Supporting Information

Visible Light-Induced three-component 1,2-Difluoroalkylarylation of Styrenes with α-Carbonyl Difluoroalkyl Bromides and Indoles


E-mail: cjzhu@nju.edu.cn

Table of Contents

1. General information ................................................................. 2
2. General experimental details..................................................... 2
3. References ................................................................................. 2
4. Characterization data of compounds ........................................ 2
5. Copies of $^1$H NMR, $^{13}$C NMR, $^{19}$F NMR .................................... 12
1. General Information

All reactions were carried out under an atmosphere of Ar with dry solvents in flame-dried
glassware unless otherwise noted. Anhydrous DMF and DMSO were purchased from J&K®
and used as received. CH₃CN and CH₂Cl₂ were distilled from CaH₂. N-substituent indoles
(1a-1v)¹, bromodifluoroacyl arenes (2b, 2c)² and difluoro amides 2d ³were prepared
according to the literature, respectively.²³ Reactions were monitored by TLC on silica gel
plates (GF254), and the analytical thin-layer chromatography (TLC) was performed on
precoated, glass-backed silica gel plates.¹ H NMR, ¹³C NMR spectra and ¹⁹F NMR spectra
were recorded on a Bruker AVANCE III–400 spectrometer at room temperature. Chemical
shifts (δ) are reported in ppm downfield from tetramethylsilane. Abbreviations for signal
couplings are: s, singlet; d, doublet; dd, double doublet; t, triplet; m, multiplet. High resolution
mass spectra were obtained on a high–resolution mass spectrometer in the ESI mode. The
36W fluorescent light bulb was directly got from the supermarket.

2. General Procedure for Three-Component 1,2-Difluoroalkylation of styrenes

An oven-dried Schlenk tube (10 mL) was equipped with a magnetic stir bar, 1 (0.2 mmol),
2 (0.4 mmol), 3 (0.4 mmol), fac-Ir(ppy)₃ (0.002mmol, 2.6 mg), AgOAc (0.4mmol). The flask
was evacuated and backfilled with Ar for 3 times. 2 ml DCM was then added with syringe
under Ar. The tube was placed at a distance (app.5 cm) from 36W white LEDs lamb, and the
resulting solution was stirred at ambient temperature under visible-light irradiation and
monitored by TLC. After the reaction was finished, the mixture was concentrated under
vacuum, and the residue was purified by chromatography on silica gel to afford the
4a-4ac.

Optimization studies show that the base was crucial for this successful transformation. The
aromatic C-H difluoroalkylation product and alkene C-H difluoroalkylation product were detected
from the reaction without base, as determined by ¹H NMR analysis of the crude reaction mixture.
Some alkenes were not suitable for this reaction:

3. References:

4. Characterization data of compounds

**ethyl 2,2-difluoro-4-(4-methoxyphenyl)-4-(1-methyl-1H-indol-3-yl)butanoate 4a**

![Chemical structure of 4a](image)

Reaction time 36h, Yield 70%, yellow oil.

^1H NMR (400 MHz, Chloroform-d): δ 7.46 (d, J = 8.0 Hz, 1H), 7.26-7.24 (m, 3H), 7.20-7.17 (m, 1H), 7.06-7.04 (m, 1H), 6.82 – 6.78 (m, 3H), 4.49 (dd J=8.2, 6.8 Hz, 1H), 3.78-3.72 (m, 8H), 3.06-2.84 (m, 2H), 1.07 (t, J = 7.2 Hz, 3H) ppm. 

^13C NMR (100MHz, Chloroform-d): δ 163.9 (t, J=32.4Hz), 158.4 , 137.4 , 134.9 , 129.0 , 126.7 , 126.5 , 121.9 , 119.4 , 119.1 , 117.1 , 116.0 (t, 248.6) , 113.8 , 109.4 , 62.6 , 56.3, 40.8 (t, J=23.0 Hz) , 36.0 (t, J=5.4 Hz), 32.7, 21.0 , 13.6 ppm. 

^19F NMR (376 MHz, Chloroform-d): δ -102.3(d, J = 267.7Hz), -104.0 (d, J = 257.6 Hz) ppm. 

HRMS (ESI) m/z calcd for C_{22}H_{23}F_{2}NO_{3}Na^+ [M+Na]^+ :410.1541; found: 410.1541.

**ethyl 4-(1-benzyl-1H-indol-3-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate 4b**

![Chemical structure of 4b](image)
Reaction time 48h, Yield 68%, yellow oil. ^1H NMR (400 MHz, Chloroform-d): \( \delta \) 7.46 (d, \( J = 8.0 \) Hz, 1H), 7.29 – 7.18 (m, 6H), 7.13 – 7.08 (m, 3H), 7.02 (t, \( J = 7.6 \) Hz, 1H), 6.90 (s, 1H), 6.80 (d, \( J = 8.8 \) Hz, 2H), 5.24 (s, 2H), 4.52 (d, \( J = 7.6 \) Hz, 1H), 3.74 (s, 2H), 3.71 – 3.69 (m, 2H), 3.06 – 2.83 (m, 2H), 1.04 (t, \( J = 7.2 \) Hz, 3H) ppm. \(^{13}\)C NMR (100 MHz, Chloroform-d): \( \delta \) 163.9 (t, \( J = 32.6 \) Hz), 158.3, 137.5, 137.0, 134.8, 129.0, 128.8, 127.6, 126.9, 126.8, 125.8, 122.1, 119.6, 119.3, 117.8, 115.9 (t, \( J = 249.9 \) Hz), 113.8, 109.9, 62.6, 55.3, 50.1, 40.8 (t, \( J = 23.7 \) Hz), 36.0 (t, \( J = 6.3 \) Hz), 13.6 ppm. \(^{19}\)F NMR (376 MHz, Chloroform-d): \( \delta \) -102.2 (d, \( J = 260.2 \) Hz), -104.3 (d, \( J = 259.8 \) Hz) ppm. HRMS (ESI) m/z calcd for C\(_{28}\)H\(_{27}\)F\(_2\)NO\(_3\)Na\(^{+}\) [M+Na\(^{+}\)] 486.1851; found: 486.1853.

