NH); ^{13}C NMR ($CDCl_3$): δ = 18.2 (CH_3, *i*-Pr), 19.5 (CH_3, *i*-Pr), 26.3 (CH_3), 26.9 (CH_3), 28.5 (CH_3, *t*-Bu), 31.0 (CH, *i*-Pr), 37.4 (C-5), 60.0 (CH), 74.0 (C-3), 80.0 (C-4), 80.5 (C, *t*-Bu), 85.0 (C-2), 104.9 (C-1), 111.7 (CMe_2), 156.2 (CO), 174.3 (CO); anal. calcd. (%) for $C_{18}H_{32}N_2O_7$: C 55.65, H 8.30, N 7.21; found: C 55.71, H 8.36, N 7.16.

L1i: Yield: 321 mg (76%); ^{1}H NMR ($CDCl_3$): δ = 1.25 (s, 3H, CH_3), 1.40 (s, 9H, CH_3, *t*-Bu), 1.42 (s, 3H, CH_3), 3.43 (m, 1H, H-5), 3.66 (m, 1H, H-5′), 3.73 (m, 1H, H-3), 3.89 (m, 1H, H-4), 4.51 (d, 1H, H-2, $^3J_{2,1}$ = 3.6 Hz), 5.27 (m, 1H, CH), 5.72 (m, 1H, NH), 5.76 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 6.89 (m, 1H, NH), 7.42 (m, 5H, CH=); ^{13}C NMR ($CDCl_3$): δ = 26.4 (CH_3), 27.1 (CH_3), 28.6 (CH_3, *t*-Bu), 37.8 (C-5), 58.1

(CH), 74.4 (C-3), 79.9 (C-4), 80.3 (C, *t*-Bu), 84.4 (C-2), 104.3 (C-1), 112.1 (CMe_2), 127.4 (CH=), 128.8 (CH=), 129.2 (CH=), 137.4 (C), 155.7 (CO), 172.7 (CO); anal. calcd. (%) for $C_{21}H_{30}N_2O_7$: C 59.70, H 7.16, N 6.63; found: C 59.72, H 7.17, N 6.61.

L2a: Yield: 330 mg (85%); ^{1}H NMR ($CDCl_3$): δ = 0.86 (d, 3H, CH_3, *i*-Pr, $^3J_{H,H}$ = 7.2 Hz), 0.91 (d, 3H, CH_3, *i*-Pr, $^3J_{H,H}$ = 7.2 Hz), 1.30 (s, 3H, CH_3), 1.39 (s, 9H, CH_3, *t*-Bu), 1.52 (s, 3H, CH_3), 2.08 (m, 1H, CH, *i*-Pr), 3.54 (m, 2H, H-5 and H-5′), 3.68 (m, 1H, H-3), 3.87 (m, 1H, H-4), 3.93 (m, 1H, CH), 4.53 (dd, 1H, H-2, $^3J_{2,1}$ = 4.0 Hz, $^3J_{2,3}$ = 3.6 Hz), 5.22 (m, 1H, NH), 5.69 (d, 1H, H-1, $^3J_{1,2}$ = 4.0 Hz), 6.72 (m, 1H, NH); ^{13}C NMR ($CDCl_3$): δ = 17.8 (CH_3, *i*Pr), 19.4 (CH_3, *i*-Pr), 26.4 (CH_3), 26.6 (CH_3), 28.4 (CH_3, *t*-Bu), 30.8 (CH, *i*Pr), 39.7 (C-5), 60.2 (CH), 72.9 (C-3), 78.5 (C-4), 79.0 (C-2), 80.1 (C, *t*-Bu), 103.8 (C-1), 112.9 (CMe_2), 156.0 (CO), 172.9 (CO); anal. calcd. (%) for $C_{18}H_{32}N_2O_7$: C 55.65, H 8.30, N 7.21; found: C 55.70, H 8.35, N 7.20.

L3a: Yield: 280 mg (72%); ^{1}H NMR ($CDCl_3$): δ = 0.93 (m, 6H, CH_3, *i*-Pr), 1.29 (s, 3H, CH_3), 1.42 (s, 9H, CH_3, *t*-Bu), 1.50 (s, 3H, CH_3), 2.06 (m, 1H, CH, *i*-Pr), 3.80 (m, 3H, H-5, H-5′ and CH), 4.31 (m, 1H, H-4), 4.41 (m, 1H, H-3), 4.53 (d, 1H, H-2, $^3J_{2,1}$ = 4.0 Hz), 5.16 (m, 1H, NH), 5.86 (d, 1H, H-1, $^3J_{1,2}$ = 4.0 Hz), 7.42 (m, 1H, NH); ^{13}C NMR ($CDCl_3$): δ = 18.4 (CH_3, *i*-Pr), 19.5 (CH_3, *i*-Pr), 26.4 (CH_3), 26.8 (CH_3), 28.5 (CH_3, *t*-Bu), 30.4 (CH, *i*-Pr), 57.1 (C-3), 59.8 (CH), 60.6 (C-5), 78.0 (C-4), 80.5 (C, *t*-Bu), 84.7 (C-2), 104.5 (C-1), 112.2 (CMe_2), 156.4 (CO), 173.0 (CO): anal. calcd. (%) for $C_{18}H_{32}N_2O_7$: C 55.65, H 8.30, N 7.21; found: C 55.66, H 8.32, N 7.22.

L3b: Yield: 346 mg (82%); ^{1}H NMR ($CDCl_3$): δ = 1.24 (s, 3H, CH_3), 1.40 (s, 9H, CH_3, *t*-Bu), 1.47 (s, 3H, CH_3), 3.05 (m, 1H, H-5), 4.08 (m, 2H, H-5' and H-3), 4.28 (m, 1H, H-4), 4.57 (m, 1H, CH), 4.60 (d, 1H, H-2, $^3J_{2,1}$ = 3.6 Hz), 5.19 (m, 1H, NH), 5.88 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 7.34 (m, 5H, CH=), 7.51 (m, 1H, NH); ^{13}C NMR ($CDCl_3$): δ = 26.4 (CH_3), 26.9 (CH_3), 28.5 (CH_3, *t*-Bu), 57.8 (C-3), 59.2 (CH), 60.0 (C-5), 77.7 (C-4), 80.6 (C, *t*-Bu), 84.4 (C-2), 104.5 (C-1), 112.2 (CMe_2), 127.3 (CH=), 128.7 (CH=), 129.2 (CH=), 137.6 (C), 155.6 (CO), 171.6 (CO); anal. calcd. (%) for $C_{21}H_{30}N_2O_7$: C 59.70, H 7.16, N 6.63; found: C 59.76, H 7.19, N 6.61.

L3d: Yield: 322 mg (80%); ^{1}H NMR ($CDCl_3$): δ = 0.93 (m, 6H, CH_3, *i*-Bu), 1.30 (s, 3H, CH_3), 1.42 (s, 9H, CH_3, *t*-Bu), 1.48 (s, 3H, CH_3), 1.51 (m, 1H, CH_2, *i*-Bu), 1.64 (m, 2H, CH and CH_2, *i*-Bu), 3.76 (m, 2H, H-5 and CH), 3.80 (m, 1H, H-5′), 4.29 (m, 1H, H-4), 4.39 (m, 1H, H-3), 4.51 (d, 1H, H-2, $^3J_{2,1}$ = 4.0 Hz), 5.11 (m, 1H, NH), 5.79 (d, 1H, H-1, $^3J_{1,2}$ = 4.0 Hz), 7.37 (m, 1H, NH); ^{13}C NMR ($CDCl_3$): δ = 21.8 (CH_3, *i*-Bu), 22.7 (CH_3, *i*-Bu), 24.7 (CH_2, *i*-Bu), 26.4 (CH_3), 26.9 (CH_3), 28.4 (CH_3, *t*-Bu), 40.4 (CH, *i*-Bu), 57.0 (C-3), 59.7 (CH), 60.3 (C-5), 78.2 (C-4), 80.6 (C, *t*-Bu), 84.9 (C-2), 103.9 (C-1), 112.4 (CMe_2), 156.2 (CO), 174.1 (CO); anal. calcd. (%) for $C_{19}H_{34}N_2O_7$: C 56.70, H 8.51, N 6.96; found: C 56.67, H 8.52, N 6.95.

