Electronic Supplementary Information

for

Dual Roles of Ethyl Bromodifluoroacetate in the Formation of Fluorine-containing Heteroaromatic Compounds

Xingxing Ma, Shaoyu Mai, Yao Zhou, Gui-Juan Cheng and Qiuling Song

\[ \text{Institute of Next Generation Matter Transformation, College of Chemical Engineering at Huaqiao University, 668 Jimei Blvd, Xiamen, Fujian, 361021, P. R. China.} \]

\[ \text{Warshel Institute for Computational Biology, School of Science and Engineering,} \]
\[ \text{The Chinese University of Hong Kong, Shenzhen, 2001 Longxiang Road, Shenzhen 51817, P. R. China.} \]

\[ \text{State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, P R China.} \]

Fax:86-592-6162990.
E-mail: qsong@hqu.edu.cn
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1. General information

All chemicals were purchased from Adamas Reagent, energy chemical company (BrCF$_2$COOEt, BrCF$_2$COOH, ClCF$_2$COONa), J&K Scientific Ltd, Bide Pharmatech Ltd and Tansoole, Shuya company (BrCF$_2$PO(OEt)$_2$). Unless otherwise stated, all experiments were conducted in a sealed tube under N$_2$ atmosphere. Reactions were monitored by TLC or GC-MS analysis. Flash column chromatography was performed over silica gel (200-300 mesh).

$^1$H-NMR and $^{13}$C-NMR spectra were recorded in CDCl$_3$ on a Bruker Avance 500 spectrometer (500 MHz $^1$H, 125 MHz $^{13}$C, 470 MHz $^9$F) at room temperature. Chemical shifts were reported in ppm on the scale relative to CDCl$_3$ ($\delta = 7.26$ for $^1$H-NMR, $\delta = 77.00$ for $^{13}$C-NMR) as an internal reference. Coupling constants ($J$) were reported in Hertz (Hz).
2. Optimization of experiment conditions for 3a

Table S1. The reaction of without the additive compared with additive

\[
\begin{align*}
\text{Ar}^3 \text{NH}_2 + \text{Br} \text{COOEt} & \xrightarrow{\text{Cu(OTf)}_2 (10 \text{ mol\%}), 
1,10\text{-phen} (12 \text{ mol\%}), 
\text{Na}_2\text{CO}_3 (3 \text{ equiv})} \text{120 \degree C, 20 h, solvent} \\
\text{1a} & \rightarrow \text{3a} 82\%
\end{align*}
\]

\[
\begin{align*}
\text{Ar}^3 \text{NH}_2 + \text{Br} \text{COOEt} & \xrightarrow{\text{Cu(OTf)}_2 (10 \text{ mol\%}), 
1,10\text{-phen} (12 \text{ mol\%}), 
\text{Na}_2\text{CO}_3 (3 \text{ equiv}) \text{ and } \text{B}_2\text{pin} (30 \text{ mol\%})} \text{120 \degree C, 20 h, solvent} \\
\text{1a} & \rightarrow \text{3a} 71\%
\end{align*}
\]

Table S2. Optimization of the bases

<table>
<thead>
<tr>
<th>entry</th>
<th>base</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>K$_2$CO$_3$</td>
<td>78%</td>
</tr>
<tr>
<td>2</td>
<td>Na$_2$CO$_3$</td>
<td>86% (82%)</td>
</tr>
<tr>
<td>3</td>
<td>NaHCO$_3$</td>
<td>73%</td>
</tr>
<tr>
<td>4</td>
<td>K$_3$PO$_4$</td>
<td>67%</td>
</tr>
<tr>
<td>5</td>
<td>Na$_3$PO$_4$</td>
<td>80%</td>
</tr>
<tr>
<td>6</td>
<td>Cs$_2$CO$_3$</td>
<td>57%</td>
</tr>
<tr>
<td>7</td>
<td>NaOAc</td>
<td>63%</td>
</tr>
<tr>
<td>8</td>
<td>Li$_2$CO$_3$</td>
<td>49%</td>
</tr>
</tbody>
</table>

Reaction condition: 1a (0.2 mmol), 2 (3 equiv), Cu(OTf)$_2$ (10 mol%), 1,10-phen (12 mol%), base (3 equiv).

GC yield, *isolated yield*
Table S3. Optimization of the Cu salt for reaction

<table>
<thead>
<tr>
<th>entry</th>
<th>[Cu]</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CuSO₄</td>
<td>67%</td>
</tr>
<tr>
<td>2</td>
<td>Cu(OTf)₂</td>
<td>86%</td>
</tr>
<tr>
<td>3</td>
<td>Cu(OAc)₂</td>
<td>68%</td>
</tr>
<tr>
<td>4</td>
<td>CuCl₂</td>
<td>60%</td>
</tr>
<tr>
<td>5</td>
<td>Cu(NO₃)₂</td>
<td>73%</td>
</tr>
<tr>
<td>6</td>
<td>Cu(acac)₂</td>
<td>70%</td>
</tr>
<tr>
<td>7</td>
<td>CuCN</td>
<td>47%</td>
</tr>
<tr>
<td>8</td>
<td>CuCl</td>
<td>58%</td>
</tr>
<tr>
<td>9</td>
<td>CuBr</td>
<td>54%</td>
</tr>
<tr>
<td>10</td>
<td>Cul</td>
<td>66%</td>
</tr>
</tbody>
</table>

Reaction conditions: 1a (0.2 mmol), 2 (3 equiv), Cu salt (10 mol%), 1,10-phen (12 mol%), Na₂CO₃ (3 equiv), 120 °C, 20 h, CH₃CN. GC yield. *isolated yield.

Table S4. Optimization of the solvent for reaction
Table S5. Optimization of the ligand for reaction

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>dioxane</td>
<td>77%</td>
</tr>
<tr>
<td>2</td>
<td>CH$_3$CN</td>
<td>86% ($^b$ 82%)</td>
</tr>
<tr>
<td>3</td>
<td>toluene</td>
<td>trace</td>
</tr>
<tr>
<td>4</td>
<td>THF</td>
<td>79%</td>
</tr>
<tr>
<td>5</td>
<td>acetone</td>
<td>68%</td>
</tr>
<tr>
<td>6</td>
<td>DCE</td>
<td>70%</td>
</tr>
<tr>
<td>7</td>
<td>DMF</td>
<td>33%</td>
</tr>
<tr>
<td>8</td>
<td>DMSO</td>
<td>trace</td>
</tr>
<tr>
<td>9</td>
<td>CH$_3$OH</td>
<td>61%</td>
</tr>
<tr>
<td>10</td>
<td>DMOE</td>
<td>42%</td>
</tr>
</tbody>
</table>

Reaction condition: 1a (0.2 mmol), 2 (3 equiv), Cu salt (10 mol%), 1,10-phen (12 mol%), Na$_2$CO$_3$ (3 equiv), 120 °C, 20 h, solvent.

$^b$ isolated yield, DMOE=1,2-Dimethoxyethane
<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>L1</td>
<td>69%</td>
</tr>
<tr>
<td>2</td>
<td>L2</td>
<td>61%</td>
</tr>
<tr>
<td>3</td>
<td>L3</td>
<td>66%</td>
</tr>
<tr>
<td>4</td>
<td>L4</td>
<td>68%</td>
</tr>
<tr>
<td>5</td>
<td>L5</td>
<td>77%</td>
</tr>
<tr>
<td>6</td>
<td>L6</td>
<td>74%</td>
</tr>
<tr>
<td>7</td>
<td>L7</td>
<td>71%</td>
</tr>
<tr>
<td>8</td>
<td>L8</td>
<td>78%</td>
</tr>
<tr>
<td>9</td>
<td>L9</td>
<td>86% (b 82%)</td>
</tr>
</tbody>
</table>

Reaction condition: 1a (0.2 mmol), 2 (3 equiv), Cu(OTf)$_2$ (10 mol%), ligand (12 mol%), Na$_2$CO$_3$ (3 equiv), GC yield. b isolated yield.
Table S6. Screening of the different difluromethyl compounds

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td></td>
</tr>
<tr>
<td>Cu(OTf)$_2$ (10 mol%)</td>
<td>1,10-phen (12 mol%)</td>
</tr>
<tr>
<td>Na$_2$CO$_3$ (3 equiv)</td>
<td>120 °C, 20 h, CH$_3$CN</td>
</tr>
</tbody>
</table>

| X=Br, R=COOEt | 2 |
| $0.32$/g |

| X=Br, R=COOH | 2-COOH |
| $3.04$/g |

| X=Br, R=P(O)(OEt)$_2$ | 7 |
| $2.29$/g |

| X=Cl, R=COONa | 2-COONa |
| $0.52$/g |

| X=Br, R=C(O)NCy$_2$ | 2-amide prepared |

| X=Br, R=O | 2-amide prepared |

| X=Br, R=O | 2-amide prepared |

| X=Br, R=O | 2-amide prepared |

**Example Entries:***

| X=Br, R=COOEt | 2 |
| $0.32$/g |

| X=Br, R=COOH | 2-COOH |
| $3.04$/g |

| X=Br, R=P(O)(OEt)$_2$ | 7 |
| $2.29$/g |

| X=Cl, R=COONa | 2-COONa |
| $0.52$/g |

| X=Br, R=C(O)NCy$_2$ | 2-amide prepared |

| X=Br, R=O | 2-amide prepared |

| X=Br, R=O | 2-amide prepared |

| X=Br, R=O | 2-amide prepared |
3. General procedure for starting materials

(1). General experimental procedures for substrates 1

GP-I: In a dry 50 mL round bottom flask, phenylboronic acid (1.3 eq.), K$_2$CO$_3$ (4.0 eq.) and Pd(PPh$_3$)$_4$ (0.1 eq.) were dissolved in a mixture of toluene / water / ethanol (3:2:1, 0.1 M). 2-Bromoaniline (1.0 eq.) was added and the resulting mixture was heated to 95 °C for 20 hours. After cooling to room temperature, the biphasic solution was diluted with saturated aqueous NH$_4$Cl and CH$_2$Cl$_2$ and the phases were separated. The aqueous phase was extracted twice with CH$_2$Cl$_2$ (50 mL) and the combined organic phases were washed with water (1 x 50 mL) and saturated aqueous NaHCO$_3$ (1 x 50 mL). The organic phases were dried over Na$_2$SO$_4$ and filtered. The filtrate was concentrated in vacuo to afford the crude product. Purification by column chromatography on silica gel (petroleum ether / ethyl acetate) afforded the corresponding products.$^1$

