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Highly Enantioselective Fluorination of Unprotected 3-Substituted Oxindoles: One-Step Synthesis of BMS 204352 (MaxiPost)

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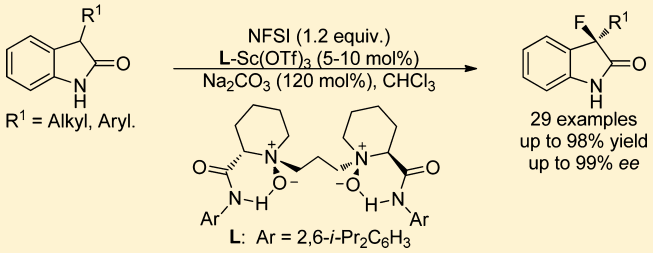
Supporting Information

ABSTRACT: The catalytic enantioselective fluorination of N−H-free 3-substituted oxindoles was accomplished by a Sc(III)/*N*,*N*′-dioxide complex. Under mild reaction conditions, a series of 3-aryl- and 3-alkyl-3-fluoro-2-oxindoles were obtained in excellent yields (up to 98%) and enantioselectivities (up to 99% ee) by using *N*-fluorobisbenzenesulfonimide (NFSI) as the fluorination agent. MaxiPost was synthesized efficiently in 81% yield with 96% ee.



INTRODUCTION

In the last decades, fluorine-containing compounds have drawn the attention of synthetic chemists, owing to their specific properties in materials and pharmaceuticals.[1] The enantioselective electrophilic fluorination of carbonyl compounds stands for one of the most efficient strategies for the construction of chiral fluorine-containing compounds.[2] The asymmetric fluorinations of 1,3-dicarbonyl compounds and aldehydes were the pioneering works in this field.[3] Subsequently, *N*-Boc-protected oxindoles were proven to be suitable substrates, and meanwhile the introduction of a fluorine atom at the 3-position of oxindoles was very fascinating in enhancing pharmaceutical efficiency. (*S*)-(+)-BMS-204352 (MaxiPost), which was identified as a promising agent for the treatment of stroke, is one such example.[4] After Shibata[5a] and Cahard[5b] independently reported a stoichiometric cinchona alkaloid derivative[6] promoted asymmetric synthesis of BMS-204352 in 2003, the catalytic enantioselective fluorination of *N*-Boc-protected oxindoles was also established using catalysts such as (*S*)-DM-BINAP-Pd(II) complex, chiral dbfox-Ph-Ni(II) or boxmi-Ni(II) complex, and bis-cinchona alkaloids.[7,8]

In comparison, unprotected 3-substituted oxindoles are relatively less acidic carbon nucleophiles.[9] Their fluorination is still limited, although it would afford the desired medicinal objects without the laborious procedures for protecting substrates and deprotection of the products (Scheme 1). In view of the purpose of ideal synthesis[10a] and protecting-group-free synthesis,[10b] direct catalytic asymmetric fluorination of unprotected oxindoles is still necessary. Herein, we report an *N*,*N*′-dioxide-Sc(OTf)$_3$ complex[11] catalyzed direct fluorination of unprotected 3-aryl- and 3-alkyloxindoles to afford the corresponding 3-fluorinated oxindoles with excellent outcomes.

RESULTS AND DISCUSSION

Initially, the asymmetric fluorination was carried out with unprotected 3-(4-methoxybenzyl)-2-oxindole **1aa**[12] and *N*-fluorobenzenesulfonimide (NFSI) using 10 mol % of **L1**-Sc(OTf)$_3$ complex as the catalyst (Figure 1). In the absence of a base additive, no product was observed (Table 1, entry 1). Considering that base might promote the enolization of oxindole, we tested a series of bases to initiate the reaction (Table 1, entries 2−6). The results indicated that the Brønsted basicity of the base played an important role in governing the rate and enantioselectivity of the fluorination reaction. The stronger the Brønsted basicity, the higher the yield and lower the enantioselectivity of the product (Table 1, entries 2−5). To our delight, when Na_2CO_3 was added, the desired fluorinated product **2aa** was obtained in 78% yield with 77% ee (Table 1, entry 3). The organic base *i*-Pr$_2$NEt gave a relatively lower yield because of the decomposition of NFSI (Table 1, entry 6 vs entry 3). Other fluorinating reagents were found to be sluggish in the catalytic system (Table 1, entries 7 and 8).

Investigation of Lewis acids[13] showed that the coordination of **L1** with $Ni(ClO_4)_2·6H_2O$, $Mg(OTf)_2$, $Y(OTf)_3$, and $La(OTf)_3$ gave low yields and enantioselectivities in this reaction (Table 2, entries 2−5 vs entry 1). The screening of the chiral amino acid backbone of the ligand suggested that the chiral *N*,*N*′-dioxide **L2** derived from (*S*)-pipecolic acid and 2,6-diisopropylaniline exhibited a superior result (84% yield, 87% ee; Table 2, entry 6 vs entries 1 and 7). Less steric hindered substituents at the ortho positions of aniline gave unsatisfactory ee's (Table 2, entry 6 vs entries 8−10). Both the ligand and the metal ion could direct a switch in enantioselectivity slightly (Table 2, entries 5 and 10).

Subsequently, the effect of solvent and temperature was surveyed as shown in Table 3. Solvents, such as methanol, diethyl ether, and toluene, gave less satisfactory results (Table 3, entries 2−4). Reactions in EtOAc and THF afforded higher yields but slightly lower enantioselectivities (Table 3, entries 5

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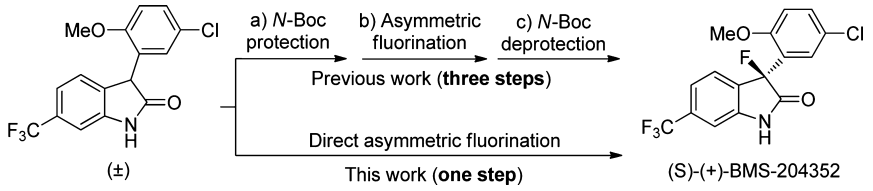
Scheme 1. Catalytic Asymmetric Synthesis of MaxiPost



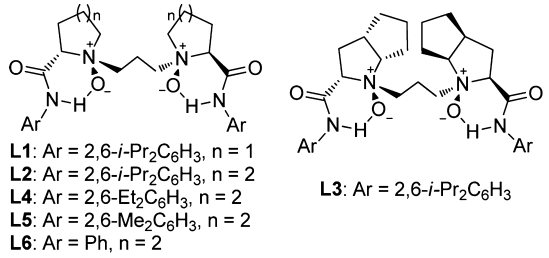
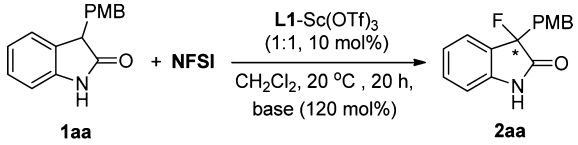


Figure 1. Ligands screened in this work.

