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Novel carbohydrate-derived pyridinecarboxylic organocatalysts for the enantioselective reduction of imines with trichlorosilane

Xin Ge [a,b], Chao Qian [a,b,*], Yunbin Chen [a], Xinzhi Chen [a,b]

[a] Department of Chemical and Biological Engineering, Zhejiang University, PR China
[b] Key Laboratory of Biomass Chemical Engineering of Ministry of Education, Zhejiang University, PR China

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ABSTRACT

A new type of carbohydrate-derived pyridinecarboxylic organocatalyst was prepared by fine-tuning a D-glucosamine backbone at the C-2 and C-3 positions. The carbohydrate-derived pyridinecarboxylic organocatalyst was used for the enantioselective reduction of imines with trichlorosilane. The reduction proceeded in high yield (up to 93%) and with moderate enantioselectivity (up to 75%).

1. Introduction

The enantioselective reduction of imines is an attractive approach for preparing chiral amines, which have a wide application in the pharmaceutical and fine chemical industry.[1] In addition to hydrogenation by the transition metal-catalyzed reduction,[1,2] an organocatalytic approach is a promising alternative method to obtain chiral amine production. A Lewis-basic organocatalytic approach with trichlorosilane reduction has been developed and this can complement Bronsted acid organocatalysis based on biomimetic reduction with a Hantzsch ester.[3] Matsumura et al. reported that *N*-formyl-L-proline anilide[3a] and *N*-picolinoyl-L-pyrrolidine[4] catalyzed the reduction of imines with trichlorosilane with moderate enantioselectivity. Later, Malkov and Kocovsky found that *N*-formyl-L-valine derived Lewis-basic organocatalysts can significantly improve the enantioselectivity.[3c] *N*-Formyl and *N*-picolinoyl chiral amino acid-based organocatalysts have also been considered to be important organocatalysts for the reduction of imines.[3a,b,e,f,4,5] Sun et al. developed *S*-chiral catalysts to reduce imines with high enantioselectivity.[6] Asymmetric organocatalysis has received much attention as an environmentally friendly approach for the preparation of enantiomerically pure organic compounds. Thus, the design of new and effective organocatalysts for asymmetric synthesis is both challenging and important.

Due to the high density of chiral information on the backbone and a number of functional groups useful for variation and optimization, carbohydrates have been intensively used in asymmetric organic synthesis.[7] The design and fine-tuning of carbohydrate-derived catalysts is facilitated by introducing additional stereodifferentiating groups.[8] In 2007, Kunz et al. reported on D-glucosamine-derived bifunctional urea Schiff base organocatalysts for enantioselective Streck and Mannich reactions.[7b] Subsequently, Machinami et al. found that aqueous asymmetric aldol reactions could be catalyzed by enanine-based carbohydrates.[7e] Highly enantioselective Michael additions of aromatic ketones with nitroolefins promoted by carbohydrate-derived bifunctional primary amine-thiourea catalysts were reported by Ma and Liu.[7c] In 2011, our research group described that carbohydrate-derived amino alcohols can catalyze the asymmetric aldol reaction of ketones with isatins in high yield and with moderate enantioselcetivity.[9] We also reported novel carbohydrate-derived prolinamides to catalyze asymmeteric aldol reactions in high yield, excellent enantioselectivity, and diastereoselectivity.[10]

Following our interests in carbohydrates[9–11] to develop novel organocatalysts for asymmeteric reactions, we herein report carbohydrate-derived pyridinecarboxylic organocatalysts for the enantioselective reduction of imines with trichlorosilane.

2. Results and discussion

Initially, we screened various carbohydrate-derivatives (Fig. 1) as organocatalysts for the reduction of imines with trichlorosilane. The results of the catalyst screening and optimizations are shown in Table 1.

We first attempted to use carbohydrate-derived amino alcohols **1a** and **1b** as catalysts and obtained moderate yields at room temperature, but the ee values were low (Table 1, entries 1–2). Carbohydrate-derived acetamide alcohols **2a** and **2b** also failed to catalyze the enantioselective reduction (Table 1, entries 3–4). Carbohydrate-derived amino alcohols and carbohydrate-derived acetamide alcohols did not catalyze the enantioselective reduction

* Corresponding author. Tel./fax: +86 571 87951615.
E-mail addresses: Qianchao@zju.edu.cn, chemtec@163.com (C. Qian).

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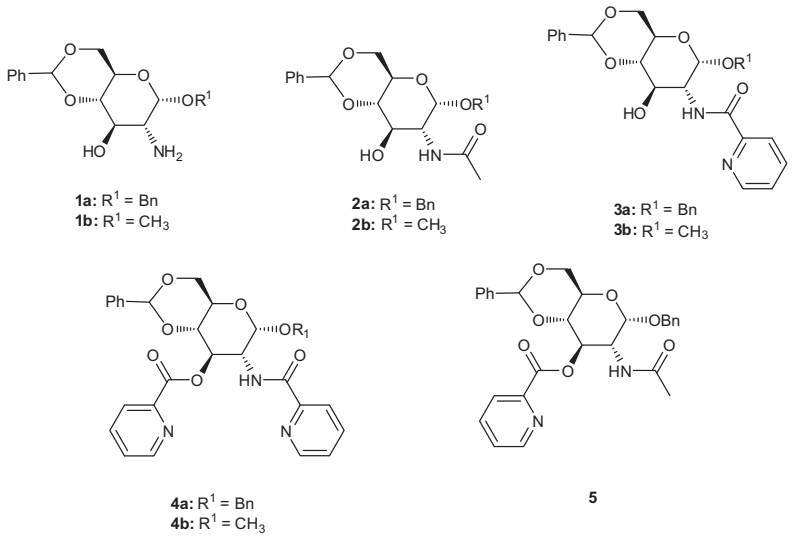


Figure 1. Structures of various carbohydrate-derived organocatalysts evaluated herein.