L3h: Yield: 319 mg (82%); ^{1}H NMR ($CDCl_3$); δ = 0.90 (d, 3H, CH_3, $^3J_{H,H}$ = 7.2 Hz), 0.97 (d, 3H, CH_3, $^3J_{H,H}$ = 7.2 Hz), 1.29 (s, 3H, CH_3), 1.43 (s, 9H, CH_3, *t*-Bu), 1.49 (s, 3H, CH_3), 2.11 (m, 1H, CH, *i*-Pr), 2.77 (m, 1H, H-5), 3.83 (d, 1H, H-3, $^3J_{3,4}$ = 1.2 Hz), 3.89 (m, 2H, H-5′ and H-4), 4.32 (m, 1H, CH), 4.55 (d, 1H, H-2, $^3J_{2,1}$ = 3.6 Hz), 5.18 (m, 1H, NH), 5.88 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 7.52 (m, 1H, NH); ^{13}C NMR ($CDCl_3$): δ = 17.8 (CH_3, *i*-Pr), 19.3 (CH_3, *i*-Pr), 26.1 (CH_3), 26.6 (CH_3), 28.3 (CH_3, *t*-Bu), 30.5 (CH, *i*-Pr), 57.4 (C-3), 60.1 (CH and C-5), 77.2 (C-4), 80.0 (C, *t*-Bu), 84.6 (C-2), 104.4 (C-1), 112.0 (CMe_2), 156.0 (CO), 172.7 (CO); anal. calcd. (%) for $C_{18}H_{32}N_2O_7$: C 55.65, H 8.30, N 7.21; found: C 55.69, H 8.33, N 7.19.

L4a: Yield: 334 mg (86%); ^{1}H NMR ($CDCl_3$): δ = 0.88 (d, 3H, CH_3, *i*-Pr, $^3J_{H;H}$ = 7.2 Hz), 0.93 (d, 3H, CH_3, *i*-Pr, $^3J_{H,H}$ = 7.2 Hz), 1.31 (s, 3H, CH_3), 1.40 (s, 9H, CH_3, *t*-Bu), 1.49 (s, 3H, CH_3), 2.11 (m, 1H, CH, *i*-Pr), 3.64 (dd, 1H, H-5, $^2J_{5,5'}$ = 13.2 Hz, $^3J_{5,4}$ = 2.8 Hz), 3.74 (m, 1H, H-4), 3.81 (dd, 1H, H-5, $^2J_{5,5'}$ = 13.2 Hz, $^3J_{5,4}$ = 2.4 Hz), 3.93 (m, 1H, CH), 4.20 (m, 1H, H-3), 4.59 (dd, 1H, H-2, $^3J_{2,1}$ = 4.0 Hz, $^3J_{2,3}$ = 3.6 Hz), 5.10 (m, 1H, NH), 5.84 (d, 1H, H-1, $^3J_{1,2}$ = 4.0 Hz), 6.59 (m, 1H, NH); ^{13}C NMR ($CDCl_3$): δ = 17.6 (CH_3, *i*-Pr), 19.2 (CH_3, *i*-Pr), 26.3 (CH_3), 26.4 (CH_3), 28.2 (CH_3, *t*-Bu), 30.5 (CH, *i*-Pr), 51.3 (C-3), 59.8 (CH), 60.5 (C-5), 78.8 (C-2), 80.1 (C, *t*-Bu), 80.4 (C-4), 104.1 (C-1), 112.5 (CMe_2), 155.8 (CO), 172.8 (CO); anal. calcd. (%) for $C_{18}H_{32}N_2O_7$: C 55.65, H 8.30, N 7.21; found: C 55.72, H 8.36, N 7.16.

Typical Procedure for the Benzoylation of L1–L4a–i

A solution of benzoyl chloride (1.1 mmol, 130 μL) in dichloromethane (0.4 mL) was slowly added to a cooled solution (0 °C) of the desired pseudodipeptide (1 mmol) in pyridine (1 mL). The reaction mixture was stirred overnight. Then ice was added and the mixture was extracted with dichloromethane (3 × 20 mL), the extract was dried over $MgSO_4$, evaporated to dryness and the residue purified by flash chromatography (pentane/ethyl acetate: 2/1) to produce the corresponding benzoylated product as white solids.

***N*-(*tert*-Butoxycarbonyl)-L-valine-(5-amide-3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose) (8a):** Yield: 374 mg (76%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (d, 3H, CH_3, *J* = 6.8 Hz), 0.95 (d, 3H, CH_3, *J* = 6.8 Hz), 1.33 (s, 3H, CH_3), 1.44 (s, 9H, CH_3), 1.53 (s, 3H, CH_3), 2.16 (m, 1H, CH), 3.58 (t, 2H, H-5, H-5′, $^3J_{5,5'-4}$ = 6.4 Hz), 3.95 (t, 1H, CH-NH, $J_{CH,NH}$ = 6.8 Hz), 4.43 (dt, 1H, H-4, $^3J_{4-5,5'}$ = 6.6 Hz, $^3J_{4,3}$ = 2.8 Hz), 4.68 (d, 1H, H-2, $^3J_{2,1}$ = 3.6 Hz), 5.09 (d, 1H, NHBoc, $J_{NH,CH}$ = 9.2 Hz), 5.42 (d, 1H, H-3, $^3J_{3,4}$ = 2.8 Hz), 6.00 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 6.41 (b, 1H, NH), 7.44–8.15 (m, 5H, CH=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.9 (CH_3), 19.5 (CH_3), 26.4 (CH_3), 26.8 (CH_3), 28.5 (CH_3), 31.1 ($CHMe_2$), 37.9 (C-5), 60.0 (CH), 77.0 (C-3), 78.2 (C-4), 83.8 (C-2), 104.9 (C-1), 112.6 (CMe_2), 128.6–134.0 (CH=), 156.0 (CMe_3), 165.7 (CO), 171.9 (CO).

***N*-(*tert*-Butoxycarbonyl)-L-phenylglycine-(5-amide-3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose) (8b):** Yield: 337 mg (64%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (s, 3H, CH_3), 1.40 (s, 9H, CH_3), 1.51 (s, 3H, CH_3), 3.44 (m, 1H, H-5′), 3.63 (m, 1H, H-5), 4.37 (sp, 1H, H-4), 4.63 (d, 1H, H-2, $^3J_{2,1}$ = 4 Hz), 5.18 (a, 1H, CH-NH), 5.26 (d, 1H, H-3, $^3J_{3,4}$ = 2.8 Hz), 5.92 (a, 1H, NHBoc), 5.95 (d, 1H, H-1, $^3J_{1,2}$ = 4 Hz), 6.42 (a, 1H, NH), 7.27–8.11 (m, 10H, CH=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4 (CH_3), 26.8 (CH_3), 28.4 (CH_3), 38.4 (C-5), 58.7 (CH-NH), 76.9 (C-3), 78.1 (C-4), 83.6 (C-2), 104.8 (C-1), 112.5 (CMe_2), 127.3–133.9 (CH=), 138.4 (CAr), 155.3 (CMe_3) 165.6 (CO), 170.6 (CO).

