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P-Spiro phosphonium salts catalyzed asymmetric fluorination of 3-substituted benzofuran-2(3*H*)-ones

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ABSTRACT

Asymmetric electrophilic fluorination of 3-substituted benzofuran-2(3*H*)-ones was realized under liquid–liquid phase-transfer catalysis with 2 mol% of chiral phosphonium salts to afford the fluorinated products with up to 96% yield and 56% ee.

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1. Introduction

The unique physical and chemical advantages resulting from the presence of fluorine atom(s) on chiral organic compounds used in pharmaceutical [1–3], agrochemical [4–6], and materials industries [7,8] have led to a rapidly increasing need for synthetic methodologies providing efficient and practical access to chiral organofluorine molecules. In this context, considerable works on catalytic enantioselective electrophilic fluorination have been reported over the last decade. Both chiral metal complex-catalyzed reactions and organocatalysis have been intensively explored in catalytic enantioselective fluorinations [9–14]. A tool of choice in asymmetric synthesis is the phase-transfer catalysis [15–19] that exploits many chiral ammonium salts and in a lesser extent chiral phosphonium salts [20–28] as powerful catalysts in many asymmetric reactions. Chiral ammonium salts have demonstrated high efficiency in asymmetric fluorination of β-keto esters [29,30]; however, to the best of our knowledge, a chiral phosphonium salt has never been reported in a catalyzed enantioselective electrophilic fluorination. Application of phase-transfer catalysis in the field of organofluorine chemistry still requires further research investigation, in particular for a comparison of ammonium versus phosphonium salts in a given reaction and a comparison of a catalyst family in different reactions. In our laboratory, we are investigating benzofuran-2(3*H*)-ones that feature a chiral quaternary center at the C3 position of the heterocyclic ring as privileged structural motifs encountered in many natural products [31–35] and potential medicines [36,37]. Enantioselective syntheses of these important chiral benzofuran-2(3*H*)-ones have been described through C-C bond formation at C3 [38–44]. However, enantioselective creation of a carbon–heteroatom bond at the C3 position is less explored. In 2011, we reported a phosphonium salt catalyzed asymmetric electrophilic amination of benzofuran-2(3*H*)-ones by (*E*)-dibenzyl diazene-1, 2-dicarboxylate leading to the corresponding amino derivatives in up to 99% ee [27]. Development of new asymmetric reactions for the synthesis of chiral fluorinated compounds has been of our interest and research objective [45–50]. As part of our ongoing studies, herein we present our results on the enantioselective electrophilic fluorination of 3-substituted benzofuran-2(3*H*)-ones with the aid of phosphonium salts as chiral catalysts.

2. Results and discussion

Our investigations started with the reaction conditions that were successful for the electrophilic amination of benzofuran-2(3*H*)-one [27]: 2 mol% of (*S*)-**3c** at room temperature in toluene for 48 h without base and in the presence of *N*-fluorobis(benzenesulfonimide) (NFSI) instead of the amination reagent. Unfortunately, we recovered the starting material quantitatively without any formation of the desired fluorinated product (Table 1, entry 1). Base-free conditions don't seem appropriate in the fluorination

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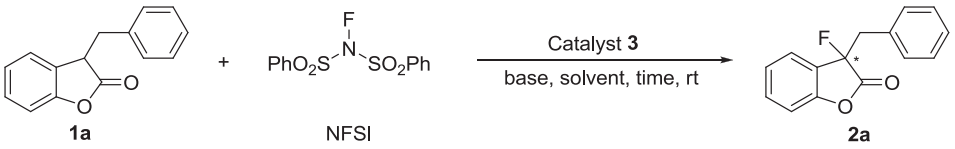
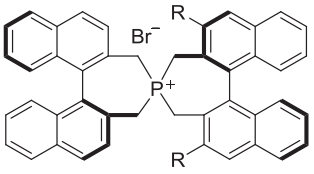
Table 1
Screening of the reaction conditions.[a]





3a (R = H),
3b (R = C_6H_5),
3c (R = 3,4,5-$F_3C_6H_2$),
3d (R = 3,5-$(CF_3)_2C_6H_3$),
3e (R = 3,5-$(3,4,5\text{-}F_3C_6H_2)_2C_6H_3$),
3f (R = 3,5-$[3,5\text{-}(CF_3)_2C_6H_3]_2C_6H_3$)

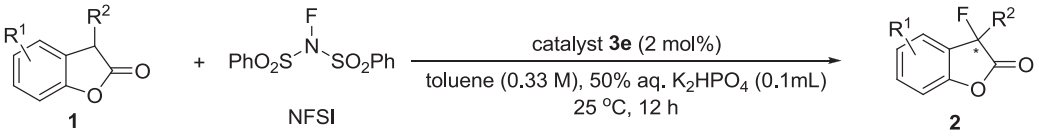
.

Entry	**3** (mol%)	Base	Solvent ([conc.] (M))	Time (h)	Yield (%)[b]	Ee (%)[c]
1	**3c** (2)	–	Toluene (0.1)	48	0	0
2	**3c** (2)	K_2HPO_4 (3 equiv)	Toluene (0.1)	144	54	40
3	**3c** (2)	K_2CO_3 (3 equiv)	Toluene (0.1)	144	23	47
4	**3c** (2)	KOH (3 equiv)	Toluene (0.1)	144	0	0
5	**3c** (2)	Et_3N (1.1 equiv)	Toluene (0.1)	72	17	3
6	**3c** (2)	DMAP (1.1 equiv)	Toluene (0.1)	12	78	12
7	**3c** (2)	K_2HPO_4 (3 equiv)	Toluene (0.2)	144	76	40
8	**3c** (2)	K_2HPO_4 (3 equiv)	Toluene (0.33)	72	76	39
9	**3c** (2)	K_2HPO_4 (3 equiv)	Toluene (1)	72	52	34
10	**3a** (2)	K_2HPO_4 (3 equiv)	Toluene (0.33)	72	76	15
11	**3b** (2)	K_2HPO_4 (3 equiv)	Toluene (0.33)	72	74	20
12	**3d** (2)	K_2HPO_4 (3 equiv)	Toluene (0.33)	72	78	33
13	**3e** (2)	K_2HPO_4 (3 equiv)	Toluene (0.33)	72	78	50
14	**3f** (2)	K_2HPO_4 (3 equiv)	Toluene (0.33)	72	78	45
15[d]	**3e** (2)	K_2HPO_4 (3 equiv)	Toluene (0.33)	72	32	20
16	**3e** (2)	10% aq. K_2HPO_4 (0.1 mL)	Toluene (0.33)	96	42	32
17	**3e** (2)	30% aq. K_2HPO_4 (0.1 mL)	Toluene (0.33)	72	88	46
18	**3e** (2)	50% aq. K_2HPO_4 (0.1 mL)	Toluene (0.33)	12	93	50
19	**3e** (2)	50% aq. K_3PO_4 (0.1 mL)	Toluene (0.33)	12	0	0
20	**3e** (2)	50% aq. K_2HPO_4 (0.05 mL)	Toluene (0.33)	24	92	49
21	**3e** (2)	50% aq. K_2HPO_4 (0.2 mL)	Toluene (0.33)	12	93	50
22	**3e** (2)	50% aq. K_2HPO_4 (0.1 mL)	Benzene (0.33)	12	90	43
23	**3e** (2)	50% aq. K_2HPO_4 (0.1 mL)	Xylene (0.33)	12	89	47
24	**3f** (2)	50% aq. K_2HPO_4 (0.1 mL)	THF (0.33)	12	88	11
25	**3e** (2)	50% aq. K_2HPO_4 (0.1 mL)	CH_2Cl_2 (0.33)	12	79	5
26	**3e** (5)	50% aq. K_2HPO_4 (0.1 mL)	Toluene (0.33)	12	93	50
27[e]	**3e** (2)	50% aq. K_2HPO_4 (0.1 mL)	Toluene (0.33)	48	60	50
28[f]	**3e** (2)	50% aq. K_2HPO_4 (0.1 mL)	Toluene (0.33)	12	87	6
29	**3e** (0.2)	50% aq. K_2HPO_4 (0.1 mL)	Toluene (0.33)	48	91	47