GP-II 2-Iodoaniline (10 mmol, 1.0 equiv), p-tolylboronic acid (12 mmol, 1.2 equiv) were added to a dry Schlenk flask. The flask was evacuated and backfilled with pure N$_2$ for 3 times. DME (10 mL) and aqueous solution of K$_2$CO$_3$ (2 M, 20 mL) were added with syringe and the mixture was stirred for 30 min at room temperature under N$_2$ atmosphere. To the stirred mixture, PdCl$_2$(PPh$_3$)$_2$ (0.2 mmol, 140 mg, 0.02 equiv) in DME (10 mL) was added with syringe at room temperature and the mixture was stirred at 80 °C for 12 h under N$_2$ atmosphere (monitored by TLC). After the reaction was complete, the mixture was then cooled to room temperature and diluted with EtOAc (20 mL). The aqueous layer was extracted with EtOAc for 3 times (20 mL × 3). Then the organic phase was combitated and dried over anhydrous MgSO$_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel by using a 30:1 mixture of petroleum ether/EtOAc as an eluent to provide amine.$^2$
(2). General experimental procedures for substrates 5

\[
\begin{align*}
\text{R} & \quad \text{S} & \quad \text{N} & \quad \text{NH}_2 \\
\text{SMe} & \quad \text{NH}_2 \\
\hline
\end{align*}
\]

To the stirred solution of KOH (6 g) in 24 mL of water, benzothiazole (3 mmol) was added and refluxed for 17 h. After cooling to room temperature, MeI (3 mmol) was added drop wise and stirring was continued for an additional 1 h. The resultant reaction mixture extracted with diethyl ether (3 x 25 mL) combined organic layers dried over Na$_2$SO$_4$, filtered and concentrated in vacuum. Purification of the crude product was achieved by flash column chromatography using petrol ether/ethyl acetate (15:1) as eluent.

4. General process for the synthesis of B

\[
\begin{align*}
\text{Ar}^1 & \quad \text{NH}_2 & \quad + & \quad \text{Br} & \quad \text{COOEt} \\
\text{2} & \quad \text{Ar}^3 & \quad \text{F} & \quad \text{F} & \quad \text{COOEt} \\
\hline
\text{Cu(OTf)}_2 (\text{10 mol\%}) & \quad 1,10\text{-phen} (\text{12 mol\%}) & \quad \text{Na}_2\text{CO}_3 (3 \text{ equiv}) & \quad 120^\circ \text{C}, 20 \text{ h}, \text{CH}_3\text{CN} \\
\text{3} & \quad \text{Ar}^2 & \quad \text{F} & \quad \text{F} & \quad \text{COOEt} \\
\hline
\end{align*}
\]

In a dried Schlenk tube were placed 1 (0.2 mol, 1 equiv), Na$_2$CO$_3$ (0.6 mol, 3 equiv), Cu(OTf)$_2$ (0.02 mmol 0.1 equiv), 1,10-phen (0.024 mmol 0.12 equiv). 2 (0.6 mmol, 3 equiv) and solvent is added the mixture under N$_2$ atmosphere. The resulting mixture was stirred at 120 °C for 20 h. Upon completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 100:1, v/v) to give the desired product 3.
5. Crystal data of 3a

Crystallographic data for compound 3a (CCDC-1820711) has been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to CCDC (Email: deposit@ccdc.cam.ac.uk).
Bond precision:  C-C = 0.0031 A  Wavelength=0.71073

| Cell:     | a=8.3324(7)  | b=18.0049(15) | c=18.9382(19) |
|          | alpha=90     | beta=90       | gamma=90       |
| Temperature: | 296 K       |               |               |

| Volume   | Calculated  | Reported  |
|          | 2841.2(4)  | 2841.2(4)  |

| Space group | P b c a      | P b c a     |
| Hall group  | -P 2ac 2ab   | -P 2ac 2ab  |

| Moiety formula | C17 H13 F2 N O2 |
| Sum formula    | C17 H13 F2 N O2 |

| Mr            | 301.28       | 301.29      |
| DX,g cm-3     | 1.409        | 1.409       |
| Z              | 8            | 8           |
| Mu (mm-1)      | 0.110        | 0.110       |
| F000           | 1248.0       | 1248.8      |
| F000’          | 1248.76      |             |
| h,k,lmax      | 9,21,22      | 9,21,22     |
| Nref          | 2494         | 2487        |
| Tmin,Tmax     | 0.419,1.000  |             |
| Tmin’         |              |             |

Correction method= # Reported T Limits: Tmin=0.419 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.997  Theta(max)= 24.990
R(reflections)= 0.0445(1797)  wR2(reflections)= 0.1237(2487)
S = 1.061  Npar= 199
6. Optimization of experiment conditions for 5

\[
\text{4a} + \text{2} \xrightarrow{\text{Cu(OTf)}_2 (10 \text{ mol\%})} \xrightarrow{1,10\text{-phen} (12 \text{ mol\%})} \text{Na}_2\text{CO}_3 (4 \text{ equiv}) \xrightarrow{\text{B}_2\text{pin}_2 (30 \text{ mol\%})} \xrightarrow{\text{CH}_3\text{CN}, 80 ^\circ\text{C}} \text{5a}
\]

<table>
<thead>
<tr>
<th>entry</th>
<th>[Cu]</th>
<th>ligand</th>
<th>additive</th>
<th>base</th>
<th>solvent</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cu(OTf)$_2$</td>
<td>1,10-phen</td>
<td>----</td>
<td>Na$_2$CO$_3$</td>
<td>CH$_3$CN</td>
<td>74</td>
</tr>
<tr>
<td>2</td>
<td>Cu(OTf)$_2$</td>
<td>1,10-phen</td>
<td>B$_2$pin$_2$</td>
<td>Na$_2$CO$_3$</td>
<td>CH$_3$CN</td>
<td>83 (78)$^b$</td>
</tr>
<tr>
<td>3</td>
<td>Cu(OTf)$_2$</td>
<td>1,10-phen</td>
<td>B$_2$pin$_2$</td>
<td>Na$_2$CO$_3$</td>
<td>THF</td>
<td>67</td>
</tr>
<tr>
<td>4</td>
<td>CuSO$_4$</td>
<td>1,10-phen</td>
<td>B$_2$pin$_2$</td>
<td>Na$_2$CO$_3$</td>
<td>CH$_3$CN</td>
<td>47</td>
</tr>
<tr>
<td>5</td>
<td>Cu(OTf)$_2$</td>
<td>Xanthos</td>
<td>B$_2$pin$_2$</td>
<td>Na$_2$CO$_3$</td>
<td>CH$_3$CN</td>
<td>60</td>
</tr>
<tr>
<td>6</td>
<td>Cu(OTf)$_2$</td>
<td>1,10-phen</td>
<td>B$_2$pin$_2$</td>
<td>K$_2$CO$_3$</td>
<td>CH$_3$CN</td>
<td>69</td>
</tr>
<tr>
<td>7</td>
<td>Cu(OTf)$_2$</td>
<td>1,10-phen</td>
<td>B$_2$pin$_2$</td>
<td>DBU</td>
<td>CH$_3$CN</td>
<td>23</td>
</tr>
<tr>
<td>8$^c$</td>
<td>Cu(OTf)$_2$</td>
<td>1,10-phen</td>
<td>B$_2$pin$_2$</td>
<td>Na$_2$CO$_3$</td>
<td>CH$_3$CN</td>
<td>54</td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions: 4a (0.2 mmol), ethyl bromodifluoroacetate (2) (3 equiv), [Cu] (10 mol%), ligand (12 mol%), B$_2$pin$_2$ (30 mol%), base (4 equiv), CH$_3$CN (2 mL) under N$_2$ atmosphere at 80 °C for 24 h. GC yields. $^b$ Isolated yields. $^c$ 12 h

7. General process for the synthesis of 5

In a dried Schlenk tube were placed 4 (0.2 mol, 1 equiv), Na$_2$CO$_3$ (0.8 mol, 4 equiv), Cu(OTf)$_2$ (0.02 mmol 0.1 equiv), 1,10-phen (0.024 mmol 0.12 equiv). 2 (0.6 mmol, 3 equiv), B$_2$pin$_2$ (0.06 mmol 0.3 equiv) and solvent CH$_3$CN is added the mixture under N$_2$ atmosphere. The resulting mixture was stirred at 80 °C for 24 h. Upon completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 100:1, v/v) to give the desired product 5.
8. Control experiments to figure out the key intermediate for this transformation

\[
\begin{align*}
\text{1a} &+ \text{Br} \xrightarrow{\text{Cu(OTf)}_2 (10 \text{ mol\%}), 1,10\text{-phen} (12 \text{ mol\%}), \text{Na}_2\text{CO}_3 (3 \text{ equiv})} \text{120 }^\circ\text{C, 20 h, CH}_3\text{CN}} \rightarrow \text{3a, 86\% (GC), 82\% (iso.)} \\
\text{1a} &+ \text{Br} \xrightarrow{\text{Cu(OTf)}_2 (10 \text{ mol\%}), 1,10\text{-phen} (12 \text{ mol\%}), \text{Na}_2\text{CO}_3 (3 \text{ equiv})} \text{120 }^\circ\text{C, 20 h, CH}_3\text{CN}} \rightarrow \text{3a', not detected}
\end{align*}
\]

