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**PAPER**

# Highly efficient asymmetric vinylogous Mannich reaction induced by *O*-pivaloylated D-galactosylamine as the chiral auxiliary†

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The diastereospecific formation of β-*N*-glycoside-linked α-amino-2(5*H*)-furanone has been achieved with high yield *via* a vinylogous Mannich reaction. The reaction was performed by using *O*-pivaloylated galactosylamine **1** as a chiral template and $ZnCl_2 \cdot Et_2O$ as a promoter in $Et_2O$. Imines **3** of aromatic compounds and trimethylsiloxyfuran **4** were converted to *N*-galactosyl α-amino-2(5H)-furanone **5**, giving ratios of diastereomers higher than 20 : 1. This procedure provides rapid access to biologically important γ-butenolide derivatives.

## Introduction

Asymmetric Mannich reactions are among the most fundamental carbon–carbon bond forming reactions in organic chemistry, and the reaction products are versatile intermediates in the synthesis of chiral, enantiomerically enriched amines.[1] On the other hand, the vinylogous Mannich reaction has gained increasing attention because in principle, it offers facile access to complicated and highly functionalized δ-amino compounds.[2] In recent years, the asymmetric Mannich-type reaction of trimethylsiloxyfuran with aldimines has proven to be a powerful synthetic protocol to prepare chiral γ-butenolide derivatives bearing an amine functionality in good yields and moderate to good enantiomeric excesses.[3] This synthetic approach allows us to obtain α,β-unsaturated γ-lactone *via* a regio- and diastereoselective four-carbon elongation of suitable imines with trimethyl siloxyfuran (TMSOF).[4]

In 1999, Martin and Lopez reported the first example of the catalytic asymmetric addition of trialkylsilyloxyfurans to the aldimines.[3f] Hoveyda and Snapper also reported a silver(I)-based catalyst using a 2-methyloxyphenyl group as an aldimine substituent, leading to the product of asymmetric vinylogous Mannich reaction of trimethylsiloxyfuran with aldimine in excellent diastereo- and enantioselectivity.[5] However, to the best of our knowledge, the chiral auxiliary asymmetric vinylogous Mannich reaction of aldimine with TMSOF has not been disclosed thus far.

Carbohydrates are valuable as enantiomerically pure starting materials in chiral pool syntheses of many chiral natural products and drugs.[6] Carbohydrate derivatives are efficient auxiliaries for stereo-differentiation in many stereoselective chiral syntheses.[7-8] A notable example is the paper by Kunz, in which the use of carbohydrates as chiral templates to promote Mannich-type reactions and the stereoselective synthesis of α-amino-phosphonic acid derivatives is reported.[9] We have developed a convenient and efficient synthetic protocol for preparation of α-aminophosphinic acid derivatives in high yields and high enantiostereoselectivity, utilizing $SnCl_4$ as the promoter and *O*-pivaloylated D-galactosylamine as the chiral auxiliary by means of Mannich-type reactions.[10] Herein we report the first example of chiral auxiliary asymmetric vinylogous Mannich reaction of aldimines with TMSOF under mild conditions to afford the corresponding adducts in moderate to good diastereomeric excesses and high yields as well as good diastereoselectivities for the production of chiral γ-butenolide derivatives.

## Results and discussion

The synthesis of β-*N*-glycosidically linked α-amino-2(5*H*)-furanone started with the condensation of arylaldehyde **2** and 2,3,4,6-tetra-*O*-pivaloyl-β-D-galactopyranosylamine **1**. The formation of the corresponding *N*-galactosylaldimines **3**[11] proceeded smoothly at room temperature under dehydrating conditions. Higher temperature and longer reaction time led preferentially to the formation of the undesired conjugated enamines.[12] In a Lewis acid catalyzed Mannich-type reaction, the aldimines **3** were reacted with trimethylsiloxyfuran **4** at low temperature to form *N*-galactosyl α-amino-2(5*H*)-furanone **5** (Scheme 1).

We initially investigated the reaction of *O*-pivaloylated *N*-galactosylimine **3h** (R = *p*-$ClC_6H_4$) with trimethylsiloxyfuran **4** in $Et_2O$ without the aid of a Lewis acid and no product **5h** was detected (Table 1, entry 1). Since the electrophilicity of imines is only moderate, the reaction between TMSOF **4** and imines requires activation by a Lewis acid to proceed. In this sense, various Lewis acids were tested in the reaction of the *N*-galactosylimine **3h** with **4** in $Et_2O$. The results revealed that CuCl, CuBr, CuI, AgOTf and $LiClO_4$ only caused anomerization of the Schiff base **3h**, and no product of **5h** was observed (Table 1, entries 2–6).

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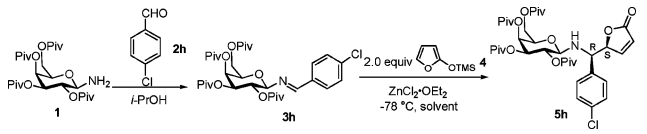
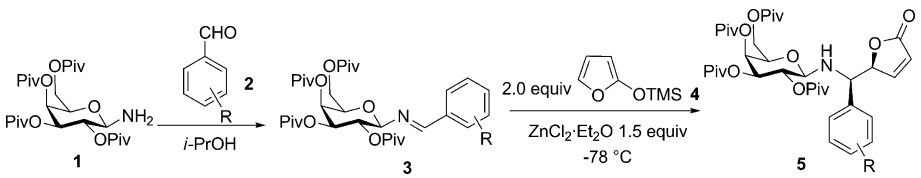
**Table 1** Survey of the conditions for the formation of **5h** according to Scheme 1[a]




| Entry | Lewis acid (equiv.) | Solvent | Time | Yields (%)[b] | dr[c] |
|---|---|---|---|---|---|
| 1 | — | $Et_2O$ | 2 d | n.r.[d] | — |
| 2 | CuCl (1) | $Et_2O$ | 2 d | n.r. | — |
| 3 | CuBr (1) | $Et_2O$ | 2 d | trace | — |
| 4 | CuI (1) | $Et_2O$ | 2 d | n.r. | — |
| 5 | $AgClO_4$ (1) | $Et_2O$ | 2 d | trace | — |
| 6 | $LiClO_4$ (1) | $Et_2O$ | 2 d | n.r. | — |
| 7 | $FeCl_3$ (1) | $Et_2O$ | 2 d | 78 | 74 : 26 : 0 : 0 |
| 8 | $AlCl_3$ (1) | $Et_2O$ | 2 d | 83 | 63 : 37 : 0 : 0 |
| 9 | $Mg(ClO_4)_2$ (1) | $Et_2O$ | 2 d | 11 | 56 : 40 : 4 : 0 |
| 10 | $Cu(OTf)_2$ (1) | $Et_2O$ | 2 h | 92 | 78 : 22 : 0 : 0 |
| 11 | $Zn(OTf)_2$ (1) | $Et_2O$ | 2 h | 81 | 89 : 11 : 0 : 0 |
| 12 | $BF_3{\cdot}Et_2O$ (1) | $Et_2O$ | 2 h | 87 | 86 : 14 : 0 : 0 |
| 13 | $SnCl_4$ (1) | $Et_2O$ | 2 h | 85 | 84 : 12 : 4 : 0 |
| 14 | $ZnCl_2{\cdot}Et_2O$ (1) | $Et_2O$ | 18 h | 89 | 91 : 9 : 0 : 0 |
| 15 | $ZnCl_2{\cdot}Et_2O$ (1) | THF | 72 h | 86 | 69 : 31 : 0 : 0 |
| 16 | $ZnCl_2{\cdot}Et_2O$ (1) | toluene | 20 h | 92 | 77 : 23 : 0 : 0 |
| 17 | $ZnCl_2{\cdot}Et_2O$ (1) | $CH_2Cl_2$ | 5 h | 87 | 68 : 32 : 0 : 0 |
| 18 | $ZnCl_2{\cdot}Et_2O$ (1) | MTBE | 72 h | 80 | 62 : 38 : 0 : 0 |
| 19 | $ZnCl_2{\cdot}Et_2O$ (1) | EDC[e] | 4 h | 91 | 62 : 38 : 0 : 0 |
| 20 | $ZnCl_2{\cdot}Et_2O$ (1.5) | $Et_2O$ | 12 h | 90 | 93 : 7 : 0 : 0 |
| 21 | $ZnCl_2{\cdot}Et_2O$ (2.0) | $Et_2O$ | 7 h | 88 | 88 : 12 : 0 : 0 |
| 22 | $ZnCl_2{\cdot}Et_2O$ (0.5) | $Et_2O$ | 60 h | 82 | 84 : 16 : 0 : 0 |

