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Catalytic enantioselective addition of alcohols to isatin-derived *N*-Boc ketimines

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ABSTRACT

The enantioselective addition of alcohols to isatin-derived *N*-Boc ketimines was investigated for the first time. Isatin-derived *N,O*-aminals were obtained in excellent yields with moderate-to-good enantioselectivities (up to 78% ee) in the presence of a quinine-based bifunctional catalyst.

1. Introduction

N,O-Aminals are important structural motifs widely found in natural products and pharmaceuticals.[1] They are also important building blocks in organic synthesis.[2] Despite the much effort made to construct *N,O*-aminals,[3] elegant examples that produce enantiomerically pure aminals have been rare.[4] The asymmetric addition of alcohols to imines represents a straightforward route to chiral *N,O*-aminal. In 2008, Antilla et al. reported a highly enantioselective alcoholysis of aldimines catalyzed by phosphoric acid.[4a] Later, List et al. extended this methodology to imines generated in situ from aldehydes and hydroxy amides, affording cyclic *N,O*-aminals in a high enantioselectivity.[4b] However, these approaches are limited to aldimines. To our knowledge, asymmetric nucleophilic additions of alcohols to ketimines are unprecedented due largely to the fact that both alcohols and ketimines are unreactive substrates while the stereoselectivity of the resulting adducts is hard to be controlled.

The asymmetric construction of a quaternary stereocenter is a challenge in organic synthesis.[5] The oxindole motifs bearing C3-quaternary structures are widely distributed in many bioactive natural products and pharmaceutically active compounds.[6] With the advancement of asymmetric organometallic and organic catalysis, rapid progress has been made in the construction of optically pure 3-substituted-hydroxyl-2-oxindoles.[7] However, asymmetric synthesis of 3-substituted-3-amino-2-oxindoles remains far less explored,[8,9] and the established methods narrowly focus on the addition of 3-substituted-2-oxindoles to nitroso or diazo compounds. Recently, isatin-derived *N*-Boc ketimines have been widely used in the asymmetric synthesis of various chiral 3-aminooxindoles.[10] We envision that these ketimines might be capable of interacting with alcohols to afford optically pure 3-alkoxy-3-amiooxindoles. Herein we report the first enantioselective addition of alcohols to *N*-Boc ketimines to afford isatin-derived *N,O*-aminals.

2. Results and discussion

The choice of a suitable catalyst that efficiently activates alcohols and ketimines may practically address their low reactivity. Tertiary amine-based bifunctional organocatalysts are widely used in asymmetric synthesis.[11] We recognize that the tertiary amine group could activate alcohol and the hydrogen bond donors activate imine through hydrogen bonding, and these synergistic interactions would help control the stereoselectivity.

Initially, the reaction of isatin-derived *N*-Boc ketimine **1a** with ethanol was chosen as a model reaction to screen the chiral organocatalysts (Fig. 1). As illustrated in Table 1, the reaction was performed smoothly in a mixed solvent of CH_2Cl_2 and EtOH with 10 mol % Takemoto catalyst **A1** at room temperature, affording the desired product in 98% yield and 39% ee (entry 1). Cinchonine-based tertiary amine-thiourea **A2** (46% ee, entry 2) provided better enantioselectivity than did A**1**. The structural difference between **A2** and **A3** seems to result in the obvious difference in their

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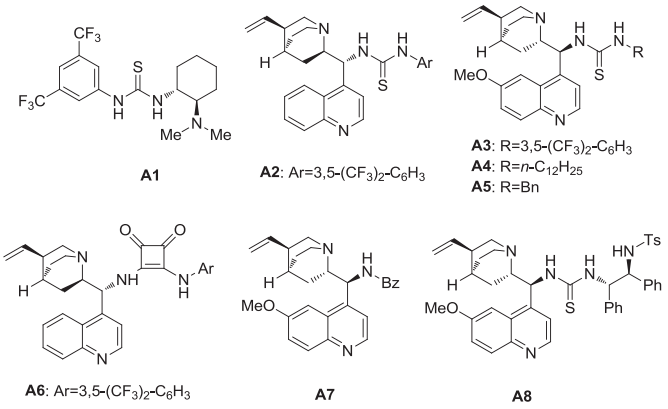
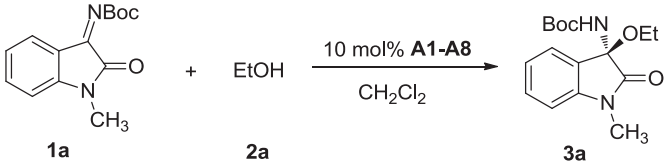


Fig. 1. Structures of organocatalysts **A1**–**A8**.

Table 1
Screening of the chiral organocatalysts[a]



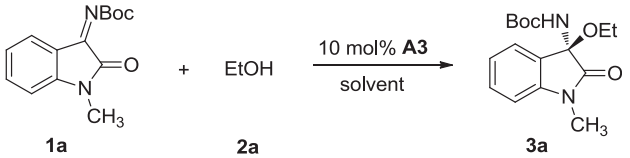
Entry	Catalyst	Time (h)	Yield[b] (%)	ee[c] (%)
1	**A1**	48	98	−39
2	**A2**	48	98	−46
3	**A3**	16	99	56
4	**A4**	84	93	2
5	**A5**	84	97	4
6	**A6**	12	99	−14
7	**A7**	120	78	9
8	**A8**	8	99	0

[a] The reactions were carried out with isatin-derived ketimines (0.2 mmol), EtOH (0.5 mL), and catalyst (0.02 mmol) in CH_2Cl_2 (0.5 mL) at room temperature.
[b] Isolated yield.
[c] The ee values were determined by chiral HPLC analysis.

catalytic behaviors. Quinine-derived aliphatic thioureas **A4** and **A5** gave the product in poor enantioselectivities. Bifunctional amine-squaramide **A6** improved the reaction rate, but gave an inferior enantioselectivity (entry 3). Using amide **A7** with a single H-bonding donor, the reaction became sluggish and resulted in a lower yield. Multifunctional organocatalyst **A8** produced the racemic adduct. These results suggest that the thiourea moiety with a strong hydrogen-bonding ability plays an important role in the asymmetric addition.