6. Control experiments to figure out the formation of isocyanides from amines

\[
\begin{align*}
\text{1a} &+ \text{Br} \xrightarrow{\text{Cu(OTf)}_2 (10 \text{ mol\%}), 1,10\text{-phen} (12 \text{ mol\%}), \text{Na}_2\text{CO}_3 (3 \text{ equiv})} \text{120 }^\circ\text{C, 20 h, CH}_3\text{CN}} \rightarrow \text{3a, 86\% (GC), 82\% (iso.)} \\
\text{1a} &+ \text{Br} \xrightarrow{\text{Cu(OTf)}_2 (10 \text{ mol\%}), 1,10\text{-phen} (12 \text{ mol\%}), \text{Na}_2\text{CO}_3 (3 \text{ equiv})} \text{120 }^\circ\text{C, 20 h, CH}_3\text{CN}} \rightarrow \text{3a', not detected}
\end{align*}
\]

9. Control experiments to figure out the formation of isocyanides from amines

\[
\begin{align*}
\text{1a} &+ \text{Br} \xrightarrow{\text{Cu(OTf)}_2 (10 \text{ mol\%}), 1,10\text{-phen} (12 \text{ mol\%}), \text{Na}_2\text{CO}_3 (2 \text{ equiv})} \text{CH}_3\text{CN (2 mL) 20 h, 120 }^\circ\text{C}} \rightarrow \text{3a, 84\% (iso. yield)} \\
\text{1a} &+ \text{Br} \xrightarrow{\text{Cu(OTf)}_2 (10 \text{ mol\%}), 1,10\text{-phen} (12 \text{ mol\%}), \text{Na}_2\text{CO}_3 (2 \text{ equiv})} \text{CH}_3\text{CN (2 mL) 20 h, 120 }^\circ\text{C}} \rightarrow \text{3a, 23\%}
\end{align*}
\]

8. Control experiments to figure out the formation of isocyanides from amines

\[
\begin{align*}
\text{1a} &+ \text{Br} \xrightarrow{\text{Cu(OTf)}_2 (10 \text{ mol\%}), 1,10\text{-phen} (12 \text{ mol\%}), \text{Na}_2\text{CO}_3 (2 \text{ equiv})} \text{CH}_3\text{CN (2 mL) 20 h, 120 }^\circ\text{C}} \rightarrow \text{3a, 23\%} \\
\text{1g} &+ \text{Br} \xrightarrow{\text{Na}_2\text{CO}_3 (2 \text{ equiv})} \text{CH}_3\text{CN (2 mL) 20 h, 120 }^\circ\text{C}} \rightarrow \text{8, 45\% (iso.) with 24\% 3g recovered}
\end{align*}
\]

(c)
10. Control experiments and radical trapping experiments.

\[
\text{NH}_2 + \text{Br}^+ \rightarrow \text{COOEt} \quad \text{Cu(OTf)}_2/1,10\text{-phen} \\
\text{Na}_2\text{CO}_3 (2 \text{ equiv}) \quad \text{CH}_3\text{CN, 20 h, 120 °C} \\
\text{N} + \text{COOEt} \\
\text{SMe} + \text{Br}^+ \\
\text{2, 3 equiv} \\
\text{1g, 0.2 mmol} \\
\text{2, 2 equiv} \\
\text{9, 2 equiv} \\
\text{10, 33% with 24% 3g, GC yield}
\]

\[
\text{N} + \text{Br}^+ \rightarrow \text{COOEt} \quad \text{Cu(OTf)}_2/1,10\text{-phen} \\
\text{Na}_2\text{CO}_3 (2 \text{ equiv}) \quad \text{CH}_3\text{CN, 20 h, 120 °C} \\
\text{N} + \text{COOEt} \\
\text{SMe} + \text{Br}^+ \\
\text{2, 1.5 equiv} \\
\text{8, 0.2 mmol} \\
\text{2, 2 equiv} \\
\text{9, 2 equiv} \\
\text{10, 62% with trace amount of 3g}
\]

\[
\text{N} + \text{Br}^+ \rightarrow \text{COOEt} \quad \text{Cu(OTf)}_2/1,10\text{-phen} \\
\text{Na}_2\text{CO}_3 (2 \text{ equiv}) \quad \text{CH}_3\text{CN, 20 h, 120 °C} \\
\text{N} + \text{COOEt} \\
\text{SMe} + \text{Br}^+ \\
\text{2, 1.5 equiv} \\
\text{9, 0.2 mmol} \\
\text{2, 1.5 equiv} \\
\text{10, 43%}
\]

11. Computation

Computational Methods

All calculations were carried out with the Gaussian 09 program. Geometries were optimized using the B3LYP density functional with the LANL2DZ basis set for Br and the 6-31G basis set for other atoms. Harmonic frequency analysis was conducted at the same level of theory to verify the stationary points to be real minima or saddle points and to obtain the thermal corrections at 298.15 K. Intrinsic reaction coordinate (IRC) calculations were carried out to ensure that the transition states connect the correct reactants and products. Single-point energies were calculated at optimized gas-phase geometries at the M06-2X/6-311G(d,p) level and solvent effects were introduced with the SMD approach. In the single-point calculations, thermal corrections were added to obtain Gibbs free energies (kcal/mol).

Computational Results

Aniline was used as model molecule of amine substrate for computational study. Free energies are given in kcal/mol.

\[
\begin{align*}
\text{ Fluoroacetyl bromide + \text{ Na}_2\text{CO}_3 } & \quad \rightarrow \quad \text{ Int1} & \quad \Delta G^\neq = 25.1 \quad \text{TS1} & \quad \rightarrow \\
 \text{ Int2} & \quad \Delta G^\neq = 26.1 \quad \text{TS2} & \quad \text{Int3} & \quad \text{Carbene} \\
\text{ + aniline + \text{ Na}_2\text{CO}_3 } & \quad \rightarrow \quad \text{ Int4} & \quad \Delta G^\neq = \quad \text{Int5} & \quad \text{TS3} \\
\text{ Int6} & \quad \Delta G^\neq = -79.7 \quad \text{Int7} & \quad \Delta G^\neq = -76.9 \quad \text{Int8} & \quad \text{TS4} \\
\text{ - NaF - NaHCO}_3 & \quad \rightarrow \quad \text{ Isocyanide} & \quad \Delta G^\neq = -128.1
\end{align*}
\]
12. Characterization data for products

**ethyl 2,2-difluoro-2-(phenanthridin-6-yl)acetate (3a)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (49.3 mg 82%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.67 (d, $J = 8.4$ Hz, 1H, 8.61 – 8.53 (m, 2H), 8.12 (dd, $J = 5.9$, 3.6 Hz, 1H), 7.94 – 7.87 (m, 1H), 7.78 – 7.71 (m, 3H), 4.57 (q, $J = 7.1$ Hz, 2H), 1.48 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.7 (t, $J = 31.3$ Hz), 150.15 (t, $J = 28.8$ Hz), 141.7, 133.8, 131.2, 130.8, 129.0, 128.9, 127.8, 126.23 (t, $J = 4.8$ Hz), 124.8, 122.5, 122.3 (t, $J = 2.5$ Hz), 122.0, 115.81 (t, $J = 25.2$ Hz), 63.0, 14.1. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -98.8.

**ethyl 2,2-difluoro-2-(8-methylphenanthridin-6-yl)acetate (3b)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (82%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.59 – 8.50 (m, 2H), 8.32 (d, $J = 0.7$ Hz, 1H), 8.15 – 8.05 (m, 1H), 7.77 – 7.68 (m, 3H), 4.57 (q, $J = 7.1$ Hz, 2H), 2.62 (s, 3H), 1.48 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) 163.7 (t, $J = 30$ Hz), 149.9 (t, $J = 30$ Hz), 141.5, 138.0, 133.1, 131.8, 130.8, 128.8, 128.5, 125.5 (t, $J = 3.8$ Hz), 125.0, 125.0 (t, $J = 2.5$ Hz), 122.4 121.9, 116.0 (t, $J = 25.2$ Hz), 63.0, 21.9, 14.1. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -98.9.

**ethyl 2-(8-ethylphenanthridin-6-yl)-2,2-difluoroacetate (3c)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (83%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.62 (d, $J = 8.5$ Hz, 1H, 8.36 (d, $J = 1.1$ Hz, 1H), 8.16 – 8.09 (m, 1H), 7.83 – 7.71 (m, 3H), 4.59 (q, $J = 7.1$ Hz, 2H), 2.95 (q, $J = 7.6$ Hz, 2H), 1.50 (t, $J = 7.1$ Hz, 3H), 1.41 (t, $J = 7.6$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.8 (t, $J = 31.3$ Hz), 150.0 (t, $J = 28.8$ Hz), 144.2, 141.5, 132.0, 132.0, 130.8, 128.8, 128.5, 125.0, 124.40 (t, $J = 5.0$ Hz), 122.6 (t, $J = 2.5$ Hz), 122.5, 121.9, 115.9 (t, $J = 251.3$ Hz), 63.0, 29.2, 15.5, 14.1. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -99.0.

HRMS (ESI, m/z) caleld for C$_{18}$H$_{16}$F$_2$NO$_2$[M+H]$^+$: 316.1149; found: 316.1145.

