Supporting Information for
Phosphine catalysed (5 + 1) cycloaddition of ynone/cinnamates with primary amines.

Jhi Ametovski,a Uttam Dutta,a,b Laura Burchill,a Debabrata Maiti,b David W. Lupton*a and Joel Hooper*a

a School of Chemistry, Monash University, Clayton 3800, Victoria, Australia
b Department of Chemistry, Indian Institute of Technology Bombay Powai, Mumbai-400 076, India.

Index

I General experimental SI-1
II Synthesis of ynone cinnamates SI-2
III Phosphine catalysed (5 + 1) annulations SI-6
IV Derivatisation studies SI-13
V NMR spectra and HPLC traces SI-15
VI References SI-48

I. General experimental

Proton (1H) and carbon (13C) NMR spectra were recorded on a Bruker DRX600 spectrometer operating at 150 MHz for carbon nuclei, a Bruker DRX400 spectrometer operating at 400 MHz for proton and 100 MHz for carbon nuclei, and a Bruker DRX300 spectrometer operating at 300 MHz for proton nuclei. 2D correlation spectra were recorded on a Bruker DRX400 spectrometer. Infrared spectra (νmax) were recorded on an Agilent Cary 630 FTIR Spectrometer. High resolution mass spectra (HRMS) (ESI) were recorded on a Bruker BioApex 47e FTMS fitted with an Analytical electrospray source using NaI for accurate mass calibration.

Analytical chiral HPLC was performed with a Perkin Elmer Series 200 HPLC using a RegisCell™ 5μm (4.6 mm x 25 cm) obtained from Regis Technologies, Inc. with visualisation at 238 or 230 nm. Flash column chromatography was performed on silica gel (Davisil LC60A, 40-63 μm silica media) using compressed air. Thin layer chromatography (TLC) was performed using aluminum-backed plates coated with 0.2 mm silica (Merck, DC-Platten, Kieselgel; 60 F254 plates). Eluted plates were visualised using a 254 nm UV lamp and/or by treatment with potassium permanganate stain or vanillin stain followed by heating. Starting materials and reagents were purchased from Sigma-Aldrich or Oakwood and were used as supplied. Tetrahydrofuran (THF) and dichloromethane (CH2Cl2) were dried by passing over activated alumina. DMF was dried by stirring with calcium hydride overnight then was filtered and distilled under reduced pressure, and stored over 3 Å molecular sieves. Unless otherwise stated, all reactions were conducted in flame-dried glassware under an atmosphere of nitrogen. Ethyl (E)-3-(2-formylphenyl)acrylate was synthesised according to the literature procedure.1
II. Synthesis of ynone cinnamates

To a solution of aryl substituted acetylene (10 mmol) in THF (20 mL) at –78 °C was added n-butyllithium solution (1.6M in hexane, 10.5 mmol) dropwise. After stirring for a further 1 h at -78 °C, ethyl (E)-3-(2-formylphenyl)acrylate (10 mmol) in THF (10 mL) was added dropwise. Stirring of the reaction at –78 °C was continued until TLC analysis of the reaction mixture indicated complete consumption of the starting material. The reaction was then quenched via slow addition of saturated NH₄Cl solution (10 mL) and then allowed to warm to room temperature. The organic phase was separated and the aqueous phase was extracted with EtOAc (3 × 10 mL), the combined organics were washed with brine, dried with Na₂SO₄, filtered and the concentrated under reduced pressure to afford the corresponding alkynol as a crude oil which was used in the next step without further purification.

2-Iodoxybenzoic acid (15 mmol) was added to a solution of the crude alkynol in EtOAc (30 mL) and the resulting suspension was heated at reflux until TLC analysis of the reaction mixture indicated complete consumption of the starting material. The reaction mixture was filtered and concentrated to afford the ynone cinnamate as a crude oil which was purified via column chromatography on silica gel (EtOAc/Hexanes).

Ethyl (E)-3-(2-(3-phenylpropioloyl)phenyl)acrylate (1a)

Following the general procedure the title compound was prepared in 58% yield as a yellow oil which solidified upon standing. Rf 0.29 (4:1, v/v hexanes : EtOAc); mp 52 – 55 °C; IR νmax 2197, 1707, 1629, 1561, 1445, 1305, 1262, 1187, 974, 758, 678 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.45 (d, J = 16.0 Hz, 1H), 8.28 (J = 8 Hz, 1H), 7.65 – 6.30 (m, 8H), 6.32 (d, J = 16.0 Hz, 1H), 4.24 (q, 2H), 1.31 (t, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 178.8, 166.4, 136.3, 136.2, 133.3, 133.1, 132.5, 130.9, 129.4, 128.7, 128.4, 121.7, 120.0, 93.5, 88.2, 60.6, 14.3 ppm; HRMS (ESI) m/z Found: (M+H)+, C₂₀H₁₇O₃, 305.1169, requires 305.1172.

Ethyl (E)-3-(2-(3-(2-methoxyphenyl)propioloyl)phenyl)acrylate (1f)

Following the general procedure the title compound was prepared in 60% yield as a yellow solid. Rf 0.07 (4:1, v/v hexanes : EtOAc); mp 78 – 82 °C; IR νmax 2185, 1709, 1628, 1594, 1562, 1492, 1460, 1435, 1248, 1164, 1002,
969, 752, 672 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 8.51-8.44 (m, 2H), 7.59-7.42 (m, 5H), 7.00-6.92 (m, 2H), 6.30 (d, J = 15.9 Hz, 1H), 4.25 (q, J = 7.2 Hz, 2H), 3.94 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 178.7, 166.3, 161.8, 143.8, 136.1, 136.0, 134.8, 133.1, 133.1, 132.8, 129.4, 128.2, 121.2, 120.6, 110.8, 109.0, 92.3, 90.7, 60.4, 55.8, 14.2 ppm; HRMS (ESI) m/z Found: (M+H)+, C₂₁H₁₈O₄, 335.1275, requires 335.1278.

Ethyl (E)-3-(2-(3-(3-methoxyphenyl)propioloyl)phenyl)acrylate (1g)

Following the general procedure the title compound was prepared in 71% yield as a viscous yellow oil. Rₜ 0.21 (4:1, v/v hexanes : EtOAc); IR νₘₐₓ 2189, 1709, 1631, 1593, 1478, 1422, 1366, 1306, 1274, 1229, 1160, 1036, 1013, 973, 897, 784, 754, 682 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.46 (d, J = 15.9 Hz, 1H), 8.29 – 8.22 (m, 1H), 7.62 – 7.48 (m, 3H), 7.30 (t, J = 7.9 Hz, 1H), 7.23 (dt, J = 7.6, 1.3 Hz, 1H), 7.15 (m, 1H), 7.02 (ddd, J = 8.2, 2.7, 1.1 Hz, 1H), 6.32 (d, J = 15.9 Hz, 1H), 4.24 (q, J = 7.1 Hz, 2H), 3.82 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 178.9, 166.6, 159.6, 143.7, 136.4, 136.3, 133.4, 132.6, 129.9, 129.6, 128.6, 125.7, 121.8, 121.0, 117.9, 117.7, 93.6, 88.0, 60.7, 55.6, 14.4 ppm; HRMS (ESI) m/z Found: (M+H)+, C₂₁H₁₈O₄, 335.1273, requires 335.1278.