***N*-(*tert*-Butoxycarbonyl)-L-phenylalanine-(5-amide-3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose) (8c):** Yield: 260 mg (48%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 3H,

CH_3), 1.40 (s, 9H, CH_3), 1.56 (s, 3H, CH_3),3.04 (m, 2H, H-8, H-8′), 3.38 (m, 1H, H-5′), 3.59 (m, 1H, H-5), 4.24 (m, 1H, H-4), 4.37 (a, 1H, CH-NH), 4.63 (d, 1H, H-2, $^3J_{2,1}=4$ Hz), 5.14 (m, 1H, H-3), 5.27 (a, 1H, NHBoc), 5.95 (d, 1H, H-1, $^3J_{1,2}=3.6$ Hz), 6.37 (a, 1H, NH), 7.20–8.11 (m, 10H, CH=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.3 (CH_3), 26.8 (CH_3), 28.4 (CH_3), 37.6 (C-5), 39.0 (CH_2), 56.2 (CH-NH), 76.8 (C-3), 77.9 (C-4), 83.7 (C-2), 104.8 (C-1), 112.5 (CMe_2), 127.1–133.9 (CH=), 136.8 (CAr), 155.6 (CMe_3) 165.7 (CO), 171.7 (CO).

***N*-(*tert*-Butoxycarbonyl)-L-leucine-(5-amide-3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose) (8d):** Yield: 213 mg (42%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (dd, 6H, CH_3, $J=8$ Hz, $J=4$ Hz), 1.34 (s, 3H,CH_3), 1.45 (s, 9H, CH_3), 1.55 (s, 3H, CH_3), 1.66 (m, 3H, CH_2, CH), 3.59 (t, 2H, H-5, H-5′, $^3J=6$ Hz), 4.13 (a, 1H, CH-NH), 4.32 (dt, 1H, H-4, $^3J_{4\text{-}5,5'}=6.5$ Hz, $^3J_{4,3}=3$ Hz), 4.69 (d, 1H, H-2, $^3J_{2,1}=3.6$ Hz), 4.84 (a, 1H, NHBoc), 5.42 (d, 1H, H-3, $^3J_{3,4}=2.8$ Hz), 6.01 (d, 1H, H-1, $^3J_{1,2}=3.6$ Hz), 6.48 (t, 1H, NH, $J=6$ Hz), 7.45–8.12 (m, 5H, CH=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.1 (CH_3), 23.2 (CH_3), 25.0 (CH_2), 26.4 (CH_3), 26.8 (CH_3), 28.5 (CH_3), 38.2 (C-5), 41.6 ($CHMe_2$), 56.8 (CH-NH), 77.4 (C-3), 78.2 (C-4), 83.8 (C-2), 104.9 (C-1), 112.6 (CMe_2), 128.7–133.9 (CH=), 150.4 (CMe_3), 165.5 (CO), 172.9 (CO).

***N*-(*tert*-Butoxycarbonyl)-L-*tert*-leucine-(5-amide-3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose) (8e):** Yield: 400 mg (79%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (s, 9H, CH_3), 1.30 (s, 3H,CH_3), 1.41 (s, 9H, CH_3), 1.51 (s, 3H, CH_3), 3.51 (m, 1H, H-5′), 3.62 (m, 1H, H-5), 3.91 (d, 1H, CH-NH, $J=9.6$ Hz), 4.43 (m, 1H, H-4), 4.66 (d, 1H, H-2, $^3J_{2,1}=4$ Hz), 5.40 (d, 1H, H-3, $^3J_{3,4}=2.4$ Hz), 5.45 (m, 1H, NHBoc), 5.98 (d, 1H, H-1, $^3J_{1,2}=4$ Hz), 6.46 (m, 1H, NH), 7.41–8.16 (m, 5H, CH=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4 (CH_3), 26.7 (CH_3), 26.8 (CH_3), 28.4 (CH_3), 37.8 (C-5), 62.5 (CH-NH), 77.0 (C-3), 78.1 (C-4), 83.7 (C-2), 104.8 (C-1), 112.5 (CMe_2), 128.4–134.7 (CH=), 156.0 (CMe_3), 165.7 (CO), 169.9 (CMe_3), 171.4 (CO).

***N*-(*tert*-Butoxycarbonyl)-L-alanine-(5-amide-3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose) (8f):** Yield: 293 mg (63%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (s, 3H,CH_3), 1.34 (d, 3H, CH_3, $J=7.2$ Hz), 1.43 (s, 9H, CH_3), 1.52 (s, 3H, CH_3), 3.59 (m, 2H, H-5, H-5′), 4.19 (a, 1H, CH-NH), 4.44 (dt, 1H, H-4, $^3J_{4\text{-}5,5'}=6.4$ Hz, $^3J_{4,3}=2.6$ Hz), 4.67 (d, 1H, H-2, $^3J_{2,1}=3.6$ Hz), 5.20 (a, 1H, NHBoc), 5.42 (d, 1H, H-3, $^3J_{3,4}=2.4$ Hz), 5.99 (d, 1H, H-1, $^3J_{1,2}=4$ Hz), 6.74 (t, 1H, NH, $J=5.6$ Hz), 7.42–8.11 (m, 5H, CH=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.6 (CH_3), 26.3 (CH_3), 26.8 (CH_3), 28.4 (CH_3), 38.0 (C-5), 50.3 (CH), 76.9 (C-3), 78.1 (C-4), 83.7 (C-2), 104.9 (C-1), 112.5 (CMe_2), 128.5–133.9 (CH=), 155.7 (CMe_3), 165.7 (CO), 171.4 (CO).

***N*-(*tert*-Butoxycarbonyl)-L-glycine-(5-amide-3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose) (8g):** Yield: 198 mg (44%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (s, 3H,CH_3), 1.45 (s, 9H, CH_3), 1.53 (s, 3H, CH_3), 3.59 (m, 2H, H-5, H-5′), 3.78 (m, 2H, CH_2-NH), 4.43 (dt, 1H, H-4, $^3J_{4\text{-}5,5'}=6.4$ Hz, $^3J_{4,3}=3.2$ Hz), 4.68 (d, 1H, H-2, $^3J_{2,1}=3.6$ Hz), 5.16 (t, 1H, NHBoc, $J=5.6$ Hz), 5.43 (d, 1H, H-3, $^3J_{3,4}=2.8$ Hz), 5.99 (d, 1H, H-1, $^3J_{1,2}=3.6$ Hz), 6.52 (a, 1H, NH), 7.43–8.02 (m, 5H, CH=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.1 (CH_3), 26.6 (CH_3), 28.3 (CH_3), 37.7 (C-5), 44.2 (CH_2-NH), 76.8 (C-3), 77.9 (C-4), 83.6 (C-2), 104.5 (C-1), 112.4 (CMe_2), 128.0–133.8 (CH=), 165.5 (CO), 169.6 (CO).

***N*-(*tert*-Butoxycarbonyl)-D-valine-(5-amide-3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose) (8h):** Yield: 305 mg (62%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (d, 6H, CH_3, $J=6.8$ Hz), 1.30 (s, 3H, CH_3), 1.41 (s, 9H, CH_3), 1.49 (s, 3H, CH_3), 2.06 (m, 1H, CH), 3.53 (m, 1H, H-5′), 3.66 (m, 1H, H-5), 3.96 (t, 1H, CH-NH, $J_{CH,NH}=7.8$ Hz), 4.59 (sp, 1H, H-4), 4.65 (d, 1H, H-2, $^3J_{2,1}=4$ Hz), 5.43 (d, 1H, H-3, $^3J_{3,4}=2.4$ Hz), 5.46 (d, 1H, NHBoc, $J=8.4$ Hz), 5.96 (d, 1H, H-1, $^3J_{1,2}=4$ Hz), 6.81 (a, 1H, NH), 7.40–8.09 (m, 5H, CH=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.1 (CH_3), 19.3 (CH_3), 26.3 (CH_3), 26.7 (CH_3), 28.4 (CH_3), 31.1 ($CHMe_2$), 38.0 (C-5), 60.2 (CH), 76.9 (C-3), 77.9 (C-4), 83.7 (C-2), 104.8 (C-1), 112.5 (CMe_2), 128.4–133.8 (CH=), 156.2 (CMe_3), 165.6 (CO), 170.4 (CO).

