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# Comparative studies on the enantioselective fluorination of oxindoles with structurally modified *N*-fluorobenzenesulfonimides

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ABSTRACT

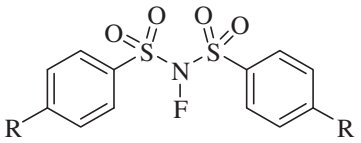
Structurally modified *N*-fluorobenzenesulfonimides (NFSIs) have been used to study the enantioselective fluorination of oxindoles in the presence of a bis-cinchona alkaloid, $(DHQD)_2PHAL$, as the catalyst. We observe that the NFSI analogues bearing two *tert*-butyl groups at the *para*-position of the symmetric phenyl rings led to an enhanced enantioselectivity in most cases (up to 96% ee) compared with the unmodified NFSIs (less than 69% ee).



## 1. Introduction

Fluorination represents a highly effective strategy in medicinal chemistry as properly fluorinated leading compounds usually exhibit good bioactivity as well as admirable pharmacological profiles.[1] However, despite some recent examples fulfilling the elegant fluorination of aldehydes, ketones, and 1,3-dicarbonyl derivatives,[2] the regioselective and, especially, stereoselective fluorination of bioactive chiral molecules remains a challenging task.

Recently, *N*-fluorobenzenesulfonimide (NFSI) has been disclosed as a promising fluorinating reagent toward the catalytic fluorination of various target compounds.[3] However, use of this reagent to give admirable enantioselectivities was scarcely reported.[4] In the context of enantioselective fluorination, besides the substrates and catalysts employed, the structure of fluorinating reagents might also impact essentially the selectivity. Recently, Yasui et al. described an improved enantioselective fluorination of silylenol ethers with *N*-fluoro-(3,5-di-*tert*-butyl-4-methoxy)benzenesulfonimide.[5] We were thus intrigued to prepare structurally modified NFSIs to yield an improved enantioselective fluorination of carbonyl derivatives. To explore the influence of different kinds of substituents on the fluorinating reactivity and selectivity, we chose structurally similar benzenesulfonimides bearing several typical substituents (Fig. 1) on the *para*-position of the symmetric phenyl ring to compare with NFSI itself. We report herein the use of these potential fluorinating reagents in the catalytic enantioselective fluorination of oxindoles, a class of interesting bioactive nucleus widely found in numerous natural products.



R = **1a**: H, **1b**: F, **1c**: $OCH_3$, **1d**: *t*-Bu , **1e**: $CF_3$, **1f**: $OCF_3$

**Fig. 1.** NFSI and structurally modified NFSIs **1a**–**1f**.

## 2. Results and discussion

The preparation of the *para*-substituted NFSIs **1a**–**1f** as illustrated in Fig. 1 was first achieved according to our previous report.[6] Then, we initiated our investigation toward the C3-fluorination of oxindole **2a** in generating the (*S*)-enantiomer **3a** under a combined system of $(DHQD)_2PHAL/NFSI/K_2CO_3$ that has already been proven to be effective for this enantioselective fluorination.[4a] All reactions

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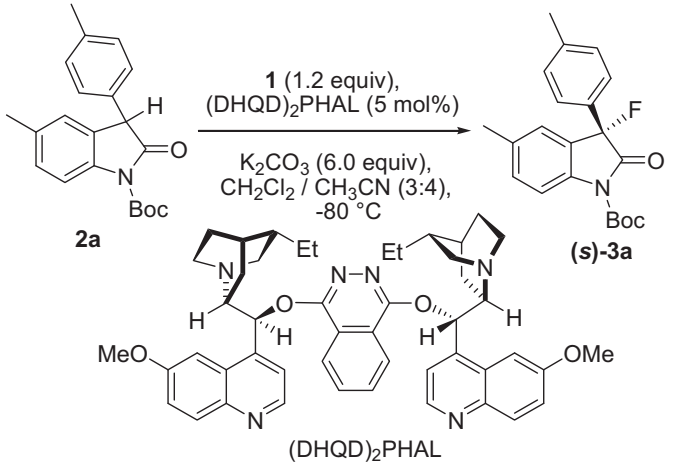
were performed at −80 °C in order to obtain better stereoselectivity and the results are complied in Table 1.

