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Enantioselective synthesis of α -tetrasubstituted (3-indoliziny) (diaryl)methanamines via chiral phosphoric acid catalysis†

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An enantioselective Friedel–Crafts reaction of cyclic α -diaryl *N*-acyl imines with indolizines catalyzed by a chiral spirocyclic phosphoric acid has been developed. The asymmetric transformation proceeds smoothly to afford α -tetrasubstituted (3-indoliziny) (diaryl)methanamines in good yields with up to 98% ee under mild conditions.

Chiral α -tetrasubstituted methanamines are frequently distributed in diverse bioactive natural products,¹ and extensive effort has been devoted to constructing these scaffolds in synthetic chemistry over the past decade.² Some excellent chiral organocatalysts³ and chiral metal salt catalysts⁴ have been developed in the asymmetric synthesis of chiral α -tetrasubstituted (diaryl) alkyl or (triaryl) methanamines. Despite these notable advances, to the best of our knowledge, there are currently no versatile protocols for the asymmetric preparation of chiral α -(3-indoliziny)(diaryl) methanamines.

Indolizines as an important class of *N*-containing heterocycles can be found in organic synthesis and numerous pharmaceuticals (Fig. 1).⁵ Many versatile strategies for the direct functionalization of indolizines have been developed.⁶ Moreover, some elegant examples toward the asymmetric synthesis of enantioenriched indolizine derivatives have been reported,⁷ as shown in Scheme 1. For instance, List and Coelho reported the first organocatalyzed asymmetric conjugate addition of indolizines to enones using the chiral BINOL-derived phosphoric acid (BINOL-PA) as a catalyst (Scheme 1a).^{7a} Zhang and Fu developed a copper-catalyzed enantioselective propargylation reaction of indolizines (Scheme 1b).^{7b} Later, Zeng's group established a highly asymmetric allylic substitution reaction of indolizine derivatives catalyzed by chiral Ir complexes (Scheme 1c).^{7c} Ni and Song described an organocatalytic highly diastereo- and enantioselective Friedel–Crafts conjugate addition of indolizines to prochiral cyclopentenones catalyzed by BINOL-PA (Scheme 1d).^{7d}

Recently, Li and Gu realized the catalytic asymmetric conjugate addition of indolizines to unsaturated ketones catalyzed by chiral Rh complexes (Scheme 1e).^{7e} Very recently, Ni

and Song reported BINOL-PA-catalyzed asymmetric atroposelective arylation of indolizines for the preparation of the axially chiral 3-arylindolizines (Scheme 1f).^{7f} Although these strategies enable direct access to asymmetric synthesis of chiral indolizine derivatives, development of new class indolizines is still a formidable target. To continue our efforts⁸ on the advancement of chiral phosphoric acid catalysis,⁹ we here present the chiral spirocyclic phosphoric acid (SPINOL-PA) catalyzed enantioselective Friedel–Crafts of indolizines with *in situ* generated cyclic α -diaryl *N*-acyl imines¹⁰ for the synthesis of chiral α -(3-indoliziny)(diaryl) methanamines.

An initial investigation for the asymmetric Friedel–Crafts reaction was carried out with methyl indolizine-2-carboxylate (**1a**) and 3-phenyl 3-hydroxyisindolinone (**2a**) in the presence of 10 mol% chiral phosphoric acid (CPA), as shown in Table 1. Chiral spirocyclic phosphoric acid (SPA) catalysts (**4a–d**) developed by our group^{8a} were firstly screened in 1,2-dichloroethane (DCE) at room temperature to afford the desired chiral α -(3-indoliziny)(diaryl) methanamine (**3a**) with acceptable yields but up to different enantioselectivities, and catalyst **4d** gave the best

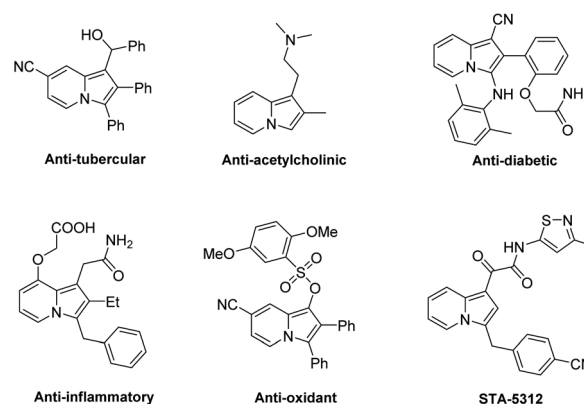


Fig. 1 Indolizine-containing bioactive compounds.

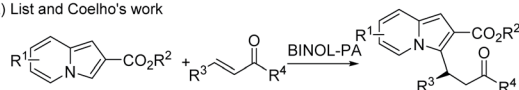
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† Electronic supplementary information (ESI) available: CCDC 2167990 (**3p**). For ESI and crystallographic data in CIF or other electronic format see <https://doi.org/10.1039/d2ra03750e>

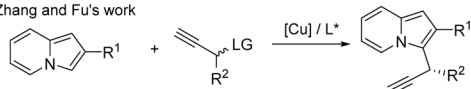


Previous work:

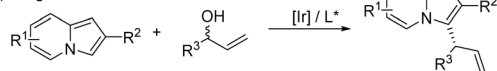
a) List and Coelho's work



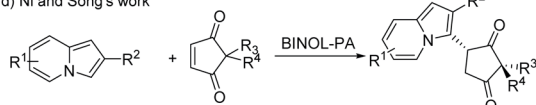
b) Zhang and Fu's work



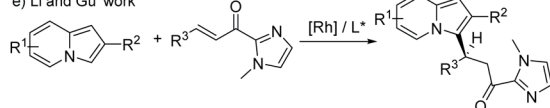
c) Zeng's work



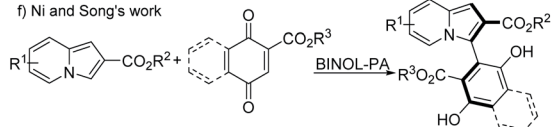
d) Ni and Song's work



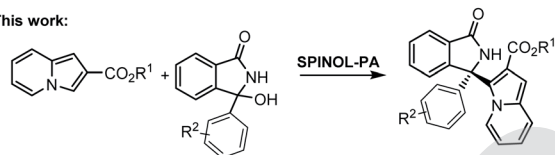
e) Li and Gu's work



f) Ni and Song's work



This work:



Scheme 1 Asymmetric functionalization of indolizines.

reaction activity and enantioselectivity (89% yield, 74% ee) (entries 1–4). In addition, we also tested BINOL-derived phosphoric acids (**5a–d**) as catalysts, only low yields (37–72%) and poor enantioselectivities (12–53% ee) were observed (entries 5–8). We believe that the efficient catalytic activity of chiral spirocyclic phosphoric acid (SPA) is due to its special skeleton. Mostly the chiral backbone of the catalyst plays a vital role in attaining high stereoinduction by regulating electronic and structural properties of substrates. On the other hand, the dual hydrogen bonding network between the SPA and other two substrates plays a crucial role in terms of reactivity and selectivity. Moreover, the influence of solvent was investigated (entries 9–13). 1,2-Dichloroethane (DCE) was still the optimal solvent, and this reaction did not even proceed in toluene, THF or EtOAc. Next, the effect of additives was also investigated (entries 14–17). In the presence of 4 Å MS, the desired product **3a** could be obtained in 91% yield with 87% ee (17). Lastly, we examined the temperature, and the reaction proceeded for 36 hours to afford the product **3a** with 92% ee but in only 9% yield when the temperature was lowered to 0 °C (entry 18). Hence, the optimized reaction conditions employed 10 mol% (*S*)-**4d** in 1,2-dichloroethane at room temperature (entry 17).