[a] The reactions were carried out with 3-benzylbenzofuran-2(3*H*)-one **1a** (0.1 mmol) and *N*-fluorobis(benzenesulfonimide) (0.15 mmol) in the presence of 2 mol% of catalyst **3**.
[b] Isolated yield.
[c] Determined by HPLC analysis using a chiral stationary phase.
[d] 4 Å MS (50 mg) was used as additive.
[e] The reaction was run at 0 °C.
[f] 1.5 equiv of Selectfluor was used as fluorinating agent.

process; indeed, when 3 equivalents of anhydrous K_2HPO_4 was employed as base, we obtained product **2a** in 54% yield and 40% ee although after a long reaction time (Table 1, entry 2). The use of other bases, e.g. K_2CO_3, KOH, Et_3N, and DMAP, resulted in either a decreased yield or a complete loss of enantioselectivity (Table 1, entries 3–6). It is worth noting that the low yield of the desired fluorinated product obtained in the presence of K_2CO_3 was partly due to the formation of 28% of 3-benzylidenebenzofuran-2(3*H*)-one (*E*/*Z* = 2/1), resulting of HF elimination on **2a** (Table 1, entry 3). Further optimization indicated that the initial concentration of the substrate was important to accelerate the reaction with $[1a]_0 = 0.33$ as optimal value (Table 1, entries 7–9). Subsequent screening with a series of phosphonium salts (Table 1, entries 10–14) revealed that increasing the steric hindrance of the 3,3′-positions of 1,1′-binaphthyl moieties led to the improvement of the enantioselectivity of the product **2a**. Accordingly, the bulky catalyst (*S*)-**3e** delivered the fluorinated product **2a** in 78% yield with 50% enantioselectivity. So far, fluorinations were run under solid–liquid phase-transfer catalysis by means of a solid base; however, traces of water may help the reaction by dissolving the base. By adding 4 Å molecular sieves as an additive, significant reductions both in yield and enantioselectivity were observed (Table 1, entry 15), thus we turned our attention to liquid–liquid phase-transfer catalysis through the use of aqueous bases (Table 1, entries 16–29). The concentration and the amount of the base were then evaluated. To our delight, the use of 50% aqueous K_2HPO_4 gave 93% yield as well as 50% ee after 12 h at room temperature (Table 1, entry 18). No desired product was obtained with 50% aqueous K_3PO_4 as base (Table 1, entry 19). With the phosphonium salt (*S*)-**3e**, the solvent effect was investigated (Table 1, entries 22–25). A polar solvent (THF) or a chlorinated one (CH_2Cl_2) led to the decrease of the enantioselectivity whereas toluene was found to be the best solvent in an aromatic series. Increasing the amount of the catalyst did not lead to an improved enantiomeric excess; however, it should be noted that as low as 0.2 mol% of (*S*)-**3e** still allowed the asymmetric fluorination (Table 1, entry 26 vs

Table 2
Asymmetric fluorination of a library of substituted benzofuran-2(3*H*)-ones.[a]



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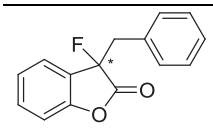
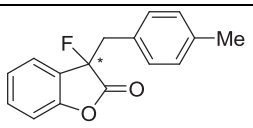
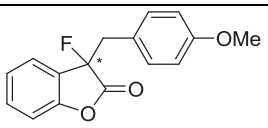
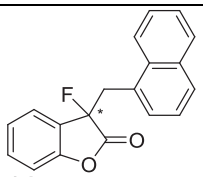