Table 1
Asymmetric reduction of ketimine **6a**[a]

6a **7a**

Entry	Catalyst	Solvent	Temp (°C)	Yield[b] (%)	ee[c] (%)	Config[d]
1	**1a**	CH_2Cl_2	rt	74	0	—
2	**1b**	CH_2Cl_2	rt	63	0	—
3	**2a**	CH_2Cl_2	rt	67	0	—
4	**2b**	CH_2Cl_2	rt	61	0	—
5	**3a**	CH_2Cl_2	rt	88	−38	(*R*)
6	**3b**	CH_2Cl_2	rt	73	−21	(*R*)
7	**4a**	CH_2Cl_2	rt	74	26	(*S*)
8	**4b**	CH_2Cl_2	rt	69	23	(*S*)
9	**5**	CH_2Cl_2	rt	93	51	(*S*)
10	**5**	Benzene	rt	13	5	(*S*)
11	**5**	CH_3Cl	rt	74	43	(*S*)
12	**5**	$ClCH_2CH_2Cl$	rt	86	44	(*S*)
13	**5**	CH_2Cl_2	0	89	62	(*S*)
14	**5**	CH_2Cl_2	−20	63	65	(*S*)

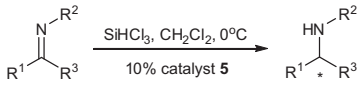
[a] The reactions were carried out with 10 mol % catalyst and 2.0 equiv of $SiHCl_3$ on a 0.5 mmol scale in 2.0 mL of solvent for 24 h.
[b] Isolated yield based on the imine.
[c] Determined by chiral HPLC.
[d] The absolute configuration was determined by comparison of the specific rotation with that in the literature.[3e]

of imines with trichlorosilane. Thus it was necessary to fine-tune carbohydrate-derivatives by introducing additional groups. Picolinoyl has been considered to be an important group in organocatalysts for the reduction of imines.[4,5] Carbohydrate-derived pyridine formamides **3a** and **3b**, which catalyze enantioselective reductions and improve yields and ee values for the (*R*)-enantiomer (Table 1, entries 5–6), were prepared by introducing a picolinoyl group. When carbohydrate-derived organocatalysts **4a** and **4b** were used for this reduction, the (*S*)-enantiomer was obtained, affording 26% ee and 23% ee separately (Table 1, entries 7–8). Encouraged by these preliminary results, we continued to optimize carbohydrate-derivatives and prepared organocatalyst **5**, which increased the ee value for the (*S*)-enantiomer to 51% (Table 1, entry 9).

We next selected catalyst **5** for further studies, and the optimization of the reaction conditions was examined. The effect of solvent was first investigated (Table 1, entries 9–12). It was found that dichloromethane was the best solvent and afforded the product with 93% yield and with 51% ee (Table 1, entry 9). Thus, we further investigated the reaction temperature using dichloromethane as the solvent. The best yield was obtained at room temperature (Table 1, entry 9). However the best enantioselectivity was observed when the reaction temperature was decreased to 0 °C (Table 1, entry 13). A further temperature decrease led to a reduction in yield without any obvious increase in the enantioselectivity (Table 1, entry 14). Based on the above results, we selected 0 °C as the best reaction temperature.

Having established the optimal reaction conditions, the substrate scope for the enantioselective reduction of imines with trichlorosilane was explored further. A range of *N*-aryl imines were reduced with $SiHCl_3$ in the presence of 10 mol % catalyst in dichloromethane at 0 °C. The results are summarized in Table 2. It was found that the results for the reduction of imines **6b–6l** were similar to imine **6a**, with satisfactory yields and moderate enantioselectivities being obtained (53–93% yield, 51–75% ee, entries 1–15). Moreover, imines **6m–6o** with an ethyl group were found

Table 2
Asymmetric reduction of ketimine **6** with catalyst **5**[a]



6 **7**

Entry	Imine	R^1	R^2	R^3	Yield[b] (%)	ee[c] (%)
1	**6a**	C_6H_5	C_6H_5	Me	89	62
2	**6b**	C_6H_5	4-FC_6H_4	Me	72	65
3	**6c**	C_6H_5	2-$CH_3C_6H_4$	Me	93	59
4	**6d**	C_6H_5	4-ClC_6H_4	Me	67	51
5	**6e**	C_6H_5	4-CH3C_6H_4	Me	92	67
6	**6f**	C_6H_5	3-ClC_6H_4	Me	74	61
7	**6g**	C_6H_5	3-BrC_6H_4	Me	72	57
8	**6h**	C_6H_5	$C_6H_4CH_2$	Me	53	59
9	**6i**	4-FC_6H_4	C_6H_5	Me	79	60
10	**6j**	4-ClC_6H_4	C_6H_5	Me	76	67
11	**6k**	4-$NO_2C_6H_4$	C_6H_5	Me	81	63
12	**6l**	4-$CH_3C_6H_4$	C_6H_5	Me	92	68
13	**6m**	C_6H_5	C_6H_5	Et	86	71
14	**6n**	4-ClC_6H_4	C_6H_5	Et	77	75
15	**6o**	4-$CH_3C_6H_4$	C_6H_5	Et	87	72

[a] The reactions were carried out with 10 mol % catalyst and 2.0 equiv of $SiHCl_3$ on a 0.5 mmol scale in 2.0 mL of solvent for 24 h.
[b] Isolated yield based on the imine.
[c] Determined by chiral HPLC.

