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Cinchona Alkaloid Catalyzed Enantioselective Chlorination of 3-Aryloxindoles

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O-Benzoylquinidine is an effective organocatalyst for the asymmetric chlorination of 3-aryloxindoles by using easily available *N*-chlorosuccinimide (NCS) as chlorine source to give the corresponding 3-aryl-3-chlorooxindoles in excellent yields and up to 93% enantiomeric excess.

Introduction

Oxindoles are important structural motifs that are found in a wide array of natural and biologically active molecules.[1] In particular, oxindole compounds bearing a quaternary stereogenic center at the 3-position are extremely useful.[2] In this context, various synthetic approaches, including fluorination,[3] hydroxylation,[4] amination,[5] aldol and Mannich reactions,[6] allylic alkylation,[7] and conjugate addition[8] with 3-substituted oxindoles as nucleophiles, have been developed in recent years for the asymmetric synthesis of 3,3-disubstituted oxindole derivatives.[9] Moreover, optically active 3-acylated oxindoles bearing a quaternary stereocenter can be generated through carboxyl migration of *O*-acylated oxindoles mediated by a chiral nucleophilic catalyst.[10]

Recently, the enantioselective construction of a carbon–halogen stereocenter has become a topical area of current asymmetric catalysis research by virtue of the fact that halogen atoms attached to a chiral stereocenter can serve as a linchpin for further stereospecific manipulations.[11] Over the past several years, electrophilic chlorination of carbonyl compounds has drawn significant interest. For example, aldehydes, ketones, acyl halides, β-oxo esters, and their derivatives are often employed as nucleophiles in these reactions.[12,13] We envisioned that a similar transformation could be achieved if oxindoles are used as nucleophiles, forming a C–Cl bond at C-3 along with the generation of a tetrasubstituted stereogenic center. The obtained product can further undergo substitution with C-[14] or O-nucleophiles[15] to produce more complex compounds. Despite intense research efforts on the aforementioned transformations,[4–9] enantioselective, asymmetric chlorination reactions of oxindoles are rare. To the best of our knowledge, only one example of a chlorination reaction of 3-aryloxindole has been described in the literature, giving the corresponding product in moderate enantioselectivity using (dbfox-Ph)Ni complex [dbfox-Ph = 4,6-dibenzofurandiyl-2,2′-bis(4-phenyloxazoline)] as the catalyst,[3e,3f] and no examples could be found for the enantioselective chlorination of 3-aryloxindoles using an organocatalyst. Herein, we wish to report our initial studies on the enantioselective chlorination of 3-aryloxindoles using *N*-chlorosuccinimide (NCS) as chlorine source in the presence of a cinchona alkaloid as an organocatalyst under mild reaction conditions.

Results and Discussion

Considering that the transformation described above relies on the deprotonation of the C-3 methine proton with a chiral amine, cinchona alkaloids were therefore used as a catalyst to effect the stereoselective chlorination. Initially, the enantioselective catalytic chlorination of *N*-Boc-3-phenyloxindole (**2a**) with NCS (1.2 equiv.) was carried out in dichloromethane in the presence of 20 mol-% quinine **1a**, affording the desired product **3a** in excellent yield (99%) with 23% *ee* (Table 1, Entry 1). Encouraged by this result, a series of cinchona alkaloids were prepared and used as catalysts to examine the reaction outcome (Figure 1); the results are summarized in Table 1. *O*-Benzylquinine **1b** and -quinidine **1i** were not effective catalysts for this reaction (Table 1, Entries 2 and 9), and quinidine **1h** also gave a poor result (Table 1, Entry 8). However, *O*-acylated catalysts, such as *O*-benzoyl-, *O*-acetyl-, and *O*-naphthoyl-derived quinidine derivatives **1j**–**l** gave better *ee* values than those of the corresponding *O*-acylated quinine catalysts

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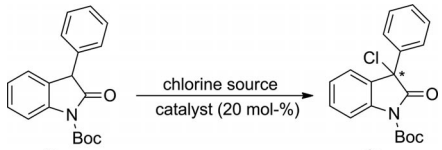
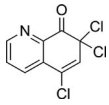
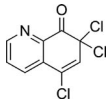
1c–**e** (Table 1, Entries 10–12 vs. 3–5), which is consistent with the previously reported result for the chlorination of 1,3-dicarbonyl compounds in which *O*-benzoylquinidine is a more effective catalyst than *O*-benzoylquinine.[13g] It should also be noted that *O*-acylcinchonidine and -cinchonine did not give satisfactory enantioselectivities in this reaction (Table 1, Entries 6–7 and 13–14). *O*-Benzoylquinidine derivative **1j** turned out to be an excellent catalyst, giving the desired product **3a** in 99% yield with 74% *ee* (Table 1, Entry 10). An alternative chlorination reagent, trichloroquinolinone, which has shown good enantioselectivity in the chlorination of 1,3-dicarbonyl compounds,[13g] did not give good results in our case (Table 1, Entry 15). The combination of 3-chloroquinolinone and an inorganic base such as $NaHCO_3$ also gave a poor result (Table 1, Entry 16).

Table 1. Catalysts and chlorine source screening for the enantioselective chlorination of oxindole **2a**.[a]



2a **3a**

Entry	Catalayst	Chlorine source	*t* [h]	Yield [%][b]	*ee* [%][c]
1	**1a**	NCS	2	99	23
2	**1b**	NCS	2	99	13
3	**1c**	NCS	2	99	51
4	**1d**	NCS	2	99	33
5	**1e**	NCS	2	94	36
6	**1f**	NCS	2	97	8
7	**1g**	NCS	2	98	5
8	**1h**	NCS	2	99	15
9	**1i**	NCS	2	99	22
10	**1j**	NCS	2	99	74
11	**1k**	NCS	2	99	66
12	**1l**	NCS	2	99	64
13	**1m**	NCS	2	99	36
14	**1n**	NCS	2	92	23
15	**1j**		24	50	66
16[d]	**1j**		24	53	58

[a] Reagents and conditions: **2a** (0.1 mmol), **1** (20 mol-%), chlorinating reagent (0.12 mmol), CH_2Cl_2 (2.0 mL), 20 °C. [b] Yield of isolated product. [c] Determined by HPLC analysis on a chiral stationary phase (Chiralcel OJ-H column). [d] $NaHCO_3$ was used as an additive.

Solvent effects were then extensively studied. It was found that, although chlorination of oxindole **2a** with NCS proceeded smoothly in a wide range of solvents, the *ee* values obtained under otherwise identical conditions varied dramatically (Table 2). For instance, in nonpolar solvent such as toluene, the reaction proceeded smoothly, giving **3a**

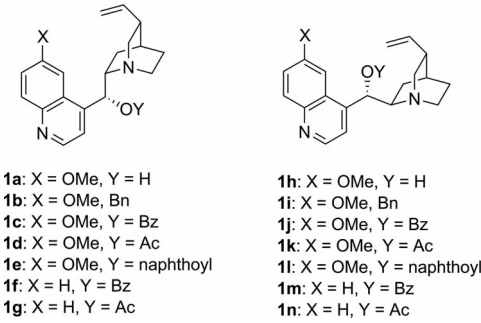


Figure 1. Catalyst screening.

in 99% yield with low enantioselectivity (Table 2, Entry 1). In polar solvents, such as acetonitrile and methanol, **3a** was obtained in moderate enantioselectivities (Table 2, Entries 2 and 3). Good enantiomeric excesses were observed in dichloromethane (CH_2Cl_2), acetone, tetrahydrofuran (THF) and 1,2-dichloroethane (DCE) (Table 1, Entry 10 and Table 2, Entries 4–6). THF was found to be the best solvent for this chlorination reaction, affording **3a** in up to 76% *ee* and good yield (Table 2, Entry 5).

Table 2. Optimization of the reaction conditions for the chlorination of oxindole **2a** mediated by catalyst **1j**.[a]

Entry	Solvent	*T* [°C]	*t* [h]	Yield [%][b]	*ee* [%][c]
1	toluene	20	2	99	37
2	CH_3CN	20	2	99	58
3[d]	MeOH	20	2	66	56
4	acetone	20	2	99	72
5	THF	20	2	99	76
6	DCE	20	2	82	70
7	CH_2Cl_2	–20	2	99	82
8	CH_2Cl_2	–30	2	99	87
9	THF	–20	2	99	85
10	THF	–30	2	99	93
11	THF	–35	2	96	91
12[e]	THF	–30	3	99	84

[a] Reagents and conditions: **2a** (0.1 mmol), **1j** (20 mol-%), NCS (0.12 mmol), solvent (2.0 mL). [b] Yield of isolated product. [c] Determined by HPLC analysis on a chiral stationary phase (Chiralcel OJ-H column). [d] 3-Methoxy-substituted oxindole was obtained. [e] 10 mol-% of catalyst **1j** was used.

