Novel Enantioselective Fluorinating Agents, (*R*)- and (*S*)-*N*-Fluoro-3-*tert*-butyl-7-nitro-3,4-dihydro-2*H*-benzo[*e*][1,2]thiazine 1,1-Dioxides

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Enantioselective fluorinating agents, (*R*)- and (*S*)-*N*-fluoro-3-*tert*-butyl-7-nitro-3,4-dihydro-2*H*-benzo[*e*][1,2]-thiazine 1,1-dioxides (BNBT-F, **2) are readily prepared in 3 steps from racemic 3-*tert*-butyl-7-nitro-3,4-dihydro-2*H*-benzo[*e*][1,2]thiazine 1,1-dioxides (**5**) via optical resolution and fluorination. These agents make accessible both enantiomers of optically active quaternary α -fluoro carbonyl compounds in modest to high enantioselectivities. X-ray crystallographic analysis of chiral **2** reveals a unique structure wherein the nitrogen atom is highly pyramidalized and fluorine occupies an axial position.**

Key words asymmetric fluorination; *N*-fluorosultam; α -fluoroketone

The extremely high reactivity of electrophilic fluorinating agents such as molecular fluorine, FCIO_3 and CF_3OF made selective fluorination reactions highly problematic. This limitation has been largely overcome by the more recent introduction of easy to handle fluorinating agents,¹⁾ of which *N*-fluoropyridinium salts,²⁾ *N*-fluoroquinolizidinium salts³⁾ and *N*-fluorosulfonamides⁴⁾ are representative. Among current issues in this field, agent-controlled enantioselective fluorination remains a major challenge.⁵⁾ Chiral *N*-fluorosulfonamide derivatives have been prepared in one approach to solving this problem.⁶⁾ For example, we recently reported a novel chiral sultam derivative, *N*-fluoro-3-cyclohexyl-3-methyl-2,3-dihydro-benzo[1,2-*d*]isothiazole 1,1-dioxide (CMIT-F, **1**), as an enantioselective fluorinating agent.⁷⁾ Unfortunately, the results to date with this class of agent have been less than satisfactory with respect to both chemical yield and enantioselectivity. In this paper, we report an additional enantioselective fluorinating agent, *N*-fluoro-3-*tert*-butyl-7-nitro-3,4-dihydro-2*H*-benzo[*e*][1,2]thiazine 1,1-dioxide (BNBT-F, **2**) which is effective in the enantioselective fluorination of cyclic ketones.

During our development of CMIT-F (**1**), we observed that the enantioselectivity of the fluorination reaction was dependent on the difference in steric bulkiness of the two substituents at the chiral center. To take advantage of this, we converted Oppolzer's sultam⁸⁾ to the *N*-fluoro sultam **3**, which has both a *tert*-butyl group and hydrogen at the chiral center. We were disappointed to find that, under the conditions of the reaction with lithium enolates, **3** furnished the corresponding imine **4**. The easy loss of HF is clearly associated with the acidity of the proton at the chiral center. With these results in mind, we designed a new N-F type fluorinating agent, BNBT-F (**2**). The proton at the chiral center in **2** should be significantly less acidic than that in **3**, and the differential bulk of two substituents at the chiral center should

be efficient enough to induce high enantioselection. Based on a precedent in the literature,⁹⁾ the electron withdrawing nitro group was introduced into the aromatic ring to increase the fluorinating ability of the agent.

Preparation of BNBT-F Chiral **2** was easily prepared from racemic 3-*tert*-butyl-7-nitro-3,4-dihydro-2*H*-benzo[*e*][1,2]thiazine 1,1-dioxide (**5**) in 3 steps, including optical resolution. The sultam **5**, prepared from 3-*tert*-butyl-3,4-dihydro-2*H*-benzo[*e*][1,2]thiazine 1,1-dioxide,⁴⁾ was derivatized with (+)-10-camphorsulfonyl chloride to furnish the diastereomeric mixture of **6** in moderate yield, accompanied by 45% of unreacted **5**. Diastereomer separation of **6** was effected by silica gel chromatography, and eluted with ethyl acetate/hexane to give the less polar isomer, (3*R*)-**6** (21%), and the more polar isomer, (3*S*)-**6** (31%). It is interesting to note that the mother liquid obtained by the recrystallization of recovered **5** (50% hexane in ethyl acetate) gave optical pure (*R*)-**5** in 20% yield. Removal of the chiral auxiliary of (3*R*)-**6** or (3*S*)-**6** was achieved with LiOH in aqueous THF to furnish (*R*)-**5** or (*S*)-**5** in 82% and 87% yield, respectively. Finally, fluorination of (*R*)-**5** with FCIO_3 in THF gave (*R*)-**2** in 66% yield. In the same way, (*S*)-**2** was obtained in 83% yield (Chart 1). X-ray crystallography was used to unambiguously determine the structure and absolute stereochemistry of (*S*)-**2**.

