Expeditious Synthesis of 3,4-Dihydro-2*H*-1λ^6-benzo[*e*][1,2]thiazine 1,1-Dioxides

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A novel pathway for the preparation of 3,4-dihydro-2*H*-1λ^6-benzo[*e*][1,2]thiazine 1,1-dioxides 3 *via* an *ortho*-methyl lithiation/cyclization reaction of *N*-acyl-*o*-toluenesulfonamides 5 is reported. Readily available *N*-acyl-*o*-toluenesulfonamides 5 were treated with 2 eq of *n*-BuLi at −78 °C—0 °C to give the corresponding sultams 6 in moderate to good yields. The resulting sultams 6 were converted to saturated sultams 3, which can be considered as one carbon-extended homologues of the Oppolzer sultams 1, in high yields by hydrogenation. Studies on the scope and limitation of this annulation for the preparation of sultams are discussed. Demonstration of the feasibility of using the sultams 3 templates for an electorophilic fluorinating agent is also described.

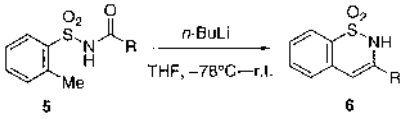
Key words sultam; lithiation; annulation; fluorination; α-fluoroketone

The Oppolzer sultams **1a** and **1b** are recognized as versatile and effective chiral auxiliaries.[1,2] Sultam **1b** substituted with a *tert*-butyl group is of particularly interest because of its consistently high stereo-induction. Enantiomerically pure **1b** is prepared from saccharin (**2**) in 4 steps *via* alkylation, reduction, chemical resolution and hydrolysis,[1a] or, alternatively, in 2 steps *via* asymmetric hydrogenation of the alkylated saccharin.[3] As a part of continuing studies aimed at the development of novel fluorinating agents based on sulfonamide templates,[4] we chose as a synthetic target the previously unknown sultam **3** (R=*tert*-Bu), which can be considered to be the one carbon-extended homologue of the Oppolzer sultam **1**. The new sultam **3** should be derived from 1,1-dioxo-1,4-dihydro-2*H*-1λ^6-benzo[*e*][1,2]thiazin-3-one (**4**), the homologue of **2**, by a procedure similar to that used by Oppolzer to prepare **1**. The only known method for preparation of **4** requires multi-step reactions and the overall yield is quite low.[5] Two groups[6,7] reported a short synthesis of the ring system **4** using lithiation of the aryl methyl group of *N*-methyl-*o*-toluenesulfonamides. However, adaption of these procedures to the preparation of **3** or **4** is limited by the difficulty of removing the methyl substituent at the nitrogen atom. Although other methods for construction of the ring systems present in **3** and **4** have been developed due to the pharmaceutical importance of such systems,[8] they are not adaptable to the synthesis of **3**. In this paper, we describe a simple synthesis of **3** using heteroannulation of *N*-acyl-*o*-toluenesulfonamides.

Results and Discussion

The 5/6-ring system **1** has been constructed in good yield by heteroannulation of *N*-acyl-2-chlorobenzenesulfonamides *via* an *ortho*-lithiation/cyclization reaction.[9] We therefore explored this method for the synthesis of the 6/6-ring system of **3** using an *ortho*-methyl lithiation/cyclization reaction of *N*-acyl-*o*-toluenesulfonamides **5**. No examples of such heteroannulations by *ortho*-methyl lithiation/cyclization of *N*-acyl-*o*-toluenesulfonamides have been reported previously. First, *N*-pivaloyl-*o*-toluenesulfonamide (**5a**), readily available from *o*-toluenesulfonamide with pivaloyl chloride in the presence of triethylamine, was treated with 2 eq of *n*-BuLi at −78 °C—0 °C to give the sultam **6a** in 74% yield. Similarly, reaction of *N*-cyclohexanecarbonyl-*o*-toluenesulfonamide (**5b**) and *N*-isobutyryl-*o*-toluenesulfonamide (**5c**) with *n*-BuLi gave the corresponding sultams **6b** and **6c** in 54% and 46%, respectively. However, a poor yield of sultam was obtained in the case of *N*-(3-methylbutanoyl)-*o*-toluenesulfonamide (**5d**) bearing a less bulky residue at the amide moiety (Table 1). Attempts to apply this procedure to the sterically unencumbered *N*-acetyl-*o*-toluenesulfonamide (**5f**) resulted in deacetylation (entry 6, Table 1), producing *o*-toluenesulfonamide (route b) rather than sultam (route a) (Fig. 2). In summary, we have demonstrated a process that leads to the formation of sultams in good yields when the groups attached to the sulfonamide nitrogen in **5** are reasonably bulky. Steric hindrance serves to prevent nucleophilic attack of *n*-BuLi on the carbonyl carbon.