Ethyl (E)-3-(2-(3-(4-methoxyphenyl)propioloyl)phenyl)acrylate (1h)

Following the general procedure the title compound was prepared in 77% yield as a yellow solid. Rₜ 0.23 (4:1, v/v hexanes : EtOAc); mp 86 – 89 °C; IR νₘₐₓ 2189, 1715, 1632, 1599, 1563, 1509, 1477, 1440, 1309, 1274, 1252, 1211, 1165, 1109, 1020, 1004, 827, 747, 680 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.37 (d, J = 15.9 Hz, 1H), 8.15 (dd, J = 7.2, 1.3 Hz, 1H), 7.54 – 7.37 (m, 5H), 6.80 (d, J = 8.9 Hz, 2H), 6.22 (d, J = 15.9 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 3.73 (s, 3H), 1.21 (t, J = 7.1 Hz, 3H); ppm ¹³C NMR (100 MHz, CDCl₃) δ 178.9, 166.5, 162.0, 143.7, 136.5, 136.1, 135.2, 133.1, 132.4, 129.5, 128.4, 121.5, 114.5, 111.7, 95.0, 88.4, 60.6, 55.6, 14.4 ppm; HRMS (ESI) m/z Found: (M+H)+, C₂₁H₁₈O₄, 335.1278, requires 335.1272.

Ethyl (E)-3-(2-(3-(4-chlorophenyl)propioloyl)phenyl)acrylate (1i)

Following the general procedure the title compound was prepared in 61% yield as a yellow solid. Rₜ 0.36 (4:1, v/v hexanes : EtOAc); mp 73 – 76 °C; IR νₘₐₓ 2195, 1710, 1632, 1589, 1561, 1475, 1305, 1267, 1161, 1088, 1004, 971, 829, 761, 713, 678 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.39 (d, J = 15.8 Hz, 1H), 8.28 (d, J = 8 Hz, 1H), 7.59 – 7.51 (m, 5H), 7.38 – 7.35 (m, 2H), 6.30 (d, J = 15.8
Hz, 1H), 4.23 (q, \( J = 7.1 \) Hz, 2H), 1.30 (t, \( J = 7.1 \) Hz, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 178.5, 166.4, 143.4, 137.3, 136.3, 135.9, 134.2, 133.4, 129.4, 129.1, 128.4, 121.7, 118.4, 92.0, 88.9, 60.6, 14.3 ppm; HRMS (ESI) \( m/z \) Found: (M+H)\(^+\), C\(_{20}\)H\(_{15}\)O\(_3\)Cl, 339.0773, requires 339.0782.

**Ethyl (E)-3-(2-(3-(4-bromophenyl)propioloyl)phenyl)acrylate (1j)**

Following the general procedure the title compound was prepared in 43% yield as a colourless solid. \( R_f \) 0.32 (4:1, v/v hexanes : EtOAc); mp 71 – 72 °C; IR \( \nu_{\text{max}} \) 2199, 1711, 1634, 1560, 1476, 1391, 1366, 1306, 1264, 1190, 1162, 1002, 966, 821 cm\(^{-1}\); \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.45 (d, \( J = 15.9 \) Hz, 1H), 8.25 (dd, \( J = 7.8, 1.0 \) Hz, 1H), 7.62 – 7.60 (m, 2H), 7.56 (d, \( J = 8.3 \) Hz, 2H), 7.51 (d, \( J = 8.4 \) Hz, 2H), 6.33 (dd, \( J = 15.8, 0.7 \) Hz, 1H), 4.26 (q, \( J = 7.2 \) Hz, 2H), 1.32 (t, \( J = 7.2 \) Hz, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 178.5, 166.4, 143.5, 136.4, 136.0, 134.3, 133.4, 132.4, 132.1, 129.4, 128.5, 125.8, 121.8, 118.9, 92.1, 88.9, 60.7, 14.3 ppm; HRMS (ESI) \( m/z \) Found: (M+H)\(^+\), C\(_{20}\)H\(_{15}\)O\(_3\)Br, 382.0274, requires 383.0277.

**Ethyl (E)-3-(2-(3-(4-cyanophenyl)propioloyl)phenyl)acrylate (1k)**

Following the general procedure the title compound was prepared in 62% yield as a viscous yellow oil. \( R_f \) 0.11 (4:1, v/v hexanes : EtOAc); IR \( \nu_{\text{max}} \) 2227, 2202, 1695, 1637, 1562, 1474, 1368, 1274, 1248, 1198, 1095, 1040, 999, 980, 940, 838, 763, 711, 674, 655 cm\(^{-1}\); \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.43 (d, \( J = 15.6 \) Hz, 1H), 8.23 (m, 1H), 7.75 – 7.69 (m, 4H), 7.63 – 7.60 (m, 2H), 7.57 – 7.53 (m, 1H), 6.32 (d, \( J = 15.6 \) Hz, 1H), 4.25 (q, \( J = 7.2 \) Hz, 2H), 1.32 (t, \( J = 7.2 \) Hz, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 178.3, 166.5, 143.4, 135.7, 135.4, 133.9, 133.5, 132.7, 132.5, 129.7, 128.8, 125.0, 122.2, 118.0, 114.3, 90.7, 90.2, 60.9, 14.5 ppm; HRMS (ESI) \( m/z \) Found: (M+H)\(^+\), C\(_{21}\)H\(_{15}\)NO\(_3\), 330.1112, requires 330.1125.

**Ethyl (E)-3-(2-(3-(6-methoxynaphthalen-2-yl)propioloyl)phenyl)acrylate (1l)**

Following the general procedure the title compound was prepared in 39% yield as an orange solid. \( R_f \) 0.21 (4:1, v/v hexanes : EtOAc); mp 100 – 101 °C; IR \( \nu_{\text{max}} \) 2182, 2171, 1619, 1480, 1390, 1255, 1175, 1123, 1009, 852 cm\(^{-1}\); \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.42 (d, \( J = 15.9 \) Hz, 1H), 8.28 – 8.22 (m, 1H), 8.07 (s, 1H), 7.75 – 7.62 (m, 3H), 7.57 – 7.46 (m, 6H), 7.36 – 7.22 (m, 2H), 7.13 (dd, \( J = 9.0, 2.5 \) Hz, 2H), 7.06 (d, \( J = 2.5 \) Hz, 2H), 6.27 (d, \( J = 15.9 \) Hz, 1H), 4.23 – 4.13 (q, \( J = 7.1 \) Hz 2H), 3.87 (s, 3H), 1.23 (t, \( J = 7.1 \) Hz, 4H) ppm; \(^{13}\)C NMR (100 MHz,
**Ethyl (E)-4,4-dimethyl-5-oxo-7-phenylhept-2-en-6-ynoate (1m)**

Following the procedure above the title compound was prepared in 53\% yield as a clear oil. R\_f 0.35 (1:4, v/v hexanes : EtOAc); IR \( \nu_{\text{max}} \) 2196, 1716, 1664, 1648, 1489, 1444, 1366, 1271, 1180, 1058, 1033, 757 cm\(^{-1}\); \(^1\)H NMR (600 MHz, CDCl\(_3\)) \( \delta \) 7.58 (dd, \( J = 8.3, 1.2 \text{ Hz}, 2\)H), 7.48 – 7.45 (m, 1H), 7.39 (t, \( J = 7.9 \text{ Hz}, 2\)H), 7.20 (dd, \( J = 16.0, 0.6 \text{ Hz}, 1\)H), 5.99 – 5.91 (m, 1H), 4.25 – 4.18 (q, \( J = 7.1 \text{ Hz}, 2\)H), 1.44 (s, 3H), 1.30 (t, \( J = 7.1 \text{ Hz}, 3\)H) ppm; \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \( \delta \) 116.5, 113.1, 93.1, 81.7, 60.4, 14.3 ppm. HRMS (ESI) \( m/z \) Found: (M+H\(^+\)), 271.1327, requires 271.1329.

