Tetrahedron 64 (2008) 11304–11312

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Development of highly enantioselective new Lewis basic *N*-formamide organocatalysts for hydrosilylation of imines with an unprecedented substrate profile

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ARTICLE INFO

Article history:
Received 23 April 2008
Received in revised form 2 September 2008
Accepted 5 September 2008
Available online 23 September 2008

Keywords:
Lewis basic organocatalysts
Acyclic ketimines
L-Pipecolinic acid
Asymmetric reduction

ABSTRACT

L-Pipecolinic acid derived *N*-formamides have been developed as new Lewis basic organocatalysts that promote the asymmetric reduction of *N*-aryl ketimines using trichlorosilane as the reducing agent. The substituent on N4 of the piperazinyl backbone and the 2-carboxamide group both proved to have profound effects on the efficacy of the catalyst. The reductions of both *N*-aryl acyclic methyl ketimines and non-methyl ketimines were catalyzed to afford the desired amines in good to high yield and enantioselectivity. In particular, catalyst **6e** enabled the reduction of the difficult bulky ketimines to be highly efficient and enantioselective, affording up to 99% yield and 97% ee. This catalyst proved to prefer the relatively bulkier non-methyl acyclic ketimines to the methyl ketimines as substrate, which is so far unprecedented in catalytic asymmetric reduction of imines.

1. Introduction

Chiral amines are fundamentally important structural motifs of natural products, drugs, and agrochemicals. Catalytic asymmetric reduction of imines is one of the most efficient and straightforward methods for their preparation and has attracted tremendous efforts in the past several decades.[1,2] However, so far only limited successes have been met with the development of catalytic asymmetric reduction of imines,[2] in contrast to the extraordinary advances that have been made in asymmetric reduction of olefins and ketones. The currently available enantioselective catalytic methods for the reduction of imines mainly rely on chiral transition metal catalysts, which often require elevated pressures and/or additives to afford high yields and ee values. On the other hand, all of these catalysts only tolerate a narrow scope of substrates, which are mostly limited to either cyclic ketimines or acyclic methyl ketimines.[2] There have been rare examples of catalysts that are tolerant to acyclic non-methyl ketimines.[3]

Recently, catalytic asymmetric reduction of imines has been effected with chiral Lewis basic organocatalysts using trichlorosilane ($HSiCl_3$) as the reducing agent (Scheme 1).[4–8] Matsumura et al. first disclosed that L-proline derived *N*-formamides **3** (Fig. 1) catalyzed the reduction of *N*-aryl ketimines in modest enantioselectivity (up to 66% ee).[4a] Later, Malkov et al. reported that L-valine derived catalysts **4** significantly improved the enantioselectivity (up to 92% ee).[5a] Very recently, our group developed an L-pipecolinic acid derived Lewis basic catalyst **5** that not only exhibited a high level of enantioselectivities (up to 96% ee), but also displayed an unprecedented substrate spectrum.[6a] Encouraged by these results, we continued to search for new highly efficient and enantioselective Lewis basic catalysts with structural diversity, particularly those with different substrate preferences and thus complementing with the existing catalysts. In a preliminary communication, we reported on an L-piperazine-2-carboxylic acid derived new catalyst **6e** (Fig. 2) that exhibited high enantioselectivity in the hydrosilylation of *N*-aryl ketimines with an interesting substrate profile.[6b] This catalyst prefers relatively bulky acyclic non-methyl ketimines as the substrate, which

1 2

Scheme 1. Asymmetric reduction of ketimines.

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doi:10.1016/j.tet.2008.09.034

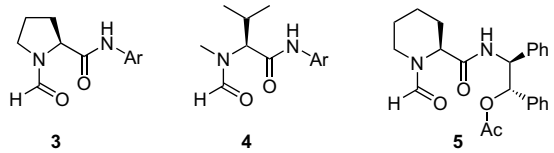


Figure 1. Structures of the Lewis basic catalysts reported previously.

is so far unprecedented. Herein, we wish to describe the details related to the development of this catalyst.

2. Result and discussion

2.1. Catalyst design and synthesis

In our previous studies, it has been shown that the six-membered cyclic 2*S*-piperdinyl backbone of **5** is preferable for the structure of chiral Lewis basic *N*-formamide catalysts.[6a] We envisioned that the analogous 2*S*-piperazinyl backbone could also be a good one for the same type of catalysts. The additional secondary amino group on the 4-position (N4) of the piperazinyl backbone should provide an excellent open site for introducing diversity elements and thus an excellent handle for fine-tuning the catalytic properties. Thus, we designed and synthesized a series of new *N*-formamide catalysts (**6**–**10**, Fig. 2) based on 2*S*-piperazinyl backbone starting from the commercially available L-piperazine-2-carboxylic acid.

The synthesis of **6**, **9**, and **10** began with the Boc- and Cbz-protected L-piperazine-2-carboxylic acid **11**, which first reacted with the corresponding amines in the presence of EDCI and HOBt to afford amides **12** (Scheme 2). *N*-Boc deprotection of **12** with trifluoroacetic acid (TFA) followed by treatment with the corresponding chloride gave intermediate **13**. After the *N*-Cbz group of **13** was removed with Pd/C, the resulting amine was subjected to N-formylation with formic acid and acetic anhydride to afford the desired *N*-formamide.

Catalysts **7** and **8** were prepared starting from the commercially available chiral 1,2-diphenyl-2-aminoethanol **14** according to Scheme 3. The coupling of **14** with **11** gave compound **15**, of which the hydroxy group was then acetylated with acetic anhydride to afford **16**. The subsequent procedures for the deprotections and the installations of R^4 and *N*-formyl groups to produce the desired catalysts **7** and **8** are similar to those shown in Scheme 2 for the preparation of **6**, **9**, and **10**.

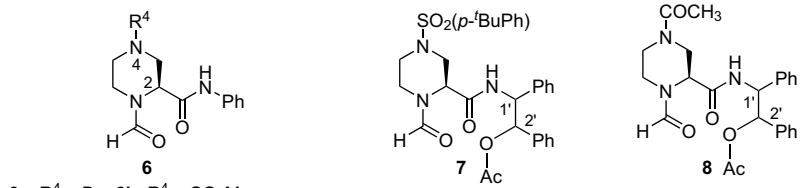
2.2. Asymmetric reduction of ketimines with $HSiCl_3$ catalyzed by chiral formamides

We first tested the catalytic efficacies of **6a**–**h** bearing various substituents R^4 on N4 in the model reaction of **1a** with $HSiCl_3$ in dichloromethane at 0 °C. As shown in Table 1, R^4 was indeed found to have significant influences on both the reactivity and the enantioselectivity of the catalyst. Catalyst **6a** with an alkyl group (Bn) on N4 gave only a moderate yield and ee value (entry 1). When this group was changed to methanesulfonyl, the resulted catalyst **6b** exhibited improved reactivity and enantioselectivity (entry 2).[9] A switch of the methanesulfonyl group to the benzenesulfonyl group (catalyst **6c**) led to further improvement of both reactivity and enantioselectivity (entry 3). Interestingly, a *para*-alkyl substitution on the benzene ring of the benzenesulfonyl group (**6d** and **6e**) has some beneficial effects on both the reactivity and the enantioselectivity of the catalyst (entries 4 and 5). The bulkier the *para*-substituent is, the stronger such effects seem to be. Compound **6e** bearing a bulky *para*-*tert*-butyl gave a high yield of 97% with 80% ee (entry 5).

A carbonyl group on N4 of the piperazinyl backbone has similar effects on the catalytic efficacies and similar substituent preference as the sulfonyl group (entries 6–8). Compound **6h** bearing a *para*-*tert*-butyl benzoyl gave good results with 87% yield and 87% ee (entry 8).

As observed with the previously reported amino acid derived diamide Lewis base catalysts,[4a,5a,b,d,6a,b,d,e] the 2-carboxlic amide group also has profound impacts on both the reactivity and the selectivity of this new catalyst system. While catalyst **10a** bearing a *para*-methoxyphenyl amide group led to slightly lowered yield and ee value, significantly decreased yield and ee value were achieved with **10b** bearing a 2-naphthyl amide group.

The (1′*S*,2′*S*)-2′-acetoxy-1′,2′-diphenylethyl amide group, a critical structural motif of **5**,[6a] was found to be unfavorable in the structure of catalysts **7**. Compound **7a** catalyzed the reaction with only 36% ee (entry 9). To check if the absolute stereochemistries in



6

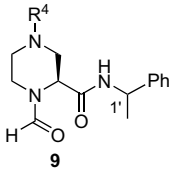
6a, R^4 = Bn; **6b**, R^4 = SO_2Me
6c, R^4 = SO_2Ph; **6d**, R^4 = $SO_2(p\text{-}MeC_6H_4)$
6e, R^4 = $SO_2(p\text{-}^tBuC_6H_4)$; **6f**, R^4 = COMe
6g, R^4 = COPh; **6h**, R^4 = $CO(p\text{-}^tBuC_6H_4)$

7

7a, (1′*S*, 2′*S*)
7b, (1′*R*, 2′*S*)
7c, (1′*S*, 2′*R*)

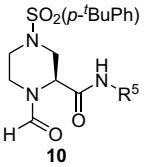
8

8a, (1′*S*, 2′*S*)
8b, (1′*R*, 2′*S*)
8c, (1′*S*, 2′*R*)



9

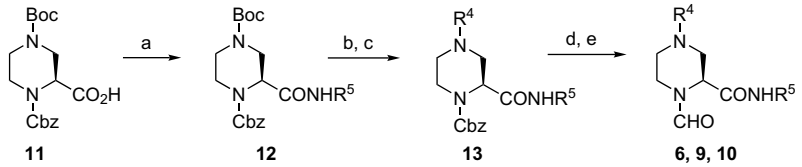
9a, 1′*R*, R^4 = COMe
9b, 1′*S*, R^4 = COMe
9c, 1′*R*, R^4 = $SO_2(p\text{-}^tBuC_6H_4)$
9d, 1′*S*, R^4 = $SO_2(p\text{-}^tBuC_6H_4)$
9e, 1′*R*, R^4 = $CO(p\text{-}^tBuC_6H_4)$
9f, 1′*R*, R^4 = $CO(p\text{-}ClC_6H_4)$
9g, 1′*R*, R^4 = COPh
9h, 1′*R*, R^4 = COEt



10

10a, R^5 = $p\text{-}MeOC_6H_4$
10b, R^5 = 2-Naphthyl

Figure 2. L-Piperazine-2-carboxylic acid derived organocatalysts.