**ethyl 2,2-difluoro-2-(8-methylphenanthridin-6-yl)acetate (3b)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (83%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.62 (d, $J = 8.5$ Hz, 1H, 8.36 (d, $J = 1.1$ Hz, 1H), 8.16 – 8.09 (m, 1H), 7.83 – 7.71 (m, 3H), 4.59 (q, $J = 7.1$ Hz, 2H), 2.95 (q, $J = 7.6$ Hz, 2H), 1.50 (t, $J = 7.1$ Hz, 3H), 1.41 (t, $J = 7.6$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.8 (t, $J = 31.3$ Hz), 150.0 (t, $J = 28.8$ Hz), 144.2, 141.5, 132.0, 132.0, 130.8, 128.8, 128.5, 125.0, 124.40 (t, $J = 5.0$ Hz), 122.6 (t, $J = 2.5$ Hz), 122.5, 121.9, 115.9 (t, $J = 251.3$ Hz), 63.0, 29.2, 15.5, 14.1. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -99.0.

HRMS (ESI, m/z) caleld for C$_{19}$H$_{18}$F$_2$NO$_2$[M+H]$^+$: 330.1306; found: 330.1302.
ethyl 2,2-difluoro-2-(8-isopropylphenanthridin-6-yl)acetate (3d)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (83%).

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.61 (d, $J = 8.6$ Hz, 1H), 8.58 – 8.52 (m, 1H), 8.37 (d, $J = 1.8$ Hz, 1H), 8.16 – 8.07 (m, 1H), 7.81 (dd, $J = 8.6$, 1.7 Hz, 1H), 7.76 – 7.63 (m, 2H), 4.56 (q, $J = 7.1$ Hz, 2H), 3.19 (dt, $J = 6.9$ Hz, 6H).

$^{13}$C NMR (125 MHz, CDCl$_3$) δ 163.8 (t, $J = 31.3$ Hz), 150.0 (t, $J = 28.8$ Hz), 148.8, 141.5, 132.2, 130.8, 130.5, 128.8, 128.5, 125.0, 123.10 (t, $J = 5.0$ Hz), 122.6 (t, $J = 5$ Hz), 121.6, 115.9 (t, $J = 252.5$ Hz), 63.0, 34.4, 23.9, 14.1.

$^{19}$F NMR (470 MHz, CDCl$_3$) δ -99.1.

HRMS (ESI, m/z) calcd for C$_{20}$H$_{20}$F$_2$NO$_2$[M+H]$^+$: 344.1462; found: 344.1460.

ethyl 2,2-difluoro-2-(8-propylphenanthridin-6-yl)acetate (3e)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a yellow oil (77%).

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.58 (d, $J = 8.5$ Hz, 1H), 8.22 – 8.01 (m, 1H), 7.79 – 7.65 (m, 3H), 4.57 (q, $J = 7.1$ Hz, 2H), 2.93 – 2.80 (m, 2H), 1.84 – 1.73 (m, 2H), 1.48 (t, $J = 7.1$ Hz, 3H), 1.01 (t, $J = 7.3$ Hz, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$) δ 163.8 (t, $J = 30$ Hz), 149.94 (t, $J = 28.8$ Hz), 142.7, 141.5, 132.4, 132.0, 130.8, 128.8, 128.5, 125.1 (t, $J = 6.3$ Hz), 125.0, 122.5 (t, $J = 2.5$ Hz), 122.4, 121.9, 115.9 (t, $J = 252.5$ Hz), 63.0, 38.2, 24.5, 14.1, 13.8.

$^{19}$F NMR (470 MHz, CDCl$_3$) δ -99.1.

HRMS (ESI, m/z) calcd for C$_{20}$H$_{20}$F$_2$NO$_2$[M+H]$^+$: 344.1462; found: 344.1458.

ethyl 2-(8-(tert-butyl)phenanthridin-6-yl)-2,2-difluoroacetate (3f)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a yellow oil (76%).

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.60 (d, $J = 8.8$ Hz, 1H), 8.54 (dd, $J = 5.7$, 3.7 Hz, 2H), 8.16 – 8.07 (m, 1H), 7.98 (dd, $J = 8.8$, 1.9 Hz, 1H), 7.76 – 7.68 (m, 2H), 4.56 (q, $J = 7.1$ Hz, 2H), 1.52 – 1.43 (m, 12H).

$^{13}$C NMR (125 MHz, CDCl$_3$) δ 163.6 (t, $J = 30$ Hz), 151.0, 150.2 (t, $J = 28.8$ Hz), 141.6, 131.8, 130.8, 129.7, 128.9, 128.6, 124.9, 122.4 (t, $J = 1.3$ Hz), 122.3, 121.9, 121.8 (t, $J = 5.0$ Hz), 115.84 (t, $J = 252.5$ Hz), 63.0, 35.3, 31.2, 14.1.

$^{19}$F NMR (470 MHz, CDCl$_3$) δ -99.2.

HRMS (ESI, m/z) calcd for C$_{21}$H$_{22}$F$_2$NO$_2$[M+H]$^+$: 358.1619; found: 358.1615.
**Ethyl 2,2-difluoro-2-(8-(methylthio)phenanthridin-6-yl)acetate (3g)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (78%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.65 – 8.39 (m, 2H), 8.25 (d, $J$ = 1.9 Hz, 1H), 8.16 – 8.01 (m, 1H), 7.72 (ddt, $J$ = 14.3, 6.8, 3.4 Hz, 3H), 4.56 (q, $J$ = 7.1 Hz, 2H), 2.64 (s, 3H), 1.47 (t, $J$ = 7.1 Hz, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.60 (t, $J$ = 31.3 Hz), 149.08 (t, $J$ = 28.8 Hz), 141.4, 139.6, 131.1, 130.9, 129.1, 128.7, 124.8, 122.9 (t, $J$ = 17.5 Hz), 122.7, 121.7, 121.1 (t, $J$ = 5.0 Hz), 115.8, 63.1, 15.4, 14.1.

$^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -99.33 (s).

HRMS (ESI, m/z) calcd for C$_{18}$H$_{16}$F$_2$NO$_2$S$^{[M+H]^+}$: 348.0870; found: 348.0876.

**ethyl 2,2-difluoro-2-(8-methoxyphenanthridin-6-yl)acetate (3h)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid ( 58.3 mg, 88%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.55 (d, $J$ = 9.2 Hz, 1H), 8.49 – 8.44 (m, 1H), 8.08 (dd, $J$ = 9.3, 2.6 Hz, 1H), 4.57 (q, $J$ = 7.1 Hz, 2H), 3.99 (s, 3H), 1.48 (t, $J$ = 7.1 Hz, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.7 (t, $J$ = 31.3 Hz), 158.8, 148.1 (t, $J$ = 28.8 Hz), 140.9, 130.7, 128.9, 128.3, 127.9, 125.0, 124.0, 123.6 (t, $J$ = 2.5 Hz), 122.3, 121.5, 115.9 (t, $J$ = 251.3 Hz), 105.7 (t, $J$ = 5 Hz), 63.0, 55.5, 14.1.

$^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -99.9.

**ethyl 2,2-difluoro-2-(8-fluorophenanthridin-6-yl)acetate (3i)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (47 mg, 74%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.63 (dd, $J$ = 9.2, 5.3 Hz, 1H), 8.52 – 8.42 (m, 1H), 8.17 (dd, $J$ = 9.7, 4.3, 2.0 Hz, 1H), 8.12 – 7.96 (m, 1H), 7.79 – 7.69 (m, 2H), 7.63 (dd, $J$ = 9.1, 8.0, 2.6 Hz, 1H), 4.58 (q, $J$ = 7.1 Hz, 2H), 1.49 (t, $J$ = 7.1 Hz, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.37 (t, $J$ = 31.3 Hz), 162.3, 160.4, 149.4 (t, $J$ = 28.8 Hz), 149.3 (t, $J$ = 30.0 Hz), 141.4, 130.9, 130.6, 129.4, 128.9, 125.1 (d, $J$ = 7.5 Hz), 124.4, 123.4 (t, $J$ = 1.25 Hz), 123.3 (t, $J$ = 1.25 Hz), 121.8, 120.8 (d, $J$ = 23.8 Hz), 115.6 (t, $J$ = 252.5 Hz), 111.2 (t, $J$ = 5 Hz), 63.1, 14.1.

$^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -99.3, -110.3.

HRMS (ESI, m/z) calcd for C$_{17}$H$_{13}$F$_3$NO$_2$[M+H]$^+$: 320.0898; found: 320.0894.
ethyl 2-(8-chlorophenanthridin-6-yl)-2,2-difluoroacetate (3j)\(^4\)

![Chemical Structure](image)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (77%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.59 (d, \(J = 8.9\) Hz, 1H), 8.55 – 8.43 (m, 2H), 8.09 (dd, \(J = 5.9, 3.6\) Hz, 1H), 7.83 (dd, \(J = 8.9, 2.1\) Hz, 1H), 7.80 – 7.71 (m, 2H), 4.58 (q, \(J = 7.1\) Hz, 2H), 1.49 (t, \(J = 7.1\) Hz, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 163.33 (t, \(J = 30.0\) Hz), 149.2 (t, \(J = 28.8\) Hz), 141.6, 134.1, 132.2, 131.9, 131.0, 129.4, 129.4, 125.6 (t, \(J = 5\) Hz), 124.3, 124.2, 123.1 (t, \(J = 1.25\) Hz), 121.9, 115.6 (t, \(J = 252.5\) Hz), 63.1, 14.1. \(^{19}\)F NMR (470 MHz, CDCl\(_3\)) \(\delta\) -98.8.

ethyl 2-(8-bromophenanthridin-6-yl)-2,2-difluoroacetate (3k)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (72%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.65 (dd, \(J = 3.7, 1.8\) Hz, 1H), 8.55 – 8.40 (m, 2H), 8.24 – 8.01 (m, 1H), 7.93 (dd, \(J = 8.9, 2.0\) Hz, 1H), 7.74 (dt, \(J = 5.5, 3.2\) Hz, 2H), 4.58 (q, \(J = 7.1\) Hz, 2H), 1.49 (t, \(J = 7.1\) Hz, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 163.32 (t, \(J = 30.0\) Hz), 149.00 (t, \(J = 31.3\) Hz), 141.6, 134.5, 132.5, 130.9, 129.4, 129.4, 128.6 (t, \(J = 5\) Hz), 124.2, 123.34 (t, \(J = 2.5\) Hz), 122.2, 121.9, 115.6 (t, \(J = 252.5\) Hz), 63.2, 14.1. \(^{19}\)F NMR (470 MHz, CDCl\(_3\)) \(\delta\) -98.6.