**Ethyl (E)-3-(1-(3-phenylpropioloyl)-1H-pyrrol-2-yl)acrylate (1n)**

Following the procedure above the title compound was prepared in 28\% yield as a yellow oil. R\_f 0.28 (1:4, v/v hexanes : EtOAc); IR \( \nu_{\text{max}} \) 2206, 1703, 1686, 1622, 1405, 1339, 1268, 1175, 1108, 1034, 986, 759 cm\(^{-1}\); \(^1\)H NMR (600 MHz, CDCl\(_3\)) \( \delta \) 8.42 (d, \( J = 15.9 \text{ Hz}, 1\)H), 7.71 – 7.62 (m, 3H), 7.54 – 7.48 (m, 1H), 7.48 – 7.39 (m, 2H), 6.79 (ddd, \( J = 3.5, 1.6, 0.8 \text{ Hz}, 1\)H), 6.34 (td, \( J = 3.4, 0.6 \text{ Hz}, 1\)H), 6.27 (d, \( J = 15.9 \text{ Hz}, 1\)H), 4.24 (q, \( J = 7.1 \text{ Hz}, 2\)H), 1.31 (t, \( J = 7.1 \text{ Hz}, 3\)H) ppm; \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \( \delta \) 116.8, 151.2, 134.2, 133.1, 131.9, 131.4, 128.8, 125.5, 119.0, 118.0, 116.6, 113.1, 93.1, 81.7, 60.4, 14.3 ppm; HRMS (ESI) \( m/z \) Found: (M+H\(^+\)), 294.1125, requires 294.1125.

**tert-Butyl (E)-3-(2-(3-phenylpropioloyl)phenyl)acrylonitrile (1o)**

Following the general procedure the title compound was prepared in 55\% yield as a pale yellow solid. R\_f 0.43 (4:1, v/v hexanes : EtOAc); mp 124 – 126 \°C; IR \( \nu_{\text{max}} \) 2195, 1691, 1626, 1592, 1369, 1286, 1252, 1209, 1154, 1027, 1011, 966, 841, 757, 690 cm\(^{-1}\); \(^1\)H NMR (600 MHz, CDCl\(_3\)) \( \delta \) 8.38 (d, \( J = 15.8 \text{ Hz}, 1\)H), 8.25 (d, \( J = 7.7 \text{ Hz}, 1\)H), 7.69 – 7.64 (m, 2H), 7.62 – 7.56 (m, 2H), 7.52 (td, \( J = 7.4 \text{ Hz}, 1.7 \text{ Hz}, 1\)H), 7.49 – 7.47 (m, 1H), 7.42 – 7.39 (m, 1H), 6.26 (d, \( J = 15.8 \text{ Hz}, 1\)H), 1.51 (s, 9H) ppm; \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \( \delta \) 179.0, 165.9, 142.5, 136.6, 136.3, 133.3, 133.2, 132.5, 131.0, 129.4, 128.8, 128.5, 123.7, 120.2, 93.7, 88.5, 80.8, 28.3 ppm; HRMS (ESI) \( m/z \) Found: (M-O\(^\text{Bu}+\text{H}_2\text{O})^+, C\text{\textsubscript{18}}\text{H}_{13}\text{O}_3, 277.0858, requires 277.0859.

(E)-3-(2-(3-phenylpropioloyl)phenyl)acrylonitrile (1p)
Following the procedure above the title compound was prepared in 53% yield as a white solid. Rf 0.29 (4:1, v/v hexanes : EtOAc); mp 192 °C (decomp.); IR νmax 2193, 1737, 1624, 1565, 1490, 1444, 1308, 1207, 1113, 1010, 995, 955 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.40 – 8.34 (m, 1H), 8.29 (d, J = 16.5 Hz, 1H), 7.68 (dd, J = 8.3, 1.4 Hz, 2H), 7.66 – 7.60 (m, 2H), 7.55 – 7.49 (m, 2H), 7.46 – 7.41 (m, 2H), 5.79 (d, J = 16.5 Hz, 1H) ppm; ¹³C NMR (150 MHz, CDCl₃) δ 178.5, 150.2, 135.3, 135.2, 133.6, 133.2, 133.1, 131.1, 130.4, 128.8, 127.9, 119.7, 117.8, 99.5, 93.9, 87.7 ppm; HRMS (ESI) m/z Found: (M+H)⁺, C₁₈H₁₁NO₂, 258.0913, requires 258.0913.

III. Phosphine catalysed (5 + 1) annulations

![Diagram](https://via.placeholder.com/150)

To a solution of ynone (0.13 mmol) and sulfonamide (0.13 mmol) in dry toluene (2.6 mL) under N₂ was added methyldiphenylphosphine (0.1M solution in toluene, 260μL, 0.026 mmol). The reaction was stirred at room temperature for 8 to 16 hours, until TLC analysis indicated complete consumption of the starting material. The reaction mixture was then concentrated under vacuum and the product purified via column chromatography on silica gel (hexanes/EtOAc or toluene/EtOAc) to afford the isoquinoline product.

**Ethyl (Z)-2-(3-benzylidene-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2a)**

Following the general procedure the title compound was prepared in 84% yield. Rf 0.29 (1:19, v/v toluene : EtOAc); mp 118 – 120 °C; IR νmax 1735, 1675, 1598, 1493, 1359, 1292, 1166, 1089, 972 cm⁻¹; ¹H NMR (300 MHz, C₆D₆) δ 8.25 (s, 1H), 8.15 – 8.04 (m, 2H), 7.64 (dd, J = 7.8, 1.3 Hz, 1H), 7.35 (d, J = 8.2 Hz, 2H), 7.15 – 7.00 (m, 3H), 6.86 (td, J = 7.4, 1.4 Hz, 1H), 6.77 (dd, J = 7.8, 1.2 Hz, 1H), 6.68 (td, J = 7.6, 1.3 Hz, 1H), 6.33 (d, J = 8.0 Hz, 2H), 6.08 (dd, J = 8.5, 5.9 Hz, 1H), 4.06 – 3.79 (m, 3H), 2.81 (dd, J = 16.1, 8.5 Hz, 1H), 2.40 (dd, J = 16.1, 5.9 Hz, 1H), 1.68 (s, 3H), 0.84 (t, J = 7.1 Hz, 3H) ppm; ¹³C-NMR (100 MHz, C₆D₆) δ 182.1, 169.3, 143.4, 141.2, 140.3, 133.3, 133.2, 131.2, 130.4, 130.1, 129.3, 128.6, 128.2, 127.7, 127.6, 126.6, 61.0, 56.6, 42.3, 21.0, 14.0 ppm; HRMS (ESI) m/z Found: (M+H)⁺, C₂₇H₂₅NO₅S, 476.1528, requires 476.1526.

