Supporting Information

Ag-catalyzed difluorohydration of β-alkynyl ketones for diastereoselective synthesis of 1,5-diconboyyl compounds

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General Information

$^1$H NMR ($^{13}$C NMR) spectra were measured on a Bruker DPX 400 MHz spectrometer in CDCl$_3$ (DMSO-$d_6$) with chemical shift ($\delta$) given in ppm relative to TMS as internal standard [(s = singlet, d = doublet, t = triplet, brs = broad singlet, m = multiplet), coupling constant (Hz)]. HRMS (ESI) was determined by using microTOF-QII HRMS/MS instrument (BRUKER). X-Ray crystallographic analysis was performed with a Siemens SMART CCD and a Siemens P4 diffractometer.

Condition optimization

Table 1. Optimization of Reaction Conditions$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>NFSI (equiv)</th>
<th>H$_2$O (equiv)</th>
<th>Cat. (mol %)</th>
<th>Solvent$^b$</th>
<th>Yield (%)$^c$</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>2.0</td>
<td>2.0</td>
<td>AgOAc (20)</td>
<td>1,4-dioxane</td>
<td>49%</td>
</tr>
<tr>
<td>2</td>
<td>2.0</td>
<td>2.0</td>
<td>AgF (20)</td>
<td>1,4-dioxane</td>
<td>31%</td>
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<tr>
<td>3</td>
<td>2.0</td>
<td>2.0</td>
<td>AgSbF$_6$ (20)</td>
<td>1,4-dioxane</td>
<td>39%</td>
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<tr>
<td>4</td>
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<td>2.0</td>
<td>AgOTf (20)</td>
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<td>5</td>
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<td>AgTFA (20)</td>
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<tr>
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<td>Ag$_2$CO$_3$ (20)</td>
<td>1,4-dioxane</td>
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</tr>
<tr>
<td>7</td>
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<td>2.0</td>
<td>AgNO$_3$ (20)</td>
<td>1,4-dioxane</td>
<td>59%</td>
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<tr>
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<td>2.5</td>
<td>2.0</td>
<td>AgNO$_3$ (20%)</td>
<td>1,4-dioxane</td>
<td>65%</td>
</tr>
<tr>
<td>9</td>
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<td>1,4-dioxane</td>
<td>73%</td>
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<tr>
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<td>CH$_3$CN</td>
<td>44%</td>
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<td>DCM</td>
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<td>THF</td>
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<td>DCE</td>
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<td>1,4-dioxane</td>
<td>74%</td>
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<td>63%</td>
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<td>1,4-dioxane</td>
<td>60%</td>
</tr>
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<td>1,4-dioxane</td>
<td>79%</td>
</tr>
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<td>1.2</td>
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<td>82%</td>
</tr>
<tr>
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<td>1.0</td>
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<td>76%</td>
</tr>
<tr>
<td>20</td>
<td>3.0</td>
<td>-</td>
<td>AgNO$_3$ (10%)</td>
<td>1,4-dioxane</td>
<td>ND$^d$</td>
</tr>
<tr>
<td>21</td>
<td>3.0</td>
<td>1.2</td>
<td>AgNO$_3$ (10%)</td>
<td>1,4-dioxane</td>
<td>50%$^e$</td>
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</tbody>
</table>

$^a$Reaction conditions: 1a (0.5 mmol), NFSI (X equiv), H$_2$O (Y equiv), Ag-catalyst (Z mol%), solvent (2.0 mL), under Ar conditions, $^b$Dry solvent. $^c$Isolated yield. $^d$Not detected (ND).$^e$Under air conditions

Our initial investigation commenced with the reaction of the preformed $\beta$-alkynyl ketones 1a with NFSI in a 1:2 mole ratio in the presence of water (2.0 equiv) using AgOAc (20 mol%) as a catalyst. The reaction was performed in 1,4-dioxane solvent at room temperature under Ar conditions, delivering the unexpected difluoride product 2a in 49% yield (Table S1, entry S1). This satisfactory result promoted us to further search the optimal
conditions for accessing product 2a. Several others silver catalysts often used in the catalytic transformation, including AgF, AgSbF6, AgOTf, AgTFA, Ag2CO3, and AgNO3, were screened for this difluorohydration by using 2.0 equivalents of NFSI as a difluorination reagent (entries S2-S7). The silver salts like AgF, AgSbF6, or AgOTf behaved lower catalytic activities than AgOAc (entries S2-S4) whereas the use of AgTFA and Ag2CO3 completely suppressed the reaction process (entries S5-S6). In another case of AgNO3, the reaction worked more efficiently, affording a higher yield of product 2a (59%) as compared with AgOAc (entry S7). The increase of the dosage of NFSI is beneficial to the transformation (entries S8-S9). Adjusting the ratio of 1a with NFSI to 1:3 improved the yield of 2a to 73%. Afterward, taking the combination of NFSI (3.0 equiv) with AgNO3 (20 mol%), we investigated the effect of the solvent. Screening followed by other aprotic solvents such as acetonitrile (CH3CN), dichloromethane (DCM), tetrahydrofuran (THF), and 1,2-dichloroethane (DCE) revealed that all these solvents did not show any improvements with respect to the reaction yield (entries S10-S13). The simultaneous decrease of the amount of AgNO3 and water is beneficial to this transformation (entries S14-S19). After careful optimizations, we found that the combination of 10 mol% of AgNO3 with 1.2 equivalents of water was proven to be most effective for this reaction, affording 82% yield (entry S18). Without water, the reaction did not work and the starting materials were recovered (entry S20). A lower conversion was detected when the identical reaction was carried out under air conditions (entry S21).

Figure 1 The ORTEP Drawing of 2w (Thermal ellipsoids are set at 30% probability level)

Figure 2 The ORTEP Drawing of 2z (Thermal ellipsoids are set at 30% probability level)
1. General Procedure for the Preparation of \( \beta \)-Alkynyl Ketones.

**Representative Procedure**: To a stirred solution of 2-((4-chlorophenyl)ethynyl)benzaldehyde (1.0 equiv, 5.0 mmol, I) in anhydrous THF (10 mL) was added by dropwise a 1.00 mol/L solution of ethylmagnesium bromide in THF (1.5 equiv, 7.5 mL, 7.5 mmol) at -10 °C. The mixture was stirred for 1 hour at -10 °C and then stirred at room temperature. After the completion of the reaction monitored by TLC, the reaction system was quenched by saturated aqueous NH\(_4\)Cl and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na\(_2\)SO\(_4\), filtered, and concentrated. After purification by flash column chromatography on silica gel, compound II (1.26 g, 4.65 mmol) was obtained in 93% yield as an oil.

In an oven dried flask, compound II (1.0 equiv, 2 mmol) and dry CH\(_2\)Cl\(_2\) (4.0 mL/mmol) were added. The resulting solution was cooled to 0 °C, and then Dess-Martin periodinane (1.5 equiv., 3 mmol) was added into this reaction system. The resulting suspension was stirred at 0 °C for 3 h. The reaction mixture was diluted with CH\(_2\)Cl\(_2\) (10.0 mL/mmol) and saturated aqueous NaHCO\(_3\) (10.0 mL/mmol). Organic layers was separated and the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (1 × 10 mL). The combined organic phase was washed with brine (1 × 10.00 mL), dried over anhydrous Na\(_2\)SO\(_4\) and concentrated under reduced pressure. Purification by column chromatography over silica gel with petroleum ether/ethyl acetate as eluent afforded 1a (0.48g, 1.8 mmol).

\[ 1\text{-}(2\text{-}((4\text{-}chlorophenyl)ethynyl)phenyl)propan-1-one (1a) \]
\[ \text{\(^1\)}H NMR (400 MHz, CDCl\(_3\)) \delta 7.70 (d, \( J = 7.6 \) Hz, 1H), 7.63 (d, \( J = 7.6 \) Hz, 1H), 7.52-7.39 (m, 4H), 7.39-7.33 (m, 2H), 3.23-3.09 (m, 2H), 1.27 (t, \( J = 7.2 \) Hz, 3H). \]
2. Isotopic labeling experiments
The isotopic labeled 1-(2-((4-chlorophenyl)ethynyl)phenyl)propan-1-one is produced as the method of 1.1.

\[
\text{\begin{align*}
\text{H NMR (400 MHz, CDCl}_3\text{) } & \delta 7.70 (d, J = 7.6\text{ Hz, } 1\text{H}), 7.63 (d, J = 7.6\text{ Hz, } 1\text{H}), 7.45 (dt, J = 14.8, 7.8\text{ Hz, } 4\text{H}), 7.36 (d, J = 8.2\text{ Hz, } 2\text{H}).
\end{align*}}
\]

In an oven-dried Schlenk tube, to a solution of isotopic labeled 1-(2-((4-chlorophenyl)ethynyl)phenyl)propan-1-one (1a, 1.0 equiv., 0.2 mmol), N-fluorobenzenesulfonimide (2.5 equiv, 0.5 mmol), AgNO\textsubscript{3} (10 mol%, 0.1 mmol) and water (1.2 equiv, 0.24 mmol) in anhydrous 1,4-dioxane (1.0 mL) under Ar atmosphere. After the reaction was completed, the product was checked by checked by \textsuperscript{1}H-NMR in DMSO-\textit{d}_6.
In an oven-dried Schlenk tube, to a solution of 1-(5-chloro-2-(phenylethynyl)phenyl)-2-(p-tolyl)ethanone (1v, 1.0 equiv., 0.2 mmol), N-fluorobenzenesulfonimide (2.5 equiv, 0.5 mmol), AgNO₃ (10 mol%, 0.1 mmol) and D₂O (1.2 equiv. 0.24 mmol) in anhydrous 1,4-dioxane (1.0 mL) under Ar atmosphere. After the reaction was completed, the product was checked by ¹H-NMR in DMSO-d₆.
3. Control experiments

In an oven-dried Schlenk tube, to a solution of isotopic labeled 1-(2-((4-chlorophenyl)ethynyl)phenyl)propan-1-one (1a, 1.0 equiv., 0.2 mmol), N-fluorobenzenesulfonimide (2.5 equiv, 0.5 mmol), AgNO₃ (10 mol%, 0.1 mmol), water (1.2 equiv, 0.24 mmol), and Phenylhydrazine (3.0 equiv, 0.6 mmol) in anhydrous 1,4-dioxane (1.0 mL) under Ar atmosphere. After the reaction was completed, the product was checked by checked by ¹H-NMR in CDCl₃.