Scheme 2. Preparation of organocatalysts **6**, **9**, and **10**. Reagents and conditions: (a) EDCI, HOBt, DIEA, R^5NH_2, rt, 80–95%; (b) TFA (20% v/v in DCM), 0 °C; (c) TEA, R^4Cl, rt, two steps 85–95%; (d) Pd/C, H_2 (g), rt, 83–96%; (e) HCO_2H, Ac_2O, rt, 60–95%.

this amide group could make any significant difference, the diastereomers **7b** and **7c** were examined. In agreement with the observation in the case of **5**, an (*S*)-configuration is distinctly preferred for C1′. Compound **7b** with (*R*)-C1′ afforded a nearly racemic product (entry 10). Interestingly, while the absolute configuration of C2′ has marginal influence on the selectivity of **5**, **7c** with (*R*)-C2′ exhibited much higher selectivity than **7b** with (*S*)-C2′ (entries 10 and 11). Thus, catalyst **7c** with the (1′*S*, 2′*R*)-2′-acetoxy-1′,2′-diphenylethyl amide group has the best-match stereochemistries. Nevertheless, the performance of **7c** is still not as good as that of **6e** bearing the same *para*-*tert*-butyl benzenesulfonyl group on N4 but a simple phenyl amide group on C2 (entries 5 and 11), which means the use of the chiral 2′-acetoxy-1′,2′-diphenylethyl amide group has no beneficial effect on the stereoselectivity of the catalysts.

When the *para*-*tert*-butyl benzenesulfonyl group on N4 was changed to a less bulky acetyl, catalysts **8** displayed similar C1′ and C2′ stereochemistry preferences as **7** (entries 12–14).

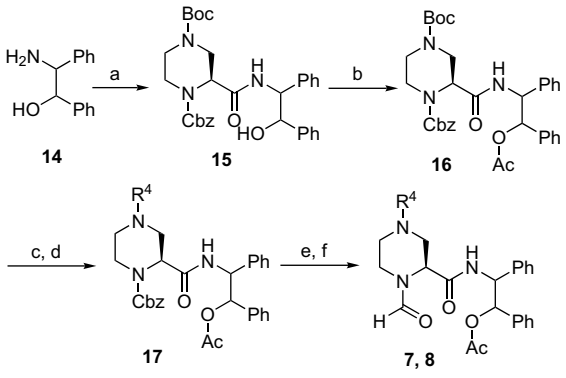
Trimming off the substituents on C2′ in **8** led to catalysts **9a** and **9b** that exhibited improved enantioselectivities (entries 15 and 16). Without the chirality of C2′, an (*R*)-configuration is preferred for C1′, with which the phenyl group virtually remains in the same β-orientation as in **7a**, **7c**, **8a**, and **8c**. As expected, such C1′ stereochemistry preference remains unchanged when R4 was replaced with *para*-*tert*-butyl benzenesulfonyl (**9c** vs **9d**, entry 17 vs 18). With the trimmed (*R*)-configured amide group, the other substituents were also examined as R^4 (**9e**–**h**). The obtained results showed that R^4 prefers a benzoyl group (**9g**, entry 21). A *para*-substituent, either *tert*-butyl (**9e**) or chloro (**9f**), on the benzene ring of this group has no obvious impact on the catalytic efficacies (entries 19 and 20).

We then selected the three catalysts **6e**, **6h**, and **9g** that displayed relatively high enantioselectivity in their classes for further study. These catalysts were first tested for the reduction of **1a** under a lowered reaction temperature at −20 °C. Interestingly, while both **6e** and **9g** gave substantially improved ee values (entries 4 and 6 vs 1 and 3, respectively, Table 2), **6h** gave slightly decreased enantioselectivity (entry 5 vs 2). Thus, **6h** became the least enantioselective among these three catalysts at −20 °C, in contrast to being the most enantioselective at 0 °C.

These catalysts were next examined with a challenging substrate, the non-methyl ketimine **1b**, at −20 °C. Similar to all the other currently available catalysts, **9g** gave no better ee value for this ketimine than for its methyl analogue **1a** (entry 9 vs 6). In contrast, substantially higher enantioselectivities were obtained for **1b** than **1a** under the catalysis of both **6e** and **6h** (entries 7 and 8 vs 4 and 5). This unprecedented observation prompted us to explore the potential of the present catalyst system for the asymmetric reduction of other relatively bulky non-methyl substrates such as **1b**–**n** (Table 3), which so far still remains a big challenge in asymmetric catalysis.

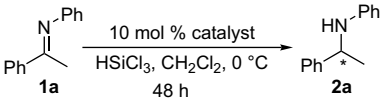
As illustrated in Table 3, in the presence of catalyst **6e**, *N*-phenyl aromatic ethyl ketimines **1b**–**g** and aliphatic ethyl ketimine **1h** all underwent smooth reductions to afford the corresponding amines in high yield and enantioselectivity (83–92% yield, 84–95% ee, entries 1–7). Moreover, ketimines **1j**–**n** with even bulkier R^2 groups were also reduced well, affording high yields and ee values (75–88% yield, 89–97% ee, entries 9–13).

To have a better picture of the substrate profile of catalyst **6e**, some other methyl ketimines **1o**–**y** besides **1a** were also examined. The results are summarized in Table 3 (entries 14–25). Although



Scheme 3. Preparation of organocatalysts **7** and **8**. Reagents and conditions: (a) **11**, EDCI, HOBt, DIEA, rt, 80–93%; (b) Ac_2O, DIEA, $CHCl_3$, reflux, 90–96%; (c) TFA (20% in DCM), 0 °C; (d) TEA, R^4Cl, rt, two steps 85–92%; (e) Pd/C, rt; (f) HCO_2H, Ac_2O, rt, two steps 60–95%.

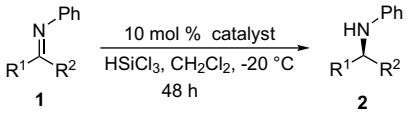
Table 1
Asymmetric hydrosilylation of ketimine **1a**[a]



Entry	Catalyst	Yield[b] (%)	ee[c] (%)	Config.
1	**6a**	65	40	*R*
2	**6b**	64	70	*R*
3	**6c**	77	74	*R*
4	**6d**	82	77	*R*
5	**6e**	**97**	**80**	*R*
6	**6f**	77	66	*R*
7	**6g**	80	78	*R*
8	**6h**	**87**	**87**	*R*
9	**7a**	80	36	*R*
10	**7b**	71	5	*S*
11	**7c**	63	71	*R*
12	**8a**	57	62	*R*
13	**8b**	52	6	*S*
14	**8c**	56	68	*R*
15	**9a**	71	80	*R*
16	**9b**	69	77	*R*
17	**9c**	79	74	*R*
18	**9d**	82	54	*R*
19	**9e**	76	83	*R*
20	**9f**	77	83	*R*
21	**9g**	**75**	**84**	*R*
22	**9h**	84	72	*R*
23	**10a**	92	73	*R*
24	**10b**	68	56	*R*

[a] Unless specified otherwise, reactions were carried out with 2.0 equiv of $HSiCl_3$ on a 0.2 mmol scale in 1.0 mL of CH_2Cl_2.
[b] Isolated yield based on the imine.
[c] The ee values were determined using chiral HPLC.

Table 2
Asymmetric hydrosilylation of ketimine **1**[a]



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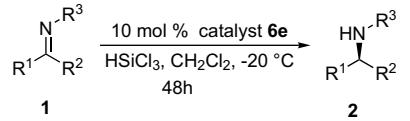
Entry	Catalyst	Imine	R^1	R^2	Temp	Yield[b] (%)	ee[c] (%)
1	**6e**	**1a**	Ph	Methyl	0	97	80
2	**6h**	**1a**	Ph	Methyl	0	87	87
3	**9g**	**1a**	Ph	Methyl	0	75	84
4	**6e**	**1a**	Ph	Methyl	−20	95	89
5	**6h**	**1a**	Ph	Methyl	−20	92	85
6	**9g**	**1a**	Ph	Methyl	−20	90	91
7	**6e**	**1b**	**Ph**	**Ethyl**	**−20**	**90**	**93**
8	**6h**	**1b**	Ph	Ethyl	−20	91	90
9	**9g**	**1b**	Ph	Ethyl	−20	80	61

[a] Unless specified otherwise, reactions were carried out with 2.0 equiv of $HSiCl_3$ on a 0.2 mmol scale in 1.0 mL of CH_2Cl_2.
[b] Isolated yield based on the imine.
[c] The ee values were determined using chiral HPLC.

moderate to high yields and ee values were obtained for these methyl ketimines, it is quite clear that these ketimines are not as good substrates as those bulkier non-methyl ketimines for the **6e** catalyzed reduction. To the best of our knowledge, such a substrate profile has not been previously reported for the asymmetric reduction of *N*-aryl ketimines. As a matter of fact, when our previous analogous catalyst **5** was used as the catalyst, a dramatically different scenario was observed (see data in parentheses in Table 3): while most of the methyl ketimines gave high ee values (89–95%, entries 15, 16, 18–22, 24, and 25), only low to moderate enantioselectivities (entries 1 and 9–13) were attained for the non-methyl ones, with only one exception of 92% ee for cyclopropanyl ketimine **1l** (entry 11).[6a] Thus, **6e** complements well with **5** and the other previously reported catalysts, which are limited to methyl ketimines for highly enantioselective reduction.