HRMS (ESI, m/z) calcd for C\(_{17}\)H\(_{13}\)BrF\(_2\)NO\(_2\)[M+H]\(^+\): 380.0098; found: 380.0093.

ethyl 2,2-difluoro-2-(8-phenylphenanthridin-6-yl)acetate (3l)\(^4\)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a yellow oil (73%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.77 (dd, \(J = 7.7, 5.4\) Hz, 2H), 8.67 – 8.59 (m, 1H), 8.23 – 8.11 (m, 2H), 7.84 – 7.76 (m, 4H), 7.61 – 7.54 (m, 2H), 7.51 – 7.44 (m, 1H), 4.61 (q, \(J = 7.1\) Hz, 2H), 1.51 (t, \(J = 7.1\) Hz, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 163.7 (t, \(J = 31.3\) Hz), 150.24 (t, \(J = 28.8\) Hz), 141.7, 140.6, 139.9, 132.9, 130.9, 130.5, 129.2, 129.0, 129.0, 128.1, 127.5, 124.7, 124.09 (t, \(J = 4.8\) Hz), 123.1, 122.7 (t, \(J = 1.7\) Hz), 122.1, 115.9 (t, \(J = 253.8\) Hz), 63.1, 14.2. \(^{19}\)F NMR (470 MHz, CDCl\(_3\)) \(\delta\) -98.8.
Ethyl 6-(2-ethoxy-1,1-difluoro-2-oxoethyl)phenanthridine-8-carboxylate (3m)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (72%).

^1H NMR (500 MHz, CDCl$_3$) $\delta$ 9.26 (d, $J = 1.6$ Hz, 1H), 8.71 (d, $J = 8.7$ Hz, 1H), 8.60 (dd, $J = 7.0$, 2.5 Hz, 1H), 8.51 (dd, $J = 8.7$, 1.5 Hz, 1H), 8.17 – 8.07 (m, 1H), 7.81 (pd, $J = 7.1$, 3.5 Hz, 2H), 4.61 (q, $J = 7.1$ Hz, 2H), 4.52 (q, $J = 7.1$ Hz, 2H), 1.51 (td, $J = 7.1$, 3.8 Hz, 6H).

^13C NMR (125 MHz, CDCl$_3$) $\delta$ 165.7, 163.4 (t, $J = 30$ Hz), 150.6 (t, $J = 30$ Hz), 142.4, 136.6, 131.1, 130.9, 129.7, 129.3, 128.4 (t, $J = 5.0$ Hz), 124.2, 122.8, 122.6, 121.8 (t, $J = 1.25$ Hz), 115.6 (t, $J = 252.5$ Hz), 63.1, 61.7, 14.4, 14.1. ^19F NMR (470 MHz, CDCl$_3$) $\delta$ -98.3.

HRMS (ESI, m/z) calcd for C$_{20}$H$_{18}$F$_2$NO$_4$ [M+H]$^+$: 374.1204; found: 374.1199.

Ethyl 2-(8-acetylphenanthridin-6-yl)-2,2-difluoroacetate (3n)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (76%).

^1H NMR (500 MHz, CDCl$_3$) $\delta$ 9.05 (d, $J = 1.6$ Hz, 1H), 8.63 (d, $J = 8.7$ Hz, 1H), 8.52 (dd, $J = 8.1$, 1.4 Hz, 1H), 8.38 (dd, $J = 8.7$, 1.7 Hz, 1H), 8.13 – 8.00 (m, 1H), 7.76 (pd, $J = 7.1$, 1.6 Hz, 2H), 4.58 (q, $J = 7.1$ Hz, 2H), 2.76 (s, 3H), 1.49 (t, $J = 7.1$ Hz, 3H).

^13C NMR (125 MHz, CDCl$_3$) $\delta$ 197.0, 163.3 (t, $J = 30$ Hz), 150.4 (t, $J = 28.8$ Hz), 142.4, 136.6, 135.7, 130.9, 130.2, 129.4, 129.4, 127.37 (t, $J = 5.0$ Hz), 124.0, 123.1, 122.6, 121.7 (t, $J = 1.3$ Hz), 115.59 (t, $J = 252.5$ Hz), 63.2, 26.6, 14.1. ^19F NMR (470 MHz, CDCl$_3$) $\delta$ -98.1.

HRMS (ESI, m/z) calcd for C$_{19}$H$_{16}$F$_2$NO$_3$ [M+H]$^+$: 344.1094; found: 344.1098.

ethyl 2,2-difluoro-2-(8-(trifluoromethyl)phenanthridin-6-yl)acetate (3o)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (71%).

^1H NMR (500 MHz, CDCl$_3$) $\delta$ 8.83 (s, 1H), 8.79 (d, $J = 8.8$ Hz, 1H), 8.59 (dd, $J = 6.7$, 2.8 Hz, 1H), 8.18 – 8.11 (m, 1H), 8.09 (dd, $J = 8.7$, 1.5 Hz, 1H), 7.86 – 7.77 (m, 2H), 4.58 (q, $J = 7.1$ Hz, 2H), 1.49 (t, $J = 7.1$ Hz, 3H). ^13C NMR (125 MHz, CDCl$_3$) $\delta$ 163.2 (t, $J = 30$ Hz), 150.1 (t, $J = 28.8$ Hz), 142.3, 136.0, 131.1, 130.3, 129.9, 129.6, 127.14 (dd, $J = 2.5$ Hz), 124.8 (t, $J = 1.3$ Hz), 123.9 (q, $J = 3.8$ Hz, 1H).
ethyl 2-(7,9-dimethylphenanthridin-6-yl)-2,2-difluoroacetate (3p)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (78%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.51 (dd, $J$ = 4.9, 3.8 Hz, 1H), 8.31 (s, 1H), 8.07 – 7.93 (m, 1H), 7.77 – 7.62 (m, 2H), 7.40 (s, 1H), 4.54 (q, $J$ = 7.1 Hz, 2H), 2.95 (t, $J$ = 2.9 Hz, 3H), 2.56 (s, 3H), 1.46 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 164.7 (t, $J$ = 32.5 Hz), 149.16 (t, $J$ = 32.5 Hz), 140.9, 140.5, 136.2, 135.8, 134.3, 130.0, 128.7, 125.1, 122.3, 121.0, 120.4, 117.14 (t, $J$ = 256.3 Hz), 62.6, 23.9 (t, $J$ = 12.5 Hz), 21.8, 14.1. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -96.1.

HRMS (ESI, m/z) calcd for C$_{18}$H$_{13}$F$_3$NO$_2$[M+H]$^+$: 370.0866; found: 370.0862.

ethyl 2-(benzo[i]phenanthridin-5-yl)-2,2-difluoroacetate (3q)$^4$

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (63%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.11 (d, $J$ = 8.5 Hz, 1H), 8.67 – 8.54 (m, 2H), 8.20 (d, $J$ = 8.9 Hz, 1H), 8.17 – 8.10 (m, 1H), 8.00 (dd, $J$ = 7.9, 1.3 Hz, 1H), 7.83 – 7.68 (m, 4H), 4.46 (q, $J$ = 7.1 Hz, 2H), 1.35 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 164.29 (t, $J$ = 32.5 Hz), 148.20 (t, $J$ = 30.0 Hz), 142.0, 135.2, 133.1, 132.9, 129.9, 129.4, 128.8, 128.4 (t, $J$ = 16.3 Hz), 128.4, 128.2, 127.4, 127.3, 124.7, 122.7, 120.8, 119.8, 117.1 (t, $J$ = 257.5 Hz), 62.7, 14.0. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -98.4.

ethyl 2-(9-chlorophenanthridin-6-yl)-2,2-difluoroacetate (3r)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (74%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.63 (d, $J$ = 2.0 Hz, 1H), 8.54 – 8.44 (m, 2H), 8.19 – 8.02 (m, 1H), 7.86 – 7.75 (m, 2H), 7.71 (dd, $J$ = 8.9, 2.1 Hz, 1H), 4.57 (q, $J$ = 7.1 Hz, 2H), 1.48 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.4 (t, $J$ = 30 Hz),149.8 (t, $H = 10.0$ Hz), 142.1, 138.0,
135.3, 131.0, 129.7, 129.2, 128.6, 127.9 (t, J = 6.3 Hz), 123.8, 122.3, 122.1, 120.6 (t, J = 1.3 Hz), 115.6 (t, J = 252.5 Hz), 63.1, 14.1. 

$^1$H NMR (470 MHz, CDCl$_3$) $\delta$ -98.6. 

HRMS (ESI, m/z) calcd for C$_{17}$H$_{13}$ClF$_2$NO$_2$[M+H]$^+$: 336.0603; found: 336.0595.

