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PAPER

Asymmetric substitutions of O-Boc-protected Morita–Baylis–Hillman adducts with pyrrole and indole derivatives†

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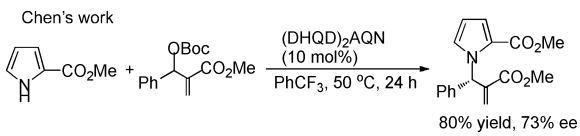
An efficient asymmetric substitution process of O-Boc-protected Morita–Baylis–Hillman adducts with various pyrrole and indole derivatives has been developed in the presence of $(DHQD)_2PYR$ in THF, affording the corresponding products in good to high yields (up to 99% yield) and moderate to high ee values (up to 92 and 96% ee) under mild conditions.

Introduction

Recently, asymmetric substitutions of Morita–Baylis–Hillman (MBH) acetates or carbonates using cinchona alkaloid derived organocatalysts have attracted much attention because this asymmetric synthetic protocol can overcome the shortages in the direct catalytic asymmetric MBH reactions in terms of substrate scope and catalytic efficiency as well as chiral induction.[1–4] In this respect, Lu[5a] and Hiemstra[5b] first independently reported (4-(3-ethyl-4-oxa-1-azatricyclo[4,4,0,$0^{3,8}$]dec-5-yl)-quinolin-6-ol (also called as β-isocupreidine) (β-ICD) catalyzed asymmetric substitution of MBH carbonates with various nucleophiles, affording the corresponding amination products in excellent yields along with modest ee values, respectively. Moreover, Chen and co-workers have recently used hydroquindine-(anthraquinone-1,4-diyl) diether ($(DHQD)_2AQN$), hydroquindine-1,4-phthalazinediyl diether ($(DHQD)_2PHAL$), hydroquinidine-2,5-diphenyl-4,6-pyrimidinediyl diether ($(DHQD)_2PYR$), and β-isocupreidine (β-ICD) in asymmetric substitutions of MBH carbonates to achieve C–C bond,[6a–6d] C–N bond[6e,6f] and C–O bond[6g,6h] formation in good yields along with high enantioselectivities under mild conditions. More recently, Wang's group also reported using cinchona alkaloids as catalysts to construct chiral allylic phosphine oxides through substitution of MBH carbonates in excellent yields along with high enantioselectivities.[7] Previously, Chen and co-workers reported that the asymmetric substitution of O-Boc-protected Morita–Baylis–Hillman adduct with methyl pyrrole-2-carboxylate provided the desired N-allylic alkylation product in 80% yield with 73% ee in the presence of $(DHQD)_2AQN$ (10 mol%) (eqn (1)).[6f] In this paper, we wish to disclose that if using 1*H*-pyrrole-2-carbonitrile instead of methyl pyrrole-2-carboxylate in the asymmetric substitution of O-Boc-protected Morita–Baylis–Hillman adducts, the corresponding products can be obtained in good yields (up to 92% yield) and high ee values (up to 92% ee) in the presence of $(DHQD)_2PYR$ under mild conditions (10 mol%) (eqn (2)).



(1)

(2)

Results and discussion

Initially, we utilized multifunctional cinchona alkaloid β-isocupreidine (β-ICD)[1k,8] (10 mol%) as the chiral catalyst to examine the reaction outcome of *tert*-butyl 2-methylene-1-(4-chlorophenyl)-3-oxobutyl carbonate **2a** (1.0 equiv) with 1*H*-pyrrole-2-carbonitrile **1a** (1.2 equiv) in tetrahydrofuran (THF) and found that the corresponding substitution product **3a** was obtained in 68% yield along with 2% ee at room temperature (25 °C) (Table 1, entry 1). We next turned our attention to screening other multifunctional cinchona alkaloids, cat. **1a–1e** and cat. **2a–2c** derived from β-ICD, in this reaction and found that the desired product **3a** was produced in 77–91% yields along with low ee values (4–20%) (Table 1, entries 2–9). Then, we found **3a** could be obtained in higher ee values (31–41%) in good yields (84–97%) in the presence of cat. **3a–3c** (Table 1, entries 10–12). Using $(DHQ)_2PHAL$, $(DHQ)_2PYR$ and $(DHQ)_2PYDZ$ as the catalysts afforded **3a** in 70–99% yields along with 38–40% ee values (Table 1, entries 13–15), while $(DHQD)_2PHAL$, $(DHQD)_2PYR$ and $(DHQD)_2PYDZ$ could afford **3a** in 34–98% yields along with

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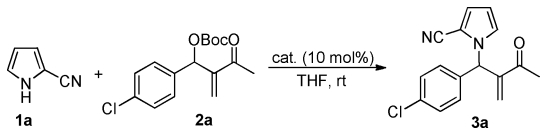
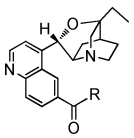
† Electronic supplementary information (ESI) available: Experimental procedures, NMR charts for all compounds and X-ray crystal data of **3h**. CCDC reference numbers 812598. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1ob06671d

Table 1 Screening of cinchona alkaloid organocatalysts for the asymmetric substitution of O-Boc-protected Morita–Baylis–Hillman adduct **2a** with **1a**

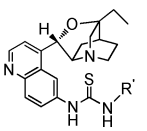


Entry[a]	Catalyst	*t* [h]	Yield [%][b]	ee [%][c]
1	**β-ICD**	48	68	–2
2	**cat. 1a**	48	78	–10
3	**cat. 1b**	48	82	–20
4	**cat. 1c**	48	87	–17
5	**cat. 1d**	48	91	–17
6	**cat. 1e**	48	93	–15
7	**cat. 2a**	48	77	–20
8	**cat. 2b**	48	87	–5
9	**cat. 2c**	48	91	–4
10	**cat. 3a**	1	85	–32
11	**cat. 3b**	1	84	–31
12	**cat. 3c**	1	97	–41
13	**(DHQ)$_2$PHAL**	48	70	–38
14	**(DHQ)$_2$PYR**	48	89	–60
15	**(DHQ)$_2$PYDZ**	48	99	–44
16	**(DHQD)$_2$PHAL**	48	62	39
17	**(DHQD)$_2$PYR**	48	98	80
18	**(DHQD)$_2$PYDZ**	48	34	41

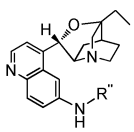
[a] Reactions were performed with **1a** (0.12 mmol), **2a** (0.10 mmol) and 10 mol% of catalyst in solvent (1.00 mL) at room temperature. [b] Yield of isolated product. [c] Determined by HPLC on a chiral stationary phase.



cat. 1a: R = NH_2
cat. 1b: R = NHPh
cat. 1c: R = NHMe
cat. 1d: R = OH
cat. 1e: R = OMe



cat. 2a: R′ = C_6H_5
cat. 2b: R′ = $CH_2C_6H_5$
cat. 2c: R′ = 3,5-$(CF_3)_2C_6H_3$



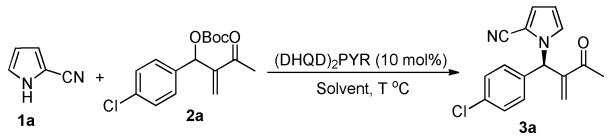
cat. 3a: R″ = H
cat. 3b: R″ = C_6H_5
cat. 3c: R″ = 3,5-$(MeO)_2C_6H_3$

39–80% ee values along with the opposite absolute configuration as those of (DHQ)$_2$PHAL, (DHQ)$_2$PYR and (DHQ)$_2$PYDZ since they are pseudo-enantiomers (Table 1, entries 16–18). In brief, (DHQD)$_2$PYR gave the best result under identical conditions.

Examination of solvent effects using (DHQD)$_2$PYR as the catalyst revealed that THF, 1,2-dichloroethane (DCE) and ethyl acetate (EtOAc) were the solvents of choice for this reaction (Table 2, entries 1–8). Lowering the reaction temperature to 0 °C in THF afforded **3a** in 92% yield along with 92% ee (Table 2, entry 9). Carrying out the reaction at 0 °C in DCE and EtOAc produced **3a** in 91% yield along with 90% ee and 80% yield along with 89% ee, respectively (Table 2, entries 10 and 11). Increasing the employed amounts of (DHQD)$_2$PYR to 15 mol% and **1a** to 2.0 equiv provided **3a** in 95% yield along with 90% ee within 72 h in 0.5 mL of THF (Table 2, entry 13). Examination of reaction temperatures under these reaction conditions indicated that the reaction should be carried out at 0 °C and the ee of **3a** could be improved at –10 °C (Table 2, entries 14–15).

Having identified the optimal conditions, we next examined the generality of this reaction with various O-Boc-protected MBH adducts **2**, and the results are summarized in Table 3. For substrates **2b–2p** bearing electron-withdrawing groups or

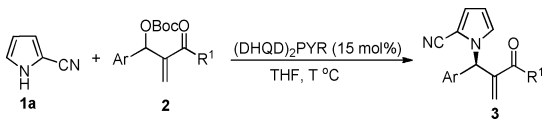
Table 2 Optimization of the reaction conditions using (DHQD)$_2$PYR as the catalyst



Entry[a]	Solvent	*t* [h]	*T* [°C]	Yield [%][b]	ee [%][c]
1	THF	48	*rt*	98	80
2	DCM	48	*rt*	89	82
3	DCE	48	*rt*	92	82
4	toluene	48	*rt*	99	75
5	$CHCl_3$	72	*rt*	97	74
6	dioxane	96	*rt*	82	67
7	DMSO	48	*rt*	89	81
8	EtOAc	72	*rt*	92	85
9	THF	168	0	92	92
10	DCE	144	0	91	90
11	EtOAc	168	0	80	89
12[d]	THF	96	0	93	90
13[d,e]	THF	72	0	95	90
14[d,e]	THF	96	–10	81	92
15[d,e]	THF	24	40	96	83

[a] Unless otherwise noted, reactions were performed with **1a** (0.12 mmol), **2a** (0.10 mmol), and 10 mol% of catalyst in solvent (1.00 mL). [b] Yield of isolated product. [c] Determined by HPLC on a chiral stationary phase. [d] Reactions were performed with **1a** (0.20 mmol), **2a** (0.10 mmol) and 10 mol% of catalyst in solvent (0.50 mL). [e] With 15 mol% catalyst.

