Methyl NFSI: Atom-economical alternative to NFSI shows higher fluorination reactivity under Lewis acid-catalysis and non-catalysis

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Experimental section

General methods

All reactions were performed in oven-dried glassware under a positive pressure of nitrogen. Solvents were transferred via syringe and were introduced into the reaction vessels though a rubber septum. All reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica-gel (60-F254). The TLC plates were visualized with UV light and 7% phosphomolybdic acid or anisaldehyde in EtOH or KMnO₄ in water/heat. Column chromatography was carried out on a column packed with silica-gel 60N spherical neutral size 63-210 μm or YAMAZENE HI-FLASH COLUMNS. The ¹H-NMR (300 MHz, 400 MHz), ¹⁹F-NMR (282 MHz), ¹³C-NMR (75.5 MHz, 100.7 MHz) spectra for solution in CDCl₃ were recorded on a Varian Mercury 300 and Bruker Avance 400. Chemical shifts (δ) are expressed in ppm downfield from internal TMS (δ = 0.00), CHCl₃ (δ = 77.0) or C₆F₆ (δ = −162.2). GC analysis were carried out SHIMADZU GC-2014 using GC Capillary Column CBP5-M25-025. Mass spectra were recorded on a SHIMADZU GCMS-QP5050A (EI-MS) and SHIMAZU LCMS-2020 (ESI-MS). High resolution mass spectrometries were recorded on a Waters Synapt G2 HDMS (ESI-MS). Infrared spectra were recorded on a JASCO FT/IR-4100 spectrometer. Melting points were recorded on a BUCHI M-565.

The β-keto esters 2a-r are known compounds, and these compounds were purchased or synthesized according to the literature procedures.³⁻⁵

The oxindoles 4a-e are synthesized according to the literature procedures.⁶⁻⁸

The malonic diesters 6a-e are known compounds, and these compounds were purchased or synthesized according to the literature procedures.¹¹

Other reagents and solvents were purchased from commercial source.
GC analysis

Table S1. GC-analysis of titanium-catalyzed fluorination of 2b

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Me-NFSI GC-Yield (%)</th>
<th>NFSI GC-Yield (%)</th>
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<tbody>
<tr>
<td>0.5</td>
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<td>21</td>
</tr>
<tr>
<td>1</td>
<td>91</td>
<td>26</td>
</tr>
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<td>98</td>
<td>45</td>
</tr>
<tr>
<td>24</td>
<td>96</td>
<td>83</td>
</tr>
</tbody>
</table>

Figure S1

The stirring mixture of *tert*-butyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate 2b (232.3 mg, 1.0 mmol), Me-NFSI (229.2 mg, 1.20 mmol, 1.2 equiv.) or NFSI (378.3 mg, 1.2 mmol, 1.2 equiv.) in CH₂Cl₂ (10.0 mL, 0.1 M) was added Ti(OiPr)₄ (30.0 μL, 0.10 mmol, 10 mol%) and stirred at room temperature under nitrogen atmosphere. The reaction mixture was added *n*-hexadecane as an initial standard. The reaction was monitored by GC.
Table S2. GC-analysis of titanium-catalyzed fluorination of 2a

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Me-NFSI GC-Yield (%)</th>
<th>NFSI GC-Yield (%)</th>
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<tbody>
<tr>
<td>(10 min)</td>
<td>–</td>
<td>52</td>
</tr>
<tr>
<td>(20 min)</td>
<td>–</td>
<td>49</td>
</tr>
<tr>
<td>0.5</td>
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<td>56</td>
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<td>1</td>
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<td>68</td>
</tr>
<tr>
<td>24</td>
<td>96</td>
<td>71</td>
</tr>
</tbody>
</table>

Figure S2

The stirring mixture of methyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate 2a (28.5 mg, 0.15 mmol), Me-NFSI (34.4 mg, 0.180 mmol, 1.2 equiv.) or NFSI (56.7 mg, 0.18 mmol, 1.2 equiv.) in CH₂Cl₂ (1.5 mL, 0.1 M) was added Ti(O’Pr)₄ (4.4 μL, 0.015 mmol, 10 mol%) and stirred at room temperature under nitrogen atmosphere. The reaction mixture was added n-dodecane as an initial standard. The reaction was monitored by GC.
Table S3. GC-analysis of fluorination of 2a under catalyst-free conditions.

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Me-NFSI GC-Yield (%)</th>
<th>NFSI GC-Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Run 1</td>
<td>Run 2</td>
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<tr>
<td>0.5</td>
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<td>53</td>
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<tr>
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</tr>
<tr>
<td>24</td>
<td>90</td>
<td>85</td>
</tr>
</tbody>
</table>

![Graph](image)

**Figure S3**
The mixture of methyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate 2a (38.0 mg, 0.2 mmol) and Me-NFSI (45.6 mg, 0.24 mmol, 1.2 equiv) or NFSI (75.7 mg, 0.24 mmol, 1.2 equiv) were cooled at \(-40\, ^\circ\text{C}\) and dissolved in \(-40\, ^\circ\text{C}\) MeOH (4.0 mL, 0.05 M) via cannula. The mixture was warm to room temperature and stirred under nitrogen atmosphere. The reaction mixture was added \(n\)-dodecane (11.3 mg) as an initial standard. The reaction was monitored by GC. This reaction was repeated four times.

Table S4. Optimization of reaction conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Lewis acid</th>
<th>Yield (%)(^b)</th>
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<tr>
<td>1</td>
<td>Ni(acac)(_2)</td>
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</tr>
<tr>
<td>2</td>
<td>Cu(acac)(_2)</td>
<td>Quant.</td>
</tr>
<tr>
<td>3</td>
<td>Zn(acac)(_2)</td>
<td>Quant.</td>
</tr>
<tr>
<td>4</td>
<td>Ti(OPr)(_4)</td>
<td>Quant.</td>
</tr>
</tbody>
</table>

\(^a\) Reaction conditions: 2b (0.1 mmol), Me-NFSI (1.2 equiv.), Lewis acid (10 mol\%), CH\(_2\)Cl\(_2\) (1 mL, 0.1 M), \(^b\) Isolated yield.
NMR experiment 1
In NMR tube, NFSI (3.2 mg, 0.01 mmol) or Me-NFSI (1.9 mg, 0.01 mmol) was dissolved in CD$_2$Cl$_2$ (0.5 mL), then, added the one drop of CF$_3$Ph as an initial standard (δ -63.000). These mixing samples were measured the $^{19}$F-NMR, then added Ti(O$i$Pr)$_4$ (3.0 μL, 0.01 mmol, 1.0 equiv.) and shaked room temperature. 30 min later, these mixing samples were measured the $^{19}$F-NMR again.

**Figure S4.** Me-NFSI: $^{19}$F-NMR (CD$_2$Cl$_2$, 282 MHz) δ 44.381.

**Figure S5.** Me-NFSI + Ti(O$i$Pr)$_4$: $^{19}$F-NMR (CD$_2$Cl$_2$, 282 MHz) δ 44.400.
Figure S6. NFSI: $^{19}$F-NMR (CD$_2$Cl$_2$, 282 MHz) $\delta$ 38.331

Figure S7. NFSI + Ti(O$^i$Pr)$_4$ (1:1): $^{19}$F-NMR (CD$_2$Cl$_2$, 282 MHz) $\delta$ 38.331
NMR experiment 2
In NMR tube, Me-NFSI (3.8 mg, 0.02 mmol) was dissolved in CDCl₃ (0.5 mL), then, added the one drop of CF₃Ph as an initial standard (δ -63.000). This mixing samples were measured the ¹⁹F-NMR, then added Ti(OPr)₄ (3.0 μL, 0.01 mmol, 0.5 equiv. or 6.0 μL, 0.02 mmol, 1.0 equiv.) and shaked room temperature. 30 min later, these mixing samples were measured the ¹⁹F-NMR again.