Table 3
Asymmetric hydrosilylation of ketimine **1** with catalyst **6e**[a]



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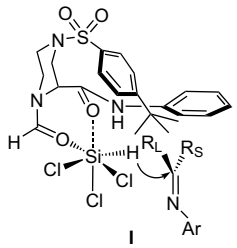
Entry	Imine	R^1	R^2	R^3	Yield[b] (%)	ee[c] (%)
1	**1b**	Ph	Et	Ph	92	94 (67)
2	**1c**	4-FPh	Et	Ph	87	95
3	**1d**	4-ClPh	Et	Ph	83	94
4	**1e**	4-BrPh	Et	Ph	89	95
5	**1f**	4-MeOPh	Et	Ph	83	90
6	**1g**	4-MePh	Et	Ph	87	88
7	**1h**	*c*-C_6H_{11}	Et	Ph	84	84
8	**1i**	Ph	Et	4-MeOPh	75	74
9	**1j**	Ph	^{n}Pr	Ph	88	90 (45)
10	**1k**	Ph	^{i}Pr	Ph	75	92 (50)
11	**1l**	Ph	^{c}Pr	Ph	85	97 (92)
12	**1m**	Ph	^{n}Bu	Ph	84	89 (29)
13	**1n**	Ph	^{i}Bu	Ph	86	91 (7)
14	**1a**	Ph	Me	Ph	95	89 (95)
15	**1o**	4-BrPh	Me	Ph	81	89 (95)
16	**1p**	4-NO_2Ph	Me	Ph	99	90 (95)
17	**1q**	4-MePh	Me	Ph	71	85
18	**1r**	4-MeOPh	Me	Ph	40	62 (93)
19	**1s**	Naphth	Me	Ph	63	88 (93)
20	**1t**	2-(6-MeO)-Naphth	Me	Ph	64	85 (90)
21	**1u**	Ph	Me	4-ClPh	84	75 (93)
22	**1v**	Ph	Me	4-MeOPh	66	55 (92)
23	**1w**	Ph	Me	4-NO_2Ph	73	56
24	**1x**	Ph	Me	2-MeOPh	33	58 (89)
25	**1y**	*c*-C_6H_{11}	Me	Ph	86	82 (95)

[a] Unless specified otherwise, reactions were carried out with 2.0 equiv of $HSiCl_3$ on a 0.2 mmol scale in 1.0 mL of CH_2Cl_2.
[b] Isolated yield based on the imine.
[c] The ee values were determined using chiral HPLC; the data in parentheses are for catalyst **5**.

2.3. Mechanistic consideration

Although detailed structural and mechanistic studies remain to be carried out, on the basis of the available experimental data, we propose a transition state model **I** for the present catalytic reaction system, which could reasonably explain the absolute configuration of the product and the profound effects of the substituent on N4 due to its steric shielding effects.



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3. Conclusion

We have developed L-pipecolinic acid derived *N*-formamides as new Lewis basic organocatalysts that promote the asymmetric reduction of *N*-aryl ketimines using trichlorosilane as the reducing agent. The substituents on N4 of the piperazinyl backbone and the 2-carboxamide group both proved to have profound effects on the efficacy of the catalyst. The reductions of both *N*-aryl acyclic methyl ketimines and non-methyl ketimines were catalyzed to afford the desired amines in good to high yield and enantioselectivity. Most remarkably, catalyst **6e** promoted the reduction of the relatively bulky non-methyl ketimines in high yields with high ee values. The preference of **6e** for the relatively bulkier non-methyl ketimines over the methyl ketimines as substrate is so far unprecedented in catalytic asymmetric reduction of imines. This feature renders the present catalyst system a good complement to the existing catalyst systems for the high enantioselective reduction of imines in terms of the substrate spectrum.

4. Experimental

4.1. General methods

All starting materials were of the highest commercially available grade and used without further purification. All solvents used in the reactions were distilled from appropriate drying agents prior to use. Reactions were monitored by thin layer chromatography using silica gel HSGF254 plates. Flash chromatography was performed using silica gel HG/T2354-92. ^1H and ^{13}C NMR (300 or 600 and 75 or 150 Hz, respectively) spectra were recorded in $CDCl_3$ or DMSO. ^1H NMR chemical shifts are reported in parts per million (δ) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$, δ7.26 ppm; DMSO, δ 2.36 ppm). Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, q=quartet, m=multiplet), coupling constants (Hz), and integration. ^{13}C NMR chemical shifts are reported in parts per million from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$, δ 77.0 ppm; DMSO, δ 40.0 ppm). ESIMS spectra were recorded on BioTOF Q. HPLC analyses were performed on PerkinElmer (Series 200 UV/VIS Detector and Series

200 Pump). Chiralpak OD-H, AD-H, and OJ-H columns were purchased from Daicel Chemical Industries, Ltd. All enantiomeric ratios have been controlled by co-injections of the pure sample with the racemic substrates. All imines were prepared according to the general procedure. Imines **1a**, **1b**, **1j**, **1k**, and **1o**–**1y** are known compounds.[4,5,6a,10] Amines **2a**–**2g** and **2j**–**2y** are also known compounds.[4,5,6a,10,11] Chemical yields refer to pure isolated substances.

4.2. General procedure for the synthesis of imines

A mixture of $NaHCO_3$ (50 mmol), amine (10 mmol), ketone (10 mmol), and activated 4 Å molecular sieves (8.0 g) in anhydrous toluene (10 mL) was heated at 80 °C for 12 h under an argon atmosphere. The mixture was filtered through Celite. The filtrate was then evaporated in vacuo and the product was crystallized from appropriate solvents or purified by distillation to give pure imine.

4.2.1. Imine **1c**

Light yellow solid; yield: 70%; mp 69–72 °C; a 15/1 mixture of *E*/*Z* isomers; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.08 (t, *J*=7.7 Hz, 3H), 2.64 (q, *J*=7.7 Hz, 2H), 6.78 (d, *J*=8.4 Hz, 2H), 7.08–7.16 (m, 3H), 7.35 (t, *J*=7.9 Hz, 2H), 7.91–7.96 (m, 2H); minor isomer: δ=1.23 (t, *J*=7.4 Hz, 3H), 2.77 (q, *J*=7.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=12.9, 23.4, 115.4, 115.5, 119.1, 123.1, 129.0, 129.8, 134.2, 151.4, 163.4, 165.0, 169.5; ESI HRMS exact mass calcd for $C_{15}H_{15}FN$ requires *m*/*z* 228.1183, found *m*/*z* 228.1176.

4.2.2. Imine **1d**

Light yellow solid; yield: 75%; mp 57–59 °C; a 12/1 mixture of *E*/*Z* isomers; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.07 (t, *J*=7.7 Hz, 3H), 2.64 (q, *J*=7.7 Hz, 2H), 6.78 (d, *J*=8.1 Hz, 2H), 7.09 (t, *J*=7.4 Hz, 1H), 7.35 (t, *J*=7.7 Hz, 2H), 7.42 (d, *J*=6.8 Hz, 2H), 7.87 (d, *J*=6.7 Hz, 2H); minor isomer: δ=1.23 (t, *J*=7.3 Hz, 3H), 2.77 (q, *J*=7.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=12.87, 23.4, 119.0, 120.8, 123.2, 128.7, 129.0, 129.4, 136.5, 151.3, 169.6; ESI HRMS exact mass calcd for $C_{15}H_{15}ClN$ requires *m*/*z* 244.0888, found *m*/*z* 244.0882.

4.2.3. Imine **1e**

Light yellow solid; yield: 75%; mp 37–39 °C; a 14/1 mixture of *E*/*Z* isomers; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.07 (t, *J*=7.7 Hz, 3H), 2.63 (q, *J*=7.7 Hz, 2H), 6.77 (d, *J*=7.3 Hz, 2H), 7.10 (t, *J*=7.4 Hz, 1H), 7.35 (t, *J*=7.7 Hz, 2H), 7.58 (d, *J*=8.6 Hz, 2H), 7.81 (d, *J*=8.7 Hz, 2H); minor isomer: δ=1.22 (t, *J*=7.2 Hz, 3H), 2.77 (q, *J*=7.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=12.87, 23.3, 118.8, 122.6, 125.0, 129.5, 129.6, 131.7, 136.9,151.3, 169.7; ESI HRMS exact mass calcd for $C_{15}H_{15}BrN$ requires *m*/*z* 288.0382, found *m*/*z* 288.0383.

4.2.4. Imine **1f**

Light yellow solid; yield: 65%; mp 51–52 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.09 (t, *J*=7.6 Hz, 3H), 2.63 (q, *J*=7.7 Hz, 2H), 3.87 (s, 3H), 6.78 (d, *J*=7.6 Hz, 2H), 6.96 (d, *J*=6.8 Hz, 2H), 6.96 (t, *J*=6.9 Hz, 1H), 7.34 (t, *J*=7.5 Hz, 2H), 7.90 (d, *J*=6.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=13.1, 23.3, 55.4, 113.8, 119.3, 122.8, 129.0, 129.3, 130.6, 151.9, 161.4, 169.8; ESI HRMS exact mass calcd for $C_{16}H_{18}NO$ requires *m*/*z* 240.1383, found *m*/*z* 240.1378.