In addition following the general procedure, however performed at 0 °C, and using (R)-SITCP catalyst (C), the title compound 2a was prepared in 85% isolated yield. HPLC RegisCell™,
hexane:iPrOH 85:15, 1 ml/min, l = 238 nm, fraction tr = 9.64 (major enantiomer) and 12.38 (minor enantiomer); ee = 15%

Ethyl (Z)-2-(3-benzylidene-2-((4-methoxyphenyl)sulfonyl)-4-oxo-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2b)

Following the general procedure the title compound was prepared in 67% yield. Rf 0.09 (4:1, v/v hexanes : EtOAc); IR νmax 1735, 1674, 1594, 1496, 1358, 1293, 1261, 1159, 1089, 1023, 835, 760, 676, 590 cm⁻¹; ¹H-NMR (400 MHz, C6D6) δ 8.29 (s, 1H), 8.17–8.06 (m, 2H), 7.73 (dd, J = 7.7, 1.4 Hz, 1H), 7.41–7.36 (m, 2H), 7.13–7.01 (m, 3H), 6.81 (td, J = 7.5, 1.4 Hz, 1H), 6.77–6.71 (m, 1H), 6.67 (td, J = 7.5, 1.4 Hz, 1H), 6.12–6.03 (m, 3H), 3.90 (ddq, J = 39.0, 10.8, 7.1 Hz, 2H), 2.93 (s, 3H), 2.82 (dd, J = 16.1, 8.3 Hz, 1H), 2.38 (dd, J = 16.1, 6.1 Hz, 1H), 0.83 (t, J = 7.1 Hz, 3H) ppm; ¹³C-NMR (100 MHz, C6D6) δ 181.9, 169.0, 162.7, 140.9, 140.0, 133.3, 132.9, 130.9, 130.2, 130.0, 129.9, 128.3, 127.3, 126.2, 113.6, 60.6, 56.3, 54.5, 42.0, 13.6 ppm; HRMS (ESI) m/z Found: (M+H)+, C27H25NO5S, 492.1471, requires 492.1475.

Ethyl (Z)-2-(3-benzylidene-4-oxo-2-(phenylsulfonyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2c)

Following the general procedure the title compound was prepared in 63% yield. Rf 0.15 (4:1, v/v hexanes : EtOAc); IR νmax 1733, 1674, 1596, 1447, 1359, 1292, 1272, 1206, 1167, 1088, 1049, 1023, 956, 840 cm⁻¹; ¹H-NMR (400 MHz, C6D6) δ 8.26 (s, 1H), 8.14–8.02 (m, 2H), 7.66 (dd, J = 7.7, 1.5 Hz, 1H), 7.45–7.35 (m, 2H), 7.13–6.97 (m, 3H), 6.78 (dd, J = 7.4, 1.3 Hz, 1H), 6.74–6.53 (m, 3H), 6.47 (t, J = 7.8 Hz, 2H), 6.07 (dd, J = 8.3, 6.1 Hz, 1H), 3.99–3.77 (m, 2H), 2.80 (dd, J = 16.2, 8.3 Hz, 1H), 2.36 (dd, J = 16.2, 6.1 Hz, 1H), 0.83 (t, J = 7.1 Hz, 3H) ppm; ¹³C-NMR (100 MHz, C6D6) δ 181.5, 168.9, 140.9, 139.7, 138.0, 133.2, 132.8, 132.8, 132.1, 130.9, 130.0, 129.5, 128.3, 128.2, 126.1, 60.6, 56.3, 41.9, 13.6 ppm; HRMS (ESI) m/z Found: (M+H)+, C26H23NO5S, 462.1367, requires 462.1370.
Ethyl (Z)-2-(3-benzylidene-2-((4-chlorophenyl)sulfonyl)-4-oxo-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2d)

Following the general procedure the title compound was prepared in 65% yield. 

Rf 0.13 (4:1, v/v hexanes : EtOAc); mp 158 – 161 ºC; IR ν max 1733, 1670, 1593, 1474, 1425, 1362, 1292, 1206, 1168, 1086, 1050, 947 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 8.23 (s, 1H), 8.06 – 8.01 (m, 2H), 7.65 (dd, J = 7.8, 1.4 Hz, 1H), 7.14 – 6.99 (m, 4H), 6.75 (td, J = 7.5, 1.4 Hz, 1H), 6.67 (td, J = 7.6, 1.2 Hz, 1H), 6.62 (dd, J = 7.7, 1.1 Hz, 1H), 6.44 – 6.39 (m, 2H), 5.96 (dd, J = 8.4, 6.0 Hz, 1H), 3.88 (ddq, J = 16.5, 8.4 Hz, 1H), 0.81 (t, J = 7.2 Hz, 3H) ppm; ¹³C-NMR (100 MHz, CDCl₃) δ 181.4, 168.8, 141.1, 139.6, 138.8, 136.2, 133.0, 130.9, 130.8, 131.0, 129.2, 129.2, 128.4, 128.3, 128.0, 126.1, 60.6, 56.3, 41.7, 13.6 ppm; HRMS (ESI) m/z Found: (M+K)⁺, C₂₇H₂₂ClNO₃S, 534.0539, requires 534.0539.

Ethyl (Z)-2-(3-benzylidene-2-((4-cyanophenyl)sulfonyl)-4-oxo-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2e)

Following the general procedure the title compound was prepared in 60% yield and purified via trituration from THF/hexanes. Rf 0.14 (4:1, v/v hexanes : EtOAc); mp 237 – 238 ºC; IR ν max 2233, 1740, 1671, 1446, 1361, 1295, 1272, 1162, 1082, 1052, 970, 838 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 8.08 – 8.05 (m, 2H), 8.05 (s, 1H), 7.56 (dd, J = 7.9, 1.4 Hz, 1H), 7.54 (d, J = 8.7 Hz, 1H), 7.49 – 7.42 (m, 4H), 7.36 – 7.33 (m, 2H), 7.24 (dd, J = 7.6, 1.2 Hz, 1H), 7.22 – 7.20 (m, 1H), 5.90 (dd, J = 8.4, 6.0 Hz, 1H), 4.11 (ddq, J = 57.7, 10.8, 7.2 Hz, 2H), 2.99 (dd, J = 16.5, 8.5 Hz, 1H), 2.68 (dd, J = 16.5, 6.1 Hz, 1H), 1.13 (t, J = 7.2 Hz, 3H) ppm; ¹³C-NMR (150 MHz, CDCl₃) δ 181.8, 169.3, 142.2, 141.5, 139.3, 134.1, 132.9, 132.5, 132.4, 132.0, 129.7, 128.8, 128.8, 128.4, 128.2, 128.0, 126.4, 117.1, 116.5, 61.5, 56.5, 41.88, 14.1 ppm; HRMS (ESI) m/z Found: (M+H)⁺, C₂₇H₂₂N₂O₃S, 487.1323, requires 487.1322.

