CCC-2014-2985

DATASET · JULY 2015

READS
18

4 AUTHORS, INCLUDING:

You-Qing Wang
Henan University
17 PUBLICATIONS **421** CITATIONS

SEE PROFILE

ChemPubSoc Europe

DOI: 10.1002/cctc.201402446

Organocatalysed Asymmetric Direct Mannich Reaction of Acetophenone Derivatives and Dibenzo[*b*,*f*][1,4]oxazepines with Azetidine-2-carboxylic Acid

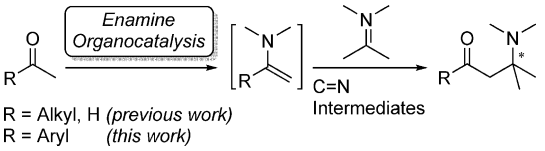
Yuan-Yuan Ren, You-Qing Wang,* Shuang Liu, and Kun Pan[a]

An enantioselective direct Mannich reaction of different acetophenone derivatives with various substituted seven-membered cyclic imines using (*S*)-azetidine-2-carboxylic acid as an organocatalyst is described, which provides an efficient access to optically active 11-substituted-10,11-dihydrodibenzo[*b*,*f*]-[1,4]oxazepine derivatives with 87–95% *ee*. For α,β-unsaturated ketone benzalacetone, the desired Mannich product was obtained with 72% *ee*. A plausible transition state is established to explain the observed absolute stereochemistry of the Mannich products. The reaction can also be performed on a gram scale with no adverse effects on the yield and enantioselectivity. Furthermore, some simple transformations involving the Wittig olefination and the decarboxylative reduction of the Mannich products were performed.

Introduction

The Mannich reaction proves to be one of the most versatile techniques for the formation of carbon–carbon bonds,[1] and an important aspect of the Mannich reaction is the construction of optically active β-amino carbonyl compounds in the presence of a chiral catalyst.[2] The search for finding other challenging and unexplored substrates for this reaction continues, with the goal of increasing the diversity of products and reaction types.

Since List, Barbas, and co-workers reported the proline-catalysed asymmetric direct Mannich reaction,[3] in the last decade much effort has been devoted to the development of the organocatalysed asymmetric direct Mannich reaction. In addition to the development of these reactions with secondary and primary amines via enamine formation,[4] significant progress has been made with chiral Brønsted base and acid organocatalysts.[2c,d,f] Among the reported non-functionalised carbonyl compounds used as Mannich donors in direct Mannich reactions, aliphatic ketones or aldehydes, such as acetone and acetaldehyde derivatives, are mainly used.[3,5] Although acetophenone derivatives are simple, cheap, and easily available chemicals used widely in organic synthesis, the use of acetophenone in the direct asymmetric Mannich reaction was limited.[6] In 2007, Gong et al.[7] and Rueping et al.[8] used, almost at the same time, acetophenone as a donor in the direct asymmetric Mannich reaction catalysed by chiral phosphoric acid catalysts. However, they investigated only two acetophenone derivatives as Mannich donors on evaluation of the substrate scope with moderate to good enantioselectivities (70–80%[7] and 34–86%[8] *ee*). Zhao et al. performed a three-component direct Mannich reaction of acetophenone and other non-functionalised aromatic ketones with 1,1,3,3-tetramethylguanidine as a base catalyst.[9] Subsequently, the same group also reported an asymmetric version of this reaction with the similar non-functionalised aromatic ketones and bifunctional cinchona alkaloid thioureas as the base catalyst, but without acetophenone.[10] As an alternative strategy, the decarboxylative Mannich reactions using aryl β-ketoacids as an enolate equivalent to acetophenone derivatives were reported.[11] Therefore, searching for a catalytic asymmetric direct Mannich reaction of acetophenone derivatives is challenging, and so far, only alkyl aldehydes or ketones have been used in the asymmetric Mannich reaction via enamine organocatalysis (Scheme 1).



Scheme 1. Mannich reaction of non-functionalised carbonyl compounds via enamine organocatalysis.

Cyclic imines have been used as electrophiles[12] in catalytic asymmetric Mannich reactions to afford the corresponding N-heterocycles with a stereogenic centre at the α position, most of which were however limited to six-membered ones.[13] Five-membered cyclic imines were also used in the asymmetric Mannich reaction catalysed by proline.[14] However, to our knowledge, seven-membered cyclic imines that were used as electrophiles in Mannich reactions have never been reported. On the basis of our previous research on the cycloaddition and Mannich reactions of six-membered cyclic imines,[15] we envisioned that the seven-membered cyclic imines dibenzo[*b*,*f*]-

[a] *Y.-Y. Ren, Dr. Y.-Q. Wang, S. Liu, K. Pan*
Provincial Key Laboratory of Natural Medicine and Immuno-Engineering
Henan University
Kaifeng 475004 (P.R. China)
E-mail: wyouqing@hotmail.com

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/cctc.201402446.

[1,4]oxazepines **1**[16] would be interesting substrates for the asymmetric Mannich reaction to afford the optically active 11-substituted-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepine derivatives, which play important roles in many physiologically active compounds.[17] Herein, we report the highly enantioselective direct Mannich reaction of **1** with acetophenone derivatives **2** via enamine organocatalysis (Scheme 1).

Results and Discussion

Because chiral phosphoric acid[7,8] and alkaloid thiourea base[10] catalysts had been used in the Mannich reaction of non-functionalised aromatic ketones, the initial studies of the Mannich reaction of imine **1a** with acetophenone **2a** focused on catalysts **C-1** and **C-2** (Figure 1) ; however, unsatisfactory results were obtained (Table 1, entries 1–4). With the (*S*)-proline catalyst system, the desired Mannich product **3aa** was obtained in 53% yield with 95% *ee*, even though some imine **1a** remained (entry 5). Then, the examination of solvents suggested that DMSO was the best solvent in terms of reactivity and enantioselectivity (entries 5–8). The effect of different amino acids and their derivatives as catalysts was also investigated (entries 9–14). The ring size of amino acids was found to play a key role, and the commercially available four-membered (*S*)-azetidine-2-carboxylic acid (**C-7**) significantly increased the reactivity to afford the product in 94% isolated yield with 93% *ee*; however, no reaction occurred with the six-membered (*S*)-pipecolinic acid (**C-8**; entry 14).

Subsequently, the substrate scope of the Mannich reaction was examined under optimal conditions. Various substituted acetophenone derivatives were investigated by using the electrophile **1a** (Table 2). The corresponding Mannich products were obtained in excellent yields with high enantioselectivities with different ketones containing either electron-donating or electron-withdrawing substituents at the *meta* and *para* positions. The *ortho*-substituted ketone **2g** gave low activity, probably owing to the steric effects. The heteroaryl ketone **2k** was also competent, and the corresponding product was obtained in excellent yield with high enantioselectivity (entry 11). Accordingly, this reaction was also applicable to α,β-unsaturated ketone **2l**, though decreased yield and enantioselectivity were observed compared with acetophenone derivatives (entry 12).

We then examined the scope of the unactivated seven-membered imines as shown in Scheme 2. Mannich reactions of various substituted dibenzo[*b*,*f*][1,4]oxazepines with acetophenone proceeded smoothly in the presence of **C-7** and yielded Mannich products **3aa**–**na** with high enantioselectivities, re-

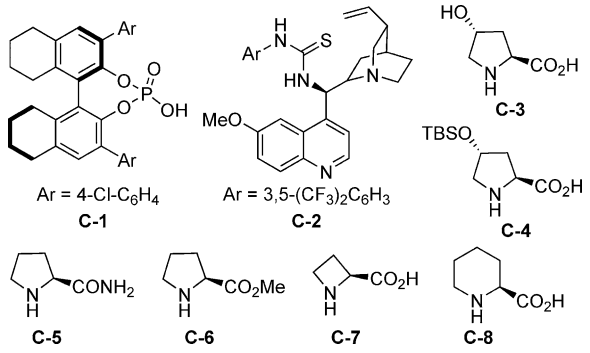
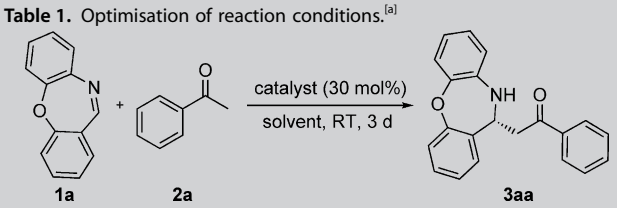


Figure 1. Catalysts screened for the Mannich reaction of imine **1a** with acetophenone **2a**. TBS = *tert*-Butyldimethylsilyl.