ethyl 2,2-difluoro-4-(5-methoxy-1H-indol-3-yl)-4-(4-methoxyphenyl)butanoate 4e

\[ \text{CO}_2\text{Et} \]
\[ \text{N} \]
\[ \text{O} \]

Reaction time 48h, Yield 46%, yellow oil. ^1H NMR (400 MHz, Chloroform-d): \( \delta \) 7.90 (s, 1H), 7.25-7.18 (m, 3H), 6.92 – 6.87 (m, 2H), 6.82-6.80 (m, 3H), 4.45 (t, \( J = 7.2 \) Hz, 1H), 3.76 – 3.72 (m, 8H), 3.06 – 2.83 (m, 2H), 1.07 (t, \( J = 7.2 \) Hz, 3H) ppm. \(^{13}\)C NMR (100 MHz, Chloroform-d): \( \delta \) 163.9 (t, \( J = 32.3 \) Hz), 158.2, 153.9, 134.6, 131.7, 129.0, 126.6, 122.4, 118.2, 115.9 (t, \( J = 249.6 \) Hz), 113.8, 112.2, 111.9, 101.3, 62.6, 55.8, 55.2, 40.5 (t, \( J = 22.6 \) Hz), 35.9 (t, \( J = 5.4 \) Hz), 13.5 ppm. \(^{19}\)F NMR (376 MHz, Chloroform-d): \( \delta \) -102.6 (d, \( J = 258.3 \) Hz), -104.1 (d, \( J = 260.2 \) Hz) ppm. HRMS (ESI) m/z calcd for C\(_{22}\)H\(_{23}\)F\(_2\)NO\(_4\)Na\(^{+}\) [M+Na\(^{+}\)] 426.1487; found: 426.1490.

ethyl 4-(1,5-dimethyl-1H-indol-3-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate 4f

\[ \text{CO}_2\text{Et} \]
\[ \text{N} \]
\[ \text{O} \]

Reaction time 48h, Yield 57%, yellow oil. ^1H NMR (400 MHz, Chloroform-d): \( \delta \) 7.25-7.23 (m, 3H), 7.13 (d, \( J = 8.4 \) Hz, 1H), 7.01-6.99 (m, 1H), 6.81 (d, \( J = 8.8 \) Hz, 2H), 6.71 (s, 1H), 4.47-4.44 (m, 1H), 3.75 (s, 3H), 3.74 – 3.70 (m, 2H), 3.66 (s, 3H), 3.05 – 2.80 (m, 2H), 2.40 (s, 3H), 1.06 (t, \( J = 7.2 \) Hz, 3H) ppm. \(^{13}\)C NMR (100 MHz, Chloroform-d): \( \delta \) 163.9 (t, \( J = 32.6 \) Hz), 158.2, 135.7, 134.9, 128.9, 128.2, 126.8, 126.5, 123.4, 118.9, 116.4, 115.9 (t, \( J = 249.5 \) Hz), 113.7, 109.0, 62.5, 55.2, 40.9 (t, \( J = 22.9 \) Hz), 35.8 (t, \( J = 6 \) Hz), 32.7, 21.5, 13.5 ppm. \(^{19}\)F NMR (376 MHz, Chloroform-d): \( \delta \) -102.5 (d, \( J = 259.1 \) Hz), -104.2 (d, \( J = 257.9 \) Hz) ppm. HRMS (ESI) m/z calcd for C\(_{23}\)H\(_{25}\)F\(_2\)NO\(_3\)Na\(^{+}\) [M+Na\(^{+}\)] 424.1695; found: 424.1698.

ethyl 2,2-difluoro-4-(5-methoxy-1-methyl-1H-indol-3-yl)-4-(4-methoxyphenyl)butanoate 4g
Reaction time 48h, Yield 59%, yellow oil. $^1$H NMR (400 MHz, Chloroform-$d$): $\delta$ 7.25-7.23 (m, 2H), 7.13 (d, $J = 8.8$ Hz, 1H), 6.88 (d, $J = 2.4$ Hz, 1H), 6.85-6.80 (m, 3H), 6.74 (s, 1H), 4.43 (dd, $J = 8.0$, 6.0 Hz, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.74 - 3.72 (m, 2H), 3.68 (s, 3H). $^1$C NMR (100 MHz, Chloroform-$d$): $\delta$ 163.9 (t, $J = 32.4$ Hz), 158.3, 153.7, 134.8, 132.7, 129.0, 127.0, 126.9, 116.5, 115.9 (t, $J = 222.4$ Hz), 113.8, 111.8, 110.1, 101.4, 62.6, 55.9, 55.3, 40.7 (t, $J = 23.7$ Hz), 35.9 (t, $J = 4.8$ Hz), 32.9, 13.6 ppm. $^{19}$F NMR (376 MHz, Chloroform-$d$): $\delta$ -102.5 (d, $J = 259.8$ Hz), -104.3 (d, $J = 257.6$ Hz) ppm. HRMS (ESI) m/z calcd for C$_{23}$H$_{25}$F$_{2}$NO$_4$Na$^+$ [M+Na$^+$] 440.1644; found: 440.1648.

