# *N*-Fluoro-3-cyclohexyl-3-methyl-2,3-dihydrobenzo[1,2-*d*]isothiazole 1,1-Dioxide: An Efficient Agent for Electrophilic Asymmetric Fluorination of Enolates

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Electrophilic fluorination of enolates with N−F-type reagents is a versatile method to directly replace hydrogen with fluorine at a specific site.[1−5] Examples of diastereoselective fluorination of chiral substrates using achiral N−F agents have led to *substrate-controlled* syntheses of chiral fluorinated compounds.[6] However, there are few successful methods for *agent-controlled* enantioselective fluorination of achiral ketones, a process that would offer many advantages over existing methods for the enantioselective preparation of chiral monofluoro organic compounds.[7] A pioneering study for the agent-controlled asymmetric fluorination was demonstrated by Lang in 1988.[8] In the fluorination of $\beta$-ketoester enolates with *N*-fluorocamphorsultam **1** (Figure 1), ee reached 70%. The enantioselectivity was improved up to 75% for the fluorination of 2-methyl-1-tetralone by the use of *N*-fluoro-3,3-dichlorocamphorsultam **2**.[9] The conveniently accessible agent **3**[10] we recently reported was neither sufficiently reactive toward carbanions nor stable enough under usual conditions to be generally useful. In this paper, we describe a simple synthesis of enantiomeric *N*-fluoro-3-cyclohexyl-3-methyl-2,3-dihydrobenzo[1,2-*d*]-isothiazole 1,1-dioxide (CMIT-F, **4**), an agent that effects asymmetric fluorinations of ketone metal enolates to furnish optically active α-fluoroketones **5** with enantioselectivity reaching 88% ee.

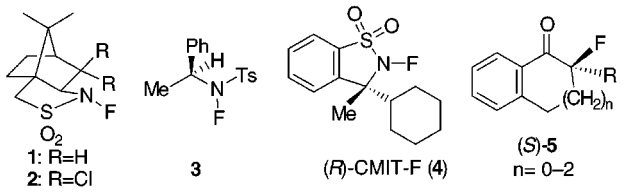
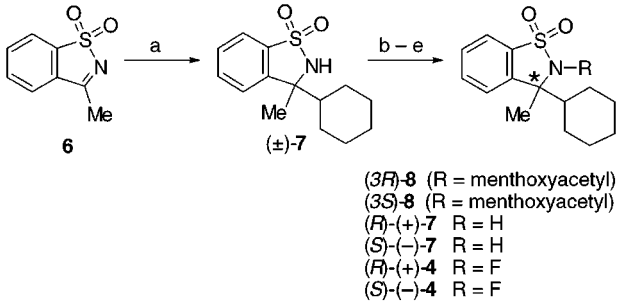



**Figure 1.**

**Scheme 1**[a]




[a] Key: (a) *c*-$C_6H_{11}MgBr$, THF (70%); (b) (−)-menthoxyacetyl chloride, NaH, THF (73%); (c) separation; (d) 2 N LiOH, aqueous THF (93−96%); (e) 15% $F_2$/He, spray-dried KF, $CHCl_3$/$CFCl_3$ (51−65%).

The structure of CMIT-F (**4**) was designed to produce a stable but reactive N−F bond and also to include steric factors that will favor asymmetric induction. In particular, the planarity present in the 2,3-dihydrobenzo[1,2-*d*]-isothiazole system seemed likely to strongly effect stereochemical orientation in an ordered transition state. This is important since no stereochemical bias can be expected in the transfer of the small fluorine atom. An important additional consideration is the fact that structural variations in these stereocontrolling groups are easy to introduce because of our synthetic design. The preparation of **4** was accomplished in good yield in five steps using a modification of the procedure reported[1e] (Scheme 1). The imine **6**, which was prepared from saccharin by Oppolzer's method,[11] was subjected to alkylation with cyclohexylmagnesium bromide to give **7** in 70% yield. Optical resolution of **7** was carried out by derivatization with (−)-menthoxyacetyl chloride followed by separation of the diastereomers (3*R*)-**8** and (3*S*)-**8** using column chromatography on silica gel.[12] Removal of the chiral auxiliary of (3*R*)-**8** and (3*S*)-**8** was achieved smoothly with