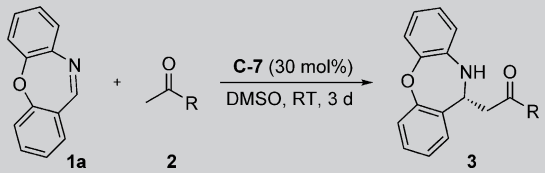
Table 1. Optimisation of reaction conditions.[a]



Entry	Catalyst	Solvent	Yield[b] [%]	*ee*[c] [%]
1	**C-1**	toluene	68	0
2	**C-1**	THF	17	0
3	**C-2**	toluene	0	–
4	**C-2**	THF	0	–
5	(*S*)-proline	DMSO	53	95
6	(*S*)-proline	DMF	10	96
7	(*S*)-proline	MeOH	60	4
8	(*S*)-proline	neat	2	83
9	**C-3**	DMSO	5	95
10	**C-4**	DMSO	76	90
11	**C-5**	DMSO	12	60
12	**C-6**	DMSO	29	79
13	**C-7**	DMSO	94	93
14	**C-8**	DMSO	0	–

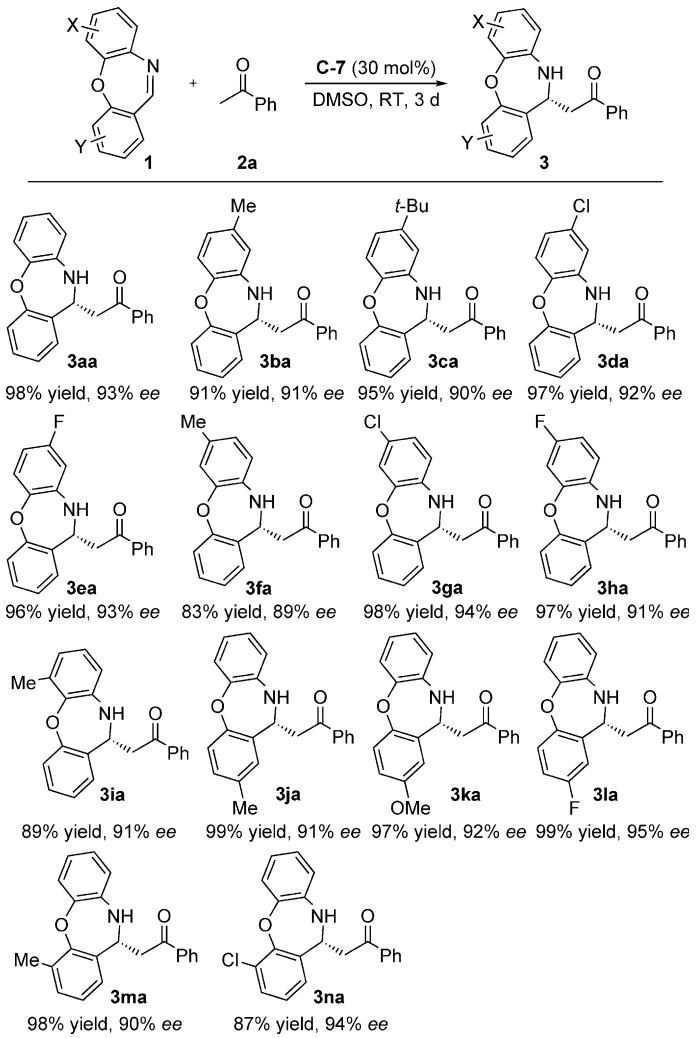
[a] Reaction conditions: 0.1 mmol of imine **1a**, 0.3 mmol of acetophenone, 0.2 mL of the solvent, and 10 mol% catalyst for entries 1–4 and 30 mol% catalyst for entries 5–14; [b] Isolated yield obtained with imine **1a**; [c] Determined from HPLC analysis with a chiral column.

Table 2. Mannich reaction of **1a** with different acetophenone derivatives **2**.[a]



Entry	**2**	R	**3**	Yield[b] [%]	*ee*[c] [%]
1	**2a**	Ph	**3aa**	98	93
2[d]	**2b**	*p*-MeO-C_6H_4	**3ab**	82	92
3	**2c**	*p*-Br-C_6H_4	**3ac**	97	91
4	**2d**	*p*-Cl-C_6H_4	**3ad**	97	90
5	**2e**	*p*-F-C_6H_4	**3ae**	91	90
6	**2f**	*p*-Me-C_6H_4	**3af**	90	93
7	**2g**	*o*-Me-C_6H_4	**3ag**	trace	–
8	**2h**	*m*-Me-C_6H_4	**3ah**	87	90
9	**2i**	3,4-Me_2-C_6H_3	**3ai**	95	90
10	**2j**	2-naphthyl	**3aj**	97	91
11	**2k**	3-thienyl	**3ak**	95	87
12	**2l**	(*E*)-CH=CHC_6H_5	**3al**	78	72

[a] Reaction conditions: 0.2 mmol of imine **1a**, 0.6 mmol of acetophenone, 0.06 mmol (30 mol%) of the catalyst, and 0.4 mL of dry DMSO; [b] Isolated yield obtained with imine **1a**; [c] Determined from HPLC analysis with a chiral column; [d] 4 days.



Scheme 2. Mannich reaction of imines **1** with acetophenone **2a**.

gardless of the position and electronic effect of the substituents on the two aryl rings of imines.

The absolute configuration of the Mannich product **3ah** was determined to be *R* from the single-crystal X-ray analysis of **3ah** (Figure 2),[18] which was recrystallised from dichloromethane and hexane. The absolute configurations of the other Mannich products were assigned by analogy on the basis of this analysis.

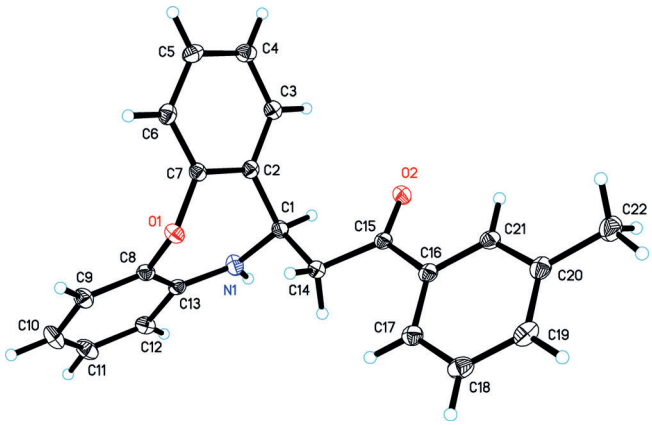


Figure 2. X-ray structure of the product **3ah**.

A transition state is proposed on the basis of the absolute configuration of Mannich products and enamine-based organocatalysis.[4] In the transition states, the *re*-face attack of the imine is favoured, probably owing to the hydrogen bonding interaction between nitrogen of the imine and carboxylic acid of the catalyst (Figure 3).

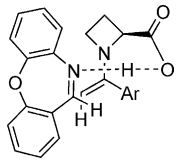
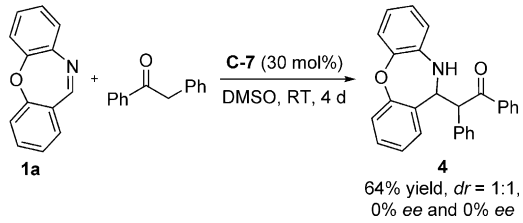


Figure 3. Transition state that gives the observed stereochemistry of the Mannich products.

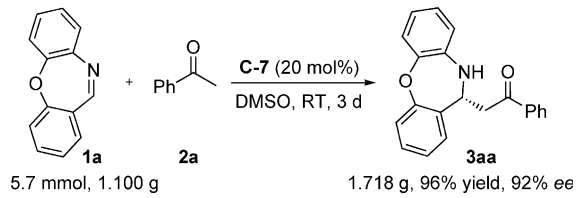
Once suitable conditions for the reaction of acetophenone and its derivatives were found, an α-substituted acetophenone was used as the Mannich donor. Under the established reaction conditions, 1,2-diphenylethanone underwent a Mannich reaction and furnished **4** in 64% yield, but with no diastereoselectivity and enantioselectivity (Scheme 3).

To further evaluate the practical use of the present catalytic system, the Mannich reaction was also performed on a gram scale (Scheme 4). The reaction proceeded smoothly with 20 mol% **C-7** to afford 1.718 g of the desired product **3aa** in 96% isolated yield with 92% *ee* after chromatographic purification.

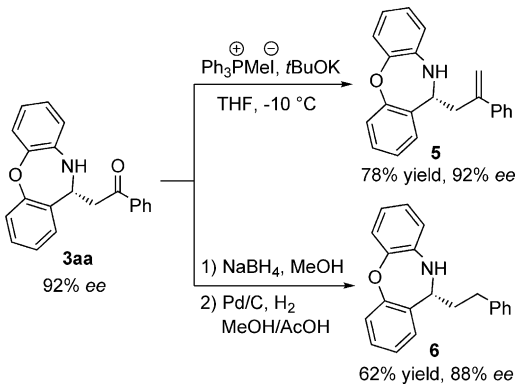
The carbonyl group in Mannich products **3** provides a convenient site for further modification. As indicated in Scheme 5, the Wittig reaction of **3aa** with methyltriphenylphosphonium iodide and *t*BuOK gave **5** in 78% yield, and the decarbonylative reduction of



Scheme 3. Mannich reaction of imines **1** with 1,2-diphenylethanone. *dr* = Diastereomeric ratio.



Scheme 4. Mannich reaction of imine **1a** with acetophenone **2a** at a gram scale.



Scheme 5. Transformation of the Mannich product **3aa**.

3aa afforded **6** in 62% yield but with slightly decreased enantioselectivity.

Conclusions

We have demonstrated the highly enantioselective direct Mannich reaction of acetophenone derivatives with dibenzo[*b*,*f*][1,4]oxazepine using commercially available four-membered (*S*)-azetidine-2-carboxylic acid as an organocatalyst, which affords optically active 11-substituted-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepine derivatives with up to 95% *ee*. This study reports the first enamine-based organocatalysis of acetophenone with secondary amine catalysts in the catalytic asymmetric Mannich reaction. This is also the first example of the asymmetric Mannich reaction using seven-membered imines as acceptors. The present study significantly extends the scope of the catalytic asymmetric Mannich reaction.