Table 1. Synthesis of Sultams **6** by Heteroannulation of **5**



5 **6**

Entry	R	Sultam	Yield (%)
1	*tert*-Bu	**6a**	74
2	*c*-Hex	**6b**	54
3	iso-Pr	**6c**	46
4	iso-Bu	**6d**	20
5	Ph	**6e**	25
6	Me	**6f**	0

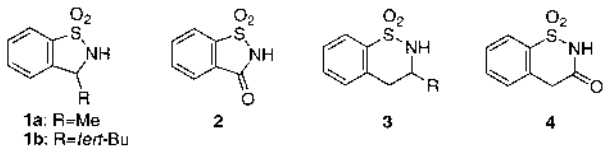


Fig. 1

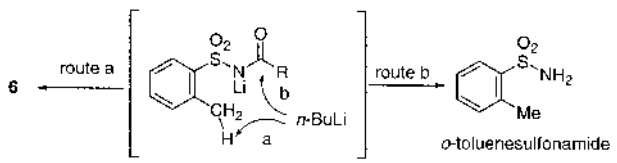


Fig. 2

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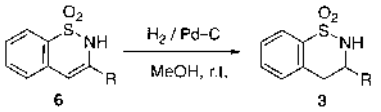
Table 2. Synthesis of Saturated Sultams **3**



Entry	R	Sultam **3**	Yield (%)
1	*tert*-Bu	**3a**	92
2	*c*-Hex	**3b**	91
3	iso-Pr	**3c**	95
4	iso-Bu	**3d**	71
5	Ph	**3e**	88

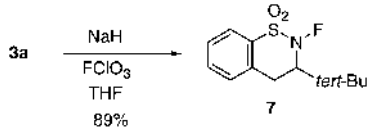
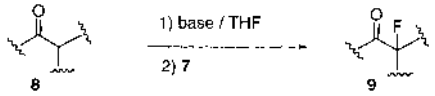
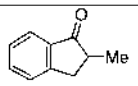
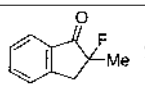
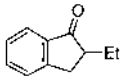
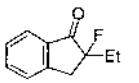
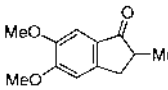
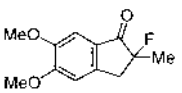
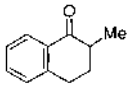
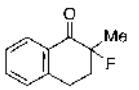
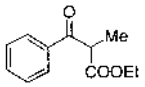
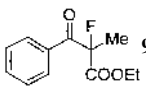


Chart 1

Table 3. Fluorination of Ketones **8** with **7**



Entry	Ketone **8**		Base	Product **9**		Yield (%)
1		**8a**	LDA		**9a**	77
2		**8b**	LDA		**9b**	56
3		**8c**	LDA		**9c**	79
4		**8d**	LDA		**9d**	56
5		**8e**	NaH		**9e**	46

The resulting sultams **6** were converted to the desired saturated sultams **3** in high yields by hydrogenation of the newly formed double bond in the presence of 10% Pd–C (Table 2).

