Electronic Supplementary Material (ESI) for Chemical Communications

Organocatalytic asymmetric synthesis of 3-difluoroalkyl 3-hydroxyoxindoles

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(Part I)

^{1}H, ^{13}C and ^{19}F NMR spectra are provided in Part II

HPLC spectra are provided in Part III

General: Reactions were monitored by thin layer chromatography using UV light to visualize the course of reaction. Purification of reaction products was carried out by flash chromatography on silica gel. Chemical yields refer to pure isolated substances. The $[\alpha]_D$ was recorded using PolAAr 3005 High Accuracy Polarimeter. Infrared (IR) spectra were obtained using a Bruker tensor 27 infrared spectrometer.^{1}H and ^{13}C NMR spectra were obtained using a Bruker DPX-400 spectrometer. Chemical shifts are reported in ppm from $CDCl_3$ or $(CD_3)_2SO$ with the solvent resonance as the internal standard. The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, m = multiplet, br = broad.

All reactions were carried out in air except noted. Anhydrous THF was prepared by distillation over sodium-benzophenone ketyl prior to use. All the chiral (thio)urea catalysts were prepared using literature procedures.[1] All the Isatins were commercially available or easily prepared using literature procedures.[2] The N-methyl protected isatins were prepared according to a literature method.[3] The aryl substituted difluoroenol silyl ethers were prepared according to the literature report[4].

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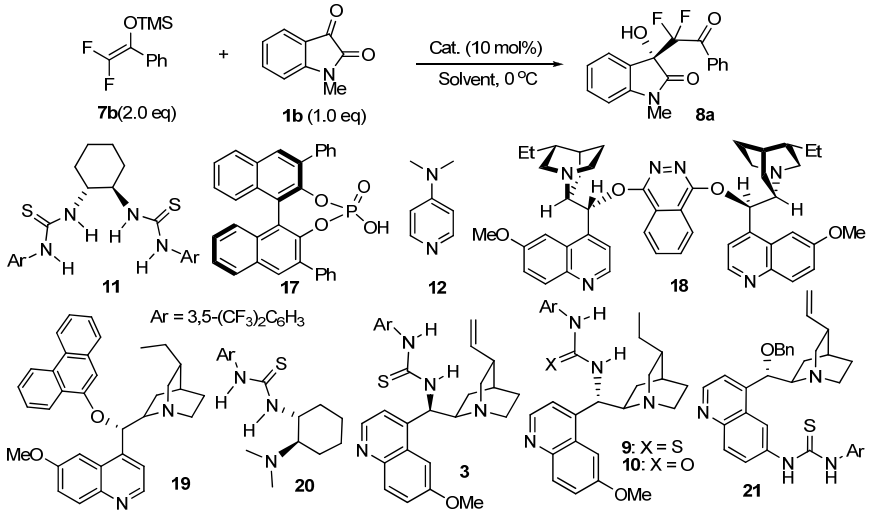
[1] a) Berkessel, A.; Mukherjee, S.; Müller, T. N.; Cleemann, F.; Roland, K.; Brandenburg, M.; Neudörfl, J.-M.; Lex, J. *Org. Biomol. Chem.* **2006**, *4*, 4319; b) Tárkányi, G.; Király, P.; Varga, S.; Vakulya, B.; Soós, T. *Chem. Eur. J.* **2008**, *14*, 6078; c) Vakulya, B.; Varga, S.; Soós, T. *J. Org. Chem.* **2008**, *73*, 3475; d) Peschiulli, A.; Quigley, C.; Tallon, S.; Gun'ko, Y. K.; Connon, S. J. *J. Org. Chem.* **2008**, *73*, 6409; e) Vakulya, B.; Varga, S.; Csámpai, A.; Soós, T. *Org. Lett.* **2005,** *7*, 1967.
[2] For a review on the synthesis of isatins, see: da Silva, J. F. M.; Garden, S. J.; Pinto, A. C. *J. Braz. Chem. Soc.* **2001**, *12*, 273.
[3] Overman, L. E; Peterson, E. A. *Tetrahedron* **2003**, *59*, 6905.
[4] a) Amii, H.; Kobayashi, T.; Hatamoto Y.; Uneyama, K. *Chem. Commun.*, **1999**, 1323; b) Prakash, G. K. S.; Hu, J.; Olah, G. A. *J. Fluorine Chem.,* **2001**, *112*, 357.

Reaction optimization



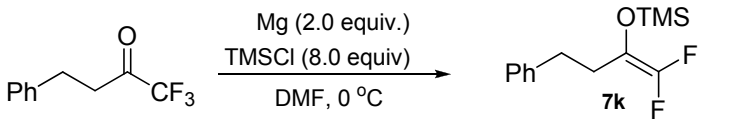
Entry[a]	Cat.	Solvent	Time (d)	Yield (%)[b]	Ee[c] (%)
1	**11**	CH_2Cl_2	3	-	-
2	**17**	CH_2Cl_2	3	24	25
3	**12**	CH_2Cl_2	1	95	-
4	**18**	CH_2Cl_2	3	75	43
5	**19**	CH_2Cl_2	3	15	15
6	**11+12**	CH_2Cl_2	3	94	11
7	**20**	CH_2Cl_2	3	65	75
8	**3**	CH_2Cl_2	3	85	79[d]
9	**9**	CH_2Cl_2	3	86	73
10	**10**	CH_2Cl_2	3	91	80
11	**21**	CH_2Cl_2	3	84	23
12	**10**	Toluene	3	7	91
13	**10**	EtOAc	3	91	94
14	**10**	THF	3	93	94

[a] On a 0.10 mmol; [b] Isolated yield; [c] Determined by chiral HPLC analysis; [d] Opposite enantiomer.

we began reaction development by evaluating different organocatalysts in the reaction of silyl enol ether **7b** and isatin **1b**, using CH_2Cl_2 as the solvent at 0°C. Brønsted acids were first examined, thiourea **11** failed in this reaction (entry 1, Table 1). Stronger acid, phosphoric acid **17**, could catalyze the reaction, but the desired product **8a** was obtained in only 24% yield with 25% ee even after 3 days (entry 2). Considering the versatility of Lewis base in the activation of trimethylsilyl nucleophiles, we tried Lewis bases as the catalyst. DMAP **12** could catalyze the reaction to give product **8a** in 95% yield (entry 3). Easily available nitrogen-based chiral Lewis bases were then examined, and up to 75% yield with 43% ee for **8a** could be obtained when using catalyst **18** (entry 4). To further improve the reactivity and ee, we tried the dual activation of both isatin **1b** and silyl enol ether **7b**. The combination of a chiral thiourea catalyst **11** and achiral Lewis base DMAP **12** indeed afforded **8a** in

11% ee (entry 6), which encouraged us to try bifunctional Brønsted acid-Lewis base catalysts **3**, **9**, **10**, **20**, **21**. Quinine derived urea catalyst **10** could afford product **8a** in 91% yield with 80% ee (entry 10). When quinidine derived thiourea catalyst **3** was used, the opposite enantiomer of product **8a** was obtained in slightly lower yield and ee (entry 8). Further optimization of solvent effects showed that up to 94% of ee for product **8a** could be achieved when using ethyl acetate or THF (entries 13-14).

Synthesis of α-aliphatic substituted difluoroenoxysilanes 7k[4] using a modified procedure.

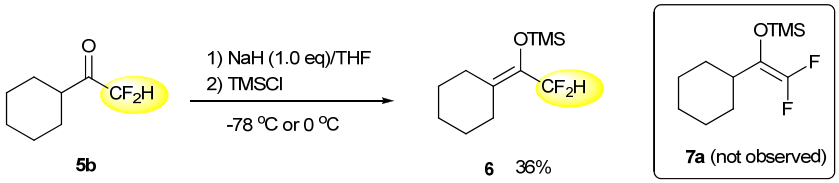


(obtained as a mixure of **7k** and DMF)

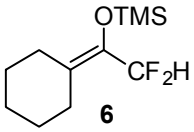
According to literature report,[4] the use of DMF as the solvent was crucial for preparing the α-aliphatic substituted difluoroenoxysilane, and only NMR yield was given. We tried in vain to isolate the desiredα-aliphatic substituted difluoroenoxysilane as a pure compound by distillation, which was contaminated by DMF according to NMR analysis. The synthesis of α-aliphatic substituted difluoroenoxysilanes from the corresponding α-CF_2H ketones also failed (see below). We found that the use of anhydrous hexane to extract difluoroenoxysilane **7k** from DMF could effectively reduce the content of DMF.

Under an atmosphere of N_2, to a 150 mL round-bottom flask was added Mg (0.76 g, 4.0 eq), followed by the addition of 25 mL of anhydrous DMF and TMSCl (2.9 mL, 8.0 eq). The mixture was cooled down to 0 ^oC, and the α-CF_3 ketone was added dropwise. The resulting then stirred at 0 ^oC for an additional 1 h. After the full completion of the ketone, the reaction mixture was extracted with the anhydrous hexane (4 × 10 mL). The combined hexane was evaporated under vacuum. The residue was distilled under reduced pressure to afford the corresponding difluoroenoxysilane **7k**. By this modification, silyl enol ether **7k** was obtained with reduced contamination of DMF. The DMF content varies from different batches. The best case we obtained **7k** as a mixture of **7k** /DMF with a ratio of 1:0.3. It should be noted that the α-aliphatic substituted difluoroenoxysilanes was not so stable as the α-aryl substituted difluoroenoxysilanes.

The synthesis of silyl enol ether 6.