**Figure S8.** Me-NFSI: ¹⁹F-NMR (CDCl₃, 282 MHz) δ 44.425

**Figure S9.** Me-NFSI+ Ti(OPr)₄ (2:1): ¹⁹F-NMR (CDCl₃, 282 MHz) δ 44.449
Figure S10. Me-NFSI+ Ti(O^Pr)_4 (1:1): $^{19}$F-NMR (CDCl$_3$, 282 MHz) $\delta$ 44.462
## Computations

### Table S5.

<table>
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<th>Ti-Me-NFSI (coformer 1)</th>
<th>Ti-Me-NFSI (conformer 2)</th>
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<tr>
<td><strong>Energy:</strong></td>
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<td>-5724150.48 kJ/mol</td>
<td>-5724148.37 kJ/mol</td>
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<tr>
<td><strong>Electrostatic:</strong></td>
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<td>+0.035</td>
<td>-0.013</td>
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<tr>
<td><strong>Mulliken:</strong></td>
<td>-0.197</td>
<td>-0.144</td>
<td>-0.132</td>
</tr>
<tr>
<td><strong>Natural:</strong></td>
<td>-0.221</td>
<td>-0.176</td>
<td>-0.172</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th></th>
<th>NFSI</th>
<th>Ti-NFSI (coformer 1)</th>
<th>Ti-NFSI (conformer 2)</th>
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<tr>
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<td>-6731078.01 kJ/mol</td>
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<td><strong>Electrostatic:</strong></td>
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<td><strong>Mulliken:</strong></td>
<td>-0.199</td>
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<tr>
<td><strong>Natural:</strong></td>
<td>-0.223</td>
<td>-0.188</td>
<td>-0.184</td>
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Calculated by B3LYP/6-31G*
Synthesis of Me-NFSI (N-Fluoromethansulfonimid)

The stirring mixture of ammonium chloride (1.38 g, 25.8 mmol) in water (16 mL) at 0 °C was slowly added a solution of mesyl chloride (5.00 mL, 64.6 mmol, 2.5 equiv.) in acetone (6 mL) and stirred at 0 °C for 1 hour. Aqueous sodium hydroxide solution (2.6 mL, 10 M) was added slowly and stirred at 0 °C. The reaction mixture was monitored by pH indicator paper turn to acidic. Aqueous sodium hydroxide solution (2.6 mL, 10 M) was added repeatedly slowly and stirred at 0 °C until reaction mixture remained basic. The reaction mixture was quenched with Conc. hydrochloric acid and extracted with ethyl acetate five times and CH₂Cl₂ five times. The organic layer was washed with brine, dried with Na₂SO₄, and concentrated under reduced pressure. The residue was purified by recrystallization (1,2-Dichloroethane) to give bismethanesulfonimide (2.73 g, 61%).

The stirring mixture of bismethanesulfonimide (1.37 g, 7.91 mmol.), NaF (3.27 g, 78.9 mmol, 10.0 equiv) in CH₃CN (100 mL) was stirred at −40 °C. A gaseous mixture of F₂ in N₂ (10% v/v) was introduced for 30 min with stirring. N₂ gas was introduced to remove the residual F₂ gas. The insoluble solid was removed by filtration with celite and washed with CH₂Cl₂. The filtrate was dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 8/2) to give N-Fluoromethansulfonimid (1.15 g, 76%) as colorless solid.

1H-NMR (CDCl₃, 300 MHz) δ 3.42 (s, 6H); 19F-NMR (CDCl₃, 282 MHz) δ −44.65 (s, 1F);
13C-NMR (CDCl₃, 75.5 MHz) δ 40.2 ; IR (KBr) 3034, 3011, 2943, 1654, 1508, 1323, 1173, 817 cm⁻¹; MS (ESI, m/z) 172 [M-F]; MP : 48.0-49.0 °C (CH₂Cl₂).

This compound has been previously prepared\(^2\)

**General procedure for the fluorination of carbonyl compounds 2.\(^2\)**

**Method A [Ti(O\(^i\)Pr\(_4\)]**

\[
\begin{align*}
\text{CH}_2\text{Cl}_2, \text{rt}, &\text{Time} \\
\beta\text{-keto esters} (0.3 \text{ mmol}), &\text{Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH}_2\text{Cl}_2 (3.0 \text{ mL, 0.1 M}) \\
&\text{was added Ti(O}\(^i\)\text{Pr}\(_4\)) (8.8 \mu\text{L, 0.030 mmol, 10 mol\%}) \\
&\text{under nitrogen atmosphere and stirred at room temperature. The reaction was monitored by TLC} \\
&\text{with UV light and KMnO}_4 \text{ in water staining until starting material was consumed maximum} \\
&\text{24 h. The resulting mixture was quenched with saturated NaHCO}_3 \text{ aqueous solution and} \\
&\text{extracted with CH}_2\text{Cl}_2 \text{ three times. The organic layer was washed with brine, dried with} \\
&\text{Na}_2\text{SO}_4 \text{ and concentrated under reduced pressure. The residue was purified by silica gel} \\
&\text{column chromatography (n-hexane/ethyl acetate) to give } \alpha\text{-fluoro-}\beta\text{-ketoesters 3.}\n\end{align*}
\]

**Method B (MeOH)**

\[
\begin{align*}
\text{MeOH, rt, &Time} \\
\beta\text{-Keto esters} (0.3 \text{ mmol}) &\text{and Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) were dissolved in} \\
&\text{MeOH (3.0 mL, 0.1 M) and the reaction mixture was stirred at room temperature under} \\
&\text{nitrogen atmosphere. The reaction was monitored by TLC with UV light and KMnO}_4 \text{ in} \\
&\text{water staining until starting material was consumed maximum 24 h. The resulting mixture} \\
&\text{was concentrated under reduced pressure. The residue was purified by silica gel column} \\
&\text{chromatography (n-hexane/ethyl acetate) to give } \alpha\text{-fluoro-}\beta\text{-ketoesters 3.}\n\end{align*}
\]

**Methyl 2-fluoro-1-oxo-2,3-dihydro-1\(H\)-indene-2-carboxylate (3a)**

\[\text{\textsuperscript{2} R. Bohlmann, DE4313664, 1994.}\]
Method A; The stirring mixture of methyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate 2a (0.30 mmol, 57.1 mg), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH₂Cl₂ (3.0 mL, 0.1 M) was added Ti(OiPr)₄ (8.8 μL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 3 h. The resulting mixture was quenched with saturated NaHCO₃ aqueous solution and extracted with CH₂Cl₂ three times. The organic layer was washed with brine, dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 9/1) to give 3a (61.7 mg, 99%) as a colorless oil.

Method B; Methyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate 2a (57.1 mg, 0.30 mmol) and Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) were dissolved in MeOH (3.0 mL, 0.1 M) and the reaction mixture was stirred at room temperature under nitrogen atmosphere for 1 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 9/1) to give 3a (60.2 mg, 96%) as a colorless oil.

¹H-NMR (CDCl₃, 300 MHz) δ 7.85 (d, J = 7.2 Hz, 1H), 7.72 (t, J = 7.1 Hz, 1H), 7.52-7.45 (m, 2H), 3.86 (s, 3H), 3.82-3.74 (m, 1H), 3.45 (dd, J = 23.1, 17.8 Hz, 1H); ¹⁹F-NMR (CDCl₃, 282 MHz) δ −165.02 (dd, J = 24.3, 12.1 Hz, 1F); MS (ESI, m/z) 247 [M+K]+.