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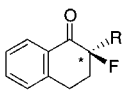
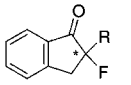
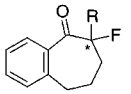
**Table 1. Enantioselective Fluorination of Ketones 9 with 4[a]**

| entry | ketone | fluorinating agent | product (5) | R | | ee (%)[b] | isolated yield (%) | configuration[c] | $[\alpha]_D^{26}$ ($CHCl_3$) | CD (EtOH) $\lambda_{ext}$ ($\Delta\varepsilon$) |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | **9a** | (*R*)-**4** |  | Me | **5a** | 74 | 67 | *S* | −18.3 ° (0.429) | 314 (−0.38) (c' = 4.34 x $10^{-3}$ M) |
| 2[d] | **9a** | (*R*)-**4** | | Me | **5a** | 14 | 65 | *S* | ND[e] | ND[e] |
| 3[f] | **9b** | (*R*)-**4** | | Et | **5b** | 72 | 70[g] | *S* | −31.3 ° (0.559) | 316 (−0.77) (c' = 2.55 x $10^{-3}$ M) |
| 4 | **9c** | (*R*)-**4** | | Bn | **5c** | 88 | 79 | *S* | −32.5 ° (0.578) | 322 (−1.25) (c' = 2.35 x $10^{-3}$ M) |
| 5 | **9d** | (*R*)-**4** |  | Me | **5d** | 54 | 54 | *S* | −23.2 ° (0.775) | 335 (−0.67) (c' = 4.73 x $10^{-3}$ M) |
| 6 | **9d** | (*S*)-**4** | | Me | **5d** | 48 | 62 | *R* | ND[e] | ND[e] |
| 7 | **9e** | (*R*)-**4** | | Et | **5e** | 20 | 73 | *S* | −9.01 ° (0.517) | 336 (−0.19) (c' = 5.80 x $10^{-3}$ M) |
| 8 | **9f** | (*R*)-**4** | | Bn | **5f** | 54 | 63 | *S* | −68.9 ° (0.961) | 336 (−1.18) (c' = 3.33 x$10^{-3}$ M) |
| 9 | **9g** | (*R*)-**4** |  | Et | **5g** | 43 | 48 | ND[e] | +16.8 ° (1.101) | 319 (+1.16) (c' = 1.18 x $10^{-3}$ M) |
| 10 | **9h** | (*R*)-**4** | | Bn | **5h** | 18 | 39 | ND[e] | +2.24 ° (0.768) | 317 (+0.39) (c' = 2.51 x $10^{-3}$ M) |

**9a**: 2-methyl-1-tetralone; **9b**: 2-ethyl-1-tetralone; **9c**: 2-benzyl-1-tetralone; **9d**: 2-methyl-1-indanone; **9e**: 2-ethyl-1-indanone; **9f**: 2-benzyl-1-indanone; **9g**: 2-ethyl-1-benzosuberone; **9h**: 2-benzyl-1-benzosuberone.

[a] Unless otherwise indicated fluorinations were carried out usng 1.1- 1.3 eq. of LDA and 1.1-1.3 eq. of fluorinating agent in THF solution. [b] Determined by HPLC analysis using a chiralcel OB- or OJ-column (hexane/*i*PrOH). [c] Ref. (9, 19). [d] The reaction was carried out in THF/HMPA (9/1). [e] ND: not determined. [f] The reaction was carried out using 0.5 eq. of (*R*)-**4**. [g] The yield was calculated based on the consumed (*R*)-**4**.

LiOH in aqueous THF[13] to furnish (*R*)-**7** and (*S*)-**7** in an optically pure state, respectively. Finally, fluorination of (*R*)-**7** and (*S*)-**7** in $CHCl_3/CFCl_3$ with 15% $F_2/He$[14] in the presence of spray-dried KF[15] as an HF scavenger afforded (*R*)-**4** and (*S*)-**4** as a stable, colorless crystalline solid, purified by silica gel column chromatography followed by recrystallization.[16] The absolute stereochemistry of (*R*)-**4** was determined through X-ray crystallographic analysis of the *N*-camphorsulfonyl derivative of (*R*)-**7**.[17]

Results of the fluorination of enolates with chiral **4** are summarized in Table 1. Fluorination of the lithium enolate of 2-methyl-1-tetralone (**9a**) with (*R*)-**4** in THF furnished (*S*)-2-fluoro-2-methyl-1-tetralone (**5a**) in 67% yield with 74% ee, after the usual workup (entry 1). The absolute stereochemistry of **5a** was determined by comparison of the specific rotation with that reported by Davis for the same compound.[9] Fluorination with **4** in the presence of HMPA resulted in a lower ee (entry 2), an observation that has mechanistic implications (see below). Similar fluorinations of other ketones, including 1-tetralones, 1-indanones, and 1-benzosuberones, with **4** were examined, and the corresponding optically active α-fluoroketones **5** were obtained (entries 3−10).