Molecular Structure of (*S*)-BNBT-F The molecular structure of (*S*)-BNBT-F (**2**) is shown in Figs. 2 and 3. The configuration of the nitrogen atom carrying fluorine in **2** is

Fig. 1

Key: (a) (+)-camphorsulfonyl chloride, NaH, THF, then separation; (b) 2M LiOH, aqueous THF; (c) NaH, THF; FCIO_3 .

Chart 1

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found to be pyramidal, with the sum of the bond angles around the nitrogen atom equaling 324.6° . The bond lengths of N(1)–S(1) and N(1)–C(1) are 1.685 (2) and 1.490 (3) Å, respectively. The length of the N(1)–F(1) bond is 1.425 (3) Å, slightly longer than that of the N–F bond of typical amines¹⁰⁾ (1.406 (16) Å for F–NR¹R²). To our slight surprise, fluorine is antiperiplanar to the hydrogen atom at the chiral center, in contrast to our previous observation.¹¹⁾ The dihedral angle F(1)–N(1)–C(1)–H(1) is 160.8° . The bulky *tert*-butyl moiety occupies the equatorial position, and the small hydrogen atom is axial. Fluorine, rather than the lone pair of nitrogens, takes an axial orientation, probably due to steric interactions with the bulky *tert*-butyl moiety.

Fig. 2. ORTEP Diagram of (*S*)-2 Fig. 3. CHARON Diagram of (*S*)-2: (a) Front View; (b) Side ViewTable 1. Enantioselective Fluorination of Ketones **7** with **2**

Ketone 7	2	Product 8	ee (%)	Yield (%)	Config. ^{d)}		
	7a	(<i>R</i>)- 2		8a	62 ^{a)}	79	<i>R</i>
	7b	(<i>S</i>)- 2		8b	44 ^{a)}	76	<i>S</i>
	7c	(<i>R</i>)- 2		8c	60 ^{a)}	59	<i>R</i>
	7d	(<i>S</i>)- 2		8d	49 ^{b)}	55	<i>R</i>
	7e	(<i>S</i>)- 2		8e	43 ^{a)}	73	ND ^{c)}
	7f	(<i>S</i>)- 2		8f	52 ^{a)}	74	<i>S</i>
	7g	(<i>R</i>)- 2		8g	57 ^{a)}	40	<i>R</i>
	7h	(<i>R</i>)- 2		8h	69 ^{b)}	70	ND ^{c)}
	7i	(<i>S</i>)- 2		8i	60 ^{c)}	56	ND ^{c)}

a) Chiralcel OB column (10% *i*PrOH/hexane). b) Chiralcel OJ column (10% *i*PrOH/hexane). c) Chiralcel OJ column (EtOH). d) Ref. 7. e) ND: not determined.

Enantioselective Fluorination of Prochiral Enolates by BNBT-F With the target agent BNBT-F (**2**) in hand, we examined the ability of **2** to effect the enantioselective fluorination of enolates of a series of tetralones and indanones **7**. Fluorination of the preformed lithium enolate of 2-methyl-1-tetralone (**7a**) with (*R*)-**2** in THF at -50°C furnished (*R*)-2-fluoro-2-methyl-1-tetralone (**8a**) in 79% yield with 62% ee. Other results of enantioselective fluorination using both (*R*)- and (*S*)-**2** are summarized in Table 1. Chiral agents **2** make accessible both enantiomers of optically active quaternary α -fluoro carbonyl compounds in modest to high enantioselectivities. The absolute stereochemistry of **8** was determined by comparison of the specific rotation with that of the authentic samples reported.⁷⁾

On the bases of the X-ray crystallographic structure of **2** and the reaction mechanism of the fluorination by CMIT-F (**1**) reported in a previous paper,⁷⁾ we propose a working model for the fluorination of **7** with (*S*)-**2**. At the asymmetric center of **2**, the bulky *tert*-butyl group occupies a pseudo-equatorial position, whereas the hydrogen atom is in an axial position. The fluorine atom occupies an axial position, and, as a consequence, the N–F bond is almost perpendicular to the benzene ring of **2**. The sulfonyl oxygen in the equatorial position can coordinate to the lithium ion of the enolate.⁷⁾ Moreover, a stacking interaction between the benzene rings of **2** and **7** is expected to be energetically favorable. Therefore, **7** is predicted to approach **2** at the less hindered α -face, as shown in Fig. 4.