This compound has been previously prepared and characterized.

 tert-Butyl 2-fluoro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (3b)

Method A; The stirring mixture of tert-butyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate 2b (69.7 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH₂Cl₂ (3.0 mL, 0.1 M) was added Ti(OiPr)₄ (8.8 μL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 3 h. The resulting mixture was quenched with saturated NaHCO₃ aqueous solution and extracted with CH₂Cl₂ three times. The organic layer was washed with brine, dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified

by silica gel column chromatography \((n\text{-hexane/ ethyl acetate} = 9/1)\) to give \(3b\) (69.1 mg, 92%) as a colorless oil.

**Method B;** tert-Butyl 1-oxo-2,3-dihydro-\(1H\)-indene-2-carboxylate \(2b\) (69.7 mg, 0.30 mmol) and Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) were dissolved in MeOH (3.0 mL, 0.1 M) and the reaction mixture was stirred at room temperature under nitrogen atmosphere for 12 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography \((n\text{-hexane/ethyl acetate} = 9/1)\) to give \(3b\) (64.6 mg, 86%) as a colorless oil.

\(^1\)H-NMR (CDCl\(_3\), 300 MHz) \(\delta\) 7.84 (\(d, J = 7.4\) Hz, 1H), 7.69 (\(t, J = 7.1\) Hz, 1H), 7.51-7.44 (m, 2H), 3.73 (dd, \(J = 17.5, 10.9\) Hz, 1H), 3.40 (dd, \(J = 22.6, 17.5\) Hz, 1H), 1.44 (s, 9H);

\(^1\)F-NMR (CDCl\(_3\), 282 MHz) \(\delta\) -164.51 (dd, \(J = 22.6, 10.4\) Hz, 1F); MS (ESI, m/z) 289 [M+K\(^+\)].

This compound has been previously prepared and characterized\(^4\)

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**1-Adamantyl 2-fluoro-2,3-dihydro-1-oxo-1\(H\)-indene-2-carboxylate (2c)**

\(\text{Method A;}\) The stirring mixture of 1-adamantyl 2,3-dihydro-1-oxo-1\(H\)-indene-2-carboxylate \(2c\) (93.1 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH\(_2\)Cl\(_2\) (3.0 mL, 0.1 M) was added Ti(O\(^\text{iPr}\))\(_4\) (8.8 \(\mu\)L, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 3 h. The resulting mixture was quenched with saturated NaHCO\(_3\) aqueous solution and extracted with CH\(_2\)Cl\(_2\) three times. The organic layer was washed with brine, dried with Na\(_2\)SO\(_4\) and concentrated under reduced pressure. The residue was purified by silica gel column chromatography \((n\text{-hexane/ ethyl acetate} = 9/1)\) to give \(3c\) (92.1 mg, 93%) as a white solid.

**Method B;** 1-Adamantyl 2,3-dihydro-1-oxo-1\(H\)-indene-2-carboxylate \(2c\) (93.1 mg, 0.30 mmol) and Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv) were dissolved in MeOH (3.0 mL, 0.1 M) and the reaction mixture was stirred at room temperature under nitrogen atmosphere for 24

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The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography $\left(n\text{-}h e x a n e / e t h y l \ a c e t a t e = 9 / 1\right)$ to give $3c$ ($67.6$ mg, $69\%$) as a colorless oil.

$^{1}H$-NMR (CDCl$_3$, 300 MHz) δ $7.84 \ (d, J = 7.4$ Hz, $1H), 7.75$-$7.64 \ (m, 1H), 7.56$-$7.35 \ (m, 2H), $3.80$-$3.71 \ (m, 1H), 3.49$-$3.35 \ (m, 1H), $2.16 \ (d, J = 12.1$ Hz, $3H), 2.06 \ (s, 6H), 1.64 \ (s, 6H);$ $^{19}F$-NMR (CDCl$_3$, 282 MHz) δ $-164.64 \ (d d, J = 24.3, 10.4$ Hz, $1F); \ M S \ (E S I, m/z) 367 [M+K]^+.$

This compound has been previously prepared and characterized.$^{3}$

**Methyl 2-fluoro-6-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (3d)**

![Chemical Structure](image)

**Method A:** The stirring mixture of methyl 6-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate $2d$ ($61.3$ mg, $0.30$ mmol), Me-NFSI ($68.8$ mg, $0.36$ mmol, $1.2$ equiv.) in CH$_2$Cl$_2$ ($3.0$ mL, $0.1$ M) was added Ti(O’Pr)$_4$ ($8.8$ μL, $0.030$ mmol, $10$ mol%) under nitrogen atmosphere and stirred at room temperature for $2$ h. The resulting mixture was quenched with saturated NaHCO$_3$ aqueous solution and extracted with CH$_2$Cl$_2$ three times. The organic layer was washed with brine, dried with Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography $\left(n\text{-}h e x a n e / e t h y l \ a c e t a t e = 8 / 2\right)$ to give $3d$ ($60.0$ mg, $90\%$) as a white solid.

**Method B:** Methyl 6-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate $2d$ ($61.3$ mg, $0.30$ mmol) and Me-NFSI ($68.8$ mg, $0.36$ mmol, $1.2$ equiv.) were dissolved in MeOH ($3.0$ mL, $0.1$ M) and the reaction mixture was stirred at room temperature under nitrogen atmosphere for $4$ h. The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography $\left(n\text{-}h e x a n e / e t h y l \ a c e t a t e = 8 / 2\right)$ to give $3d$ ($60.3$ mg, $90\%$) as a white solid.

$^{1}H$-NMR (CDCl$_3$, 300 MHz) δ $7.64 \ (s, 1H), 7.52 \ (d, J = 7.7$ Hz, $1H), 7.39 \ (d, J = 7.7$ Hz, $1H), 3.81 \ (s, 3H), 3.81$-$3.70 \ (m, 1H), $3.39 \ (d d, J = 23.2, 17.9$ Hz, $1H), 2.43 \ (s, 3H);$ $^{19}F$-NMR (CDCl$_3$, 282 MHz) δ $-164.92 \ (d d, J = 22.6, 10.4$ Hz, $1F); \ M S \ (E S I, m/z) 261 [M+K]^+.$

This compound has been previously prepared and characterized.$^{4}$
**Methyl 2-fluoro-6-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (3e)**

**Method A:** The stirring mixture of methyl 6-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate 2e (66.1 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH₂Cl₂ (3.0 mL, 0.1 M) was added Ti(OiPr)₄ (8.8 μL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 2 h. The resulting mixture was quenched with saturated NaHCO₃ aqueous solution and extracted with CH₂Cl₂ three times. The organic layer was washed with brine, dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 8/2) to give 3e (70.3 mg, 98%) as a white solid.

**Method B:** Methyl 6-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate 2e (66.1 mg, 0.30 mmol) and Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) were dissolved in MeOH (3.0 mL, 0.1 M) and the reaction mixture was stirred at room temperature under nitrogen atmosphere for 4 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 8/2) to give 3e (70.1 mg, 98%) as a white solid.