Ethyl (Z)-2-(3-(2-methoxybenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2f)

Following the general procedure the title compound was prepared in 68% yield as a bright yellow crystalline solid. Rf 0.21 (4:1, v/v hexanes : EtOAc); mp 109 – 114 ºC; IR ν max 1710, 1672, 1594, 1488, 1462, 1359, 1291, 1241, 1145, 1085, 1022, 974 cm⁻¹; ¹H-NMR (300 MHz, CDCl₃) δ 9.26 (s, 1H), 9.12 (dd, J = 8.0, 1.7 Hz, 1H), 7.67 (dd, J = 7.8, 1.4 Hz, 1H), 7.38 (d, J = 8.3 Hz, 2H), 7.09 (ddd, J = 8.3, 7.3, 1.7 Hz, 1H), 6.97 – 6.91 (m, 1H), 6.83 (td, J = 7.4, 1.4 Hz, 1H), 6.76 (dd, J = 7.7, 1.3 Hz, 1H), 6.67 (td, J = 7.5, 1.4 Hz, 1H), 6.44 (dd, J = 8.3, 1.1 Hz, 1H), 6.34 – 6.29 (m, 2H), 6.14 (dd, J = 8.3,
6.0 Hz, 1H), 4.09 – 3.86 (m, 2H), 3.22 (s, 3H), 2.90 (dd, J = 16.1, 8.3 Hz, 1H), 2.42 (dd, J = 16.1, 6.1 Hz, 1H), 1.68 (s, 3H), 0.92 (t, J = 7.1 Hz, 3H) ppm; \(^1^3\)C-NMR (100 MHz, \(\text{C}_6\text{D}_6\)) \(\delta\) 181.8, 169.1, 159.7, 142.7, 139.9, 135.2, 134.1, 132.5, 132.4, 131.9, 130.4, 129.3, 129.1, 128.8, 127.1, 126.4, 126.1, 122.5, 120.4, 110.5, 60.6, 56.3, 54.8, 41.9, 20.5, 13.7 ppm; HRMS (ESI) m/z Found: (M+Na)\(^+\), \(\text{C}_{28}\text{H}_{27}\text{NO}_6\text{S}\), 528.1452, requires 528.1451.

**Ethyl \((Z)-2-(3-(3-methoxybenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2g)\)**

Following the general procedure the title compound was prepared in 84% yield as a yellow crystalline solid. \(R_f\) 0.21 (4:1, v/v hexanes : EtOAc); mp 118–120 °C; IR \(\nu_{\text{max}}\) 1729, 1673, 1598, 1469, 1433, 1295, 1280, 1255, 1164, 1086, 1032, 977 cm\(^{-1}\); H-NMR (300 MHz, \(\text{C}_6\text{D}_6\)) \(\delta\) 8.42 (s, 1H), 8.26 (d, \(J = 2.2 \) Hz, 1H), 7.77 (dd, \(J = 7.7, 1.5 \) Hz, 1H), 7.57 (d, \(J = 7.5 \) Hz, 1H), 7.47 (d, \(J = 8.3 \) Hz, 2H), 7.12 (t, \(J = 7.9 \) Hz, 1H), 7.01 – 6.83 (m, 2H), 6.75 (td, \(J = 7.8, 6.4 \) Hz, 3H), 6.41 (d, \(J = 8.0 \) Hz, 3H), 6.17 (dd, \(J = 8.9, 5.5 \) Hz, 1H), 4.11 – 3.90 (m, 2H), 3.76 (s, 2H), 2.91 (dd, \(J = 16.3, 8.9 \) Hz, 1H), 2.44 (dd, \(J = 16.3, 5.6 \) Hz, 1H), 1.77 (s, 4H), 0.91 (t, \(J = 7.1 \) Hz, 2H) ppm; \(^1^3\)C-NMR (100 MHz, \(\text{C}_6\text{D}_6\)) \(\delta\) 181.8, 169.0, 159.8, 142.9, 141.1, 140.0, 135.3, 134.4, 132.8, 130.34, 129.9, 129.2, 129.0, 127.2, 126.3, 126.1, 118.8, 116.3, 60.6, 56.4, 55.0, 41.8, 20.6, 13.6 ppm; HRMS (ESI) m/z Found: (M+Na)\(^+\), \(\text{C}_{28}\text{H}_{27}\text{NO}_6\text{S}\), 528.1447, requires 528.1451.

**Ethyl \((Z)-2-(3-(4-methoxybenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2h)\)**

Following the general procedure the title compound was prepared in 87% yield as a yellow crystalline solid. \(R_f\) 0.24 (4:1, v/v hexanes : EtOAc); mp 111–112 °C; IR \(\nu_{\text{max}}\) 1735, 1671, 1593, 1551, 1510, 1356, 1300, 1257, 1164, 1085, 1025, 956 cm\(^{-1}\); H-NMR (300 MHz, \(\text{C}_6\text{D}_6\)) \(\delta\) 8.33 (s, 1H), 8.11 (d, \(J = 8.9 \) Hz, 2H), 7.69 (dd, \(J = 7.8, 1.4 \) Hz, 1H), 7.39 (d, \(J = 8.3 \) Hz, 2H), 6.85 – 6.60 (m, 5H), 6.31 (d, \(J = 8.0 \) Hz, 2H), 6.19 – 6.07 (m, 1H), 4.05 – 3.79 (m, 2H), 3.20 (s, 3H), 2.87 (dd, \(J = 16.1, 8.3 \) Hz, 1H), 2.40 (dd, \(J = 16.1, 6.1 \) Hz, 1H), 1.66 (s, 3H), 0.84 (t, \(J = 7.1 \) Hz, 3H) ppm; \(^1^3\)C-NMR (100 MHz, \(\text{C}_6\text{D}_6\)) \(\delta\) \(^{1^3}\)C NMR (75 MHz, \(\text{C}_6\text{D}_6\)) \(\delta\) 181.9, 169.2, 162.3, 141.1, 139.9, 135.2, 132.6, 130.6, 129.0, 128.0, 127.2, 126.2, 126.2, 126.1, 118.8, 116.3, 60.6, 56.4, 55.0, 41.8, 20.6, 13.6 ppm; HRMS (ESI) m/z Found: (M+Na)\(^+\), \(\text{C}_{28}\text{H}_{27}\text{NO}_6\text{S}\), 528.1447, requires 528.1451.
**Ethyl (Z)-2-(3-(4-chlorobenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2i)**

Following the general procedure the title compound was prepared in 72% yield. *R*<sub>t</sub> 0.27 (4:1, v/v hexanes : EtOAc); mp 170 – 173 °C; IR ν<sub>max</sub> 1729, 1672, 1596, 1489, 1456, 1358, 1292, 1209, 1164, 1086, 1012, 959, 669 cm<sup>-1</sup>; <sup>1</sup>H-NMR (400 MHz, C<sub>6</sub>D<sub>6</sub>) δ 8.13 (s, 1H), 7.86 (d, *J* = 8.6 Hz, 2H), 7.68 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.36 (d, *J* = 8.3 Hz, 2H), 7.05 (d, *J* = 8.6 Hz, 2H), 6.82 (td, *J* = 7.5, 1.5 Hz, 1H), 6.72 – 6.64 (m, 2H), 6.36 – 6.27 (m, 2H), 6.05 (dd, *J* = 8.6, 5.8 Hz, 1H), 4.03 – 3.79 (m, 2H), 2.74 (dd, *J* = 16.1, 8.7 Hz, 1H), 2.34 (dd, *J* = 16.2, 5.8 Hz, 1H), 1.68 (s, 3H), 0.86 (t, *J* = 7.1 Hz, 3H) ppm; <sup>13</sup>C-NMR (100 MHz, C<sub>6</sub>D<sub>6</sub>) δ 181.5, 168.8, 143.1, 139.9, 139.2, 136.8, 135.0, 133.9, 132.9, 131.7, 130.0, 130.0, 128.9, 128.5, 127.8, 127.3, 126.2, 60.7, 56.3, 42.0, 20.6, 13.6 ppm; HRMS (ESI) *m/z* Found: (M+Na)<sup>+</sup>, C<sub>25</sub>H<sub>23</sub>CINO<sub>3</sub>S, 532.0951, requires 532.0956.