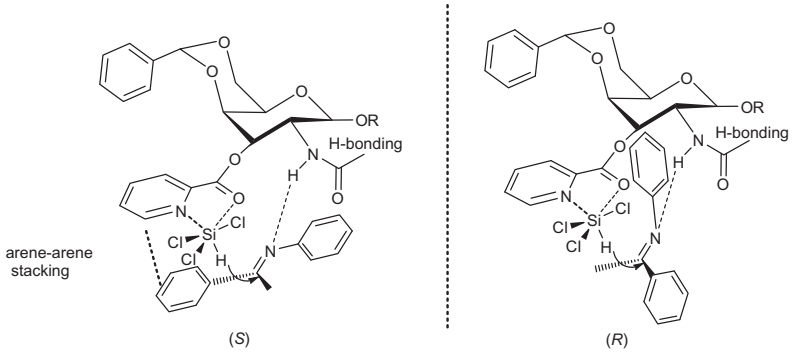


Figure 2. A proposed mechanism for the imine reduction catalyzed by **5**.

to be good substrates for organocatalyst **5**, affording 77–87% yield and 71–75% ee. When imines with electron-withdrawing groups were reduced, the yield decreased. The electronic effect on the enantioselectivity was probed by substitution of the phenyl ring with electron-donating and electron-withdrawing groups and was found to be negligible.

We have proposed a mechanism, which is shown in Figure 2. It can be seen that the enantioselective reduction of imines with trichlorosilane is catalyzed by the carbohydrate-derived pyridinecarboxylic organocatalyst **5**. Organocatalyst **5** could coordinate with trichlorosilane via the nitrogen atom of the pyridine ring and the carbonyl oxygen atom. The imine is activated by a hydrogen bond of the amide group. Consequently, the proposed arene–arene interactions between the pyridine of the catalyst and the benzene ring of the substrate aid the catalyst assembly with the reaction partners, leading to the (*S*)-enantiomer, being favoured. This is similar to the transition state proposed by Zhang et al.[5b]

3. Conclusion

In conclusion, we have described a new type of carbohydrate-derived pyridinecarboxylic organocatalyst for the enantioselective reduction of imines with trichlorosilane, which were constructed from commercial D-glucosamine as an inexpensive natural chiral pool starting material. The fine-tuning of carbohydrate-derived catalysts was carried out by introducing pyridinecarboxylic groups. We also screened the reaction conditions and proposed a plausible mechanism.

4. Experimental

4.1. General

Melting points were determined on an X4-Data microscopic melting point apparatus and are uncorrected. Optical rotation values were measured on a PerkinElmer P241 polarimeter operating at 589 nm. Nuclear magnetic resonance (NMR) spectra were measured at 400 MHz (^{1}H) or at 100 MHz (^{13}C) on a Bruker Avance DRX-400 spectrometer. All reactions were monitored by analytical thin-layer chromatography (TLC) from Merck with detection by spraying with 5% (w/v) phosphomolybdic acid in ethanol and subsequent heating or UV. All reagents and solvents were general reagent grade unless otherwise stated. All reactions were carried out in predried glassware (150 °C, 5 h) cooled under vacuum.

4.2. The synthesis of carbohydrate derived organocatalyst 1a–b, 2a–b

The carbohydrate derived organocatalysts **1a**–**b** and **2a**–**b** were prepared according to the literature.[7a,9–11]

4.2.1. Benzyl-4,6-*O*-benzylidene-2-amino-2-deoxy-α-D-glucopyranoside 1a

White solid. Mp 172.4–173.8 °C. $[\alpha]_D^{20} = +59.7$ (*c* 1.05, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80–6.91 (m, 10H), 5.53 (s, 1H), 4.90 (d, *J* = 3.6 Hz, 1H), 4.75 (d, *J* = 11.7 Hz, 1H), 4.52 (d, *J* = 11.8 Hz, 1H), 4.24 (dd, *J* = 10.1, 4.8 Hz, 1H), 3.88 (td, *J* = 9.9, 4.8 Hz, 1H), 3.83–3.66 (m, 2H), 3.49 (t, *J* = 9.3 Hz, 1H), 2.81 (dd, *J* = 9.7, 3.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.86, 137.67, 128.97, 128.42, 128.06, 127.89, 127.76, 126.62, 101.47, 99.58, 82.08, 71.70, 69.33, 68.74, 63.30, 57.06. Anal. Calcd (%) for $C_{20}H_{23}NO_5$: C, 67.21; H, 6.49; N, 3.92; O, 22.38. Found: C, 67.12; H, 6.32; N, 3.81.