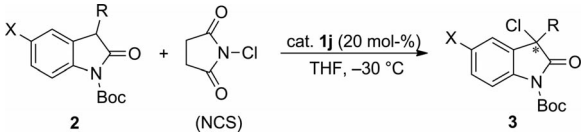
Examination of the effect of temperature revealed that lowering of the temperature could significantly improve the enantioselectivity of **3a** without sacrificing the yield (99%) (Table 2, Entries 7–11); the best enantioselectivity for **3a** was obtained in THF at –30 °C. The effect of catalyst loading was also examined, and it was found that the use of 10 mol-% catalyst led to a decrease in enantioselectivity and required a longer reaction time (Table 2, Entry 12). Thus, 20 mol-% catalyst was employed in subsequent studies.

The substrate scope of the reaction was then examined under the optimized conditions (Table 3). Generally, all of the 3-aryloxindoles underwent this chlorination reaction smoothly within short reaction times. Both the electronic and steric nature of the substituents on the oxindoles and the aromatic ring at the C-3 position played important roles in determining the reaction outcome. The *N*-Boc-3-phenyl-substituted oxindoles gave the corresponding products **3a**–**c**

in excellent yields (>96%) and excellent enantioselectivities, regardless of the electron-withdrawing or -donating nature of the substituents on the 5-position of the oxindoles (90–93% *ee*; Table 3, Entries 1–3). However, *N*-Boc-3-aryl-substituted oxindoles gave the corresponding products in lower enantioselectivities, and substrates with an electron-donating group on the aromatic ring at the C-3 position required longer times to complete the reaction than the corresponding substrates with electron-withdrawing groups (Table 3, Entries 7–9 vs. 4–6). Substrates **2j** and **2k**, bearing a bulky 2-naphthyl group at the C-3 position of the oxindole, also gave the corresponding products **3j** and **3k**, respectively, in lower enantioselectivities (Table 3, Entries 10–11). In the case of 3-(*m*-tolyl)-substituted oxindole **2l**, the desired product **3l** was obtained in 99% yield and 84% *ee*, which is very similar to the case of 3-(*p*-tolyl)-substituted substrate **2h** (Table 3, Entries 12 vs. 8). However, only 7% *ee* of product **3m** was observed for 3-(*o*-tolyl)-substituted oxindole **2m**, presumably due to steric hindrance (Table 3, Entry 13). It should be noted that when 3-alkyloxindoles **2n** and **2o** were used, the corresponding chlorinated products **3n** and **3o** were obtained in high yields, but with lower enantioselectivities (Table 3, Entries 14 and 15).

Several oxindoles with different *N*-protecting groups were also examined. As shown in Scheme 1, *N*-benzyl- and *N*-phenyl-substituted 3-phenyloxindoles **2p** and **2q**, respectively, gave the corresponding products **3p** and **3q** with lower *ee* values under the optimized conditions. In sharp contrast, *N*-(9*H*-fluoren-9-yloxycarbonyl)-substituted oxindole **2r** gave the desired product **3r** in acceptable yield and *ee*, indicating that the presence of a bulky *N*-protecting group is crucial for a satisfactory stereochemical outcome (Scheme 1).

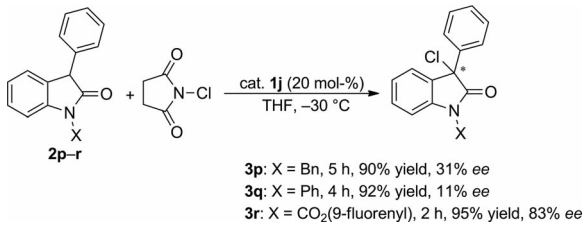
Table 3. Enantioselective chlorination of oxindoles **2** mediated by catalyst **1j**.[a]



2 (NCS) **3**

Entry	Substrate **2**	X	R	Product **3**	*t* [h]	Yield [%][b]	*ee* [%]
1	**2a**	H	Ph	**3a**	2	99	93[c]
2	**2b**	F	Ph	**3b**	2	99	90[d]
3	**2c**	Me	Ph	**3c**	3	96	91[d]
4	**2d**	H	*p*-FC_6H_4	**3d**	2.5	99	81[d]
5	**2e**	F	*p*-FC_6H_4	**3e**	1	99	84[d]
6	**2f**	Me	*p*-FC_6H_4	**3f**	2	98	65[d]
7	**2g**	H	*p*-MeC_6H_4	**3g**	3	92	73[d]
8	**2h**	F	*p*-MeC_6H_4	**3h**	2	98	84[e]
9	**2i**	Me	*p*-MeC_6H_4	**3i**	5	81	70[e]
10	**2j**	H	2-naphthyl	**3j**	2	97	72[d]
11	**2k**	F	2-naphthyl	**3k**	2	96	66[c]
12	**2l**	F	*m*-MeC_6H_4	**3l**	2	99	84[c]
13	**2m**	F	*o*-MeC_6H_4	**3m**	2	99	7[f]
14	**2n**	H	Me	**3n**	5	91	22[e]
15	**2o**	H	Bn	**3o**	5	85	29[e]

[a] Reagents and conditions: **2** (0.1 mmol), **1j** (20 mol-%), NCS (0.12 mmol), THF (2.0 mL), –30 °C. [b] Yield of isolated product. [c] Determined by HPLC analysis on a chiral stationary phase (Chiralcel OJ-H column). [d] Determined by HPLC analysis on a chiral stationary phase (Chiralpak AS-H column). [e] Determined by HPLC analysis on a chiral stationary phase (Chiralpak AD-H column). [f] Determined by HPLC analysis on a chiral stationary phase (Chiralpak IC column).



Scheme 1. Effect of alternative 3-aryloxindole *N*-protecting groups.

Conclusions

A highly effective asymmetric α-chlorination reaction of oxindoles has been developed by using an inexpensive cinchona alkaloid as the organocatalyst and NCS as the chlorination reagent under mild conditions, providing an operationally simple protocol to access enantiomerically highly enriched chloro-substituted compounds. Investigations aimed at fully understanding the reaction mechanism and developing more effective catalysts with broad substrate scope are ongoing.

Experimental Section

General Remarks: NMR spectra were recorded with a Bruker Avance III 400 MHz or a Varian Mercury vx 300 MHz spectrometer with solutions in $CDCl_3$ and tetramethylsilane (TMS) as an internal standard; *J* values are reported in Hz. IR spectra were recorded with a Bio-Rad FTS-185 spectrometer. Chiral HPLC was performed with a Shimadzu SPD-10A series instrument with chiral columns. MS and HRMS (EI) were measured with a Finnigan MA^+ instrument. Flash column chromatography was performed using silica gel (300–400 mesh). Unless otherwise noted, all commercially obtained reagents were used without further purification. All reactions were carried out under air in a closed system. Catalysts **1b**–**g** and **1i**–**n** were synthesized according to literature methods.[6c,16] Substrates **2a**,[3d] **2b**,[7c,8b] **2c**,[4a] **2d**,[3d] **2f**,[4a] **2g**,[3d] **2i**,[4a] **2j**,[8b,8e] **2n**,[3d] **2o**,[3d] **2p**,[17] and **2q**,[18] and product **3a**[3e] are known compounds.

General Procedure for the Synthesis of 3-Aryl-*N*-Boc-oxindoles 2:[3d,3g] A solution of ArBr (51 mmol) in THF (20 mL) was added to a mixture of magnesium (1.2 g, 51 mmol) and a trace amount of iodine under argon. The mixture was stirred at room temperature until complete consumption of the magnesium was observed. To a stirred, cold (–40 °C) suspension of isatins (20.4 mmol) in THF (40 mL) under argon was added dropwise the above solution of ArMgBr (2.5 equiv.) in THF (20 mL). The reaction mixture was allowed to warm to room temperature and stirred for 5 h, then the reaction mixture was quenched with 2 N HCl and extracted with ethyl acetate. The combined organic layers were washed with saturated aqueous Na_2CO_3 and brine, and then dried with Na_2SO_4. After the solvent was evaporated under reduced pressure, purifica-

tion by silica gel column chromatography was carried out to give the 3-aryl-3-hydroxyoxindole.

To a solution of 3-aryl-3-hydroxyoxindole (17.8 mmol) in CH_2Cl_2 (80 mL) was added $(Boc)_2O$ (35.5 mmol) and DMAP (0.22 g, 1.8 mmol). The reaction mixture was stirred at room temperature for 3 h and then quenched with saturated aqueous NH_4Cl. The aqueous layer was extracted with dichloromethane and then dried with Na_2SO_4. After removal of the solvent, the crude product was purified by silica gel column chromatography to give the 3-aryl-*N*-Boc-3-[(*tert*-butoxycarbonyl)oxy]oxindole.