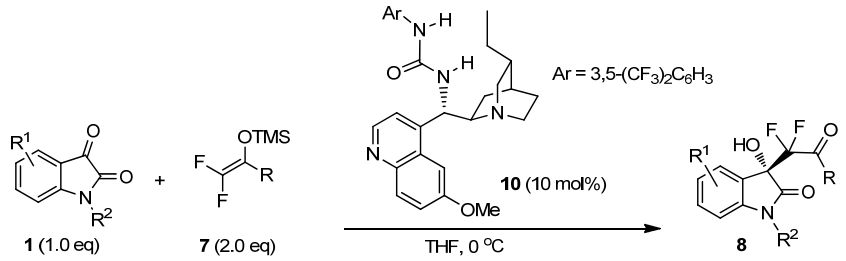
Under an atmosphere of N_2, to a 100 mL round-bottom flask was added 20 mL of anhydrousTHF, α-CF_2H ketone **5b** (774.0 mg, 4.8 mmol), and then NaH (192 mg, 1.0 eq) was added at 0 °C over 5 min. The mixture was stirred at 0 °C for an additional 2 h before TMSCl (0.43 mL, 2.0 eq) was added dropwise at 0 °C for a period of 2 h. After the full completion of ketone **5b**, the reaction mixture was concentrated under vacuum, and the residue was distilled under reduced pressure to afford the corresponding silyl enol ether **6** (401.2 mg). **No matter the reaction was run at -78 or 0 °C, only silyl enol ether ii was obtained by ^{1}H NMR analysis, and no difluoroenoxysilane 7a was detected.**



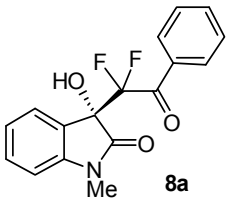
6

Reduced pressure distillation afforded the desired product **6** in 36% yield as colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.20 (s, 9H), 1.14-1.32 (m, 3H), 1.69-1.80 (m, 3H), 2.19 (s, 4H), 6.43 (t, J = 54 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 134.34 (t, J = 20 Hz), 128.27, 109.36 (t, J = 232 Hz), 71.01, 36.05, 28.00, 27.82, 27.66, 26.83, 26.38, 25.52, 25.26, 24.49, 0.12; ^{19}F NMR (376 MHz, $CDCl_3$): δ -118.2 (s, 1F); MS (EI): 234 (M^+, 43), 73 (100), 214 (1), 183 (41), 142 (16), 109 (65), 81 (86), 67 (59), 199 (12); HRMS (EI): Exact mass calcd for $C_{11}H_{20}OF_2Si[M]^+$:234.1252, Found: 234.1254.

General procedure for the Mukaiyama aldol reaction of difluoroenoxysilanes with isatins.

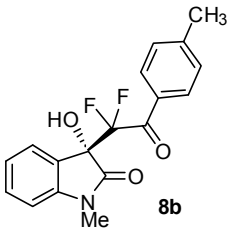


To a 10 mL vial were added catalyst **10** (14.5 mg, 0.025 mmol) and isatins **1** (0.25 mmol), followed by 2.5 mL of anhydrous THF (5.0 mL of solvent was used when unprotected isatins have a poor solubility in THF, which was indicated in the following). The reaction mixture was stirred vigorously at room temperature until the full dissolution of isatins **1**, and then cooled to 0 ^{o}C for about 20 minutes before the freshly prepared difluoroenoxysilanes **7** (0.50 mmol) was added. After the addition of difluoroenoxysilanes **7**, the reaction was kept at 0 ^{o}C till the completion of isatins **1** by TLC analysis, and the solvent was removed under vacuum. The residue was directly subjected to column chromatography using CH_2Cl_2/ethyl acetate (from 100:1 to 10:1) as the eluent, affording the desired product **8**.



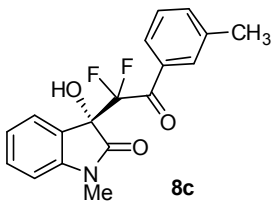
8a

The reaction was run at 0 ^{o}C for 3 days, affording the product **8a** in 89% yield as white solid (m.p. 136-138 ^{o}C); HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 19.06 min, t_r (minor) = 14.07 min) gave the isomeric composition of the product: 94% ee, $[\alpha]^{25}_{D}$ = -105.5 (c = 0.58, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.24 (s, 3H), 4.24 (s, 1H), 6.88 (d, J = 8.0 Hz, 1H), 7.07-7.11 (m, 1H), 7.39-7.43 (m, 1H), 7.45-7.48 (m, 2H), 7.53 (d, J = 7.6 Hz, 1H), 7.61-7.64 (m, 1H), 8.02 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 188.63 (t, J = 30 Hz), 172.69, 144.72, 134.68, 132.00, 131.17, 130.20, 130.17, 130.13, 128.59, 128.29, 126.01, 124.20, 123.21, 115.56 (t, J = 263 Hz), 108.75, 76.36 (t, J = 24 Hz), 26.42; ^{19}F NMR (376 MHz, $CDCl_3$): δ -107.8 (d, J = 301 Hz, 1F), -108.7 (d, J = 301 Hz, 1F); IR (ATR): 3383, 2925, 2854, 1788, 1699, 1614, 1549, 1452, 1422, 820; MS (EI): 317 (M^+, 11), 318 [$(M+H)^+$, 2], 162 (100), 105 (44), 77 (42), 51 (11), 78 (8), 104 (6), 156 (3); HRMS (EI): Exact mass calcd for $C_{17}H_{13}NO_3F_2$ $[M]^+$: 317.0863, Found: 317.0870.



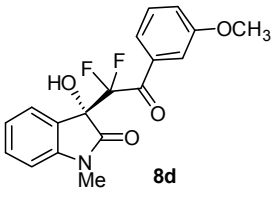
8b

The reaction was run at 0 °C for 5 days, affording the desired product **8b** in 86% yield as white solid (m.p. 146-148 °C); HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 25/75, 1.0 mL/min, 230 nm; t_r (major) = 11.08 min, t_r (minor) = 9.79 min) gave the isomeric composition of the product: 93% ee, $[\alpha]^{25}_{D}$ = -108.9 (c = 0.46, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.41 (s, 3H), 3.24 (s, 3H), 4.33 (s, 1H), 6.88 (d, *J* = 7.6 Hz, 1H), 7.06-7.10 (m, 1H), 7.20-7.35 (m, 2H), 7.38-7.42 (m, 1H), 7.52 (d, *J* = 7.2 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 188.14 (t, *J* = 30 Hz), 172.86, 146.09, 144.74, 131.13, 130.36, 130.20, 129.35, 129.06, 126.00, 124.33, 123.20, 115.67 (t, *J* = 264 Hz), 108.74, 76.40 (t, *J* = 24 Hz), 26.43, 21.80; ^{19}F NMR (376 MHz, $CDCl_3$): *δ* -108.2 (d, *J* = 301 Hz, 1F), -109.2 (d, *J* = 301 Hz, 1F); IR (ATR): 3365, 2974, 2892, 1702, 1607, 1529, 1470, 1381, 1188, 1084, 828; MS (EI): 331 (M^+, 8.0), 332 [$(M+H)^+$, 2], 162 (100), 119 (84), 91 (58), 65 (25), 170 (15), 77 (14), 92 (13); HRMS (EI): Exact mass calcd for $C_{18}H_{15}NO_3F_2$ $[M]^+$: 331.1020, Found: 331.1024.



8c

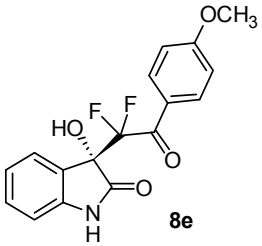
The reaction was carried out at 0 °C for 5 days, affording the desired product **8c** in 79% yield as white solid (m.p. 58-60 °C); HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 20/80, 1.0 mL/min, 230 nm; t_r (major) = 12.58 min, t_r (minor) = 8.93 min) gave the isomeric composition of the product: 95% ee, $[\alpha]^{25}_{D}$ = -96.0 (c = 0.80, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 3H), 3.23 (s, 3H), 4.28 (s, 1H), 6.88 (d, *J* = 7.6 Hz, 1H), 7.07-7.10 (m, 1H), 7.33-7.44 (m, 3H), 7.51-7.53 (m, 1H), 7.81-7.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 188.69 (t, *J* = 29 Hz), 172.82, 144.63, 138.43, 138.03, 135.48, 134.04, 131.92, 131.07, 130.62, 130.49, 128.41, 128.17, 127.39, 127.24, 125.91, 124.34, 123.15, 115.65 (t, *J* = 264 Hz), 108.72, 76.30 (t, *J* = 24 Hz), 26.37, 21.17; ^{19}F NMR (376 MHz, $CDCl_3$): *δ* -108.3 (d, *J* = 301 Hz, 1F), -109.2 (d, *J* = 301 Hz, 1F); IR (ATR): 3336, 2974, 2920, 1711, 1614, 1584, 1495, 1473, 1188, 1048, 794; MS (EI): 331 (M^+, 8.0), 332 [$(M+H)^+$, 2], 162 (100), 119 (58), 91 (50), 65 (21), 77 (13), 92 (10), 170 (6); HRMS (EI): Exact mass calcd for $C_{18}H_{15}NO_3F_2$ $[M]^+$: 331.1020, Found: 331.1021.



8d

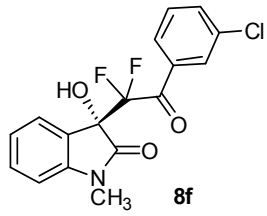
The reaction was carried out at 0 °C for 3 days. Column chromatography afforded the desired product **8d** in 89% yield as white solid (m.p. 120-121 °C); HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 25/75, 1.0 mL/min, 230 nm; t_r (major) = 12.53 min, t_r (minor) = 9.29 min) gave the isomeric composition

of the product: 95% ee, $[\alpha]^{25}_D$ = -112.8 (c = 0.98, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.24 (s, 3H), 3.82 (s, 3H), 4.19 (s, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 7.07-7.11 (m, 1H), 7.16-7.18 (m, 1H), 7.35-7.43 (m, 2H), 7.49-7.54 (m, 2H), 7.65-7.67 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 188.31 (t, *J* = 29 Hz), 172.66, 159.52, 144.67, 133.06, 131.14, 129.58, 125.96, 124.25, 123.18, 122.92, 121.61, 115.58 (t, *J* = 265 Hz), 113.93, 108.73, 76.28 (t, *J* = 24 Hz), 55.37, 26.39; ^{19}F NMR (376 MHz, $CDCl_3$): *δ* -108.2 (d, *J* = 301 Hz, 1F), -109.2 (d, *J* = 301 Hz, 1F); IR (ATR): 3379, 2968, 2925, 1700, 1615, 1594, 1470, 1429, 1363, 1087, 765; MS (EI): 347 (M^+, 8.0), 348 [$(M+H)^+$, 2], 162 (100), 135 (47), 77 (34), 107 (21), 92 (20), 64 (11), 186 (10); HRMS (EI): Exact mass calcd for $C_{18}H_{15}NO_4F_2$ $[M]^+$: 347.0969, Found: 347.0972.