ethyl 2,2-difluoro-4-(5-fluoro-1-methyl-1H-indol-3-yl)-4-(4-methoxyphenyl)butanoate

Reaction time 48h, Yield 78%, yellow oil. $^1$H NMR (400 MHz, Chloroform-$d$): $\delta$ 7.24-7.20 (m, 2H), 7.14 (dd, $J = 9.0$, 4.0 Hz, 1H), 6.94-6.91 (m, 1H), 6.85 (s, 1H), 4.41 (t, $J = 7.6$ Hz, 1H), 3.76-3.73 (m, 5H), 3.68 (s, 3H). $^{13}$C NMR (100 MHz, Chloroform-$d$): $\delta$ 163.8 (t, $J = 32.5$ Hz), 158.7, 158.3, 156.3, 134.5, 134.0, 128.9, 128.0, 126.8, 116.9, 115.9 (t, $J = 4.3$ Hz), 113.9, 110.3, 110.0 (d, $J = 3.5$ Hz), 109.9, 104.4, 104.2, 62.6, 55.3, 40.6 (t, $J = 22.5$ Hz), 35.8 (t, $J = 4.6$ Hz), 33.0, 13.6 ppm. $^{19}$F NMR (376 MHz, Chloroform-$d$): $\delta$ -102.6 (d, $J = 259.7$ Hz), -104.1 (d, $J = 256.2$ Hz) ppm. HRMS (ESI) m/z calcd for C$_{22}$H$_{22}$F$_3$NO$_3$Na$^+$ [M+Na$^+$] 428.1448; found: 428.1448.

ethyl 4-(5-chloro-1-methyl-1H-indol-3-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate

Reaction time 48h, Yield 84%, yellow oil. $^1$H NMR (400 MHz, Chloroform-$d$): $\delta$ 7.40 (d, $J = 1.6$ Hz, 1H), 7.22-7.19 (m, 2H), 7.13-7.09 (m, 2H), 6.82 - 6.80 (m, 3H), 6.42 (t, $J = 7.2$ Hz, 1H), 3.78-3.73 (m, 5H), 6.82-6.80 (m, 2H), 1.08 (t, $J = 7.2$ Hz, 3H) ppm. $^{13}$C NMR (100MHz, Chloroform-$d$): $\delta$ 163.8 (t, $J = 32.5$ Hz), 158.7, 158.3, 156.3, 134.5, 134.0, 128.9, 128.0, 126.8, 116.9, 115.9 (t, $J = 4.3$ Hz), 113.9, 110.3, 110.0 (d, $J = 3.5$ Hz), 109.9, 104.4, 104.2, 62.6, 55.3, 40.6 (t, $J = 22.5$ Hz), 35.8 (t, $J = 4.6$ Hz), 33.0, 13.6 ppm. $^{19}$F NMR (376 MHz, Chloroform-$d$): $\delta$ -102.6 (d, $J = 259.7$ Hz), -104.1 (d, $J = 256.2$ Hz) ppm. HRMS (ESI) m/z calcd for C$_{22}$H$_{22}$ClF$_2$NO$_3$Na$^+$ [M+Na$^+$] 444.1148; found: 444.1150.

ethyl 4-(5-bromo-1-methyl-1H-indol-3-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate
Reaction time 48h, Yield 90%, yellow oil. \(^1\)H NMR (400 MHz, Chloroform-\(d\)): \(\delta \) 7.56 (d, \(J = 2.0 \text{ Hz}, 1H\)), 7.26-7.19 (m, 3H), 7.10 (d, \(J = 8.4 \text{ Hz}, 1H\)), 6.83 – 6.81 (m, 3H), 4.42 (t, \(J =7.2 \text{ Hz}, 1H\)), 3.76-3.71 (m, 5H), 3.68 (s, 3H), 3.01-2.79 (m, 2H), 1.09 (t, \(J = 7.2 \text{ Hz}, 3H\)) ppm. \(^1\)C NMR (100MHz, Chloroform-\(d\)): \(\delta \) 163.8 (t, \(J = 32.3 \text{ Hz} \)), 158.3 , 135.9 , 134.4 , 128.8 , 128.2 , 127.6 , 124.7 , 121.8 , 116.6 , 115.7 (t, \(J = 249.5 \text{ Hz} \)), 113.9 , 112.5 , 110.8 , 62.6 , 55.2, 40.7 (t, \(J = 23.1 \text{ Hz} \)), 35.7 (t, \(J = 4.5 \text{ Hz} \)), 32.9, 13.6 ppm. \(^1\)F NMR (376 MHz, Chloroform-\(d\)): \(\delta \) -102.7 (d, \(J = 259.4 \text{ Hz} \)), -104.0 (d, \(J = 259.4 \text{ Hz} \)) ppm. HRMS (ESI) m/z calcd for C\(_{22}\)H\(_{22}\)BrF\(_2\)NO\(_3\)Na\([\text{M+Na}]^+\) 488.0643; found: 488.0644.

ethyl 4-(5-cyano-1-methyl-1H-indol-3-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate 4k