***N*-(*tert*-Butoxycarbonyl)-D-phenylglycine-(5-amide-3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose) (8i):** Yield: 337 mg (64%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (s, 3H,CH_3), 1.40 (s, 9H, CH_3), 1.48 (s, 3H, CH_3), 3.45 (m, 1H, H-5′), 3.64 (m, 1H, H-5), 4.36 (dt, 1H, H-4, $^3J_{4\text{-}5,5'}=6.5$ Hz, $^3J_{4,3}=2.8$ Hz), 4.65 (d, 1H, H-2, $^3J_{2,1}=4$ Hz), 5.16 (a, 1H, CH-NH), 5.39 (d, 1H, H-3, $^3J_{3,4}=3.2$ Hz), 5.88 (d, 1H, NHBoc, $J=7.2$ Hz), 5.94 (d, 1H, H-1, $^3J_{1,2}=3.2$ Hz), 6.42 (t, 1H, NH, $J=5.6$ Hz), 7.27–8.10 (m, 10H, CH=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4 (CH_3), 26.8 (CH_3), 28.4 (CH_3), 38.1 (C-5), 58.6 (CH-NH), 76.9 (C-3), 77.8 (C-4), 83.6 (C-2), 104.8 (C-1), 112.5 (CMe_2), 127.3–133.9 (CH=), 138.3 (CAr), 155.3 (CMe_3) 165.8 (CO), 170.2 (CO).

***N*-(*tert*-Butoxycarbonyl)-L-valine-(5-amide-3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-ribofuranose) (9a):** Yield: 374 mg (76%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (d, 3H, CH_3, $J=8$ Hz), 0.95 (d, 3H, CH_3, $J=4$ Hz), 1.33 (s, 3H, CH_3), 1.45 (s, 9H, CH_3), 1.56 (s, 3H, CH_3), 2.15 (m, 1H, CH), 3.52 (m, 1H, H-5′), 3.76 (m, 1H, H-5), 3.93 (t, 1H, CH-NH, $J_{CH,NH}=6$ Hz), 4.36 (sp, 1H, H-4), 4.71 (dd, 1H, H-3, $^3J_{3,2}=8$ Hz , $^3J_{3,4}=4$ Hz), 4.94 (t, 1H, H-2, $^3J_{2\text{-}1,3}=6$ Hz), 5.00 (a, 1H, NHBoc), 5.85 (d, 1H, H-1, $^3J_{1,2}=4$ Hz), 6.26 (a, 1H, NH), 7.43–8.09 (m, 5H, CH=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.5 (CH_3), 19.5 (CH_3), 26.7 (CH_3), 28.5 (CH_3), 31.0 ($CHMe_2$), 39.7 (C-5), 60.1 (CH), 73.7 (C-3), 76.4 (C-4), 77.7 (C-2), 104.3 (C-1), 113.4 (CMe_2), 128.6–133.7 (CH=), 149.8 (CMe_3), 166.1 (CO), 172.0 (CO).

***N*-(*tert*-Butoxycarbonyl)-L-valine-(3-amide-5-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose) (10a):** Yield: 251 mg (51%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (d, 3H, CH_3, $J=4$ Hz), 0.95 (d, 3H, CH_3, $J=8$ Hz), 1.33 (s, 3H, CH_3), 1.45 (s, 9H, CH_3), 1.55 (s, 3H, CH_3), 2.21 (m, 1H, CH), 3.86 (t, 1H, CH-NH, $J_{CH,NH}=8$ Hz), 4.49 (m, 1H, H-3), 4.52 (d, 1H, H-2, $^3J_{2,1}=4$ Hz), 4.60 (m, 1H, H-4), 4.66 (dd, 2H, H-5, H-5′, $^2J_{5,5'}=8$ Hz , $^3J_{5,5\text{-}4}=4$ Hz), 4.86 (a, 1H, NHBoc), 5.90 (d, 1H, H-1, $^3J_{1,2}=4$ Hz), 6.41 (d, 1H, NH, $J=8$ Hz), 7.44–8.11 (m, 5H, CH=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.8 (CH_3), 19.6 (CH_3), 26.3 (CH_3), 26.7 (CH_3), 28.4 (CH_3), 29.8 ($CHMe_2$), 55.7 (C-5), 59.6 (CH), 62.0 (C-3), 76.1 (C-4), 84.6 (C-2), 104.7 (C-1), 112.5 (CMe_2), 128.6–133.4 (CH=), 146.9 (CMe_3), 166.2 (CO), 171.7 (CO).

***N*-(*tert*-Butoxycarbonyl)-L-phenylglycine-(3-amide-5-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose) (10b):** Yield: 342 mg (65%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (s, 3H,CH_3), 1.41 (s, 9H, CH_3), 1.52 (s, 3H, CH_3), 4.39 (s, 1H, H-2), 4.53 (d, 1H, H-3, $^3J_{3,4}=6$ Hz), 4.58 (m, 1H, H-4), 4.63 (dd, 2H, H-5, H-5′, $^2J_{5,5'}=8.8$ Hz, $^3J_{5,5'\text{-}4}=3.2$ Hz), 5.19 (a, 1H, CH-NH), 5.71 (a, 1H, NHBoc), 5.77 (s, 1H, H-1),

6.66 (a, 1H, NH), 7.29–8.12 (m, 10H, CH=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.3 (CH_3), 26.7 (CH_3), 28.4 (CH_3), 56.2 (C-5), 59.2 (CH-NH), 62.0 (C-3), 76.2 (C-4), 84.4 (C-2), 104.6 (C-1), 112.5 (CMe_2), 127.3–133.7 (CH=), 137.5 (CAr), 155.6 (CMe_3) 166.3 (CO), 170.7 (CO).

***N*-(*tert*-Butoxycarbonyl)-L-leucine-(3-amide-5-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose) (10d):** Yield: 288 mg (57%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (d, 3H, CH_3, J = 4 Hz), 0.95 (d, 3H, CH_3, J = 8 Hz), 1.33 (s, 3H, CH_3), 1.45 (s, 9H, CH_3), 1.55 (s, 3H, CH_3), 1.66 (m, 3H, CH_2, CH), 3.86 (t, 1H, CH-NH, $J_{CH,NH}$ = 8 Hz), 4.49 (m, 1H, H-3), 4.52 (d, 1H, H-2, $^3J_{2,1}$ = 4 Hz), 4.60 (m, 1H, H-4), 4.66 (dd, 2H, H-5, H-5′, $^2J_{5,5'}$ = 8 Hz , $^3J_{5,5'\text{-}4}$ = 4 Hz), 4.86 (a, 1H, NHBoc), 5.90 (d, 1H, H-1, $^3J_{1,2}$ = 4 Hz), 6.41 (d, 1H, NH, J = 8 Hz), 7.44–8.11 (m, 5H, CH=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.1 (CH_3), 23.2 (CH_3), 26.3 (CH_3), 27.2 (CH_3), 28.4 (CH_3), 32.8 ($CHMe_2$), 55.7 (C-5), 59.6 (CH), 62.0 (C-3), 76.1 (C-4), 84.6 (C-2), 104.7 (C-1), 112.5 (CMe_2), 128.6–133.4 (CH=), 146.9 (CMe_3), 166.2 (CO), 171.7 (CO).