8e

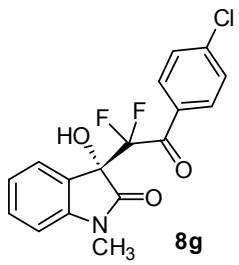
The reaction was run at 0 °C for 6 days. Column chromatography afforded the desired product **8e** in 88% yield as yellow solid (m.p. 152-154 °C); HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 48.48 min, t_r (minor) = 25.45 min) gave the isomeric composition of the product: 90% ee, $[\alpha]^{25}_D$ = -73.6 (c = 0.69, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.87 (s, 3H), 6.85-6.87 (m, 1H), 6.94-6.98 (m, 1H), 7.09-7.11 (m, 2H), 7.27-7.31 (m, 3H), 8.06-8.08 (m, 2H), 10.57 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): 186.28 (t, *J* = 28 Hz), 173.96, 167.57, 164.77, 163.32, 143.48, 133.47, 131.83, 131.02, 127.02, 126.15, 125.65, 123.48, 122.18, 117.66 (t, *J* = 261 Hz), 114.55, 114.25, 110.48, 76.15 (t, *J* = 25 Hz), 56.17, 55.85; ^{19}F NMR (376 MHz, $CDCl_3$): *δ* -108.1 (d, *J* = 278 Hz, 1F), -108.8 (d, *J* = 274 Hz, 1F); IR (ATR): 3366, 2932, 2844, 1715, 1682, 1620, 1600, 1573, 1473, 1314, 1180, 850; MS (EI): 333 (M^+, 8.0), 135 (100), 92 (31), 186 (30), 77 (30), 148 (26), 107 (13), 43 (13); HRMS (EI): Exact mass calcd for $C_{17}H_{13}NO_4F_2$ $[M]^+$: 333.0813, Found: 333.0811



8f

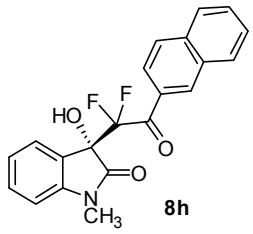
The reaction was carried out at 0 °C for 5 days. Column chromatography afforded the desired product **8f** in 74% yield as white solid (m.p. 64-66 °C); HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 14.67 min, t_r (minor) = 10.63 min) gave the isomeric composition of the product: 96% ee, $[\alpha]^{25}_D$ = -109.3 (c = 0.61, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.24 (s, 3H), 4.15 (s, 1H), 6.89 (d, *J* = 7.2 Hz, 1H), 7.08-7.12 (m, 1H), 7.40-7.44 (m, 2H), 7.51-7.53 (m, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.91-7.93 (m, 1H), 7.97 (s, 1H); ^{13}C NMR (100

MHz, $CDCl_3$): 187.40 (t, J = 29 Hz), 172.68, 144.54, 134.85, 134.53, 134.42, 133.49, 133.31, 131.25, 130.14, 130.01, 129.89, 129.64, 128.28, 125.96, 124.10, 123.32, 115.57 (t, J = 264 Hz), 108.84, 76.27 (t, J = 23 Hz), 26.45; ^{19}F NMR (376 MHz, $CDCl_3$): δ -108.8 (d, J = 301 Hz, 1F), -109.8 (d, J = 301 Hz, 1F); IR (ATR): 3369, 2987, 2923, 1710, 1699, 1614, 1569, 1473, 1427, 1379, 1086, 889; MS (EI): 351 (M^+, 5.0), 352 [$(M+H)^+$, 1], 162 (100), 111 (23), 139 (20), 77 (13), 163 (10), 104 (8), 190 (1); HRMS (EI): Exact mass calcd for $C_{17}H_{12}NO_3F_2{}^{35}Cl$ $[M]^+$: 351.0474, Found: 351.0474.



8g

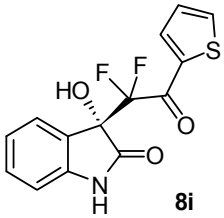
The reaction was carried out at 0 ^{o}C for 5 days. Column chromatography afforded the desired product **8g** in 90% yield as white solid (m.p. 158-160 ^{o}C); HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 15.53 min, t_r (minor) = 13.88 min) gave the isomeric composition of the product: 95% ee, $[\alpha]^{25}_D$ = -138.2 (c = 1.20, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.24 (s, 3H), 4.20 (s, 1H), 6.89 (d, J = 7.6 Hz, 1H), 7.08-7.12 (m, 1H), 7.40-7.45 (m, 3H), 7.51-7.52 (m, 1H), 7.96-7.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 187.37 (t, J = 30 Hz), 172.73, 144.57, 141.43, 139.83, 131.61, 131.49, 131.20, 130.34, 128.98, 128.67, 125.95, 124.19, 123.30, 115.67 (t, J = 264 Hz), 108.83, 76.29 (t, J = 24 Hz), 26.45; ^{19}F NMR (376 MHz, $CDCl_3$): δ -108.6 (d, J = 301 Hz, 1F), -109.5 (d, J = 300 Hz, 1F); IR (ATR): 3333, 2974, 2892, 1715, 1703, 1614, 1589, 1489, 1473, 1378, 1088, 1047, 879; MS (EI): 351 (M^+, 5.0), 352 [$(M+H)^+$, 1], 162 (100), 43 (29), 139 (28), 77 (24), 111 (23), 130 (23), 190 (1); HRMS (EI): Exact mass calcd for $C_{17}H_{12}NO_3F_2{}^{35}Cl$ $[M]^+$: 351.0474, Found: 351.0476.



8h

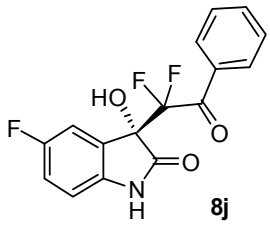
The reaction was carried out at 0 ^{o}C for 5 days. Column chromatography afforded the desired product **8h** in 71% yield as white solid (m.p. 130-132 ^{o}C); HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 25/75, 1.0 mL/min, 230 nm; t_r (major) = 11.61 min, t_r (minor) = 10.37 min) gave the isomeric composition of the product: 94% ee, $[\alpha]^{25}_D$ = -141.0 (c = 060, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.24 (s, 3H), 4.30 (s, 1H), 6.89 (d, J = 7.6 Hz, 1H), 7.08-7.12 (m, 1H), 7.39-7.43 (m, 1H), 7.55-7.59 (m, 2H), 7.63-7.66 (m, 1H), 7.86-7.89 (m, 2H), 7.95-7.99 (m, 2H), 8.66 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 188.31 (t, J = 30 Hz), 172.85, 144.64, 135.99, 133.22, 132.34, 132.02, 131.83, 131.09, 130.10, 129.49, 129.36, 129.15, 128.37, 128.02, 127.62, 126.93, 126.51, 125.95, 125.47, 124.51, 124.37, 123.18, 115.94 (t, J = 264 Hz), 108.74, 76.41 (t, J = 24 Hz), 26.38; ^{19}F NMR (376

MHz, $CDCl_3$): δ -107.8 (d, J = 297 Hz, 1F), -108.7 (d, J = 301 Hz, 1F); IR (ATR): 3346, 2973, 2899, 1701, 1615, 1587, 1482, 1471, 1380, 1086, 1048, 881; MS (EI): 367 (M^+, 18), 368 [$(M+H)^+$, 4], 127 (100), 155 (86), 162 (80), 206 (41), 128 (29), 77 (29), 126 (19); HRMS (EI): Exact mass calcd for $C_{21}H_{15}NO_3F_2$ $[M]^+$: 367.1020, Found: 367.1019.



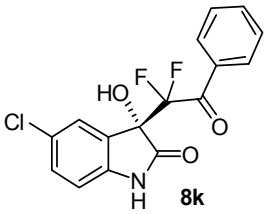
8i

The reaction was run at 0 °C for 6 days. Column chromatography afforded the desired product **8i** in 45% yield as white solid (m.p. 78-80 °C); HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 25/75, 1.0 mL/min, 230 nm; t_r (major) = 14.99 min, t_r (minor) = 9.32 min) gave the isomeric composition of the product: 88% ee, $[\alpha]^{25}_D$ = -66.7 (c = 0.15, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.84-6.86 (m, 1H), 6.96-7.00 (m, 1H), 7.28-7.36 (m, 4H), 8.10 (s, 1H), 8.21-8.22 (m, 1H), 10.62 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): 180.69 (t, J = 29 Hz), 173.50, 143.29, 139.09, 138.61, 138.56, 138.04, 137.99, 131.16, 129.76, 126.29, 126.24, 122.21, 116.85 (t, J = 260 Hz), 110.44, 76.22 (t, J = 25 Hz); ^{19}F NMR (376 MHz, DMSO-d_6): δ -105.6 (d, J = 267 Hz, 1F), -106.5 (d, J = 263 Hz, 1F); IR (ATR): 3357, 2933, 2827, 1711, 1673, 1619, 1511, 1473, 1413, 1182, 1090, 986, 935, 781; MS (EI): 309 (M^+, 7.0), 310 [$(M+H)^+$, 1], 111 (100), 148 (90), 162 (64), 92 (24), 65 (20), 83 (18), 84 (11); HRMS (EI): Exact mass calcd for $C_{14}H_9NO_3F_2S$ $[M]^+$: 309.0271, Found: 309.0271.



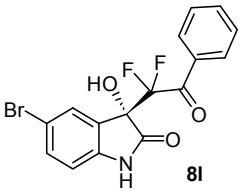
8j

This reaction was carried out in 5.0 mL of anhydrous THF at 0 °C for 4 days. Column chromatography afforded the desired product **8j** in 82% yield as white solid (m.p. 175-178 °C); HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 13.01 min, t_r (minor) = 8.61 min) gave the isomeric composition of the product: 93% ee, $[\alpha]^{25}_D$ = -83.9 (c = 0.82, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.88-6.89 (m, 1H), 7.15-7.19 (m, 2H), 7.50 (s, 1H), 7.57-7.60 (m, 2H), 7.72-7.76 (m, 1H), 8.07-8.09 (m, 2H), 10.67 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): 188.11 (t, J = 28 Hz), 173.60, 159.34, 156.97, 139.62, 135.10, 132.94, 130.68, 129.13, 128.26, 128.18, 117.59, 117.36, 117.10 (t, J = 259 Hz), 113.96, 113.71, 111.50, 111.42, 76.52 (t, J = 25 Hz); ^{19}F NMR (376 MHz, DMSO-d_6): δ -108.6 (d, J = 271 Hz, 1F), -109.6 (d, J = 274 Hz, 1F), -121.39 (s, 1F); IR (ATR): 3213, 2924, 2850, 1731, 1708, 1687, 1631, 1596, 1488, 1449, 1182, 1090, 985, 869; MS (EI): 321 (M^+, 15), 322 [$(M+H)^+$, 3], 105 (100), 77 (82), 166 (64), 156 (41), 51 (26), 110 (14), 78 (12); HRMS (EI): Exact mass calcd for $C_{16}H_{10}NO_3F_3$ $[M]^+$: 321.0613, Found: 321.0613.