Table 1. Screen of the Base Additives and Fluorinating Agents



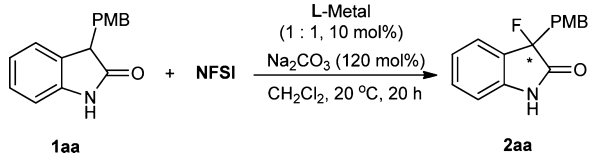
entry[a]	base	yield[b] (%)	ee[c] (%)
1	no	n.r.	n.d.
2	Li_2CO_3	13	62
3	Na_2CO_3	78	77
4	K_2CO_3	80	71
5	Cs_2CO_3	85	21
6[d]	*i*-Pr_2NEt	15	12
7[e]	Na_2CO_3	n.r.	n.d.
8[f]	Na_2CO_3	17	10

[a]Unless otherwise noted, all reactions were performed with **L1**-Sc(OTf)$_3$ (1/1, 10 mol %), base (0.12 mmol), **1aa** (0.1 mmol, PMB = *p*-methoxybenzyl), and NFSI (*N*-fluorobenzenesulfonimide, 0.12 mmol) in CH_2Cl_2 (0.5 mL) under N_2 at 20 °C for 20 h. [b]Isolated yield; n.r. = no reaction. [c]Determined by HPLC analysis; n.d. = not determined. [d]*i*-Pr_2NEt led to the decomposition of NFSI. [e]*N*-Fluoropyridinium triflate was used instead of NFSI. [f]Selectfluor was used instead of NFSI.

and 6). Comparatively, chlorinated alkanes gave better results (Table 3, entries 7−9). Pleasingly, the enantioselectivity increased to 95% ee using $CHCl_3$ as the solvent (Table 3, entry 9). Meanwhile, the reaction temperature was found to have a slight effect on the reaction under these conditions. Lowering the reaction temperature to 0 °C further improved the ee to 97% (Table 3, entries 10 and 11). Importantly, the catalyst loading could decrease to 5 mol % without loss of the yield and enantioselectivity in a prolonged reaction time (Table 3, entry 12).

With the optimized reaction conditions in hand (Table 3, entry 12), the generality of the protocol for different unprotected 3-substituted oxindoles was explored. As shown in Table 4, the reactions performed well with a series of 3-benzyl-substituted oxindoles. The electronic nature and the position of substituents on the C3-benzyl ring had little influence on the yields and enantiomeric excesses (80−98% yields, 96−99% ee's; Table 4, entries 1−14). Remarkably, variation of the C3-substituent to thienylmethyl, pyridylmethyl, or naphthylmethyl was satisfied to deliver the desired products in 84−90% yields with 91−99% ee's (Table 4, entries 15−18). The 3-alkyl-2-oxindoles were also tolerated for this reaction

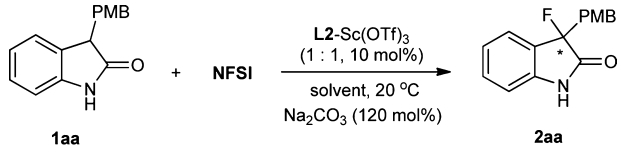
Table 2. Screen of Lewis Acids and *N,N′*-Dioxide Ligands



entry[a]	metal	ligand	yield[b] (%)	ee[c] (%)
1	$Sc(OTf)_3$	**L1**	78	77
2	$Ni(ClO_4)_2{\cdot}6H_2O$	**L1**	20	<5
3	$Mg(OTf)_2$	**L1**	16	<5
4	$Y(OTf)_3$	**L1**	19	17
5	$La(OTf)_3$	**L1**	11	−13
6	$Sc(OTf)_3$	**L2**	84	87
7	$Sc(OTf)_3$	**L3**	75	88
8	$Sc(OTf)_3$	**L4**	80	75
9	$Sc(OTf)_3$	**L5**	80	50
10	$Sc(OTf)_3$	**L6**	95	−13

[a]All reactions were performed with **L**-Sc(OTf)$_3$ (1/1, 10 mol %), Na_2CO_3 (0.12 mmol), **1aa** (0.1 mmol), and NFSI (0.12 mmol) in CH_2Cl_2 (0.5 mL) under N_2 at 20 °C for 20 h. [b]Isolated yield. [c]Determined by HPLC analysis.

Table 3. Screen of Solvents



entry[a]	solvent	time (h)	yield[b] (%)	ee[c] (%)
1	CH_2Cl_2	20	84	87
2	CH_3OH	20	6	22
3	Et_2O	20	28	73
4	toluene	20	68	80
5	EtOAc	20	98	85
6	THF	20	92	85
7	Cl_3CCH_3	20	95	85
8	CH_2ClCH_2Cl	20	85	87
9	$CHCl_3$	20	90	95
10[d]	$CHCl_3$	48	86	97
11[d,e]	$CHCl_3$	48	95	97
12[d–f]	$CHCl_3$	72	96	97

[a]Unless otherwise noted, all reactions were performed with **L2**-Sc(OTf)$_3$ (1/1, 10 mol %), Na_2CO_3 (0.12 mmol), **1aa** (0.1 mmol), and NFSI (0.12 mmol) in solvent (0.5 mL) under N_2 at 20 °C for 20 h. [b]Isolated yield. [c]Determined by HPLC analysis. [d]At 0 °C. [e]In $CHCl_3$ (0.25 mL). [f]5 mol % catalyst loading.

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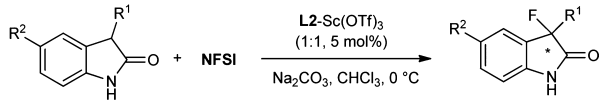
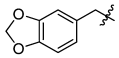
Table 4. Substrate Scope of the Catalytic Asymmetric Fluorination of Unprotected 3-Substituted Oxindoles



1
1aa-1ba, R^2 = H; **1bb**, R^2 = Cl

2aa-2bb

entry[a]	R^1	time (days)	product	yield[b] (%)	*ee*[c] (%)
1	4-$MeOC_6H_4CH_2$	3	**2aa**	96	97
2	Bn	3	**2ab**	95	99
3	2-$MeC_6H_4CH_2$	2	**2ac**	87	99
4	3-$MeC_6H_4CH_2$	3	**2ad**	96	96
5	4-$MeC_6H_4CH_2$	3	**2ae**	96	96
6	2-$ClC_6H_4CH_2$	2	**2af**	82	98
7	3-$ClC_6H_4CH_2$	2	**2ag**	84	97
8	4-$ClC_6H_4CH_2$	3	**2ah**	98	98
9	4-$FC_6H_4CH_2$	2	**2ai**	80	97
10	4-$BrC_6H_4CH_2$	3	**2aj**	92	96
11	3-$NO_2C_6H_4CH_2$	3	**2ak**	98	96
12	4-$NO_2C_6H_4CH_2$	3	**2al**	94	97
13	2,4-$Cl_2C_6H_3CH_2$	2	**2am**	85	97
14		2	**2an**	91	97
15[d]		3	**2ao**	90	97 (*R*)
16		2	**2ap**	84	91
17	1-Naphthylmethyl	2	**2aq**	90	99
18	2-Naphthylmethyl	2	**2ar**	88	97
19[e]	Me	2	**2as**	80	90
20[e,f]	Et	2	**2at**	87	92
21[e,f]	*n*-Pr	2	**2au**	83	93
22[e,f]	*n*-Bu	2	**2av**	82	93
23[e,f]	*i*-Bu	2	**2aw**	85	93
24[e,f]	3-Ethylbutyl	2	**2ax**	87	90
25[e]	Allyl	2	**2ay**	81	95
26[g,h]	Ph	3	**2az**	85	89 (*R*)
27[g]	4-ClC_6H_4	3	**2ba**	89	89
28[g]	Ph	2	**2bb**	98	93

[a]Unless otherwise noted, the reactions were performed with **1** (0.1 mmol), **L2**-Sc(III) complex (1/1, 5 mol %) and Na_2CO_3 (0.12 mmol, 12.7 mg), NFSI (0.12 mmol, 37.8 mg) in $CHCl_3$ (0.25 mL) at 0 °C for the indicated time. [b]Isolated yield. [c]Determined by HPLC analysis (see Supporting Information for details). [d]The absolute configuration of **2ao** was *R* as determined by X-ray analysis. [e]In 0.5 mL of $CHCl_3$ and at 20 °C. [f]10 mol % catalyst loading. [g]In 2.0 mL of $CHCl_3$ at −20 °C with 10 mol % of **L3**-Sc(III) complex (1/1). [h]The absolute configuration of **2az** was *R* determined by comparison with literature.