For the determination of absolute stereochemistry of **5d**, an alternative preparation was attempted, by treatment of (*S*)-2-hydroxy-2-methyl-1-indanone (**10**, 73% ee)[18] with DAST in $CH_2Cl_2$ at −78 °C, to give (*R*)-**5d** in 72% yield with 66% ee, according to the similar method for preparation of (*S*)-**5a** (Scheme 2).[9] The absolute stereochemistry of the other products was tentatively assigned using the CD octant rule.[19]

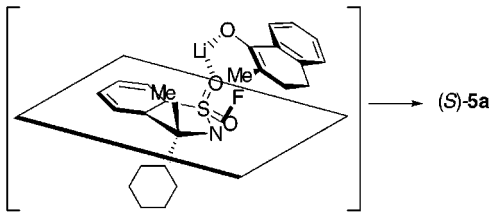
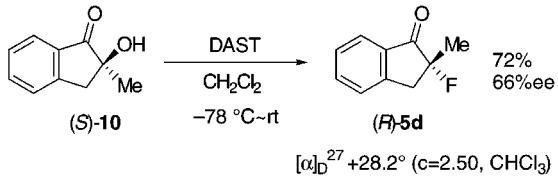



**Figure 2.** Possible transition-state model for the fluorination of the lithium enolate of **9a** with (*R*)-**4**.

**Scheme 2**




On the basis of the X-ray crystallographic structure of **4** reported in a previous communication,[17] the working model for the *S* selectivity in the fluorination of **9a** with (*R*)-**4** is shown in Figure 2. The nitrogen atom of **4** is found to be highly pyramidalized, and the fluorine is almost antiperiplanar with the bulky cyclohexyl group. The chelation structure of lithium enolate of **9a** in THF solution is strongly indicated by the fact that addition of HMPA resulted in lowering the enantioselectivity (Table 1, entry 2).

Advances in techniques of asymmetric syntheses have resulted in the development of methodologies that give complete enantioselection (>99% ee),[20] a standard of selectivity that is consonant with the requirements of modern synthetic chemistry. Nonetheless, since the previous maximum ee for asymmetric fluorinations was

(12) Reaction of (±)-**7** with (+)-camphorsulfonyl chloride [see, ref 17] was difficult to carry to completion when carried out on a large scale. For large scale optical resolution, condensation of (±)-**7** with (−)-menthoxyacetyl chloride as a chiral auxiliary was much more effective. Each diastereomer obtained was separated easily by column chromatography on silica gel and subsequent hydrolysis with LiOH furnished (*R*)-**7** and (*S*)-**7** in good yield.

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(16) (*R*)-**4**: mp 126−127 °C ($CH_2Cl_2$/hexane); $[\alpha]^{26}_D$ +48.0° (*c* 0.95, $CHCl_3$). (*S*)-**4**: mp 124−127 °C ($CH_2Cl_2$/hexane); $[\alpha]^{29}_D$ −49.2° (*c* 1.05, $CHCl_3$).

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75%, in a reaction that proceeded in low chemical yield, CMIT-F (**4**), with ee as high as 88%, represents a significant advance in agent-controlled asymmetric fluorination. Further structural modifications of **4** are currently under investigation with the goal of achieving the synthesis of optically pure α-fluoroketones.

## Experimental Section

**General Information.** Melting points were determined on a Yanagimoto micro-melting-point apparatus and uncollected. IR spectra ($cm^{-1}$) were recorded on a Perkin-Elmer 1600 spectrometer. $^1H$ NMR spectra were measured as solutions in $CDCl_3$, and chemical shifts are expressed in ppm relative to internal $Me_4Si$ (0.00 ppm) and were recorded on a JEOL GX-270 (270 MHz) or a Varian Gemini 300 (300 MHz) spectrometer. $^{19}F$ NMR spectra were measured with $CFCl_3$ as an internal standard and were taken with a JEOL GX-270 (254 MHz) spectrometer. Upfield shifts are quoted as negative $\delta$ values. EI mass spectra were taken with a JEOL JMS-D300 spectrometer. Column chromatography and preparative TLC were performed on BW-200 (Fuji Silysia) and Kieselgel 60 (Merck, art. 7748), respectively. All reactions involving oxygen- or moisture-sensitive compounds were carried out under a dry $N_2$ atmosphere. Unless otherwise noted, reagents were added by syringe. THF was distilled from sodium/benzophenone immediately prior to use.