4.2.5. Imine **1g**

Light yellow solid; yield: 60%; mp 47–48 °C; an 11/1 mixture of *E*/*Z* isomers; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.08 (t, *J*=7.6 Hz, 3H), 2.41 (s, 3H), 2.64 (q, *J*=7.6 Hz, 2H), 6.79 (d, *J*=8.4 Hz, 2H), 7.10 (t, *J*=7.5 Hz, 1H), 7.24–7.31 (m, 2H), 7.34 (t, *J*=7.6 Hz, 2H), 7.83 (d, *J*=8.2 Hz, 2H); minor isomer: δ=1.23 (t, *J*=7.4 Hz, 3H), 2.78 (q, *J*=7.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=13.1, 21.4, 23.4, 119.2, 120.9, 122.9, 127.6, 128.9, 129.2, 135.3, 140.6, 151.8, 170.5; ESI HRMS exact mass calcd for $C_{16}H_{18}N$ requires *m*/*z* 224.1434, found *m*/*z* 224.1433.

4.2.6. Imine **1h**

Light yellow oil; yield: 61%; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.0 (t, *J*=7.7 Hz, 3H), 1.17–1.92 (m, 10H), 2.37 (m, 1H), 2.45 (q, *J*=7.3 Hz, 2H), 6.65 (d, *J*=7.3 Hz, 2H), 6.99 (t, 1H), 7.26 (t, *J*=7.7 Hz, 2H); minor isomer: 2.14 (q, *J*=7.7 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=11.8, 25.2, 26.4, 28.6, 30.8, 46.0, 119.2, 122.4, 128.7, 151.7, 179.7; ESI HRMS exact mass calcd for $C_{15}H_{22}N$ requires *m*/*z* 216.1747, found *m*/*z* 216.1736.

4.2.7. Imine **1l**

Light yellow oil; yield: 62%; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.02–1.07 (m, 2H), 1.22–1.28 (m, 2H), 2.67 (m, 1H), 6.56–7.57 (m, 8H), 8.00–8.04 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=9.5, 11.6, 17.1, 120.1, 122.6, 128.0, 128.5, 132.7, 138.1, 151.1, 172.9; ESI HRMS exact mass calcd for $C_{16}H_{16}N$ requires *m*/*z* 222.1277, found *m*/*z* 222.1275.

4.2.8. Imine **1m**

Light yellow oil; yield: 70%; a 12/1 mixture of *E*/*Z* isomers; ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.77 (t, *J*=7.2 Hz, 3H), 1.19–1.25 (m, 2H), 1.40–1.60 (m, 2H), 2.64 (t, *J*=7.9 Hz, 3H), 6.78 (d, *J*=8.4 Hz, 2H), 7.07 (t, *J*=7.42 Hz, 1H), 7.34 (t, *J*=8.0 Hz, 2H), 7.44–7.46 (m, 3H), 7.89–7.92 (m, 2H); minor isomer: δ=2.76 (t, *J*=7.88 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=13.6, 22.7, 30.3, 38.3, 119.2, 122.9, 127.5, 128.4, 128.9, 130.2, 138.6, 151.6, 169.9; ESI HRMS exact mass calcd for $C_{17}H_{20}N$ requires *m*/*z* 238.1590, found *m*/*z* 238.1592.

4.2.9. Imine **1n**

Light yellow oil; yield: 55%; an 8/1 mixture of *E*/*Z* isomers; ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.78 (d, *J*=6.7 Hz, 6H), 1.86–1.93 (m, 1H), 2.59 (d, *J*=7.4 Hz, 2H), 6.78–6.79 (m, 2H), 7.04–7.11 (m, 1H), 7.26–7.56 (m, 5H), 7.84–7.98 (m, 2H); minor isomer: δ=1.00 (d, *J*=6.7 Hz, 6H), 2.68 (d, *J*=7.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=22.5, 22.8, 27.0, 38.9, 119.5, 122.9, 127.6, 128.4, 128.8, 130.1, 139.1, 151.4, 169.8; ESI HRMS exact mass calcd for $C_{17}H_{20}N$ requires *m*/*z* 238.1590, found *m*/*z* 238.1600.

4.3. General procedure for catalytic hydrosilylation of imines

Under an argon atmosphere, trichlorosilane (40 μL, 0.4 mmol) was added dropwise to a stirred solution of imine **1** (0.20 mmol) and catalyst (0.02 mmol) in anhydrous CH_2Cl_2 at 0 °C. The mixture was allowed to stir at the same temperature for 48 h. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (5 mL) and was extracted with EtOAc. The combined extracts were washed with brine and dried over anhydrous $MgSO_4$. Solvents were evaporated. The crude product was purified by column chromatography (silica gel, hexane/EtOAc) to afford pure amine. The ee values were determined by using established HPLC techniques with chiral stationary phases.

4.3.1. Amine **2a**

Light yellow oil; yield: 95%, purification by flash chromatography (hexane/EtOAc=98/2); ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.54 (d, *J*=6.72 Hz, 3H), 4.05 (br s, 1H), 4.51 (q, *J*=6.72 Hz, 1H), 6.53 (m, 2H), 6.66 (m, 1H), 7.08–7.14 (m, 2H), 7.26–7.40 (m, 5H) in agreement with the literature data.[4,5a] The enantiomers were analyzed by HPLC using a chiral OD-H column (*n*-heptane/2-propanol=99/1, flow rate=1.0 mL/min, wavelength=254 nm); minor enantiomer: t_R=11.82 min, major enantiomer: t_R=16.05 min; 89% ee.

4.3.2. Amine **2b**

Light yellow oil; yield: 92%, purification by flash chromatography (2% EtOAc in hexane); ^{1}H NMR (600 MHz, $CDCl_3$): δ=0.93–0.96 (t, *J*=7.4 Hz, 3H), 1.79–1.83 (q, *J*=7.3 Hz, 4H), 4.20–4.22 (t, *J*=6.7 Hz, 1H), 6.50 (t, *J*=7.8 Hz, 2H), 6.60 (t, *J*=7.3 Hz, 1H), 7.05 (t, *J*=8.5 Hz, 2H), 7.20–7.33 (m, 5H) in agreement with the literature data.[10a] The enantiomers were analyzed by HPLC using a chiral OD-H column

(*n*-heptane/2-propanol=99/1, flow rate=1.0 mL/min, wavelength=254 nm); minor enantiomer: t_R=8.15 min, major enantiomer: t_R=10.27 min; 94% ee.

4.3.3. Amine **2c**

Light yellow oil; yield: 87%, purification by flash chromatography (hexane/EtOAc=98/2); $[\alpha]_D^{20}$ −4.85 (*c* 0.676, EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.95 (t, *J*=7.4 Hz, 3H), 1.72–1.89 (m, 2H), 4.06 (s, 1H), 4.21 (t, *J*=6.5 Hz, 1H), 6.50 (d, *J*=8.3 Hz, 2H), 6.67 (t, *J*=7.3 Hz, 1H), 7.01 (t, *J*=8.7 Hz, 2H), 7.10 (t, *J*=7.7 Hz, 2H), 7.28–7.33 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=10.8, 31.8, 59.2, 113.3, 115.3, 115.4, 117.4, 128.0, 129.2, 139.7, 147.4, 161.0, 162.7; ESI HRMS exact mass calcd for $C_{15}H_{17}FN$ requires *m*/*z* 230.1340, found *m*/*z* 230.1345. The enantiomers were analyzed by HPLC using a chiral OD-H column (*n*-heptane/2-propanol=99/1, flow rate=1.0 mL/min, wavelength=254 nm); minor enantiomer: t_R=9.13 min, major enantiomer: t_R=13.30 min; 95% ee.

4.3.4. Amine **2d**

Light yellow oil; yield: 83%, purification by flash chromatography (hexane/EtOAc=98/2); $[\alpha]_D^{20}$ −7.89 (*c* 0.57, EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.95 (t, *J*=7.4 Hz, 3H), 1.74–1.86 (m, 2H), 4.05 (s, 1H), 4.21 (t, *J*=6.6 Hz, 1H), 6.48 (d, *J*=7.7 Hz, 2H), 6.65 (t, *J*=7.3 Hz, 1H), 7.09 (t, *J*=7.5 Hz, 2H), 7.26–7.34 (m, 4H) in agreement with the literature data.[11a–c] The enantiomers were analyzed by HPLC using a chiral OD-H column (*n*-heptane/2-propanol=99/1, flow rate=1.0 mL/min, wavelength=254 nm); minor enantiomer: t_R=9.95 min, major enantiomer: t_R=15.12 min; 94% ee.

4.3.5. Amine **2e**

Light yellow oil; yield: 89%, purification by flash chromatography (hexane/EtOAc=98/2); $[\alpha]_D^{20}$ −2.31 (*c* 0.736, EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.95 (t, *J*=7.4 Hz, 3H), 1.75–1.85 (m, 2H), 4.05 (s, 1H), 4.18 (br s, 1H), 6.47 (d, *J*=7.7 Hz, 2H), 6.67 (t, *J*=7.3 Hz, 1H), 7.08 (t, *J*=7.4 Hz, 2H), 7.24 (t, *J*=8.8 Hz, 2H), 7.43 (d, *J*=6.5 Hz, 2H) in agreement with the literature data.[11c] The enantiomers were analyzed by HPLC using a chiral OD-H column (*n*-heptane/2-propanol=95/5, flow rate=1.0 mL/min, wavelength=254 nm); minor enantiomer: t_R=7.72min, major enantiomer: t_R=11.02min; 95% ee.

4.3.6. Amine **2f**

Light yellow oil; yield: 83%, purification by flash chromatography (hexane/EtOAc=98/2); $[\alpha]_D^{20}$ −10.94 (*c* 0.384, EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.95 (t, *J*=7.4 Hz, 3H), 1.75–1.85 (m, 2H), 3.79 (s, 3H), 4.19 (t, *J*=6.68 Hz, 1H), 6.53 (d, *J*=7.7 Hz, 2H), 6.64 (t, *J*=7.3 Hz, 1H), 6.87 (d, *J*=8.6 Hz, 2H), 7.10 (t, *J*=7.5 Hz, 2H), 7.27 (d, *J*=8.6 Hz, 2H) in agreement with the literature data.[6a,11b] The enantiomers were analyzed by HPLC using a chiral OD-H column (*n*-heptane/2-propanol=99/1, flow rate=1.0 mL/min, wavelength=254 nm); minor enantiomer: t_R=10.74 min, major enantiomer: t_R=13.92 min; 90% ee.