With the optimal conditions in hand, we set out to explore the substrate scope and limitations of this asymmetric

transformation, as summarized in Table 2. In general, a range of 3-aryl 3-hydroxyisoindolinones **2** with different substituents were amenable to this strategy, and reacted efficiently with methyl indolizine-2-carboxylate **1a** to provide good yields and high enantioselectivities (**3a–j**, up to 94% yield, up to 98% ee). When two methyl groups were placed around the 3-aryl ring, we observed a small drop in enantioselectivity as the corresponding product **3f** was obtained in 82% yield and 78% ee. Interestingly, when methoxy group was introduced in *ortho* position of the 3-aryl, the enantioselectivity was dramatically improved (**3e**, 91% yield, 98% ee). Furthermore, CF₃ group on the 3-aryl substituent proceeded smoothly to afford the desired product **3h** in good yield with excellent enantioselectivity (94% ee). We found that 3-alkyl 3-hydroxyisoindolinones were not tolerated and the reactions did not run with **1a** under the standard reaction conditions, such as methyl, allyl or benzyl substituent on the isoindolinone alcohol. We tried carrying out the reactions of 3-alkyl 3-hydroxyisoindolinones with substrate **1a** in HFIP, and found that the reactions still could not run.

We next examined the scope of indolizines **1**. Ethyl indolizine-2-carboxylate **1b** also gave the desired products (**3k–m**) in good yields with excellent enantioselectivities (up to 94% ee). However, indolizine with a 5-methyl or 5-phenyl substituent depressed the reactivity and failed to provide the desired product under standard conditions because of the steric hindrance. Furthermore, methyl pyrrolo[1,2-*a*]quinoline-2-carboxylate **1c** also gave the desired products (**3n–q**) with high enantioselectivities (up to 94% ee). The absolute configuration in product **3p** (CCDC 2167990†) was clearly determined to be (*R*) by X-ray diffraction analysis of a single crystal, and the absolute configuration of products **3** was assigned as (*R*) by analogy.

To further explore the synthetic practicality of the developed protocol, we investigated a 1 mmol scale reaction of this asymmetric Friedel–Crafts reaction, as shown in Scheme 2. Under the optimized reaction conditions, the reaction of methyl pyrrolo[1,2-*a*]quinoline-2-carboxylate **1c** (1 mmol) and 3-(4-chlorophenyl)-3-hydroxyisoindolin-1-one **2i** (1 mmol) afforded the desired product **3p** in 61% yield with 94% ee.

We attempted to extend the reaction by treating product **3p** with NaOH and obtained the corresponding product **4** in 81% yield and 98% ee, as shown in Scheme 3.

Conclusions

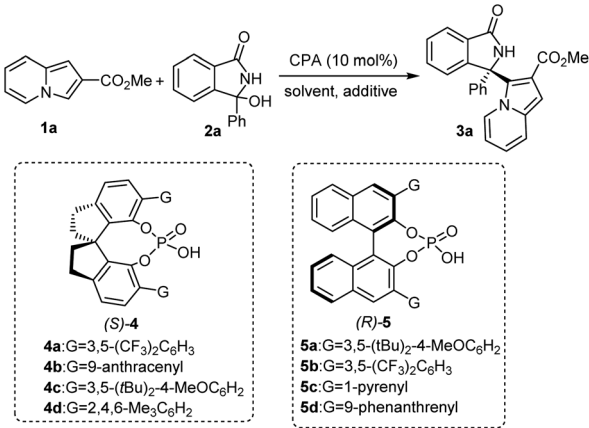
In summary, we have reported a metal free protocol for chiral spirocyclic phosphoric acid-catalyzed enantioselective Friedel–Crafts reaction of cyclic α -diaryl *N*-acyl imines with indolizines, providing convenient access to a range of α -tetrasubstituted (3-indoliziny) (diaryl)methanamines in good yields with up to 98% ee under mild conditions.

Experimental

General information

All reactions were carried out in oven-dried glassware with magnetic stirring under ambient conditions. Unless otherwise noted, all reagents, including the chiral phosphoric acid



Table 1 Optimization of the reaction conditions^a


Entry	CPA	Solvent	Additive	Yield ^b (%)	ee ^c (%)
1	(S)-4a	DCE	None	49	15
2	(S)-4b	DCE	None	71	41
3	(S)-4c	DCE	None	78	6
4	(S)-4d	DCE	None	89	74
5	(R)-5a	DCE	None	55	-12
6	(R)-5b	DCE	None	37	-19
7	(R)-5c	DCE	None	61	-23
8	(R)-5d	DCE	None	72	-53
9	(S)-4d	DCM	None	91	37
10	(S)-4d	MeCN	None	55	23
11	(S)-4d	Toluene	None	N.R.	—
12	(S)-4d	THF	None	N.R.	—
13	(S)-4d	EtOAc	None	N.R.	—
14	(S)-4d	MeOH	None	N.R.	—
15	(S)-4d	DCE	Na ₂ SO ₄	82	78
16	(S)-4d	DCE	MgSO ₄	79	74
17	(S)-4d	DCE	3 Å MS	80	84
18	(S)-4d	DCE	4 Å MS	91	87
19 ^d	(S)-4d	DCE	4 Å MS	9	91

^a Reactions were performed with **1a** (0.05 mmol), **2a** (0.05 mmol) and CPA catalyst (10 mol%) in the presence of additive (100 mg) in solvent (1 mL) for 24 hours at room temperature. ^b Isolated yields. ^c Determined by chiral HPLC analysis. ^d At 0 °C for 36 hours.

catalysts **4** and **5**, were purchased from commercial supplies and used without further purification, and all solvents were dried and purified according to standard methods prior to use. Substrates **1** (ref. 11) and **2** (ref. 12) were synthesized according to the literature methods. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker AVANCE III 400 MHz spectrometer instrument at 400 MHz and 100 MHz spectrometer, respectively. The chemical shifts (δ) were quoted in parts per million (ppm) downfield relative to internal standard TMS (0.0 ppm) and referenced to solvent peaks in the NMR solvent (CDCl₃ = δ 7.26 ppm; δ 77.00 ppm; δ 77.00 ppm; δ 77.00 ppm; δ 40.00 ppm). Spin multiplicity were reported using the following abbreviations: s = singlet, d = doublet, t = triplet, dd = doublet of doublet, td = triplet of doublet, m = multiplet. Infrared spectra were recorded on an ATR-FTIR spectrometer. ESI-HRMS were recorded on a Water Micromass GCT Premier mass

spectrometer. Optical rotations were measured on a PerkinElmer Model 341 polarimeter at 20 °C. Enantiomeric excess (ee) were measured by chiral HPLC analysis.

General procedure for the asymmetric synthesis of **3** via chiral phosphoric acid-catalyzed reaction of indolizine-2-carboxylate **1** and quinone methyl ester **2**