**3-Cyclohexyl-3-methyl-2,3-dihydrobenzo[1,2-*d*]isothiazole 1,1-Dioxide (7).** A mixture of **6** (1.00 g, 5.52 mmol) and a 1.0 M solution of cyclohexylmagnesium bromide in ether (10.0 mL, 10.0 mmol) in THF (100 mL) was stirred at −40 °C for 24 h. HCl (10%, 10 mL) was added, stirring was continued for 5 min, and the organic layer was washed with water (20 mL). The organic layer was washed with 10% sodium thiosulfate and brine and dried over $MgSO_4$. The solvent was evaporated to give a solid, which was purified by recrystallization with AcOEt to furnish **7** obtained as a colorless crystals (1.02 g, 70%): mp 181−183 °C (AcOEt/hexane); IR (KBr) 3242, 1276, 1155 $cm^{-1}$; $^1H$ NMR (270 MHz) $\delta$ 0.98−2.02 (m, 11H, *c*-Hex), 1.61 (s, 3H, Me), 4.34 (brs, 1H, NH), 7.33 (d, $J$ = 7.8 Hz, 1H, ArH), 7.51 (t, $J$ = 7.4 Hz, 1H, ArH), 7.63 (t, $J$ = 7.4 Hz, 1H, ArH), 7.75 (d, $J$ = 7.8 Hz, 1H, ArH); MS *m*/*z* 266 ($M^+ + 1$). Anal. Calcd for $C_{14}H_{19}NO_2S$: C, 63.36; H, 7.22; N, 5.28. Found: C, 63.02; H, 7.19; N, 5.20.

***N*-Menthoxyacetyl-3-cyclohexyl-3-methyl-2,3-dihydrobenzo[1,2-*d*]isothiazole 1,1-Dioxide (8).** A solution of **7** (3.30 g, 12.5 mmol) in THF (200 mL) was treated with NaH (60% oil dispersion, 697 mg, 17.4 mmol) at 0 °C, and the resulting mixture was stirred at room temperature for 1.5 h. (−)-Menthoxyacetyl chloride (3.19 g, 13.7 mmol) was then added at 0 °C. The reaction mixture was allowed to warm slowly, stirred overnight at room temperature, and then poured onto 5% NaOH solution (50 mL). The mixture was extracted with ether (4 × 100 mL). The combined organic layers were washed with 5% NaOH solution (50 mL), water (50 mL), and saturated $NH_4Cl$ (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed ($CH_2Cl_2$/acetone 1:1) to give **8a** and **8b** (4.20 g, 73%) as a mixture of diastereomers. Each diastereoisomer was isolated by flash chromatography as a colorless oil.

**(3*R*)-*N*-Menthoxyacetyl-3-cyclohexyl-3-methyl-2,3-dihydrobenzo[1,2-*d*]isothiazole 1,1-Dioxide [(3*R*)-8].** Less polar isomer (3*R*)-**8**: $[\alpha]^{28}_D$ −69.3° ($c$ = 0.49, $CHCl_3$); IR (neat) 2930, 1718, 1321, 1233, 1124 $cm^{-1}$; $^1H$ NMR (300 MHz) $\delta$ 0.30 (qd, $J$ = 12.6, 3 Hz, 1H, C*H*HCH$_2$), 0.82 (d, $J$ = 6.6 Hz, 3H, MeCH), 0.84−1.45, 1.51−1.86, 1.93−2.16 (each m, total 17H, CH*HCH*$_2$, >CH−, $CH_2$, *c*-Hex), 0.92 (d, $J$ = 7.1 Hz, 6H, $Me_2CH$), 1.97 (s, 3H, MeC), 2.37 (heptet d, $J$ = 7.1, 3 Hz, 1H, C*H*Me$_2$), 2.76 (m, 1H, >CH−), 3.25 (td, $J$ = 10, 4 Hz, 1H, >CHO), 4.71, 4.81 (ABq, $J$ = 16.5 Hz, 2H, $OCH_2O$), 7.47 (d, $J$ = 7.7 Hz, 1H, ArH), 7.60 (t, $J$ = 7.7 Hz, 1H, ArH), 7.71 (t, $J$ = 7.7 Hz, 1H, ArH), 7.79 (d, $J$ = 7.7 Hz, 1H, ArH); HRMS calcd for $C_{26}H_{39}NO_4S$ 461.2600, found 461.2590. Anal. Calcd for $C_{26}H_{39}NO_4S$: C, 67.64; H, 8.51; N, 3.03. Found: C, 67.43; H, 8.49; N, 3.34.

