Supporting Information
for

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

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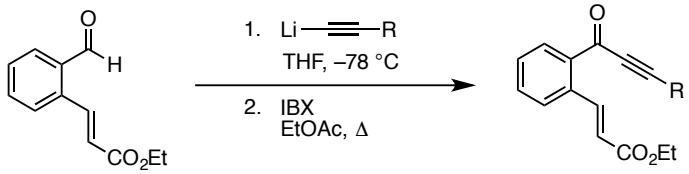
I. General experimental

Proton (^{1}H) and carbon (^{13}C) 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 (ν_{max}) 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 (CH_2Cl_2) 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]

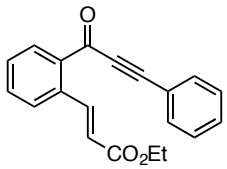
II. Synthesis of ynone cinnamates



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 NH_4Cl 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 Na_2SO_4, 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.

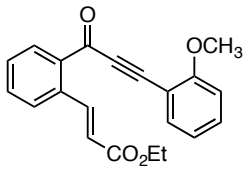
2-Iodoxybenzoic acid (15 mmol) was added to a solution of the crude alkynol in EtOAc (30 mL) and the resulting suspension was heated at reflux until TLC analysis of the reaction mixture indicated complete consumption of the starting material. The reaction mixture was filtered and concentrated to afford 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. R_f 0.29 (4:1, v/v hexanes : EtOAc); mp 52 – 55 °C; IR ν_{max} 2197, 1707, 1629, 1561, 1445, 1305, 1262, 1187, 974, 758, 678 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 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; ^{13}C NMR (100 MHz, $CDCl_3$) 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: $(M+H)^+$, $C_{20}H_{17}O_3$, 305.1169, requires 305.1172.

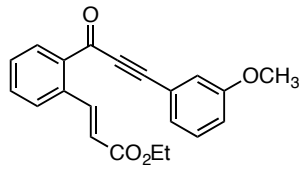
Ethyl (*E*)-3-(2-(3-(2-methoxyphenyl)propioloyl)phenyl)acrylate (1f)



Following the general procedure the title compound was prepared in 60% yield as a yellow solid. R_f 0.17 (4:1, v/v hexanes : EtOAc); mp 78 – 82 °C; IR ν_{max} 2185, 1709, 1628, 1594, 1562, 1492, 1460, 1435, 1248, 1164, 1002,

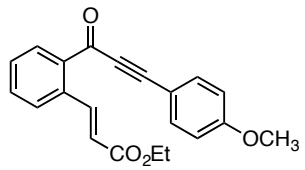
969, 752, 672 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.51-8.44 (m, 2H), 7.59-7.42 (m, 5H), 7.00-6.92 (m, 2H), 6.30 (d, *J* = 15.9 Hz, 1H), 4.25 (q, *J* = 7.2 Hz, 2H), 3.94 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.7, 166.3, 161.8, 143.8, 136.1, 136.0, 134.8, 133.1, 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: $(M+H)^+$, $C_{21}H_{18}O_4$, 335.1275, requires 335.1278.

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



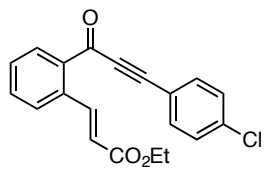
Following the general procedure the title compound was prepared in 71% yield as a viscous yellow oil. R_f 0.21 (4:1, v/v hexanes : EtOAc); IR ν_{max} 2189, 1709, 1631, 1593, 1573, 1478, 1422, 1366, 1306, 1274, 1229, 1160, 1036, 1013, 973, 897, 784, 754, 682 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.46 (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; ^{13}C NMR (100 MHz, $CDCl_3$) 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: $(M+H)^+$, $C_{21}H_{18}O_4$, 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. R_f 0.23 (4:1, v/v hexanes : EtOAc); mp 86 – 89 °C; IR ν_{max} 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, $CDCl_3$) 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 ^{13}C NMR (100 MHz, $CDCl_3$) 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: $(M+H)^+$, $C_{21}H_{18}O_4$, 335.1278, requires 335.1272.

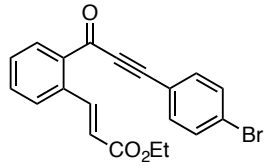
Ethyl (*E*)-3-(2-(3-(4-chlorophenyl)propioloyl)phenyl)acrylate (1i)



Following the general procedure the title compound was prepared in 61% yield as a yellow solid. R_f 0.36 (4:1, v/v hexanes : EtOAc); mp 73 – 76 °C; IR ν_{max} 2195, 1710, 1632, 1589, 1561, 1475, 1305, 1267, 1161, 1088, 1004, 971, 829, 761, 713, 678 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 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

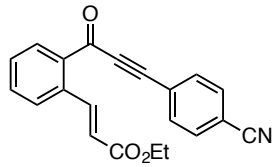
Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.5, 166.4, 143.4, 137.3, 136.3, 135.9, 134.2, 133.4, 132.4, 129.4, 129.1, 128.4, 121.7, 118.4, 92.0, 88.9, 60.6, 14.3 ppm; HRMS (ESI) *m/z* Found: $(M+H)^+$, $C_{20}H_{15}O_3Cl$, 339.0773, requires 339.0782.

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



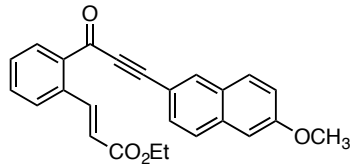
Following the general procedure the title compound was prepared in 43% yield as a colourless solid. R_f 0.32 (4:1, v/v hexanes : EtOAc); mp 71 – 72 °C; IR ν_{max} 2199, 1711, 1634, 1560, 1476, 1391, 1366, 1306, 1264, 1190, 1162, 1002, 966, 821 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ^{1}H NMR (600 MHz, Chloroform-*d*) δ 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, 2H), 1.32 (t, *J* = 7.2, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ ^{13}C NMR (151 MHz, $CDCl_3$) δ 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: $(M+H)^+$, $C_{20}H_{15}O_3Br$, 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 ν_{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 (600 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 178.3, 166.5, 143.4, 136.7, 135.7, 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.

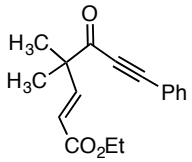
Ethyl (*E*)-3-(2-(3-(6-methoxynaphthalen-2-yl)propioloyl)phenyl)acrylate (1l)



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 ν_{max} 2182, 1717, 1619, 1480, 1390, 1255, 1175, 1123, 1009, 852 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 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,

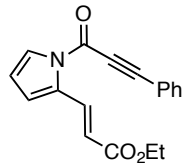
$CDCl_3$) δ 178.8, 166.5, 159.5, 143.7, 136.5, 136.3, 135.7, 134.4, 133.1, 132.4, 129.9, 129.4, 129.1, 128.4, 128.2, 127.3, 121.6, 120.0, 114.6, 106.0, 95.0, 88.5, 60.6, 55.5, 14.3 ppm; HRMS (ESI) *m/z* Found: $(M+H)^+$, $C_{25}H_{20}O_4$, 385.1437, requires 385.1434.

Ethyl (*E*)-4,4-dimethyl-5-oxo-7-phenylhept-2-en-6-ynoate (1m)



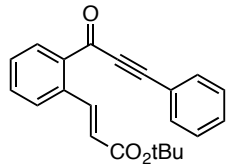
Following the procedure above the title compound was prepared in 53% yield as a clear oil. R_f 0.35 (1:4, v/v hexanes : EtOAc); IR ν_{max} 2196, 1716, 1664, 1648, 1489, 1444, 1366, 1271, 1180, 1058, 1033, 757 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.48 – 7.45 (m, 1H), 7.39 (t, *J* = 7.9 Hz, 2H), 7.20 (dd, *J* = 16.0, 0.6 Hz, 1H), 5.99 – 5.91 (m, 1H), 4.25 – 4.18 (q, *J* = 7.1 Hz, 2H), 1.44 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.13, 166.26, 150.30, 133.18, 130.98, 128.67, 121.20, 119.75, 94.26, 85.98, 60.59, 50.90, 23.54, 14.25 ppm; HRMS (ESI) *m/z* Found: $(M+H)^+$, $C_{17}H_{18}O_3$, 271.1327, requires 271.1329.

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



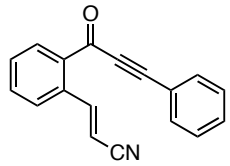
Following the procedure above the title compound was prepared in 28% yield as a yellow oil. R_f 0.28 (1:4, v/v hexanes : EtOAc); IR ν_{max} 2206, 1703, 1686, 1622, 1405, 1339, 1268, 1175, 1108, 1034, 986, 759 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.42 (d, *J* = 15.9 Hz, 1H), 7.72 – 7.62 (m, 3H), 7.55 – 7.48 (m, 1H), 7.48 – 7.39 (m, 2H), 6.79 (ddd, *J* = 3.5, 1.6, 0.8 Hz, 1H), 6.34 (td, *J* = 3.4, 0.6 Hz, 1H), 6.27 (d, *J* = 15.9 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.8, 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: $(M+H)^+$, $C_{18}H_{15}NO_3$, 294.1122, requires 294.1125.

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



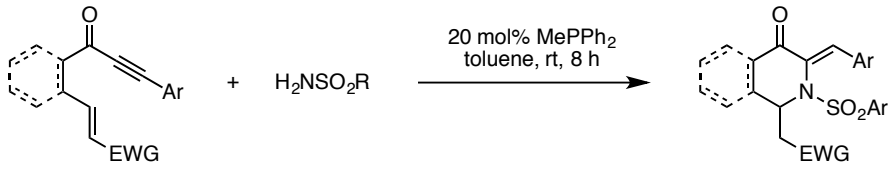
Following the general procedure the title compound was prepared in 55% yield as a pale yellow solid. R_f 0.43 (4:1, v/v hexanes : EtOAc); mp 124 – 126 °C; IR ν_{max} 2195, 1691, 1626, 1592, 1369, 1286, 1252, 1209, 1154, 1027, 1011, 966, 841, 757, 690 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.38 (d, *J* = 15.8 Hz, 1H), 8.25 (d, *J* = 7.7 Hz, 1H), 7.69 – 7.64 (m, 2H), 7.62 – 7.56 (m, 2H), 7.52 (td, *J* = 7.4 Hz, 1.7 Hz, 1H), 7.49 – 7.47 (m, 1H), 7.42 – 7.39 (m, 1H), 6.26 (d, *J* = 15.8 Hz, 1H), 1.51 (s, 9H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ 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: $(M-O^tBu+H_2O)^+$, $C_{18}H_{13}O_3$, 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. R_f 0.29 (4:1, v/v hexanes : EtOAc); mp 192 °C (decomp.); IR ν_{max} 2193, 1737, 1624, 1565, 1490, 1444, 1308, 1207, 1113, 1010, 995, 955 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) 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; ^{13}C NMR (150 MHz, $CDCl_3$) 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: $(M+H)^+$, $C_{18}H_{11}NO$, 258.0913, requires 258.0913.

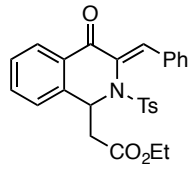
III. Phosphine catalysed (5 + 1) annulations



SI-2

To a solution of ynone (0.13 mmol) and sulfonamide (0.13 mmol) in dry toluene (2.6 mL) under N_2 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 isoquinolone product.

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

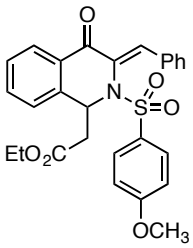


Following the general procedure the title compound was prepared in 84% yield. R_f 0.29 (1:19, v/v toluene : EtOAc); mp 118 – 120 °C; IR ν_{max} 1735, 1675, 1598, 1493, 1359, 1292, 1166, 1089, 972 cm^{-1}; ^1H-NMR (300 MHz, C_6D_6) δ 8.25 (s, 1H), 8.15 – 8.04 (m, 2H), 7.64 (dd, *J* = 7.8, 1.3 Hz, 1H), 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; ^{13}C-NMR (100 MHz, C_6D_6) 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: $(M+H)^+$, $C_{27}H_{25}NO_5S$, 476.1528, requires 476.1526.

In addition following the general procedure, however performed at 0 ºC, and using (*R*)-SITCP catalyst (**C**), the title compound **2a** was prepared in 85% isolated yield. HPLC RegisCell™,

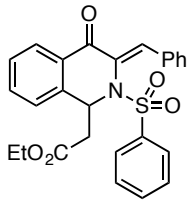
hexane:iPrOH 85:15, 1 ml/min, l = 238 nm, fraction tr = 9.64 (major enantiomer) and 12.38 (minor enantiomer); ee = 15%

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



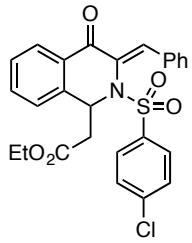
Following the general procedure the title compound was prepared in 67% yield. R_f 0.09 (4:1, v/v hexanes : EtOAc); IR ν_{max} 1735, 1674, 1594, 1496, 1358, 1293, 1261, 1159, 1089, 1023, 835, 760, 676, 590 cm^{-1}; ^{1}H-NMR (400 MHz, C_6D_6) δ 8.29 (s, 1H), 8.17 – 8.06 (m, 2H), 7.73 (dd, *J* = 7.7, 1.4 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; ^{13}C-NMR (100 MHz, C_6D_6) δ 181.9, 169.0, 162.7, 140.9, 140.0, 133.3, 132.9, 132.9, 130.9, 130.2, 130.0, 129.9, 129.8, 128.3, 127.3, 126.2, 113.6, 60.6, 56.3, 54.5, 42.0, 13.6 ppm; HRMS (ESI) *m/z* Found: $(M+H)^+$, $C_{27}H_{25}NO_5S$, 492.1471, requires 492.1475.

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



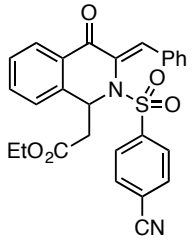
Following the general procedure the title compound was prepared in 63% yield. R_f 0.15 (4:1, v/v hexanes : EtOAc); IR ν_{max} 1733, 1674, 1596, 1447, 1359, 1292, 1272, 1206, 1167, 1088, 1049, 1023, 956, 840 cm^{-1}; ^{1}H-NMR (400 MHz, C_6D_6) δ 8.26 (s, 1H), 8.14 – 8.02 (m, 2H), 7.66 (dd, *J* = 7.7, 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; ^{13}C-NMR (100 MHz, C_6D_6) 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: $(M+H)^+$, $C_{26}H_{23}NO_5S$, 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)



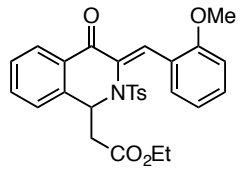
Following the general procedure the title compound was prepared in 65% yield. R_f 0.13 (4:1, v/v hexanes : EtOAc); mp 158 – 161 °C; IR ν_{max} 1733, 1670, 1593, 1474, 1425, 1362, 1292, 1206, 1168, 1086, 1050, 947 cm^{-1}; ^{1}H-NMR (600 MHz, C_6D_6) δ 8.23 (s, 1H), 8.06 – 8.01 (m, 2H), 7.65 (dd, *J* = 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* = 55.9, 10.8, 7.2 Hz, 2H), 2.75 (dd, *J* = 16.3, 8.4 Hz, 1H), 2.31 (dd, *J* = 16.3, 6.1 Hz, 1H), 0.81 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C-NMR (100 MHz, C_6D_6) δ 181.4, 168.8, 141.1, 139.6, 138.8, 136.26, 133.0, 132.9, 132.8, 131.0, 130.0, 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: $(M+K)^+$, $C_{26}H_{22}ClNO_5S$, 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. R_f 0.14 (4:1, v/v hexanes : EtOAc); mp 237 – 238 °C; IR ν_{max} 2233, 1740, 1671, 1446, 1361, 1295, 1272, 1162, 1082, 1052, 970, 838 cm^{-1}; ^{1}H-NMR (600 MHz, C_6D_6) 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; ^{13}C-NMR (150 MHz, C_6D_6) 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: $(M+H)^+$, $C_{27}H_{22}N_2O_5S$, 487.1323, requires 487.1322.

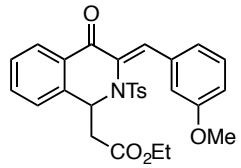
Ethyl (*Z*)-2-(3-(2-methoxybenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2f)



Following the general procedure the title compound was prepared in 68% yield as a bright yellow crystalline solid. R_f 0.21 (4:1, v/v hexanes : EtOAc); mp 109 – 114 °C; IR ν_{max} 1710, 1672, 1594, 1488, 1462, 1359, 1291, 1241, 1145, 1085, 1022, 974 cm^{-1}; ^{1}H-NMR (300 MHz, C_6D_6) 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,

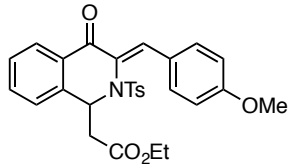
6.0 Hz, 1H), 4.09 – 3.86 (m, 2H), 3.22 (s, 3H), 2.90 (dd, *J* = 16.1, 8.3 Hz, 1H), 2.42 (dd, *J* = 16.1, 6.1 Hz, 1H), 1.68 (s, 3H), 0.92 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C-NMR (100 MHz, C_6D_6) δ 181.8, 169.1, 159.7, 142.7, 139.9, 135.2, 134.1, 132.5, 132.4, 131.9, 130.4, 129.3, 129.1, 128.8, 127.1, 126.4, 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: $(M+Na)^+$, $C_{28}H_{27}NO_6S$, 528.1452, requires 528.1451.

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



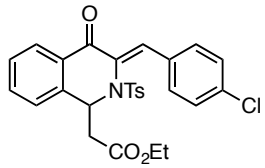
Following the general procedure the title compound was prepared in 84% yield as a yellow crystalline solid. R_f 0.21 (4:1, v/v hexanes : EtOAc); mp 118– 120 °C; IR ν_{max} 1729, 1673, 1598, 1469, 1433, 1295, 1280, 1255, 1232, 1164, 1086, 1032, 977 cm^{-1}; ^{1}H-NMR (300 MHz, C_6D_6) δ 8.42 (s, 1H), 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; ^{13}C-NMR (100 MHz, C_6D_6) δ 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: $(M+Na)^+$, $C_{28}H_{27}NO_6S$, 528.1447, requires 528.1451.

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



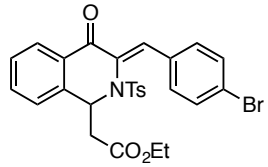
Following the general procedure the title compound was prepared in 87% yield as a yellow crystalline solid. R_f 0.24 (4:1, v/v hexanes : EtOAc); mp 111 – 112 °C; IR ν_{max} 1735, 1671, 1593, 1551, 1510, 1356, 1300, 1257, 1164, 1085, 1025, 956 cm^{-1}; ^{1}H-NMR (300 MHz, C_6D_6) δ 8.33 (s, 1H), 8.11 (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; ^{13}C-NMR (100 MHz, C_6D_6) δ ^{13}C NMR (75 MHz, C_6D6) δ 181.9, 169.2, 162.3, 142.8, 141.1, 139.9, 135.2, 132.6, 130.6, 129.0, 128.0, 127.2, 126.2, 126.2, 114.0, 60.6, 56.5, 41.9, 20.7, 13.7 ppm; HRMS (ESI) *m/z* Found: $(M+Na)^+$, $C_{28}H_{27}NO_6S$, 528.1449, requires 528.1451.

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



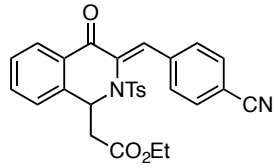
Following the general procedure the title compound was prepared in 72% yield. R_f 0.27 (4:1, v/v hexanes : EtOAc); mp 170 – 173 °C; IR ν_{max} 1729, 1672, 1596, 1489, 1456, 1358, 1292, 1209, 1164, 1086, 1012, 959, 669 cm^{-1}; ^{1}H-NMR (400 MHz, C_6D_6) δ 8.13 (s, 1H), 7.86 (d, *J* = 8.6 Hz, 2H), 7.68 (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; ^{13}C-NMR (100 MHz, C_6D_6) 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: $(M+Na)^+$, $C_{27}H_{24}ClNO_5S$, 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_f 0.28 (4:1, v/v hexanes : EtOAc); mp 167 – 175 °C; IR ν_{max} 1735, 1677, 1598, 1584, 1487, 1402, 1359, 1294, 1166, 1074, 1010, 957, 675 cm^{-1}; ^{1}H-NMR (400 MHz, C_6D_6) 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; ^{13}C-NMR (100 MHz, C_6D_6) δ 181.5, 168.8, 143.0, 139.9, 139.3, 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: $(M+H)^+$, $C_{27}H_{24}BrNO_5S$, 554.0632, requires 554.0631.

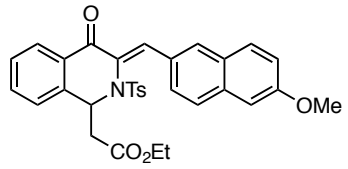
Ethyl (*Z*)-2-(3-(4-cyanobenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2k)



Following the general procedure the title compound was prepared in 60% yield. R_f 0.26 (4:1, v/v hexanes : EtOAc); mp 178 – 182 °C; IR ν_{max} 2229, 1737, 1673, 1595, 1457, 1347, 1293, 1164, 1086, 1042, 964 cm^{-1}; ^{1}H-NMR (300 MHz, C_6D_6) 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; ^{13}C-NMR (75 MHz, C_6D_6) δ 181.9, 169.4, 144.0, 140.6, 138.6, 137.5, 135.6, 134.0, 133.8,

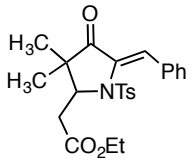
133.0, 132.6, 132.2, 131.9, 131.7, 130.3, 129.7, 126.9, 118.9, 114.5, 61.5, 56.9, 42.87, 21.2, 14.3 ppm; HRMS (ESI) *m/z* Found: $(M+Na)^+$, $C_{28}H_{24}N_2O_5S$, 523.1292, requires 523.1298.

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



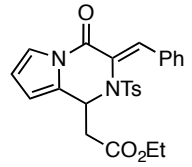
Following the general procedure the title compound was prepared in 60% yield as a bright orange waxy solid. R_f 0.12 (19:1, v/v toluene : EtOAc); IR ν_{max} 1734, 1671, 1588, 1481, 1392, 1356, 1263, 1196, 1135, 1087, 1026, 813 cm^{-1}; ^{1}H-NMR (600 MHz, C_6D_6) δ ^{1}H NMR (600 MHz, Benzene-d_6) δ 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; ^{13}C-NMR (150 MHz, C_6D_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: $(M+H)^+$, $C_{32}H_{29}NO_6S$, 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}; ^{1}H-NMR (400 MHz, C_6D_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; ^{13}C-NMR (100 MHz, C_6D_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: $(M+H)^+$, $C_{24}H_{27}NO_5S$, 442.1681, requires 442.1683.

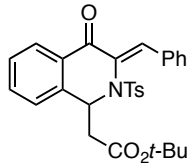
Ethyl (*Z*)-2-(3-benzylidene-4-oxo-2-tosyl-1,2,3,4-tetrahydropyrrolo[1,2-*a*]pyrazin-1-yl)acetate (2n)



Following the general procedure the title compound was prepared in 73% yield as a white crystalline solid. R_f 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}; ^{1}H-NMR (600 MHz, C_6D_6) δ 8.00 (s, 1H), 7.85 – 7.77 (m, 1H), 7.31 (d, *J* =

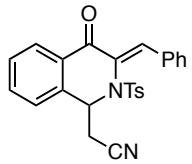
8.3 Hz, 2H), 6.92 – 6.87 (m, 2H), 6.86 – 6.83 (m, 1H), 6.70 (dd, *J* = 3.3, 1.5 Hz, 1H), 6.33 – 6.28 (m, 2H), 5.94 (ddd, *J* = 7.8, 7.0, 0.8 Hz, 1H), 5.53 (ddd, *J* = 3.3, 1.6, 0.8 Hz, 1H), 5.47 (t, *J* = 3.2 Hz, 1H), 3.77 – 3.60 (m, 2H), 2.49 (dd, *J* = 16.1, 7.0 Hz, 1H), 2.17 (dd, *J* = 16.1, 7.9 Hz, 1H), 1.55 (s, 3H), 0.65 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C-NMR (150 MHz, C_6D_6) 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: $(M+H)^+$, $C_xH_xNO_xS$, 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}; ^{1}H-NMR (600 MHz, C_6D_6) 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 (td, *J* = 7.4, 1.4 Hz, 1H), 6.77 (dd, *J* = 7.7, 1.3 Hz, 1H), 6.66 (td, *J* = 7.5, 1.3 Hz, 1H), 6.32 – 6.27 (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; ^{13}C-NMR (150 MHz, C_6D_6) 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: $(M+H)^+$, $C_{29}H_{29}NO_5S$, 504.1847, requires 504.1839.