2a: 94% yield, 50% ee

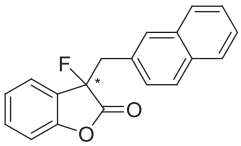


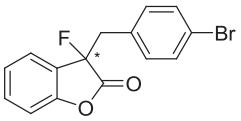
2b: 91% yield, 48% ee



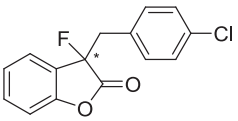
2c: 95% yield, 49% ee


2d: 93% yield, 45% ee

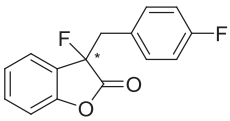

2e: 93% yield, 46% ee



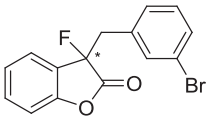
2f: 95% yield, 46% ee



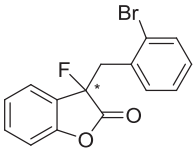
2g: 90% yield, 47% ee



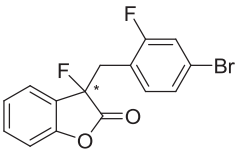
2h: 96% yield, 56% ee



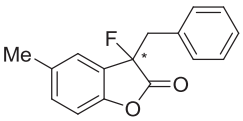
2i: 93% yield, 44% ee



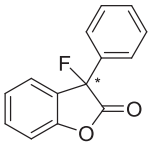
2j: 93% yield, 44% ee

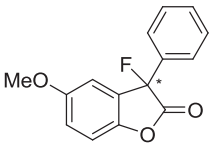


2k: 94% yield, 50% ee

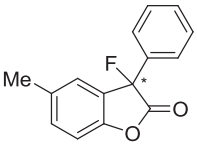


2l: 96% yield, 46% ee

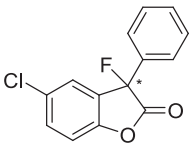

2m: 92% yield, 19% ee



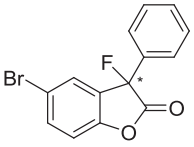
2n: 92% yield, 19% ee



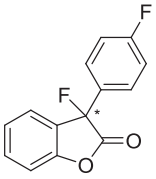
2o: 97% yield, 24% ee

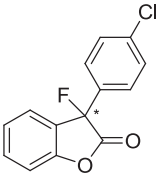


2p: 96% yield, 29% ee

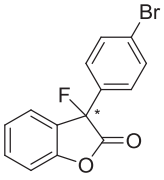


2q: 97% yield, 32% ee


2r: 97% yield, 14% ee



2s: 93% yield, 14% ee



2t: 90% yield, 9% ee

[a] Unless specified, the reaction was carried out with 1.5 equiv. of *N*-fluorobis(benzensulfonimide) in the presence of 2 mol% of **3e** and 50% aq. K_2HPO_4 (0.1 mL) in toluene (0.3 M) at 25 °C. Yields are for isolated products after column chromatography. Enantiopurity of the fluorinated products was determined by HPLC analysis using chiral columns with hexane–isopropanol as eluent.

entry 29). A fluorination run at 0 °C required longer reaction time and gave an important decline of yield but without any increase of the enantioselectivity (Table 1, entry 27). Replacement of *N*-fluorobis(benzenesulfonimide) by Selectfluor gave the product **2a** in high yield but almost as racemic product (Table 1, entry 28).

In order to provide a comparison between ammonium and phosphonium salts, we conducted the fluorination with Maruoka's catalyst, (*S*)-4,4-dibutyl-2,6-bis(3,4,5-trifluorophenyl)-4,5-dihydro-3*H*-dinaphtho[7,6,1,2-cde]azepinium bromide), and various cinchona alkaloid derived quaternary ammonium salts. Very poor enantioselectivities were observed (up to 8% ee) with these quaternary ammonium salt catalysts. These results indicated the superiority of phosphonium salts **3** in this fluorination reaction.

Under the optimal conditions, the generality of the current catalytic asymmetric electrophilic fluorination was evaluated by employing a variety of benzofuran-2(3*H*)-ones. The results are summarized in Table 2. Substrates with electron-donating and electron-neutral groups on the benzyl group gave the desired products in high yields and moderate enantioselectivites **(2a–e)**. Halogen substitution on the *para*-, *meta*-, *ortho*- or disubstitution of the benzyl group had no impact on the activity and enantioselectivity **(2f–k)**. In addition, the desired adduct was obtained in good yield and moderate ee value for 5-methyl-substituted benzofuranone **(2l)**. When we applied this methodology to 3-aryl-substituted benzofuran-2(3*H*)-ones, excellent yields were observed while the enantioselectivity decreased substantially due to the higher reactivity of the substrates **(2m–t)**. Substrates with electron-withdrawing groups on the benzofuranone ring gave

higher enantioselectivities than those with electron-donating groups **(2m–q)**. Poor enantioselectivites were obtained for 3-arylbenzofuranones **(2r–t)**. The scope of the reaction was further extended to the fluorination of 3-methylbenzofuran-2(3*H*)-one, 3-isopropylbenzofuran-2(3*H*)-one, and 3-butylbenzofuran-2(3*H*)-one with *N*-fluorobis(benzenesulfonimide). These substrates were found to be unsuitable for this asymmetric transformation and no desired product was observed.

From a mechanistic viewpoint, the current electrophilic fluorination is clearly distinct from our previously reported electrophilic amination of 3-substituted benzofuran-2(3*H*)-ones [27]. Indeed, the fluorination required a base to proceed whereas the amination was conducted under base-free conditions. In the amination case, the favorable enol formation combined with the electrophilic activation of the nitrogen donor reagent explained the high enantioselection, whereas the fluorination in the presence of a base proceeds through a phosphonium enolate probably without any cooperative activation of the fluorinating agent.

3. Conclusions

We have developed a mild and practical catalytic enantioselective fluorination reaction using chiral phosphonium salt catalysts and *N*-fluorobis(benzenesulfonimide). These *P*-spiro phosphonium salts have showed high efficiency under phase transfer catalysis conditions in the fluorination reaction. A series of the fluorinated benzofuran-2(3*H*)-ones were obtained with up to 96% yield and 56% ee. Further improvement of enantioselectivity of this transformation and additional mechanistic studies are ongoing in our laboratory and will be reported in due course.

4. Experimental

4.1. General information

All purchased reagents were used without further purification. Analytical thin layer chromatography was performed on 0.20 mm Qingdao Haiyang silica gel plates. Silica gel (200–300 mesh) (from Qingdao Haiyang Chem. Company, Ltd.) was used for flash chromatography. ^{1}H, ^{13}C and ^{19}F NMR were recorded on Bruker AV 400 MHz spectrometer at 400 MHz (^{1}H), 100 MHz (^{13}C), 376 MHz (^{19}F) or Varian 600 MHz spectrometer at 600 MHz (^{1}H), 150 MHz (^{13}C), 565 MHz (^{19}F). Chemical shifts were reported in parts per million (ppm) from the solvent resonance as the internal standard ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm). High resolution mass spectrometry (HRMS) spectra were obtained on a micrOTOF-QII Instrument. Optical rotations were determined using an Autopol IV automatic polarimeter. IR spectra were recorded on an AVATAR 360 FT-IR spectrometer. HPLC analysis were carried out on a Hewlett Packard Model HP 1200 instrument. Melting points were measured on a WRS-1A digital melting point apparatus and are uncorrected.

4.2. General procedure for catalyzed fluorination

A mixture of substituted benzofuran-2(3H)-one (0.1 mmol), N-fluorobis(benzenesulfonimide) (47.2 mg, 0.15 mmol), 50% aqueous K_2HPO_4 (0.1 mL) and (*S*, *S*)-**3e** (2.7 mg, 2 mol%) in toluene (0.3 mL) was stirred vigorously at 25 °C for 12 h. The resulting mixture was purified by column chromatography on silica gel (ethyl acetate/petroleum ether = 1/50 as eluent) to afford the desired **2**. The product was identified by NMR spectroscopy. The enantiomeric excess of the product was determined by HPLC using a chiral column.