Table 3 Substrate scope in the (DHQD)$_2$PYR-catalyzed asymmetric substitution of O-Boc-protected Morita–Baylis–Hillman adducts **2** with **1a**



Entry[a]	**2**	R^1	Ar	*t* [h]	*T* [°C]	yield [%][b]	ee [%][c]
1	**2b**	Me	4-FC_6H_4	96	0	**3b**, 78	82
2	**2c**	Me	4-$CF_3C_6H_4$	110	–10	**3c**, 91	88
3	**2d**	Me	3-ClC_6H_4	100	–10	**3d**, 88	85
4	**2e**	Me	2-ClC_6H_4	100	–10	**3e**, 95	89
5	**2f**	Me	3,4-$Cl_2C_6H_3$	72	0	**3f**, 91	90
6	**2g**	Me	2,3-$Cl_2C_6H_3$	48	0	**3g**, 90	91
7	**2h**	Me	4-BrC_6H_4	72	0	**3h**, 82	91
8	**2i**	Me	3-BrC_6H_4	72	0	**3i**, 97	84
9	**2j**	Me	2-BrC_6H_4	72	0	**3j**, 95	83
10	**2k**	Me	4-$NO_2C_6H_4$	96	–10	**3k**, 99	92
11	**2l**	Me	3-$NO_2C_6H_4$	110	–10	**3l**, 84(89)[d]	78 (60)[d]
12	**2m**	Me	4-CNC_6H_4	72	–10	**3m**, 99	88
13	**2n**	Me	C_6H_5	110	–10	**3n**, 68(88)[d]	82 (79)[d]
14	**2o**	Me	4-MeC_6H_4	100	0	**3o**, 80	76
15	**2p**	Me	2-$MeOC_6H_4$	100	–10	**3p**, 93	88
16	**2q**	Me	2-furyl	48	0	**3q**, 89	39
17	**2r**	Me	2-thienyl	72	0	**3r**, 75	62
18	**2s**	Et	4-$NO_2C_6H_4$	120	–10	**3s**, 61(80)[d]	92 (90)[d]
19	**2t**	OMe	4-ClC_6H_4	120	*rt*	**3t**, 73	83

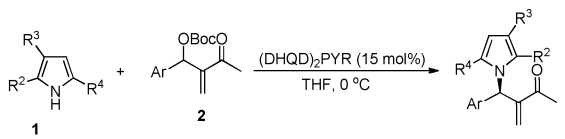
[a] Reactions were performed with **1** (0.20 mmol), **2**(0.10 mmol) and 15 mol% of catalyst in solvent (0.50 mL). [b] Yield of isolated product. [c] Determined by HPLC on a chiral stationary phase. [d] Reactions were carried out at 0 °C.

electron-donating groups on their aromatic rings, the asymmetric substitution reactions with **1a** proceeded smoothly to give the corresponding products **3b–3p** in 68–99% yields along with

60–92% ee at 0 °C or −10 °C, suggesting that the electronic property of substituents at the aromatic rings of **2** did not have a significant impact on the reaction outcomes (Table 3, entries 1–15). Only in the case of substrate **2l** having a 3-nitrophenyl group, the desired product **3l** was formed in 89% yield along with 60% ee at 0 °C in THF (Table 3, entry 11). Furthermore, in the asymmetric substitution reaction of O-Boc-protected MBH adducts **2q** and **2r** having heteroaromatic groups, the corresponding products **3q** and **3r** were obtained in good yields along with moderate ee values (39% ee and 62% ee), presumably due to the electronic property of the heteroaromatic ring of MBH adducts (Table 3, entries 16 and 17). Using substrates **2s** and **2t**, in which R^1 = Et and OMe, in this reaction also afforded the desired products **3s** and **3t** in 61% yield along with 92% ee at 0 °C and 73% yield along with 83% ee at room temperature, respectively (Table 3, entries 18 and 19). Carrying out the reaction of **2s** with **1a** at −10 °C could improve the ee value of **3s** but along with a sacrifice in yield, presumably due to the steric effect of the ethyl group in MBH adduct **2** and the electronic properties of the OMe group in MBH adduct **2**, respectively (Table 3, entry 18).

We next attempted to use various pyrrole derivatives including 4-(2-phenylacetyl)-1*H*-pyrrole-2-carbonitrile **1b**, 4-acetyl-1*H*-pyrrole-2-carbonitrile **1c**, 2,2,2-trichloro-1-(1*H*-pyrrol-2-yl)-ethanone **1d**, 1-(4-bromo-1*H*-pyrrol-2-yl)-2,2,2-trichloro-ethanone **1e**, 1*H*-pyrrole-2,4-dicarbonitrile **1f** and 1*H*-pyrrole-2-carbaldehyde **1g** in this reaction and the results of these experiments are summarized in Table 4. Base on the relatively better results obtained from Table 3, we focused on the use of *p*-substituted substrates in this reaction. As can be seen from Table 4, these reactions proceeded smoothly to give the desired products **4a–4j** in good yields with good to high ee values (up to

Table 4 $(DHQD)_2PYR$-catalyzed asymmetric substitution of O-Boc-protected Morita–Baylis–Hillman Adducts **2** with various pyrrole derivatives **1**

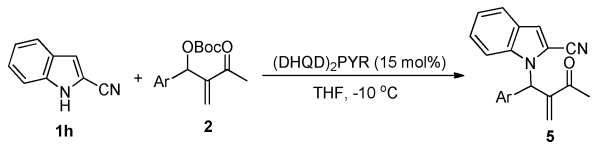


1b, R^2 = H, R^3 = BnCO, R^4 = CN;
1c, R^2 = H , R^3 = Ac, R^4 = CN;
1d, R^2 = R^3 = H, R^4 = $COCCl_3$;
1e, R^2 = H, R^3 = Br, R^4 = $COCCl_3$;
1f, R^2 = H, R^3 = R^4 = CN;
1g, R^2 = R^3 = H, R^4 = CHO.

Entry[a]	1	Ar	*t* [h]	Yield [%][b]	ee [%][c]
1	**1b**	4-ClC_6H_4, **2a**	100	**4a**, 75	96
2	**1b**	4-FC_6H_4, **2b**	100	**4b**, 70	91
3	**1b**	4-$CF_3C_6H_4$, **2c**	100	**4c**, 46	91
4	**1b**	4-BrC_6H_4, **2h**	100	**4d**, 77	94
5	**1b**	4-$NO_2C_6H_4$, **2j**	100	**4e**, 63	93
6	**1b**	C_6H_5, **2m**	100	**4f**, 58	89
7	**1c**	4-ClC_6H_4, **2a**	100	**4g**, 76	94
8	**1d**	4-ClC_6H_4, **2a**	72	**4h**, 83	90
9	**1e**	4-ClC_6H_4, **2a**	72	**4i**, 71	84
10	**1f**	4-ClC_6H_4, **2a**	100	**4j**, 84	85
11	**1g**	4-ClC_6H_4, **2a**	100	**4k**, 70	92

[a] Reactions were performed with **1** (0.20 mmol), **2** (0.10 mmol) and 15 mol% of catalyst in THF (0.50 mL) at 0 °C. [b] Yield of isolated product. [c] Determined by HPLC on a chiral stationary phase.

Table 5 $(DHQD)_2PYR$-catalyzed asymmetric substitution of O-Boc-protected Morita–Baylis–Hillman adducts **2** with 1*H*-indole-2-carbonitrile **1h**



Entry[a]	Ar	*t* [h]	Yield [%][b]	ee [%][c]
1	4-ClC_6H_4, **2a**	72	**5a**, 99	95
2	4-FC_6H_4, **2b**	96	**5b**, 91	96
3	4-$CF_3C_6H_4$, **2c**	96	**5c**, 67	92
4	4-BrC_6H_4, **2h**	96	**5d**, 98	96
5	4-$NO_2C_6H_4$, **2j**	96	**5e**, 93	95
6	4-CNC_6H_4, **2l**	72	**5f**, 98	92

[a] Reactions were performed with **1** (0.20 mmol), **2** (0.10 mmol) and 15 mol% of catalyst in THF (0.50 mL) at −10 °C. [b] Yield of isolated product. [c] Determined by HPLC on a chiral stationary phase.

96%) under standard conditions (Table 4, entries 1–11), except substrate **4c**, bearing a *p*-CF_3 group. The reason for its lower yield may be due to the steric interaction between the CF_3 substituent and the BnC(O) substituent at the pyrrole ring (Table 4, entry 3). To be noted, when the R^3 group was replaced by bromine or a cyano group, the ee values of the corresponding products decreased although their yields were still good, perhaps due to the electronic effect of the pyrrole moiety (Table 4, entries 9 and 10).

1*H*-Indole-2-carbonitrile **1h** is also a suitable substrate in this asymmetric substitution reaction. As shown in Table 5, the corresponding products **5a–5f** were obtained in 67–99% yields along with 92–96% ee in the reactions with **2a–2c**, **2h**, **2j** and **2l** under the standard conditions (Table 5, entries 1–6), further suggesting the wide substrate scope in this asymmetric substitution reaction. Notably, the main reason for the relatively low yield of **5c** having a *p*-CF_3 group may be also due to the steric interaction between the CF_3 substituent with the indole ring as mentioned above (Table 5, entry 3).

The absolute configuration of product **3** was unequivocally assigned as (*R*)-configuration by X-ray diffraction of **3h** bearing a bromine atom on the benzene ring. Its ORTEP drawing is shown in Fig. 1 and its CIF data are presented in the Supporting Information.†[9]

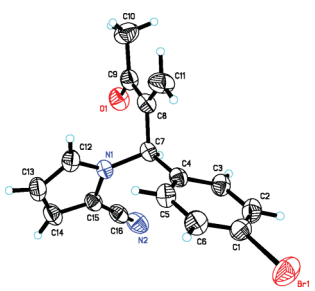


Fig. 1 ORTEP drawing of **3h**.

In light of the experimental results described above and recent studies,[10] we proposed a possible transition state for this asymmetric substitution reaction although there are several possible conformations of cinchona alkaloids in solution. The proposed possible

model to account for the high enantioselectivity is shown in Fig. 2. In the chiral pocket of the catalyst, the formed $(DHQD)_2PYR$-MBH adduct just above the 2,5-diphenylpyrimidine linker blocks the rear face of this *E* isomer. While, on the other hand, the aromatic ring of MBH substrate might be stabilized through π–π stacking with the linker (we speculate that this may be the main reason for the relatively low enantioselectivity for this reaction catalyzed by the other bis(cinchona alkaloid) catalysts). Subsequently the attack of the incoming nucleophile would presumably take place on the re-face, which is consistent with the experimental results.

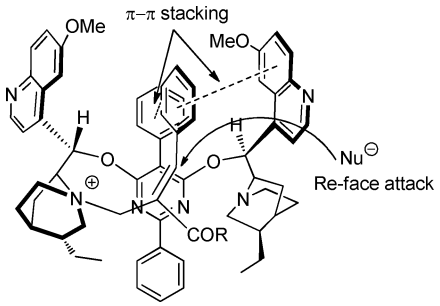


Fig. 2 Proposed model of the reaction transition state.