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Reaction time 48h, Yield 52%, yellow oil. \(^1\)H NMR (400 MHz, Chloroform-\(d\)): \(\delta \) 7.75-7.74 (m, 1H), 7.40 (dd, \(J = 8.6,1.6 \text{ Hz} \), 1H), 7.30 (d, \(J = 8.4 \text{ Hz}, 1H\)), 7.19 (d, \(J = 8.8 \text{ Hz}, 1H\)), 6.98 (s, 1H), 6.83 (d, \(J = 8.8 \text{ Hz}, 2H\)), 4.47 (t, \(J =8.4 \text{ Hz}, 1H\)), 3.87-3.80 (m, 2H), 3.78 (m, 6H), 3.01-2.82 (m, 2H), 1.12 (t, \(J = 7.2 \text{ Hz}, 3H\)) ppm. \(^1\)C NMR (100MHz, Chloroform-\(d\)): \(\delta \) 163.8 (t, \(J = 32.0 \text{ Hz} \)), 158.5 , 138.7 , 134.0 , 128.8 , 128.4 , 126.4, 125.1 , 124.8 , 120.7 , 118.4 , 115.6 (t, \(J = 250.4 \text{ Hz} \)), 114.0 , 110.2 , 102.1 , 62.7 , 55.3, 40.5 (t, \(J = 23.1 \text{ Hz} \)), 35.6 (t, \(J = 5.2 \text{ Hz} \)), 33.0 , 13.6 ppm. \(^1\)F NMR (376 MHz, Chloroform-\(d\)): \(\delta \) -102.3 (d, \(J = 262.1 \text{ Hz} \)), -104.6 (d, \(J = 261.7 \text{ Hz} \)) ppm. HRMS (ESI) m/z calcd for C\(_{23}\)H\(_{22}\)F\(_2\)N\(_2\)O\(_3\)Na\([\text{M+Na}]^+\) 435.1491; found: 435.1492.

ethyl 2,2-difluoro-4-(4-methoxyphenyl)-4-(1-methyl-5-((methylperoxy)carbonyl)-1H-indol-3-yl)butanoate 4l

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Reaction time 48h, Yield 77%, yellow oil. \(^1\)H NMR (400 MHz, Chloroform-\(d\)): \(\delta \) 8.25 (d, \(J = 0.8 \text{ Hz}, 1H\)), 7.89 (dd, \(J = 8.8,1.6 \text{ Hz} \), 1H), 7.25-7.22 (m, 3H), 6.88 (s, 1H), 6.83-6.80 (m, 2H), 4.53 (t, \(J =7.2 \text{ Hz}, 1H\)), 3.90 (s, 3H), 3.78-3.76 (m, 2H), 3.74 (s, 3H), 3.72 (s, 3H), 3.05-2.83 (m, 2H), 1.07 (t, \(J = 7.2 \text{ Hz}, 3H\)) ppm. \(^1\)C NMR (100MHz, Chloroform-\(d\)): \(\delta \) 168.1 , 163.9 (t, \(J = 32.6 \text{ Hz} \)), 158.4 , 139.7 , 134.5 , 128.8 , 127.7 , 126.2 , 123.3 , 122.3 , 121.2 , 118.6 , 115.8 (t, \(J = 249.2 \text{ Hz} \)), 113.9 , 109.0 , 62.6 , 55.2, 51.9, 40.9 (t, \(J = 23.3 \text{ Hz} \)), 35.7 (t, \(J = 5.8 \text{ Hz} \)), 32.9, 13.6 ppm. \(^1\)F NMR (376 MHz, Chloroform-\(d\)): \(\delta \) -102.5 (d, \(J = 259.4 \text{ Hz} \)), -104.6 (d, \(J = 261.7 \text{ Hz} \)) ppm. HRMS (ESI) m/z calcd for C\(_{24}\)H\(_{25}\)F\(_2\)N\(_2\)O\(_5\)Na\([\text{M+Na}]^+\) 468.1593; found: 468.1596.

ethyl 4-(4-(benzyloxy)-1-methyl-1H-indol-3-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate 4m
Reaction time 48h, Yield 54%, yellow oil. $^1$H NMR (400 MHz, Chloroform-d): $\delta$ 7.36 – 7.30 (m, 5H), 7.05 – 7.01 (m, 3H), 6.83 (d, $J = 8.0$ Hz, 1H), 6.71 – 6.68 (m, 3H), 6.46 (d, $J = 8.0$ Hz, 1H), 5.14 (dd, $J = 21.6, 12.0$ Hz, 2H), 4.90 (t, $J = 7.6$ Hz, 1H), 3.72 (s, 3H), 3.68 – 3.62 (m, 5H), 3.13 - 3.02 (m, 1H), 2.81 - 2.68 (m, 1H), 1.02 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, Chloroform-d): $\delta$ 164.2 (t, $J = 32.4$ Hz), 157.8 , 153.5 , 138.9 , 137.3 , 136.0 , 129.1 , 128.4 , 127.8 , 125.5 , 122.5 , 117.6 , 116.8 , 116.0 (t, $J = 249.1$ Hz), 113.3 , 102.6 , 100.6 , 69.8 , 62.3 , 55.2 , 41.7 (t, $J = 22.5$ Hz), 36.1 (t, $J = 4.7$ Hz), 32.9, 13.5 ppm.