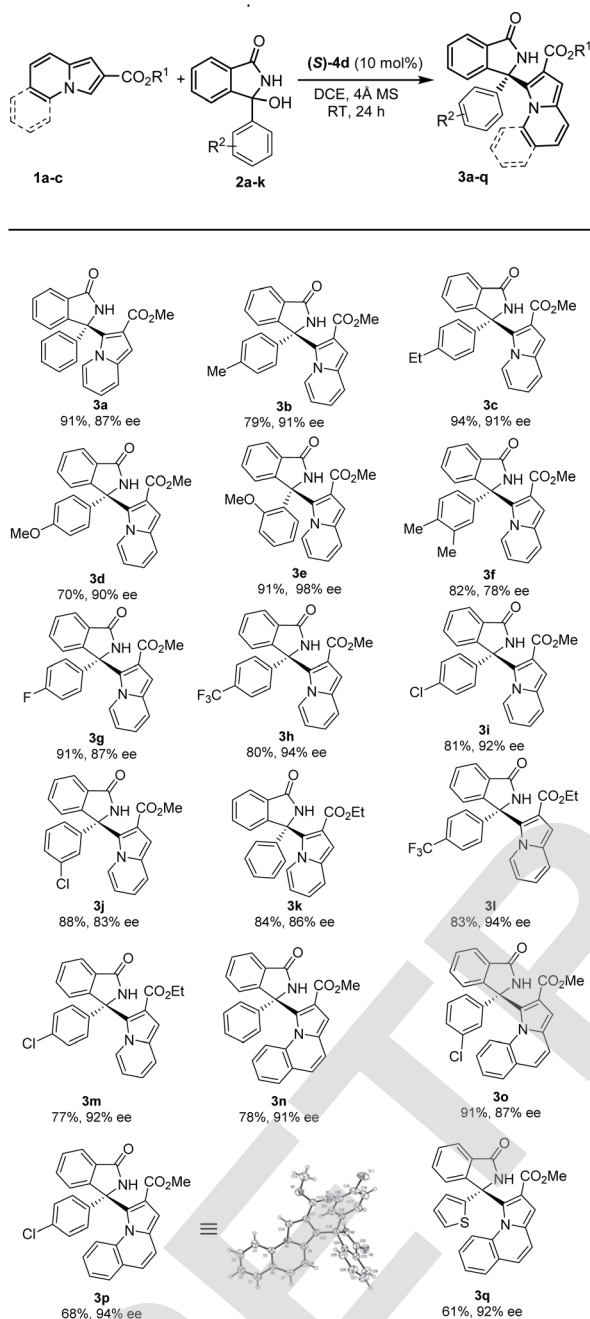
To a mixture of indolizine-2-carboxylate **1** (0.05 mmol), 3-hydroxyisoindolinones **2** (0.05 mmol, 1 equiv.) and catalyst (S)-**4a** (0.005 mmol, 10 mol%) in DCE (1 mL) was added 4 Å MS (100 mg). After stirring at room temperature for 24 hours, the residue was purified by flash column chromatography with acetate/petroleum ether 1 : 2 (v/v) on silica gel to give the desired product **3**.

(R)-Methyl 3-(3-oxo-1-phenylisoindolin-1-yl) indolizine-2-carboxylate (3a). White solid (17.4 mg, 91%). Mp 119–120 °C. 87% ee, determined by HPLC [Daicel Chiralcel] AD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 60/40, 1.0 mL min⁻¹, 254 nm, t_{major} = 14.566 min, t_{minor} = 9.524 min. $[\alpha]_{\text{D}}^{20}$ = -440.3° (c 0.36, CH₂Cl₂). ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.02 (s, 1H), 8.26 (d, *J* = 6.9 Hz, 1H), 8.08 (s, 1H), 7.76 (d, *J* = 6.8 Hz, 1H), 7.59–7.50 (m, 3H), 7.25 (m, 5H), 6.55 (m, 2H), 6.12 (d, *J* = 9.3 Hz, 1H), 3.25 (s, 3H) ppm. ¹³C NMR (101 MHz, DMSO) δ 168.9, 165.3, 158.8, 151.1, 145.7, 132.3, 131.6, 130.4, 129.0, 128.6, 127.4, 127.2, 125.6, 125.5, 123.7, 119.6, 119.4, 119.2, 118.1, 112.3, 112.0, 67.1, 60.2, 51.5 ppm. IR (film): γ = 3393, 2949, 1694, 1610, 1541, 1503, 1466, 1370, 1313, 1266, 1222, 1159, 1075, 745, 702 cm⁻¹. HRMS *m/z* (ESI⁺): calcd for C₂₄H₁₈N₂NaO₃ ([M + Na]⁺) 405.1210, found 405.1211.

(R)-Methyl 3-(3-oxo-1-(*p*-tolyl)isoindolin-1-yl)indolizine-2-carboxylate (3b). White solid (15.7 mg, 79%). Mp 118–120 °C. 91% ee, determined by HPLC [Daicel Chiralcel] AD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 60/40, 1.0 mL min⁻¹, 254 nm, t_{major} = 14.365 min, t_{minor} = 7.750 min. $[\alpha]_{\text{D}}^{20}$ = -571.1° (c 0.30, CH₂Cl₂). ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.98 (s, 1H), 8.26 (d, *J* = 6.8 Hz, 1H), 8.07 (s, 1H), 7.75 (d, *J* = 6.9 Hz, 1H), 7.55–7.48 (m, 3H), 7.15 (d, *J* = 8.2 Hz, 2H), 7.06 (d, *J* = 8.2 Hz, 2H), 6.53 (m, 2H), 6.15 (d, *J* = 9.3 Hz, 1H), 3.27 (s, 3H), 2.23 (s, 3H) ppm. ¹³C NMR (101 MHz, DMSO) δ 168.9, 165.4, 151.4, 142.7, 136.5, 132.3, 131.6, 130.4, 129.2, 128.9, 127.2, 125.6, 125.4, 123.7, 119.6, 119.4, 119.3, 118.0, 112.4, 112.0, 66.9, 51.6, 26.8, 21.2, 21.0 ppm. IR (film): γ = 3403, 2949, 1694, 1541, 1508, 1466, 1437, 1364, 1314, 1267, 1221, 1159, 1069, 815, 755, 692 cm⁻¹. HRMS *m/z* (ESI⁺): calcd for C₂₅H₂₀N₂NaO₃ ([M + Na]⁺) 419.1366, found 419.1364.

(R)-Methyl 3-(1-(4-ethylphenyl)-3-oxoisoindolin-1-yl) indolizine-2-carboxylate (3c). White solid (19.3 mg, 94%). Mp 105–107 °C. 91% ee, determined by HPLC [Daicel Chiralcel] AD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 60/40, 1.0 mL min⁻¹, 254 nm, t_{major} = 14.463 min, t_{minor} = 7.273 min. $[\alpha]_{\text{D}}^{20}$ = -486.6° (c 0.38, CH₂Cl₂). ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.99 (s, 1H), 8.26 (d, *J* = 6.9 Hz, 1H), 8.06 (s, 1H), 7.75 (d, *J* = 6.8 Hz, 1H), 7.55 (m, 2H), 7.53–7.48 (m, 1H), 7.17 (d, *J* = 8.3 Hz, 2H), 7.09 (d, *J* = 8.3 Hz, 2H), 6.59–6.47 (m, 2H), 6.15 (d, *J* = 9.3 Hz, 1H), 3.25 (s, 3H), 2.58–2.52 (m, 2H), 1.12 (t, *J* = 7.6 Hz, 3H) ppm. ¹³C NMR (101 MHz, DMSO) δ 168.9, 165.4, 151.3,



Table 2 Substrates scope^a

^a Reactions were performed with **1** (0.05 mmol), **2** (0.05 mmol) and **(S)-4d** (10 mol%) in the presence of 4 Å MS (100 mg) in DCE (1 mL) at room temperature for 24 hours. Isolated yield was given. The ee was determined by chiral HPLC analysis.

142.9, 142.9, 132.3, 131.6, 130.3, 128.9, 128.0, 127.2, 125.7, 125.4, 123.7, 119.7, 119.4, 119.3, 117.9, 112.5, 111.9, 66.9, 51.6, 31.6, 30.3, 28.2, 16.1 ppm. IR (film): γ = 3398, 2961, 1694, 1610, 1540, 1504, 1466, 1437, 1364, 1313, 1267, 1221, 1159, 1097, 828, 753, 692 cm^{-1} . HRMS m/z (ESI^+): calcd for $\text{C}_{26}\text{H}_{22}\text{N}_2\text{NaO}_3$ ($[\text{M} + \text{Na}]^+$) 433.1523, found 433.1526.