Next, the effect of the reaction solvents was investigated using 10 mol % of **A3** as chiral catalyst (Table 2). In all the solvents examined except DMF, product **3a** was obtained in excellent yields. In DMF, however, the reaction proceeded slowly and resulted in moderate yield and stereoselectivity (entry 8). Non-polar solvents, such as toluene and CH_2Cl_2 led to inferior enantioselectivities (entries 1 and 2). CH_3CN turns out to be the most suitable solvent, which afforded **3a** in nearly quantitative yield and the highest ee, though required a longer reaction time (99% yield, 69% ee, entry 7). When the reaction was carried out in EtOH, compound **3a** was obtained in 96% yield with 66% ee (entry 9). The ratio of EtOH to CH_3CN has no significant effect on the enantioselectivity (entries 10 and 11). The amount of EtOH could be reduced down to 5 equiv, but with an extended reaction time of 24 h (entry 12). Low reaction temperatures provided better enantioselectivity (entries 14 and 15 vs 9). Varying the substrate concentration affected the reaction time but not the enantioselectivity (entries 15 and 16 vs 13). On the

Table 2
Optimization of the reaction conditions[a]



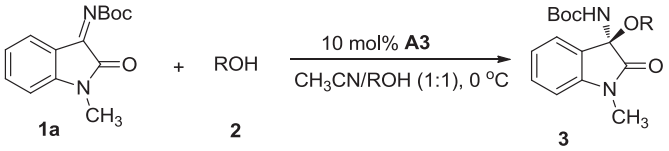
Entry	Solvent	Temp (°C)	Time (h)	Yield[b] (%)	ee[c] (%)
1	Toluene	25	6	93	60
2	CH_2Cl_2	25	16	99	56
3	THF	25	6	97	67
4	TBME	25	6	99	65
5	Ether	25	6	91	68
6	EtOAc	25	6	90	66
7	CH_3CN	25	12	99	69
8	DMF	25	24	60	62
9	EtOH	25	6	96	66
10[d]	CH_3CN	25	13	99	68
11[e]	CH_3CN	25	12	98	69
12[f]	CH_3CN	25	24	94	67
13	CH_3CN	0	60	97	76
14	CH_3CN	−20	120	93	79
15[g]	CH_3CN	0	48	99	75
16[h]	CH_3CN	0	96	97	74

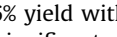
[a] Unless stated otherwise, the reactions were carried out with **1a** (0.2 mmol), EtOH (0.5 mL), **A3** (0.02 mmol), and solvent (0.5 mL).
[b] Isolated yield.
[c] The ee values were determined by chiral HPLC analysis.
[d] Using 1 mL EtOH/CH_3CN (1/2).
[e] Using 1 mL EtOH/CH_3CN (2/1).
[f] Using 5 equiv EtOH and 1 mL CH_3CN.
[g] Using 0.5 mL EtOH/CH_3CN (1/1).
[h] Using 2.0 mL EtOH/CH_3CN (1/1).

basis of the above-results, the optimal reaction condition was established to be the presence of 0.2 M ketimine **1** in CH_3CN/EtOH (1/1) with 10 mol % catalyst **A3** at 0 °C.

With the optimal reaction condition in hand, we examined the scope of the method using different alcohols as the nucleophile (Table 3). The steric properties of alcohol are determined to have a remarkable effect on the reaction. A series of primary alcohols are suitable substrates for this reaction (entries 1–6). Isopropanol exhibited a significantly low reactivity (80% yield, 74% ee, entry 7).

Table 3
Asymmetric addition of different alcohols to isatin-derived ketimine **1a**[a]



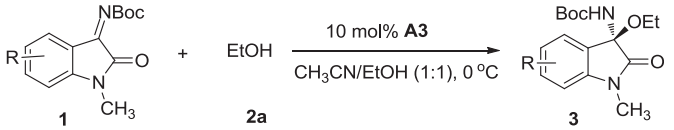
Entry	ROH	Product	Yield[b] (%)	ee[c] (%)
1	MeOH	**3b**	98	67
2	EtOH	**3a**	97	76
3	*n*-PrOH	**3c**	95	75
4	*n*-BuOH	**3d**	94	77
5[d]	$C_{12}H_{25}OH$	**3e**	96	73
6[e]	$C_6H_5CH_2CH_2OH$	**3f**	95	71
7	*i*-PrOH	**3g**	80	74
8	*t*-BuOH	**3h**	Trace	n.d.
9[e]		**3i**	79	76
10[e]		**3j**	94	74
11[e]		**3k**	91	56

[a] Unless stated otherwise, the reactions were carried out with **1a** (0.2 mmol), alcohol (0.5 mL), and **A3** (0.02 mmol) in CH_3CN (0.5 mL) at 0 °C.
[b] Isolated yields.
[c] The ee values were determined by chiral HPLC analysis.
[d] Using 5 equiv of alcohol and 1 mL ether.
[e] Using 5 equiv of alcohol and 1 mL CH_3CN.

Tertiary alcohols, such as *tert*-butanol could not react with **1a** under the typical reaction condition (entry 8). Due to its solubility, when lauryl alcohol was used as nucleophile, the reaction was performed in ether. Unsaturated alcohols, such as allyl alcohol and *trans*-cinnamyl alcohol were also well tolerated, leading to a good selectivity (entries 9–11). However, a relatively lower yield was obtained when allyl alcohol was used as nucleophile (entry 9). The *N*,*O*-aminal decorated with a propargyl alcohol was provided in high yield but with the lowest ee (entry 11).

Further exploration of the reaction scope was focused on varying the substituents on the isatin-derived ketimines (Table 4). Excellent yields were obtained in all the examined cases (90–98% yields), whereas the enantioselectivity varied in terms of the location of the substituents. Introduction of substituents at 6-position had a slightly positive effect (entries 5 and 6). The enantioselectivity decreased dramatically when substituents were introduced to the 7-position (entries 7–9).

Table 4
Asymmetric addition of ethanol to different isatin-derived ketimines **1**[a]



Entry	R	Product	Yield[b] (%)	ee[c] (%)
1	5-Me	**3l**	90	77
2	5-F	**3m**	98	77
3	5-Cl	**3n**	97	76
4	5-Br	**3o**	95	74
5	6-Cl	**3p**	98	78
6	6-Br	**3q**	92	77
7	7-F	**3r**	93	69
8	7-Cl	**3s**	96	63
9	7-Me	**3t**	94	65

[a] The reactions were carried out with **1** (0.2 mmol), EtOH (0.5 mL), and **A3** (0.02 mmol) in CH_3CN (0.5 mL) at 0 °C.
[b] Isolated yields.
[c] The ee values were determined by chiral HPLC analysis.

The absolute configuration of product **3q** was determined to be *R* by X-ray analysis (Fig. 2). And the configurations of other *N*,*O*-aminals were tentatively assigned by referring to that of **3q**. According to the above-mentioned experimental results and the related reports,[10a,12] a probable transition-state structure was proposed. As shown in Fig. 3, the thiourea moiety activates the ketimine through hydrogen-bonding interactions while the alcohol activated by the tertiary amine then attacks the ketimine from the *re*-face to generate the product with an (*R*)-configuration.