4.2.1. 3-Benzyl-3-fluorobenzofuran-2(3H)-one (**2a**)

22.8 mg, light yellow solid, mp 60−62 °C, 94% yield, $[\alpha]_D^{25}$ −5.8 (*c* 1.0, CH_2Cl_2); 50% ee, determined by HPLC analysis [Daicel chiralcel AD-H, *n*-hexane/*i*-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 8.3 min, t_{minor} = 7.8 min]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (t, *J* = 8.0 Hz, 1H), 7.23–7.29 (m, 3H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.08–7.10 (m, 3H), 7.03 (d, *J* = 8.0 Hz, 1H), 3.66 (dd, *J* = 10.8, 10.8 Hz, 1H), 3.34 (dd, *J* = 22.0, 22.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6 (d, J = 22.5 Hz), 153.7 (d, J = 6.5 Hz), 132.2 (d, J_{F-C} = 2.9 Hz), 131.5 (d, J_{F-C} = 6.5 Hz), 130.6, 128.5, 127.8, 125.9, 124.6 (d, *J* = 2.4 Hz), 123.5 (d, *J* = 19.9 Hz), 111.4, 92.0 (d, J_{F-C} = 193.2 Hz), 41.7 (d, J_{F-C} = 28.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −147.35 (dd, *J* = 8.4, 8.4 Hz); IR (KBr) ν 3031, 2963, 2934, 1816, 1620, 1603, 1465, 1334, 1296, 1225, 1130, 1070, 1034, 880, 756 cm^{-1}; HRMS (ESI) found: *m/z* 265.0632 $[M+Na]^+$, Calcd for $C_{15}H_{11}FO_2$ + Na 265.0641.

4.2.2. 3-Fluoro-3-(4-methylbenzyl)benzofuran-2(3H)-one (**2b**)

23.3 mg, light yellow solid, mp 49–50 °C, 91% yield, $[\alpha]_D^{25}$ −12.6 (*c* 1.0, CH_2Cl_2); 48% ee, determined by HPLC analysis [Daicel chiralcel IC-H, *n*-hexane/*i*-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 8.1 min, t_{minor} = 8.4 min]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.43 (d, *J* = 7.8 Hz, 1H), 7.12–7.20 (m, 2H), 6.95–7.06 (m, 5H), 3.62 (dd, *J* = 10.8, 10.4 Hz, 1H), 3.32 (dd, *J* = 21.6, 21.6 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7 (d, J = 22.8 Hz), 153.7 (d, *J* = 6.6 Hz), 137.4, 132.2 (d, J_{F-C} = 2.8 Hz), 130.4, 129.2, 128.3 (d, J_{F-C} = 6.8 Hz), 125.9, 124.6 (d, *J* = 2.1 Hz), 123.7 (d, *J* = 19.9 Hz), 111.4, 92.1 (d, J_{F-C} = 193.0 Hz), 41.3 (d, J_{F-C} = 27.9 Hz), 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ −147.16 (dd, *J* = 8.4, 8.4 Hz, 1F); IR (KBr) ν 3052, 2967, 2924, 1820, 1724, 1622, 1602, 1464, 1333, 1294, 1221, 1132, 1077, 1032, 880, 772 cm^{-1}; HRMS (ESI) found: *m/z* 279.0790 $[M+Na]^+$, Calcd for $C_{16}H_{13}FO_2$ + Na 279.0797.

4.2.3. 3-Fluoro-3-(4-methoxybenzyl)benzofuran-2(3H)-one (**2c**)

25.8 mg, light yellow oil, 95% yield, $[\alpha]_D^{25}$ −14.0 (*c* 1.0, CH_2Cl_2); 49% ee, determined by HPLC analysis [Daicel chiralcel IB-H, *n*-hexane/*i*-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 8.7 min, t_{minor} = 9.7 min]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.43 (d, *J* = 7.8 Hz, 1H), 6.98–7.19 (m, 5H), 6.76–6.78 (m, 2H), 3.78 (s, 3H), 3.60 (dd, *J* = 10.4, 10.4 Hz, 1H), 3.29 (dd, *J* = 21.6, 21.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7 (d, *J* = 22.8 Hz), 159.2, 153.7 (d, *J* = 6.6 Hz), 132.2 (d, J_{F-C} = 2.8 Hz), 131.6, 125.8, 124.6 (d, J_{F-C} = 2.5 Hz), 123.7 (d, *J* = 19.8 Hz), 123.3 (d, *J* = 5.8 Hz), 113.9, 111.4, 92.2 (d, J_{F-C} = 192.8 Hz), 55.2, 40.9 (d, J_{F-C} = 28.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −147.47 (dd, *J* = 8.1, 8.1 Hz); IR (KBr) ν 3051, 2960, 2931, 1820, 1615, 1516, 1464, 1333, 1300, 1257, 1218, 1181, 1078, 1032, 881, 775 cm^{-1}; HRMS (ESI) found: *m/z* 295.0737 $[M+Na]^+$, Calcd for $C_{16}H_{13}FO_3$ + Na 295.0746.

4.2.4. 3-Fluoro-3-(naphthalen-1-ylmethyl)benzofuran-2(3H)-one (**2d**)

27.2 mg, light yellow solid, mp 107–108 °C, 93% yield, $[\alpha]_D^{25}$ −19.7 (*c* 1.0, CH_2Cl_2); 45% ee, determined by HPLC analysis [Daicel chiralcel AD-H, *n*-hexane/*i*-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 11.7 min, t_{minor} = 9.7 min]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95–7.97 (d, *J* = 7.6 Hz, 1H), 7.83–7.88 (m, 2H), 7.28–7.50 (m, 5H), 7.06–7.09 (d, *J* = 8.4 Hz, 1H), 6.93–6.97 (t, *J* = 7.6 Hz, 1H), 6.73–6.75 (d, *J* = 7.6 Hz, 1H), 4.18 (dd, *J* = 12.0, 12.0 Hz, 1H), 3.73 (dd, *J* = 27.6, 27.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0 (d, *J* = 22.6 Hz), 153.6 (d, *J* = 6.7 Hz), 133.9, 132.6, 132.1 (d, J_{F-C} = 2.8 Hz), 129.7, 128.7 (d, J_{F-C} = 6.3 Hz), 128.2 (d, J_{F-C} = 3.0 Hz), 126.4, 126.1, 125.8, 125.0, 124.3 (d, *J* = 2.4 Hz), 124.1 (d, *J* = 2.3 Hz), 123.6 (d, *J* = 20.5 Hz), 111.3, 91.9 (d, J_{F-C} = 194.2 Hz), 37.9 (d, J_{F-C} = 28.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −148.70 (dd, *J* = 9.3, 9.6 Hz); IR (KBr) ν 3051, 2958, 2926, 1819, 1623, 1600, 1510, 1461, 1397, 1293, 1226, 1133, 1075,

1030, 876, 776 cm^{-1}; HRMS (ESI) found: *m/z* 315.0795 $[M+Na]^+$, Calcd for $C_{19}H_{13}FO_2$ + Na 315.0797.