4.2.2. Methyl-4,6-*O*-benzylidene-2-amino-2-deoxy-α-D-glucopyranoside 1b

White solid. Mp 166–167 °C; $[\alpha]_D^{20} = +103.1$ (*c* 0.905, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.41 (m, 2H), 7.41–7.35 (m, 3H), 5.61 (s, 1H), 4.62 (d, *J* = 3.6 Hz, 1H), 4.18 (dd, *J* = 9.9, 4.8 Hz, 1H), 3.76 3.56 (m, 3H), 3.48 (t, *J* = 9.2 Hz, 1H), 3.29 (s, 3H), 2.81 (dd, *J* = 9.7, 3.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.99, 134.09, 133.24, 131.63, 106.13, 103.97, 87.27, 73.27, 72.63, 67.68, 59.96, 59.35. Anal. Calcd (%) for $C_{14}H_{19}NO_5$: C, 59.78; H, 6.81; N, 4.98; O, 28.44. Found: C, 59.764; H, 6.75; N, 4.81.

4.2.3. Benzyl-4,6-*O*-benzylidene-2-acetylamino-2-deoxy-α-D-glucopyranoside 2a

White solid. Mp 189–192 °C; $[\alpha]_D^{20} = +56$ (*c* 0.21, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 8.00 (d, *J* = 8.2 Hz, 1H), 7.49–7.43 (m, 2H), 7.42–7.33 (m, 7H), 7.30 (ddd, *J* = 8.4, 3.6, 1.8 Hz, 1H), 5.62 (s, 1H), 5.19 (d, *J* = 5.8 Hz, 1H), 4.80 (d, *J* = 3.6 Hz, 1H), 4.70 (d, *J* = 12.6 Hz, 1H), 4.49 (d, *J* = 12.6 Hz, 1H), 4.18–4.11 (m, 1H), 3.86 (ddd, *J* = 10.6, 8.3, 3.7 Hz, 1H), 3.72 (ddd, *J* = 21.9, 12.6, 7.9 Hz, 3H), 3.51 (t, *J* = 9.0 Hz, 1H), 1.84 (d, *J* = 9.8 Hz, 3H). ^{13}C NMR (100 MHz, DMSO) δ 169.93, 138.19 (d, *J* = 3.3 Hz), 129.34, 128.7, 128.49, 128.07 (d, *J* = 7.3 Hz), 126.86, 101.34, 97.43, 69.06, 68.48, 67.73, 63.33 54.67, 23.00. Anal. Calcd (%) for $C_{22}H_{25}NO_6$: C, 66.15; H, 6.31; N, 3.51; O, 24.03. Found: C, 66.04; H, 6.15; N, 3.48.

4.2.4. Methyl-4,6-*O*-benzylidene-2-acetylamino-2-deoxy-α-D-glucopyranoside 2b

White solid. Mp 250–252 °C; $[\alpha]_D^{20} = +90$ (*c* 0.11, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 7.90 (d, *J* = 8.4 Hz, 1H), 7.46 (dd, *J* = 6.6, 3.2 Hz, 2H), 7.41–7.35 (m, 3H), 5.61 (s, 1H), 4.62 (d, *J* = 3.6 Hz, 1H), 4.18 (dd, *J* = 9.9, 4.8 Hz, 1H), 3.89–3.80 (m, 1H), 3.74 (t, *J* = 10.1 Hz, 1H), 3.69–3.63 (m, 1H), 3.63–3.56 (m, 1H), 3.48 (t, *J* = 9.2 Hz, 1H), 3.29 (s, 3H), 1.85 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 169.43, 137.74, 128.84, 127.99, 126.37, 100.87, 98.71, 82.01, 68.02, 67.37, 62.43, 54.71, 54.10, 22.57. Anal. Calcd (%) for $C_{16}H_{21}NO_6$: C, 59.43; H, 6.55; N, 4.33; O, 29.69 Found: C, 59.67; H, 6.72; N, 4.21.

4.3. General procedure for the synthesis of carbohydrate derived organocatalyst 3a–b, 4a–b, 5

To a stirred solution of picolinic acid (246 mg, 2.0 mmol) in CH_2Cl_2 (20 mL) were added the corresponding carbohydrate derived organocatalyst (2.0 mmol), carbonyldiiazole (CDI, 356 mg, 2.2 mmol), and 4-dimethylamiopyridine (DMAP, 24 mg, 0.2 mmol) at 0 °C and the reaction mixture was stirred at room temperature for 24 h. The organic phase was evaporated under reduced pressure to give the crude product, which was purified by column chromatography through silica gel to give a pure product.