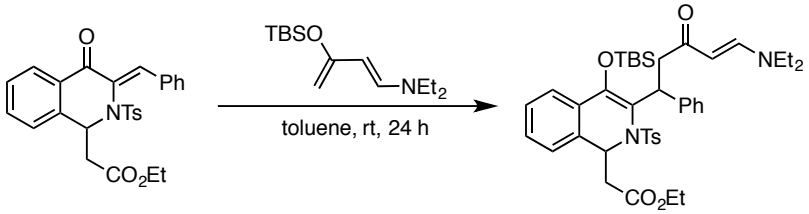
(*Z*)-2-(3-Benzylidene-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (2p)



Following the general procedure the title compound was prepared in 46% yield as a pale yellow oil. R_f 0.22 (19:1, v/v toluene : EtOAc); IR ν_{max} 1676, 1597, 1493, 1449, 1361, 1292, 1186, 1167, 1087, 969 cm^{-1}; ^{1}H-NMR (600 MHz, C_6D_6) δ 8.23 (s, 1H), 8.15 – 8.10 (m, 1H), 7.63 (dd, *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; ^{13}C-NMR (150 MHz, C_6D_6) 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: $(M+H)^+$, $C_{25}H_{20}N_2O_3S$, 429.1271, requires 429.1267.

IV. Derivatisation studies

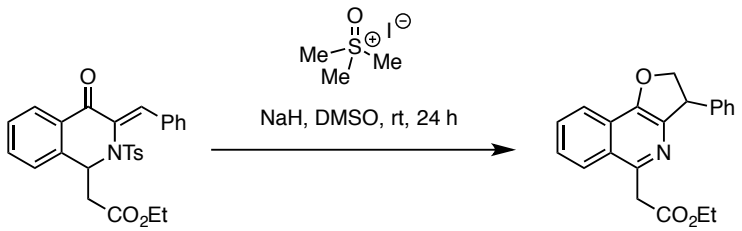
Ethyl (*E*)-2-(4-((*tert*-butyldimethylsilyl)oxy)-3-(5-(diethylamino)-3-oxo-1-phenylpent-4-en-1-yl)-2-tosyl-1,2-dihydroisoquinolin-1-yl)acetate (6)



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 N_2 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).

R_f 0.54 (4:1, v/v hexanes : EtOAc); IR ν_{max} 2931, 1735, 1600, 1560, 1466, 1358, 1250, 1196, 1097, 960 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.58 (m, 2H), 7.50 (d, *J* = 12.9 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.30 – 7.26 (m, 2H), 7.25 – 7.20 (m, 1H), 7.05 – 6.83 (m, 6H), 5.28 (dd, *J* = 9.8, 5.0 Hz, 1H), 5.17 (dd, *J* = 12.3, 8.3 Hz, 2H), 4.12 (dd, *J* = 15.6, 11.9 Hz, 1H), 4.00 (qd, *J* = 7.2, 5.0 Hz, 2H), 3.21 (d, *J* = 7.7 Hz, 4H), 3.00 (dd, *J* = 15.6, 3.2 Hz, 1H), 2.40 – 2.24 (m, 4H), 1.98 (dd, *J* = 15.5, 5.0 Hz, 1H), 1.24 – 1.03 (m, 9H), 0.47 (s, 3H), 0.00 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.8, 172.1, 152.2, 148.5, 144.9, 142.5, 137.2, 136.1, 132.5, 131.7, 130.5, 130.2, 129.9, 129.8, 128.6, 128.4, 128.2, 126.0, 124.7, 62.8, 57.4, 43.5, 40.4, 28.5, 23.6, 20.7, 16.3, 0.0, -0.3 ppm; HRMS (ESI) *m/z* Found: $(M+H)^+$, $C_{41}H_{54}N_2O_6SSi$, 731.3545, requires 731.3545.

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



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 Et_2O (2 x 5 mL). The organic

extract was washed with water (2 x 5 mL), brine, dried with $MgSO_4$, 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)

R_f 0.35 (4:1, v/v hexanes : EtOAc); mp 118 – 122 °C; IR ν_{max} 1731, 1632, 1587, 1509, 1495, 1444, 1384, 1320, 1259, 1161, 1088, 1030, 1009, 916, 762 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.91 (m, 2H), 7.62 (ddd, *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; ^{13}C NMR (100 MHz, $CDCl_3$) 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: $(M+H)^+$, $C_{21}H_{20}NO_3$, 334.1442, requires 334.1438.

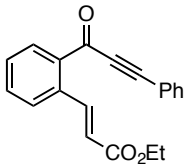
Ethyl 2-(3-((dodecylthio)(phenyl)methyl)-4-hydroxyisoquinolin-1-yl)acetate (8)

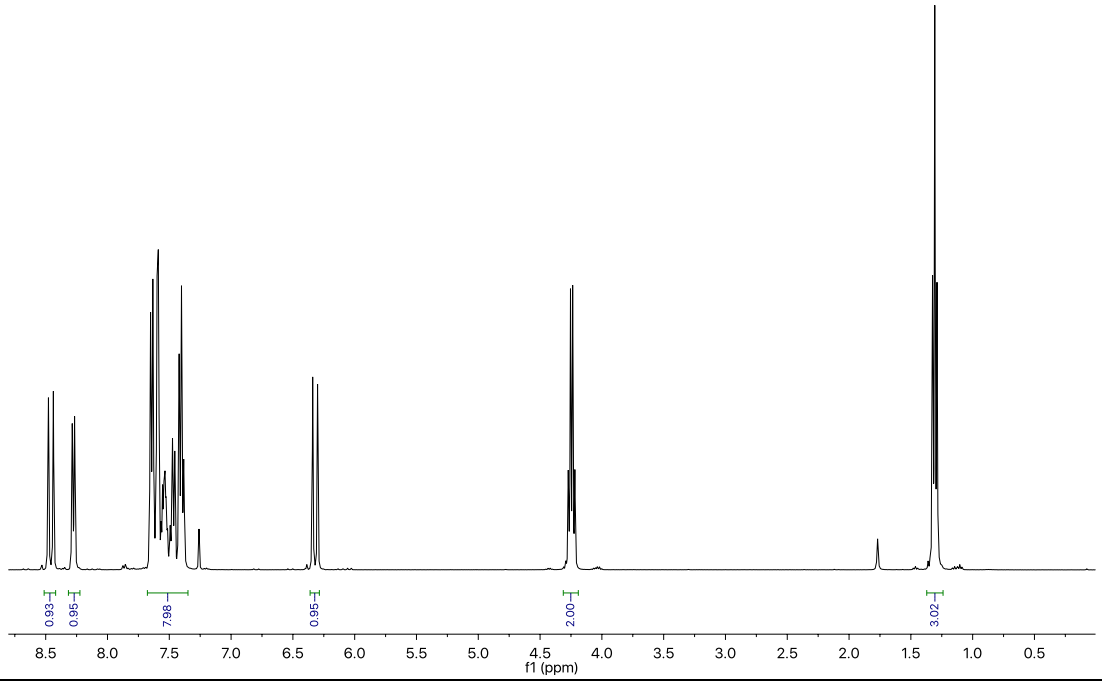
Adapted from the literature procedure[2]: N_2 was bubbled through a solution of **2e** (60 mg, 0.13 mmol) and 1-dodecanethiol (160 μL, 0.66 mmol) in dimethylformamide (2 mL) for 10 minutes and then DBU (95 μL, 0.63 mmol) was added dropwise. The solution became yellow and was stirred for 30 mins under N_2 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 Na_2SO_4, filtered and then purified via column chromatography on silica gel to provide the product as a pale yellow oil (57 mg, 84% yield).

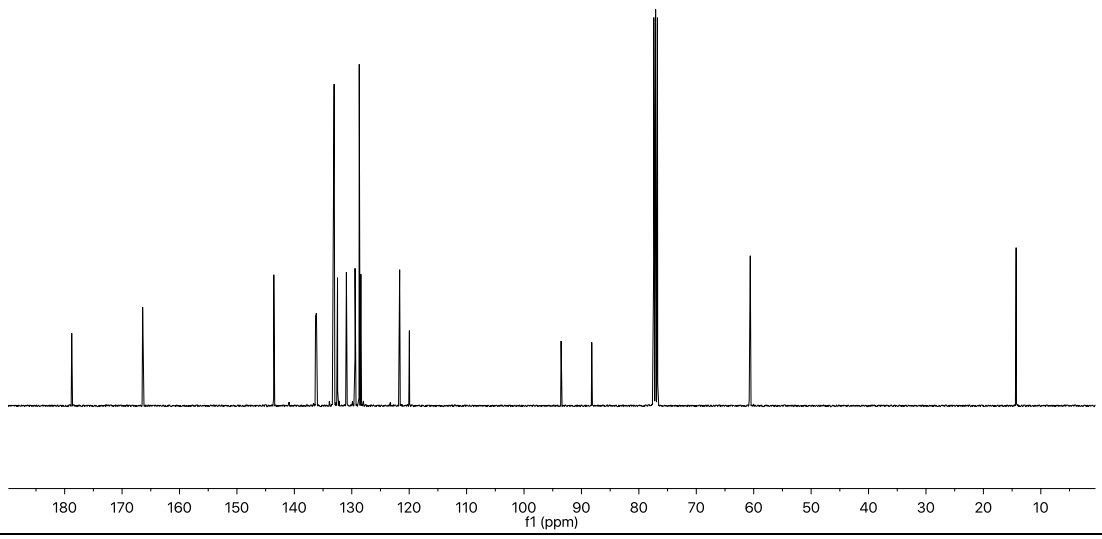
R_f 0.61 (4:1, v/v hexanes : EtOAc); IR ν_{max} 2923, 2853, 1735, 1582, 1450, 1390, 1252, 1155, 1030, 765 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.74 (s, 1H), 8.34 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.70 (t, *J* = 7.7 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 7.6 Hz, 2H), 7.28 (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; ^{13}C NMR (100 MHz, $CDCl_3$) 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, 29.0, 23.0, 14.1, 14.1 ppm; HRMS (ESI) *m/z* Found: $(M-H)^-$, $C_{32}H_{43}NO_3S$, 520.2896, requires 520.2891.

V. NMR spectra and HPLC traces

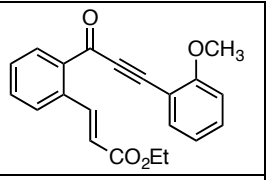
Ethyl (*E*)-3-(2-(3-phenylpropioloyl)phenyl)acrylate (1a)

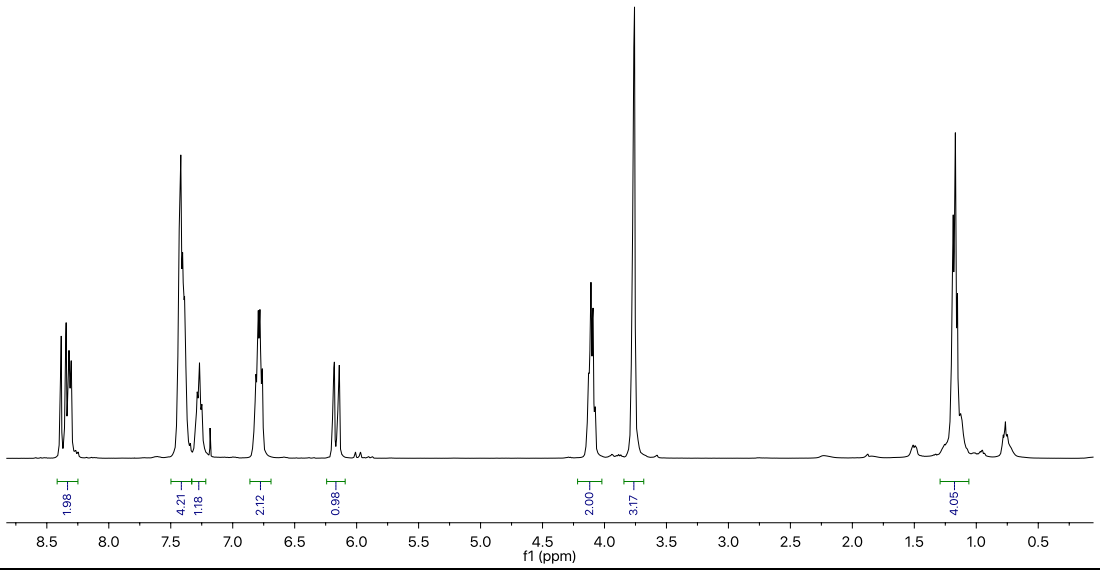


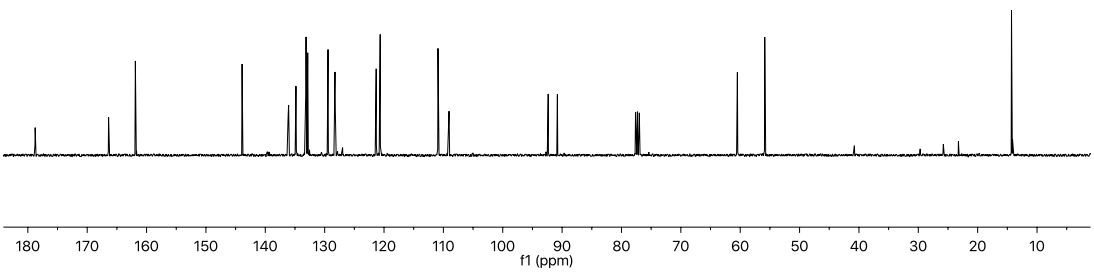




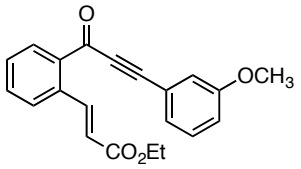
Ethyl (*E*)-3-(2-(3-(2-methoxyphenyl)propioloyl)phenyl)acrylate (1f)

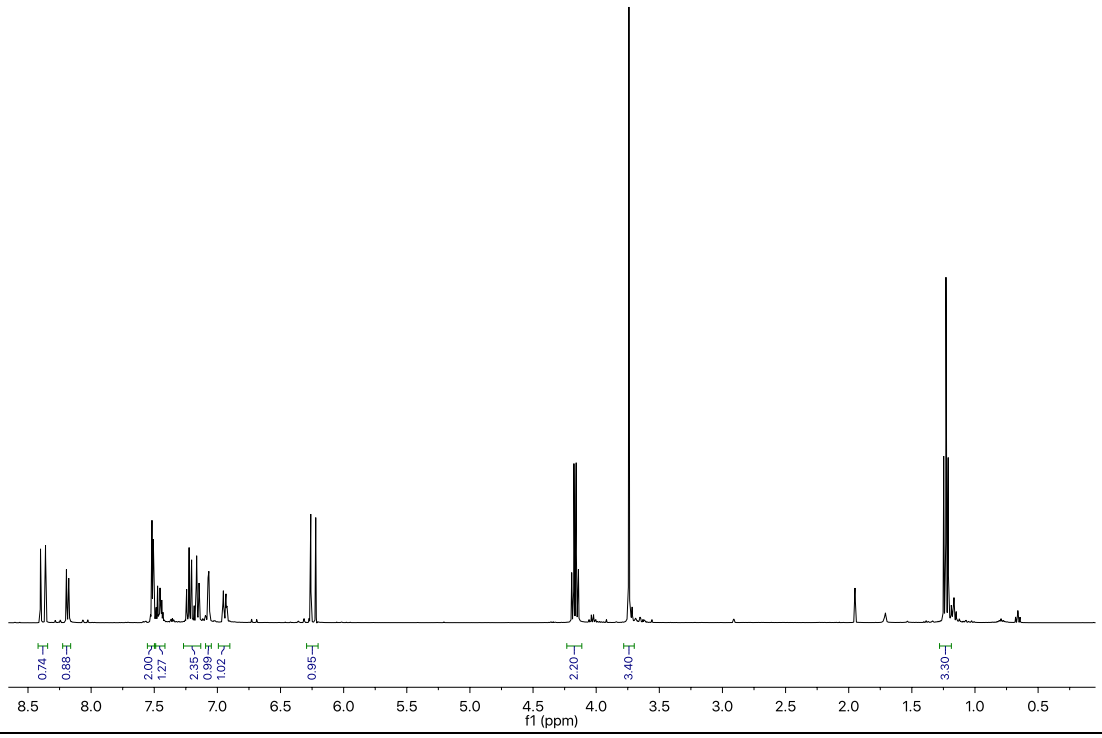


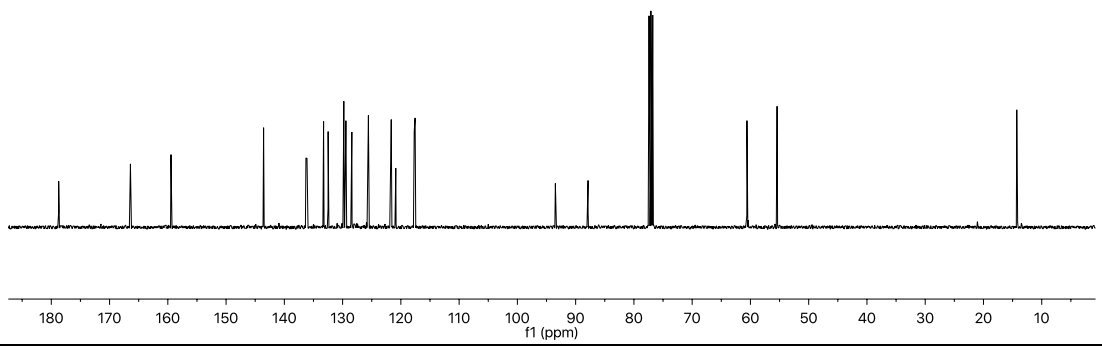




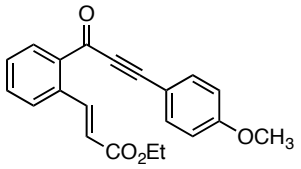
Ethyl (*E*)-3-(2-(3-(3-methoxyphenyl)propioloyl)phenyl)acrylate (1g)

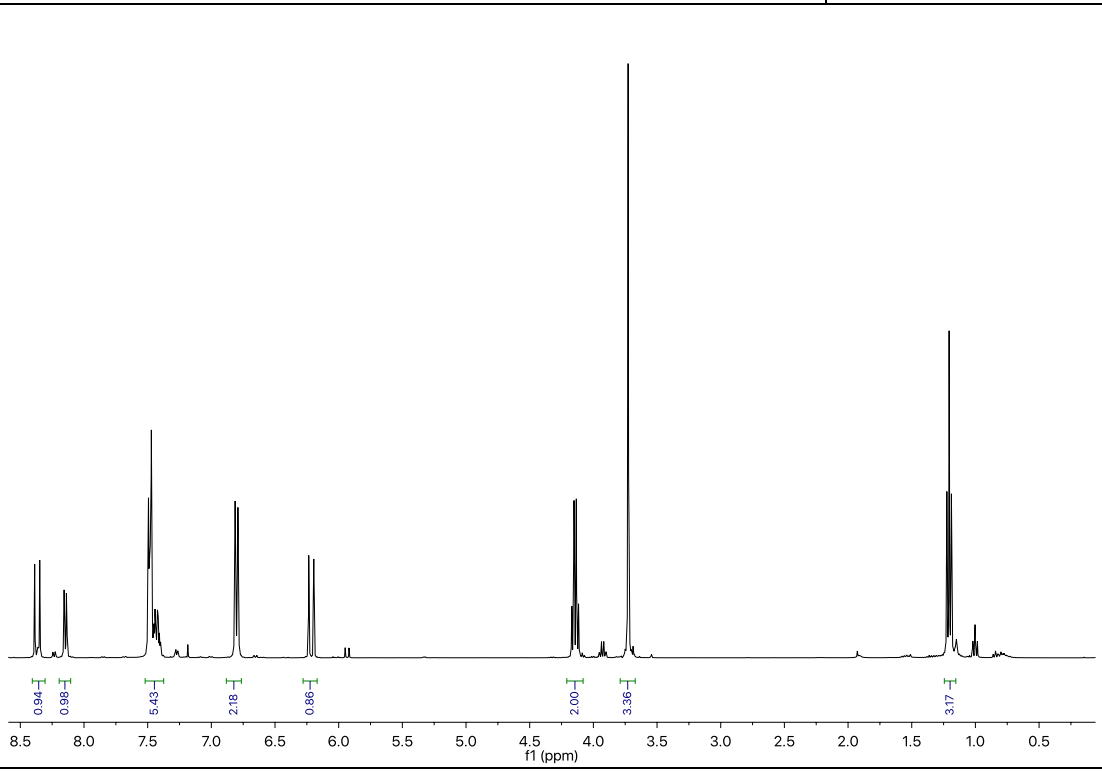


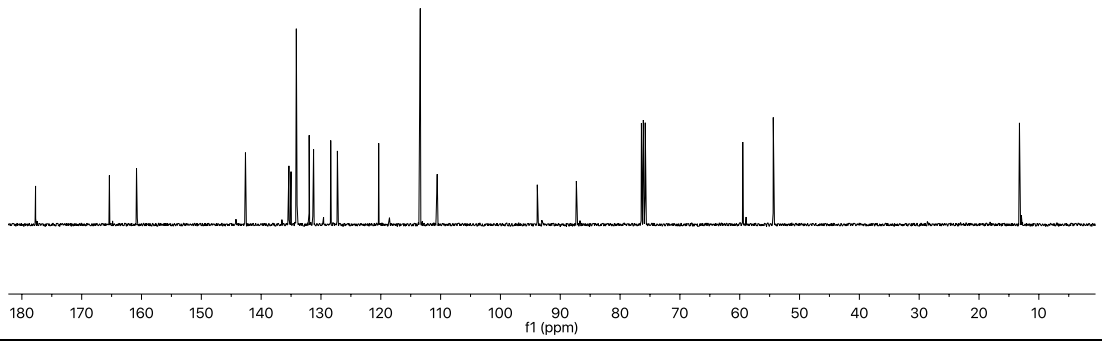




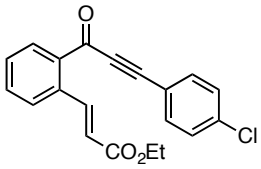
Ethyl (*E*)-3-(2-(3-(4-methoxyphenyl)propioloyl)phenyl)acrylate (1h)

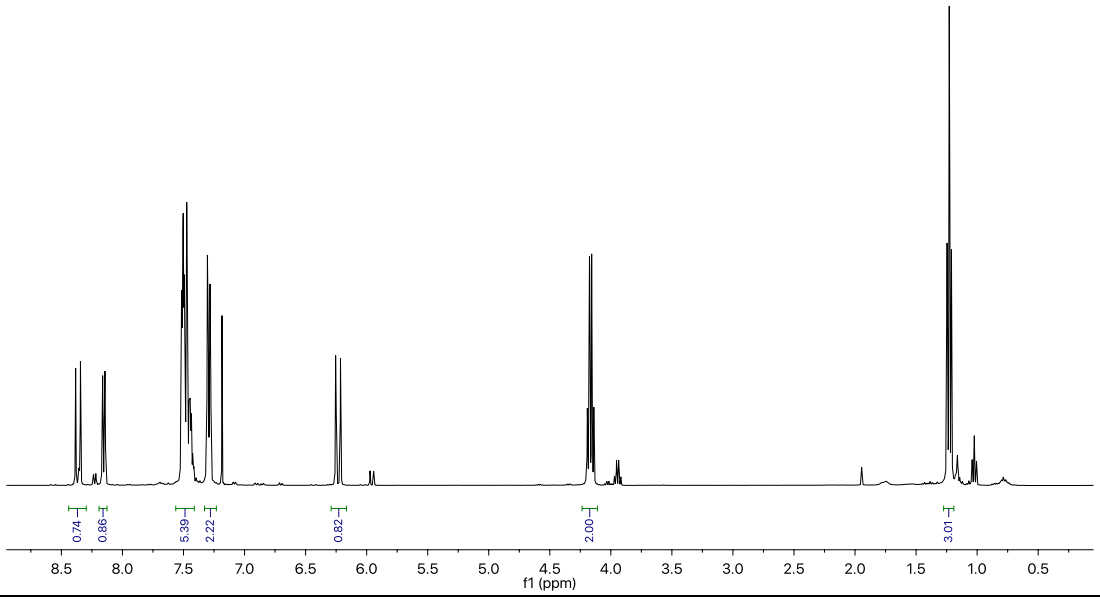


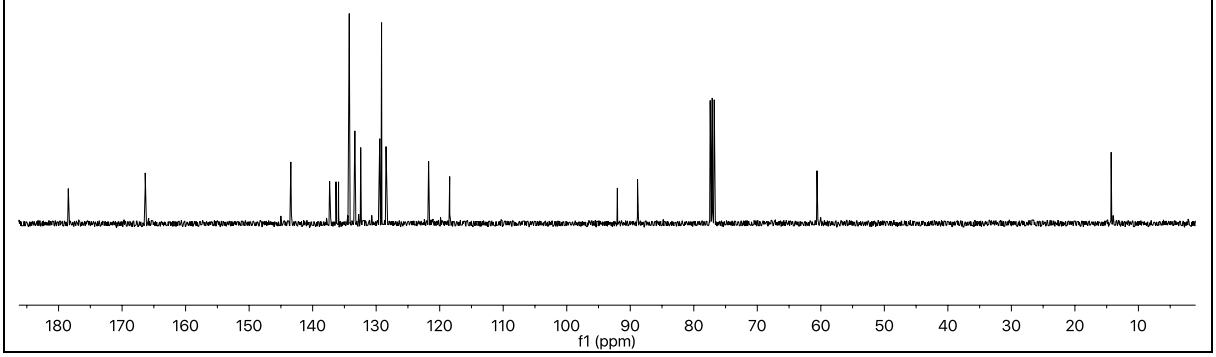




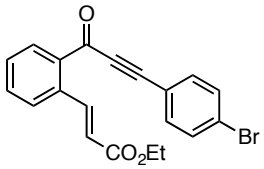
Ethyl (*E*)-3-(2-(3-(4-chlorophenyl)propioloyl)phenyl)acrylate (1i)