**Ethyl 2-([1,3]dioxolo[4,5-j]phenanthridin-6-yl)-2,2-difluoroacetate (3s)**

![Image](image1)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (84%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.35 (dd, J = 6.2, 3.5 Hz, 1H), 8.06 (dd, J = 6.2, 3.4 Hz, 1H), 7.94 (s, 1H), 7.85 (s, 1H), 7.68 (dd, J = 6.3, 3.3 Hz, 2H), 6.19 (s, 2H), 4.56 (q, J = 7.1 Hz, 2H), 1.48 (t, J = 7.1 Hz, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.69 (t, J = 31.3 Hz), 151.5, 148.6 (t, J = 12.5 Hz), 141.5, 132.2, 130.7, 128.5, 128.4, 125.0, 121.9, 118.9 (t, J = 1.3 Hz), 116.0 (t, J = 252.5 Hz), 103.5 (t, J = 5.0 Hz), 102.3, 100.3, 63.0, 14.1. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -99.1.

HRMS (ESI, m/z) calcd for C$_{18}$H$_{14}$F$_2$NO$_4$[M+H]$^+$: 346.0891; found: 346.0886.

**ethyl 2,2-difluoro-2-(9-methoxyphenanthridin-6-yl)acetate (3t)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (85%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.51 – 8.41 (m, 2H), 8.08 (d, J = 7.7 Hz, 1H), 7.93 (d, J = 2.0 Hz, 1H), 7.77 – 7.65 (m, 2H), 7.32 (dd, J = 9.2, 2.5 Hz, 1H), 4.56 (q, J = 7.1 Hz, 2H), 4.04 (s, 3H), 1.47 (t, J = 7.1 Hz, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.75 (t, J = 31.3 Hz), 161.6, 149.5 (t, J = 28.8 Hz), 142.1, 136.3, 130.8, 129.1, 128.3, 128.1 (t, J = 5 Hz), 124.6, 122.1, 118.2, 117.12 (t, J = 1.3 Hz), 115.8 (t, J = 252.5 Hz), 103.1, 63.0, 55.6, 14.1. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -99.1.

HRMS (ESI, m/z) calcd for C$_{18}$H$_{16}$F$_2$NO$_3$[M+H]$^+$: 332.1098; found: 332.1098.

**ethyl 2-(2-cyanophenanthridin-6-yl)-2,2-difluoroacetate (3u)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (71%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.90 (d, J = 1.5 Hz, 1H), 8.61 (dd, J = 19.9, 8.3 Hz, 2H), 8.18 (d, J = 8.4 Hz, 1H), 8.05 – 7.97 (m, 1H), 7.92 (dd, J = 8.4, 1.7 Hz, 1H), 7.89 – 7.81 (m, 1H), 4.57 (q, J = 7.1 Hz, 2H), 1.47 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.1 (t, J = 31.3 Hz), 153.1 (t, J = 28.8 Hz), 143.2, 132.9, 132.5, 132.0, 130.6, 129.3, 127.8, 126.7 (t, J = 5.0 Hz), 125.0,
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (86%).

1H NMR (500 MHz, CDCl₃) δ 8.50 (t, J = 7.2 Hz, 2H), 8.45 (dd, J = 9.1, 5.7 Hz, 1H), 7.84 (ddd, J = 8.3, 7.1, 1.1 Hz, 1H), 7.77 – 7.61 (m, 2H), 7.45 (ddd, J = 9.0, 8.1, 2.7 Hz, 1H), 4.58 (q, J = 7.1 Hz, 2H), 1.48 (t, J = 7.1 Hz, 3H). 13C NMR (125 MHz, CDCl₃) δ 163.6, 163.5 (t, J = 15.4 Hz), 161.6, 151.4 (t, J = 28.8 Hz), 142.9 (d, J = 11.3 Hz), 133.6, 131.6, 127.7, 126.3 (t, J = 5.0 Hz), 124.1 (d, J = 8.8 Hz) 122.2, 121.8, 121.5 (d, J = 2.5 Hz), 118.1 (d, J = 23.8 Hz), 115.7 (t, J = 253.8 Hz), 115.1 (d, J = 21.3 Hz), 63.1, 14.1. 19F NMR (470 MHz, CDCl₃) δ -98.7, -111.2.

HRMS (ESI, m/z) calcd for C₁₇H₁₇F₉N₃O₂[M+H]^+: 327.0945; found: 327.0942.

diagram of ethyl 2,2-difluoro-2-(3-fluorophenanthridin-6-yl)acetate (3v)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (78%).

1H NMR (500 MHz, CDCl₃) δ 8.56 (d, J = 8.4 Hz, 1H), 8.51 (d, J = 8.2 Hz, 1H), 8.45 (d, J = 9.1 Hz, 1H), 7.85 (dd, J = 8.3, 7.1, 1.1 Hz, 1H), 7.67 (ddd, J = 8.2, 7.0, 1.1 Hz, 1H), 7.49 (d, J = 2.7 Hz, 1H), 7.37 (dd, J = 9.0, 2.7 Hz, 1H), 4.56 (q, J = 7.1 Hz, 2H), 3.97 (s, 3H), 1.46 (t, J = 7.1 Hz, 3H). 13C NMR (125 MHz, CDCl₃) δ 163.8 (t, J = 31.3 Hz), 160.3, 150.5 (t, J = 27.5 Hz), 143.5, 134.1, 131.2, 126.8, 126.2 (t, J = 5.0 Hz), 123.2, 122.0, 121.4 (t, J = 1.3 Hz), 120.1, 119.0, 115.7 (t, J = 252.5 Hz), 110.4, 63.0, 55.7, 14.1. 19F NMR (470 MHz, CDCl₃) δ -98.8.

HRMS (ESI, m/z) calcd for C₁₀H₁₄N₃O₂[M+H]^+: 208.1081; found: 208.1080.

ethyl 2,2-difluoro-2-(3-fluorophenanthridin-6-yl)acetate (3v)

ethyl 2,2-difluoro-2-(3-methoxyphenanthridin-6-yl)acetate (3w)

ethyl 2,2-difluoro-2-(2-(trifluoromethyl)phenanthridin-6-yl)acetate (3x)
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (79%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.85 (s, 1H), 8.70 (d, $J$ = 8.4 Hz, 1H), 8.60 (d, $J$ = 8.3 Hz, 1H), 8.23 (d, $J$ = 8.5 Hz, 1H), 8.04 – 7.89 (m, 2H), 7.83 (ddd, $J$ = 8.2, 7.1, 1.0 Hz, 1H), 4.57 (q, $J$ = 7.1 Hz, 2H), 1.48 (t, $J$ = 7.1 Hz, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.3 (t, $J$ = 30 Hz), 152.4 (t, $J$ = 28.8 Hz), 143.1, 133.6, 131.8, 130.6 (dd, $J$ = 32.5 Hz), 128.8, 126.61 (t, $J$ = 5.0 Hz), 125.1 (m, $J$ = 2.5 Hz), 124.6, 122.9, 122.6, 120.8 (t, $J$ = 3.8 Hz), 119.9 (q, $J$ = 5 Hz), 115.4 (t, $J$ = 253.8 Hz), 63.2, 14.1. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -62.1, -98.9.

HRMS (ESI, m/z) calcd for C$_{18}$H$_{13}$F$_5$NO$_2$ [M+H]$^+$: 370.0866; found: 370.0859.

ethyl 2,2-difluoro-2-(4-fluorophenanthridin-6-yl)acetate (3y)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (86%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.63 – 8.54 (m, 2H), 8.29 (d, $J$ = 8.4 Hz, 1H), 7.90 (ddd, $J$ = 8.3, 7.1, 1.2 Hz, 1H), 7.77 (ddd, $J$ = 8.3, 7.1, 1.1 Hz, 1H), 7.66 (td, $J$ = 8.1, 5.2 Hz, 1H), 7.40 (ddd, $J$ = 9.3, 7.9, 1.0 Hz, 1H), 4.60 (q, $J$ = 7.2 Hz, 2H), 1.50 (t, $J$ = 7.2 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.5 (t, $J$ = 30.0 Hz), 160.0, 157.9, 150.3 (t, $J$ = 31.3 Hz), 133.3, 131.7, 131.5 (d, $J$ = 10.0 Hz), 129.1 (d, $J$ = 8.8 Hz) 128.5, 126.7, 126.4 (t, $J$ = 5.0 Hz), 122.9, 122.4 (t, $J$ = 2.5 Hz), 117.5 (d, $J$ = 3.8 Hz), 115.8 (t, $J$ = 252.5 Hz), 114.1 (d, $J$ = 18.8 Hz), 63.3, 14.0. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -98.7, -122.3.

HRMS (ESI, m/z) calcd for C$_{17}$H$_{13}$F$_3$NO$_2$ [M+H]$^+$: 320.0898; found: 320.0891.

ethyl 2,2-difluoro-2-(2-(trifluoromethoxy)phenanthridin-6-yl)acetate (3z)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (76%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.68 – 8.55 (m, 2H), 8.39 (d, $J$ = 1.8 Hz, 1H), 8.18 (d, $J$ = 8.9 Hz, 1H), 8.05 – 7.91 (m, 1H), 7.89 – 7.79 (m, 1H), 7.63 (dd, $J$ = 8.9, 1.5 Hz, 1H), 4.59 (q, $J$ = 7.1 Hz, 2H), 1.50 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.4 (t, $J$ = 30.0 Hz), 160.0, 157.9, 150.3 (t, $J$ = 31.3 Hz), 133.3, 131.7, 131.5 (d, $J$ = 10.0 Hz), 129.1 (d, $J$ = 8.8 Hz) 128.5, 126.7, 126.4 (t, $J$ = 5.0 Hz), 122.9, 122.4 (t, $J$ = 2.5 Hz), 117.5 (d, $J$ = 3.8 Hz), 115.8 (t, $J$ = 252.5 Hz), 114.1 (d, $J$ = 18.8 Hz), 63.3, 14.0. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -98.7, -122.3.