We subsequently demonstrated the feasibility of using the sultams **3** as templates for new electrophilic fluorinating agents. The sultam **3a** was smoothly fluorinated with $FClO_3$[10] in the presence of NaH in tetrahydrofuran (THF) to generate *N*-fluorosultam **7** in 89% yield, which was used as a new agent for electrophilic fluorination. Results of the fluorination of aryl ketones with **7** are summarized in Table 3. As expected, sultam **7** was found to be a good agent for electrophilic fluorination[11] of certain aryl ketones.

Conclusions

We have developed a novel pathway for the preparation of 3,4-dihydro-2*H*-1λ^6-benzo[*e*][1,2]thiazine 1,1-dioxides **3** *via* an *ortho*-methyl lithiation/cyclization reaction of *N*-acyl-*o*-toluenesulfonamides **5**. Our method is the most expeditious among the previously reported methods[5—8] for construction of similar ring systems. Analytical scale optical resolution of the racemic sultam **3a** was successful using chiralcel OJ column (Rs=20.6, retention time of enantiomers: 8.27 and 45.78 min, conditions: hexane/isopropanol/trifluoroacetic acid (TFA)=80/20/0.1, flow rate=1.0 ml/min). The asymmetric synthesis of **3** as a template for enantioselective fluorination[4,12] 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. ^{1}H-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. Electron ionization (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.

General Procedure for Heteroannulation of 5: 3-*tert*-Butyl-2*H*-1λ^6-benzo[*e*][1,2]thiazine 1,1-Dioxide (6a) To a mechanically stirred solution of *N*-pivaloyl-*o*-toluenesulfonamide (225 mg, 1.00 mmol) in THF (5.0 ml) was added under nitrogen at −78 °C a 1.68 M solution of *n*-BuLi in hexane (1.30 ml, 2.20 mmol). The reaction mixture was allowed to warm to room temperature over 1 h and stirred for an additional 3—4 h at room temperature. Saturated aqueous NH_4Cl (20 ml) was added to the reaction mixture. The mixture was extracted with AcOEt (3×50 ml). The combined organic layers were washed with brine (10 ml), dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed (10% AcOEt in hexane) to give **6a** (175 mg, 74%).

Colorless crystals. mp 196—199 °C (CH_2Cl_2/hexane); IR (KBr) cm^{-1} 3252, 2965, 1624, 1314, 1180; ^{1}H-NMR (300 MHz) δ 1.30 (9H, s, *tert*-Bu), 6.19 (1H, s, PhCH=), 7.05 (1H, br s, NH), 7.36 (1H, d, J=7.7 Hz, ArH), 7.42 (1H, t, J=7.7 Hz, ArH), 7.55 (1H, t, J=7.7 Hz, ArH), 7.85 (1H, d, J=7.7 Hz, ArH); MS *m/z* 238 (M^++1), 237 (M^+). HR-MS Calcd for $C1_2H_{15}NO_2S$: 237.0824. Found 237.0834. *Anal.* Calcd for $C_{12}H_{15}NO_2S$: C, 60.73; H, 6.37; N, 5.90. Found: C, 60.57; H, 6.26; N, 5.91.

3-Cyclohexyl-2*H*-1λ^6-benzo[*e*][1,2]thiazine 1,1-Dioxide (**6b**): Colorless crystals. mp 203 °C (CH_2Cl_2/hexane); IR (KBr) cm^{-1} 3217, 2936, 1636, 1304, 1176; ^{1}H-NMR (300 MHz) δ 1.20—2.27 (11H, m, *c*-Hex), 6.08 (1H, s, PhCH=), 6.69 (1H, br s, NH), 7.33 (1H, d, J=7.7 Hz, ArH), 7.41 (1H, t, J=7.7 Hz, ArH), 7.55 (1H, t, J=7.7 Hz, ArH), 7.86 (1H, d, J=7.7 Hz, ArH); MS *m/z* 264 (M^++1), 263 (M^+); *Anal.* Calcd for $C_{14}H_{17}NO_2S$: C, 63.85; H, 6.51; N, 5.32. Found: C, 63.95; H, 6.36; N, 5.39.