Experimental Section

General

All commercially available compounds were used as received without further purification unless otherwise noted. Compounds **2a** and **d**–**i** were purified by using column chromatography on silica gel before use. DMSO, DMF, and (*S*)-azetidine-2-carboxylic acid (**C-7**) were purchased from Acros and used as received without further purification. Other solvents were distilled from appropriate drying agents before use unless otherwise noted. The ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded in $CDCl_3$ on Bruker DRX-400 spectrometers with tetramethylsilane as an internal standard. Enantiomeric excess was determined from HPLC analysis with a chiral column (see below for details). Optical rotations were measured with a polarimeter. Flash column chromatography was performed on silica gel (200–300 mesh). All reactions were monitored by using TLC or NMR spectroscopy.

Experimental methods and characterisation data for seven-membered cyclic imines **1**, copies of ^{1}H and ^{13}C NMR spectra of all compounds, and HPLC chromatograms are given in the Supporting Information.

Catalytic asymmetric Mannich reaction

General procedure: Aromatic ketone (0.6 mmol) was added to the mixture of imine (0.2 mmol), (*S*)-azetidine-2-carboxylic acid (30 mol%, 0.06 mmol), and DMSO (0.4 mL). This reaction mixture was stirred at RT for the time shown in Table 2 and Schemes 2–4. Direct purification of the reaction mixture by using column chromatography on silica gel (petroleum ether/EtOAc 40:1–5:1) gave the desired Mannich adducts. Racemic Mannich adducts were obtained from racemic proline.

(*R*)-2-(10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-phenylethanone (**3aa**): Pale yellow oil; yield 98% (61.8 mg); R_f = 0.50 (petroleum ether/EtOAc 5:1); 93% *ee*; $[\alpha]_D^{20} = +74.5$ (c = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, J = 7.6 Hz, 2H), 7.50 (t, J = 7.3 Hz, 1H), 7.38 (t, J = 7.6 Hz, 2H), 7.30--7.13 (m, 3H), 7.06 (dd, J = 17.6, 7.8 Hz, 2H), 6.80 (t, J = 7.4 Hz, 1H), 6.65 (t, J = 7.4 Hz, 1H), 6.52 (d, J = 7.8 Hz, 1H), 4.94 (d, J = 8.7 Hz, 1H), 4.61 (s, 1H), 4.10 (dd, J = 18.0, 9.6 Hz, 1H), 3.44 ppm (dd, J = 18.0, 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.0, 157.1, 143.7, 137.1, 136.7, 133.3, 132.6, 129.2, 128.5, 128.3, 128.0, 124.7, 124.3, 121.7, 121.2, 119.0, 119.0, 54.5, 44.2 ppm; HRMS (ESI): m/z: calcd for $C_{21}H_{18}NO_2$: 316.1332 $[M+H]^+$; found: 316.1328; HPLC (Chiralcel IA column, hexane/*i*PrOH 85:15, 0.8 mL min^{-1}, 254 nm): t_1 = 13.8 min, t_2 = 16.6 min (major, *R*).

(*R*)-2-(10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-(4-methoxyphenyl)ethanone (**3ab**): Pale yellow oil; yield 82% (56.7 mg; R_f = 0.10 (petroleum ether/EtOAc 10:1); 92% *ee*; $[\alpha]_D^{20} = +80.2$ (c = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, J = 8.8 Hz, 2H), 7.31--7.12 (m, 3H), 7.06 (dd, J = 16.7, 7.8 Hz, 2H), 6.90--6.73 (m, 3H), 6.64 (t, J = 7.5 Hz, 1H), 6.52 (d, J = 7.9 Hz, 1H), 4.94 (dd, J = 9.5, 3.0 Hz, 1H), 4.64 (s, 1H), 4.04 (dt, J = 23.5, 11.7 Hz, 1H), 3.80 (s, 3H), 3.38 ppm (dd, J = 17.7, 3.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.5, 163.6, 157.1, 143.6, 137.2, 132.6, 130.3, 129.7, 129.1, 128.3, 124.6, 124.3, 121.6, 121.2, 119.0, 118.9, 113.7, 55.4, 54.5, 43.7 ppm; HRMS (ESI): m/z: calcd for $C_{22}H_{20}NO_3$: 346.1438 $[M+H]^+$; found: 346.1410; HPLC (Chiralcel IA column, hexane/*i*PrOH 80:20, 0.8 mL min^{-1}, 254 nm): t_1 = 19.2 min, t_2 = 22.5 min (major, *R*).

(*R*)-1-(4-bromophenyl)-2-(10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)ethanone (**3ac**): Pale yellow oil; yield 97% (76.7 mg); R_f = 0.35 (petroleum ether/EtOAc 10:1); 91% *ee*; $[\alpha]_D^{20} = +68.4$ (c = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.4 Hz, 2H), 7.28--7.14 (m, 3H), 7.06 (dd, J = 17.0, 8.2 Hz, 2H), 6.80 (t, J = 7.5 Hz, 1H), 6.65 (t, J = 7.5 Hz, 1H), 6.51 (d, J = 7.9 Hz, 1H), 4.90 (dd, J = 9.4, 3.3 Hz, 1H), 4.57 (s, 1H), 4.07 (dd, J = 17.9, 9.5 Hz, 1H), 3.40 ppm (dd, J = 17.9, 3.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.0, 157.1, 143.6, 137.0, 135.4, 132.4, 131.8, 129.5, 129.3, 128.5, 128.3, 124.7, 124.4, 121.7, 121.2, 119.1, 118.9, 54.4, 44.2 ppm; HRMS (ESI): m/z: calcd for $C_{21}H_{17}BrNO_2$: 394.0437 $[M+H]^+$; found: 394.0421; HPLC (Chiralcel AD-H column, hexane/*i*PrOH 85:15, 1.0 mL min^{-1}, 254 nm): t_1 = 16.6 min, t_2 = 19.3 min (major, *R*).

(*R*)-1-(4-Chlorophenyl)-2-(10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)ethanone (**3ad**): Pale yellow oil; yield 97% (68.2 mg); R_f = 0.27 (petroleum ether/EtOAc 10:1); 90% *ee*; $[\alpha]_D^{20} = +75.1$ (c = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, J = 8.5 Hz, 2H), 7.33 (d, J = 8.5 Hz, 2H), 7.29--7.21 (m, 1H), 7.18 (d, J = 7.8 Hz, 2H), 7.07 (dt, J = 14.8, 7.7 Hz, 2H), 6.80 (t, J = 7.6 Hz, 1H), 6.65 (t, J = 7.6 Hz, 1H), 6.50 (d, J = 7.9 Hz, 1H), 4.89 (dd, J = 9.4, 3.3 Hz, 1H), 4.59 (s, 1H), 4.07 (dd, J = 18.0, 9.5 Hz, 1H), 3.39 ppm (dd, J = 18.0, 3.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.8, 157.1, 143.5, 139.7, 137.0, 134.9, 132.4, 129.4, 129.3, 128.8, 128.3, 124.7, 124.4, 121.7, 121.2, 119.0, 118.8, 54.4, 44.2 ppm; HRMS (ESI): m/z: calcd for

$C_{21}H_{17}ClNO_2$: 350.0942 $[M+H]^+$; found: 350.0937; HPLC (Chiralcel AD-H column, hexane/*i*PrOH 80:20, 0.8 mL min^{-1}, 254 nm): t_1 = 17.0 min, t_2 = 19.1 min (major, *R*).

(*R*)-2-(10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-(4-fluorophenyl)ethanone (**3 ae**): Yellow solid; yield 91% (60.4 mg; R_f = 0.25 (petroleum ether/EtOAc 10:1); m.p. 87–88 °C (petroleum ether/EtOAc); 90% *ee*; $[\alpha]_D^{20}$ = +76.5 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98--7.85 (m, 2H), 7.29--7.13 (m, 3H), 7.13--6.96 (m, 4H), 6.80 (td, *J* = 7.9, 1.3 Hz, 1H), 6.71--6.60 (m, 1H), 6.51 (dd, *J* = 7.9, 1.3 Hz, 1H), 4.91 (dd, *J* = 9.5, 3.5 Hz, 1H), 4.59 (s, 1H), 4.07 (dd, *J* = 17.8, 9.5 Hz, 1H), 3.41 ppm (dd, *J* = 17.8, 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.4, 165.8 (d, $^1J_{C-F}$ = 255.3 Hz), 157.1, 143.6, 137.1, 133.1 (d, $^4J_{C-F}$ = 3.0 Hz), 132.5, 130.7 (d, $^3J_{C-F}$ = 9.4 Hz), 129.3, 128.3, 124.7, 124.2, 121.7, 121.2, 119.0, 118.9, 115.6 (d, $^2J_{C-F}$ = 21.9 Hz), 54.5, 44.2 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −104.4 ppm; HRMS (ESI): *m*/*z*: calcd for $C_{21}H_{17}FNO_2$: 334.1238 $[M+H]^+$; found: 334.1234; HPLC (Chiralcel AD-H column, hexane/*i*PrOH 80:20, 1.0 mL min^{-1}, 254 nm): t_1 = 13.4 min, t_2 = 14.5 min (major, *R*).