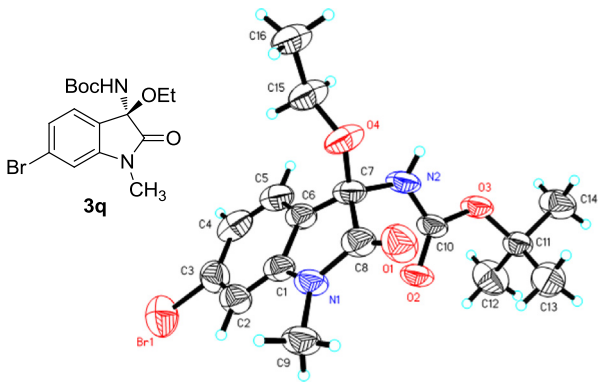


Fig. 2. X-ray crystal structure of *N*,*O*-aminal **3q**.

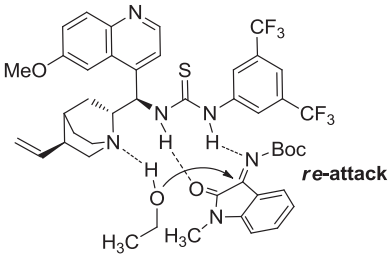


Fig. 3. Proposed transition state.

3. Conclusion

In summary, we have described the first example of enantioselective addition of alcohols to isatin-derived ketimines. In the presence of 10 mol % of a quinine-based bifunctional catalyst, chiral *N*,*O*-aminals were achieved in excellent yields and with moderate-to-good enantioselectivities. The method established here represents a new protocol for the asymmetric construction of isatin-derived *N*,*O*-aminals.

4. Experimental section

4.1. General methods

Melting points were taken without correction. Optical rotations were measured on a WZZ-2A digital polarimeter at the wavelength of the sodium D-line (589 nm). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker 400 spectrometer and the chemical shifts were referenced to tetramethylsilane (δ 0.00 ppm) using acetone-d_6 as solvent. IR spectra were recorded on Nicolet Magna-I 550 spectrometer. High Resolution Mass spectra (HRMS) were recorded on Micromass GCT with Electron Spray Ionization (ESI) resource. HPLC analysis was performed on Waters equipment using Chiralpak AS-H or AD-H column.

Toluene, THF, TBME, and ether were freshly distilled from sodium–benzophenone. CH_2Cl_2, ethyl acetate, and CH_3CN were freshly distilled from CaH_2. All alcohols were commercially available and were purified by standard methods. Thin-layer chromatography (TLC) was performed on 10–40 μm silica gel plates. Column chromatography was performed, using silica gel (300–400 mesh) eluted with ethyl acetate and CH_2Cl_2.

All substituted *N*-Boc ketimines were synthesized according to literature.[10a] Catalyst **A1** was commercially available; **A2** (cinchonine-thiourea), **A3**, **A4**, **A5** (quinine-thiourea), **A6** (cinchonine-squaramide), **A7** (quinine-amide), and **A8** were prepared according to literature procedures.[13]

4.2. Typical experimental procedure for the asymmetric reactions

To a solution of catalyst **A3** (0.02 mmol, 11.9 mg) in 1.0 mL CH_3CN/EtOH (1/1) was added isatin-derived *N*-Boc ketimine (0.2 mmol) at 0 °C, and the resulting mixture was stirred at this temperature until the reaction completed (monitored by TLC). The solvent was removed under reduced pressure and the residue was purified by column chromatography (20/1 CH_2Cl_2/acetate) to give the desired product **3**.

*4.2.1. (R)-tert-Butyl (3-ethoxy-1-methyl-2-oxoindolin-3-yl) carbamate (**3a**).* White solid, 97% yield, 76% ee, mp 121.0–121.2 °C; $[\alpha]_D^{20}$ +17.8 (*c* 2.61, CH_2Cl_2); ^{1}H NMR (400 MHz, acetone-d_6): δ 7.52 (d, *J*=7.2 Hz, 1H), 7.38 (td, *J*=7.6, 1.2 Hz, 1H), 7.11–7.07 (m, 1H), 6.99 (d, *J*=7.6 Hz, 1H), 3.62–3.50 (m, 1H), 3.18 (s, 1H), 3.11 (s, 1H), 1.24 (s, 1H), 1.07 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6): δ 172.8,

154.3, 145.2, 131.1, 128.4, 125.3, 123.3, 109.3, 85.3, 80.1, 60.1, 28.3, 26.4, 15.6; IR (KBr, cm^{-1}): ν 3261, 2976, 2931, 1728, 1614, 1471, 1369, 1250, 1157, 1061, 752; HRMS (ESI) calcd for $C_{16}H_{22}N_2O_4Na$ ($[M+Na]^+$): 329.1477, found: 329.1477; HPLC analysis (AS-H column, λ=254 nm, eluent: hexane/2-propanol=95/5, flow rate: 0.5 mL/min): t_R=31.77 min (minor), 34.63 min (major).

*4.2.2. (R)-tert-Butyl (3-methoxy-1-methyl-2-oxoindolin-3-yl) carbamate (**3b**).* White solid, 98% yield, 67% ee, mp 105.2–106.4 °C; $[\alpha]_D^{20}$ +28.4 (*c* 2.93, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.54 (d, *J*=7.2 Hz, 1H), 7.39 (td, *J*=8.0, 1.2 Hz, 1H), 7.18–7.08 (m, 1H), 7.00 (d, *J*=8.0 Hz, 1H), 3.30 (s, 3H), 3.19 (s, 3H), 3.13 (s, 1H), 1.26 (s, 9H); ^{13}C NMR (100 MHz, acetone-d_6): δ 172.5, 154.2, 145.2, 131.2, 127.9, 125.5, 123.3, 109.3, 85.5, 80.1, 51.6, 28.3, 26.3; IR (KBr, cm^{-1}): ν 3442, 2981, 1736, 1616, 1495, 1473, 1373, 1250, 1167, 1093, 756; HRMS (ESI) calcd for $C_{15}H_{20}N_2O_4K$ ($[M+K]^+$): 331.1060, found: 331.1063; HPLC analysis (AD-H column, λ=254 nm, eluent: hexane/2-propanol=90/10, flow rate: 0.9 mL/min): t_R=25.06 min (minor), 38.13 min (major).