**1H-NMR (CDCl₃, 400 MHz)** δ 7.40 (d, J = 8.3 Hz, 1H), 7.31-7.27 (m, 1H), 7.24 (d, J = 2.4 Hz, 1H), 3.86 (s, 3H), 3.81 (s, 3H), 3.72 (dd, J = 17.3, 10.6 Hz), 3.36 (dd, J = 23.0, 17.3 Hz, 1H); **19F-NMR (CDCl₃, 282 MHz)** δ -164.68 (dd, J = 22.4, 10.3 Hz, 1F); **13C-NMR (CDCl₃, 100.7 MHz)** δ 195.06 (d, J = 19.1 Hz), 167.71 (d, J = 27.9 Hz), 160.15, 143.76 (d, J = 4.4 Hz), 134.35, 127.27, 126.27, 106.41, 95.21 (d, J = 201.7 Hz), 55.68, 53.19, 37.60 (d, J = 23.5 Hz); IR (KBr) 3077, 3014, 2962, 2843, 1764, 1719, 1493, 1170, 1024, 896, 768, 674 cm⁻¹; MS (ESI, m/z) 277 [M+K]⁺; HRMS (ESI) C₁₂H₁₁FNaO₄ [M+Na]⁺ 261.0539 calcd for 261.0543; MP : 117.0-117.9 °C (n-hexane/CH₂Cl₂).

**Methyl 2-fluoro-5,6-dimethoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (3f).**
**Method A:** The stirring mixture of methyl 5,6-dimethoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate 2f (75.1 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH$_2$Cl$_2$ (3.0 mL, 0.1 M) was added Ti(OiPr)$_4$ (8.8 μL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 4 h. The resulting mixture was quenched with saturated NaHCO$_3$ aqueous solution and extracted with CH$_2$Cl$_2$ three times. The organic layer was washed with brine, dried with Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography ($n$-hexane/CH$_2$Cl$_2$ = 2/8) to give 3f (75.3 mg, 94%) as a white solid.

**Method B:** Methyl 5,6-dimethoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate 2f (75.1 mg, 0.30 mmol) and Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) were dissolved in MeOH (3.0 mL, 0.1 M) and the reaction mixture was stirred at room temperature under nitrogen atmosphere for 8 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography ($n$-hexane/CH$_2$Cl$_2$ = 2/8) to give 3f (53.1 mg, 66%) as a white solid.

$^1$H-NMR (CDCl$_3$, 300 MHz) δ 7.23 (s, 1H), 6.90 (s, 1H), 4.01 (s, 3H), 3.93 (s, 3H), 3.82 (s, 3H), 3.71 (dd, $J$ = 17.5, 10.4 Hz, 1H), 3.35 (dd, $J$ = 22.2, 17.5 Hz, 1H); $^{19}$F-NMR (CDCl$_3$, 282 MHz) δ −164.35 (dd, $J$ = 22.4, 10.3 Hz, 1F); $^{13}$C-NMR (CDCl$_3$, 100.7 MHz) δ 193.29 (d, $J$ = 18.3 Hz), 167.95 (d, $J$ = 27.9 Hz), 157.17, 150.29, 146.82 (d, $J$ = 4.4 Hz), 125.89, 107.26, 105.39, 95.04 (d, $J$ = 201.0 Hz), 56.43, 56.14, 53.12, 37.88 (d, $J$ = 23.8 Hz); IR (KBr) 3013, 2954, 2834, 1771, 1705, 1185, 1044, 861, 771, 658 cm$^{-1}$; MS (ESI, m/z) 307 [M+K]$^{+}$; HRMS (ESI) C$_{13}$H$_{13}$FNaO$_5$[M+Na]$^{+}$ 291.0645 calcd for 291.0642; MP : 118.4-119.7 °C ($n$-hexane/CH$_2$Cl$_2$).

Methyl 5-chloro-2-fluoro-2,3-dihydro-1-oxo-1H-indene-2-carboxylate (3g)

**Method A:** The stirring mixture of methyl 5-chloro-2,3-dihydro-1-oxo-1H-indene-2-carboxylate 2g (67.4 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in

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CH₂Cl₂ (3.0 mL, 0.1 M) was added Ti(O’Pr)₄ (8.8 μL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 3 h. The resulting mixture was quenched with saturated NaHCO₃ aqueous solution and extracted with CH₂Cl₂ three times. The organic layer was washed with brine, dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 9/1) to give 3g (69.0 mg, 95%) as a brown solid.

**Method B:** Methyl 5-chloro-2,3-dihydro-1-oxo-1H-indene-2-carboxylate 2g (67.4 mg, 0.30 mmol) and Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) were dissolved in MeOH (3.0 mL, 0.1 M) and the reaction mixture was stirred at room temperature under nitrogen atmosphere for 8 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 9/1) to give 3g (60.3 mg, 83%) as a brown solid.

¹H-NMR (CDCl₃, 300 MHz) δ 7.78 (d, J = 8.2 Hz, 1H), 7.51-7.45 (m, 2H), 3.82 (s, 3H), 3.82-3.74 (m, 1H), 3.49-3.36 (m, 1H); ¹⁹F-NMR (CDCl₃, 282 MHz) −164.56 (dd, J = 22.4, 10.3 Hz, 1F); MS (ESI, m/z) 281 [M+K]+.

This compound has been previously prepared and characterized³

**Methyl 5-bromo-2-fluoro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (3h)**

**Method A:** The stirring mixture of methyl 5-bromo-1-oxo-2,3-dihydro-1H-indene-2-carboxylate 2h (86.1 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH₂Cl₂ (3.0 mL, 0.1 M) was added Ti(O’Pr)₄ (8.8 μL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 8 h. The resulting mixture was quenched with saturated NaHCO₃ aqueous solution and extracted with CH₂Cl₂ three times. The organic layer was washed with brine, dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 8/2) to give 3h (79.2 mg, 92%) as a brown solid.

**Method B:** Methyl 5-bromo-1-oxo-2,3-dihydro-1H-indene-2-carboxylate 2h (86.1 mg, 0.30
mmol) and Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) were dissolved in MeOH (3.0 mL, 0.1 M) and the reaction mixture was stirred at room temperature under nitrogen atmosphere for 12 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 8/2) to give 3h (74.3 mg, 86%) as a brown solid.

\[^1\text{H-NMR (CDCl}_3, 300 \text{ MHz}) \delta 7.69-7.61 (m, 3H), 3.82 (s, 3H), 3.82-3.74 (m, 1H), 3.49-3.36 (m, 1H); ^{19}\text{F-NMR (CDCl}_3, 282 \text{ MHz}) \delta -164.66 (dd, J = 22.4, 10.3 Hz, 1F); \text{MS (ESI, m/z) 325 [M+K]^+}.

This compound has been previously prepared and characterized\(^4\)

**Methyl 2-fluoro-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (3i)**

![Structure of 3i]

**Method A:** The stirring mixture of methyl 1-oxo-1,2,3,4-tetrahydronaphthalene -2-carboxylate 2i (61.3 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH\(_2\)Cl\(_2\) (3.0 mL, 0.1 M) was added Ti(O\(^\text{iPr}\)\(_4\)) (8.8 \(\mu\)L, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 6 h. The resulting mixture was quenched with saturated NaHCO\(_3\) aqueous solution and extracted with CH\(_2\)Cl\(_2\) three times. The organic layer was washed with brine, dried with Na\(_2\)SO\(_4\) and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 8/2) to give 3i (56.8 mg, 85%) as a colorless oil.