4.2.5. 3-Fluoro-3-(naphthalen-2-ylmethyl)benzofuran-2(3H)-one (**2e**)

27.2 mg, light yellow solid, mp 74–75 °C, 93% yield, $[\alpha]_D^{25}$ −14.3 (*c* 1.0, CH_2Cl_2); 46% ee, determined by HPLC analysis [Daicel chiralcel AD-H, *n*-hexane/*i*-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 11.2 min, t_{minor} = 11.8 min]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72–7.83 (m, 3H), 7.59 (s, 1H), 7.48–7.50 (m, 2H), 7.37–7.41 (t, *J* = 8.0 Hz, 1H), 7.09–7.21 (m, 3H), 7.01 (d, *J* = 8.0 Hz, 1H), 3.84 (dd, *J* = 10.0, 10.0 Hz, 1H), 3.51 (dd, *J* = 18.0, 18.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6 (d, *J* = 22.5 Hz), 153.7 (d, *J* = 6.5 Hz), 133.2, 132.7, 132.3 (d, J_{F-C} = 3.0 Hz), 129.8, 129.0 (d, J_{F-C} = 6.3 Hz), 128.1 (d, J_{F-C} = 5.2 Hz), 127.8, 127.6, 126.2 (d, *J* = 5.7 Hz), 125.9, 124.6 (d, *J* = 2.3 Hz), 123.6 (d, *J* = 20.0 Hz), 111.5, 92.1 (d, J_{F-C} = 193.1 Hz), 41.9 (d, J_{F-C} = 28.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −146.85 (dd, *J* = 8.1, 8.4 Hz); IR (KBr) ν 3056, 2959, 2927, 1816, 1623, 1601, 1508, 1464, 1438, 1295, 1220, 1128, 1077, 1028, 877, 774 cm^{-1}; HRMS (ESI) found: *m/z* 315.0790 $[M+Na]^+$, Calcd for $C_{19}H_{13}FO_2$ + Na 315.0797.

4.2.6. 3-(4-Bromobenzyl)-3-fluorobenzofuran-2(3H)-one (**2f**)

30.5 mg, light yellow solid, mp 39–40 °C, 95% yield, $[\alpha]_D^{25}$ −7.3 (*c* 1.0, CH_2Cl_2); 46% ee, determined by HPLC analysis [Daicel chiralcel IC-H, *n*-hexane/*i*-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 8.2 min, t_{minor} = 8.7 min]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.45 (m, 3H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.05–7.11 (m, 2H), 6.96–6.98 (m, 2H), 3.60 (dd, *J* = 10.8, 10.8 Hz, 1H), 3.29 (dd, *J* = 21.6, 21.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3 (d, *J* = 22.7 Hz), 153.7 (d, *J* = 6.5 Hz), 132.4 (d, J_{F-C} = 2.9 Hz), 132.2, 131.5, 130.5 (d, J_{F-C} = 6.5 Hz), 125.7, 124.7 (d, *J* = 2.5 Hz), 123.2 (d, *J* = 19.9 Hz), 122.1, 111.6, 91.0 (d, J_{F-C} = 192.5 Hz), 41.2 (d, J_{F-C} = 28.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −147.57 (dd, *J* = 8.4, 8.4 Hz); IR (KBr) ν 3029, 2925, 2854, 1821, 1622, 1600, 1488, 1461, 1331, 1289, 1227, 1142, 1070, 1018, 875, 756 cm^{-1}; HRMS (ESI) found: *m/z* 342.9738 $[M+Na]^+$, Calcd for $C_{15}H_{10}BrFO_2$ + Na 342.9746.

4.2.7. 3-(4-Chlorobenzyl)-3-fluorobenzofuran-2(3H)-one (**2g**)

24.9 mg, light yellow solid, mp 67–68 °C, 90% yield, $[\alpha]_D^{25}$ −21.1 (*c* 1.0, CH_2Cl_2); 47% ee, determined by HPLC analysis [Daicel chiralcel AD-H, *n*-hexane/*i*-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 7.8 min, t_{minor} = 8.3 min]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.45 (t, *J* = 8.0 Hz, 1H), 7.17–7.24 (m, 3H), 7.02–7.11 (m, 4H), 3.62 (dd, *J* = 10.8, 10.8 Hz, 1H, 3.31 (dd, *J* = 21.6, 21.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3 (d, *J* = 22.7 Hz), 153.7 (d, *J* = 6.6 Hz), 133.9, 132.4 (d, J_{F-C} = 2.9 Hz), 131.9, 130.0 (d, J_{F-C} = 6.4 Hz), 128.7, 125.7, 124.7 (d, J_{F-C} = 2.4 Hz), 123.3 (d, *J* = 20.0 Hz), 111.6, 91.8 (d, J_{F-C} = 193.7 Hz), 41.1 (d, J_{F-C} = 28.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −147.62 (dd, *J* = 7.8, 8.4 Hz); IR (KBr) ν 3111, 2961, 2928, 1824, 1621, 1601, 1492, 1466, 1409, 1295, 1228, 1107, 1074, 1018, 879, 754 cm^{-1}; HRMS (ESI) found: *m/z* 299.0253 $[M+Na]^+$, Calcd for $C_{15}H_{10}ClFO_2$ + Na 299.0251.