4.3.1. Benzyl-4,6-*O*-benzylidene-2-picolinamide-2-deoxy-α-D-glucopyranoside 3a

White solid. Yield 81%. Mp 187.6–188.5 °C. $[\alpha]_D^{20} = +40.0$ (*c* 1.08, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68–8.56 (m, 1H), 8.49 (d, *J* = 9.2 Hz, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 7.86 (td, *J* = 7.7, 1.7 Hz, 1H), 7.50 (d, *J* = 1.8 Hz, 2H), 7.46 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.42–7.33 (m, 4H), 7.33–7.23 (m, 5H), 5.60 (s, 1H), 5.00 (d, *J* = 3.9 Hz, 1H), 4.82 (dd, *J* = 19.0, 9.3 Hz, 1H), 4.59 (d, *J* = 12.1 Hz, 1H), 4.49–4.37 (m, 1H), 4.28 (dd, *J* = 10.2, 4.9 Hz, 1H), 4.16 (t, *J* = 9.6 Hz, 1H), 3.98 (td, *J* = 9.9, 4.9 Hz, 1H), 3.81 (t, *J* = 10.3 Hz, 1H), 3.70 (t, *J* = 9.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.32, 149.27, 148.20, 137.38, 137.11, 136.83, 129.23, 128.50, 128.32, 128.10, 126.36, 122.60, 102.03, 97.33, 82.18, 70.65, 69.94, 68.91, 62.78, 54.15. Anal. Calcd (%) for $C_{26}H_{26}N_2O_6$: C, 67.52; H, 5.67; N, 6.06; O, 20.76. Found: C, 67.41; H, 5.59; N, 6.18.

4.3.2. Methyl-4,6-*O*-benzylidene-2-picolinamide-2-deoxy-α-D-glucopyranoside 3b

White solid. Yield 74%. Mp 177.8–178.5 °C. $[\alpha]_D^{20} = +24.9$ (*c* 0.95, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 4.3 Hz, 1H), 8.37 (d, *J* = 9.0 Hz, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.85 (td, *J* = 7.7, 1.6 Hz, 1H), 7.55–7.32 (m, 5H), 7.26 (s, 1H), 5.60 (s, 1H), 4.83 (d, *J* = 3.8 Hz, 1H), 4.43 (td, *J* = 9.7, 3.8 Hz, 1H), 4.32 (dd, *J* = 9.8, 4.4 Hz, 1H), 4.10 (t, *J* = 8.8 Hz, 1H), 3.96–3.77 (m, 2H), 3.68 (t, *J* = 9.2 Hz, 1H), 3.46 (s, 3H), 3.04 (d, *J* = 2.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.42, 148.26, 137.37, 129.22, 128.31, 126.47, 126.36, 122.66, 102.04, 99.09, 82.20, 70.68, 68.95, 62.40, 55.46, 54.20. Anal. Calcd (%) for $C_{20}H_{22}N_2O_6$: C, 62.17; H, 5.74; N, 7.25; O, 24.84. Found: C, 62.12; H, 5.69; N, 7.21.

4.3.3. Benzyl-4,6-*O*-benzylidene-3-*O*-(pyridinecarboxylic)-2-picolinamide-2-deoxy-α-D-glucopyranoside 4a

White solid. Yield 91%. Mp 142.1–143.3 °C. $[\alpha]_D^{20} = +47.2$ (*c* 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73–8.63 (m, 1H), 8.62–8.45 (m, 2H), 8.14–7.95 (m, 2H), 7.76 (dtd, *J* = 22.9, 7.7, 1.6 Hz, 2H), 7.46–7.35 (m, 6H), 7.35–7.31 (m, 1H), 7.29 (dd, *J* = 3.6, 2.5 Hz, 1H), 7.27 (dd, *J* = 6.5, 2.8 Hz, 2H), 7.25–7.17 (m, 2H), 5.91 (t, *J* = 10.0 Hz, 1H), 5.68–5.45 (m, 1H), 5.04 (dd, *J* = 7.0, 3.8 Hz, 1H), 4.87–4.71 (m, 2H), 4.31 (dt, *J* = 10.3, 5.2 Hz, 1H), 4.21–4.07 (m, 1H), 4.07–3.91 (m, 1H), 3.85 (t, *J* = 10.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.48, 164.43, 149.92, 149.07, 148.34, 147.51, 137.36, 137.09, 136.91, 136.64, 128.98, 128.56, 128.45, 128.29, 128.24, 128.18, 128.17, 128.09, 126.82, 126.32, 126.18, 126.15, 125.53, 122.13, 101.52, 97.39, 79.44, 71.66, 70.05, 68.92, 63.26, 52.36. Anal. Calcd (%) for $C_{32}H_{29}N_3O_7$: C, 67.71; H, 5.15; N, 7.40; O, 19.73. Found: C, 67.54; H, 5.21; N, 7.35.

4.3.4. Methyl-4,6-*O*-benzylidene-3-*O*-(pyridinecarboxylic)-2-picolinamide-2-deoxy-α-D-glucopyranoside 4b

White solid. Yield 94%. Mp 197.5–199.2 °C. $[\alpha]_D^{20} = +45.0$ (*c* 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62–8.56 (m, 1H), 8.47 (d, *J* = 4.2 Hz, 1H), 8.35 (d, *J* = 10.0 Hz, 1H), 7.95 (dd, *J* = 16.5, 7.8 Hz, 2H), 7.70–7.60 (m, 2H), 7.38–7.31 (m, 2H), 7.28 (ddd, *J* = 13.7, 7.4, 5.1 Hz, 2H), 7.25–7.17 (m, 3H), 5.90–5.69 (m, 1H), 5.50 (s, 1H), 4.82 (t, *J* = 5.8 Hz, 1H), 4.72 (td, *J* = 10.2, 3.7 Hz, 1H), 4.28 (dd, *J* = 10.3, 4.5 Hz, 1H), 4.04–3.89 (m, 2H), 3.80 (t, *J* = 10.0 Hz, 1H), 3.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.48, 163.44, 148.88, 148.04, 147.38, 146.45, 136.05, 135.93, 135.89, 127.95, 127.14, 125.78, 125.30, 125.15, 124.48, 121.12, 100.51, 98.27, 78.38, 70.60, 67.94, 61.89, 54.45, 51.36. Anal. Calcd (%) for $C_{26}H_{25}N_3O_7$: C, 63.54; H, 5.13; N, 8.55; O, 22.79. Found: C, 63.26; H, 5.29; N, 8.41.