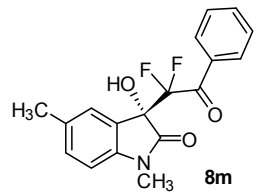
8k

The reaction was carried out in 5.0 mL of anhydrous THF at 0 °C for 5 days. Column chromatography afforded the desired product **8k** in 88% yield as white solid (m.p. 203-206 °C); HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 20/80, 1.0 mL/min, 230 nm; t_r (major) = 9.36 min, t_r (minor) = 6.24 min) gave the isomeric composition of the product: 93% ee, $[\alpha]^{25}_{D}$ = -66.1 (c = 0.72, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.90-6.92 (m, 1H), 7.31 (s, 1H), 7.37-7.39 (m, 1H), 7.53 (s, 1H), 7.57-7.61 (m, 2H), 7.73-7.76 (m, 1H), 8.07-8.09 (m, 2H), 10.79 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): 188.10 (t, *J* = 28 Hz), 173.37, 142.34, 135.19, 132.84, 130.98, 130.71, 129.18, 128.66, 126.21, 126.12, 117.09 (t, *J* = 259 Hz), 112.11, 76.29 (t, *J* = 25 Hz); ^{19}F NMR (376 MHz, DMSO-d_6): *δ* -108.5 (d, *J* = 274 Hz, 1F), -109.5 (d, *J* = 274 Hz, 1F); IR (ATR): 3216, 2962, 2923, 2361, 2335, 1731, 1712, 1632, 1597, 1488, 1378, 1179, 1090, 841; MS (EI): 337 (M^+, 16), 338 [$(M+H)^+$, 3], 105 (100), 77 (83), 182 (55), 156 (52), 51 (27), 184 (22), 78 (13); HRMS (EI): Exact mass calcd for $C_{16}H_{10}NO_3F_2{}^{35}Cl$ $[M]^+$: 337.0317, Found: 337.0316.



8l

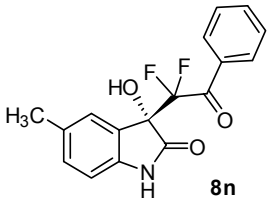
The reaction was carried out in 5.0 mL of anhydrous THF at 0 °C for 5 days. Column chromatography afforded the desired product **8l** in 85% yield as white solid (m.p. 206-208 °C); HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 13.55 min, t_r (minor) = 8.60 min) gave the isomeric composition of the product: 93% ee, $[\alpha]^{25}_{D}$ = -49.1 (c = 1.12, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.85-6.87 (m, 1H), 7.43 (s, 1H), 7.50-7.61 (m, 4H), 7.73-7.77 (m, 1H), 8.07-8.08 (m, 2H), 10.80 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): 188.08 (t, *J* = 28 Hz), 173.23, 142.74, 135.19, 133.82, 132.82, 130.70, 129.17, 129.04, 128.82, 117.08 (t, *J* = 263 Hz), 113.75, 112.61, 76.22 (t, *J* = 26 Hz); ^{19}F NMR (376 MHz, DMSO-d_6): *δ* -108.5 (d, *J* = 274 Hz, 1F), -109.4 (d, *J* = 274 Hz, 1F); IR (ATR): 3226, 2961, 2922, 1720, 1707, 1631, 1598, 1487, 1451, 1381, 1263, 1090, 801; MS (EI): 381 (M^+, 9), 382 [$(M+H)^+$, 2], 105 (100), 77 (81), 156 (51), 228 (32), 226 (31), 51 (25), 78 (12); HRMS (EI): Exact mass calcd for $C_{16}H_{10}NO_3F_2{}^{79}Br$ $[M]^+$: 380.9812, Found: 380.9811.



8m

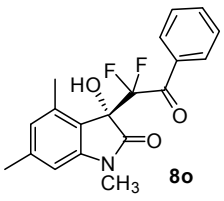
The reaction was carried out at 0 °C for 5 days. Column chromatography afforded the desired product **8m** in 90% yield as white oil. HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 25/75, 1.0 mL/min, 230 nm; t_r (major) = 9.58 min, t_r (minor) = 8.06 min) gave the isomeric composition of the product: 95% ee, $[\alpha]^{25}_{D}$ = -76.4 (c = 1.21, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.31 (s, 3H), 3.20 (s, 3H), 4.30 (s,

1H), 6.77 (d, *J* = 7.6 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.34 (s, 1H), 7.44-7.48 (m, 2H), 7.60-7.64 (m, 1H), 8.03 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 188.71 (t, *J* = 31 Hz), 172.60, 142.33, 134.66, 132.92, 132.08, 131.39, 130.22, 130.19, 130.16, 128.59, 128.30, 126.82, 124.10, 115.52 (t, *J* = 263 Hz), 108.51, 76.51 (t, *J* = 24 Hz), 26.45, 20.98; ^{19}F NMR (376 MHz, $CDCl_3$): δ -108.5 (d, *J* = 301 Hz, 1F), -109.4 (d, *J* = 297 Hz, 1F); IR (ATR): 3363, 2971, 2918, 2359, 1708, 1697, 1621, 1600, 1501, 1449, 1361, 1047, 821; MS (EI): 331 (M^+, 8), 332 [$(M+H)^+$, 2], 176 (100), 77 (46), 105 (37), 51 (12), 177 (12), 118 (7), 156 (1); HRMS (EI): Exact mass calcd for $C_{18}H_{15}NO_3F_2$ $[M]^+$: 331.1020, Found: 331.1019.



8n

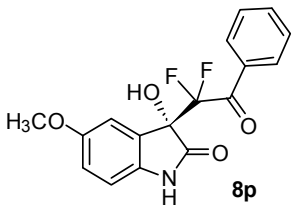
The reaction was carried out at 0 °C for 5 days. Column chromatography afforded the desired product **8n** in 90% yield as white solid (m.p. 174-176 °C); HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 25/75, 1.0 mL/min, 230 nm; t_r (major) = 12.40 min, t_r (minor) = 6.29 min) gave the isomeric composition of the product: 90% ee, $[\alpha]^{25}_D$ = -78.7 (c = 0.53, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.24 (s, 3H), 6.75-6.78 (m, 1H), 7.10-7.12 (m, 1H), 7.15 (s, 1H), 7.29 (s, 1H), 7.56-7.59 (m, 2H), 7.71-7.75 (m, 1H), 8.06-8.08 (m, 2H), 10.51 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): 188.28 (t, *J* = 28 Hz), 173.73, 140.91, 134.93, 133.16, 131.26, 131.14, 130.70, 129.68, 129.05, 128.97, 126.79, 117.37 (t, *J* = 262 Hz), 110.23, 76.40 (t, *J* = 26 Hz), 20.97; ^{19}F NMR (376 MHz, DMSO-d_6): δ -108.6 (d, *J* = 271 Hz, 1F), -109.6 (d, *J* = 271 Hz, 1F); IR (ATR): 3257, 2922, 2848, 2258, 1731, 1703, 1628, 1597, 1494, 1449, 1207, 974, 843; MS (EI): 317 (M^+, 12), 318 [$(M+H)^+$, 2], 162 (100), 77 (61), 105 (51), 51 (18), 78 (12), 163 (11), 156 (7); HRMS (EI): Exact mass calcd for $C_{17}H_{13}NO_3F_2$ $[M]^+$: 317.0863, Found: 317.0865.



8o

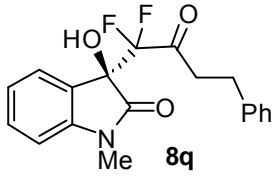
The reaction was carried out in 5.0 mL of anhydrous THF at 0 °C for 5 days. Column chromatography afforded the desired product **8o** in 80% yield as white solid (m.p. 130-133 °C); HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 15.05 min, t_r (minor) = 14.21 min) gave the isomeric composition of the product: 90% ee, $[\alpha]^{25}_D$ = -110.9 (c = 0.69, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26 (s, 3H), 2.52 (s, 3H), 3.46 (s, 3H), 4.22 (s, 1H), 6.93 (s, 1H), 7.19 (s, 1H), 7.44-7.48 (m, 2H), 7.60-7.64 (m, 1H), 8.02 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 188.80 (t, *J* = 30 Hz), 173.41, 139.86, 135.35, 134.55, 133.26, 132.75, 132.26, 130.20, 130.17, 130.14, 128.53, 128.29, 12472, 124.63, 120.05, 115.59 (t, *J* = 264 Hz), 75.88 (t, *J* = 24 Hz), 29.82, 20.56, 18.76; ^{19}F NMR

(376 MHz, $CDCl_3$): δ -108.7 (d, J = 297 Hz, 1F), -109.7 (d, J = 297 Hz, 1F); IR (ATR): 3364, 2987, 2921, 2360, 2338, 1704, 1693, 1606, 1467, 1450, 1380, 1083, 866, 780; MS (EI): 345 (M^+, 10), 346 [$(M+H)^+$, 2], 190 (100), 77 (47), 105 (33), 191 (12), 51 (11), 91 (10), 156 (1); HRMS (EI): Exact mass calcd for $C_{19}H_{17}NO_3F_2$ $[M]^+$: 345.1177, Found: 345.1177.



8p

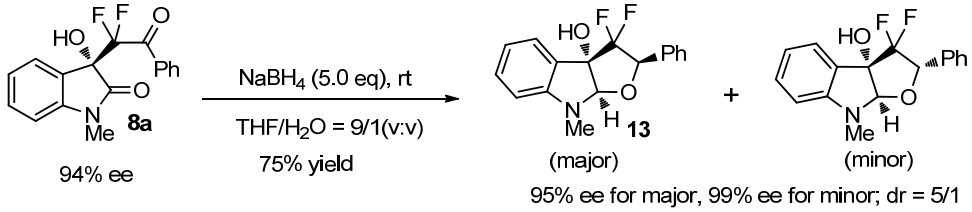
The reaction was carried out at 0 ^oC for 5 days. Column chromatography afforded the desired product **8p** in 78% yield as white solid (m.p. 166-168 ^oC); HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 20/80, 1.0 mL/min, 230 nm; t_r (major) = 19.31 min, t_r (minor) = 10.30 min) gave the isomeric composition of the product: 91% ee, $[\alpha]^{25}_D$ = -83.8 (c = 0.66, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.69 (s, 3H), 6.78-6.80 (m, 1H), 6.88-6.91 (m, 2H), 7.37 (s, 1H), 7.56-7.59 (m, 2H), 7.71-7.75 (m, 1H), 8.07-8.09 (m, 2H), 10.45 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): 188.29 (t, J = 29 Hz), 173.62, 155.22, 136.58, 135.02, 133.20, 130.73, 129.13, 127.83, 117.37 (t, J = 262 Hz), 115.80, 113.15, 111.04, 76.73 (t, J = 26 Hz), 56.00; ^{19}F NMR (376 MHz, DMSO-d_6): δ -108.8 (d, J = 271 Hz, 1F), -109.8 (d, J = 271 Hz, 1F); IR (ATR): 3358, 2943, 2837, 2257, 1716, 1687, 1598, 1492, 1469, 1283, 1209, 1164, 832; MS (EI): 333 (M^+, 26), 334 [$(M+H)^+$, 5], 178 (100), 77 (67), 105 (52), 149 (20), 106 (18), 122 (14), 156 (6); HRMS (EI): Exact mass calcd for $C_{17}H_{13}NO_4F_2$ $[M]^+$: 333.0813, Found: 333.0815.