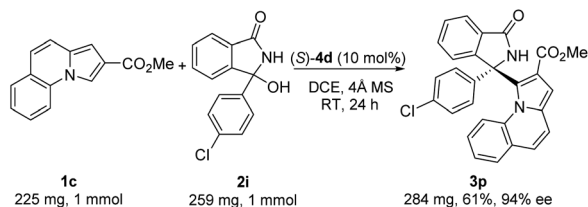
(R)-Methyl 3-(1-(4-methoxyphenyl)-3-oxoisindolin-1-yl)indolizine-2-carboxylate (3d). White solid (14.4 mg, 70%). Mp 113–115 °C. 90% ee, determined by HPLC [Daicel Chiralcel] AD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 60/40, 1.0 mL min⁻¹, 254 nm, t_{major} = 12.837 min, t_{minor} = 6.504 min. $[\alpha]_{\text{D}}^{20}$ = -434.1° (c 0.26, CH_2Cl_2). ¹H NMR (400 MHz, $\text{DMSO}-d_6$) δ 9.01 (s, 1H), 8.25 (d, J = 6.7 Hz, 1H), 8.06 (s, 1H), 7.74 (d, J = 7.1 Hz, 1H), 7.56 (m, 2H), 7.53–7.48 (m, 1H), 7.18 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 8.8 Hz, 2H), 6.54 (m, 2H), 6.19 (d, J = 9.1 Hz, 1H), 3.70 (s, 3H), 3.30 (s, 3H) ppm. ¹³C NMR (101 MHz, DMSO) δ 168.8, 165.4, 158.6, 151.5, 137.6, 132.3, 131.6, 130.4, 128.8, 127.3, 127.2, 127.0, 125.3, 123.7, 119.6, 119.4, 117.9, 113.9, 112.6, 111.9, 100.0, 66.6, 60.3, 55.6, 51.7 ppm. IR (film): γ = 3393, 2950, 1694, 1608, 1508, 1466, 1437, 1370, 1313, 1297, 1266, 1221, 1177, 1096, 1033, 829, 745, 693 cm^{-1} . HRMS m/z (ESI^+): calcd for $\text{C}_{25}\text{H}_{20}\text{N}_2\text{NaO}_4$ ($[\text{M} + \text{Na}]^+$) 435.1315, found 435.1317.

(R)-Methyl 3-(1-(2-methoxyphenyl)-3-oxoisindolin-1-yl)indolizine-2-carboxylate (3e). White solid (18.8 mg, 91%). Mp 111–112 °C. 98% ee, determined by HPLC [Daicel Chiralcel] AD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 60/40, 1.0 mL min⁻¹, 254 nm, t_{major} = 8.571 min, t_{minor} = 9.692 min. $[\alpha]_{\text{D}}^{20}$ = -412.3° (c 0.39, CH_2Cl_2). ¹H NMR (500 MHz, CD_2Cl_2) δ 7.86–7.83 (m, 1H), 7.81 (d, J = 6.7 Hz, 1H), 7.73 (s, 1H), 7.64 (s, 1H), 7.61 (s, 1H), 7.53 (m, 2H), 7.28 (m, 3H), 6.94–6.84 (m, 2H), 6.43 (d, J = 6.7 Hz, 2H), 3.49 (s, 3H), 3.46 (s, 3H) ppm. ¹³C NMR (101 MHz, DMSO) δ 169.4, 165.9, 157.4, 149.8, 131.65, 131.6, 129.4, 129.3, 128.6, 125.7, 125.5, 124.0, 120.3, 119.6, 119.0, 118.1, 116.1, 113.3, 112.6, 111.6, 65.7, 55.7, 51.8, 49.9, 29.7 ppm. IR (film): γ = 3393, 2949, 1694, 1610, 1541, 1503, 1466, 1370, 1313, 1266, 1222, 1159, 1075, 745, 702 cm^{-1} . HRMS m/z (ESI^+): calcd for $\text{C}_{25}\text{H}_{20}\text{N}_2\text{NaO}_4$ ($[\text{M} + \text{Na}]^+$) 435.1315, found 435.1318.

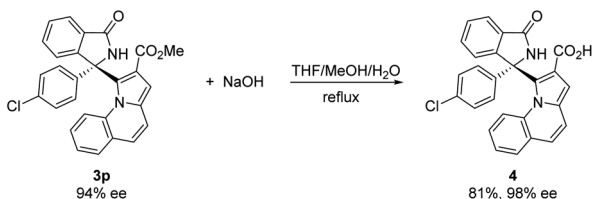
(R)-Methyl 3-(1-(3,4-dimethylphenyl)-3-oxoisindolin-1-yl)indolizine-2-carboxylate (3f). White solid (16.8 mg, 82%). Mp 113–114 °C. 78% ee, determined by HPLC [Daicel Chiralcel] AD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 60/40, 1.0 mL min⁻¹, 254 nm, t_{major} = 10.419 min, t_{minor} = 6.636 min. $[\alpha]_{\text{D}}^{20}$ = -421.9° (c 0.33, CH_2Cl_2). ¹H NMR (500 MHz, CDCl_3) δ 7.92 (d, J = 6.6 Hz, 1H), 7.79 (m, 3H), 7.54–7.43 (m, 2H), 7.34 (d, J = 7.0 Hz, 1H), 7.08 (s, 1H), 6.99 (m, 2H), 6.43 (t, J = 6.7 Hz, 1H), 6.40–6.30 (m, 1H), 5.88 (d, J = 9.5 Hz, 1H), 3.45 (s, 3H), 2.15 (d, J = 9.1 Hz, 6H) ppm. ¹³C NMR (101 MHz, DMSO) δ 169.5, 165.6, 150.6, 142.2, 136.4, 135.3, 131.6, 131.0, 130.2, 129.5, 128.6, 126.0, 125.8, 125.7, 124.3, 122.5, 119.7, 119.6, 118.8, 117.6, 113.0, 111.8, 66.7, 51.6, 20.0, 19.4 ppm. IR (film): γ = 3402, 2948, 1694, 1610, 1541, 1500, 1437, 1364, 1313, 1266, 1220, 1159, 1098, 816, 755, 692 cm^{-1} . HRMS m/z (ESI^+): calcd for $\text{C}_{26}\text{H}_{22}\text{N}_2\text{NaO}_3$ ($[\text{M} + \text{Na}]^+$) 433.1523, found 433.1521.

(R)-Methyl 3-(1-(4-fluorophenyl)-3-oxoisindolin-1-yl)indolizine-2-carboxylate (3g). White solid (18.2 mg, 91%). Mp 106–107 °C. 87% ee, determined by HPLC [Daicel Chiralcel] AD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 60/40, 1.0 mL min⁻¹, 254 nm, t_{major} = 11.698 min, t_{minor} = 7.095 min. $[\alpha]_{\text{D}}^{20}$ = -440.4° (c 0.27, CH_2Cl_2). ¹H NMR (400 MHz, $\text{DMSO}-d_6$) δ 9.08 (s, 1H), 8.30–8.24 (m, 1H), 8.11 (s, 1H), 7.77 (d, J = 7.1 Hz, 1H), 7.62–7.50 (m, 3H), 7.29 (m, 2H), 7.09 (t, J = 8.8 Hz, 2H),





Scheme 2 1 mmol scale reaction.



Scheme 3 Derivatization experiment.

6.60–6.52 (m, 2H), 6.20 (d, $J = 8.6$ Hz, 1H), 3.33 (s, 3H) ppm. ^{13}C NMR (101 MHz, DMSO) δ 168.8, 165.2, 162.8, 160.4, 151.0, 142.0, 132.5, 131.5, 130.3, 129.1, 127.7 (d, $J = 8.0$ Hz), 127.2, 125.5, 123.8, 119.6, 119.3, 119.2, 118.4, 115.4, 115.2, 112.3, 112.0, 66.7, 51.6 ppm. ^{19}F NMR (376 MHz, CDCl₃) δ –116.43 (s) ppm. IR (film): $\gamma = 3403, 2950, 1694, 1601, 1504, 1466, 1437, 1365, 1314, 1267, 1222, 1158, 1093, 1051, 832, 744, 692\text{ cm}^{-1}$. HRMS m/z (ESI⁺): calcd for C₂₄H₁₇FN₂NaO₃ ([M + Na]⁺) 423.1115, found 423.1116.