4.3.5. Benzyl-4,6-*O*-benzylidene-3-*O*-(pyridinecarboxylic)-2-acetylamino-2-deoxy-α-D-glucopyranoside 5

White solid. Yield 87%. Mp 179–181 °C. $[\alpha]_D^{20} = +19.2$ (*c* 0.97, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 4.1 Hz, 1H), 8.10 (dd, *J* = 7.0, 4.9 Hz, 2H), 7.85–7.75 (m, 2H), 7.43–7.24 (m, 10H), 5.67 (t, *J* = 10.0 Hz, 1H), 5.53 (s, 1H), 4.97 (d, *J* = 3.6 Hz, 1H), 4.77 (d, *J* = 11.8 Hz, 1H), 4.56 (dd, *J* = 16.9, 7.7 Hz, 2H), 4.26 (dd, *J* = 10.3, 4.7 Hz, 1H), 4.03 (d, *J* = 4.7 Hz, 1H), 3.90 (t, *J* = 9.5 Hz, 1H), 3.80 (t, *J* = 10.2 Hz, 1H), 1.81 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.40, 165.00, 149.88, 147.12, 137.34, 136.83, 136.55, 131.53, 129.54, 129.09, 128.71, 128.41, 128.32, 128.20, 128.07, 127.31, 126.16, 125.64, 121.30, 101.54, 97.33, 79.08, 71.88, 70.24, 68.82, 63.21, 52.37, 23.04. Anal. Calcd (%) for $C_{28}H_{28}N_2O_7$: C, 66.66; H, 5.59; N, 5.55; O, 22.20. Found: C, 66.69; H, 5.53; N, 5.51.

4.4. General experimental procedure for the the enantioselective reduction of imines with trichlorosilane catalyzed by 5

To a stirred solution of imine **6** (0.5 mmol) and catalyst **5** (25 mg, 0.05 mmol) in dry CH_2Cl_2 (2 mL) was added the trichlorosilane (0.1 ml, 1 mmol) at 0 °C and the reaction mixture was stirred at 0 °C for 24 h. Saturated $NaHCO_3$ (2 ml) was then added and extracted with CH_2Cl_2 (3 × 5 ml). The combined organic phases were washed with saturated brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by column chromatography through silica gel, eluting with a 1:99 ethyl acetate/petroleum ether solvent mixture to give pure **7**. The ee value of the reduction product was determined by HPLC on a chiral column (Daicel, Chiralpak, OD-H).

4.4.1. (*S*)-*N*-Phenyl-1-phenylethylamine 7a[3a,3b,4]

Yield 89%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.18 (m, 4H), 7.14 (t, *J* = 7.1 Hz, 1H), 7.01 (t, *J* = 7.6 Hz, 2H), 6.56 (t, *J* = 7.2 Hz, 1H), 6.43 (d, *J* = 7.6 Hz, 2H), 4.41 (q, *J* = 6.6 Hz, 1H), 1.43 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.26, 144.20, 128.07, 127.60, 125.83, 124.82, 116.21, 112.29, 52.43, 23.98. HPLC analysis: Chiralcel OD-H (Hexane/*i*-PrOH = 99/1, 1.0 mL/min, 254 nm, 25 °C): t_{major} = 10.193 min, t_{minor} = 11.987 min, ee: 62%.

4.4.2. (*S*)-4-Fluoro-*N*-(1-phenylethyl)aniline 7b[12]

Yield 72%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.19 (m, 4H), 7.17–7.10 (m, 1H), 6.76–6.65 (m, 2H), 6.39–6.27 (m, 2H), 4.36–4.27 (m, 1H), 3.83 (s, 1H), 1.41 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.63 (d, *J* = 234.7 Hz), 144.01, 142.59, 127.64, 125.92, 124.78, 114.46 (d, *J* = 22.2 Hz), 113.06 (d, *J* = 7.3 Hz), 113.02, 53.03, 24.03. HPLC analysis: Chiralcel OD-H (Hexane/*i*-PrOH = 99/1, 1.0 mL/min, 254 nm, 25 °C): t_{minor} = 11.332 min, t_{major} = 12.671 min, ee: 65%.

4.4.3. (*S*)-2-Methyl-*N*-(1-phenylethyl)aniline 7c[13]

Yield 93%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (dd, *J* = 8.2, 1.2 Hz, 2H), 7.24–7.18 (m, 2H), 7.12 (ddd, *J* = 12.1, 6.4, 3.2 Hz, 1H), 6.95 (d, *J* = 7.3 Hz, 1H), 6.90–6.81 (m, 1H), 6.51 (td, *J* = 7.4, 0.9 Hz, 1H), 6.28 (d, *J* = 7.9 Hz, 1H), 4.44 (q, *J* = 6.7 Hz, 1H), 3.75 (s, 1H), 2.13 (s, 3H), 1.46 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.17 (d, *J* = 12.5 Hz), 128.92, 127.59, 125.87 (d, *J* = 15.1 Hz), 124.73, 120.49, 115.79, 109.99, 52.25, 24.20,

16.57. HPLC analysis: Chiralcel OD-H (Hexane/*i*-PrOH = 99/1, 1.0 mL/min, 254 nm, 25 °C): t_{major} = 9.847 min, t_{minor} = 10.467 min, ee: 59%.