1-(2-(2-(4-chlorophenyl)-1-fluoro-2-oxoethyl)phenyl)propan-1-one (10)

¹H NMR (400 MHz, CDCl₃) δ 8.11 (d, J = 8.4 Hz, 2H), 7.99 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.71-7.64 (m, 1H), 7.58-7.49 (m, 3H), 7.42-7.28 (m, 1H), 3.12-2.90 (m, 2H), 1.15 (t, J = 7.2 Hz, 3H).

Scheme S1. Plausible mechanism for forming 2
LC-MS experiments for reaction solution containing intermediate B, C and D.

LC-MS Spectra of Intermediate B

LC-MS Spectra of Intermediate D
Typical Procedure for the Synthesis of Products 2

In an oven-dried Schlenk tube, to a solution of β-alkynyl ketones (1, 1.0 equiv, 0.5 mmol), N-fluorobenzenesulfonimide (3.0 equiv, 1.5 mmol), AgNO₃ (10 mol%, 0.05 mmol) and water (1.2 equiv, 0.60 mmol) in anhydrous 1,4-dioxane (2.0 mL) under Ar atmosphere. The reaction mixture was stirred at room temperature for 12.0 hours. After the reaction monitored by TLC was completed, the organic solvent was removed under vacuum, and the residue was purified by silica gel column with petroleum ether/ethyl acetate to afford pure products 2.

1-(2-(2-(4-Chlorophenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoropropan-1-one (2a)

![Structure of 2a]

white solid, mp 71-73 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.14 (d, J = 8.4 Hz 2H), 7.97-7.90 (m, 1H), 7.81 (m, 1H), 7.75-7.67 (m, 2H), 7.59-7.50 (m, 3H), 7.39 (d, J = 47.6 Hz, 1H), 5.85-5.62 (m, 1H). ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 198.9 (d, J = 19.5 Hz), 191.2 (d, J = 22.1 Hz), 140.2, 136.8 (d, J = 18.1 Hz), 133.6, 133.4 (d, J = 1.7 Hz), 131.9 (d, J = 1.9 Hz), 130.7 (d, J = 1.9 Hz), 130.0 (d, J = 5.5 Hz), 129.1, 128.5, 127.3 (d, J = 15.9 Hz), 90.3 (d, J = 181.3 Hz), 89.6 (d, J = 179.1 Hz), 17.8 (d, J = 22.5 Hz). ¹⁹F NMR (376 MHz, CDCl₃; δ, ppm) -179.3 (d, J = 47.4 Hz, 1F), -179.9 -180.4 (m, 1F, major), -181.2 -181.5 (m, 1F), -181.6 (d, J = 47.4 Hz, 1F, major). IR (film, ν, cm⁻¹) 3068, 3028, 1725, 1590, 1507, 1448, 1359, 1220, 1199, 1173, 1155, 1083, 844. HR-MS (ESI) m/z calcd for C₁₇H₁₃ClF₂O₂ [M+Na]⁺ 345.0470, found 345.0468.

1-(2-(2-(3-Chlorophenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoropropan-1-one (2b)

![Structure of 2b]

oil; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.11 (s, 1H), 8.04 (d, J = 7.6 Hz, 1H), 7.98-7.92 (m, 1H), 7.85-7.77 (m, 1H), 7.73 (t, J = 7.6 Hz, 1H), 7.66-7.59 (m, 1H), 7.56 (t, J = 7.6 Hz, 1H), 7.52-7.45 (m, 1H), 7.33 (d, J = 47.2 Hz, 1H), 5.85-5.62 (m, 1H). ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 198.8 (d, J = 19.9 Hz), 191.1 (d, J = 22.2 Hz), 136.7 (d, J = 18.9 Hz), 135.1 (d, J = 2.0 Hz), 133.6, 131.8 (d, J = 2.6 Hz), 130.1, 130.0 (d, J = 5.4 Hz), 129.2 (d, J = 2.1 Hz), 128.6, 127.7 (d, J = 14.8 Hz), 127.3 (d, J = 6.8 Hz), 127.2, 89.9 (d, J = 176.9 Hz), 89.6 (d, J = 179.1 Hz), 17.8 (d, J = 22.5 Hz). ¹⁹F NMR (376 MHz, CDCl₃; δ, ppm) -179.77 (d, J = 1.5 Hz, 1F), -180.34 (s, 1F, major), -181.44 (s, 1F), -181.81 (d, J = 1.9 Hz, 1F, major). HR-MS (ESI) m/z calcd for C₁₇H₁₃ClF₂O₂ [M+Na]⁺ 345.0470, found 345.0471.

1-(2-(2-(4-Bromophenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoropropan-1-one (2c)

![Structure of 2c]

white solid, mp 81-82 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.01 (d, J = 8.4 Hz, 2H), 7.97-7.91 (m, 1H), 7.79
(t, J = 7.6 Hz, 1H), 7.74-7.65 (m, 3H), 7.56 (t, J = 7.6 Hz, 1H), 7.29 (d, J = 47.6 Hz, 1H), 5.85-5.60 (m, 1H), 1.62 (dd, J = 24.4, 6.8 Hz, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 198.9 (d, J = 19.7 Hz), 191.4 (d, J = 22.0 Hz), 136.8 (d, J = 18.3 Hz), 133.6 (d, J = 7.1 Hz), 132.1, 130.7 (d, J = 2.1 Hz), 130.0 (d, J = 5.5 Hz), 129.8 (d, J = 5.4 Hz), 129.0, 128.6, 127.8 (d, J = 14.3 Hz), 127.3 (d, J = 16.0 Hz), 89.8 (d, J = 176.8 Hz), 89.7 (d, J = 179.0 Hz), 17.8 (d, J = 22.5 Hz). \(^{19}\)F NMR (376 MHz, CDCl\(_3\); \(\delta\), ppm) -179.27 (s, 1F), -180.21 (s, 1F, major), -181.36 (s, 1H), -181.52 (s, 1F, major). IR (film, \(\nu\), cm\(^{-1}\)) 3068, 3028, 1725, 1590, 1507, 1448, 1359, 1220, 1199, 1173, 1155, 1083, 844. HR-MS (ESI) m/z calcd for C\(_{17}\)H\(_{13}\)BrF\(_2\)O\(_2\) [M+Na]\(^+\) 388.9965, found 388.9962.

2-Fluoro-1-(2-(1-fluoro-2-(4-fluorophenyl)-2-oxoethyl)phenyl)propan-1-one (2d)

![Image of 2-Fluoro-1-(2-(1-fluoro-2-(4-fluorophenyl)-2-oxoethyl)phenyl)propan-1-one](image)

white solid, mp 66-68 °C; \(^{1}\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 8.19 (d, J = 8.4 Hz, 2H), 8.00-7.89 (m, 1H), 7.84-7.77 (m, 1H), 7.72 (t, J = 7.6 Hz, 1H), 7.56 (t, J = 7.6 Hz, 1H), 7.41-7.14 (m, 3H), 5.85-5.60 (m, 1H), 1.64 (dd, J = 24.0, 6.8 Hz, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 199.0(d, J = 19.7 Hz), 190.8 (d, J = 21.9 Hz), 166.1 (d, J = 254.3 Hz), 136.9 (d, J = 18.2 Hz), 133.5 (d, J = 1.7 Hz), 132.1 (d, J = 2.5 Hz), 132.0 (d, J = 2.5 Hz), 131.5 (d, J = 4.7 Hz), 129.9 (d, J = 5.5 Hz), 128.5, 127.3 (d, J = 15.9 Hz), 116.0 (d, J = 21.8 Hz), 89.8 (d, J = 176.9 Hz), 89.7 (d, J = 179.1 Hz), 17.8 (d, J = 22.5 Hz). \(^{19}\)F NMR (376 MHz, CDCl\(_3\); \(\delta\), ppm) -103.8 (s, 1F, major), -103.9(s, 1F, major), -178.9 (s, 1F), -180.3 (s, 1F, major), -181.3 (d, J = 5.3 Hz, 1F, major), -181.4 (d, J = 5.3 Hz, 1F). IR (film, \(\nu\), cm\(^{-1}\)) 3000, 1702, 1683, 1595, 1506, 1240, 1212, 1160, 1086, 991, 839. HR-MS (ESI) m/z calcd for C\(_{17}\)H\(_{13}\)F\(_2\)O\(_2\) [M+Na]\(^+\) 329.0765, found 329.0764.

2-Fluoro-1-(2-(1-fluoro-2-oxo-2-phenylethyl)phenyl)propan-1-one (2e)

![Image of 2-Fluoro-1-(2-(1-fluoro-2-oxo-2-phenylethyl)phenyl)propan-1-one](image)

white solid, mp 67-69 °C; \(^{1}\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 8.14 (d, J = 7.6 Hz, 2H), 7.96-7.90 (m, 1H), 7.84-7.77 (m, 1H), 7.74-7.61 (m, 2H), 7.59-7.50 (m, 3H), 7.46-7.20 (m, 1H), 5.89-5.62 (m, 1H), 1.63 (dd, J = 24.4, 6.8 Hz, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 199.0 (d, J = 19.7 Hz), 192.5 (d, J = 21.9 Hz), 137.0 (d, J = 18.5 Hz), 135.0 (d, J = 1.7 Hz), 133.7, 133.4, 132.2 (d, J = 3.3 Hz), 129.8 (d, J = 5.5 Hz), 129.2 (d, J = 2.2 Hz), 128.8, 128.4, 127.3 (d, J = 15.8 Hz), 89.8 (d, J = 177.5 Hz), 89.4 (d, J = 176.6 Hz), 17.8 (d, J = 22.5 Hz). \(^{19}\)F NMR (376 MHz, CDCl\(_3\); \(\delta\), ppm) -178.85 (s, 1F), -180.33 (s, 1F, major), -181.38 (s, 1F, major), -181.39 (s, 1F). IR (film, \(\nu\), cm\(^{-1}\)) 3069, 2987, 1689, 1596, 1573, 1450, 1318, 1239, 1218, 1114, 1081, 1012,977, 824. HR-MS (ESI) m/z calcd for C\(_{17}\)H\(_{14}\)F\(_2\)O\(_2\) [M+Na]\(^+\) 311.0860, found 311.0864.