**Method B:** Methyl 1-oxo-1,2,3,4-tetrahydronaphthalene -2-carboxylate 2i (61.3 mg, 0.30 mmol) and Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) were dissolved in MeOH (3.0 mL, 0.1 M) and the reaction mixture was stirred at room temperature under nitrogen atmosphere for 24 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 8/2) to give 3i (60.5 mg, 91%) as a colorless oil.

\[^1\text{H-NMR (CDCl}_3, 300 \text{ MHz}) \delta 8.08 (d, J = 7.5 Hz, 1H), 7.56 (dd, J = 7.5, 1.4 Hz, 1H), 7.38 (t, J = 7.5 Hz, 1H), 7.31-7.26 (m, 1H), 3.84 (s, 3H), 3.25-3.03 (m, 2H), 2.83-2.66 (m, 1H), 2.62-2.49 (m, 1H); ^{19}\text{F-NMR (CDCl}_3, 282 \text{ MHz}) \delta -164.66 (dd, J = 23.3, 11.2 Hz, 1F); \text{MS (ESI, m/z) 325 [M+K]^+}.

\(^4\)
This compound has been previously prepared and characterized\(^4\).

Methyl 2-fluoro-6-methoxy-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (3j)

Method A: The stirring mixture of methyl 6-methoxy-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate 2j (70.3 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH\(_2\)Cl\(_2\) (3.0 mL, 0.1 M) was added Ti(O\(_i\)Pr\(_4\)) (8.8 \(\mu\)L, 0.030 mmol, 10 mol\%) under nitrogen atmosphere and stirred at room temperature for 6 h. The resulting mixture was quenched with saturated NaHCO\(_3\) aqueous solution and extracted with CH\(_2\)Cl\(_2\) three times. The organic layer was washed with brine, dried with Na\(_2\)SO\(_4\) and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (\(n\)-hexane/ethyl acetate = 8/2) to give 3j (72.0 mg, 95%) as a colorless oil.

Method B: Methyl 6-methoxy-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate 2j (70.3 mg, 0.30 mmol) and Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) were dissolved in MeOH (3.0 mL, 0.1 M) and the reaction mixture was stirred at room temperature under nitrogen atmosphere for 12 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (\(n\)-hexane/ethyl acetate = 8/2) to give 3j (64.3 mg, 85%) as a colorless oil.

\(^1\)H-NMR (CDCl\(_3\), 300 MHz) \(\delta\) 8.05 (d, \(J = 8.8\) Hz, 1H), 6.89 (dd, \(J = 8.8, 2.2\) Hz, 1H), 6.72 (d, \(J = 2.2\) Hz, 1H), 3.88 (s, 3H), 3.84 (s, 3H), 3.21-3.00 (m, 2H), 2.97-2.63 (m, 1H), 2.59-2.46 (m, 1H); \(^19\)F-NMR (CDCl\(_3\), 282 MHz) \(\delta\) –164.45 (dd, \(J = 23.3, 11.2\) Hz, 1F); \(^{13}\)C-NMR (CDCl\(_3\), 100.7 MHz) \(\delta\) 186.92 (d, \(J = 19.1\) Hz), 168.11 (d, \(J = 26.4\) Hz), 164.60, 145.78, 131.14, 123.86, 114.08, 112.54, 93.17 (d, \(J = 193.7\) Hz), 55.57, 52.99, 31.88 (d, \(J = 22.0\) Hz), 25.12 (d, \(J = 7.3\) Hz); IR (neat) 3012, 2954, 2854, 1765, 1682, 1600, 1228, 1069, 942, 837, 780 cm\(^{-1}\); MS (ESI, m/z) 291 [M+K]\(^+\); HRMS (ESI) C\(_{13}\)H\(_{13}\)FNaO\(_4\) [M+Na]\(^+\) 275.0696 calcd for 275.0696.
Methyl 7-chloro-2-fluoro-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (3k)

**Method A:** The stirring mixture of methyl 7-chloro-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate 2k (71.6 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH₂Cl₂ (3.0 mL, 0.1 M) was added Ti(OiPr)₄ (8.8 μL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 12 h. The resulting mixture was quenched with saturated NaHCO₃ aqueous solution and extracted with CH₂Cl₂ three times. The organic layer was washed with brine, dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 8/2) to give 3k (56.2 mg, 73%) as a white solid.

**Method B:** Methyl 7-chloro-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate 2k (71.6 mg, 0.30 mmol) and Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) were dissolved in MeOH (3.0 mL, 0.1 M) and the reaction mixture was stirred at room temperature under nitrogen atmosphere for 24 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 8/2) to give 3k (69.3 mg, 90%) as a white solid.

^{1}H-NMR (CDCl₃, 300 MHz) δ 8.04 (d, J = 2.4 Hz, 1H), 7.52 (dd, J = 8.2, 2.4 Hz, 1H), 7.26-7.24 (m, 1H), 3.84 (s, 3H), 3.20-3.01 (m, 2H), 2.81-2.65 (m, 1H), 2.61-2.50 (m, 1H);
^{19}F-NMR (CDCl₃, 282 MHz) δ −164.90 (dd, J = 21.6, 11.2 Hz, 1F); ^{13}C-NMR (CDCl₃, 75.5 MHz) δ 187.52 (d, J = 19.2 Hz), 167.45 (d, J = 26.1 Hz), 141.29, 134.54, 133.55, 131.63, 130.35, 128.00, 92.95 (d, J = 194.5 Hz), 53.21, 31.65 (d, J = 22.3 Hz), 24.41 (d, J = 7.7 Hz) IR (KBr) 3090, 3011, 2956, 2846, 1760, 1719, 1691, 1595, 1310, 1089, 958, 842, 768 cm⁻¹; MS (ESI, m/z) 295 [M+K]; HRMS (ESI) C₁₂H₁₀ClFNaO₃ [M+Na]^+ 279.0200 calcd for 279.0201; MP: 91.9-92.6 °C (n-hexane/CH₂Cl₂).

Methyl 6-fluoro-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-6-carboxylate (3l)

![Methyl 6-fluoro-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-6-carboxylate (3l)](image-url)
**Method A:** The stirring mixture of methyl 5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-6-carboxylat 2l (65.5 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH₂Cl₂ (3.0 mL, 0.1 M) was added Ti(OiPr)₄ (8.8 μL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 24 h. The resulting mixture was quenched with saturated NaHCO₃ aqueous solution and extracted with CH₂Cl₂ three times. The organic layer was washed with brine, dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 9/1) to give 3l (65.0 mg, 92%) as a colorless oil.

**Method B:** Methyl 5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-6-carboxylat 2l (65.5 mg, 0.30 mmol) and Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) were dissolved in MeOH (3.0 mL, 0.1 M) and the reaction mixture was added and stirred at room temperature under nitrogen atmosphere for 24 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 9/1) to give 3l (24.7 mg, 35%) as a colorless oil.

1H-NMR (CDCl₃, 300 MHz) δ 7.55 (dd, J = 7.6, 1.5 Hz, 1H), 7.44 (td, J = 7.5, 1.5 Hz, 1H), 7.31 (t, J = 7.2 Hz, 1H), 7.22 (d, J = 7.6 Hz, 1H), 3.83 (s, 3H), 3.17-3.07 (m, 1H), 2.98-2.90 (m, 1H), 2.63 (dqd, J = 36.0, 7.4, 5.4 Hz, 1H), 2.37-2.09 (m, 2H), 1.97-1.85 (m, 1H);

13C-NMR (CDCl₃, 75.5 MHz) δ 198.71 (d, J = 35.3, 14.7 Hz, 1F); IR (neat) 2953, 2835, 1756, 1693, 1598, 1245, 1136, 1094, 961, 741 cm⁻¹; MS (ESI, m/z) 259 [M+Na]+; HRMS (ESI) C₁₃H₁₂FNaO₃ [M+Na]+ 259.0746 calcd for 259.0754.