**Table 1**
The enantioselective fluorination of **2a** with different kinds of *para*-substituted NFSI analogues catalyzed by $(DHQD)_2PHAL$




| Entry | Reagent **1** (R) | *t* (h) | Yield[a] (%) | ee[e] (%) |
|---|---|---|---|---|
| 1 | **1a** (H) | 36[b] | 99 | 70 |
| 2 | **1b** (F) | 36[b] | 98 | 75 |
| 3 | **1c** (OMe) | 96[c] | 57 | 70 |
| 4 | **1d** (*t*-Bu) | 96[c] | 40 | 88 |
| 5 | **1e** ($CF_3$) | 84[d] | — | — |
| 6 | **1f** (O $CF_3$) | 72[d] | — | — |

[a] Isolated yield of **3**.
[b] Complete conversion as indicated by TLC.
[c] Incomplete conversion as indicated by TLC.
[d] No target product generating.
[e] The absolute configurations of products **3a** were determined by comparison with the HPLC data in the literature.[4a]

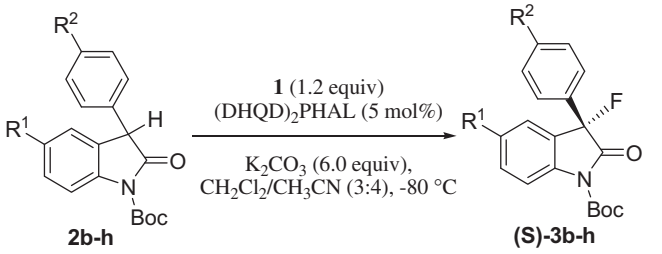
In using the unmodified **1a** (NFSI) as the reference fluorinating reagent, **3a** was afforded with a 70% ee and an almost quantitative yield (99%) in 36 h (Table 1, entry 1). In contrast, in the presence of *para*-fluoro-substituted NFSI **1b** (R=F), **3a** was obtained with a slightly improved ee of 75% in 98% yield in 36 h (Table 1, entry 2), whereas **1c** with an OMe substitution led to an identical ee of 70% with a decreased yield of 57% in 96 h (Table 1, entry 3). Interestingly, a higher enantioselectivity could be obtained with 88% ee in the presence of **1d** (R=*t*-Bu) (Table 1, entry 4), albeit with an incomplete conversion of **2a** to yield 40% of **3a** in 96 h. However, NFSIs with strong electron-withdrawing substituents including **1e** (R=$CF_3$, entry 5) and **1f** (R=$OCF_3$, entry 6) failed to afford the fluorinated product **3a** even by reacting over days.

A further investigation was carried out in order to comparatively test the substrate scope of reagents **1a**, **1b**, **1c**, and **1d** under the same condition. The results are listed in Table 2.

We notice that the substitution of different functional groups on the phenyl rings of substrates **2** obviously influences the reactivity and stereoselectivity. Oxindole **2c** ($R^1$=F, $R^2$=Me) is not a suitable substrate for the fluorinating reagents selected under the condition (Table 2, entries 5–8). In the case of substrate **2b** ($R^1$=H, $R^2$=Me), NFSI analogues **1b** (60% ee), **1c** (49% ee), and **1d** (51% ee) led to better enantioselectivity comparing with NFSI **1a** that gave a low ee value (38%) of **3b** in 68% yield. Nevertheless, the fluorination of **2b** with **1c** and **1d** was incomplete as indicated by TLC monitoring, whereas reagents **1a** and **1b** gave a complete conversion to product **3b** (Table 2, entries 1–4).