3-Isopropyl-2*H*-1λ^6-benzo[*e*][1,2]thiazine 1,1-Dioxide (**6c**): Colorless crystals. IR (KBr) cm^{-1} 3181, 2960, 1643, 1302, 1166; ^{1}H-NMR (300 MHz) δ 1.27 (6H, d, J=7.1 Hz, $CH(C\underline{H}_3)_2$), 2.62 (1H, septet, J=7.1 Hz, $C\underline{H}(CH_3)_2$), 6.09 (1H, s, PhCH=), 7.13 (1H, br s, NH), 7.34 (1H, d, J=7.7 Hz, ArH), 7.41 (1H, t, J=7.7 Hz, ArH), 7.55 (1H, t, J=7.7 Hz, ArH), 7.86 (1H, d, J=7.7 Hz, ArH); MS *m/z* 224 (M^++1), 223 (M^+). HR-MS Calcd for $C_{11}H_{13}NO_2S$: 223.0667. Found 223.0685.

3-Isobutyl-2*H*-1λ^6-benzo[*e*][1,2]thiazine 1,1-Dioxide (**6d**): Colorless crystals. mp 129—131 °C (CH_2Cl_2/hexane); IR (KBr) cm^{-1} 3202, 2954, 1640, 1304, 1155; ^{1}H-NMR (300 MHz) δ 1.00 (6H, d, J=6.6 Hz, $CH(C\underline{H}_3)_2$), 2.00 (1H, m, $C\underline{H}(CH_3)_2$), 2.26 (2H, d, J=7.7 Hz, CH_2), 6.06 (1H, s, PhCH=), 6.69 (1H, br s, NH), 7.32 (1H, d, J=7.7 Hz, ArH), 7.42 (1H, t, J=7.7 Hz, ArH), 7.55 (1H, t, J=7.7 Hz, ArH), 7.87 (1H, d, J=7.7 Hz, ArH); MS *m/z* 238 (M^++1), 237 (M^+); *Anal.* Calcd for $C_{12}H_{15}NO_2S$: C, 60.73; H, 6.37; N, 5.90. Found: C, 60.57; H, 6.26; N, 5.91.

3-Phenyl-2*H*-1λ^6-benzo[*e*][1,2]thiazine 1,1-Dioxide (**6e**): Colorless crystals. mp 211—213 °C (CH_2Cl_2/hexane); IR (KBr) cm^{-1} 3190, 1623, 1313, 1167; ^{1}H-NMR (300 MHz) δ 6.69 (1H, s, PhCH=), 6.80 (1H, br s, NH), 7.48—7.95 (9H, m, ArH); MS *m/z* 258 (M^++1), 257 (M^+). HR-MS Calcd for $C_{14}H_{11}NO_2S$: 257.0510. Found 257.0516.

General Procedure for Hydrogenation of 6: 3-*tert*-Butyl-3,4-dihydro-2*H*-1λ^6-benzo[*e*][1,2]thiazine 1,1-Dioxide (3a) A solution of **6a** (224 mg,

0.950 mmol) and 10% Pd on charcoal (30 mg) in methanol (10 ml) was stirred at 20 °C under a H_2 atmosphere for 24 h. Filtration through celite, evaporation, and flash column chromatography on silica gel yielded **3a** (207 mg, 92%) which precipitated from CH_2Cl_2/hexane as colorless crystals. mp 161 °C (CH_2Cl_2/hexane); IR (KBr) cm^{-1} 3245, 2967, 1328, 1166; ^{1}H-NMR (300 MHz) δ 1.06 (9H, s, *tert*-Bu), 2.89 (1H, dd, J=17, 11 Hz, CHHAr), 2.96 (1H, dd, J=17, 5.5 Hz, CHHAr), 3.60 (1H, ddd, J=12, 11, 5.5 Hz, NCH<), 4.22 (1H, br d, J=12 Hz, NH), 7.25 (1H, d, J=7.7 Hz, ArH), 7.37 (1H, t, J=7.7 Hz, ArH), 7.45 (1H, t, J=7.7 Hz, ArH), 7.81 (1H, d, J=7.7 Hz, ArH); MS *m/z* 240 (M^++1), 239 (M^+), 182 (M^+−*tert*-Bu). HR-MS Calcd for $C_{12}H_{17}NO_2S$: 239.0980. Found 239.0991. *Anal.* Calcd for $C_{12}H_{17}NO_2S$: C, 60.22; H, 7.16; N, 5.85. Found: C, 60.53; H, 7.28; N, 5.90.