4.4.4. (*S*)-4-Chloro-*N*-(1-phenylethyl)aniline 7d[3f,6a]

Yield 67%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.19 (m, 4H), 7.19–7.11 (m, 1H), 6.99–6.88 (m, 2H), 6.39–6.29 (m, 2H), 4.35 (q, J = 6.7 Hz, 1H), 4.08 (s, 1H), 1.42 (d, J = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.57, 143.53, 127.79 (d, J = 19.7 Hz). 126.03, 124.77, 120.96, 113.50, 52.70, 23.86. HPLC analysis: Chiralcel OD-H (Hexane/*i*-PrOH = 95/5, 1.0 mL/min, 254 nm, 25 °C): t_{minor} = 7.563 min, t_{major} = 9.026 min, ee: 51%.

4.4.5. (*S*)-4-Methyl-*N*-(1-phenylethyl)aniline 7e[3f,12]

Yield 92%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.16 (m, 4H), 7.15–7.08 (m, 1H), 6.80 (d, J = 8.1 Hz, 2H), 6.37–6.28 (m, 2H), 4.35 (q, J = 6.7 Hz, 1H), 3.77 (s, 1H), 2.09 (s, 3H), 1.39 (d, J = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.37, 143.97, 128.54, 127.55, 125.73, 125.27, 124.80, 112.38, 52.61, 23.98, 19.30. HPLC analysis: Chiralcel OD-H (Hexane/*i*-PrOH = 99/1, 1.0 mL/min, 254 nm, 25 °C): t_{minor} = 20.440 min, t_{major} = 22.681 min, ee: 67%.

4.4.6. (*S*)-3-Chloro-*N*-(1-phenylethyl)aniline 7f

Yield 74%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.19 (m, 4H), 7.18–7.10 (m, 1H), 6.88 (t, J = 8.0 Hz, 1H), 6.51 (ddd, J = 7.9, 1.9, 0.8 Hz, 1H), 6.40 (t, J = 2.1 Hz, 1H), 6.27 (ddd, J = 8.2, 2.3, 0.8 Hz, 1H), 4.36 (q, J = 6.7 Hz, 1H), 4.05 (s, 1H), 1.41 (d, J = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.41, 144.57, 134.83, 130.13, 128.80, 127.14, 125.81, 117.17, 113.10, 111.52, 53.38, 24.89. HPLC analysis: Chiralcel OD-H (Hexane/*i*-PrOH = 95/5, 1.0 mL/min, 254 nm, 25 °C): t_{major} = 8.075 min, t_{minor} = 10.059 min, ee: 61%.

4.4.7. (*S*)-3-Bromo-*N*-(1-phenylethyl)aniline 7g

Yield 72%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.19 (m, 4H), 7.19–7.10 (m, 1H), 6.83 (t, J = 8.0 Hz, 1H), 6.65 (dddd, J = 8.3, 6.4, 2.5, 1.3 Hz, 1H), 6.58 (t, J = 2.1 Hz, 1H), 6.34–6.27 (m, 1H), 4.43–4.28 (m, 1H), 4.04 (s, 1H), 1.42 (t, J = 5.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.43, 143.40, 129.34, 127.71, 126.06, 124.72, 122.01, 119.01, 114.97, 110.79, 52.28, 23.76. HPLC analysis: Chiralcel OD-H (Hexane/*i*-PrOH = 95/5, 1.0 mL/min, 254 nm, 25 °C): t_{major} = 8.644 min, t_{minor} = 10.835 min, ee: 57%.

4.4.8. (*S*)-*N*-Benzyl-1-phenylethanamine 7h[14]

Yield 53%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.21 (m, 10H), 4.57 (d, J = 9.0 Hz, 1H), 3.81–3.62 (m, 2H), 2.00 (d, J = 1.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.61, 140.53, 128.57, 128.40, 127.31, 127.09, 127.04, 60.04, 51.43, 16.43. HPLC analysis: Chiralcel OD-H (Hexane/*i*-PrOH = 99/1, 1.0 mL/min, 254 nm, 25 °C): t_{minor} = 6.072 min, t_{major} = 7.286 min, ee: 59%.

4.4.9. (*S*)-*N*-Phenyl-*N*-[1-(4-fluorophenyl)ethyl]amine 7i[15]

Yield 79%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.24 (m, 2H), 7.08 (t, J = 7.9 Hz, 2H), 7.01–6.90 (m, 2H), 6.64 (t, J = 7.3 Hz, 1H), 6.47 (d, J = 7.9 Hz, 2H), 4.43 (d, J = 6.7 Hz, 1H), 4.01 (s, 1H), 1.46 (d, J = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$)δ 161.82 (d, J = 244.3 Hz), 147.13, 140.97, 140.94, 129.22,127.41 (d, J = 8.0 Hz), 117.54, 115.50 (d, J = 21.3 Hz), 113.44, 52.98, 25.22. HPLC analysis: Chiralcel OD-H (Hexane/*i*-PrOH = 95/5, 1.0 mL/min, 254 nm, 25 °C): t_{major} = 12.998 min, t_{minor} = 14.982 min, ee: 60%.