In summary, we have synthesized BNBT-F (**2**) and have found it to be a new agent for enantioselective fluorination with moderate to high enantioselectivity. X-ray crystallographic analysis of **2** revealed that the N–F bond [1.425(3) Å] is slightly longer than that of Davis's (–)-*N*-fluoro-2,10-(3,3-dichlorocamphorsultam) 1.420(6) Å,^{6c)} and slightly shorter than that of CMIT-F [1.435(3) Å].¹¹⁾ A relationship between N–F bond lengths and fluorination efficiency is now under investigation.

Experimental

General Methods Melting points were determined on a Yanagimoto micro-melting point apparatus and are uncorrected. 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 δ 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 N_2 atmosphere. Unless otherwise noted, reagents were added by syringe. THF was distilled from sodium/benzophenone immediately prior to use.

3-*tert*-Butyl-7-nitro-3,4-dihydro-2H-benzo[e][1,2]-thiazine 1,1-Dioxide (5**)** A mixture of fuming HNO_3 (1.76 ml, 42 mmol) and conc. H_2SO_4 (6 ml) was dropped into a solution of 3-*tert*-butyl-3,4-dihydro-2H-benzo[e][1,2]-thiazine 1,1-dioxide⁴⁾ (5.02 g, 21 mmol) at -20°C and stirred for 1 h. The reaction mixture was poured onto crashed ice and extracted with AcOEt (150 ml $\times$ 3). The combined organic layer was washed with water, brine, and dried (MgSO_4), then concentrated *in vacuo*. The residue was chromatographed (50% CH_2Cl_2 in hexane, then 50% AcOEt in hexane) to give **5** (4.06 g, 68%) as a white powder. mp 194°C (AcOEt/hexane). IR (KBr) cm^{-1} : 3264, 3019, 2967, 1328, 1215, 758, 669. ^1H -NMR (CDCl_3) δ : 1.06 (s, 9H, *tert*-Bu), 2.96 (dd, $J=17.3$, 11.7 Hz, 1H, CHHAr), 3.08 (dd, $J=17.3$, 4.1 Hz, 1H, CHHAr), 3.61 (ddd, $J=12$, 11, 4.1 Hz, 1H, NCH<), 4.42 (d,

Fig. 4. Schematic Representation of the Transition State in the Fluorination of Enolates with (*S*)-**2**

$J=11.7$ Hz, 1H, NH), 7.45 (d, $J=8.5$ Hz, 1H, ArH), 8.24 (dd, $J=8.5$, 2.4 Hz, 1H, ArH), 8.60 (d, $J=2.4$ Hz, 1H, ArH). MS m/z : 284 (M^+), 269 ($\text{M}^+ - \text{Me}$), 227 ($\text{M}^+ - \text{tert-Bu}$). HRMS Calcd for $\text{C}_{12}\text{H}_{16}\text{N}_2\text{O}_4\text{S}$: 284.0830. Found 284.0838. Anal. Calcd for $\text{C}_{12}\text{H}_{16}\text{N}_2\text{O}_4\text{S}$: C, 50.69; H, 5.67; N, 9.85. Found: C, 50.54; H, 5.60; N, 9.89.

***N*-Camphorsulfonyl-3-*tert*-butyl-7-nitro-3,4-dihydro-benzo[e][1,2]-thiazine 1,1-Dioxide (**6**)** A solution of **5** (1.04 g, 3.66 mmol) in THF (50 ml) was treated with NaH (60% oil dispersion, 292 mg, 7.72 mmol) at 0°C and stirred at room temperature for 1.5 h. (+)-10-Camphorsulfonyl chloride (1.38 g, 5.49 mmol) was added to the mixture, followed by stirring overnight. Cold saturated aqueous NH_4Cl was added, and the resulting mixture was extracted with AcOEt (50 ml $\times$ 3). The combined organic layer was washed with water, brine, and dried (MgSO_4), then concentrated *in vacuo*. The residue was chromatographed (40% CH_2Cl_2 in hexane, then 30% AcOEt in hexane) to give the less polar isomer (*R*)-**6** (0.38 g, 21%), the more polar isomer (*S*)-**6** (0.56 g, 31%) and 0.47 g of unreacted **5** as a white powder. The recovered **5** was recrystallized (50% AcOEt in hexane) to give racemic colorless crystals (0.26 g, 25%) and the enantiopure (*R*)-**5** (0.21 g, 20%) from the mother liquid.