HRMS (ESI, m/z) calcd for C$_{18}$H$_{13}$F$_5$NO$_3$ [M+H]$^+$: 386.0816; found: 386.0812.
ethyl 2-(benzo[c][1,5]naphthyridin-6-yl)-2,2-difluoroacetate (3aa)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (77%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.36 – 9.27 (m, 1H), 9.07 (dd, $J$ = 4.3, 1.7 Hz, 1H), 8.58 (d, $J$ = 8.3 Hz, 1H), 8.41 (dd, $J$ = 8.2, 7.1, 1.0 Hz, 1H), 7.88 (ddd, $J$ = 8.4, 7.1, 1.3 Hz, 1H), 7.70 (dd, $J$ = 8.3, 4.3 Hz, 1H), 4.58 (q, $J$ = 7.1 Hz, 2H), 1.48 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.4 (t, $J$ = 30.0 Hz), 151.2, 151.1 (t, $J$ = 28.8 Hz), 141.5, 137.8, 136.6, 134.8, 131.8, 129.6, 125.6 (t, $J$ = 5.0 Hz), 124.35 (t, $J$ = 1.3 Hz), 124.2, 124.1, 115.3 (t, $J$ = 25.2 Hz), 63.2. 19F NMR (470 MHz, CDCl$_3$) $\delta$ -99.0. HRMS (ESI, m/z) calcd for C$_{16}$H$_{13}$F$_2$N$_2$O$_2$[M+H]$^+$: 303.0945; found: 303.0942.

Diethyl 2,2'-(pyrrolo[1,2-a]quinoxaline-1,4-diyl)bis(2,2-difluoroacetate) (3ab)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (73%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.19 (d, $J$ = 8.6 Hz, 1H), 8.03 (dd, $J$ = 8.0, 1.5 Hz, 1H), 7.31 – 7.22 (m, 2H), 4.48 (q, $J$ = 7.1 Hz, 2H), 4.37 (q, $J$ = 7.1 Hz, 2H), 1.40 (t, $J$ = 7.1 Hz, 3H), 1.26 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 162.9 (t, $J$ = 33.8 Hz), 162.6 (t, $J$ = 31.3 Hz), 135.1, 131.5, 130.1, 128.0, 126.4, 125.7, 122.4 (t, $J$ = 31.3 Hz), 118.7 (t, $J$ = 6.3 Hz), 116.8 (t, $J$ = 7.5 Hz), 115.1, 113.1, 111.1 (t, $J$ = 246.3 Hz), 107.34 (t, $J$ = 3.8 Hz), 64.0, 63.4, 14.0, 13.8. 19F NMR (470 MHz, CDCl$_3$) $\delta$ -92.7, -105.1. HRMS (ESI, m/z) calcd for C$_{19}$H$_{17}$F$_4$N$_2$O$_4$[M+H]$^+$: 413.1124; found: 413.1117.

ethyl 2-(benzo[d]thiazol-2-yl)-2,2-difluoroacetate (5a)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (78%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.16 (d, $J$ = 7.8 Hz, 1H), 8.02 – 7.96 (m, 1H), 7.58 – 7.5 (m, 1H), 7.31 – 7.22 (m, 2H), 4.44 (q, $J$ = 7.1 Hz, 2H), 1.37 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 161.7 (t, $J$ = 32.5 Hz), 160.3 (t, $J$ = 32.5 Hz), 152.5, 135.1, 127.0, 127.0, 124.8, 122.0, 110.3 (t, $J$ = 251.3 Hz), 64.0, 13.9. 19F NMR (470 MHz, CDCl$_3$) $\delta$ -98.4. HRMS (ESI, m/z) calcd for C$_{11}$H$_{10}$F$_2$NO$_2$S[+M]$^+$: 258.0400; found: 258.0396.
ethyl 2,2-difluoro-2-(5-methoxybenzo[d]thiazol-2-yl)acetate (5b)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (77%). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.01 (d, $J = 9.0$ Hz, 1H), 7.37 (d, $J = 2.5$ Hz, 1H), 7.16 (dd, $J = 9.1$, 2.5 Hz, 1H), 4.44 (q, $J = 7.1$ Hz, 2H), 3.90 (s, 3H), 1.37 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 161.9 (t, $J = 31.3$ Hz), 159.0, 157.3 (t, $J = 32.5$ Hz), 147.0, 136.8, 125.3, 117.0, 110.3 (t, $J = 25.3$ Hz), 103.6, 63.9, 55.9, 13.9. $^{19}$F NMR (470 MHz, CDCl$_3$) δ -98.0. HRMS (ESI, m/z) calcd for C$_{12}$H$_{12}$F$_2$NO$_3$S[M+H]$^+$: 288.0506; found: 288.0502.

ethyl 2-(5-ethoxybenzo[d]thiazol-2-yl)-2,2-difluoroacetate (5c)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (82%). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.00 (d, $J = 9.0$ Hz, 1H), 7.36 (d, $J = 2.5$ Hz, 1H), 7.15 (dd, $J = 9.0$, 2.5 Hz, 1H), 4.44 (q, $J = 7.1$ Hz, 2H), 4.11 (q, $J = 7.0$ Hz, 2H), 1.47 (t, $J = 7.0$ Hz, 3H), 1.37 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 161.9 (t, $J = 32.5$ Hz), 158.4, 157.1 (t, $J = 32.5$Hz), 146.9, 136.8, 125.3, 117.4, 108.3 (t, $J = 251.3$ Hz), 64.2, 63.9, 14.7, 13.9. $^{19}$F NMR (470 MHz, CDCl$_3$) δ -98.0. HRMS (ESI, m/z) calcd for C$_{13}$H$_{14}$F$_2$NO$_3$S[M+H]$^+$: 302.0662; found: 302.0658.

ethyl 2,2-difluoro-2-(5-(trifluoromethoxy)benzo[d]thiazol-2-yl)acetate (5d)

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (85%). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.16 (d, $J = 9.0$ Hz, 1H), 7.85 (d, $J = 1.2$ Hz, 1H), 7.45 (dd, $J = 9.0$, 1.6 Hz, 1H), 4.44 (q, $J = 7.1$ Hz, 2H), 1.38 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 161.5 (t, $J = 32.5$ Hz), 161.4 (t, $J = 31.3$ Hz), 150.8, 147.8, 136.1, 125.8, 121.1, 114.3, 109.9 (t, $J = 252.5$ Hz), 64.1, 13.9. $^{19}$F NMR (470 MHz, CDCl$_3$) δ -58.0, -98.5. HRMS (ESI, m/z) calcd for C$_{12}$H$_9$F$_3$NO$_3$S[M+H]$^+$: 342.0223; found: 342.0220.

ethyl 2,2-difluoro-2-(5-methylbenzo[d]thiazol-2-yl)acetate (5e)
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (79%).

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.02 (d, \(J = 8.4\) Hz, 1H), 7.75 (s, 1H), 7.37 (dd, \(J = 8.4, 1.5\) Hz, 1H), 4.44 (q, \(J = 7.1\) Hz, 2H), 2.52 (s, 3H), 1.37 (t, \(J = 7.1\) Hz, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 161.8 (t, \(J = 31.3\) Hz), 159.1 (t, \(J = 32.5\) Hz), 150.6, 137.5, 135.4, 128.7, 124.2, 121.5, 110.3 (t, \(J = 251.3\) Hz), 63.9, 21.7, 13.9. \(^{19}\)F NMR (470 MHz, CDCl\(_3\)) \(\delta\) -98.3.

HRMS (ESI, m/z) calcd for C\(_{12}\)H\(_{12}\)F\(_2\)NO\(_2\)S\([\text{M}+\text{H}]^+\): 272.0557; found: 272.0556.

**ethyl 2-(5-bromobenzo[d]thiazol-2-yl)-2,2-difluoroacetate (5f)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a white solid (67%).

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.13 (d, \(J = 1.8\) Hz, 1H), 8.00 (d, \(J = 8.8\) Hz, 1H), 7.68 (dd, \(J = 8.8, 1.9\) Hz, 1H), 4.44 (q, \(J = 7.1\) Hz, 2H), 1.37 (t, \(J = 7.1\) Hz, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 161.5 (t, \(J = 32.5\) Hz), 160.8 (t, \(J = 32.5\) Hz), 151.3, 136.7, 130.7, 125.8, 124.7, 121.0, 110.0 (t, \(J = 252.5\) Hz), 64.1, 13.9. \(^{19}\)F NMR (470 MHz, CDCl\(_3\)) \(\delta\) -98.43 (s).

HRMS (ESI, m/z) calcd for C\(_{11}\)H\(_{10}\)BrF\(_2\)NO\(_2\)S\([\text{M}+\text{H}]^+\): 335.9505; found: 335.9507.

**ethyl 2-(6-chlorobenzo[d]thiazol-2-yl)-2,2-difluoroacetate (5g)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a yellow oil (75%).