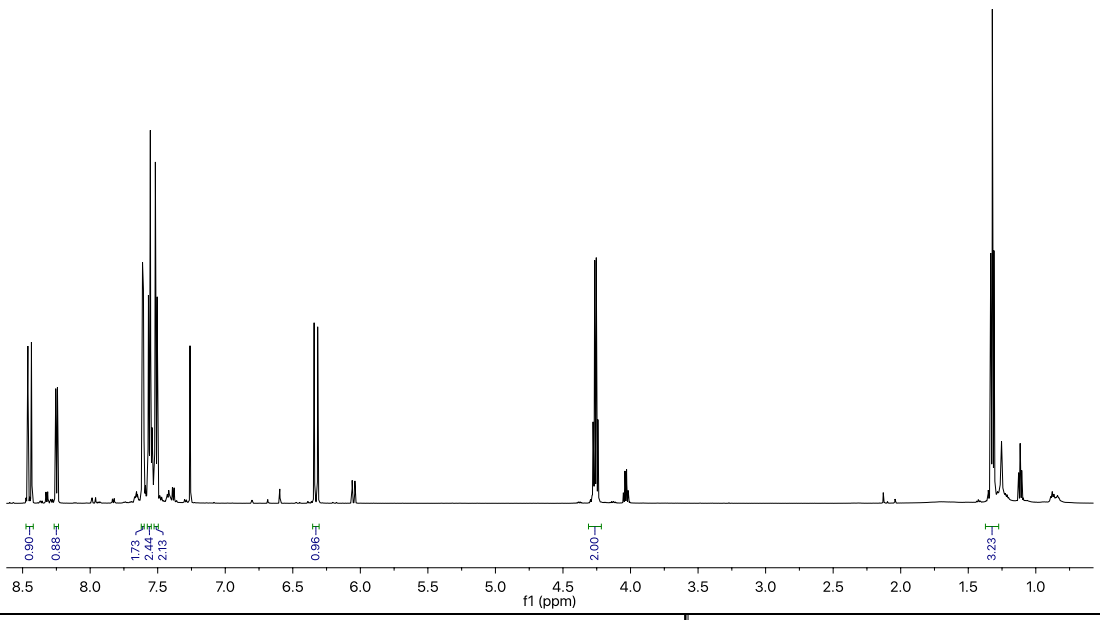


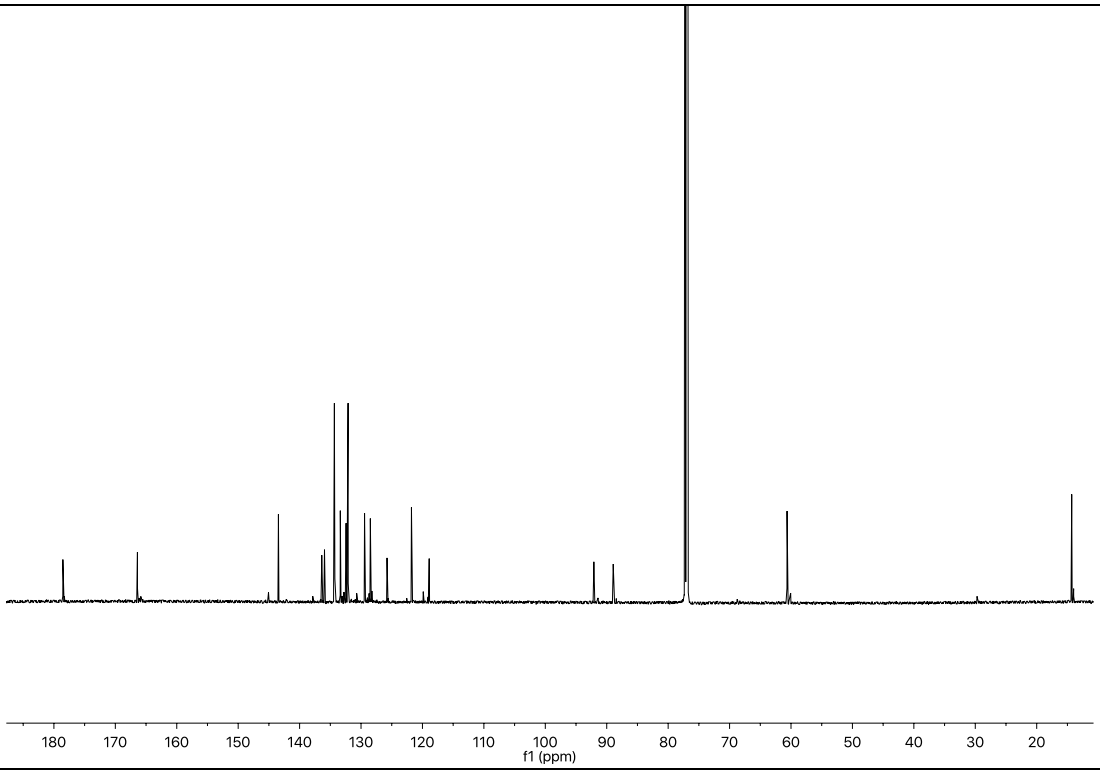




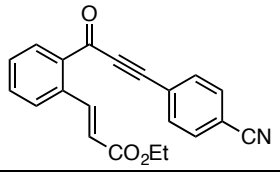
Ethyl (*E*)-3-(2-(3-(4-bromophenyl)propioloyl)phenyl)acrylate (1j)

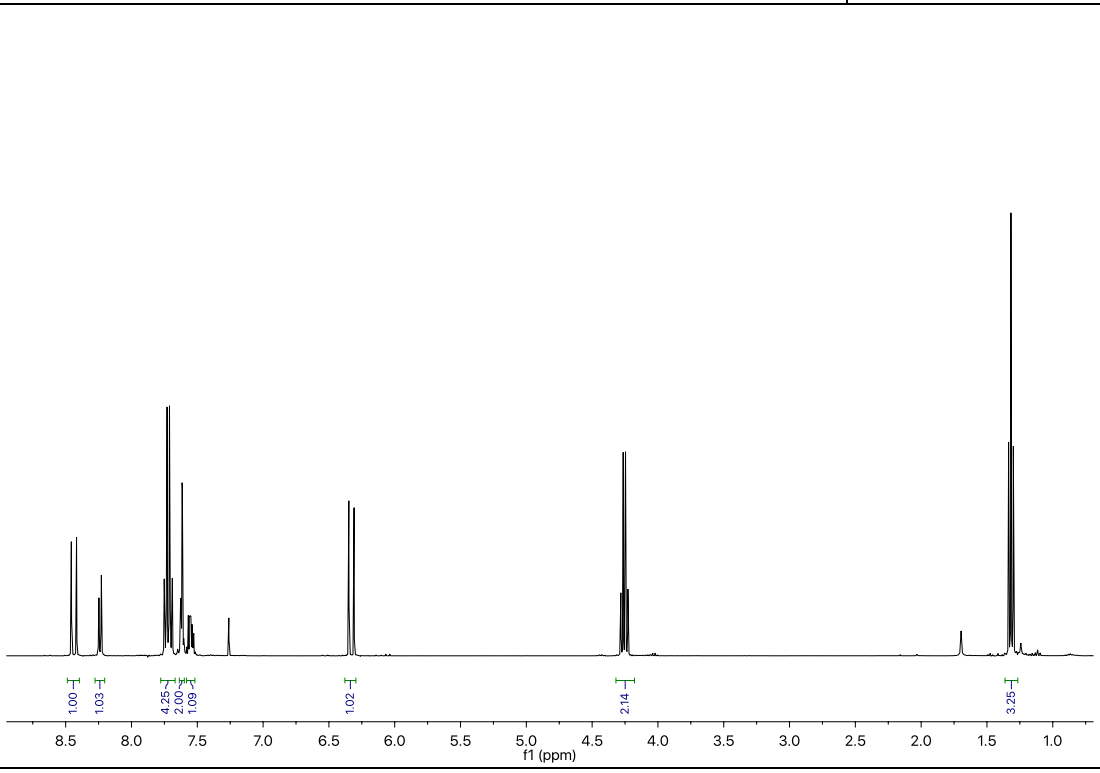


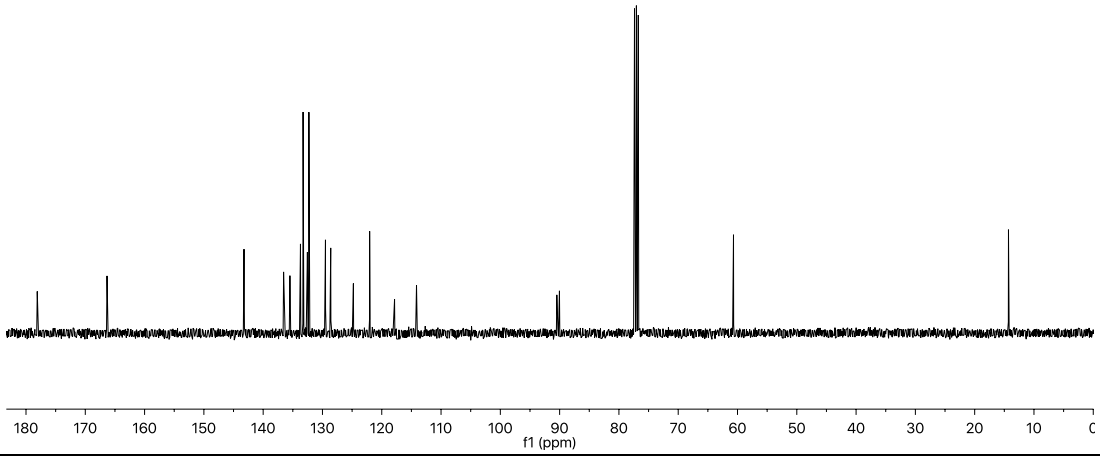




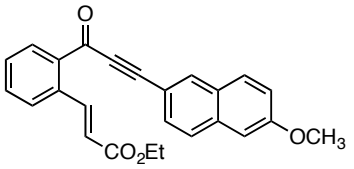
Ethyl (*E*)-3-(2-(3-(4-cyanophenyl)propioloyl)phenyl)acrylate (1k)

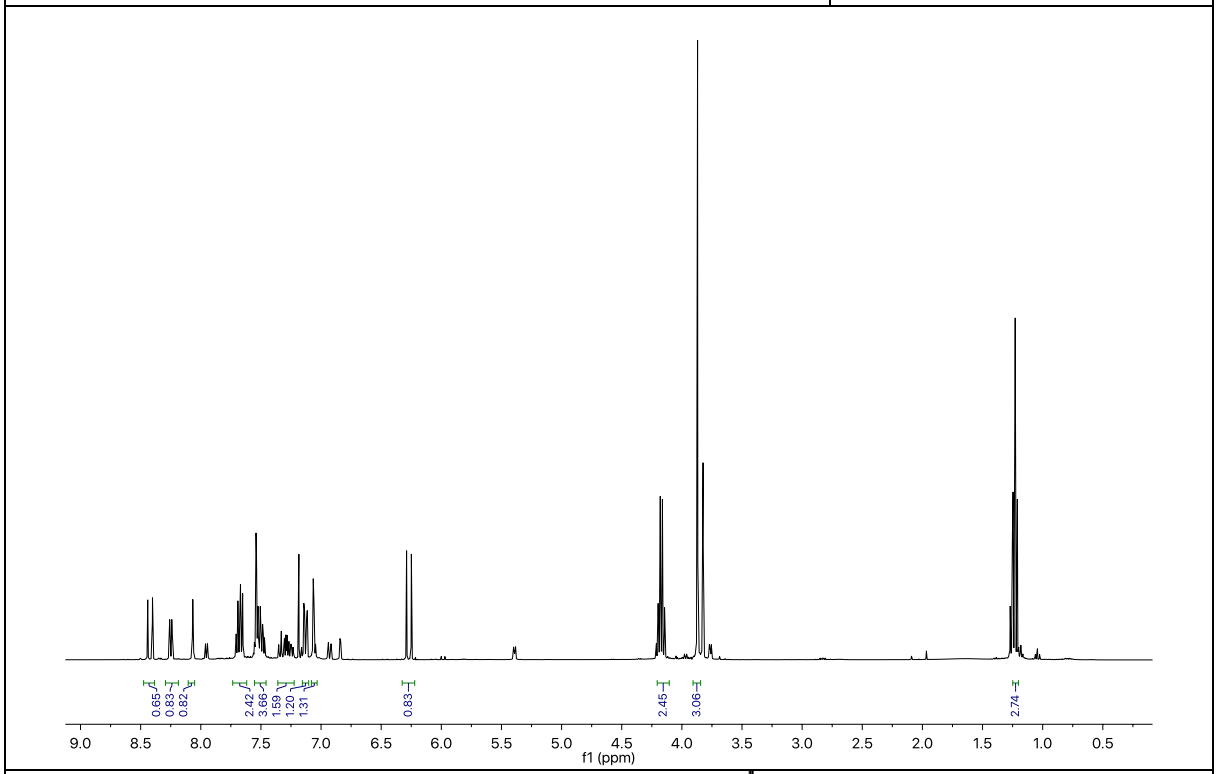


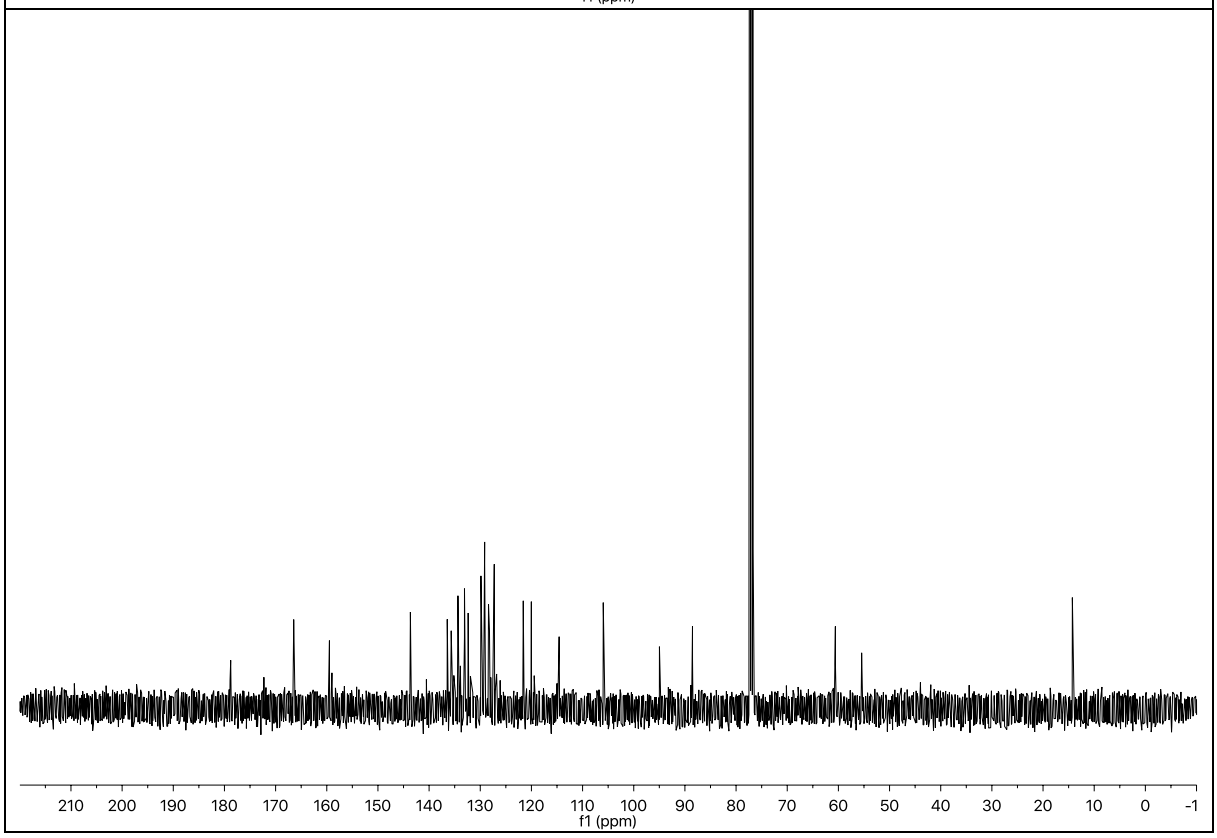




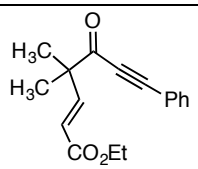
Ethyl (*E*)-3-(2-(3-(6-methoxynaphthalen-2-yl)propioloyl)phenyl)acrylate (1l)

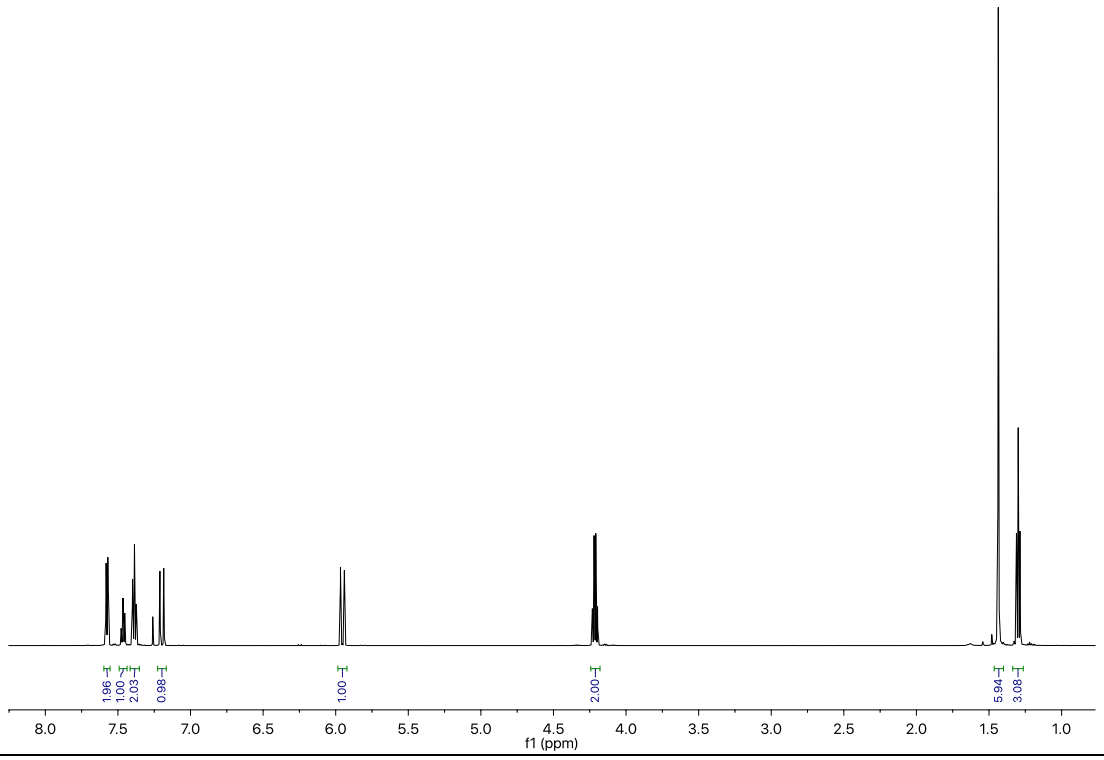


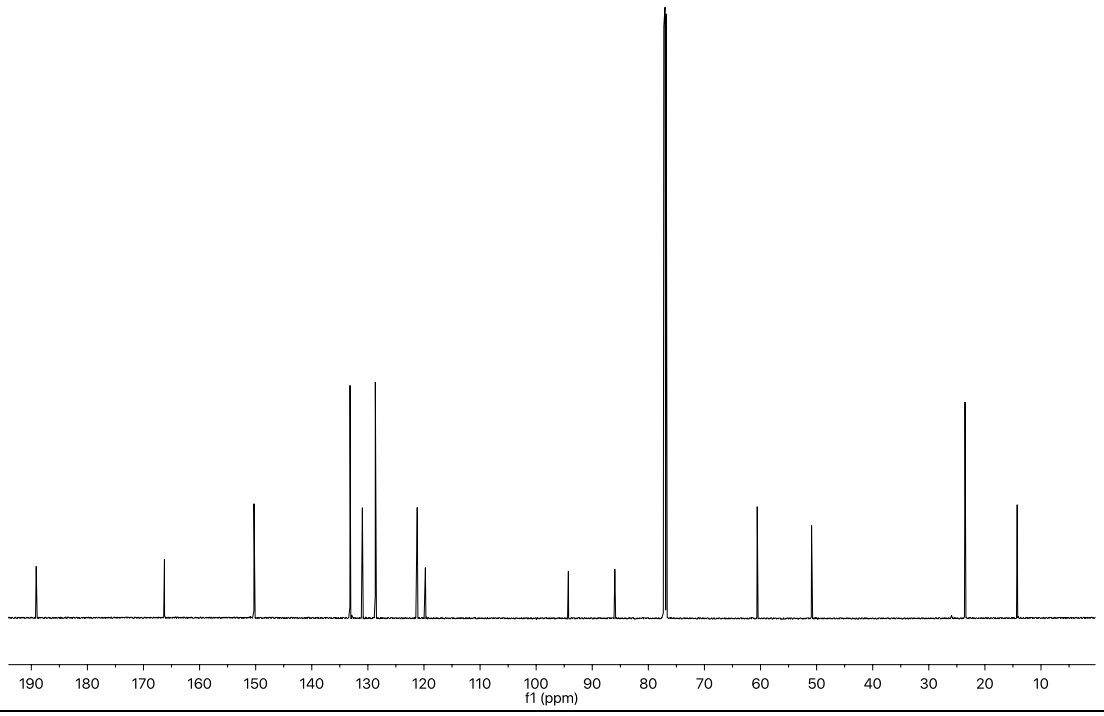




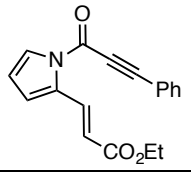
Ethyl (*E*)-4,4-dimethyl-5-oxo-7-phenylhept-2-en-6-ynoate (1m)