In summary, we have developed an interesting asymmetric substitution process of O-Boc-protected Morita–Baylis–Hillman adducts with various pyrrole and indole derivatives in the presence of $(DHQD)_2PYR$, affording the corresponding products in good to high yields (up to 99% yield) and moderate to high ee values (up to 92% ee and 96% ee) under mild conditions, which is applicable to a wide range of substrates from MBH adducts. This new asymmetric catalytic system can overcome the drawback in the asymmetric substitution of Morita–Baylis–Hillman carbonates with methyl pyrrole-2-carboxylate.[6f] Current efforts are in progress to use these novel multifunctional quinidine derived organocatalysts for other asymmetric catalysis.

Experimental section

General remarks

^{1}H NMR spectra were recorded on a Bruker AM-300 or AM-400 spectrometer for solution in $CDCl_3$ with tetramethylsilane (TMS) as internal standard; *J*-values are in Hz. Mass spectra were recorded with a HP-5989 instrument. All of the compounds reported in this paper gave satisfactory HRMS analytic data. Melting points were determined on a digital melting point apparatus and temperatures were uncorrected. Optical rotations were determined at 589 nm (sodium D line) using a Perkin-Elmer-341 MC digital polarimeter; $[\alpha]_D$-values are given in units of 10 deg^{-1} cm^2 g^{-1}. Infrared spectra were recorded on a Perkin-Elmer PE-983 spectrometer with absorption in cm^{-1}. Chiral HPLC was performed on a SHIMADZU SPD-10A vp series with chiral columns (Chiralpak AD-H, IC-H columns 4.6 × 250 mm, (Daicel Chemical Ind., Ltd.)). THF, toluene and Et_2O were distilled from sodium (Na) under argon (Ar) atmosphere. CH_3CN, 1,2-dichloroethane and dichloromethane were distilled from CaH_2 under argon (Ar) atmosphere. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai GF254 silica gel coated plates. Flash column chromatography was carried out using 300–400 mesh silica gel at increased pressure. Cinchona alkaloids catalysts β-ICD[8a] and catalysts cat. **1a–1e**, cat. **2a–2c** and cat. **3a** were prepared according to the literature procedure.[4h] Catalysts cat. **3b** and cat. **3c** were prepared based on Buchwald and Hartwig's Pd-catalyzed amination reaction.[11] O-Boc-Protected Morita–Baylis–Hillman products were prepared according to the literature procedure.[4g]

General procedure for the preparation of the catalysts

The reaction procedure for the preparation of the catalysts has been summarized in the ESI† and the spectroscopic data of **cat. 3b–3c** are shown below.

4-((1S,5*S*)-3-Ethyl-4-oxa-1-azatricyclo[4.4.0.03,8]decan-5-yl)-*N*-phenylquinolin-6-amine cat. 3b: a yellow solid; $[\alpha]_D^{20}$ = +141.2 (c 0.72, $CHCl_3$); m.p. 166–168 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.03 (t, *J* = 7.5 Hz, 3H), 1.47 (dd, *J* = 12.8 Hz, 6.0 Hz, 1H), 1.69–1.80 (m, 4H), 1.94 (dd, *J* = 12.8 Hz, 6.0 Hz, 1H), 2.71 (d, *J* = 12.8 Hz, 1H), 3.40–3.46 (m, 2H), 4.15 (d, *J* = 12.8 Hz, 1H), 4.25 (d, *J* = 6.0 Hz, 1H), 5.28 (brs, 3H), 6.08 (s, 1H), 6.93 (t, *J* = 6.4 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 2H), 7.23 (t, *J* = 7.2 Hz, 2H), 7.45 (s,1H), 7.52 (d, *J* = 4.0 Hz, 1H), 7.72 (dd, *J* = 9.2 Hz, 2.0 Hz, 1H), 7.92–7.94 (m, 2H), 8.68 (d, *J* = 4.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.1, 21.5, 21.8, 27.1, 32.5, 45.7, 53.5, 58.0, 71.5, 76.1, 107.0, 118.6, 118.9, 120.1, 121.8, 126.2, 129.3, 130.8, 138.6, 142.2, 143.1, 143.4, 146.5; IR (neat) *v* 3445, 2935, 2360, 2342, 1601,1508, 1593, 1480, 1458, 1279, 1203. 1152, 1069, 822 cm^{-1}; MS (%) *m*/*z* 385 (45), 328 (100), 346 (6), 285 (9), 233 (6), 166 (9); HRMS (EI) for $C_{25}H_{26}N_3O$: 385.2154; Found: 385.2158.

***N*-(3,5-Dimethoxyphenyl)-4-((1S,5*S*)-3-ethyl-4-oxa-1-azatricyclo[4.4.0.03,8]decan-5-yl)quinolin-6-amine cat. 3c**: a yellow solid; $[\alpha]_D^{20}$ = +63.6 (c 0.31, $CHCl_3$); m.p. 179–182 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.06 (t, *J* = 7.2 Hz, 3H), 1.50 (dd, *J* = 13.2 Hz, 6.8 Hz, 1H), 1.73–1.86 (m, 4H), 1.98 (dd, *J* = 13.2 Hz, 6.8 Hz, 1H), 2.38 (s, 1H), 3.04 (d, *J* = 13.2 Hz, 1H), 3.41–3.43 (m, 2H), 3.75 (s, 6H), 4.16 (d, *J* = 13.2 Hz, 1H), 4.24 (d, *J* = 6.4 Hz, 1H), 5.00 (brs, 2H), 6.09 (s, 2H), 6.34 (s, 2H), 7.31 (s, 1H), 7.55 (d, *J* = 4.0 Hz, 1H), 7.78 (d, *J* = 9.2 Hz, 1H), 7.92–7.96 (m, 2H), 8.70 (d, *J* = 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.2, 23.2, 23.9, 27.2, 32.7, 46.3, 54.3, 55.2, 56.3, 72.8, 93.6, 96.2, 107.6, 119.1, 122.0, 126.6, 131.0, 141.4, 142.1, 143.8, 144.5, 147.3, 161.5; IR (neat) *v* 3396, 2928, 2359, 1608, 1508, 1480, 1463, 1279, 1204, 1152, 1069, 1014, 860, 823 cm^{-1}; MS (%) *m*/*z* 445 (65), 388 (100), 346 (6), 223 (6), 166 (6); HRMS (EI) for $C_{27}H_{31}N_3O_3$: 445.2365; Found: 445.2371.

Typical procedure for the preparation of Boc-protected Morita–Baylis–Hillman adducts

The reaction procedure for the preparation of Boc-protected Morita–Baylis–Hillman adducts has been summarized in the ESI† and their spectroscopic data are shown below.

***tert*-Butyl (1-(4-fluorophenyl)-2-methylene-3-oxobutyl) carbonate 2b**: a white solid (2.99 g, 74% yield); m.p. 84–87 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.45 (s, 9H), 2.32 (s, 3H), 6.16 (d, *J* = 1.2 Hz, 1H), 6.24 (s, 1H), 6.52 (s, 1H), 7.00 (t, *J* = 8.4 Hz, 2H), 7.37 (dd, *J* = 5.2 Hz, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 27.7, 74.4, 82.7, 115.3 (d, $J_{C\text{-}F}$ = 21.5 Hz), 125.2, 129.3 (d, $J_{C\text{-}F}$ = 8.1 Hz), 133.8 (d,

$J_{C\text{-}F}$ = 2.9 Hz), 147.6, 152.2, 162.5 (d, $J_{C\text{-}F}$ = 245.4 Hz), 197.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ −113.803– −113.728 (m, 1F); IR (neat) ν 2982, 2935, 1747, 1682, 1606, 1510, 1082, 973, 839 cm^{-1}; MS (ESI) m/z 317.2 M + Na); HRMS (ESI) for $C_{16}H_{19}FNa_1O_4$ (M + Na): 317.1160; Found: 317.1173.

***tert*-Butyl (1-(2,3-dichlorophenyl)-2-methylene-3-oxobutyl) carbonate 2g**: a white solid (1.14 g, 33% yield); m.p. 114–117 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.47 (s, 9H), 2.39 (s, 3H), 5.81 (d, J = 1.2 Hz, 1H), 6.31 (s, 1H), 6.94 (s, 1H), 7.22 (t, J = 8.0 Hz, 1H), 7.29 (dd, J = 1.6 Hz, J = 8.0 Hz, 1H), 7.43 (dd, J = 1.6 Hz, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.0, 27.6, 72.0, 83.0, 126.0, 127.3, 128.2, 130.2, 131.6, 133.6, 138.1, 145.6, 152.0, 196.8; IR (neat) ν 2979, 2920, 2351, 1744, 1670, 1566, 1414, 1279, 959, 847 cm^{-1}; MS (ESI) m/z 367.1 (M + Na); HRMS (ESI) for $C_{16}H_{18}Cl_2Na_1O_4$ (M + Na): 367.0474; Found: 367.0492.

General procedure for the preparation of 3 from the reaction of 1a with 2a using 3a as an example in the presence of (DHQD)$_2$PYR

A solution of compound **1a** (0.2 mmol, 17 μL) and compound **2a** (0.1 mmol, 31 mg) in THF (0.5 mL) was stirred at −10 °C for 96 h in the presence of organocatalyst (DHQD)$_2$PYR (0.015 mmol, 13 mg) under an argon atmosphere. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (elution with petroleum ether/EtOAc = 16 : 1–8 : 1) to provide the corresponding product **3a**.

(*R*)-1-(1-(4-Chlorophenyl)-2-methylene-3-oxobutyl)-1*H*-pyrrole-2-carbonitrile 3a: a white solid (23 mg, 81% yield); m.p. 91–92 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 5.40 (s, 1H), 6.17 (dd, J = 2.4 Hz, 4.0 Hz, 1H), 6.44 (s, 1H), 6.60 (dd, J = 1.6 Hz, 2.4 Hz, 1H), 6.63 (s, 1H), 6.86 (dd, J = 1.6 Hz, 4.0 Hz, 1H), 7.09 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.4, 104.4, 109.5, 113.2, 121.0, 125.5, 128.7, 129.2, 129.3, 134.7, 134.9, 147.0, 196.4; IR (neat) ν 2924, 2854, 2215, 1678, 1490, 1367, 1225, 1088, 1070, 969, 861, 815, 735 cm^{-1}; MS (%) m/z 284 (35), 242 (4), 193 (11), 149 (4), 115 (22), 89 (4), 57 (6), 43 (100); HRMS (EI) for $C_{16}H_{13}N_2OCl$: 284.0716; Found: 284.0718; $[\alpha]_D^{20}$ −116.6 (c 0.35, $CHCl_3$) (92% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 12.10 min, t_{minor} = 9.65 min.