**Methyl 1-fluoro-2-oxocyclopentane-1-carboxylate (3m)**

![Methyl 1-fluoro-2-oxocyclopentane-1-carboxylate (3m)](image)

**Method A:** The stirring mixture of methyl 2-oxocyclopentane-1-carboxylate 2m (37.2 μL, 42.6 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH₂Cl₂ (3.0 mL, 0.1 M) was added Ti(OiPr)₄ (8.8 μL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at...
room temperature for 6 h. The resulting mixture was quenched with saturated NaHCO₃ aqueous solution and extracted with CH₂Cl₂ three times. The organic layer was washed with brine, dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (CH₂Cl₂) to give 3m (23.3 mg, 48%) as a colorless oil.

1H-NMR (CDCl₃, 300 MHz) δ 3.85 (s, 3H), 2.60-2.49 (m, 3H), 2.41-2.29 (m, 1H), 2.21-2.11 (m, 2H); 19F-NMR (CDCl₃, 282 MHz) δ −164.63 (t, J = 20.7 Hz, 1F); MS (EI, m/z) 160 [M]+.

This compound has been previously prepared and characterized⁴

**Benzyl 1-fluoro-2-oxocyclopentane-1-carboxylate (3n)**

\[
\begin{align*}
\text{Method A:} & \quad \text{The stirring mixture of benzyl 2-oxocyclopentane-1-carboxylate 2n (65.5 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH₂Cl₂ (3.0 mL, 0.1 M) was added Ti(O^iPr)₄ (8.8 µL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 24 h. The resulting mixture was quenched with saturated NaHCO₃ aqueous solution and extracted with CH₂Cl₂ three times. The organic layer was washed with brine, dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (CH₂Cl₂) to give 3n (38.3 mg, 54%) as a colorless oil.} \\
\text{1H-NMR (CDCl₃, 300 MHz) δ 7.40-7.32 (m, 5H), 5.25 (dd, J = 15.6, 12.0 Hz, 2H), 2.60-2.46 (m, 3H), 2.42-2.24 (m, 1H), 2.17-2.07 (m, 2H); 19F-NMR (CDCl₃, 282 MHz) δ −164.47 (t, J = 20.7 Hz, 1F); MS (ESI, m/z) 259 (M+Na+).} \\
\text{This compound has been previously prepared and characterized}³
\end{align*}
\]

**Methyl 1-fluoro-2-oxocyclohexane-1-carboxylate (3o)**

\[
\begin{align*}
\text{Method A:} & \quad \text{The stirring mixture of methyl 2-oxocyclohexane-1-carboxylate 2o (42.2 µL, 46.9 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH₂Cl₂ (3.0 mL, 0.1 M) was added Ti(O^iPr)₄ (8.8 µL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at}\n\end{align*}
\]
room temperature for 24 h. The resulting mixture was quenched with saturated NaHCO₃ aqueous solution and extracted with CH₂Cl₂ three times. The organic layer was washed with brine, dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (CH₂Cl₂) to give 3o (12.2 mg, 23%) as a colorless oil.

**1H-NMR (CDCl₃, 400 MHz) δ 3.85 (s, 3H), 2.78-2.69 (m, 1H), 2.64-2.58 (m, 1H), 2.53-2.40 (m, 1H), 2.22-2.12 (m, 1H), 1.98-1.81 (m, 4H); 19F-NMR (CDCl₃, 282 MHz) δ −161.60 (m, 1F); 13C-NMR (CDCl₃, 100.7 MHz) δ 201.68 (d, J = 19.8 Hz), 167.36 (d, J = 24.9 Hz), 96.42 (d, J = 197.3 Hz), 52.99, 39.46, 35.97 (d, J = 22.0 Hz), 26.53, 20.82 (d, J = 5.1 Hz); IR (neat) 2952, 2870, 1758, 1730, 1439, 1309, 1179, 1094, 891, 839, 736, 682 cm⁻¹; MS (EI, m/z) 174 [M]+; HRMS (EI) C₈H₁₁FO₃ [M]+ 174.0692 calcd for 174.0691.

**Methyl 1-fluoro-2-oxocycloheptane-1-carboxylate (3p)**

**Method A:** The stirring mixture of methyl 2-oxocycloheptane-1-carboxylate 2p (42.8 μL, 51.1 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH₂Cl₂ (3.0 mL, 0.1 M) was added Ti(O(iPr)₄ (8.8 μL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 24 h. The resulting mixture was quenched with saturated NaHCO₃ aqueous solution and extracted with CH₂Cl₂ three times. The organic layer was washed with brine, dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (CH₂Cl₂) to give 3p (10.3 mg, 18%) as a colorless oil.

**1H-NMR (CDCl₃, 300 MHz) δ 3.82 (s, 3H), 2.85-2.69 (m, 2H), 2.33-2.18 (m, 2H), 2.00-1.85 (m, 3H), 1.66-1.42 (m, 3H); 19F-NMR (CDCl₃, 282 MHz) δ −164.20 (dd, J = 34.5, 19.0 Hz, 1F); 13C-NMR (CDCl₃, 75.5 MHz) δ 204.29 (d, J = 20.8 Hz), 167.74 (d, J = 25.4 Hz), 99.00 (d, J = 198.4 Hz), 53.22, 40.75, 33.82 (d, J = 23.1 Hz), 29.03, 25.76, 23.72; IR (neat) 2934, 2862, 1766, 1727, 1453, 1278, 1151, 1043, 939, 888, 843, 743, 619 cm⁻¹; MS (ESI, m/z) 211 [M+Na]+; HRMS (ESI) C₉H₁₃FNaO₃ [M+Na]+ 211.0746 calcd for 211.0748

**Ethyl 2-fluoro-3-oxo-3-phenylpropanoate (3q)**

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**Method A:** The stirring mixture of ethyl 3-oxo-3-phenylpropanoate 2q (52.0 μL, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH₂Cl₂ (3.0 mL, 0.1 M) was added Ti(OiPr)₄ (8.8 μL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 24 h. The resulting mixture was quenched with saturated NaHCO₃ aqueous solution and extracted with CH₂Cl₂ three times. The organic layer was washed with brine, dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 8/2) to give 3q (40.0 mg, 63%) as a colorless oil.

¹H-NMR (CDCl₃, 300 MHz) δ 8.04 (d, J = 7.6 Hz, 2H), 7.65-7.62 (m, 1H), 7.53-7.48 (m, 2H), 5.87 (d, J = 48.8 Hz, 1H), 4.30 (q, J = 6.9 Hz, 2H), 1.26 (t, J = 7.2 Hz, 3H); ¹⁹F-NMR (CDCl₃, 282 MHz) δ -190.81 (d, J = 48.3 Hz, 1F); MS (ESI, m/z) 209 [M-H]⁻.

This compound has been previously prepared and characterized³

**Methyl 2-Fluoro-2-methyl-3-oxo-3-phenylpropionate (3r)**

The stirring mixture of methyl 2-methyl-3-oxo-3-phenylpropionate 2r (57.7 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH₂Cl₂ (3.0 mL, 0.1 M) was added Ti(OiPr)₄ (88 μL, 0.30 mmol, 1.0 equiv) under nitrogen atmosphere and stirred at room temperature for 24 h. The resulting mixture was quenched with saturated NaHCO₃ aqueous solution and extracted with CH₂Cl₂ three times. The organic layer was washed with brine, dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 8/2) to give 3r (42.1 mg, 67%) as a colorless oil.