4.3.7. Amine **2g**

Light yellow oil; yield: 87%, purification by flash chromatography (hexane/EtOAc=98/2); $[\alpha]_D^{20}$ −6.16 (*c* 0.406, EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.96 (t, *J*=7.4 Hz, 3H), 1.76–1.87 (m, 2H), 2.33 (s, 3H), 4.20 (t, *J*=6.7 Hz, 1H), 6.51 (d, *J*=8.6 Hz, 2H), 6.63 (t, *J*=7.3 Hz, 1H), 7.06–7.26 (m, 6H) in agreement with the literature data.[6a,11d] The enantiomers were analyzed by HPLC using a chiral OD-H column (*n*-heptane/2-propanol=99/1, flow rate=1.0 mL/min, wavelength=254 nm); minor enantiomer: t_R=6.71 min, major enantiomer: t_R=8.60 min; 88% ee.

4.3.8. Amine **2h**

Light yellow oil; yield: 84%, purification by flash chromatography (hexane/EtOAc=98/2); $[\alpha]_D^{20}$ +10.53 (*c* 0.38, EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.93 (t, *J*=7.4 Hz, 3H), 1.11–1.22 (m, 5H), 1.65–1.77 (m, 8H), 3.10–3.16 (m, 1H), 3.44 (br s, 1H), 6.56–6.65 (m, 3H), 7.12–7.26 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=10.8, 24.7, 26.5, 26.6, 26.7, 29.0, 29.5, 41.6, 59.2, 112.7, 116.2, 129.3, 148.9; ESI HRMS exact mass calcd for $C_{15}H_{24}N$ requires *m*/*z* 218.1903, found *m*/*z* 218.1912. Compound **2h** was N-formylated and the resulted *N*-formyl-**2h** enantiomers were successfully analyzed using a chiral OJ-H column (*n*-heptane/2-propanol=98/2, flow rate=1.0 mL/min, wavelength=254 nm); minor enantiomer: t_R=8.28 min, major enantiomer: t_R=9.98 min; 84% ee.

N-Formyl-**2h**: ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.91 (t, *J*=7.3 Hz, 3H), 1.03–1.25 (m, 6H), 1.72–2.04 (m, 7H), 4.09 (dt, *J*=3.1, 10.7 Hz, 1H), 7.16 (d, *J*=8.0 Hz, 2H), 7.21–7.42 (m, 3H), 8.43 (s, 1H).

4.3.9. Amine **2i**

Light yellow oil; yield: 75%, purification by flash chromatography (hexane/EtOAc=95/5); $[\alpha]_D^{25}$ +11.9 (*c* 0.74, EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.96 (t, *J*=7.4 Hz, 3H), 1.82 (m, 2H), 3.69 (s, 3H), 4.17 (t, *J*=6.7 Hz, 1H), 6.49 (d, *J*=9.0 Hz, 2H), 6.70 (d, *J*=9.0 Hz, 2H), 7.24 (m, 1H), 7.31 (m, 4H) in agreement with the literature data.[6a,10a] The enantiomers were analyzed by HPLC using a chiral AD-H column (*n*-heptane/2-propanol=98/2, flow rate=1.0 mL/min, wavelength=254 nm); minor enantiomer: t_R=11.05 min, major enantiomer: t_R=12.17 min; 74% ee.

4.3.10. Amine **2j**

Light yellow oil; yield: 88%, purification by flash chromatography (hexane/EtOAc=98/2); $[\alpha]_D^{25}$ +14.1 (*c* 0.34, EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$): δ=0.93 (t, *J*=7.3 Hz, 3H), 1.31–1.49 (m, 2H), 1.75 (m, 1H), 4.07 (br s, 1H), 4.30 (t, *J*=6.8 Hz, 1H), 6.50 (d, *J*=7.7 Hz, 2H), 6.62 (t, *J*=7.1 Hz, 1H), 7.07 (t, *J*=7.5 Hz, 2H), 7.21 (m, 1H), 7.31 (m, 4H) in agreement with the literature data.[10b,c] The enantiomers were analyzed by HPLC using a chiral OD-H column (*n*-heptane/2-propanol=99/1, flow rate=1.0 mL/min, wavelength=254 nm); minor enantiomer: t_R=7.30 min, major enantiomer: t_R=9.17 min; 90% ee.

4.3.11. Amine **2k**

Light yellow oil; yield: 75%, purification by flash chromatography (hexane/EtOAc=98/2); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.92 (d, *J*=6.8 Hz, 3H), 0.98 (d, *J*=6.8 Hz, 3H), 2.03–2.05 (m, 1H), 4.11 (s, 2H), 6.50 (d, *J*=7.9 Hz, 2H), 6.60 (t, *J*=7.3 Hz, 1H), 7.07 (t, *J*=7.7 Hz, 2H), 7.20–7.30 (m, 5H) in agreement with the literature data.[10c] The enantiomers were analyzed by HPLC using a chiral OD-H column (*n*-heptane/2-propanol=99/1, flow rate=1.0 mL/min, wavelength=254 nm); minor enantiomer: t_R=6.22 min, major enantiomer: t_R=7.26 min; 92% ee.

4.3.12. Amine **2l**

Light yellow oil; yield: 85%, purification by flash chromatography (hexane/EtOAc=98/2); $[\alpha]_D^{20}$ −80.10 (*c* 0.412, EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.40–0.60 (m, 4H), 1.18–1.29 (m, 1H), 3.65 (d, *J*=8.4 Hz, 1H), 4.41 (br s, 1H), 6.48 (d, *J*=7.6 Hz, 2H), 6.64 (t, *J*=7.4 Hz, 1H), 7.09 (t, *J*=7.4 Hz, 2H), 7.25–7.43 (m, 5H) in agreement with the literature data.[11e] The enantiomers were analyzed by HPLC using a chiral OD-H column (*n*-heptane/2-propanol=99/1, flow rate=1.0 mL/min, wavelength=254 nm); minor enantiomer: t_R=9.08 min, major enantiomer: t_R=10.42 min; 97% ee.

4.3.13. Amine **2m**

Light yellow oil; yield: 84%, purification by flash chromatography (hexane/EtOAc=98/2); $[\alpha]_D^{20}$ −23.86 (*c* 0.352, EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$): δ=0.88 (t, *J*=7.7 Hz, 3H), 1.25–1.43 (m, 4H), 1.73–1.83 (m, 2H), 4.07 (br s, 1H), 4.28 (t, *J*=6.8 Hz, 1H), 6.50 (d, *J*=7.7 Hz, 2H), 6.61 (t, *J*=7.3 Hz, 1H), 7.07 (t, *J*=7.1 Hz, 2H), 7.21 (t, *J*=6.9 Hz, 1H), 7.29–7.34 (m, 4H) in agreement with the literature data.[10c,11f] The enantiomers were analyzed by HPLC using a chiral OD-H

column (*n*-heptane/2-propanol=99/1, flow rate=1.0 mL/min, wavelength=254 nm); minor enantiomer: t_R=6.73 min, major enantiomer: t_R=8.23 min; 89% ee.

4.3.14. Amine **2n**

Light yellow oil; yield: 86%, purification by flash chromatography (hexane/EtOAc=98/2); $[\alpha]_D^{20}$ −18.78 (*c* 0.362, EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.94 (d, *J*=6.2 Hz, 3H), 0.99 (d, *J*=6.1 Hz, 3H), 1.57–1.62 (m, 1H), 1.65–1.74 (m, 2H), 4.04 (br s, 1H), 4.38 (t, *J*=7.5 Hz, 1H), 6.52 (d, *J*=7.6 Hz, 2H), 6.63 (t, *J*=7.3 Hz, 1H), 7.06–7.11 (m, 2H), 7.22–7.37 (m, 5H) in agreement with the literature data.[11g] The enantiomers were analyzed by HPLC using a chiral OD-H column (*n*-heptane/2-propanol=99/1, flow rate=1.0 mL/min, wavelength=254 nm); minor enantiomer: t_R=6.68min, major enantiomer: t_R=7.55min; 91% ee.

4.4. General procedure for the synthesis of catalysts 6, 9, and 10

To a solution of **11** (10 g, 27.4 mmol) in CH_2Cl_2 (70 mL) were added amine (32.9 mmol), DIEA (5.8 mL, 32.9 mmol), HOBt (4.8 g, 32.9 mmol), and EDCI (6.3 g, 32.9 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 12 h and then concentrated under reduced pressure. The residue was diluted with EtOAC (200 mL) and the solution was washed with saturated aqueous $NaHCO_3$ (40 mL), aqueous HCl (1.0 M, 20 mL), and brine (20 mL) and dried over anhydrous Na_2SO_4 After removal of solvents under reduced pressure, the residue was purified through column chromatography on silica gel to give pure amide **12**.

Compound **12** (2.28 mmol) was dissolved in 20 v/v% TFA in CH_2Cl_2 (40 mL) and stirred at room temperature for an hour, and then concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 and the resulting solution was cooled to 0 °C. TEA (480 μL, 3.42 mmol) was added followed by the addition of R^4Cl. The mixture was allowed to stir at room temperature overnight. After removal of solvents under reduced pressure, the residue was purified through column chromatography on silica gel to afford pure intermediate **13**.

Compound **13** (1.0 mmol), 5% Pd/C (50 mg), and methanol (15 mL) were charged in a two-neck flask (100 mL). The mixture was stirred under hydrogen (1 atm) until the starting material completely disappeared (monitored by TLC), and then filtered through Celite. The filtrate was concentrated under reduced pressure. The residue was dissolved in formic acid (1.5 mL) and the resulting solution was cooled to 0 °C. Acetic anhydride (1 mL) was added dropwise and the mixture was allowed to stir at room temperature overnight. After removal of solvents under reduced pressure, the residue was purified through column chromatography on silica gel to give pure catalyst.