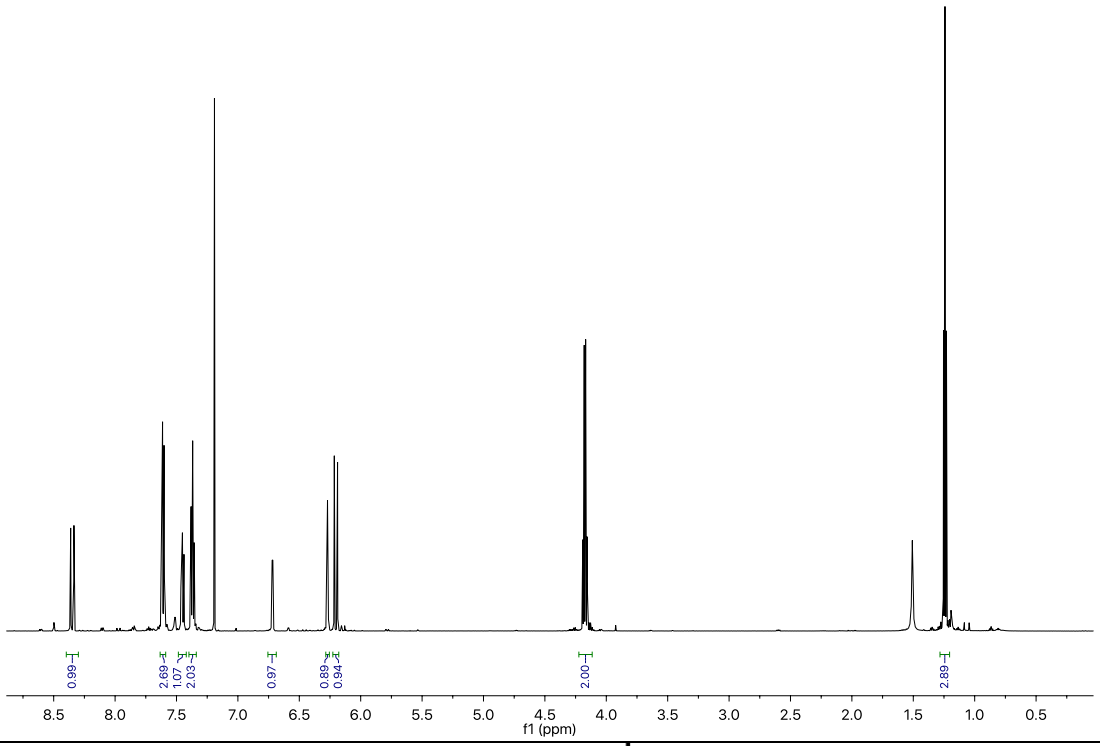


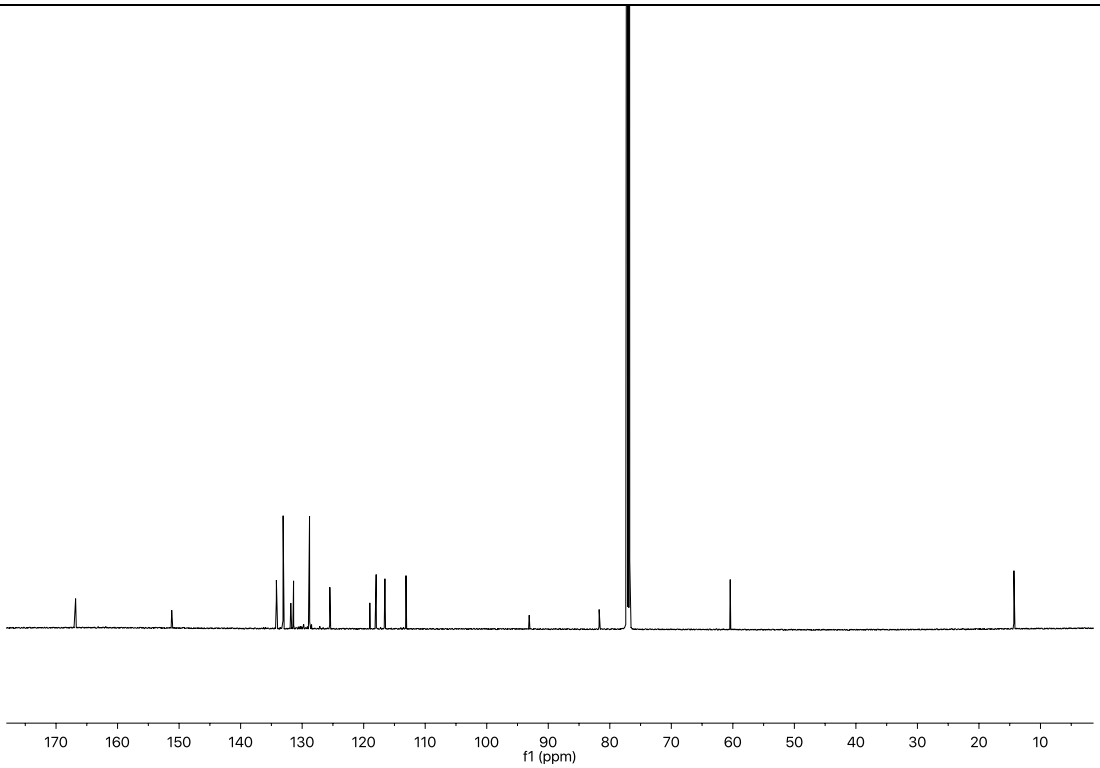




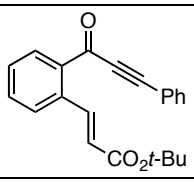
Ethyl (*E*)-3-(1-(3-phenylpropioloyl)-1*H*-pyrrol-2-yl)acrylate (1n)

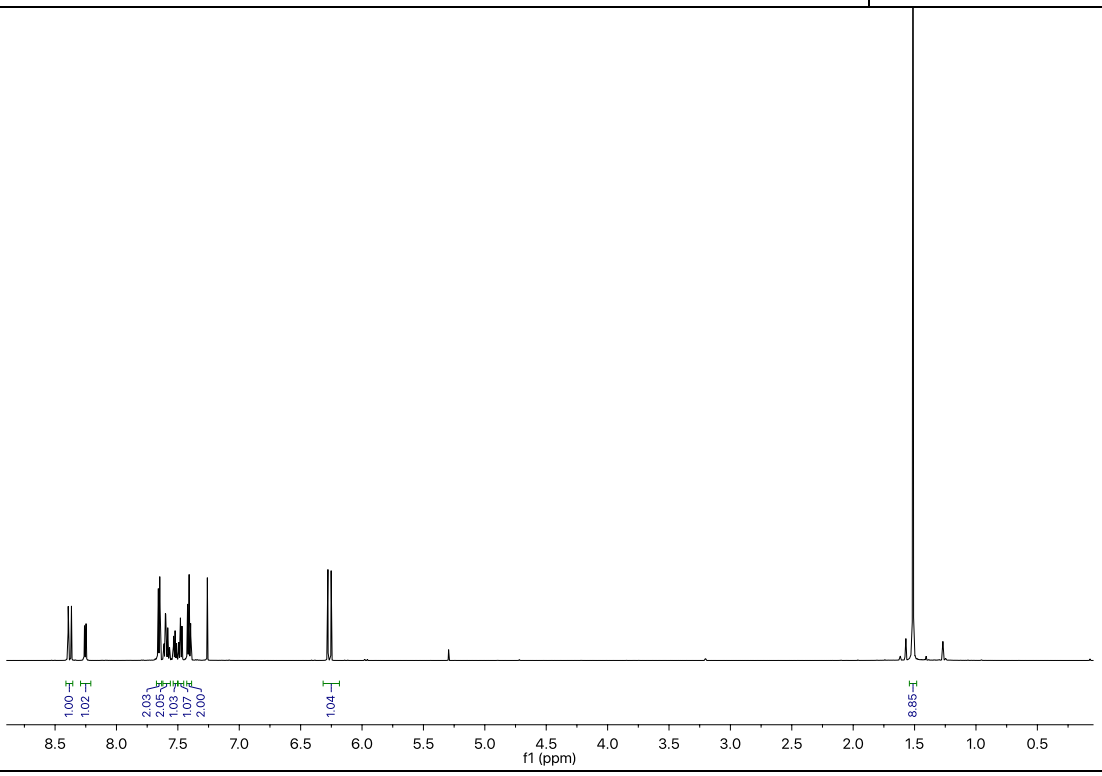


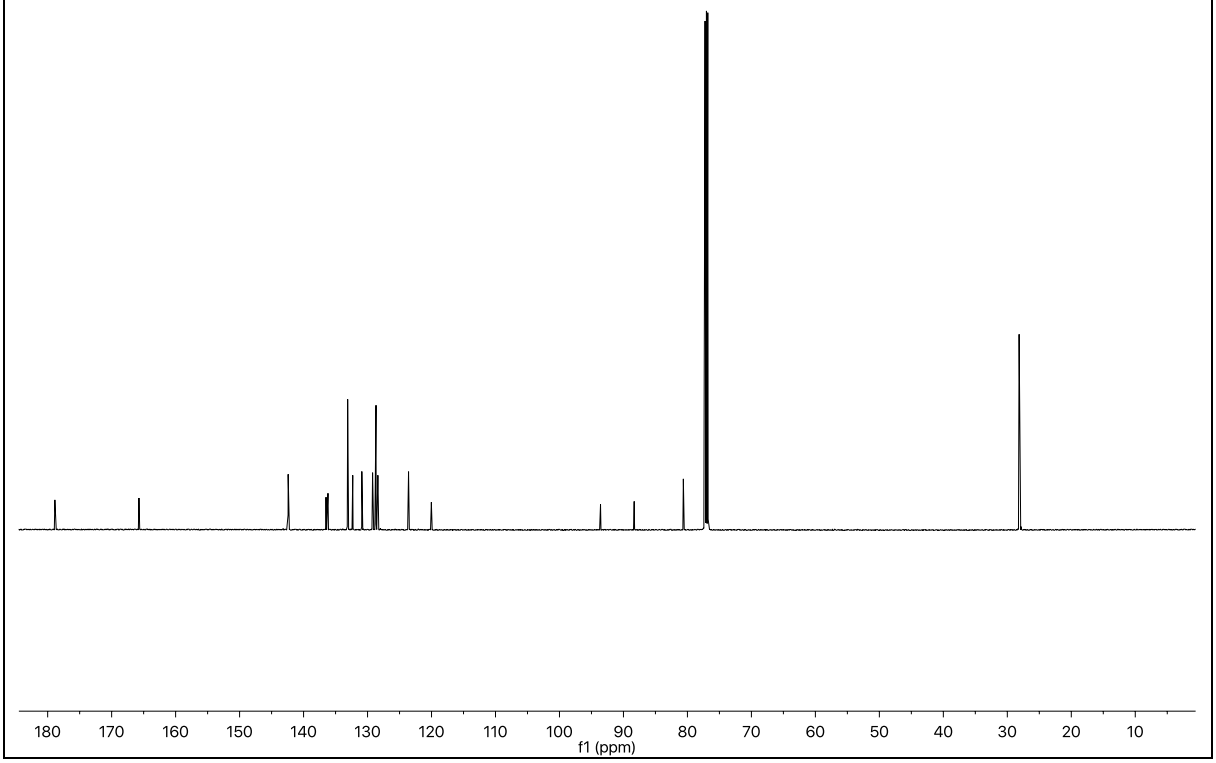




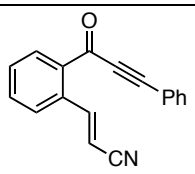
***tert*-Butyl (*E*)-3-(2-(3-phenylpropioloyl)phenyl)acrylate (1o)**

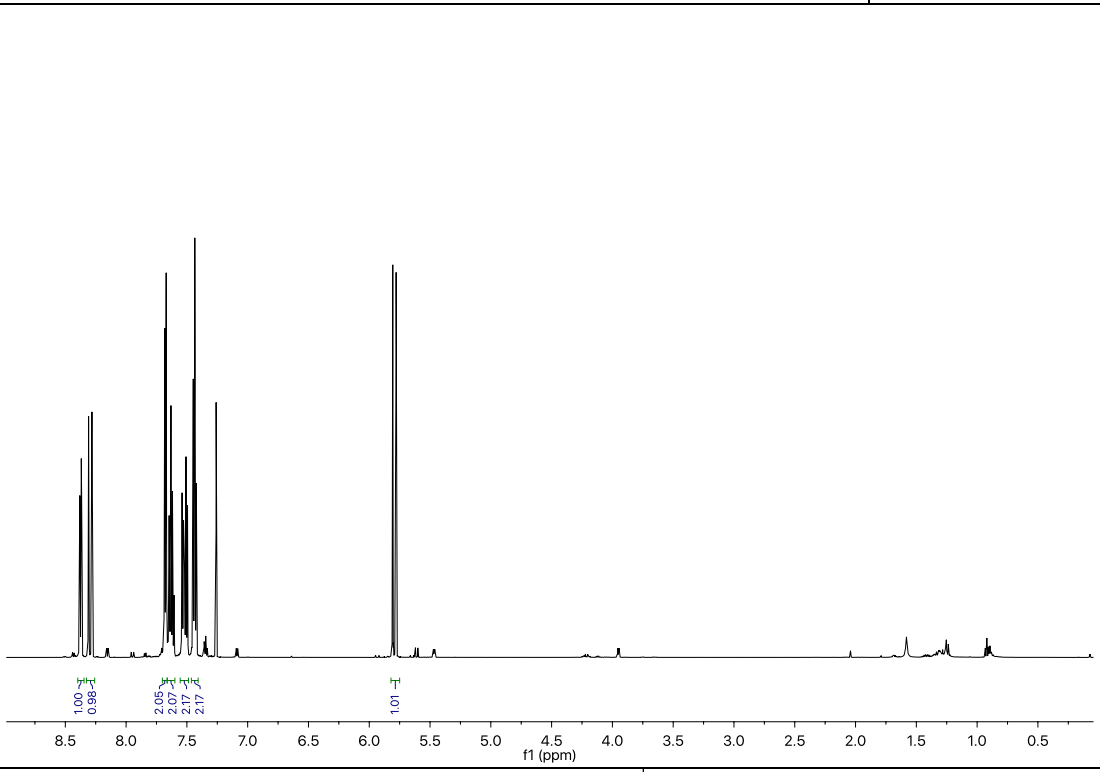


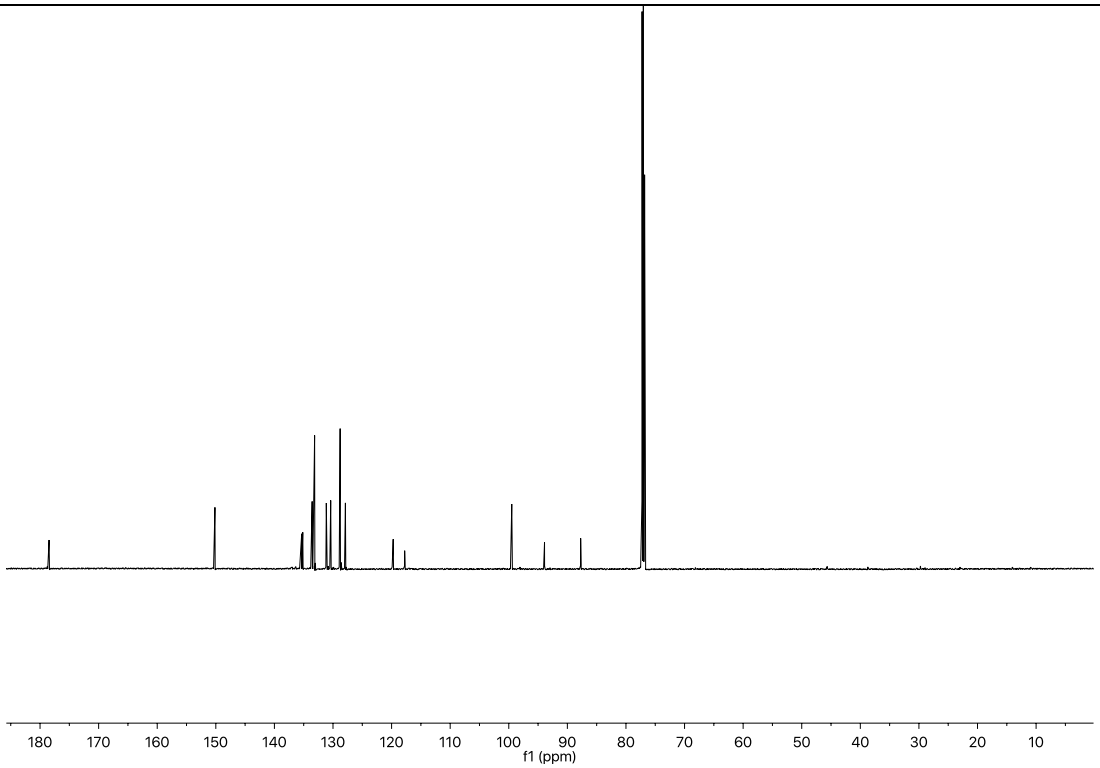




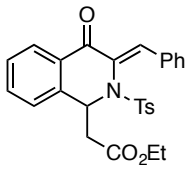
(*E*)-3-(2-(3-phenylpropioloyl)phenyl)acrylonitrile (1p)

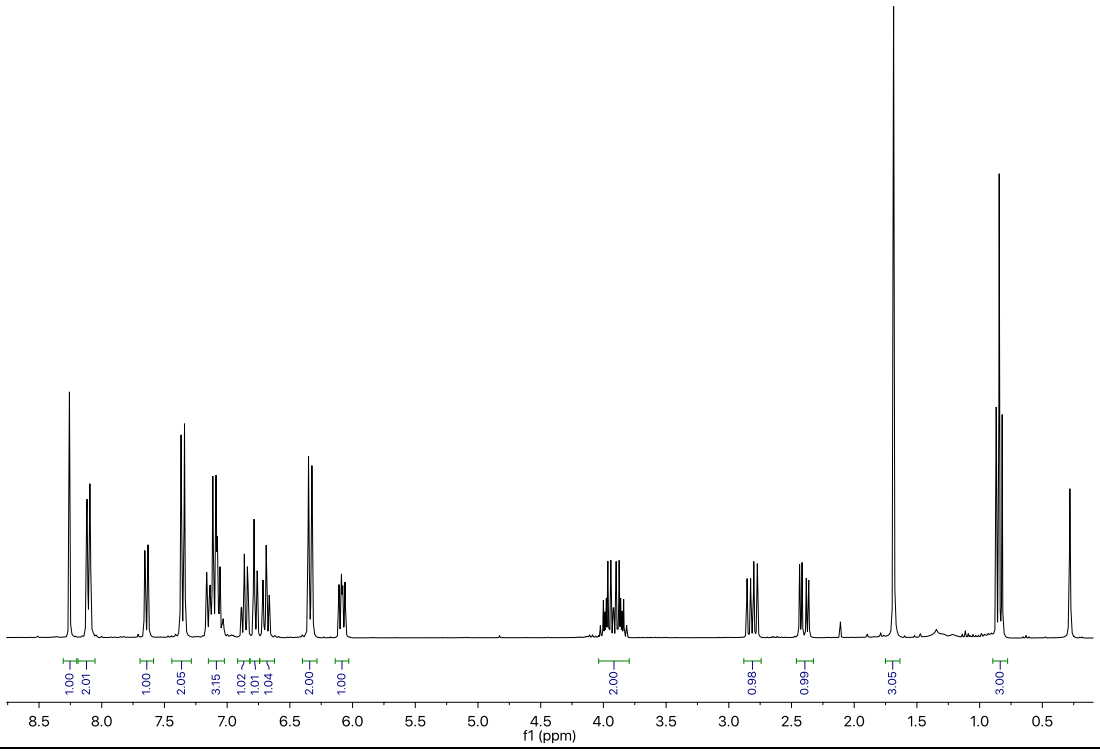


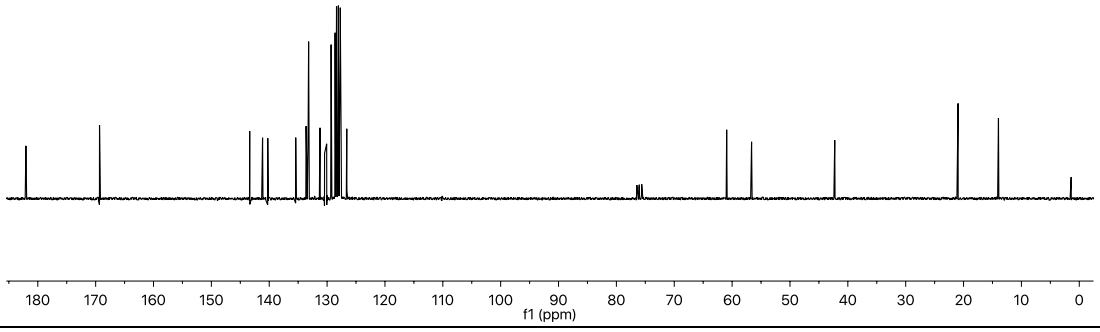




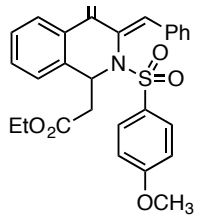
Ethyl (*Z*)-2-(3-benzylidene-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2a)

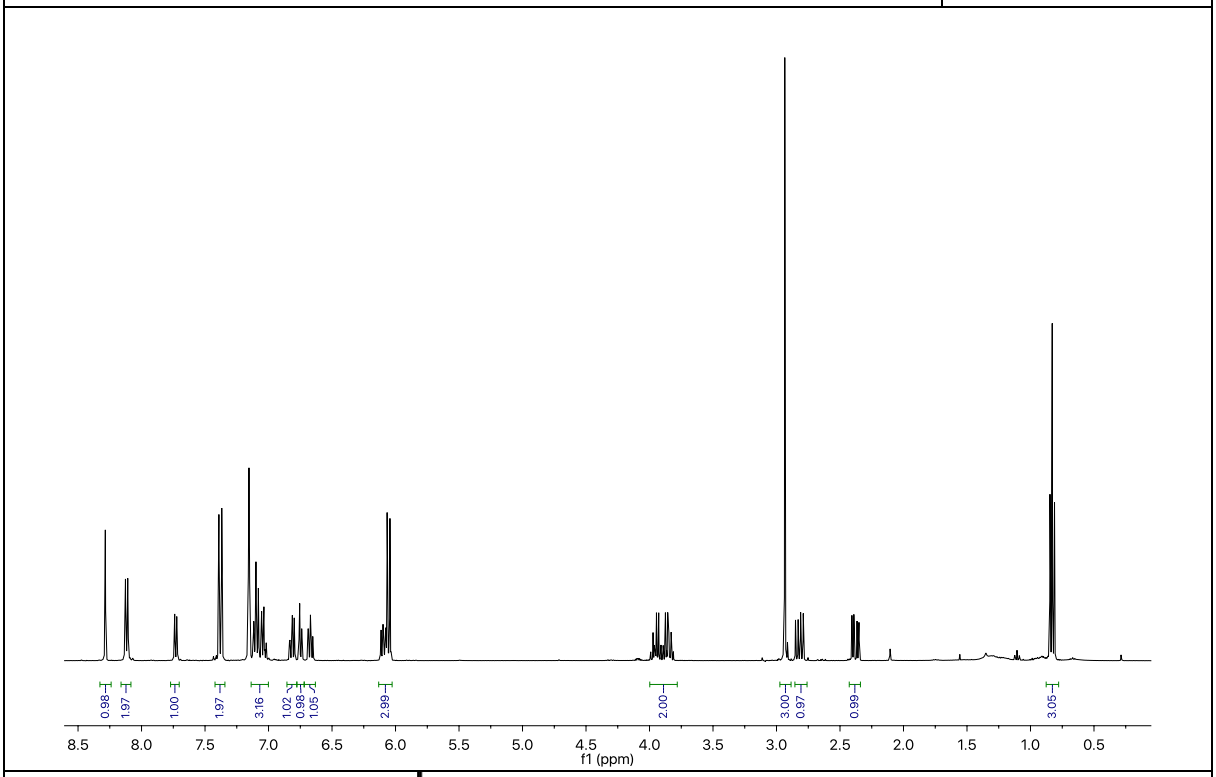


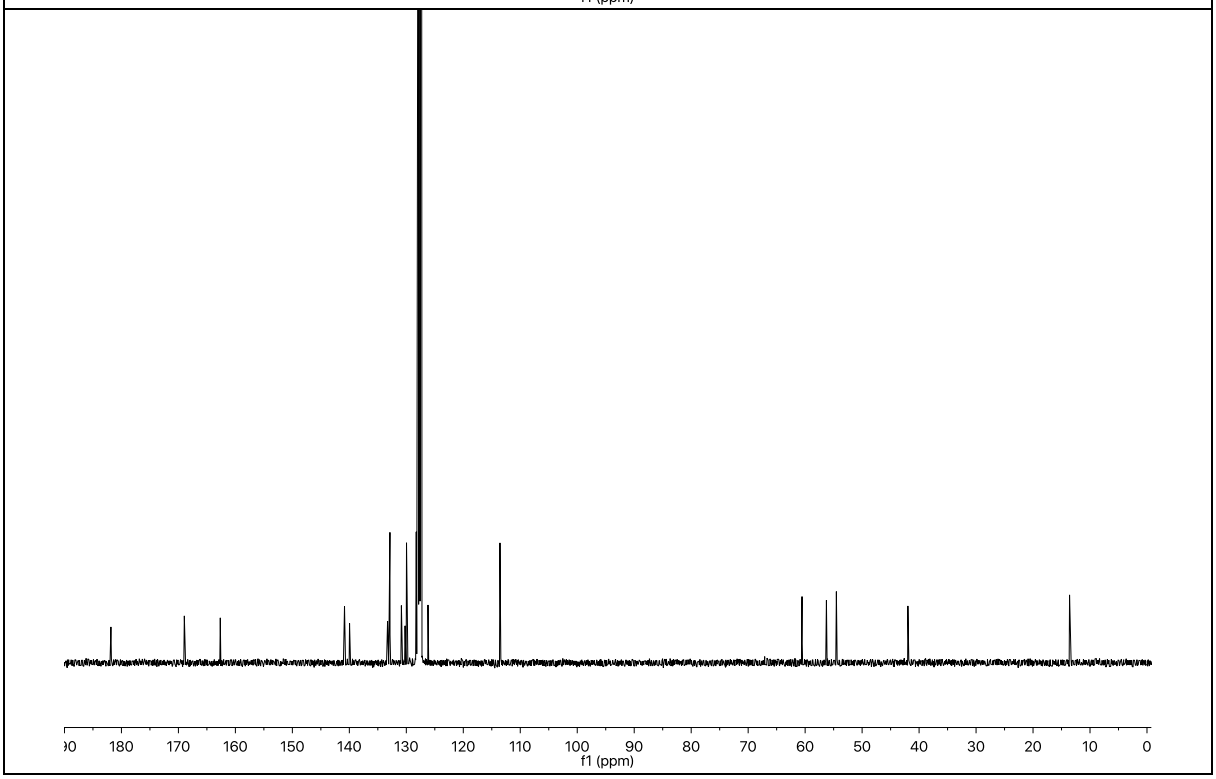




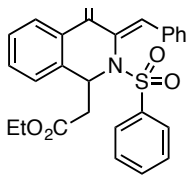
tetrahydroisoquinolin-1-yl)acetate (2b)