For the fluorination of substrate **2d** ($R^1$=OMe, $R^2$=Me), the unmodified NFSI led to **3d** in 49% ee and 80% isolated yield. In

**Table 2**
The enantioselective fluorination of different substrates with *para*-substituted NFSIs in the catalysis of $(DHQD)_2PHAL$ in comparison with NFSI itself




| Entry | Substrate ($R^1$, $R^2$) | Reagent **1** (R) | *t* (h) | Yield[a] (%) | ee[d] (%) |
|---|---|---|---|---|---|
| 1 | **2b** (H, Me) | **1a** (H) | 48[b] | 68 | 38 |
| 2 | **2b** (H, Me) | **1b** (F) | 48[b] | 60 | 60 |
| 3 | **2b** (H, Me) | **1c** (OMe) | 96[c] | 44 | 49 |
| 4 | **2b** (H, Me) | **1d** (*t*-Bu) | 96[c] | 20 | 51 |
| 5 | **2c** (F, Me) | **1a** (H) | 96[e] | — | — |
| 6 | **2c** (F, Me) | **1b** (F) | 96[e] | — | — |
| 7 | **2c** (F, Me) | **1c** (OMe) | 96[e] | — | — |
| 8 | **2c** (F, Me) | **1d** (*t*-Bu) | 96[e] | — | — |
| 9 | **2d** (OMe,Me) | **1a** (H) | 48[b] | 80 | 49 |
| 10 | **2d** (OMe, Me) | **1b** (F) | 48[b] | 78 | 37 |
| 11 | **2d** (OMe, Me) | **1c** (OMe) | 96[c] | 59 | 30 |
| 12 | **2d** (OMe, Me) | **1d** (*t*-Bu) | 96[c] | 76 | 76 |
| 13 | **2e** (H, H) | **1a** (H) | 48[b] | 66 | 56 |
| 14 | **2e** (H, H) | **1b** (F) | 48[b] | 60 | 76 |
| 15 | **2e** (H, H) | **1c** (OMe) | 96[c] | 49 | 94 |
| 16 | **2e** (H, H) | **1d** (*t*-Bu) | 96[c] | 17 | 96 |
| 17 | **2f** (Me, H) | **1a** (H) | 48[b] | 64 | 22 |
| 18 | **2f** (Me, H) | **1b** (F) | 48[b] | 61 | 86 |
| 19 | **2f** (Me, H) | **1c** (OMe) | 96[c] | 40 | 78 |
| 20 | **2f** (Me, H) | **1d** (*t*-Bu) | 96[c] | 49 | 86 |
| 21 | **2g** (Me, F) | **1a** (H) | 48[b] | 68 | 22 |
| 22 | **2g** (Me, F) | **1b** (F) | 48[b] | 61 | 49 |
| 23 | **2g** (Me, F) | **1c** (OMe) | 96[c] | 50 | 74 |
| 24 | **2g** (Me, F) | **1d** (*t*-Bu) | 96[c] | 25 | 94 |
| 25 | **2h** (H, F) | **1a** (H) | 48[b] | 66 | 69 |
| 26 | **2h** (H, F) | **1b** (F) | 48[b] | 72 | 47 |
| 27 | **2h** (H, F) | **1c** (OMe) | 96[b] | 79 | 21 |
| 28 | **2h** (H, F) | **1d** (*t*-Bu) | 96[b] | 69 | 39 |

[a] Isolated yield of **3**.
[b] Complete conversion as indicated by TLC.
[c] Incomplete conversion as indicated by TLC.
[d] The absolute configurations of products **3** were determined by comparison with the HPLC data in the literature.[3g,4a]
[e] Reaction was carried out at −80 °C for 3 days, and then at −20 °C for 1 day, but no target product generating with **2c** remaining.

contrast, **1b** (37% ee) and **1c** (30% ee) proved to be less effective in selectively fluorinating the same substrate. Interestingly, the use of reagent **1d** with a *t*-Bu substitution on NFSI resulted in a higher ee value (76%) of **3d** in an isolated yield of 76% (entries 9–12 in Table 2). And surprisingly, the fluorination of substrate **2e** ($R^1$=H, $R^2$=H) with *t*-Bu and OMe substitution on NFSI afforded considerably higher ee value (96 and 94%, respectively), though in lower yields than NFSI **1a** itself, which led to 56% ee value and 66% yield (entries 13–16 in Table 2). For substrate **2f** ($R^1$=Me, $R^2$=H), although NFSI **1a** gave a much lower ee value (22%), the modified NFSI analogues **1b**, **1c**, and **1d** supplied **3f** in rather good enantioselectivity with ee values of 86, 78, and 86%, respectively (entries 17–20, Table 2).