(80−87% yields, 90−93% ee's; Table 4, entries 19−24). Moreover, oxindole with an unsaturated allyl group at the C3 position was compatible with this method, giving a moderate yield with 95% ee (Table 4, entry 25). By the use of *N*,*N*′-dioxide **L3** instead of **L2**,[14] 3-aryl-2-oxindoles were also suitable substrates for this reaction (85−98% yields, 89−93% ee's; Table 4, entries 26−28).

Encouraged by these results, we next applied this method to synthesize Maxipost. Excitingly, the desired Maxipost **2bc** was achieved in 81% yield with 96% ee (Scheme 2).[15] The absolute configuration of Maxipost was determined to be *S* by comparing the optical rotation with the literature value.[5a] Without introduction and removal of protecting groups, this direct synthesis approach is atom-economical and efficient.

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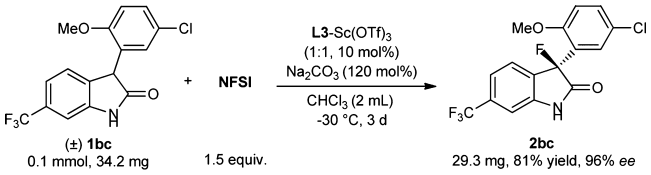
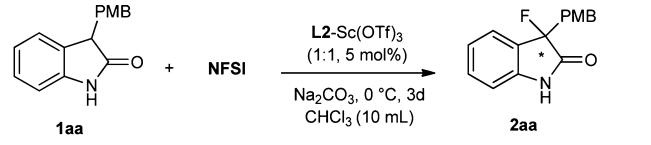
Scheme 2. One-Step Synthesis of Optically Active Maxipost



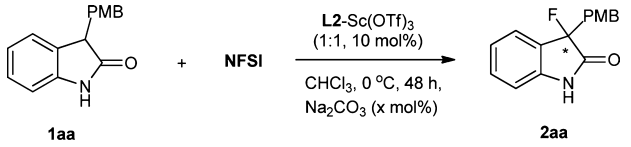
To show the synthetic utility of the catalyst system, fluorination of oxindole **1aa** was expanded to a gram scale. The desired 3-fluorooxindole **2aa** was obtained in 93% yield with 97% ee (Scheme 3).

Scheme 3. Asymmetric Fluorination of Oxindole 1aa on a Gram Scale



Control experiments were performed to verify the specific effect of the base on the fluorination (Scheme 4). No reaction

Scheme 4. Control Experiments



x =	2aa yield (%)	2aa ee (%)
0	n.r.	n.d.
10	12	96
50	79	97
120	95	97
200	97	96

was observed without a base. Also a catalytic amount of Na_2CO_3 exhibited low reactivity. These results indicated that base accelerated the enolization of oxindole and the formation of sodium dibenzenesulfonimide was beneficial to the equilibrium toward the fluorinated product. When 200 mol % of Na_2CO_3 was added, the product **2aa** was obtained with lower ee, possibly due to the background reaction promoted by excess Na_2CO_3.[16]

In light of the X-ray structure of the *N,N′*-dioxide-Sc(III) complex[17] and the absolute configurations of the product **2ao**[18] and **2az**, a catalytic model for the fluorination of the 3-substituted oxindole was proposed. As shown in Figure 2, the oxophilic metal Sc(III)[19] coordinates with four oxygens of the *N,N′*-dioxide ligand, oxygen of the enolized oxindole and one sulfonic oxygen of the NFSI. The *Si* face of the enolized oxindole was shielded by the rear 2,6-diisopropylphenyl group. Therefore, *Re*-face attack at the fluorine of NFSI yields the corresponding *R*-configured product **2ao**.

CONCLUSIONS

In summary, we have developed a highly enantioselective fluorination of N-unprotected 3-substituted 2-oxindoles in the presence of a chiral Sc(III)-*N,N′*-dioxide complex and Na_2CO_3. A variety of useful N−H-free 3-fluorooxindole derivatives could be obtained in good yields (up to 98%) with excellent enantioselectivities (up to 99% ee) under mild reaction conditions. Optically active MaxiPost was directly synthetized in one step. Further application of this catalyst system to other reactions of the unprotected 3-substituted oxindoles is in progress.

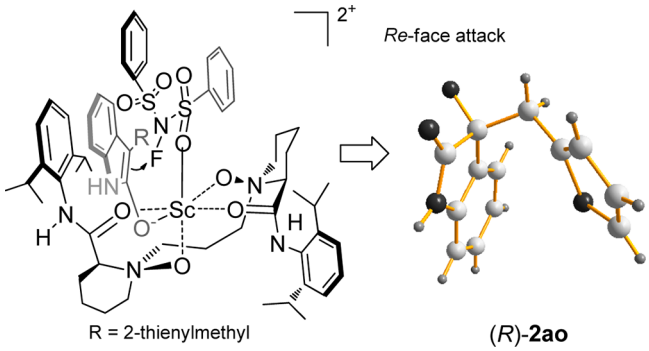


Figure 2. Proposed catalytic model and the X-ray crystallographic structure of **2ao**.

EXPERIMENTAL SECTION

General Remarks. Reactions were carried out using commercial available reagents in overdried apparatus. $CHCl_3$ was directly distilled before use. Enantiomeric excesses (ee) were determined by HPLC analysis using the corresponding commercial chiral column as stated in the experimental procedures at 23 °C with UV detection at 254 nm. Optical rotations were reported as follows: $[\alpha]^{25}_D$ (*c* in g/100 mL, solvent). ^1H NMR spectra were recorded on commercial instruments (400 MHz). ^{13}C NMR spectra was collected on commercial instruments (100 MHz) with complete proton decoupling. ^{19}F NMR was measured at 376 MHz; HRMS was recorded on a commercial apparatus (ESI Source). The *N,N′*-dioxide ligands **L1**−**L6** were synthesized by the same procedure in the literature.[20]

General Procedure for the Catalytic Asymmetric Fluorination Reaction. A dry reaction tube was charged with $Sc(OTf)_3$ (2.5 mg, 5 mol %), **L2** (3.3 mg, 5 mol %), and **1** (0.1 mmol) under an N_2 atmosphere. Then, $CHCl_3$ (0.25 mL) was added and the mixture was stirred at 35 °C for 0.5 h. Finally, NFSI (0.12 mmol, 37.8 mg) and Na_2CO_3 (0.12 mmol, 12.7 mg) were added with stirring at the indicated temperature. The reaction mixture was stirred at the indicated temperature for 2−3 days. The residue was purified by flash chromatography (eluent CH_2Cl_2, then petroleum ether/AcOEt 4/1) on silica gel to afford the products. The enantiomeric excess (ee) was determined by high-performance liquid chromatography (HPLC).