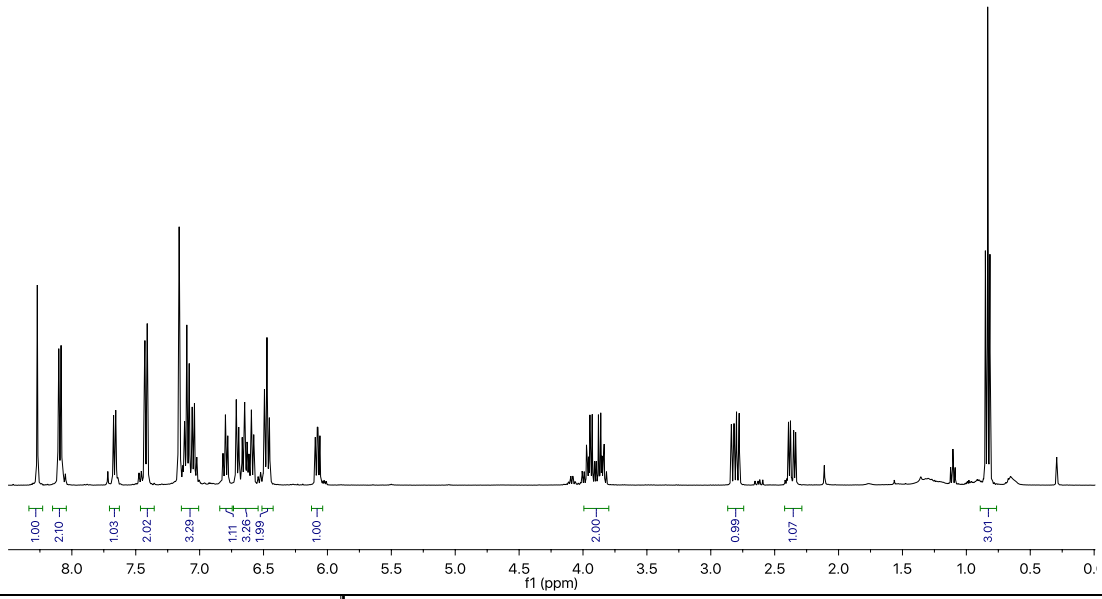


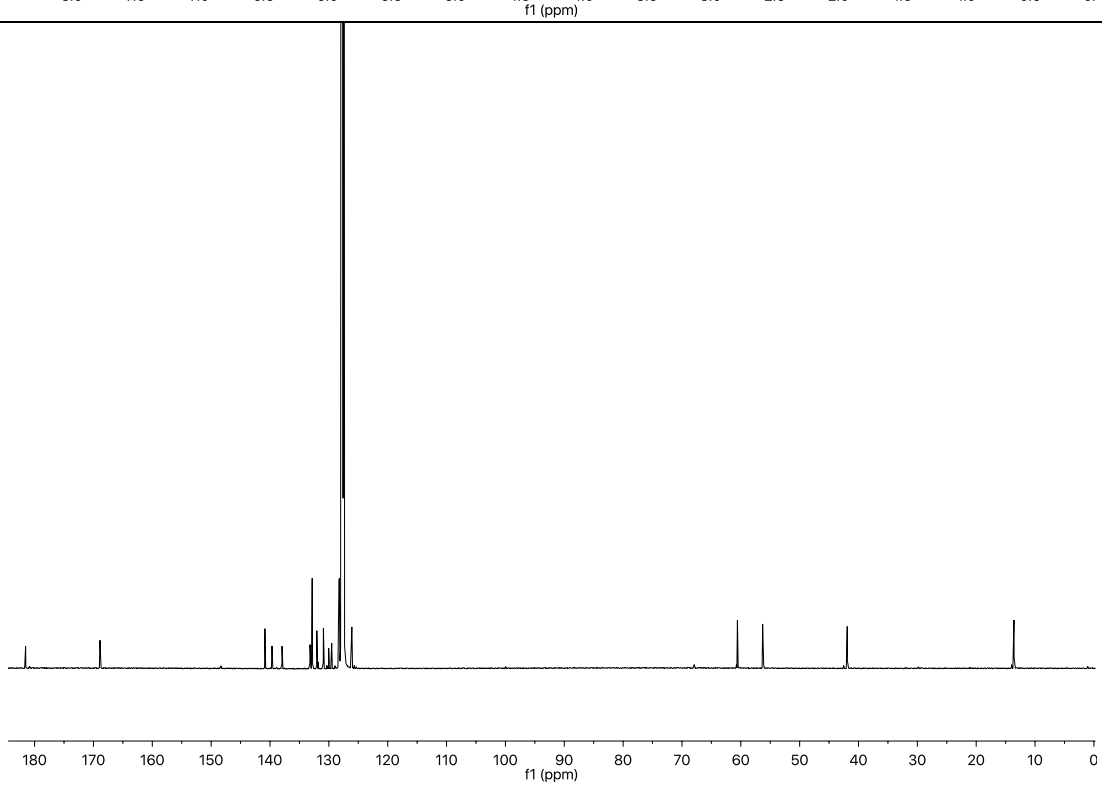




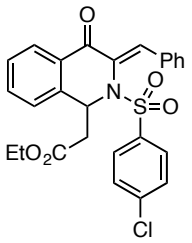
Ethyl (*Z*)-2-(3-benzylidene-4-oxo-2-(phenylsulfonyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2c)

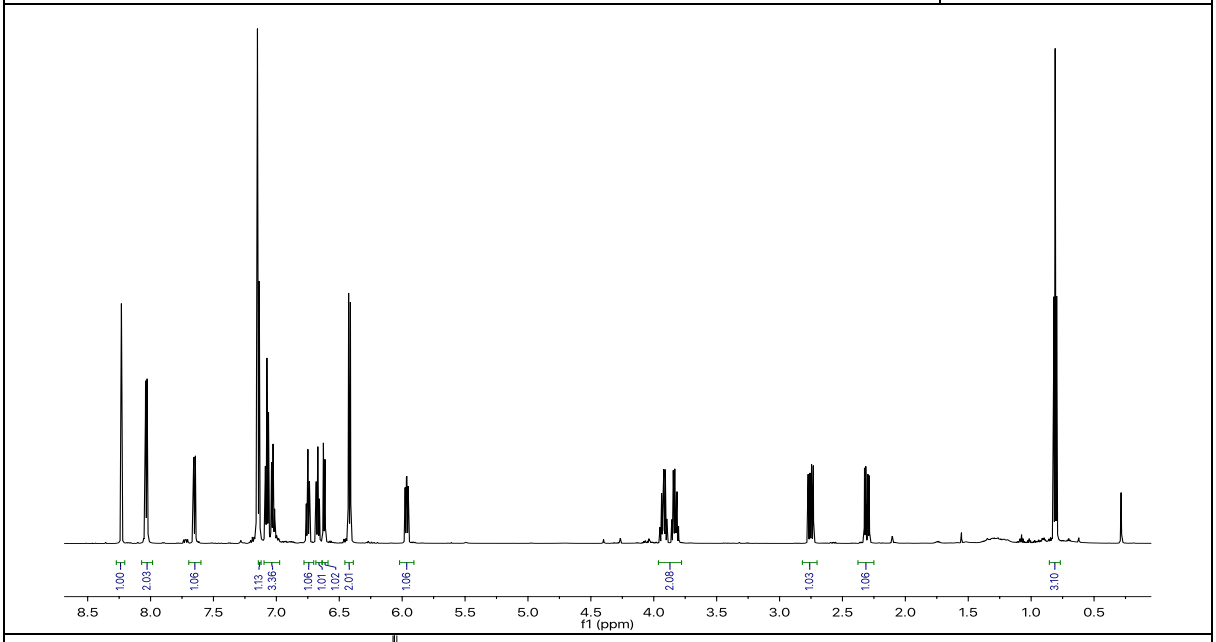


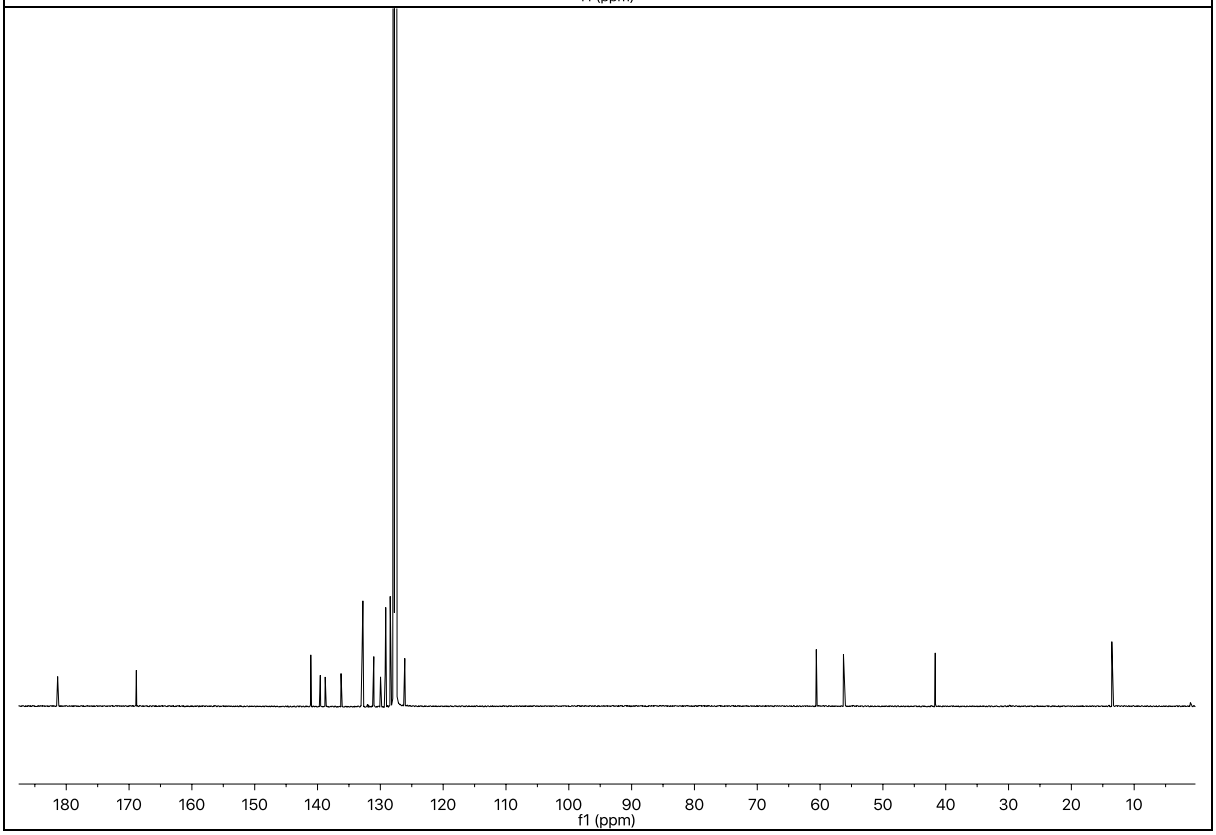




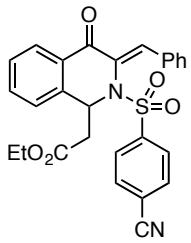
Ethyl (*Z*)-2-(3-benzylidene-2-((4-chlorophenyl)sulfonyl)-4-oxo-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2d)

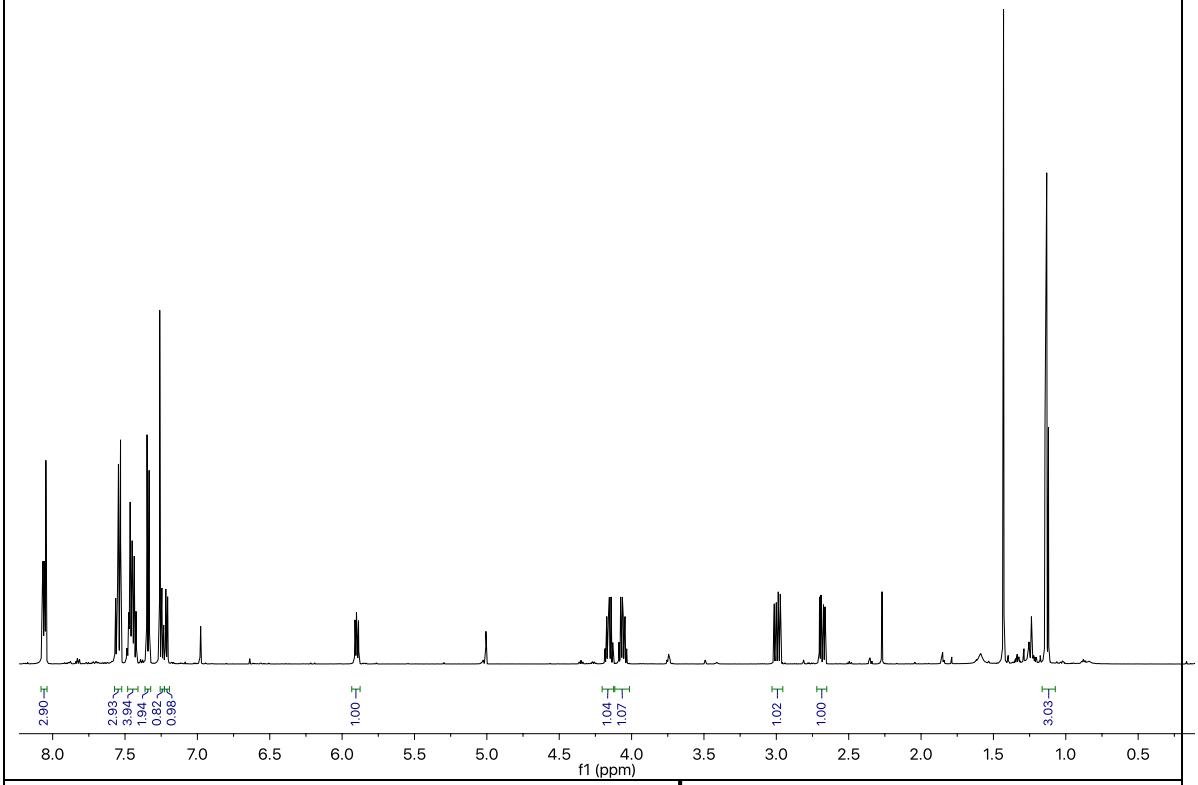


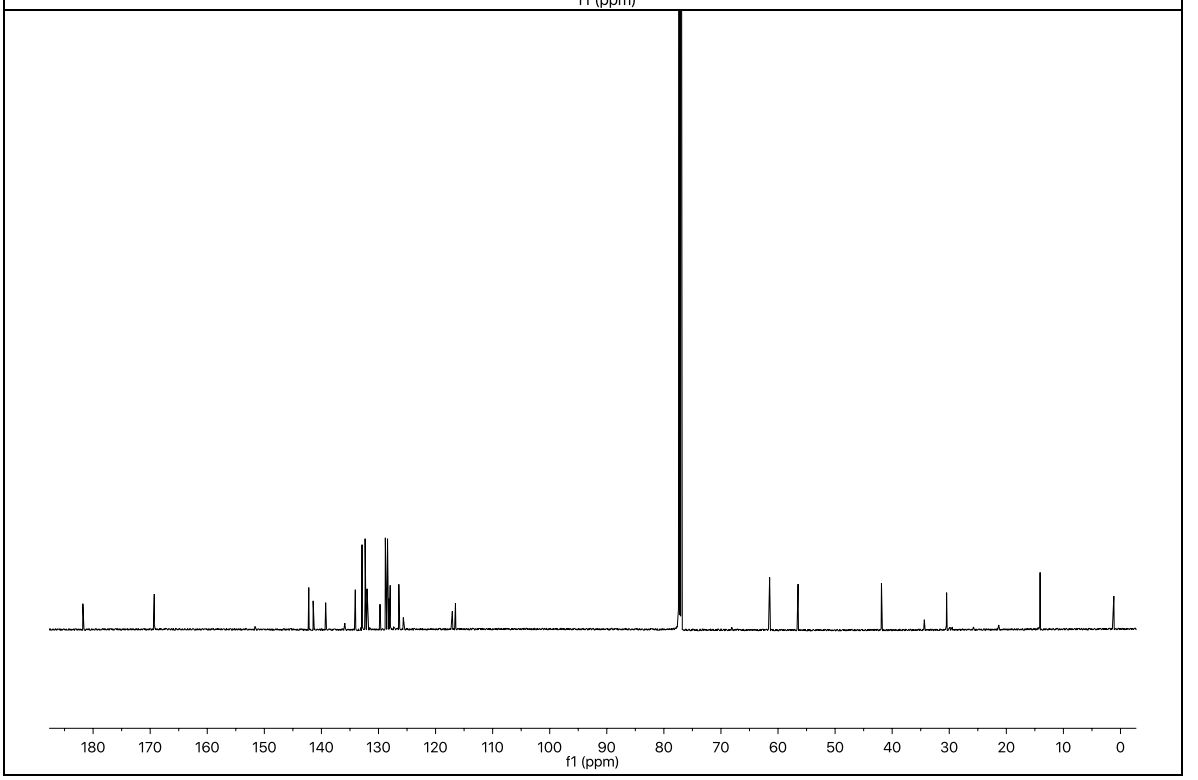




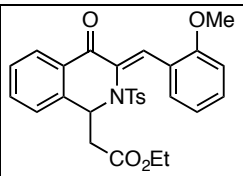
Ethyl (*Z*)-2-(3-benzylidene-2-((4-cyanophenyl)sulfonyl)-4-oxo-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2e)

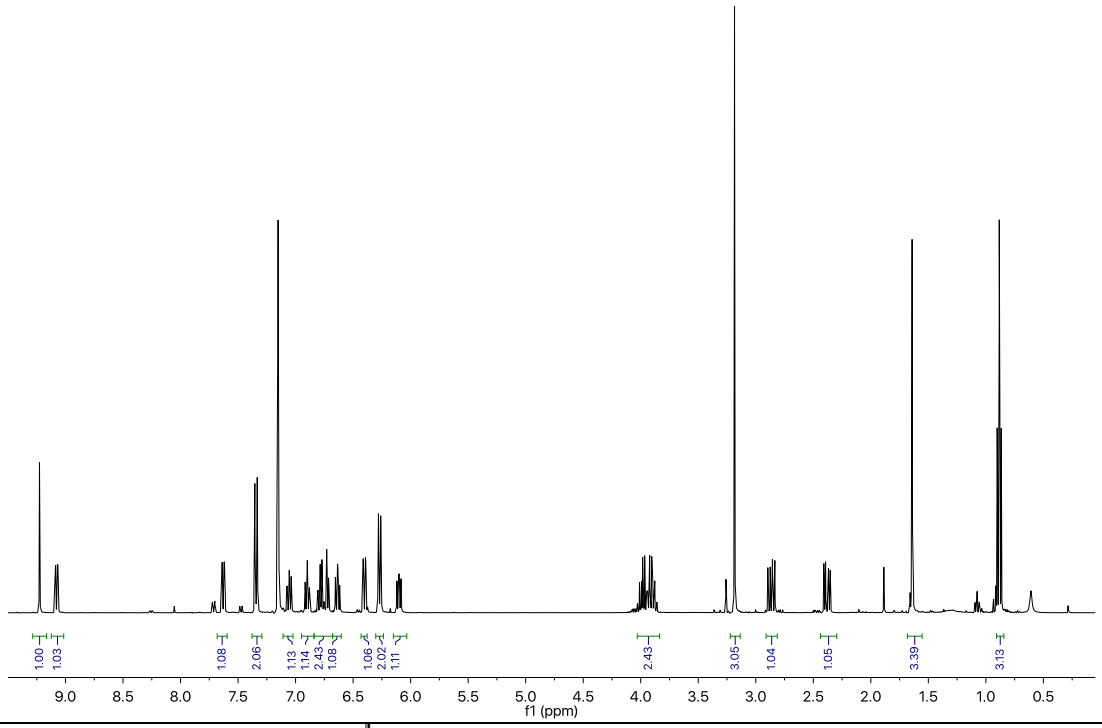


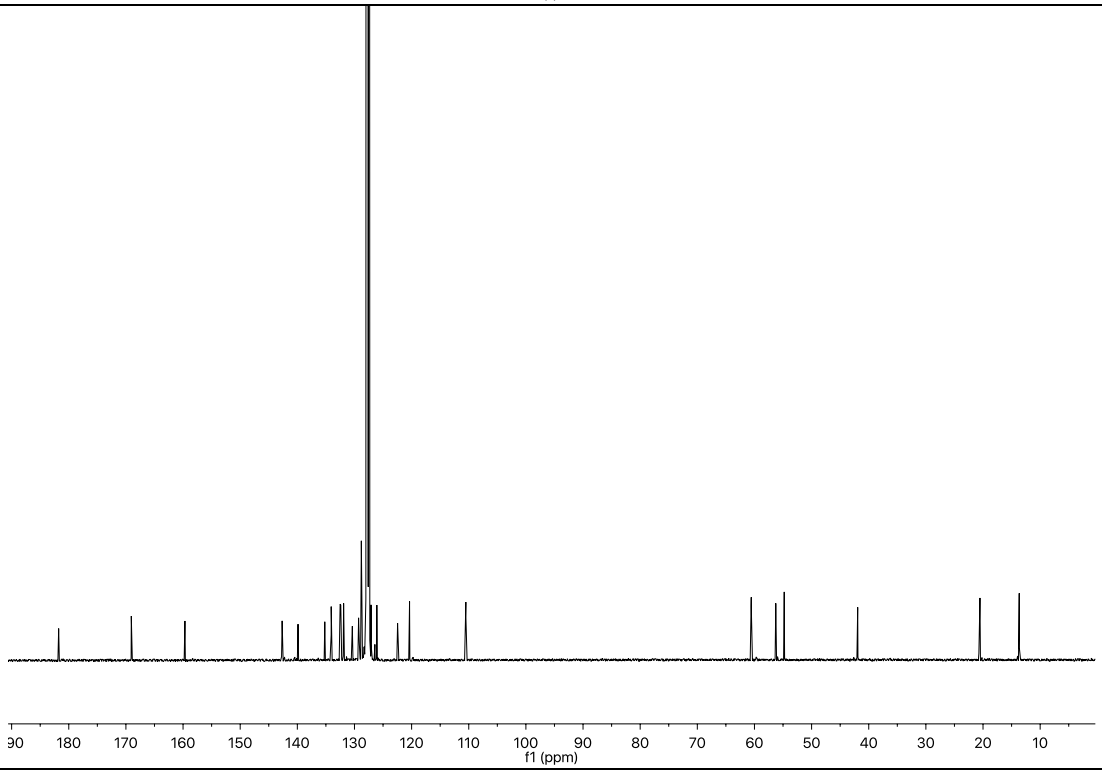




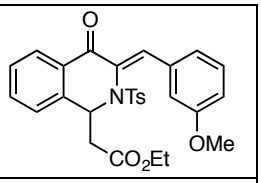
Ethyl (*Z*)-2-(3-(2-methoxybenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2f)