Similarly, the fluorination results of oxindole **2g** with **1b**, **1c**, and **1d** provided higher ee value than unmodified NFSI, among which the *t*-Bu-substituted NFSI resulted in an ee value of 94% (entries 21–24, Table 2). Unfortunately, in the case of **2h**, inconsistent results occurred. NFSI analogues **1b** (47% ee, 72%), **1c** (21% ee, 79%), and **1d** (39% ee, 69%) led to worse reactivity and enantioselectivity comparing with NFSI **1a** that gave a higher value (69%) of **3h** in 66% yield. As a whole, the fluorinating enantioselectivity largely

depends on the substrates except for fluorinating reagent itself. In most cases, **1d**, an NFSI analogue with a *t*-Bu substituent, shows much better enantioselectivity than NFSI itself.

The plausible catalytic cycle was proposed in Fig. 2 according to the literature.[4a,7] Firstly, NFSI analogue **1** reacts with cinchona alkaloid and intermediate **I** was afforded. Secondly, intermediate **I**, as a phase transfer catalyst, shifts the base to the organic phase to get intermediate **II**, which then promotes enolization of substrate **2** to form enolate **III** and intermediate **IV**. Finally, the intermediate **I** or **II**, or compound **1** fluorinates **III** to produce the target molecule **3**, finalizing the catalytic cycle of cinchona alkaloid. The enantioselectivity of this reaction was determined by the competition of N–F cinchona alkaloid salt (intermediates **I**) against NFSI analogue (compound **1**) for the fluorination of enolate **III**. Naturally, the different substituents on the phenyl ring of $(ArSO_2)_2N^-$ anion of intermediate **III** influence the reaction yield or ee value.

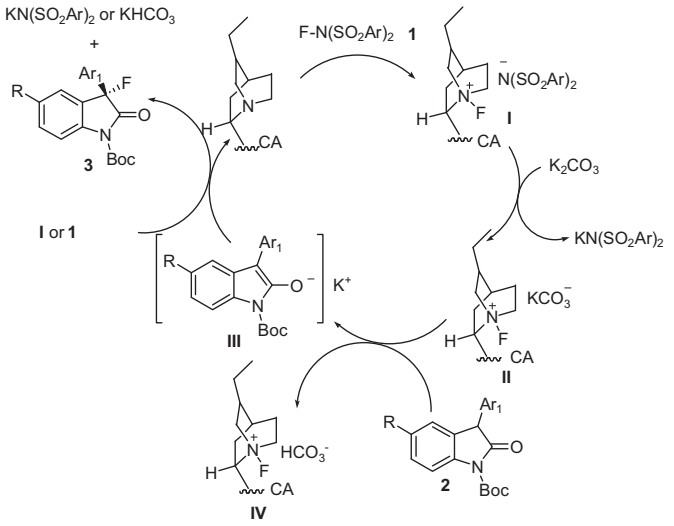



**Fig. 2.** A proposed catalytic cycle for cinchona alkaloids-catalyzed enantioselective fluorination of **2** with fluorinating reagents **1**.

Then, according to this mechanism, efforts were paid to explain the reaction results. Theoretically, electron-donating substitution on the *para*-position of phenyl rings of the NFSI analogue weakens its fluorinating reactivity, and on the contrary, electron-withdrawing substitution activates the reactivity.[8] In agreement with this contention, employing **1b** (OMe) and **1c** (*t*-Bu) led to incomplete conversion of **2**, and NFSI exhibited higher fluorinating reactivity. However, because of their instability and bad compatibility,[10] utilizing electron-withdrawing reagents **1e** ($CF_3$–NFSI) and **1f** ($CF_3O$–NFSI) led to decomposition under this circumstance and failed to give target products.