8q

The reaction was carried out at 0 ^oC for 3 days. Column chromatography afforded the desired product **8q** in 27% yield as yellow oil; HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 15.59 min, t_r (minor) = 14.04 min) gave the isomeric composition of the product: 65% ee, $[\alpha]^{25}_D$ = -9.5 (c = 0.80, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.87-3.10 (m, 4H), 3.19 (s, 3H), 4.19 (s, 1H), 6.83-6.85 (m, 1H), 7.10-7.15 (m, 3H), 7.18-7.22 (m, 1H), 7.26-7.29 (m, 2H), 7.39-7.44 (m, 1H), 7.46-7.48 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 200.4 (q, J = 25 Hz), 172.48, 144.48, 139.87, 131.44, 128.93, 128.51, 128.43, 128.30, 126.30, 126.15, 123.50, 123.26, 113.23 (t, J = 260 Hz), 108.88, 39.92, 28.25, 26.44; ^{19}F NMR (376 MHz, $CDCl_3$): δ -115.9 (d, J = 278 Hz, 1F), -119.3 (d, J = 278 Hz, 1F); IR (ATR): 3060, 2880, 2830, 2335, 1715, 1614, 1507, 1496, 1472, 1302, 1191, 1111, 754; MS (EI): 345 (M^+, 8), 162 (100), 325 (8), 308 (10), 287 (3), 184 (11), 133 (23), 91 (74), 105 (54); HRMS (EI): Exact mass calcd for $C_{19}H_{17}NO_3F_2$ $[M]^+$:345.1177, Found: 345.1175.

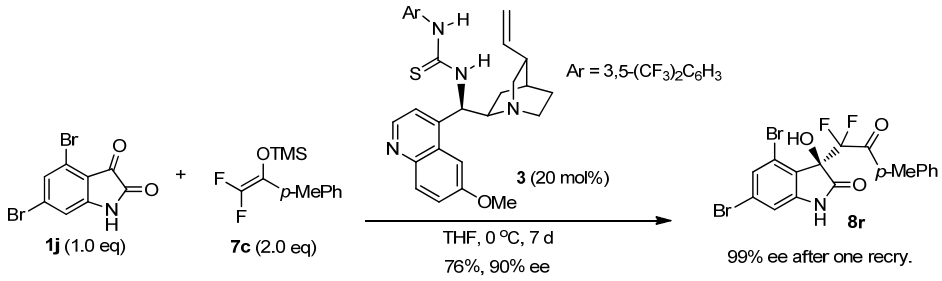
General Procedure for the preparation of 13 from 8a.[5]



To a stirred solution of **8a (**31.7 mg, 0.10 mmol, 94% ee) in 1.0 mL of mixture solvent of THF/ H_2O (9/1, v/v) was added $NaBH_4$ (19.0 mg, 0.5 mmol) at room temperature in two portions. The resulting mixture was stirred until the completion of **8a** as indicated by TLC (about 1 h). The reaction was quenched by the addition of 0.5 mL of saturated NH_4Cl aqueous solution, and the resulting mixture was stirred at room temperature until the generation of gas ceased. Then the mixture was extracted with ethyl acetate (5.0 mL × 4), the combined organic layer was dried over anhydrous Na_2SO_4, and concentrated under vacuum. The crude mixture was purified by silica gel column chromatography (using DCM as the eluent) to give product **13** (22.6 mg) in 75% yield as white solid(m.p. 128-130 ^oC); The relative configuration of product **13** was determined by NOE analysis**.** HPLC analysis [Chiralcel OJ-H, ^{i}PrOH/hexane = 20/80, 1.0 mL/min, 230 nm; major diastereomer: τ_R = 20.47 min (major enantiomer), τ_R = 16.35 min (minor enantiomer); minor diastereomer: τ_R = 23.10 min (major enantiomer), τ_R = 19.11 min (minor enantiomer)] gave the isomeric composition of major diastereomer: 95% ee, minor diastereomer: 99% ee; $[\alpha]^{25}_D$ = 24.2 (c = 0.32, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.83 (s, 1H), 3.04 (s, 3H), 5.07 (t, *J* = 12.0 Hz, 1H), 5.22 (s, 1H), 6.49-6.51 (m, 1H), 6.71-6.74 (m, 1H), 7.20-7.39 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.38, 132.71, 132.21, 131.72, 131.40, 129.00, 128.71, 128.24, 128.06, 127.39, 127.20, 126.25, 126.22, 125.71, 125.69, 125.54, 124.15, 124.13, 122.97, 122.94, 120.37, 118.74, 118.41, 107.51, 106.31, 101.71, 84.85 (t, *J* = 21 Hz), 81.05 (t, *J* = 31 Hz), 31.45; ^{19}F NMR (376 MHz, $CDCl_3$): δ -112.8 (d, *J* = 229 Hz), -113.9 (d, *J* = 233 Hz,), -122.7 (d, *J* = 229 Hz), -127.4 (d, *J* = 226 Hz); IR (ATR): 3272, 3036, 2927, 2845, 1613, 1494, 1469, 1378, 1230, 1022, 920, 844, 699; MS (EI): 303 (M^+, 99), 304 [$(M+H)^+$, 18], 77 (100), 178 (78), 147 (64), 106 (62), 91 (39), 162 (29), 234 (7); HRMS (EI): Exact mass calcd for $C_{17}H_{15}NO_2F_2$ $[M]^+$: 303.1071, Found: 303.1069.

[5] P. Shanmugam, V. Vaithiyanathan, and B. Viswambharan, *Aust. J. Chem.* **2007**, 60, 296.

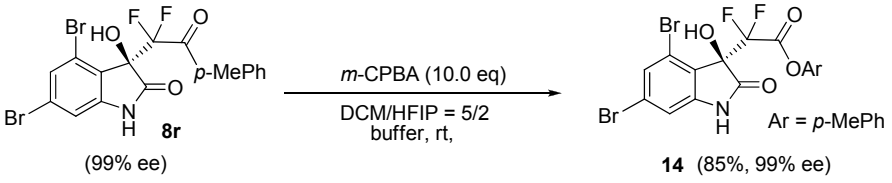
The synthesis of (*R*)-8r using catalyst 3



Following the general procedure, in the presence of 20 mol% of the pseudo-enantiomeric catalyst **3**, the reaction of silane **7c** with 4,6-dibromoisatin **1j** could readily provide the *R*-enantiomer of product **8r** in 76% yield with 90% ee, as white solid (m.p. 160-162 ^{o}C). HPLC analysis (Chiralcel IC-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 25.05 min, t_r (minor) = 10.41 min) gave the isomeric composition of the product: 90% ee, $[\alpha]^{25}_{D}$ = 139.6 (c = 1.00, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.28 (s, 3H), 4.96 (brs, 1H), 6.91 (s, 1H), 7.19-7.25 (m, 2H), 7.32-7.33 (m, 1H), 7.73-7.78 (m, 2H), 8.95 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 189.19 (t, *J* = 29 Hz), 174.36, 170.45, 144.56, 138.51, 138.24, 135.65, 134.39, 132.42, 130.75, 130.63, 130.55, 129.13, 128.49, 128.33, 127.75, 127.29, 125.38, 122.52, 121.27, 115.58 (t, *J* = 264 Hz), 113.63, 79.38 (t, *J* = 28 Hz), 21.26; ^{19}F NMR (376 MHz, $CDCl_3$): *δ* -103.9 (d, *J* = 282 Hz, 1F), -105.3 (d, *J* = 278 Hz, 1F); IR (ATR): 3338, 2930, 2815, 2322, 1742, 1690, 1605, 1571, 1426, 1281, 1120, 926, 846; MS (EI): 475 (M^+, 3), 476 [$(M+H)^+$, 1], 170 (100), 119 (88), 91 (57), 306 (30), 65 (22), 308 (17), 92 (16); HRMS (EI): Exact mass calcd for $C_{17}H_{11}NO_3F_2{}^{79}Br_2$ $[M]^+$: 472.9074, Found: 472.9073.

The enantiopure (*R*)-**8r** could be easily obtained by a single recrystallization.

The preparation of 14 from 8r[6].

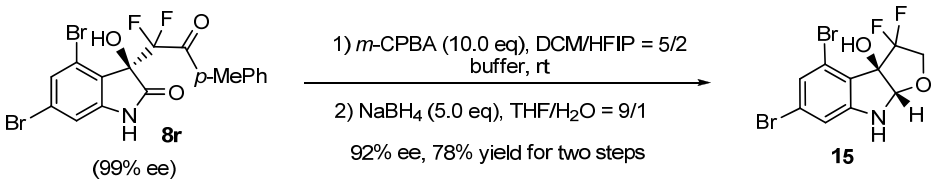


The **8r** (18.0 mg, 0.038 mmol, 99% ee) was dissolved in DCM/HFIP (5:2, 1.4 mL), followed by the addition of *m*-CPBA (77.0 mg, 0.38 mmol, 85%) and Phosphate buffer (24.0 μL) at ambient temperature. The mixture was stirred until the complete consumption of **8r** by TLC analysis (about 24 h). Then the reaction mixture was quenched by the addition of saturated aqueous $Na_2S_2O_3$. The

[6] S. Kobayashi; H. Tanaka, H. Amii and K. Uneyama, *Tetrahedron,* **2003**, *59*, 1547.

mixture was extracted with AcOEt for three times. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine for two times respectively, dried over Na_2SO_4, and concentrated in vacuum. The crude residue was purified by silica gel column chromatography (using DCM/EA = 15/1 as eluent) to give product **14** (15.7 mg) as white oil in 85% yield. HPLC analysis [Chiralcel OD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 12.97 min, t_r (minor) = 14.97 min)] gave the isomeric composition of the product: 99% ee; $[\alpha]^{25}_D$ = 40.0 (c = 0.21, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.32 (s, 3H), 6.85 (s, 1H), 6.93-6.95 (m, 1H), 7.10 (s, 1H), 7.14-7.16 (m, 1H), 7.32-7.36 (m, 1H), 7.50-7.51 (m, 2H), 11.14 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.31, 160.50 (t, *J* = 32 Hz), 149.90, 146.67, 140.29, 130.12, 129.33, 128.10, 125.05, 124.01, 121.71, 121.60, 114.07 (t, *J* = 262 Hz), 113.21, 78.96 (t, *J* = 26 Hz), 21.29; ^{19}F NMR (376 MHz, DMSO-d_6): δ -110.6 (d, *J* = 248 Hz), -111.4 (d, *J* = 248 Hz); IR (ATR): 3281, 2919, 2850, 1795, 1755, 1708, 1606, 1571, 1468, 1423, 1167, 903, 844; MS (EI): 489 (M^+, 2), 108 (100), 306 (54), 308 (34), 304 (28), 91 (23), 77 (17), 65 (10); HRMS (EI): Exact mass calcd for $C_{17}H_{11}NO_4F_2{}^{79}Br_2$ $[M]^+$: 488.9023, Found: 488.9021.