4.4.1. Catalyst **6a**

White solid; yield: 80%; $[\alpha]_D^{20}$ −83.0 (*c* 0.10, $CHCl_3$); mp 54.0–55.0 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=2.15–2.20 (m, 1H), 2.23 and 2.42 (dd, *J*=4.0, 12.2 Hz, 1H), 3.03–3.09 (m, 1H), 3.38 and 3.46 (d, *J*=12.2 Hz, 1H), 3.55–3.68 (m, 3H), 4.13 and 5.09 (s, 1H), 4.34 (dd, *J*=2.7, 12.6 Hz, 1H), 7.11–7.15 (m, 1H), 7.28–7.40 (m, 7H), 7.48–7.51 (m, 2H), 8.20 and 8.26 (s, 1H), 8.58 and 9.90 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=37.4, 43.7, 52.2, 53.4, 63.0, 120.2, 124.8, 128.2, 128.9, 129.1, 129.4, 136.1, 137.2, 161.9, 166.9; ESI HRMS exact mass calcd for $(C_{19}H_{21}N_3O_2+Na)^+$ requires *m*/*z* 346.1526, found *m*/*z* 346.1506.

4.4.2. Catalyst **6b**

White solid; yield: 70%; $[\alpha]_D^{20}$ −42.1 (*c* 0.12, MeOH); mp 198.0–202.0 °C; ^{1}H NMR (600 MHz, DMSO): δ=2.71 and 2.83 (td, *J*=3.4, 11.8 Hz, 1H), 2.90 (s, 3H), 3.05 and 3.10 (dd, *J*=4.6, 12.7 Hz, 1H), 3.17 and 3.66 (td, *J*=3.6, 12.7 Hz, 1H), 3.54 and 3.58 (d, *J*=11.6 Hz, 1H), 3.82 and 4.20 (d, *J*=12.2 Hz, 1H), 4.12 and 4.26 (d, *J*=12.5 Hz, 1H), 4.74 and 5.01 (s, 1H), 7.10 (t, *J*=7.5 Hz, 1H), 7.34 (t, *J*=7.5 Hz, 2H), 7.56 and 7.60 (d, *J*=7.7 Hz, 2H), 8.18 and 8.23 (s, 1H), 10.01 and 10.05 (s, 1H); ^{13}C NMR (150 MHz, DMSO): δ=35.3, 43.3, 45.8, 47.0, 51.0, 120.4, 124.3, 129.2, 138.8, 163.4, 167.2; ESI HRMS exact mass calcd for $(C_{13}H_{17}N_3O_4S+Na)^+$ requires *m*/*z* 334.0832, found *m*/*z* 334.0835.

4.4.3. Catalyst **6c**

White solid; yield: 70%; $[\alpha]_D^{20}$ −62.0 (*c* 0.11, $CHCl_3$); mp 211.0–212.0 °C; ^{1}H NMR (600 MHz, $CDCl_3$/CD_3OD): δ=2.44–2.51 (m, 1H), 2.61 and 2.71 (dd, *J*=4.3, 12.5 Hz, 1H), 3.66 and 3.72 (d, *J*=11.5 Hz, 1H), 3.80–3.85 (m, 2H), 4.38–4.41 (m, 1H), 5.09 (s, 1H), 7.12–7.17 (m, 1H), 7.31–7.36 (m, 2H), 7.51–7.57 (m, 4H), 7.62–7.66 (m, 1H), 7.77 (d, *J*=7.6 Hz, 2H), 8.12 and 8.08 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$/CD_3OD): δ=37.7, 43.2, 45.6, 51.1, 120.5, 124.6, 127.4, 128.7, 129.2, 133.3, 135.5, 137.4, 162.8, 165.8; ESI HRMS exact mass calcd for $(C_{18}H_{19}N_3O_4S+Na)^+$ requires *m*/*z* 396.0988, found *m*/*z* 396.0972.

4.4.4. Catalyst **6d**

White solid; yield: 86%; $[\alpha]_D^{20}$ −61.2 (*c* 0.15, $CHCl_3$); mp 96.0–100.0 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=2.43 (s, 3H), 2.37–2.48 (m, 1H), 2.52 and 2.57 (dd, *J*=12.6, 3.7 Hz, 1H), 3.61 (m, 1H), 3.80 (d, *J*=9.0 Hz, 1H), 4.38 (m, 1H), 4.26 and 5.14 (s, 1H), 7.12 and 7.16 (t, *J*=7.4 Hz, 1H), 7.29–7.36 (m, 4H), 7.51 and 7.66 (d, *J*=7.6 Hz, 2H), 7.66 (d, *J*=7.4 Hz, 2H), 7.97 and 8.33 (s, 1H), 8.17 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=21.6, 37.7, 43.2, 45.8, 51.4, 120.2, 124.8, 127.8, 129.0, 130.0, 132.6, 137.2, 144.4, 162.3, 165.0; ESI HRMS exact mass calcd for $(C_{19}H_{21}N_3O_4S+Na)^+$ requires *m*/*z* 410.1145, found *m*/*z* 410.1139.

4.4.5. Catalyst **6e**

White solid; yield: 90%; $[\alpha]_D^{20}$ −48.0 (*c* 0.10, $CHCl_3$); mp 212.0–214.0 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.34 (s, 9H), 2.43 and 2.50 (td, *J*=3.1, 11.5 Hz, 1H), 2.54 and 2.60 (dd, *J*=3.7, 12.7 Hz, 1H), 3.61–3.64 (m, 1H), 3.80–3.84 (m, 1H), 4.39–4.43 (m, 2H), 4.27 and 5.16 (br s, 1H), 7.12 and 7.16 (d, *J*=7.3 Hz, 1H), 7.31 and 7.35 (d, *J*=7.9 Hz, 2H), 7.52–7.63 (m, 4H), 7.70 (d, *J*=8.3 Hz, 2H), 7.97 and 8.35 (s, 1H), 8.18 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$/CD_3OD): δ=30.9, 35.2, 37.7, 43.3, 45.7, 51.3, 57.1, 120.3, 124.7, 126.3, 127.5, 128.9, 129.0, 132.4, 137.4, 157.3, 162.6; ESI HRMS exact mass calcd for $(C_{22}H_{27}N_3O_4S+Na)^+$ requires *m*/*z* 452.1614, found *m*/*z* 452.1619.

4.4.6. Catalyst **6f**

White solid; yield: 91%; $[\alpha]_D^{20}$ −167.0 (*c* 0.10, $CHCl_3$); mp 79–81 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=2.34 (s, 3H), 2.68–2.73 (dt, *J*=3.3, 13.0 Hz, 1H), 3.22–3.25 (dd, *J*=4.4, 13.8 Hz, 1H), 3.33–3.38 (dt, *J*=3.4, 12.9 Hz, 1H), 3.63–3.65 (m, 1H), 4.58–4.60 (d, *J*=13.7 Hz, 1H), 4.72–4.74 (d, *J*=13.7 Hz, 1H), 5.09 (d, *J*=3.9 Hz, 1H), 7.14 (t, *J*=7.3 Hz, 1H), 7.30–7.64 (m, 4H), 8.02 (s, 1H), 8.30 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=21.3, 40.2, 43.6, 45.0, 51.9, 120.4, 124.9, 129.0, 137.1, 163.1, 166.1, 170.4; ESI HRMS exact mass calcd for $(C_{14}H_{17}N_3O_3+Na)^+$ requires *m*/*z* 298.1162, found *m*/*z* 298.1154.

4.4.7. Catalyst **6g**

White solid; yield: 78%; $[\alpha]_D^{20}$ −220.0 (*c* 0.10, $CHCl_3$); mp 33–35 °C; ^{1}H NMR (600 MHz, $CHCl_3$): δ=2.70–2.74 (dt, *J*=3.7, 12.5 Hz, 1H), 3.02–3.26 (m, 1H), 3.70–3.73 (m, 1H), 4.30–4.35 (m, 2H), 4.67–4.71 (m, 1H), 4.94–4.97 (m, 1H), 7.05–7.11 (m, 2H), 7.29–7.34 (m, 4H), 7.51–7.59 (m, 4H), 8.21 (s, 1H), 10.08 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=38.1, 43.2, 50.6, 52.1, 120.3, 124.7, 127.4, 128.6, 128.9, 130.2, 137.6, 163.0, 166.3, 171.7; ESI HRMS exact mass calcd for $(C_{19}H_{19}N_3O_3+Na)^+$ requires *m*/*z* 360.1319, found *m*/*z* 360.1318.

4.4.8. Catalyst **6h**

White solid; yield: 74%; $[\alpha]_D^{20}$ −43.0 (*c* 0.10, MeOH); mp 90–92 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.30 (s, 9H), 3.13–3.26 (m, 2H), 3.59–4.02 (m, 2H), 4.24–4.35 (m, 2H), 5.23 (m, 1H), 7.09–7.13 (t,

J=7.4 Hz, 1H), 7.26–7.48 (m, 8H), 8.26 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$):δ=30.1, 34.2, 43.1, 56.9, 124.0, 125.2, 126.5, 128.5, 163.6, 167.6, 172.0; ESI HRMS exact mass calcd for $(C_{23}H_{27}N_3O_3+Na)^+$ requires m/z 416.1945, found m/z 416.1947.