2-Fluoro-1-(2-(1-fluoro-2-oxo-2-(p-toly)ethyl)phenyl)propan-1-one (2f)

![Image of 2-Fluoro-1-(2-(1-fluoro-2-oxo-2-(p-toly)ethyl)phenyl)propan-1-one](image)

white solid, mp 88-90 °C; \(^{1}\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 8.03 (d, J = 8.0 Hz, 2H), 7.97-7.88 (m, 1H), 7.79
(m, 1H), 7.68 (m, 1H), 7.55 (t, J = 7.6 Hz, 1H), 7.44-7.17 (m, 3H), 5.84-5.59 (m, 1H), 2.46 (s, 3H), 1.64 (dd, J = 24.0, 6.8 Hz, 3H). \(^1\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 199.1 (d, J = 19.7 Hz), 192.1 (d, J = 21.7 Hz), 144.7, 137.0 (d, J = 18.5 Hz), 133.4 (d, J = 1.2 Hz), 132.3 (d, J = 3.1 Hz), 129.8 (d, J = 5.4 Hz), 129.5, 129.4 (d, J = 2.1 Hz), 128.8 (d, J = 1.1 Hz), 127.4 (d, J = 15.5 Hz), 89.7 (d, J = 176.8 Hz), 89.3 (d, J = 176.5 Hz), 21.8, 17.9 (d, J = 22.4 Hz). \(^19\)F NMR (376 MHz, CDCl\(_3\); \(\delta\), ppm) -178.30 (s, 1F), -180.26 (s, 1F), -180.95 (s, 1F), -181.31 (s, 1F). IR (film, \(\nu\), cm\(^{-1}\)) 3069, 2997, 2940, 1696, 1603, 1575, 1223, 1213, 1087, 978. HR-MS (ESI) m/z calcld for C\(_{18}\)H\(_{16}\)F\(_2\)O\(_2\) [M+Na\(^+\)] 325.1016, found 325.1021.

2-Fluoro-1-(2-(1-fluoro-2-oxo-2-(m-tolyl)ethyl)phenyl)propan-1-one (2g)

white solid, mp 67-69 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 7.98-7.89 (m, 3H), 7.84-7.76 (m, 1H), 7.74-7.66 (m, 1H), 7.55 (t, J = 7.6 Hz, 1H), 7.49-7.18 (m, 3H), 5.72 (m, 1H), 2.46 (s, 3H), 1.63 (dd, J = 24.0, 6.8 Hz, 3H). \(^1\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 199.0 (d, J = 19.4 Hz), 192.6 (d, J = 21.7 Hz), 138.6, 137.0 (d, J = 18.4 Hz), 135.1 (d, J = 1.6 Hz), 134.6, 133.4 (d, J = 1.6 Hz), 132.2 (d, J = 2.4 Hz), 129.8 (d, J = 5.4 Hz), 129.7 (d, J = 1.9 Hz), 128.6, 128.4 (d, J = 1.1 Hz), 127.3 (d, J = 15.7 Hz), 126.5 (d, J = 2.3 Hz), 89.8 (d, J = 179.5 Hz), 89.7 (d, J = 176.7 Hz), 21.4, 17.9 (d, J = 22.6 Hz). \(^19\)F NMR (376 MHz, CDCl\(_3\); \(\delta\), ppm) -178.32--178.77 (m, 1F), -180.33 (s, 1F, major), -181.08--181.19 (m, 1F, major), -181.23 (s, 1F). IR (film, \(\nu\), cm\(^{-1}\)) 3028, 2994, 1688, 1603, 1575, 1314, 1240, 1164, 1114, 1075, 1037, 986. HR-MS (ESI) m/z calcld for C\(_{18}\)H\(_{16}\)F\(_2\)O\(_2\) [M+Na\(^+\)] 325.1016, found 325.1017.

1-(2-(2-(4-Ethylphenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoropropan-1-one (2h)

white solid, mp 88-82 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 8.07 (d, J = 8.0 Hz, 2H), 7.95-7.88 (m, 1H), 7.83-7.76 (m, 1H), 7.73-7.66 (m, 1H), 7.54 (t, J = 7.6 Hz, 1H), 7.44-7.19 (m, 3H), 5.84-5.59 (m, 1H), 2.81-2.68 (m, 2H), 1.62 (dd, J = 24.0, 6.8 Hz, 3H), 1.34-1.26 (m, 3H). \(^1\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 199.1 (d, J = 19.9 Hz), 192.1 (d, J = 21.5 Hz), 150.9, 137.1 (d, J = 18.4 Hz), 133.4, 132.7 (d, J = 1.6 Hz), 132.5 (d, J = 1.0 Hz), 132.3 (d, J = 2.4 Hz), 129.74 (d, J = 5.3 Hz), 129.5 (d, J = 1.9 Hz), 128.3, 127.4 (d, J = 15.6 Hz), 89.6 (d, J = 176.9 Hz), 89.3 (d, J = 176.4 Hz), 29.1, 17.85 (d, J = 22.6 Hz), 15.2. \(^19\)F NMR (376 MHz, CDCl\(_3\); \(\delta\), ppm) -178.3 (s, 1F), -180.3 (s, 1F, major), -180.9 (s, 1F, major), -181.3 (s, 1F). IR (film, \(\nu\), cm\(^{-1}\)) 3052, 2965, 2930, 2869, 1683, 1604, 1574, 1240, 1219, 1010, 980. HR-MS (ESI) m/z calcld for C\(_{19}\)H\(_{18}\)F\(_2\)O\(_2\) [M+Na\(^+\)] 339.1172, found 339.1174.

1-(2-(2-(4-(tert-Butyl)phenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoropropan-1-one (2i)
white solid, mp 85-87 °C; ^1H NMR (400 MHz, CDCl$_3$; δ, ppm) 8.09 (d, J = 8.4 Hz, 2H), 7.92 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.74-7.67 (m, 1H), 7.59-7.52 (m, 3H), 7.40 (d, J = 47.6 Hz, 1H), 5.84-5.63 (m, 1H), 1.64 (dd, J = 24.0, 6.8 Hz, 3H), 1.39 (s, 9H). ^13C NMR (100 MHz, CDCl$_3$; δ, ppm) 199.1 (d, J = 19.8 Hz), 192.1 (d, J = 21.6 Hz), 157.6, 137.0 (d, J = 18.4 Hz), 133.3 (d, J = 1.4 Hz), 132.4 (d, J = 1.6 Hz), 132.3 (d, J = 2.5 Hz), 129.7 (d, J = 5.3 Hz), 129.24 (d, J = 2.1 Hz), 128.4, 127.4 (d, J = 15.6 Hz), 125.8, 89.8 (d, J = 179.2 Hz), 89.8 (d, J = 179.6 Hz), 35.2, 31.1, 17.9 (d, J = 22.5 Hz). ^19F NMR (376 MHz, CDCl$_3$; δ, ppm) -178.4 (s, 1F), -179.6 (s, 1F), -180.3 (s, 1F, major), -181.0 (s, 1F, major). IR (film, ν, cm$^{-1}$) 3037, 2971, 2873, 1697, 1682, 1600, 1572, 1317, 1222, 1190, 1085, 1014, 973. HR-MS (ESI) m/z calcd for C$_{21}$H$_{22}$F$_{2}$O$_{2}$ [M+Na]$^+$ 367.1486, found 367.1480.

2-Fluoro-1-(2-(1-fluoro-2-oxo-2-((thiophen-3-yl)ethyl)phenyl)propan-1-one (2j)

oil; ^1H NMR (400 MHz, CDCl$_3$; δ, ppm) 8.44-8.38 (m, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.81-7.72 (m, 1H), 7.71-7.62 (m, 2H), 7.57-7.49 (m, 1H), 7.41-7.33 (m, 1H), 7.10 (d, J = 47.6 Hz, 1H), 5.83-5.62 (m, 1H), 1.64 (dd, J = 24.0, 6.8 Hz, 3H). ^13C NMR (100 MHz, CDCl$_3$; δ, ppm) 199.7 (d, J = 20.1 Hz), 187.1 (d, J = 22.7 Hz), 139.2 (d, J = 2.1 Hz), 136.1 (d, J = 18.5 Hz), 134.6 (d, J = 5.9 Hz), 133.1 (d, J = 1.0 Hz), 132.8 (d, J = 2.7 Hz), 129.5 (d, J = 5.3 Hz), 128.6 (d, J = 1.4 Hz), 127.7 (d, J = 1.5 Hz), 127.4 (d, J = 14.3 Hz), 126.2, 91.1 (d, J = 178.8 Hz), 90.0 (d, J = 179.6 Hz), 17.91 (d, J = 22.5 Hz). ^19F NMR (376 MHz, CDCl$_3$; δ, ppm) -177.55--177.65 (m, 1F), -180.20 (s, 1F, major), -180.76--180.83 (m, 1F, major), -181.00 (s, 1F). IR (film, ν, cm$^{-1}$) 3110, 2991, 1690, 1575, 1509, 1415, 1232, 1180, 1082, 879. HR-MS (ESI) m/z calcd for C$_{18}$H$_{12}$F$_{2}$O$_{2}$S [M+Na]$^+$ 317.0424, found 317.0430.