(*R*)-1-(1-(4-Fluorophenyl)-2-methylene-3-oxobutyl)-1*H*-pyrrole-2-carbonitrile 3b: a yellow oil (21 mg, 78% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 5.38 (s, 1H), 6.16 (dd, J = 3.2 Hz, 4.0 Hz, 1H), 6.43 (s, 1H), 6.59 (t, J = 2.0 Hz, 1H), 6.64 (s, 1H), 6.86 (dd, J = 1.6 Hz, 4.0 Hz, 1H), 7.07 (t, J = 8.8 Hz, 2H), 7.15 (dd, J = 5.2 Hz, 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.4, 104.4, 109.4, 113.2, 116.0 (d, $J_{C\text{-}F}$ = 21.5 Hz), 121.0, 125.5, 128.3, 129.8 (d, $J_{C\text{-}F}$ = 8.2 Hz), 132.1 (d, $J_{C\text{-}F}$ = 3.0 Hz), 147.3, 162.7 (d, $J_{C\text{-}F}$ = 246.9 Hz), 196.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ −112.674 (s, 1F); IR (neat) ν 2925, 2853, 2216, 1681, 1509, 1410, 1366, 1293, 1226, 1172, 977, 823, 739 cm^{-1}; MS (ESI) m/z 291.2 (M + Na); HRMS (ESI) for $C_{16}H_{13}FN_2NaO$ (M + Na): 291.0904; Found: 291.0914; $[\alpha]_D^{20}$ −197.9 (c 0.60, $CHCl_3$) (82% ee); Chiralcel AD-H, hexane/^{i}PrOH = 70 : 30, 0.6 mL min^{-1}, 214 nm, t_{major} = 7.62 min, t_{minor} = 8.42 min.

(*R*)-1-(2-Methylene-3-oxo-1-(4-(trifluoromethyl)phenyl)butyl)-1*H*-pyrrole-2-carbonitrile 3c: a colorless oil (29 mg, 91% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.42 (s, 3H), 5.45 (d, J = 1.2 Hz, 1H), 6.20 (dd, J = 2.8 Hz, 4.0 Hz, 1H), 6.49 (s, 1H), 6.63 (dd, J = 1.6 Hz, 2.8 Hz, 1H), 6.72 (s, 1H), 6.88 (dd, J = 1.6 Hz, 4.0 Hz, 1H), 7.25 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 8.4 Hz, 2H);^{13}C NMR (100 MHz, $CDCl_3$): δ 25.9, 60.5, 104.6, 109.8, 113.1, 121.1, 123.7 (q, $J_{C\text{-}F}$ = 270.7 Hz), 125.4, 126.0 (q, $J_{C\text{-}F}$ = 3.7 Hz), 128.2, 129.3, 130.5 (q, $J_{C\text{-}F}$ = 32.7 Hz), 140.6, 146.7, 196.4; ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$): δ −62.759 (s, 3F); IR (neat) ν 2925, 2218, 1740, 1682, 1621, 1523, 1418, 1323, 1264, 1166, 1114, 1068, 823, 738 cm^{-1}; MS (%) m/z 318 (11), 115 (8), 89 (4), 57 (7), 43 (100); HRMS (EI) for $C_{17}H_{13}N_2OF_3$: 318.0980; Found: 318.0981; $[\alpha]_D^{20}$ −80.3 (c 1.50, $CHCl_3$) (88% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 11.20 min, t_{minor} = 8.56 min.

(*R*)-1-(1-(3-Chlorophenyl)-2-methylene-3-oxobutyl)-1*H*-pyrrole-2-carbonitrile 3d: a yellow oil (25 mg, 88% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.41 (s, 3H), 5.42 (s, 1H), 6.18 (t, J = 3.2 Hz, 1H), 6.45 (s, 1H), 6.61 (t, J = 2.0 Hz, 1H), 6.63 (s, 1H), 6.87 (dd, J = 1.6 Hz, 4.0 Hz, 1H), 7.03–7.05 (m, 1H), 7.11–7.12 (m, 1H), 7.30–7.35 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 60.5, 104.5, 109.6, 113.2, 121.0, 125.5, 126.2, 128.0, 128.9, 129.0, 130.3, 135.0, 138.5, 146.9, 196.4; IR (neat) ν 2925, 2854, 2216, 1679, 1575, 1429, 1365, 1286, 1227, 1116, 1072, 977, 736 cm^{-1}; MS (%) m/z 284 (34), 242 (4), 193 (5), 115 (19), 89 (7), 57 (6), 43 (100); HRMS (EI) for $C_{16}H_{13}N_2OCl$: 284.0716; Found: 284.0719; $[\alpha]_D^{20}$ −198.5 (c 0.80, $CHCl_3$) (85% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 12.20 min, t_{minor} = 10.92 min.

(*S*)-1-(1-(2-Chlorophenyl)-2-methylene-3-oxobutyl)-1*H*-pyrrole-2-carbonitrile 3e: a yellow oil (27 mg, 95% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.42 (s, 3H), 5.36 (d, J = 0.8 Hz, 1H), 6.18 (dd, J = 2.8 Hz, 4.0 Hz, 1H), 6.44 (s, 1H), 6.58 (dd, J = 1.6 Hz, 2.8 Hz, 1H), 6.87 (dd, J = 1.6 Hz, 4.0 Hz, 1H), 6.88–6.91 (m, 1H), 6.96 (s, 1H), 7.23–7.34 (m, 2H), 7.43–7.45 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 58.4, 104.8, 109.5, 113.1, 120.9, 125.5, 127.1 128.1, 128.7, 130.1, 130.4, 134.1, 134.7, 146.2, 196.2; IR (neat) ν 2924, 2854, 2216, 1679, 1469, 1409, 1365, 1290, 1116, 1052, 976, 855, 738 cm^{-1}; MS (%) m/z 284 (4), 249 (36), 193 (5), 115 (15), 84 (9), 57 (7), 43 (100); HRMS (EI) for $C_{16}H_{13}N_2OCl$: 284.0716; Found: 284.0715; $[\alpha]_D^{20}$ −72.9 (c 1.35, $CHCl_3$) (90% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 13.61 min, t_{minor} = 12.34 min.

(*R*)-1-(1-(3,4-Dichlorophenyl)-2-methylene-3-oxobutyl)-1*H*-pyrrole-2-carbonitrile 3f: a yellow oil (29 mg, 91% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.42 (s, 3H), 5.44(s, 1H), 6.20 (dd, J = 2.4 Hz, 4.0 Hz, 1H), 6.47 (s, 1H), 6.60–6.61 (m, 2H), 6.88 (dd, J = 1.6 Hz, 4.0 Hz, 1H), 6.99 (dd, J = 2.4 Hz, 8.0 Hz, 1H), 7.21 (d, J = 2.4 Hz, 1H), 7.46 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.1, 104.6, 109.8, 113.1, 121.2, 125.4, 127.3, 129.1, 129.8, 131.0, 133.1, 133.4, 136.7, 146.7, 196.3; IR (neat) ν 2925, 2855, 2216, 1677, 1523, 1470, 1365, 1285, 1115, 1073, 961, 879, 817, 737 cm^{-1}; MS (%) m/z 318 (17), 227 (4), 149 (10), 57 (3), 43 (100); HRMS (EI) for $C_{16}H_{12}N_2OCl_2$: 318.0327; Found: 318.0323; $[\alpha]_D^{20}$ −154.5 (c 1.20, $CHCl_3$) (90% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 13.01 min, t_{minor} = 9.69 min.

(*S*)-1-(1-(2,3-Dichlorophenyl)-2-methylene-3-oxobutyl)-1*H*-pyrrole-2-carbonitrile 3g: a white solid (29 mg, 91% yield); m.p. 124–126 °C ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.43 (s, 3H), 5.40 (s, 1H), 6.20 (s, 1H), 6.46 (s, 1H), 6.60 (s, 1H), 6.78 (d, J = 7.8 Hz, 1H), 6.88 (s, 1H), 6.97 (s, 1H), 7.21 (t, J = 7.8 Hz, 1H), 7.48 (d, J = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.9, 58.9, 104.8, 109.7, 113.0, 121.1, 125.4, 126.2, 127.5, 129.1, 130.8, 132.4, 134.4, 137.2,

145.9, 196.1; IR (neat) ν 2923, 2850, 2214, 1676, 1447, 1411, 1365, 1290, 1177, 1121, 1047, 963, 876, 745 cm^{-1}; MS (%) m/z 318 (4), 283 (37), 149 (11), 113 (5), 43 (100); HRMS (EI) for $C_{16}H_{12}N_2OCl_2$: 318.0327; Found: 318.0325; $[\alpha]_D^{20}$ −119.5 (c 0.90, $CHCl_3$) (91% ee); Chiralcel AD-H, hexane/^{i}PrOH = 90 : 10, 0.7 mL min^{-1}, 230 nm, t_{major} = 11.88 min, t_{minor} = 10.92 min.

(*R*) - 1 - (1 - (4 - Bromophenyl) - 2 - methylene - 3 - oxobutyl)-1*H*-pyrrole-2-carbonitrile 3h: a white solid (27 mg, 82% yield); m.p. 87–89 °C ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 5.41 (s, 1H), 6.17 (dd, J = 2.4 Hz, 3.6 Hz, 1H), 6.44 (s, 1H), 6.60–6.62 (m, 1H), 6.85 (dd, J = 1.6 Hz, 3.6 Hz, 1H), 7.01 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.5, 104.5, 109.6, 113.2, 121.0, 122.9, 125.5, 128.9, 129.6, 132.2, 135.6, 146.9, 196.5; IR (neat) ν 2925, 2215, 1940, 1680, 1521, 1367, 1440, 1350, 1224, 1170, 1069, 818, 737 cm^{-1}; MS (%) m/z 328 (8), 237 (4), 158 (13), 115 (17), 89 (4), 84 (4), 63 (4), 43 (100); HRMS (EI) for $C_{16}H_{13}N_2OBr$: 328.0211; Found: 328.0209; $[\alpha]_D^{20}$ −177.0 (c 0.25, $CHCl_3$) (91% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 12.42 min, t_{minor} = 9.91 min.