To a solution of 3-aryl-*N*-Boc-3-[(*tert*-butoxycarbonyl)oxy]oxindole (7.1 mmol) in MeOH (60 mL), Pd/C (0.3 g) was added, and the mixture was stirred under hydrogen at room temperature for 4 h. The reaction mixture was filtered through Celite to remove Pd/C. After removal of the solvent, the crude product was purified by silica gel column chromatography to give the 3-aryl-*N*-Boc-oxindole.

3-Aryl-*N*-Boc-oxindole 2e: Yield: 2.0 g (75%; total yield); white solid; m.p. 106.7–107.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93 (dd, J = 8.8, 4.4 Hz, 1 H, ArH), 7.18–7.14 (m, 2 H, ArH), 7.09–7.02 (m, 3 H, ArH), 6.87 (ddd, J = 7.6, 2.8, 1.2 Hz, 1 H, ArH), 4.69 (s, 1 H, CH), 1.62 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.3, 162.5 (d, J = 245.7 Hz), 160.0 (d, J = 242.7 Hz), 149.2, 136.4 (d, J = 2.4 Hz), 131.3 (d, J = 3.2 Hz), 130.2 (d, J = 8.2 Hz), 128.8 (d, J = 8.4 Hz), 116.6 (d, J = 7.8 Hz), 116.0 (d, J = 21.6 Hz), 115.4 (d, J = 22.7 Hz), 112.4 (d, J = 24.3 Hz), 84.7, 51.8 (d, J = 1.5 Hz), 28.0 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –113.9, –117.4 ppm. IR (film): $\tilde{\nu}$ = 1759, 1728, 1509, 1485, 1345, 1295, 1270, 1255, 1228, 1146, 1091 cm^{-1}. MS (EI): *m*/*z* (%) = 345 (1) $[M]^+$, 245 (82), 216 (100), 201 (5), 169 (6), 57 (10). HRMS: calcd. for $C_{19}H_{17}F_2NO_3$ $[M]^+$ 345.1177; found 345.1179.

3-Aryl-*N*-Boc-oxindole 2h: Yield: 1.9 g (70%; total yield); white solid; m.p. 120.4–121.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (dd, J = 8.8, 4.4 Hz, 1 H, ArH), 7.16 (d, J = 8.0 Hz, 2 H, ArH), 7.06 (d, J = 8.0 Hz, 2 H, ArH), 7.09–7.04 (m, 1 H, ArH), 6.87 (ddd, J = 7.6, 2.8, 1.2 Hz, 1 H, ArH), 4.66 (s, 1 H, CH), 2.33 (s, 3 H, CH_3), 1.62 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.6, 160.0 (d, J = 242.3 Hz), 149.3, 137.9, 136.4 (d, J = 2.2 Hz), 132.6, 129.7, 129.4 (d, J = 8.4 Hz), 128.4, 116.4 (d, J = 7.8 Hz), 115.1 (d, J = 22.7 Hz), 112.4 (d, J = 24.4 Hz), 84.5, 52.3 (d, J = 1.6 Hz), 28.0, 21.1 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –117.7 ppm. IR (film): $\tilde{\nu}$ = 1769, 1727, 1478, 1294, 1268, 1251, 1143, 1090 cm^{-1}. MS (EI): *m*/*z* (%) = 341 (1) $[M]^+$, 241 (100), 226 (11), 212 (47), 198 (43), 183 (6), 170 (4), 57 (6). HRMS: calcd. for $C_{20}H_{20}FNO_3$ $[M]^+$ 341.1427; found 341.1426.

3-Aryl-*N*-Boc-oxindole 2k: Yield: 1.8 g (57%; total yield); white solid; m.p. 129.4–129.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (dd, J = 8.8, 4.4 Hz, 1 H, ArH), 7.84–7.77 (m, 3 H, ArH), 7.66 (d, J = 1.2 Hz, 1 H, ArH), 7.50–7.45 (m, 2 H, ArH), 7.25 (dd, J = 8.4, 2.0 Hz, 1 H, ArH), 7.09 (tdd, J = 8.8, 2.8, 0.8 Hz, 1 H, ArH), 6.91 (ddd, J = 8.0, 2.8, 0.8 Hz, 1 H, ArH), 4.87 (s, 1 H, CH), 1.62 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.4, 160.0 (d, J = 242.5 Hz), 149.3, 136.4 (d, J = 2.3 Hz), 133.3, 132.96, 132.92, 129.2 (d, J = 8.3 Hz), 129.0, 127.82, 127.79, 127.7, 126.4, 126.3, 125.9, 116.5 (d, J = 7.8 Hz), 115.3 (d, J = 22.7 Hz), 112.5 (d, J = 24.4 Hz), 84.6, 52.8 (d, J = 1.6 Hz), 28.0 ppm. ^{19}F NMR (376 MHz, $CDCl_3$, non-decoupled): δ = –117.443, –117.456, –117.464, –117.477, –117.486, –117.498 ppm. IR (film): $\tilde{\nu}$ = 1764, 1727, 1483, 1345, 1295, 1271, 1145, 1090 cm^{-1}. MS (EI): *m*/*z* (%) = 377 (1) $[M]^+$, 277 (100), 248 (77), 233 (4), 220 (5). HRMS: calcd. for $C_{23}H_{20}FNO_3$ $[M]^+$ 377.1427; found 377.1426.

3-Aryl-*N*-Boc-oxindole 2l: Yield: 1.7 g (65%; total yield); white solid; m.p. 125.4–125.9 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.92 (dd, J = 9.0, 4.5 Hz, 1 H, ArH), 7.23 (t, J = 7.5 Hz, 1 H, ArH), 7.12 (d, J = 7.5 Hz, 1 H, ArH), 7.05 (td, J = 9.0, 2.7 Hz, 1 H, ArH), 6.97–6.95 (m, 2 H, ArH), 6.87 (ddd, J = 7.5, 2.4, 0.9 Hz, 1 H, ArH), 4.66 (s, 1 H, CH), 2.32 (s, 3 H, CH_3), 1.62 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.5, 160.0 (d, J = 242.3 Hz), 149.3, 138.8, 136.3 (d, J = 2.3 Hz), 135.5, 129.3 (d, J = 8.5 Hz), 129.1, 128.8, 125.5, 116.3 (d, J = 7.9 Hz), 115.1 (d, J = 22.7 Hz), 112.4 (d, J = 24.3 Hz), 84.5, 52.6 (d, J = 1.7 Hz), 28.0, 21.3 ppm. ^{19}F NMR (376 MHz, $CDCl_3$, non-decoupled): δ = –117.593, –117.605, –117.614, –117.626, –117.636, –117.648 ppm. IR (film): $\tilde{\nu}$ = 1761, 1727, 1479, 1369, 1341, 1293, 1268, 1250, 1141, 1093 cm^{-1}. MS (EI): *m*/*z* (%) = 341 (1) $[M]^+$, 241 (100), 212 (28), 198 (32), 183 (4), 57 (6). HRMS: calcd. for $C_{20}H_{20}FNO_3$ $[M]^+$ 341.1427; found 341.1429.

3-Aryl-*N*-Boc-oxindole 2m: Yield: 2.1 g (72%; total yield); white solid; m.p. 104.5–105.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (dd, J = 8.8, 4.4 Hz, 1 H, ArH), 7.25–7.18 (m, 2 H, ArH), 7.13–7.09 (m, 1 H, ArH), 7.03 (ddt, J = 8.8, 2.8, 0.8 Hz, 1 H, ArH), 6.85–6.81 (m, 1 H, ArH), 6.78 (dd, J = 7.6, 2.0 Hz, 1 H, ArH), 4.96 (s, 1 H, CH), 2.38 (s, 3 H, CH_3), 1.62 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.4, 160.0 (d, J = 242.3 Hz), 149.3, 137.2, 136.3, 134.5, 131.1, 129.7 (d, J = 8.3 Hz), 128.1, 126.4, 125.5, 116.3, 116.2, 114.9 (d, J = 22.6 Hz), 112.0 (d, J = 24.3 Hz), 84.5, 28.0, 19.8 ppm. ^{19}F NMR (376 MHz, $CDCl_3$, non-decoupled): δ = –117.577, –117.601, –117.612, –117.647 ppm. IR (film): $\tilde{\nu}$ = 1766, 1724, 1481, 1346, 1294, 1268, 1252, 1141, 1086, 848, 813, 736, 629 cm^{-1}. MS (EI): *m*/*z* (%) = 341 (2) $[M]^+$, 241 (100), 226 (8), 212 (17), 198 (15), 183 (4), 57 (22). HRMS: calcd. for $C_{20}H_{20}FNO_3$ $[M]^+$ 341.1427; found 341.1432.