***N*-(*tert*-Butoxycarbonyl)-D-valine-(3-amide-5-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose) (10h):** Yield: 290 mg (59%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (d, 6H, CH_3, J = 6.8 Hz), 1.30 (s, 3H, CH_3), 1.44 (s, 9H, CH_3), 1.53 (s, 3H, CH_3), 2.03 (m, 1H, CH), 3.88 (t, 1H, CH-NH, $J_{CH,NH}$ = 8 Hz), 4.42 (m, 1H, H-3), 4.50 (d, 1H, H-2, $^3J_{2,1}$ = 4 Hz), 4.60 (m, 1H, H-4), 4.68 (dd, 2H, H-5, H-5′, $^2J_{5,5'}$ = 9.4 Hz , $^3J_{5,5'\text{-}4}$ = 3.4 Hz), 5.27 (d, 1H, NHBoc, J = 7.6 Hz), 5.93 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 6.79 (d, 1H, NH, J = 8.4 Hz), 7.41–8.12 (m, 5H, CH=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.8 (CH_3), 19.3 (CH_3), 26.1 (CH_3), 26.5 (CH_3), 28.3 (CH_3), 30.6 ($CHMe_2$), 55.6 (C-5), 60.4 (CH), 62.1 (C-3), 75.9 (C-4), 84.5 (C-2), 104.6 (C-1), 112.2 (CMe_2), 128.4–133.4 (CH=), 156.2 (CMe_3), 166.1 (CO), 172.1 (CO).

***N*-(*tert*-Butoxycarbonyl)-L-valine-(3-amide-5-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-ribofuranose) (11a):** Yield: 399 mg (81%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (d, 3H, CH_3, J = 8 Hz), 1.00 (d, 3H, CH_3, J = 4 Hz), 1.38 (s, 3H, CH_3), 1.47 (s, 9H, CH_3), 1.59 (s, 3H, CH_3), 2.17 (m, 1H, CH), 3.99 (a, 1H, CH-NH), 4.09 (m, 1H, H-4), 4.3 (dd, 1H, H-5′, $^2J_{5,5'}$ = 12 Hz, $^3J_{5,5'\text{-}4}$ = 4 Hz), 4.46 (m, 1H, H-3), 4.65 (t, 1H, H-2, $^3J_{2\text{-}1,3}$ = 4 Hz), 4.74 (dd, 1H, H-5, $^2J_{5,5'}$ = 12 Hz, $^3J_{5,5'\text{-}4}$ = 4 Hz), 5.09 (a, 1H, NHBoc), 5.91 (d, 1H, H-1, $^3J_{1,2}$ = 4 Hz), 6.36 (d, 1H, NH, J = 12 Hz), 7.44–8.12 (m, 5H, CH=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.8 (CH_3), 19.6 (CH_3), 26.5 (CH_3), 26.8 (CH_3), 28.5 (CH_3), 31.0 ($CHMe_2$), 52.0 (C-3), 59.9 (CH), 63.6 (C-5), 78.5 (C-4), 78.9 (C-2), 104.7 (C-1), 117.7 (CMe_2), 128.5–133.2 (CH=), 149.8 (CMe_3), 166.4 (CO), 171.9 (CO).

Typical Procedure for the Preparation of Thioamide Ligands L5–L8a–i

To a cooled solution of the desired benzoylated product (1 mmol) in THF (4 mL) Lawesson's reagent (0.8 mmol, 317 mg) was added. The reaction was stirred overnight at 60 °C. Then, the reaction mixture was evaporated and chromatographed (pentane/ethyl acetate: 3/1) to produce the corresponding thioamides as white solids.

L5a: Yield: 232 mg (57%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (dd, 6H, CH_3, $^2J_{5,5'}$ = 10.6 Hz, $^3J_{5,5'\text{-}4}$ = 6.8 Hz), 1.33 (s, 3H, CH_3), 1.44 (s, 9H, CH_3), 1.53 (s, 3H, CH_3), 2.28 (m, 1H, CH), 3.97 (m, 1H, H-5′), 4.02 (m, 1H, H-5), 4.08 (m, 1H, CH-NH), 4.63 (sp, 1H, H-4), 4.70 (d, 1H, H-2, $^3J_{2,1}$ = 4 Hz), 5.26 (a, 1H, NHBoc), 5.42 (d, 1H, H-3, $^3J_{3,4}$ = 2.8 Hz), 6.01 (d, 1H, H-1, $^3J_{1,2}$ = 4 Hz), 7.45–8.04 (m, 5H, CH=), 8.25 (m, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.9 (CH_3), 19.8 (CH_3), 26.4 (CH_3), 26.8 (CH_3), 28.5 (CH_3), 33.5 ($CHMe_2$), 43.8 (C-5), 55.7 (CH), 76.4 (C-4), 77.2 (C-3), 83.7 (C-2), 104.9 (C-1), 112.7 (CMe_2), 128.8–134.2 (CH=), 155.8 (CMe_3), 165.8 (CO), 205.2 (CS); anal. calcd. (%) for $C_{25}H_{36}N_2O_7S$: C 59.03, H 7.13, N 5.51, S 6.30; found: C 59.00, H 7.08, N 5.49, S 6.28.

L5b: Yield: 287 mg (66%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (s, 3H, CH_3), 1.42 (s, 9H, CH_3), 1.51 (s, 3H, CH_3), 3.83 (m, 1H, H-5′), 4.11 (m, 1H, H-5), 4.59 (m, 1H, H-4), 4.66 (d, 1H, H-2, $^3J_{2,1}$ = 4 Hz), 5.31 (d, 1H, H-3, $^3J_{3,4}$ = 2.4 Hz), 5.47 (a, 1H, CH-NH), 5.97 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 6.16 (d, 1H, NHBoc, J = 6.4 Hz), 7.27–8.12 (m, 10H, CH=), 8.41 (a, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4 (CH_3), 26.8 (CH_3), 28.4 (CH_3), 44.2 (C-5), 64.0 (CH-NH), 76.4 (C-4), 77.1 (C-3), 83.6 (C-2), 104.8 (C-1), 112.7 (CMe_2), 127.1–133.9 (CH=), 139.5 (CAr), 154.9 (CMe_3) 165.7 (CO), 202.9 (CS); anal. calcd. (%) for $C_{28}H_{34}N_2O_7S$: C 61.97, H 6.32, N 5.16, S 5.91; found: C 61.92, H 6.30, N 5.18, S 5.88.

L5c: Yield: 361 mg (81%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34 (s, 3H,CH_3), 1.42 (s, 9H, CH_3), 1.57 (s, 3H, CH_3), 3.10 (m, 1H, H-8′), 3.20 (m, 1H, H-8), 3.67 (m, 1H, H-5′), 4.00 (m, 1H, H-5), 4.31 (m, 1H, H-4), 4.56 (a, 1H, CH-NH), 4.64 (d, 1H, H-2, $^3J_{2,1}$ = 4 Hz), 5.01 (m, 1H, H-3), 5.43 (a, 1H, NHBoc), 5.94 (d, 1H, H-1, $^3J_{1,2}$ = 4 Hz), 7.23–8.09 (m, 10H, CH=), 7.80 (a, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4 (CH_3), 26.9 (CH_3), 28.5 (CH_3), 42.4 (CH_2), 43.3 (C-5), 60.6 (CH-NH), 76.3 (C-4), 77.4 (C-3), 83.8 (C-2), 104.8 (C-1), 112.8 (CMe_2), 127.3–134.1 (CH=), 136.8 (CAr), 155.2 (CMe_3) 165.9 (CO), 204.2 (CS); anal. calcd. (%) for $C_{29}H_{36}N_2O_7S$: C 62.57, H 6.52, N 5.03, S 5.76; found: C 62.54, H 6.49, N 4.98, S 5.71.

L5d: Yield: 96 mg (23%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (dd, 6H, CH_3, J = 6.2 Hz, J = 1.8 Hz), 1.33 (s, 3H,CH_3), 1.44 (s, 9H, CH_3), 1.54 (s, 3H, CH_3), 1.58–1.74 (m, 3H, CH_2, CH), 3.93 (m, 1H, H-5′), 4.06 (m, 1H, H-5), 4.39 (m, 1H, CH-NH), 4.62 (sp, 1H, H-4), 4.70 (d, 1H, H-2, $^3J_{2,1}$ = 4 Hz), 5.13 (d, 1H, NHBoc, J = 7.6 Hz), 5.42 (d, 1H, H-3, $^3J_{3,4}$ = 2.8 Hz), 6.01 (d, 1H, H-1, $^3J_{1,2}$ = 4 Hz), 7.45–8.04 (m, 5H, CH=), 8.36 (a, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.1 (CH_3), 23.1 (CH_3), 25.1 (CH_2), 26.4 (CH_3), 26.8 (CH_3), 28.5 (CH_3), 44.0 (C-5), 44.8 ($CHMe_2$), 59.6 (CH-NH), 76.5 (C-4), 77.2 (C-3), 83.8 (C-2), 104.9 (C-1), 112.7 (CMe_2), 128.3–134.0 (CH=), 155.7 (CMe_3), 165.7 (CO), 206.3 (CS); anal. calcd. (%) for $C_{26}H_{38}N_2O_7S$: C 59.75, H 7.33, N 5.36, S 6.14; found: C 59.77, H 7.29, N 5.34, S 6.11.