(R)-Methyl 3-(3-oxo-1-(4-(trifluoromethyl)phenyl)isoindolin-1-yl)indolizine-2-carboxylate (3h). White solid (18.0 mg, 80%). Mp 110–111 °C. 94% ee, determined by HPLC [Daicel Chiralcel] AD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 60/40, 1.0 mL min^{−1}, 254 nm, $t_{\text{major}} = 9.671$ min, $t_{\text{minor}} = 5.479$ min. $[\alpha]_{\text{D}}^{20} = -459.6^\circ$ (c 0.30, CH₂Cl₂). ^1H NMR (400 MHz, DMSO-*d*₆) δ 9.12 (s, 1H), 8.29 (d, $J = 6.6$ Hz, 1H), 8.16 (s, 1H), 7.79 (d, $J = 6.9$ Hz, 1H), 7.64 (d, $J = 8.2$ Hz, 2H), 7.57 (m, 3H), 7.48 (d, $J = 8.1$ Hz, 2H), 6.64–6.52 (m, 2H), 6.14 (d, $J = 9.0$ Hz, 1H), 3.28 (s, 3H) ppm. ^{13}C NMR (101 MHz, CDCl₃) δ 169.3, 165.0, 149.4, 149.2, 131.7, 131.2, 130.4, 129.4, 129.2, 129.1, 125.9, 125.5, 125.3 (d, $J = 3.6$ Hz), 124.7, 122.8, 119.5, 119.4, 119.2, 117.8, 112.3, 112.0, 66.7, 60.9, 29.7, 14.0 ppm. ^{19}F NMR (376 MHz, CDCl₃) δ –62.92 (d, $J = 11.9$ Hz) ppm. IR (film): $\gamma = 3404, 2961, 1694, 1616, 1541, 1503, 1467, 1438, 1411, 1364, 1326, 1263, 1223, 1194, 1163, 1098, 1068, 1017, 802, 757, 744, 695\text{ cm}^{-1}$. HRMS m/z (ESI⁺): calcd for C₂₅H₁₇F₃N₂NaO₃ ([M + Na]⁺) 473.1083, found 473.1086.

(R)-Methyl 3-(1-(4-chlorophenyl)-3-oxoisoindolin-1-yl)indolizine-2-carboxylate (3i). White solid (16.8 mg, 81%). Mp 126–127 °C. 92% ee, determined by HPLC [Daicel Chiralcel] AD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 60/40, 1.0 mL min^{−1}, 254 nm, $t_{\text{major}} = 13.252$ min, $t_{\text{minor}} = 7.570$ min. $[\alpha]_{\text{D}}^{20} = -530.6^\circ$ (c 0.39, CH₂Cl₂). ^1H NMR (400 MHz, DMSO-*d*₆) δ 9.06 (s, 1H), 8.27 (d, $J = 6.2$ Hz, 1H), 8.12 (s, 1H), 7.77 (d, $J = 6.8$ Hz, 1H), 7.60–7.51 (m, 3H), 7.29 (m, 4H), 6.61–6.51 (m, 2H), 6.18 (d, $J = 9.0$ Hz, 1H), 3.33 (s, 3H) ppm. ^{13}C NMR (101 MHz,

DMSO) δ 168.8, 165.1, 150.7, 144.9, 132.5, 132.0, 131.4, 130.4, 129.2, 128.7, 128.6, 128.0, 127.5, 127.3, 125.5, 123.9, 119.7, 119.2, 119.1, 118.5, 112.1, 111.9, 66.8, 51.6 ppm. IR (film): $\gamma = 3403, 2950, 1697, 1637, 1488, 1467, 1437, 1364, 1314, 1268, 1221, 1159, 1093, 1055, 1012, 824, 745, 690\text{ cm}^{-1}$. HRMS m/z (ESI⁺): calcd for C₂₄H₁₇ClN₂NaO₃ ([M + Na]⁺) 439.0820, found 439.0821.

(R)-Methyl 3-(1-(3-chlorophenyl)-3-oxoisoindolin-1-yl)indolizine-2-carboxylate (3j). White solid (18.3 mg, 88%). Mp 104–105 °C. 83% ee, determined by HPLC [Daicel Chiralcel] AD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 60/40, 1.0 mL min^{−1}, 254 nm, $t_{\text{major}} = 9.524$ min, $t_{\text{minor}} = 14.566$ min. $[\alpha]_{\text{D}}^{20} = -521.8^\circ$ (c 0.43, CH₂Cl₂). ^1H NMR (400 MHz, DMSO-*d*₆) δ 9.11 (s, 1H), 8.28 (d, $J = 6.1$ Hz, 1H), 8.13 (s, 1H), 7.78 (d, $J = 6.8$ Hz, 1H), 7.64–7.51 (m, 3H), 7.28 (t, $J = 4.1$ Hz, 3H), 7.25–7.18 (m, 1H), 6.61–6.52 (m, 2H), 6.18 (d, $J = 8.7$ Hz, 1H), 3.32 (s, 3H) ppm. ^{13}C NMR (101 MHz, DMSO) δ 168.8, 165.1, 150.5, 148.3, 133.4, 132.6, 131.4, 130.6, 130.4, 129.3, 127.4, 127.3, 125.5, 125.4, 124.5, 123.9, 119.7, 119.2, 119.1, 118.5, 112.1, 111.6, 66.9, 51.6 ppm. IR (film): $\gamma = 3398, 2950, 1698, 1611, 1591, 1541, 1503, 1467, 1437, 1370, 1314, 1266, 1221, 1191, 1079, 746, 729, 630\text{ cm}^{-1}$. HRMS m/z (ESI⁺): calcd for C₂₄H₁₇ClN₂NaO₃ ([M + Na]⁺) 439.0820, found 439.0823.

(R)-Ethyl 3-(3-oxo-1-phenylisoindolin-1-yl)indolizine-2-carboxylate (3k). White solid (16.6 mg, 84%). Mp 115–116 °C. 86% ee, determined by HPLC [Daicel Chiralcel] AD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 60/40, 1.0 mL min^{−1}, 254 nm, $t_{\text{major}} = 15.741$ min, $t_{\text{minor}} = 9.017$ min. $[\alpha]_{\text{D}}^{20} = -290.1^\circ$ (c 0.91, CH₂Cl₂). ^1H NMR (400 MHz, CDCl₃) δ 7.93 (d, $J = 6.5$ Hz, 1H), 7.88 (s, 1H), 7.80 (d, $J = 9.1$ Hz, 2H), 7.50 (m, 2H), 7.33 (d, $J = 7.1$ Hz, 3H), 7.24–7.16 (m, 3H), 6.44 (t, $J = 6.3$ Hz, 1H), 6.36 (m, 1H), 5.89 (d, $J = 9.5$ Hz, 1H), 4.00 (m, 1H), 3.85 (m, 1H), 1.06 (t, $J = 7.1$ Hz, 3H) ppm. ^{13}C NMR (101 MHz, CDCl₃) δ 169.4, 165.1, 150.3, 145.0, 131.5, 131.2, 130.3, 128.7, 128.2, 127.0, 125.9, 125.7, 125.1, 124.4, 119.9, 119.6, 118.8, 117.5, 112.9, 111.8, 66.9, 60.7, 31.5, 30.2, 14.0 ppm. IR (film): $\gamma = 3403, 2949, 1693, 1610, 1560, 1466, 1437, 1369, 1314, 1267, 1222, 1159, 745, 702\text{ cm}^{-1}$. HRMS m/z (ESI⁺): calcd for C₂₅H₂₀N₂NaO₃ ([M + Na]⁺) 419.1366, found 419.1366.