Procedure for the Synthesis of the *N*-(9*H*-Fluoren-9-yloxycarbonyl)-3-phenyloxindole (2r):[3d] $BF_3{\cdot}OEt_2$ (1.9 mL, 15 mmol) was added to a solution of 3-hydroxy-3-phenyloxindole (1.7 g, 7.5 mmol) and triethylsilane (2.4 mL, 15 mmol) in CH_2Cl_2 (30 mL) at 0 °C. After 15 min, the reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was quenched with saturated aqueous Na_2CO_3, extracted with CH_2Cl_2,and the combined organic layers were dried with Na_2SO_4. After removal of the solvent, the crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate, 2:1) to give 3-phenyloxindole (63%, 1.0 g).

To a stirred, cold (–40 °C) suspension of 3-phenyloxindole (0.42 g, 2 mmol) in THF (10 mL) under argon, was added dropwise a prepared solution of EtMgBr (2.2 mmol, 1.1 equiv.) in THF (10 mL). After 10 min, a solution of 9*H*-fluoren-9-yl 1*H*-imidazole-1-carboxylate[3d] (0.61 g, 2.2 mmol) in THF (3 mL) was added to the reaction vessel at –40 °C. The reaction mixture was warmed to room temperature and stirred for 4 h. The reaction was quenched with saturated aqueous NH_4Cl solution and the mixture extracted with ethyl acetate. The combined organic layers were washed with brine and then dried with Na_2SO_4. After removal of the solvent, the crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate, 8:1) to give **2r** (52%, 0.44 g) as a white solid. M.p. 166.9–168.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, J = 8.0 Hz, 1 H, ArH), 7.74–7.72 (m, 2 H, ArH), 7.65 (d, J = 7.6 Hz, 2 H, ArH), 7.41 (dt, J = 7.2, 2.4 Hz, 2 H, ArH), 7.34–7.25 (m, 6 H, ArH), 7.17–7.14 (m, 4 H, ArH), 6.90 (s, 1 H, CH), 4.74 (s, 1 H, CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.5, 151.6, 141.1, 141.1, 140.9, 140.9, 139.8, 135.9, 129.8, 128.9, 128.8, 128.5, 128.0, 127.9, 127.4, 126.3, 126.3, 125.2, 124.9, 120.0, 115.2, 78.0, 52.3 ppm. IR (film): $\tilde{\nu}$ = 1766, 1721, 1478, 1452, 1353,

1285, 1238, 1181, 1151, 1089, 1040, 1000, 935, 753, 742, 696 cm^{-1}. MS (EI): *m*/*z* (%) = 373 (13) [M]$^+$, 208 (41), 180 (8), 165 (100). HRMS: calcd. for $C_{27}H_{19}NO$ [M]$^+$ 373.1467; found 373.1468.

General Procedure for the Chlorination of Oxindoles 2: To a solution of oxindole **2** (0.1 mmol) in THF (1.5 mL) was added *O*-benzoylquinidine (8.6 mg, 0.02 mmol) with stirring. The mixture was cooled to –30 °C (bath temperature) for 20 min; then a solution of NCS (16 mg, 0.12 mmol) in THF (0.5 mL) was added dropwise. The resulting mixture was stirred at –30 °C for 1–5 h (monitored by TLC until no oxindole remained), concentrated, and purified by silica gel column chromatography to give compound **3**.

3-Aryl-3-chlorooxindole 3a:[3e] Yield: 34.0 mg (99%); pale-yellow oil; $[\alpha]_D^{25}$ = +107.2 (*c* = 1.0, $CHCl_3$); 93% *ee* (Chiralcel OJ-H; hexane/2-propanol, 90:10; 0.5 mL/min; 254 nm; t_{major} = 11.98 min, t_{minor} = 14.07 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 8.4 Hz, 1 H, ArH), 7.52–7.50 (m, 2 H, ArH), 7.48–7.42 (m, 2 H, ArH), 7.38–7.35 (m, 3 H, ArH), 7.30–7.26 (m, 1 H, ArH), 1.62 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 148.9, 139.1, 136.3, 130.7, 129.1, 128.9, 128.5, 127.8, 126.1, 125.4, 115.6, 85.2, 66.5, 28.0 ppm.

3-Aryl-3-chlorooxindole 3b: Yield: 35.8 mg (99%); pale-yellow oil; $[\alpha]_D^{25}$ = +129.5 (*c* = 1.0, $CHCl_3$); 90% *ee* (Chiralpak AS-H; hexane/2-propanol, 98:2; 0.6 mL/min; 214 nm; t_{major} = 9.28 min, t_{minor} = 9.88 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (dd, *J* = 8.8, 4.4 Hz, 1 H, ArH), 7.50–7.48 (m, 2 H, ArH), 7.39–7.36 (m, 3 H, ArH), 7.18–7.12 (m, 2 H, ArH), 1.62 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.5, 160.1 (d, *J* = 244.1 Hz), 148.9, 135.8, 135.0 (d, *J* = 2.5 Hz), 130.6 (d, *J* = 8.3 Hz), 129.3, 128.7, 127.6, 117.6 (d, *J* = 22.8 Hz), 117.2 (d, *J* = 7.7 Hz), 113.3 (d, *J* = 24.8 Hz), 85.3, 66.1 (d, *J* = 1.6 Hz), 28.0 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –115.8 ppm. IR (film): $\tilde{\nu}$ = 1778, 1734, 1483, 1339, 1293, 1262, 1144, 1098 cm^{-1}. MS (EI): *m*/*z* (%) = 361 (1) [M]$^+$, 261 (26), 226 (100), 198 (16), 170 (7), 57 (69), 41 (10). HRMS: calcd. for $C_{19}H_{17}ClFNO_3$ [M]$^+$ 361.0881; found 361.0886.

3-Aryl-3-chlorooxindole 3c: Yield: 34.4 mg (96%); pale-yellow oil; $[\alpha]_D^{25}$ = +119.6 (*c* = 1.0, $CHCl_3$); 91% *ee* (Chiralpak AS-H; hexane/2-propanol, 99:1; 0.3 mL/min; 254 nm; t_{major} = 17.13 min, t_{minor} = 18.33 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.4 Hz, 1 H, ArH), 7.52–7.50 (m, 2 H, ArH), 7.37–7.35 (m, 3 H, ArH), 7.26–7.22 (m, 2 H, ArH), 2.38 (s, 3 H, CH_3), 1.62 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 149.0, 136.7, 136.5, 135.2, 131.3, 129.1, 128.8, 128.5, 127.8, 126.4, 115.4, 84.9, 66.8, 28.0, 21.0 ppm. IR (film): $\tilde{\nu}$ = 1777, 1733, 1489, 1332, 1299, 1276, 1248, 1149, 1113 cm^{-1}. MS (EI): *m*/*z* (%) = 357 (1) [M]$^+$, 257 (20), 222 (100), 207 (13), 194 (18), 165 (7), 57 (18). HRMS: calcd. for $C_{20}H_{20}ClNO_3$ [M]$^+$ 357.1132; found 357.1136.

3-Aryl-3-chlorooxindole 3d: Yield: 35.8 mg (99%); pale-yellow oil; $[\alpha]_D^{25}$ = +175.7 (*c* = 1.0, $CHCl_3$); 81% *ee* (Chiralpak AS-H; hexane/2-propanol, 200:1; 0.2 mL/min; 230 nm; t_{major} = 26.38 min, t_{minor} = 27.78 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 8.4 Hz, 1 H, ArH), 7.53–7.42 (m, 4 H, ArH), 7.32–7.28 (m, 1 H, ArH), 7.07–7.02 (m, 2 H, ArH), 1.62 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.7, 163.1 (d, *J* = 248.2 Hz), 148.8, 139.1, 132.2 (d, *J* = 3.2 Hz), 130.9, 130.0 (d, *J* = 8.6 Hz), 128.5, 125.7 (d, *J* = 57.6 Hz), 115.7, 115.6, 115.4, 85.3, 65.8, 28.0 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –112.2 ppm. IR (film): $\tilde{\nu}$ = 1775, 1735, 1507, 1467, 1340, 1287, 1249, 1144, 1093 cm^{-1}. MS (EI) *m*/*z* (%) = 361 (1) [M]$^+$, 261 (18), 226 (100), 198 (9), 170 (4), 57 (11). HRMS: calcd. for $C_{19}H_{17}ClFNO_3$ [M]$^+$ 361.0881; found 361.0889.