The preparation of 15 from 8r:

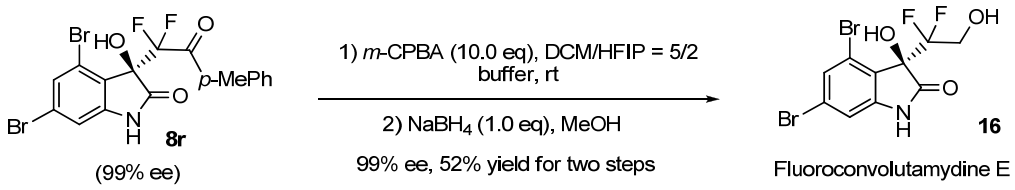


The **8r** (15.6 mg, 0.034 mmol, 99% ee) was dissolved in DCM/HFIP (5:2, 1.4 mL), followed by the addition of *m*-CPBA (68.0 mg, 0.34 mmol, 85%) and Phosphate buffer (22.0 μL) at ambient temperature. The reaction mixture was stirred until the complete consumption of **8r** by TLC analysis (about 24 h), and then quenched by addition of saturated aqueous $Na_2S_2O_3$. The mixture was extracted with AcOEt for three times (5.0 mL × 3). The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine for two times (5.0 mL × 2) respectively, dried over Na_2SO_4, and concentrated in vacuum. The crude residue was directly used for the next step without further purification.

To a stirred solution of crude ester **14** in 1.0 mL of mixed solvent of THF/H_2O (9/1, v/v) was added $NaBH_4$ (6.5 mg, 0.17 mmol) at room temperature in two portions. The resulting mixture was stirred until the completion of the starting material as indicated by TLC (about 1.0 h). The reaction was

quenched by the addition of 0.5 mL of saturated NH_4Cl aqueous solution, and the resulting mixture was stirred at room temperature until the generation of gas ceased. Then the reaction mixture was extracted with ethyl acetate (5.0 mL × 4), the combined organic layer was dried over anhydrous Na_2SO_4, and concentrated under vacuum. The crude mixture was purified by silica gel column chromatography (using DCM as eluent) to give product **15** (9.8 mg) in 78% yield as white oil. HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 25/75, 1.0 mL/min, 230 nm; t_r (major) = 9.31 min, t_r (minor) = 5.42 min) gave the isomeric composition of the product: 92% ee, $[\alpha]^{25}_D$ = -24.4 (c = 0.50, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.82-4.03 (m, 2H), 5.37 (s, 1H), 6.64 (brs, 1H), 6.77 (s, 1H), 7.00 (s, 1H), 7.57 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 153.96, 127.62, 126.49, 125.09, 125.00, 124.31, 123.75, 123.67, 122.47, 122.41, 111.04, 100.77, 86.53 (q, J = 96 Hz), 68.75 (t, J = 30 Hz); ^{19}F NMR (376 MHz, DMSO-d_6): δ -110.01 (d, J = 229 Hz, 1 F), -114.63 (d, J = 229 Hz, 1 F); IR (ATR): 3381, 2924, 2855, 1778, 1598, 1568, 1444, 1377, 1338, 1207, 776; MS (EI): 369 (M^+, 12), 44 (100), 306 (58), 303 (33), 90 (36), 251 (24), 170 (23), 265 (18), 227 (10); HRMS (EI): Exact mass calcd for $C_{10}H_7NO_2F_2Br_2$ $[M]^+$: 368.8812, Found: 368.8815.

The preparation of fluoroconvolutamydine E 16 from 8r:



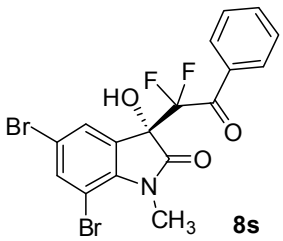
The **8r** (17.6 mg, 0.038 mmol, 99% ee) was dissolved in DCM/HFIP (5:2, 1.4 mL), followed by the addition of *m*-CPBA (77.0 mg, 0.38 mmol, 85%) and Phosphate buffer (24.0 μL) at ambient temperature. The mixture was stirred until the complete consumption of **8r** by TLC analysis (about 24 h), and then quenched by addition of saturated aqueous $Na_2S_2O_3$. The mixture was extracted with AcOEt for three times (5.0 mL × 3). The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine for two times (5.0 mL × 2) respectively, dried over Na_2SO_4, and concentrated in vacuum. The crude residue was directly used for the next step without further purification.

To a stirred solution of ester **14** in MeOH (1.0 mL) was added $NaBH_4$ (1.5 mg, 0.038 mmol) at room temperature in one portion. The reaction mixture was stirred until the completion of the starting material as indicated by TLC (about 1.0 h), and then quenched by the addition of 0.5 mL of saturated

NH_4Cl aqueous solution. After the generation of gas ceased, the solvent was removed under reduced pressure, and the residue was extracted with ethyl acetate (5.0 mL × 5). The combined organic layer was dried over anhydrous Na_2SO_4, and concentrated under vacuum. The crude mixture was purified by silica gel column chromatography (using DCM/EA = 5/1 as eluent) to give product **16** (7.0 mg) in 52% total yield as white solid. m.p. 115-118 ^oC.The NMR data of **16:** HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 20/80, 1.0 mL/min, 230 nm; t_r (major) = 16.17 min, t_r (minor) = 10.09 min) gave the isomeric composition of the product: 98% ee, $[\alpha]^{25}_D$ = 15.0 (c = 0.20, MeOH);^{1}H NMR (400 MHz, DMSO-d_6): δ 3.86-4.09 (m, 2H), 5.27 (t, *J* = 5.6 Hz, 1H), 6.97 (s, 1H), 7.01 (s, 1H), 7.41 (s, 1H), 10.86 (brs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.12, 175.05, 146.58, 128.86, 125.15, 124.44, 124.00, 122.03, 121.85, 121.60, 119.45, 112.61, 79.70 (q, *J* = 122 Hz), 58.93 (t, *J* = 23 Hz); ^{19}F NMR (376 MHz, DMSO-d_6): δ -110.71 (d, *J* = 244 Hz, 1 F), -117.41 (d, *J* = 256 Hz, 1 F); IR (ATR): 3424, 3185, 2923, 2854, 1786, 1726, 1606, 1568, 1338, 1212, 925; MS (EI): 385 (M^+, 4), 306 (100), 304 (53), 308 (50), 170 (11), 168 (10), 90 (9); HRMS (EI): Exact mass calcd for $C_{10}H_7NO_3F_2{}^{79}Br_2$ $[M]^+$: 384.8761, Found: 384.8763.

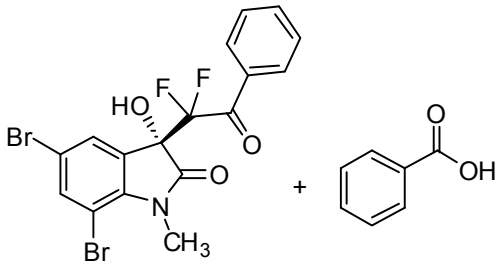
Determination of the absolute configuration.

The absolute configuration of product **8s** was determined to be *S* by X-ray analysis.[7] The configurations of other compounds were tentatively assigned by comparing the sign of their optical rotations to that of **8s**. Following the general procedure, compound **8s** was obtained in 58% yield with 73% ee as white solid. After a single recrystalization, the enantioselectivity of compound **8s** could be enriched to 99%. We tried in vain to obtain the homochiral single crystal of product **8s** when using enantiopure product **8s**. Fortunately, we obtained single crystal of the 1:1 complex of enantiopure **8s** and benzoic acid, and determined the absolute configuration of product **8s**.



8s

HPLC analysis (Chiralcel OZ-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; t_r (major) = 6.73 min, t_r (minor) = 7.53 min); $[\alpha]^{25}_{D}$ = -133.4 (c = 0.90, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.46 (s, 3H), 7.50 (s, 1H), 7.57-7.61 (m, 2H), 7.74-7.78 (m, 2H), 7.86 (s, 1H), 8.04-8.06 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): 187.84 (t, *J* = 29 Hz), 172.24, 141.44, 138.03, 135.53, 132.31, 131.01, 130.64, 129.33, 127.98, 116.79 (t, *J* = 265 Hz), 115.24, 103.33, 75.19 (t, *J* = 24 Hz), 30.19; ^{19}F NMR (376 MHz, DMSO-d_6): δ -108.3 (d, *J* = 282 Hz, 1F), -109.1 (d, *J* = 286 Hz, 1F); IR (ATR): 3238, 2986, 2930, 2854, 1708, 1685, 1620, 1597, 1474, 1450, 1252, 1089, 851; MS (EI): 473 (M^+, 6), 474 [$(M+H)^+$, 1], 105 (100), 77 (86), 320 (44), 156 (26), 51 (24), 318 (22); HRMS (EI): Exact mass calcd for $C_{17}H_{11}NO_3F_2{}^{79}Br_2$ $[M]^+$: 472.9074, Found: 472.9076.



Data intensity of **this complex on the left** was collected using a Bruker SMART APEX II (Mo radiation). The X-ray condition of was 50 kV × 30 mA. Data collection and reduction were done by using the Bruker ApexII software package. The structure was solved by direct methods and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for non-H atoms using SHELX-97. Hydrogen atoms were added at their geometrically idea positions and refined isotropically. Crystal data for **this complex**: C_{24} $H_{17}Br_2F_2NO_5$, M = 597.21, T = 173(2) K, λ = 0.71073 Å, Monoclinic, space group P2(1), a = 12.4308(5) Å, b = 7.9993(3) Å, c = 12.8452(6) Å, V = 1168.96(8) Å^3, z = 2, d_{calc} = 1.697 mg/m^3, 13398 reflections measured, 3692 unique [R(int) = 0.0222], R_1 = 0.0198, wR_2 =

[7] Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center. (CCDC 835881)

0.0478 ($I > 2\sigma(I)$), final R_1 = 0.0215, wR_2 = 0.0482 (all data), GOF = 1.049, and 309 parameters.