L5f: Yield: 299 mg (78%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.44 (s, 9H, CH_3), 1.54 (s, 3H, CH_3), 3.95 (m, 1H, H-5′), 4.05 (m, 1H, H-5), 4.43 (m, 1H, CH-NH), 4.61 (sp, 1H, H-4), 4.70 (d, 1H, H-2, $^3J_{2,1}$ = 4 Hz), 5.15 (a, 1H, NHBoc), 5.43 (d, 1H, H-3, $^3J_{3,4}$ = 4 Hz), 6.01 (d, 1H, H-1, $^3J_{1,2}$ = 4 Hz), 7.45–8.03 (m, 5H, CH=), 8.28 (a, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.9 (CH_3), 26.4 (CH_3), 26.9 (CH_3), 28.5 (CH_3), 44.0 (C-5), 52.5 (CH), 76.5 (C-3), 77.4 (C-4), 83.8 (C-2), 104.9 (C-1), 112.7 (CMe_2), 128.8–134.0 (CH=), 157.7 (CMe_3), 165.8 (CO), 206.2 (CS); anal. calcd. (%) for $C_{23}H_{32}N_2O_7S$: C 57.48, H 6.71, N 5.83, S 6.67; found: C 57.44, H 6.70, N 5.81, S 6.64.

L5g: Yield: 295 mg (79%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (s, 3H, CH_3), 1.45 (s, 9H, CH_3), 1.52 (s, 3H, CH_3), 3.95 (m, 1H, H-5′), 4.09 (m, 1H, H-5), 4.15 (d, 2H, H-7, H-7′, $^2J_{7,7'}$ = 7.2 Hz), 4.62 (sp, 1H, H-4), 4.69 (d, 1H, H-2, $^3J_{2,1}$ = 4 Hz), 5.31 (a, 1H, NHBoc), 5.44 (d, 1H, H-3, $^3J_{3,4}$ = 3.2 Hz), 5.99 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 7.43–8.01 (m, 5H, CH=), 8.55 (a, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4 (CH_3), 26.8 (CH_3), 28.4 (CH_3), 43.8 (C-5), 52.3 (CH_2-NH), 76.5 (C-4), 77.2 (C-3), 83.7 (C-2), 104.9 (C-1), 112.6 (CMe_2), 128.7–133.9 (CH=), 165.6 (CO), 200.8 (CS); anal. calcd. (%) for $C_{22}H_{30}N_2O_7S$: C 56.64, H 6.48, N 6.00, S 6.87; found: C 56.60, H 6.45, N 5.99, S 6.84.

L5h: Yield: 260 mg (64%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (d, 6H, CH_3, J = 6 Hz), 1.31 (s, 3H, CH_3), 1.43 (s, 9H, CH_3), 1.49 (s, 3H, CH_3), 2.19 (m, 1H, CH), 3.84 (m, 1H, H-5′),4.09 (t, 1H, CH-NH, $J_{CH,NH}$ = 7.6 Hz), 4.17 (m, 1H, H-5), 4.65 (sp, 1H, H-4), 4.67 (d, 1H, H-2, $^3J_{2,1}$ = 4 Hz), 5.32 (a, 1H, NHBoc), 5.42 (d, 1H, H-3, $^3J_{3,4}$ = 2.4 Hz), 5.96 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 7.44–8.01 (m, 5H, CH=), 8.48 (a, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.3 (CH_3), 19.6 (CH_3), 26.5 (CH_3), 26.8 (CH_3), 28.5 (CH_3), 33.6 ($CHMe_2$), 44.0 (C-5), 66.7 (CH), 76.3 (C-4), 76.9 (C-3), 83.7 (C-2), 104.8 (C-1), 112.6 (CMe_2), 128.8–133.9 (CH=), 156.1 (CMe_3), 165.7 (CO), 205.1 (CS); anal. calcd. (%) for $C_{25}H_{36}N_2O_7S$: C 59.03, H 7.13, N 5.51, S 6.30; found: C 59.02, H 7.12, N 5.50, S 6.28.

L5i: Yield: 321 mg (74%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (s, 3H, CH_3), 1.43 (s, 9H, CH_3), 1.47 (s, 3H, CH_3), 3.87 (t, 1H, H-5′, J = 7 Hz), 3.98 (t, 1H, H-5, J = 5.8 Hz), 4.54 (m, 1H, H-4), 4.68 (d, 1H, H-2, $^3J_{2,1}$ = 3.6 Hz), 5.40 (d, 1H, H-3, $^3J_{3,4}$ = 2.4 Hz), 5.47 (a, 1H, CH-NH), 5.95 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 6.12 (a, 1H, NHBoc), 7.27–8.10 (m, 10H, CH=), 8.37 (a, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4 (CH_3), 26.8 (CH_3), 28.4 (CH_3), 44.1 (C-5), 63.9 (CH-NH), 76.3 (C-4), 76.9 (C-3), 83.6 (C-2), 104.8 (C-1), 112.7 (CMe_2), 127.0–134.0 (CH=), 139.4 (CAr), 155.1 (CMe_3) 165.8 (CO), 202.9 (CS); anal. calcd. (%) for $C_{28}H_{34}N_2O_7S$: C 61.97, H 6.32, N 5.16, S 5.91; found: C 61.95, H 6.30, N 5.15, S 5.89.

L6a: Yield: 93 mg (23%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (d, 3H, CH_3, J = 8 Hz), 0.95 (d, 3H, CH_3, J = 4 Hz), 1.34 (s, 3H, CH_3), 1.46 (s, 9H, CH_3), 1.56 (s, 3H, CH_3), 2.33 (m, 1H, CH), 3.98 (m, 1H, H-5′), 4.17 (m, 1H, H-5), 4.20 (a, 1H, CH-NH), 4.52 (sp, 1H, H-4), 4.73 (dd, 1H, H-3, $^3J_{3,2}$ = 10 Hz , $^3J_{3,4}$ = 6 Hz), 4.98 (t, 1H, H-2, $^3J_{2\text{-}1,3}$ = 4 Hz), 5.18 (a, 1H, NHBoc), 5.87 (d, 1H, H-1, $^3J_{1,2}$ = 4 Hz), 7.45–8.09 (m, 5H, CH=), 8.11 (a, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.6 (CH_3), 20.0 (CH_3), 26.7 (CH_3), 28.5 (CH_3), 33.2 ($CHMe_2$), 45.8 (C-5), 67.4 (CH), 74.0 (C-3), 75.5 (C-4), 77.6 (C-2), 104.5 (C-1), 113.6 (CMe_2), 128.6–133.7 (CH=), 155.8 (CMe_3), 166.0 (CO), 205.3 (CS); anal. calcd. (%) for $C_{25}H_{36}N_2O_7S$: C 59.03, H 7.13, N 5.51, S 6.30; found: C 59.00, H 7.11, N 5.48, S 6.27.