$^{19}$F NMR (376 MHz, Chloroform-d): $\delta$ -102.5 (d, $J = 257.2$ Hz), -104.3 (d, $J = 258.7$ Hz) ppm. HRMS (ESI) m/z calcd for C$_{29}$H$_{29}$F$_2$NO$_3$Na$^+ [M+Na]^+$ 516.1957; found: 516.1960.

ethyl 4-(4-chloro-1-methyl-1H-indol-3-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate 4n

Reaction time 48h, Yield 58%, yellow oil. $^1$H NMR (400 MHz, Chloroform-d): $\delta$ 7.26-7.24 (m, 2H), 7.14 (dd, $J = 9.4, 1.2$ Hz, 1H), 7.09-7.02 (m, 2H), 6.83-6.81 (m, 3H), 5.20 (t, $J = 7.6$ Hz, 1H), 3.83-3.74 (m, 5H), 3.70 (s, 3H), 3.04-2.77 (m, 2H), 1.12 (t, $J = 7.2$ Hz, 3H) ppm. $^{13}$C NMR (100MHz, Chloroform-d): $\delta$ 164.2 (t, $J = 32.7$ Hz), 158.1 , 138.5 , 135.2 , 129.2 , 128.2 , 126.3 , 123.3 , 122.3 , 120.5 , 117.7 , 115.7 (t, $J = 249.4$ Hz), 113.7 , 118.2 , 62.6 , 55.2, 42.1 (t, $J = 22.5$ Hz), 35.2 (t, $J = 5.0$ Hz), 33.1, 13.6 ppm. $^{19}$F NMR (376 MHz, Chloroform-d): $\delta$ -102.5 (d, $J = 257.2$ Hz), -104.3 (d, $J = 258.7$ Hz) ppm. HRMS (ESI) m/z calcd for C$_{22}$H$_{22}$ClF$_2$NO$_3$Na$^+ [M+Na]^+$ 444.1148; found: 444.1150.

ethyl 2,2-difluoro-4-(6-fluoro-1-methyl-1H-indol-3-yl)-4-(4-methoxyphenyl)butanoate 4o

Reaction time 48h, Yield 88%, yellow oil. $^1$H NMR (400 MHz, Chloroform-d): $\delta$ 7.30 – 7.29 (m, 2H), 6.90 (dd, $J = 9.8, 2.4$ Hz, 1H), 6.82 – 6.76 (m, 4H), 4.45 (t, $J = 8.0$ Hz, 1H), 3.78-3.73 (m, 5H), 3.65 (s, 3H), 3.02-2.80 (m, 2H), 1.08 (t, $J = 7.2$ Hz, 3H) ppm. $^{13}$C NMR (100MHz, Chloroform-d): $\delta$ 163.8 (t, $J = 32.3$ Hz), 161.1 , 158.8 , 158.3 , 137.4 , 137.3 , 134.6 , 128.9 , 126.6 (d, $J = 3.2$ Hz), 123.1 , 120.2 (d, $J = 9.7$ Hz) , 117.4 , 115.8 (t, $J = 249.6$ Hz), 113.8 , 107.7 (d, $J = 24.4$ Hz), 95.6 (d, $J = 24.9$ Hz), 62.6 , 55.2 , 40.7 (t, $J = 23.1$ Hz), 35.8 (t, $J = 6.0$ Hz), 32.8 , 13.6 ppm. $^{19}$F NMR (376 MHz, Chloroform-d): $\delta$ -102.4 (d, $J = 259.8$ Hz), -104.4 (d, $J = 259.8$ Hz), -120.7 ppm. HRMS (ESI) m/z calcd for C$_{22}$H$_{22}$ClF$_3$NO$_3$Na$^+ [M+Na]^+$ 428.1444; found: 428.1447.

ethyl 4-(1,7-dimethyl-1H-indol-3-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate 4p
Reaction time 48h, Yield 70%, yellow oil.\(^1\)H NMR (400 MHz, Chloroform-d): \(\delta\) 7.29 (d, \(J = 6.8\) Hz, 1H), 7.22 (d, \(J = 8.4\) Hz, 2H), 6.65 (s, 1H), 4.45 (dd, \(J = 8.4, 4.0\) Hz, 1H), 3.75 (m, 5H), 3.02 – 2.79 (m, 2H), 2.71 (s, \(J = 32.5\) Hz), 1.09 (t, \(J = 7.2\) Hz, 3H) ppm.

\(^13\)C NMR (100 MHz, Chloroform-d): \(\delta\) 163.9 (t, \(J = 32.5\) Hz), 158.2, 136.0, 134.7, 129.0, 128.0, 124.5, 121.3, 119.3, 117.4, 116.8, 115.9 (t, \(J = 249.7\) Hz), 113.7, 62.6, 55.2, 40.7, 13.6 ppm.

\(^19\)F NMR (376 MHz, Chloroform-d): \(\delta\) -102.1 (d, \(J = 259.8\) Hz), -104.6 (d, \(J = 259.1\) Hz) ppm. HRMS (ESI) m/z calcd for C\(_{23}\)H\(_{25}\)F\(_2\)NO\(_3\)Na\(^+\) [M+Na\(^+\)] 424.1695; found: 424.1697.

ethyl 4-(1,2-dimethyl-1H-indol-3-yl)-2,2-difluoro-4-(4-methoxyphenyl)butanoate 4q

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Reaction time 48h, Yield 62%, yellow oil.\(^1\)H NMR (400 MHz, Chloroform-d): \(\delta\) 7.34 (d, \(J = 8.0\) Hz, 1H), 7.24-7.19 (m, 3H), 7.08 (t, \(J = 7.6\) Hz, 1H), 6.95 (s, \(J = 7.6\) Hz, 1H), 6.79-6.78 (m, 2H), 4.49 (dd, \(J = 11.0, 4.0\) Hz, 1H), 3.72 (s, 3H), 3.61 (s, 3H), 3.56-3.48 (m, 1H), 3.35-3.20 (m, 1H), 3.01-2.83 (m, 2H), 2.37 (s, 3H), 0.76 (t, \(J = 7.2\) Hz, 3H) ppm.