*3-Fluoro-3-(4-methoxybenzyl)indolin-2-one (**2aa**):* yield 26.0 mg, 96%; light yellow oil; $[\alpha]^{25}_D$ = −31.9° (*c* 0.47, CH_2Cl_2); HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r (major) = 11.78 min, t_r (minor) = 9.68 min, ee = 97%; ^1H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.25−7.15 (m, 1H), 6.97−6.85 (m, 4H), 6.73 (d, *J* = 7.7 Hz, 1H), 6.66 (d, *J* = 8.3 Hz, 2H), 3.68 (s, 3H), 3.50−3.37 (m, 1H), 3.09 (dd, *J* = 22.6, 13.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1 (d, *J* = 21.0 Hz), 157.7, 140.0 (d, *J* = 5.6 Hz), 130.6, 130.0 (d, *J* = 2.8 Hz), 124.8, 124.6 (d, *J* = 19.3 Hz), 123.4 (d, *J* = 7.2 Hz), 121.8 (d, *J* = 2.4 Hz), 112.5, 109.6, 92.5 (d, *J* = 190.6 Hz), 54.1, 39.2 (d, *J* = 27.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −155.8 (dd, *J* = 22.8, 10.6 Hz, 1F); HRMS (ESI) calcd for $C_{16}H_{14}FNO_2$ ([M] + Na^+) 294.0906, found 294.0910.

*3-Benzyl-3-fluoroindolin-2-one (**2ab**):* yield 22.9 mg, 95%; white solid, mp 105−107 °C; $[\alpha]^{25}_D$ = −52.3° (*c* 0.26, CH_2Cl_2); HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ 254 nm) t_r (major) = 14.12 min, t_r(minor) = 12.60 min, ee = 99%; ^1H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.35−7.14 (m, 4H), 7.13−7.04 (m, 2H), 7.03−6.91 (m, 2H), 6.80 (d, *J* = 7.8 Hz,1H), 3.64−3.46

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(m, 1H), 3.22 (dd, J = 22.7, 13.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.9 (d, J = 21.0 Hz), 141.0 (d, J = 5.7 Hz), 132.5 (d, J = 6.9 Hz), 131.1 (d, J = 2.9 Hz), 130.7, 128.2, 127.3, 125.9, 125.5 (d, J = 19.1 Hz), 122.9 (d, J = 2.5 Hz), 110.6, 93.5 (d, J = 191.0 Hz), 41.1 (d, J = 27.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −155.2 (dd, J = 22.5, 10.6 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{15}H_{12}FNO$ ([M] + Na^+) 264.0801, found 264.0801.

3-Fluoro-3-(2-methylbenzyl)indolin-2-one ***(2ac)****:* yield 22.2 mg, 87%; colorless oil; $[\alpha]^{25}_D$ = −25.3° (c 0.45, CH_2Cl_2); HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm) t_r(major) = 14.20 min, t_r(minor) = 12.57 min, ee = 99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 7.35−7.27 (m, 1H), 7.23 (t, J = 6.5 Hz, 2H), 7.17 (t, J = 6.1 Hz, 2H), 6.97−6.87 (m, 2H), 6.68 (d, J = 7.4 Hz, 1H), 3.64 (t, J = 13.9 Hz, 1H), 3.18 (dd, J = 31.6, 14.5 Hz, 1H), 2.10 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.8 (d, J = 21.2 Hz), 140.8 (d, J = 5.9 Hz), 137.8, 131.6 (d, J = 1.3 Hz), 131.5 (d, J = 2.3 Hz), 131.0 (d, J = 2.6 Hz), 130.4, 127.6, 125.9 (d, J = 29.9 Hz), 125.6 (d, J = 19.7 Hz), 122.9 (d, J = 2.4 Hz), 110.7, 93.5 (d, J = 192.3 Hz), 37.6 (d, J = 27.2 Hz), 19.9 (d, J = 1.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −155.2 (dd, J = 22.7, 10.7 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{16}H_{14}FNO$ ([M] + Na^+) 278.0957, found 278.0965.

3-Fluoro-3-(3-methylbenzyl)indolin-2-one ***(2ad)****:* yield 24.5 mg, 96%; white solid, mp 96−98 °C; $[\alpha]^{25}_D$ = −38.8° (c 0.40, CH_2Cl_2); HPLC (Chiralcel ID, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 7.44 min, t_r(minor) = 6.74 min, ee = 96%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.35−7.25 (m, 1H), 7.15−6.98 (m, 4H), 6.95 (s, 1H), 6.90 (d, J = 7.3 Hz, 1H), 6.85 (d, J = 7.7 Hz, 1H), 3.65−3.50 (m, 1H), 3.19 (dd, J = 23.4, 13.5 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1 (d, J = 21.0 Hz), 141.0 (d, J = 5.7 Hz), 137.8, 132.4 (d, J = 6.4 Hz), 131.5, 131.1 (d, J = 2.8 Hz), 128.0 (d, J = 4.4 Hz), 127.7, 126.0, 125.6 (d, J = 19.2 Hz), 122.9 (d, J = 2.5 Hz), 110.6, 93.5 (d, J = 191.0 Hz), 41.0 (d, J = 27.7 Hz), 21.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ −155.3 (dd, J = 23.0, 10.8 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{16}H_{14}FNO$ ([M] + Na^+) 278.0957, found 278.0963.

3-Fluoro-3-(4-methylbenzyl)indolin-2-one ***(2ae)****:* yield 24.5 mg, 96%; white solid, mp 108−110 °C; $[\alpha]^{25}_D$ = −32.9° (c 0.49, CH_2Cl_2); HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 8.22 min, t_r(minor) = 7.03 min, ee = 96%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 7.25−7.10 (m, 1H), 7.00−6.85 (m, 6H), 6.73 (d, J = 7.7 Hz, 1H), 3.61−3.39 (m, 1H), 3.11 (dd, J = 22.6, 13.5 Hz, 1H), 2.21 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1 (d, J = 20.8 Hz), 141.1 (d, J = 5.6 Hz), 136.9, 131.1 (d, J = 2.8 Hz), 130.5, 129.3 (d, J = 6.9 Hz), 128.9, 125.9, 125.6 (d, J = 19.0 Hz), 122.9 (d, J = 2.4 Hz), 110.6, 93.5 (d, J = 190.5 Hz), 40.7 (d, J = 27.7 Hz), 21.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ −155.2 (dd, J = 22.3, 10.5 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{16}H_{14}FNO$ ([M] + Na^+) 278.0957, found 278.0962.

3-(2-Chlorobenzyl)-3-fluoroindolin-2-one ***(2af)****:* yield 22.6 mg, 82%; yellow solid, mp 118−120 °C; $[\alpha]^{25}_D$ = −2.4° (c 0.45, CH_2Cl_2); HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 9.89 min, t_r(minor) = 8.50 min, ee = 98%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 7.53−7.45 (m, 1H), 7.37−7.20 (m, 4H), 6.96 (t, J = 7.6 Hz, 1H), 6.90 (d, J = 7.8 Hz, 1H), 6.83 (d, J = 7.4 Hz, 1H), 3.73 (t, J = 14.8 Hz, 1H), 3.51 (dd, J = 27.6, 14.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1 (d, J = 21.0 Hz), 140.7 (d, J = 5.9 Hz), 135.3 (s), 132.5 (d, J = 1.7 Hz), 131.2 (d, J = 3.1 Hz), 131.2 (d, J = 2.9 Hz), 129.5, 128.9, 126.8, 125. 9, 125.3 (d, J = 19.2 Hz), 123.0 (d, J = 2.5 Hz), 110.6, 92.9 (d, J = 192.2 Hz), 37.4 (d, J = 27.7 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −157.2 (dd, J = 26.7, 15.0 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{15}H_{11}Cl^{34.9689}FNO$ ([M] + Na^+) 298.0411, found 298.0415.