3-Aryl-3-chlorooxindole 3e: Yield: 37.6 mg (99%); pale-yellow oil; $[\alpha]_D^{25}$ = +128.0 (*c* = 0.96, $CHCl_3$); 84% *ee* (Chiralpak AS-H; hexane/2-propanol, 95:5; 0.6 mL/min; 254 nm; t_{major} = 5.92 min, t_{minor} = 6.35 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (dd, *J* = 8.8, 4.4 Hz, 1 H, ArH), 7.51–7.46 (m, 2 H, ArH), 7.20–7.13 (m, 2 H, ArH), 7.07 (tt, *J* = 8.8, 2.0 Hz, 2 H, ArH), 1.62 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 163.2 (d, *J* = 248.8 Hz), 160.2 (d, *J* = 244.4 Hz), 148.8, 135.0 (d, *J* = 2.6 Hz), 131.6 (d, *J* = 3.2 Hz), 130.1 (d, *J* = 8.2 Hz), 129.8 (d, *J* = 8.6 Hz), 117.8 (d, *J* = 22.9 Hz), 117.4 (d, *J* = 7.8 Hz), 115.7 (d, *J* = 21.8 Hz), 113.2 (d, *J* = 24.8 Hz), 85.5, 65.5 (d, *J* = 1.5 Hz), 28.0 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –111.7 (d, *J* = 1.5 Hz), –115.6 (d, *J* = 1.5 Hz) ppm. IR (film): $\tilde{\nu}$ = 1776, 1736, 1507, 1484, 1339, 1295, 1262, 1144, 1095 cm^{-1}. MS (EI): *m*/*z* (%) = 379 (1) [M]$^+$, 279 (17), 244 (100), 216 (51), 188 (7), 169 (5), 57 (10). HRMS: calcd. for $C_{19}H_{16}ClF_2NO_3$ [M]$^+$ 379.0787; found 379.0790.

3-Aryl-3-chlorooxindole 3f: Yield: 36.8 mg (98%); pale-yellow oil; $[\alpha]_D^{25}$ = +101.8 (*c* = 1.0, $CHCl_3$); 65% *ee* (Chiralpak AS-H; hexane/2-propanol, 99:1; 0.3 mL/min; 254 nm; t_{major} = 15.38 min, t_{minor} = 17.43 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.4 Hz, 1 H, ArH), 7.52–7.48 (m, 2 H, ArH), 7.27–7.22 (m, 2 H, ArH), 7.07–7.03 (m, 2 H, ArH), 2.39 (s, 3 H, CH_3), 1.62 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 163.1 (d, *J* = 248.1 Hz), 148.9, 136.7, 135.4, 132.3 (d, *J* = 3.2 Hz), 131.5, 130.0 (d, *J* = 8.4 Hz), 128.4, 126.3, 115.5 (d, *J* = 7.0 Hz), 115.4, 85.1, 66.1, 28.0, 21.1 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –112.4 ppm. IR (film): $\tilde{\nu}$ = 1774, 1735, 1506, 1491, 1332, 1300, 1277, 1248, 1149, 1113 cm^{-1}. MS (EI): *m*/*z* = 375 (1) [M]$^+$, 275 (13), 240 (100), 225 (11), 212 (28), 183 (7), 57 (7). HRMS: calcd. for $C_{20}H_{19}ClFNO_3$ [M]$^+$ 375.1037; found 375.1039.

3-Aryl-3-chlorooxindole 3g: Yield: 32.9 mg (92%); pale-yellow oil; $[\alpha]_D^{25}$ = +87.6 (*c* = 0.9, $CHCl_3$); 73% *ee* (Chiralpak AS-H; hexane/2-propanol, 95:5; 0.6 mL/min; 214 nm; t_{major} = 7.63 min, t_{minor} = 8.18 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 8.4 Hz, 1 H, ArH), 7.47–7.38 (m, 4 H, ArH), 7.30–7.26 (m, 1 H, ArH), 7.17 (d, *J* = 8.4 Hz, 2 H, ArH), 2.34 (s, 3 H, CH_3), 1.62 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 149.0, 139.2, 139.1, 133.3, 130.6, 129.2, 129.0, 127.8, 126.1, 125.3, 115.6, 85.0, 66.5, 28.0, 21.1 ppm. IR (film): $\tilde{\nu}$ = 1777, 1734, 1478, 1467, 1341, 1288, 1249, 1145, 1093 cm^{-1}. MS (EI): *m*/*z* (%) = 357 (1) [M]$^+$, 257 (17), 222 (100), 194 (9), 57 (12). HRMS: calcd. for $C_{20}H_{20}ClNO_3$ [M]$^+$ 357.1132; found 357.1139.

3-Aryl-3-chlorooxindole 3h: Yield: 36.8 mg (98%); pale-yellow oil; $[\alpha]_D^{25}$ = +83.9 (*c* = 0.95, $CHCl_3$); 84% *ee* (Chiralpak AD-H; hexane/2-propanol, 95:5; 0.6 mL/min; 250 nm; t_{major} = 6.29 min, t_{minor} = 6.82 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (dd, *J* = 8.8, 4.0 Hz, 1 H, ArH), 7.37 (d*t*, *J* = 8.4, 1.6 Hz, 2 H, ArH), 7.19–7.17 (m, 2 H, ArH), 7.14 (dt, *J* = 8.4, 1.6 Hz, 2 H, ArH), 2.35 (s, 3 H, CH_3), 1.61 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.6, 160.1 (d, *J* = 243.8 Hz), 148.9, 139.5, 135.0 (d, *J* = 2.5 Hz), 132.8, 130.7 (d, *J* = 8.3 Hz), 129.4, 127.6, 117.5 (d, *J* = 22.8 Hz), 117.2 (d, *J* = 7.7 Hz), 113.2 (d, *J* = 24.7 Hz), 85.3, 66.1 (d, *J* = 1.5 Hz), 28.0, 21.1 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –116.0 ppm. IR (film): $\tilde{\nu}$ = 1780, 1734, 1483, 1340, 1294, 1262, 1144, 1096 cm^{-1}. MS (EI): *m*/*z* (%) = 375 (1) [M]$^+$, 275 (17), 240 (100), 212 (13), 57 (15). HRMS: calcd. for $C_{20}H_{19}ClFNO_3$ [M]$^+$ 375.1037; found 375.1039.

3-Aryl-3-chlorooxindole 3i: Yield: 30.1 mg(81%); pale-yellow oil; $[\alpha]_D^{25}$ = +86.8 (*c* = 0.91, $CHCl_3$); 70% *ee* (Chiralpak AD-H; hexane/2-propanol, 99:1; 0.5 mL/min; 230 nm; t_{major} = 12.79 min, t_{minor} = 13.82 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 8.4 Hz, 1 H, ArH), 7.39 (d, *J* = 8.4 Hz, 2 H, ArH), 7.25–7.22 (m, 2 H, ArH), 7.17 (d, *J* = 8.4 Hz, 2 H, ArH), 2.37 (s, 3 H, CH_3), 2.34 (s, 3 H, CH_3), 1.61 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz,

$CDCl_3$): δ = 171.2, 149.0, 139.2, 136.7, 135.2, 133.5, 131.2, 129.2, 128.9, 127.8, 126.4, 115.3, 84.9, 66.8, 28.0, 21.1, 21.0 ppm. IR (film): ṽ = 1778, 1733, 1491, 1333, 1298, 1277, 1248, 1150, 1108 cm^{-1}. MS (EI): *m/z* (%) = 371 (1) $[M]^+$, 271 (17), 236 (100), 208 (16), 194 (11), 57 (11). HRMS: calcd. for $C_{21}H_{22}ClNO_3$ $[M]^+$ 371.1288; found 371.1292.

3-Aryl-3-chlorooxindole 3j: Yield: 38.2 mg (97%); pale-yellow solid; m.p. 146.1–147.0 °C; $[\alpha]_D^{25}$ = +64.9 (*c* = 0.96, $CHCl_3$); 72% *ee* (Chiralpak AS-H; hexane/2-propanol, 95:5; 0.7 mL/min; 230 nm; t_{major} = 7.33 min, t_{minor} = 7.93 min). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.03 (dd, *J* = 0.8, 8.4 Hz, 1 H, ArH), 7.87 (d, *J* = 8.8 Hz, 1 H, ArH), 7.83–7.81 (m, 2 H, ArH), 7.78–7.74 (m, 2 H, ArH), 7.52–7.46 (m, 4 H, ArH), 7.33–7.29 (m, 1 H, ArH), 1.62 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 148.9, 139.1, 133.5, 133.2, 132.4, 130.8, 128.8, 128.7, 128.4, 127.5, 127.3, 127.1, 126.6, 126.1, 125.4, 125.1, 115.6, 85.1, 66.7, 27.9 ppm. IR (film): ṽ = 1771, 1732, 1606, 1479, 1465, 1339, 1290, 1253, 1163, 1148, 1090 cm^{-1}. MS (EI): *m/z* (%) = 393 (1) $[M]^+$, 316 (4), 293 (8), 259 (100), 230 (63), 215 (7), 202 (7), 57 (6). HRMS: calcd. for $C_{23}H_{20}ClNO_3$ $[M]^+$ 393.1132; found 393.1139.