4.4.9. Catalyst ***9a***

White solid; yield: 67%; $[\alpha]_D^{20}$ −7.6 (c 0.9, MeOH); mp 187–189 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.47 (d, J=6.8 Hz, 3H), 2.25 (s, 3H), 2.58–2.63 (dt, J=3.3, 12.8 Hz, 1H), 2.93–3.12 (dt, J=3.5, 13.6 Hz, 1H), 3.13–3.16 (dd, J=4.4, 13.6 Hz, 1H), 3.49–3.52 (m, 1H), 4.56–4.58 (d, J=13.6 Hz, 1H), 4.63–4.65 (d, J=13.2 Hz, 1H), 4.96–4.98 (d, J=3.9 Hz, 1H), 5.04–5.14 (m, 1H), 6.28 (d, J=7.8 Hz, 1H), 7.20–7.36 (m, 5H), 8.19 (s, 1H); ^{13}C NMR (150 MHz, MeOD): δ=19.7, 41.3, 42.9, 46.2, 49.1, 51.8, 56.9, 125.6, 126.7, 128.2, 143.4, 163.8, 168.0, 170.7; ESI HRMS exact mass calcd for $(C_{16}H_{21}N_3O_3+Na)^+$ requires m/z 326.1475, found m/z 326.1480.

4.4.10. Catalyst ***9b***

White solid; yield: 73%; $[\alpha]_D^{20}$ −8.3 (c 0.1, MeOH); mp 182–184 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ=1.50 (d, J=6.9 Hz, 3H), 2.26 (s, 3H), 2.59–2.63 (dt, J=3.3, 12.9 Hz, 1H), 3.06–3.12 (dt, J=3.5, 12.9 Hz, 1H), 3.13–3.16 (dd, J=4.6, 13.7 Hz, 1H), 3.50 (d, J=11.9 Hz, 1H), 4.58 (d, J=13.6 Hz, 1H), 4.99 (d, J=4.1 Hz, 1H), 5.06–5.13 (m, 1H), 6.25 (d, J=7.1 Hz, 1H), 7.21–7.36 (m, 5H), 8.20 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=22.3, 41.4, 43.4, 47.1, 47.8, 56.2, 126.4, 127.1, 127.8, 144.6, 163.3, 168.7, 169.1; ESI HRMS exact mass calcd for $(C_{16}H_{21}N_3O_4+Na)^+$ requires m/z 326.1475, found m/z 326.1473.

4.4.11. Catalyst ***9c***

White solid; yield: 85%; $[\alpha]_D^{20}$ +51.4 (c 0.7, MeOH); mp 178–180 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.34 (s, 9H), 1.53–1.57 (dd, J=6.9, 8.2 Hz, 3H), 2.35–2.42 (dq, J=3.4, 9.0 Hz, 1H), 2.53 and 2.56 (dd, J=3.6, 12.4 Hz, 1H), 3.45–3.52 (m, 1H), 3.76 (t, J=10.8 Hz, 1H), 4.31 (d, J=12.5 Hz, 1H), 4.08 and 5.02 (s, 1H), 5.15 (q, J=7.4 Hz, 1H), 6.25 and 6.75 (d, J=7.7 Hz, 1H), 7.24–7.39 (m, 5H), 7.53–7.57 (m, 2H), 7.67 (d, J=7.5 Hz, 2H), 8.07 (d, J=2.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=22.7, 31.2, 35.4, 43.1, 46.2, 48.7, 50.2, 55.8, 126.6, 126.8, 127.2, 127.9, 128.7, 144.6, 156.9, 163.0 167.5; ESI HRMS exact mass calcd for $(C_{27}H_{27}N_3O_4+Na)^+$ requires m/z 480.1894, found m/z 480.1905.

4.4.12. Catalyst ***9d***

White solid; yield: 75%; $[\alpha]_D^{20}$ −31.3 (c 0.9, MeOH); mp 95–97 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.34 (s, 9H), 1.52–1.56 (dd, J=7.0, 16.8 Hz, 3H), 2.31–2.39 (m, 1H), 2.49–2.52 (dd, J=3.8, 12.4 Hz, 1H), 3.47–3.54 (m, 1H), 3.73–3.75 (d, J=11.3 Hz, 1H), 4.33–4.36 (q, J=7.4 Hz, 1H), 4.08 and 5.02 (d, J=2.5 Hz, 1H), 5.10–5.16 (m, 1H), 6.38 and 6.82 (d, J=7.7 Hz, 1H), 7.23–7.28 (m, 1H), 7.33–7.35 (q, J=4.5 Hz, 4H), 7.53–7.57 (q, J=8.6 Hz, 2H), 7.67 (d, J=7.5 Hz, 2H), 8.07 (d, J=2.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=21.9, 31.0, 35.2, 43.1, 46.0, 49.3, 50.1, 56.2, 126.1, 126.3, 127.6, 128.7, 132.4, 142.9, 157.4, 162.0, 165.9; ESI HRMS exact mass calcd for $(C_{27}H_{27}N_3O_4+Na)^+$ requires m/z 480.1894, found m/z 480.1915.

4.4.13. Catalyst ***9e***

White solid; yield: 75%; $[\alpha]_D^{20}$ +43 (c 0.8, MeOH); mp 110–112 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.35 (s, 9H), 1.46 (d, J=7.0 Hz, 1H), 2.51–2.51–2.53 (m, 1H), 3.10–3.28 (m, 2H), 3.60–3.80 (m, 2H), 4.17–4.18 (t, J=8.3 Hz, 1H), 4.95–5.10 (m, 2H), 7.22–7.36 (m, 7H), 7.50–7.52 (m, 2H), 8.17 (s, 1H); ^{13}C NMR (150 MHz, MeOD):δ=20.8, 30.2, 34.4, 43.0, 49.3, 51.4, 125.3, 125.7, 126.7, 128.1, 131.9, 163.5, 168.5, 171.9; ESI HRMS exact mass calcd for $(C_{25}H_{31}N_3O_3+Na)^+$ requires m/z 444.2258, found m/z 444.2265.

4.4.14. Catalyst ***9f***

White solid; yield: 75%; $[\alpha]_D^{20}$ +34 (c 0.9, MeOH); mp 78–90 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.44 (d, J=6.0 Hz, 3H), 1.49–1.52 (m, 1H), 1.64 (s, 1H), 3.16–3.20 (m, 2H), 3.41–3.44 (m, 1H), 4.11–4.14 (m, 1H), 5.06–5.29 (m, 2H), 7.26–7.49 (m, 9H), 8.17 (s, 1H); ^{13}C NMR (150 MHz, MeOD): δ=20.7, 42.9, 49.1, 51.4, 56.5, 125.7, 126.7, 128.2, 129.9, 133.5, 134.9, 135.9, 143.6, 163.5, 168.4; 171.6; ESI HRMS exact mass calcd for $(C_{21}H_{22}Cl_1N_3O_3+Na)^+$ requires m/z 422.1242, found m/z 422.1256.

4.4.15. Catalyst ***9g***

White solid; yield: 81%; $[\alpha]_D^{20}$ +45 (c 0.1, MeOH); mp 62–64 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.52 (d, J=4.6 Hz, 3H), 1.77–1.83 (m, 1H), 3.18–3.21 (q, J=3.7 Hz, 2H), 3.43 (m, 1H), 3.84 (m, 1H), 4.17 (m, 1H), 5.09–5.16 (m, 1H), 7.26–7.43 (m, 10H), 8.18 (s, 1H); ^{13}C NMR (150 MHz, MeOD): δ=22.4, 43.0, 48.8, 50.9, 126.4, 127.1, 128.7, 130.1, 136.0, 144.8, 163.0, 168.1, 170.0; ESI HRMS exact mass calcd for $(C_{21}H_{23}N_3O_3+Na)^+$ requires m/z 388.1632, found m/z 388.1629.

4.4.16. Catalyst ***9h***

White solid; yield: 60%; $[\alpha]_D^{20}$ +9.3 (c 0.9, MeOH); mp 179–181 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=0.90–0.89 (q, J=7.0 Hz, 3H), 1.30–1.33 (dd, J=6.6, 15.6 Hz, 3H), 2.26–2.30 (m, 1H), 2.65 (m, 1H), 2.85–3.08 (m, 1H), 3.25–3.27 (q, J=14.8 Hz, 2H), 3.78–3.84 (m, 1H), 3.92–4.05 (m, 1H), 4.25–4.32 (m, 1H), 4.35–4.44 (m, 1H), 4.66–4.71 (m, 1H), 4.81–4.89 (m, 1H), 7.20–7.26 (m, 5H), 8.21 (s, 1H); ^{13}C NMR (150 MHz, MeOD): δ=20.2, 25.3, 37.9, 43.1, 45.3, 49.3, 51.9, 56.9, 125.8, 126.8, 128.2, 143.4, 163.8, 168.0, 173.9; ESI HRMS exact mass calcd for $(C_{17}H_{23}N_3O_3+Na)^+$ requires m/z 340.1632, found m/z 340.1639.

4.4.17. Catalyst ***10a***

White solid; yield: 80%; $[\alpha]_D^{20}$ −36.0 (c 0.10, MeOH); mp 126.0–127.0 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.35 (s, 9H), 2.40–2.45 (m, 1H), 2.53 and 2.53 (dd, J=12.6, 3.8 Hz, 1H), 3.60–3.62 (m, 1H), 3.79 and 3.81 (s, 3H), 3.82–3.84 (m, 1H), 4.40 (d, J=12.4 Hz, 1H), 5.14 and 4.25 (s, 1H), 6.85 and 6.88 (d, J=8.8 Hz, 2H), 7.44 (d, J=8.8 Hz, 1H), 7.52–7.58 (m, 3H), 7.70 (d, J=8.4 Hz, 2H), 7.84 and 8.24 (s, 1H), 8.17 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=31.0, 35.3, 43.2, 45.4, 45.8, 51.3, 55.5, 114.2, 122.0, 126.4, 127.6, 130.3, 132.5, 157.3, 162.3, 164.8; ESI HRMS exact mass calcd for $(C_{23}H_{29}N_3O_5S+Na)^+$ requires m/z 482.1720, found m/z 482.1725.