**Ethyl (Z)-2-(3-(4-bromobenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2j)**

Following the general procedure the title compound was prepared in 70% yield. *R*<sub>t</sub> 0.28 (4:1, v/v hexanes : EtOAc); mp 167 – 175 °C; IR ν<sub>max</sub> 1735, 1677, 1598, 1584, 1487, 1402, 1359, 1294, 1166, 1074, 1010, 957, 675 cm<sup>-1</sup>; <sup>1</sup>H-NMR (400 MHz, C<sub>6</sub>D<sub>6</sub>) δ 8.12 (s, 1H), 7.78 (d, *J* = 8.6 Hz, 2H), 7.69 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.37 (d, *J* = 8.3 Hz, 2H), 7.22 (d, *J* = 8.6 Hz, 2H), 6.85 – 6.78 (m, 1H), 6.71 – 6.65 (m, 2H), 6.35 – 6.30 (m, 2H), 6.06 (dd, *J* = 8.6, 5.8 Hz, 1H), 3.91 (ddq, *J* = 38.8, 10.8, 7.1 Hz, 2H), 2.74 (dd, *J* = 16.1, 8.7 Hz, 1H), 2.34 (dd, *J* = 16.1, 5.8 Hz, 1H), 1.68 (s, 3H), 0.86 (t, *J* = 7.1 Hz, 3H) ppm; <sup>13</sup>C-NMR (100 MHz, C<sub>6</sub>D<sub>6</sub>) δ 181.5, 168.8, 143.0, 139.9, 139.2, 136.8, 135.0, 134.0, 132.9, 132.0, 131.5, 130.2, 130.0, 128.9, 126.1, 125.5, 60.7, 56.2, 41.95, 20.6, 13.6 ppm; HRMS (ESI) *m/z* Found: (M+H)<sup>+</sup>, C<sub>27</sub>H<sub>25</sub>BrNO<sub>3</sub>S, 554.0632, requires 554.0631.

**Ethyl (Z)-2-(3-(4-cyanobenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2k)**

Following the general procedure the title compound was prepared in 60% yield. *R*<sub>t</sub> 0.26 (4:1, v/v hexanes : EtOAc); mp 178 – 182 °C; IR ν<sub>max</sub> 2229, 1737, 1673, 1595, 1457, 1347, 1293, 1164, 1086, 1042, 964 cm<sup>-1</sup>; <sup>1</sup>H-NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>) δ 7.99 (s, 1H), 7.77 – 7.70 (m, 2H), 7.65 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.29 (d, *J* = 8.3 Hz, 2H), 6.98 (d, *J* = 8.5 Hz, 2H), 6.82 – 6.74 (m, 1H), 6.64 (td, *J* = 7.4, 1.0 Hz, 2H), 6.31 – 6.25 (m, 2H), 5.97 (dd, *J* = 8.6, 5.6 Hz, 1H), 4.15 – 3.56 (m, 2H), 2.65 (dd, *J* = 16.1, 8.6 Hz, 1H), 2.29 (dd, *J* = 16.1, 5.7 Hz, 1H), 1.65 (s, 3H), 0.84 (t, *J* = 7.1 Hz, 3H) ppm; <sup>13</sup>C-NMR (75 MHz, C<sub>6</sub>D<sub>6</sub>) δ 181.9, 169.4, 144.0, 140.6, 138.6, 137.5, 135.6, 134.0, 133.8,
133.0, 132.6, 132.2, 131.9, 131.7, 130.3, 129.7, 126.9, 118.9, 114.5, 61.5, 56.9, 42.87, 21.2, 14.3 ppm; HRMS (ESI) m/z Found: (M+Na)+, C_{28}H_{28}N_{2}O_{5}S, 523.1292, requires 523.1298.

**Ethyl (Z)-2-(3-((6-methoxynaphthalen-2-yl)methylene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2l)**

Following the general procedure the title compound was prepared in 60% yield as a bright orange waxy solid. Rf 0.12 (19:1, v/v toluene : EtOAc); IR ν_{max} 1734, 1671, 1588, 1481, 1392, 1356, 1263, 1196, 1135, 1087, 1026, 813 cm⁻¹; ¹H-NMR (600 MHz, C_{6}D_{6}) δ ¹H NMR (600 MHz, Benzene-d₆) δ 8.64 (dd, J = 8.7, 1.8 Hz, 1H), 8.49 (s, 1H), 8.17 – 8.14 (m, 1H), 7.73 (dd, J = 7.7, 1.4 Hz, 1H), 7.54 (dd, J = 17.4, 8.8 Hz, 2H), 7.42 (d, J = 8.2 Hz, 2H), 7.10 (dd, J = 8.8, 2.5 Hz, 1H), 6.85 – 6.79 (m, 2H), 6.75 – 6.67 (m, 2H), 6.34 – 6.31 (m, 2H), 6.17 (dd, J = 8.6, 5.9 Hz, 1H), 3.92 (ddq, J = 75.0, 10.6, 7.1 Hz, 2H), 3.33 (s, 3H), 2.92 (dd, J = 16.3, 8.6 Hz, 1H), 2.43 (dd, J = 16.3, 5.9 Hz, 1H), 1.66 (s, 3H), 0.78 (t, J = 7.2 Hz, 3H) ppm; ¹³C-NMR (150 MHz, C_{6}D_{6}) δ 181.8, 169.1, 159.6, 142.8, 141.4, 140.0, 136.4, 135.3, 132.6, 130.9, 130.4, 129.1, 128.9, 128.7, 128.6, 127.4, 127.2, 126.7, 126.1, 119.1, 105.8, 60.6, 56.3, 54.5, 41.9, 20.6, 13.5 ppm; HRMS (ESI) m/z Found: (M+H)+, C_{32}H_{29}NO_{5}S, 556.1783, requires 556.1788.

**Ethyl (Z)-2-(5-benzylidene-3,3-dimethyl-4-oxo-1-tosylpyrrolidin-2-yl)acetate (2m)**

Following the general procedure the title compound was prepared in 34% yield as a pale yellow oil. IR ν_{max} 1729, 1597, 1447, 1347, 1163, 1135, 1028, 811 cm⁻¹; ¹H-NMR (400 MHz, C_{6}D_{6}) δ 7.79 (s, 1H), 7.75 (dd, J = 8.2, 2.0 Hz, 4H), 7.12 (dd, J = 8.3, 6.9 Hz, 2H), 7.08 – 7.01 (m, 1H), 6.61 (d, J = 8.2 Hz, 2H), 4.47 (dd, J = 8.3, 3.8 Hz, 1H), 3.90 (qd, J = 7.1, 4.8 Hz, 2H), 2.80 (dd, J = 16.7, 3.8 Hz, 1H), 2.64 (dd, J = 16.7, 8.3 Hz, 1H), 1.76 (s, 3H), 0.92 (t, J = 7.2 Hz, 3H), 0.89 (s, 3H), 0.46 (s, 3H) ppm; ¹³C-NMR (100 MHz, C_{6}D_{6}) δ 200.5, 170.2, 144.0, 135.5, 133.8, 130.7, 130.6, 129.5, 128.7, 124.2, 64.4, 60.4, 46.7, 38.6, 25.3, 20.7, 17.8, 13.7 ppm; HRMS (ESI) m/z Found: (M+H)+, C_{32}H_{29}NO_{5}S, 442.1681, requires 442.1683.