*4.2.3. (R)-tert-Butyl (1-methyl-2-oxo-3-propoxyindolin-3-yl) carbamate (**3c**).* Colorless oil, 95% yield, 75% ee; $[\alpha]_D^{20}$ +15.2 (*c* 2.70, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.53 (d, *J*=7.2 Hz, 1H), 7.38 (dd, *J*=7.6, 1.2 Hz), 7.11–7.07 (m, 1H), 6.99 (d, *J*=7.6 Hz, 1H), 3.48–3.39 (m, 1H), 3.19 (s, 3H), 3.11 (s, 1H), 1.52–1.43 (m, 2H), 1.25 (s, 9H), 0.82 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6): δ 172.6, 154.1, 145.1, 131.0, 128.2, 125.3, 123.2, 109.2, 85.2, 80.0, 65.8, 28.2, 26.3, 23.5, 10.7; IR (KBr, cm^{-1}): ν 3425, 2974, 1736, 1318, 1495, 1398, 1248, 1165, 1092, 1057, 754; HRMS (ESI) calcd for $C_{17}H_{24}N_2O_4K$ ($[M+K]^+$): 359.1373, found: 359.1370; HPLC analysis (AS-H column, λ=254 nm, eluent: hexane/2-propanol=90/10, flow rate: 0.5 mL/min): t_R=21.48 min (major), 23.28 min (minor).

*4.2.4. (R)-tert-Butyl (3-butoxy-1-methyl-2-oxoindolin-3-yl) carbamate (**3d**).* Colorless oil, 94% yield, 77% ee; $[\alpha]_D^{20}$ +13.2 (*c* 2.65, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.54 (d, *J*=7.2 Hz, 1H), 7.38 (td, *J*=8.0, 1.2 Hz, 1H), 7.11–7.07 (m, 1H), 6.99 (d, *J*=8.0 Hz, 1H), 3.51–3.43 (m, 2H), 3.19 (s, 3H), 3.11 (s, 1H), 1.48–1.41 (m, 3H), 3.19 (s, 3H), 3.11 (s, 1H), 1.48–1.41 (m, 2H), 1.34–1.20 (m, 11H), 0.82 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6): δ 172.7, 154.1, 145.1, 131.0, 128.2, 125.3, 123.2, 109.2, 85.1, 80.0, 63.8, 32.4, 28.3, 26.3, 19.6, 14.0; IR (KBr, cm^{-1}): ν 3311, 2960, 2933, 2874, 1732, 1616, 1471, 1369, 1248, 1161, 1092, 752; HRMS (ESI) calcd for $C_{18}H_{26}N_2O_4Na$ ($[M+Na]^+$): 357.1790, found: 357.1787; HPLC analysis (AS-H column, λ=254 nm, eluent: hexane/2-propanol=90/10, flow rate: 0.5 mL/min): t_R=11.66 min (minor), 14.13 min (major).

*4.2.5. (R)-tert-Butyl (3-(dodecyloxy)-1-methyl-2-oxoindolin-3-yl) carbamate (**3e**).* Colorless oil, 96% yield, 73% ee; $[\alpha]_D^{20}$ +8.38 (*c* 3.25, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.40 (d, *J*=7.2 Hz, 1H), 7.25 (dd, *J*=7.6, 1.2 Hz, 1H), 6.98–6.94 (m, 1H), 6.86 (d, *J*=8.0 Hz, 1H), 3.78–3.30 (m, 2H), 3.08 (s, 1H), 3.06 (s, 3H), 1.36–1.29 (m, 2H), 1.13–1.12 (m, 26H), 0.74 (t, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6): δ 172.8, 154.2, 145.2, 131.1, 128.3, 125.4, 123.3, 109.3, 85.2, 80.1, 64.3, 32.7, 30.5, 30.4, 30.3, 30.1, 30.1, 30.0, 30.0, 28.3, 26.6, 26.4, 23.4, 14.4; IR (KBr, cm^{-1}): ν 3396, 2926, 2855, 1727, 1717, 1376, 1249, 1090, 1051, 880, 752; HRMS (ESI) calcd for $C_{26}H_{42}N_2O_4$ ($[M+H]^+$): 447.3223, found: 447.3224; HPLC analysis (AD-H column, λ=254 nm, eluent: hexane/2-propanol=90/10, flow rate: 0.9 mL/min): t_R=6.92 min (minor), 17.71 min (major).

*4.2.6. (R)-tert-Butyl (1-methyl-2-oxo-3-phenethoxyindolin-3-yl)carbamate (**3f**).* Semi-solid, 95% yield, 71% ee; $[\alpha]_D^{20}$ +6.28 (*c* 3.25, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.47 (d, *J*=7.2 Hz, 1H), 7.36 (td, *J*=8.0, 1.2 Hz, 1H), 7.26–7.22 (m, 2H), 7.19–7.15 (m, 3H), 7.06 (d, *J*=7.6 Hz, 1H), 3.75 (t, *J*=7.2 Hz, 2H), 3.16 (s, 3H), 3.13 (s, 1H), 2.79 (t, *J*=7.2 Hz, 2H), 1.24 (s, 9H); ^{13}C NMR (100 MHz, acetone-d_6): δ 172.6, 154.2, 145.1, 139.5, 131.2, 129.9, 129.1, 128.2, 127.1, 125.4, 123.3, 109.3, 85.2, 80.2, 65.5, 36.9, 28.4, 26.4; IR (KBr, cm^{-1}): ν 3321, 2924, 2872, 1738, 1711, 1614, 1471, 1367, 1252, 1101, 760, 706; HRMS (ESI) calcd for $C_{22}H_{26}N_2O_4Na$ ($[M+Na]^+$): 405.1790, found: 405.1785; HPLC analysis (AD-H column, λ=254 nm, eluent: hexane/2-propanol=90/10, flow rate: 0.9 mL/min): t_R=18.63 min (minor), 39.76 min (major).

*4.2.7. (R)-tert-Butyl (3-isopropoxy-1-methyl-2-oxoindolin-3-yl) carbamate (**3g**).* White solid, 80% yield, 74% ee, mp 109.7–110.0 °C; $[\alpha]_D^{20}$ +6.14 (*c* 2.49, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.61 (d, *J*=7.2 Hz, 1H), 7.40 (td, *J*=8.0, 1.2 Hz, 1H), 7.10–7.07 (m, 1H), 6.99 (d, *J*=8.0 Hz, 1H), 4.16–4.05 (m, 1H), 3.20 (s, 3H), 3.08 (s, 1H), 1.26 (s, 9H), 1.07 (d, *J*=6.4 Hz, 3H), 0.97 (d, *J*=6 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6): δ 173.3, 154.1, 145.0, 131.0, 128.9, 125.8, 123.3, 109.3, 84.7, 80.1, 67.5, 28.4, 26.4, 24.2, 24.0; IR (KBr, cm^{-1}): ν 3329, 2979, 2935, 1736, 1616, 1495, 1473, 1371, 1248, 1165, 1092, 754; HRMS (ESI) calcd for $C_{17}H_{24}N_2O_4Na$ ($[M+Na]^+$): 343.1634, found: 343.1638; HPLC analysis (AD-H column, λ=254 nm, eluent: hexane/2-propanol=80/20, flow rate: 0.5 mL/min): t_R=7.65 min (minor), 10.95 min (major).