(3*R*)-*N*-Camphorsulfonyl-3-*tert*-butyl-7-nitro-3,4-dihydro-benzo[e][1,2]-thiazine 1,1-Dioxide (*R*)-6**** Colorless crystals. mp 152°C (AcOEt/hexane). $[\alpha]_{\text{D}}^{26} -14.1^{\circ}$ ($c=0.88$, CHCl_3). IR (KBr) cm^{-1} : 3020, 2966, 1747, 1534, 1216, 758, 669. ^1H -NMR (CDCl_3) δ : 0.87 (s, 3H, gem Me), 1.07 (s, 3H, gem Me), 1.14 (s, 9H, *tert*-Bu), 1.39 (m, 1H), 1.61 (m, 1H), 2.03 (m, 1H), 2.35 (m, 2H), 3.22 (dd, $J=14.9$, 7.3 Hz, 1H, CHHAr), 3.33 (dd, $J=14.9$, 11 Hz, 1H, CHHAr), 3.83, 4.04 (ABq, $J=14.9$ Hz, 2H, CH_2), 4.55 (dd, $J=11$, 7.3 Hz, 1H, NCH<), 7.56 (d, $J=8.3$ Hz, 1H, ArH), 8.38 (dd, $J=8.3$, 2.2 Hz, 1H, ArH), 8.67 (d, $J=2.2$ Hz, 1H, ArH). MS m/z : 499 ($\text{M}^+ + 1$), 498 (M^+), 483 ($\text{M}^+ - \text{Me}$), 441 ($\text{M}^+ - \text{tert-Bu}$). HRMS Calcd for $\text{C}_{22}\text{H}_{30}\text{N}_2\text{O}_7\text{S}_2$: 498.1495. Found 498.1463. Anal. Calcd for $\text{C}_{22}\text{H}_{30}\text{N}_2\text{O}_7\text{S}_2$: C, 52.99; H, 6.06; N, 5.62. Found: C, 52.76; H, 5.89; N, 5.44.

(3*S*)-*N*-Camphorsulfonyl-3-*tert*-butyl-7-nitro-3,4-dihydro-benzo[e][1,2]-thiazine 1,1-Dioxide (*S*)-6**** Colorless crystals. mp 223°C (AcOEt/hexane). $[\alpha]_{\text{D}}^{26} +58.6^{\circ}$ ($c=0.48$, CHCl_3). IR (KBr) cm^{-1} : 3020, 2967, 1745, 1534, 1216, 758, 668. ^1H -NMR (CDCl_3) δ : 0.90 (s, 3H, gem Me), 1.10 (s, 3H, gem Me), 1.14 (s, 9H, *tert*-Bu), 1.40 (m, 1H), 1.64 (m, 1H), 2.05 (m, 3H), 2.36 (m, 2H), 3.24 (dd, $J=14.9$, 7.3 Hz, 1H, CHHAr), 3.35 (dd, $J=14.9$, 11.0 Hz, 1H, CHHAr), 3.39, 4.38 (ABq, $J=14.9$ Hz, 2H, CH_2), 4.56 (dd, $J=11.0$, 7.6 Hz, 1H, NCH<), 7.58 (d, $J=8.3$ Hz, 1H, ArH), 8.40 (dd, $J=8.3$, 2.4 Hz, 1H, ArH), 8.71 (d, $J=2.4$ Hz, 1H, ArH). MS m/z : 499 ($\text{M}^+ + 1$), 498 (M^+), 483 ($\text{M}^+ - \text{Me}$), 441 ($\text{M}^+ - \text{tert-Bu}$). HRMS Calcd for $\text{C}_{22}\text{H}_{30}\text{N}_2\text{O}_7\text{S}_2$: 498.1495. Found 498.1463. Anal. Calcd for $\text{C}_{22}\text{H}_{30}\text{N}_2\text{O}_7\text{S}_2$: C, 52.99; H, 6.06; N, 5.62. Found: C, 52.98; H, 6.05; N, 5.60.