**(3*S*)-*N*-Menthoxyacetyl-3-cyclohexyl-3-methyl-2,3-dihydrobenzo[1,2-*d*]isothiazole 1,1-Dioxide [(3*S*)-8].** More polar isomer (3*S*)-**8**: $[\alpha]^{27}_D$ −23.5 ° ($c$ = 1.37, $CHCl_3$); IR (neat) 2933, 1718, 1320, 1216 $cm^{-1}$; $^1H$ NMR (300 MHz) $\delta$ 0.28 (qd, $J$ = 12.6, 3 Hz, 1H, C*H*HCH$_2$), 0.82 (d, $J$ = 6.6 Hz, 3H, MeCH), 0.85−1.43, 1.55−1.87, 1.94−2.19 (each m, total 17H, CH*HCH*$_2$, >CH−, $CH_2$, *c*-Hex), 0.93 (d, $J$ = 7.1 Hz, 6H, $Me_2CH$), 1.97 (s, 3H, MeC), 2.37 (heptet d, $J$ = 7.1, 3 Hz, 1H, C*H*Me$_2$), 2.75 (m, 1H, >CH−), 3.25 (td, $J$ = 10, 4 Hz, 1H, >CHO), 4.77 (s, 2H, $OCH_2O$), 7.47 (d, $J$ = 7.7 Hz, 1H, ArH), 7.60 (t, $J$ = 7.7 Hz, 1H, ArH), 7.71 (t, $J$ = 7.7 Hz, 1H, ArH), 7.79 (d, $J$ = 7.7 Hz, 1H, ArH); HRMS calcd for $C_{26}H_{39}NO_4S$ 461.2600, found 461.2596. Anal. Calcd for $C_{26}H_{39}NO_4S$: C, 67.64; H, 8.51; N, 3.03. Found: C, 67.83; H, 8.62; N, 2.87.

**(3*R*)-3-Cyclohexyl-3-methyl-2,3-dihydrobenzo[1,2-*d*]isothiazole 1,1-Dioxide [(*R*)-7].** A solution of (3*R*)-**8** (1.56 g, 3.40 mmol) in THF (25 mL) was treated with 2 N LiOH (25 mL), and the resulting mixture was stirred for 3 h. The mixture was extracted with $CH_2Cl_2$ (500 mL). The organic layer was washed with saturated $NaHCO_3$ (100 mL) and brine (100 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by recrystallization (AcOEt/hexane) to give (*R*)-**7** (832 mg, 93%) as colorless crystals. The product exhibited the same spectroscopic properties (NMR, IR and MS) as racemic **7**: $[\alpha]^{29}_D$ +29.47° ($c$ = 0.97, $CHCl_3$); mp 221 °C (AcOEt/hexane).

**(3*S*)-3-Cyclohexyl-3-methyl-2,3-dihydrobenzo[1,2-*d*]isothiazole 1,1-Dioxide [(*S*)-7].** A solution of (3*S*)-**8** (1.52 g, 3.30 mmol) in THF (25 mL) was treated with 2 N LiOH (25 mL), and the resulting mixture was stirred for 3 h. The mixture was extracted with $CH_2Cl_2$ (500 mL). The organic layer was washed with saturated $NaHCO_3$ (100 mL) and brine (100 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by recrystallization (AcOEt/hexane) to give (*S*)-**7** (841 mg, 96%) as colorless crystals. The product exhibited the same spectroscopic properties (NMR, IR, and MS) as racemic **7**: $[\alpha]^{29}_D$ −22.58° ($c$ = 1.01, $CHCl_3$); mp 216−219 °C (AcOEt/hexane).

**(3*R*)-*N*-Fluoro-3-cyclohexyl-3-methyl-2,3-dihydrobenzo-[1,2-*d*]isothiazole 1,1-Dioxide [(*R*)-4].** To a stirred solution of (*S*)-**7** (810 mg, 3.06 mmol) in $CFCl_3$/$CFCl_3$ (1:1, 20 mL) in the presence of spray-dried KF (532 mg, 9.18 mmol) was introduced 15% $F_2$ gas in helium at −40 °C for 2−3 h. Insoluble materials were removed by filtration, and concentration of the filtrate gave a solid, which was purified by recrystallization ($CH_2Cl_2$/hexane) to give (*R*)-**4** (445 mg, 51%) as colorless crystals: mp 77−79 °C; $[\alpha]^{26}_D$ +48.0° ($c$ = 0.95, $CHCl_3$); IR (KBr) 2935, 1359, 1184 $cm^{-1}$; $^{19}F$ NMR $\delta$ −58.5 (s); $^1H$ NMR (270 MHz) $\delta$ 1.11−2.05 (m, 11H, *c*-Hex), 1.65 (d, $J$ = 5.9 Hz, 3H, Me), 7.27−7.82 (m, 4H, ArH); MS *m*/*z* 283 ($M^+$), 264 ($M^+$ − F), 200 ($M^+$ − *c*-Hex); HRMS calcd for $C_{14}H_{18}FNO_2S$ 283.1041, found 283.1017. Anal. Calcd for $C_{14}H_{18}FNO_2S$: C, 59.34; H, 6.40; N, 4.94. Found: C, 59.14; H, 6.64; N, 4.86.