3-Cyclohexyl-3,4-dihydro-2*H*-1λ^6-benzo[*e*][1,2]thiazine 1,1-Dioxide (**3b**): Colorless crystals. mp 123 °C (CH_2Cl_2/hexane); IR (KBr) cm^{-1} 3233, 2929, 1307, 1164; ^{1}H-NMR (300 MHz) δ 1.04—2.01 (11H, m, *c*-Hex), 2.83 (1H, dd, J=17, 11 Hz, CHHAr), 2.91 (1H, dd, J=17, 5 Hz, CHHAr), 3.64 (1H, tdd, J=11, 6.6, 5 Hz, NCH<), 4.49 (1H, br d, J=11 Hz, NH), 7.19 (1H, d, J=7.7 Hz, ArH), 7.32 (1H, t, J=7.7 Hz, ArH), 7.40 (1H, t, J=7.7 Hz, ArH), 7.74 (1H, d, J=7.7 Hz, ArH); MS *m/z* 266 (M^++1), 265 (M^+), 182 (M^+−*c*-Hex); *Anal.* Calcd for $C_{14}H_{19}NO_2S$: C, 63.36; H, 7.22; N, 5.28. Found: C, 63.16; H, 7.18; N, 5.16.

3,4-Dihydro-3-isopropyl-2*H*-1λ^6-benzo[*e*][1,2]thiazine 1,1-Dioxide (**3c**): Colorless crystals. mp 109—110 °C (CH_2Cl_2/hexane); IR (KBr) cm^{-1} 3210, 2961, 1316, 1160; ^{1}H-NMR (300 MHz) δ 1.06 (3H, d, J=6.6 Hz, CH(CH$_3$)$_2$), 1.08 (3H, d, J=6.6 Hz, CH(CH$_3$)$_2$), 1.86 (1H, octet, J=6.6 Hz, CH(CH$_3$)$_2$), 2.85 (1H, dd, J=17, 11.5 Hz, CHHAr), 2.93 (1H, dd, J=17, 5 Hz, CHHAr), 3.65 (1H, tdd, J=11.5, 6.6, 5 Hz, NCH<), 4.37 (1H, br d, J=11.5 Hz, NH), 7.22 (1H, d, J=7.7 Hz, ArH), 7.36 (1H, t, J=7.7 Hz, ArH), 7.43 (1H, t, J=7.7 Hz, ArH), 7.78 (1H, d, J=7.7 Hz, ArH); MS *m/z* 226 (M^++1), 225 (M^+), 182 (M^+−iso-Pr); *Anal.* Calcd for $C_{11}H_{15}NO_2S$: C, 58.64; H, 6.71; N, 6.22. Found: C, 58.43; H, 6.87; N,6.17.

3,4-Dihydro-3-isobutyl-2*H*-1λ^6-benzo[*e*][1,2]thiazine 1,1-Dioxide (**3d**): Colorless crystals. mp 119—121 °C (CH_2Cl_2/hexane); IR (KBr) cm^{-1} 3248, 2961, 1316, 1164; ^{1}H-NMR (300 MHz) δ 0.96 (6H, d, J=6 Hz, CH(CH$_3$)$_2$), 1.41 (1H, ddd, J=14, 8, 5.5 Hz, CHH), 1.59 (1H, ddd, J=14, 8, 5.5 Hz, CHH), 1.92 (1H, m, CH(CH$_3$)$_2$), 2.76 (1H, dd, J=17, 11.5 Hz, CHHAr), 2.92 (1H, dd, J=17, 4 Hz, CHHAr), 3.95 (1H, m, NCH<), 4.34 (1H, br d, J=12 Hz, NH), 7.19 (1H, d, J=7.7 Hz, ArH), 7.35 (1H, t, J=7.7 Hz, ArH), 7.42 (1H, t, J=7.7 Hz, ArH), 7.78 (1H, d, J=7.7 Hz, ArH); MS *m/z* 240 (M^++1), 239 (M^+), 182 (M^+−iso-Bu). *Anal.* Calcd for $C_{12}H_{17}NO_2S$: C, 60.22; H, 7.16; N, 5.85. Found: C, 59.99; H, 6.95; N, 5.65.