3-Aryl-3-chlorooxindole 3k: Yield: 39.5 mg (96%); pale-yellow solid; m.p. 138.6–139.1 °C; $[\alpha]_D^{25}$ = +40.1 (*c* = 0.9, $CHCl_3$); 66% *ee* (Chiralcel OJ-H; hexane/2-propanol, 90:10; 0.7 mL/min; 230 nm; t_{major} = 12.13 min, t_{minor} = 8.38 min). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.04 (dd, *J* = 9.6, 4.4 Hz, 1 H, ArH), 7.88 (d, *J* = 8.8 Hz, 1 H, ArH), 7.84–7.79 (m, 3 H, ArH), 7.72 (dd, *J* = 8.8, 2.0 Hz, 1 H, ArH), 7.54–7.48 (m, 2 H, ArH), 7.22–7.17 (m, 2 H, ArH), 1.61 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.5, 160.2 (d, *J* = 244.1 Hz), 148.9, 135.1 (d, *J* = 2.6 Hz), 133.3, 132.9, 132.4, 130.5 (d, *J* = 8.3 Hz), 128.9, 128.5, 127.6, 127.3, 127.1, 126.8, 124.8, 117.7 (d, *J* = 22.9 Hz), 117.3 (d, *J* = 7.7 Hz), 113.4 (d, *J* = 24.8 Hz), 85.4, 66.4 (d, *J* = 1.6 Hz), 28.0 ppm. ^{19}F NMR (376 MHz, $CDCl_3$, non-decoupled): δ = –115.673, –115.685, –115.695, –115.707, –115.715, –115.727 ppm. IR (film): ṽ = 1776, 1733, 1484, 1339, 1295, 1261, 1144, 1124, 1095, 1020 cm^{-1}. MS (EI): *m/z* (%) = 411 (2) $[M]^+$, 311 (17), 276 (100), 248 (40), 233 (4), 220 (6), 57 (8). HRMS: calcd. for $C_{23}H_{19}ClFNO_3$ $[M]^+$ 411.1037; found 411.1042.

3-Aryl-3-chlorooxindole 3l: Yield: 37.2 mg (99%); pale-yellow oil; $[\alpha]_D^{25}$ = +86.5 (*c* = 0.97, $CHCl_3$); 84% *ee* (Chiralcel OJ-H; hexane/2-propanol, 90:10; 0.5 mL/min; 230 nm; t_{major} = 10.38 min, t_{minor} = 9.21 min). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.99 (q, *J* = 8.8, 4.4 Hz, 1 H, ArH), 7.32 (s, 1 H, ArH), 7.28–7.21 (m, 2 H, ArH), 7.19–7.11 (m, 3 H, ArH), 2.36 (s, 3 H, CH_3), 1.62 (s, 9 H, 3×CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.6, 160.1 (d, *J* = 244.0 Hz), 148.9, 138.6, 135.6, 135.0 (d, *J* = 2.3 Hz), 130.8 (d, *J* = 8.3 Hz), 130.2, 128.5, 128.2, 124.6, 117.5 (d, *J* = 22.9 Hz), 117.1 (d, *J* = 7.8 Hz), 113.2 (d, *J* = 24.8 Hz), 85.3, 66.2 (d, *J* = 1.5 Hz), 28.0, 21.5 ppm. ^{19}F NMR (376 MHz, $CDCl_3$, non-decoupled): δ = –115.887, –115.900, –115.908, –115.919, –115.929, –115.942 ppm. IR (film): ṽ = 1779, 1735, 1483, 1370, 1339, 1294, 1263, 1251, 1145, 1101 cm^{-1}. MS (EI): *m/z* (%) = 375 (1) $[M]^+$, 275 (24), 240 (100), 225 (4), 212 (8), 197 (5), 57 (12). HRMS: calcd. for $C_{20}H_{19}ClFNO_3$ $[M]^+$ 375.1037; found 375.1042.

3-Aryl-3-chlorooxindole 3m: Yield: 37.2 mg (99%); pale-yellow oil; $[\alpha]_D^{25}$ = +4.7 (*c* = 0.99, $CHCl_3$); 7% *ee* (Chiralpak IC; hexane/2-propanol, 70:30; 0.5 mL/min; 214 nm; t_{major} = 9.71 min, t_{minor} = 10.38 min). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.13 (dd, *J* = 7.6, 1.2 Hz, 1 H, ArH), 7.95 (dd, *J* = 8.8, 4.4 Hz, 1 H, ArH), 7.38–7.29 (m, 2 H, ArH), 7.12–7.07 (m, 2 H, ArH), 6.75 (dd, *J* = 7.6, 2.8 Hz, 1 H, ArH), 1.80 (s, 3 H, CH_3), 1.66 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.6, 160.2 (d, *J* = 244.2 Hz), 149.0, 134.9, 134.7, 132.5, 131.8, 131.3, 131.2, 129.3 (d, *J* = 31.8 Hz), 126.4, 117.4, 117.1, 117.1, 117.0, 111.9 (d, *J* = 24.8 Hz), 85.4, 28.0, 20.0 ppm. ^{19}F NMR (376 MHz, $CDCl_3$, non-decoupled): δ = –115.831, –115.843, –115.853, –115.864, –115.873, –115.885 ppm. IR (film): ṽ = 1778, 1735, 1484, 1339, 1294, 1263, 1250, 1142, 1094, 851, 731 cm^{-1}. MS (EI): *m/z* (%) = 375 (1) $[M]^+$, 275 (70), 240 (100), 211 (17), 197 (16), 183 (8), 57 (62), 41 (8). HRMS: calcd. for $C_{20}H_{19}ClFNO_3$ $[M]^+$ 375.1037; found 375.1038.

3-Chloro-3-methyloxindole 3n: Yield: 25.6 mg (91%); colorless oil; $[\alpha]_D^{25}$ = +12.5 (*c* = 0.9, $CHCl_3$); 22% *ee* (Chiralpak AD-H; hexane/2-propanol, 98:2; 0.5 mL/min; 230 nm; t_{major} = 9.54 min, t_{minor} = 11.21 min). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.4 Hz, 1 H, ArH), 7.46 (dd, *J* = 7.6, 0.8 Hz, 1 H, ArH), 7.38 (td, *J* = 7.6, 1.6 Hz, 1 H, ArH), 7.23 (td, *J* = 7.6, 1.2 Hz, 1 H, ArH), 1.95 (s, 3 H, CH_3), 1.65 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.2, 148.9, 138.2, 130.5, 129.7, 125.2, 123.8, 115.5, 85.0, 61.9, 28.0, 26.4 ppm. IR (film): ṽ = 1781, 1736, 1609, 1468, 1344, 1290, 1250, 1151 cm^{-1}. MS (EI): *m/z* (%) = 281 (4) $[M]^+$, 181 (71), 146 (100), 128 (11), 57 (31). HRMS: calcd. for $C_{14}H_{16}ClNO_3$ $[M]^+$ 281.0819; found 281.0821.

3-Chloro-3-benzyloxindole 3o: Yield: 30.4 mg (85%); pale-yellow oil; $[\alpha]_D^{25}$ = +4.1 (*c* = 0.91, $CHCl_3$); 29% *ee* (Chiralpak AD-H; hexane/2-propanol, 90:10; 0.7 mL/min; 214 nm; t_{major} = 5.99 min, t_{minor} = 6.68 min). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 8.0 Hz, 1 H, ArH), 7.34–7.27 (m, 2 H, ArH), 7.21–7.10 (m, 4 H, ArH), 6.94 (d, *J* = 7.2 Hz, 2 H, ArH), 3.61 (d, *J* = 13.2 Hz, 1 H, CH), 3.54 (d, *J* = 13.2 Hz, 1 H, CH), 1.58 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.8, 148.5, 138.9, 133.0, 130.5, 130.4, 128.1, 127.5, 124.9, 124.7, 115.2, 84.8, 65.4, 46.1, 28.0 ppm. IR (film): ṽ = 1780, 1738, 1607, 1467, 1370, 1348, 1290, 1252, 1150 cm^{-1}. MS (EI): *m/z* (%) = 357 (4) $[M]^+$, 257 (100), 222 (10), 204 (8), 165 (8), 91 (89), 57 (31). HRMS: calcd. for $C_{20}H_{20}ClNO_3$ $[M]^+$ 357.1132; found 357.1134.