[a] Unless otherwise noted all the reactions were performed with 0.3 mmol of **3**, 0.6 mmol TMSOF in 2 mL solvent at -78 °C. [b] After purification by chromatography. [c] Diastereomeric ratio (dr) values were determined by HPLC of unpurified products. [d] no reaction. [e] EDC = 1,2-dichloroethane.



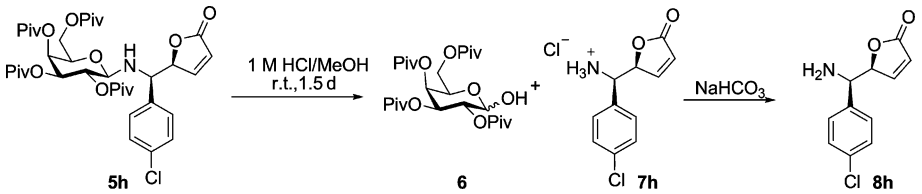

**Scheme 1** Reaction of aldimines with trimethylsiloxyfuran.

Other Lewis acids tested (*e.g.*, $FeCl_3$, $AlCl_3$, $Mg(ClO_4)_2$, $Cu(OTf)_2$, $Zn(OTf)_2$, $BF_3{\cdot}Et_2O$, $SnCl_4$ and $ZnCl_2{\cdot}Et_2O$) were able to promote the addition (Table 1, entries 7–14). Since $ZnCl_2{\cdot}Et_2O$ gave the higher diastereoselectivity (d.r. = 91 : 9 : 0 : 0) compared with other Lewis acids, it was used in further investigations. The ratio of diastereomers **5h** was determined by HPLC.

With the best Lewis acid $ZnCl_2{\cdot}Et_2O$ being identified, we next carried out the asymmetric vinylogous Mannich reaction of **3h** with **4** in different solvents to determine the best solvent for this reaction. The results showed that THF, toluene, $CH_2Cl_2$, methyl *tert*-butyl ether (MTBE) and 1,2-dichloroethane were providing **5h** in lower yields and diastereomeric ratio (Table 1, entries 15–19). Therefore, the tentatively optimized reaction conditions were determined to use $Et_2O$ as the solvent in further investigations.

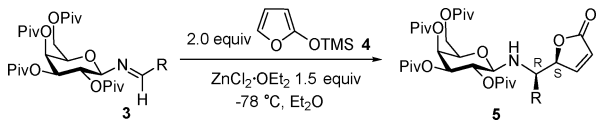
To determine the optimal conditions, imine **3h** was reacted with two equivalents of trimethylsiloxyfuran **4** in the presence of different concentrations of $ZnCl_2{\cdot}Et_2O$ in $Et_2O$ at −78 °C. An increase in the concentration of Lewis acid (1.5 equiv) resulted in a higher yield of **5h** and a slight increase in the diastereoselectivity. A further increase in the concentration (2 equiv) had no significant effect on the yield or the selectivity. The reaction time will extend to 60 h when the catalyst concentration decreases to 0.5 equivalent (Table 1, entries 20–22).

Under these optimum conditions, we next examined the generality of this reaction with various aldimines **3** with siloxyfuran **4** and the results were summarized in Table 2. It was found that *O*-pivaloylated *N*-galactosylimine **3**, bearing both electron-rich and electron-poor aromatic groups, gave the corresponding asymmetric vinylogous Mannich products **5b–n** in good to high yields and diastereoselectivities (Table 2, **5b–n**). As for the aldimine in which R was a phenyl group, relatively lower yield and diastereoselectivity was realized under identical conditions (Table 2, **5a**). Particularly, this process was efficient for cinnamaldehyde and afforded the desired product with 54% diastereoselectivity in 76% yield (Table 2, **5o**). Notably, the aldimine derived from heteroaromatic aldehydes gave the adducts in good yields with high diastereoselectivities (Table 2, **5p–q**). Furthermore, the reaction of Schiff base **3** of aliphatic aldehyde with trimethylsiloxyfuran **4** led to the product in very poor yield, only anomerization and decomposition occurred.




**Scheme 2** Synthesis of (*S*)-5-((*R*)-amino(4-chlorophenyl) methyl)-5*H*-furan-2-one **8b**.

**Table 2** The vinylogous Mannich reaction of *N*-(2,3,4,6-tetra-*O*-pivaloylated-D-galactosyl)aldimines **5a–q**




| Product | R | Time (h) | Yield (%)[a] | dr[b] | de(%)[c] |
|---|---|---|---|---|---|
| **5a** | $C_6H_5$ | 36 | 54 | 61 : 39 : 0 : 0 | 22 |
| **5b** | *o*-$CH_3C_6H_4$ | 18 | 87 | 95 : 5 : 0 : 0 | 90 |
| **5c** | *o*-$ClC_6H_4$ | 24 | 72 | 80 : 17 : 3 : 0 | 60 |
| **5d** | *o*-$BrC_6H_4$ | 18 | 83 | 87 : 13 : 0 : 0 | 74 |
| **5e** | *m*-$ClC_6H_4$ | 18 | 75 | 93 : 7 : 0 : 0 | 86 |
| **5f** | *m*-$FC_6H_4$ | 24 | 88 | 94 : 6 : 0 : 0 | 88 |
| **5g** | *m*-$CH_3C_6H_4$ | 16 | 73 | 89 : 11 : 0 : 0 | 78 |
| **5h** | *p*-$ClC_6H_4$ | 12 | 90 | 93 : 7 : 0: 0 | 86 |
| **5i** | *p*-$OCH_3C_6H_4$ | 96 | 66 | 69 : 13 : 8 : 10 | 38 |
| **5j** | *p*-$FC_6H_4$ | 26 | 94 | 97 : 3 : 0 : 0 | 94 |
| **5k** | *p*-$NO_2C_6H_4$ | 108 | 60 | 90 : 10 : 0 : 0 | 80 |
| **5l** | *p*-$BrC_6H_4$ | 44 | 84 | 98 : 2 : 0 : 0 | 96 |
| **5m** | *p*-$CH_3C_6H_4$ | 12 | 66 | 90 : 5 : 5 : 0 | 80 |
| **5n** | *p*-$CF_3C_6H_4$ | 24 | 88 | 94 : 6 : 0 : 0 | 88 |
| **5o** | phCH═CH | 12 | 76 | 77 : 23 : 0 : 0 | 54 |
| **5p** | 2-furyl | 18 | 63 | 86 : 8 : 6 : 0 | 72 |
| **5q** | 3-pyridyl | 12 | 54 | 93 : 7 : 0 : 0 | 86 |

[a] After purification by chromatography. [b] Diastereomeric ratio determined from the crude product by HPLC. [c] Reference 8c.