3,4-Dihydro-3-phenyl-2*H*-1λ^6-benzo[*e*][1,2]thiazine 1,1-Dioxide (**3e**): Colorless crystals. mp 135—136 °C (CH_2Cl_2/hexane); IR (KBr) cm^{-1} 3225, 1317, 1159; ^{1}H-NMR (300 MHz) δ 3.25 (1H, d, J=6.6 Hz, CHHAr), 3.26 (1H, d, J=10 Hz, CHHAr), 4.84 (1H, br d, J=10 Hz, NH), 4.98 (1H, td, J=10, 6.6 Hz, NCH<), 7.28 (1H, d, J=7.7 Hz, ArH), 7.36—7.51 (7H, m, ArH), 7.84 (1H, d, J=7.7 Hz, ArH); MS *m/z* 260 (M^++1), 259 (M^+); *Anal.* Calcd for $C_{14}H_{13}NO_2S$: C, 64.84; H, 5.05; N, 5.40. Found: C, 64.45; H, 5.05; N,5.25.

3-*tert*-Butyl-3,4-dihydro-2-fluoro-2*H*-1λ^6-benzo[*e*][1,2]thiazine 1,1-Dioxide (7) A solution of **3a** (48 mg, 0.20 mmol) in THF (3.0 ml) was treated with NaH (60% dispersion in mineral oil, 12.0 mg, 0.30 mmol) under N_2 at 0 °C and the mixture was stirred at 0 °C for 1 h. To the mixture was introduced freshly generated $FClO_3$ gas at 0 °C for 3 h. Insoluble materials were removed by filtration and concentration of the filtrate gave a residue, which was chromatographed on silica gel (25% AcOEt in hexane) to give **7** (46.0 mg, 89%) as colorless crystals. mp 104—106 °C (CH_2Cl_2/hexane); IR (KBr) cm^{-1} 2967, 1360, 1183; ^{19}F-NMR δ −72.4 (br s, NF); ^{1}H-NMR (270 MHz) δ 1.16 (9H, s, *tert*-Bu), 2.93, 3.30, 4.12 (total 1H, br d, [J=17 Hz], br m, br, CH$_2$Ar, NCH<), 7.35 (1H, d, J=7.6 Hz, ArH), 7.47 (1H, t, J=7.6 Hz, ArH), 7.57 (1H, t, J=7.6 Hz, ArH), 7.93 (1H, d, J=7.6 Hz, ArH); MS *m/z* 258 (M^++1), 257 (M^+), 237 (M^+−HF), 200 (M^+−*tert*-Bu); *Anal.* Calcd for $C_{12}H_{16}FNO_2S$: C, 56.01; H, 6.27; N, 5.44. Found: C, 55.77; H, 6.18; N, 5.41.