*4.2.8. (R)-tert-Butyl (3-(allyloxy)-1-methyl-2-oxoindolin-3-yl) carbamate (**3i**).* Colorless oil, 79% yield, 76% ee; $[\alpha]_D^{20}$ +17.8 (*c* 2.40, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.57 (d, *J*=7.2 Hz, 1H), 7.39 (td, *J*=8.0, 1.2 Hz, 1H), 7.10 (td, *J*=7.6, 0.8 Hz, 1H), 7.00 (d, *J*=7.6 Hz, 1H), 5.87–5.77 (m, 1H), 5.22–5.17 (m, 1H), 5.06–5.03 (m, 1H), 4.15–4.05 (m, 2H), 3.19 (s, 3H), 3.09 (s, 1H), 1.26 (s, 9H); ^{13}C NMR (100 MHz, acetone-d_6): δ 172.5, 154.1, 145.0, 135.3, 131.1, 128.0, 125.4, 123.3, 116.6, 109.3, 85.0, 80.1, 65.4, 28.3, 26.3; IR (KBr, cm^{-1}): ν 3425, 2981, 2370, 1724, 1616, 1473, 1373, 1250, 1163, 1092, 1057, 754; HRMS (ESI) calcd for $C_{17}H_{22}N_2O_4Na$ ($[M+Na]^+$): 341.1477, found: 341.1475; HPLC analysis (AD-H column, λ=254 nm, eluent: hexane/2-propanol=80/20, flow rate: 0.9 mL/min): t_R=11.41 min (minor), 18.44 min (major).

*4.2.9. (R,E)-tert-Butyl (3-(cinnamyloxy)-1-methyl-2-oxoindolin-3-yl) carbamate (**3j**).* Semi-solid, 94% yield, 74% ee; $[\alpha]_D^{20}$ +25.7 (*c* 2.62, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.61 (d, *J*=7.2 Hz, 1H), 7.42–7.37 (m, 3H), 7.32–7.29 (m, 2H), 7.24–7.21 (m, 1H), 7.13–7.09 (m, 1H), 7.00 (d, *J*=8.0 Hz, 1H), 6.55 (d, *J*=12.0 Hz, 1H), 6.25 (dt, *J*=12.0, 6.0 Hz, 1H), 4.33–4.23 (m, 2H), 3.18 (s, 9H), 3.13 (s, 1H), 1.27 (s, 9H); ^{13}C NMR (100 MHz, acetone-d_6): δ 172.7, 154.3, 145.2, 137.7, 132.8, 131.3, 129.5, 128.5, 128.1, 127.3, 126.5, 125.6, 123.4, 109.4, 85.1, 80.2, 65.4, 28.4, 26.4; IR (KBr, cm^{-1}): ν 3232, 3120, 2982, 1730, 2378, 1703, 1616, 1473, 1373, 1248, 1055, 752, 692; HRMS (ESI) calcd for $C_{23}H_{26}N_2O_4Na$ ($[M+Na]^+$): 395.1971, found: 395.1920; HPLC analysis (AS-H column, λ=254 nm, eluent: hexane/2-propanol=90/10, flow rate: 0.9 mL/min): t_R=10.87 min (minor), 12.13 min (major).

*4.2.10. (R)-tert-Butyl (1-methyl-2-oxo-3-(prop-2-yn-1-yloxy) indolin-3-yl)carbamate (**3k**).* White solid, 91% yield, 56% ee, mp 92.2–93.5 °C; $[\alpha]_D^{20}$ +25.4 (*c* 2.77, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.62 (d, *J*=7.2 Hz, 1H), 7.40 (td, *J*=8.0, 1.2 Hz, 1H), 7.12–7.08 (m, 1H), 7.01 (d, *J*=8.0 Hz, 1H), 4.46 (dd, *J*=15.2, 2.4 Hz, 1H), 7.35 (dd, *J*=15.2, 2.4 Hz, 1H), 3.19 (s, 3H), 3.14 (s, 1H), 2.93 (t, *J*=2.4 Hz, 1H), 1.28 (s, 9H); ^{13}C NMR (100 MHz, acetone-d_6): δ 172.0, 154.2, 144.9, 131.4, 127.6, 125.7, 123.4, 109.4, 84.6, 80.3, 76.0, 52.5, 30.6, 28.2, 26.3; IR (KBr, cm^{-1}): ν 3294, 2979, 2937, 2125, 1724, 1616, 1473, 1373, 1250, 1161, 1092, 1055, 754; HRMS (ESI) calcd for $C_{17}H_{20}N_2O_4Na$ ($[M+Na]^+$): 339.1321, found: 339.1317; HPLC analysis (AD-H column, λ=254 nm, eluent: hexane/2-propanol=80/20, flow rate: 0.9 mL/min): t_R=34.67 min (minor), 37.55 min (major).

*4.2.11. (R)-tert-Butyl (3-ethoxy-1,5-dimethyl-2-oxoindolin-3-yl) carbamate (**3l**).* White solid, 90% yield, 77% ee, mp 109.0–111.6 °C;

$[\alpha]_D^{20}$ +4.21 (*c* 1.95, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.21 (s, 1H), 7.05 (d, *J*=7.6 Hz, 1H), 6.73 (d, *J*=7.6 Hz, 1H), 3.47–3.35 (m, 2H), 3.02 (s, 3H), 2.94 (s, 1H), 2.18 (s, 3H), 1.11 (s, 9H), 0.93 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6): δ 172.7, 154.2, 142.8, 132.6, 131.23, 128.4, 126.0, 109.0, 85.3, 80.0, 60.0, 28.3, 26.3, 21.1, 15.5; IR (KBr, cm^{-1}): ν 3425, 2979, 1732, 1624, 1504, 1398, 1369, 1250, 1167, 1101, 422; HRMS (ESI) calcd for $C_{17}H_{24}N_2O_4Na$ ($[M+Na]^+$): 343.1634, found: 343.1637; HPLC analysis (AD-H column, λ=254 nm, eluent: hexane/2-propanol=90/10, flow rate: 0.9 mL/min): t_R=13.06 min (minor), 36.96 min (major).