**Ethyl (Z)-2-(3-benzylidene-4-oxo-2-tosyl-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazin-1-yl)acetate (2n)**

Following the general procedure the title compound was prepared in 73% yield as a white crystalline solid. Rf 0.28 (1:19, v/v toluene : EtOAc); mp 163 – 164 °C; IR ν_{max} 1713, 1699, 1617, 1407, 1360, 1302, 1259, 1165, 1086, 1016, 948, 863 cm⁻¹; ¹H-NMR (600 MHz, C_{6}D_{6}) δ 8.00 (s, 1H), 7.85 – 7.77 (m, 1H), 7.31 (d, J =
8.3 Hz, 2H), 6.92 – 6.87 (m, 2H), 6.86 – 6.83 (m, 1H), 6.70 (dd, J = 3.3, 1.5 Hz, 1H), 6.33 – 6.28 (m, 2H), 5.94 (ddd, J = 7.8, 7.0, 0.8 Hz, 1H), 5.53 (ddd, J = 3.3, 1.6, 0.8 Hz, 1H), 5.47 (t, J = 3.2 Hz, 1H), 3.77 – 3.60 (m, 2H), 2.49 (dd, J = 16.1, 7.0 Hz, 1H), 2.17 (dd, J = 16.1, 7.9 Hz, 1H), 1.55 (s, 3H), 0.65 (t, J = 7.1 Hz, 3H) ppm; 13C-NMR (150 MHz, C₆D₆) δ 167.8, 157.1, 142.9, 142.5, 133.4, 131.9, 131.8, 130.4, 128.4, 127.5, 122.7, 115.7, 111.5, 108.9, 59.6, 50.7, 40.1, 19.9, 12.8 ppm; HRMS (ESI) m/z Found: (M+H)⁺, CₓHₓNₒₓOₓS, 465.1472, requires 465.1479.

tert-Butyl (Z)-2-(3-benzylidene-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2o)

Following the general procedure the title compound was prepared in 73% yield.

IR ν max 1727, 1675, 1596, 1449, 1360, 1293, 1207, 1165, 1088, 956 cm⁻¹; 1H-NMR (600 MHz, C₆D₆) δ 8.29 (s, 1H), 8.17 – 8.07 (m, 2H), 7.67 (dd, J = 7.8, 1.3 Hz, 1H), 7.35 (d, J = 8.2 Hz, 2H), 7.13 (d, J = 7.9 Hz, 2H), 7.08 – 7.03 (m, 1H), 6.81 – 6.77 (m, 2H), 6.12 – 6.07 (m, 1H), 2.88 (dd, J = 16.2, 7.7 Hz, 1H), 2.42 (dd, J = 16.1, 6.3 Hz, 1H), 1.66 (s, 3H), 1.36 (s, 9H) ppm; 13C-NMR (150 MHz, C₆D₆) δ 181.7, 168.3, 142.8, 140.7, 140.2, 135.2, 133.4, 132.8, 132.7, 130.8, 130.1, 129.7, 128.9, 128.3, 127.3, 127.1, 126.3, 80.8, 56.3, 43.2, 27.7, 20.5 ppm; HRMS (ESI) m/z Found: (M+H)⁺, C₂₉H₂₉N₂O₅S, 504.1847, requires 504.1839.

(Z)-2-(3-Benzylidene-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (2p)

Following the general procedure the title compound was prepared in 46% yield as a pale yellow oil. Rf 0.22 (19:1, v/v toluene : EtOAc); IR ν max 1676, 1597, 1493, 1449, 1361, 1292, 1186, 1167, 1087, 969 cm⁻¹; 1H-NMR (600 MHz, C₆D₆) δ 8.23 (s, 1H), 8.15 – 8.10 (m, 1H), 7.63 (d, J = 7.7, 1.4 Hz, 1H), 7.26 (d, J = 8.3 Hz, 2H), 7.19 (d, J = 7.7 Hz, 2H), 7.09 – 7.05 (m, 1H), 6.76 (td, J = 7.5, 1.4 Hz, 1H), 6.63 (td, J = 7.6, 1.2 Hz, 1H), 6.50 (dd, J = 7.7, 1.0 Hz, 1H), 6.27 (d, J = 8.0 Hz, 2H), 5.41 (t, J = 7.6 Hz, 1H), 2.12 (dd, J = 16.9, 7.3 Hz, 1H), 1.74 (dd, J = 16.8, 7.7 Hz, 1H), 1.62 (s, 3H) ppm; 13C-NMR (150 MHz, C₆D₆) δ 180.1, 142.5, 141.0, 136.2, 133.6, 132.0, 130.6, 129.0, 128.1, 127.7, 127.5, 126.6, 126.5, 125.8, 115.1, 54.9, 23.9, 19.7 ppm; HRMS (ESI) m/z Found: (M+H)⁺, C₂₉H₂₉N₂O₃S, 429.1271, requires 429.1267.
IV. Derivatisation studies

**Ethyl (E)-2-(4-((tert-butyldimethylsilyl)oxy)-3-(5-(diethylamino)-3-oxo-1-phenylpent-4-en-1-yl)-2-tosyl-1,2-dihydroisoquinolin-1-yl)acetate (6)**

![Chemical structure](image)

To a solution of ethyl (Z)-2-(3-benzylidene-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate 2a (60 mg, 13 mmol) in toluene (5 mL) under N₂ was added diene 5 (160 mg, 0.63 mmol) at rt. The reaction mixture was stirred for 24 h, at which point TLC analysis of the reaction mixture indicated complete consumption of the starting material. The reaction mixture was concentrated under reduced pressure and the crude residue was purified via column chromatography on silica gel to provide the product as a light brown oil (47 mg, 51% yield).