2-Fluoro-1-(4-fluoro-2-(1-fluoro-2-oxo-2-(p-tolyl)ethyl)phenyl)propan-1-one (2l)

white solid, mp 115-117 °C; ^1H NMR (400 MHz, CDCl$_3$; δ, ppm) 8.10-7.98 (m, 3H), 7.55 (d, J = 10.0 Hz, 1H), 7.44-7.29 (m, 3H), 7.25-7.18 (m, 1H), 5.78-5.50 (m, 1H), 2.48 (s, 3H), 1.64 (dd, J = 24.4, 6.8 Hz, 3H). ^13C NMR (100 MHz, CDCl$_3$; δ, ppm) 197.1 (d, J = 19.7 Hz), 191.0 (d, J = 21.5 Hz), 165.7 (d, J = 255.3 Hz), 144.9, 141.8 (dd, J = 18.6, 9.0 Hz), 132.8 (dd, J = 9.5, 6.9 Hz), 132.4 (d, J = 1.7 Hz), 129.6, 129.4 (d, J = 1.9 Hz), 115.3 (d, J = 16.2 Hz), 115.1 (dd, J = 24.6, 18.9 Hz), 89.8 (d, J = 178.9 Hz), 89.3 (d, J = 177.8 Hz), 21.8, 17.7 (d, J = 21.5 Hz). ^19F NMR (376 MHz, CDCl$_3$; δ, ppm) -102.2 (s, 1F), -102.3 (s, 1F, major), -179.2 (s, 1F, major), -179.6 (s, 1F), -179.8 (s, 1F), -181.1 (s, 1F, major). IR (film, ν, cm$^{-1}$) 3059, 2995, 2944, 1689, 1608, 1586, 1244, 1226, 1188, 1106, 1092, 996. HR-MS (ESI) m/z calcd for C$_{18}$H$_{15}$F$_{2}$O$_{2}$ [M+Na]$^+$ 343.0922, found 343.0925.

2-Fluoro-1-(5-fluoro-2-(1-fluoro-2-oxo-2-phenylethyl)phenyl)propan-1-one (2m)
white solid, mp 78-80°C; 1H NMR (400 MHz, CDCl3; δ, ppm) 8.12 (d, J = 7.6 Hz, 2H), 7.80-7.73 (m, 1H), 7.69-7.62 (m, 2H), 7.55 (t, J = 7.6 Hz, 2H), 7.43-7.36 (m, 1H), 7.24 (d, J = 47.6 Hz, 1H), 5.74-5.50 (m, 1H), 1.63 (dd, J = 24.4, 6.8 Hz, 3H). 13C NMR (100 MHz, CDCl3; δ, ppm) 198.3 (d, J = 18.8 Hz), 192.4 (d, J = 21.8 Hz), 162.0 (d, J = 248.4 Hz), 134.8 (d, J = 1.7 Hz), 133.9, 132.6 (dd, J = 18.8, 3.4 Hz), 129.4 (dd, J = 15.8, 8.1 Hz), 129.2 (d, J = 2.3 Hz), 128.8, 128.4 (d, J = 3.3 Hz), 120.2 (dd, J = 21.0, 1.4 Hz), 117.0 (dd, J = 23.2, 6.8 Hz), 90.1 (d, J = 179.9 Hz), 89.5 (d, J = 177.6 Hz), 17.6 (d, J = 22.3 Hz). 19F NMR (376 MHz, CDCl3; δ, ppm) -111.4 (s, 1F), -111.9 (s, 1F, major), -111.3--111.4 (m, 1F), -178.3--178.5 (m, 1F, major), -180.3--180.4 (m, 1F), -180.4--180.6(m, 1F, major). IR (film, ν, cm⁻¹) 3000, 2946, 2924, 1693, 1582, 1495, 1450, 1256, 1212, 1196, 1093, 1013, 1002, 913. HR-MS (ESI) m/z calcd for C17H13F3O2 [M+Na]+ 329.0765, found 329.0767.

I-(2-(2-(4-Chlorophenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluorohexan-1-one (2n)

oil; 1H NMR (400 MHz, CDCl3; δ, ppm) 8.12-8.05 (m, 2H), 7.96-7.89 (m, 1H), 7.82-7.76 (m, 1H), 7.72 (t, J = 7.6 Hz, 1H), 7.60-7.48 (m, 3H), 7.25 (d, J = 47.6 Hz, 1H), 5.66-5.48 (m, 1H), 2.07-1.81 (m, 2H), 1.59-1.28 (m, 4H), 0.93 (dd, J = 13.2, 7.2 Hz, 3H). 13C NMR (100 MHz, CDCl3; δ, ppm) 199.1 (d, J = 19.7 Hz), 191.1 (d, J = 21.8 Hz), 140.2, 136.7 (d, J = 18.3 Hz), 133.5 (d, J = 3.9 Hz), 133.2 (d, J = 1.3 Hz), 132.3 (d, J = 2.9 Hz), 130.6 (d, J = 2.3 Hz), 129.8 (d, J = 5.6 Hz), 129.1, 128.5, 127.3 (d, J = 16.0 Hz), 93.3 (d, J = 182.0 Hz), 89.8 (d, J = 177.0 Hz), 32.0 (d, J = 21.1 Hz), 26.9 (d, J = 2.9 Hz), 22.2 (d, J = 5.3 Hz), 13.8 (s, 1H). 19F NMR (376 MHz, CDCl3; δ, ppm) -178.41 (d, J = 47.4 Hz, 1F), -181.35 (d, J = 47.4 Hz, 1F, major), -188.40--188.99 (m, 1F, major), -189.46--189.88 (m, 1F). IR (film, ν, cm⁻¹) 3068, 3028, 1725, 1590, 1507, 1448, 1359, 1220, 1199, 1173, 1155, 1083, 844. HR-MS (ESI) m/z calcd for C20H15F5ClO2 [M+Na]+ 387.0939, found 387.0931.

I-(2-(2-(4-Chlorophenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoror-3-methylbutan-1-one (2o)

oil; 1H NMR (400 MHz, CDCl3; δ, ppm) 8.09 (d, J = 8.4 Hz, 2H), 7.97 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.76-7.68 (m, 1H), 7.61-7.46 (m, 3H), 7.26 (d, J = 48.0 Hz, 1H), 5.53-5.28 (m, 1H), 2.57-2.14 (m, 1H), 1.10 (d, J = 6.8 Hz, 3H), 0.96 (d, J = 6.8 Hz, 3H). 13C NMR (100 MHz, CDCl3; δ, ppm) 198.9 (d, J = 20.1 Hz), 191.2 (d, J = 21.7 Hz), 140.2, 136.8 (d, J = 18.1 Hz), 133.6 (d, J = 1.8 Hz), 132.4 (d, J = 2.4 Hz), 130.6 (d, J = 2.1 Hz), 130.1 (d, J = 6.2 Hz), 129.2, 129.1, 128.5, 127.3 (d, J = 16.3 Hz), 97.1 (d, J = 185.5 Hz), 89.8 (d, J = 176.8 Hz), 31.4 (d, J = 20.5 Hz), 19.0 (d, J = 4.0 Hz), 16.0 (d, J = 5.5 Hz). 19F NMR (376 MHz, CDCl3; δ, ppm) -177.53 (s, 1F), -180.84 (s, 1F, major), -198.53 (s, 3F, major), -199.65 (s, 1F). IR (film, ν, cm⁻¹) 3072, 2969, 2935, 2878, 1698, 1590, 1574, 1489, 1402, 1231, 1214, 1093, 101, 928. HR-MS (ESI) m/z calcd for C19H17ClF3O2 [M+Na]+ 373.0783, found 373.0786.

I-(2-(2-(4-Chlorophenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoror-3,3-dimethylbutan-1-one (2p)
white solid, mp 95-97 ºC; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.09 (d, J = 8.4 Hz, 2H), 8.04 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.74-7.67 (m, 1H), 7.58-7.49 (m, 3H), 7.33 (d, J = 47.6 Hz, 1H), 5.32 (d, J = 48.4 Hz, 1H), 1.03 (s, 9H). ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 199.4 (d, J = 20.8 Hz), 191.5 (d, J = 21.7 Hz), 140.1, 136.4 (d, J = 17.9 Hz), 134.1 (d, J = 2.4 Hz), 133.6 (d, J = 1.7 Hz), 133.4 (d, J = 1.6 Hz), 130.6 (d, J = 2.1 Hz), 130.5, (d, J = 6.0 Hz), 129.1, 128.4, 127.3 (d, J = 16.2 Hz), 98.1 (d, J = 186.2 Hz), 89.97 (d, J = 176.9 Hz), 35.86 (d, J = 19.7 Hz), 25.9 (d, J = 4.6 Hz). ¹⁹F NMR (376 MHz, CDCl₃; δ, ppm) -180.17 (s, 1F), -190.40 (s, 1F). IR (film, ν, cm⁻¹) 3049, 2979, 2942, 2876, 1698, 1671, 1591, 1574, 1403, 1314, 1249, 1213, 1095, 1013, 985. HR-MS (ESI) m/z calcd for C₂₉H₁₉Cl₂F₂O₂ [M+Na]⁺ 387.0939, found 387.0944.

I-(4-Chlorophenyl)-2-(2-(2-cyclobutyl-2-fluoroacetyl)phenyl)-2-fluoroethane (2g)

oil; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.06 (d, J = 8.4 Hz, 2H), 7.92 (d, J = 7.6 Hz, 1H), 7.80-7.66 (m, 2H), 7.58-7.46 (m, 3H), 7.21 (d, J = 48.0 Hz, 1H), 5.62-5.45 (m, 1H), 3.02-2.80 (m, 1H), 2.20-1.78 (m, 6H). ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 198.2 (d, J = 19.9 Hz), 191.23 (d, J = 21.7 Hz), 140.1, 136.64 (d, J = 18.2 Hz), 133.5 (d, J = 1.6 Hz), 133.4, 130.6 (d, J = 2.0 Hz), 129.9 (d, J = 5.3 Hz), 129.1, 128.9 (d, J = 1.8 Hz), 128.5, 127.3 (d, J = 16.0 Hz), 94.2 (d, J = 182.8 Hz), 89.8 (d, J = 176.8 Hz), 37.1 (d, J = 22.4 Hz), 22.5 (d, J = 4.6 Hz), 18.1 (d, J = 12.3 Hz). ¹⁹F NMR (376 MHz, CDCl₃; δ, ppm) -177.4 (d, J = 47.8 Hz, 1F), -181.1 (d, J = 47.4 Hz, 1F, major), -196.8 (dd, J = 49.6, 26.7 Hz, 1F, major), -197.5 (dd, J = 49.6, 26.7 Hz, 1F). IR (film, ν, cm⁻¹) 3071, 2983, 2945, 2866, 1697, 1590, 1574, 1489, 1402, 1245, 1214, 1093, 1012, 976. HR-MS (ESI) m/z calcd for C₂₉H₁₉Cl₂F₂O₂ [M+Na]⁺ 385.0783, found 385.0777.