Furthermore, electrochemical measurements of these NFSI analogues were carried out to assess their ordering of fluorinating reactivity.[9] The measured $E_p$ values by cyclic voltammetry were listed in Table 3. In accordance with our reaction results, it indicated that **1c** (MeO–NFSI) and especially **1d** (*t*-Bu–NFSI) held an appreciably weaker fluorinating ability than NFSI (entries 1, 3, and 4, Table 3), and F-NFSI had a similar fluorinating reactivity to NFSI (entry 2, Table 3), However, the measured data for **1e** ($CF_3$–NFSI) and **1f** ($CF_3O$–NFSI), were higher than that of **1a** (entries 5 and 6, Table 3), which led to their instability and decomposition in the presence of a strong alkali $K_2CO_3$ in this fluorinating reaction, which agrees with our observation and literature.[10] We note that, for the CV test, these fluorination reactions were proceeded under different circumstances with distinct mechanisms, and the CV data for these fluorinating agents can only supply a rough relative evaluation for their fluorinating reactivity.

**Table 3**
The measured peak reduction potentials of NFSI analogues

| Entry | Reagent **1** (R) | $E_p$, reduction[a] (V) |
|---|---|---|
| 1 | **1a** (H) | −1.08 |
| 2 | **1b** (F) | −1.06 |
| 3 | **1c** (OMe) | −1.16 |
| 4 | **1d** (*t*-Bu) | −1.46 |
| 5 | **1e**[b] ($CF_3$) | −0.89 |
| 6 | **1f**[b] ($OCF_3$) | −0.91 |
| 7 | Selectfluor | +0.21 |

[a] The data were obtained in acetonitrile containing 0.1 M $Bu_4NBF_4$, at 0.5 V $s^{-1}$ on a 2 $cm^2$ platinum disk working electrode at room temperature.
[b] Compounds **1d** ($CF_3$) and **1e** ($OCF_3$) had an apparently bad solubility in MeCN.

## 3. Conclusion

In conclusion, we have attempted the fluorinating efficiency of benzenesulfonimides bearing different substituents such as F, *t*-Bu, OMe, $CF_3$, and $OCF_3$ on the *para*-position of the symmetric phenyl ring to compare with NFSI itself in the context of the enantioselective fluorination of various oxindole substrates. We disclose that reactions with differently substituted NFSIs may lead to enhanced enantioselectivity compared with unmodified NFSI. Reagents containing a *p*-*t*-Bu substituent on the phenyl ring have been proven to lower the fluorinating reactivity but to considerably increase the fluorinating enantioselectivity in most cases.

## 4. Experimental section

### 4.1. General methods

All the starting chemicals and catalyst $(DHQD)_2PHAL$ were commercially available and used without further purification, fluorinating reagents **1a**–**e**[6] and substrates **2a**–**h**[4a] were prepared according to procedures known in the literature. $^1H$ NMR, $^{13}C$ NMR and $^{19}F$ NMR spectra were recorded on a Bruker 400 MHz instrument; *J* values are reported in hertz (Hz). Flash column chromatography was performed using silica gel (300–400 mesh). Melting points were uncorrected. Unless otherwise noted, analytical high-performance liquid chromatography (HPLC) was carried out on WATERS equipment with chiral column.

### 4.2. General procedure for the synthesis of fluorinating reagent 1a–f

The mixture of benzenesulfonimides (compound **4**) (19.6 mmol) and 2% sodium hydroxide aqueous solution (350 mL, 175 mmol) was stirred for 20 min, the precipitate was filtered and the solid benzenesulfonimide sodium salt (compound **5**) was air-dried. The mixture of compound **5** and acetonitrile (150 mL) was stirred and cooled to −30 °C. A 5–8 L gaseous mixture of 10% $F_2$ in nitrogen (volume percent) was introduced at a rate of 150 mL/min to the solution. The insoluble solid was removed by filtration. The filtrate was evaporated under vacuum and washed with water, a yellow solid was obtained. After recrystallization pure compound **1** was afforded.

*4.2.1. N-Fluoro-p-fluorobenzenesulfonimde (**1b**).* White crystal. mp 114.8–116.0 °C; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 8.08–8.05 (m, 4H), 7.33–7.29 (m, 4H); $^{19}F$ NMR ($CDCl_3$, 376 MHz) $\delta$ −36.42 (s, 1F), −98.36 (s, 2F).