(*R*)-2-(10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-p-tolylethanone (**3 af**): Pale yellow oil; yield 90% (59.0 mg); R_f = 0.27 (petroleum ether/EtOAc 10:1); 93% *ee*; $[\alpha]_D^{20}$ = +80.5 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 8.1 Hz, 2H), 7.29--7.22 (m, 1H), 7.21--7.13 (m, 4H), 7.06 (dd, *J* = 17.3, 7.5 Hz, 2H), 6.80 (t, *J* = 7.5 Hz, 1H), 6.64 (t, *J* = 7.5 Hz, 1H), 6.52 (d, *J* = 7.9 Hz, 1H), 4.94 (dd, *J* = 9.7, 3.1 Hz, 1H), 4.64 (s, 1H), 4.08 (dd, *J* = 18.0, 9.7 Hz, 1H), 3.40 (dd, *J* = 17.9, 3.2 Hz, 1H), 2.35 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.6, 157.1, 144.2, 143.6, 137.1, 134.1, 132.6, 129.2, 129.1, 128.3, 128.1, 124.6, 124.3, 121.6, 121.2, 119.0, 118.9, 54.4, 44.0, 21.6 ppm; HRMS (ESI): *m*/*z*: calcd for $C_{22}H_{20}NO_2$: 330.1489 $[M+H]^+$; found: 330.1482; HPLC (Chiralcel IA column, hexane/*i*PrOH 80:20, 0.8 mL min^{-1}, 254 nm): t_1 = 13.4 min, t_2 = 15.2 min (major, *R*).

(*R*)-2-(10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1 m-tolylethanone (**3 ah**): White solid; yield 87% (57.0 mg); R_f = 0.32 (petroleum ether/EtOAc 10:1); m.p. 151–153 °C (dichloromethane/hexane); 90% *ee*; $[\alpha]_D^{20}$ = +69.9 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 7.6 Hz, 2H), 7.34--7.18 (m, 5H), 7.14--7.00 (m, 2H), 6.81 (td, *J* = 7.9, 1.4 Hz, 1H), 6.65 (td, *J* = 7.9, 1.4 Hz, 1H), 6.53 (dd, *J* = 7.9, 1.4 Hz, 1H), 4.94 (dd, *J* = 9.5, 2.5 Hz, 1H), 4.60 (s, 1H), 4.11 (dd, *J* = 17.9, 9.7 Hz, 1H), 3.42 (dd, *J* = 17.9, 3.4 Hz, 1H), 2.35 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.3, 157.1, 143.7, 138.4, 137.1, 136.7, 134.1, 132.7, 129.2, 128.6, 128.5, 128.3, 125.3, 124.7, 124.3, 121.7, 121.2, 119.0, 119.0, 54.5, 44.3, 21.2 ppm; HRMS (ESI): *m*/*z*: calcd for $C_{22}H_{20}NO_2$: 330.1489 $[M+H]^+$; found: 330.1483; HPLC (Chiralcel AD-H column, hexane/*i*PrOH 85:15, 1.0 mL min^{-1}, 254 nm): t_1 = 11.6 min, t_2 = 13.3 min (major, *R*).

(*R*)-2-(10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-(3,4-dimethylphenyl)ethanone (**3 ai**): Pale yellow oil; yield 95% (65.6 mg); R_f = 0.27 (petroleum ether/EtOAc 10:1); 90% *ee*; $[\alpha]_D^{20}$ = +72.4 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71--7.58 (m, 2H), 7.29--7.22 (m, 1H), 7.20--7.00 (m, 5H), 6.80 (t, *J* = 7.4 Hz, 1H), 6.64 (t, *J* = 7.4 Hz, 1H), 6.52 (d, *J* = 7.7 Hz, 1H), 4.93 (d, *J* = 9.3 Hz, 1H), 4.63 (s, 1H), 4.09 (dd, *J* = 17.8, 9.8 Hz, 1H), 3.39 (d, *J* = 17.8 Hz, 1H), 2.25 ppm (d, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.9, 157.1, 143.7, 142.9, 137.2, 136.9, 134.6, 132.6, 129.8, 129.2, 129.1, 128.3, 125.7, 124.6, 124.3, 121.6, 121.2, 119.0, 118.9, 54.5, 44.0, 19.9, 19.6 ppm; HRMS (ESI): *m*/*z*: calcd for $C_{23}H_{22}NO_2$: 344.1645 $[M+H]^+$; found: 344.1635; HPLC (Chiralcel AD-H column, hexane/*i*PrOH 85:15, 1.0 mL min^{-1}, 254 nm): t_1 = 13.1 min, t_2 = 15.8 min (major, *R*).

(*R*)-2-(10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-(naphthalen-2-yl)ethanone (**3 aj**): Yellow solid; yield 97% (71.0 mg); R_f = 0.30 (petroleum ether/EtOAc 10:1); m.p. 140–141 °C (petroleum ether/EtOAc); 91% *ee*; $[\alpha]_D^{20}$ = +46.9 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.35 (s, 1H), 7.95 (d, *J* = 8.6 Hz, 1H), 7.79 (t, *J* = 9.4 Hz, 3H), 7.49 (dt, *J* = 14.6, 7.0 Hz, 2H), 7.29--7.17 (m, 3H), 7.16--7.00 (m, 2H), 6.79 (t, *J* = 7.3 Hz, 1H), 6.65 (t, *J* = 7.2 Hz, 1H), 6.52 (d, *J* = 7.6 Hz, 1H), 4.98 (d, *J* = 8.8 Hz, 1H), 4.65 (s, 1H), 4.24 (dd, *J* = 17.7, 9.6 Hz, 1H), 3.54 ppm (dd, *J* = 17.8, 3.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.9, 157.1, 143.7, 137.1, 135.6, 134.0, 132.7, 132.4, 130.0, 129.5, 129.2, 128.5, 128.4, 128.3, 127.7, 126.7, 124.7, 124.3, 123.5, 121.7, 121.2, 119.0, 119.0, 54.7, 44.3 ppm; HRMS (ESI): *m*/*z*: calcd for $C_{25}H_{20}NO_2$: 366.1489 $[M+H]+$; found: 366.1471; HPLC (Chiralcel AD-H column, hexane/*i*PrOH 80:20, 0.8 mL min^{-1}, 254 nm): t_1 = 21.0 min, t_2 = 30.1 min (major, *R*).

(*R*)-2-(10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-(thiophen-3-yl)ethanone (**3 ak**): Yellow solid; yield 95% (61.4 mg; R_f = 0.23 (petroleum ether/EtOAc 10:1); m.p. 79–80 °C (petroleum ether/EtOAc); 87% *ee*; $[\alpha]_D^{20}$ = +62.4 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 1.8 Hz, 1H), 7.48 (dd, *J* = 5.1, 0.8 Hz, 1H), 7.29--7.13 (m, 4H), 7.13--6.99 (m, 2H), 6.86--6.75 (m, 1H), 6.70--6.60 (m, 1H), 6.51 (dd, *J* = 7.9, 1.2 Hz, 1H), 4.90 (dd, *J* = 9.5, 3.4 Hz, 1H), 4.57 (s, 1H), 3.99 (dd, *J* = 17.5, 9.6 Hz, 1H), 3.36 ppm (dd, *J* = 17.5, 3.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.2, 157.1, 143.6, 142.1, 137.1, 132.5, 132.5, 129.2, 128.2, 126.6, 126.4, 124.7, 124.3, 121.7, 121.2, 119.0, 118.9, 54.5, 45.4 ppm; HRMS (ESI): *m*/*z*: calcd for $C_{19}H_{16}NO_2S$: 322.0896 $[M+H]^+$; found: 322.0890; HPLC (Chiralcel AD-H column, hexane/*i*PrOH 85:15, 1.0 mL min^{-1}, 254 nm): t_1 = 19.0 min, t_2 = 20.5 min (major, *R*).

(*R*,*E*)-1-(10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-4-phenylbut-3-en-2-one (**3 al**): Yellow oil; yield 78% (53.0 mg); R_f = 0.18 (petroleum ether/EtOAc 10:1); 72% *ee*; $[\alpha]_D^{20}$ = +64.2 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58--7.41 (m, 3H), 7.41--7.30 (m, 3H), 7.29--7.24 (m, 1H), 7.23--7.14 (m, 2H), 7.14--7.00 (m, 2H), 6.83 (t, *J* = 7.5 Hz, 1H), 6.67 (dd, *J* = 15.5, 7.4 Hz, 2H), 6.54 (d, *J* = 7.9 Hz, 1H), 4.87 (dd, *J* = 9.6, 3.4 Hz, 1H), 4.54 (s, 1H), 3.82 (dd, *J* = 17.4, 9.8 Hz, 1H), 3.17 ppm (dd, *J* = 17.4, 3.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.0, 157.1, 143.8, 143.4, 137.1, 134.3, 132.6, 130.6, 129.2, 128.9, 128.3, 128.2, 126.4, 124.7, 124.3, 121.7, 121.2, 119.1, 119.1, 54.5, 45.9 ppm; HRMS (ESI): *m*/*z*: calcd for $C_{23}H_{19}NNaO_2$: 364.1308 $[M+Na]^+$; found: 364.1293; HPLC (Chiralcel AD-H column, hexane/*i*PrOH 85:15, 1.0 mL min^{-1}, 254 nm): t_1 = 16.3 min, t_2 = 21.1 min (major, *R*).

(*R*)-2-(8-methyl-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-phenylethanone (**3 ba**): Pale yellow oil; yield 91% (59.8 mg); R_f = 0.36 (petroleum ether/EtOAc 10:1); 91% *ee*; $[\alpha]_D^{20}$ = +55.3 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 7.4 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 2H), 7.28--7.13 (m, 3H), 7.04 (td, *J* = 7.4, 1.2 Hz, 1H), 6.97 (d, *J* = 8.1 Hz, 1H), 6.44 (dd, *J* = 8.1, 1.4 Hz, 1H), 6.33 (s, 1H), 4.92 (dd, *J* = 9.6, 3.4 Hz, 1H), 4.55 (s, 1H), 4.11 (dd, *J* = 18.0, 9.6 Hz, 1H), 3.42 (dd, *J* = 18.0, 3.4 Hz, 1H), 2.11 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.1, 157.3, 141.7, 136.7, 136.6, 134.2, 133.3, 132.6, 129.2, 128.5, 128.3, 128.0, 124.2, 121.4, 121.1, 119.7, 119.3, 54.4, 44.2, 20.5 ppm; HRMS (ESI): *m*/*z*: calcd for $C_{22}H_{20}NO_2$: 330.1489 $[M+H]^+$; found: 330.1485; HPLC (Chiralcel IA column, hexane/*i*PrOH 85:15, 0.8 mL min^{-1}, 254 nm): t_1 = 12.7 min, t_2 = 13.6 min (major, *R*).