The ratio of the obtained diastereomers **5** was determined by HPLC from the crude mixture of the reaction. It should be noted that because of the anomeric carbon and one stereogenic centre created at the α-position of the 2(5H)-furanone, the eight diastereomers were βSS, βRS, αSS, αRS, βSR, βRR, αSR and αRR. The determination of the diasteriomeric ratios (dr) from HPLC illustrated that the aldimines derived from arylaldehydes with electron-withdrawing groups afforded moderate to good diastereoselectivities. The experimental results showed that only the corresponding β-anomers were obtained in this reaction. The mixture **5h** was treated with 1 M hydrogen chloride in methanol at room temperature giving the easily separable carbohydrate template **6** and the enantiomerically pure (*S*)-5-((*R*)-amino(4-chlorophenyl)methyl)-5*H*-furan-2-one hydrochloride **7h** in quantitative yield. The diastereomers **7h** could be hydrolyzed by using saturated $NaHCO_3$ to give the γ-butenolide **8h** with (–)-optical rotations in 90% yield. The $^1$H NMR spectrum of **8h** showed that the two diastereomers of **5h** (ratio 93 : 7, Table 2) contain enantiomers of the γ-butenolide **8h** (Scheme 2).

In order to determine the absolute configuration of the main isomer of the trimethylsiloxyfuran addition to *N*-galactosylaldimines **3**, a single crystal X-ray diffraction study of **5h** was performed. The molecular structure of **5h** is shown in Fig. 1, and the structure

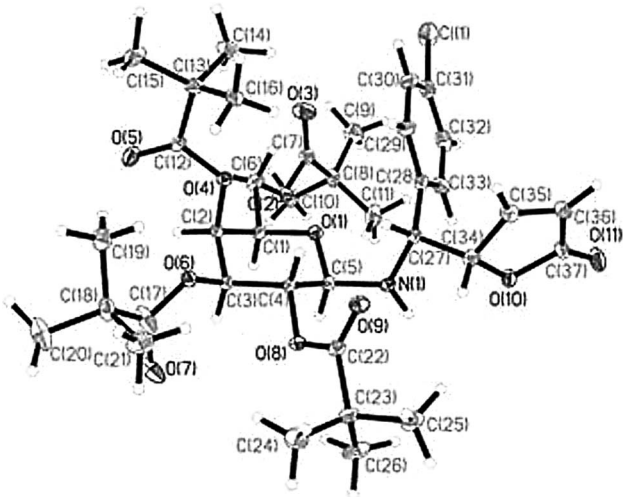



**Fig. 1**

shows that the relative configuration of β-*N*-glycoside-α-amino-2(5*H*)-furanone main product can be assigned as βRS.

The possible mechanism for the reactions is shown in Fig. 2. The preferred formation of the configured diastereomer of **5** can be rationalized by an attack of trimethylsiloxyfuran from the Si side of *N*-galactosylaldimines **3**. In the transition state, the zinc atom has tetra-coordination of which the sites are occupied by the imine nitrogen and carbonyloxygen (C-2) of the pivaloyloxy group respectively, and one of the two chlorines may be removed when trimethylsiloxyfuran was introduced. According to this rationalization, the $S_N2'$-type attack of trimethylsiloxyfuran from the back side of the plane of C═N is initiated. Based on these results, this hypothesis would explain the course of the main isomer synthesis. The mechanism indicates that the pivaloyl group in the aldimines **3** plays a significant role in controlling the diastereoselective addition of trimethylsiloxyfuran to *N*-galactosylaldimines **3**.

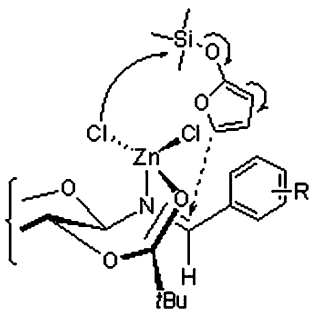



**Fig. 2**

## Conclusion

In conclusion, we have developed a new efficient synthetic protocol for preparation of chiral γ-butenolide derivatives in high yields and high enantiostereoselectivity, utilizing $ZnCl_2 \cdot Et_2O$ as the promoter and *O*-pivaloylated D-galactosylamine **1** as chiral auxiliary *via* vinylogous Mannich reactions. The *O*-pivaloylated galactosylamine **1** is an effective chiral template in the synthesis of chiral *N*-galactosyl α-amino-2(5*H*)-furanone **5**. $ZnCl_2 \cdot Et_2O$ can form the tetra-coordination intermediate inducing the *S* configuration at the Cα centre by attack at the Si-side of the C═N plane of the imine carbon atom. (*S*)-5-((*R*)-amino(phenyl)methyl)-5*H*-furan-2-one **8** can be detached easily from the carbohydrate template, which can be recycled.

## Experimental

### General remarks

All reactions were carried out under an inert atmosphere and in heat-dried glassware. Anhydrous $Et_2O$ was obtained by distillation from sodium. Flash column chromatography was performed on silica gel (particle size 10–40 μm, Ocean Chemical Factory of Qingdao, China). $^1H$ and $^{13}C$ NMR spectra were recorded on Brucker-400 (400 MHz for $^1H$, 75 MHz for $^{13}C$). Chemical shifts were reported in ppm downfield from internal $Si(CH_3)_4$. The crystal structure was determined on a Bruker SMART 1000 CCD diffractometer. Mass spectra were recorded on a LCQ advantage spectrometer with ESI resource. HR-MS were recorded on APEXII and ZAB-HS spectrometers. Melting points were determined on a T-4 melting point apparatus (uncorrected). Optical rotations were recorded on a Perkin Elemer 241 Polarimeter. HPLC analyses were recorded on a C18 column.

**General procedure for the preparation of *O*-pivaloyiated *N*-Galactosylimines 3 of Aromatic Aldhydes.** To a solution of 2,3,4,6-tetra-*O*-pivaloyl-β-D-galactopyranosylamine **1** (0.515 g, 1 mmol) and aldehyde **2** (1.3 mmol) in 2-propanol (2.5 ml), 2–3 drops of acetic acid were added and the mixture was stirred at room temperature for about 0.5 h. The appearance of a precipitate from the solution indicated the formation of **3**, after the precipitate was filtered off, then washed with ice cold 2-propanol and dried in vacuum, *N*-galactosylaldimines **3** was isolated as a colorless solid.

**General procedure for the synthesis of β-*N*-glycosidic linkages γ-butenolide derivatives 5.** A solution of *N*-galactosylaldimines **3** (0.3 mmol) in $Et_2O$ (2 ml) was cooled to −78 °C, and trimethylsiloxy furan (0.094 g, 0.6 mmol) and $ZnCl_2 \cdot OEt_2$ (0.45 mL, 0.45 mmol) were added. The mixture was stirred for corresponding time at −78 °C. The mixture was hydrolyzed with saturated aqueous $NH_4Cl$ (5 ml). The aqueous phase was extracted with $Et_2O$ (3 × 10 ml), and the organic layers were dried with anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude products **5**, which were purified by flash column chromatography on silica gel [petroleum ether/ethyl acetate, 5 : 1(v/v)] to provide pure products **5**.