L7a: Yield: 49 mg (12%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.79 (d, 3H, CH_3, J = 8 Hz), 0.93 (d, 3H, CH_3, J = 4 Hz), 1.34 (s, 3H, CH_3), 1.44 (s, 9H, CH_3), 1.57 (s, 3H, CH_3), 2.44 (m, 1H, CH), 4.09 (t, 1H, CH-NH, $J_{CH,NH}$ = 8 Hz), 4.57 (m, 1H, H-3), 4.62 (d, 1H, H-2, $^3J_{2,1}$ = 4 Hz), 4.68 (m, 1H, H-4), 5.02 (d, 1H, NHBoc, J = 8 Hz), 5.25 (dd, 2H, H-5, H-5′, $^2J_{5,5'}$ = 8 Hz, $^3J_{5,5'-4}$ = 4 Hz), 5.88 (d, 1H, H-1, $^3J_{1,2}$ = 4 Hz), 7.44–8.06 (m, 5H, CH=), 8.40 (a, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.5 (CH_3), 19.3 (CH_3), 26.3 (CH_3), 26.7 (CH_3), 28.4 (CH_3), 32.0 ($CHMe_2$), 61.3 (C-5), 61.7 (C-3), 68.3 (CH), 75.7 (C-4), 83.7 (C-2), 104.6 (C-1), 112.7 (CMe_2), 128.6–134.3 (CH=), 156.1 (CMe_3), 166.1 (CO), 205.3 (CS); anal. calcd. (%) for $C_{25}H_{36}N_2O_7S$: C 59.03, H 7.13, N 5.51, S 6.30; found: C 58.99, H 7.11, N 5.45, S 6.26.

L7b: Yield: 103 mg (19%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (s, 3H, CH_3), 1.44 (s, 9H, CH_3), 1.54 (s, 3H, CH_3), 4.51 (d, 1H, H-2, $^3J_{2,1}$ = 3.2 Hz), 4.62 (d, 1H, H-3, $^3J_{3,4}$ = 5.2 Hz), 4.68 (m, 1H, H-4), 5.20 (dd, 1H, H-5, H-5′, $^2J_{5,5'}$ = 8.2 Hz, $^3J_{5,5'-4}$ = 3.4 Hz), 5.51 (d, 1H, CH-NH), 5.69 (a, 1H, NHBoc), 5.75 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 7.25–8.11 (m, 10H, CH=), 8.45 (a, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4 (CH_3), 26.7 (CH_3), 28.4 (CH_3), 61.6 (C-5), 61.7 (C-3), 65.8 (CH), 75.5 (C-4), 83.5 (C-2), 104.6 (C-1), 112.8 (CMe_2), 127.0–133.8 (CH=), 138.5 (CAr), 155.3 (CMe_3) 166.2 (CO), 203.2 (CS); anal. calcd. (%) for $C_{28}H_{34}N_2O_7S$: C 61.97, H 6.32, N 5.16, S 5.91; found: C 61.94, H 6.30, N 5.11, S 5.89.

L7d: Yield: 67 mg (16%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (dd, 6H, CH_3, J = 6.2 Hz, J = 1.8 Hz), 1.35 (s, 3H,CH_3), 1.42 (s, 9H, CH_3), 1.51 (s, 3H, CH_3), 1.6–1.8 (m, 3H, CH_2, CH), 4.06 (t, 1H, CH-NH, $J_{CH,NH}$ = 8 Hz), 4.61 (m, 1H, H-3), 4.65 (m, 2H, H-2 and H-4), 5.01 (d, 1H, NHBoc, J = 8 Hz), 5.26 (dd, 2H, H-5, H-5′, $^2J_{5,5'}$ = 8 Hz , $^3J_{5,5'-4}$ = 4 Hz), 5.92 (d, 1H, H-1, $^3J_{1,2}$ = 4 Hz), 7.44–8.06 (m, 5H, CH=), 8.42 (a, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.1 (CH_3), 23.1 (CH_3), 25.1 (CH_2), 26.4 (CH_3), 26.8 (CH_3), 32.0 ($CHMe_2$), 61.2 (C-5), 61.9 (C-3), 68.6 (CH), 75.9 (C-4), 83.3 (C-2), 104.1 (C-1), 112.2 (CMe_2), 128.6–134.3 (CH=), 156.1 (CMe_3), 166.3 (CO), 205.6 (CS); anal. calcd. (%) for $C_{26}H_{38}N_2O_7S$: C 59.75, H 7.33, N 5.36, S 6.14; found: C 59.74, H 7.30 N 5.34, S 6.12.

L7h: Yield: 85 mg (21%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83 (d, 3H, CH_3, J = 6.8 Hz), 0.91 (d, 3H, CH_3, J = 6.4 Hz), 1.32 (s, 3H, CH_3), 1.44 (s, 9H, CH_3), 1.56 (s, 3H, CH_3), 2.87 (m, 1H, CH), 3.48 (t, 1H, CH-NH, $J_{CH,NH}$ = 5 Hz), 3.67 (t, 1H, NHBoc, J = 5 Hz), 4.51 (m, 1H, H-3), 4.59 (d, 1H, H-2, $^3J_{2,1}$ = 3.6 Hz), 4.69 (m, 1H, H-4), 5.26 (dd, 2H, H-5, H-5′, $^2J_{5,5'}$ = 8.2 Hz, $^3J_{5,5'-4}$ = 3.8 Hz), 5.94 (d, 1H, H-1, $^3J_{1,2}$ = 3.6 Hz), 7.44–8.14 (m, 5H, CH=), 8.54 (a, 1H, NH); anal. calcd. (%) for $C_{25}H_{36}N_2O_7S$: C 59.03, H 7.13, N 5.51, S 6.30; found: C 59.00, H 7.09, N 5.47, S 6.26.

L8a: Yield: 154 mg (38%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (dd, 6H, CH_3, J = 10.6 Hz, J = 6.6 Hz), 1.36 (s, 3H, CH_3), 1.44 (s, 9H, CH_3), 1.59 (s, 3H, CH_3), 2.29 (m, 1H, CH), 4.11 (t, 1H, CH-NH, $J_{CH,NH}$ = 7.8 Hz), 4.23 (m, 1H, H-4), 4.34 (dd, 1H, H-5′, $^2J_{5,5'}$ = 12.6 Hz, $^3J_{5,5'-4}$ = 5.8 Hz), 4.76 (t, 1H, H-2, $^3J_{2\text{-}1,3}$ = 1 Hz), 4.78 (dd, 1H, H-5, $^2J_{5,5'}$ = 5.4 Hz , $^3J_{5,5'-4}$ = 2 Hz), 5.20 (m, 1H, H-3), 5.28 (a, 1H, NHBoc), 5.93 (d, 1H, H-1, $^3J_{1,2}$ = 4 Hz), 7.41–8.08 (m, 5H, CH=); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.8 (CH_3), 19.7 (CH_3), 26.3 (CH_3), 26.6 (CH_3), 28.3 (CH_3), 33.2 ($CHMe_2$), 56.5 (C-3), 63.7 (C-5), 67.1 (CH), 78.1 (C-4), 78.3 (C-2), 104.6 (C-1), 113.1 (CMe_2), 128.1–133.0 (CH=), 155.6 (CMe_3), 166.2 (CO), 205.7 (CS); anal. calcd. (%) for $C_{25}H_{36}N_2O_7S$: C 59.03, H 7.13, N 5.51, S 6.30; found: C 58.99, H 7.08, N 5.47, S 6.24.

Typical Procedure for the ATH of Ketones

The desired ligand (0.0055 mmol), catalyst precursor {[$RuCl_2$(p-cymene)$_2$]$_2$ or [$RhCl_2Cp^*_2$]$_2$} (0.0025 mmol), and LiCl

(4.2 mg, 0.1 mmol) were treated under vacuum for 10 min. Under argon, substrate (1 mmol), propan-2-ol (2 mL) and THF (2.5 mmol) were sequentially added. The reaction was initiated by adding *i*-PrONa (0.1 M, 0.5 mL, 0.05 mmol) to the solution. After completion of the reaction the solution was filtered through a plug of silica and eluted with Et_2O, and the solvents were evaporated. The products were analyzed by GC (CP Chirasil DEX CB).[7a,b,d]

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References

[1] See, for example: a) *Asymmetric Catalysis in Industrial Scale: Challenges, Approaches and Solutions*, (Eds.: H. U. Blaser, E. Schmidt), Wiley, Weinheim, Germany, **2003**; b) I. Ojima, (Ed.), in: *Catalytic Asymmetric Synthesis* Wiley-VCH, New York, **2000**; c) J. M. Brown, in: *Comprehensive Asymmetric Catalysis*, (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer-Verlag, Berlin, **1999**, Vol. I, pp 121–182; d) R. Noyori, in: *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, **1994**; e) *Applied Homogeneous Catalysis with Organometallic Compounds*, 2nd edn., (Eds.: B. Cornils, W. A. Herrmann), Wiley-VCH, Weinheim, **2002**.