\(^13\)C NMR (100 MHz, Chloroform-d): \(\delta\) 163.1 (dd, \(J = 35.0, 30.8\) Hz), 157.8, 136.9, 135.3, 134.7, 128.2, 126.2, 120.5, 119.4, 118.9, 116.2 (dd, \(J = 249.2, 245.6\) Hz), 113.7, 110.6, 108.7, 62.0, 55.2, 39.1 (t, \(J = 22.7\) Hz), 34.6 (dd, \(J = 32.2, 12.4\) Hz), 29.6, 13.2, 10.4 ppm. \(^19\)F NMR (376 MHz, Chloroform-d): \(\delta\) 99.7 (d, \(J = 260.2\) Hz), -107.0 (d, \(J = 259.8\) Hz) ppm. HRMS (ESI) m/z calcd for C\(_{23}\)H\(_{25}\)F\(_2\)NO\(_3\)Na\(^+\) [M+Na\(^+\)] 424.1695; found: 424.1697.

ethyl 2,2-difluoro-4-(4-methoxyphenyl)-4-(1-methyl-2-phenyl-1H-indol-3-yl)butanoate 4r

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Reaction time 48h, Yield 68%, yellow oil.\(^1\)H NMR (400 MHz, Chloroform-d): \(\delta\) 7.60 (d, \(J = 7.6\) Hz, 1H), 7.44-7.30 (m, 6H), 7.20-7.18 (m, 3H), 7.11-7.07 (m, 1H), 6.78-6.74 (m, 2H), 4.35 (dd, \(J = 10.2, 5.2\) Hz, 1H), 3.72 (s, 3H), 3.64-3.56 (m, 1H), 3.50 (s, 3H), 3.34-3.20 (m, 1H), 3.10-3.02 (m, 1H), 2.94-2.82 (m, 1H), 0.92 (t, \(J = 7.2\) Hz, 3H) ppm. \(^13\)C NMR (100 MHz, Chloroform-d): \(\delta\) 163.4 (dd, \(J = 34.7, 31.7\) Hz), 157.8, 139.2, 137.3, 135.8, 131.5, 130.9, 128.5, 128.4, 128.3, 125.0, 121.4, 120.5, 119.4, 116.0 (dd, \(J = 250.1, 246.2\) Hz), 113.7, 112.5, 109.6, 62.1, 55.2, 39.7 (t, \(J = 22.1\) Hz), 35.2 (dd, \(J = 6.2, 3.9\) Hz), 30.7, 13.4 ppm. \(^19\)F NMR (376 MHz, Chloroform-d): \(\delta\) 99.7 (d, \(J = 260.2\) Hz), -107.0 (d, \(J = 259.8\) Hz) ppm. HRMS (ESI) m/z calcd for C\(_{28}\)H\(_{27}\)F\(_2\)NO\(_3\)Na\(^+\) [M+Na\(^+\)] 486.1851; found: 486.1853.
ethyl 2,2-difluoro-4-(4-methoxyphenyl)-4-(1-methyl-2-phenyl-1H-indol-3-yl)butanoate 4s

Reaction time 48h, Yield 51%, yellow oil. 'H NMR (400 MHz, Chloroform-d): δ
7.60 (d, J = 8.4 Hz, 1H), 7.33-7.27 (m, 4H), 7.07-7.02 (m, 3H), 6.81-6.79 (m, 2H), 5.52 (dd, J=9.4,5.2 Hz, 1H), 4.53-4.38 (m, 2H), 3.97 (s, 3H), 3.79-3.74 (m, 4H), 3.50-3.42 (m, 1H), 3.31-3.02 (m, 2H), 1.44 (t, J= 7.2 Hz, 3H), 0.97 (t, J = 7.2 Hz, 3H) ppm.

'13C NMR (100MHz, Chloroform-d): δ 163.5 (t, J = 32.5 Hz), 162.5, 157.9, 138.9, 135.1, 128.4, 126.0, 125.0, 124.9, 123.6, 120.1, 116.0 (dd, J = 250.2,247.4 Hz), 113.7, 110.4, 62.4, 61.1, 55.2, 39.1 (t, J = 23.1 Hz), 33.9 (dd, J= 6.0,3.1 Hz), 32.3, 14.3, 13.4 ppm.

'19F NMR (376 MHz, Chloroform-d): δ -101.2 (d, J = 259.4 Hz), -106.7 (d, J = 259.1 Hz) ppm. HRMS (ESI) m/z calcd for C26H27F2NO5Na+ [M+Na]+ 482.1750; found: 482.1753.

ethyl 2,2-difluoro-4-(4-methoxyphenyl)-4-(1-methyl-1H-pyrrolo[2,3-b]pyridin-3-yl)butanoate 4u

Reaction time 48h, Yield 53%, yellow oil. 'H NMR (400 MHz, Chloroform-d): δ
8.28 (dd, J= 4.6,1.6 Hz, 1H), 7.69 (dd, J = 8.0,1.6 Hz, 1H), 7.22-7.20 (m, 2H), 6.98-6.95 (m, 2H), 6.83-6.81 (m, 2H), 4.46 (t, J = 7.2 Hz, 1H), 3.83 (s, 3H), 3.81 – 3.77 (m, 5H), 3.04 – 2.81 (m, 2H), 1.08 (t, J = 7.2 Hz, 3H), 1.08 (s, 3H), 3.81 ppm. '13C NMR (100 MHz, Chloroform-d): δ 163.5 (t, J = 31.3 Hz), 158.4, 148.1, 143.1, 134.4, 128.9, 127.6, 126.3, 119.1, 115.7 (t, J = 248.4 Hz), 156.8, 115.2, 113.9, 62.6, 55.3, 40.5 (t, J = 22.7 Hz), 36.0 (t, J = 4.0 Hz), 31.1, 13.6 ppm. '19F NMR (376 MHz, Chloroform-d): δ -101.2 ppm (d, J = 259.4 Hz), -106.7 (d, J = 259.1 Hz) ppm. HRMS (ESI) m/z calcd for C20H21F2N2O3Na+ [M+Na]+ 389.1669; found: 389.1669.