(*R*)-2-(8-tert-butyl-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-phenylethanone (**3 ca**): Pale yellow oil; yield 95% (73.8 mg); R_f = 0.43 (petroleum ether/EtOAc 10:1); 90% *ee*; $[\alpha]_D^{20}$ = +27.9 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00--7.85 (m, 2H), 7.50 (dd, *J* = 10.5, 4.2 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 2H), 7.27--7.23 (m, 1H), 7.22--7.13 (m, 2H), 7.10--6.95 (m, 2H), 6.68 (dd, *J* = 8.4, 2.3 Hz, 1H),

6.53 (d, $J=2.3$ Hz, 1H), 4.95 (d, $J=7.3$ Hz, 1H), 4.58 (s, 1H), 4.23--4.00 (m, 1H), 3.43 (dd, $J=18.0$, 3.5 Hz, 1H), 1.17 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=199.2$, 157.3, 147.7, 141.6, 136.7, 136.2, 133.3, 132.6, 129.2, 128.5, 128.3, 128.0, 124.2, 121.2, 121.1, 116.3, 116.1, 54.5, 44.3, 34.0, 31.2 ppm; HRMS (ESI): *m/z*: calcd for $C_{25}H_{26}NO_2$: 372.1958 $[M+H]^+$; found: 372.1986; HPLC (Chiralcel IA column, hexane/*i*PrOH 90:10, 0.7 mL min^{-1}, 254 nm): $t_1=11.5$ min, $t_2=12.2$ min (major, *R*).

(*R*)-2-(8-chloro-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-phenylethanone (**3 da**): Yellow solid; yield 97% (68.0 mg); $R_f=0.14$ (petroleum ether/EtOAc=20:1); m.p. 225–226 °C (petroleum ether/EtOAc); 92% *ee*; $[\alpha]_D^{20}=+30.6$ ($c=1.0$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.91$ (d, $J=7.5$ Hz, 2H), 7.52 (t, $J=7.4$ Hz, 1H), 7.40 (t, $J=7.7$ Hz, 2H), 7.32--7.13 (m, 3H), 7.08 (t, $J=7.3$ Hz, 1H), 6.99 (d, $J=8.5$ Hz, 1H), 6.56 (dd, $J=8.5$, 2.3 Hz, 1H), 6.49 (d, $J=2.3$ Hz, 1H), 4.93 (d, $J=9.3$ Hz, 1H), 4.69 (s, 1H), 4.13 (dd, $J=18.0$, 9.7 Hz, 1H), 3.44 ppm (dd, $J=18.0$, 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=$ 198.8, 157.0, 142.0, 138.4, 136.6, 133.4, 132.5, 129.5, 129.5, 128.6, 128.3, 128.1, 124.7, 122.8, 121.1, 118.3, 117.9, 54.2, 44.3 ppm; HRMS (ESI): *m/z*: calcd for $C_{21}H_{17}ClNO_2$: 350.0942 $[M+H]^+$; found: 350.0941; HPLC (Chiralcel AD-H column, hexane/*i*PrOH 80:20, 0.8 mL min^{-1}, 254 nm): $t_1=15.7$ min (major, *R*), $t_2=16.8$ min.

(*R*)-2-(8-fluoro-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-phenylethanone (**3 ea**): Pale yellow oil; yield 96% (64.0 mg); $R_f=0.17$ (petroleum ether/EtOAc 20:1); 93% *ee*; $[\alpha]_D^{20}=+92.4$ ($c=1.0$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.92$ (d, $J=7.3$ Hz, 2H), 7.52 (t, $J=7.4$ Hz, 1H), 7.40 (t, $J=7.7$ Hz, 2H), 7.31--7.14 (m, 3H), 7.08 (td, $J=7.4$, 0.9 Hz, 1H), 7.01 (dd, $J=8.8$, 5.7 Hz, 1H), 6.35--6.25 (m, 1H), 6.21 (dd, $J=10.2$, 2.9 Hz, 1H), 5.08--4.85 (m, 1H), 4.70 (d, $J=4.6$ Hz, 1H), 4.17 (dd, $J=18.0$, 9.7 Hz, 1H), 3.44 ppm (dd, $J=18.0$, 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=198.9$, 159.7 (d, $^1J_{C-F}=$ 240.5 Hz), 157.3, 139.6 (d, $^4J_{C-F}=2.3$ Hz), 138.5 (d, $^3J_{C-F}=10.9$ Hz), 136.6, 133.4, 132.6, 129.5, 128.6, 128.3, 128.1, 124.7, 122.5 (d, $^3J_{C-F}=$ 10.2 Hz), 121.1, 104.7 (d, $^2J_{C-F}=15.2$ Hz), 104.5 (d, $^2J_{C-F}=18.3$ Hz), 54.1, 44.4 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-118.91$ ppm; HRMS (ESI): *m/z*: calcd for $C_{21}H_{17}FNO_2$: 334.1238 $[M+H]^+$; found: 334.1235; HPLC (Chiralcel IA column, hexane/*i*PrOH 85:15, 0.8 mL min^{-1}, 254 nm): $t_1=15.5$ min, $t_2=18.5$ min (major, *R*).

(*R*)-2-(7-methyl-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-phenylethanone (**3 fa**): Pale yellow oil; yield 83% (59.9 mg); $R_f=0.32$ (petroleum ether/EtOAc 10:1); 89% *ee*; $[\alpha]_D^{20}=+49.4$ ($c=1.0$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.92$--7.83 (m, 2H), 7.47 (d, $J=7.4$ Hz, 1H), 7.36 (t, $J=7.7$ Hz, 2H), 7.22 (d, $J=7.7$ Hz, 1H), 7.17 (dd, $J=5.6$, 1.5 Hz, 2H), 7.04 (dd, $J=7.4$, 1.1 Hz, 1H), 6.92 (d, $J=1.1$ Hz, 1H), 6.61 (dd, $J=8.0$, 1.3 Hz, 1H), 6.43 (d, $J=8.0$ Hz, 1H), 4.91 (dd, $J=9.6$, 3.4 Hz, 1H), 4.50 (s, 1H), 4.03 (dd, $J=18.0$, 9.6 Hz, 1H), 3.41 (dd, $J=18.0$, 3.5 Hz, 1H), 2.18 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=199.0$, 157.0, 143.8, 136.7, 134.3, 133.2, 132.5, 129.0, 128.5, 128.4, 128.0, 125.1, 124.1, 121.9, 121.1, 119.2, 54.6, 44.0, 20.1 ppm; HRMS (ESI): *m/z*: calcd for $C_{22}H_{20}ClNO_2$: 330.1489 $[M+H]^+$; found: 330.1484; HPLC (Chiralcel IA column, hexane/*i*PrOH 85:15, 0.8 mL min^{-1}, 254 nm): $t_1=14.5$ min, $t_2=16.5$ min (major, *R*).

(*R*)-2-(7-chloro-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-phenylethanone (**3 ga**): Yellow solid; yield 98% (68.7 mg); $R_f=0.21$ (petroleum ether/EtOAc 10:1); m.p. 97–98 °C (petroleum ether/EtOAc); 94% *ee*; $[\alpha]_D^{20}=+39.9$ ($c=1.0$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.96$--7.83 (m, 2H), 7.52 (t, $J=7.4$ Hz, 1H), 7.40 (t, $J=7.7$ Hz, 2H), 7.26 (tt, $J=8.8$, 4.4 Hz, 1H), 7.19 (dd, $J=13.3$, 4.9 Hz, 2H), 7.14--7.03 (m, 2H), 6.76 (dd, $J=8.6$, 2.3 Hz, 1H), 6.43 (d, $J=8.6$ Hz, 1H), 4.92 (d, $J=8.8$ Hz, 1H), 4.65 (s, 1H), 4.24--3.95 (m, 1H), 3.41 ppm (dd, $J=18.1$, 3.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=$ 198.8, 156.7, 143.7, 136.5, 135.9, 133.4, 132.4, 129.4, 128.6, 128.3, 128.0, 124.7, 124.5, 122.8, 121.7, 121.2, 119.5, 54.3, 44.0 ppm; HRMS (ESI): *m/z*: calcd for $C_{21}H_{17}ClNO_2$: 350.0942 $[M+H]^+$; found: 350.0934; HPLC (Chiralcel IA column, hexane/*i*PrOH 85:15, 0.8 mL min^{-1}, 254 nm): $t_1=14.8$ min, $t_2=19.8$ min (major, *R*).