I-(4-Chlorophenyl)-2-(2-(2-cyclohexyl-2-fluoroacetyl)phenyl)-2-fluoroethane (2r)

white solid, mp 88-90 ºC; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.08 (d, J = 8.8 Hz, 2H), 7.97 (d, J = 7.6 Hz, 1H), 7.80 (d, J = 7.6 Hz, 1H), 7.72 (t, J = 7.6 Hz, 1H), 7.56 (t, J = 7.6 Hz, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.25 (d, J = 47.6 Hz, 1H), 5.45-5.19 (m, 1H), 2.13-1.94 (m, 1H), 1.84-1.56 (m, 5H), 1.42-1.09 (m, 5H). ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 199.2 (d, J = 20.1 Hz), 191.3 (d, J = 21.8 Hz), 140.2, 136.6 (d, J = 18.1 Hz), 133.5, 132.6 (d, J = 2.0 Hz), 130.6 (d, J = 2.2 Hz), 130.1 (d, J = 6.6 Hz), 129.1, 128.5, 127.3 (d, J = 16.0 Hz), 97.0 (d, J = 184.8 Hz), 89.8 (d, J = 177.0 Hz), 40.7 (d, J = 19.9 Hz), 29.1 (d, J = 3.3 Hz), 26.0, 25.7 (d, J = 21.4 Hz). ¹⁹F NMR (376 MHz, CDCl₃; δ, ppm) -177.4 (s, 1F), -180.8 (s, 1F, major), -195.9 (s, 1F, major), -197.0 (s, 1F). IR (film, ν, cm⁻¹) 3092, 2935, 2853, 1701, 1682, 1588, 1572, 1450, 1403, 1229, 1216, 1093, 1014, 989. HR-MS (ESI) m/z calcd for C₂₃H₁₁Cl₂F₂O₂ [M+Na]⁺ 413.1096, found 413.1107.
I-(4-Chlorophenyl)-2-fluoro-2-(2-(2-fluoro-2-phenylacetyl)phenyl)ethanone (2s)

white solid, mp 145-147 °C; $^1$H NMR (400 MHz, CDCl$_3$; δ, ppm) 8.11 (d, J = 8.4 Hz, 2H), 7.88 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.53 (d, J = 8.4 Hz, 2H), 7.50-7.38 (m, 6H), 7.24 (d, J = 47.6 Hz, 1H), 6.51 (d, J = 48.4 Hz, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$; δ, ppm) 196.2 (d, J = 22.0 Hz), 190.9 (d, J = 21.7 Hz), 140.2, 136.9 (d, J = 19.0 Hz), 133.8 (d, J = 20.1 Hz), 133.6, 133.2 (d, J = 1.3 Hz), 131.9 (d, J = 2.9 Hz), 130.6 (d, J = 1.8 Hz), 130.1 (d, J = 3.3 Hz), 129.8 (d, J = 2.4 Hz), 129.2, 128.6 (d, J = 1.5 Hz), 127.8, 127.7 (d, J = 4.5 Hz), 127.1 (d, J = 5.5 Hz), 93.7 (d, J = 186.1 Hz), 89.3 (d, J = 176.4 Hz). $^{19}$F NMR (376 MHz, CDCl$_3$; δ, ppm) -173.1 (s, 1F), -175.9 (s, 1F, major), -179.2 (s, 1F, major), -180.9 (s, 1F). IR (film, ν, cm$^{-1}$) 3066, 2962, 1686, 1589, 1574, 1489, 1402, 1229, 1214, 1092, 1053, 1012, 972. HR-MS (ESI) m/z calcd for C$_{25}$H$_{15}$ClF$_2$O$_2$ [M+Na]$^+$ 407.0626, found 407.0621.

I-(4-Chlorophenyl)-2-fluoro-2-(2-fluoro-2-(m-tolyl)acetyl)phenyl)ethanone (2t)

oil; $^1$H NMR (400 MHz, CDCl$_3$; δ, ppm) 8.09 (d, J = 8.0 Hz, 2H), 7.84 (d, J = 7.6 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.56-7.49 (m, 2H), 7.48-7.39 (m, 1H), 7.36-7.29 (m, 1H), 7.27-7.14 (m, 4H), 6.48 (d, J = 48.8 Hz, 1H), 2.38 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$; δ, ppm) 196.2 (d, J = 21.8 Hz), 190.9 (d, J = 21.8 Hz), 140.2, 139.1 (d, J = 1.1 Hz), 137.0 (d, J = 18.1 Hz), 133.8 (d, J = 9.4 Hz), 133.5 (d, J = 17.3 Hz), 130.7 (d, J = 2.7 Hz), 130.8 (d, J = 2.9 Hz), 130.7, 130.3 (d, J = 2.9 Hz), 129.1, 128.5 (d, J = 1.1 Hz), 128.4 (d, J = 4.9 Hz), 127.8 (dd, J = 10.2, 4.7 Hz), 127.3 (d, J = 15.9 Hz), 124.9 (d, J = 5.2 Hz), 93.7 (d, J = 184.4 Hz), 89.8 (d, J = 177.1 Hz), 21.4. $^{19}$F NMR (376 MHz, CDCl$_3$; δ, ppm) -172.30 (s, 1F, major), -175.13 (s, 1F), -179.18 (s, 1F), -180.88 (s, 1F, major). IR (film, ν, cm$^{-1}$) 3067, 2961, 2922, 2863, 1686, 1589, 1574, 1489, 1401, 1247, 1213, 1093, 1012, 973. HR-MS (ESI) m/z calcd for C$_{23}$H$_{17}$ClF$_2$O$_2$ [M+Na]$^+$ 421.0783, found 421.0791.

2-(4-Bromophenyl)-1-(2-(2-(4-chlorophenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoroethanone (2u)

white solid, mp 124-126°C; $^1$H NMR (400 MHz, CDCl$_3$; δ, ppm) 8.06 (d, J = 8.4 Hz, 2H), 7.89-7.74 (m, 2H), 7.72-7.66 (m, 1H), 7.61-7.43 (m, 5H), 7.39-7.29 (m, 2H), 7.27-7.02 (m, 1H), 6.46 (d, J = 48.0 Hz, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$; δ, ppm) 195.8 (d, J = 21.8 Hz), 191.0 (d, J = 21.9 Hz), 140.3, 137.1 (d, J = 18.3 Hz), 133.9, 133.3 (d, J = 1.8 Hz), 132.9 (d, J = 20.1 Hz), 132.4, 131.5 (d, J = 2.8 Hz), 130.7 (d, J = 2.2 Hz), 130.2 (d, J = 3.6 Hz), 129.2 (d, J = 1.8 Hz), 129.2, 128.5, 127.4 (d, J = 16.1 Hz), 124.3 (d, J = 3.3 Hz), 92.9 (d, J = 185.7 Hz), 89.9 (d, J = 177.7 Hz). $^{19}$F NMR (376 MHz, CDCl$_3$; δ, ppm) -174.35 (s, 1F, major), -176.83 (s, 1F), -179.45 (s, 1F), -181.50 (s, 1F, major). IR (film, ν, cm$^{-1}$) 3089, 2966, 1690, 1588, 1573, 1489, 1403, 1315, 1227, 1212, 1095, 1012, 971. HR-MS (ESI) m/z calcd for C$_{24}$H$_{16}$BrClF$_2$O$_2$ [M+Na]$^+$ 484.9713, found 484.9729.
1-(5-Chloro-2-(1-fluoro-2-oxo-2-phenylethyl)phenyl)-2-fluoro-2-(p-tolyl)ethanone (2v)

white solid, mp 92-94 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.13 (dd, J = 12.8, 7.6 Hz, 2H), 7.79 (s, 1H), 7.75-7.51 (m, 5H), 7.37-7.29 (m, 2H), 7.28-7.02 (m, 3H), 6.41 (d, J = 48.4 Hz, 1H), 2.39 (s, 3H). ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 195.5 (d, J = 22.6 Hz), 191.8 (d, J = 21.6 Hz), 140.3 (d, J = 3.0 Hz), 135.5 (d, J = 18.8 Hz), 134.6 (d, J = 1.7 Hz), 134.5 (d, J = 2.0 Hz), 133.9, 133.4 (d, J = 2.7 Hz), 133.3 (d, J = 1.7 Hz), 130.5 (d, J = 20.1 Hz), 130.0, 129.8 (d, J = 3.5 Hz), 129.3 (d, J = 14.6 Hz), 128.8 (d, J = 3.5 Hz), 127.6 (d, J = 5.0 Hz), 93.8 (d, J = 185.7 Hz), 89.5 (d, J = 178.0 Hz), 21.3. ¹⁹F NMR (376 MHz, CDCl₃; δ, ppm) -172.16 (d, J = 4.1 Hz, 1F, major), -174.40 (d, J = 3.1 Hz, 1F), -179.09 (s, 1F), -180.75 (s, 1F, major). IR (film, ν, cm⁻¹) 3071, 2922, 1694, 1597, 1562, 1449, 1219, 1182, 1115, 1062, 1014, 977. HR-MS (ESI) m/z calcd for C₂₃H₁₇ClF₂O₂ [M+Na]+ 421.0783, found 421.0788.