ethyl 2,2-difluoro-4-(2-methoxyphenyl)-4-(1-methyl-1H-indol-3-yl)butanoate 4v

Reaction time 48h, Yield 75%, yellow oil. 'H NMR (400 MHz, Chloroform-d): δ
7.56 (d, J = 7.6 Hz, 1H), 7.24-7.21 (m, 2H), 7.14-7.10 (m, 2H), 7.06-7.01 (m, 1H), 6.86-6.82 (m, 3H), 5.01 (t, J = 7.2 Hz, 1H), 3.85 (s, 3H), 3.73 – 3.66 (m, 5H), 3.04 – 2.84 (m, 2H), 1.04 (t, J = 7.2 Hz, 3H) ppm. '13C NMR (100 MHz, Chloroform-d): δ 164.2 (t, J = 32.5 Hz), 156.8, 137.1, 131.3, 128.6, 127.7, 127.1, 126.9, 121.7, 120.4, 119.5, 118.9, 116.3, 116.1 (t, J = 249.7 Hz), 110.8, 109.2, 62.4, 55.5, 39.9 (t, J = 23.3 Hz), 32.7, 29.5 (t, J = 5.8 Hz), 13.6 ppm. '19F NMR (376 MHz, Chloroform-d): δ -103.3, -103.4 ppm. HRMS (ESI) m/z calcd for C20H21F2NO3Na+ [M+Na]+ 410.1538; found: 410.1539.
ethyl 2,2-difluoro-4-(1-methyl-1H-indol-3-yl)-4-(p-tolyl)butanoate 4w

React. time 48h, Yield 58%, yellow oil. \( ^1H \) NMR (400 MHz, Chloroform-d): \( \delta \) 7.48 (d, \( J = 8.0 \text{ Hz} \), 1H), 7.26-7.16 (m, 4H), 7.09-7.02 (m, 3H), 4.50 (t, \( J = 7.2 \text{ Hz} \), 1H), 3.75 – 3.66 (m, 5H), 3.08 – 2.83 (m, 2H), 2.29 (s, 3H), 1.05 (t, \( J = 7.2 \text{ Hz} \), 3H) ppm. \( ^{13}C \) NMR (100 MHz, Chloroform-d): \( \delta \) 163.9 (t, \( J = 32.1 \text{ Hz} \)), 139.8 , 137.3 , 136.1 , 129.1 , 127.8 , 126.6 , 126.5 , 121.8 , 119.4 , 119.0 , 116.9 , 115.9 (t, \( J = 249.7 \text{ Hz} \)), 109.2 , 62.5 , 40.7 (t, \( J = 23.2 \text{ Hz} \)), 36.3 (t, \( J = 5.2 \text{ Hz} \)), 32.7 , 21.0 , 13.5 ppm. \( ^{19}F \) NMR (376 MHz, Chloroform-d): \( \delta \) -102.8 (d, \( J = 257.6 \text{ Hz} \)), -104.0 (d, \( J = 258.3 \text{ Hz} \)) ppm. HRMS (ESI) m/z calcd for C_{22}H_{23}F_{2}NO_{2}Na\(^{+}\) [M+Na\(^{+}\)] 394.1589; found: 394.1590.

ethyl 2,2-difluoro-2-(1-(1-methyl-1H-indol-3-yl)-1,2,3,4-tetrahydronaphthalen-2-yl)acetate 4x

React. time 48h, Yield 65%, yellow oil. \( ^1H \) NMR (400 MHz, Chloroform-d): \( \delta \) 7.28-7.26 (m, 2H), 7.19-7.10 (m, 3H), 7.02-6.96 (m, 3H), 6.72 (s, 1H), 4.50 (d, \( J = 8.4 \text{ Hz} \), 1H), 3.73 – 3.68 (m, 4H), 3.22 – 3.06 (m, 2H), 3.02 (t, \( J = 6.4 \text{ Hz} \), 2H), 2.34-2.27 (m, 1H), 1.90-1.81 (m, 1H), 0.84 (t, \( J = 7.6 \text{ Hz} \), 3H) ppm. \( ^{13}C \) NMR (100 MHz, Chloroform-d): \( \delta \) 163.9 (dd, \( J = 33.6 \), 32.2 Hz), 137.8 , 137.4 , 135.8 , 129.7 , 128.3 , 126.3 , 126.0 , 125.9 , 121.6 , 119.8 , 119.1 , 117.0 (dd, \( J = 253.0 \), 247.9 Hz), 116.1 , 109.2 , 62.1 , 44.0 (t, \( J = 21.3 \text{ Hz} \)), 36.3 (dd, \( J = 5.4 \), 2.2 Hz), 32.7 , 27.9 , 20.5 (dd, \( J = 5.8 \), 3.8 Hz), 13.3 ppm. \( ^{19}F \) NMR (376 MHz, Chloroform-d): \( \delta \) -106.3 (d, \( J = 257.6 \text{ Hz} \)), -116.1 (d, \( J = 257.2 \text{ Hz} \)) ppm. HRMS (ESI) m/z calcd for C_{23}H_{23}F_{2}NO_{3}Na\(^{+}\) [M+Na\(^{+}\)] 406.1589; found: 406.1590.