4.4.10. (*S*)-*N*-Phenyl-*N*-[1-(4-chlorophenyl)ethyl]amine 7j[15]

Yield 76%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.20 (m, 4H), 7.12–7.00 (m, 2H), 6.64 (t, J = 7.3 Hz, 1H), 6.52–6.36 (m, 2H), 4.42 (q, J = 6.7 Hz, 1H), 4.01 (s, 1H), 1.45 (d, J = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.03, 143.90, 132.45, 129.23, 128.87, 127.35, 117.61, 113.43, 53.06, 25.14. HPLC analysis: Chiralcel OD-H (Hexane/*i*-PrOH = 95/5, 1.0 mL/min, 254 nm, 25 °C): t_{major} = 7.499 min, t_{minor} = 8.319 min, ee: 61%.

4.4.11. (*S*)-*N*-Phenyl-*N*-[1-(4-nitrophenyl)ethyl]amine 7k[3e]

Yield 81%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14–7.95 (m, 2H), 7.46 (d, J = 8.7 Hz, 2H), 7.01 (dd, J = 8.5, 7.4 Hz, 2H), 6.61 (d, J = 7.3 Hz, 1H), 6.47–6.20 (m, 2H), 4.48 (q, J = 6.8 Hz, 1H), 4.02 (s, 1H), 1.46 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.21, 147.08, 146.55, 129.26, 126.73, 124.09, 117.99, 113.32, 53.33, 24.94. HPLC analysis: Chiralcel OD-H (Hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm, 25 °C): t_{major} = 18.570 min, t_{minor} = 22.780 - min, ee: 63%.

4.4.12. (*S*)-*N*-Phenyl-*N*-[1-(4-methylphenyl)ethyl]amine 7l[3e]

Yield 92%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, J = 8.1 Hz, 2H), 7.12–7.00 (m, 4H), 6.61 (tt, J = 7.4, 1.0 Hz, 1H), 6.51–6.44 (m, 2H), 4.42 (q, J = 6.7 Hz, 1H), 3.95 (s, 1H), 2.28 (s, 3H), 1.45 (d, J = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.26, 141.14, 135.27, 128.13 (d, J = 23.1 Hz), 124.69, 116.09, 112.24, 52.05, 23.92, 19.99. HPLC analysis: Chiralcel OD-H (Hexane/*i*-PrOH = 99/1, 1.0 mL/min, 254 nm, 25 °C): t_{major} = 5.330 min, t_{minor} = 5.861 min, ee: 68%.

4.4.13. (*S*)-*N*-Benzyl-1-phenylpropylamine 7m[3e]

Yield 86%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.21 (m, 10H), 4.57 (d, J = 9.0 Hz, 1H), 3.81–3.62 (m, 2H), 2.00 (d, J = 1.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.48, 142.88, 128.03, 127.44, 125.82, 125.44, 116.08, 112.22, 58.67, 30.59, 9.77. HPLC analysis: Chiralcel OD-H (Hexane/*i*-PrOH = 99/1, 1.0 mL/min, 254 nm, 25 °C): t_{major} = 8.143 min, t_{minor} = 9.720 min, ee: 71%.

4.4.14. (*S*)-*N*-phenyl-*N*-[1-(4-chlorophenyl)propyl]amine 7n[3e]

Yield 77%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, J = 10.4 Hz, 4H), 7.00 (dd, J = 8.5, 7.4 Hz, 2H), 6.57 (t, J = 7.3 Hz, 1H), 6.40 (dd, J = 8.5, 0.9 Hz, 2H), 4.12 (t, J = 6.7 Hz, 1H), 3.95 (s, 1H), 1.82–1.59 (m, 2H), 0.87 (t, J = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.19, 141.50, 131.42, 128.10, 127.64, 126.83, 116.40, 112.25, 58.15, 30.64, 9.66. HPLC analysis: Chiralcel OD-H (Hexane/*i*-PrOH = 99/1, 1.0 mL/min, 254 nm, 25 °C): t_{major} = 9.873 min, t_{minor} = 14.328 min, ee: 75%.

4.4.15. (*S*)-*N*-Phenyl-*N*-[1-(4-methylphenyl)propyl]amine 7o[3e]

Yield 87%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21–7.12 (m, 3H), 7.08–6.96 (m, 3H), 6.55 (d, J = 7.3 Hz, 1H), 6.44 (dd, J = 8.6, 0.9 Hz, 2H), 4.12 (t, J = 6.7 Hz, 1H), 3.97 (s, 1H), 2.24 (s, 3H), 1.74 (td, J = 14.4, 7.1 Hz, 2H), 0.87 (t, J = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.58, 139.86, 135.35, 128.16, 128.04, 125.36, 116.02, 112.21, 58.42, 30.61, 20.04, 9.81. HPLC analysis: Chiralcel OD-H (Hexane/*i*-PrOH = 99/1, 1.0 mL/min, 254 nm, 25 °C): t_{major} = 6.522 min, t_{minor} = 8.431 min, ee: 72%.

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