3-(3-Chlorobenzyl)-3-fluoroindolin-2-one ***(2ag)****:* yield 23.2 mg, 84%; yellow oil; $[\alpha]^{25}_D$ = −32.5° (c 0.46, CH_2Cl_2); HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 16.37 min, t_r(minor) = 14.97 min, ee = 97%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 7.32 (t, J = 7.6 Hz, 1H), 7.27−7.22 (m, 1H), 7.19−7.13 (m, 2H), 7.08−6.94 (m, 3H), 6.87 (d, J = 7.8 Hz, 1H), 3.62−3.51 (m, 1H), 3.20 (dd, J = 23.0, 13.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.7 (d, J = 20.7 Hz), 141.0 (d, J = 5.7 Hz), 134.6 (d, J = 6.4 Hz), 134.0, 131.4 (d, J = 2.8 Hz), 130.7, 129. 5, 128.9, 127.7, 125.8, 125.1 (d, J = 19.1 Hz), 123.1 (d, J = 2.5 Hz), 110.8, 93.1 (d, J = 191.8 Hz), 40.7 (d, J = 28.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ= −155.7 (dd, J = 22.7, 10.9 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{15}H_{11}Cl^{34.9689}FNO$ ([M] + Na^+) 298.0411, found 298.0418.

3-(4-Chlorobenzyl)-3-fluoroindolin-2-one ***(2ah)****:* yield 27.0 mg, 98%; white solid, mp 138−140 °C; $[\alpha]^{25}_D$ = −28.6° (c 0.39, CH_2Cl_2); HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 8.94 min, t_r(minor) = 7.53 min, ee = 98%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.27−7.17 (m, 1H), 7.14−7.07 (m, 2H), 7.04−6.85 (m, 4H), 6.74 (d, J = 7.8 Hz, 1H), 3.50−3.40 (m, 1H), 3.14 (dd, J = 21.8, 13.5 Hz,1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.5 (d, J = 21.0 Hz), 141.0 (d, J = 5.6 Hz), 133.4, 132.0, 131.3 (d, J = 2.8 Hz), 131.0 (d, J = 7.1 Hz), 128.4, 125.7, 125.2 (d, J = 19.1 Hz), 123.1 (d, J = 2.5 Hz), 110.7, 93.2 (d, J = 191.5 Hz), 40.5 (d, J = 28.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −155.3 (dd, J = 21.6, 10.3 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{15}H_{11}Cl^{34.9689}FNO$ ([M] + Na^+) 298.0411, found 298.0417.

3-Fluoro-3-(4-fluorobenzyl)indolin-2-one ***(2ai)****:* yield 20.7 mg, 80%; white solid, mp 115−117 °C; $[\alpha]^{25}_D$ = −39.2° (c 0.43, CH_2Cl_2); HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 9.32 min, t_r(minor) = 8.01 min, ee = 97%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.24−7.16 (m, 1H), 7.06−6.89 (m, 4H), 6.82 (t, J = 8.6 Hz, 2H), 6.74 (d, J = 7.8 Hz, 1H), 3.41−3.51 (m, 1H), 3.13 (dd, J = 22.1, 13.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.8 (d, J = 20.8 Hz), 163.4, 161.0, 141.0 (d, J = 5.7 Hz), 132.2 (d, J = 7.5 Hz), 131.3 (d, J = 2.8 Hz), 128.2 (dd, J = 7.1, 3.3 Hz), 125.7, 125.3 (d, J = 19.2 Hz), 123.0 (d, J = 2.5 Hz), 115.1 (d, J = 21.3 Hz), 110.7, 93.3 (d, J = 190.1 Hz), 40.3 (d, J = 28.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −115.0 to −115.3 (m, 1F), −155.5 (dd, J = 21.7, 10.3 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{15}H_{11}F_2NO$ ([M] + Na^+) 282.0706, found 282.0706.

3-(4-Bromobenzyl)-3-fluoroindolin-2-one ***(2aj)****:* yield 29.4 mg, 92%; white solid, mp 116−118 °C; $[\alpha]^{25}_D$ = −21.6° (c 0.59, CH_2Cl_2); HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 9.35 min, t_r(minor) = 8.03 min, ee = 96%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.40−7.25 (m, 3H), 7.14−6.88 (m, 4H), 6.83 (d, J = 7.7 Hz, 1H), 3.56−3.43 (m, 1H), 3.19 (dd, J = 21.9, 13.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.7 (d, J = 20.6 Hz), 141.0 (d, J = 5.6 Hz), 132.3, 131.5 (d, J = 7.2 Hz), 131.4, 125.7, 125.2 (d, J = 19.1 Hz), 123.1, 121.6, 110.8, 93.1 (d, J = 191.1 Hz), 40.5 (d, J = 28.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −155.2 (dd, J = 21.5, 10.3 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{15}H_{11}{}^{78.9183}BrFNO$ ([M] + H^+) 320.0086, found 320.0092.

3-Fluoro-3-(3-nitrobenzyl)indolin-2-one ***(2ak)****:* yield 28.0 mg, 98%; white solid, mp 79−81 °C; $[\alpha]^{25}_D$ = −23.0° (c 0.57, CH_2Cl_2); HPLC (Chiralcel IA, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 17.69 min, t_r(minor) = 16.44 min, ee = 96%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.12 (d, J = 7.6, 1H), 7.97 (s, 1H), 7.60−7.37 (m, 2H), 7.33 −7.27(m, 1H), 7.06−7.01 (m, 2H), 6.85 (d, J = 7.6 Hz, 1H), 3.64 (t, J = 12.6 Hz, 1H), 3.36 (dd, J = 21.4, 13.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.3 (d, J = 20.8 Hz), 148.0, 140.9 (d, J = 5.6 Hz), 136.9, 134.7 (d, J = 6.5 Hz), 131.7 (d, J = 2.7 Hz), 129.2, 125.5 (d, J = 2.6 Hz), 124.8 (d, J = 19.1 Hz), 123.3 (d, J = 2.4 Hz), 122.6, 111.0, 92.8 (d, J = 192.6 Hz), 40.7 (d, J = 28.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −156.1 (dd, J = 21.1, 11.5 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{15}H_{11}FN_2O_3$ ([M] + Na^+) 309.0651, found 309.0652.

3-Fluoro-3-(4-nitrobenzyl)indolin-2-one ***(2al)****:* yield 26.9 mg, 94%; yellow solid, mp 152−154 °C; $[\alpha]^{25}_D$ = −10.8° (c 0.54, CH_2Cl_2); HPLC (Chiralcel OJ-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 43.21 min, t_r(minor) = 33.43 min, ee = 97%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.09 (d, J = 8.4 Hz, 2H), 7.33−7.27 (m, 3H), 7.07−7.01 (m, 2H), 6.83 (d, J = 7.8 Hz, 1H), 3.65 (t, J = 12.2 Hz, 1H), 3.36 (dd, J = 21.3, 13.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0 (d, J = 20.8 Hz), 147.4, 140.8 (d, J = 5.6 Hz), 140.3 (d, J = 6.5 Hz), 131.7 (d, J = 2.7 Hz), 131.6, 125.6, 124.8 (d, J = 19.3 Hz), 123.4, 123.3 (d, J = 2.3 Hz), 110.9, 92.7 (d, J =

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193.0 Hz), 40.9 (d, J = 28.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −155.0 (dd, J = 21.0, 10.9 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{15}H_{11}FN_2O_3$ ([M] + Na^+) 309.0651, found 309.0649.