4.4.18. Catalyst ***10b***

White solid; yield: 70%; $[\alpha]_D^{20}$ −42.7 (c 0.10, MeOH); mp 129.0–130.0 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.33 (s, 9H), 2.44–2.58 (m, 2H), 3.63–3.80 (m, 3H), 4.49–4.53 (m, 1H), 5.26 and 4.48 (s, 1H), 7.42–7.56 (m, 5H), 7.66–7.87 (m, 6H), 8.17 and 8.18 (s, 1H), 8.37 and 8.64 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=21.0, 31.0, 35.2, 43.2, 45.8, 45.8, 60.4, 120.9, 125.6, 126.1, 126.3, 126.5, 126.6, 127.7, 128.6, 131.9, 132.5, 134, 157.2, 162.5, 171.1; ESI HRMS exact mass calcd for $(C_{26}H_{29}N_3O_4S+Na)^+$ requires m/z 502.1771, found m/z 502.1759.

4.5. General procedure for the synthesis of catalysts 7 and 8

To a solution of **11** (10 g, 27.4 mmol) in DCM (70 mL) were added **14** (7.0 g, 32.9 mmol), DIEA (5.8 mL, 32.9 mmol), HOBt (4.8 g, 32.9 mmol), and EDCI (6.3 g, 32.9 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 12 h and then concentrated under reduced pressure. The residue was diluted with EtOAC (200 mL) and the solution was washed with saturated aqueous $NaHCO_3$ (40 mL), aqueous HCl (1.0 M, 20 mL), and brine (20 mL) and dried over anhydrous Na_2SO_4 After removal of solvents under reduced pressure, the residue was purified through column chromatography on silica gel (eluent: hexane/EtOAc=5/1) to give pure **15**.

Acetic anhydride (2 mL, 21.3 mmol) was added dropwise to a solution of **15** (4.3 mmol) in chloroform. The mixture was refluxed for 5 h and then concentrated under reduced pressure. The residue

was purified by column chromatography on silica gel (eluent: hexane/EtOAc=10/1) to give pure acetate **16**.

The rest of the procedures are similar to those for the synthesis of **6**, **9**, and **10** from intermediates **12**.

4.5.1. Catalyst ***7a***

White solid; yield: 81%; $[\alpha]_D^{20}$ +38.0 (*c* 0.10, MeOH); mp 116.0–118.0 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.35 and 1.36 (s, 9H), 2.03–2.06 (m, 1H), 2.159 and 2.164 (s, 3H), 2.24–2.48 (m, 3H), 3.40 and 4.10 (d, *J*=13.7 Hz, 1H), 3.72 and 3.73 (d, *J*=11.2 Hz, 1H), 3.94 and 4.98 (s, 1H), 4.20 (m, 1H), 5.46 and 5.54 (dd, *J*=8.3, 5.64 Hz and 8.64, 3.7 Hz, 1H), 6.08 and 6.16 (d, *J*=5.6, 3.6 Hz, 1H), 7.21–7.72 (m, 14H), 7.95 and 8.02 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=20.8, 31.0, 35.3, 42.5, 45.4, 50.6, 56.2, 58.3, 60.4, 125.9, 126.3, 126.6, 126.9, 127.0, 127.1, 127.7, 128.0, 128.2, 128.4, 128.6, 128.7, 131.3, 137.4, 157.9, 161.5, 166.4, 169.8; ESI HRMS exact mass calcd for $(C_{32}H_{37}N_3O_6S+Na)^+$ requires *m*/*z* 614.2295, found *m*/*z* 614.2291.

4.5.2. Catalyst ***7b***

White solid; yield: 86%; $[\alpha]_D^{20}$ +14.7 (*c* 0.10, MeOH); mp 105.0–107.0 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.35 and 1.36 (s, 9H), 2.09 and 2.13 (s, 3H), 2.20–2.54 (m, 2H), 3.00–3.01 (m, 1H), 3.39 and 4.18 (d, *J*=13.9 Hz, 1H), 3.68 (d, *J*=11.2 Hz, 1H), 4.24–4.30 (m, 1H), 4.91 and 4.05 (s, 1H), 5.42–5.46 (m, 1H), 6.10 and 6.17 (d, *J*=5.40 Hz, 1H), 7.11–7.18 (m, 4H), 7.28–7.35 (m, 6H), 7.52–7.69 (m, 4H), 8.0 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=21.0, 31.0, 35.2, 42.8, 44.8, 45.7, 50.9, 57.6, 60.4, 126.3, 126.4, 127.1, 127.6, 127.9, 128.2, 128.4, 128.5, 132.4, 136.8, 157.4, 162.0, 165.9, 170.7; ESI HRMS exact mass calcd for $(C_{32}H_{37}N_3O_6S+Na)^+$ requires *m*/*z* 614.2295, found *m*/*z* 614.2290.

4.5.3. Catalyst ***7c***

White solid; yield: 76%; $[\alpha]_D^{20}$ +43.8 (*c* 0.10, MeOH); mp 222.0–223.0 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.35 (s, 9H), 2.04 and 2.10 (s, 3H), 2.20–2.41 (m, 2H), 3.01–4.19 (m, 4H), 5.00 and 3.9 (s, 1H), 5.47–5.49 (m, 1H), 6.21 and 6.18 (d, *J*=6.7 Hz, 1H), 7.15–7.18 (m, 2H), 7.26–7.36 (m, 8H), 7.53–7.57 (m, 2H), 7.65–7.68 (m, 2H), 8.01 and 8.05 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=21.0, 31.1, 35.3, 36.7, 42.7, 45.2, 46.0, 50.7, 57.6, 126.4, 126.5, 127.3, 127.6, 127.8, 128.0, 128.2, 128.5, 131.6, 136.7, 157.6, 161.9, 166.0, 170.1; ESI HRMS exact mass calcd for $(C_{32}H_{37}N_3O_6S+Na)^+$ requires *m*/*z* 614.2295, found *m*/*z* 614.2301.

4.5.4. Catalyst ***8a***

White solid; yield: 87%; $[\alpha]_D^{20}$ −37.5 (*c* 0.8, MeOH); mp 101–103 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.97 (s, 3H), 2.12 (s, 3H), 2.64 (dt, *J*=3.1, 12.8 Hz, 1H), 3.14 (dd, *J*=4.7, 13.8 Hz, 1H), 3.22 (dt, *J*=3.6, 16.2 Hz, 1H), 3.63 (d, *J*=13.4 Hz, 1H), 4.40 (d, *J*=13.8 Hz, 1H), 4.63 (d, *J*=13.4 Hz, 1H), 4.90 (d, *J*=4.1 Hz, 1H), 5.23 (t, *J*=7.5 Hz, 1H), 5.30 (t, *J*=7.3 Hz, 1H), 6.00 and 6.08 (d, *J*=6.4 Hz, 1H), 7.00–7.29 (m, 10H), 8.31 and 8.2 (s, 1H); ^{13}C NMR (150 MHz, MeOD): δ=19.8, 41.3, 42.7, 45.8, 51.6, 56.6, 58.4, 77.3, 126.7, 127.1, 127.4, 128.0, 163.7, 168.9, 170.7; ESI HRMS exact mass calcd for $(C_{24}H_{27}N_3O_5+Na)^+$ requires *m*/*z* 460.1843, found *m*/*z* 460.1833.

4.5.5. Catalyst ***8b***

White solid; yield: 75%; $[\alpha]_D^{20}$ −46.2 (*c* 0.8, MeOH); mp 87–89 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=2.04 (s, 3H), 2.16 (s, 3H), 2.58 and 2.78 (dt, *J*=3.2, 13.0 Hz, 1H), 3.04–3.08 (dd, *J*=4.4, 13.7 Hz 1H), 3.12–3.15 (dd, *J*=4.6, 14.0 Hz, 1H), 3.38 (d, *J*=12.4 Hz, 1H), 4.39 (t, *J*=13.4 Hz, 1H) 4.60 (t, *J*=13.7 Hz, 1H), 4.80 (d, *J*=4.0 Hz, 1H), 5.30–5.34 (m, 1H), 6.01 (d, *J*=6.3 Hz, 1H), 6.86 (d, *J*=9.0 Hz, 1H), 7.11–7.35 (m, 10H), 8.5 (s, 1H); ^{13}C NMR (150 MHz, MeOD): δ=21.0, 38.5, 42.2, 44.0, 46.8, 52.7, 57.5, 77.7, 129.0, 129.5, 130.0, 164.9, 169.0, 171.2, 172.0; ESI HRMS exact mass calcd for $(C_{24}H_{27}N_3O_5+Na)^+$ requires *m*/*z* 460.1843, found *m*/*z* 460.1853.

4.5.6. Catalyst ***8c***

White solid; yield: 95%; $[\alpha]_D^{20}$ −75 (*c* 0.7, MeOH); mp 93–95 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ=2.04 (s, 3H), 2.16 (s, 3H), 2.60 and 2.75 (dt, *J*=9.5, 12.8 Hz, 1H), 2.97–3.01 (dt, *J*=3.2, 12.8 Hz, 1H), 3.12–3.15 (dd, *J*=4.6, 14.0 Hz, 1H), 3.46–3.49 (t, *J*=13.8 Hz, 1H), 3.63 (m, 1H), 4.39–4.60 (t, *J*=13.7 Hz, 2H), 5.30–5.34 (m, 1H), 6.08–6.16 (m, 1H), 6.90–7.16 (m, 5H), 7.24–7.33 (m, 5H), 8.15and 8.21 (s, 1H); ^{13}C NMR (600 MHz, MeOD): δ=19.8, 37.2, 41.0, 42.6, 45.7, 51.3, 57.7, 76.7, 127.1, 127.6, 127.9, 128.1, 163.4, 168.2, 170.0, 170.7; ESI HRMS exact mass calcd for $(C_{24}H_{27}N_3O_5+Na)^+$ requires *m*/*z* 460.1843, found *m*/*z* 460.1826.

Acknowledgements

We are grateful for financial supports from National Natural Science Foundation of China (Projects 20672107 and 20732006).

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