¹H-NMR (CDCl₃, 300 MHz) δ 8.04 (d, J = 7.4 Hz, 2H), 7.62-7.58 (m, 1H), 7.50-7.45 (m, 2H), 3.80 (s, 3H), 1.89 (d, J = 22.6 Hz, 3H); ¹⁹F-NMR (CDCl₃, 282 MHz) δ -152.30 (q, J = 22.4 Hz, 1F); MS (ESI, m/z) 249 [M+K]⁺.
This compound has been previously prepared and characterized

**General procedure for the fluorination of oxindoles 4**

The stirring mixture of oxindoles 4 (0.3 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH₂Cl₂ (3.0 mL, 0.1 M) was added Ti(O″Pr)₄ (8.8 μL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 1 hour. The resulting mixture was quenched with saturated NaHCO₃ aqueous solution and extracted with CH₂Cl₂ three times. The organic layer was washed with brine, dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give fluorinated oxindoles 5.

**tert-Butyl 3-fluoro-3-methyl-2-oxoindoline-1-carboxylate (5a)**

The stirring mixture of tert-butyl 3-methyl-2-oxoindoline-1-carboxylate 4a (74.2 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH₂Cl₂ (3.0 mL, 0.1 M) was added Ti(O″Pr)₄ (8.8 μL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 1 hour. The resulting mixture was quenched with saturated NaHCO₃ aqueous solution and extracted with CH₂Cl₂ three times. The organic layer was washed with brine, dried with Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 9/1) to give 5a (68.2 mg, 86%) as a colorless oil.

$^1$H-NMR (CDCl₃, 300 MHz) δ 7.90 (d, $J = 8.2$ Hz, 1H), 7.46-7.41 (m, 2H), 7.24 (t, $J = 7.6$ Hz, 2H), 1.79 (d, $J = 21.8$ Hz, 3H), 1.65 (s, 9H); $^{19}$F-NMR (CDCl₃, 282 MHz) δ −145.52 (q, $J = 21.8$ Hz, 1F); MS (ESI, m/z) 288 [M+Na]+.

This compound has been previously prepared and characterized

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**tert-Butyl 3-fluoro-2-oxo-3-phenylindoline-1-carboxylate (5b)**

![Structure of 5b]

The stirring mixture of *tert*-butyl 2-oxo-3-phenylindoline-1-carboxylate 4b (92.8 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH$_2$Cl$_2$ (3.0 mL, 0.1 M) was added Ti(O'iPr)$_4$ (8.8 μL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 1 hour. The resulting mixture was quenched with saturated NaHCO$_3$ aqueous solution and extracted with CH$_2$Cl$_2$ three times. The organic layer was washed with brine, dried with Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (*n*-hexane/ethyl acetate = 8/2) to give 5b (90.3 mg, 92%) as a white solid.

$^1$H-NMR (CDCl$_3$, 300 MHz) δ 8.01 (d, $J$ = 8.5 Hz, 1H), 7.51-7.26 (m, 8H), 1.62 (s, 9H); $^{19}$F-NMR (CDCl$_3$, 282 MHz) δ −145.88 (s, 1F); MS (ESI, m/z) 350 [M+Na]$^+$. This compound has been previously prepared and characterized.$^6$

**tert-Butyl 3-fluoro-5-methyl-2-oxo-3-phenylindoline-1-carboxylate (5c)**

![Structure of 5c]

The stirring mixture of *tert*-butyl 5-methyl-2-oxo-3-phenylindoline-1-carboxylate 4c (97.0 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH$_2$Cl$_2$ (3.0 mL, 0.1 M) was added Ti(O'iPr)$_4$ (8.8 μL, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 1 hour. The resulting mixture was quenched with saturated NaHCO$_3$ aqueous solution and extracted with CH$_2$Cl$_2$ three times. The organic layer was washed with brine, dried with Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (*n*-hexane/ethyl acetate = 9/1) to give 5c (83.1 mg, 81%) as a colorless oil.

$^1$H-NMR (CDCl$_3$, 300 MHz) δ 7.88 (d, $J$ = 8.2 Hz, 1H), 7.44-7.26 (m, 6H), 7.17 (s, 1H), 2.36


SI-27
(s, 3H), 1.62 (s, 9H); \(^{19}\text{F-NMR (CDCl}_3, 282 \text{ MHz)} \delta -146.17 \text{ (s, 1F); MS (ESI, m/z) 380 [M+K]}^+.

This compound has been previously prepared and characterized\(^7\)

**tert-Butyl 5-chloro-3-fluoro-2-oxo-3-phenylindoline-1-carboxylate (5d)**

![Image of the compound](https://example.com/compound_image)

The stirring mixture of tert-butyl 5-chloro-2-oxo-3-phenylindoline-1-carboxylate 4d (103.1 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH\(_2\)Cl\(_2\) (3.0 mL, 0.1 M) was added Ti(O\(_i\)Pr\(_4\)) (8.8 \(\mu\)L, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 1 hour. The resulting mixture was quenched with saturated NaHCO\(_3\) aqueous solution and extracted with CH\(_2\)Cl\(_2\) three times. The organic layer was washed with brine, dried with Na\(_2\)SO\(_4\) and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate = 9/1) to give 5d (80.3 mg, 74%) as a colorless oil.

\(^1\text{H-NMR (CD}_3\text{CN, 300 MHz)} \delta 8.33 (d, J = 8.2 \text{ Hz, 1H}), 7.92 (t, J = 7.8 \text{ Hz, 1H}), 7.79-7.63 \text{ (m, 6H), 1.94 (s, 9H)}; \(^{19}\text{F-NMR (CD}_3\text{CN, 282 MHz)} \delta -145.73 \text{ (s, 1F).}

This compound has been previously prepared and characterized\(^7\)

**tert-Butyl 3-fluoro-5-methyl-2-oxo-3-(4-tolyl)indoline-1-carboxylate (5e)**

![Image of the compound](https://example.com/compound_image)

The stirring mixture of tert-butyl 5-methyl-2-oxo-3-(4-tolyl)indoline-1-carboxylate 4e (101.2 mg, 0.30 mmol), Me-NFSI (68.8 mg, 0.36 mmol, 1.2 equiv.) in CH\(_2\)Cl\(_2\) (3.0 mL, 0.1 M) was added Ti(O\(_i\)Pr\(_4\)) (8.8 \(\mu\)L, 0.030 mmol, 10 mol%) under nitrogen atmosphere and stirred at room temperature for 1 hour. The resulting mixture was quenched with saturated NaHCO\(_3\) aqueous solution and extracted with CH\(_2\)Cl\(_2\) three times. The organic layer was washed with brine, dried with Na\(_2\)SO\(_4\) and concentrated under reduced pressure. The residue was purified

by silica gel column chromatography \((n\text{-}\text{hexane/ ethyl acetate} = 9/1)\) to give 5e (92.5 mg, 87\%) as a white solid.

\[^1\text{H}-\text{NMR (CDCl}_3, 300 \text{ MHz)} \delta 7.87 \text{ (d, } J = 8.2 \text{ Hz, 1H), } 7.31-7.18 \text{ (m, 6H), 2.36 (s, 6H), 1.60 (s, 9H); } ^{19}\text{F}-\text{NMR (CDCl}_3, 282 \text{ MHz)} \delta −146.15 \text{ (s, 1F); MS (ESI, m/z) 394 [M+K]^+.}

This compound has been previously prepared and characterized\(^8\)

**General procedure for the fluorination of malonic diesters 6.**

The stirring mixture of malonic diesters 6 (0.3 mmol), Me-NFSI (114.7 mg, 0.60 mmol, 2.0 equiv.) in Toluene (3.0 mL, 0.1 M) was added Ti(O\(^{i}\)Pr\(_4\)) (17.7 \(\mu\)L, 0.060 mmol, 20 mol\%) under nitrogen atmosphere and stirred for 12 hours at reflux. The resulting mixture was cooled to room temperature and quenched with saturated NaHCO\(_3\) aqueous solution and extracted with CH\(_2\)Cl\(_2\) three times. The organic layer was washed with brine, dried with Na\(_2\)SO\(_4\) and concentrated under reduced pressure. The residue was purified by silica gel column chromatography \((n\text{-}\text{hexane/ethyl acetate})\) to give fluorinated malonicesters 7.