**(*S*)-5-((*R*)-(2,3,4,6-tetra-*O*-pivaloyl-β-D-galactopyranosyl)-amino(phenylmethyl)-5*H*-furan-2-one (5a).** White solid; Mp 64–68 °C; $[\alpha]_D^{25} = -2.6°$ ($c = 0.5$, $CH_2Cl_2$); $^1H$-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.02 (s, 9H, $C(CH_3)_3$), 1.09 (s, 18H, $2C(CH_3)_3$), 1.21 (s, 9H, $C(CH_3)_3$), 2.33 (d, $^3J_{H-H} = 11.4$ Hz, 1H, NH), 3.63 (t, $^3J_{H-H} = 6.0$ Hz, 1H, CH), 3.88 (dd, $^3J_{H-H} = 11.4$ Hz, $^3J_{H-H} = 6.0$ Hz, 2H, 2CH), 4.00 (dd, $^3J_{H-H} = 10.2$ Hz, $^3J_{H-H} = 7.2$ Hz, 1H, CH), 4.51 (s, 1H, CH), 4.96–5.07 (m, 3H, 3CH), 5.41 (d, $^3J_{H-H} = 7.2$ Hz, 1H, CH), 5.96 (d, $^3J_{H-H} = 4.4$ Hz, 1H, CH), 7.19–7.31 (m, 6H, Ph); $^{13}C$-NMR (75 MHz, $CDCl_3$): $\delta$ = 26.07, 26.18, 26.21, 26.26, 37.66, 37.69, 37.77, 38.06, 52.50, 58.60, 66.19, 67.62, 70.17, 70.70, 85.05, 85.59, 121.79, 127.09, 127.67, 127.99, 134.90, 152.13, 171.45, 175.89, 176.11, 176.50, 176.80; ESI-MS: 710.8 ([M + Na]$^+$); HRMS calcd for $C_{37}H_{53}NO_{11}$: 710.3511 [M + Na]$^+$. found: 710.3514.

**(*S*)-5-((*R*)-(2,3,4,6-tetra-*O*-pivaloyl-β-D-galactopyranosyl)-amino(2-methylphenyl)methyl)-5*H*-furan-2-one (5b).** White solid; Mp 71–72 °C; $[\alpha]_D^{25} = -48.4°$ ($c = 0.5$, $CH_2Cl_2$); $^1H$-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.02 (s, 9H, $C(CH_3)_3$), 1.07 (s, 9H, $C(CH_3)_3$), 1.09 (s, 9H, $C(CH_3)_3$), 1.21 (s, 9H, $C(CH_3)_3$), 2.19 (d, $^3J_{H,H} = 10.9$ Hz, 1H, NH), 2.30 (s, 3H, $CH_3$), 3.60 (t, $^3J_{H,H} = 6.6$ Hz, 1H, CH), 3.82–3.92 (m, 2H, 2CH), 3.97 (dd, $^3J_{H,H} = 10.9$ Hz, $^3J_{H,H} = 6.6$ Hz, 1H, CH), 4.84 (s, 1H, CH), 4.97–4.99 (m, 2H, 2CH), 5.02 (s, 1H, CH), 5.27 (s, 1H, CH), 6.03 (d, $^3J_{H,H} = 5.2$ Hz, 1H, CH), 7.13–7.15 (m, 3H, Ph), 7.30–7.31 (m, 2H, Ph, CH); $^{13}C$-NMR (75 MHz, $CDCl_3$): $\delta$ = 18.47, 26.07, 26.12, 26.16, 26.21, 37.64, 37.70, 37.78, 38.06, 53.43, 60.21, 66.03, 67.71, 70.13, 70.60, 84.04, 85.32, 121.99, 125.31, 126.22, 127.13, 130.04, 132.89, 135.49, 151.91, 171.34, 175.84, 176.09, 176.40, 176.80; ESI-MS: 724.9 ([M + Na]$^+$); HRMS calcd for $C_{38}H_{55}NO_{11}$: 724.3667 [M + Na]$^+$. found: 724.3674.

**(*S*)-5-((*R*)-(2,3,4,6-tetra-*O*-pivaloyl-β-D-galactopyranosyl)-amino(*o*-chlorophenyl)methyl)-5*H*-furan-2-one (5c).** White solid; Mp 87–89 °C; $[\alpha]_D^{25} = -22.5°$ ($c = 0.5$, $CH_2Cl_2$); $^1H$-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.03 (s, 18H, $2C(CH_3)_3$), 1.10 (s, 9H, $C(CH_3)_3$), 1.21(s, 9H, $C(CH_3)_3$), 2.57 (dd, $^3J_{H-H} = 11.1$ Hz, $^3J_{H-H} = 4.8$ Hz, 1H, NH), 3.75 (t, $^3J_{H-H} = 6.8$ Hz, 1H, CH), 3.90 (dd, $^3J_{H-H} = 11.1$ Hz, $^3J_{H-H} = 7.0$ Hz, 1H, CH), 3.96–4.02 (m, 2H, 2CH), 5.00–5.07 (m, 3H, 3CH), 5.31 (s, 2H, 2CH), 5.88 (dd, $^3J_{H-H} = 5.6$ Hz, $^3J_{H-H} = 1.4$ Hz, 1H, CH), 7.13–7.19 (m, 2H, Ph), 7.25 (d, $^3J_{H-H} = 5.6$ Hz, 1H, CH), 7.32–7.37 (m, 2H, Ph); $^{13}C$-NMR (75 MHz, $CDCl_3$): $\delta$ = 26.07, 26.16, 26.20, 26.25, 37.66, 37.71, 37.78, 38.07, 54.76, 60.34, 66.06, 67.45, 70.11, 70.76, 84.12, 86.72, 121.83, 125.98, 128.33, 128.50, 128.53, 132.18, 132.88, 151.55, 171.34, 175.89, 176.12, 176.54, 176.84; ESI-MS: 744.9 ([M + Na]$^+$); HRMS calcd for $C_{37}H_{52}ClNO_{11}$: 744.3121 [M + Na]$^+$. found: 744.3126.

**(*S*)-5-((*R*)-(2,3,4,6-tetra-*O*-pivaloyl-β-D-galactopyranosyl)-amino(*o*-bromophenyl)methyl)-5*H*-furan-2-one (5d).** White solid; Mp 64–66 °C; $[\alpha]_D^{25} = -22.6°$ ($c = 0.5$, $CH_2Cl_2$); $^1H$-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.03 (s, 18H, $2C(CH_3)_3$), 1.10 (s, 9H, $C(CH_3)_3$), 1.22 (s, 9H, $C(CH_3)_3$), 2.53 (dd, $^3J_{H-H} = 4.0$ Hz, $^3J_{H-H} = 3.3$ Hz, 1H, NH), 3.74 (t, $^3J_{H-H} = 6.9$ Hz, 1H, CH), 3.91 (dd, $^3J_{H-H} = 10.8$ Hz, $^3J_{H-H} = 7.6$ Hz, 2H, 2CH), 4.01 (dd, $^3J_{H-H} = 10.8$ Hz, $^3J_{H-H} = 6.9$ Hz, 1H, CH), 4.99–5.04 (m, 3H, 3CH), 5.27–5.31 (m, 2H, 2CH), 5.89 (dd, $^3J_{H-H} = 5.7$ Hz, $^3J_{H-H} = 1.5$ Hz, 1H, CH), 7.08 (t, $^3J_{H-H} = 7.7$ Hz, 1H, Ph), 7.16–7.25 (m, 1H, Ph), 7.33 (d, $^3J_{H-H} = 7.7$ Hz, 1H, Ph), 7.36 (d, $^3J_{H-H} = 5.7$ Hz, 1H, CH), 7.45 (d, $^3J_{H-H} = 7.7$ Hz, 1H, Ph); $^{13}C$-NMR (75 MHz, $CDCl_3$): $\delta$ = 26.10, 26.19, 26.22, 26.26, 37.68, 37.73, 37.79, 38.08, 57.30, 60.22, 66.00, 67.49, 70.09, 70.74, 84.06, 86.59, 121.88, 122.89, 126.58, 128.68, 128.73, 131.91, 134.36, 151.42, 171.33, 175.90, 176.16, 176.55, 176.88;

ESI-MS: 788.9 ([M + Na]$^+$); HRMS calcd for $C_{37}H_{52}BrNO_{11}$: 788.2616 [M + Na]$^+$. found: 788.2614.