(R)-Ethyl 3-(3-oxo-1-(4-(trifluoromethyl)phenyl)isoindolin-1-yl)indolizine-2-carboxylate (3l). White solid (19.3 mg, 83%). Mp 97–99 °C. 94% ee, determined by HPLC [Daicel Chiralcel] AD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 60/40, 1.0 mL min^{−1}, 254 nm, $t_{\text{major}} = 8.130$ min, $t_{\text{minor}} = 4.912$ min. $[\alpha]_{\text{D}}^{20} = -343.0^\circ$ (c 0.37, CH₂Cl₂). ^1H NMR (400 MHz, CDCl₃) δ 7.96 (d, $J = 7.8$ Hz, 2H), 7.82 (d, $J = 7.7$ Hz, 2H), 7.58–7.45 (m, 6H), 7.31 (d, $J = 7.4$ Hz, 1H), 6.47 (t, $J = 6.7$ Hz, 1H), 6.39 (m, 1H), 5.90 (d, $J = 9.5$ Hz, 1H), 4.02 (m, 1H), 3.96–3.87 (m, 1H), 1.06 (t, $J = 7.1$ Hz, 3H) ppm. ^{13}C NMR (101 MHz, CDCl₃) δ 169.3, 165.0, 149.4, 149.2, 131.7, 131.2, 130.4, 129.4, 129.2, 129.1, 126.8, 125.9, 125.5, 125.3 (d, $J = 3.6$ Hz), 124.7, 122.8, 119.5, 119.4, 119.2, 117.8, 112.3, 112.0, 66.7, 60.9, 29.7, 14.0 ppm. ^{19}F NMR (376 MHz, CDCl₃) δ –62.99 (s) ppm. IR (film): $\gamma = 3403, 2959, 1694, 1615, 1503, 1467, 1326, 1268, 1220, 1163, 1122, 1081, 1017, 837, 744, 695\text{ cm}^{-1}$. HRMS m/z (ESI⁺): calcd for C₂₆H₁₉F₃N₂NaO₃ ([M + Na]⁺) 487.1240, found 487.1241.



(R)-Ethyl 3-(1-(4-chlorophenyl)-3-oxoisindolin-1-yl)indolizine-2-carboxylate (3m). White solid (16.6 mg, 77%). Mp 93–94 °C. 92% ee, determined by HPLC [Daicel Chiralcel] AD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 60/40, 1.0 mL min^{−1}, 254 nm, *t*_{major} = 13.446 min, *t*_{minor} = 6.167 min. $[\alpha]_D^{20} = -507.3^\circ$ (c 0.25, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ 7.94 (d, *J* = 6.9 Hz, 1H), 7.88 (s, 1H), 7.81 (d, *J* = 4.8 Hz, 2H), 7.52 (m, 2H), 7.32 (d, *J* = 6.0 Hz, 2H), 7.22 (d, *J* = 3.7 Hz, 1H), 7.15 (d, *J* = 4.8 Hz, 2H), 6.45 (t, *J* = 6.7 Hz, 1H), 6.40–6.34 (m, 1H), 5.87 (d, *J* = 9.5 Hz, 1H), 4.07 (m, 1H), 3.92 (m, 1H), 1.10 (t, *J* = 7.1 Hz, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 169.3, 165.0, 149.6, 147.3, 134.3, 131.7, 131.2, 130.3, 129.6, 129.1, 127.3, 125.9, 125.8, 125.3, 124.6, 123.4, 119.6, 119.4, 119.1, 117.8, 112.1, 111.9, 66.6, 60.9, 14.1 ppm. IR (film): γ = 3398, 2963, 1694, 1610, 1504, 1466, 1370, 1313, 1267, 1219, 1158, 1096, 830, 745, 692 cm^{−1}. HRMS *m/z* (ESI⁺): calcd for C₂₅H₁₉ClN₂NaO₃ ([M + Na]⁺) 453.0976, found 453.0977.

(R)-Methyl 1-(3-oxo-1-phenylisindolin-1-yl)pyrrolo[1,2-*a*]quinoline-2-carboxylate (3n). White solid (16.8 mg, 78%). Mp 156–157 °C. 91% ee, determined by HPLC [Daicel Chiralcel] OD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 85/15, 0.8 mL min^{−1}, 254 nm, *t*_{major} = 48.470 min, *t*_{minor} = 34.766 min. $[\alpha]_D^{20} = -525.4^\circ$ (c 0.20, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ 8.43 (s, 1H), 7.99–7.94 (m, 1H), 7.91–7.85 (m, 2H), 7.58–7.49 (m, 5H), 7.38–7.33 (m, 4H), 7.25–7.19 (m, 2H), 6.72 (d, *J* = 9.9 Hz, 1H), 5.86 (d, *J* = 10.0 Hz, 1H), 3.49 (s, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 150.1, 144.9, 132.7, 131.7, 131.1, 128.9, 128.9, 128.7, 128.5, 128.4, 127.9, 127.1, 125.9, 125.2, 124.9, 124.5, 123.5, 120.9, 118.8, 118.1, 117.5, 116.4, 114.3, 66.9, 51.6, 31.5, 29.7, 14.2 ppm. IR (film): γ = 3403, 2962, 1694, 1609, 1560, 1513, 1466, 1291, 1261, 1213, 1091, 1030, 799, 752, 701 cm^{−1}. HRMS *m/z* (ESI⁺): calcd for C₂₈H₂₀N₂NaO₃ ([M + Na]⁺) 455.1366, found 455.1367.

(R)-Methyl 1-(1-(3-chlorophenyl)-3-oxoisindolin-1-yl)pyrrolo[1,2-*a*]quinoline-2-carboxylate (3o). White solid (21.2 mg, 91%). Mp 144–145 °C. 87% ee, determined by HPLC [Daicel Chiralcel] OD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 85/15, 0.8 mL min^{−1}, 254 nm, *t*_{major} = 27.451 min, *t*_{minor} = 23.576 min. $[\alpha]_D^{20} = -550.8^\circ$ (c 0.19, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ 8.45 (d, *J* = 5.0 Hz, 1H), 7.96 (t, *J* = 6.4 Hz, 2H), 7.92–7.88 (m, 1H), 7.59 (d, *J* = 5.1 Hz, 1H), 7.55 (m, 3H), 7.41–7.38 (m, 1H), 7.34 (d, *J* = 6.2 Hz, 2H), 7.27 (d, *J* = 1.9 Hz, 1H), 7.18 (t, *J* = 4.5 Hz, 2H), 6.73 (m, 1H), 5.84 (m, 1H), 3.57 (m, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 169.7, 169.4, 165.2, 149.5, 149.4, 147.1, 142.2, 131.9, 129.9, 129.7, 129.2, 128.8, 128.7, 127.4, 126.0, 125.9, 125.3, 125.1, 124.7, 123.9, 123.5, 122.9, 121.2, 117.9, 114.4, 87.7, 66.6, 51.8 ppm. IR (film): γ = 3403, 2960, 1694, 1610, 1591, 1513, 1438, 1377, 1291, 1261, 1214, 1128, 1088, 794, 750, 699 cm^{−1}. HRMS *m/z* (ESI⁺): calcd for C₂₈H₁₉ClN₂NaO₃ ([M + Na]⁺) 489.0976, found 489.0981.

(R)-Methyl 1-(1-(4-chlorophenyl)-3-oxoisindolin-1-yl)pyrrolo[1,2-*a*]quinoline-2-carboxylate (3p). White solid (15.8 mg, 68%). Mp 156–157 °C. 94% ee, determined by HPLC [Daicel Chiralcel] OD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 85/15, 0.8 mL min^{−1}, 254 nm, *t*_{major} = 31.845 min, *t*_{minor} = 21.607 min. $[\alpha]_D^{20} = -550.8^\circ$ (c 0.12, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃)

δ 8.44 (s, 1H), 7.98–7.87 (m, 3H), 7.55 (d, *J* = 7.0 Hz, 4H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.31 (d, *J* = 7.5 Hz, 3H), 7.21 (d, *J* = 8.5 Hz, 2H), 6.73 (d, *J* = 9.9 Hz, 1H), 5.86 (d, *J* = 9.9 Hz, 1H), 3.58 (s, 3H) ppm. ¹³C NMR (151 MHz, CDCl₃) δ 171.9, 167.8, 152.1, 149.7, 136.9, 135.9, 135.2, 134.4, 133.7, 132.2, 131.8, 131.6, 131.4, 131.3, 129.9, 128.5, 127.9, 127.8, 127.3, 126.1, 125.8, 123.7, 120.9, 120.5, 118.3, 116.9, 69.2, 54.3 ppm. IR (film): γ = 3398, 2951, 1694, 1610, 1560, 1514, 1486, 1438, 1359, 1291, 1246, 1213, 1150, 1091, 1014, 793, 752, 692 cm^{−1}. HRMS *m/z* (ESI⁺): calcd for C₂₈H₁₉ClN₂NaO₃ ([M + Na]⁺) 489.0976, found 489.0980.