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.92 (dd, \(J = 8.9, 5.0\) Hz, 1H), 7.83 (dd, \(J = 9.1, 2.5\) Hz, 1H), 7.31 (td, \(J = 8.8, 2.5\) Hz, 1H), 4.44 (q, \(J = 7.1\) Hz, 2H), 1.38 (t, \(J = 7.1\) Hz, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 163.0, 162.7 (t, \(J = 32.5\) Hz), 161.5 (t, \(J = 31.3\) Hz), 161.0, 153.4 (d, \(J = 12.2\) Hz), 130.6, 122.9 (d, \(J = 9.9\) Hz), 116.3 (d, \(J = 25\) Hz), 110.82 (d, \(J = 23.8\) Hz), 110.00 (t, \(J = 251.3\) Hz), 64.1, 13.9. \(^{19}\)F NMR (470 MHz, CDCl\(_3\)) \(\delta\) -98.6, -114.0.

HRMS (ESI, m/z) calcd for C\(_{11}\)H\(_{9}\)F\(_3\)NO\(_2\)S\([\text{M}+\text{H}]^+\): 276.0301; found: 276.0303.

**ethyl 2-(4,6-difluorobenzo[d]thiazol-2-yl)-2,2-difluoroacetate (5h)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a yellow oil (75%).

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.92 (dd, \(J = 8.9, 5.0\) Hz, 1H), 7.83 (dd, \(J = 9.1, 2.5\) Hz, 1H), 7.31 (td, \(J = 8.8, 2.5\) Hz, 1H), 4.44 (q, \(J = 7.1\) Hz, 2H), 1.38 (t, \(J = 7.1\) Hz, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 163.0, 162.7 (t, \(J = 32.5\) Hz), 161.5 (t, \(J = 31.3\) Hz), 161.0, 153.4 (d, \(J = 12.2\) Hz), 130.6, 122.9 (d, \(J = 9.9\) Hz), 116.3 (d, \(J = 25\) Hz), 110.82 (d, \(J = 23.8\) Hz), 110.00 (t, \(J = 251.3\) Hz), 64.1, 13.9. \(^{19}\)F NMR (470 MHz, CDCl\(_3\)) \(\delta\) -98.6, -114.0.

HRMS (ESI, m/z) calcd for C\(_{11}\)H\(_{9}\)F\(_3\)NO\(_2\)S\([\text{M}+\text{H}]^+\): 276.0301; found: 276.0303.
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 100:1, v/v) to give the product as a yellow oil (75%).

\[ \text{H NMR (500 MHz, CDCl}_3\text{)} \delta 7.48 (\text{dd}, J = 7.5, 2.3, 1.3 \text{ Hz}, 1\text{H}), 7.09 (\text{ddd}, J = 9.9, 9.2, 2.3 \text{ Hz}, 1\text{H}), 4.45 (\text{q}, J = 7.1 \text{ Hz}, 2\text{H}), 1.38 (\text{t}, J = 7.1 \text{ Hz}, 3\text{H}). \]

\[ \text{C NMR (125 MHz, CDCl}_3\text{)} \delta 160.63 – 160.16 (\text{m}), 138.1, 109.8 (\text{t}, J = 250 \text{ Hz}), 104.14 (\text{d}, J = 5.0 \text{ Hz}), 104.03 (\text{dd}, J = 26.8, 5.0 \text{ Hz}), 104.28 – 103.46 (\text{m}), 64.2, 13.9. \]

\[ \text{F NMR (470 MHz, CDCl}_3\text{)} \delta -97.9, -108.45 (\text{d}, J = 7.0 \text{ Hz}), -114.71 (\text{d}, J = 7.1 \text{ Hz}). \]

HRMS (ESI, m/z) calcd for C_{11}H_{8}F_{4}NO_{2}S[M+H]^+: 294.0212; found: 294.0208.

(2'-isocyano-[1,1'-biphenyl]-4-yl)(methyl)sulfane (8)

\[ \text{H NMR (500 MHz, CDCl}_3\text{)} \delta 7.51 – 7.32 (\text{m}, 8\text{H}), 2.54 (\text{s}, 3\text{H}). \]

\[ \text{C NMR (125 MHz, CDCl}_3\text{)} \delta 166.5, 139.3, 138.2, 133.5, 130.4 129.6, 129.3, 128.0, 126.2, 15.5. \]

(2'-isocyano-[1,1'-biphenyl]-4-yl)(methyl)sulfane (11)

\[ \text{H NMR (500 MHz, CDCl}_3\text{)} \delta 7.49 – 7.31 (\text{m}, 4\text{H}), 7.01 – 6.95 (\text{m}, 2\text{H}), 6.92 (\text{t}, J = 5.0 \text{ Hz}, 1\text{H}), 6.03 (\text{s}, 2\text{H}). \]

\[ \text{C NMR (125 MHz, CDCl}_3\text{)} \delta 166.5, 147.5, 138.5, 130.8, 130.5, 129.5, 127.9, 122.9, 109.5, 108.5, 101.4. \]

1-(difluoromethyl)-1H-benzo[d]imidazole (10)

\[ \text{H NMR (500 MHz, CDCl}_3\text{)} \delta 8.12 (\text{s}, 1\text{H}), 7.93 – 7.76 (\text{m}, 1\text{H}), 7.61 (\text{dd}, J = 5.4, 3.6 \text{ Hz}, 1\text{H}), 7.37 (\text{ddd}, J = 85.8, 55.8, 43.2 \text{ Hz}, 3\text{H}). \]

\[ \text{C NMR (125 MHz, CDCl}_3\text{)} \delta 143.9, 139.1, 130.6, 124.8, 124.2, 121.0, 111.1, 109.0 (\text{t}, J = 248.8 \text{ Hz}) \text{F NMR (470 MHz, CDCl}_3\text{)} \delta -93.7. \]

13. References:


14. NMR spectroscopic data
ethyl 2,2-difluoro-2-(phenanthridin-6-yl)acetate (3a)
ethyl 2,2-difluoro-2-(8-methylphenanthridin-6-yl)acetate (3b)
ethyl 2-(8-ethylphenanthridin-6-yl)-2,2-difluoroacetate (3c)
ethyl 2,2-difluoro-2-(8-isopropylphenanthridin-6-yl)acetate (3d)
ethyl 2,2-difluoro-2-(8-propylphenanthridin-6-yl)acetate (3e)
ethyl 2-(8-(tert-butyl)phenanthridin-6-yl)-2,2-difluoroacetate (3f)
ethyl 2,2-difluoro-2-(8-(methylthio)phenanthridin-6-yl)acetate (3g)
ethyl 2,2-difluoro-2-(8-methoxyphenanthridin-6-yl)acetate (3h)
ethyl 2,2-difluoro-2-(8-fluorophenanthridin-6-yl)acetate (3i)
ethyl 2-(8-chlorophenanthridin-6-yl)-2,2-difluoroacetate (3j)
ethyl 2-(8-bromophenanthridin-6-yl)-2,2-difluoroacetate (3k)
ethyl 2,2-difluoro-2-(8-phenylphenanthridin-6-yl)acetate (3l)
Ethyl 6-(2-ethoxy-1,1-difluoro-2-oxoethyl)phenanthridine-8-carboxylate (3m)
ethyl 2-(8-acetylphenanthridin-6-yl)-2,2-difluoroacetate(3n)
ethyl 2,2-difluoro-2-(8-(trifluoromethyl)phenanthridin-6-yl)acetate

(3o)
ethyl 2-(7,9-dimethylphenanthridin-6-yl)-2,2-difluoroacetate (3p)
ethyl 2-(benzo[i]phenanthridin-5-yl)-2,2-difluoroacetate (3q)
ethyl 2-(9-chlorophenanthridin-6-yl)-2,2-difluoroacetate (3r)
Ethyl 2-([1,3]dioxolo[4,5-j]phenanthridin-6-yl)-2,2-difluoroacetate (3s)
ethyl 2,2-difluoro-2-(9-methoxyphenanthridin-6-yl)acetate (3t)
ethyl 2-(2-cyanophenanthridin-6-yl)-2,2-difluoroacetate (3u)
ethyl 2,2-difluoro-2-(3-fluorophenanthridin-6-yl)acetate (3v)
ethyl 2,2-difluoro-2-(3-methoxyphenanthridin-6-yl)acetate (3w)
ethyl 2,2-difluoro-2-(2-(trifluoromethyl)phenanthridin-6-yl)acetate (3x)
ethyl 2,2-difluoro-2-(4-fluorophenanthridin-6-yl)acetate (3y)
ethyl 2,2-difluoro-2-(2-(trifluoromethoxy)phenanthridin-6-yl)acetate (3z)
ethyl 2-(benzo[c][1,5]naphthyridin-6-yl)-2,2-difluoroacetate (3aa)
diethyl2,2'-((pyrrolo[1,2-a]quinoxaline-1,4-diyl)bis(2,2-difluoroacetate)
(3ab)
ethyl 2-(benzo[d]thiazol-2-yl)-2,2-difluoroacetate (5a)
ethyl 2,2-difluoro-2-(5-methoxybenzo[d]thiazol-2-yl)acetate (5b)
ethyl 2-(5-ethoxybenzo[d]thiazol-2-yl)-2,2-difluoroacetate (5c)
ethyl 2,2-difluoro-2-(5-(trifluoromethoxy)benzo[d]thiazol-2-yl)acetate (5d)
ethyl 2,2-difluoro-2-(5-methylbenzo[d]thiazol-2-yl)acetate (5e)
ethyl 2-(5-bromobenzo[d]thiazol-2-yl)-2,2-difluoroacetate (5f)
ethyl 2-(6-chlorobenzo[d]thiazol-2-yl)-2,2-difluoroacetate (5g)
ethyl 2-(4,6-difluorobenzo[d]thiazol-2-yl)-2,2-difluoroacetate (5h)
(2'-isocyano-[1,1'-biphenyl]-4-yl)(methyl)sulfane (8)
(2'-isocyano-[1,1'-biphenyl]-4-yl)(methyl)sulfane (11)
1-(difluoromethyl)-1H-benzo[d]imidazole (10)