**(*S*)-5-((*R*)-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-galactopyranosyl)-amino(*m*-chlorophenyl)methyl)-5*H*-furan-2-one (5e).** White solid; Mp 83–85 °C; $[\alpha]_D^{25} = -37.5°$ ($c$ = 0.5, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.03 (s, 1H, $C(CH_3)_3$), 1.10 (s, 18H, $2C(CH_3)_3$), 1.21 (s, 1H, $C(CH_3)_3$), 2.36 (d, $^3J_{H-H}$ = 10.7 Hz, 1H, NH), 3.66 (t, $^3J_{H-H}$ = 7.0 Hz, 1H, CH), 3.89 (dd, $^3J_{H-H}$ = 10.7 Hz, $^3J_{H-H}$ = 6.7 Hz, 2H, 2CH), 3.99 (dd, $^3J_{H-H}$ = 11.3 Hz, $^3J_{H-H}$ = 7.0 Hz, 1H, CH), 4.47 (s, 1H, CH), 4.98–5.05 (m, 2H, 2CH), 5.11 (t, $^3J_{H-H}$ = 1.7 Hz, 1H, CH), 5.29 (s, 1H, CH), 5.99 (dd, $^3J_{H-H}$ = 5.6 Hz, $^3J_{H-H}$ = 1.7 Hz, 1H, CH), 7.09 (d, $^3J_{H-H}$ = 5.9 Hz, 1H, Ph), 7.19–7.24 (m, 3H, Ph), 7.27 (d, $^3J_{H-H}$ = 5.6 Hz, 1H, CH); $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 26.07, 26.15, 26.21, 26.30, 37.67, 37.70, 37.79, 38.07, 58.02, 60.45, 66.09, 67.44, 70.06, 70.81, 84.57, 85.45, 122.11, 125.34, 127.00, 128.97, 133.70, 137.22, 151.56, 171.08, 175.88, 176.11, 176.54, 176.82; ESI-MS: 722.9 ([M + H]$^+$); HRMS calcd for $C_{37}H_{52}ClNO_{11}$: 744.3121 [M + Na]$^+$. found: 744.3125.

**(*S*)-5-((*R*)-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-galactopyranosyl)-amino(*m*-fluorophenyl)methyl)-5*H*-furan-2-one (5f).** White solid; Mp 79–81 °C; $[\alpha]_D^{25} = -31.5°$ ($c$ = 0.5, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.03 (s, 9H, $C(CH_3)_3$), 1.09 (s, 18H, $2C(CH_3)_3$), 1.21 (s, 9H, $C(CH_3)_3$), 2.35 (s, 1H, NH), 3.64 (t, $^3J_{H-H}$ = 6.7 Hz, 1H, CH), 3.89 (dd, $^3J_{H-H}$ = 11.4 Hz, $^3J_{H-H}$ = 6.6 Hz, 2H, 2CH), 3.99 (dd, $^3J_{H-H}$ = 11.4 Hz, $^3J_{H-H}$ = 6.7 Hz, 1H, CH), 4.49 (d, $^3J_{H-H}$ = 3.2 Hz, 1H, CH), 4.98–5.05 (m, 2H, 2CH), 5.12 (d, $^3J_{H-H}$ = 2.1 Hz, 1H, CH), 5.29 (s, 1H, CH), 5.99 (dd, $^3J_{H-H}$ = 5.7 Hz, $^3J_{H-H}$ = 2.1 Hz, 1H, CH), 6.92–6.99 (m, 3H, Ph), 7.21–7.29 (m, 2H, Ph, CH); $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 26.07, 26.11, 26.17, 26.21, 37.68, 37.72, 37.79, 38.08, 58.12, 60.45, 66.11, 67.49, 70.08, 70.83, 84.60, 85.55, 113.86, 114.09, 114.43, 114.64, 122.08, 122.79, 129.23, 129.32, 137.71, 137.77, 151.60, 160.65, 163.11, 171.11, 175.89, 176.13, 176.57, 176.83; ESI-MS: 728.9 ([M + Na]$^+$); HRMS calcd for $C_{37}H_{52}FNO_{11}$: 728.3417 [M + Na]$^+$. found: 728.3418.

**(*S*)-5-((*R*)-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-galactopyranosyl)-amino(*m*-methylphenyl)methyl)-5*H*-furan-2-one (5g).** White solid; Mp 69–72 °C; $[\alpha]_D^{25} = -37.4°$ ($c$ = 0.5, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.03 (s, 9H, $C(CH_3)_3$), 1.10 (s, 18H, $2C(CH_3)_3$), 1.21 (s, 9H, $C(CH_3)_3$), 2.23 (br, 1H, NH), 2.27 (s, 1H, $CH_3$), 3.62 (t, $^3J_{H,H}$ = 6.6 Hz, 1H, CH), 3.87–3.93 (m, 2H, 2CH), 4.00 (dd, $^3J_{H,H}$ = 11.1 Hz, $^3J_{H,H}$ = 6.6 Hz, 1H, CH), 4.49 (t, $^3J_{H,H}$ = 3.4 Hz, 1H, CH), 4.92–5.03 (m, 2H, 2CH), 5.08 (d, $^3J_{H,H}$ = 1.3 Hz, 1H, CH), 5.27 (d, $^3J_{H,H}$ = 2.3 Hz, 1H, CH), 5.97 (d, $^3J_{H,H}$ = 5.8 Hz, 1H, CH), 7.00 (d, $^3J_{H,H}$ = 7.5 Hz, 1H, Ph), 7.03 (s, 1H, Ph), 7.05 (d, $^3J_{H,H}$ = 6.9 Hz, 1H, Ph), 7.16 (t, $^3J_{H,H}$ = 7.5 Hz, 1H, Ph), 7.26 (d, 5.8 Hz, 1H, CH); $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 20.41, 26.07, 26.16, 26.21, 26.28, 37.67, 37.70, 37.78, 38.07, 58.27, 60.50, 66.18, 67.59, 70.14, 70.70, 85.09, 85.34, 121.76, 124.17, 127.58, 127.63, 128.31, 134.75, 137.43, 152.05, 171.43, 175.94, 176.16, 176.41, 176.84; ESI-MS: 724.9 ([M + Na]$^+$).]$^+$); HRMS calcd for $C_{38}H_{55}NO_{11}$: 724.3667 [M + Na]$^+$, found: 724.3669.