(3*R*)-3-*tert*-Butyl-7-nitro-3,4-dihydro-2H-benzo[e][1,2]-thiazine 1,1-Dioxide [(*R*)-5**]** A solution of (*R*)-**6** (0.79 g, 1.58 mmol) in THF (15 ml) was treated with 2 M LiOH (7 ml) at room temperature and stirred for 1 h. The mixture was poured into 10% aqueous HCl solution and extracted with AcOEt (50 ml $\times$ 3). The combined organic layer was washed with water, brine, and dried (MgSO_4), then concentrated *in vacuo*. The residue was chromatographed (20% AcOEt in hexane) to give (*R*)-**5** (0.37 g, 82%) as colorless crystals. mp 223°C (AcOEt/hexane). $[\alpha]_{\text{D}}^{26} +52.4^{\circ}$ ($c=0.96$, CHCl_3). The optical pure (*R*)-**5** exhibited the same spectral properties (IR, MS and ^1H -NMR) as the racemic **5**.

(3*S*)-3-*tert*-Butyl-7-nitro-3,4-dihydro-2H-benzo[e][1,2]-thiazine 1,1-Dioxide [(*S*)-5**]** In the same way, 0.6 g (1.2 mmol) of (*S*)-**6** was treated with 2 M LiOH (5 ml) to give (*S*)-**5** (0.30 g, 87%) as colorless crystals. $[\alpha]_{\text{D}}^{26} -52.8^{\circ}$ ($c=0.98$, CHCl_3). The optical pure (*S*)-**5** exhibited the same spectral properties (IR, MS and ^1H -NMR) as (*R*)-**5**.

(3*R*)-*N*-Fluoro-3-*tert*-butyl-7-nitro-3,4-dihydro-2H-benzo[e][1,2]-thiazine 1,1-Dioxide [(*R*)-BNBT-F(2**)]** A solution of (*R*)-**5** (1.83 g, 6.44 mmol) in THF (50 ml) was treated with NaH (60% dispersion in min-

eral oil, 386 mg, 9.66 mmol) under N_2 at $0^\circ C$, and the mixture was stirred at room temperature for 1 h. To this mixture was introduced freshly prepared $FCIO_3$ gas generated from $KClO_4$ (4.46 g, 32.2 mmol) and FSO_3H (32.2 g, 322 mmol) for 3 h. The reaction was quenched by a saturated aqueous NH_4Cl solution and the resulting mixture was extracted with $AcOEt$ (50 ml $\times$ 3). The combined organic layer was washed with water, brine, and dried ($MgSO_4$), then concentrated *in vacuo*. The residue was chromatographed on silica gel (30% $AcOEt$ in hexane) to give (R)-BNBTF(2) (1.28 g, 66%) as colorless crystals. mp $143-145^\circ C$ ($AcOEt$ /hexane). $[\alpha]_D^{26} + 50.8^\circ$ ($c=0.61$, $CHCl_3$). IR (KBr) cm^{-1} : 3019, 2968, 1534, 1215, 758, 669. ^{19}F -NMR ($CDCl_3$, $CFCl_3$) δ : -70.9 (brs, NF). ^1H -NMR ($CDCl_3$) δ : 1.18 (s, 9H, *tert*-Bu), 3.07 (m, 1H, $CHHAr$), 3.37 (m, 1H, $CHHAr$), 4.14 (brs, 1H, $NCH<$), 7.60 (d, $J=8.5$ Hz, 1H, ArH), 8.41 (dd, $J=8.5$, 2.2 Hz, 1H, ArH), 8.85 (d, $J=2.2$ Hz, 1H, ArH). MS m/z : 302 (M^+), 282 ($M^+ - HF$), 244 ($M^+ - tert$ -Bu). HRMS Calcd for $C_{12}H_{15}FN_2O_4S$: 302.0736. Found 302.0736. Anal. Calcd for $C_{12}H_{15}FN_2O_4S$: C, 47.67; H, 5.00; N, 9.27. Found: C, 47.83; H, 4.97; N, 9.39.

(3S)-N-Fluoro-3-*tert*-butyl-7-nitro-3,4-dihydro-2H-benzo[e][1,2]-thiazine 1,1-Dioxide [(S)-BNBTF(2)] In the same way, (S)-(2) (0.82 g, 83%) was obtained from (S)-5 (0.93 g, 3.26 mmol) as colorless crystals. $[\alpha]_D^{26} - 47.3^\circ$ ($c=0.69$, $CHCl_3$). (S)-(2) exhibited the same spectral properties (IR, MS, ^1H -NMR and ^{19}F -NMR) as (R)-(2).