*4.2.12. (R)-tert-Butyl (3-ethoxy-5-fluoro-1-methyl-2-oxoindolin-3-yl)carbamate (**3m**).* White solid, 98% yield, 77% ee, mp 108.5–109.7 °C; $[\alpha]_D^{20}$ +26.8 (*c* 2.77, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.38 (d, *J*=7.6 Hz, 1H), 7.17 (td, *J*=8.4, 2.4 Hz, 1H), 7.03–7.00 (m, 1H), 3.65–3.53 (m, 2H), 3.17 (s, 3H), 3.10 (s, 1H), 1.28 (s, 9H), 1.09 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6): δ 172.5, 161.1, 158.8, 154.3, 141.2, 130.1 (d, *J*=7.5 Hz), 117.1 (d, *J*=23.4 Hz), 113.4 (d, *J*=25.9 Hz), 110.3 (d, *J*=7.9 Hz), 85.1, 80.3, 60.2, 28.3, 26.5, 15.5; IR (KBr, cm^{-1}): ν 3300, 2982, 2931, 2461, 1728, 1678, 1497, 1271, 1111, 868, 808, 554; HRMS (ESI) calcd for $C_{16}H_{21}FN_2O_4Na$ ($[M+Na]^+$): 347.1383, found: 347.1387; HPLC analysis (AD-H column, λ=254 nm, eluent: hexane/2-propanol=90/10, flow rate: 0.9 mL/min): t_R=11.69 min (minor), 29.21 min (major).

*4.2.13. (R)-tert-Butyl (5-chloro-3-ethoxy-1-methyl-2-oxoindolin-3-yl)carbamate (**3n**).* White solid, 97% yield, 76% ee, mp 117.7–119.2 °C; $[\alpha]_D^{20}$ +3.90 (*c* 3.23, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.42 (s, 1H), 7.27 (dd, *J*=8.4, 2.4 Hz, 1H), 6.90 (d, *J*=8.4 Hz, 1H), 3.46 (m, 2H), 3.06 (s, 3H), 2.97 (s, 1H), 1.14 (s, 9H), 0.95 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6): δ 172.3, 154.3, 143.9, 130.9, 130.4, 128.2, 125.6, 110.8, 85.0, 80.4, 60.2, 28.3, 26.5, 15.5; IR (KBr, cm^{-1}): ν 3431, 2981, 2939, 1736, 1614, 1493, 1367, 1261, 1165, 1105, 1057, 689; HRMS (ESI) calcd for $C_{16}H_{22}ClN_2O_4$ ($[M+H]^+$): 341.1268, found: 341.1266; HPLC analysis (AD-H column, λ=254 nm, eluent: hexane/2-propanol=90/10, flow rate: 0.9 mL/min): t_R=14.75 min (minor), 28.43 min (major).

*4.2.14. (R)-tert-Butyl (5-bromo-3-ethoxy-1-methyl-2-oxoindolin-3-yl)carbamate (**3o**).* White solid, 95% yield, 74% ee, mp 100.6–101.3 °C; $[\alpha]_D^{20}$ +3.33 (*c* 3.15, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.68 (s, 1H), 7.56 (dd, *J*=8.4, 2.4 Hz, 1H), 6.99 (d, *J*=8.4 Hz, 1H), 3.66–3.54 (m, 2H), 3.19 (s, 3H), 3.13 (s, 1H), 1.28 (s, 9H), 1.09 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6): δ 172.2, 154.2, 144.3, 133.7, 130.6, 128.2, 115.3, 111.2, 84.8, 80.3, 60.2, 28.3, 26.4, 15.4; IR (KBr, cm^{-1}): ν 3284, 2978, 2931, 1740, 1686, 1608, 1491, 1367, 1115, 1020, 878, 812, 532; HRMS (ESI) calcd for $C_{16}H_{21}BrN_2O_4Na$ ($[M+Na]^+$): 407.0582, found: 407.0581; HPLC analysis (AD-H column, λ=254 nm, eluent: hexane/2-propanol=90/10, flow rate: 0.9 mL/min): t_R=15.18 min (minor), 27.68 min (major).

*4.2.15. (R)-tert-Butyl (6-chloro-3-ethoxy-1-methyl-2-oxoindolin-3-yl)carbamate (**3p**).* White solid, 98% yield, 78% ee, mp 131.4–131.7 °C; $[\alpha]_D^{20}$ +29.9 (*c* 3.15, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.37 (d, *J*=8.0 Hz, 1H), 6.97 (dd, *J*=8.0, 1.6 Hz, 1H), 6.94 (d, *J*=1.6 Hz, 1H), 3.50–3.38 (m, 2H), 3.07 (s, 3H), 2.92 (s, 1H), 1.13 (s, 9H), 0.94 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6): δ 172.7, 154.2, 146.7, 136.2, 127.2, 126.5, 122.9, 109.9, 84.8, 80.3, 60.3, 28.3, 26.5, 15.5; IR (KBr, cm^{-1}): ν 3336, 2981, 2935, 1741, 1614, 1496, 1371, 1242, 1074, 905, 820, 733; HRMS (ESI) calcd for $C_{16}H_{22}ClN_2O_4$ ($[M+H]^+$): 341.1268, found: 341.1270; HPLC analysis (AD-H column, λ=254 nm, eluent: hexane/2-propanol=90/10, flow rate: 0.9 mL/min): t_R=13.31 min (minor), 16.79 min (major).

*4.2.16. (R)-tert-Butyl (6-bromo-3-ethoxy-1-methyl-2-oxoindolin-3-yl) carbamate (**3q**).* White solid, 92% yield, 77% ee, mp 135.6–127.7 °C; $[\alpha]_D^{20}$ +11.8 (*c* 2.42, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.44 (d, *J*=8.0 Hz, 1H), 7.27 (dd, *J*=8.0, 1.6 Hz, 1H), 7.21 (d, *J*=1.6 Hz, 1H), 3.64–3.51 (m, 2H), 3.21 (s, 3H), 3.12 (s, 1H), 1.27 (s, 9H), 1.07 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6): δ 172.6, 154.2, 146.7, 127.6, 126.8, 126.0, 124.2, 112.7, 84.8, 80.3, 60.2, 28.3, 26.5, 15.5; IR (KBr, cm^{-1}): ν 3329, 2978, 1739, 1682, 1608, 1496, 1371, 1290, 1111, 1066, 1020, 895, 717; HRMS (ESI) calcd for $C_{16}H_{21}BrN_2O_4K$ ($[M+K]^+$): 423.0322, found: 423.0320; HPLC analysis (AD-H column, λ=254 nm, eluent: hexane/2-propanol=90/10, flow rate: 0.9 mL/min): t_R=13.10 min (minor), 16.53 min (major).