**Diethyl 2-Fluoro-2-methylmalonate (7a)**

The stirring mixture of diethyl methylmalonatea 6a (51.0 \(\mu\)L, 0.30 mmol), Me-NFSI (114.7 mg, 0.60 mmol, 2.0 equiv.) in Toluene (3.0 mL, 0.1 M) was added Ti(O\(^{i}\)Pr\(_4\)) (17.7 \(\mu\)L, 0.060 mmol, 20 mol\%) under nitrogen atmosphere and stirred for 12 hours at reflux. The resulting mixture was cooled to room temperature and quenched with saturated NaHCO\(_3\) aqueous solution and extracted with CH\(_2\)Cl\(_2\) three times. The organic layer was washed with brine, dried with Na\(_2\)SO\(_4\) and concentrated under reduced pressure. The residue was purified by silica gel column chromatography \((n\text{-}\text{hexane/ethyl acetate} = 9/1)\) to give 7a (52.4 mg, 91\%)

as a colorless oil.

$^1$H-NMR (CDCl$_3$, 300 MHz) δ 4.30 (q, $J = 7.2$ Hz, 4H), 1.79 (d, $J = 22.1$ Hz, 3H), 1.31 (t, $J = 7.2$ Hz, 6H); $^{19}$F-NMR (CDCl$_3$, 282 MHz) δ −158.00 (q, $J = 22.4$ Hz, 1F); MS (ESI, m/z) 193 [M+H]$^+$. 

This compound has been previously prepared and characterized$^9$

Diethyl 2-Fluoro-2-phenylmalonate (7b)

The stirring mixture of diethyl phenylmalonate 6b (64.7 μL, 0.30 mmol), Me-NFSI (114.7 mg, 0.60 mmol, 2.0 equiv.) in Toluene (3.0 mL, 0.1 M) was added Ti(OiPr)$_4$ (17.7 μL, 0.060 mmol, 20 mol%) under nitrogen atmosphere and stirred for 12 hours at reflux. The resulting mixture was cooled to room temperature and quenched with saturated NaHCO$_3$ aqueous solution and extracted with CH$_2$Cl$_2$ three times. The organic layer was washed with brine, dried with Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography ($n$-hexane/ethyl acetate = 9/1) to give 7b (40.0 mg, 52%) as a colorless oil.

$^1$H-NMR (CDCl$_3$, 300 MHz) δ 7.58 (s, 2H), 7.41 (s, 3H), 4.33 (q, $J = 7.0$ Hz, 4H), 1.32 (t, $J = 7.0$ Hz, 6H); $^{19}$F-NMR (CDCl$_3$, 282 MHz) δ −161.50 (s, 1F); MS (ESI, m/z) 255 [M+H]$^+$. 

This compound has been previously prepared and characterized$^{10}$

Diethyl 2-Benzyl-2-fluoromalonate (7c)

The stirring mixture of diethyl benzylmalonatea 6c (51.0 μL, 0.30 mmol), Me-NFSI (114.7 mg, 0.60 mmol, 2.0 equiv.) in Toluene (3.0 mL, 0.1 M) was added Ti(OiPr)$_4$ (17.7 μL, 0.060 mmol, 20 mol%) under nitrogen atmosphere and stirred for 12 hours at reflux. The resulting mixture was cooled to room temperature and quenched with saturated NaHCO$_3$ aqueous

solution and extracted with CH$_2$Cl$_2$ three times. The organic layer was washed with brine, dried with Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography ($n$-hexane/ethyl acetate = 9/1) to give 7c (61.8 mg, 77%) as a colorless oil.

$^1$H-NMR (CDCl$_3$, 300 MHz) δ 7.33-7.26 (m, 5H), 4.24 (q, $J = 7.2$ Hz, 4H), 3.47 (d, $J = 25.6$ Hz, 2H), 1.24 (t, $J = 7.2$ Hz, 6H); $^{19}$F-NMR (CDCl$_3$, 282 MHz) δ −165.18 (t, $J = 25.0$ Hz, 1F); $^{13}$C-NMR (CDCl$_3$, 75.5 MHz) δ 165.76 (d, $J = 25.4$ Hz), 132.92, 130.30, 128.35, 127.52, 94.62 (d, $J = 201.5$ Hz), 62.66, 40.15 (d, $J = 20.0$ Hz), 13.92; IR (neat) 3033, 2984, 2908, 1759, 1455, 1305, 1057, 748 cm$^{-1}$; MS (ESI, m/z) 269 [M+H]$^+$; HRMS (ESI) C$_{14}$H$_{17}$FNaO$_4$ [M+Na]$^+$ 291.1009 calcd for 291.1021.

**Dibenzyl 2-Benzylfluoro-malonate (7d)**

\[
\begin{align*}
\text{Bn} & \text{O} \\
\text{F} & \text{OBn}
\end{align*}
\]

The stirring mixture of dibenzyl 2-benzylmalonate $^{11}$ 6d (95.2 μL, 0.30 mmol), Me-NFSI (114.7 mg, 0.60 mmol, 2.0 equiv.) in Toluene (3.0 mL, 0.1 M) was added Ti(O'Pr)$_4$ (17.7 μL, 0.060 mmol, 20 mol%) under nitrogen atmosphere and stirred for 12 hours at reflux. The resulting mixture was cooled to room temperature and quenched with saturated NaHCO$_3$ aqueous solution and extracted with CH$_2$Cl$_2$ three times. The organic layer was washed with brine, dried with Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography ($n$-hexane/ethyl acetate = 8/2) to give 7d (60.4 mg, 51%) as a colorless oil.

$^1$H-NMR (CDCl$_3$, 300 MHz) 7.36-7.32 (m, 6H), 7.24-7.17 (m, 7H), 7.15-7.12 (m, 2H), 5.17 (s, 4H), 5.16 (s, 2H), 3.47 (d, $J = 25.6$ Hz, 2H); $^{19}$F-NMR (CDCl$_3$, 282 MHz) δ −164.84 (t, $J = 25.9$ Hz, 1F); $^{13}$C-NMR (CDCl$_3$, 75.5 MHz) δ 165.46 (d, $J = 26.1$ Hz), 134.43, 132.63, 130.24, 128.59, 128.38, 128.33, 127.51, 94.64 (d, $J = 202.3$ Hz), 68.07, 40.15 (d, $J = 20.8$ Hz) (No resolution one Carbon atom.); IR (neat) 3087, 3033, 2959, 1754, 1497, 1283, 1137, 1054, 949, 748, 698 cm$^{-1}$; MS (ESI, m/z) 415 [M+Na]$^+$; HRMS (ESI) C$_{24}$H$_{21}$FNaO$_4$ [M+Na]$^+$

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415.1322 calcd for 415.1325.
NMR spectrum

X: parts per Million : 1H

X: parts per Million : 10F

SI-33
SI-35
X: parts per Million : 19F

X: parts per Million : 1H

SI-38
SI-41
N
Boc
O
Ph
F
5b

X: parts per Million : 1H

N
Boc
O
Ph
F
5b

X: parts per Million : 19F

SI-57
7a