**(*S*)-5-((*R*)-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-galactopyranosyl)-amino(4-chlorophenyl)methyl)-5*H*-furan-2-one (5h).** White solid; Mp 96–98 °C; $[\alpha]_D^{25} = -37.9°$ ($c$ = 0.5, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.03 (s, 9H, $C(CH_3)_3$), 1.08 (s, 9H, $C(CH_3)_3$), 1.10 (s, 9H, $C(CH_3)_3$), 1.21 (s, 9H, $C(CH_3)_3$), 2.39 (dd, $^3J_{H,H}$ = 11.8 Hz, $^3J_{H,H}$ = 2.9 Hz, 1H, NH), 3.65 (t, $^3J_{H,H}$ = 6.8 Hz, 1H, CH), 3.86–3.90 (m, 2H, 2CH), 4.00 (dd, $^3J_{H,H}$ = 11.8 Hz, $^3J_{H,H}$ = 6.8 Hz, 1H, CH), 4.46 (t, $^3J_{H,H}$ = 2.9 Hz, 1H, CH), 4.98–5.05 (m, 2H, 2CH), 5.12 (t, $^3J_{H,H}$ = 1.7 Hz, 1H, CH), 5.29 (d, $^3J_{H,H}$ = 1.7 Hz, 1H, CH), 5.96 (dd, $^3J_{H,H}$ = 5.7 Hz, $^3J_{H,H}$ = 1.7 Hz, 1H, CH), 7.13 (d, $^3J_{H,H}$ = 8.3 Hz, 2H, Ph), 7.23–7.26 (m, 3H, Ph, CH); $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 26.07, 26.08, 26.17, 26.20, 37.66, 37.70, 37.77, 38.06, 58.11, 60.43, 66.10, 67.51, 70.06, 70.76, 84.65, 85.61, 122.06, 127.83, 128.46, 133.28, 133.47, 151.71, 171.15, 175.85, 176.07, 176.52, 176.78; ESI-MS: 744.9 ([M + Na]$^+$); HRMS calcd for $C_{37}H_{52}ClNO_{11}$: 744.3121 [M + Na]$^+$. found: 744.3121.

**(*S*)-5-((*R*)-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-galactopyranosyl)-amino(4-methoxyphenyl)methyl)-5*H*-furan-2-one (5i).** White solid; Mp 80–82 °C; $[\alpha]_D^{25} = -20.2°$ ($c$ = 0.5, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.02 (s, 9H, $C(CH_3)_3$), 1.10 (s, 18H, $2C(CH_3)_3$), 1.21 (s, 9H, $C(CH_3)_3$), 2.26 (d, $^3J_{H,H}$ = 1.4 Hz, 1H, NH), 3.61 (t, $^3J_{H,H}$ = 6.7 Hz, 1H, CH), 3.74 (s, 3H, $CH_3$), 3.87–3.91 (m, 2H, 2CH), 3.99 (dd, $^3J_{H,H}$ = 11.1 Hz, $^3J_{H,H}$ = 6.7 Hz, 1H, CH), 4.48 (s, 1H, CH), 4.95–5.03 (m, 2H, 2CH), 5.08 (s, 1H, CH), 5.27 (d, $^3J_{H,H}$ = 1.7 Hz, 1H, CH), 5.96 (dd, $^3J_{H,H}$ = 5.8 Hz, $^3J_{H,H}$ = 1.7 Hz, 1H, CH), 6.80 (d, $^3J_{H,H}$ = 6.4 Hz, 2H, Ph), 7.11 (d, $^3J_{H,H}$ = 6.4 Hz, 2H, Ph), 7.26 (d, $^3J_{H,H}$ = 5.8 Hz, 1H, CH); $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 26.08, 26.16, 26.20, 26.27, 37.66, 37.69, 37.77, 38.06, 54.26, 57.83, 60.47, 66.17, 67.56, 70.14, 70.68, 85.15, 85.32, 113.06, 121.80, 126.42, 128.26, 152.11, 158.62, 171.46, 175.90, 176.12, 176.46, 176.81; ESI-MS: 740.9 ([M + Na]$^+$); HRMS calcd for $C_{38}H_{55}NO_{12}$: 740.3617 [M + Na]$^+$. found: 740.3623.

**(*S*)-5-((*R*)-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-galactopyranosyl)-amino(4-fluorophenyl)methyl)-5*H*-furan-2-one (5j).** White solid; Mp 133–135 °C; $[\alpha]_D^{25} = -40.0°$ ($c$ = 0.5, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.03 (s, 9H, $C(CH_3)_3$), 1.08 (s, 9H, $C(CH_3)_3$), 1.10 (s, 9H, $C(CH_3)_3$), 1.21 (s, 9H, $C(CH_3)_3$), 2.36 (d, $^3J_{H,H}$ = 11.7 Hz, $^3J_{H,H}$ = 2.5 Hz, 1H, NH), 3.64 (t, $^3J_{H,H}$ = 6.6 Hz, 1H, CH), 3.88 (dd, $^3J_{H,H}$ = 11.7 Hz, $^3J_{H,H}$ = 7.2 Hz, 2H, 2CH), 4.00 (dd, $^3J_{H,H}$ = 11.1 Hz, $^3J_{H,H}$ = 6.6 Hz, 1H, CH), 4.47 (t, $^3J_{H,H}$ = 2.5 Hz, 1H, CH), 4.97–5.05 (m, 2H, 2CH), 5.12 (s, 1H, CH), 5.29 (s, 1H, CH), 5.96 (dd, $^3J_{H,H}$ = 5.8 Hz, $^3J_{H,H}$ = 1.3 Hz, 1H, CH), 6.96 (t, $^3J_{H,H}$ = 8.4 Hz, 2H, Ph), 7.16–7.19 (m, 2H, Ph), 7.26 (d, $^3J_{H,H}$ = 5.8 Hz, 1H, CH); $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 26.07, 26.16, 26.20, 26.32, 37.66, 37.70, 37.76, 38.06, 58.01, 60.41, 66.08, 67.49, 70.04, 70.73, 84.81, 85.59, 114.51, 114.73, 122.01, 128.69, 128.77, 130.61, 151.77, 160.33, 162.79, 171.21, 175.86, 176.10, 176.51, 176.80. ESI-MS: 728.9 ([M + Na]$^+$); HRMS calcd for $C_{37}H_{52}FNO_{11}$: 728.3417 [M + Na]$^+$. found: 728.3411.

**(*S*)-5-((*R*)-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-galactopyranosyl)-amino(4-nitrophenyl)methyl)-5*H*-furan-2-one (5k).** White solid; Mp 177–179 °C; $[\alpha]_D^{25} = -49.1°$ ($c$ = 0.5, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.03 (s, 9H, $C(CH_3)_3$), 1.08 (s, 9H, $C(CH_3)_3$), 1.10 (s, 9H, $C(CH_3)_3$), 1.22 (s, 9H, $C(CH_3)_3$), 2.61 (dd, $^3J_{H,H}$ = 11.5 Hz, $^3J_{H,H}$ = 3.7 Hz, 1H, NH), 3.68 (t, $^3J_{H,H}$ = 6.6 Hz, 1H, CH), 3.84–3.95 (m, 2H, 2CH), 4.00 (dd, $^3J_{H,H}$ = 11.5 Hz, $^3J_{H,H}$ = 6.6 Hz, 1H, CH), 4.53 (t, $^3J_{H,H}$ = 3.7 Hz, 1H, CH), 5.00–5.08 (m, 2H, 2CH), 5.31 (s, 1H, CH), 5.96 (d, $^3J_{H,H}$ = 5.4 Hz, 1H, CH), 7.28 (d, $^3J_{H,H}$ = 5.4 Hz, 1H, CH), 7.37 (d, $^3J_{H,H}$ = 8.3 Hz, 2H, Ph), 8.12 (d, $^3J_{H,H}$ = 8.3 Hz, 2H, Ph); $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 26.06,

26.15, 26.20, 26.25, 37.68, 37.72, 37.80, 38.07, 58.58, 60.30, 65.94, 67.35, 69.90, 70.86, 84.20, 86.08, 122.41, 122.66, 128.03, 142.67, 146.87, 151.22, 170.72, 175.79, 176.08, 176.66, 176.79; ESI-MS: 755.9 ([M + Na]$^+$); HRMS calcd for $C_{37}H_{52}N_2O_{13}$: 755.3362 [M + Na]$^+$. found: 755.3358.