*4.2.2. N-Fluoro-p-methoxyphenylsulfonimide (**1c**).* White crystal, mp 138.2–138.8 °C; H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.93 (d, *J*=9.2 Hz,

4H), 7.03 (d, *J*=9.2 Hz, 4H), 3.91 (s, 6H); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ −37.43 (s, 1F).

*4.2.3. N-Fluoro-p-tert-butylbenzenesulfonimde (**1d**).* White crystal, mp 149.5–150.3 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.95 (d, *J*=8.8 Hz, 4H), 7.61 (d, *J*=8.8, 4H), 1.36 (s, 18H); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ −36.43 (s, 1F).

*4.2.4. N-Fluoro-p-trifluoromethylbenzene sulfonimide(**1e**).* White crystal, mp 127.9–128.6 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.17 (d, *J*=8.4 Hz, 4H), 7.92 (d, *J*=8.4 Hz, 4H); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ −36.00 (s, 1F), −63.51 (s, 6F).

*4.2.5. N-Fluoro-p-trifluoromethoxylbenzenesulfonimide (**1f**).* White crystal, mp 81.5–82.4 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.86 (d, *J*=8.8 Hz, 4H), 7.76 (d, *J*=8.8 Hz, 4H); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ −36.23 (s, 1F), −57.65 (s, 6F).

### 4.3. General procedure for the catalytic enantioselective fluorination of oxindole

$(DHQD)_2PHAL$ (5 mol %) and NFSI analogues (1.2 equiv) in $CH_3CN$/$CH_2Cl_2$ (v/v=3:4, 1.5 mL) were stirred under argon atmosphere at room temperature for 30 min. $K_2CO_3$ (6.0 equiv) was then added to the solution, and the reaction mixture stirred for 30 min at −80 °C. A solution of oxindole **2a**–**h** (0.148 mmol) in $CH_3CN/CH_2Cl_2$ (v/v=3:4, 1 mL) was added to the above solution. The solution was stirred at the temperature for 1.5–4 days with monitoring by TLC, and it was stopped by the addition of water. The reaction mixture was then diluted with AcOEt, washed with 2 N HCl, saturated aqueous sodium bicarbonate solution, brine, dried over $Na_2SO_4$, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel to give **3a**–**h**.[4a] The ee of the products **3a**–**h** was determined by chiral HPLC on CHIRALCEL OD-H or Phenomenex Lux 5u Cellulose-1 column.

*4.3.1. (S)-N-tert-Butoxycarbonyl-3-fluoro-3-(4-methylphenyl)-5-methyl-2-oxindole (**3a**).* White solid; mp: 110–112 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.53 (s, 9H), 2.28 (s, 6H), 7.10 (d, *J*=4.0 Hz, 2H), 7.13–7.23 (m, 4H), 7.79 (d, *J*=8.8 Hz, 1H); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ −144.9 (s, 1F); HPLC: (OD-H, hexane/*i*-PrOH=99:1, 0.9 mL/min, 254 nm), $t_R$ (*R*-isomer)=5.99 min, $t_R$ (*S*-isomer)=7.33 min.

*4.3.2. (S)-N-tert-butoxycarbonyl-3-fluoro-3-(4-methylphenyl)-2-oxindole (**3b**).* White solid; Mp: 90–92 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.61 (s, 9H), 2.35 (s, 3H), 7.19 (d, *J*=8.4 Hz, 2H), 7.26–7.28 (m, 1H), 7.25 (d, *J*=7.9 Hz, 2H), 7.37 (d, *J*=7.6 Hz, 1H), 7.48–7.52 (m, 1H), 8.00 (d, *J*=8.2 Hz, 1H); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ −144.55 (s, 1F); HPLC: (OD-H, hexane/*i*-PrOH=99:1, 0.5 mL/min, 254 nm), $t_R$ (*R*-isomer)=11.16 min, $t_R$ (*S*-isomer)=13.16 min.