(*R*)-2-(7-fluoro-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-phenylethanone (**3 ha**): Pale yellow oil; yield 97% (65.0 mg); $R_f=0.20$ (petroleum ether/EtOAc 10:1); 91% *ee*; $[\alpha]_D^{20}=+51.9$ ($c=1.0$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.91$ (d, $J=7.4$ Hz, 2H), 7.53 (t, $J=7.4$ Hz, 1H), 7.41 (t, $J=7.7$ Hz, 2H), 7.30--7.23 (m, 1H), 7.19 (dd, $J=10.5$, 4.4 Hz, 2H), 7.08 (dd, $J=7.9$, 7.0 Hz, 1H), 6.85 (dd, $J=9.3$, 2.8 Hz, 1H), 6.60--6.52 (m, 1H), 6.47 (dd, $J=8.8$, 5.7 Hz, 1H), 5.05--4.83 (m, 1H), 4.53 (s, 1H), 3.99 (dd, $J=18.0$, 9.9 Hz, 1H), 3.40 ppm (dd, $J=18.0$, 3.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=$ 199.0, 156.4, 156.3 (d, $^1J_{C-F}=239.4$), 144.3 (d, $^3J_{C-F}=10.7$ Hz), 136.6, 133.4, 133.3 (d, $^4J_{C-F}=2.7$ Hz), 132.1, 129.2, 128.6, 128.4, 128.0, 124.4, 121.2, 119.7 (d, $^3J_{C-F}=8.8$ Hz), 111.2 (d, $^2J_{C-F}=22.1$ Hz), 108.8 (d, $^2J_{C-F}=24.5$ Hz), 54.7, 43.8 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=$ -124.5 ppm; HRMS (ESI): *m/z*: calcd for $C_{21}H_{17}FNO_2$: 334.1238 $[M+H]^+$; found: 334.1240; HPLC (Chiralcel IA column, hexane/*i*PrOH 85:15, 0.8 mL min^{-1}, 254 nm): $t_1=14.1$ min, $t_2=18.6$ min (major, *R*).

(*R*)-2-(6-methyl-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-phenylethanone (**3 ia**): Pale yellow oil; yield 89% (67.5 mg); $R_f=0.30$ (petroleum ether/EtOAc 10:1); 91% *ee*; $[\alpha]_D^{20}=+49.4$ ($c=1.0$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.94$--7.82 (m, 2H), 7.48 (t, $J=7.4$ Hz, 1H), 7.42--7.30 (m, 2H), 7.27--7.22 (m, 1H), 7.21--7.13 (m, 2H), 7.04 (td, $J=7.5$, 1.9 Hz, 1H), 6.68 (t, $J=7.7$ Hz, 1H), 6.54 (d, $J=7.3$ Hz, 1H), 6.37 (d, $J=7.2$ Hz, 1H), 4.94 (dd, $J=9.6$, 3.3 Hz, 1H), 4.57 (s, 1H), 4.03 (dd, $J=18.0$, 9.6 Hz, 1H), 3.40 (dd, $J=18.0$, 3.4 Hz, 1H), 2.42 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=199.0$, 157.0, 142.8, 137.4, 136.6, 133.2, 132.8, 130.5, 129.0, 128.5, 128.3, 128.0, 124.2, 124.0, 121.5, 120.9, 117.0, 54.3, 44.8, 17.1 ppm; HRMS (ESI): *m/z*: calcd for $C_{22}H_{20}NO_2$: 330.1489 $[M+H]^+$; found: 330.1485; HPLC (Chiralcel IA column, hexane/*i*PrOH 85:15, 0.8 mL min^{-1}, 254 nm): $t_1=11.2$ min, $t_2=13.1$ min (major, *R*).

(*R*)-2-(2-methyl-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-phenylethanone (**3 ja**): Pale yellow oil; yield 99% (65.2 mg); $R_f=0.32$ (petroleum ether/EtOAc 10:1); 91% *ee*; $[\alpha]_D^{20}=+89.6$ ($c=1.0$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.98$--7.90 (m, 2H), 7.58--7.51 (m, 1H), 7.42 (dd, $J=10.6$, 4.7 Hz, 2H), 7.15--7.01 (m, 4H), 6.83 (td, $J=7.9$, 1.5 Hz, 1H), 6.68 (td, $J=7.9$, 1.5 Hz, 1H), 6.55 (dd, $J=7.9$, 1.5 Hz, 1H), 4.92 (dd, $J=9.6$, 3.4 Hz, 1H), 4.64 (s, 1H), 4.16 (dd, $J=18.0$, 9.6 Hz, 1H), 3.48 (dd, $J=18.0$, 3.4 Hz, 1H), 2.32 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=199.1$, 155.0, 143.8, 137.1, 136.7, 133.9, 133.26, 132.2, 129.6, 128.8, 128.5, 128.0, 124.6, 121.6, 120.9, 118.9, 54.4, 44.3, 20.7 ppm; HRMS (ESI): *m/z*: calcd for $C_{22}H_{20}NO_2$: 330.1489 $[M+H]^+$; found: 330.1486; HPLC (Chiralcel IA column, hexane/*i*PrOH 85:15, 0.8 mL min^{-1}, 254 nm): $t_1=12.0$ min, $t_2=$ 17.5 min (major, *R*).

(*R*)-2-(2-methoxy-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-phenylethanone (**3 ka**): Pale yellow oil; yield 97% (67.3 mg); $R_f=$ 0.21 (petroleum ether/EtOAc 10:1); 92% *ee*; $[\alpha]_D^{20}=+75.4$ ($c=1.0$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.94$ (d, $J=7.4$ Hz, 2H), 7.54 (t, $J=7.4$ Hz, 1H), 7.42 (t, $J=7.7$ Hz, 2H), 7.18--7.06 (m, 2H), 6.89--6.76 (m, 3H), 6.71--6.62 (m, 1H), 6.55 (dd, $J=7.9$, 1.1 Hz, 1H), 4.92 (dd, $J=9.5$, 3.2 Hz, 1H), 4.64 (s, 1H), 4.19 (dd, $J=17.9$, 9.6 Hz, 1H), 3.78 (s, 3H), 3.50 ppm (dd, $J=17.9$, 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=199.0$, 156.0, 151.0, 143.8, 137.1, 136.7, 133.5, 133.3, 128.5, 128.0, 124.6, 121.9, 121.5, 118.8, 113.8, 113.5, 55.6,

54.3, 44.1 ppm; HRMS (ESI): *m/z*: calcd for $C_{22}H_{20}NO_3$: 346.1438 $[M+H]^+$; found: 346.1436; HPLC (Chiralcel IA column, hexane/*i*PrOH 85:15, 0.8 mL min^{-1}, 254 nm): $t_1=17.5$ min, $t_2=22.0$ min (major, *R*).

(*R*)-2-(2-fluoro-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-phenylethanone (**3la**): Pale yellow oil; yield 99% (66.2 mg); $R_f=0.40$ (petroleum ether/EtOAc 10:1); 95% *ee*; $[\alpha]_D^{20}=+60.8$ ($c=1.0$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.98$--7.91 (m, 2H), 7.55 (t, $J=7.4$ Hz, 1H), 7.43 (t, $J=7.7$ Hz, 2H), 7.17 (dd, $J=9.6$, 4.8 Hz, 1H), 7.11 (dd, $J=8.0$, 1.4 Hz, 1H), 6.99--6.91 (m, 2H), 6.86 (td, $J=7.9$, 1.4 Hz, 1H), 6.69 (td, $J=7.9$, 1.5 Hz, 1H), 6.56 (dd, $J=7.9$, 1.4 Hz, 1H), 4.93 (d, $J=7.0$ Hz, 1H), 4.63 (s, 1H), 4.12 (dd, $J=18.0$, 9.4 Hz, 1H), 3.51 ppm (dd, $J=18.0$, 3.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=198.6$, 158.8 (d, $^1J_{C-F}=243.5$ Hz), 153.2 (d, $^4J_{C-F}=2.7$ Hz), 143.5, 137.0, 136.5, 134.2 (d, $^3J_{C-F}=7.3$ Hz), 133.4, 128.6, 128.0, 124.9, 122.5 (d, $^3J_{C-F}=8.4$ Hz), 121.6, 119.1, 118.9, 115.4 (d, $^2J_{C-F}=22.9$ Hz), 114.8 (d, $^2J_{C-F}=23.6$ Hz), 53.9, 43.9 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-118.1$ ppm; HRMS (ESI): *m/z*: calcd for $C_{21}H_{17}FNO_2$: 334.1238 $[M+H]^+$; found: 334.1233; HPLC (Chiralcel IA column, hexane/*i*PrOH 85:15, 0.8 mL min^{-1}, 254 nm): $t_1=13.1$ min, $t_2=16.6$ min (major, *R*).

(*R*)-2-(4-methyl-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-phenylethanone (**3ma**): Yellow solid; yield 98% (77.7 mg); $R_f=0.24$ (petroleum ether/EtOAc 10:1); m.p. 91–92 °C (petroleum ether/EtOAc); 90% *ee*; $[\alpha]_D^{20}=+85.0$ ($c=1.0$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.97$ (d, $J=7.5$ Hz, 2H), 7.54 (t, $J=7.3$ Hz, 1H), 7.43 (t, $J=7.7$ Hz, 2H), 7.17 (dd, $J=6.1$, 5.0 Hz, 2H), 7.09 (d, $J=7.0$ Hz, 1H), 7.01 (t, $J=7.5$ Hz, 1H), 6.86 (dd, $J=11.1$, 4.0 Hz, 1H), 6.73--6.63 (m, 1H), 6.60--6.50 (m, 1H), 4.98 (dd, $J=9.4$, 3.2 Hz, 1H), 4.67 (s, 1H), 4.25 (dd, $J=17.9$, 9.6 Hz, 1H), 3.52 (dd, $J=17.9$, 3.4 Hz, 1H), 2.49 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=199.1$, 155.4, 142.7, 137.6, 136.7, 133.2, 132.9, 130.7, 130.5, 128.5, 128.0, 125.8, 124.7, 124.2, 121.9, 118.6, 118.4, 54.1, 44.1, 16.2 ppm; HRMS (ESI): *m/z*: calcd for $C_{22}H_{20}NO_2$: 330.1489 $[M+H]^+$; found: 330.1493; HPLC (Chiralcel IA column, hexane/*i*PrOH 85:15, 0.8 mL min^{-1}, 254 nm): $t_1=9.8$ min, $t_2=12.1$ min (major, *R*).