General Procedure for Asymmetric Fluorination of Ketones with 2: (R)-2-Fluoro-2-methyl-1-tetralone (8a) To a stirred solution of 2-methyl-1-tetralone (16 mg, 0.10 mmol) in THF (1.0 ml) was added a 1.0 M solution of LHMDS in THF (0.15 ml, 0.15 mmol) under nitrogen at $-78^\circ C$. The mixture was stirred for 10 min at $-78^\circ C$, warmed to $0^\circ C$, stirred for an additional 1 h, and cooled to $-50^\circ C$. A solution of (R)-2 (36 mg, 0.12 mmol) in THF (1 ml) was added to the reaction mixture. After the reaction was complete, as indicated by TLC, the reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (1 ml). The aqueous layer was extracted with $AcOEt$ (5 ml $\times$ 3), the combined organic phase was washed with water (10 ml), brine (10 ml), and dried ($MgSO_4$), then concentrated to give an oil which was purified by preparative TLC (10% $AcOEt$ in hexane) to give **8a** (14.1 mg, 79%, 62% ee) as a colorless oil: $[\alpha]_D^{26} + 21.7^\circ$ ($c=0.63$, $CHCl_3$); IR (neat) cm^{-1} : 2938, 1701. ^{19}F -NMR δ : -153.2 (m). ^1H -NMR ($CDCl_3$) δ : 1.60 (d, $J=22.2$ Hz, 3H, Me), 2.21-2.36 (m, 1H, $CHHAr$), 2.43-2.57 (m, 1H, $CHHAr$), 3.01 (ddd, $J=17.3$, 9.3, 5.1 Hz, 1H, $CHHAr$), 3.20 (dt, $J=17.3$, 5.3 Hz, 1H, $CHHAr$), 7.26 (d, $J=7.6$ Hz, 1H, ArH), 7.35 (t, $J=7.3$, 1.5 Hz, 1H, ArH), 7.52 (td, $J=7.3$, 1.5 Hz, 1H, ArH), 8.07 (dd, $J=7.6$, 1.5 Hz, 1H, ArH). MS m/z 178 (M^+). HRMS Calcd for $C_{11}H_{11}FO$ 178.0794. Found 178.0801.

(S)-2-Ethyl-2-fluoro-1-tetralone (8b) Fluorination of 2-ethyl-1-tetralone (15.4 mg, 0.1 mmol) with a 1 M solution of LHMDS (1.5 ml, 1.5 mmol) and (S)-2 (36 mg, 1.2 mmol) gave **8b** (14.6 mg, 79%, 44% ee) as a light yellow oil after purification by silica gel column chromatography (15% $AcOEt$ in hexane). $[\alpha]_D^{26} - 27.6^\circ$ ($c=0.62$, $CHCl_3$). IR (neat) cm^{-1} : 3019, 1700. ^{19}F -NMR ($CDCl_3$, $CFCl_3$) δ : -163.2 (m); ^1H -NMR ($CDCl_3$) δ : 1.04 (t, $J=7.3$ Hz, 3H, Me), 1.93 (m, 2H, CH_2), 2.39 (m, 2H, CH_2), 3.09 (m, 2H, CH_2Ar), 7.25 (d, $J=7.6$ Hz, 1H, ArH), 7.35 (t, $J=7.6$ Hz, 1H, ArH), 7.52 (t, $J=7.6$ Hz, 1H, ArH), 8.06 (d, $J=7.8$ Hz, 1H, ArH). MS m/z : 192 (M^+), 173 ($M^+ - HF$), 163 ($M^+ - Et$). HRMS Calcd for $C_{12}H_{13}FO$: 192.0950. Found 192.0967.

(R)-5-Methoxy-2-ethyl-2-fluoro-1-tetralone (8c) Fluorination of 5-methoxy-2-ethyl-1-tetralone (21 mg, 0.1 mmol) with a 1 M solution of LHMDS (1.5 ml, 1.5 mmol) and (R)-2 (36 mg, 1.2 mmol) gave **8c** (13.2 mg, 59%, 60% ee) as a light yellow oil after purification by silica gel column chromatography (15% $AcOEt$ in hexane). $[\alpha]_D^{26} + 16.8^\circ$ ($c=0.43$, $CHCl_3$). IR (neat) cm^{-1} : 3019, 1700. ^{19}F -NMR ($CDCl_3$, $CFCl_3$) δ : -163.9 (m). ^1H -NMR ($CDCl_3$) δ : 1.02 (t, $J=7.3$ Hz, 3H, Me), 1.89 (m, 2H, CH_2), 2.34 (m, 2H, CH_2), 2.78 (m, 1H, $CHHAr$), 3.15 (m, 1H, $CHHAr$), 3.87 (s, 3H, OMe), 7.04 (d, $J=8.1$ Hz, 1H, ArH), 7.32 (t, $J=7.8$ Hz, 1H, ArH), 7.65 (d, $J=7.8$ Hz, 1H, ArH). MS m/z : 223 ($M^+ + 1$), 222 (M^+), 202 ($M^+ - HF$), 202 ($M^+ - Et$). HRMS Calcd for $C_{13}H_{15}FO_2$: 222.1056. Found 222.1065.