4.2.8. 3-Fluoro-3-(4-fluorobenzyl)benzofuran-2(3H)-one (**2h**)

25.0 mg, light yellow oil, 96% yield, $[\alpha]_D^{25}$ −17.3 (*c* 1.0, CH_2Cl_2); 56% ee, determined by HPLC analysis [Daicel chiralcel IC-H, *n*-hexane/*i*-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 7.9 min, t_{minor} = 8.4 min]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.46 (t, *J* = 8.0 Hz, 1H), 7.17–7.20 (t, *J* = 7.6 Hz, 1H), 7.04–7.11 (m, 4H), 6.92–6.96 (m, 1H), 3.62 (dd, *J* = 10.8, 10.4 Hz, 1H), 3.32 (dd, *J* = 21.2, 21.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4 (d, *J* = 22.6 Hz), 162.4 (d, *J* = 245.2 Hz), 153.7 (d, *J* = 6.7 Hz), 132.4 (d, *J* = 2.8 Hz), 132.2 (d, *J* = 8.0 Hz), 127.2 (q, *J* = 3.3 Hz), 125.7, 124.7 (d, J_{F-C} = 2.2 Hz), 123.4 (d, J_{F-C} = 20.3 Hz), 115.4 (d, J_{F-C} = 21.3 Hz), 111.5, 91.9 (d, J_{F-C} = 192.8 Hz), 40.9 (d, J_{F-C} = 28.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −114.26 to −114.34 (m, 1F), −147.81 (dd, *J* = 8.1, 8.4 Hz); IR (KBr) ν 3046, 2964, 2933, 1825, 1621, 1603, 1510, 1466, 1440, 1290, 1261, 1126, 1132, 1072, 879, 762 cm^{-1}; HRMS (ESI) found: *m/z* 283.0543 $[M+Na]^+$, Calcd for $C_{15}H_{10}F_2O_2$ + Na 283.0547.

4.2.9. 3-(3-Bromobenzyl)-3-fluorobenzofuran-2(3H)-one (**2i**)

29.9 mg, light yellow solid, mp 42–43 °C, 93% yield, $[\alpha]_D^{25}$ −10.1 (*c* 1.0, CH_2Cl_2); 44% ee, determined by HPLC analysis [Daicel chiralcel AD-H, *n*-hexane/*i*-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 9.9 min, t_{minor} = 9.2 min]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.46 (m, 2H), 7.13–7.25 (m, 3H), 7.04–7.09 (m, 3H), 3.62 (dd, *J* = 11.2, 11.2 Hz, 1H), 3.27 (dd, *J* = 22.8, 22.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2 (d, *J* = 22.5 Hz), 153.7 (d, *J* = 6.5 Hz), 133.8 (d, J_{F-C} = 5.7 Hz), 133.6, 132.5 (d, J_{F-C} = 3.0 Hz), 131.0, 130.0, 129.2, 125.8, 124.7 (d, J_{F-C} = 2.3 Hz), 123.2 (d, *J* = 20.1 Hz), 122.4, 111.6, 91.5 (d, J_{F-C} = 193.9 Hz), 41.3 (d, J_{F-C} = 28.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −147.87 (dd, *J* = 87, 8.7 Hz); IR (KBr) ν 3067, 2963, 2927, 1818, 1725, 1621, 1599, 1463, 1332, 1294, 1261, 1227, 1078, 1023, 879, 803 cm^{-1}; HRMS (ESI) found: *m/z* 342.9736 $[M+Na]^+$, Calcd for $C_{15}H_{10}BrFO_2$ + Na 342.9746.

4.2.10. 3-(2-Bromobenzyl)-3-fluorobenzofuran-2(3H)-one (**2j**)

29.5 mg, light yellow oil, 92% yield, $[\alpha]_D^{25}$ −9.5 (*c* 1.0, CH_2Cl_2); 47% ee, determined by HPLC analysis [Daicel chiralcel AD-H, *n*-hexane/*i*-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 7.5 min, t_{minor} = 7.0 min]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53–7.55 (d, *J* = 8.0 Hz, 1H), 7.41–7.49 (m, 2H), 7.32–7.36 (t, *J* = 7.2 Hz, 1H), 7.18–7.22 (m, 1H), 7.08–7.12 (m, 2H), 6.86–6.88 (d, *J* = 7.2 Hz, 1H), 3.77–3.84 (m, 1H), 3.61 (dd, *J* = 27.6, 27.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4 (d, *J* = 22.6 Hz), 153.5 (d, *J* = 7.0 Hz), 133.0, 132.3 (d, J_{F-C} = 1.7 Hz), 132.2 (d, J_{F-C} = 2.8 Hz), 132.1 (d, J_{F-C} = 2.0 Hz), 129.5, 127.6, 126.1, 124.6 (d, J_{F-C} = 2.5 Hz), 123.2 (d, *J* = 20.1 Hz), 111.3, 91.6 (d, J_{F-C} = 194.0 Hz), 40.8 (d, J_{F-C} = 27.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −149.47 (dd, *J* = 12.6, 12.6 Hz); IR (KBr) ν 3028, 2926, 1823, 1725, 1623, 1601, 1466, 1333, 1288, 1227, 1141, 1070, 1031, 875, 755 cm^{-1}; HRMS (ESI) found: *m/z* 342.9742 $[M+Na]^+$, Calcd for $C_{15}H_{10}BrFO_2$ + Na 342.9746.

4.2.11. 3-(4-Bromo-2-fluorobenzyl)-3-fluorobenzofuran-2(3H)-one (**2k**)

31.9 mg, light yellow solid, mp 71–72 °C, 94% yield, $[\alpha]_D^{25}$ −27.1 (*c* 1.0, CH_2Cl_2); 50% ee, determined by HPLC analysis [Daicel chiralcel IC-H, *n*-hexane/*i*-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 7.7 min, t_{minor} = 8.1 min]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.45 (m, 1H), 7.14–7.28 (m, 5H), 7.07–7.09 (d, *J* = 8.0 Hz, 1H), 3.61–3.68 (m, 1H), 3.41 (dd, *J* = 20.0, 20.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2 (d, *J* = 22.3 Hz), 160.9 (d, *J* = 250.7 Hz), 153.6 (d, *J* = 8.5 Hz), 133.4 (d, J_{F-C} = 3.8 Hz), 132.3 (d, J_{F-C} = 2.9 Hz), 127.7 (d, J_{F-C} = 3.7 Hz), 125.6, 124.9, 123.1 (d, J_{F-C} = 19.8 Hz), 122.3 (d, *J* = 9.5 Hz), 119.2 (d, *J* = 25.5 Hz), 118.3 (dd, *J* = 5.7, 5.7 Hz), 111.5, 91.1 (d, J_{F-C} = 193.7 Hz), 34.9 (d, J_{F-C} = 29.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.72 to −112.77 (m, 1F), −147.39 to −147.48 (m, 1F); IR (KBr) ν 3057, 2962, 2937, 1830, 1607, 1577, 1485, 1463, 1400, 1289, 1226, 1147, 1091, 1027, 871, 755 cm^{-1}; HRMS (ESI) found: *m/z* 360.9643 $[M+Na]^+$, Calcd for $C_{15}H_9BrF_2O_2$ + Na 360.9652.