*4.2.17. (R)-tert-Butyl (3-ethoxy-7-fluoro-1-methyl-2-oxoindolin-3-yl)carbamate (**3r**).* White solid, 93% yield, 69% ee, mp 80.1–81.2 °C; $[\alpha]_D^{20}$ +16.8 (*c* 2.64, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.18 (d. *J*=7.2 Hz, 1H), 7.08–7.03 (m, 1H), 6.98–6.93 (m, 1H), 3.49–3.38 (m, 2H), 3.24 (d, *J*=2.8 Hz, 3H), 2.93 (s, 1H), 1.22 (s, 1H), 0.93 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6): δ 172.6, 154.2, 149.7, 147.3, 131.6 (t, *J*=10.5 Hz), 124.2 (d, *J*=6.2 Hz), 121.1, 118.9 (d, *J*=19.5 Hz), 85.1, 80.3, 60.2, 28.9 (d, *J*=5.6 Hz), 28.3, 15.5; IR (KBr, cm^{-1}): ν 3333, 2976, 1736, 1633, 1481, 1369, 1292, 1240, 1053, 879, 781, 731, 561; HRMS (ESI) calcd for $C_{16}H_{21}FN_2O_4K$ ($[M+K]^+$): 363.1122, found: 363.1118; HPLC analysis (AD-H column, λ=254 nm, eluent: hexane/2-propanol=90/10, flow rate: 0.9 mL/min): t_R=13.11 min (minor), 28.47 min (major).

*4.2.18. (R)-tert-Butyl (7-chloro-3-ethoxy-1-methyl-2-oxoindolin-3-yl)carbamate (**3s**).* White solid, 96% yield, 63% ee, mp 103.1–104.2 °C; $[\alpha]_D^{20}$ +28.0 (*c* 3.15, CH_2Cl_2); ^1H NMR (400 MHz, d_6-acetone): δ 7.28 (d, *J*=7.2 Hz, 1H), 7.21 (dd, *J*=8.0, 1.2 Hz, 1H), 6.97–6.93 (m, 1H), 3.46–3.40 (m, 5H), 2.94 (s, 1H), 1.11 (s, 9H), 0.93 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6): δ 173.1, 154.1, 140.9, 133.1, 124.6, 123.7, 115.9, 84.6, 80.3, 60.3, 29.8, 28.3, 15.5; IR (KBr, cm^{-1}): ν 3271, 2978, 2931, 2887, 1722, 1608, 1466, 1165, 1134, 1053, 878, 789, 627; HRMS (ESI) calcd for $C_{16}H_{21}ClN_2O_4Na$ ($[M+Na]^+$): 363.1088, found: 363.1089; HPLC analysis (AD-H column, λ=254 nm, eluent: hexane/2-propanol=90/10, flow rate: 0.9 mL/min): t_R=13.05 min (minor), 32.95 min (major).

*4.2.19. (R)-tert-Butyl (3-ethoxy-1,7-dimethyl-2-oxoindolin-3-yl) carbamate (**3t**).* White solid, 94% yield, 65% ee, mp 104.5–105.7 °C; $[\alpha]_D^{20}$ +15.8 (*c* 2.99, CH_2Cl_2); ^1H NMR (400 MHz, acetone-d_6): δ 7.31 (d, *J*=7.2 Hz, 1H), 7.11 (d, *J*=7.6 Hz, 1H), 6.98–6.94 (m, 1H), 3.56–3.49 (m, 2H), 3.46 (s, 3H), 3.13 (s, 1H), 2.58 (s, 3H), 1.25 (s, 9H), 1.05 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6): δ 173.5, 154.2, 142.8, 134.7, 129.2, 123.3, 122.9, 120.8, 84.6, 80.0, 59.9, 29.8, 28.3, 19.1, 15.5; IR (KBr, cm^{-1}): ν 3306, 2978, 2465, 1682, 1606, 1504, 1363, 1296, 1176, 1122, 858, 771, 764; HRMS (ESI) calcd for $C_{17}H_{24}N_2O_4Na$ ($[M+Na]^+$): 343.1634, found: 343.1637; HPLC analysis (AD-H column, λ=254 nm, eluent: hexane/2-propanol=90/10, flow rate: 0.9 mL/min): t_R=18.25 min (minor), 50.32 min (major).

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.06.076.

References and notes

1. For examples, see: (a) Perry, N. B.; Blunt, J. W.; Munro, M. H. G.; Pannell, L. K. *J. Am. Chem. Soc.* **1988**, *110*, 4850–4851; (b) Sakemi, S.; Ichiba, T.; Kohmoto, S.;

Saucy, G.; Higa, T. *J. Am. Chem. Soc.* **1988**, *110*, 4851–4853; (c) Fusetani, N.; Sugawara, T.; Matsunaga, S. *J. Org. Chem.* **1992**, *57*, 3828–3832; (d) Tanaka, J.-I.; Higa, T. *Tetrahedron Lett.* **1996**, *37*, 5535–5538; (e) Cichewicz, R. H.; Valeriote, F. A.; Crews, P. *Org. Lett.* **2004**, *6*, 1951–1954; (f) Pettit, G. R.; Xu, J.-P.; Chapuis, J.-C.; Pettit, R. K.; Tackett, L. P.; Doubek, D. L.; Hooper, J. N. A.; Schmidt, J. M. *J. Med. Chem.* **2004**, *47*, 1149–1152; (g) Gao, H.; Liu, W.; Zhu, T.; Mo, X.; Mandi, A.; Kurtan, T.; Li, J.; Ai, J.; Gu, Q.; Li, D. *Org. Biomol. Chem.* **2012**, *10*, 9501–9506.