**(*S*)-5-((*R*)-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-galactopyranosyl)-amino(4-bromophenyl)methyl)-5*H*-furan-2-one (5l).** White solid; Mp 171–173 °C; $[\alpha]_D^{25}$ = –60.8° (*c* = 0.5, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.10 (s, 9H, $C(CH_3)_3$), 1.16 (s, 9H, $C(CH_3)_3$), 1.17 (s, 9H, $C(CH_3)_3$), 1.28 (s, 9H, $C(CH_3)_3$), 2.42 (dd, $^3J_{H,H}$ = 12.3 Hz, $^3J_{H,H}$ = 3.5 Hz, 1H, NH), 3.70 (t, $^3J_{H,H}$ = 6.8 Hz, 1H, CH), 3.94 (dd, $^3J_{H,H}$ = 11.1 Hz, $^3J_{H,H}$ = 6.9 Hz, 2H, 2CH), 4.07 (dd, $^3J_{H,H}$ = 11.1 Hz, $^3J_{H,H}$ = 6.8 Hz, 1H, CH), 4.51 (t, $^3J_{H,H}$ = 3.5 Hz, 1H, CH), 5.03–5.09 (m, 2H, 2CH), 5.16–5.19 (m, 1H, CH), 5.36 ($^3J_{H,H}$ = 2.4 Hz, 1H, CH), 6.04 (dd, $^3J_{H,H}$ = 5.8 Hz, $^3J_{H,H}$ = 1.0 Hz, 1H, CH), 7.14 (d, $^3J_{H,H}$ = 8.4 Hz, 2H, Ph), 7.30 (dd, $^3J_{H,H}$ = 5.8 Hz, $^3J_{H,H}$ = 1.5 Hz, 1H, CH), 7.48 (d, $^3J_{H,H}$ = 8.4 Hz, 2H, Ph); $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 26.07, 26.18, 26.20, 26.33, 37.66, 37.69, 37.77, 38.06, 58.12, 60.40, 66.06, 67.48, 70.01, 70.77, 84.54, 85.55, 121.47, 122.12, 128.75, 130.82, 133.90, 151.56, 171.11, 175.85, 176.08, 176.52, 176.79; ESI-MS: 788.9 ([M + Na]$^+$); HRMS calcd for $C_{38}H_{55}NO_{11}$: 788.2616 [M + Na]$^+$. found: 788.2612.

**(*S*)-5-((*R*)-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-galactopyranosyl)-amino(*p*-methylphenyl)methyl)-5*H*-furan-2-one (5m).** White solid; Mp 75–77 °C; $[\alpha]_D^{25}$ = –36.6° (*c* = 0.5, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.02 (s, 9H, $C(CH_3)_3$), 1.10 (s, 18H, $2C(CH_3)_3$), 1.21 (s, 9H, $C(CH_3)_3$), 2.24 (s, br, 1H, NH), 3.28 (s, 3H, $CH_3$), 3.60 (t, $^3J_{H-H}$ = 6.8 Hz, 1H, CH), 3.88 (dd, $^3J_{H-H}$ = 11.1 Hz, $^3J_{H-H}$ = 6.8 Hz, 2H, 2CH), 3.99 (dd, $^3J_{H-H}$ = 11.0 Hz, $^3J_{H-H}$ = 6.8 Hz, 1H, CH), 4.49 (d, $^3J_{H-H}$ = 3.7 Hz, 1H, CH), 4.94–5.00 (m, 2H, 2CH), 5.08 (t, $^3J_{H-H}$ = 7.0 Hz, 1H, CH), 5.27 (d, $^3J_{H-H}$ = 2.2 Hz, 1H, CH), 5.97 (dd, $^3J_{H-H}$ = 5.7 Hz, $^3J_{H-H}$ = 1.7 Hz, 1H, CH), 7.07–7.11 (m, 4H, Ph), 7.25 (d, $^3J_{H-H}$ = 5.7 Hz, 1H, CH); $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 20.10, 26.08, 26.14, 26.17, 26.22, 37.67, 37.71, 37.78, 38.07, 58.15, 60.51, 66.21, 67.61, 70.18, 70.72, 85.12, 85.35, 121.81, 127.03, 128.40, 131.63, 137.33, 152.04, 171.42, 175.92, 176.13, 176.45, 176.83; ESI-MS: 724.9 ([M + Na]$^+$); HRMS calcd for $C_{38}H_{55}NO_{11}$: 724.3667 [M + Na]$^+$. found: 724.3667.

**(*S*)-5-((*R*)-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-galactopyranosyl)-amino(*p*-trifluoromethylphenyl)methyl)-5*H*-furan-2-one (5n).** White solid; Mp 160–161 °C; $[\alpha]_D^{25}$ = –41.2° (*c* = 0.5, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.03 (s, 9H, $C(CH_3)_3$), 1.08 (s, 9H, $C(CH_3)_3$), 1.10 (s, 9H, $C(CH_3)_3$), 1.21 (s, 9H, $C(CH_3)_3$), 2.46 (d, $^3J_{H-H}$ = 8.8 Hz, 1H, NH), 3.65 (t, $^3J_{H-H}$ = 6.8 Hz, 1H, CH), 3.88 (dd, $^3J_{H-H}$ = 11.1 Hz, $^3J_{H-H}$ = 6.8 Hz, 2H, 2CH), 4.00 (dd, $^3J_{H-H}$ = 11.1 Hz, $^3J_{H-H}$ = 6.7 Hz, 1H, CH), 4.52 (d, $^3J_{H-H}$ = 3.8 Hz, 1H, CH), 4.99–5.06 (m, 2H, 2CH), 5.16 (dd, $^3J_{H-H}$ = 3.8 Hz, $^3J_{H-H}$ = 1.3 Hz, 1H, CH), 5.29 (d, $^3J_{H-H}$ = 2.1 Hz, 1H, CH), 5.97 (dd, $^3J_{H-H}$ = 5.8 Hz, $^3J_{H-H}$ = 2.0 Hz, 1H, CH), 7.26 (dd, $^3J_{H-H}$ = 5.8 Hz, $^3J_{H-H}$ = 1.3 Hz, 1H, CH), 7.33 (d, $^3J_{H-H}$ = 8.1 Hz, 2H, Ph), 7.53 (d, $^3J_{H-H}$ = 8.1 Hz, 2H, Ph); $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 26.06, 26.14, 26.20, 26.24, 37.67, 37.71, 37.78, 38.07, 58.47, 60.37, 66.03, 67.47, 69.99, 70.81, 84.45, 85.76, 121.47, 122.22, 124.17, 124.56, 124.60, 127.49, 129.58, 129.91, 139.26, 151.44, 170.99, 175.85, 176.09, 176.59, 176.81; ESI-MS: 778.9 ([M + Na]$^+$); HRMS calcd for $C_{38}H_{52}F_3NO_{11}$: 778.3385 [M + Na]$^+$. found: 778.3381.