4.2.12. 3-Benzyl-3-fluoro-5-methylbenzofuran-2(3H)-one (**2l**)

24.6 mg, light yellow solid, mp 82–83 °C, 96% yield, $[\alpha]_D^{25}$ −11.3 (*c* 1.0, CH_2Cl_2); 46% ee, determined by HPLC analysis [Daicel chiralcel IC-H, *n*-hexane/*i*-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 8.4 min, t_{minor} = 8.9 min]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.19–7.28 (m, 4H), 7.08–7.09 (m, 2H), 6.90–6.92 (m, 2H), 3.63 (dd, *J* = 10.8, 10.4 Hz, 1H), 3.33 (dd, *J* = 21.2, 21.2 Hz, 1H), 2.33

(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9 (d, J = 22.7 Hz), 151.6 (d, J = 6.6 Hz), 134.4 (d, J_{F-C} = 2.4 Hz), 132.6 (d, J_{F-C} = 3.0 Hz), 131.6 (d, J_{F-C} = 5.6 Hz), 130.6, 128.4, 127.7, 126.1, 123.3 (d, J = 19.7 Hz), 111.0, 92.3 (d, J_{F-C} = 193.1 Hz), 41.8 (d, J_{F-C} = 28.1 Hz), 21.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ −147.04 (dd, J = 8.4, 8.4 Hz); IR (KBr) ν 2948, 2927, 1815, 1620, 1485, 1455, 1433, 1296, 1211, 1136, 1089, 1032, 869, 743 cm^{-1}; HRMS (ESI) found: m/z 279.0792 [M+Na]$^+$, Calcd for $C_{16}H_{13}FO_2$ + Na 279.0797.

4.2.13. 3-Fluoro-3-phenylbenzofuran-2(3H)-one (**2m**)

21.0 mg, colorless oil, 92% yield, $[\alpha]_D^{25}$ −21.1 (c 1.0, CH_2Cl_2); 19% ee, determined by HPLC analysis [Daicel chiralcel AD-H, n-hexane/i-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 12.1 min, t_{minor} = 9.5 min]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51–7.53 (t, J = 7.8 Hz, 1H), 7.40–7.41 (m, 6H), 7.21–7.29 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.8 (d, J = 26.6 Hz), 154.4 (d, J = 6.5 Hz), 134.7 (d, J = 27.3 Hz), 132.8, 130.0, 128.9, 126.6, 126.1 (d, J_{F-C} = 5.6 Hz), 125.4, 124.8 (d, J_{F-C} = 18.6 Hz), 111.7, 92.0 (d, J_{F-C} = 190.2 Hz); ^{19}F NMR (565 MHz, $CDCl_3$) δ −144.24 (s); IR (KBr) ν 3065, 3034, 1822, 1621, 1603, 1464, 1324, 1290, 1224, 1134, 1076, 1023, 948, 871, 759 cm^{-1}; HRMS (ESI) found: m/z 251.0475 [M+Na]$^+$, Calcd for $C_{14}H_9FO_2$ + Na 251.0484.

4.2.14. 3-Fluoro-5-methoxy-3-phenylbenzofuran-2(3H)-one (**2n**)

24.5 mg, colorless oil, 95% yield, $[\alpha]_D^{25}$ −38.8 (c 1.0, CH_2Cl_2); 25% ee, determined by HPLC analysis [Daicel chiralcel AD-H, n-hexane/i-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 15.6 min, t_{minor} = 14.1 min]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41–7.42 (m, 5H), 7.15 (d, J = 9.0 Hz, 1H), 7.04–7.06 (m, 1H), 6.92 (s, 1H), 3.79 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.2 (d, J = 26.3 Hz), 157.3, 148.1 (d, J = 6.9 Hz), 134.8 (d, J = 27.6 Hz), 129.9, 128.8, 126.0 (d, J = 5.9 Hz), 125.4 (d, J = 18.8 Hz), 118.7 (d, J_{F-C} = 2.9 Hz), 112.4, 111.3, 92.1 (d, J_{F-C} = 190.7 Hz), 56.0; ^{19}F NMR (565 MHz, $CDCl_3$) δ −145.30 (s); IR (KBr) ν 3070, 3015, 2973, 2941, 1820, 1726, 1617, 1488, 1312, 1290, 1219, 1135, 1094, 1022, 952, 869, 767 cm^{-1}; HRMS (ESI) found: m/z 281.0583 [M+Na]$^+$, Calcd for $C_{15}H_{11}FO_2$ + Na 281.0590.

4.2.15. 3-Fluoro-5-methyl-3-phenylbenzofuran-2(3H)-one (**2o**)

23.5 mg, colorless oil, 97% yield, $[\alpha]_D^{25}$ −40.3 (c 1.0, CH_2Cl_2); 24% ee, determined by HPLC analysis [Daicel chiralcel AD-H, n-hexane/i-PrOH = 95/5, 0.8 mL/min, 254 nm UV detector, t_{major} = 6.8 min, t_{minor} = 6.2 min]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31–7.35 (m, 5H), 7.24 (d, J = 7.8 Hz, 1H), 7.13 (s, 1H), 7.03 (d, J = 8.4 Hz, 1H), 2.30 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.2 (d, J = 26.6 Hz), 152.3 (d, J = 6.6 Hz), 135.2 (d, J = 2.1 Hz), 134.9 (d, J = 27.6 Hz), 133.3 (d, J = 3.2 Hz), 129.9, 128.8, 126.8, 126.0 (d, J_{F-C} = 5.6 Hz), 124.7 (d, J_{F-C} = 18.9 Hz), 111.3, 92.2 (d, J_{F-C} = 189.8 Hz), 21.1; ^{19}F NMR (565 MHz, $CDCl_3$) δ −144.65 (s); IR (KBr) ν 3064, 3030, 2924, 2866, 1821, 1620, 1487, 1450, 1285, 1225, 1137, 1074, 1003, 947, 816, 760 cm^{-1}; HRMS (ESI) found: m/z 265.0635 [M+Na]$^+$, Calcd for $C_{15}H_{11}FO_2$ + Na 265.0641.

4.2.16. 5-Chloro-3-fluoro-3-phenylbenzofuran-2(3H)-one (**2p**)

25.2 mg, colorless oil, 96% yield, $[\alpha]_D^{25}$ −47.2 (c 1.0, CH_2Cl_2); 29% ee, determined by HPLC analysis [Daicel chiralcel AD-H, n-hexane/i-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 10.1 min, t_{minor} = 9.2 min]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40–7.41 (m, 1H), 7.33–7.35 (m, 3H), 7.29–7.30 (m, 3H), 7.09 (d, J = 8.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.1 (d, J = 26.0 Hz), 152.7 (d, J = 6.6 Hz), 134.1 (d, J = 27.4 Hz), 132.9, 130.7 (d, J = 3.2 Hz), 130.3, 129.0, 126.7, 126.4 (d, J_{F-C} = 19.1 Hz), 125.9 (d, J_{F-C} = 7.2 Hz), 113.1, 91.8 (d, J_{F-C} = 192.2 Hz); ^{19}F NMR (565 MHz, $CDCl_3$) δ −145.13 (s); IR (KBr) ν 3067, 3037, 1828, 1727, 1618, 1468, 1423, 1290, 1228, 1140, 1085, 1033, 947, 821, 709 cm^{-1}; HRMS (ESI) found: m/z 285.0092 [M+Na]$^+$, Calcd for $C_{14}H_8ClFO_2$ + Na 285.0095.