(*R*)-1-(1-(3-Bromophenyl)-2-methylene-3-oxobutyl)-1*H*-pyrrole-2-carbonitrile 3i: a yellow oil (32 mg, 97% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.41 (s, 3H), 5.42 (s, 1H), 6.18 (t, J = 2.8 Hz, 1H), 6.45 (s, 1H), 6.62 (s, 2H), 6.86 (d, J = 2.8 Hz, 1H), 7.08 (d, J = 8.0 Hz, 1H), 7.23–7.27 (m, 2H), 7.49 (d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.5, 104.6, 109.7, 113.2, 121.0, 123.1, 125.6, 126.7, 129.0, 130.6, 130.9, 132.0, 138.7, 146.9, 196.4; IR (neat) ν 2925, 2853, 2216, 1679, 1570, 1456, 1409, 1365, 1286, 1226, 1116, 1072, 976, 738, 688 cm^{-1}; MS (%) m/z 328 (6), 253 (4), 207 (1), 158 (8), 115 (15), 84 (8), 57 (5), 43 (100); HRMS (EI) for $C_{16}H_{13}N_2OBr$: 328.0211; Found: 328.0215; $[\alpha]_D^{20}$ −107.1 (c 1.50, $CHCl_3$) (84% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 16.58 min, t_{minor} = 15.28 min.

(*S*)-1-(1-(2-Bromophenyl)-2-methylene-3-oxobutyl)-1*H*-pyrrole-2-carbonitrile 3j: a yellow oil (31 mg, 94% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.42 (s, 3H), 5.35 (s, 1H), 6.18 (dd, J = 2.8 Hz, 4.0 Hz, 1H), 6.45 (s, 1H), 6.57 (dd, J = 1.6 Hz, 2.8 Hz, 1H), 6.87 (dd, J = 1.6 Hz, 4.0 Hz, 1H), 6.88–6.91 (m, 1H), 6.92 (s, 1H), 7.21–7.32 (m, 2H), 7.62–7.64 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.8, 104.9, 109.5, 113.0, 120.9, 124.5, 125.5, 127.7, 128.3, 128.8, 130.2, 133.8, 136.3, 146.4, 196.2; IR (neat) ν 2367, 2218, 1678, 1521, 1406, 1281, 1220, 1111, 1074, 978, 751 cm^{-1}; MS (ESI) m/z 351.2 (M + Na); HRMS (ESI) for $C_{16}H_{13}BrN_2NaO$ (M + Na): 351.0104; Found: 351.0116; $[\alpha]_D^{20}$ −84.2 (c 0.67, $CHCl_3$) (84% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 11.07 min, t_{minor} = 9.88 min.

(*R*)-1-(2-Methylene-1-(4-nitrophenyl)-3-oxobutyl)-1*H*-pyrrole-2-carbonitrile 3k: a yellow oil (30 mg, 99% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.45 (s, 3H), 5.52 (s, 1H), 6.24 (t, J = 2.8 Hz, 3.6 Hz, 1H), 6.54 (s, 1H), 6.66 (d, J = 1.2 Hz, 1H), 6.75 (s, 1H), 6.90 (dd, J = 1.2 Hz, 4.0 Hz, 1H), 7.29 (d, J = 8.8 Hz, 2H), 8.24 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.3, 104.7, 110.1, 113.0, 121.3, 124.2, 125.3, 128.7, 129.8, 143.8, 146.3, 147.9, 196.3; IR (neat) ν 2923, 2853, 2216, 1679, 1605, 1520, 1440, 1346, 1227, 1173, 976, 856, 735 cm^{-1}; MS (%) m/z 295 (465), 278 (49), 236 (15), 162 (18), 115 (9), 92 (11), 43 (100); HRMS (EI) for $C_{16}H_{13}N_3O_3$: 295.0957; Found: 295.0956; $[\alpha]_D^{20}$ −87.9 (c 1.50, $CHCl_3$) (93% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 31.61 min, t_{minor} = 22.63 min.

(*R*)-1-(2-Methylene-1-(3-nitrophenyl)-3-oxobutyl)-1*H*-pyrrole-2-carbonitrile 3l: a yellow oil (25 mg, 84% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.45 (s, 3H), 5.51 (t, J = 1.2 Hz, 1H), 6.24 (dd, J = 2.8 Hz, 4.0 Hz, 1H), 6.55 (s, 1H), 6.64 (dd, J = 1.6 Hz, 2.8 Hz, 1H), 6.76 (s, 1H), 6.90 (dd, J = 1.6 Hz, 4.0 Hz, 1H), 7.49–7.51 (m, 1H), 7.59–7.63 (m, 1H), 7.96–7.97 (m, 1H), 8.22–8.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.3, 104.6, 110.1, 113.0, 121.3, 122.5, 123.7, 125.4, 129.7, 130.2, 134.1, 138.9, 146.3, 148.6, 196.4; IR (neat) ν 2926, 2855, 2216, 1679, 1529, 1456, 1409, 1349, 1291, 1073, 967, 808, 730 cm^{-1}; MS (%) m/z 295 (14), 278 (32), 162 (6), 115 (14), 92 (11), 43 (100); HRMS (EI) for $C_{16}H_{13}N_3O_3$: 295.0957; Found: 295.0953; $[\alpha]_D^{20}$ −122.5 (c 1.10, $CHCl_3$) (78% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 23.20 min, t_{minor} = 18.43 min.

(*R*)-1-(1-(4-Cyanophenyl)-2-methylene-3-oxobutyl)-1*H*-pyrrole-2-carbonitrile 3m: a colorless oil (27.3 mg, 99% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.43 (s, 3H), 5.49 (s, 1H), 6.22 (dd, J = 2.8 Hz, 4.0 Hz, 1H), 6.52 (s, 1H), 6.64 (dd, J = 1.6 Hz, 2.8 Hz, 1H), 6.71 (s, 1H), 6.88 (dd, J = 1.6 Hz, 4.0 Hz, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.68 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 60.4, 104.6, 110.0, 112.6, 113.0, 118.0, 121.1, 125.3, 128.4, 129.8, 132.7, 141.9, 146.3, 196.3; IR (neat) ν 2925, 2854, 2216, 1678, 1454, 1410, 1366, 1295, 1115, 1073, 976, 818, 740 cm^{-1}; MS (%) m/z 275 (85), 260 (12), 232 (11), 184 (15), 142 (51), 92 (11), 43 (100); HRMS (EI) for $C_{17}H_{13}N_3O$: 275.1059; Found: 275.1055; $[\alpha]_D^{20}$ −121.1 (c 1.50, $CHCl_3$) (88% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 26.84 min, t_{minor} = 19.98 min.

(*R*)-1-(2-Methylene-3-oxo-1-phenylbutyl)-1*H*-pyrrole-2-carbonitrile 3n: a yellow oil (17 mg, 68% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.39 (s, 3H), 5.38 (t, J = 0.8 Hz, 1H), 6.15 (t, J = 3.2 Hz, 1H), 6.41 (s, 1H), 6.60–6.61 (m, 1H), 6.66 (s, 1H), 6.85 (dd, J = 1.2 Hz, 3.2 Hz, 1H), 7.14–7.16 (m, 2H), 7.34–7.39 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 61.2, 104.4, 109.3, 113.4, 120.9, 125.7, 128.0, 128.3, 128.8, 129.0, 136.3, 147.4, 196.6; IR (neat) ν 3124, 2216, 1740, 1680, 1598, 1451, 1365, 1292, 1171, 976, 734, 699 cm^{-1}; MS (%) m/z 250 (18), 235 (4), 207 (3), 159 (7), 115 (14), 91 (4), 57 (8), 43 (100); HRMS (EI) for $C_{16}H_{14}N_2O$: 250.1106; Found: 250.1103; $[\alpha]_D^{20}$ −165.6 (c 0.75, $CHCl_3$) (82% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 16.49 min, t_{minor} = 14.90 min.

(*R*)-1-(2-Methylene-3-oxo-1-(p-tolyl)butyl)-1*H*-pyrrole-2-carbonitrile 3o: a white solid (21 mg, 80% yield); m.p. 63–65 °C ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.34 (s, 3H), 2.38 (s, 3H), 5.34 (d, J = 1.2 Hz, 1H), 6.13 (dd, J = 2.8 Hz, 4.0 Hz, 1H), 6.39 (s, 1H), 6.59 (dd, J = 1.6 Hz, 2.8 Hz, 1H), 6.61 (s, 1H), 6.84 (dd, J = 1.6 Hz, 4.0 Hz, 1H), 7.05 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 26.1, 61.0, 104.3, 109.1, 113.4, 120.8, 125.8, 127.9, 128.0, 129.7, 133.2, 138.7, 147.6, 196.6; IR (neat) ν 2925, 2854, 1718, 1622, 1560, 1467, 1380, 1259, 1186, 1082, 965, 763 cm^{-1}; MS (%) m/z 264 (20), 249 (7), 173 (10), 131 (7), 115 (7), 91 (3), 84 (3), 43 (100); HRMS (EI) for $C_{17}H_{16}N_2O$: 264.1263; Found: 264.1267; $[\alpha]_D^{20}$ −142.1 (c 1.00, $CHCl_3$) (76% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 13.81 min, t_{minor} = 10.92 min.

(*R*)-1-(1-(2-Methoxyphenyl)-2-methylene-3-oxobutyl)-1*H*-pyrrole-2-carbonitrile 3p: a white solid (26 mg, 93% yield); m.p. 95–97 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.38 (s, 3H), 3.80 (s, 3H), 5.31 (d, J = 1.2 Hz, 1H), 6.12 (dd, J = 2.8 Hz, 4.0 Hz, 1H),

6.35 (s, 1H), 6.60 (dd, J = 1.6 Hz, 2.8 Hz, 1H), 6.83 (dd, J = 1.6 Hz, 4.0 Hz, 1H), 6.85–6.87 (m, 1H), 6.90–6.93 (m, 2H), 6.96 (s, 1H), 7.31–7.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 55.6, 104.4, 108.8, 113.4, 120.4, 120.5, 125.0, 125.5, 127.3, 127.5, 130.1, 147.1, 156.7, 196.5; IR (neat) ν 2924, 2854, 1713, 1671, 1598, 1490, 1463, 1361, 1250, 1111, 1022, 970, 745 cm^{-1}; MS (%) m/z 280 (19), 189 (12), 147 (14), 115 (7), 91 (7), 71 (13), 57 (17), 43 (100); HRMS (EI) for $C_{17}H_{16}N_2O_2$: 280.1212; Found: 280.1210; $[\alpha]_D^{20}$ −183.1 (c 0.50, $CHCl_3$) (89% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 12.91 min, t_{minor} = 11.29 min.