(S)-2-Benzyl-2-fluoro-1-tetralone (8d) Fluorination of 2-benzyl-1-tetralone (23.6 mg, 0.1 mmol) with a 1 M solution of LHMDS (1.5 ml, 1.5 mmol) and (S)-2 (36 mg, 1.2 mmol) gave **8d** (14 mg, 55%, 49% ee) as a light yellow oil after purification by silica gel column chromatography (15% $AcOEt$ in hexane). $[\alpha]_D^{26} - 28.6^\circ$ ($c=0.54$, $CHCl_3$). IR (neat) cm^{-1} : 3019, 1734. ^{19}F -NMR ($CDCl_3$, $CFCl_3$) δ : -158.02 (m); ^1H -NMR ($CDCl_3$) δ : 1.98-2.25 (m, 2H, CH_2), 2.89-3.07 (m, 3H, CH_2Ar , $CHHAr$), 3.26 (dd, $J=17.6$, 14.6 Hz, 1H, $CHHAr$), 7.19-7.26 (m, 6H, ArH), 7.30 (t, $J=7.6$ Hz, 1H, ArH), 7.47 (td, 1H, $J=7.6$, 1.5 Hz, ArH), 8.03 (dd, 1H, $J=7.6$, 1.5 Hz, ArH). MS m/z : 192 (M^+), 173 ($M^+ - HF$), 163 ($M^+ - Et$). HRMS Calcd for

$C_{17}H_{15}FO$: 254.1107. Found 254.1103.

(-)-2-Carbomethoxy-2-fluoro-1-tetralone (8e) Fluorination of 2-ethyl-1-tetralone (20.4 mg, 0.1 mmol) with a 1 M solution of LHMDS (1.5 ml, 1.5 mmol) and (S)-2 (36 mg, 1.2 mmol) gave **8e** (16.2 mg, 73%, 43% ee) as a light yellow oil after purification by silica gel column chromatography (30% $AcOEt$ in hexane). $[\alpha]_D^{26} - 6.7^\circ$ ($c=0.71$, $CHCl_3$). IR (neat) cm^{-1} : 3020, 1765, 1696. ^{19}F -NMR ($CDCl_3$, $CFCl_3$) δ : -164.68 (dd, $J=22.2$, 11.1 Hz). ^1H -NMR ($CDCl_3$) δ : 2.51-2.85 (m, 2H, CH_2), 3.02-3.28 (m, 2H, CH_2Ar), 3.84 (s, 3H, OCH₃), 7.28 (d, $J=7.6$ Hz, 1H, ArH), 7.38 (t, $J=7.6$ Hz, 1H, ArH), 7.56 (td, $J=7.6$, 1.5 Hz, 1H, ArH), 8.09 (dd, $J=7.6$, 1.5 Hz, 1H, ArH). MS m/z : 192 (M^+), 173 ($M^+ - HF$), 163 ($M^+ - Et$). HRMS Calcd for $C_{12}H_{11}FO_3$: 222.2123. Found 222.2116.

(S)-2-Methyl-2-fluoro-1-indanone (8f) Fluorination of 2-methyl-1-indanone (14.6 mg, 0.1 mmol) with a 1 M solution of LHMDS (1.5 ml, 1.5 mmol) and (S)-2 (36 mg, 1.2 mmol) gave **8f** (12.1 mg, 74%, 52% ee) as a light yellow oil after purification by silica gel column chromatography (10% $AcOEt$ in hexane). $[\alpha]_D^{26} - 20.7^\circ$ ($c=0.60$, $CHCl_3$). IR (neat) cm^{-1} : 3023, 1730. ^{19}F -NMR δ : -152.8 (quintet d, $J=22.5$, 11 Hz). ^1H -NMR (270 MHz) δ : 1.63 (d, $J=22.7$ Hz, 3H, Me), 3.30 (dd, $J=17.6$, 11.3 Hz, 1H, $CHHAr$), 3.47 (dd, $J=22.1$, 17.6 Hz, 1H, $CHHAr$), 7.43 (t, $J=7.6$ Hz, 2H, ArH), 7.66 (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.