(R)-Methyl 1-(3-oxo-1-(thiophen-2-yl)isindolin-1-yl)pyrrolo[1,2-*a*]quinoline-2-carboxylate (3q). Yellow solid (13.4 mg, 61%). Mp 144–145 °C. 92% ee, determined by HPLC [Daicel Chiralcel] OD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH = 85/15, 0.8 mL min^{−1}, 254 nm, *t*_{major} = 38.232 min, *t*_{minor} = 26.609 min. $[\alpha]_D^{20} = -550.8^\circ$ (c 0.19, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ 8.41 (s, 1H), 8.01–7.95 (m, 2H), 7.89 (d, *J* = 8.7 Hz, 1H), 7.58–7.51 (m, 4H), 7.44 (m, 1H), 7.36 (t, *J* = 7.3 Hz, 1H), 7.11–7.08 (m, 1H), 6.85 (d, *J* = 3.2 Hz, 2H), 6.72 (d, *J* = 9.9 Hz, 1H), 5.80 (d, *J* = 9.9 Hz, 1H), 3.64 (s, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 168.9, 165.6, 150.5, 149.8, 132.6, 131.9, 130.6, 129.2, 128.8, 128.7, 128.5, 126.9, 125.7, 125.2, 124.5, 124.2, 123.9, 123.4, 121.1, 119.3, 117.9, 117.3, 115.6, 114.4, 64.6, 51.9 ppm. IR (film): γ = 3403, 2950, 1694, 1601, 1504, 1466, 1437, 1365, 1314, 1267, 1222, 1158, 1093, 1051, 832, 744, 692 cm^{−1}. HRMS *m/z* (ESI⁺): calcd for C₂₆H₁₈N₂NaO₃ ([M + Na]⁺) 461.0930, found 461.0931.

Procedure for the 1.0 mmol scale reaction

To a mixture of indolizine-2-carboxylate **1c** (225 mg, 1 mmol), 3-hydroxyisindolinones **2i** (259 mg, 1 mmol, 1 equiv.) and catalyst (**S**)-**4a** (0.1 mmol, 10 mol%) in DCE (20 mL) was added 4 Å MS (2 g). After stirring at room temperature for 24 hours, the residue was purified by flash column chromatography with acetate/petroleum ether 1 : 2 (v/v) on silica gel to give the desired product **3p** (284 mg) in 61% yield with 94% ee.

Procedure for the derivatization experiment

To a 100 mL round-bottomed flask, **3p** (292 mg, 0.63 mmol), NaOH (125 mg, 3.2 mmol) and 30 mL mixed solvent [THF/MeOH/H₂O 2 : 2 : 0.5 (v/v/v)] were added. After refluxing for 5 hours, adjusted the pH to 2 with 1 M HCl and extracted three times with ethyl acetate. The residue was purified by flash column chromatography with acetate/petroleum ether/formic acid 1 : 1 : 1.5% (v/v/v) on silica gel to give the desired product **4** (230 mg) in 81% yield with 98% ee.

(R)-1-(1-(4-chlorophenyl)-3-oxoisindolin-1-yl)pyrrolo[1,2-*a*]quinoline-2-carboxylic acid. Yellow solid (230 mg, 81%). Mp 212–213 °C. 98% ee, determined by HPLC [Daicel] AD-H column (250 × 4.6 mm), *n*-hexane/*i*-PrOH/HCOOH = 80/20/0.1, 1.0 mL min^{−1}, 254 nm, *t*_{major} = 21.848 min, *t*_{minor} = 12.595 min. $[\alpha]_D^{20} = -568.889^\circ$ (c 0.13, CH₂Cl₂). ¹H NMR (400 MHz, CD₂Cl₂) δ 13.31 (s, 1H), 10.37 (s, 1H), 8.56 (s, 1H), 7.92 (m, 2H), 7.59 (m, 2H), 7.53 (m, 2H), 7.47–7.43 (m, 1H), 7.38–7.24 (m, 5H), 6.74 (d, *J* = 10.0 Hz, 1H), 6.10 (d, *J* = 10.0 Hz, 1H) ppm. ¹³C NMR (101 MHz, CD₂Cl₂) δ 171.5, 167.9, 150.1, 144.1, 133.13, 133.09, 132.2, 131.6, 129.7, 129.5, 129.1, 128.9, 128.5, 127.0, 126.8, 125.5,



124.7, 123.8, 121.2, 119.6, 118.4, 116.6, 114.8, 68.4, 54.4, 54.1, 53.8, 53.5, 53.3 ppm. IR (film): $\gamma = 3290, 2924, 1689, 1661, 1610, 1540, 1488, 1441, 1379, 1329, 1290, 1213, 1154, 1014, 918, 828, 791, 750, 704 \text{ cm}^{-1}$. HRMS m/z (ESI⁺): calcd for C₂₇H₁₇ClN₂NaO₃ ([M + Na]⁺) 475.0820, found 475.0820.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