3-(2,4-Dichlorobenzyl)-3-fluoroindolin-2-one (**2am**): yield 26.4 mg, 85%; white solid, mp 119−121 °C; $[\alpha]^{25}_D$ = +19.4° (c 0.53, CH_2Cl_2); HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 9.83 min, t_r(minor) = 7.42 min, ee = 97%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 7.32 (d, J = 8.2 Hz, 1H), 7.29−7.19 (m, 2H), 7.19−7.15 (m, 1H), 6.90 (t, J = 7.5 Hz, 1H), 6.80 (t, J = 7.6 Hz, 2H), 3.58 (t, J = 15.0 Hz, 1H), 3.36 (dd, J = 26.6, 14.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.9 (d, J = 21.5 Hz), 140.7 (d, J = 5.8 Hz), 136.0, 134.1, 133.3 (d, J = 1.7 Hz), 131.4 (d, J = 2.7 Hz), 129.8 (d, J = 2.9 Hz), 129.3, 127.2, 125.7, 125.1 (d, J = 19.2 Hz), 123.2, 110.8, 92.6 (d, J = 192.5 Hz), 37.1 (d, J = 27.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −157.32 (dd, J = 26.2, 15.4 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{15}H_{10}{}^{34.9689}Cl_2FNO$ ([M] + Na^+) 332.0021, found 332.0024.

3-(Benzo[d][1,3]dioxol-5-ylmethyl)-3-fluoroindolin-2-one (**2an**): yield 25.9 mg, 91%; white solid, mp 132−134 °C; $[\alpha]^{25}_D$ = −23.0° (c 0.52, CH_2Cl_2); HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 13.76 min, t_r(minor) = 12.17 min, ee = 97%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.36−7.22 (m, 1H), 7.09−6.96 (m, 2H), 6.84 (d, J = 7.8 Hz, 1H), 6.72−6.57 (m, 2H), 6.55−6.49 (m, 1H), 5.90 (s, 2H), 3.53−3.43 (m, 1H), 3.14 (dd, J = 22.6, 13.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1 (d, J = 20.9 Hz), 147.4, 146.8, 141.1 (d, J = 5.7 Hz), 131.2 (d, J = 2.9 Hz), 126.1 (d, J = 7.0 Hz), 125.8, 125.5 (d, J = 19.1 Hz), 124.0, 123.0(d, J = 2.5 Hz), 110.8 (d, J = 15.9 Hz), 108.0, 101.0, 93.5 (d, J = 190.8 Hz), 40.7 (d, J = 27.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −154.9 (dd, J = 21.8, 10.4 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{16}H_{12}FNO_3$ ([M] + Na^+) 308.0699, found 308.0705.

(R)-3-Fluoro-3-(thiophen-2-ylmethyl)indolin-2-one (**2ao**): yield 22.2 mg, 90%; white solid, mp 152−154 °C; $[\alpha]^{25}_D$ = +0.9° (c 0.35, CH_2Cl_2); HPLC (Chiralcel IA, hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 17.48 min, t_r(minor) = 15.79 min, ee = 98%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.24−6.96 (m, 3H), 6.96−6.53 (m, 3H), 3.74 (dd, J = 14.5, 9.6 Hz, 1H), 3.53 (dd, J = 21.0, 14.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.4 (d, J = 20.8 Hz), 141.3 (d, J = 5.6 Hz), 133.7 (d, J = 8.4 Hz), 131.5 (d, J = 2.9 Hz), 128.4, 126.8, 125.6 (d, J = 20.9 Hz), 125.2 (d, J = 18.9 Hz), 123.2 (d, J = 2.5 Hz), 110.7, 92.7 (d, J = 190.8 Hz), 35.3 (d, J = 30.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −154.2 to −154.7 (m, 1F); HRMS (ESI-TOF) calcd for $C_{13}H_{10}FNOS$ ([M] + Na^+) 270.0365, found 270.0371.

3-Fluoro-3-(pyridin-2-ylmethyl)indolin-2-one (**2ap**): yield 20.3 mg, 84%; yellow solid, mp 121−123 °C; $[\alpha]^{25}_D$ = −2.2° (c 0.41, CH_2Cl_2); HPLC (Chiralcel OJ-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 13.58 min, t_r(minor) = 12.28 min, ee = 91%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.42 (d, J = 4.3, 1H), 7.61−7.54 (m, 1H), 7.30−7.25 (m, 1H), 7.24−7.18 (m, 1H), 7.17−7.06 (m, 1H), 7.05−6.86 (m, 2H), 6.78 (d, J = 7.8 Hz, 1H), 3.74 (t, J = 13.2 Hz, 1H), 3.59 (dd, J = 20.3, 13.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.8 (d, J = 20.8 Hz), 153.9 (d, J = 8.0 Hz), 149.1, 141.4 (d, J = 5.8 Hz), 136.4, 131.2 (d, J = 3.0 Hz), 125.7, 125.3 (d, J = 18.6 Hz), 124.9 (d, J = 1.9 Hz), 122.8 (d, J = 2.7 Hz), 122.3, 110.6, 92.9 (d, J = 188.7 Hz), 43.0 (d, J = 28.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −154.2 (dd, J = 20.0, 12.8 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{14}H_{11}FN_2O$ ([M] + Na^+) 265.0753, found 265.0749.

3-Fluoro-3-(naphthalen-1-ylmethyl)indolin-2-one (**2aq**): yield 26.2 mg, 90%; yellow solid, mp 132−134 °C; $[\alpha]^{25}_D$ = −86.5° (c 0.52, CH_2Cl_2); HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 12.19 min, t_r(minor) = 11.02 min, ee = 99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.90−7.79 (m, 2H), 7.56−7.17 (m, 5H), 6.95−6.74 (m, 2H), 6.67 (d, J = 7.4 Hz, 1H), 4.16−4.05 (m, 1H), 3.65 (dd, J = 28.8, 14.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.7 (d, J = 20.9 Hz), 140.8 (d, J = 5.8 Hz), 133.8, 132.9, 131.0 (d, J = 2.7 Hz), 129.7, 129.3 (d, J = 3.2 Hz), 128.4 (d, J = 21.3 Hz), 126.4, 125.9, 125.6, 125.4, 125.0, 124.5 (d, J = 2.5 Hz), 122.7 (d, J = 2.4 Hz), 110.7, 93.60 (d, J = 192.7 Hz), 37.3 (d, J = 27.7 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −157.0 (dd, J = 28.4, 11.9 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{19}H_{14}FNO$ ([M] + Na^+) 314.0957, found 314.0952.

3-Fluoro-3-(naphthalen-2-ylmethyl)indolin-2-one (**2ar**): yield 25.6 mg, 88%; white solid, mp 112−114 °C; $[\alpha]^{25}_D$ = −48.0° (c 0.51, CH_2Cl_2); HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 10.64 min, t_r(minor) = 8.88 min, ee = 97%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.85−7.73 (m, 1H), 7.68 (m,2 H), 7.55 (s, 1H), 7.45−7.40 (m, 2H), 7.31−7.13 (m, 2H), 6.98 (m, 2H), 6.76 (d, J = 7.8 Hz, 1H), 3.75−3.65 (m, 1H), 3.37 (dd, J = 22.6, 13.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.9 (d, J = 20.9 Hz), 141.0 (d, J = 5.7 Hz), 133.2, 132.5, 131.2 (d, J = 2.8 Hz), 130.1 (d, J = 6.8 Hz), 129.7, 128.6, 127.8 (d, J = 8.0 Hz), 127.6, 126.0, 125.9 (d, J = 4.9 Hz), 125.5 (d, J = 19.2 Hz), 123.0 (d, J = 2.5 Hz), 110.7, 93.5 (d, J = 191.2 Hz), 41.2 (d, J = 27.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −154.8 (dd, J = 22.2, 10.5 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{19}H_{14}FNO$ ([M] + Na^+) 314.0957, found 314.0953.