I-(5-Chloro-2-(1-fluoro-2-oxo-2-phenylethyl)phenyl)-2-fluoro-3-methylbut-3-en-1-one (2w)

white solid, mp 77-79 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.18-8.08 (m, 2H), 7.97 (s, 1H), 7.76-7.62 (m, 3H), 7.59-7.50 (m, 2H), 7.27 (d, J = 47.6 Hz, 1H), 5.80 (d, J = 48.4 Hz, 1H), 5.38-5.22 (m, 2H), 1.81-1.73 (m, 1H). ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 195.7 (d, J = 22.1 Hz), 191.7 (d, J = 21.6 Hz), 138.5 (d, J = 18.0 Hz), 135.4 (d, J = 4.8 Hz), 134.8 (d, J = 1.7 Hz), 134.6 (d, J = 2.1 Hz), 133.9, 133.4 (d, J = 1.6 Hz), 130.1 (d, J = 5.4 Hz), 129.3 (d, J = 2.5 Hz), 128.8, 128.7 (d, J = 16.2 Hz), 118.0 (d, J = 9.1 Hz), 96.0 (d, J = 186.8 Hz), 89.0 (d, J = 177.1 Hz), 17.8 (d, J = 2.7 Hz). ¹¹BF NMR (376 MHz, CDCl₃; δ, ppm) -178.54 (s, 1F), -181.42 (s, 1F), -181.81 (s, 1F), -182.33 (s, 1F). IR (film, ν, cm⁻¹) 3071, 2987, 1694, 1597, 1562, 1451, 1219, 1117, 1062, 1016, 992. HR-MS (ESI) m/z calcd for C₁₀H₁₂ClF₂O [M+Na]+ 371.0626, found 371.0631.

2-Fluoro-1-(2-(1-fluoro-2-(4-fluorophenyl)-2-oxoethyl)phenyl)-3,3-dimethylbutan-1-one (2x)

white solid, mp 62-64 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.19 (dd, J = 8.0, 5.6 Hz, 2H), 8.03 (d, J = 7.6 Hz, 1H), 7.79 (d, J = 7.6 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 7.43-7.17 (m, 3H), 5.33 (d, J = 48.0 Hz, 1H), 1.03 (s, 9H). ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 199.5 (d, J = 20.7 Hz), 191.1 (d, J = 21.5 Hz), 166.1 (d, J = 254.2 Hz), 136.5 (d, J = 18.0 Hz), 134.1 (d, J = 2.4 Hz), 133.4 (d, J = 1.5 Hz), 131.9 (dd, J = 9.4, 2.2 Hz), 131.6 (dd, J = 2.7, 2.0 Hz), 130.5 (d, J = 7.3 Hz), 128.4, 127.3 (d, J = 16.2 Hz), 116.0 (d, J = 21.8 Hz), 98.0 (d, J = 186.1 Hz), 89.98 (d, J = 176.9 Hz), 35.9 (d, J = 19.7 Hz), 25.9 (d, J = 4.6 Hz). ¹¹BF NMR (376 MHz, CDCl₃; δ, ppm) -103.95 (s, 1F), -180.03 (s, 1F), -190.48 (s, 1F). IR (film, ν, cm⁻¹) 3080, 2964, 1703, 1680, 1599, 1575, 1508, 1309, 1221, 1160, 1019, 983. HR-MS (ESI) m/z calcd for C₁₉H₁₉F₃O₂ [M+Na]+ 371.1235,
2-Fluoro-1-(2-(1-fluoro-2-oxo-2-phenylethyl)phenyl)-3,3-dimethylbutan-1-one (2y)

![Chemical Structure](structure1.png)

white solid, mp 84-86 °C; $^1$H NMR (400 MHz, CDCl$_3$; δ, ppm) 8.12 (d, $J = 7.6$ Hz, 2H), 8.00 (d, $J = 8.0$ Hz, 1H), 7.77 (d, $J = 7.6$ Hz, 1H), 7.70-7.58 (m, 2H), 7.51 (t, $J = 7.6$ Hz, 3H), 7.38 (d, $J = 48.0$ Hz, 1H), 5.29 (d, $J = 48.4$ Hz, 1H), 1.02 (s, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$; δ, ppm) 199.5 (d, $J = 21.0$ Hz), 192.7 (d, $J = 21.5$ Hz), 136.6 (d, $J = 18.0$ Hz), 135.2 (d, $J = 1.5$ Hz), 134.3 (d, $J = 2.3$ Hz), 133.7, 133.3 (d, $J = 1.1$ Hz), 130.4 (d, $J = 7.3$ Hz), 129.2 (d, $J = 2.0$ Hz), 128.8, 128.3, 127.4 (d, $J = 16.0$ Hz), 98.2 (d, $J = 186.2$ Hz), 89.9 (d, $J = 176.8$ Hz), 35.9 (d, $J = 19.7$ Hz), 25.9 (d, $J = 4.6$ Hz). $^{19}$F NMR (376 MHz, CDCl$_3$; δ, ppm) -174.92 (s, 1F), -179.92 (s, 1F major), -190.19 (s, 1F), -190.41 (s, 1F major). IR (film, μ, cm$^{-1}$) 3076, 2985, 2967, 2944, 2875, 1702, 1671, 1598, 1571, 1452, 1314, 1239, 1215, 1183, 1068, 1016, 984. HR-MS (ESI) m/z calc for C$_{20}$H$_{20}$F$_2$O$_2$ [M+Na]$^+$ 353.1329, found 353.1329.

2-fluoro-1-(2-(1-fluoro-2-oxo-2-(p-tolyl)ethyl)phenyl)-3,3-dimethylbutan-1-one (2z)

![Chemical Structure](structure2.png)

white solid, mp 100-102 °C; $^1$H NMR (400 MHz, CDCl$_3$; δ, ppm) 8.04 (d, $J = 8.0$ Hz, 2H), 8.00 (d, $J = 8.0$ Hz, 1H), 7.78 (d, $J = 8.0$ Hz, 1H), 7.67 (t, $J = 7.6$ Hz, 1H), 7.53 (t, $J = 7.6$ Hz, 1H), 7.47-7.31 (m, 3H), 5.31 (d, $J = 48.0$ Hz, 1H), 2.46 (s, 3H), 1.04 (s, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$; δ, ppm) 199.6 (d, $J = 20.8$ Hz), 192.3 (d, $J = 21.2$ Hz), 144.7, 136.6 (d, $J = 18.2$ Hz), 134.4 (d, $J = 2.5$ Hz), 133.2 (d, $J = 1.1$ Hz), 132.7 (d, $J = 1.4$ Hz), 130.3 (d, $J = 7.4$ Hz), 129.5, 129.3 (d, $J = 2.0$ Hz), 128.3, 127.4 (d, $J = 15.7$ Hz), 98.3 (d, $J = 186.2$ Hz), 89.9 (d, $J = 176.8$ Hz), 35.9 (d, $J = 19.6$ Hz), 25.9 (d, $J = 4.6$ Hz), 21.8. $^{19}$F NMR (376 MHz, CDCl$_3$; δ, ppm) -179.55 (s, 1F), -190.33 (s, 1F). IR (film, μ, cm$^{-1}$) 3011, 2988, 1686, 1671, 1607, 1571, 1370, 1319, 1241, 1225, 1209, 1067, 1017, 983. HR-MS (ESI) m/z calc for C$_{21}$H$_{22}$F$_2$O$_2$ [M+Na]$^+$ 367.1486, found 367.1488.

1-(2-(2-(4-ethylphenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoro-3,3-dimethylbutan-1-one (2aa)

![Chemical Structure](structure3.png)

white solid, mp 85-87 °C; $^1$H NMR (400 MHz, CDCl$_3$; δ, ppm) 8.07 (d, $J = 8.0$ Hz, 2H), 8.00 (d, $J = 7.6$ Hz, 1H), 7.78 (d, $J = 8.0$ Hz, 1H), 7.68 (t, $J = 7.6$ Hz, 1H), 7.53 (t, $J = 7.6$ Hz, 1H), 7.46-7.32 (m, 3H), 5.32 (d, $J = 48.4$ Hz, 1H), 2.75 (q, $J = 7.6$ Hz, 1H), 1.30 (t, $J = 7.6$ Hz, 3H), 1.04 (s, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$; δ, ppm) 199.6 (d, $J = 21.1$ Hz), 192.3 (d, $J = 21.3$ Hz), 150.7, 136.6 (d, $J = 18.1$ Hz), 134.4 (d, $J = 2.6$ Hz), 133.2, 132.8 (d, $J = 1.5$ Hz), 130.3 (d, $J = 7.4$ Hz), 129.4 (d, $J = 2.0$ Hz), 128.3, 127.4 (d, $J = 15.6$ Hz), 98.3 (d, $J = 186.3$ Hz), 89.9 (d, $J = 176.8$ Hz), 35.9 (d, $J = 19.7$ Hz), 29.1, 25.9 (d, $J = 4.6$ Hz), 15.1. $^{19}$F NMR (376 MHz,
1-(2-(2-(4-(tert-butyl)phenyl)-1-fluoro-2-oxoethyl)phenyl)-2-fluoro-3,3-dimethylbutan-1-one (2bb)

oil; \(^1\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 8.09 (d, J = 8.0 Hz, 2H), 8.01 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 7.6 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.58-7.50 (m, 3H), 7.40 (d, J = 48.0 Hz, 1H), 5.33 (d, J = 48.4 Hz, 1H), 1.38 (s, 9H), 1.04 (s, 9H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 199.7 (d, J = 20.9 Hz), 192.3 (d, J = 21.3 Hz), 157.5, 136.6 (d, J = 18.0 Hz), 134.4 (d, J = 2.4 Hz), 133.2, 132.5, 130.3 (d, J = 7.2 Hz), 129.2 (d, J = 2.0 Hz), 128.3, 127.4 (d, J = 15.8 Hz), 125.8, 98.3 (d, J = 186.2 Hz), 93.18 (d, J = 176.7 Hz), 35.9 (d, J = 19.6 Hz), 35.2, 31.1, 25.9 (d, J = 4.6 Hz). \(^{19}\)F NMR (376 MHz, CDCl\(_3\); \(\delta\), ppm) -179.59 (s, 1F), -190.48 (s, 1F). IR (film, \(\nu\), cm\(^{-1}\)). HR-MS (ESI) m/z calcd for C\(_{22}\)H\(_{18}\)F\(_2\)O\(_2\) [M+Na]\(^+\) 409.1955, found 409.1958.