2. For a review on the application of *N*,*O*-aminals, see: Warriner, S. *Category 4: Compounds with Two Carbon-heteroatom Bonds in Science of Synthesis: Houben-Weyl Methods of Molecular Transformations*; Georg Thieme: Stuttguart, 2007; Vol. 30, pp 7–46.
3. For selected references of the non-stereoselective synthesis of *N*,*O*-aminals, see: (a) Huang, X.; Shao, N.; Palani, A.; Aslanian, R. *Tetrahedron Lett.* **2007**, *48*, 1967–1971; (b) Kiren, S.; Shangguan, N.; Williams, L. J. *Tetrahedron Lett.* **2007**, *48*, 7456–7459; (c) Wan, S.; Green, M. E.; Park, J.-H.; Floreancig, P. E. *Org. Lett.* **2007**, *9*, 5385–5388; (d) Fujioka, H.; Kubo, O.; Senami, K.; Okamoto, K.; Okitsu, T.; Kita, Y. *Heterocycles* **2009**, *79*, 1113–1120; (e) Yin, P.; Ma, W.-B.; Chen, Y.; Huang, W.-C.; Deng, Y.; He, L. *Org. Lett.* **2009**, *11*, 5482–5485; (f) Downey, C. W.; Fleisher, A. S.; Rague, J. T.; Safran, C. L.; Venable, M. E.; Pike, R. D. *Tetrahedron Lett.* **2011**, *52*, 4756–4759; (g) Naud, S.; Macnaughton, S. J.; Dyson, B. S.; Woollaston, D. J.; Dallimore, J. W. P.; Robertson, J. *Org. Biomol. Chem.* **2012**, *10*, 3506–3518.
4. For the catalytic asymmetric synthesis of chiral *N*,*O*-aminals, see: (a) Li, G.; Fronczek, F. R.; Antilla, J. C. *J. Am. Chem. Soc.* **2008**, *130*, 12216–12217; (b) Vellalath, S.; Coric, I.; List, B. *Angew. Chem., Int. Ed.* **2010**, *49*, 9749–9752; (c) Kim, H.; Rhee, Y. H. *J. Am. Chem. Soc.* **2012**, *134*, 4011–4014; (d) Zhou, F.; Zeng, X.-P.; Wang, C.; Zhao, X.-L.; Zhou, J. *Chem. Commun.* **2013**, *49*, 2022–2024.
5. Christoffers, J.; Baro, A. *Quaternary Stereocentres: Challenges and Solutions for Organic Synthesis*; Wiley-VCH: Weinheim. 2005.
6. For reviews, see: (a) Hibino, S.; Choshi, T. *Nat. Prod. Rep.* **2001**, *18*, 66–87; (b) Lin, H.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 36–51; (c) Marti, C.; Carreira, E. M. *Eur. J. Org. Chem.* **2003**, 2209–2219; (d) Galliford, C. V.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 8748–8758; (e) Peddibhotla, S. *Curr. Bioact. Compd.* **2009**, *5*, 20–38.
7. For reviews, see: (a) Zhou, F.; Liu, Y.-L.; Zhou, J. *Adv. Synth. Catal.* **2010**, *352*, 1381–1407; (b) Klein, J.; Taylor, R. J. K. *Eur. J. Org. Chem.* **2011**, 6821–6841; (c) Dalpozzo, R.; Bartoli, G.; Bencivenni, G. *Chem. Soc. Rev.* **2012**, *41*, 7247–7290; (d) Shen, K.; Liu, X.; Lin, L.; Feng, X. *Chem. Sci.* **2012**, *3*, 327–334.
8. For diastereoselective approaches using chiral auxiliaries, see: (a) Lesma, G.; Landoni, N.; Pilati, T.; Sacchetti, A.; Silvani, A. *J. Org. Chem.* **2009**, *74*, 4537–4541; (b) Jung, H. H.; Buesking, A. W.; Ellman, J. A. *Org. Lett.* **2011**, *13*, 3912–3915; (c) Yan, W.; Wang, D.; Feng, J.; Li, P.; Wang, R. *J. Org. Chem.* **2012**, *77*, 3311–3317.
9. For selected catalytic asymmetric α-amination, see: (a) Cheng, L.; Liu, L.; Wang, D.; Chen, Y.-J. *Org. Lett.* **2009**, *11*, 3874–3877; (b) Qian, Z.-Q.; Zhou, F.; Du, T.-P.; Wang, B.-L.; Ding, M.; Zhao, X.-L.; Zhou, J. *Chem. Commun.* **2009**, 6753–6755; (c) Bui, T.; Hernandez-Torres, G.; Milite, C.; Barbas, C. F. *Org. Lett.* **2010**, *12*, 5696–5699; (d) Mouri, S.; Chen, Z.; Mitsunuma, H.; Furutachi, M.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2010**, *132*, 1255–1257; (e) Yang, Z.; Wang, Z.; Bai, S.; Shen, K.; Chen, D.; Liu, X.; Lin, L.; Feng, X. *Chem.—Eur. J.* **2010**, *16*, 6632–6637; (f) Shen, K.; Liu, X.; Wang, G.; Lin, L.; Feng, X. *Angew. Chem., Int. Ed.* **2011**, *50*, 4684–4688.
10. (a) Yan, W.; Wang, D.; Feng, J.; Li, P.; Zhao, D.; Wang, R. *Org. Lett.* **2012**, *14*, 2512–2515; (b) Feng, J.; Yan, W.; Wang, D.; Li, P.; Sun, Q.; Wang, R. *Chem. Commun.* **2012**, *48*, 8003–8005; (c) Hara, N.; Nakamura, S.; Sano, M.; Tamura, R.; Funahashi, Y.; Shibata, N. *Chem.—Eur. J.* **2012**, *18*, 9276–9280; (d) Lv, H.; Tiwari, B.; Mo, J.; Xing, C.; Chi, Y. R. *Org. Lett.* **2012**, *14*, 5412–5415; (e) Hu, F.-L.; Wei, Y.; Shi, M.; Pindi, S.; Li, G. *Org. Biomol. Chem.* **2013**, *11*, 1921–1924; (f) Chauhan, P.; Chimni, S. S. *Tetrahedron: Asymmetry* **2013**, *24*, 343–356.
11. For selected reviews on bifunctional catalysis, see: (a) Connon, S. J. *Chem. Commun.* **2008**, 2499–2510; (b) Takemoto, Y. *Chem. Pharm. Bull.* **2010**, *58*, 593–601; (c) Lu, L. Q.; An, X. L.; Chen, J. R.; Xiao, W. J. *Synlett* **2012**, 490–508.
12. Wang, S.-X.; Chen, F.-E. *Adv. Synth. Catal.* **2009**, *351*, 547–552.
13. (a) Vakulya, B.; Varga, S.; Csámpai, A.; Soós, T. *Org. Lett.* **2005**, *7*, 1967–1969; (b) Shi, M.; Lei, Z.-Y.; Zhao, M.-X.; Shi, J.-W. *Tetrahedron Lett.* **2007**, *48*, 5743–5746; (c) Yang, W.; Du, D.-M. *Org. Lett.* **2010**, *12*, 5450–5453; (d) Li, W.; Wu, W.; Yu, F.; Huang, H.; Liang, X.; Ye, J. *Org. Biomol. Chem.* **2011**, *9*, 2505–2511.