**(*S*)-5-((*R*,*E*)-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-galactopyranosyl)-1-amino-3-phenylallyl)-5*H*-furan-2-one (5o).** White solid; Mp 54–57 °C; $[\alpha]_D^{25}$ = –29.9° (*c* = 0.5, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.03 (s, 9H, $C(CH_3)_3$), 1.09 (s, 9H, $C(CH_3)_3$), 1.11 (s, 9H, $C(CH_3)_3$), 1.21 (s, 9H, $C(CH_3)_3$), 2.13 (s, br, 1H, NH), 3.79 (dd, $^3J_{H-H}$ = 13.0 Hz, $^3J_{H-H}$ = 6.3 Hz, 1H, CH), 3.91 (dd, $^3J_{H-H}$ = 11.1 Hz, $^3J_{H-H}$ = 7.1 Hz, 1H, CH), 4.01–4.08 (m, 2H, 2CH), 4.12 (d, $^3J_{H-H}$ = 8.4 Hz, 1H, CH), 5.01 (q, $^3J_{H-H}$ = 8.4 Hz, 1H, CH), 5.06 (dd, $^3J_{H-H}$ = 10.4 Hz, $^3J_{H-H}$ = 3.3 Hz, 1H, CH), 5.11 (t, $^3J_{H-H}$ = 1.5 Hz, 1H, CH), 5.33 (d, $^3J_{H-H}$ = 3.3 Hz, 1H, CH), 5.78 (dd, $^3J_{H-H}$ = 15.9 Hz, $^3J_{H-H}$ = 8.4 Hz, 1H, CH), 6.08 (dd, $^3J_{H-H}$ = 5.8 Hz, $^3J_{H-H}$ = 1.8 Hz, 1H, CH), 6.55 (d, $^3J_{H-H}$ = 15.9 Hz, 1H, CH), 7.22–7.29 (m, 5H, Ph), 7.36 (dd, $^3J_{H-H}$ = 5.8 Hz, $^3J_{H-H}$ = 1.4 Hz, 1H, CH); $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 26.06, 26.09, 26.11, 26.19, 37.69, 37.73, 37.87, 38.05, 57.37, 60.42, 66.08, 67.49, 70.13, 70.69, 84.77, 86.28, 122.02, 122.98, 125.48, 127.35, 127.73, 134.06, 134.68, 152.17, 171.48, 175.90, 176.10, 176.41, 176.81; ESI-MS: 736.9 ([M + Na]$^+$); HRMS calcd for $C_{39}H_{55}NO_{11}$: 736.3667 [M + Na]$^+$. found: 736.3659.

**(*S*)-5-((*S*)-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-galactopyranosyl)-amino(2-furyl)methyl)-5*H*-furan-2-one (5p).** White solid; Mp 39–42 °C; $[\alpha]_D^{25}$ = –11.9° (*c* = 0.5, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.03 (s, 9H, $C(CH_3)_3$), 1.06 (s, 9H, $C(CH_3)_3$), 1.11 (s, 9H, $C(CH_3)_3$), 1.21 (s, 9H, $C(CH_3)_3$), 2.23 (dd, $^3J_{H,H}$ = 12.7 Hz, $^3J_{H,H}$ = 4.7 Hz, 1H, NH), 3.71 (t, $^3J_{H,H}$ = 7.1 Hz, 1H, CH), 3.90 (dd, $^3J_{H,H}$ = 12.7 Hz, $^3J_{H,H}$ = 11.9 Hz, 2H, 2CH), 4.24 (t, $^3J_{H,H}$ = 6.3 Hz, 1H, CH), 4.55 (t, $^3J_{H,H}$ = 4.5 Hz, 1H, CH), 4.93–5.04 (m, 2H, 2CH), 5.19 (s, 1H, CH), 5.30 (s, 1H, CH), 6.03 (d, $^3J_{H,H}$ = 5.4 Hz, 1H, CH), 6.21–6.32 (m, 2H, 2CH), 7.21 (s, 1H, CH), 7.41–7.48 (m, 1H, 1CH); $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 26.04, 26.06, 26.17, 26.19, 37.67, 37.69, 37.83, 38.04, 53.26, 60.31, 66.05, 67.32, 70.14, 70.66, 83.55, 86.10, 108.34, 109.47, 121.67, 141.57, 148.92, 152.60, 171.37, 175.85, 176.07, 176.44, 176.76; ESI-MS: 700.33 ([M + Na]$^+$); HRMS calcd for $C_{35}H_{51}NO_{12}$: 700.3298 [M + Na]$^+$. found: 700.3303.

**(*S*)-5-((*R*)-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-galactopyranosyl)-amino(3-pyridyl)methyl)-5*H*-furan-2-one (5q).** White solid; Mp 67–69 °C; $[\alpha]_D^{25}$ = –11.4° (*c* = 0.5, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.10 (s, 9H, $C(CH_3)_3$), 1.12 (s, 9H, $C(CH_3)_3$), 1.18 (s, 9H, $C(CH_3)_3$), 1.29 (s, 9H, $C(CH_3)_3$), 2.12 (d, $^3J_{H,H}$ = 10.1 Hz, 1H, NH), 3.77 (t, $^3J_{H,H}$ = 6.6 Hz, 1H, CH), 3.98–4.06 (m, 2H, 2CH), 4.32 (d, $^3J_{H,H}$ = 5.2 Hz, 1H, CH), 4.53 (d, $^3J_{H,H}$ = 3.3 Hz, 1H, CH), 5.08–5.12 (m, 2H, 2CH), 5.30 (s, 1H, CH), 5.35 (d, $^3J_{H,H}$ = 3.0 Hz, 1H, CH), 6.02 (d, $^3J_{H,H}$ = 5.8 Hz, 1H, CH), 7.39 (t, $^3J_{H,H}$ = 5.8 Hz, 2H, Ph), 7.71 (d, $^3J_{H,H}$ = 6.5 Hz, 1H, CH), 8.47–8.68 (m, 2H, Ph); $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 26.07, 26.09, 26.13, 26.23, 37.69, 37.72, 37.78, 38.08, 56.96, 60.31, 65.99, 67.35, 69.93, 70.88, 84.49, 86.32, 122.49, 122.72, 127.83, 129.89, 131.31, 135.66, 151.47, 170.77, 175.80, 176.08, 176.71, 176.81; ESI-MS: 689.3 ([M + H]$^+$); HRMS calcd for $C_{36}H_{52}N_2O_{11}$: 711.3460 [M + Na]$^+$. found: 711.3463.

**General Procedure for the synthesis of (*S*)-5-((*R*)-amino(phenyl)-methyl)-5*H*-furan-2-one 8.** A solution of compound **5h** (0.2 mmol) in dry methanol (2 ml) was treated with freshly prepared (1 M) solution of HCl/MeOH (0.5 ml). The solution

was stirred for 1.5 d (TLC control). Then methanol was evaporated *in vacuo* and the remaining residue dissolved in 0.5 M HCl (5 ml) and extracted with pentane (3 × 10 ml). The aqueous solution was neutralized using saturated $NaHCO_3$ aqueous solution until a pH value of 7 was achieved for the solution. Then, $CH_2Cl_2$ (5.0 ml) was added, the organic layer was separated, and the aqueous layer was washed with $CH_2Cl_2$ (3 × 5 ml). The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent evaporated, giving **8h** as yellow oil.

**(S)-5-((R)-amino(4-chlorophenyl)methyl)furan-2(5H)-one (8h).** Yellow oil; $[\alpha]_D^{25} = -92.9°$ ($c = 0.5$, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$): $\delta$ = 1.70 (bs, 2H, $NH_2$), 4.33 (d, $^3J_{H-H}$ = 4.4 Hz, 1H, CH), 5.11 (t, $^3J_{H-H}$ = 2.1 Hz, 1H, CH), 6.06 (dd, $^3J_{H-H}$ = 2.4 Hz, $^3J_{H-H}$ = 5.6 Hz, 1H, CH), 4.51 (s, 1H, CH), 7.20–7.23 (m, 3H, Ph, CH), 7.27–7.29 (d, $^3J_{H-H}$ = 8.4 Hz, 2H, Ph); $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 55.61, 85.61, 122.40, 127.12, 127.97, 132.99, 136.95, 151.93, 171.50; ESI-MS: 206.5 ($M^+$ - $NH_3$); HRMS calcd for $C_{38}H_{52}F_3NO_{11}$: 224.0473 $[M + H]^+$. found: 224.0476.

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