3-Aryl-3-chlorooxindole 3p: Yield: 30.0 mg (90%); pale-yellow oil; $[\alpha]_D^{25}$ = +76.4 (*c* = 0.7, $CHCl_3$); 31% *ee* (Chiralpak AS-H; hexane/2-propanol, 90:10; 0.7 mL/min; 214 nm; t_{major} = 14.23 min, t_{minor} = 15.23 min). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.58–7.56 (m, 2 H, ArH), 7.41–7.24 (m, 10 H, ArH), 7.11 (dt, *J* = 7.6, 0.4 Hz, 1 H, ArH), 6.77 (d, *J* = 8.0 Hz, 1 H, ArH), 4.94 (s, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.6, 141.9, 136.6, 135.1, 130.4, 130.3, 128.9, 128.6, 127.8, 127.5, 127.1, 126.0, 123.6, 109.9, 66.3, 44.2 ppm. IR (film): ṽ = 1726, 1610, 1486, 1468, 1344, 1187, 1164, 928, 878, 750, 692 cm^{-1}. MS (EI): *m/z* (%) = 333 (16) $[M]^+$, 298 (100), 270 (10), 242 (12), 208 (9), 179 (13), 165 (12), 152 (5), 91 (71), 65 (6). HRMS: calcd. for $C_{21}H_{16}ClNO$ $[M]^+$ 333.0920; found 333.0927.

3-Aryl-3-chlorooxindole 3q: Yield: 29.4 mg (92%); white solid; m.p. 127.6–129.4 °C; $[\alpha]_D^{25}$ = +13.4 (*c* = 1.0, $CHCl_3$); 11% *ee* (Chiralpak AS-H; hexane/2-propanol, 90:10; 1.0 mL/min; 230 nm; t_{major} = 7.18 min, t_{minor} = 10.08 min). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.63 (dd, *J* = 8.0, 2.0 Hz, 2 H, ArH), 7.54–7.30 (m, 10 H, ArH), 7.21–7.17 (m, 1 H, ArH), 6.89 (d, *J* = 8.0 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.6, 142.8, 136.7, 133.8, 130.3, 130.1, 129.7, 129.0, 128.6, 128.4, 127.6, 126.5, 126.3, 124.0, 110.2, 66.4 ppm. IR (film): ṽ = 1728, 1593, 1496, 1468, 1361, 1200, 1167, 877, 758, 732, 695 cm^{-1}. MS (EI): *m/z* (%) = 319 (11) $[M]^+$, 284 (100), 256 (31), 178 (7), 152 (7), 128 (6), 77 (7). HRMS: calcd. for $C_{20}H_{14}ClNO$ $[M]^+$ 319.0764; found 319.0771.

3-Aryl-3-chlorooxindole 3r: Yield: 42.9 mg (95%); white solid; m.p. 167.8–169.1 °C; $[\alpha]_D^{25}$ = +58.8 (*c* = 1.01, $CHCl_3$); 83% *ee* (Chiralpak IC; hexane/2-propanol, 90:10; 0.7 mL/min; 214 nm; t_{major} = 13.58 min, t_{minor} = 14.78 min). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 8.4 Hz, 1 H, ArH), 7.74–7.71 (m, 2 H, ArH), 7.67 (d,

J = 7.2 Hz, 2 H, ArH), 7.50–7.47 (m, 2 H, ArH), 7.44–7.40 (m, 4 H, ArH), 7.37–7.27 (m, 6 H, ArH), 6.89 (s, 1 H, CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.6, 151.3, 141.2, 141.1, 140.6, 140.6, 138.4, 136.0, 130.9, 130.0, 129.2, 129.0, 128.6, 128.1, 128.0, 127.8, 126.4, 126.3, 126.2, 125.8, 120.1, 115.7, 78.5, 66.3 ppm. IR (film): $\tilde{\nu}$ = 1783, 1733, 1469, 1348, 1280, 1234, 1152, 1094, 1039, 1002, 952, 757, 742, 724, 698 cm^{-1}. MS (EI): *m/z* (%) = 407 (1) $[M]^+$, 373 (6), 298 (10), 208 (19), 180 (5), 165 (100), 91 (7). HRMS: calcd. for $C_{27}H_{18}ClNO$ $[M]^+$ 407.1077; found 407.1084.

Supporting Information (see footnote on the first page of this article): NMR spectra of new compounds and HPLC traces for the determination of the enantiomeric excess for compounds **3**.

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[1] a) A. U. Rahman, A. Basha, *Indole Alkaloid*, Harwood Academic Publishers, Amsterdam, **1997**; b) C. Marti, E. M. Carreira, *Eur. J. Org. Chem.* **2003**, *12*, 2209–2219; c) A. B. Dounay, L. E. Overman, *Chem. Rev.* **2003**, *103*, 2945–2964; d) C. V. Galliford, K. A. Scheidt, *Angew. Chem.* **2007**, *119*, 8902; *Angew. Chem. Int. Ed.* **2007**, *46*, 8748–8758; e) B. M. Trost, M. K. Brennan, *Synthesis* **2009**, 3003–3025.

[2] a) M. Ochi, K. Kawasaki, H. Kataoka, Y. Uchio, *Biochem. Biophys. Res. Commun.* **2001**, *283*, 1118–1123; b) P. Hewawasam, M. Erway, S. L. Moon, J. Knipe, H. Weiner, C. G. Boissard, D. J. Post-Munson, Q. Gao, S. Huang, V. K. Gribkoff, N. A. Meanwell, *J. Med. Chem.* **2002**, *45*, 1487–1499; c) X. Z. Wearing, J. M. Cook, *Org. Lett.* **2002**, *4*, 4237–4240; d) G. Gilles, S. L. Claudine, *Stress* **2003**, *6*, 199–206; e) H. Suzuki, H. Morita, M. Shiro, J. I. Kobayashi, *Tetrahedron* **2004**, *60*, 2489–2495; f) K. Bernard, S. Bogliolo, J. Ehrenfeld, *Br. J. Pharmacol.* **2005**, *144*, 1037–1050; g) A. H. Abadi, S. M. Abou-Seri, D. E. Abdel-Rahman, C. Klein, O. Lozach, L. Meijer, *Eur. J. Med. Chem.* **2006**, *41*, 296–305; h) S. E. Reisman, J. M. Ready, M. M. Weiss, A. Hasuoka, M. Hirata, K. Tamaki, T. V. Ovaska, C. J. Smith, J. L. Wood, *J. Am. Chem. Soc.* **2008**, *130*, 2087–2100.

[3] a) N. Shibata, E. Suzuki, T. Asahi, M. Shiro, *J. Am. Chem. Soc.* **2001**, *123*, 7001–7009; b) L. Zoute, C. Audouard, J.-C. Plaquevent, D. Cahard, *Org. Biomol. Chem.* **2003**, *1*, 1833–1834; c) N. Shibata, T. Ishimaru, E. Suzuki, K. L. Kirk, *J. Org. Chem.* **2003**, *68*, 2494–2497; d) Y. Hama shima, T. Suzuki, H. Takano, Y. Shimura, M. Sedeoka, *J. Am. Chem. Soc.* **2005**, *127*, 10164–10165; e) N. Shibata, J. Kohno, K. Takai, T. Ishimaru, S. Nakamura, T. Toru, S. Kanemasa, *Angew. Chem.* **2005**, *117*, 4276; *Angew. Chem. Int. Ed.* **2005**, *44*, 4204–4207; f) T. Toru, T. Shibata, JP 2006290789; g) T. Ishimaru, N. Shibata, T. Horikawa, N. Yasuda, S. Nakamura, T. Toru, M. Shiro, *Angew. Chem.* **2008**, *120*, 4225; *Angew. Chem. Int. Ed.* **2008**, *47*, 4157–4161.

[4] a) T. Ishimaru, N. Shibata, J. Nagai, S. Nakamura, T. Toru, S. Kanemasa, *J. Am. Chem. Soc.* **2006**, *128*, 16488–16489; b) D. Sano, K. Nagata, T. Itoh, *Org. Lett.* **2008**, *10*, 1593–1595; c) T. Bui, N. R. Candeias, C. F. Barbas III, *J. Am. Chem. Soc.* **2010**, *132*, 5574–5575.