(*R*)-2-(4-chloro-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-phenylethanone (**3na**): Pale yellow oil; yield 87% (66.7 mg); $R_f=0.18$ (petroleum ether/EtOAc 10:1); 94% *ee*; $[\alpha]_D^{20}=+121.5$ ($c=1.0$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.03$--7.87 (m, 2H), 7.55 (t, $J=7.4$ Hz, 1H), 7.43 (t, $J=7.7$ Hz, 2H), 7.36 (dd, $J=8.0$, 1.5 Hz, 1H), 7.31 (d, $J=8.0$ Hz, 1H), 7.15 (dd, $J=7.6$, 1.5 Hz, 1H), 7.02 (t, $J=7.8$ Hz, 1H), 6.87 (td, $J=8.0$, 1.3 Hz, 1H), 6.69 (td, $J=8.0$, 1.3 Hz, 1H), 6.55 (dd, $J=8.0$, 1.3 Hz, 1H), 5.09--4.89 (m, 1H), 4.65 (s, 1H), 4.23 (dd, $J=18.0$, 9.4 Hz, 1H), 3.51 ppm (dd, $J=18.0$, 3.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=198.7$, 152.8, 142.3, 137.1, 136.5, 134.9, 133.4, 129.8, 128.6, 128.0, 126.6, 125.3, 125.0, 122.4, 118.7, 118.4, 54.0, 44.0 ppm; HRMS (ESI): *m/z*: calcd for $C_{21}H_{17}ClNO_2$: 350.0942 $[M+H]^+$; found: 350.0934; HPLC (Chiralcel IA column, hexane/*i*PrOH 85:15, 0.8 mL min^{-1}, 254 nm): $t_1=11.2$ min, $t_2=13.9$ min (major, *R*).

2-(10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1,2-diphenylethanone (**4**): Pale yellow oil, Yield 64% (50.0 mg), $R_f=0.36$, 0.41 (petroleum ether/EtOAc 10:1); diastereomeric ratio = 1:1; 0% *ee* and 0% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): mixture of diastereomers; $\delta=7.94$--7.87 (m, 2H), 7.85--7.78 (m, 2H), 7.44--7.21 (m, 13H), 7.19--6.97 (m, 11H), 6.82--6.66 (m, 4H), 6.63--6.57 (m, 1H), 6.54 (dd, $J=7.5$, 1.3 Hz, 1H), 6.45 (dd, $J=8.0$, 1.4 Hz, 1H), 6.23 (dd, $J=7.9$, 1.4 Hz, 1H), 5.94 (d, $J=10.6$ Hz, 1H), 5.84 (d, $J=10.3$ Hz, 1H), 5.04--4.85 (m, 2H), 4.68 (s, 1H), 3.87 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): mixture of diastereomers; $\delta=199.7$, 199.0, 157.2, 156.9, 143.2, 137.2, 137.0, 136.7, 136.5, 133.1, 132.9, 132.0, 130.6, 130.5, 129.9, 129.3, 129.1, 129.0, 128.9, 128.7, 128.5, 128.45, 128.4, 128.2, 127.7, 127.29, 124.8, 124.6, 124.5, 124.0, 121.8, 121.7, 121.1, 120.7, 118.7, 118.5, 118.3, 118.2, 62.0, 61.8, 58.6, 57.9 ppm; HRMS (ESI): *m/z*: calcd for $C_{27}H_{22}NO_2$: 392.1645 $[M+H]^+$; found: 392.1648; HPLC (Chiralcel AD-H column, hexane/*i*PrOH 85:15, 0.7 mL min^{-1}, 254 nm): $t_1=14.4$ min, $t_2=21.3$ min, $t_3=19.1$ min, $t_4=19.9$ min.

Transformations of the Mannich product 3aa

(*R*)-11-(2-phenylallyl)-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepine (**5**): Dry THF (2.5 mL) was added to a mixture of methyltriphenylphosphonium iodide (235.0 mg, 0.58 mmol) and *t*BuOK (0.58 mmol) in a flame-dried flask, and the suspension was stirred at RT for 80 min. The yellow suspension was then cooled to −10 °C, and then a solution of **3aa** (61.1 mg, 0.19 mmol) in THF (2.5 mL) that was cooled previously to −10 °C was added dropwise to the yellow suspension. After 5 h, another portion of the mixture of methyltriphenylphosphonium iodide (76.8 mg, 0.19 mmol) and *t*BuOK (0.19 mmol) in THF, was added to the reaction system. The reaction was stirred for another 8 h. Water was added, and the aqueous layer was extracted with DCM. The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4; the solvent was evaporated under reduced pressure. The resulting residue was purified by using column chromatography and **5** was afforded as a pale yellow oil: yield 78% (47.5 mg); 92% *ee*; $[\alpha]_D^{20}=+0.2$ ($c=1.0$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.40$ (d, $J=6.9$ Hz, 2H), 7.37–7.19 (m, 4H), 7.15 (d, $J=7.7$ Hz, 1H), 7.06 (ddd, $J=9.0$, 7.5, 1.0 Hz, 3H), 6.87–6.76 (m, 1H), 6.70–6.60 (m, 1H), 6.46 (dd, $J=7.9$, 1.3 Hz, 1H), 5.37 (d, $J=1.0$ Hz, 1H), 5.11 (s, 1H), 4.47 (dd, $J=9.0$, 5.4 Hz, 1H), 3.98 (s, 1H), 3.38–3.13 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=157.2$, 145.3, 143.9, 140.2, 137.5, 133.5, 128.9, 128.6, 127.8, 127.1, 126.3, 124.3, 124.1, 121.7, 121.1, 118.9, 118.7, 115.9, 55.2, 41.0 ppm; HRMS (ESI): *m/z*: calcd for $C_{22}H_{20}NO$: 314.1539 $[M+H]^+$; found: 314.1541; HPLC (Chiralcel AD-H column, hexane/*i*PrOH 95:5, 0.8 mL min^{-1}, 254 nm): $t_1=10.2$ min, $t_2=15.4$ min (major, *R*).

(*R*)-11-phenethyl-10,11-dihydrodibenzo[*b*,*f*][1,4]oxazepine (**6**): $NaBH_4$ (25.0 mg, 0.66 mmol) was added to a solution of **3aa** (105.6 mg, 0.33 mmol) in methanol (3.0 mL) at 25 °C. After the resulting mixture was stirred for 1 h, water was added. The mixture was extracted with dichloromethane. The organic layer was washed with brine and dried over anhydrous Na_2SO_4. After removal of the solvent, the crude product obtained was dissolved in MeOH (5.0 mL), and 5% Pd on charcoal (106.1 mg) and AcOH (0.5 mL) were added to the solution. The reaction was performed with H_2 gas at an initial pressure of 4.1 MPa and 50 °C for 48 h. The catalyst was filtered off, and the filtrate was concentrated by rotary evaporation. The crude product was purified by using column chromatography and **6** was afforded as a pale yellow oil: yield 62% (61.3 mg); 88% *ee*; $[\alpha]_D^{20}=+19.0$ ($c=1.0$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.34$–7.0 (m, 10H), 6.99 (m, 1H), 6.84 (dd, $J=10.9$, 4.3 Hz, 1H), 6.66 (t, $J=7.6$ Hz, 1H), 6.52 (d, $J=7.9$ Hz, 1H), 4.35 (t, $J=7.3$ Hz, 1H), 3.95 (s, 1H), 2.87–2.61 (m, 2H), 2.52–2.29 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=157.2$, 143.9, 141.4, 137.4, 133.9, 128.8, 128.5, 128.4, 127.3, 126.0, 124.4, 124.1, 121.7, 121.1, 118.8, 118.6, 56.8, 36.4, 33.0 ppm; HRMS (ESI): *m/z*: calcd for $C_{21}H_{20}NO$: 302.1539 $[M+H]^+$; found: 302.1552; HPLC (Chiralcel IA column, hexane/*i*PrOH 95:5, 0.6 mL min^{-1}, 254 nm): $t_1=18.2$ min, $t_2=19.4$ min (major, *R*).

Acknowledgements

We acknowledge financial support from the National Natural Science Foundation of China (21002022) and the international scientific and technological cooperation program of Henan province (124300510032).

Keywords: acetophenone derivatives · asymmetric catalysis · Mannich reaction · nitrogen heterocycles · organocatalysis

[1] M. Arend, B. Westermann, N. Risch, *Angew. Chem. Int. Ed.* **1998**, *37*, 1044 – 1070; *Angew. Chem.* **1998**, *110*, 1096 – 1122.

[2] For reviews on asymmetric Mannich reactions, see: a) A. Córdova, *Acc. Chem. Res.* **2004**, *37*, 102 – 112; b) M. M. B. Marques, *Angew. Chem. Int. Ed.* **2006**, *45*, 348 – 352; *Angew. Chem.* **2006**, *118*, 356 – 360; c) A. Ting, S. E. Schaus, *Eur. J. Org. Chem.* **2007**, 5797 – 5815; d) J. M. M. Verkade, L. J. C. van Hemert, P. J. L. M. Quaedflieg, F. P. J. T. Rutjes, *Chem. Soc. Rev.* **2008**, *37*, 29 – 41; e) R. G. Arrayás, J. C. Carretero, *Chem. Soc. Rev.* **2009**, *38*, 1940 – 1948; f) S. J. Greco, V. Lacerda, R. B. Santos, *Aldrichimica Acta* **2011**, *44*, 15 – 24; g) B. Karimi, D. Enders, E. Jafari, *Synthesis* **2013**, *45*, 2769 – 2812.