(R)-2-Benzyl-2-fluoro-1-indanone (8g) Fluorination of 2-benzyl-1-indanone (22.2 mg, 0.1 mmol) with a 1 M solution of LHMDS (1.5 ml, 1.5 mmol) and (R)-2 (36 mg, 1.2 mmol) gave **8g** (9.6 mg, 40%, 57% ee) as a light yellow oil after purification by silica gel column chromatography (benzene): $[\alpha]_D^{26} + 32.9^\circ$ ($c=0.75$, $CHCl_3$). IR (neat) cm^{-1} : 3023, 1726. ^{19}F -NMR δ : -154.72 (m). ^1H -NMR (270 MHz) δ : 2.95 (dd, $J=30.3$, 14.2 Hz, 1H, $CHHAr$), 3.15 (dd, $J=22.9$, 17.8 Hz, 1H, $CHHAr$), 3.39 (dd, $J=17.8$, 12.5 Hz, 1H, $CHHAr$), 3.41 (t, $J=14.1$ Hz, 1H, $CHHAr$), 7.25-7.30 (m, 5H, ArH), 7.43 (m, 2H, ArH), 7.61 (td, $J=7.6$, 1.2 Hz, 1H, ArH), 7.81 (d, $J=7.6$ Hz, 1H, ArH). MS m/z 240 (M^+), 221 ($M^+ - HF$). HRMS Calcd for $C_{16}H_{13}FO$: 240.0950. Found 240.0953.

(+)-2-*p*-Methoxybenzyl-2-fluoro-1-indanone (8h) Fluorination of 2-*p*-methoxybenzyl-1-indanone (25.2 mg, 0.1 mmol) with a 1 M solution of LHMDS (1.5 ml, 1.5 mmol) and (R)-2 (36 mg, 1.2 mmol) gave **8h** (19 mg, 70%, 69% ee) as a light yellow oil after purification by silica gel column chromatography (50% CH_2Cl_2 in hexane). $[\alpha]_D^{26} + 46.2^\circ$ ($c=0.56$, $CHCl_3$). IR (neat) cm^{-1} : 3018, 1726. ^{19}F -NMR ($CDCl_3$, $CFCl_3$) δ : -154.8 (m). ^1H -NMR ($CDCl_3$) δ : 2.92 (dd, $J=29.7$, 14.3 Hz, 1H, $CHHAr$), 3.15 (dd, $J=22.8$, 17.3 Hz, 1H, $CHHAr$), 3.35 (m, 2H, CH_2Ar), 3.78 (s, 3H, OMe), 6.82 (d, $J=8.6$ Hz, 2H, ArH), 7.18 (d, $J=8.6$ Hz, 2H, ArH), 7.39 (dd, $J=13.2$, 7.6 Hz, 2H, ArH), 7.61 (t, $J=7.6$ Hz, 1H, ArH), 7.80 (d, $J=7.6$ Hz, 1H, ArH). MS m/z : 271 ($M^+ + 1$), 270 (M^+), 250 ($M^+ - HF$). HRMS Calcd for $C_{17}H_{15}FO_2$: 270.1056. Found 270.1051.

(-)-5,6-Dimethoxy-2-benzyl-2-fluoro-1-indanone (8i) Fluorination of 5,6-dimethoxy-2-benzyl-1-indanone (28.2 mg, 0.1 mmol) with a 1 M solution of LHMDS (1.5 ml, 1.5 mmol) and (S)-2 (36 mg, 1.2 mmol) gave **8i** (16.8 mg, 56%, 60% ee) as a light yellow oil after purification by silica gel column chromatography (50% CH_2Cl_2 in hexane). $[\alpha]_D^{26} - 57.8^\circ$ ($c=0.55$, $CHCl_3$). IR (neat) cm^{-1} : 3021, 1710. ^{19}F -NMR ($CDCl_3$, $CFCl_3$) δ : -153.5 (m); ^1H -NMR ($CDCl_3$) δ : 2.89 (dd, $J=29.8$, 14.1 Hz, 1H, $CHHAr$), 2.98 (dd, $J=22.9$, 17.5 Hz, 1H, $CHHAr$), 3.23 (dd, $J=17.5$, 12.0 Hz, 1H, $CHHAr$), 3.33 (t, $J=13.5$ Hz, 1H, $CHHAr$), 3.84 (s, 1H, OMe), 3.87 (s, 1H, OMe), 6.68 (s, 1H, ArH), 7.13 (s, 1H, ArH), 7.20 (m, 5H, ArH). MS m/z : 301 ($M^+ + 1$), 300 (M^+), 280 ($M^+ - HF$). HRMS Calcd for $C_{18}H_{17}FO_3$: 300.1162. Found 300.1174.

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