- (a) P. M. Dewick, *Medicinal Natural Products: A Biosynthetic Approach*, Wiley, Chichester, UK, 2009; (b) P. S. Sidhu, N. Nassif, M. M. McCallum, K. Teske, B. Feleke, N. Y. Yuan, P. Nandhikonda, J. M. Cook, R. K. Singh, D. D. Bickle and L. A. Arnold, *ACS Med. Chem. Lett.*, 2014, **5**, 199; (c) J. Zhu, H. Chen, X.-E. Guo, X.-L. Qiu, C.-M. Hu, A. R. Chamberlin and W.-H. Lee, *Eur. J. Med. Chem.*, 2015, **96**, 196.
- (a) S. Kobayashi, Y. Mori, J. S. Fossey and M. M. Salter, *Chem. Rev.*, 2011, **111**, 2626; (b) S.-L. You, Q. Cai and M. Zeng, *Chem. Soc. Rev.*, 2009, **38**, 2190; (c) J. Vesely and R. Rios, *Chem. Soc. Rev.*, 2014, **43**, 611; (d) Z.-H. Kang, Y.-H. Wang, D. Zhang, R.-B. Wu, X.-F. Xu and W.-H. Hu, *J. Am. Chem. Soc.*, 2019, **141**, 1473; (e) Z.-H. Kang, D. Zhang, J.-Y. Shou and W.-H. Hu, *Org. Lett.*, 2018, **20**, 983; (f) J.-Y. Chen, H.-Y. Wu, Q.-W. Gui, S. Yan, J. Deng, Y.-W. Lin, Z. Cao and W.-M. He, *Chin. J. Catal.*, 2021, **42**, 1445; (g) Y. Wu, J.-Y. Chen, J. Ning, X. Jiang, J. Deng, Y. Deng, R. Xu and W.-M. He, *Green Chem.*, 2021, **23**, 3950; (h) Z.-L. Wu, J.-Y. Chen, X.-Z. Tian, W.-T. Ouyang, Z.-T. Zhang and W.-M. He, *Chin. Chem. Lett.*, 2022, **33**, 1501; (i) Q.-W. Gui, B. Wang, S. Zhu, F.-L. Li, M.-X. Zhu, M. Yi, J.-L. Yu, Z.-L. Wu and W.-M. He, *Green Chem.*, 2021, **23**, 4430.
- (a) M. Terada and K. Sorimachi, *J. Am. Chem. Soc.*, 2007, **129**, 292; (b) Q. Kang, Z. Zhao and S.-L. You, *J. Am. Chem. Soc.*, 2007, **129**, 1484; (c) G. B. Rowland, E. B. Rowland, Y. Liang, J. A. Perman and J. C. Antilla, *Org. Lett.*, 2007, **9**, 2609; (d) S. Nakamura, N. Matsuda and M. Ohara, *Chem.-Eur. J.*, 2016, **22**, 9478; (e) J. Feng, W. Yan, D. Wang, P. Li, Q. Sun and R. Wang, *Chem. Commun.*, 2012, **48**, 8003; (f) D. Glavac, C. Zheng, I. Dokli, S.-L. You and M. Gredicak, *J. Org. Chem.*, 2017, **82**, 8752.
- (a) M. Johannsen, *Chem. Commun.*, 1999, 2233; (b) S. Saaby, X. Fang, N. Gathergood and K. A. Jørgensen, *Angew. Chem., Int. Ed.*, 2000, **39**, 4114; (c) S. Saaby, P. Bayon, P. S. Aburel and K. A. Jørgensen, *J. Org. Chem.*, 2002, **67**, 4352; (d) L. Wu, R. Liu, G. Zhang, D. Wang, H. Wu, J. Gao and Y. Jia, *Adv. Synth. Catal.*, 2015, **357**, 709; (e) K. Tsuchida, Y. Senda, K. Nakajima and Y. Nishibayashi, *Angew. Chem.*, 2016, **128**, 9880; (f) S. Dasgupta, J. Liu, C. A. Shoffler, G. P. A. Yap and M. P. Watson, *Org. Lett.*, 2016, **18**, 6006.
- (a) J. Kluza, M. A. A. Gallego, J. C. Loyens, J. M. Beauvillain, F. Sousa-Faro, C. Cuevas, P. Marchetti and C. Bailly, *Cancer Res.*, 2006, **66**, 3177; (b) G. S. Singh and E. E. Mmatli, *Eur. J. Med. Chem.*, 2011, **46**, 5237; (c) T. Weide, L. Arve, H. Prinz, H. Waldmann and H. Kessler, *Bioorg. Med. Chem. Lett.*, 2006, **16**, 59; (d) I. Macsari, Y. Besidski, G. Csajernyk, L. I. Nilsson, L. Sandberg, U. Yngve, K. Åhlin, T. Bueters, A. B. Eriksson, P. E. Lund, E. Venyike, S. Oerther, K. H. Blakeman, L. Luo and P. I. Arvidsson, *J. Med. Chem.*, 2012, **55**, 6866.
- (a) X. Chen, X. Hu, Y. Deng, H. Jiang and W.-A. Zeng, *Org. Lett.*, 2016, **18**, 4742; (b) S. A. Roy, J. Zgheib, C. Zhou and B. A. Arndtsen, *Chem. Sci.*, 2021, **12**, 2251; (c) I. V. Nechaev, G. V. Cherkaev, P. N. Solov'yev and N. V. Boev, *J. Org. Chem.*, 2021, **86**, 4220; (d) K. Su, X. Guo, L. Zhu, Y. Liu, Y. Lu and B. Chen, *Org. Chem. Front.*, 2021, **8**, 4177; (e) D. Zhang, Z. Su, Q. He, Z. Wu, Y. Zhou, C. Pan, X. Liu and X. Feng, *J. Am. Chem. Soc.*, 2020, **142**, 15975; (f) X. Huang and T.-X. Zhang, *Tetrahedron Lett.*, 2009, **50**, 208; (g) J. Jaung and Y.-S. Jung, *Bull. Korean Chem. Soc.*, 2003, **24**, 1565; (h) Y.-X. Yao, M. Alami, A. Hamze and O. Provot, *Org. Biomol. Chem.*, 2021, **19**, 3509; (i) C.-S. Xie, Y.-H. Zhang and P.-X. Xu, *Synlett*, 2008, **20**, 3115; (j) D. C. Rogness, N. A. Markina, J. P. Waldo and R. C. Larock, *J. Org. Chem.*, 2012, **77**, 2743.
- (a) J. T. M. Corriea, B. List and F. Coelho, *Angew. Chem., Int. Ed.*, 2017, **56**, 7967; (b) L. Yang, X. Pu, D.-W. Niu, Z.-Y. Fu and X. Zhang, *Org. Lett.*, 2019, **21**, 8553; (c) J.-M. Lu, M.-F. Wang, R.-G. Xu, H.-Z. Sun, X. Zheng, G.-F. Zhong and X.-F. Zeng, *Asian J. Org. Chem.*, 2021, **10**, 1500; (d) Q.-J. Ni, Z.-M. Zhu, Y.-J. Fan, X.-Y. Chen and X.-X. Song, *Org. Lett.*, 2021, **23**, 9548; (e) C. Huang, Z.-F. Zhao, S.-W. Li, J.-X. Zhao, L.-F. Wu and C.-Z. Gu, *Org. Chem. Front.*, 2022, **9**, 1932; (f) X.-X. Song, Y.-J. Fan, Z.-M. Zhu and Q.-J. Ni, *Org. Lett.*, 2022, **24**, 2315.
- (a) F. Xu, D. Huang, C. Han, W. Shen, X.-F. Lin and Y.-G. Wang, *Org. Chem.*, 2010, **75**, 8677; (b) D. Huang, X. Li, F. Xu, L. Li and X.-F. Lin, *ACS Catal.*, 2013, **3**, 2244; (c) L. Wang, J.-L. Zhong and X.-F. Lin, *Angew. Chem., Int. Ed.*, 2019, **58**, 15824; (d) J. Luo, T. Zhang, L. Wang, G. Liao, Q. Yao, Y. Wu, B. Zhan, Y. Lan, X.-F. Lin and B.-F. Shi, *Angew. Chem., Int. Ed.*, 2019, **58**, 6708; (e) B. Zhan, L. Wang, J. Luo, X.-F. Lin and B.-F. Shi, *Angew. Chem., Int. Ed.*, 2020, **59**, 3568; (f) A. B. Woldegiorgis, Z. Han and X.-F. Lin, *Org. Lett.*, 2021, **23**, 6606; (g) L. Wang, J.-L. Zhong and X.-F. Lin, *Synlett*, 2021, **32**, 417; (h) Z. Chen, L. Wang, Y. Qian and X.-F. Lin, *Synlett*, 2021, **32**, 1231; (i) X.-F. Lin, L. Wang, Z. Han and Z.-L. Chen, *Chin. J. Chem.*, 2021, **39**, 602.
- (a) T. Akiyama, J. Itoh, K. Yokota and K. Fuchibe, *Angew. Chem., Int. Ed.*, 2004, **43**, 1566; (b) D. Uruguchi and M. Terada, *J. Am. Chem. Soc.*, 2004, **126**, 5356. For reviews, see: (c) T. Akiyama, *Chem. Rev.*, 2007, **107**, 5744; (d)



- M. Terada, *Chem. Commun.*, 2008, 4097; (e) G. Adair, S. Mukherjee and B. List, *Aldrichimica Acta*, 2008, **41**, 31; (f) S.-L. You, Q. Cai and M. Zeng, *Chem. Soc. Rev.*, 2009, **38**, 2190; (g) D. Parmar, E. Sugiono, S. Raja and M. Rueping, *Chem. Rev.*, 2014, **114**, 9047; (h) A. B. Woldegiorgis and X.-F. Lin, *Beilstein J. Org. Chem.*, 2021, **17**, 2729.
- 10 (a) A. U. Rajshekhar, M. S. Milon, K. R. Sumit, G. B. Rayhan and K. S. A. Vinod, *Chem. Commun.*, 2018, **54**, 3516; (b) C.-X. Qian, W.-W. Liu, J.-W. Sun and P.-F. Li, *Org. Chem. Front.*, 2022, **9**, 1234; (c) L. Chen and Y. Zou, *Adv. Synth. Catal.*, 2021, **363**, 4159; (d) M. Rong, J. Li, Y. Zhou, F. Zhang and J.-A. Ma, *Org. Lett.*, 2020, **22**, 9010.
- 11 Q.-J. Ni, Z.-M. Zhu, Y.-J. Fan, X.-Y. Chen and X.-X. Song, *Org. Lett.*, 2021, **23**, 9548.
- 12 M. M. Sadhu, S. K. Ray, R. A. Unhale and V. K. Singh, *Org. Biomol. Chem.*, 2022, **20**, 410.