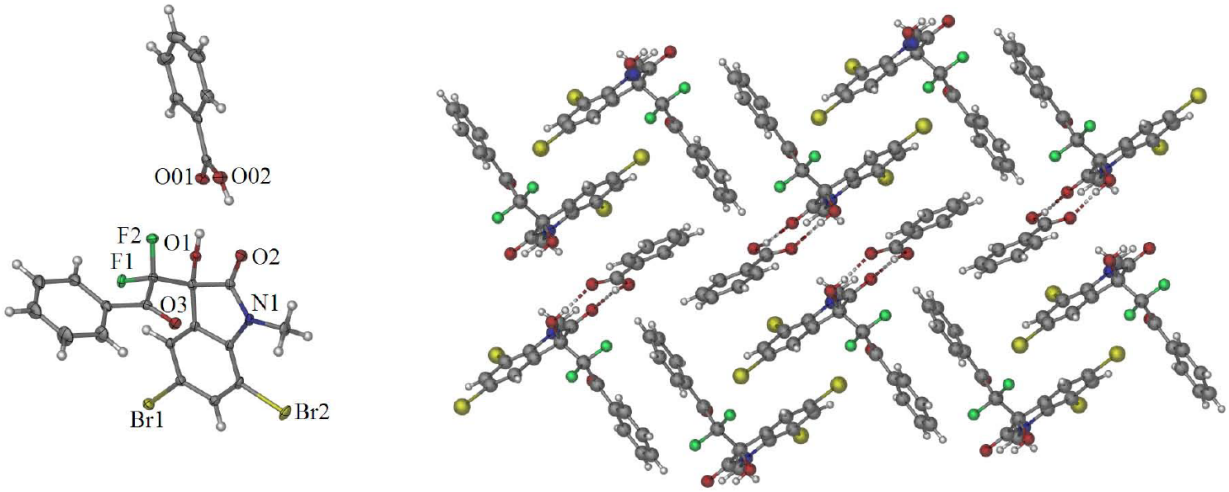


Table 1. Crystal data and structure refinement for z.

Identification code	z
Empirical formula	$C_{24}H_{17}Br_2F_2NO_5$
Formula weight	597.21
Temperature	173(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 12.4308(5) A alpha = 90 deg.
	b = 7.9993(3) A beta = 113.7680(10) deg.
	c = 12.8452(6) A gamma = 90 deg.
Volume	1168.96(8) A^3
Z, Calculated density	2, 1.697 Mg/m^3
Absorption coefficient	3.520 mm^-1
F(000)	592
Crystal size	0.48 x 0.26 x 0.20 mm
Theta range for data collection	2.95 to 25.01 deg.
Limiting indices	-14<=h<=14, -9<=k<=9, -15<=l<=15
Reflections collected / unique	13398 / 3692 [R(int) = 0.0222]
Completeness to theta = 25.01	99.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.5395 and 0.2829
Refinement method	Full-matrix least-squares on F^2

Data / restraints / parameters	3692 / 1 / 309
Goodness-of-fit on F^2	1.049
Final R indices [I>2sigma(I)]	R1 = 0.0198, wR2 = 0.0478
R indices (all data)	R1 = 0.0215, wR2 = 0.0482
Absolute structure parameter	0.011(5)
Largest diff. peak and hole	0.295 and -0.196 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for z.
U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Br(1)	-399(1)	-2628(1)	-6901(1)	35(1)
Br(2)	-2298(1)	3381(1)	-6164(1)	47(1)
O(1)	-3401(1)	-3293(2)	-4572(1)	28(1)
O(2)	-3699(1)	-423(2)	-3183(2)	35(1)
O(3)	-867(1)	-141(2)	-2329(2)	35(1)
F(1)	-1130(1)	-4149(2)	-3193(1)	35(1)
F(2)	-2191(1)	-3465(2)	-2259(1)	36(1)
N(1)	-2950(2)	798(2)	-4360(2)	28(1)
C(1)	-2309(2)	271(3)	-5000(2)	26(1)
C(2)	-1989(2)	1100(3)	-5777(2)	30(1)
C(3)	-1397(2)	234(3)	-6325(2)	30(1)
C(4)	-1142(2)	-1427(3)	-6095(2)	28(1)
C(5)	-1448(2)	-2286(3)	-5319(2)	27(1)
C(6)	-2031(2)	-1418(3)	-4788(2)	25(1)
C(7)	-2555(2)	-2069(3)	-3995(2)	25(1)
C(8)	-3129(2)	-483(3)	-3769(2)	27(1)
C(9)	-1638(2)	-2824(3)	-2904(2)	28(1)
C(10)	-685(2)	-1613(4)	-2134(2)	30(1)
C(11)	373(2)	-2248(4)	-1180(2)	34(1)
C(12)	511(2)	-3914(4)	-820(2)	42(1)
C(13)	1512(3)	-4382(5)	120(3)	55(1)
C(14)	2365(3)	-3218(6)	687(3)	66(1)
C(15)	2239(3)	-1590(7)	338(3)	72(1)
C(16)	1241(2)	-1089(5)	-599(3)	55(1)
C(17)	-3324(2)	2502(4)	-4243(2)	40(1)
O(01)	-4734(1)	-4473(3)	-3525(2)	38(1)
O(02)	-4565(2)	-2664(3)	-2146(2)	44(1)
C(01)	-5557(2)	-6945(4)	-2486(2)	40(1)
C(02)	-6004(3)	-8095(5)	-1963(3)	58(1)
C(03)	-6306(2)	-7594(7)	-1080(3)	65(1)
C(04)	-6154(3)	-5971(6)	-737(3)	62(1)
C(05)	-5693(2)	-4816(4)	-1233(2)	45(1)
C(06)	-5386(2)	-5303(4)	-2113(2)	35(1)
C(07)	-4873(2)	-4122(3)	-2670(2)	32(1)

Table 3. Bond lengths [A] and angles [deg] for z.

Br(1)-C(4)	1.901(2)
Br(2)-C(2)	1.889(2)
O(1)-C(7)	1.409(3)
O(1)-H(1A)	0.8400
O(2)-C(8)	1.226(3)
O(3)-C(10)	1.206(3)
F(1)-C(9)	1.360(3)
F(2)-C(9)	1.372(3)
N(1)-C(8)	1.346(3)
N(1)-C(1)	1.420(3)
N(1)-C(17)	1.467(3)
C(1)-C(2)	1.383(4)
C(1)-C(6)	1.394(3)
C(2)-C(3)	1.392(4)
C(3)-C(4)	1.370(4)
C(3)-H(3A)	0.9500
C(4)-C(5)	1.384(3)
C(5)-C(6)	1.368(3)
C(5)-H(5A)	0.9500
C(6)-C(7)	1.506(3)
C(7)-C(9)	1.530(3)
C(7)-C(8)	1.540(3)
C(9)-C(10)	1.541(4)
C(10)-C(11)	1.480(3)
C(11)-C(16)	1.389(4)
C(11)-C(12)	1.398(4)
C(12)-C(13)	1.390(4)
C(12)-H(12A)	0.9500
C(13)-C(14)	1.379(6)
C(13)-H(13A)	0.9500
C(14)-C(15)	1.365(6)
C(14)-H(14A)	0.9500
C(15)-C(16)	1.394(5)
C(15)-H(15A)	0.9500
C(16)-H(16A)	0.9500
C(17)-H(17A)	0.9800
C(17)-H(17B)	0.9800
C(17)-H(17C)	0.9800
O(01)-C(07)	1.212(3)
O(02)-C(07)	1.324(3)
O(02)-H(02A)	0.8400
C(01)-C(02)	1.381(4)
C(01)-C(06)	1.385(4)
C(01)-H(01A)	0.9500
C(02)-C(03)	1.391(5)
C(02)-H(02B)	0.9500
C(03)-C(04)	1.359(7)
C(03)-H(03A)	0.9500
C(04)-C(05)	1.372(5)
C(04)-H(04A)	0.9500
C(05)-C(06)	1.386(4)

C(05)-H(05A)	0.9500
C(06)-C(07)	1.476(4)
C(7)-O(1)-H(1A)	109.5
C(8)-N(1)-C(1)	111.05(19)
C(8)-N(1)-C(17)	121.2(2)
C(1)-N(1)-C(17)	127.6(2)
C(2)-C(1)-C(6)	119.0(2)
C(2)-C(1)-N(1)	131.8(2)
C(6)-C(1)-N(1)	109.1(2)
C(1)-C(2)-C(3)	119.4(2)
C(1)-C(2)-Br(2)	124.49(19)
C(3)-C(2)-Br(2)	116.11(19)
C(4)-C(3)-C(2)	119.8(2)
C(4)-C(3)-H(3A)	120.1
C(2)-C(3)-H(3A)	120.1
C(3)-C(4)-C(5)	122.0(2)
C(3)-C(4)-Br(1)	119.54(18)
C(5)-C(4)-Br(1)	118.42(19)
C(6)-C(5)-C(4)	117.5(2)
C(6)-C(5)-H(5A)	121.2
C(4)-C(5)-H(5A)	121.2
C(5)-C(6)-C(1)	122.2(2)
C(5)-C(6)-C(7)	128.5(2)
C(1)-C(6)-C(7)	109.09(19)
O(1)-C(7)-C(6)	108.57(19)
O(1)-C(7)-C(9)	109.32(19)
C(6)-C(7)-C(9)	112.97(17)
O(1)-C(7)-C(8)	111.56(17)
C(6)-C(7)-C(8)	101.64(18)
C(9)-C(7)-C(8)	112.6(2)
O(2)-C(8)-N(1)	125.8(2)
O(2)-C(8)-C(7)	125.1(2)
N(1)-C(8)-C(7)	109.1(2)
F(1)-C(9)-F(2)	105.94(19)
F(1)-C(9)-C(7)	108.29(19)
F(2)-C(9)-C(7)	109.33(16)
F(1)-C(9)-C(10)	110.11(17)
F(2)-C(9)-C(10)	106.88(18)
C(7)-C(9)-C(10)	115.8(2)
O(3)-C(10)-C(11)	122.4(2)
O(3)-C(10)-C(9)	116.7(2)
C(11)-C(10)-C(9)	120.8(2)
C(16)-C(11)-C(12)	119.5(3)
C(16)-C(11)-C(10)	117.0(3)
C(12)-C(11)-C(10)	123.4(2)
C(13)-C(12)-C(11)	119.4(3)
C(13)-C(12)-H(12A)	120.3
C(11)-C(12)-H(12A)	120.3
C(14)-C(13)-C(12)	120.4(4)
C(14)-C(13)-H(13A)	119.8
C(12)-C(13)-H(13A)	119.8
C(15)-C(14)-C(13)	120.5(3)
C(15)-C(14)-H(14A)	119.7