(*S*)-1-(1-(Furan-2-yl)-2-methylene-3-oxobutyl)-1*H*-pyrrole-2-carbonitrile 3q: a yellow oil (18 mg, 75% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 5.50 (t, J = 1.2 Hz, 1H), 6.17 (dd, J = 2.8 Hz, J = 4.0 Hz, 1H), 6.28 (dd, J = 0.8 Hz, J = 4.0 Hz, 1H), 6.36 (s, 1H), 6.38 (dd, J = 1.6 Hz, J = 4.0 Hz, 1H), 6.67 (s, 1H), 6.69 (dd, J = 1.6 Hz, J = 2.8 Hz, 1H), 6.85 (dd, J = 1.6 Hz, J = 4.0 Hz, 1H), 7.44 (dd, J = 0.8 Hz, J = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 55.0, 103.8, 109.4, 110.6, 110.7, 113.1, 121.0, 125.8, 127.6, 143.6, 145.5, 149.0, 196.2; IR (neat) ν 2924, 2855, 2217, 1680, 1454, 1409, 1366, 1286, 1142, 1116, 1071, 1015, 961, 808, 815 cm^{-1}; MS (ESI) m/z 263.1 (M + Na); HRMS (ESI) for $C_{20}H_{20}N_2NaO_7S$ (M + Na): 263.0791; Found: 263.0801; $[\alpha]_D^{20}$ = +134 (c 0.17, $CHCl_3$) (62% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 17.58 min, t_{minor} = 24.15 min.

(*S*)-1-(2-Methylene-3-oxo-1-(thiophen-2-yl)butyl)-1*H*-pyrrole-2-carbonitrile 3r: a yellow oil (23 mg, 89% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 5.48 (s, 1H), 6.16 (t, J = 3.2 Hz, 1H), 6.37 (s, 1H), 6.71 (d, J = 1.6 Hz, 1H), 6.85 (dd, J = 1.6 Hz, 4.0 Hz, 1H), 6.87 (s, 1H), 6.95–6.96 (m, 1H), 7.00–7.02 (m, 1H), 7.34–7.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 56.3, 104.0, 109.4, 113.2, 121.1, 125.7, 127.0, 127.2, 127.3, 128.0, 138.9, 147.7, 196.2; IR (neat) ν 2925, 2854, 2216, 1669, 1574, 1468, 1359, 1254, 1082, 1065, 972, 851, 760 cm^{-1}; MS (ESI) m/z 279.1 (M + Na); HRMS (ESI) for $C_{20}H_{20}N_2NaO_7S$ (M + Na): 279.0563; Found: 279.0576; $[\alpha]_D^{20}$ = +84.4 (c 1.1, $CHCl_3$) (39% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 10.47 min, t_{minor} = 12.70 min.

(*R*)-1-(2-Methylene-1-(4-nitrophenyl)-3-oxobutyl)-1*H*-pyrrole-2-carbonitrile 3s: a yellow oil (19 mg, 61% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.11 (t, J = 7.2 Hz, 3H), 2.81 (q, J = 7.2 Hz, 2H), 5.46 (dd, J = 0.8 Hz, 1.2 Hz, 1H), 6.23 (dd, J = 2.8 Hz, 4.0 Hz, 1H), 6.52 (s, 1H), 6.65 (dd, J = 1.6 Hz, 2.8 Hz, 1H), 6.76 (s, 1H), 6.90 (dd, J = 1.6 Hz, 4.0 Hz, 1H), 7.29 (d, J = 8.8 Hz, 2H), 8.24 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.9, 31.2, 60.6, 104.8, 110.1, 113.0, 121.3, 124.2, 125.3, 128.5, 128.7, 143.9, 146.0, 147.9, 199.1; IR (neat) ν 2981, 2940, 2218, 1682, 1607, 1522, 1456, 1345, 1225, 1073, 979, 839, 739 cm^{-1}; MS (ESI) m/z 332.3 (M + Na); HRMS (ESI) for $C_{17}H_{15}N_3NaO_3S$ (M + Na): 332.1006; Found: 332.1015; $[\alpha]_D^{20}$ −116.3 (c 1.00, $CHCl_3$) (93% ee); Chiralcel OD-H, hexane/^{i}PrOH = 90 : 10, 0.7 mL min^{-1}, 230 nm, t_{major} = 32.22 min, t_{minor} = 29.03min.

(*R*)-Methyl 2-((4-chlorophenyl)(2-cyano-1*H*-pyrrol-1-yl)methyl)acrylate 3t: a colorless oil (22 mg, 73% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 3.73 (s, 3H), 5.22 (d, J = 1.2 Hz, 1H), 6.19 (dd, J = 2.8 Hz, 4.0 Hz, 1H), 6.56 (s, 1H), 6.59 (s, 1H), 6.65 (dd, J = 1.6 Hz, 2.8 Hz, 1H), 6.87 (dd, J = 1.6 Hz, 4.0 Hz, 1H), 7.11 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.4, 61.3, 104.5, 109.6, 113.1, 120.9, 125.2, 129.1, 129.2, 129.3, 134.7, 134.8, 139.1, 164.9; IR (neat) ν 2923, 2853, 2216, 1679, 1605, 1520, 1440, 1346, 1227, 1173, 976, 856, 735 cm^{-1}; MS (%) m/z 300 (58), 209 (47), 177 (16), 149 (69), 130 (27), 115 (100), 91 (15), 59 (50), 49 (15); HRMS (EI) for $C_{16}H_{13}N_2O_2Cl$: 300.0666; Found: 300.0663; $[\alpha]_D^{20}$ −110.0 (c 1.00, $CHCl_3$) (83% ee); Chiralcel AD, hexane/^{i}PrOH = 70 : 30, 0.6 mL min^{-1}, 214 nm, t_{major} = 7.37 min, t_{minor} = 8.31 min.

General procedure for the preparation of 4 from the reaction of 1b with 2a using 4a as an example in the presence of $(DHQD)_2PYR$

A solution of compound **1b** (0.2 mmol, 42 mg) and compound **2a** (0.1 mmol, 31 mg) in THF (0.5 mL) was stirred at 0 °C in the presence of organocatalyst $(DHQD)_2PYR$ (0.015 mmol, 13 mg) under argon atmosphere. The reaction solution was monitored by TLC. After the reaction complete, the solvent was removed under reduced pressure and the residue was chromatographed on silica gel (elution with petroleum ether/EtOAc = 4 : 1–2 : 1) to provide the corresponding product **4a**.

(*R*)-1-(1-(4-Chlorophenyl)-2-methylene-3-oxobutyl)-4-(2-phenylacetyl)-1*H*-pyrrole-2-carbonitrile 4a: a white oil (30 mg, 75% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 3.97 (s, 2H), 5.44 (t, J = 1.2 Hz, 1H), 6.47 (s, 1H), 6.59 (s, 1H), 7.03 (d, J = 8.4 Hz, 2H), 7.11 (d, J = 1.6 Hz, 1H), 7.18–7.20 (m, 2H), 7.25–7.32 (m, 4H), 7.37 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 47.0, 60.9, 106.3, 111.8, 121.1, 124.8, 127.0, 128.7, 129.2, 129.3, 129.6, 133.6, 134.2, 135.3, 146.1, 191.8, 196.1; IR (neat) ν 2925, 2855, 2222, 1674, 1538, 1491, 1367, 1277, 1216, 1157, 1068, 977, 931, 863, 835, 724, 637 cm^{-1}; MS (%) m/z 311 (48), 193 (28), 115 (13), 91 (31), 65 (8), 43 (100); HRMS (EI) for $C_{24}H_{19}N_2O_2Cl$: 402.1135; Found: 402.1138; $[\alpha]_D^{20}$ −10.1 (c 0.60, $CHCl_3$) (96% ee); Chiralcel IC, hexane/^{i}PrOH = 70 : 30, 0.7 mL min^{-1}, 214 nm, t_{major} = 36.70 min, t_{minor} = 32.15 min.

(*R*)-1-(1-(4-Fluorophenyl)-2-methylene-3-oxobutyl)-4-(2-phenylacetyl)-1*H*-pyrrole-2-carbonitrile 4b: a white oil (27 mg, 70% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 3.97 (s, 2H), 5.42 (s, 1H), 6.46 (s, 1H), 6.60 (s, 1H) 7.08–7.32 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 47.0, 61.0, 106.2, 111.9, 116.4 (d, $J_{C\text{-}F}$ = 21.6 Hz), 121.1, 124.8, 127.0, 128.7, 128.8, 129.2, 129.8 (d, $J_{C\text{-}F}$ = 8.1 Hz), 130.8 (d, $J_{C\text{-}F}$ = 3.0 Hz), 145.2, 146.3, 162.9 (d, $J_{C\text{-}F}$ = 248.4 Hz), 191.8, 196.2;^{19}F NMR (376 MHz, $CDCl_3$): δ −111.681–−111.610 (m, 1F); IR (neat) ν 2925, 2854, 2222, 1674, 1538, 1510, 1367, 1319, 1224, 1158, 978, 931, 868, 832, 764, 724, 637 cm^{-1}; MS (ESI) m/z 409.3 (M + Na); HRMS (ESI) for $C_{24}H_{19}FN_2NaO_2$ (M + Na): 409.1323; Found: 409.1341; $[\alpha]_D^{20}$ −11.1 (c 0.50, $CHCl_3$) (91% ee); Chiralcel IC, hexane/^{i}PrOH = 70 : 30, 0.7 mL min^{-1}, 214 nm, t_{major} = 33.90 min, t_{minor} = 33.29 min.

(*R*)-1-(2-Methylene-3-oxo-1-(4-(trifluoromethyl)phenyl)butyl)-4-(2-phenylacetyl)-1*H*-pyrrole-2-carbonitrile 4c: a white oil (27 mg, 46% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.41 (s, 3H), 3.98 (s, 2H), 5.49 (t, J = 1.2 Hz, 1H), 6.52 (s, 1H), 6.68 (s, 1H), 7.14 (d, J = 1.6 Hz, 1H), 7.14–7.31 (m, 8H), 7.64 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.8, 47.0, 60.9, 106.3, 111.7, 119.5, 123.1 (q, $J_{C\text{-}F}$ = 270.7 Hz), 125.0, 126.2 (q, $J_{C\text{-}F}$ = 3.7 Hz), 127.0, 128.1, 128.6, 128.7, 129.2, 130.3, 131.3 (q, $J_{C\text{-}F}$ = 32.7 Hz), 134.2, 139.2, 145.7, 191.7, 196.1; ^{19}F NMR (376 MHz, $CDCl_3$): δ −62.797 (s, 3F); IR (neat) ν 3121, 2223, 1676, 1539, 1510, 1367, 1319, 1224, 1161, 1112, 1068, 978, 931, 863, 827, 722, 637 cm^{-1}; MS (ESI) m/z 459.3 (M + Na); HRMS (ESI) for $C_{25}H_{19}F_3N_2NaO_2$ (M + Na): 459.1291; Found: 459.1307; $[\alpha]_D^{20}$ = +21.1 (c 0.90, $CHCl_3$) (91%

ee); Chiralcel IC, hexane/^{i}PrOH = 70 : 30, 0.7 mL min^{-1}, 214 nm, t_{major} = 16.26 min, t_{minor} = 14.73 min.