4.2.17. 5-Bromo-3-fluoro-3-phenylbenzofuran-2(3H)-one (**2q**)

29.8 mg, colorless oil, 97% yield, $[\alpha]_D^{25}$ −37.6 (c 1.0, CH_2Cl_2); 32% ee, determined by HPLC analysis [Daicel chiralcel AD-H, n-hexane/i-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 12.2 min, t_{minor} = 11.3 min]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55–7.56 (m, 1H), 7.44 (s, 1H), 7.29–7.35 (m, 5H), 7.03–7.04 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.0 (d, J = 27.0 Hz), 153.2 (d, J = 6.3 Hz), 135.8, 134.1 (d, J = 27.0 Hz), 130.3, 129.6, 129.0, 126.8 (d, J_{F-C} = 19.4 Hz), 125.8 (d, J_{F-C} = 5.6 Hz), 117.9, 113.5, 91.7 (d, J_{F-C} = 192.2 Hz); ^{19}F NMR (565 MHz, $CDCl_3$) δ −145.05 (s); IR (KBr) ν 3061, 2963, 2926, 1826, 1722, 1617, 1454, 1408, 1262, 1227, 1140, 1088, 1025, 945, 812, 698 cm^{-1}; HRMS (EI) found: m/z 305.9693 [M]$^+$, Calcd for $C_{14}H_8BrFO_2$ 305.9692.

4.2.18. 3-Fluoro-3-(4-fluorophenyl)benzofuran-2(3H)-one (**2r**)

23.4 mg, colorless oil, 95% yield, $[\alpha]_D^{25}$ −16.1 (c 1.0, CH_2Cl_2); 14% ee, determined by HPLC analysis [Daicel chiralcel AD-H, n-hexane/i-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 11.6 min, t_{minor} = 9.4 min]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53–7.55 (m, 1H), 7.41–7.43 (m, 3H), 7.31 (q, J = 7.2 Hz, 1H), 7.23 (t, J = 7.2 Hz, 1H), 7.09–7.11 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.6 (d, J = 28.2 Hz), 163.7 (d, J = 249.0 Hz), 154.4 (d, J = 6.8 Hz), 133.0, 130.5 (d, J = 27.3 Hz), 128.5 (q, J = 4.6 Hz), 126.6, 125.4, 124.4 (d, J = 19.2 Hz), 116.0 (d, J_{F-C} = 21.9 Hz), 111.8, 91.4 (d, J_{F-C} = 190.4 Hz); ^{19}F NMR (565 MHz, $CDCl_3$) δ −110.62 (s), −141.61 to −141.63 (m, 1F); IR (KBr) ν 3080, 1825, 1621, 1604, 1510, 1464, 1290, 1229, 1134, 1079, 1020, 954, 872, 759 cm^{-1}; HRMS (ESI) found: m/z 259.0781 [M+Na+NH_4–CO]$^+$, Calcd for $C_{14}H_8F_2O_2$ + -Na + NH_4–CO 259.0785.

4.2.19. 3-(4-Chlorophenyl)-3-fluorobenzofuran-2(3H)-one (**2s**)

24.4 mg, colorless oil, 93% yield, $[\alpha]_D^{25}$ −23.3 (c 1.0, CH_2Cl_2); 14% ee, determined by HPLC analysis [Daicel chiralcel AD-H, n-hexane/i-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 11.5 min, t_{minor} = 9.7 min]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44–7.47 (m, 1H), 7.29–7.32 (m, 3H), 7.25–7.26 (m, 2H), 7.21 (t, J = 7.2 Hz, 1H), 7.14 (d, J = 7.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.4 (d, J = 27.2 Hz), 154.4 (d, J = 6.6 Hz), 136.3 (d, J = 2.0 Hz), 133.3, 133.1, 129.1, 127.7 (d, J = 5.4 Hz), 126.5, 125.5, 124.3 (d, J_{F-C} = 19.2 Hz), 111.9, 91.5 (d, J_{F-C} = 192.0 Hz); ^{19}F NMR (565 MHz, $CDCl_3$) δ −143.31 (s); IR (KBr) ν 3067, 2924, 1822, 1621, 1600, 1491, 1465, 1323, 1290, 1225, 1135, 1076, 1016, 937, 873, 759 cm^{-1}; HRMS (ESI) found: m/z 285.0092 [M+Na]$^+$, Calcd for $C_{14}H_8ClFO_2$ + Na 285.0095.

4.2.20. 3-(4-Bromophenyl)-3-fluorobenzofuran-2(3H)-one (**2t**)

27.6 mg, colorless oil, 90% yield, $[\alpha]_D^{25}$ −25.7 (c 1.0, CH_2Cl_2); 9% ee, determined by HPLC analysis [Daicel chiralcel AD-H, n-hexane/i-PrOH = 98/2, 0.8 mL/min, 254 nm UV detector, t_{major} = 10.7 min, t_{minor} = 9.4 min]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53–7.56 (m, 3H), 7.40 (d, J = 7.8 Hz, 1H), 7.23–7.32 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.3 (d, J = 26.6 Hz), 154.4 (d, J = 6.6 Hz), 133.7 (d, J = 28.2 Hz), 133.1 (d, J = 3.2 Hz), 132.1, 127.8 (d, J = 5.4 Hz), 126.6, 125.5, 124.6 (d, J_{F-C} = 2.1 Hz), 124.2 (d, J_{F-C} = 18.8 Hz), 111.9, 91.5 (d, J_{F-C} = 190.4 Hz); ^{19}F NMR (565 MHz, $CDCl_3$) δ −143.80 (s); IR (KBr) ν 3061, 2955, 2924, 2853, 1821, 1621, 1599, 1488, 1461, 1323, 1289, 1225, 1135, 1075, 1011, 873, 756 cm^{-1}; HRMS (ESI) found: m/z 328.9596 [M+Na]$^+$, Calcd for $C_{14}H_8BrFO_2$ + Na 328.9589.

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