2,2-difluoro-4-(4-methoxyphenyl)-4-(1-methyl-1H-indol-3-yl)-1-phenylbutan-1-one 4aa

React. time 48h, Yield 80%, yellow oil. \( ^1H \) NMR (400 MHz, Chloroform-d): \( \delta \) 7.87 (d, \( J = 7.6 \text{ Hz} \), 2H), 7.54-7.50 (m, 1H), 7.38-7.34 (m, 2H), 7.22-7.16 (m, 4H), 7.03-7.00 (m, 1H), 6.76-6.74 (m, 2H), 6.71 (s, 1H), 4.62 (dd, \( J = 8.2 \), 6.0 Hz, 1H), 3.73 (s, 3H), 3.64 (s, 3H), 3.22-2.94 (m, 2H) ppm. \( ^{13}C \) NMR (100 MHz, Chloroform-d): \( \delta \) 189.3 (t, \( J = 30.9 \text{ Hz} \)), 158.1 , 137.3 , 135.6 , 133.9 , 129.9 (t, \( J = 4.1 \text{ Hz} \)), 128.9 , 128.4 , 126.7 , 126.5 , 121.8 , 119.5 (t, \( J = 251.3 \text{ Hz} \)), 119.4 , 119.0 , 117.7 , 113.8 , 109.2 , 55.2 , 40.8 (t, \( J = 23.0 \text{ Hz} \)), 35.8 (t, \( J = 3.9 \text{ Hz} \)), 32.7 ppm. \( ^{19}F \) NMR (376 MHz,
Chloroform-\(d\): \(\delta\) -98.2, -98.3 ppm. HRMS (ESI) m/z calcd for C_{26}H_{24}F_{2}NO_{3}Na\(^+\) [M+Na]\(^+\) 442.1589; found: 442.1591.

2,2-difluoro-4-(4-methoxyphenyl)-4-(1-methyl-1H-indol-3-yl)-1-(thiophen-2-yl)butan-1-one \(4ab\)

\[
\text{Reaction time 48h, Yield 76%, yellow oil. } \quad \text{H NMR (400 MHz, Chloroform-\(d\))}: \begin{align*}
\delta & 7.68 (d, J = 2.8Hz, 1H), 7.56-7.54 (m, 1H), 7.38 (d, J = 8.0Hz, 1H), 6.96-6.92 (m, 2H), 6.68-6.60 (m, 2H), 6.63 (s, 1H), 4.52 (t, J = 8.0 Hz, 1H), 3.65 (s, 3H), 3.56 (s, 3H), 3.12-2.83 (m, 2H) ppm. \\
\text{C NMR (100 MHz, Chloroform-\(d\))}: \begin{align*}
\delta & 182.9 (t, J = 30.8 Hz), 158.1, 138.5, 137.2, 135.9, 135.4 (t, J = 6.2 Hz), 128.9, 128.4, 128.0, 126.7, 126.6, 121.8, 119.3, 119.5 (t, J = 252.7 Hz), 119.0, 117.4, 113.8, 109.2, 55.2, 40.9 (t, J = 23.0 Hz), 35.8 (t, J = 3.6Hz), 32.7 ppm. \\
\text{F NMR (376 MHz, Chloroform-\(d\))}: \begin{align*}
\delta & -98.9 (J = 268.8Hz), -100.1 (J = 270.3Hz) ppm. HRMS (ESI) m/z calcd for C_{24}H_{20}F_{2}NO_{3}Na\(^+\) [M+Na]\(^+\) 448.1153; found: 448.1154.
\end{align*}
\end{align*}
\]

2,2-difluoro-4-(4-methoxyphenyl)-4-(1-methyl-1H-indol-3-yl)-N-phenylbutanamide \(4ac\)

\[
\text{Reaction time 48h, Yield 30%, yellow oil. } \quad \text{H NMR (400 MHz, Chloroform-\(d\))}: \begin{align*}
\delta & 7.53 (d, J = 8.0Hz, 1H), 7.42 (s, 1H), 7.28-7.24 (m, 4H), 7.19-7.04 (m, 6H), 6.81 (s, 1H), 6.77-6.75 (m, 2H), 4.54 (t, J = 7.6 Hz, 1H), 3.67 (s, 3H), 3.54 (s, 3H), 3.22-3.09 (m, 1H), 3.02-2.89 (m, 1H) ppm. \\
\text{C NMR (100 MHz, Chloroform-\(d\))}: \begin{align*}
\delta & 162.0 (t, J = 27.9 Hz), 158.2, 137.0, 135.8, 135.0, 128.8, 128.7, 126.8, 126.4, 125.2, 121.8, 119.8, 119.1, 119.0, 117.9 (t, J = 254.0 Hz), 116.5, 113.9, 109.4, 55.1, 40.2 (t, J = 22.4 Hz), 35.9 (t, J = 5.8 Hz), 32.5 ppm. \\
\text{F NMR (376 MHz, Chloroform-\(d\))}: \begin{align*}
\delta & -101.8 (J = 255.7Hz), -103.8 (J = 254.9Hz) ppm. HRMS (ESI) m/z calcd for C_{26}H_{24}F_{2}NO_{3}Na\(^+\) [M+Na]\(^+\) 457.1698; found: 457.1699.
\end{align*}
\end{align*}
\]
5. Copies of $^1$H NMR, $^{13}$C NMR, $^{19}$F NMR