General Procedure for Fluorination of Ketones with 7: 2-Fluoro-2-methyl-1-indanone (9a) To a mechanically stirred solution of diisopropylamine (0.048 ml, 0.37 mmol) in THF (1.0 ml) was added under nitrogen at 0 °C a 1.68 M solution of *n*-BuLi in hexane (0.22 ml, 0.37 mmol). After the mixture was stirred for 15 min at 0 °C and then cooled to −78 °C, a solution of the 2-methyl-1-indanone (**8a**) (45.0 mg, 0.31 mmol) in THF (1.0 ml) was added. The reaction mixture was stirred for 1 h at 0 °C and then re-cooled to −40 °C. A solution of **7** (87.0 mg, 0.34 mmol) in THF (1 ml) was slowly added and the reaction mixture 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), brine (10 ml), dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed (10% AcOEt in hexane) by preparative TLC to give **9a** (38.9 mg, 77%) as a light-yellow oil. IR (neat) cm^{-1} 3023, 1730, 1218; ^{19}F-NMR δ −152.8 (quintet d, J=22.5, 11 Hz); ^{1}H-NMR (270 MHz) δ 1.63 (d, J=22.5 Hz, 3H, Me), 3.30 (dd, J=17, 11 Hz, 1H, CHHAr), 3.47 (dd, J=22.5, 17 Hz, 1H, CHHAr), 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); HR-MS Calcd for $C_{10}H_9FO$: 164.0637. Found 164.0626; $C_{10}H_{10}FO$: 165.0715. Found 165.0694.

2-Ethyl-2-fluoro-1-indanone (**9b**): Light-yellow oil. IR (neat) cm^{-1} 3021, 1727, 1216; ^{19}F-NMR δ −160.0 (tdd, J=26, 19, 15 Hz); ^{1}H-NMR (270 MHz) δ 1.01 (t, J=7.4 Hz, 3H, Me), 1.75—2.13 (m, 2H, CH$_2$), 2.35 (d, J=19 Hz, 1H, CHHAr), 3.36 (d, J=15 Hz, 1H, CHHAr), 7.43 (m, 2H, ArH), 7.66 (t, J=7.6 Hz, 1H, ArH); HR-MS Calcd for $C_{11}H_{11}FO$: 178.0794. Found 178.0793.

5,6-Dimethoxy-2-fluoro-2-methyl-1-indanone (**9c**): Colorless crystals. mp 132 °C (CH_2Cl_2/hexane); ^{19}F-NMR δ −151.7 (quintet d, J=22.5, 11 Hz); ^{1}H-NMR (270 MHz) δ 1.62 (3H, d, J=22.5 Hz, CH$_3$), 3.21 (1H, dd, J=17, 11 Hz, CHHAr), 3.37 (1H, dd, J=22.5, 17 Hz, CHHAr), 3.92 (3H, s, OCH$_3$), 3.99 (3H, s, OCH$_3$), 6.85 (1H, s, ArH), 7.22 (1H, s, ArH); MS *m/z* 225 (M^++1), 224 (M^+), 209 (M^+−CH$_3$), 204 (M^+−HF); *Anal.* Calcd for $C_{12}H_{13}FO_3$: C, 64.28; H, 5.84. Found: C, 63.99; H, 5.79.

2-Fluoro-2-methyl-1-tetralone (**9d**): Colorless oil. IR (neat) cm^{-1} 2938, 1701; ^{19}F-NMR δ −155.1 (qdd, J=22, 16.6, 9.2 Hz); ^{1}H-NMR (270 MHz) δ 1.60 (t, J=22 Hz, 3H, Me), 2.21—2.57 (m, 2H, CH$_2$), 2.95—3.23 (m, 2H, CH$_2$Ar), 7.25—8.09 (m, 4H, ArH); MS *m/z* 178 (M^+); HR-MS Calcd for $C_{11}H_{11}FO$: 178.0794. Found 178.0801.

Ethyl 2-Benzoyl-2-fluoropropionate (9e) To a stirred solution of ethyl 2-benzoylpropionate (40 mg, 0.19 mmol) in dry THF (2.0 ml) was added 60% NaH (10 mg, 0.23 mmol) at 0 °C. After stirring for 1 h, a solution of **7** (0.21 mmol) in THF (1.0 ml) was added and stirred overnight. Usual work-up and column chromatography gave ethyl 2-benzoyl-2-fluoropropionate (19.9 mg, 46%) as a colorless oil. Spectral data for **9e** (^{1}H-NMR, ^{19}F-NMR, IR, mass) corresponded to literature value.[4a)]

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