(*R*)-1-(1-(4-Bromophenyl)-2-methylene-3-oxobutyl)-4-(2-phenylacetyl)-1*H*-pyrrole-2-carbonitrile 4d: a white oil (34 mg, 76% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 3.97 (s, 2H), 5.45 (s, 1H), 6.47 (s, 1H), 6.57 (s, 1H), 6.96 (d, J = 8.4 Hz, 2H), 7.11 (d, J = 1.6 Hz, 1H), 7.18–7.32 (m, 6H), 7.52 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 47.1, 61.0, 106.3, 111.8, 121.1, 123.5, 124.9, 127.0, 128.7, 129.2, 129.5, 129.6, 132.5, 134.2, 134.3, 146.1, 191.8, 196.1; IR (neat) ν 2925, 2855, 2222, 1673, 1538, 1489, 1387, 1367, 1217, 1158, 1072, 1011, 978, 931, 859, 723, 637 cm^{-1}; MS (%) m/z 355 (27), 237 (14), 158 (17), 115 (12), 91 (21), 65 (8), 43 (100); HRMS (EI) for $C_{24}H_{19}N_2O_2Br$: 446.0630; Found: 446.0633; $[\alpha]_D^{20}$ −4.8 (c 0.90, $CHCl_3$) (94% ee); Chiralcel IC, hexane/^{i}PrOH = 70 : 30, 0.7 mL min^{-1}, 214 nm, t_{major} = 38.74 min, t_{minor} = 33.76 min.

(*R*)-1-(2-Methylene-1-(4-nitrophenyl)-3-oxobutyl)-4-(2-phenylacetyl)-1*H*-pyrrole-2-carbonitrile 4e: a white solid (26 mg, 63% yield); m.p. 150–152 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.43 (s, 3H), 3.99 (s, 2H), 5.54 (s, 1H), 6.56 (s, 1H), 6.72 (s, 1H), 7.17–7.33 (m, 9H), 8.24 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.8, 47.1, 60.7, 106.4, 111.6, 124.4, 125.3, 127.1, 128.5, 128.6, 128.7, 129.3, 130.8, 134.1, 142.4, 145.4, 148.2, 191.7, 196.0; IR (neat) ν 2925, 2855, 2221, 1679, 1538, 1493, 1462, 1376, 1325, 1278, 1197, 1161, 979, 932, 853, 764,750, 637 cm^{-1}; MS (%) m/z 322 (72), 158 (13), 119 (42), 115 (9), 91 (46), 71 (14), 57 (20), 43 (100); HRMS (EI) for $C_{24}H_{19}N_3O_4$: 413.1376; Found: 413.1371; $[\alpha]_D^{20}$ = +22.4 (c 0.55, $CHCl_3$) (93% ee); Chiralcel OD-H, hexane/^{i}PrOH = 70 : 30, 0.7 mL min^{-1}, 214 nm, t_{major} = 47.40 min, t_{minor} = 35.17 min.

(*R*)-1-(2-Methylene-3-oxo-1-phenylbutyl)-4-(2-phenylacetyl)-1*H*-pyrrole-2-carbonitrile 4f: a yellow oil (23 mg, 58% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 3.97 (s, 2H), 5.43 (s, 1H), 6.46 (s, 1H), 6.63 (s, 1H), 7.09–7.30 (m, 9H), 7.38–7.40 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 46.9, 61.6, 106.3, 112.0, 121.0, 124.6, 127.0, 127.9, 128.7, 129.0, 129.2, 129.3, 130.8, 134.3, 134.9, 146.4, 191.8, 196.2; IR (neat) ν 2924, 2854, 2223, 1666, 1537, 1455, 1379, 1276, 1215, 1158, 978, 955, 931, 859, 749, 696 cm^{-1}; MS (%) m/z 277 (84), 159 (46), 119 (15), 115 (14), 91 (18), 71 (4), 57 (7), 43 (100); HRMS (EI) for $C_{24}H_{20}N_2O_2$: 368.1525; Found: 368.1523; $[\alpha]_D^{20}$ −4.1 (c 1.00, $CHCl_3$) (89% ee); Chiralcel OD-H, hexane/^{i}PrOH = 70 : 30, 0.6 mL min^{-1}, 214 nm, t_{major} = 27.99 min, t_{minor} = 24.04 min.

(*R*)-4-Acetyl-1-(1-(4-chlorophenyl)-2-methylene-3-oxobutyl)-1*H*-pyrrole-2-carbonitrile 4g: a white solid (25 mg, 76% yield); m.p. = 122–124 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.38 (s, 3H), 2.43 (s, 3H), 5.51 (s, 1H), 6.52 (s, 1H), 6.63 (s, 1H), 7.08 (d, J = 8.4 Hz, 2H), 7.18 (d, J = 1.6 Hz, 1H), 7.25 (d, J = 1.6 Hz, 1H), 7.39 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 27.2, 60.9, 106.3, 111.8, 121.0, 125.8, 128.0, 129.2, 129.5, 129.7, 133.6, 135.3, 146.1, 192.1, 196.2; IR (neat) ν 3114, 2924, 2223, 1669, 1538, 1489, 1391, 1372, 1205, 1118, 1092, 1014, 974, 936, 809, 780, 659, 643 cm^{-1}; MS (%) m/z 326 (45), 193 (16), 115 (8), 85 (13), 71 (13), 57 (14), 43 (100); HRMS (EI) for $C_{18}H_{15}N_2O_2Cl$: 326.0822; Found: 326.0820; $[\alpha]_D^{20}$ −2.1 (c 1.00, $CHCl_3$) (94% ee); Chiralcel AD-H, hexane/^{i}PrOH = 70 : 30, 0.6 mL min^{-1}, 214 nm, t_{major} = 10.39 min, t_{minor} = 14.88 min.

(*R*)-3-((4-Chlorophenyl)(3-(2,2,2-trichloroacetyl)-1*H*-pyrrol-1-yl)methyl)but-3-en-2-one 4h: a white solid (33.6 mg, 83% yield); m.p. = 152–124 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.39 (s, 3H), 5.17 (d, J = 1.2 Hz, 1H), 6.23 (dd, J = 2.8 Hz, 4.4 Hz, 1H), 6.29 (s, 1H), 6.73 (dd, J = 1.6 Hz, 2.8 Hz, 1H), 7.15 (d, J = 8.4 Hz, 2H), 7.33 (s, 1H), 7.35 (d, J = 8.4 Hz, 1H), 7.64 (dd, J = 1.6 Hz, 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 61.2, 96.3, 109.2, 121.5, 125.4, 126.4, 129.2, 129.5, 130.1, 131.2, 134.6, 135.5, 148.5, 172.3, 196.6; IR (neat) ν 2925, 2855, 2224, 1677, 1538, 1489, 1408, 1373, 1326, 1230, 1168, 1132, 1068, 979, 946, 865, 851, 765, 726, 689 cm^{-1}; MS (%) m/z 286 (24), 258 (9), 244 (9), 193 (5), 115 (10), 84 (11), 71 (13), 57 (5), 43 (100); HRMS (EI) for $C_{17}H_{13}NO_2Cl_4$: 402.9700; Found: 402.9705; $[\alpha]_D^{20}$ −216.4 (c 0.65, $CHCl_3$) (90% ee); Chiralcel IC, hexane/^{i}PrOH = 70 : 30, 0.5 mL min^{-1}, 214 nm, t_{major} = 11.17 min, t_{minor} = 14.50 min.

(*R*)-3-((2-Bromo-4-(2,2,2-trichloroacetyl)-1*H*-pyrrol-1-yl)(4-chlorophenyl)methyl)but-3-en-2-one 4i: a white solid (34.0 mg, 71% yield); m.p. = 168–170 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 5.26 (t, J = 0.8 Hz, 1H), 6.32 (s, 1H), 6.69 (d, J = 1.6 Hz, 1H), 7.14 (d, J = 8.4 Hz, 2H), 7.30 (s, 1H), 7.37 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 61.5, 96.8, 121.9, 126.0, 126.8, 129.4, 130.0, 130.4, 134.8, 134.9, 148.0, 171.7, 196.3; IR (neat) ν 2925, 2855, 2224, 1679, 1366, 1326, 1191, 1169, 1068, 979, 955, 922, 861, 836, 765, 732, 683 cm^{-1}; MS (%) m/z 364 (5), 193 (5), 115 (8), 84 (12), 43 (100); HRMS (EI) for $C_{17}H_{12}NO_2Cl_4Br$: 480.8806; Found: 480.8802; $[\alpha]_D^{20}$ −111.3 (c 0.50, $CHCl_3$) (84% ee); Chiralcel IC, hexane/^{i}PrOH = 70 : 30, 0.5 mL min^{-1}, 214 nm, t_{major} = 9.07 min, t_{minor} = 10.65 min.

(*R*)-1-(1-(4-Chlorophenyl)-2-methylene-3-oxobutyl)-1*H*-pyrrole-2,4-dicarbonitrile 4j: a white solid (26 mg, 84% yield); m.p. = 117–119 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.44 (s, 3H), 5.51 (t, J = 0.8 Hz, 1H), 6.54 (s, 1H), 6.64 (s, 1H), 7.05 (d, J = 1.6 Hz, 1H), 7.07 (d, J = 8.4 Hz, 2H), 7.11 (d, J = 1.6 Hz, 1H), 7.41 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 61.5, 94.8, 106.7, 110.8, 113.8, 123.2, 129.2, 129.7, 129.8, 130.7, 133.1, 135.7, 145.9, 196.0; IR (neat) ν 2930, 2859, 2222, 1669, 1263, 1112, 1022, 910, 803, 662 cm^{-1}; MS (%) m/z 309 (36), 274 (8), 193 (11), 115 (18), 85 (11), 71 (14), 57 (25), 43 (100); HRMS (EI) for $C_{17}H_{12}N_3OCl$: 309.0669; Found: 309.0668; $[\alpha]_D^{20}$ −1.3 (c 0.50, $CHCl_3$) (85% ee); Chiralcel IC, hexane/^{i}PrOH = 70 : 30, 0.7 mL min^{-1}, 214 nm, t_{major} = 30.62 min, t_{minor} = 25.64 min.