[5] a) Z.-Q. Qian, F. Zhou, T.-P. Du, B.-L. Wang, M. Ding, X.-L. Zhao, J. Zhou, *Chem. Commun.* **2009**, 6753–6755; b) L. Cheng, L. Liu, D. Wang, Y.-J. Chen, *Org. Lett.* **2009**, *11*, 3874–3877; c) T. Bui, M. Borregan, C. F. Barbas III, *J. Org. Chem.* **2009**, *74*, 8935–8938; d) S. Mouri, Z. Chen, H. Mitsunuma, M. Furutachi, S. Matsunaga, M. Shibasaki, *J. Am. Chem. Soc.* **2010**, *132*, 1255–1257.

[6] a) S. Ogawa, N. Shibata, J. Inagaki, S. Nakamura, T. Toru, M. Shiro, *Angew. Chem.* **2007**, *119*, 8820; *Angew. Chem. Int. Ed.* **2007**, *46*, 8666–8669; b) X. Tian, K. Jiang, J. Peng, W. Du, Y.-C. Chen, *Org. Lett.* **2008**, *10*, 3583–3586; c) L. Cheng, L. Liu, H. Jia, D. Wang, Y.-J. Chen, *J. Org. Chem.* **2009**, *74*, 4650–4653; d) X.-L. Liu, Y.-H. Liao, Z.-J. Wu, L.-F. Cun, X.-M. Zhang, W.-C. Yuan, *J. Org. Chem.* **2010**, *75*, 4872–4875; e) K. Shen, X. Liu, K. Zheng, W. Li, X. Hu, L. Lin, X. Feng, *Chem. Eur. J.* **2010**, *16*, 3736–3742.

[7] a) B. M. Trost, M. U. Frederiksen, *Angew. Chem.* **2005**, *117*, 312; *Angew. Chem. Int. Ed.* **2005**, *44*, 308–310; b) B. M. Trost, Y. Zhang, *J. Am. Chem. Soc.* **2007**, *129*, 14548–14549; c) K. Jiang, J. Peng, H.-L. Cui, Y.-C. Chen, *Chem. Commun.* **2009**, 3955–3957; d) B. M. Trost, Y. Zhang, *Chem. Eur. J.* **2010**, *16*, 296–303.

[8] a) T. Bui, S. Syed, C. F. Barbas III, *J. Am. Chem. Soc.* **2009**, *131*, 8758–8759; b) R. He, C. Ding, K. Maruoka, *Angew. Chem.* **2009**, *121*, 4629; *Angew. Chem. Int. Ed.* **2009**, *48*, 4559–4561; c) Y. Kato, M. Furutachi, Z. Chen, H. Mitsunuma, S. Matsunaga, M. Shibasaki, *J. Am. Chem. Soc.* **2009**, *131*, 9168–9169; d) P. Galzerano, G. Bencivenni, F. Pesciaioli, A. Mazzanti, B. Giannichi, L. Sambri, G. Bartoli, P. Melchiorre, *Chem. Eur. J.* **2009**, *15*, 7846–7849; e) R. He, S. Shirakawa, K. Maruoka, *J. Am. Chem. Soc.* **2009**, *131*, 16620–16621; f) X. Li, Z.-G. Xi, S. Luo, J.-P. Cheng, *Org. Biomol. Chem.* **2010**, *8*, 77–82; g) X. Li, B. Zhang, Z.-G. Xi, S. Luo, J.-P. Cheng, *Adv. Synth. Catal.* **2010**, *352*, 416–424; h) Y.-H. Liao, X.-L. Liu, Z.-J. Wu, L.-F. Cun, X.-M. Zhang, W.-C. Yuan, *Org. Lett.* **2010**, *12*, 2896–2899.

[9] F. Zhou, Y.-L. Liu, J. Zhou, *Adv. Synth. Catal.* **2010**, *352*, 1381–1407.

[10] a) S. A. Shaw, P. Aleman, E. Vedeis, *J. Am. Chem. Soc.* **2003**, *125*, 13368–13369; b) I. D. Hills, G. C. Fu, *Angew. Chem.* **2003**, *115*, 4051; *Angew. Chem. Int. Ed.* **2003**, *42*, 3921–3924; c) S. A. Shaw, P. Aleman, J. Christy, J. W. Kampf, P. Va, E. Vedejs, *J. Am. Chem. Soc.* **2006**, *128*, 925–934; d) T. A. Duffey, S. A. Shaw, E. Vedejs, *J. Am. Chem. Soc.* **2009**, *131*, 14–15.

[11] a) J. March, *Advanced Organic Chemistry: Reactions, Mechanisms and Structure*, 4th ed., Wiley, New York, **1992**; b) N. De Kimpe, R. Verhé, *The Chemistry of α-Haloketones, α-Haloaldehydes, and α-Haloimines*, Wiley, New York, **1990**.

[12] For Lewis acid catalyzed chlorination, see: a) L. Hintermann, A. Togni, *Helv. Chim. Acta* **2000**, *83*, 2425–2435; b) M. Marigo, N. Kumaragurubaran, K. A. Jørgensen, *Chem. Eur. J.* **2004**, *10*, 2133–2137; c) L. Bernardi, K. A. Jørgensen, *Chem. Commun.* **2005**, 1324–1326; d) M. Kawatsura, S. Hayashi, Y. Komatsu, S. Hayase, T. Itoh, *Chem. Lett.* **2010**, *39*, 466–467.

[13] For organocatalyzed chlorination, see: a) H. Wack, A. E. Taggi, A. M. Hafez, W. J. Drury III, T. Lectka, *J. Am. Chem. Soc.* **2001**, *123*, 1531–1532; b) S. France, H. Wack, A. E. Taggi, A. M. Hafez, T. R. Wagerle, M. H. Shah, C. L. Dusich, T. Lectka, *J. Am. Chem. Soc.* **2004**, *126*, 4245–4255; c) M. P. Brochu, S. P. Brown, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2004**, *126*, 4108–4109; d) N. Halland, A. Braunton, S. Bachmann, M. Marigo, K. A. Jørgensen, *J. Am. Chem. Soc.* **2004**, *126*, 4790–4791; e) M. Marigo, S. Bachmann, N. Halland, A. Braunton, K. A. Jørgensen, *Angew. Chem.* **2004**, *116*, 5623; *Angew. Chem. Int. Ed.* **2004**, *43*, 5507–5510; f) S. France, A. Weatherwax, T. Lectka, *Eur. J. Org. Chem.* **2005**, 475–479; g) G. Bartoli, M. Bosco, A. Carlone, M. Locatelli, P. Melchiorre, L. Sambri, *Angew. Chem.* **2005**, *117*, 6375; *Angew. Chem. Int. Ed.* **2005**, *44*, 6219–6222; h) E. C. Lee, K. M. McCauley, G. C. Fu, *Angew. Chem.* **2007**, *119*, 995; *Angew. Chem. Int. Ed.* **2007**, *46*, 977–979; i) M. Ueda, T. Kano, K. Maruoka, *Org. Biomol. Chem.* **2009**, *7*, 2005–2012; j) Y. Cai, W. Wang, K. Shen, J. Wang, X. Hu, L. Lin, X. Liu, X. Feng, *Chem. Commun.* **2010**, *46*, 1250–1252.

[14] a) C. D. Grant, M. J. Krische, *Org. Lett.* **2009**, *11*, 4485–4487; b) S. Ma, X. Han, S. Krishnan, S. C. Virgil, B. M. Stoltz, *An-*

gew. Chem. **2009**, *121*, 8181; *Angew. Chem. Int. Ed.* **2009**, *48*, 8037–8041.
[15] F. W. Goldberg, P. Magnus, R. Turnbull, *Org. Lett.* **2005**, *7*, 4531–4534.
[16] a) H. Li, Y. Wang, L. Tang, F. Wu, X. Liu, C. Guo, B. M. Foxman, L. Deng, *Angew. Chem.* **2005**, *117*, 107; *Angew. Chem. Int. Ed.* **2005**, *44*, 105–108; b) M. Shi, Z.-Y. Lei, M.-X. Zhao, J.-W. Shi, *Tetrahedron Lett.* **2007**, *48*, 5743–5746.
[17] A. Huang, J. J. Kodanko, L. E. Overman, *J. Am. Chem. Soc.* **2004**, *126*, 14043–14053.
[18] a) T. Minami, K. Yamataka, Y. Ohshiro, T. Agawa, N. Yasuoka, N. Kasai, *J. Org. Chem.* **1972**, *37*, 3810–3818; b) G. C. H. Chiang, T. Olsson, *Org. Lett.* **2004**, *6*, 3079–3082.

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