*4.3.3. N-tert-Butoxycarbonyl-3-fluoro-3-(4-methylphenyl)-5-fluoro-2-oxindole (**3c**).* White solid; mp: 132–133 °C; IR (KBr): 2962, 1784, 1730, 1489, 1344, 1297, 1261, 1156, 878, 810 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.60 (s, 9H), 2.36 (s, 3H), 7.08–7.10 (m, 1H), 7.21–7.26 (m, 5H), 8.01 (m, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 168.9 (d, *J*=25.0 Hz), 160.3 (dd, *J*=160.3, 31.5 Hz), 147.9, 138.9 (d, *J*=1.6 Hz), 135.8 (dd, *J*=5.3, 2.7 Hz), 131.2, 130.9, 126.2 (dd, *J*=56.0, 8.0 Hz), 125.1 (d, *J*=5.7 Hz), 117.4 (dd, *J*=22.8, 2.9 Hz), 116.2 (d, *J*=7.2 Hz), 112.5 (d, *J*=24.6 Hz), 92.3 (dd, *J*=188.3, 1.7 Hz), 84.2, 28.7, 27.0, 20.2; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ −145.66 (s, 1F), −116.08 (s, 1F); MS (EI): *m*/*z* (%): 359 ($M^+$, 2), 230 (20), 244 (21), 258 (20), 259 (100). HRMS (EI) calcd for $C_{20}H_{19}F_2NO_3$: 359.1333, found: 359.1335.

*4.3.4. (S)-N-tert-Butoxycarbonyl-3-fluoro-3-(4-methylphenyl)-5-methoxy-2-oxindole (**3d**).* White solid; mp: 128–130 °C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 1.60 (s, 9H), 2.35 (s, 3H), 3.79 (s, 3H), 6.89 (t, *J*=2.4 Hz, 1H), 7.01 (dt, *J*=9.0, 2.4 Hz, 1H), 7.20 (d, *J*=8.4 Hz, 2H), 7.25 (d, *J*=8.6 Hz, 2H), 7.92 (dd, *J*=9.0, 1.4 Hz, 1H); $^{19}$F NMR ($CDCl_3$, 376 MHz): $\delta$ −145.35 (s, 1F); HPLC: (OD-H, hexane/*i*-PrOH=99:1, 0.5 mL/min, 254 nm), $t_R$ (*R*-isomer)=14.5 min, $t_R$ (*S*-isomer)=16.8 min.

*4.3.5. (S)-N-tert-Butoxycarbonyl-3-fluoro-3-phenyl-2-oxindole (**3e**).* White solid; mp: 71–73 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.62 (s, 9H), 7.27 (d, *J*=6.0 Hz, 1H), 7.29–7.40 (m, 6H), 7.51–7.53 (m, 1H), 8.01 (d, *J*=8.4 Hz, 1H); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ −145.37 (s, 1F); HPLC: (Lux 5u Cellulose-4, hexane/*i*-PrOH=98:2, 0.7 mL/min, 214 nm), $t_R$ (*S*-isomer)=9.2 min, $t_R$ (*R*-isomer)=10.3 min; $[\alpha]_D^{25}$ +78.4 (*c* 0.900, $CHCl_3$) 96% ee, *S*; lit.[4a] $[\alpha]_D^{25}$ +82.9 (*c* 0.450, $CHCl_3$) 87% ee, *S*.

*4.3.6. (S)-N-tert-Butoxycarbonyl-3-fluoro-3-phenyl-5-methyl-2-oxindole (**3f**).* White solid; mp: 126–128 °C; IR (KBr): 2922, 2854, 1781, 1734, 1597, 1490, 1371, 1332, 1277, 1250, 1151, 1124 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.61 (s, 9H), 2.36 (s, 3H), 7.17 (s, 1H), 7.30 (d, *J*=8.6 Hz, 1H), 7.34–7.40 (m, 5H), 7.87 (d, *J*=8.4 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 169.4 (d, *J*=24.9 Hz), 147.9, 137.5 (d, *J*=5.2 Hz), 134.7 (d, *J*=27.6 Hz), 134.2 (d, *J*=2.7 Hz), 131.3 (d, *J*=3.5 Hz), 127.6, 125.6, 125.1 (d, *J*=6.0 Hz), 124.5 (d, *J*=17.6 Hz), 114.4, 91.8 (d, *J*=186.5 Hz), 83.8, 28.7, 26.0, 19.9; $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ −145.64 (s, 1F); MS (EI): *m*/*z* (%) 341 ($M^+$, 3), 212 (59), 241 (100). HRMS (EI) calcd for $C_{20}H_{20}FNO_3$: 341.1427, found: 341.1425; HPLC: (Lux 5u Cellulose-4, hexane/*i*-PrOH=80:20, 0.4 mL/min, 214 nm), $t_R$ (*S*-isomer)=13.4 min, $t_R$ (*R*-isomer)=14.0; $[\alpha]_D^{25}$ +69.9 (*c* 0.500, $CHCl_3$) 86% ee.