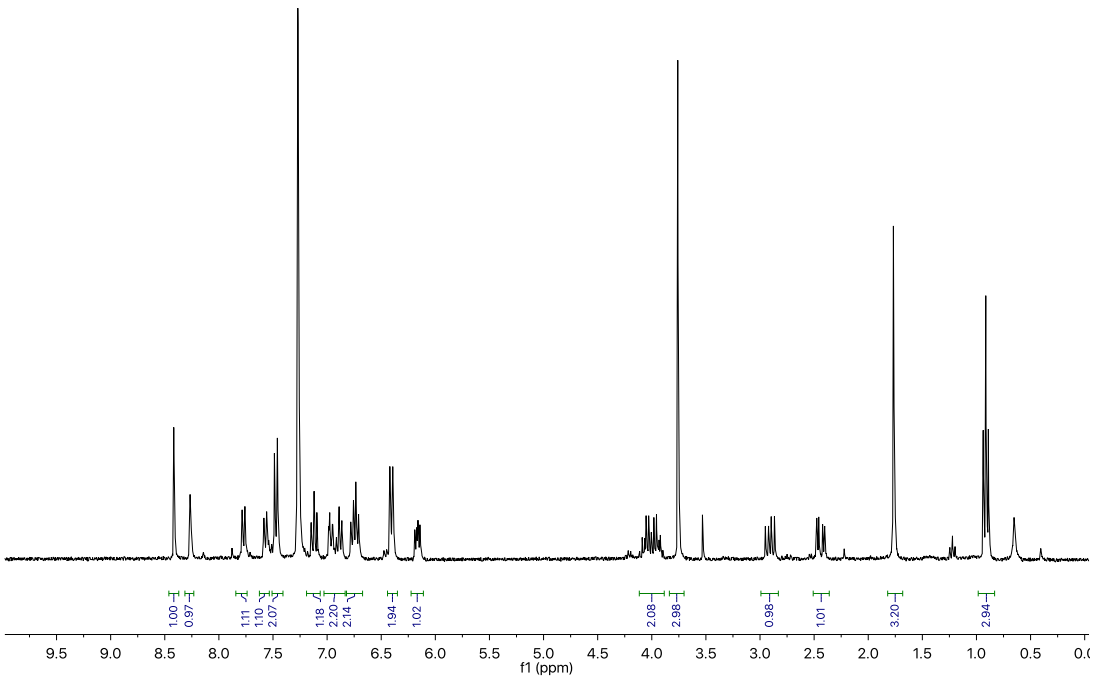


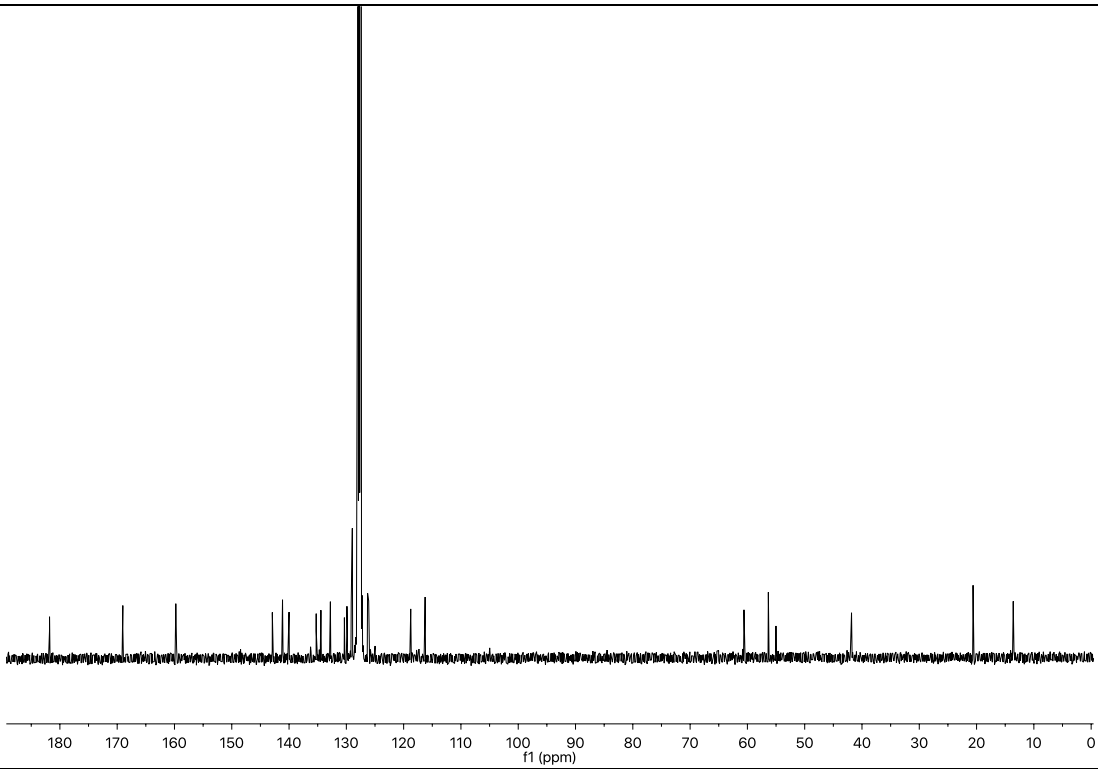




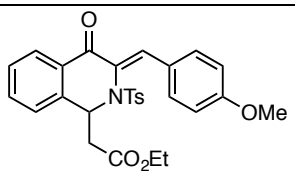
Ethyl (*Z*)-2-(3-(3-methoxybenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2g)

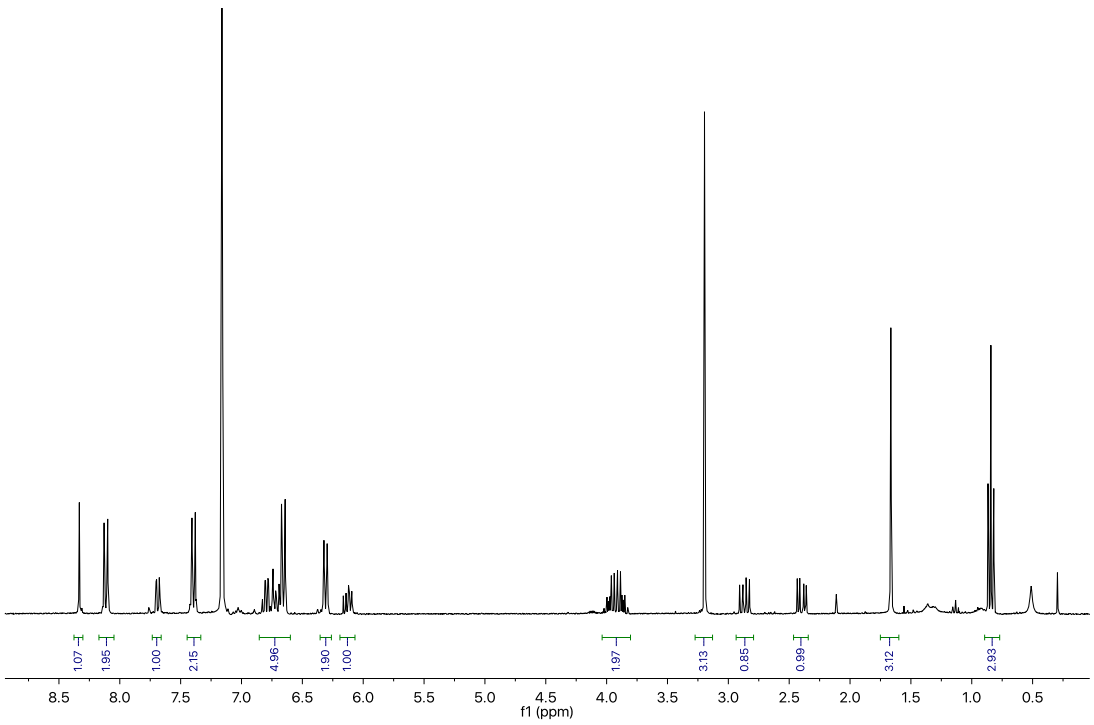


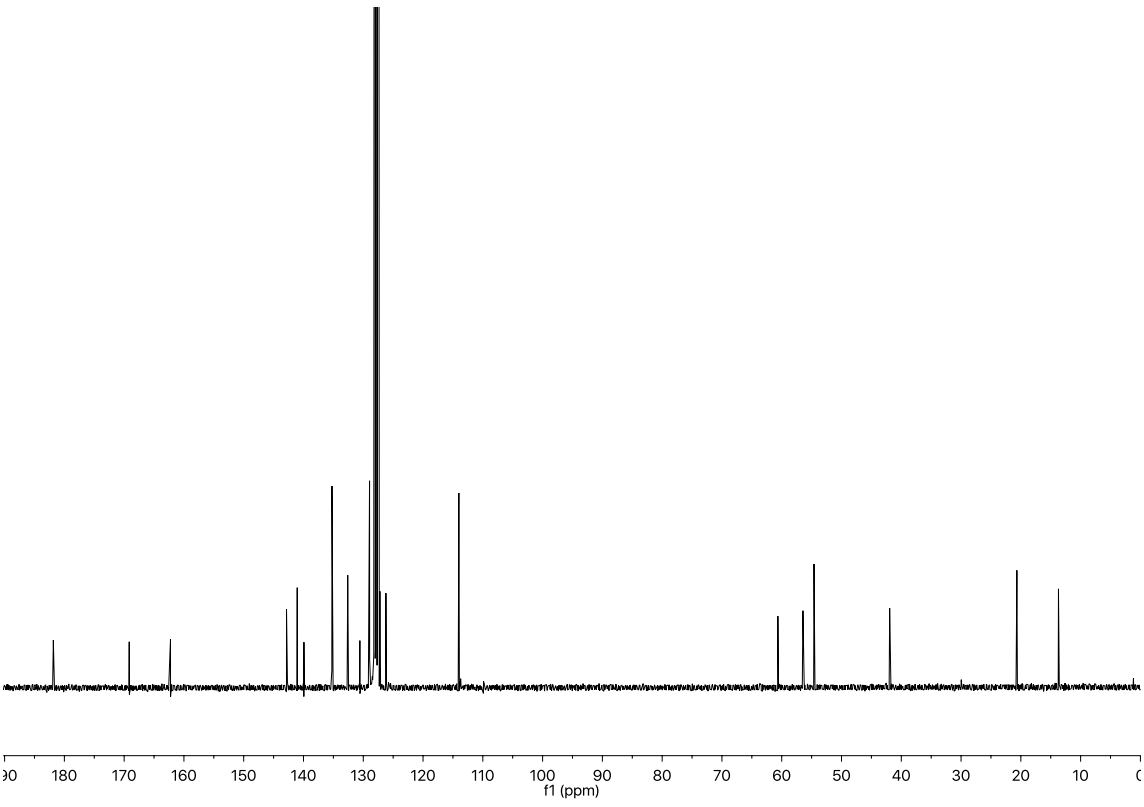




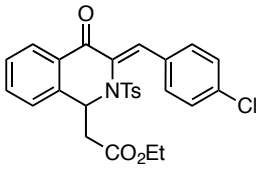
Ethyl (*Z*)-2-(3-(4-methoxybenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2h)

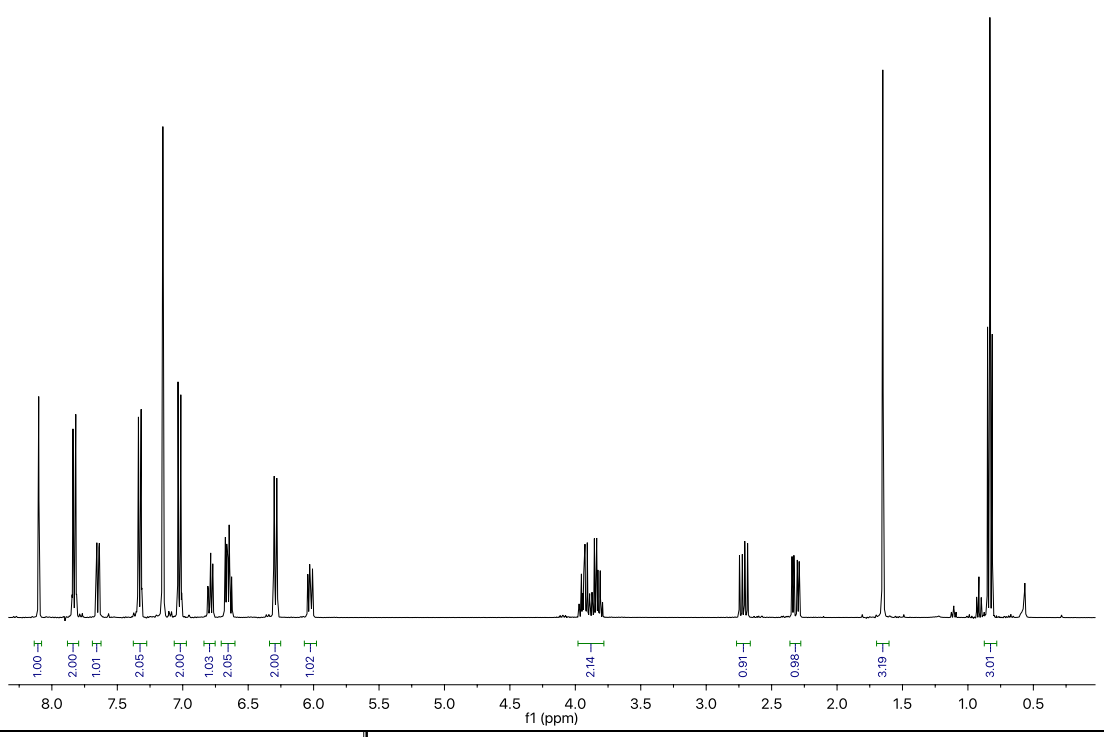


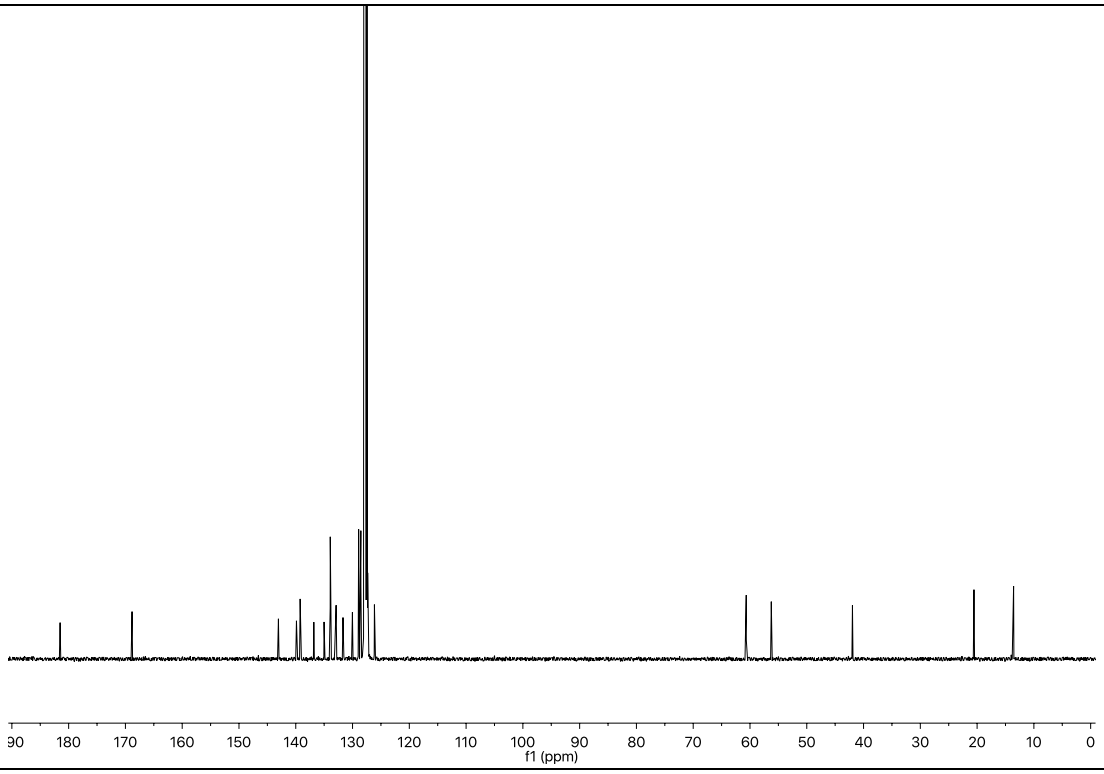




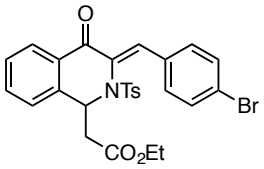
Ethyl (*Z*)-2-(3-(4-chlorobenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2i)

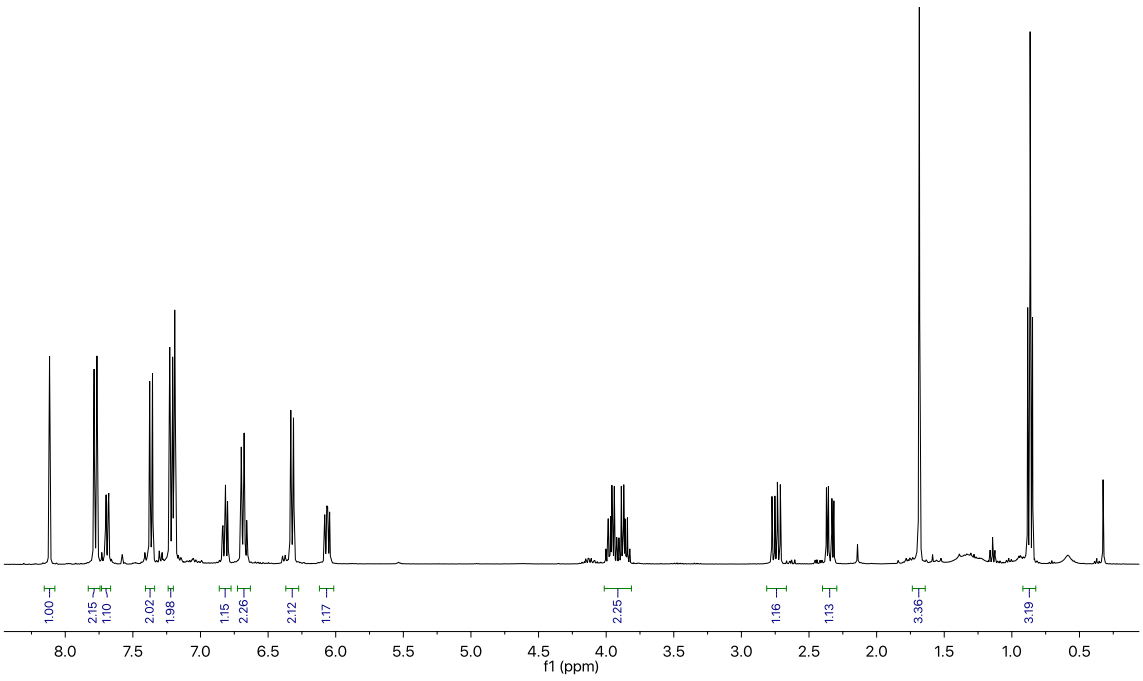


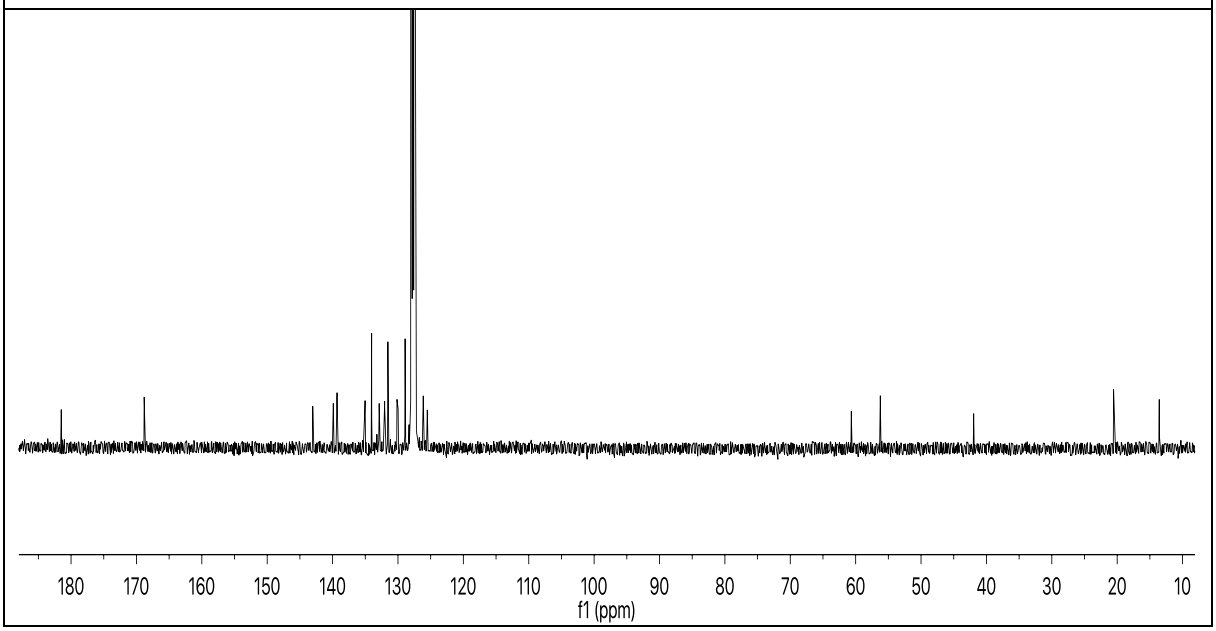




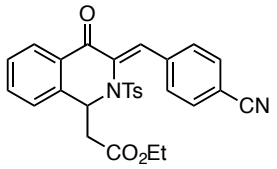
Ethyl (*Z*)-2-(3-(4-bromobenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2j)

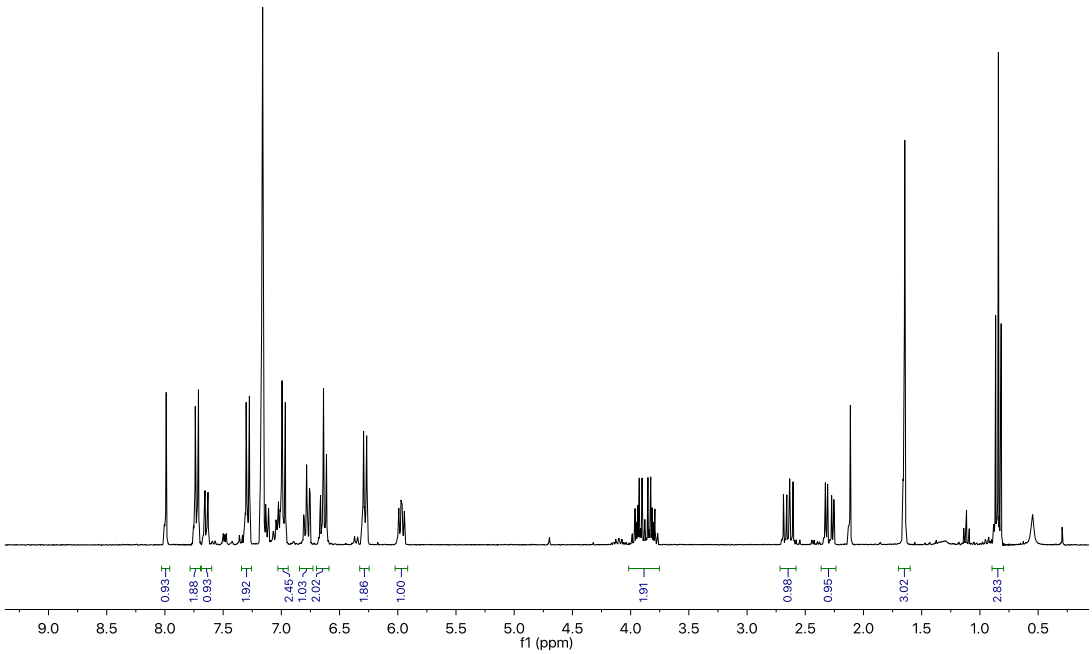


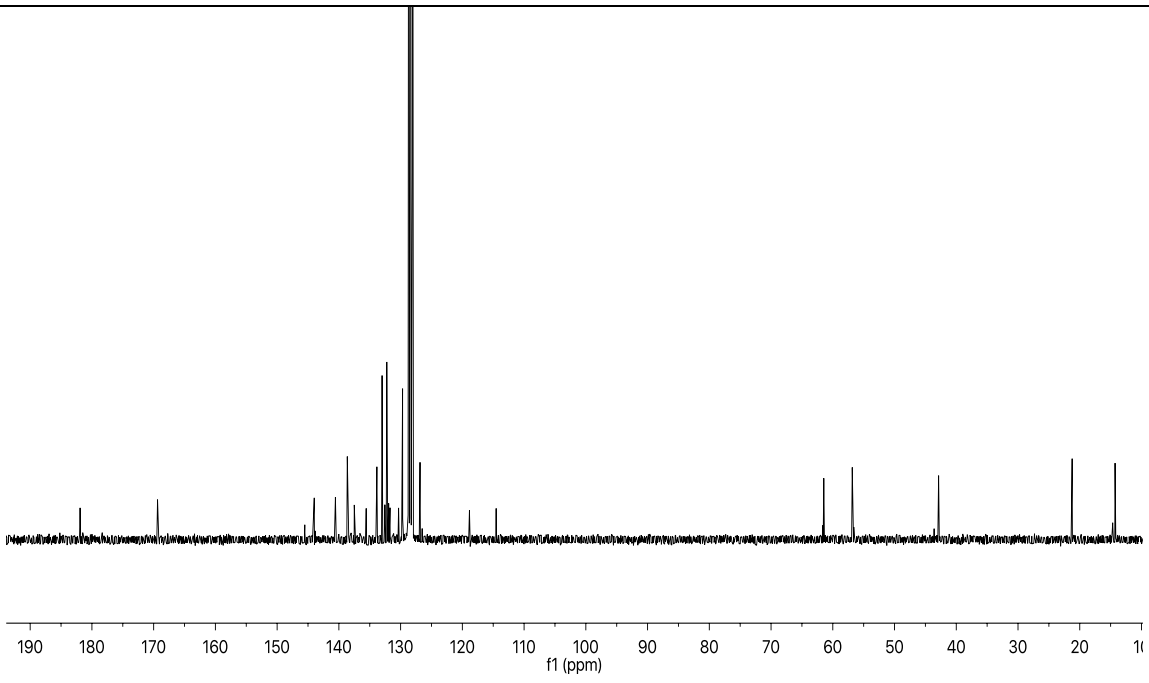




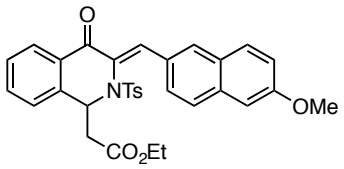
Ethyl (*Z*)-2-(3-(4-cyanobenzylidene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2k)