(*R*)-1-(1-(4-Chlorophenyl)-2-methylene-3-oxobutyl)-1*H*-pyrrole-2-carbaldehyde 4k: a white solid (20.0 mg, 70% yield); m.p. = 140–143 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.36 (s, 3H), 5.19 (d, J = 1.2 Hz, 1H), 6.22 (dd, J = 2.8 Hz, 4.0 Hz, 1H), 6.29 (s, 1H), 6.71 (t, J = 0.8 Hz, 1H), 7.01 (dd, J = 1.6 Hz, 4.0 Hz, 1H), 7.12 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 7.39 (s, 1H), 9.52 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 60.1, 109.8, 125.5, 126.8, 129.0, 129.4, 129.8, 131.4, 134.3, 135.7, 148.3, 179.1, 196.7; IR (neat) ν 2803, 2346, 1675, 1651, 1460, 1327, 1220, 1058, 956, 861, 741 cm^{-1}; MS (%) m/z 287 (6), 258 (9), 244 (25), 115 (15), 43 (100); HRMS (EI) for $C_{16}H_{14}NO_2Cl$: 287.0713; Found: 287.0716; $[\alpha]_D^{20}$ −193.1 (c 0.75, $CHCl_3$) (92% ee); Chiralcel OD, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 30.62 min, t_{minor} = 25.64 min.

General procedure for the preparation of 5 from the reaction of 1h with 2a using 5a as an example in the presence of $(DHQD)_2PYR$

A solution of compound **1h** (0.2 mmol, 14 mg) and compound **2a** (0.1 mmol, 31 mg) in THF (0.5 mL) was stirred at −10 °C for 96 h in the presence of organocatalyst $(DHQD)_2PYR$ (0.015 mmol,

13 mg) under argon atmosphere. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (elution with petroleum ether/EtOAc = 16 : 1–8 : 1) to provide the corresponding product **5a**.

1-(1-(4-Chlorophenyl)-2-methylene-3-oxobutyl)-1*H*-indole-2-carbonitrile 5a: a white solid (33 mg, 99% yield); m.p. 144–146 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.43 (s, 3H), 5.78 (dd, J = 0.8 Hz, 1.2 Hz, 1H), 6.51 (t, J = 0.8 Hz, 1H), 7.02 (s, 1H), 7.07 (d, J = 8.0 Hz, 2H), 7.17–7.21 (m, 1H), 7.24–7.32 (m, 5H), 7.64–7.66 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 58.5, 109.6, 111.4, 113.6, 115.6, 121.7, 122.4, 126.1, 126.4, 129.0, 129.2, 130.2, 134.4, 135.0, 137.6, 145.9, 197.3; IR (neat) ν 2925, 2855, 2221, 1680, 1444, 1406, 1343, 1320, 1277, 1226, 1164, 948, 853, 750 cm^{-1}; MS (%) m/z 334 (50), 299 (4), 193 (13), 142 (8), 115 (13), 84 (5), 71 (2), 57 (3), 43 (100); HRMS (EI) for $C_{20}H_{15}N_2OCl$: 334.0873; Found: 334.0874; $[\alpha]_D^{20}$ –49.6 (c 1.10, $CHCl_3$) (95% ee); Chiralcel AD-H, hexane/^{i}PrOH = 70 : 30, 0.6 mL min^{-1}, 214 nm, t_{major} = 9.10 min, t_{minor} = 10.07 min.

1-(1-(4-Fluorophenyl)-2-methylene-3-oxobutyl)-1*H*-indole-2-carbonitrile 5b: a white foam (32 mg, 99% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.43 (s, 3H), 5.74 (s, 1H), 6.49 (s, 1H), 7.01–7.05 (m, 3H), 7.11–7.18 (m, 3H), 7.20–7.32 (m, 3H), 7.65 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 58.5, 109.5, 111.4, 113.5, 115.6 (d, $J_{C\text{-}F}$ = 3.7 Hz), 115.9, 121.7, 122.4, 126.1, 126.4, 129.7 (d, $J_{C\text{-}F}$ = 8.3 Hz), 129.9, 132.2 (d, $J_{C\text{-}F}$ = 3.8 Hz), 137.6, 146.2, 162.5 (d, $J_{C\text{-}F}$ = 246.5 Hz), 197.4; ^{19}F NMR (376 MHz, $CDCl_3$): δ –113.075– –113.003 (m, 1F); IR (neat) ν 2923, 2855, 2219, 1675, 1510, 1365, 1319, 1226, 1160, 972, 846, 750 cm^{-1}; MS (%) m/z 318 (35), 275 (4), 177 (21), 142 (8), 133 (13), 115 (5), 84 (5), 57 (3), 43 (100); HRMS (EI) for $C_{20}H_{15}N_2OF$: 318.1168; Found: 318.1171; $[\alpha]_D^{20}$ –82.0 (c 0.50, $CHCl_3$) (96% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 13.97 min, t_{minor} = 9.40 min.

1-(2-methylene-3-oxo-1-(4-(trifluoromethyl)phenyl)butyl)-1*H*-indole-2-carbonitrile 5c: a white foam (25 mg, 68% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.44 (s, 3H), 5.82 (s, 1H), 6.56 (s, 1H), 7.11 (s, 1H), 7.18–7.22 (m, 1H), 7.24–7.31 (m, 5H), 7.60 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 58.6, 109.6, 111.3, 113.6, 115.7, 121.8, 122.5, 123.8 (q, $J_{C\text{-}F}$ = 270.7 Hz), 125.8 (q, $J_{C\text{-}F}$ = 2.9 Hz), 126.2, 126.4, 128.2, 130.6 (q, $J_{C\text{-}F}$ = 32.6 Hz), 130.7, 137.6, 140.6, 145.6, 197.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.692– –62.680 (m, 3F); IR (neat) ν 2925, 2854, 2221, 1681, 1618, 1445, 1321, 1247, 1165, 1120, 1168, 977, 877, 750 cm^{-1}; MS (%) m/z 368 (44), 349 (3), 325 (7), 299 (3), 227 (8), 142 (20), 133 (2), 115 (14), 84 (2), 63 (3), 43 (100); HRMS (EI) for $C_{21}H_{15}N_2OF_3$: 368.1136; Found: 368.1141; $[\alpha]_D^{20}$ –36.4 (c 0.50, $CHCl_3$) (92% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 9.75 min, t_{minor} = 8.35 min.

1-(1-(4-Bromophenyl)-2-methylene-3-oxobutyl)-1*H*-indole-2-carbonitrile 5d: a white solid (38 mg, 99% yield); m.p. 151–153 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.43 (s, 3H), 5.79 (s, 1H), 6.52 (s, 1H), 7.00–7.02 (m, 3H), 7.17–7.21 (m, 1H), 7.25–7.32 (m, 3H), 7.47 (d, J = 8.4 Hz, 2H), 7.65 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 58.5, 109.6, 111.4, 113.6, 115.7, 121.8, 122.5, 122.6, 126.1, 126.4, 129.6, 130.3, 132.0, 135.6, 137.6, 145.9, 197.3; IR (neat) ν 2925, 2854, 2221, 1680, 1444, 1402, 1346, 1319, 1278, 1225, 1163, 1070, 948, 852, 749 cm^{-1}; MS (%) m/z 378 (28), 299 (5), 237 (8), 158 (22), 142 (9), 115 (47), 89 (6), 63 (7), 43 (100); HRMS (EI) for $C_{20}H_{15}N_2OBr$: 378.0368; Found: 378.0363; $[\alpha]_D^{20}$ –38.6 (c 1.10, $CHCl_3$) (96% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, t_{major} = 10.20 min, t_{minor} = 12.25 min.

1-(2-Methylene-1-(4-nitrophenyl)-3-oxobutyl)-1*H*-indole-2-carbonitrile 5e: a yellow solid (32 mg, 93% yield); m.p. 90–93 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.47 (s, 3H), 5.84 (s, 1H), 6.60 (s, 1H), 7.15 (s, 1H), 7.20–7.35 (m, 6H), 7.68 (d, J = 7.6 Hz, 2H), 8.20 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 58.3, 109.4, 111.1, 113.5, 116.1, 122.0, 122.6, 124.0, 126.5, 128.9, 130.8, 137.5, 143.8, 145.2, 147.7, 197.2; IR (neat) ν 2925, 2855, 2221, 1680, 1517, 1446, 1344, 1318, 1279, 1228, 1192, 1165, 964, 850, 750 cm^{-1}; MS (%) m/z 345 (56), 328 (15), 299 (5), 256 (8), 162 (15), 142 (31), 115 (28), 89 (7), 63 (8), 43 (100); HRMS (EI) for $C_{20}H_{15}N_3O_3$: 345.1113; Found: 345.1111; $[\alpha]_D^{20}$ –69.5 (c 1.40, $CHCl_3$) (95% ee); Chiralcel AD-H, hexane/^{i}PrOH = 70 : 30, 0.6 mL min^{-1}, 214 nm, t_{major} = 13.69 min, t_{minor} = 18.09 min.

1-(2-Methylene-1-(4-nitrophenyl)-3-oxobutyl)-1*H*-indole-2-carbonitrile 5f: a colorless oil (32 mg, 98% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.45 (s, 3H), 5.81 (t, J = 1.2 Hz, 1H), 6.58 (s, 1H), 7.10 (s, 1H), 7.20–7.35 (m, 7H), 7.63–7.68 (m, 3H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 58.4, 109.5, 111.1, 112.4, 113.5, 116.0, 118.1, 122.0, 122.6, 126.3, 126.4, 128.6, 130.7, 132.6, 137.5, 141.8, 145.2, 197.2; IR (neat) ν 2924, 2854, 2221, 1680, 1446, 1401, 1363, 1345, 1317, 1278, 1229, 1194, 967, 851, 750 cm^{-1}; MS (%) m/z 325 (40), 310 (5), 282 (7), 184 (6), 142 (51), 115 (9), 84 (4), 63 (4), 43 (100); HRMS (EI) for $C_{21}H_{15}N_3O$: 325.1215; Found: 325.1214; $[\alpha]_D^{20}$ –51.8 (c 1.60, $CHCl_3$) (93% ee); Chiralcel AD-H, hexane/^{i}PrOH = 70 : 30, 0.6 mL min^{-1}, 214 nm, t_{major} = 12.94 min, t_{minor} = 15.17 min.

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9 The crystal data of **3h** have been deposited to the CCDC with reference number 812598.† Empirical formula: $C_{16}H_{13}BrN_2O$; Formula weight: 329.19; Crystal color, habit: colorless, Crystal dimensions: 0.26 × 0.18 × 0.13 mm; Crystal system: Orthorhombic; Lattice parameters: a = 8.5810(18) Å, b = 9.4511(19) Å, c = 18.265(4) Å, α = 90°, β = 90°, γ = 90°, V = 1481.3(5) Å^3; Space group: $P2(1)2(1)2(1)$; Z = 4; D_c = 1.476 g cm^{-3}; F_{000} = 664; Final R induces [$I > 2\sigma(I)$]: R_1 = 0.0407; w R_2 = 0.1105.

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