**Ethyl 2-(3-phenyl-2,3-dihydrofuro[3,2-c]isoquinolin-5-yl)acetate (7)**

![Chemical structure](image)

To a dry Schlenk flask containing NaH (60% dispersion in mineral oil) (4 mg, 0.17 mmol) and trimethylsulfoxonium iodide (37 mg, 0.17 mmol) was added dry DMSO (1 mL). The resulting suspension was stirred for 30 minutes at which point a solution of 2a (40 mg, 0.08 mmol) in dry DMSO (1 mL) was added dropwise. The reaction mixture was allowed to stir overnight until TLC analysis of the reaction mixture indicated complete consumption of the starting material. The reaction was cooled and quenched with water (4 mL), extracted with Et₂O (2 x 5 mL). The organic
extract was washed with water (2 x 5 mL), brine, dried with MgSO₄, filtered and then concentrated under reduced pressure. The crude residue was purified via column chromatography on silica gel to afford the product as a white solid (27 mg, 96% yield)

Rₜ 0.35 (4:1, v/v hexanes : EtOAc); mp 118 – 122 °C; IR νₘₐₓ 1731, 1632, 1587, 1509, 1495, 1444, 1384, 1320, 1259, 1161, 1088, 1030, 1009, 916, 762 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.98 – 7.91 (m, 2H), 7.62 (dd, J = 8.0, 6.8, 1.2 Hz, 1H), 7.52 (ddd, J = 8.5, 6.9, 1.3 Hz, 1H), 7.27 – 7.21 (m, 2H), 7.17 – 7.13 (m, 2H), 5.12 (dd, J = 9.9, 9.0 Hz, 1H), 4.85 (dd, J = 9.9, 6.1 Hz, 1H), 4.66 (dd, J = 9.0, 6.1 Hz, 1H), 4.24 – 4.10 (m, 2H), 4.04 (qd, J = 7.1, 1.7 Hz, 2H), 1.08 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 170.9, 147.3, 142.4, 129.5, 128.8, 127.9, 127.4, 127.3, 127.0, 125.1, 123.8, 121.4, 79.7, 61.0, 49.2, 41.9, 14.1 ppm; HRMS (ESI) m/z Found: (M+H)+, C₂₁H₂₈NO₃, 334.1442, requires 334.1438.

Ethyl 2-(3-((dodecylthio)(phenyl)methyl)-4-hydroxyisoquinolin-1-yl)acetate (8)

Adapted from the literature procedure²: N₂ was bubbled through a solution of 2e (60 mg, 0.13 mmol) and 1-dodecanethiol (160 μL, 0.66 mmol) in dimethylformamide (2 mL) for 10 minutes and then DBU (95 μL, 0.63 mmol) was added dropwise. The solution became yellow and was stirred for 30 mins under N₂ at which point TLC analysis indicated complete consumption of the starting material. This was followed by the addition of water (2 mL), the layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 5 mL). The combined organic extracts were dried with Na₂SO₄, filtered and then purified via column chromatography on silica gel to provide the product as a pale yellow oil (57 mg, 84% yield).

Rₜ 0.61 (4:1, v/v hexanes : EtOAc); IR νₘₐₓ 2923, 2853, 1735, 1582, 1450, 1390, 1252, 1155, 1030, 765 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.74 (s, 1H), 8.34 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.70 (t, J = 7.7 Hz, 1H), 7.62 (t, J = 7.8 Hz, 1H), 7.39 (d, J = 7.6 Hz, 2H), 7.28 (d, J = 7.2 Hz, 1H), 7.24 – 7.20 (m, 1H), 5.71 (s, 1H), 4.27 – 4.15 (m, 2H), 4.12 (q, J = 7.1 Hz, 2H), 2.62 (dt, J = 13.6, 7.1 Hz, 1H), 2.49 (dt, J = 12.6, 7.6 Hz, 1H), 1.69 – 1.55 (m, 3H), 1.37 – 1.18 (m, 17H), 1.16 (t, J = 7.1 Hz, 3H), 0.88 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 170.7, 145.4, 138.5, 129.1, 128.6, 128.1, 127.8, 127.6, 124.8, 122.2, 60.9, 54.5, 41.7, 32.4, 31.9, 29.6, 29.6, 29.4, 29.3, 29.1, 14.1, 14.1 ppm; HRMS (ESI) m/z Found: (M-H)-, C₃₉H₃₅NO₃S, 520.2896, requires 520.2891.

SI-14
V. NMR spectra and HPLC traces

Ethyl (E)-3-(2-(3-phenylpropioyl)phenyl)acrylate (1a)
Ethyl (E)-3-(2-(3-(2-methoxyphenyl)propionoyl)phenyl)acrylate (1f)
Ethyl (E)-3-(2-(3-(3-methoxyphenyl)propioyl)phenyl)acrylate (1g)
Ethyl (E)-3-(2-(3-(4-methoxyphenyl)propioloyl)phenyl)acrylate (1h)
Ethyl (E)-3-(2-(3-(4-chlorophenyl)propioloyl)phenyl)acrylate (1i)
Ethyl (E)-3-(2-(3-(4-bromophenyl)propioyl)phenyl)acrylate (1j)
Ethyl (E)-3-(2-(3-(4-cyanophenyl)propioyl)phenyl)acrylate (1k)
Ethyl\(\text{CO}_2\text{Et}\)
\((E)-3-(2-(3-(6\text{-methoxynaphthalen-2-yl})\text{propioloyl})\text{phenyl})\text{acrylate (II)}\)
Ethyl (E)-4,4-dimethyl-5-oxo-7-phenylept-2-en-6-ynoate (1m)
Ethyl (E)-3-(1-(3-phenylpropioyl)-1H-pyrrol-2-yl)acrylate (1n)
** tert-Butyl (E)-3-(2-(3-phenylpropioyloxy)phenyl)acrylate (1o) **
(E)-3-[(2-(3-phenylpropionyl)phenyl)acrylonitrile (lp)
Ethyl (Z)-2-(3-benzylidene-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2a)
Ethyl (Z)-2-(3-benzylidene-2-((4-methoxyphenyl)sulfonyl)-4-oxo-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2b)
Ethyl (Z)-2-(3-benzylidene-4-oxo-2-(phenylsulfonyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2c)
Ethyl (Z)-2-(3-benzylidene-2-((4-chlorophenyl)sulfonyl)-4-oxo-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2d)
Ethyl (Z)-2-(3-benzylidene-2-((4-cyanophenyl)sulfonyl)-4-oxo-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2e)
Ethyl (Z)-2-(3-(2-methoxybenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2f)
Ethyl (Z)-2-(3-(3-methoxybenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2g)
Ethyl \((Z)-2-(3-(4\text{-methoxybenzylidene})-4\text{-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl})\text{acetate (2h)}\)
Ethyl (Z)-2-(3-(4-chlorobenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2i)
Ethyl (Z)-2-(3-(4-bromobenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2j)
Ethyl (Z)-2-(3-(4-cyanobenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2k)
Ethyl (Z)-2-(3-(((6-methoxynaphthalen-2-yl)methylene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2l)
Ethyl (Z)-2-(5-benzylidene-3,3-dimethyl-4-oxo-1-tosylpyrrolidin-2-yl)acetate (2m)
Ethyl (Z)-2-(3-benzylidene-4-oxo-2-tosyl-1,2,3,4-tetrahydropyrrolo[1,2-α]pyrazin-1-yl)acetate (2n)
tert-Butyl (Z)-2-(3-benzylidene-4-oxo-2-tosyl-1,2,3,4-
tetrahydroisoquinolin-1-yl)acetate (2o)
(Z)-2-(3-Benzylidene-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (2p)
Ethyl \((E)\)-2-(4-((tert-butyldimethylsilyl)oxy)-3-(5-(diethylamino)-3-oxo-1-phenylpent-4-en-1-yl)-2-tosyl-1,2-dihydroisoquinolin-1-yl)acetate (6)
Ethyl 2-(3-phenyl-2,3-dihydrofuro[3,2-c]isoquinolin-5-yl)acetate (7)
Ethyl 2-(3-((dodecylthio)(phenyl)methyl)-4-hydroxyisoquinolin-1-yl)acetate (8)
References

(1) G. Satyanarayana, H. Madhurima, J. Krishna, Synthesis 2015, 47, 1245.