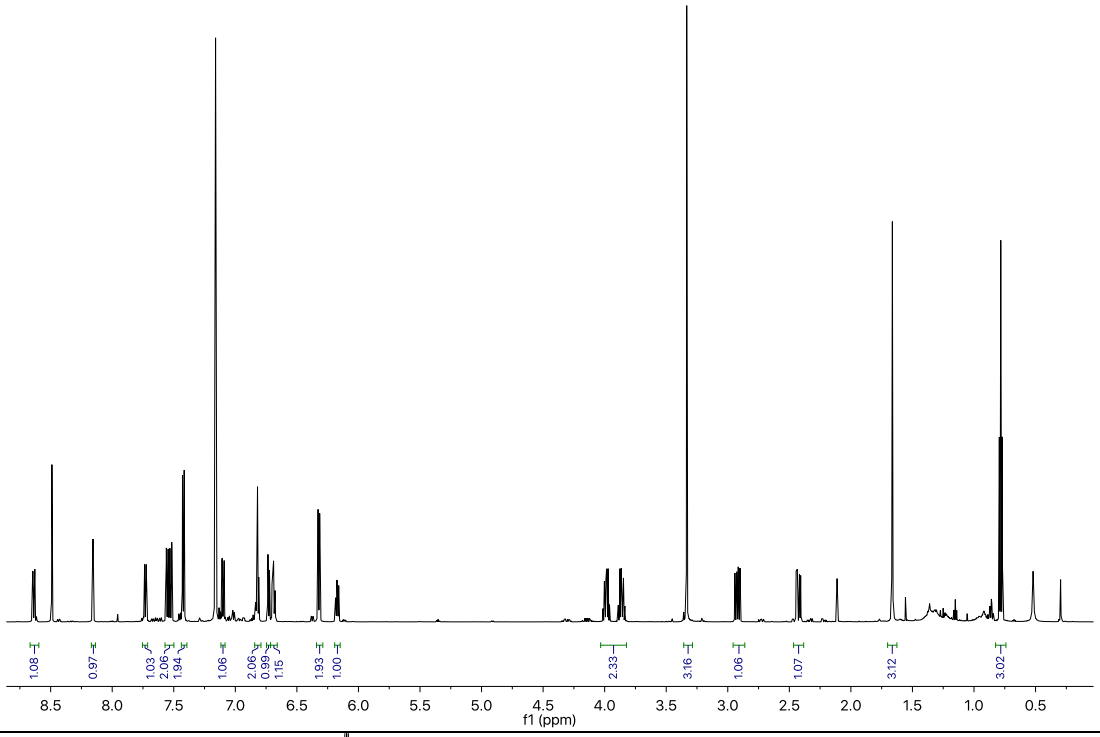


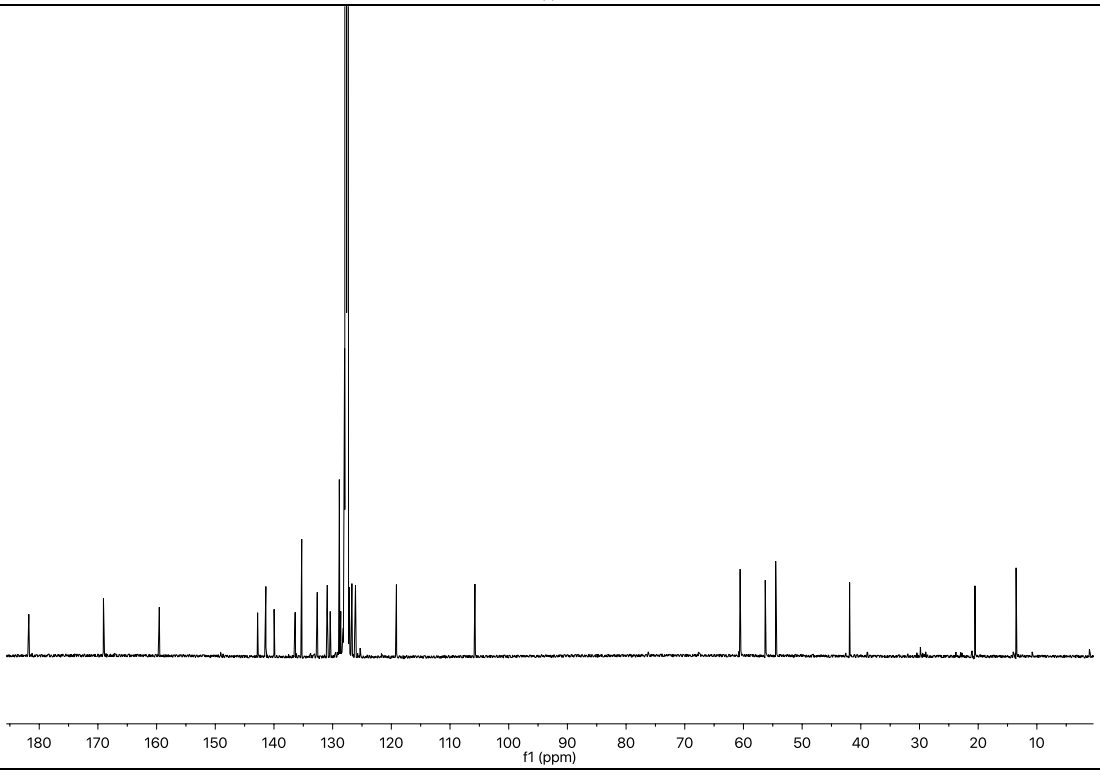




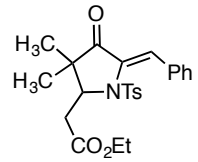
Ethyl (*Z*)-2-(3-((6-methoxynaphthalen-2-yl)methylene)-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2l)

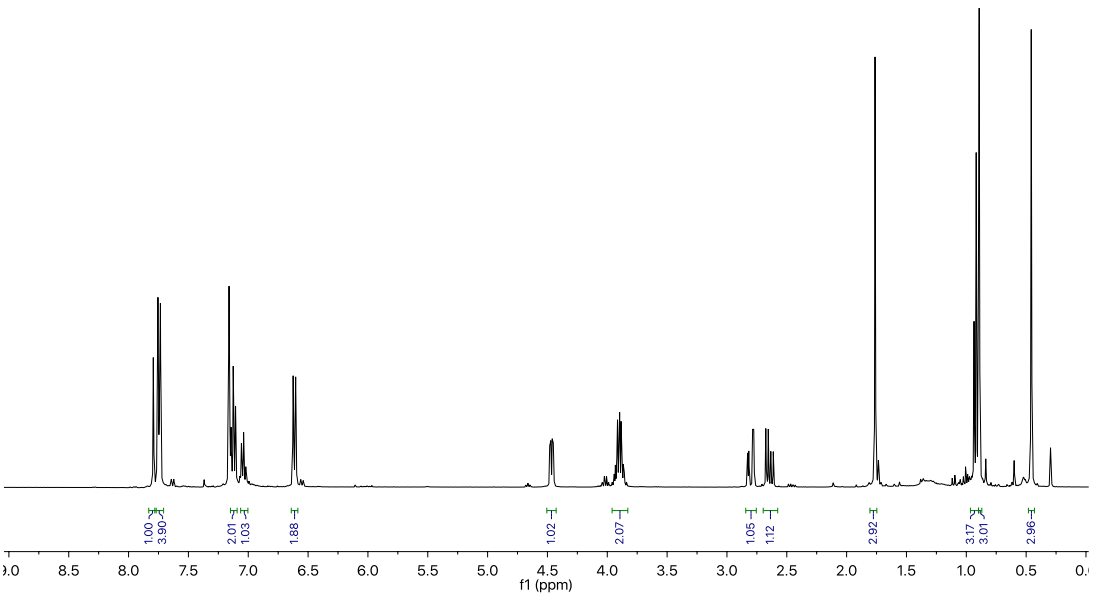


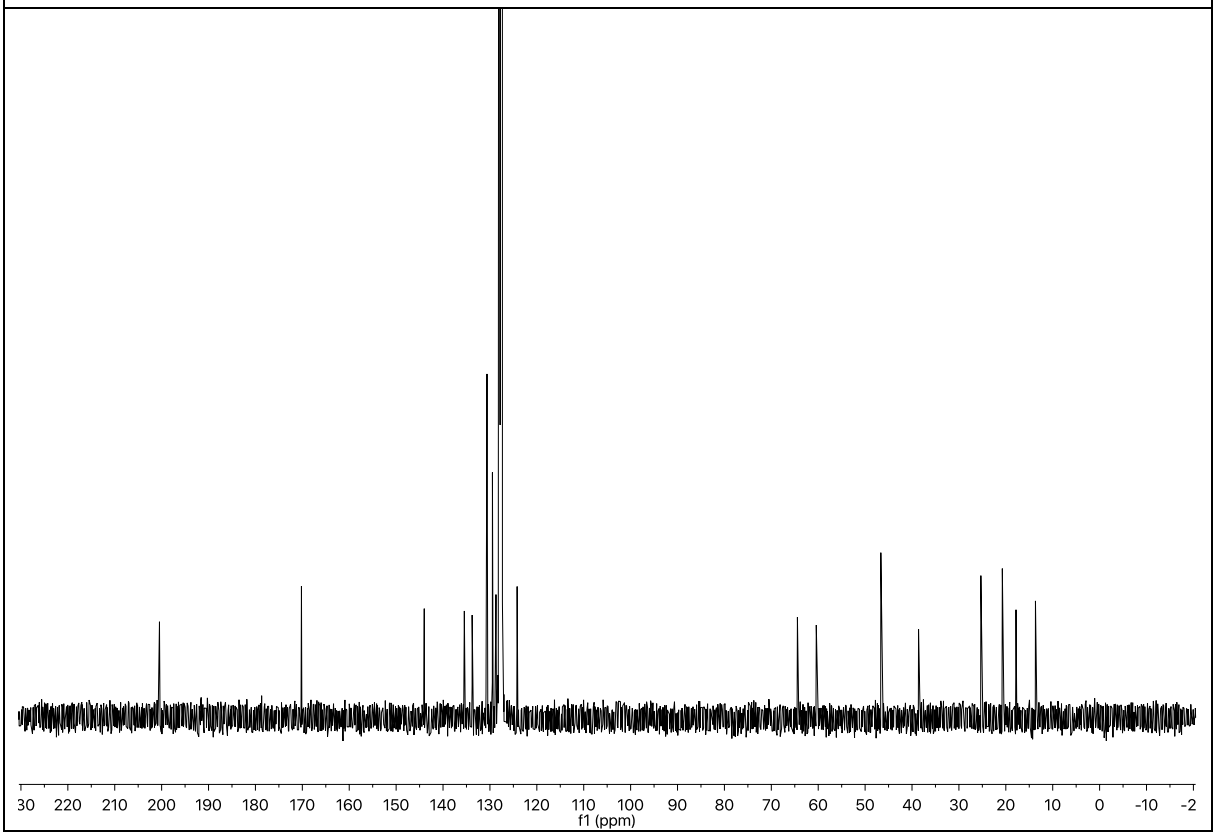




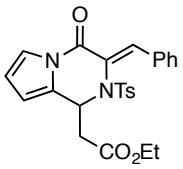
Ethyl (*Z*)-2-(5-benzylidene-3,3-dimethyl-4-oxo-1-tosylpyrrolidin-2-yl)acetate (2m)

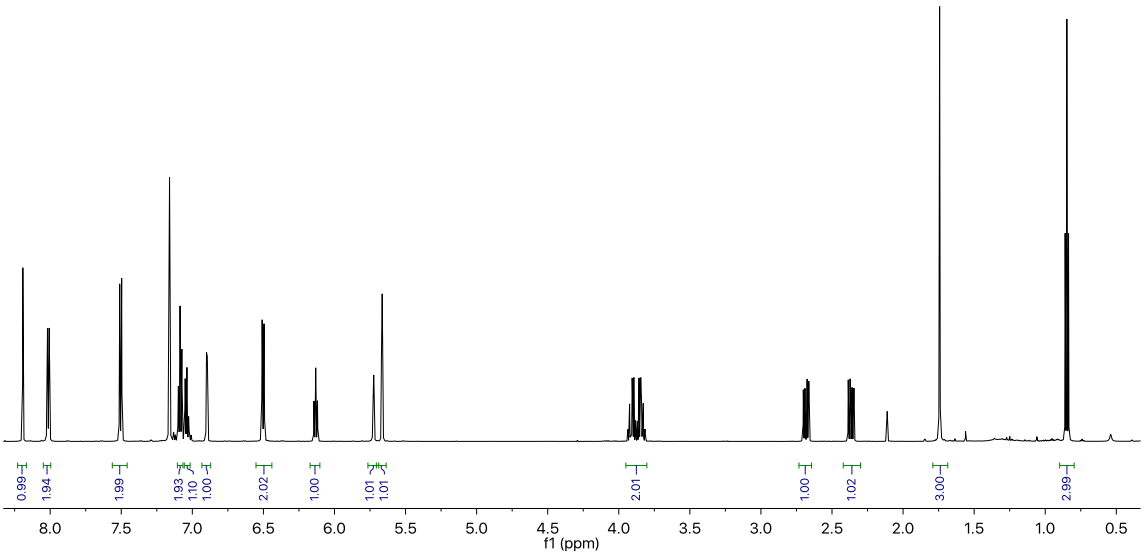


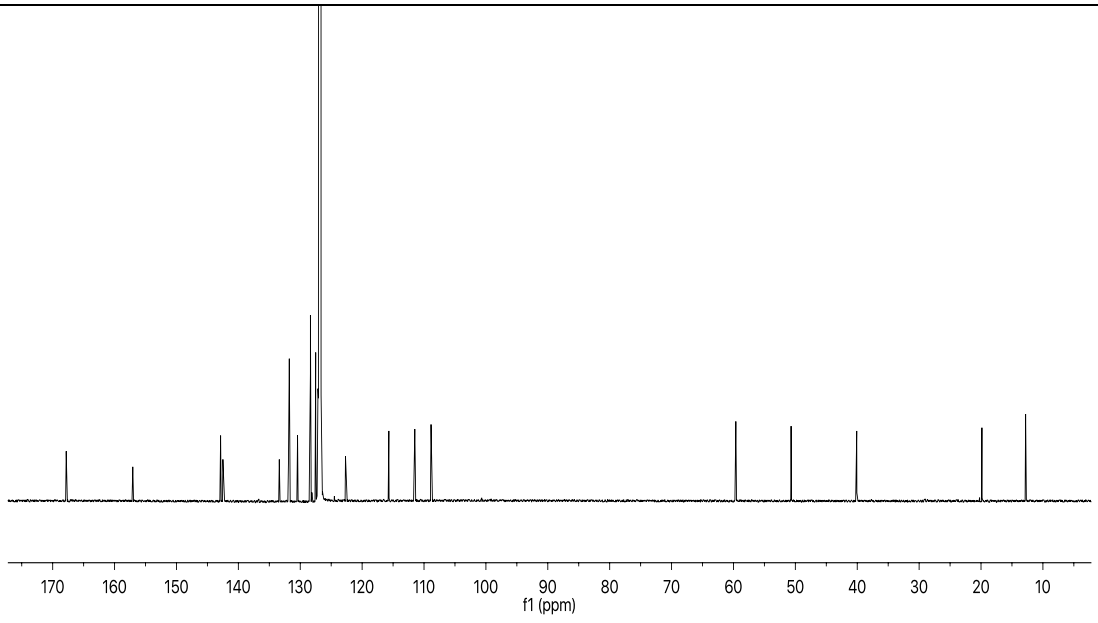




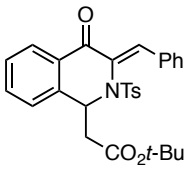
Ethyl (*Z*)-2-(3-benzylidene-4-oxo-2-tosyl-1,2,3,4-tetrahydropyrrolo[1,2-*a*]pyrazin-1-yl)acetate (2n)

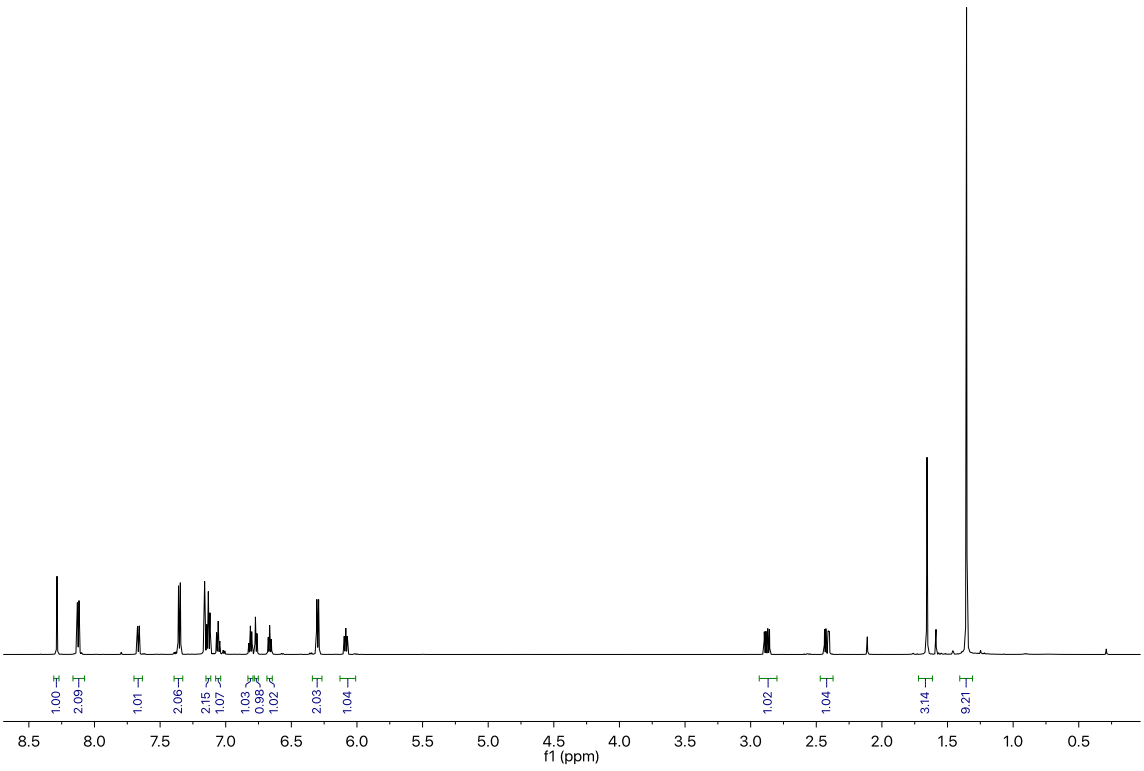


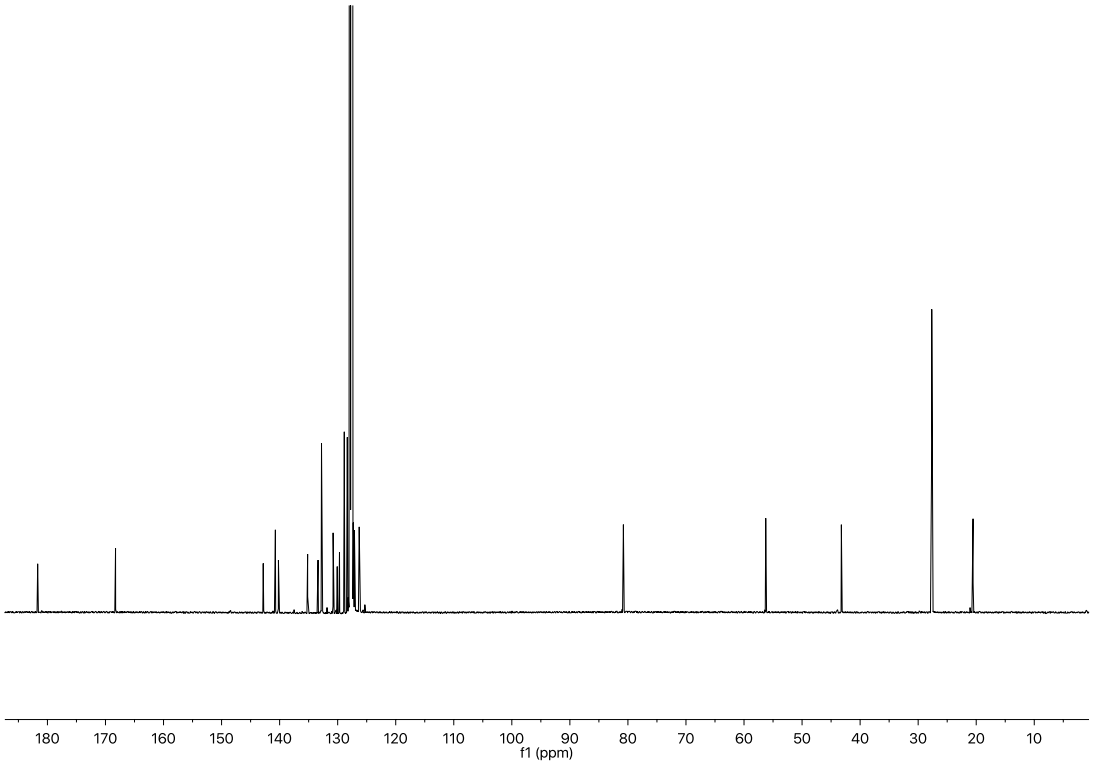




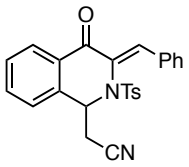
***tert*-Butyl (*Z*)-2-(3-benzylidene-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (2o)**