**(3*S*)-*N*−Fluoro-3-cyclohexyl-3-methyl-2,3-dihydrobenzo-[1,2-*d*]isothiazole 1,1-Dioxide [(*S*)-4].** To a stirred solution of (*S*)-**7** (338 mg, 1.27 mmol) in $CFCl_3$/$CFCl_3$ (1:1, 10 mL) in the presence of spray-dried KF (221 mg, 3.81 mmol) was introduced 15% $F_2$ gas in helium at −40 °C for 2−3 h. Insoluble materials were removed by filtration, and concentration of the filtrate gave a solid, which was purified by recrystallization ($CH_2Cl_2$/hexane) to give (*S*)-**4** (234 mg, 65%) as colorless crystals. The product exhibited the same spectroscopic properties (NMR, IR, and MS) as (*R*)-**4**: mp 77−79 °C; $[\alpha]^{29}_D$ −49.2° ($c$ = 1.05, $CHCl_3$).

**General Procedure for Fluorination of 9: (*S*)-2-Fluoro-2-methyl-1-tetralone (5a).** To a mechanically stirred solution of diisopropylamine (0.042 mL, 0.30 mmol) in THF (1.0 mL) was added under nitrogen at 0 °C a 1.54 M solution of *n*-BuLi in hexane (0.19 mL, 0.30 mmol). After the mixture was stirred for 15 min at 0 °C and then chilled to −78 °C, a solution of the 2-methyl-1-tetralone (**9a**) (40.0 mg, 0.25 mmol) in THF (1.0 mL) was added. The reaction mixture was stirred for 1 h at 0 °C and then chilled to −40 °C. A solution of (*R*)-**4** (78.0 mg, 0.28 mmol) in THF (1 mL) was slowly added. The reaction mixture was stirred overnight at −40 °C and then poured onto saturated aqueous $NH_4Cl$ (5 mL). The aqueous layer was extracted with AcOEt (3 × 50 mL). The combined organic layers were washed with water (10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed (10% AcOEt in hexane) by preparative TLC to give (*S*)-**5a** (29.6 mg, 67%, 74% ee) as a colorless oil: IR (neat) 2938, 1701 $cm^{-1}$; $^{19}F$ NMR $\delta$ −155.1 (qdd, $J$ = 22, 16.6, 9.2 Hz); $^1H$ NMR (270 MHz)

$\delta$ 1.60 (t, $J$ = 22 Hz, 3H, Me), 2.21−2.57 (m, 2H, $CH_2$), 2.95−3.23 (m, 2H, $CH_2Ar$), 7.25−8.09 (m, 4H, ArH); MS $m/z$ 178 ($M^+$); HRMS calcd for $C_{11}H_{11}FO$ 178.0794, found 178.0801 (ref 9).

**(*S*)-2-Ethyl-2-fluoro-1-tetralone (5b).** Fluorination of 2-ethyl-1-tetralone (**9b**) (100 mg, 0.58 mmol) with diisopropylamine (0.083 mL, 0.63 mmol), a 1.54 M solution of *n*-BuLi in hexane (0.42 mL, 0.63 mmol), and (*R*)-**4** (81.2 mg, 0.29 mmol) gave after chromatography (10% AcOEt in hexane) (*S*)-**5b** (31 mg, 70% based on **4**, 72% ee) as a light yellow oil: IR (neat) 3020, 1700, 1216 $cm^{-1}$; $^{19}F$ NMR $\delta$ −163.3 (m); $^1H$ NMR (270 MHz) $\delta$ 1.04 (t, $J$ = 7.4 Hz, 3H, Me), 1.79 (m, 2H, $CH_2$), 2.40 (m, 2H, $CH_2$), 3.06 (m, 2H, $CH_2Ar$), 7.25 (d, $J$ = 7.6 Hz, 1H, ArH), 7.35 (d, $J$ = 7.6 Hz, 1H, ArH), 7.52 (d, $J$ = 7.6 Hz, 1H, ArH), 8.06 (d, $J$ = 7.6 Hz, 1H, ArH); HRMS calcd for $C_{12}H_{13}FO$ 192.0950, found 192.0967.