*4.3.7. (S)-N-tert-Butoxycarbonyl-3-fluoro-3-(4-fluorophenyl)-5-methyl-2-oxindole (**3g**).* Oil; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.61 (s, 9H), 2.37 (s, 3H), 7.07 (d, *J*=8.5 Hz, 2H), 7.17 (s, 1H), 7.30–7.37 (m, 3H), 7.87 (d, *J*=8.4 Hz, 1H); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ −111.71 (s, 1F), −143.17 (s, 1F); HPLC: (AD-H, hexane/*i*-PrOH=98:2, 0.7 mL/min, 214 nm), $t_R$ (*S*-isomer)=8.7 min, $t_R$ (*R*-isomer)=9.3 min; $[\alpha]_D^{20}$ +95.7 (*c* 0.750, $CHCl_3$) 94% ee, *S*; lit.[3g] $[\alpha]_D^{25}$ +78.6 (*c* 0.87, $CHCl_3$) 98% ee, *S*.

*4.3.8. (S)-N-tert-Butoxycarbonyl-3-fluoro-3-(4-fluorophenyl)-2-oxindole (**3h**).* Oil; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.62 (s, 9H), 7.08 (d, 2H, *J*=8.4 Hz), 7.28–7.30 (m, 1H), 7.34–7.37 (m, 3H), 7.53 (tt, 1H, *J*=1.8, 7.8 Hz), 8.01 (d, 1H, *J*=8.4 Hz); $^{19}$F NMR ($CDCl_3$, 376 MHz) $\delta$ −111.53 111.54 (s, 1F), −142.95 (s, 1F); HPLC: (Phenomenex Lux 5u Cellulose-1, hexane/*i*-PrOH=96:4, 1.0 mL/min, 230 nm), $t_R$ (*R*-isomer)=4.23 min, $t_R$ (*S*-isomer)=4.82 min.

### 4.4. The procedure for electrochemical measurement of the fluorinating ability of N–F fluorinating reagents by cyclic voltammetry

*4.4.1. Cells and electrodes.* Working electrodes for cyclic voltammetry were a platinum disk electrodes with an area of 2 cm$^2$ (purchased from Tianjin Aidahongsheng Technology Co. Ltd), the auxiliary electrode was a coiled platinum wire, and the reference electrode was a Ag|AgCl reference (silver wire in contact with AgCl+saturated KCl aqueous solution). All electrodes for voltammetry were polished for 5 min prior to use with 50–75 μm silica gel in acetonitrile. The cells used in these experiments were some 100 mL glass flasks.

*4.4.2. Experimental procedure.* In a 100 mL three-neck flask was added $Bu_4NF_4$ acetonitrile solution (0.1 M, 30 mL), a platinum disk working electrode, a coiled platinum wire auxiliary electrode, and a Ag|AgCl reference electrode were inserted into the solution, and

connected to electrochemical system (PARSTAT2273, Ametek Inc). The system was scanned at 500 mV/s ranging from −2.0 to +1.5 V for three cycles. The measured voltammogram was recorded as background. Then the N–F fluorinating reagent was added to the above solution to get 5.0 mmol/L sample solution, scanned under the same conditions, voltammogram was recorded.

The final voltammogram was obtained by subtracting background from the recorded voltammogram.

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## Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.04.037.

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