2-fluoro-1-(2-(1-fluoro-2-(4-methoxyphenyl)-2-oxoethyl)phenyl)-3,3-dimethylbutan-1-one (2cc)

white solid, mp 91-93 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 8.13 (d, J = 8.8 Hz, 2H), 7.99 (d, J = 7.6 Hz, 1H), 7.77 (d, J = 7.6 Hz, 1H), 7.71-7.63 (m, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.36 (d, J = 48.4 Hz, 1H), 7.00 (d, J = 8.8 Hz, 2H), 5.31 (d, J = 48.4 Hz, 1H), 3.91 (s, 3H), 1.04 (s, 9H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 199.8 (d, J = 21.3 Hz), 191.2 (d, J = 21.3 Hz), 164.0, 136.6 (d, J = 17.9 Hz), 134.6 (d, J = 2.8 Hz), 133.1 (d, J = 0.9 Hz), 131.6 (d, J = 2.1 Hz), 130.2 (d, J = 7.5 Hz), 128.2, 128.1 (d, J = 1.5 Hz), 127.4 (d, J = 15.3 Hz), 114.0, 98.4 (d, J = 186.3 Hz), 89.8 (d, J = 176.9 Hz), 55.5, 35.9 (d, J = 19.7 Hz), 25.9 (d, J = 4.7 Hz). \(^{19}\)F NMR (376 MHz, CDCl\(_3\); \(\delta\), ppm) -179.04 (s, 1F), -190.34 (s, 1F). IR (film, \(\nu\), cm\(^{-1}\)) 3072, 2976, 1686, 1673, 1602, 1575, 1423, 1263, 1248, 1033, 1016, 983. HR-MS (ESI) m/z calcd for C\(_{21}\)H\(_{18}\)F\(_2\)O\(_3\) [M+Na]\(^+\) 383.1435, found 383.1429.

2-Fluoro-1-(2-(1-fluoro-2-oxo-2-(thiophen-3-yl)ethyl)phenyl)-3,3-dimethylbutan-1-one (2dd)

white solid, mp 82-84 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 8.44-8.40 (m, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.76-7.62 (m, 3H), 7.57-7.49 (m, 1H), 7.39-7.33 (m, 1H), 7.13 (d, J = 48.0 Hz, 1H), 5.29 (d, J = 48.0 Hz, 1H), 1.06 (s, 9H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 200.2 (d, J = 21.7 Hz, 1H), 187.3 (d, J = 22.3 Hz), 139.4 (d, J = 2.0 Hz), 135.6 (d, J = 18.2 Hz), 135.0 (d, J = 2.7 Hz), 134.5 (d, J = 5.6 Hz), 132.9, 130.0 (d, J = 7.6 Hz), 128.5, 127.7 (d, J = 13.7 Hz), 127.6, 126.2, 98.7 (d, J = 186.9 Hz), 91.2 (d, J = 179.0 Hz), 35.9 (d, J = 19.6 Hz), 25.9 (d, J = 4.6 Hz). \(^{19}\)F NMR (376 MHz, CDCl\(_3\); \(\delta\), ppm) -178.87 (s, 1F), -190.04 (s, 1F). IR (film, \(\nu\), cm\(^{-1}\))
Typical Procedure for the Synthesis of Products 3.
In an oven-dried Schlenk tube, to a methanol solution (1.0 mL) of products 2 (1.0 equiv, 0.2 mmol), NH$_4$OAc (3 equiv, 0.6 mmol) was added under air condition. The reaction mixture was stirred at room temperature for 8 hours. After the reaction monitored by TLC was completed, the organic solvent was removed under vacuum, and the residue was purified by silica gel column with petroleum ether/ethyl acetate to afford products.

3-(4-Chlorophenyl)-4-fluoro-1-(1-fluoroethyl)isoquinoline (3a)

![Chemical Structure]

white solid, mp 106-107 °C; $^1$H NMR (400 MHz, CDCl$_3$; δ ppm) 8.44 (d, J = 8.8 Hz, 1H), 8.22 (d, J = 8.4 Hz, 1H), 8.16 (d, J = 8.4 Hz, 2H), 7.82 (t, J = 7.6 Hz, 1H), 7.75-7.67 (m, 1H), 7.51 (d, J = 8.8 Hz, 2H), 6.48-6.23 (m, 1H), 2.00 (dd, J = 24.0, 6.4 Hz, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$; δ ppm) 152.7 (dd, J = 19.7, 5.7 Hz), 152.5 (d, J = 266.6 Hz), 152.4 (d, J = 264.4 Hz), 134.7 (d, J = 1.4 Hz), 134.0 (d, J = 6.1 Hz), 133.0 (d, J = 10.2 Hz), 130.5 (d, J = 1.8 Hz), 130.2 (d, J = 7.2 Hz), 128.7, 128.2 (d, J = 16.3 Hz), 127.3 (d, J = 2.6 Hz), 125.2 (dd, J = 6.0, 1.2 Hz), 120.7 (d, J = 6.6 Hz), 90.8 (d, J = 166.6 Hz), 19.8 (d, J = 23.1 Hz). $^{19}$F NMR (376 MHz, CDCl$_3$; δ ppm) -135.86 (d, J = 4.9 Hz, 1F), -167.18 (d, J = 4.5 Hz, 1F).

IR (film, ν, cm$^{-1}$) 3052, 2985, 1623, 1591, 1502, 1450, 1319, 1264, 1182, 1070, 1054, 1011, 988. HR-MS (ESI) m/z calcd for C$_{18}$H$_{18}$F$_2$O$_2$S[M+Na]$^+$ 359.0893, found 359.0898.

4-Fluoro-1-(1-fluoroethyl)-3-(m-toly)isoquinoline (3b)

![Chemical Structure]

white solid, mp 73-75 °C; $^1$H NMR (400 MHz, CDCl$_3$; δ ppm) 8.46 (d, J = 8.4 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 10.0 Hz, 2H), 7.81 (t, J = 7.6 Hz, 1H), 7.75-7.66 (m, 1H), 7.45 (t, J = 7.6 Hz, 1H), 7.28 (d, J = 7.6 Hz, 1H), 6.49-6.27 (m, 1H), 2.51 (s, 3H), 2.01 (dd, J = 24.0, 6.4 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$; δ ppm) 152.6 (d, J = 20.8 Hz), 152.6 (d, J = 20.7 Hz), 152.34 (dd, J = 263.7, 1.7 Hz), 138.1, 135.5 (d, J = 5.8 Hz), 134.6 (d, J = 10.8 Hz), 130.3 (d, J = 1.8 Hz), 129.6 (d, J = 6.0 Hz), 129.5, 128.4, 127.9, 127.1 (d, J = 2.4 Hz), 126.1 (d, J = 6.7 Hz), 125.2 (dd, J = 6.3, 1.3 Hz), 120.7 (d, J = 6.6 Hz), 91.2 (d, J = 166.5 Hz), 21.7, 20.0 (d, J = 23.2 Hz). $^{19}$F NMR (376 MHz, CDCl$_3$; δ ppm) -136.52 (d, J = 4.9 Hz, 1F), -167.18 (d, J = 4.5 Hz, 1F). IR (film, ν, cm$^{-1}$) 3051, 2921, 1622, 1588, 1373, 1263, 1162, 1059, 1040, 989. HR-MS (ESI) m/z calcd for C$_{18}$H$_{12}$ClF$_2$N [M+Na]$^+$ 326.0524, found 326.0528.

3-(4-Chlorophenyl)-4-fluoro-1-(1-fluoro-2-methylpropyl)isoquinoline (3c)

![Chemical Structure]
3-(4-Chlorophenyl)-4-fluoro-1-(1-fluoropentyl)isoquinoline (3d)

white solid, mp 68-69 °C; 1H NMR (400 MHz, CDCl3; δ, ppm) 8.44 (d, J = 8.8 Hz, 1H), 8.23 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.8 Hz, 2H), 7.85-7.77 (m, 1H), 7.75-7.66 (m, 1H), 7.52 (d, J = 8.4 Hz, 2H), 6.24-5.97 (m, 1H), 2.50-2.15 (m, 2H), 1.76-1.60 (m, 1H), 1.58-1.41 (m, 3H), 1.02-0.92 (m, 3H). 13C NMR (100 MHz, CDCl3; δ, ppm) 152.69 (dd, J = 21.0, 5.7 Hz), 152.5 (dd, J = 264.1, 1.6 Hz) 134.7 (d, J = 6.0 Hz), 133.1 (d, J = 10.2 Hz), 130.5 (d, J = 1.8 Hz), 130.2 (d, J = 7.1 Hz), 128.7, 128.3 (d, J = 16.2 Hz), 128.1, 127.4 (d, J = 2.5 Hz), 125.2 (dd, J = 6.5, 1.1 Hz), 120.7 (d, J = 6.7 Hz), 94.9 (d, J = 170.9 Hz), 34.1 (d, J = 21.6 Hz), 27.6 (d, J = 4.7 Hz), 22.5, 14.0. 19F NMR (376 MHz, CDCl3; δ, ppm) -136.20 (d, J = 4.1 Hz, 1F), -174.65 (d, J = 4.1 Hz, 1F). IR (film, ν, cm⁻¹) 3073, 2976, 1624, 1590, 1503, 1377, 1251, 1187, 1091, 1011, 996. HR-MS (ESI) m/z calcd for C20H18ClF3N [M+Na]⁺ 368.0994, found 368.0986.