C(13)-C(14)-H(14A)	119.7
C(14)-C(15)-C(16)	120.2(4)
C(14)-C(15)-H(15A)	119.9
C(16)-C(15)-H(15A)	119.9
C(11)-C(16)-C(15)	120.0(4)
C(11)-C(16)-H(16A)	120.0
C(15)-C(16)-H(16A)	120.0
N(1)-C(17)-H(17A)	109.5
N(1)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
N(1)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
C(07)-O(02)-H(02A)	109.5
C(02)-C(01)-C(06)	120.0(3)
C(02)-C(01)-H(01A)	120.0
C(06)-C(01)-H(01A)	120.0
C(01)-C(02)-C(03)	119.9(4)
C(01)-C(02)-H(02B)	120.0
C(03)-C(02)-H(02B)	120.0
C(04)-C(03)-C(02)	119.4(3)
C(04)-C(03)-H(03A)	120.3
C(02)-C(03)-H(03A)	120.3
C(03)-C(04)-C(05)	121.5(3)
C(03)-C(04)-H(04A)	119.2
C(05)-C(04)-H(04A)	119.2
C(04)-C(05)-C(06)	119.6(3)
C(04)-C(05)-H(05A)	120.2
C(06)-C(05)-H(05A)	120.2
C(01)-C(06)-C(05)	119.6(3)
C(01)-C(06)-C(07)	118.4(2)
C(05)-C(06)-C(07)	122.0(3)
O(01)-C(07)-O(02)	123.2(2)
O(01)-C(07)-C(06)	122.6(3)
O(02)-C(07)-C(06)	114.2(2)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for z.
The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
Br(1)	34(1)	35(1)	38(1)	0(1)	17(1)	1(1)
Br(2)	60(1)	20(1)	52(1)	8(1)	15(1)	2(1)
O(1)	26(1)	24(1)	31(1)	-6(1)	9(1)	-6(1)
O(2)	36(1)	29(1)	44(1)	-7(1)	19(1)	0(1)
O(3)	32(1)	32(1)	34(1)	0(1)	4(1)	-6(1)
F(1)	36(1)	25(1)	39(1)	2(1)	10(1)	9(1)
F(2)	31(1)	40(1)	38(1)	9(1)	14(1)	-4(1)
N(1)	26(1)	18(1)	33(1)	-4(1)	5(1)	3(1)
C(1)	20(1)	20(1)	28(1)	-1(1)	0(1)	-1(1)
C(2)	29(1)	16(1)	33(2)	2(1)	0(1)	-1(1)
C(3)	29(1)	29(1)	28(2)	3(1)	7(1)	-4(1)
C(4)	25(1)	26(1)	31(1)	-3(1)	10(1)	-1(1)
C(5)	23(1)	20(1)	33(1)	-1(1)	6(1)	0(1)
C(6)	21(1)	20(1)	29(1)	-2(1)	4(1)	-4(1)
C(7)	24(1)	21(1)	27(1)	-4(1)	7(1)	-2(1)
C(8)	22(1)	22(1)	30(1)	-6(1)	3(1)	-2(1)
C(9)	26(1)	24(1)	33(1)	2(1)	13(1)	2(1)
C(10)	26(1)	35(2)	27(1)	-1(1)	12(1)	-4(1)
C(11)	26(1)	46(2)	27(1)	3(1)	8(1)	2(1)
C(12)	35(1)	54(2)	34(2)	9(1)	12(1)	3(1)
C(13)	46(2)	72(2)	45(2)	20(2)	17(2)	16(2)
C(14)	38(2)	106(4)	40(2)	17(2)	1(1)	9(2)
C(15)	42(2)	88(3)	54(2)	-3(2)	-12(2)	-3(2)
C(16)	37(2)	61(2)	45(2)	2(2)	-4(1)	-4(1)
C(17)	45(1)	21(1)	52(2)	-6(1)	18(1)	7(1)
O(01)	35(1)	46(1)	35(1)	-7(1)	17(1)	-10(1)
O(02)	52(1)	39(1)	49(1)	-8(1)	28(1)	-3(1)
C(01)	30(1)	49(2)	36(2)	-1(1)	6(1)	-8(1)
C(02)	47(2)	58(2)	53(2)	5(2)	4(2)	-21(1)
C(03)	42(2)	103(3)	42(2)	17(2)	9(1)	-21(2)
C(04)	54(2)	92(3)	47(2)	5(2)	28(2)	-2(2)
C(05)	38(1)	64(2)	33(2)	-1(1)	14(1)	2(1)
C(06)	17(1)	52(2)	26(1)	3(1)	1(1)	1(1)
C(07)	20(1)	39(2)	30(2)	-1(1)	3(1)	3(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for z.

	x	y	z	U(eq)
H(1A)	-3805	-3509	-4200	61(10)
H(3A)	-1169	793	-6857	36
H(5A)	-1259	-3435	-5161	32
H(12A)	-73	-4719	-1214	50
H(13A)	1607	-5510	372	66
H(14A)	3046	-3551	1327	79
H(15A)	2832	-798	733	86
H(16A)	1154	45	-839	65
H(17A)	-3751	2488	-3747	60
H(17B)	-3840	2931	-4994	60
H(17C)	-2632	3224	-3911	60
H(02A)	-4396	-1995	-2562	77(13)
H(01A)	-5367	-7280	-3101	48
H(02B)	-6104	-9228	-2206	69
H(03A)	-6617	-8379	-719	78
H(04A)	-6372	-5628	-141	74
H(05A)	-5584	-3690	-975	54

Table 6. Torsion angles [deg] for z.

C(8)-N(1)-C(1)-C(2)	175.3(2)
C(17)-N(1)-C(1)-C(2)	-9.1(4)
C(8)-N(1)-C(1)-C(6)	-1.8(3)
C(17)-N(1)-C(1)-C(6)	173.9(2)
C(6)-C(1)-C(2)-C(3)	-0.1(3)
N(1)-C(1)-C(2)-C(3)	-176.9(2)
C(6)-C(1)-C(2)-Br(2)	179.95(17)
N(1)-C(1)-C(2)-Br(2)	3.1(4)
C(1)-C(2)-C(3)-C(4)	0.3(4)
Br(2)-C(2)-C(3)-C(4)	-179.78(18)
C(2)-C(3)-C(4)-C(5)	-0.6(4)
C(2)-C(3)-C(4)-Br(1)	177.01(18)
C(3)-C(4)-C(5)-C(6)	0.7(3)
Br(1)-C(4)-C(5)-C(6)	-176.96(16)
C(4)-C(5)-C(6)-C(1)	-0.5(3)
C(4)-C(5)-C(6)-C(7)	174.1(2)
C(2)-C(1)-C(6)-C(5)	0.2(3)
N(1)-C(1)-C(6)-C(5)	177.72(19)
C(2)-C(1)-C(6)-C(7)	-175.29(19)
N(1)-C(1)-C(6)-C(7)	2.2(2)
C(5)-C(6)-C(7)-O(1)	-59.2(3)
C(1)-C(6)-C(7)-O(1)	116.0(2)
C(5)-C(6)-C(7)-C(9)	62.2(3)
C(1)-C(6)-C(7)-C(9)	-122.6(2)
C(5)-C(6)-C(7)-C(8)	-176.9(2)
C(1)-C(6)-C(7)-C(8)	-1.7(2)
C(1)-N(1)-C(8)-O(2)	-176.5(2)

C(17)-N(1)-C(8)-O(2)	7.5(4)
C(1)-N(1)-C(8)-C(7)	0.6(3)
C(17)-N(1)-C(8)-C(7)	-175.4(2)
O(1)-C(7)-C(8)-O(2)	62.3(3)
C(6)-C(7)-C(8)-O(2)	177.8(2)
C(9)-C(7)-C(8)-O(2)	-61.0(3)
O(1)-C(7)-C(8)-N(1)	-114.9(2)
C(6)-C(7)-C(8)-N(1)	0.7(2)
C(9)-C(7)-C(8)-N(1)	121.8(2)
O(1)-C(7)-C(9)-F(1)	59.2(2)
C(6)-C(7)-C(9)-F(1)	-61.8(2)
C(8)-C(7)-C(9)-F(1)	-176.25(17)
O(1)-C(7)-C(9)-F(2)	-55.8(2)
C(6)-C(7)-C(9)-F(2)	-176.82(19)
C(8)-C(7)-C(9)-F(2)	68.8(2)
O(1)-C(7)-C(9)-C(10)	-176.59(17)
C(6)-C(7)-C(9)-C(10)	62.4(2)
C(8)-C(7)-C(9)-C(10)	-52.0(2)
F(1)-C(9)-C(10)-O(3)	137.5(2)
F(2)-C(9)-C(10)-O(3)	-107.8(2)
C(7)-C(9)-C(10)-O(3)	14.3(3)
F(1)-C(9)-C(10)-C(11)	-44.8(3)
F(2)-C(9)-C(10)-C(11)	69.9(2)
C(7)-C(9)-C(10)-C(11)	-168.05(19)
O(3)-C(10)-C(11)-C(16)	-8.6(4)
C(9)-C(10)-C(11)-C(16)	173.9(2)
O(3)-C(10)-C(11)-C(12)	168.9(2)
C(9)-C(10)-C(11)-C(12)	-8.6(4)
C(16)-C(11)-C(12)-C(13)	0.5(4)
C(10)-C(11)-C(12)-C(13)	-176.9(3)
C(11)-C(12)-C(13)-C(14)	-0.5(5)
C(12)-C(13)-C(14)-C(15)	0.2(6)
C(13)-C(14)-C(15)-C(16)	0.1(6)
C(12)-C(11)-C(16)-C(15)	-0.2(5)
C(10)-C(11)-C(16)-C(15)	177.4(3)
C(14)-C(15)-C(16)-C(11)	-0.1(6)
C(06)-C(01)-C(02)-C(03)	1.5(4)
C(01)-C(02)-C(03)-C(04)	-0.2(5)
C(02)-C(03)-C(04)-C(05)	-0.9(5)
C(03)-C(04)-C(05)-C(06)	0.8(5)
C(02)-C(01)-C(06)-C(05)	-1.6(4)
C(02)-C(01)-C(06)-C(07)	178.2(2)
C(04)-C(05)-C(06)-C(01)	0.5(4)
C(04)-C(05)-C(06)-C(07)	-179.3(3)
C(01)-C(06)-C(07)-O(01)	9.5(3)
C(05)-C(06)-C(07)-O(01)	-170.8(2)
C(01)-C(06)-C(07)-O(02)	-169.6(2)
C(05)-C(06)-C(07)-O(02)	10.1(3)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for z [A and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1A)...O(01)	0.84	1.87	2.690(2)	166.7
O(02)-H(02A)...O(2)	0.84	1.88	2.701(3)	166.6

Symmetry transformations used to generate equivalent atoms: