Electronic Supplementary Information

A Pd(II)-catalyzed C-H activation approach to densely functionalized N-heteroaromatics related to neocryptolepine: Their evaluation as potential inducers of apoptosis

Rajnikanth Sunke, a Vimal Kumar, a Mohd Ashraf Ashfaq, a Swapna Yellangi, a,b Raghavender Medisetti, a,b Pushkar Kulkarni, a,b E. V. Venkat Shivaji Ramaraoo, a Nasreen Z. Ehtesham, c and Manojit Pal a,*

a Dr. Reddy’s Institute of Life Sciences, University of Hyderabad Campus, Gachibowli, Hyderabad 500 046, India
b Zephase Therapeutics (an incubated company at the DRILS), University of Hyderabad Campus, Gachibowli, Hyderabad 500046, India.
c National Institute of Pathology, Safdarjang Hospital Campus, New Delhi – 110029, India

E-mail: manojitpal@rediffmail.com
Scheme S-1. The complete scheme for the synthesis of compound 4.

Table S-1: Iodine mediated synthesis of Compound 3.\textsuperscript{a}

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<th>Entry</th>
<th>Indole (1)</th>
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<th>Product (3)</th>
<th>Yield\textsuperscript{b} (%)</th>
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Legend:
- **2a**: 2-aminocinnamic acid
- **3a**: 2-aminocinnamic acid
- **2b**: 2-bromo-4-fluorobenzylamine
- **3b**: 2-bromo-4-fluorobenzylamine
- **2c**: 2-bromo-4-fluorobenzylamine
- **3c**: 2-bromo-4-fluorobenzylamine
- **2d**: 2-bromo-4-fluorobenzylamine
- **3d**: 2-bromo-4-fluorobenzylamine
- **2e**: 2-bromo-4-fluorobenzylamine
- **3e**: 2-bromo-4-fluorobenzylamine
- **2f**: 2-bromo-4-fluorobenzylamine
- **3f**: 2-bromo-4-fluorobenzylamine
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All the reactions were carried out using compound 1 (1.2 mmol), 2 (1.0 mmol), I₂ (1.2 mmol) and Cs₂CO₃ (1.5 mmol) in CH₃CN (5.0 mL) at room temperature under nitrogen.

<table>
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<th>Entry</th>
<th>Indole (1)</th>
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All the reactions were carried out using compound 1 (1.2 mmol), 2 (1.0 mmol), I₂ (3 mmol) and Cs₂CO₃ (1.5 mmol) in CH₃CN (5.0 mL) at room temperature under nitrogen.

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<th>Entry</th>
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\(^a\) Isolated yield.

**Table S-3:** Iodine mediated synthesis of Compound 3t-v.\(^a\)
All the reactions were carried out using compound 1 (1.2 mmol), 2 (1.0 mmol), I₂ (1.2 mmol) and Cs₂CO₃ (1.5 mmol) in CH₃CN (5.0 mL) at room temperature under nitrogen.

Isolated yield.

**Table S-4: Synthesis of compound 4.**

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*aAll the reactions are carried out using compound 3 (1 mmol), Pd(OAc)$_2$ (5 mol%), Cu(OAc)$_2$ (1.5 mmol) and TFA (1.2 mmol) in CH$_3$CN (2.5 mL) at 60 °C, 6h under air. bIsolated yield.*
Experimental Chemistry

**General methods:** Unless stated otherwise, reactions were performed under nitrogen atmosphere using oven dried glassware. Reactions were monitored by thin layer chromatography (TLC) on silica gel plates (60 F254), visualizing with ultraviolet light or iodine spray. Flash chromatography was performed on silica gel (230-400 mesh) using distilled hexane, ethyl acetate. $^1$H and $^{13}$C NMR spectra were recorded in CDCl$_3$ or DMSO-$d_6$ solution by using a 400 MHz spectrometer. Proton chemical shifts ($\delta$) are relative to tetramethylsilane (TMS, $\delta$ = 0.00) as internal standard and expressed in ppm. Spin multiplicities are given as s (singlet), d (doublet), dd (doublet of doublet), td (triplet of doublet), t (triplet) and m (multiplet) as well as b (broad). Coupling constants ($J$) are given in hertz. MS spectra were obtained on a Agilent 6430 series Triple Quard LC-MS / MS spectrometer. Melting points (mp) were by using Buchi B-540 melting point apparatus and are uncorrected. Chromatographic purity by HPLC (Agilent 1200 series Chem Station software) was determined by using area normalization method and the condition specified in each case: column, mobile phase (range used), flow rate, detection wavelength, and retention times.

**General Procedure for the preparation of 4-substituted-2-iodoanilines (S-1)$^1$**

![Chemical reaction diagram](image)

A mixture of 4-substituted aniline (1 mmol), iodine (1 mmol) and sodium bicarbonate (1.5 mmol) in toluene, H$_2$O (10 mL, 9:1) was stirred at room temperature for 3 hours. After completion of the reaction, the mixture was diluted with ethyl acetate (30 mL), washed with sodium thiosulphate solution (2 x 20 mL), followed by brine solution (20 mL), dried over anhydrous Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography using ethylacetate–hexane to give the desired compound S-1.
General Procedure for the preparation of \((E)\)-Alkyl 3-(2-amino-5-substituted phenyl)acrylate (S-2)

![Reaction Scheme]

The compound S-2 was prepared according to a procedure described in the literature\(^2\)

\( (E)\)-Methyl 3-(2-amino-5-methylphenyl)acrylate (S-2a)

![Methyl Acrylate Structure]

Yield: 75%; yellow solid; mp: 77-78 °C; \( R_f = 0.2 \) (10% EtOAc/ n-hexane); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta: 7.83 \) (d, \( J = 16.0 \) Hz, 1H), 7.21 (s, 1H), 7.01 (dd, \( J = 8.2, 2.4 \) Hz, 1H), 6.64 (d, \( J = 8.0 \) Hz, 1H), 6.36 (d, \( J = 16.0 \) Hz, 1H), 3.85 (s, 2H), 3.81 (s, 3H), 2.26 (s, 3H); \(^13\)C NMR (100 MHz, CDCl\(_3\)): 167.7, 143.2, 140.3, 132.2, 128.1 (2C), 119.8, 117.3, 116.9, 51.6, 20.3; MS (ES mass): 192.2 (M+1); HPLC: 99.4%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH\(_3\)CN (T/%B): 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 270.0 nm, retention time 2.5 min.

\( (E)\)-Ethyl 3-(2-amino-5-chlorophenyl)acrylate (S-2b)

![Ethyl Acrylate Structure]
Yield: 66%; yellow solid; mp: 85-87 °C; R_f = 0.2 (10% EtOAc/ n-hexane); ^1H NMR (400 MHz, CDCl_3) δ: 7.72 (d, J = 16.0 Hz, 1H), 7.35 (s, 1H), 7.12 (dd, J = 8.4, 2.4 Hz, 1H), 6.65 (d, J = 8.4 Hz, 1H), 6.35 (d, J = 16.0 Hz, 1H), 4.27 (q, J = 7.2 Hz, 2H), 4.02 (s, 2H), 1.34 (t, J = 7.2 Hz, 3H); ^13C NMR (100 MHz, CDCl_3): 166.8, 143.9, 138.5, 130.8, 127.2, 123.5, 121.1, 119.3, 117.8, 60.6, 14.2; MS (ES mass): 226.1 (M+1); HPLC: 99.6%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH_3CN (T/%B): 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 255.0 nm, retention time 3.4 min.

(E)-Ethyl 3-(2-amino-5-fluorophenyl)acrylate (S-2c)

Yield: 83%; yellow solid; mp: 80-82 °C; R_f = 0.2 (10% EtOAc/ n-hexane); ^1H NMR (400 MHz, CDCl_3) δ: 7.76 (d, J = 16.0 Hz, 1H), 7.09 (dd, J = 9.6, 2.8 Hz, 1H), 6.93-6.89 (m, 1H), 6.66 (dd, J = 8.8, 4.8 Hz, 1H), 6.34 (d, J = 16.0 Hz, 1H), 4.28 (q, J = 7.2 Hz, 2H), 3.83 (s, 2H), 1.35 (t, J = 7.2 Hz, 3H); ^13C NMR (100 MHz, CDCl_3): 166.8, 157.3 (C-F J = 235.7 Hz), 155.0, 141.7, 138.8, 120.8, 119.3, 118.3 (C-F J = 22.6 Hz), 118.0, 117.9 (C-F J = 7.6 Hz), 117.8, 113.4 (C-F J = 22.6 Hz), 113.2, 60.5, 14.2; MS (ES mass): 210.1 (M+1); HPLC: 99.3%, Column: Symmetry C-18 75 * 4.6 mm, 3.5 μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH_3CN (T/%B): 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 270.0 nm, retention time 3.0 min.

(E)-Ethyl 3-(2-amino-5-bromophenyl)acrylate (S-2d)
Yield: 58%; yellow solid; mp: 88-90 °C; R_f = 0.2 (10% EtOAc/ n-hexane); ^1^H NMR (400 MHz, CDCl_3) δ: 7.71 (d, J = 16.0 Hz, 1H), 7.49 (s, 1H), 7.25 (dd, J = 8.8, 2.4 Hz, 1H), 6.60 (d, J = 8.4 Hz, 1H), 6.35 (d, J = 16.0 Hz, 1H), 4.27 (q, J = 7.2 Hz, 2H), 3.97 (s, 2H), 1.34 (t, J = 7.2 Hz, 3H); ^1^3^C NMR (100 MHz, CDCl_3): 166.8, 144.4, 138.4, 133.6, 130.2, 121.6, 119.4, 118.2, 110.5, 60.6, 14.2; MS (ES mass): 272.1 (M+3); HPLC: 98.4%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH_3CN (T/%B): 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 250.0 nm, retention time 3.5 min.

(E)-Methyl 3-(2-amino-5-bromophenyl)acrylate (S-2e)

Yield: 69%; yellow solid; mp: 90-92 °C; R_f = 0.2 (10% EtOAc/ n-hexane); ^1^H NMR (400 MHz, CDCl_3) δ: 7.71 (d, J = 16.0 Hz, 1H), 7.48 (s, 1H), 7.26-7.22 (m, 1H), 6.59 (d, J = 8.4 Hz, 1H), 6.34 (d, J = 16.0 Hz, 1H), 3.97 (s, 2H), 3.81 (s, 3H); ^1^3^C NMR (100 MHz, CDCl_3): 167.2, 144.4, 138.7, 133.7, 130.2, 121.5, 118.9, 118.2, 110.6, 51.7; MS (ES mass): 257.9 (M+3); HPLC: 96.1%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH_3CN (T/%B): 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 250.0 nm, retention time 3.3 min.

General Procedure for the preparation of (E)-Alkyl 3-(5-substituted-2-(4-methylphenylsulfonamido)phenyl)acrylate (2)

Compounds 2a–2j were prepared according to a procedure described in the literature^3
(E)-Methyl 3-(5-methyl-2-(4-methylphenylsulfonamido)phenyl)acrylate (2a)

Yield: 95%; white solid; mp: 160-162 °C; R_f = 0.2 (20% EtOAc/ n-hexane); ^1H NMR (400 MHz, CDCl3) δ: 7.56 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 16.0 Hz, 1H), 7.27 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 7.19-7.14 (m, 1H), 6.69 (s, 1H), 6.13 (d, J = 16.0 Hz, 1H), 3.80 (s, 3H), 2.38 (s, 3H), 2.34 (s, 3H); ^13C NMR (100 MHz, CDCl3): 166.9, 143.8, 139.3, 137.3, 135.8, 132.0, 131.7, 130.6, 129.5 (2C), 127.9, 127.3, 127.2 (2C), 119.7, 51.8, 21.4, 20.9; MS (ES mass): 344.2 (M-1); HPLC: 98.5%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH3CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 270.0 nm, retention time 3.4 min.

(E)-Ethyl 3-(5-methyl-2-(4-methylphenylsulfonamido)phenyl)acrylate (2b)

Yield: 97%; white solid; mp: 145-147 °C; R_f = 0.2 (20% EtOAc/ n-hexane); ^1H NMR (400 MHz, CDCl3) δ: 7.54 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 15.6 Hz, 1H), 7.29 (d, J = 8.4 Hz, 1H), 7.25 (s, 1H), 7.17 (t, J = 8.4 Hz, 3H), 6.70 (s, 1H), 6.10 (d, J = 15.6 Hz, 1H), 4.23 (q, J = 7.2 Hz, 2H), 2.36 (s, 3H), 2.32 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H); ^13C NMR (100 MHz, CDCl3): 166.6, 143.6, 139.3, 137.2, 135.8, 132.1, 131.6, 130.8, 129.5 (2C), 128.2, 127.3, 127.2 (2C), 119.9, 60.7, 21.4, 20.9, 14.2; MS (ES mass): 358.2 (M-1); HPLC: 99.5%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH3CN (T/%B): 0/20, 0.5/20,
2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 270.0 nm, retention time 3.5 min.

*(E)*-Ethyl 3-(5-fluoro-2-(4-methylphenylsulfonamido)phenyl)acrylate (2c)

![Chemical structure of 2c]

Yield: 91%; white solid; mp: 161-163 °C; R\textsubscript{f} = 0.2 (20% EtOAc/ n-hexane); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\): 7.54 (d, \(J = 8.4\) Hz, 2H), 7.43 (d, \(J = 15.6\), 1H), 7.39 (dd, \(J = 7.8, 4.2\) Hz, 1H), 7.21 (d, \(J = 8.0\) Hz, 2H), 7.14 (dd, \(J = 9.2, 2.8\) Hz, 1H), 7.09-7.05 (m, 1H), 6.81 (s, 1H), 6.09 (d, \(J = 15.6\) Hz, 1H), 4.25 (q, \(J = 7.2\) Hz, 2H), 2.38 (s, 3H), 1.34 (t, \(J = 7.2\) Hz, 3H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): 166.2, 162.6 (C-F \(J = 24.6\) Hz), 160.1, 144.0, 138.0 (2C), 135.5, 133.3 (C-F \(J = 8.3\) Hz), 133.2, 130.7, 130.6, 129.6, 127.2, 121.4, 117.9, 117.7, 113.3 (C-F \(J = 23.3\)Hz), 113.1, 60.9, 21.4, 14.2; MS (ES mass): 362.2 (M-1); HPLC: 99.1%, Column: Symmetry C-18 75 * 4.6 mm, 3.5\(\mu\)m, mobile phase A: 0.1 % TFA in water, mobile phase B: CH\textsubscript{3}CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 230.0 nm, retention time 3.5 min.

*(E)*-Methyl 3-(5-fluoro-2-(thiophene-2-sulfonamido)phenyl)acrylate (2d)

![Chemical structure of 2d]

Yield: 85%; white solid; mp: 171-173 °C; R\textsubscript{f} = 0.2 (20% EtOAc/ n-hexane); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\): 7.56-7.54 (m, 1H), 7.50 (d, \(J = 15.8\), 1H), 7.41-7.35 (m, 2H), 7.20 (dd, \(J = 9.2, 2.8\) Hz, 1H), 7.13-7.05 (m, 1H), 7.01-6.99 (m, 1H), 6.79 (s, 1H), 6.20 (d, \(J = 15.8\) Hz, 1H), 3.79 (s, 3H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): 166.4, 162.8 (C-F \(J = 247.4\) Hz), 160.3, 138.9, 137.6, 133.4 (C-F \(J = 8.2\) Hz), 133.3, 133.0, 132.8, 130.5 (C-F \(J = 8.8\) Hz), 130.4, 130.1, 127.5, 121.4, 118.0
(C-F $J = 22.6 \text{ Hz}$), 117.8, 113.4 (C-F $J = 23.5 \text{ Hz}$), 113.2, 51.9; MS (ES mass): 342.2 (M+1); HPLC: 99.4%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH$_3$CN (T/%B): 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (80:20); UV 260.0 nm, retention time 3.2 min.

**(E)-Methyl 3-(5-bromo-2-(4-methylphenylsulfonamido)phenyl)acrylate (2e)**

![Chemical structure of 2e]

Yield: 97%; white solid; mp: 192-194 °C; $R_f = 0.2$ (20% EtOAc/ n-hexane); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.58 (s, 1H), 7.56-7.55 (m, 2H), 7.46 (dd, $J = 8.8, 2.4 \text{ Hz}$, 1H), 7.42 (d, $J = 15.8 \text{ Hz}$, 1H), 7.30 (d, $J = 8.8 \text{ Hz}$, 1H), 7.22 (d, $J = 8.0 \text{ Hz}$, 2H), 6.72 (s, 1H), 6.13 (d, $J = 15.8 \text{ Hz}$, 1H), 3.80 (s, 3H), 2.36 (s,3H); $^{13}$C NMR (100 MHz, CDCl$_3$): 166.4, 144.2, 137.7, 135.5, 133.7 (2C), 132.0, 129.8, 129.7 (2C), 128.7, 127.2 (2C), 121.5, 120.7, 52.0, 21.4; MS (ES mass): 410.1 (M+1); HPLC: 99.7%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH$_3$CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 230.0 nm, retention time 3.5 min.

**(E)-Ethyl 3-(5-bromo-2-(4-methylphenylsulfonamido)phenyl)acrylate (2f)**

![Chemical structure of 2f]

Yield: 98%; white solid; mp: 146-149 °C; $R_f = 0.2$ (20% EtOAc/ n-hexane); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.56 (d, $J = 8.2 \text{ Hz}$, 3H), 7.46 (dd, $J = 8.6, 2.2 \text{ Hz}$, 1H), 7.38 (d, $J = 16.0 \text{ Hz}$, 1H), 7.33 (d, $J = 8.4 \text{ Hz}$, 1H), 7.22 (d, $J = 8.0 \text{ Hz}$, 2H), 6.70 (s, 1H), 6.11 (d, $J = 16.0 \text{ Hz}$, 1H), 4.24 (q, $J = 7.2 \text{ Hz}$, 2H), 2.38 (s, 3H), 1.33 (t, $J = 7.2 \text{ Hz}$, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): 166.2, 144.0, 137.7, 135.6, 133.8, 133.6, 132.4, 129.8, 129.7 (2C), 129.2, 127.2 (2C), 121.6, 120.7, 61.0, 21.4, 14.2; MS (ES mass): 424.1 (M+1); HPLC: 99.4%, Column: Symmetry C-18 75 * 4.6
mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 230.0 nm, retention time 3.7 min.

(E)-Methyl 3-(5-chloro-2-(4-methylphenylsulfonamido)phenyl)acrylate (2g)

![Chemical Structure](image)

Yield: 98%; white solid; mp: 149-151 °C; R_f = 0.2 (20% EtOAc/ n-hexane); ^1H NMR (400 MHz, CDCl₃) δ: 7.56 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 16.4 Hz, 1H), 7.41 (s, 1H), 7.38 (d, J = 8.8 Hz, 1H), 7.32 (dd, J = 8.6, 2.4 Hz, 1H), 7.22 (d, J = 8.0 Hz, 2H), 6.77 (s, 1H), 6.13 (d, J = 16.4 Hz, 1H), 3.80 (s, 3H), 2.38 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): 166.6, 144.1, 138.1, 135.5, 133.2, 133.0, 132.1, 130.7, 129.7 (2C), 129.0, 127.2 (2C), 126.8, 121.1, 52.0, 21.4; MS (ES mass): 364.2 (M-1); HPLC: 98.9%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 230.0 nm, retention time 3.5 min.

(E)-Ethyl 3-(2-(4-methylphenylsulfonamido)phenyl)acrylate (2h)

![Chemical Structure](image)

Yield: 98%; white solid; mp: 140-143 °C; R_f = 0.2 (20% EtOAc/ n-hexane); ^1H NMR (400 MHz, CDCl₃) δ: 7.56 (d, J = 8.4 Hz, 2H), 7.48 (d, J = 15.6 Hz, 1H), 7.45-7.42 (m, 2H), 7.24 (d, J = 8.0 Hz, 1H), 7.19 (d, J = 8.0 Hz, 2H), 6.72 (s, 1H), 6.13 (d, J = 15.6 Hz, 1H), 4.24 (q, J = 7.2 Hz, 2H), 2.36 (s, 3H), 1.33 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): 166.5, 143.8, 138.9, 135.8, 134.7, 130.8, 130.4, 129.6 (2C), 127.5, 127.2 (2C), 127.1, 127.0, 120.5, 60.8, 21.4, 14.2; MS (ES mass): 344.2 (M-1); HPLC: 99.3%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm,
mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 270.0 nm, retention time 3.4 min.

**(E)-Ethyl 3-(5-chloro-2-(4-methylphenylsulfonamido)phenyl)acrylate (2i)**

![Diagram of (E)-Ethyl 3-(5-chloro-2-(4-methylphenylsulfonamido)phenyl)acrylate (2i)]

Yield: 95%; white solid; mp: 169-171 °C; R_f = 0.2 (20% EtOAc/ n-hexane); ¹H NMR (400 MHz, CDCl₃) δ: 7.58 (d, J = 8.4 Hz, 2H), 7.41-7.38 (m, 2H), 7.38-7.36 (m, 1H), 7.32 (dd, J = 8.8, 2.4 Hz, 1H), 7.23 (d, J = 8.0 Hz, 2H), 6.79 (s, 1H), 6.13 (d, J = 15.7 Hz, 1H), 4.25 (q, J = 7.2 Hz, 2H), 2.39 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): 166.1, 144.1, 137.6, 135.6, 133.2, 132.9, 132.0, 130.7, 129.7 (2C), 128.9, 127.2 (2C), 126.8, 121.7, 61.0, 21.4, 14.2; MS (ES mass): 378.2 (M-1); HPLC: 99.5%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 270.0 nm, retention time 3.6 min.

**(E)-Methyl 3-(5-fluoro-2-(4-methylphenylsulfonamido)phenyl)acrylate (2j)**

![Diagram of (E)-Methyl 3-(5-fluoro-2-(4-methylphenylsulfonamido)phenyl)acrylate (2j)]

Yield: 93%; white solid; mp: 156-158 °C; R_f = 0.2 (20% EtOAc/ n-hexane); ¹H NMR (400 MHz, CDCl₃) δ: 7.54 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 15.6 Hz, 1H), 7.35-7.32 (m, 1H), 7.22 (d, J = 8.4 Hz, 2H), 7.15 (dd, J = 8.8, 2.8 Hz, 1H), 7.10-7.03 (m, 1H), 6.45 (s, 1H), 6.11 (d, J = 15.6 Hz, 1H), 3.79 (s, 3H), 2.39 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): 166.7, 162.6 (C-F J = 246.7 Hz), 160.1, 144.0, 138.5, 138.4, 135.5, 133.4 (C-F J = 8.1 Hz), 133.3, 130.7, 130.6, 129.6, 127.2,
120.8, 117.9, 117.7, 113.3 (C-F $J = 23.3$Hz), 113.1, 52.0, 21.4; MS (ES mass): 348.2 (M-1); HPLC: 99.4%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH$_3$CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 230.0 nm, retention time 3.3 min.

(\textit{E})-Ethyl 3-(3,5-dimethyl-2-(4-methylphenylsulfonamido)phenyl)acrylate (2k)

\begin{center}
\includegraphics[width=0.5\textwidth]{2k.png}
\end{center}

Yield: 93%; white solid; mp: 142-144 °C; $R_f = 0.2$ (20% EtOAc/ n-hexane); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.52 (d, $J = 8.0$ Hz, 2H), 7.43 (d, $J = 16.0$ Hz, 1H), 7.18-7.09 (m, 4H), 6.22 (s, 1H), 6.01 (d, $J = 16.0$ Hz, 1H), 4.18 (q, $J = 7.2$ Hz, 2H), 2.37 (s, 3H), 2.31 (s, 3H), 2.29 (s, 3H), 1.31 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): 166.8, 143.5, 140.8, 139.3, 137.8, 136.2, 133.8, 133.7, 130.7, 129.5 (2C), 127.4 (2C), 125.2, 118.2, 60.6, 21.4, 21.0, 18.8, 14.2; MS (ES mass): 372.2 (M-1); HPLC: 99.8%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH$_3$CN (T/%B): 0/20, 0.5/20, 2/95, 10/95, 10.5/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (80:20); UV 230.0 nm, retention time 3.7 min.

(\textit{E})-Ethyl 3-(4-methyl-2-(4-methylphenylsulfonamido)phenyl)acrylate (2l)

\begin{center}
\includegraphics[width=0.5\textwidth]{2l.png}
\end{center}

Yield: 95%; white solid; mp: 132-134 °C; $R_f = 0.2$ (20% EtOAc/ n-hexane); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.56 (d, $J = 8.4$ Hz, 2H), 7.35 (d, $J = 15.6$ Hz, 2H), 7.26 (s, 1H), 7.19 (d, $J = 8.4$ Hz, 2H),
7.04 (d, J = 7.6 Hz, 1H), 6.56 (s, 1H), 6.07 (d, J = 15.6, 1H), 4.22 (q, J = 7.2 Hz, 2H), 2.36 (s, 3H), 2.34 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl3): 166.6, 143.8, 141.6, 138.7 (2C), 135.7, 134.5, 129.5, 128.2, 128.1, 127.5, 127.2, 126.7, 119.4, 119.3, 60.7, 21.4, 21.3, 14.2; MS (ES mass): 358.2 (M-1); HPLC: 99.9%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH3CN (T%/B): 0/20, 0.5/20, 2/95, 10/95, 10.5/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (80:20); UV 230.0 nm, retention time 3.7 min.

General Procedure for synthesis of (E)-Alkyl 3-(5-substituted-2-(N-(1-alkyl-1H-indol-2-yl)-4-methylphenylsulfonamido)phenyl)acrylate (3)4

To a mixture of (E)-alkyl 3-(5-substituted-2-(4-methylphenylsulfonamido)phenyl)acrylate derivative 2 (1.0 mmol), Cs2CO3 (1.5 mmol), I2 (1.2 mmol) in acetonitrile (2.5 mL) added indole derivative 1 (1.2 mmol), then stirred at room temperature under nitrogen for 6-8 h. The progress of the reaction was monitored by TLC. Upon completion, the reaction was quenched with a saturated solution of Na2S2O3 (5 mL) and extracted with ethyl acetate (3 × 30 mL). The organic layers were collected, combined washed with brine (50 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under a reduced pressure. The residue was purified by column chromatography over silica gel using ethyl acetate–hexane to give the desired product (3).

(E)-Methyl-3-(2-(N-(1-ethyl-1H-indol-2-yl)-4-methylphenylsulfonamido)-5-methylphenyl)acrylate (3a)
Yield: 85%; white solid; mp: 180-182 °C; R<sub>f</sub> = 0.2 (10% EtOAc/ n-hexane); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 8.47 (d, J = 16.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.52 (d, J = 8.0 Hz, 2H), 7.33-7.27 (m, 3H), 7.24-7.19 (m, 1H), 7.17 (d, J = 7.6 Hz, 1H), 7.14-7.09 (m, 1H), 7.10-7.06 (m, 1H), 6.42 (d, J = 16.0 Hz, 1H), 6.30 (s, 1H), 4.29 (q, J = 7.2 Hz, 2H), 3.86 (s, 3H), 2.47 (s, 3H), 2.36 (s, 3H), 1.21 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl<sub>3</sub>): 166.9, 144.5, 141.0, 138.9, 136.9, 134.4, 134.3 (2C), 133.8, 131.4, 129.9 (2C), 129.3 (2C), 129.2, 127.6, 125.9, 122.6, 121.0, 199.8, 119.4, 109.9, 100.3, 51.7, 37.6, 21.6, 21.1, 14.8; MS (ES mass): 489.2 (M+1); HPLC: 98.6%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH<sub>3</sub>CN (T%/B): 0/50, 1/50, 6/98, 12/98, 13/50, 15/50; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 220.0 nm, retention time 4.2 min.

(E)-Ethyl-3-(2-(N-(1-ethyl-1H-indol-2-yl)-4-methylphenylsulfonamido)-5-methylphenyl)acrylate (3b)

Yield: 87%; white solid; mp: 147-149 °C; R<sub>f</sub> = 0.2 (10% EtOAc/ n-hexane); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 8.44 (d, J = 16.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.52 (d, J = 8.0 Hz, 2H), 7.32-7.26 (m, 3H), 7.22 (d, J = 7.2 Hz, 1H), 7.18 (d, J = 8.0 Hz, 1H), 7.13-7.10 (m, 1H), 7.08 (t, J = 6.8 Hz, 1H), 6.41 (d, J = 16.0 Hz, 1H), 6.31 (s, 1H), 4.35-4.30 (q, J = 7.2 Hz, 2H), 4.30-4.24 (m, 2H), 2.46 (s, 3H), 2.36 (s, 3H), 1.39 (t, J = 7.2 Hz, 3H), 1.21 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl<sub>3</sub>): 166.5, 144.5, 140.6, 138.9, 136.8, 134.4, 134.3 (2C), 133.8, 131.3, 129.9, 129.3 (2C), 129.1 (2C), 127.6, 125.9, 122.5, 121.0, 119.9, 119.8, 109.9, 100.3, 60.5, 37.6, 21.6, 21.1,
(E)-Ethyl-3-(2-(N-(1-ethyl-1H-indol-2-yl)-4-methylphenylsulfonamido)-5-fluorophenyl)acrylate (3c)

Yield: 83%; white solid; mp: 156-158 °C; Rf = 0.2 (10% EtOAc/ n-hexane); ¹H NMR (400 MHz, CDCl₃) δ: 8.41 (d, J = 16.0 Hz, 1H), 7.59 (d, J = 8.4 Hz, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.38 (dd, J = 9.2, 2.8 Hz, 1H), 7.31-7.27 (m, 4H), 7.25-7.21 (m, 1H), 7.11-7.07 (m, 1H), 7.04-6.99 (m, 1H), 6.40 (d, J = 16.0 Hz, 1H), 6.32 (s, 1H), 4.33 (q, J = 7.2 Hz, 2H), 4.28-4.25 (m, 2H), 2.47 (s, 3H), 1.40 (t, J = 7.2 Hz, 3H), 1.22 (t, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): 166.0, 163.2 (C-F J = 250.0 Hz), 160.7, 144.8, 139.5, 139.4, 137.0, 136.9, 134.0 (C-F J = 7 Hz), 133.8, 132.1, 129.5 (2C), 129.1 (2C), 125.8, 122.8, 121.4, 121.0, 119.9, 117.6, 117.4, 113.6, 113.4 (C-F J = 22.5 Hz), 109.9, 100.4, 60.7, 37.6, 21.6, 14.9, 14.3; MS (ES mass): 507.2 (M+1); HPLC: 99.6%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 225.0 nm, retention time 4.2 min.

(E)-Methyl-3-(2-(N-(1-ethyl-1H-indol-2-yl)thiophene-2-sulfonamido)-5-fluorophenyl)acrylate (3d)
Yield: 68%; white solid; mp: 173-175 °C; Rf = 0.2 (10% EtOAc/ n-hexane); 1H NMR (400 MHz, CDCl₃) δ: 8.41 (d, J = 16.4 Hz, 1H), 7.72-7.71 (m, 1H), 7.57-7.55 (m, 2H), 7.40-7.37 (m, 2H), 7.30 (d, J = 8.0 Hz, 1H), 7.25 (dd, J = 8.0, 1.2 Hz, 1H), 7.17-7.15 (m, 1H), 7.12-7.09 (m, 1H), 7.08-7.03 (m, 1H), 6.48 (s, 1H), 6.43 (d, J = 16.4 Hz, 1H), 4.28 (q, J = 7.2 Hz, 2H), 3.87 (s, 3H), 1.22 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl₃) δ: 166.5, 163.4 (C-F J = 249.2 Hz), 160.9, 139.6, 137.0, 136.9, 135.1, 134.9 (C-F J = 5.6 Hz), 134.9, 134.0, 133.9, 133.5, 131.9, 127.5, 125.8, 123.0, 121.2, 121.1, 120.1, 117.8 (C-F J = 23.0 Hz), 117.6, 113.8 (C-F J = 23.1 Hz), 113.6, 110.0, 100.5, 51.9, 37.7, 14.8; MS (ES mass): 485.2 (M+1); HPLC: 97.9%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (80:20); UV 220.0 nm, retention time 3.8 min.

(E)-Methyl-3-(5-bromo-2-(N-(1-ethyl-1H-indol-2-yl)-4-methylphenylsulfonamido)phenyl)acrylate (3e)

Yield: 75%; white solid; mp: 199-201 °C; Rf = 0.2 (10% EtOAc/ n-hexane); 1H NMR (400 MHz, CDCl₃) δ: 8.40 (d, J = 16.0 Hz, 1H), 7.83 (s, 1H), 7.59 (d, J = 8.4 Hz, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.42 (dd, J = 8.8, 2.4 Hz, 1H), 7.32-7.29 (m, 3H), 7.24-7.20 (m, 1H), 7.16 (d, J = 8.8 Hz, 1H), 7.11-7.07 (m, 1H), 6.43 (d, J = 16.0 Hz, 1H), 6.29 (s, 1H), 4.25 (q, J = 7.6 Hz, 2H), 3.87 (s, 3H), 2.47 (s, 3H), 1.20 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl₃): 166.5, 144.9, 139.5,
138.3, 136.6, 134.0, 133.8, 133.6, 133.4, 131.6, 130.1, 129.5 (2C), 129.1 (2C), 125.7, 122.9, 122.8, 121.1, 120.9, 119.9, 109.9, 100.5, 51.9, 37.6, 21.6, 14.8; MS (ES mass): 555.1 (M+3); HPLC: 98.8%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/50, 1/50, 6/98, 12/98, 13/50, 15/50; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 210.5 nm, retention time 7.9 min.

\((E)\)-Ethyl-3-(5-bromo-2-(N-(1-ethyl-1H-indol-2-yl)-4-methylphenylsulfonamido)phenyl)acrylate (3f)

Yield: 80%; white solid; mp: 163-165 °C; \(R_f = 0.2 \) (10% EtOAc/ n-hexane); \(^1\)H NMR (400 MHz, CDCl₃) \(\delta\): 8.38 (d, \(J = 16.0 \) Hz, 1H), 7.83 (s, 1H), 7.59 (d, \(J = 8.4 \) Hz, 2H), 7.52 (d, \(J = 7.6 \) Hz, 1H), 7.43 (dd, \(J = 8.4, 2.0 \) Hz, 1H), 7.33-7.26 (m, 3H), 7.23 (t, \(J = 7.6 \) Hz, 1H), 7.17 (d, \(J = 8.4 \) Hz, 1H), 7.09 (t, \(J = 7.6 \) Hz, 1H), 6.42 (d, \(J = 16.00 \) Hz, 1H), 6.29 (s, 1H), 4.32 (q, \(J = 7.2 \) Hz, 2H), 4.25 (q, \(J = 7.2 \) Hz, 2H), 2.47 (s, 3H), 1.39 (t, \(J = 7.2 \) Hz, 3H), 1.21 (t, \(J = 7.2 \) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl₃): 166.0, 144.9, 139.2, 138.2, 136.7, 134.0, 133.8, 133.6, 133.3, 131.6, 130.1, 129.5 (2C), 129.1 (2C), 125.7, 122.9, 122.8, 121.4, 121.1, 119.9, 109.9, 100.6, 60.7, 37.6, 21.7, 14.9, 14.3; MS (ES mass): 567.2 (M+1); HPLC: 98.9%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 225.0 nm, retention time 4.5 min.

\((E)\)-Methyl-3-(5-methyl-2-(4-methyl-N-(1-methyl-1H-indol-2-yl)phenylsulfonamido)phenyl)acrylate (3g)
(E)-Ethyl-3-(5-methyl-2-(4-methyl-N-(1-methyl-1H-indol-2-yl)phenylsulfonamido)phenyl)acrylate (3h)

Yield: 71%; white solid; mp: 172-173 °C; R<sub>f</sub> = 0.2 (10% EtOAc/ n-hexane); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 8.40 (d, J = 16.0 Hz, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 8.0 Hz, 1H), 7.45 (s, 1H), 7.30 (d, J = 8.0 Hz, 2H), 7.26-7.21 (m, 2H), 7.11 (s, 2H), 7.10-7.06 (m, 1H), 6.35 (d, J = 16.0 Hz, 1H), 6.28 (s, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 2.48 (s, 3H), 2.35 (s, 3H); 13C NMR (100 MHz, CDCl<sub>3</sub>): 166.9, 144.5, 141.2, 139.1, 137.2, 135.1, 135.0, 134.6, 134.4, 131.4, 129.8, 129.3 (2C), 129.0 (2C), 127.8, 125.6, 122.6, 120.8, 119.8 (2C), 109.8, 100.2, 51.7, 30.0, 21.6, 21.0; MS (ES mass): 475.2 (M+1); HPLC: 99.0%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH<sub>3</sub>CN (T/%B): 0/50, 1/50, 6/98, 12/98, 13/50, 15/50; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 220.0 nm, retention time 7.8 min.

(E)-Ethyl-3-(5-methyl-2-(4-methyl-N-(1-methyl-1H-indol-2-yl)phenylsulfonamido)phenyl)acrylate (3h)

Yield: 83%; white solid; mp: 184-186 °C; R<sub>f</sub> = 0.2 (10% EtOAc/ n-hexane); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 8.39 (d, J = 16.0 Hz, 1H), 7.59 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.0 Hz, 1H), 7.45 (s, 1H), 7.32-7.20 (m, 5H), 7.11-7.04 (m, 2H), 6.33 (d, J = 16.0 Hz, 1H), 6.30 (s, 1H), 4.30 (q, J = 7.2 Hz, 2H), 3.87 (s, 3H), 2.47 (s, 3H), 2.35 (s, 3H), 1.38 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl<sub>3</sub>): 166.4, 144.4, 140.8, 139.1, 137.2, 135.2, 135.0, 134.6, 134.5, 131.3, 129.8, 129.3 (2C), 129.0 (2C), 127.7, 125.6, 122.6, 120.8, 120.2, 119.8, 109.2, 100.2, 60.5, 30.0, 21.6, 21.0, 14.3; MS (ES mass): 489.2 (M+1); HPLC: 98.1%, Column: Symmetry C-18 75 * 4.6 mm,
3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH3CN  (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 220.0 nm, retention time 4.3 min.

**(E)-Methyl-3-(5-chloro-2-(4-methyl-N-(1-methyl-1H-indol-2-yl)phenylsulfonamido)phenyl)acrylate (3i)**

![Image of compound 3i](image)

Yield: 68%; white solid; mp: 178-180 °C; Rf = 0.2 (10% EtOAc/ n-hexane); 1H NMR (400 MHz, CDCl3) δ: 8.35 (d, J = 16.0 Hz, 1H), 7.61 (d, J = 8.0 Hz, 2H), 7.57 (s, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.33-7.26 (m, 4H), 7.25-7.22 (m, 1H), 7.17 (d, J = 8.8 Hz, 1H), 7.11-7.07 (m, 1H), 6.35 (d, J = 16.0Hz, 1H), 6.27 (s, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 2.48 (s, 3H); 13C NMR (100 MHz, CDCl3): 166.5, 144.9, 139.8, 138.1, 136.5, 135.1, 135.0, 134.5, 134.2, 131.3, 130.4, 129.5 (2C), 129.0 (2C), 127.3, 125.6, 122.9, 121.3, 120.9 (2C), 109.9, 100.4, 52.0, 30.0, 21.7; MS (ES mass): 495.0 (M+1); HPLC: 96.4%, Column: Symmetry C-18 250 * 4.6 mm, 5μm, mobile phase A: 5mm Ammonium Acetate in water, mobile phase B: CH3CN  (T/%B): 0/20, 3/20, 12/95, 23/95, 25/20, 30/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 230.4 nm, retention time 15.0 min.

**(E)-Methyl-3-(5-bromo-2-(4-methyl-N-(1-methyl-1H-indol-2-yl)phenylsulfonamido)phenyl)acrylate (3j)**

![Image of compound 3j](image)
Yield: 60%; white solid; mp: 204-206 °C; Rf = 0.2 (10% EtOAc/ n-hexane); 1H NMR (400 MHz, CDCl3) δ: 8.34 (d, J = 16.0 Hz, 1H), 7.77 (s, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 8.0 Hz, 1H), 7.43 (dd, J = 8.8, 2.4 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.27 (s, 1H), 7.26-7.24 (m, 1H), 7.12-7.07 (m, 2H), 6.35 (d, J = 16.0 Hz, 1H), 6.26 (s, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 2.48 (s, 3H); 13C NMR (100 MHz, CDCl3): 166.4, 144.8, 139.7, 138.6, 136.8, 135.1, 134.4, 134.2, 133.4, 131.5, 130.3, 129.5 (2C), 129.0 (2C), 125.5, 123.0, 122.9, 121.3, 120.9, 120.0, 109.8, 100.4, 51.9, 30.0, 21.6; MS (ES mass): 541.1 (M+3); HPLC: 97.7%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH3CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 220.0 nm, retention time 4.2 min.

**(E)-Ethyl 3-(2-(4-methyl-N-(1-methyl-1H-indol-2-yl)phenylsulfonamido)phenyl)acrylate (3k)**

Yield: 73%; white solid; mp: 167-169 °C; Rf = 0.2 (10% EtOAc/ n-hexane); 1H NMR (400 MHz, CDCl3) δ: 8.44 (d, J = 16.0 Hz, 1H), 7.66 (dd, J = 7.2, 2.0 Hz, 1H), 7.59 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 7.6 Hz, 1H), 7.37-7.27 (m, 6H), 7.23 (d, J = 8.4 Hz, 1H), 7.12-7.06 (m, 1H), 6.35 (d, J = 16.0 Hz, 1H), 6.31 (s, 1H), 4.31 (q, J = 7.2 Hz, 2H), 3.87 (s, 3H), 2.48 (s, 3H), 1.38 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl3): 166.4, 144.6, 140.7, 139.7, 135.1, 135.0, 134.9, 134.6, 130.5, 130.1, 129.4 (2C), 129.1, 129.0 (2C), 127.3, 125.6, 122.8, 120.9, 120.5, 119.9, 109.8, 100.4, 60.6, 30.0, 21.6, 14.3; MS (ES mass): 475.1 (M+1); HPLC: 99.4%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH3CN (T/%B): 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 220.0 nm, retention time 4.2 min.

**(E)-Methyl-3-(2-(N-(1-benzyl-1H-indol-2-yl)-4-methylphenylsulfonamido)-5-methylphenyl)acrylate (3l)**
Yield: 84%; white solid; mp: 161-163 °C; \( R_f = 0.2 \) (10% EtOAc/\( n \)-hexane); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \): 8.18 (d, \( J = 16.0 \) Hz, 1H), 7.61 (d, \( J = 8.0 \) Hz, 2H), 7.56-7.54 (m, 1H), 7.29 (d, \( J = 8.0 \) Hz, 3H), 7.13-7.06 (m, 4H), 7.06-6.98 (m, 4H), 6.64 (d, \( J = 7.2 \) Hz, 2H), 6.48 (s, 1H), 6.04 (d, \( J = 16.0 \) Hz, 1H), 5.51 (s, 2H), 3.72 (s, 3H), 2.48 (s, 3H), 2.30 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): 166.5, 144.6, 140.6, 138.9, 136.9, 136.6, 135.4, 134.6 (2C), 134.3, 131.2, 129.9, 129.4 (2C), 129.2 (2C), 128.0 (2C), 127.6, 126.7, 125.9, 125.6 (2C), 122.9, 120.9, 120.2, 119.7, 110.7, 100.8, 51.5, 46.4, 21.7, 21.0; MS (ES mass): 551.2 (M+1); HPLC: 98.7%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH\(_3\)CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 270.0 nm, retention time 4.3 min.

\((E)-\text{Ethyl-3-(2-}\left(\text{N-(1-benzyl-1H-indol-2-yl)-4-methylphenylsulfonamido-5-chlorophenyl}\right)\text{acrylate (3m)}\)

Yield: 83%; white solid; mp: 135-137 °C; \( R_f = 0.2 \) (10% EtOAc/\( n \)-hexane); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \): 8.16 (d, \( J = 16.0 \) Hz, 1H), 7.62 (d, \( J = 8.0 \) Hz, 2H), 7.59-7.54 (m, 1H), 7.41 (s, 1H), 7.31 (d, \( J = 8.0 \) Hz, 2H), 7.17 (d, \( J = 4.36 \) Hz, 2H), 7.14-7.06 (m, 3H), 7.05-6.97 (m, 3H), 6.58 (d, \( J = 7.2 \) Hz, 2H), 6.48 (s, 1H), 6.05 (d, \( J = 16.0 \) Hz, 1H), 5.48 (s, 2H), 4.21 (q, \( J = 7.2 \) Hz, 2H), 2.48 (s, 3H), 1.33 (t, \( J = 7.2 \) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): 165.7, 144.9, 139.0,
137.3, 136.7, 136.6, 134.7 (3C), 134.1, 131.5, 130.0, 129.6 (2C), 129.1, 128.1 (2C), 127.0, 126.9 (2C), 126.8, 125.8, 125.4, 123.2, 121.4, 121.0, 120.3, 110.6, 101.2, 60.5, 46.1, 21.7, 14.3; MS (ES mass): 585.2 (M+1); HPLC: 97.8%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 215.0 nm, retention time 4.6 min.

*(E)-Methyl-3-(2-(N-(1-benzyl-1H-indol-2-yl)-4-methylphenylsulfonamido)-5-fluorophenyl)acrylate (3n)*

![Chemical Structure](image)

Yield: 82%; white solid; mp: 139-141 °C; Rᵢ = 0.2 (10% EtOAc/ n-hexane); ¹H NMR (400 MHz, CDCl₃) δ: 8.12 (d, J = 16.4 Hz, 1H), 7.61 (d, J = 8.0 Hz, 2H), 7.58-7.56 (m, 1H), 7.31 (d, J = 8.0 Hz, 2H), 7.23-7.19 (m, 1H), 7.16-7.06 (m, 4H), 7.02 (t, J = 7.2 Hz, 3H), 6.96-6.86 (m, 1H), 6.60 (d, J = 7.6 Hz, 2H), 6.47 (s, 1H), 6.00 (d, J = 16.4 Hz, 1H), 5.51 (s, 2H), 3.75 (s, 3H), 2.48 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): 166.1, 163.2 (C-F J = 248.7 Hz), 160.7, 144.9, 139.4, 137.2, 137.1, 136.8, 135.0, 134.7, 134.0, 132.1, 132.0, 129.5 (2C), 129.1, 128.1 (2C), 126.8, 125.8 (2C), 125.4, 123.2, 121.0, 120.9, 120.4, 117.3 (C-F J = 22.8Hz), 117.1, 113.6 (C-F J = 23.5Hz), 113.3, 110.7, 101.0, 51.7, 46.2, 21.7; MS (ES mass): 555.2 (M+1); HPLC: 98.4%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 270.0 nm, retention time 4.1 min.

*(E)-Ethyl-3-(2-(N-(1-benzyl-1H-indol-2-yl)-4-methylphenylsulfonamido)-5-fluorophenyl)acrylate (3o)*
Yield: 79%; white solid; mp: 149-151 °C; Rf = 0.2 (10% EtOAc/ n-hexane); ¹H NMR (400 MHz, CDCl₃) δ: 8.12 (d, J = 16.0 Hz, 1H), 7.62 (d, J = 8.4 Hz, 2H), 7.57-7.55 (m, 1H), 7.30 (d, J = 8.0 Hz, 2H), 7.26-7.22 (m, 1H), 7.13-7.07 (m, 4H), 7.02 (t, J = 6.5 Hz, 3H), 6.92-6.87 (m, 1H), 6.60 (d, J = 7.6 Hz, 2H), 6.49 (s, 1H), 6.00 (d, J = 16.0 Hz, 1H), 5.50 (s, 2H), 4.22 (q, J = 7.2 Hz, 2H), 2.47 (s, 3H), 1.34 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): 165.7, 163.2 (C-F J = 250.0 Hz), 160.7, 144.8, 139.2 (2C), 136.7, 134.9 (2C), 134.7, 134.1, 129.5 (2C), 129.1 (2C), 128.1 (2C), 126.8, 125.8, 125.4 (2C), 123.2, 121.4, 121.0, 120.3, 117.2 (C-F J = 20.0 Hz), 117.0, 113.5, 113.3, 110.7, 101.1, 60.5, 46.2, 21.7, 14.3; MS (ES mass): 569.1 (M+1); HPLC: 99.0%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 270.0 nm, retention time 4.3 min.

(E)-Ethyl-3-(2-(N-(1-benzyl-1H-indol-2-yl)-4-methylphenylsulfonamido)-5-bromophenyl)acrylate (3p)

Yield: 76%; white solid; mp: 145-147 °C; Rf = 0.2 (10% EtOAc/ n-hexane); ¹H NMR (400 MHz, CDCl₃) δ: 8.09 (d, J = 16.0 Hz, 1H), 7.62 (d, J = 8.0 Hz, 2H), 7.66-7.60 (m, 2H), 7.30 (d, J = 8.0 Hz, 3H), 7.13-7.08 (m, 4H), 7.02 (t, J = 7.2 Hz, 3H), 6.58 (d, J = 7.6 Hz, 2H), 6.48 (s, 1H), 6.02 (d, J = 16.0 Hz, 1H), 5.47 (s, 2H), 4.21 (q, J = 7.2 Hz, 2H), 2.48 (s, 3H), 1.33 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): 165.7, 144.9, 138.9, 137.8, 136.9, 136.6, 134.7, 134.6,
134.1, 133.0, 131.7, 130.0 (2C), 129.6 (2C), 129.1 (2C), 128.1, 126.8, 125.8, 125.4 (2C), 123.2, 122.8, 121.4, 121.0, 120.3, 110.6, 101.2, 60.5, 46.1, 21.7, 14.2; MS (ES mass): 631.1 (M+3); HPLC: 98.1%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 275.0 nm, retention time 4.6 min.

(E)-Ethyl -3-(2-(N-(1-hexyl-1H-indol-2-yl)-4-methylphenylsulfonamido)phenyl)acrylate (3q)

![Chemical Structure](image)

Yield: 55%; white solid; mp: 125-127 °C; R_f = 0.2 (10% EtOAc/ n-hexane); ¹H NMR (400 MHz, CDCl₃) δ: 8.45 (d, J = 16.0 Hz, 1H), 7.73 (dd, J = 7.6, 2.4 Hz, 1H), 7.63 (d, J = 8.0 Hz, 2H), 7.54 (d, J = 8.0 Hz, 1H), 7.42-7.32 (m, 3H), 7.30 (d, J = 8.0 Hz, 2H), 7.26-7.18 (m, 2H), 7.06 (m, 1H), 6.45 (d, J = 16.0 Hz, 2H), 4.32 (q, J = 7.2 Hz, 2H), 4.13-4.04 (m, 2H), 1.56 (s, 2H), 1.40 (t, J = 7.2 Hz, 3H), 1.32-1.16 (m, 6H), 0.85 (t, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): 166.3, 144.5, 140.6, 139.0, 134.6, 134.5, 134.1 (2C), 130.5, 130.2, 129.4 (2C), 129.1 (2C), 128.7, 127.1, 125.7, 122.5, 121.0, 119.9, 119.8, 110.0, 100.9, 60.5, 43.0, 31.5, 29.9, 26.5, 22.4, 21.6, 14.3, 13.9; MS (ES mass): 545.2 (M+1); HPLC: 98.9%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 225.0 nm, retention time 5.1 min.

(E)-Ethyl-3-(2-(N-(1-ethyl-1H-indol-2-yl)-4-methylphenylsulfonamido)-5-iodophenyl)acrylate (3r)
Yield: 73%; white solid; mp: 173-175 °C; \( R_f = 0.2 \) (10% EtOAc/ \( n \)-hexane); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \): 8.35 (d, \( J = 16.0 \) Hz, 1H), 8.03 (s, 1H), 7.65-7.57 (m, 3H), 7.52 (d, \( J = 8.0 \) Hz, 1H), 7.31 (d, \( J = 8.0 \) Hz, 3H), 7.23 (t, \( J = 7.2 \) Hz, 1H), 7.09 (t, \( J = 7.2 \) Hz, 1H), 7.03 (d, \( J = 8.4 \) Hz, 1H), 6.41 (d, \( J = 16.0 \) Hz, 1H), 6.29 (s, 1H), 4.32 (q, \( J = 7.2 \) Hz, 2H), 4.25 (q, \( J = 6.8 \) Hz, 2H), 2.47 (s, 3H), 1.39 (t, \( J = 7.2 \) Hz, 3H), 1.21 (t, \( J = 7.2 \) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \): 166.0, 144.8, 139.3, 139.1, 139.0, 136.9, 136.2, 134.1, 133.9, 131.7, 129.5 (2C), 129.1 (2C), 125.8, 122.8, 121.3, 121.1, 119.9, 109.9 (2C), 100.6, 94.5, 60.7, 37.6, 21.6, 14.9, 14.3; MS (ES mass): 615.1 (M+1); HPLC: 99.5%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH\(_3\)CN (T/%B): 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 225.0 nm, retention time 4.6 min.

\((E)\)-Ethyl-3-(5-iodo-2-(4-methyl-\( N\)-(1-methyl-1\( H\)-indol-2-\( yl\))phenylsulfonamido)phenyl)acrylate (3s)

Yield: 68%; white solid; mp: 163-165 °C; \( R_f = 0.2 \) (10% EtOAc/ \( n \)-hexane); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \): 8.29 (d, \( J = 16.0 \) Hz, 1H), 7.97 (s, 1H), 7.62 (dd, \( J = 8.4, 2.4 \) Hz, 1H), 7.59 (d, \( J = 8.0 \) Hz, 2H), 7.50 (d, \( J = 8.0 \) Hz, 1H), 7.31 (d, \( J = 8.0 \) Hz, 2H), 7.29 (s, 1H), 7.24 (d, \( J = 8.0 \) Hz, 1H), 7.12-7.07 (m, 1H), 6.96 (d, \( J = 8.4 \) Hz, 1H), 6.33 (d, \( J = 16.0 \) Hz, 1H), 6.26 (s, 1H), 4.30 (q, \( J = 7.2 \) Hz, 2H), 3.84 (s, 3H), 2.47 (s, 3H), 1.37 (t, \( J = 7.2 \) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \): 165.9, 144.8, 139.3 (2C), 139.2, 137.0, 136.3, 135.1, 134.4, 134.3, 131.6, 129.5 (2C),
129.0 (2C), 125.5, 122.9, 121.7, 120.9, 120.0, 109.8, 100.4, 94.7, 60.7, 30.0, 21.6, 14.3; MS (ES mass): 601.1 (M+1); HPLC: 96.1%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 220.0 nm, retention time 4.6 min.

**(E)-Ethyl 3-(2-(N-(5-bromo-1-methyl-1H-indol-2-yl)-4-methylphenylsulfonamido)-3,5-dimethylphenyl)acrylate (3t)**

![Chemical Structure](image)

Yield: 84%; pink solid; mp: 213-215 °C; Rᵣ = 0.2 (10% EtOAc/ n-hexane); ¹H NMR (400 MHz, CDCl₃) δ: 8.06 (d, J = 16.0 Hz, 1H), 7.72 (d, J = 8.4 Hz, 2H), 7.62 (s, 1H), 7.32-7.26 (m, 3H), 7.24 (s, 1H), 7.12 (s, 1H), 7.03 (d, J = 8.8 Hz, 1H), 6.62 (s, 1H), 6.25 (d, J = 16.0 Hz, 1H), 4.34-4.14 (m, 2H), 3.50 (s, 3H), 2.47 (s, 3H), 2.41 (s, 3H), 2.33 (s, 3H), 1.34 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): 166.4, 144.7, 141.9, 139.7, 139.0, 135.6, 135.4, 135.1, 134.9, 134.8, 133.7, 129.6 (2C), 128.9 (2C), 127.2, 126.1, 125.1, 123.1, 119.6, 113.0, 110.9, 100.3, 60.4, 30.8, 21.6, 20.9, 20.5, 14.4; MS (ES mass): 581.1 (M+1); HPLC: 98.4%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 10/95, 10.5/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (80:20); UV 230.0 nm, retention time 5.1 min.

**(E)-Ethyl 3-(2-(N-(5-methoxy-1-methyl-1H-indol-2-yl)-4-methylphenylsulfonamido)-4-methylphenyl)acrylate (3u)**
Yield: 87%; white solid; mp: 180-182 °C; \( R_f = 0.2 \) (20% EtOAc/ n-hexane); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \): 8.35 (d, \( J = 16.0 \) Hz, 1H), 7.62 (d, \( J = 8.2 \) Hz, 2H), 7.55 (d, \( J = 8.0 \) Hz, 1H), 7.31 (t, \( J = 8.0 \) Hz, 2H), 7.20-7.12 (m, 2H), 7.06 (s, 1H), 6.98 (t, \( J = 4.3 \) Hz, 1H), 6.90 (dd, \( J = 8.8, 2.4 \)Hz, 1H), 6.36-6.26 (m, 2H), 4.29 (q, \( J = 7.2 \) Hz, 2H), 3.81 (s, 3H), 3.80 (s, 3H), 2.46 (s, 3H), 2.30 (s, 3H), 1.37 (t, \( J = 7.2 \) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): 166.6, 154.2, 144.5, 141.2, 140.6, 139.4, 135.1, 134.6, 131.8, 130.7, 130.3, 129.9, 129.3 (2C), 129.0 (2C), 127.0, 125.8, 119.3, 113.2, 110.7, 102.3, 100.1, 60.5, 55.7, 30.1, 21.7. 21.3, 14.3; MS (ES mass): 519.2 (M+1); HPLC: 94.5%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH\(_3\)CN (T/%B): 0/20, 0.5/20, 2/95, 10/95, 10.5/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (80:20); UV 230.0 nm, retention time 4.2 min.

\((E)\)-Ethyl-3-(2-(N-(6-chloro-1-methyl-1H-indol-2-yl)-4-methylphenylsulfonamido)phenyl)acrylate (3v)

Yield: 82%; white solid; mp: 157-159 °C; \( R_f = 0.2 \) (20% EtOAc/ n-hexane); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \): 8.38 (d, \( J = 16.0 \) Hz, 1H), 7.69 (dd, \( J = 7.2, 2.0 \) Hz, 1H), 7.57 (d, \( J = 8.0 \) Hz, 2H), 7.41 (d, \( J = 8.4 \) Hz, 1H), 7.38-7.32 (m, 2H), 7.30 (d, \( J = 8.0 \) Hz, 2H), 7.27 (s, 1H), 7.26-7.22 (m, 1H), 7.05 (dd, \( J = 8.4, 2.0 \) Hz, 1H), 6.35 (d, \( J = 16.0 \) Hz, 1H), 6.31 (s, 1H), 4.30 (q, \( J = 7.2 \) Hz, 2H), 3.82 (s, 3H), 2.47 (s, 3H), 1.38 (t, \( J = 7.2 \) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): 166.3, 144.8, 140.6, 139.4, 135.6, 135.4, 134.9, 134.3, 130.6, 130.1, 129.5 (2C), 129.2, 129.0 (2C), 128.7, 127.4, 124.1, 121.9, 120.7 (2C), 109.8, 100.6, 60.6, 30.2, 21.7, 14.3; MS (ES mass): 509.2
Typical procedure for synthesis of methyl-2-(6-ethyl-2-methyl-6H-indolo[2,3-b]quinolin-11-yl)acetate (4a)

\[(E)-\text{Methyl-3-(2-(N-(1-ethyl-1H-indol-2-yl)-4-methylphenylsulfonamido)-5-methylphenyl)acrylate 3a (0.20 mmol), Pd (OAc)}_2 (5 \text{ mol%}), \text{Cu(OAc)}_2 (0.30 \text{ mmol)}, \text{TFA (0.24 mmol) and CH}_3\text{CN (2.5 mL) was heated at 60 °C in air for 5h. The progress of the reaction was monitored by TLC. After completion of the reaction, reaction mixture was cooled to RT, diluted with ethyl acetate (15 mL) and passed through celite. The resulting solution was washed with water (3 x 15 mL) followed by brine solution (25 mL), dried over anhydrous Na}_2\text{SO}_4, \text{ and concentrated under reduced pressure. The residue was purified by column chromatography using ethyl acetate–hexane to give desired compound 4a.}

Yield: 86%; light yellow solid; mp: 183-186 °C; \(R_f = 0.2\) (10% EtOAc/ n-hexane); \(^1\text{H NMR (400 MHz, CDCl}_3\):} δ: 8.29 (d, \(J = 8.0 \text{ Hz}, 1\text{H}), 8.05 (d, \(J = 8.4 \text{ Hz}, 1\text{H}), 7.99 (s, 1\text{H}), 7.60-7.55 (m, 2\text{H}), 7.46 (d, \(J = 8.0 \text{ Hz}, 1\text{H}), 7.31 (t, \(J = 7.6 \text{ Hz}, 1\text{H}), 4.69 (s, 2\text{H}), 4.60 (q, \(J = 7.2 \text{ Hz}, 2\text{H}), 3.69 (s, 3\text{H}), 2.61 (s, 3\text{H}), 1.50 (t, \(J = 7.2 \text{ Hz}, 3\text{H}); \(^{13}\text{C NMR (100 MHz, CDCl}_3\):} δ: 170.4, 151.2, 145.2, 141.9, 132.8, 132.6, 130.8, 128.0, 127.6, 123.5, 123.4, 122.6, 120.6, 119.7, 117.1, 108.7, 52.4, 35.9, 34.8, 21.8, 13.6; MS (ES mass): 333.1 (M+1); HPLC: 99.0%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH}_3\text{CN (T/%B):} 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 230.0 nm, retention time 3.0 min.
Ethyl-2-(6-ethyl-2-methyl-6H-indolo[2,3-b]quinolin-11-yl)acetate (4b)

Compound 4b was synthesized from 3b following a procedure similar to that of compound 4a
Yield: 89%; yellow solid; mp: 285-287 °C; Rf = 0.2 (10% EtOAc/ n-hexane); 1H NMR (400 MHz, CDCl3) δ: 8.31 (d, J = 8.0 Hz, 1H), 8.05 (d, J = 8.8 Hz, 1H), 8.01 (s, 1H), 7.61-7.54 (m, 2H), 7.46 (d, J = 8.0 Hz, 1H), 7.30 (t, J = 8.0 Hz, 1H), 4.68 (s, 2H), 4.60 (q, J = 7.2 Hz, 2H), 4.18 (q, J = 7.2 Hz, 2H), 2.61 (s, 3H), 1.50 (t, J = 8.0 Hz, 1H), 1.20 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ: 169.9, 151.2, 145.2, 141.9, 133.0, 132.5, 130.8, 127.9, 127.6, 123.5 (2C), 122.8, 120.6, 119.6, 117.1, 108.6, 61.3, 35.9, 35.0, 21.8, 14.1, 13.6; MS (ES mass): 347.1 (M+1); HPLC: 96.4%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH3CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 275.0 nm, retention time 3.2 min.

Ethyl-2-(6-ethyl-2-fluoro-6H-indolo[2,3-b]quinolin-11-yl)acetate (4c)

Compound 4c was synthesized from 3c following a procedure similar to that of compound 4a
Yield: 78%; orange solid; mp: 133-135 °C; Rf = 0.2 (10% EtOAc/ n-hexane); 1H NMR (400 MHz, CDCl3) δ: 8.35 (d, J = 7.6 Hz, 1H), 8.13 (dd, J = 9.2, 5.6 Hz, 1H), 7.88 (dd, J = 10.8, 2.7 Hz, 1H), 7.65-7.57 (m, 1H), 7.53-7.46 (m, 2H), 7.35-7.31 (m, 1H), 4.63 (s, 2H), 4.62 (q, J = 7.2 Hz, 2H), 4.19 (q, J = 7.2 Hz, 2H), 1.51 (t, J = 7.2 Hz, 3H), 1.22 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ: 169.5, 151.2, 143.6, 142.1, 132.9, 130.2 (C-F J = 8.8 Hz), 130.1, 128.1,
123.8 (3C), 120.1, 119.8, 118.6 (C-F J = 25.6 Hz), 118.3, 117.7, 108.7, 107.5 (C-F J = 22.9 Hz), 107.3, 61.5, 35.2, 29.6, 14.1, 13.5; MS (ES mass): 351.2 (M+1); HPLC: 93.4%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 225.0 nm, retention time 3.8 min.

**Methyl-2-(6-ethyl-2-fluoro-6H-indolo[2,3-b]quinolin-11-yl)acetate (4d)**

![Chemical Structure](image)

Compound 4d was synthesized from 3d following a procedure similar to that of compound 4a
Yield: 52%; off white solid; mp: 163-175 °C; Rf = 0.2 (10% EtOAc/ n-hexane); ¹H NMR (400 MHz, CDCl₃) δ: 8.32 (d, J = 8.0 Hz, 1H), 8.13 (dd, J = 9.2, 5.6 Hz, 1H), 7.86 (dd, J = 10.6, 2.6 Hz, 1H), 7.61 (t, J = 7.2 Hz, 1H), 7.55-7.44 (m, 2H), 7.33 (t, J = 7.6 Hz, 1H), 4.64 (s, 2H), 4.59 (q, J = 7.2 Hz, 2H), 3.70 (s, 3H), 1.50 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ: 170.0, 159.8 (C-F J = 241.6 Hz), 157.4, 151.2, 143.6, 142.1, 132.7 (2C), 130.2 (C-F J = 8.8 Hz), 130.2, 128.2, 123.8 (2C), 120.0, 119.9, 118.6 (C-F J = 25.6 Hz), 118.4, 108.8, 107.4 (C-F J = 22.8 Hz), 107.2, 52.5, 36.0, 35.0, 13.5; MS (ES mass): 337.2 (M+1); HPLC: 95.7%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 275.0 nm, retention time 3.8 min.

**Methyl-2-(2-bromo-6-ethyl-6H-indolo[2,3-b]quinolin-11-yl)acetate (4e)**

![Chemical Structure](image)
Compound 4e was synthesized from 3e following a procedure similar to that of compound 4a
Yield: 80%; white solid; mp: 186-189 °C; Rf = 0.2 (10% EtOAc/ n-hexane); 
1H NMR (400 MHz, CDCl3) δ: 8.37 (s, 1H), 8.30 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.8 Hz, 1H), 7.77 (dd, J = 9.0, 2.0 Hz, 1H), 7.61 (t, J = 7.6 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.34 (t, J = 7.2 Hz, 1H), 4.65 (s, 2H), 4.55 (q, J = 7.2 Hz, 2H), 4.31 (s, 3H), 1.51 (t, J = 7.2 Hz, 3H); 
13C NMR (100 MHz, CDCl3) δ: 169.9, 151.6, 145.3, 142.1, 132.5, 131.7, 129.9, 128.2, 126.0, 124.7, 123.8, 120.2, 120.1, 117.8, 116.5, 108.9, 52.6, 36.0, 34.7, 13.5; MS (ES mass): 399.1 (M+3); HPLC: 99.5%, Column: Symmetry C18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH3CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 225.0 nm, retention time 4.0 min.

**Ethyl-2-(2-bromo-6-ethyl-6H-indolo[2,3-b]quinolin-11-yl)acetate (4f)**

![Image of Compound 4f](image)

Compound 4f was synthesized from 3f following a procedure similar to that of compound 4a
Yield: 88%; yellow solid; mp: 187-189 °C; Rf = 0.2 (10% EtOAc/ n-hexane); 
1H NMR (400 MHz, CDCl3) δ: 8.39 (s, 1H), 8.32 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.8 Hz, 1H), 7.77 (dd, J = 8.8, 2.4 Hz, 1H), 7.64-7.57 (m, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.34-7.30 (m, 1H), 4.63 (s, 2H), 4.58 (q, J = 7.2 Hz, 2H), 4.19 (q, J = 7.2 Hz, 2H), 1.50 (t, J = 7.2 Hz, 3H), 1.22 (t, J = 7.2 Hz, 3H); 
13C NMR (100 MHz, CDCl3) δ: 169.4, 151.6, 145.2, 142.1, 132.7, 131.7, 129.9, 128.2, 126.2, 124.8, 123.8, 120.2, 120.0, 117.8, 116.4, 108.9, 61.5, 36.0, 35.0, 14.1, 13.5; MS (ES mass): 411.1 (M+3); HPLC: 99.2%, Column: Symmetry C18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH3CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 275.0 nm, retention time 4.3 min.

**Methyl-2-(2,6-dimethyl-6H-indolo[2,3-b]quinolin-11-yl)acetate (4g)**
Compound 4g was synthesized from 3g following a procedure similar to that of compound 4a
Yield: 75%; yellow floppy solid; mp: 208-210 °C; R\textsubscript{f} = 0.2 (10% EtOAc/ n-hexane); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\): 8.28 (d, \(J = 8.0\) Hz, 1H), 8.06 (d, \(J = 8.8\) Hz, 1H), 7.99 (s, 1H), 7.61-7.56 (m, 2H), 7.44 (d, \(J = 8.0\) Hz, 1H), 7.32 (t, \(J = 7.2\) Hz, 1H), 4.70 (s, 2H), 3.99 (s, 3H), 3.69 (s, 3H), 2.61 (s, 3H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\): 170.4, 151.9, 145.1, 142.9, 132.9, 132.7, 130.9, 127.8, 127.7, 123.4, 123.3, 122.7, 120.4, 119.9, 117.1, 108.5, 52.4, 34.8, 27.6, 21.8; MS (ES mass): 319.2 (M+1); HPLC: 98.0%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH\textsubscript{3}CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 225.0 nm, retention time 2.9 min.

Ethyl-2-(2,6-dimethyl-6\textsubscript{H}-indolo[2,3-b]quinolin-11-yl)acetate (4h)

Compound 4h was synthesized from 3h following a procedure similar to that of compound 4a
Yield: 82%; yellow solid; mp: 145-147 °C; R\textsubscript{f} = 0.2 (10% EtOAc/ n-hexane); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\): 8.31 (d, \(J = 8.0\) Hz, 1H), 8.05 (d, \(J = 8.8\) Hz, 1H), 8.01 (s, 1H), 7.61-7.55 (m, 2H), 7.44 (d, \(J = 8.0\) Hz, 1H), 7.32 (t, \(J = 8.0\) Hz, 1H), 4.68 (s, 2H), 4.17 (q, \(J = 7.2\) Hz, 2H), 3.99 (s, 3H), 2.61 (s, 3H), 1.19 (t, \(J = 7.2\) Hz, 3H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\): 169.8, 151.9, 145.1, 142.9, 133.2, 132.6, 130.9, 129.7, 128.9, 127.8, 127.7, 123.4, 122.8, 119.8, 117.1, 108.5, 61.3, 35.0, 27.6, 21.8, 14.1; MS (ES mass): 333.2 (M+1); HPLC: 94.8%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH\textsubscript{3}CN (T/%B):
0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 225.0 nm, retention time 3.0 min.

**Methyl-2-(2-chloro-6-methyl-6H-indolo[2,3-b]quinolin-11-yl)acetate (4i)**

![Methyl-2-(2-chloro-6-methyl-6H-indolo[2,3-b]quinolin-11-yl)acetate (4i)](image)

Compound 4i was synthesized from 3i following a procedure similar to that of compound 4a

Yield: 85%; white solid; mp: 167-169 °C; R<sub>f</sub> = 0.2 (10% EtOAc/ n-hexane); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 8.29 (d, <i>J</i> = 8.0 Hz, 1H), 8.20 (s, 1H), 8.08 (d, <i>J</i> = 8.8 Hz, 1H), 7.66 (dd, <i>J</i> = 8.8, 2.4 Hz, 1H), 7.63-7.60 (m, 1H), 7.45 (d, <i>J</i> = 8.0 Hz, 1H), 7.36-7.32 (m, 1H), 4.65 (s, 2H), 3.98 (s, 3H), 3.70 (s, 3H);<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 169.8, 152.2, 145.0, 143.1, 132.7, 129.6, 129.3, 128.7, 128.3, 124.1, 123.6, 122.8, 120.3, 120.0, 117.8, 108.8, 52.6, 34.8, 27.6; MS (ES mass): 339.0 (M+1); HPLC: 96.4%, column: Symmetry C-18 250 x 4.6 mm 5μm, mobile phase A: 5 mm Ammonium Acetate in water, mobile phase B: CH<sub>3</sub>CN, gradient (T/%B): 0/20, 3/20, 12/95, 23/95, 25/20, 30/20; flow rate: 1.0 mL/min; UV 260 nm, retention time 14.4 min.

**Methyl-2-(2-bromo-6-methyl-6H-indolo[2,3-b]quinolin-11-yl)acetate (4j)**

![Methyl-2-(2-bromo-6-methyl-6H-indolo[2,3-b]quinolin-11-yl)acetate (4j)](image)

Compound 4j was synthesized from 3j following a procedure similar to that of compound 4a

Yield: 77%; light green solid; mp: 201-203 °C; R<sub>f</sub> = 0.2 (10% EtOAc/ n-hexane); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 8.37 (s, 1H), 8.29 (d, <i>J</i> = 8.0 Hz, 1H), 8.02 (d, <i>J</i> = 8.8 Hz, 1H), 7.78 (dd, <i>J</i> = 8.8, 2.4 Hz, 1H), 7.66-7.60 (m, 1H), 7.46 (d, <i>J</i> = 8.0 Hz, 1H), 7.35 (t, <i>J</i> = 7.6 Hz, 1H), 4.65 (s, 2H), 3.99 (s, 3H), 3.71 (s, 3H);<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 169.8, 152.3, 145.2, 143.1, 132.6,
131.8, 129.8, 128.3, 126.1, 124.7, 123.6, 120.4, 120.0, 117.8, 116.6, 108.8, 52.6, 34.7, 27.6; MS (ES mass): 385.0 (M+3); HPLC: 98.8%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 280.0 nm, retention time 3.8 min.

**Ethyl-2-(6-methyl-6H-indolo[2,3-b]quinolin-11-yl)acetate (4k)**

![Chemical Structure](image)

Compound 4k was synthesized from 3k following a procedure similar to that of compound 4a

Yield: 84%; off white solid; mp: 145-147 °C; Rᵢ = 0.2 (10% EtOAc/ n-hexane); ¹H NMR (400 MHz, CDCl₃) δ: 8.33 (d, J = 8.0 Hz, 1H), 8.27 (d, J = 8.0 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.75-7.71 (m, 1H), 7.61 (t, J = 8.0 Hz, 1H), 7.54-7.50 (m, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.33 (t, J = 7.2 Hz, 1H), 4.70 (s, 2H), 4.16 (q, J = 7.2 Hz, 2H), 4.01 (s, 3H), 1.18 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ:169.7, 152.2, 146.7, 143.0, 133.9, 128.6, 128.0, 127.9, 123.9, 123.6, 123.5, 123.1, 120.4, 120.0, 117.2, 108.6, 61.4, 35.1, 27.6, 14.1; MS (ES mass): 319.2 (M+1); HPLC: 99.5%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 275.0 nm, retention time 3.2 min.

**Methyl-2-(6-benzyl-2-methyl-6H-indolo[2,3-b]quinolin-11-yl)acetate (4l)**

![Chemical Structure](image)

Compound 4l was synthesized from 3l following a procedure similar to that of compound 4a
Yield: 89%; yellow solid; mp: 202-204 °C; R_f = 0.2 (10% EtOAc/ n-hexane); ¹H NMR (400 MHz, CDCl₃) δ: 8.29 (d, J = 7.6 Hz, 1H), 8.06 (t, J = 8.4 Hz, 1H), 8.02 (s, 1H), 7.57 (dd, J = 8.6, 1.6 Hz, 1H), 7.51-7.44 (m, 1H), 7.33-7.27 (m, 5H), 7.24-7.19 (m, 2H), 5.77 (s, 2H), 4.71 (s, 2H), 3.71 (s, 3H), 2.62 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ: 170.4, 151.7, 145.2, 142.1, 137.2, 133.0, 132.9, 130.9, 128.6 (2C), 128.1, 127.7, 127.2, 127.1 (2C), 123.7, 123.4, 122.7, 120.7, 120.1, 117.0, 109.5, 52.5, 44.8, 34.8, 21.9; MS (ES mass): 395.2 (M+1); HPLC: 97.1%, Column: Symmetry C-18 75 * 4.6 mm, 3.5µm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 275.0 nm, retention time 3.8 min.

Ethyl-2-(6-benzyl-2-chloro-6H-indolo[2,3-b]quinolin-11-yl)acetate (4m)

Compound 4m was synthesized from 3m following a procedure similar to that of compound 4a

Yield: 75%; yellow solid; mp: 154-156 °C; R_f = 0.2 (10% EtOAc/ n-hexane); ¹H NMR (400 MHz, CDCl₃) δ: 8.33 (d, J = 8.0 Hz, 1H), 8.25 (s, 1H), 8.07 (d, J = 8.8 Hz, 1H), 7.65 (dd, J = 8.8, 2.4 Hz, 1H), 7.51 (t, J = 8.0 Hz, 1H), 7.34-7.27 (m, 6H), 7.24-7.22 (m, 1H), 5.77 (s, 2H), 4.66 (s, 2H), 4.21 (q, J = 7.2 Hz, 2H), 1.23 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ: 169.4, 152.2, 145.1, 142.3, 137.0, 133.0, 129.8, 129.3, 128.8, 128.6 (2C), 128.3, 127.4, 127.1 (2C), 124.5, 123.7, 122.9, 120.4, 120.3, 117.7, 109.7, 61.6, 44.9, 35.1, 14.1; MS (ES mass): 429.2 (M+1); HPLC: 94.1%, Column: Symmetry C-18 75 * 4.6 mm, 3.5µm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 275.0 nm, retention time 4.6 min.

Methyl-2-(6-benzyl-2-fluoro-6H-indolo[2,3-b]quinolin-11-yl)acetate (4n)
Compound 4n was synthesized from 3n following a procedure similar to that of compound 4a. 
Yield: 81%; yellow solid; mp: 171-173 °C; Rf = 0.2 (10% EtOAc/n-hexane); 1H NMR (400 MHz, CDCl3) δ: ppm 8.33 (d, J = 7.6 Hz, 1H), 8.13 (dd, J = 9.2, 5.6 Hz, 1H), 7.88 (dd, J = 10.4, 2.8 Hz, 1H), 7.54-7.49 (m, 2H), 7.36-7.27 (m, 6H), 7.25-7.22 (m, 1H), 5.77 (s, 2H), 4.66 (s, 2H), 4.66 (s, 2H), 3.72 (s, 3H); 13C NMR (100 MHz, CDCl3) δ: 170.0, 143.6, 142.3, 137.0, 136.6, 130.4 (C-F J = 8.8 Hz), 130.3, 128.7, 128.6, 128.2, 127.3, 127.1, 123.7, 123.6, 120.7, 120.3, 120.1, 118.7, 118.5 (C-F J = 25.5 Hz), 117.6, 109.6, 107.7, 107.5, 107.2, 52.6, 44.8, 35.0; MS (ES mass): 399.1 (M+1); HPLC: 93.7%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1% TFA in water, mobile phase B: CH3CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 275.0 nm, retention time 4.1 min.

Ethyl 2-(6-benzyl-2-fluoro-6H-indolo[2,3-b]quinolin-11-yl)acetate (4o)

Compound 4o was synthesized from 3o following a procedure similar to that of compound 4a. 
Yield: 83%; yellow solid; mp: 174-176 °C; Rf = 0.2 (10% EtOAc/n-hexane); 1H NMR (400 MHz, CDCl3) δ: ppm 8.34 (d, J = 8.0 Hz, 1H), 8.12 (dd, J = 9.2, 5.6 Hz, 1H), 7.90 (dd, J = 10.4, 2.4 Hz, 1H), 7.52-7.47 (m, 2H), 7.34-7.28 (m, 6H), 7.25-7.20 (m, 1H), 5.75 (s, 2H), 4.64 (s, 2H), 4.20 (q, J = 7.2 Hz, 2H), 1.22 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ: 169.5, 151.8, 143.6, 142.4, 137.1, 133.2, 130.4, 130.3, 128.6 (2C), 128.2, 127.3, 127.1, 123.7, 120.3, 120.2, 118.7, 118.4, 117.7, 109.6, 107.6, 107.3, 61.5, 44.8, 35.3, 14.1; MS (ES mass): 413.2 (M+1);
HPLC: 93.3%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 2/20, 10/95, 20/95, 10/20, 25/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 275.0 nm, retention time 4.2 min.

**Ethyl 2-(6-benzyl-2-bromo-6H-indolo[2,3-b]quinolin-11-yl)acetate (4p)**

![Chemical Structure Image]

Compound 4p was synthesized from 3p following a procedure similar to that of compound 4a

Yield: 77%; yellow solid; mp: 166-168 °C; Rf = 0.2 (10% EtOAc/ n-hexane); ¹H NMR (400 MHz, CDCl₃) δ: 8.42 (s, 1H), 8.33 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 9.2 Hz, 1H), 7.77 (dd, J = 8.8, 2.4 Hz, 1H), 7.51 (t, J = 8.0 Hz, 1H), 7.39-7.28 (m, 6H), 7.24-7.21 (m, 1H), 5.77 (s, 2H), 4.66 (s, 2H), 4.21 (q, J = 7.2 Hz, 2H), 1.24 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ: 169.4, 145.3, 142.3, 136.9, 133.0, 131.8, 130.1, 130.0, 128.7, 128.6, 128.3, 127.4, 127.1, 126.2, 125.1, 123.7, 120.4, 120.3, 117.7, 116.7, 109.9, 109.7, 61.6, 44.9, 35.1, 14.1; MS (ES mass): 473.1 (M+1); HPLC: 90.1%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 225.0 nm, retention time 4.8 min.

**Ethyl 2-(6-hexyl-6H-indolo[2,3-b]quinolin-11-yl)acetate (4q)**

![Chemical Structure Image]
Compound 4q was synthesized from 3q following a procedure similar to that of compound 4a. Yield: 67%; light yellow solid; mp: 132-135 °C; R_f = 0.2 (10% EtOAc/ n-hexane); ^1^H NMR (400 MHz, CDCl_3) δ: 8.34 (d, J = 8.0 Hz, 1H), 8.27 (d, J = 7.6 Hz, 1H), 8.15 (d, J = 8.8 Hz, 1H), 7.75-7.70 (m, 1H), 7.62-7.56 (m, 1H), 7.53-7.59 (m, 1H), 7.46 (d, J = 8.0 Hz, 1H), 7.33-7.30 (m, 1H), 4.70 (s, 2H), 4.56-4.51 (t, J = 7.2 Hz, 2H), 4.18 (q, J = 7.2 Hz, 2H), 2.00-1.90 (m, 2H), 1.46 (dd, J = 10.53, 5.83 Hz, 2H), 1.41-1.35 (m, 2H), 1.33-1.29 (m, 2H), 1.19 (t, J = 7.2 Hz, 3H), 0.88 (t, J = 7.2 Hz, 3H); ^1^C NMR (100 MHz, CDCl_3) δ: 169.8, 152.0, 146.7, 142.4, 133.6, 128.4, 128.3, 127.7, 123.9, 123.6, 123.0, 120.5, 119.7, 117.1, 109.9, 108.9, 61.3, 41.3, 35.1, 31.5, 28.3, 26.7, 22.5, 14.1, 14.0; MS (ES mass): 389.2 (M+1); HPLC: 91.6%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH_3CN (T/%B): 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 220.0 nm, retention time 4.0 min.

**Ethyl 2-(6-ethyl-2-iodo-6H-indolo[2,3-b]quinolin-11-yl)acetate (4r)**

![Ethyl 2-(6-ethyl-2-iodo-6H-indolo[2,3-b]quinolin-11-yl)acetate (4r)](image)

Compound 4r was synthesized from 3r following a procedure similar to that of compound 4a. Yield: 72%; light yellow solid; mp: 159-161 °C; R_f = 0.2 (10% EtOAc/ n-hexane); ^1^H NMR (400 MHz, CDCl_3) δ: 8.60 (s, 1H), 8.32 (d, J = 8.0 Hz, 1H), 7.93 (dd, J = 8.8, 1.6 Hz, 1H), 7.87 (d, J = 8.8 Hz, 1H), 7.65-7.57 (m, 1H), 7.47 (d, J = 8.4 Hz, 1H), 7.36-7.29 (m, 1H), 4.63 (s, 2H), 4.59 (q, J = 7.2 Hz, 2H), 4.20 (q, J = 7.2 Hz, 2H), 1.50 (t, J = 7.2 Hz, 3H), 1.23 (t, J = 7.2 Hz, 3H); ^1^C NMR (100 MHz, CDCl_3) δ: 169.4, 145.6, 142.1, 139.8, 136.9, 132.8, 132.6, 130.0, 128.2, 125.5, 123.8, 120.3, 120.1, 117.6, 108.9, 87.3, 61.5, 36.0, 35.0, 14.1, 13.5; MS (ES mass): 459.1 (M+1); HPLC: 96.7%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH_3CN (T/%B): 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 280.0 nm, retention time 4.3 min.

**Ethyl 2-(2-iodo-6-methyl-6H-indolo[2,3-b]quinolin-11-yl)acetate (4s)**
Compound 4s was synthesized from 3s following a procedure similar to that of compound 4a.

Yield: 69%; light yellow solid; mp: 167-171 °C; \( R_f = 0.2 \) (10% EtOAc/\( n\)-hexane); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta: 8.60 \) (s, 1H), 8.31 (d, \( J = 8.0 \) Hz, 1H), 7.98-7.91 (m, 1H), 7.88 (d, \( J = 8.8 \) Hz, 1H), 7.61 (d, \( J = 8.0 \) Hz, 1H), 7.45 (d, \( J = 8.0 \) Hz, 1H), 7.37-7.31 (m, 1H), 4.63 (s, 2H), 4.19 (q, \( J = 7.2 \) Hz, 2H), 3.99 (s, 3H), 1.22 (t, \( J = 7.2 \) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta: 169.3, 152.3, 145.6, 143.1, 137.0, 132.9, 132.7, 129.8, 128.3, 125.5, 123.6, 120.3, 120.1, 117.6, 108.8, 87.4, 61.5, 35.0, 27.6, 14.1; MS (ES mass): 445.1 (M+1); HPLC: 91.3%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH\(_3\)CN (T/%B): 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (90:10); UV 280.0 nm, retention time 4.2 min.

**Ethyl 2-(9-bromo-2,4,6-trimethyl-6H-indolo[2,3-b]quinolin-11-yl)acetate (4t)**

Compound 4t was synthesized from 3t following a procedure similar to that of compound 4a.

Yield: 87%; yellow solid; mp: 213-215 °C; \( R_f = 0.2 \) (20% EtOAc/\( n\)-hexane); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta: 8.40 \) (s, 1H), 7.86 (s, 1H), 7.66 (dd, \( J = 8.8, 2.0 \) Hz, 1H), 7.46 (s, 1H), 7.29 (d, \( J = 8.8 \) Hz, 1H), 4.60 (s, 2H), 4.18 (q, \( J = 7.2 \) Hz, 2H), 3.96 (s, 3H), 2.85 (s, 3H), 2.56 (s, 3H), 1.23 (t, \( J = 7.2 \) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): 169.7, 150.6, 144.4, 141.4, 135.4, 133.8, 132.3, 131.4, 129.9, 125.9, 123.2, 122.0, 120.6, 115.3, 112.1, 109.6, 61.4, 35.1, 27.3, 21.8, 18.3, 14.1; MS (ES mass): 425.1 (M+1); HPLC: 99.7%, Column: Symmetry C-18 75 * 4.6 mm,
3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 10/95, 10.5/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (80:20); UV 285.0 nm, retention time 5.7 min.

**Ethyl 2-(9-methoxy-3,6-dimethyl-6H-indolo[2,3-b]quinolin-11-yl)acetate (4u)**

![Structure of 4u](image)

Compound 4u was synthesized from 3u following a procedure similar to that of compound 4a
Yield: 84%; white solid; mp: 180-182 °C; Rᵣ = 0.2 (20% EtOAc/ n-hexane); ¹H NMR (400 MHz, CDCl₃) δ: 8.15 (d, J = 8.8 Hz, 1H), 7.91-7.89 (m, 2H), 7.33 (d, J = 8.4 Hz, 2H), 7.21 (dd, J = 8.8, 2.8 Hz, 1H), 4.64 (s, 2H), 4.16 (q, J = 7.2 Hz, 2H), 3.96 (s, 6H), 2.60 (s, 3H), 1.18 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): 169.8, 154.1, 152.6, 147.0, 139.0, 137.5, 133.8, 127.1, 125.2, 123.7, 121.4, 120.9, 116.5, 115.1, 108.8, 108.2, 61.4, 56.2, 35.1, 27.6, 21.7, 14.1; MS (ES mass): 363.2 (M+1); HPLC: 99.5%, Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN (T/%B): 0/20, 0.5/20, 2/95, 10/95, 10.5/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (80:20); UV 230.0 nm, retention time 3.6 min.

**Ethyl 2-(8-chloro-6-methyl-6H-indolo[2,3-b]quinolin-11-yl)acetate (4v)**

![Structure of 4v](image)

Compound 4v was synthesized from 3v following a procedure similar to that of compound 4a
Yield: 81%; off white solid; mp: 173-175 °C; Rᵣ = 0.2 (20% EtOAc/ n-hexane); ¹H NMR (400 MHz, CDCl₃) δ: 8.27 (d, J = 8.4 Hz, 1H), 8.22 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H),
7.76-7.72 (m, 1H), 7.54 (t, J = 7.2 Hz, 1H), 7.42 (s, 1H), 7.29 (dd, J = 8.4, 2.0 Hz, 1H), 4.64 (s, 2H), 4.15 (q, J = 7.2 Hz, 2H), 3.97 (s, 3H), 1.17 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl₃): 169.5, 152.2, 146.6, 143.5, 133.8, 133.7, 128.9, 128.1, 124.1, 123.9, 123.4, 120.2, 118.8, 116.4, 109.9, 108.8, 61.4, 35.0, 27.6, 14.1; MS (ES mass): 353.1 (M+1); HPLC: 98.6%,
Column: Symmetry C-18 75 * 4.6 mm, 3.5μm, mobile phase A: 0.1 % TFA in water, mobile phase B: CH₃CN  (T/%B): 0/20, 0.5/20, 2/95, 10/95, 10.5/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: WATER (80:20); UV 270.0 nm, retention time 3.9 min.

References:


**Sulphorhodamine B (SRB) Assay:**

**The principle:** The anti-proliferative activity and cancer cell selectivity of the synthesized compounds on cancer cells was evaluated using the SRB (Sulforhodamine B) cell proliferation assay. This assay was chosen because of its sensitivity, large dynamic range and the ability to measure cell proliferation over three days with normalization to initial cell number as well as to vehicle-treated cells. Further, this assay is the standardized assay of choice for screening of anticancer compounds at the National Cancer Institute (NIH). The SRB assay provides a colorimetric readout which can be spectrophotometrically measured and does not involve antibodies or toxic reagents. The assay is based on detection of total protein content of cells, which increases or decreases in proportion with cell number.
The methodology: Cancer cells (around 5000 in number) were seeded in 96-well plates and incubated overnight. The optimum cell number to be seeded was determined by a growth curve analysis for the cell line. Compounds (dissolved in 100% DMSO to a stock concentration of 200mM) were added to the adhered cells at a final concentration of 10µM. After 72h of treatment, the cells were washed with phosphate-buffered saline and ice-cold 10% trichloroacetic acid was added to the cells to precipitate the proteins. It was incubated for 1h at 4°C. The cells were then washed with water and air-dried. Cellular proteins were then stained using 0.4% SRB solution in 1% acetic acid for 30 min at room temperature. The unbound dye was washed away by destaining with 1% acetic acid and bound dye was solubilized with 10mM Tris solution (pH 10.5). Absorbance of solubilized dye was measured at a wavelength of 590 nm. Percentage growth was determined by the formula

$$\frac{[(At-A0/Ac-A0)\times100]}{\text{[(At-A0/Ac-A0) X 100]}$$

where At=absorbance after 72h of test compound treatment,
A0=Absorbance at time 0,
Ac=Absorbance after 72h without treatment.

The known cytotoxic agent, gemcitabine was used as a positive control in the assay.

Zebrafish embryo studies:

Materials and Methods:

Husbandry:
Zebrafish obtained from a local vendor were maintained in in-house built re-circulatory system under 14-10 h light dark cycle and 28 °C temperature as described earlier (Banote et al., 2013). Breeding was carried out using females and males in ratio of 2:3 and the embryos obtained were collected in petridishes and maintained at 28°C. (Westerfield et al., 2000, Nakhi et al.,2013).

Apoptosis Assay:
24hpf embryos were de-chorinated manually. 6 embryos were distributed as two sets in each well of 24 well plates with 250 µl of 0.1% DMSO. The working stock solutions were prepared by serial dilution as described earlier. Each well was added with 250µl of respective concentration to obtain final working concentration. Embryos were incubated at 28°C for 24 hrs and 48hrs. Check apoptotic effect at 24 h and 48 h by washing drug exposed embryos thrice with
E3 medium. Acridine orange (2µg/ml) solution of dye in E3 medium was added and incubated for 30 min. The embryos were rinsed thoroughly twice in fresh E3 medium to wash the acridine orange solution. Stained embryos were anesthetized with tricaine and photographed under UV illumination using Zeiss AxioCamMR camera attached to a Zeiss florescence microscope (GFP filter set: excitation 473, emission 520) under 5X magnification. The Images were taken and analyzed using Image J software.

Teratogenicity assay:
In this assay, 1dpf embryos at same developmental stage were sorted out and dechorionated using protease K. Test compounds stock solutions were prepared by dissolving in 100% DMSO. By serial dilution from stock solutions various concentrations were prepared and the final concentration of DMSO becomes 0.1%. The embryos were distributed in 24 well plate (3/well) and concentrations of test compounds starting from 1µM to 30µM compound was added to each well accordingly where n=6. The plate was incubated at 28°C until 5dpf. The embryos were washed with PBS and anesthetized using tricaine (0.008%). Morphological scoring was done based on the procedure previously described (Panzica-Kelly et al, 2010).

Results:
Apoptosis Assay:
The compound 4k showed significant increase in apoptotic activity from 1µM to 30µM, where as 4j showed significant apoptotic activity at 30µM. In case of 4a the increased apoptotic activity was seen upto 10µM & embryos were dead at 30µM. The Percentage induction of apoptosis (Graph S-1) and EC₅₀ of compounds was calculated (Graph S-2).
Graph S-1. The qualitative data of percentage induction of apoptosis of the compounds 4k, 4j and 4a at different concentrations and Methotrexate. All the statistical analysis was done using GraphPad Prism® software.

Graph S-2. EC₅₀ (apoptosis) of compounds 4k, 4j and 4a.

Teratogenicity assay:
Results of teratogenicity assay are presented in Graph S-3 and Fig S-1. The compound 4k showed toxicity at 30µM and found to be safe at 1, 3 and 10µM. The compound 4j was found to be safe at 1 & 3µM and toxic at 10 and 30 µM. In case of compound 4a toxicity was observed at 3 and 10 µM. Embryos were found to be dead at 30µM.
Graph S-3. Results of teratogenicity assay using compounds 4k, 4j and 4a. Statistical analysis for scoring was done using GraphPad Prism® software using two-way ANOVA.

Fig S-1. Representative images of teratogenicity assay

Table S-4. Results of zebrafish embryo toxicity study with toxicological indices and major organs/systems affected in positive control and test compounds at maximum test concentration (MTC).

(- no effect, x- slightly toxic, xx-moderately toxic, xxx-severely toxic).
Compound 4k was found to be safe at all concentrations. At higher concentrations compound 4j showed mild toxicity whereas compound 4a was found to be toxic.

**Table S-5. Summary of results in Zebrafish assay**

<table>
<thead>
<tr>
<th>Pharmacological Evaluations</th>
<th>Test Compounds Data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tests</strong></td>
<td><strong>Endpoint</strong></td>
</tr>
<tr>
<td>Apoptosis</td>
<td>Acridine Orange staining of apoptotic cells</td>
</tr>
<tr>
<td>Teratogenicity</td>
<td>Morphological assessment of Phenotypic changes</td>
</tr>
<tr>
<td>Overall Therapeutic</td>
<td>Ratio of NOAEL/EC50</td>
</tr>
<tr>
<td>Index</td>
<td>Overall NOAEL = lowest NOAEL</td>
</tr>
<tr>
<td>-------</td>
<td>-----------------------------</td>
</tr>
</tbody>
</table>

**References:**


Copies of $^1$H and $^{13}$C NMR spectra

Fig. 1: $^1$H NMR spectra of compound **S-2a** (CDCl$_3$, 400 MHz)
Fig. 2: $^{13}$C NMR spectra of compound S-2a (CDCl$_3$, 100 MHz)
Fig. 3: $^1$H NMR spectra of compound S-2b (CDCl$_3$, 400 MHz)
Fig. 4: $^{13}$C NMR spectra of compound S-2b (CDCl$_3$, 100 MHz)
Fig. 5: $^1$H NMR spectra of compound S-2c (CDCl$_3$, 400 MHz)
Fig. 6: $^{13}$C NMR spectra of compound S-2e (CDCl$_3$, 100 MHz)
Fig. 7: $^1$H NMR spectra of compound S-2d (CDCl$_3$, 400 MHz)
Fig. 8: $^{13}$C NMR spectra of compound S-2d (CDCl$_3$, 100 MHz)
Fig. 9: $^1$H NMR spectra of compound S-2e \((\text{CDCl}_3, 400 \text{ MHz})\)
Fig. 10: $^{13}$C NMR spectra of compound S-2e (CDCl$_3$, 100 MHz)
Fig. 11: $^1$H NMR spectra of compound $2a$ (CDCl$_3$, 400 MHz)
Fig. 12: $^{13}$C NMR spectra of compound 2a (CDCl$_3$, 100 MHz)
Fig. 13: $^1$H NMR spectra of compound 2b (CDCl$_3$, 400 MHz)
Fig. 14: $^{13}$C NMR spectra of compound 2b (CDCl$_3$, 100 MHz)
Fig. 15: $^1$H NMR spectra of compound 2c (CDCl$_3$, 400 MHz)
Fig. 16: $^{13}$C NMR spectra of compound 2c (CDCl$_3$, 100 MHz)
Fig. 17: $^1$H NMR spectra of compound 2d (CDCl$_3$, 400 MHz)
Fig. 18: $^{13}$C NMR spectra of compound 2d (CDCl$_3$, 100 MHz)
Fig. 19: $^1$H NMR spectra of compound 2e (CDCl$_3$, 400 MHz)
Fig. 20: $^{13}$C NMR spectra of compound 2e (CDCl$_3$, 100 MHz)
Fig. 21: $^1$H NMR spectra of compound 2f (CDCl$_3$, 400 MHz)
Fig. 22: $^{13}$C NMR spectra of compound 2f (CDCl$_3$, 100 MHz)
Fig. 23: $^1$H NMR spectra of compound 2g (CDCl$_3$, 400 MHz)
Fig. 24: $^{13}$C NMR spectra of compound 2g (CDCl$_3$, 100 MHz)
Fig. 25: $^1$H NMR spectra of compound 2h (CDCl$_3$, 400 MHz)
Fig. 26: $^{13}$C NMR spectra of compound 2h (CDCl$_3$, 100 MHz)
Fig. 27: $^1$H NMR spectra of compound 2i (CDCl$_3$, 400 MHz)
Fig. 28: $^{13}$C NMR spectra of compound 2i (CDCl$_3$, 100 MHz)
Fig. 29: $^1$H NMR spectra of compound 2j (CDCl$_3$, 400 MHz)
Fig. 30: $^{13}$C NMR spectra of compound 2j (CDCl$_3$, 100 MHz)
Fig. 31: $^1$H NMR spectra of compound 2k (CDCl$_3$, 400 MHz)
Fig. 32: $^{13}$C NMR spectra of compound 2k (CDCl$_3$, 100 MHz)
Fig. 33: $^1$H NMR spectra of compound 2l (CDCl$_3$, 400 MHz)
Fig. 34: $^{13}$C NMR spectra of compound 2l (CDCl$_3$, 100 MHz)
Fig. 35: $^1$H NMR spectra of compound 3a (CDCl$_3$, 400 MHz)
Fig. 36: $^{13}$C NMR spectra of compound 3a (CDCl$_3$, 100 MHz)
Fig. 37: $^1$H NMR spectra of compound 3b (CDCl$_3$, 400 MHz)
Fig. 38: $^{13}$C NMR spectra of compound 3b (CDCl$_3$, 100 MHz)
Fig. 39: $^1$H NMR spectra of compound 3c (CDCl$_3$, 400 MHz)
Fig. 40: $^{13}$C NMR spectra of compound 3c (CDCl$_3$, 100 MHz)
Fig. 41: $^1$H NMR spectra of compound 3d (CDCl$_3$, 400 MHz)
Fig. 42: $^{13}$C NMR spectra of compound 3d (CDCl$_3$, 100 MHz)
Fig. 43: $^1$H NMR spectra of compound 3e (CDCl$_3$, 400 MHz)
Fig. 44: $^{13}$C NMR spectra of compound 3e (CDCl$_3$, 100 MHz)
Fig. 45: $^1$H NMR spectra of compound 3f (CDCl$_3$, 400 MHz)
Fig. 46: $^{13}$C NMR spectra of compound 3f (CDCl$_3$, 100 MHz)
Fig. 47: $^1$H NMR spectra of compound 3g (CDCl$_3$, 400 MHz)
Fig. 48: $^{13}$C NMR spectra of compound 3g (CDCl$_3$, 100 MHz)
Fig. 49: $^1H$ NMR spectra of compound 3h (CDCl$_3$, 400 MHz)
Fig. 50: $^{13}$C NMR spectra of compound 3h (CDCl$_3$, 100 MHz)
Fig. 51: $^1$H NMR spectra of compound 3i (CDCl$_3$, 400 MHz)
Fig. 52: $^{13}$C NMR spectra of compound 3i (CDCl$_3$, 100 MHz)
Fig. 53: $^1$H NMR spectra of compound 3j (CDCl$_3$, 400 MHz)
Fig. 54: $^{13}$C NMR spectra of compound 3j (CDCl$_3$, 100 MHz)
Fig. 55: $^1$H NMR spectra of compound 3k (CDCl$_3$, 400 MHz)
Fig. 56: $^{13}$C NMR spectra of compound 3k (CDCl$_3$, 100 MHz)
Fig. 57: $^1$H NMR spectra of compound 3l (CDCl$_3$, 400 MHz)
Fig. 58: $^{13}$C NMR spectra of compound 31 (CDCl$_3$, 100 MHz)
Fig. 59: $^1$H NMR spectra of compound 3m (CDCl$_3$, 400 MHz)
Fig. 60: $^{13}$C NMR spectra of compound 3m (CDCl$_3$, 100 MHz)
Fig. 61: $^1$H NMR spectra of compound 3n (CDCl$_3$, 400 MHz)
Fig. 62: $^{13}$C NMR spectra of compound 3n (CDCl$_3$, 100 MHz)
Fig. 63: $^1$H NMR spectra of compound 3o (CDCl$_3$, 400 MHz)
Fig. 64: $^{13}$C NMR spectra of compound 3o (CDCl$_3$, 100 MHz)
Fig. 65: $^1$H NMR spectra of compound 3p (CDCl$_3$, 400 MHz)
Fig. 66: $^{13}$C NMR spectra of compound 3p (CDCl$_3$, 100 MHz)
Fig. 67: $^1$H NMR spectra of compound 3q (CDCl$_3$, 400 MHz)
Fig. 68: $^{13}$C NMR spectra of compound 3q (CDCl$_3$, 100 MHz)
Fig. 69: $^1$H NMR spectra of compound 3r (CDCl$_3$, 400 MHz)
Fig. 70: $^{13}$C NMR spectra of compound 3r (CDCl$_3$, 100 MHz)
Fig. 71: $^1$H NMR spectra of compound 3s (CDCl$_3$, 400 MHz)
Fig. 72: $^{13}$C NMR spectra of compound 3s (CDCl$_3$, 100 MHz)
Fig. 73: $^1$H NMR spectra of compound 3t (CDCl$_3$, 400 MHz)
Fig. 74: $^{13}$C NMR spectra of compound 3t (CDCl$_3$, 100 MHz)
Fig. 75: $^1$H NMR spectra of compound 3u (CDCl$_3$, 400 MHz)
Fig. 76: $^{13}$C NMR spectra of compound 3u (CDCl$_3$, 100 MHz)
Fig. 77: $^1$H NMR spectra of compound 3v (CDCl$_3$, 400 MHz)
Fig. 78: $^{13}$C NMR spectra of compound 3v (CDCl$_3$, 100 MHz)
Fig. 79: $^1$H NMR spectra of compound 4a (CDCl$_3$, 400 MHz)
Fig. 80: $^{13}$C NMR spectra of compound 4a (CDCl$_3$, 100 MHz)
Fig. 81: $^1$H NMR spectra of compound 4b (CDCl$_3$, 400 MHz)
Fig. 82: $^{13}$C NMR spectra of compound 4b (CDCl$_3$, 100 MHz)
Fig. 83: $^1$H-$^1$H COSY spectra of compound 4b
Fig. 84: 2D NOESY spectra of compound 4b
Fig. 85: 1D-NOE spectra of compound 4b
Fig. 86: DEPT spectra of compound 4b
Fig. 87: $^1$H NMR spectra of compound 4c (CDCl$_3$, 400 MHz)
Fig. 88: $^{13}$C NMR spectra of compound 4c (CDCl$_3$, 100 MHz)
Fig. 89: $^1$H NMR spectra of compound 4d (CDCl$_3$, 400 MHz)
Fig. 90: $^{13}$C NMR spectra of compound 4d (CDCl$_3$, 100 MHz)
Fig. 91: $^1$H NMR spectra of compound 4e (CDCl$_3$, 400 MHz)
Fig. 92: $^{13}$C NMR spectra of compound 4e (CDCl$_3$, 100 MHz)
Fig. 93: $^1$H NMR spectra of compound 4f (CDCl$_3$, 400 MHz)
Fig. 94: $^{13}$C NMR spectra of compound 4f (CDCl$_3$, 100 MHz)
Fig. 95: $^1$H NMR spectra of compound 4g (CDCl$_3$, 400 MHz)
Fig. 96: $^{13}$C NMR spectra of compound 4g (CDCl$_3$, 100 MHz)
Fig. 97: $^1$H NMR spectra of compound 4h (CDCl$_3$, 400 MHz)
Fig. 98: $^{13}$C NMR spectra of compound 4h (CDCl$_3$, 100 MHz)
Fig. 99: $^1$H NMR spectra of compound 4i (CDCl$_3$, 400 MHz)
Fig. 100: $^{13}$C NMR spectra of compound 4i (CDCl$_3$, 100 MHz)
Fig. 101: $^1$H NMR spectra of compound 4j (CDCl$_3$, 400 MHz)
Fig. 102: $^{13}$C NMR spectra of compound 4j (CDCl$_3$, 100 MHz)
Fig. 103: $^1$H NMR spectra of compound 4k (CDCl$_3$, 400 MHz)
Fig. 104: $^{13}$C NMR spectra of compound 4k (CDCl$_3$, 100 MHz)
Fig. 105: $^1$H NMR spectra of compound 4l (CDCl$_3$, 400 MHz)
Fig. 106: $^{13}$C NMR spectra of compound 41 (CDCl$_3$, 100 MHz)
Fig. 107: $^1$H NMR spectra of compound 4m (CDCl$_3$, 400 MHz)
Fig. 108: $^{13}$C NMR spectra of compound 4m (CDCl$_3$, 100 MHz)
Fig. 109: $^1$H NMR spectra of compound 4n (CDCl$_3$, 400 MHz)
Fig. 110: $^{13}$C NMR spectra of compound 4n (CDCl$_3$, 100 MHz)
Fig. 111: $^1$H NMR spectra of compound 40 (CDCl$_3$, 400 MHz)
Fig. 112: $^{13}$C NMR spectra of compound 40 (CDCl$_3$, 100 MHz)
Fig. 113: $^1$H NMR spectra of compound 4p (CDCl$_3$, 400 MHz)
Fig. 114: $^{13}$C NMR spectra of compound 4p (CDCl$_3$, 100 MHz)
Fig. 115: $^1$H NMR spectra of compound 4q (CDCl$_3$, 400 MHz)
Fig. 116: $^{13}$C NMR spectra of compound 4q (CDCl$_3$, 100 MHz)
Fig. 117: $^1$H NMR spectra of compound 4r (CDCl$_3$, 400 MHz)
Fig. 118: $^{13}$C NMR spectra of compound 4r (CDCl$_3$, 100 MHz)
Fig. 119: $^1$H NMR spectra of compound 4s (CDCl$_3$, 400 MHz)
Fig. 120: $^{13}$C NMR spectra of compound 4s (CDCl$_3$, 100 MHz)
Fig. 121: $^1$H NMR spectra of compound 4t (CDCl$_3$, 400 MHz)
Fig. 122: $^{13}$C NMR spectra of compound 4t (CDCl$_3$, 100 MHz)
Fig. 123: $^1$H NMR spectra of compound 4u (CDCl$_3$, 400 MHz)
Fig. 124: $^{13}$C NMR spectra of compound 4u (CDCl$_3$, 100 MHz)
Fig. 125: $^1$H NMR spectra of compound 4v (CDCl$_3$, 400 MHz)
Fig. 126: $^{13}$C NMR spectra of compound 4v (CDCl$_3$, 100 MHz)