**(*S*)-2-Benzyl-2-fluoro-1-tetralone (5c).** Fluorination of 2-benzyl-1-tetralone (**9c**) (60.0 mg, 0.250 mmol) with diisopropylamine (0.0430 mL, 0.310 mmol), a 1.54 M solution of *n*-BuLi in hexane (0.200 mL, 0.310 mmol), and (*R*)-**4** (79.0 mg, 0.280 mmol) gave after chromatography (10% AcOEt in hexane) (*S*)-**5c** (50.7 mg, 79%, 88% ee) as a light yellow oil: IR (neat) 2927, 1698 $cm^{-1}$; $^{19}F$ NMR $\delta$ −158.8 (dddd, $J$ = 31.3, 16.6, 16.5, 5.5 Hz); $^1H$ NMR (270 MHz) $\delta$ 2.04−2.35 (m, 2H, $CH_2$), 2.96−3.14 (m, 3H, $CH_2$-Ph, C*H*HAr), 3.23 (dd, $J$ = 17.3, 14.9 Hz, 1H, CH*H*Ar), 7.26−7.57 (m, 8H, ArH), 8.10 (d, $J$ = 7.8 Hz, 1H, ArH); MS $m/z$ 254 ($M^+$), 235 ($M^+$ − F), 163 ($M^+$ − Bn); HRMS calcd for $C_{17}H_{15}FO$ 254.1107, found 254.1106.

**(*S*)-2-Fluoro-2-methyl-1-indanone (5d).** Fluorination of 2-methyl-1-tetralone (**9d**) (40.0 mg, 0.270 mmol) with diisopropylamine (0.0430 mL, 0.330 mmol), a 1.54 M solution of *n*-BuLi in hexane (0.21 mL, 0.330 mmol), and (*R*)-**4** (85.0 mg, 0.300 mmol) gave after chromatography (15% hexane in $CH_2Cl_2$) (*S*)-**5d** (24.3 mg, 54%, 54% ee) as a light yellow oil: IR (neat) 3023, 1730, 1218 $cm^{-1}$; $^{19}F$ NMR $\delta$ −152.8 (quintet d, $J$ = 22.5, 11 Hz); $^1H$ NMR (270 MHz) $\delta$ 1.63 (d, $J$ = 22.5 Hz, 3H, Me), 3.30 (dd, $J$ = 17, 11 Hz, 1H, C*H*HAr), 3.47 (dd, $J$ = 22.5, 17 Hz, 1H, CH*H*Ar), 7.43 (t, $J$ = 7.6 Hz, 2H, ArH), 7.67 (t, $J$ = 7.6 Hz, 1H, ArH), 7.82 (d, $J$ = 7.6 Hz, 1H, ArH); MS $m/z$ 165 ($M^+$ + 1), 164 ($M^+$), 149 ($M^+$ − Me); HRMS calcd for $C_{10}H_9FO$ 164.0637, found 164.0626; $C_{10}H_{10}FO$ 165.0715, found 165.0694.

**(*S*)-2-Ethyl-2-fluoro-1-indanone (5e).** Fluorination of 2-ethyl-1-tetralone (**9e**) (40.0 mg, 0.250 mmol) with diisopropylamine (0.0420 mL, 0.300 mmol), a 1.54 M solution of *n*-BuLi in hexane (0.19 mL, 0.300 mmol), and (*R*)-**4** (78.0 mg, 0.280 mmol) gave after chromatography (15% hexane in $CH_2Cl_2$) (*S*)-**5e** (32.7 mg, 73%, 20% ee) as a light yellow oil: IR (neat) 3021, 1727, 1216 $cm^{-1}$; $^{19}F$ NMR $\delta$ −160.0 (tdd, $J$ = 26, 19, 15 Hz); $^1H$ NMR (270 MHz) $\delta$ 1.01 (t, $J$ = 7.4 Hz, 3H, Me), 1.75−2.13 (m, 2H, $CH_2$), 2.35 (d, $J$ = 19 Hz, 1H, C*H*HAr), 3.36 (d, $J$ = 15 Hz, 1H, CH*H*Ar), 7.43 (m, 2H, ArH), 7.66 (t, $J$ = 7.6 Hz, 1H, ArH); HRMS calcd for $C_{11}H_{11}FO$ 178.0794, found 178.0793.