[3] a) B. List, *J. Am. Chem. Soc.* **2000**, *122*, 9336 – 9337; b) W. Notz, K. Sakthivel, T. Bui, G. Zhong, C. F. Barbas, III, *Tetrahedron Lett.* **2001**, *42*, 199 – 201.

[4] a) S. Mukherjee, J. W. Yang, S. Hoffmann, B. List, *Chem. Rev.* **2007**, *107*, 5471 – 5569; b) L.-W. Xu, J. Luo, Y. Lu, *Chem. Commun.* **2009**, 1807 – 1821; c) O. V. Serdyuk, C. M. Heckel, S. B. Tsogoeva, *Org. Biomol. Chem.* **2013**, *11*, 7051 – 7071.

[5] For selected examples of the organocatalytic asymmetric Mannich-type reaction with the non-functionalised aliphatic ketones or aldehydes as donors, see: a) Y. Hayashi, W. Tsuboi, M. Shoji, N. Suzuki, *J. Am. Chem. Soc.* **2003**, *125*, 11208 – 11209; b) I. Ibrahem, W. Zou, M. Engqvist, Y. Xu, A. Córdova, *Chem. Eur. J.* **2005**, *11*, 7024 – 7029; c) A. J. A. Cobb, D. M. Shaw, D. A. Longbottom, J. B. Gold, S. V. Ley, *Org. Biomol. Chem.* **2005**, *3*, 84 – 96; d) S. Mitsumori, H. Zhang, P. H.-Y. Cheong, K. N. Houk, F. Tanaka, C. F. Barbas III., *J. Am. Chem. Soc.* **2006**, *128*, 1040 – 1041; e) H. Zhang, M. Mifsud, F. Tanaka, C. F. Barbas III., *J. Am. Chem. Soc.* **2006**, *128*, 9630 – 9031; f) L. Cheng, X. Han, H. Huang, M. W. Wong, Y. Lu, *Chem. Commun.* **2007**, 4143 – 4145; g) J. W. Yang, C. Chandler, M. Stadler, D. Kampen, B. List, *Nature* **2008**, *452*, 453 – 455; h) T. Kano, Y. Yamaguchi, K. Maruoka, *Angew. Chem. Int. Ed.* **2009**, *48*, 1838 – 1840; *Angew. Chem.* **2009**, *121*, 1870 – 1872; i) J. Pietruszka, R. C. Simon, *ChemCatChem* **2010**, *2*, 505 – 508; j) Q.-X. Guo, Y.-W. Liu, X.-C. Li, L.-Z. Zhong, Y.-G. Peng, *J. Org. Chem.* **2012**, *77*, 3589 – 3594; k) T. Kano, R. Sakamoto, M. Akakura, K. Maruoka, *J. Am. Chem. Soc.* **2012**, *134*, 7516 – 7520.

[6] For the asymmetric Mannich-type reaction of the unmodified 2-hydroxyacetophenone derivatives donors using metal catalysts, see: a) B. M. Trost, L. R. Terrell, *J. Am. Chem. Soc.* **2003**, *125*, 338 – 339; b) S. Matsunaga, N. Kumagai, S. Harada, M. Shibasaki, *J. Am. Chem. Soc.* **2003**, *125*, 4712 – 4713; c) S. Matsunaga, T. Yoshida, H. Morimoto, N. Kumagai, M. Shibasaki, *J. Am. Chem. Soc.* **2004**, *126*, 8777 – 8785; d) T. Yoshida, H. Morimoto, N. Kumagai, S. Matsunaga, M. Shibasaki, *Angew. Chem. Int. Ed.* **2005**, *44*, 3470 – 3474; *Angew. Chem.* **2005**, *117*, 3536 – 3540; e) M. Sugita, A. Yamaguchi, N. Yamagiwa, S. Handa, S. Matsunaga, M. Shibasaki, *Org. Lett.* **2005**, *7*, 5339 – 5342; f) B. M. Trost, J. Jaratjaroonphong, V. Reutrakul, *J. Am. Chem. Soc.* **2006**, *128*, 2778 – 2779; g) A. Yamaguchi, S. Matsunaga, M. Shibasaki, *Tetrahedron Lett.* **2006**, *47*, 3985 – 3989; h) S. Matsunaga, M. Sugita, N. Yamagiwa, S. Handa, A. Yamaguchi, M. Shibasaki, *Bull. Chem. Soc. Jpn.* **2006**, *79*, 1906 – 1912.

[7] Q.-X. Guo, H. Liu, C. Guo, S.-W. Luo, Y. Gu, L.-Z. Gong, *J. Am. Chem. Soc.* **2007**, *129*, 3790 – 3791.

[8] M. Rueping, E. Sugiono, F. R. Schoepke, *Synlett* **2007**, *9*, 1441 – 1445.

[9] Q. Guo, J. C.-G. Zhao, H. Arman, *Tetrahedron Lett.* **2012**, *53*, 4866 – 4869.

[10] Q. Guo, J. C.-G. Zhao, *Org. Lett.* **2013**, *15*, 508 – 511.

[11] a) C. Jiang, F. Zhong, Y. Lu, *Beilstein J. Org. Chem.* **2012**, *8*, 1279 – 1283; b) C.-F. Yang, C. Shen, J.-Y. Wang, S.-K. Tian, *Org. Lett.* **2012**, *14*, 3092 – 3095; c) H.-N. Yuan, S. Wang, J. Nie, W. Meng, Q. Yao, J.-A. Ma, *Angew. Chem. Int. Ed.* **2013**, *52*, 3869 – 3873; *Angew. Chem.* **2013**, *125*, 3961 – 3965; d) H.-X. Zhang, J. Nie, H. Cai, J.-A. Ma, *Org. Lett.* **2014**, *16*, 2542 – 2545.

[12] a) S. Kobayashi, H. Ishitani, *Chem. Rev.* **1999**, *99*, 1069 – 1094; b) S. Kobayashi, Y. Mori, J. S. Fossey, M. M. Salter, *Chem. Rev.* **2011**, *111*, 2626 – 2704.

[13] a) T. Itoh, M. Yokoya, K. Miyauchi, K. Nagata, A. Ohsawa, *Org. Lett.* **2003**, *5*, 4301 – 4304; b) W. Zhuang, S. Saaby, K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2004**, *43*, 4476 – 4478; *Angew. Chem.* **2004**, *116*, 4576 – 4578; c) T. Itoh, M. Yokoya, K. Miyauchi, K. Nagata, A. Ohsawa, *Org. Lett.* **2006**, *8*, 1533 – 1535; d) B. Jiang, J. J. Dong, Y. G. Si, X. L. Zhao, Z. G. Huang, M. Xu, *Adv. Synth. Catal.* **2008**, *350*, 1360 – 1366; e) B. T. Hahn, R. Frőhlich, K. Harms, F. Glorius, *Angew. Chem. Int. Ed.* **2008**, *47*, 9985 – 9988; *Angew. Chem.* **2008**, *120*, 10134 – 10137; f) K. Schulz, L. Ratjen, J. Martens, *Tetrahedron* **2011**, *67*, 546 – 553; g) M. R. Monaco, P. Renzi, D. M. S. Schietroma, M. Bella, *Org. Lett.* **2011**, *13*, 4546 – 4549; h) T. Kano, S. Song, Y. Kubota, K. Maruoka, *Angew. Chem. Int. Ed.* **2012**, *51*, 1191 – 1194; *Angew. Chem.* **2012**, *124*, 1217 – 1220.

[14] a) L. Li, M. Han, M. Xiao, Z. Xie, *Synlett* **2011**, 1727 – 1730; b) D.-J. Cheng, S.-K. Tian, *Adv. Synth. Catal.* **2013**, *355*, 1715 – 1718.

[15] a) Y.-Q. Wang, Y. Zhang, H. Dong, J. Zhang, J. Zhao, *Eur. J. Org. Chem.* **2013**, 3764 – 3770; b) Y.-Q. Wang, Y. Zhang, K. Pan, J. You, J. Zhao, *Adv. Synth. Catal.* **2013**, *355*, 3381 – 3386.

[16] a) A. W. H. Wardrop, G. L. Sainsbury, J. M. Harrison, T. D. Inch, *J. Chem. Soc. Perkin Trans. 1* **1976**, 1279 – 1285; b) V. G. Noskov, L. N. Kalinina, M. N. Noskova, Y. L. Kruglyak, O. G. Strukov, A. P. Bezrukov, V. K. Kurochkin, *Pharm. Chem. J.* **1997**, *31*, 431 – 434; c) Y. R. Jorapur, G. Rajagopal, P. J. Saikia, R. R. Pal, *Tetrahedron Lett.* **2008**, *49*, 1495 – 1497. The corresponding seven-membered cyclic ketimines dibenzo[*b*,*f*][1,4]oxazepine were used as substrates in the catalytic asymmetric hydrogenation: d) K. Gao, C.-B. Yu, W. Li, Y.-G. Zhou, X. Zhang, *Chem. Commun.* **2011**, *47*, 7845 – 7847.

[17] a) P. P. M. A. Dols, B. J. B. Folmer, H. Hamersma, C. W. Kuil, H. Lucas, L. Ollero, J. B. M. Rewinkel, P. H. H. Hermkens, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 1461 – 1467; b) R. J. Riley, P. Roberts, N. R. Kitteringham, B. K. Park, *Biochem. Pharmacol.* **1990**, *39*, 1951 – 1958.

[18] CCDC 981947 (**3 ah**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Received: June 12, 2014
Revised: July 7, 2014
Published online on August 26, 2014