3-Fluoro-3-methylindolin-2-one (**2as**): yield 13.2 mg, 80%; white solid, mp 128−130 °C; $[\alpha]^{25}_D$ = −14.3° (c 0.27, CH_2Cl_2); HPLC (Chiralcel IA, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 7.93 min, t_r(minor) = 6.84 min, ee = 90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ= 8.80 (s, 1H), 7.42 (d, J = 7.2 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.11 (t, J = 7.4 Hz, 1H), 6.95 (d, J = 7.7 Hz, 1H), 1.84−1.74 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ= 175.7 (d, J = 21.7 Hz), 140.7 (d, J = 5.1 Hz), 131.2 (d, J = 2.9 Hz), 127.6 (d, J = 18.7 Hz), 124.5, 123.4 (d, J = 2.5 Hz), 110.9, 91.4 (d, J = 184.8 Hz), 21.3 (d, J = 29.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −148.7 to −161.9 (m, 1F); HRMS (ESI-TOF) calcd for C_9H_8FNO ([M] + Na^+) 188.0488, found 188.0491.

3-Ethyl-3-fluoroindolin-2-one (**2at**): yield 15.6 mg, 87%; yellow oil; $[\alpha]^{25}_D$ = +13.5° (c 0.23, CH_2Cl_2); HPLC (Chiralcel IA, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 6.20 min, t_r(minor) = 7.61 min, ee = 92%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 7.32 (d, J = 7.4 Hz, 1H), 7.30−7.22 (m, 1H), 7.03 (t, J = 7.6 Hz, 1H), 6.86 (d, J = 7.8 Hz, 1H), 2.19−2.07 (m, 2H), 0.82 (t, J = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.5 (d, J = 21.3 Hz), 141.3 (d, J = 5.6 Hz), 131.1 (d, J = 2.9 Hz), 126.2 (d, J = 19.0 Hz), 124.9, 123.3 (d, J = 2.6 Hz), 110.7, 94.4 (d, J = 187.3 Hz), 28.2 (d, J = 27.7 Hz), 7.0 (d, J = 8.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −157.2 (t, J = 14.1 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{10}H_{10}FNO$ ([M] + Na^+) 202.0644, found 202.0648.

3-Fluoro-3-propylindolin-2-one (**2au**): yield 16.0 mg, 83%; white solid, mp 88−90 °C; $[\alpha]^{25}_D$ = +25.8° (c 0.25, CH_2Cl_2); HPLC (Chiralcel IA, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 7.43 min, t_r(minor) = 6.23 min, ee = 93%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (s, 1H), 7.39 (d, J = 7.4 Hz, 1H), 7.36−7.29 (m, 1H), 7.10 (t, J = 7.6 Hz, 1H), 6.93 (d, J = 7.8 Hz, 1H), 2.25−2.04 (m, 2H), 1.41−1.17 (m, 2H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.7 (d, J = 21.3 Hz), 141.2 (d, J = 5.7 Hz), 131.1 (d, J = 2.9 Hz), 126.5 (d, J = 18.9 Hz), 124.9, 123.3 (d, J = 2.6 Hz), 110.8, 93. Nine (d, J = 186.9 Hz), 37.1 (d, J = 26.4 Hz), 16.1 (d, J = 7.3 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ −155.6 (t, J = 14.4 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{11}H_{12}FNO$ ([M] + Na^+) 216.0801, found 216.0802.

3-Butyl-3-fluoroindolin-2-one (**2av**): yield 17.0 mg, 82%; white solid, mp 83−85 °C; $[\alpha]^{25}_D$ = +16.2° (c 0.30, CH_2Cl_2); HPLC (Chiralcel IA, hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 5.82 min, t_r(minor) = 6.66 min, ee = 93%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 7.57−7.28 (m, 1H), 7.10 (t, J = 7.6 Hz, 1H), 6.93 (d, J = 7.8 Hz, 1H), 2.36−1.87 (m, 1H), 1.44−1.24 (m, 1H), 1.22−1.09 (m, 1H), 0.86 (t, J = 7.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.6 (d, J = 21.4 Hz), 141.2 (d, J = 5.7 Hz), 131.1 (d, J = 2.9 Hz), 126.5 (d, J = 18.9 Hz), 124.9, 123.3 (d, J = 2.5 Hz), 110.7, 93.9 (d, J = 187.0 Hz), 34.8 (d, J = 26.6 Hz), 24.6 (d, J = 6.8 Hz), 22.7, 13.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −155.5 (t, J = 14.3 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{12}H_{14}FNO$ ([M] + Na^+) 230.0957, found 230.0961.

3-Fluoro-3-isobutylindolin-2-one (**2aw**): yield 17.6 mg, 85%; white solid, mp 84−86 °C; $[\alpha]^{25}_D$ = + 31.2° (c 0.25, CH_2Cl_2); HPLC (Chiralcel IA, hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ 254

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nm) t_r(major) = 6.75 min, t_r(minor) = 5.96 min, ee = 93%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 7.39 (d, J = 7.3 Hz, 1H), 7.37−7.29 (m, 1H), 7.10 (t, J = 7.5 Hz, 1H), 6.94 (d, J = 7.8 Hz, 1H), 2.14 (d, J = 6.6 Hz, 1H), 2.10 (d, J = 6.6 Hz, 1H), 1.75−1.63 (m, 1H), 0.90 (d, J = 6.6 Hz, 3H), 0.85 (d, J = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.8 (d, J = 21.4 Hz), 141.2 (d, J = 5.7 Hz), 131.2 (d, J = 3.1 Hz), 126.5 (d, J = 18.6 Hz), 125.4, 123.2 (d, J = 2.7 Hz), 110.8, 94.0 (d, J = 184.8 Hz), 43.0 (d, J = 25.5 Hz), 23.8 (d, J = 6.6 Hz), 23.6 (d, J = 16.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −150.6 (t, J = 16.2 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{12}H_{14}FNO$ ([M] + Na^+) 230.0957, found 230.0956.

*3-(2-Ethylbutyl)-3-fluoroindolin-2-one (**2ax**):* yield 20.4 mg, 87%; colorless oil; $[\alpha]^{25}_D$ = +23.0° (c 0.24, CH_2Cl_2); HPLC (Chiralcel IC, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 6.37 min, t_r(minor) = 7.41 min, ee = 90%.; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (s, 1H), 7.39 (d, J = 7.3 Hz, 1H), 7.36−7.29 (m, 1H), 7.09 (t, J = 7.6 Hz, 1H), 6.93 (d, J = 7.8 Hz, 1H), 2.28−1.94 (m, 2H), 1.36−1.20 (m, 5H), 0.81− 0.76 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.8 (d, J = 21.5 Hz), 141.2 (d, J = 5.7 Hz), 131.1 (d, J = 3.0 Hz), 126.6 (d, J = 18.8 Hz), 125.3, 123.1 (d, J = 2.6 Hz), 110.8, 94.2 (d, J = 185.5 Hz), 38.0 (d, J = 25.6 Hz), 35.2 (d, J = 5.7 Hz), 25.8 (d, J = 15.5 Hz), 10.3 (d, J = 6.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −151.4 to −152.2 (m, 1F); HRMS (ESI-TOF) calcd for $C_{14}H_{18}FNO$ ([M] + Na^+) 258.1270, found 258.1271.