3-(4-Chlorophenyl)-4-fluoro-1-(fluoro(phenyl)methyl)isoquinoline (3e)

white solid, mp 114-116 °C; 1H NMR (400 MHz, CDCl3; δ, ppm) 8.31 (d, J = 8.0 Hz, 1H), 8.22 (d, J = 8.4 Hz, 1H), 8.16 (d, J = 8.4 Hz, 2H), 7.80-7.75 (m, 1H), 7.63-7.57 (m, 1H), 7.55-7.46 (m, 3H), 7.4-7.31 (m, 3H), 7.15 (d, J = 47.6 Hz, 1H). 13C NMR (100 MHz, CDCl3; δ, ppm) 152.6 (d, J = 264.9, 1.6 Hz), 152.3 (d, J = 22.1 Hz), 152.2 (d, J = 22.1 Hz), 138.5 (d, J = 21.7 Hz), 134.8, 133.8 (d, J = 6.0 Hz), 133.3 (d, J = 10.2 Hz), 130.6 (d, J = 1.8 Hz), 130.2 (d, J = 7.1 Hz), 128.8 (d, J = 34.9 Hz), 128.7, 128.5, 128.3 (d, J = 1.4 Hz), 128.2, 127.1 (d, J = 2.7 Hz), 125.8 (d, J = 6.7 Hz), 120.7 (d, J = 6.7 Hz), 96.0 (d, J = 175.2 Hz). 19F NMR (376 MHz, CDCl3; δ, ppm) -135.63 (d, J = 3.6 Hz, 1F), -174.68 (d, J = 3.6 Hz, 1F). IR (film, ν, cm⁻¹) 3061, 1622, 1592, 1502, 1448, 1372, 1175, 1162, 1093, 1057, 1012, 961. HR-MS (ESI) m/z calcd for C22H14ClF3N [M+Na]⁺ 388.0681, found 388.0676.

4-Fluoro-1-(1-fluoro-2,2-dimethylpropyl)-3-(thiophen-3-yl)isoquinoline (3f)
white solid, mp 89-91 °C; $^1$H NMR (400 MHz, CDCl$_3$; $\delta$, ppm) 8.45 (d, $J$ = 8.4 Hz, 1H), 8.20 (d, $J$ = 8.4 Hz, 2H), 7.99 (d, $J$ = 4.8 Hz, 1H), 7.80-7.72 (m 1H), 7.67-7.58 (m, 1H), 7.46 (dd, $J$ = 4.4, 3.2 Hz, 1H), 5.90 (d, $J$ = 46.4 Hz, 1H), 1.16 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 151.3 (dd, $J$ = 21.8, 6.0 Hz), 150.84 (dd, $J$ = 263.1, 1.2 Hz), 137.2 (d, $J$ = 6.5 Hz), 130.7 (dd, $J$ = 11.3, 1.1 Hz), 130.1 (d, $J$ = 1.8 Hz), 128.0 (d, $J$ = 15.6 Hz), 127.9 (d, $J$ = 6.0 Hz), 127.8 (d, $J$ = 1.2 Hz), 127.3 (d, $J$ = 1.7 Hz), 126.3 (dd, $J$ = 10.8, 1.2 Hz), 125.6 (d, $J$ = 9.8 Hz), 125.4 (d, $J$ = 1.0 Hz), 120.3 (d, $J$ = 6.9 Hz), 101.2 (d, $J$ = 179.6 Hz), 36.6 (d, $J$ = 20.5 Hz), 26.4 (d, $J$ = 4.3 Hz). $^{19}$F NMR (376 MHz, CDCl$_3$; $\delta$, ppm) -136.29 (s, 1F), -185.14 (d, $J$ = 1.9 Hz, 1F). IR (film, $\nu$, cm$^{-1}$) 3067, 2970, 1623, 1591, 1476, 1395, 1213, 1174, 1057, 995. HR-MS (ESI) m/z calcd for C$_{18}$H$_{17}$F$_2$NS [M+Na]$^+$ 340.0947, found 340.0948.
Copies of $^1$H, $^{13}$C and $^{19}$F NMR Spectra for Compounds

$^1$H NMR Spectrum of Compound 2a

$^{13}$C NMR Spectrum of Compound 2a
\[ \text{\(^{19}\text{F NMR Spectrum of Compound 2a}\)} \]

\[ \text{\(^{1}\text{H NMR Spectrum of Compound 2b}\)} \]

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$^{13}$C NMR Spectrum of Compound 2b

$^{19}$F NMR Spectrum of Compound 2b
$^{1}H$ NMR Spectrum of Compound 2c

$^{13}C$ NMR Spectrum of Compound 2c
$^{19}$F NMR Spectrum of Compound 2c

$^1$H NMR Spectrum of Compound 2d
$^{13}$C NMR Spectrum of Compound 2d

$^{19}$F NMR Spectrum of Compound 2d
$^1$H NMR Spectrum of Compound 2e

$^{13}$C NMR Spectrum of Compound 2e
$^{19}$F NMR Spectrum of Compound 2e

$^1$H NMR Spectrum of Compound 2f
$^{13}$C NMR Spectrum of Compound 2f

$^{19}$F NMR Spectrum of Compound 2f
$^1$H NMR Spectrum of Compound 2g

$^{13}$C NMR Spectrum of Compound 2g
$^{19}$F NMR Spectrum of Compound 2g

$^1$H NMR Spectrum of Compound 2h
$^{13}$C NMR Spectrum of Compound 2h

$^{19}$F NMR Spectrum of Compound 2h
$^1$H NMR Spectrum of Compound 2i

$^{13}$C NMR Spectrum of Compound 2i
$^1$F NMR Spectrum of Compound 2i

$^1$H NMR Spectrum of Compound 2j
\( ^{13}\text{C NMR Spectrum of Compound 2j} \)

\( ^{19}\text{F NMR Spectrum of Compound 2j} \)
$^1$H NMR Spectrum of Compound 2m

$^{13}$C NMR Spectrum of Compound 2m
$^{19}$F NMR Spectrum of Compound 2m

$^1$H NMR Spectrum of Compound 2l
$^{13}$C NMR Spectrum of Compound 2l

$^{19}$F NMR Spectrum of Compound 2l
$^1$H NMR Spectrum of Compound 2n

$^{13}$C NMR Spectrum of Compound 2n
$^{19}$F NMR Spectrum of Compound 2n

$^1$H NMR Spectrum of Compound 2o
$^{13}$C NMR Spectrum of Compound 2o

$^{19}$F NMR Spectrum of Compound 2o
$\text{H NMR Spectrum of Compound 2p}$

$\text{C NMR Spectrum of Compound 2p}$
19F NMR Spectrum of Compound 2p

1H NMR Spectrum of Compound 2q
$^{13}$C NMR Spectrum of Compound 2q

$^{19}$F NMR Spectrum of Compound 2q
$^1$H NMR Spectrum of Compound 2r

$^{13}$C NMR Spectrum of Compound 2r
$^{19}\text{F NMR Spectrum of Compound 2r}$

$^{1}\text{H NMR Spectrum of Compound 2s}$
$^{13}$C NMR Spectrum of Compound 2s

$^{19}$F NMR Spectrum of Compound 2s
$^{1}H$ NMR Spectrum of Compound 2t

$^{13}C$ NMR Spectrum of Compound 2t
$^{19}$F NMR Spectrum of Compound 2t

$^1$H NMR Spectrum of Compound 2u
$^{13}$C NMR Spectrum of Compound 2u

$^{19}$F NMR Spectrum of Compound 2u
$^1$H NMR Spectrum of Compound 2v

$^{13}$C NMR Spectrum of Compound 2v
$^{19}$F NMR Spectrum of Compound 2v

$^1$H NMR Spectrum of Compound 2w
$^{13}$C NMR Spectrum of Compound 2w

$^{19}$F NMR Spectrum of Compound 2w
H NMR Spectrum of Compound 2x

13C NMR Spectrum of Compound 2x
$\text{F NMR Spectrum of Compound 2x}$

$\text{H NMR Spectrum of Compound 2y}$
$^{13}$C NMR Spectrum of Compound 2y

$^{19}$F NMR Spectrum of Compound 2y
**1H NMR Spectrum of Compound 2z**

**13C NMR Spectrum of Compound 2z**
$^{19}$F NMR Spectrum of Compound 2z

$^1$H NMR Spectrum of Compound 2aa
$^{13}$C NMR Spectrum of Compound 2aa

$^{19}$F NMR Spectrum of Compound 2aa
$^{\text{1}}\text{H NMR Spectrum of Compound 2bb}$

$^{\text{13C NMR Spectrum of Compound 2bb}}$
$^{19}$F NMR Spectrum of Compound 2bb

$^1$H NMR Spectrum of Compound 2cc
$^{13}$C NMR Spectrum of Compound 2cc

$^{19}$F NMR Spectrum of Compound 2cc
$^{1}H$ NMR Spectrum of Compound 2dd

$^{13}$C NMR Spectrum of Compound 2dd
$^{19}$F NMR Spectrum of Compound 2dd

$^{1}$H NMR Spectrum of Compound 3a
$^{13}$C NMR Spectrum of Compound 3a

$^{19}$F NMR Spectrum of Compound 3a
$^{1}$H NMR Spectrum of Compound 3b

$^{13}$C NMR Spectrum of Compound 3b
$^{19}$F NMR Spectrum of Compound 3b

$^1$H NMR Spectrum of Compound 3c
$^1$C NMR Spectrum of Compound 3c

$^{19}$F NMR Spectrum of Compound 3c
$^1$H NMR Spectrum of Compound 3d

$^{13}$C NMR Spectrum of Compound 3d
$^1$H NMR Spectrum of Compound 3e

$^{19}$F NMR Spectrum of Compound 3d
$^{13}$C NMR Spectrum of Compound 3e

$^{19}$F NMR Spectrum of Compound 3e
H NMR Spectrum of Compound 3f

^1^H NMR Spectrum of Compound 3f

13C NMR Spectrum of Compound 3f

^1^3^C NMR Spectrum of Compound 3f
$^{19}$F NMR Spectrum of Compound 3f