[2] V. Farina, J. T. Reeves, C. H. Senanayake, J. J. Song, *Chem. Rev.* **2006**, *106*, 2734.

[3] See for example: a) C. Wang, X. Wu, J. Xiao, *Chem. Asian J.* **2008**, *3*, 1750; b) S. Gladiali, E. Alberico, *Chem. Soc. Rev.* **2006**, *35*, 226; c) K. Everaere, A. Mortreux, J.-F. Carpentier, *Adv. Synth. Catal.* **2003**, *345*, 67; d) T. Ohkuma, R. Noyori, in: *Comprehensive Asymmetric Catalysis*, Vol. 1, (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**, p 199; e) M. J. Palmer, M. Wills, *Tetrahedron: Asymmetry* **1999**, *10*, 2045; f) R. Noyori, S. Hashiguchi, *Acc. Chem. Res.* **1997**, *30*, 97; g) G. Zassinovich, G. Mestroni, S. Gladiali, *Chem. Rev.* **1992**, *92*, 1051.

[4] a) C. P. Casey, H. Guan, *J. Am. Chem. Soc.* **2007**, *129*, 5816; b) S. Zhou, S. Fleischer, K. Junge, S. Das, D. Addis, M. Beller, *Angew. Chem.* **2010**, *122*, 8298; *Angew. Chem. Int. Ed.* **2010**, *49*, 8121; c) A. A. Mikhailine, R. H. Morris, *Inorg. Chem.* **2010**, *49*, 11039; d) A. Naik, T. Maji, O. Reiser, *Chem. Commun.* **2010**, *46*, 4475; e) A. Mikhailine, A. L. Lough, R. H. Morris, *J. Am. Chem. Soc.* **2009**, *131*, 1394.

[5] a) S. Hashiguchi, A. Fujii, J. Takahara, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1995**, *117*, 7562; b) A. Fujii, S. Hashiguchi, N. Uematsu, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1996**, *118*, 2521.

[6] See, for example: a) S. J. Nordin, P. Roth, T. Tarnai, D. A. Alonso, P. Brandt, P. G. Andersson, *Chem. Eur. J.* **2001**, *7*, 1431; b) D. A. Alonso, S. J. Nordin, P. Roth, T. Tarnai, P. G. Andersson, M. Thommen, U. Pittelkow, *J. Org. Chem.* **2000**, *65*, 3116; c) D. A. Alonso, D. Guijarro, P. Pinho, O. Temme, P. G. Andersson, *J. Org. Chem.* **1998**, *63*, 2749; d) A. Schlatter, W.-D. Woggon, *Adv. Synth. Catal.* **2008**, *350*, 995; e) A. Schlatter, M. K. Kundu, W.-D. Woggon, *Angew. Chem.* **2004**, *116*, 6899; *Angew. Chem. Int. Ed.* **2004**, *43*, 6731; f) M. T. Reetz, X. Li, *J. Am. Chem. Soc.* **2006**, *128*, 1044; g) Y. Jiang, Q. Jiang, X. Zhang, *J. Am. Chem. Soc.* **1998**, *120*, 3817; h) D. S. Matharu, D. J. Morris, A. M. Kawamoto, G. J. Clarkson, M. Wills, *Org. Lett.* **2005**, *7*, 5489; i) I. M. Pastor, P. Västilä, H. Adolfsson, *Chem. Commun.* **2002**, 2046; j) A. B. Zaitsev, H. Adolfsson, *Org. Lett.* **2006**, *8*, 5129.

[7] a) I. M. Pastor, P. Västilä, H. Adolfsson, *Chem. Eur. J.* **2003**, *9*, 4031; b) A. Bøgevig, I. M. Pastor, H. Adolfsson, *Chem. Eur. J.* **2004**, *10*, 294; c) P. Västilä, J. Wettergren, H. Adolfsson, *Chem. Commun.* **2005**, 4039; d) J. Wettergren, A. Bøgevig, M. Portier, H. Adolfsson, *Adv. Synth. Catal.* **2006**, *348*, 1277; e) P. Västilä, A. B. Zaitsev, J. Wettergren, T. Privalov, H. Adolfsson, *Chem. Eur. J.* **2006**, *12*, 3218; f) J. Wettergren, A. B. Zaitsev, H. Adolfsson, *Adv. Synth. Catal.* **2007**, *349*, 2556; g) J. Wettergren, E. Buitrago, P. Ryberg, H. Adolfsson, *Chem. Eur. J.* **2009**, *15*, 5709.

[8] a) K. Ahlford, J. Ekström, A. B. Zaitsev, P. Ryberg, L. Eriksson, H. Adolfsson, *Chem. Eur. J.* **2009**, *15*, 11197; b) F. Tinnis, H. Adolfsson, *Org. Biomol. Chem.* **2010**, *8*, 4536; c) K. Ahlford, M. Livendahl, H. Adolfsson, *Tetrahedron Lett.* **2009**, *50*, 6321.

[9] a) M. Diéguez, O. Pàmies, C. Claver, *Chem. Rev.* **2004**, *104*, 3189; b) M. Diéguez, O. Pàmies, A. Ruiz, Y. Díaz, S. Castillón, C. Claver, *Coord. Chem. Rev.* **2004**, *248*, 2165; c) M. Diéguez, A. Ruiz, C. Claver, *Dalton Trans.* **2003**, 2957; d) S. Castillón, Y. Díaz, C. Claver, *Chem. Soc. Rev.* **2005**, *34*, 702; e) M. Diéguez, C. Claver, O. Pàmies, *Eur. J. Org. Chem.* **2007**, 4621; f) M. M. K. Boysen, *Chem. Eur. J.* **2007**, *13*, 8648; g) V. Benessere, R. Del Litto, A. De Roma, F. Ruffo, *Coord. Chem. Rev.* **2010**, *254*, 390; h) S. Woodward, M. Diéguez, O. Pàmies, *Coord. Chem. Rev.* **2010**, *254*, 2007.

[10] For a recent successful application of ligands **3**, see: M. Coll, O. Pàmies, H. Adolfsson, M. Diéguez, *Chem. Commun.* **2011**, *47*, 12188.

[11] There are few other examples on the use of carbohydrate-based ligands in this transformation with low-to-moderate enantioselectivities (<78% *ee*). See: a) S. Guillarme, T. X. Mai Nguyen, C. Saluzzo, *Tetrahedron: Asymmetry* **2008**, *19*, 1450; b) K.-D. Huynh, H. Ibrahim, M. Toffano, G. Vo-Thanh, *Tetrahedron: Asymmetry* **2010**, *21*, 1542.

[12] E. Raluy, O. Pàmies, M. Diéguez, *Adv. Synth. Catal.* **2009**, *351*, 1648, and references cited therein.

[13] R. O. Hancock, *J. Chem. Educ.* **1992**, *69*, 615.

[14] The related non-sugar based thioamide ligands **2** afforded 79% *ee* for **S2**, 92% *ee* for **S3**, 81% *ee* for **S4**, 89% *ee* for **S5**, 94% *ee* for **S6**, 92% *ee* for **S7**, 97% *ee* for **S9** and 97% for **S10**. There are no data reported for substrate **S8**. See refs.[6j,8]