*3-Allyl-3-fluoroindolin-2-one (**2ay**):* yield 15.5 mg, 81%; white solid, mp 80−82 °C; $[\alpha]^{25}_D$ = −22.9° (c 0.31, CH_2Cl_2); HPLC (Chiralcel IA, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 7.81 min, t_r(minor) = 6.60 min, ee = 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 7.42 (d, J = 7.4 Hz, 1H), 7.37−7.30 (m, 1H), 7.09 (t, J = 7.6 Hz, 1H), 6.93 (d, J = 7.8 Hz, 1H), 5.69−5.59 (m, 1H), 5.19−5.13 (m, 2H), 3.09−2.93 (m, 1H), 2.87−2.77 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.9 (d, J = 21.0 Hz), 141.1 (d, J = 5.6 Hz), 131.2 (d, J = 2.9 Hz), 128.8 (d, J = 8.4 Hz), 125. Nine (d, J = 18.9 Hz), 125.3, 123.2 (d, J = 2.5 Hz), 121.2, 110.8, 92.8 (d, J = 189.9 Hz), 39.4 (d, J = 28.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −156.9 (dd, J = 17.8, 11.9 Hz, 1F); HRMS (ESI-TOF) calcd for $C_{11}H_{10}FNO$ ([M] + Na^+) 214.0644, found 214.0642.

*(R)-3-Fluoro-3-phenylindolin-2-one (**2az**):* yield 19.3 mg, 85%; white solid, mp 137−139 °C; $[\alpha]^{25}_D$ = −136.7° (c 0.35, CH_2Cl_2); HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 8.20 min, t_r(minor) = 13.04 min, ee = 89%; the absolute configuration of the **2az** was determined to be *R* by comparing the value of optical rotation of *tert*-butyl 3-fluoro-2-oxo-3-phenylindoline-1-carboxylate with the reported value[7a] ($[\alpha]^{25}_D$ = −71.7° (c 0.75, $CHCl_3$), 89% ee; lit[7a] $[\alpha]^{27}_D$ = −70.4° (c 0.77, $CHCl_3$), 79% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.56−9.36 (m, 1H), 7.46−7.34 (m, 5H), 7.33−7.29 (m, 1H), 7.27 (d, J = 7.6 Hz, 1H), 7.08 (t, J = 7.6 Hz, 1H), 6.94 (d, J = 7.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.4 (d, J = 23.8 Hz), 142.0 (d, J = 5.7 Hz), 135.8 (d, J = 27.0 Hz), 131.6 (d, J = 3.0 Hz), 129.3 (d, J = 1.4 Hz), 128.7, 127.4 (d, J = 18.1 Hz), 126.3 (d, J = 19.5 Hz), 125.8 (d, J = 6.4 Hz), 123.7 (d, J = 2.7 Hz), 111.3, 93.9 (d, J = 188.7 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −154.4 (s, 1F); HRMS (ESI-TOF) calcd for $C_{14}H_{10}FNO$ ([M] + Na^+) 250.0644, found 250.0643.

*3-(4-Chlorophenyl)-3-fluoroindolin-2-one (**2ba**):* yield 23.3 mg, 89%; white solid, mp 144−146 °C; $[\alpha]^{25}_D$ = −90.5° (c 0.45, CH_2Cl_2); HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 6.15 min, t_r(minor) = 10.37 min, ee = 89%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85−8.65 (m, 1H), 7.46−7.23 (m, 5H), 7.21 (d, J = 7.4 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 6.94−6.83 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4 (d, J = 18.7 Hz), 140.7 (d, J = 4.9 Hz), 134.5 (d, J = 2.1 Hz), 133.2 (d, J = 27.5 Hz), 130.8 (d, J = 3.1 Hz), 127.9, 126.3 (d, J = 6.3 Hz), 125.7 (d, J = 18.0 Hz), 125.4, 122.8 (d, J = 2.7 Hz), 110.1, 92.2 (d, J = 191.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −153.2 (s, 1F); HRMS (ESI-TOF) calcd for $C_{14}H_9{}^{34.9689}ClFNO$ ([M] + Na^+) 284.0254, found 284.0254.

*5-Chloro-3-fluoro-3-phenylindolin-2-one (**2bb**):* yield 25.6 mg, 98%; white solid, mp 156−158 °C; $[\alpha]^{25}_D$ = −178.3° (c 0.51, CH_2Cl_2); HPLC (Chiralcel IC, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 6.54 min, t_r(minor) = 7.37 min, ee = 93%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 7.53−7.23 (m, 6H), 7.19 (s, 1H), 6.82 (d, J = 8.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.7 (d, J = 23.7 Hz), 140.2 (d, J = 5.6 Hz), 135.1 (d, J = 26.8 Hz), 131.6 (d, J = 2.9 Hz), 129.6 (d, J = 1.0 Hz), 129.1 (d, J = 3.1 Hz), 129.0, 128.8, 126.8, 125.5 (d, J = 6.5 Hz), 112.2, 93.5 (d, J = 190.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −155.1 (s, 1F); HRMS (ESI-TOF) calcd for $C_{14}H_9{}^{34.9689}ClFNO$ ([M] + Na^+) 284.0254, found 284.0256.

*(S)-3-(5-Chloro-2-methoxyphenyl)-3-fluoro-6-(trifluoromethyl)-indolin-2-one (MaxiPost **2bc**).* MaxiPost **2bc** was purified by flash column chromatography (eluent pure CH_2Cl_2) to give a white solid: 81% yield, 29.3 mg; mp 196−198 °C; HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ 254 nm) t_r(major) = 6.38 min, t_r(minor) = 9.57 min, ee = 96%; $[\alpha]^{25}_D$ = +134.1° (c 0.59, MeOH), 96% ee (lit.[5a] $[\alpha]^{28}_D$ = +168° (c 0.132, MeOH)), >99% ee, *S* enantiomer; by comparing the value of optical rotation with the reported value,[5a] the absolute configuration of MaxiPost was determined to be *S*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.9−8.45 (m, 1H), 7.73 (s, 1H), 7.28 (d, J = 8.7 Hz, 1H), 7.21−7.17 (m, 1H), 7.18−7.04 (m, 2H), 6.70 (d, J = 8.7 Hz, 1H), 3.47 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4 (d, J = 20.1 Hz), 152.6 (d, J = 6.1 Hz), 141.6 (d, J = 5.5 Hz), 132.4 (d, J = 32.0 Hz), 129.3, 125.6 (d, J = 1.9 Hz), 125.5, 125.4, 124.9 (d, J = 26.8 Hz), 124.5 (d, J = 1.7 Hz), 121.1, 119.2, 111.7, 106.1, 90.1 (d, J = 185.5 Hz), 55.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.0 (d, J = 2.3 Hz, 3F), −159.5 (s, 1F).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Text, figures, tables, and a CIF file giving crystallographic data for **2ao**, full optimization details, ^{1}H and ^{13}C NMR spectra, and HPLC data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(13) Other metals were screened; see the Supporting Information for details.

(14) The desired fluorinated 3-phenyl-substituted oxindole was obtained in 93% yield with 84% ee using 10 mol % of **L2**-Sc(III) complex.

(15) The experiment about scaling up the Maxipost synthesis (3.5 mmol) resulted in decreased yield and enantioselectivity (53% yield, 86% ee) due to the low solubility of the substrate.

(16) The product **2aa** was obtained in 9% yield using 120 mol % of Na_2CO_3 without **L2**-Sc$(OTf)_3$ complex.

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