**(*S*)-2-Benzyl-2-fluoro-1-indanone (5f).** Fluorination of 2-benzyl-1-tetralone (**9f**) (50.0 mg, 0.230 mmol) with diisopropylamine (0.0350 mL, 0.270 mmol), a 1.54 M solution of *n*-BuLi in hexane (0.180 mL, 0.270 mmol), and (*R*)-**4** (70.0 mg, 0.250 mmol) gave after chromatography (10% AcOEt in hexane) (*S*)-**5f** (34 mg, 63%, 54% ee) as a light yellow oil: IR (neat) 3019, 1727, 1215 $cm^{-1}$; $^{19}F$ NMR $\delta$ -154.7 (dddd, $J$ = 30, 23, 14, 13 Hz); $^1H$ NMR (270 MHz) $\delta$ 2.95 (dd, $J$ = 30, 14 Hz, 1H, C*H*HAr), 3.15 (dd, $J$ = 23, 18 Hz, 1H, C*H*HAr), 3.38 (dd, $J$ = 18, 13 Hz, 1H, CH*H*Ar), 3.41 (t, $J$ = 14 Hz, 1H, CH*H*Ar), 7.38 (q, $J$ = 7.6 Hz, 2H, ArH), 7.62 (t, $J$ = 7.6 Hz, 1H, ArH), 7.81 (d, $J$ = 7.6 Hz, 1H, ArH); HRMS calcd for $C_{16}H_{13}FO$ 240.0950, found 240.0953.

**2-Ethyl-2-fluoro-1-benzosuberone (5g).** Fluorination of 2-ethyl-1-benzosuberone (**9g**) (50.0 mg, 0.270 mmol) with diisopropylamine (0.0500 mL, 0.320 mmol), a 1.54 M solution of *n*-BuLi in hexane (0.210 mL, 0.320 mmol), and (*R*)-**4** (83.0 mg, 0.290 mmol) gave after chromatography (15% hexane in $CH_2Cl_2$) **5g** (26.0 mg, 48%, 43% ee, note: **5g** was obtained as an inseparable mixture of **5g** and **9g** (32 mg, **5g**:**9g** = 88:12) as a light yellow oil): IR (neat) 3019, 1215 $cm^{-1}$; $^{19}F$ NMR $\delta$ −158.1 (m); $^1H$ NMR (270 MHz) $\delta$ 0.92 (t, $J$ = 7.6 Hz, 3H, Me), 1.75−2.25 (m, 6H, Me × 3), 2.84−3.17 (m, 2H, $CH_2Ar$), 7.18−7.48 (m, 4H, ArH); HRMS calcd for $C_{13}H_{15}FO$ 206.1107, found 206.1112.

**2-Benzyl-2-fluoro-1-benzosuberone (5h).** Fluorination of 2-benzyl-1-benzosuberone (**9h**) (50.0 mg, 0.200 mmol) with diisopropylamine (0.0300 mL, 0.240 mmol), a 1.54 M solution of *n*-BuLi in hexane (0.160 mL, 0.240 mmol), and (*R*)-**4** (62.0 mg, 0.220 mmol) gave after chromatography (15% hexane in benzene) **5h** (21 mg, 39%, 18% ee) as a light yellow oil: IR (neat) 3019, 1690, 1216 $cm^{-1}$; $^{19}F$ NMR $\delta$ −153.8 (pentet, $J$ = 25 Hz); $^1H$ NMR (270 MHz) $\delta$ 1.70−2.15 (m, 4H, $CH_2CH_2$), 2.91, 3.13 (each m, total 3H, C*H*HAr, $CH_2Ph$), 3.30 (dt, $J$ = 17, 15 Hz, 1H, CH*H*Ar), 7.16−7.40 (m, 9H, ArH); HRMS calcd for $C_{18}H_{17}FO$ 268.1263, found 268.1282.

**Preparation of (*R*)-5d from (*S*)-10.** To a stirred solution of (*S*)-**10**[18] (83 mg, 0.512 mmol, 73% ee) in dry $CH_2Cl_2$ (3 mL) was added DAST (124 mg, 0.769 mmol) at −78 °C. The temperature was allowed to warm to room temperature over 1 h. The reaction mixture was poured into water and extracted with AcOEt. The organic extract was washed with brine, dried, and concentrated in vacuo. The residue was purified by preparative TLC eluting with 30% AcOEt in hexane to give (*R*)-**5d** (60.4 mg, 72%, 66% ee) as a colorless oil. The product has the same spectroscopic data (NMR, IR and MS) as (*S*)-**5d** from fluorination of **9d** with (*R*)-**4**: $[\alpha]^{27}_D$ +28.2° ($c$ = 2.50, $CHCl_3$).

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**Supporting Information Available:** Experimental procedures for the camphorsulfonylation of **7** and hydrolysis of the camphorsulfonyl derivative of **7.** This material is available free of charge via the Internet at http://pubs.acs.org.

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