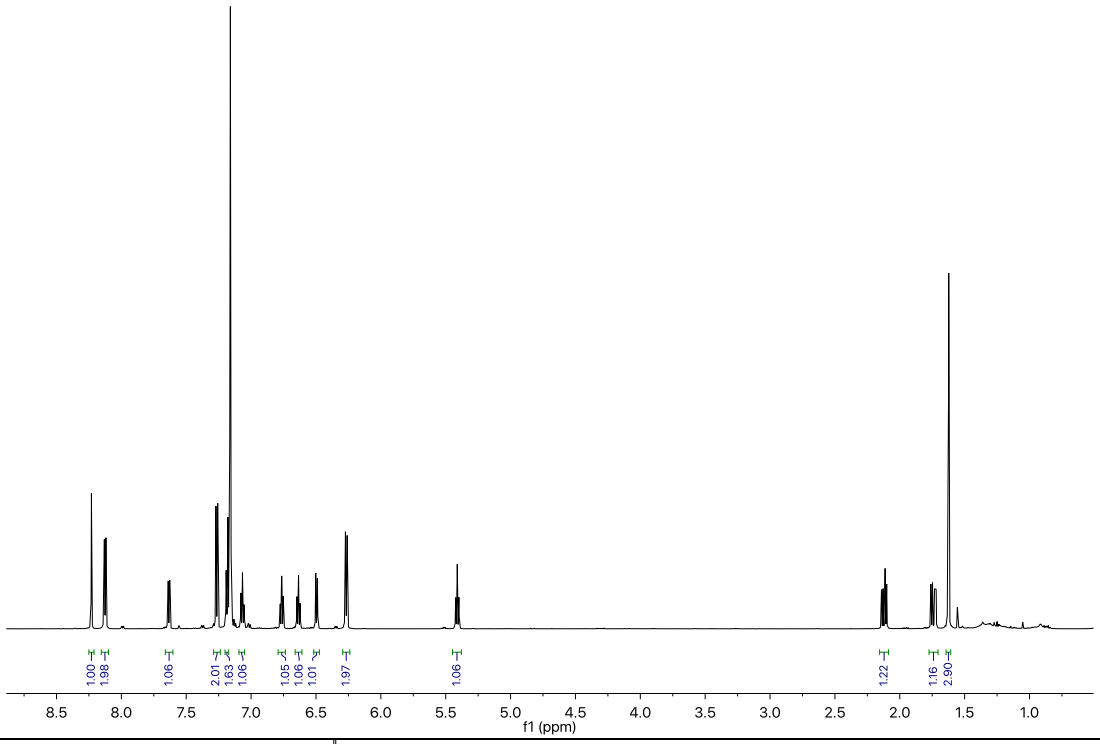


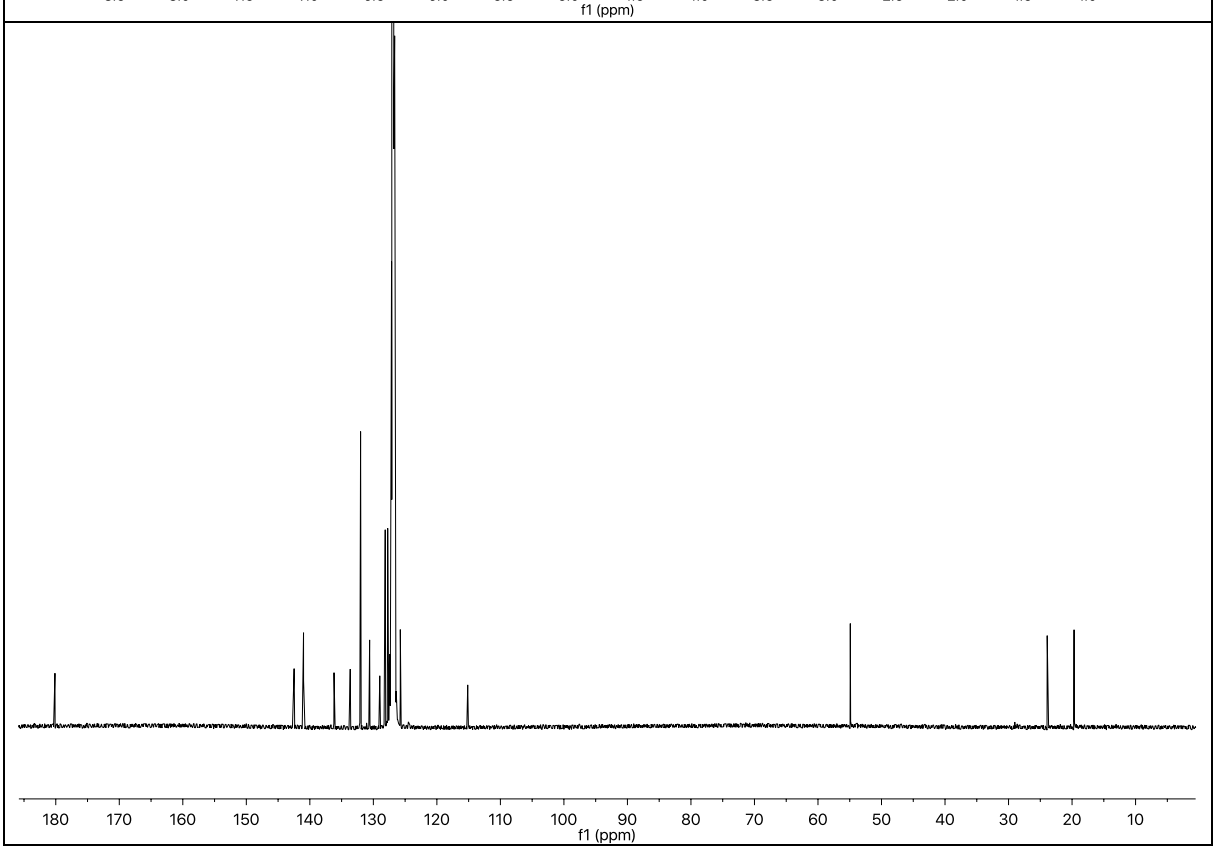




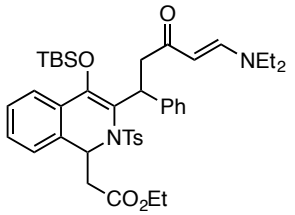
(*Z*)-2-(3-Benzylidene-4-oxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (2p)

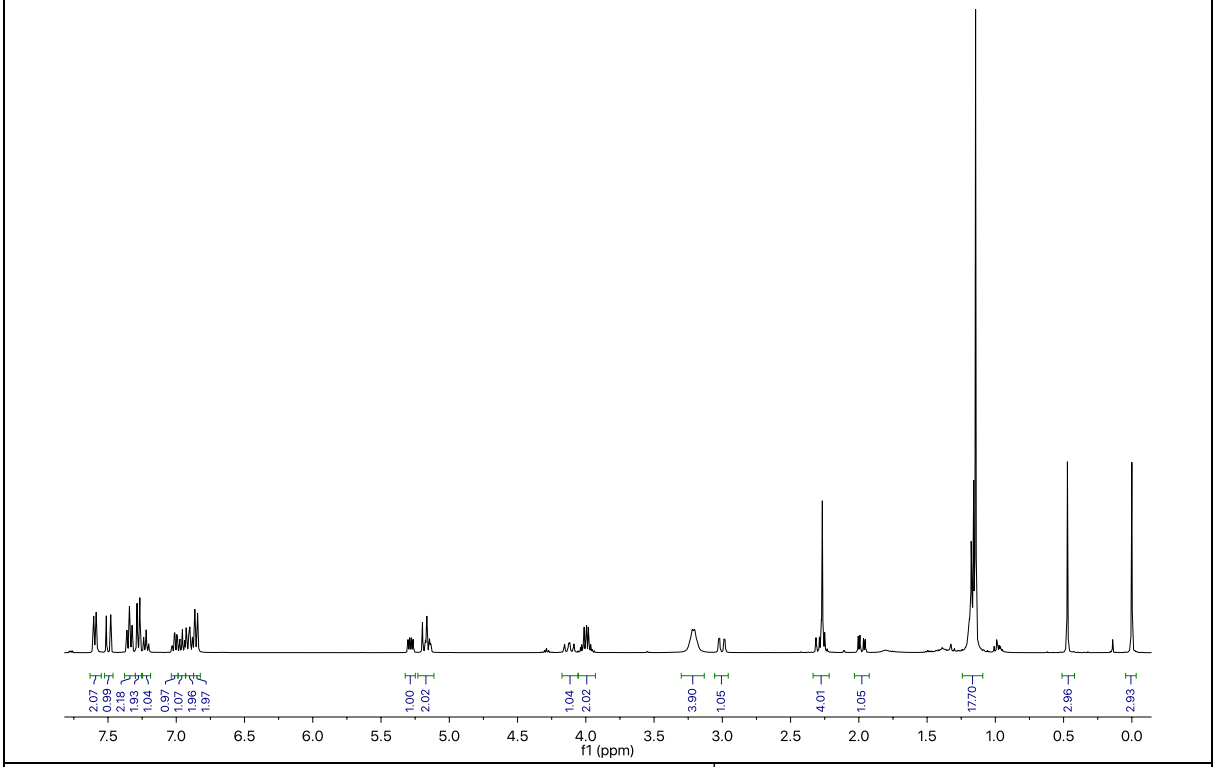


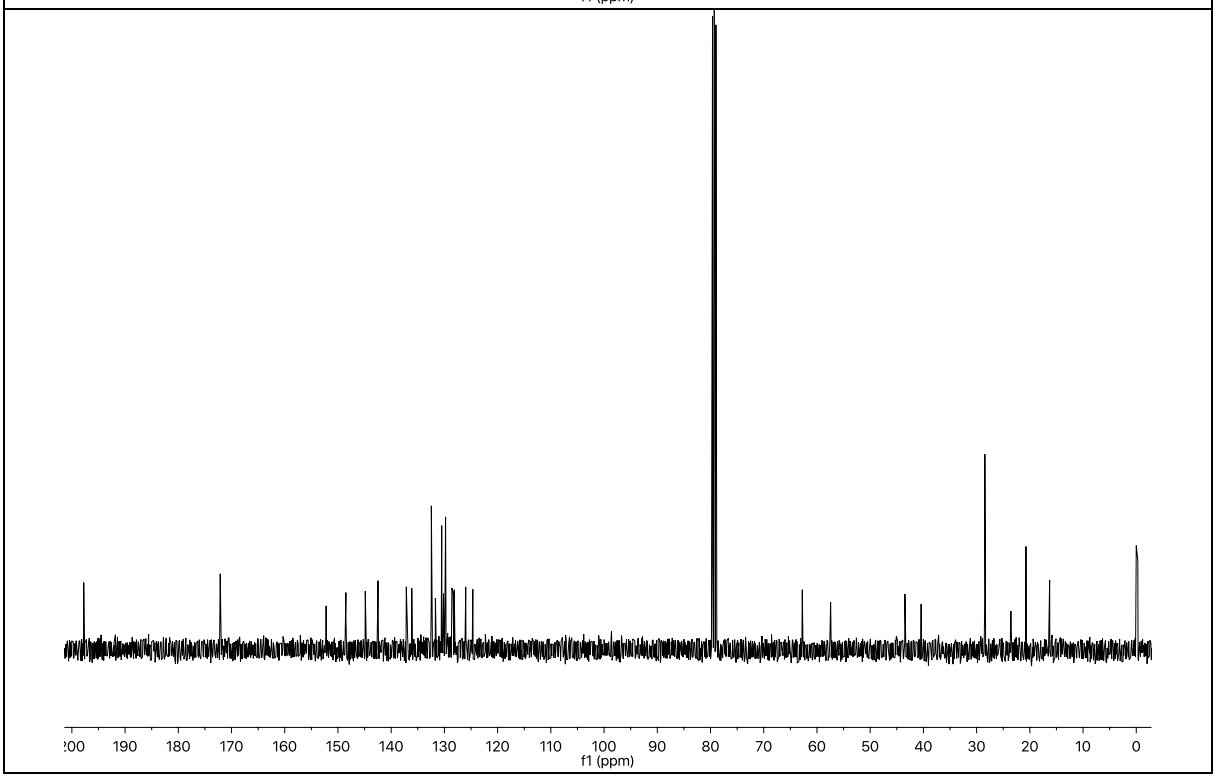




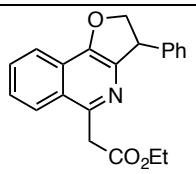
Ethyl (*E*)-2-(4-((*tert*-butyldimethylsilyl)oxy)-3-(5-(diethylamino)-3-oxo-1-phenylpent-4-en-1-yl)-2-tosyl-1,2-dihydroisoquinolin-1-yl)acetate (6)

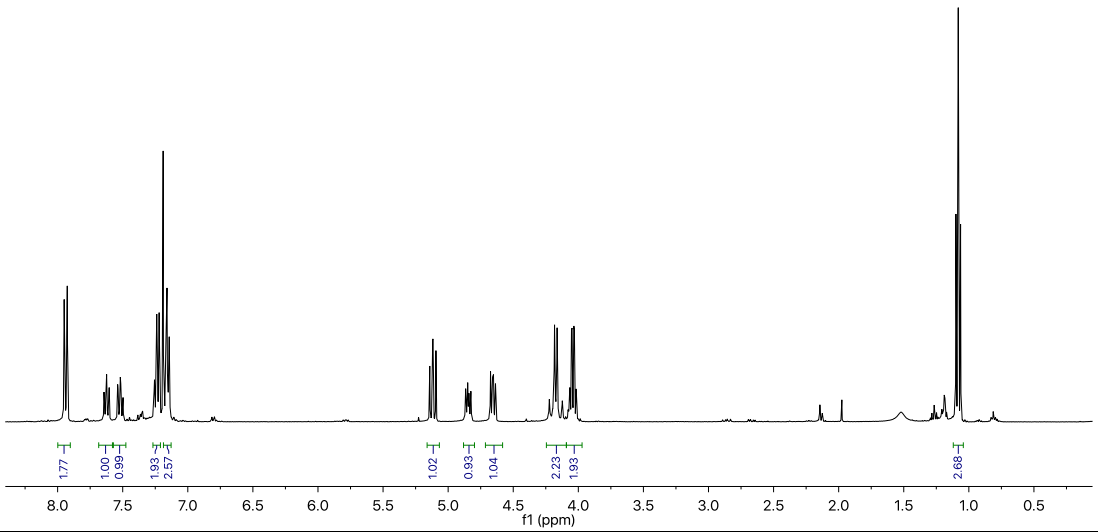


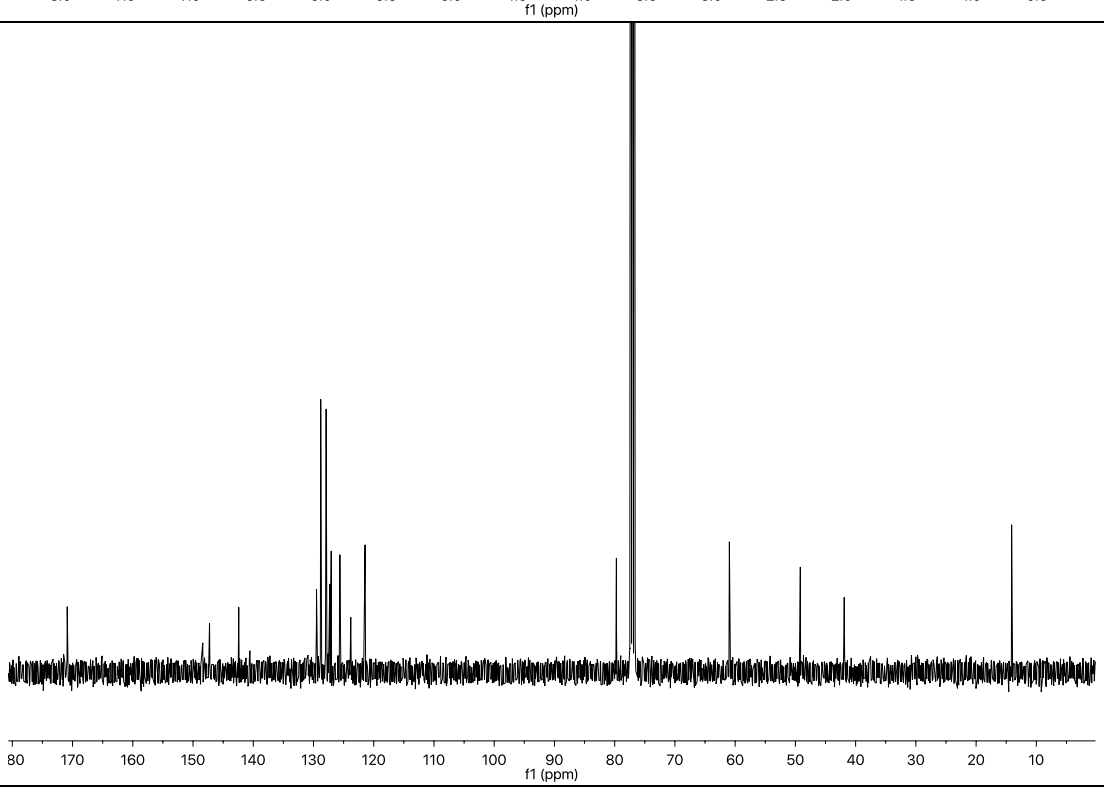




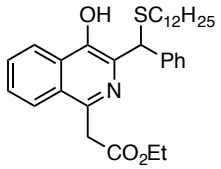
Ethyl 2-(3-phenyl-2,3-dihydrofuro[3,2-*c*]isoquinolin-5-yl)acetate (7)

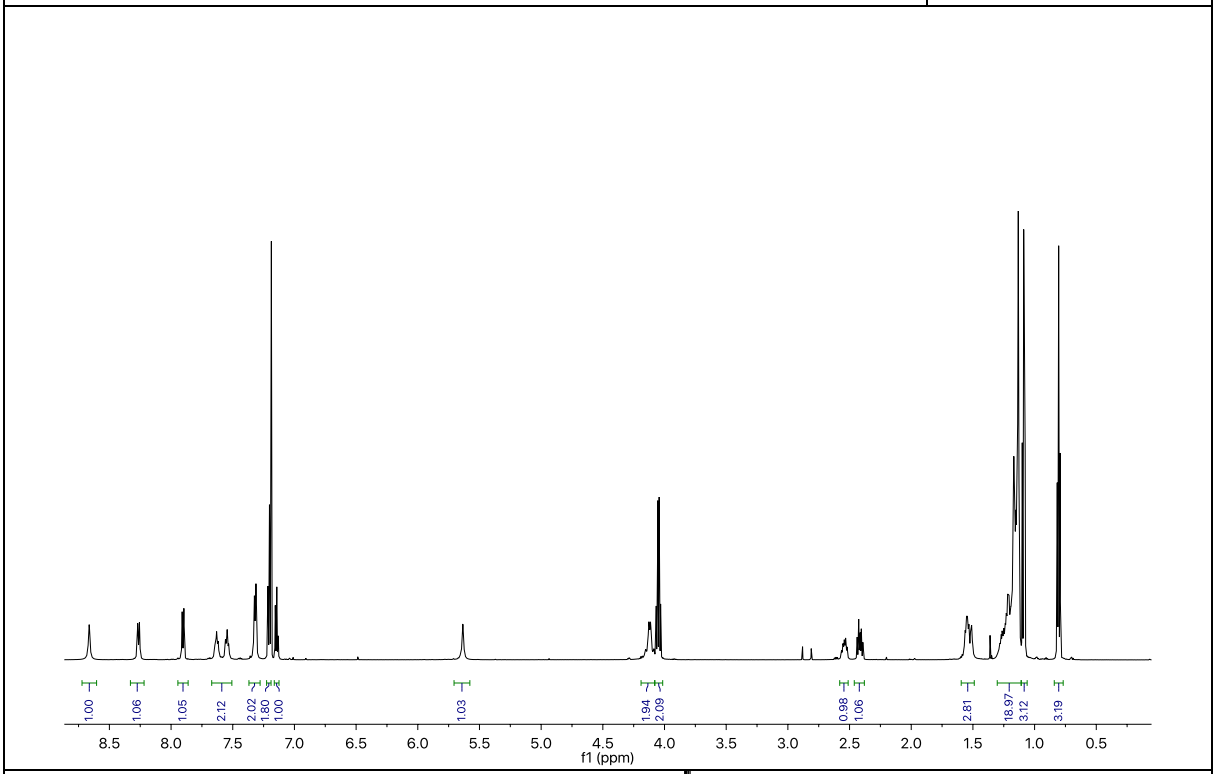


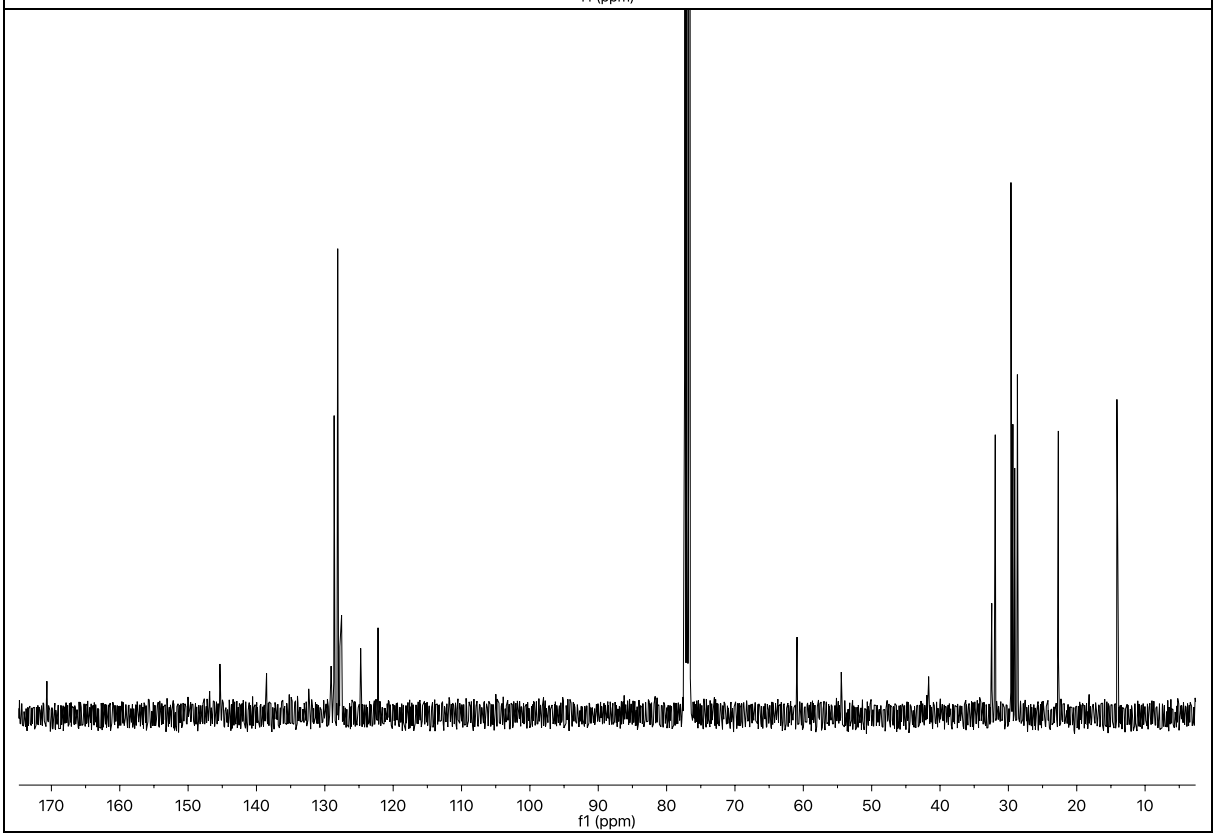


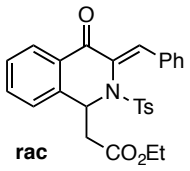


Ethyl 2-(3-((dodecylthio)(phenyl)methyl)-4-hydroxyisoquinolin-1-yl)acetate (8)









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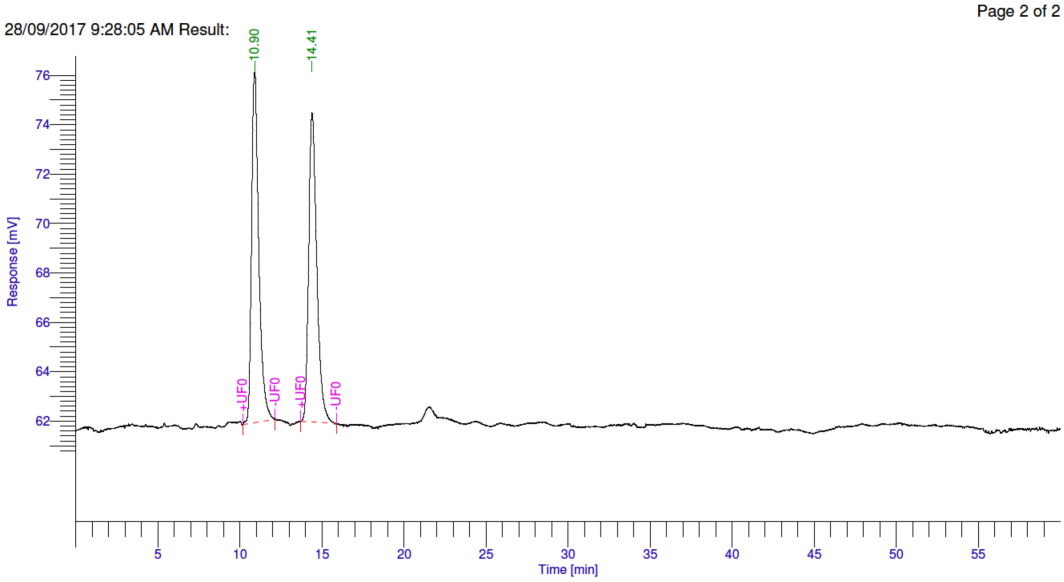
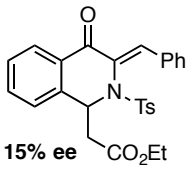
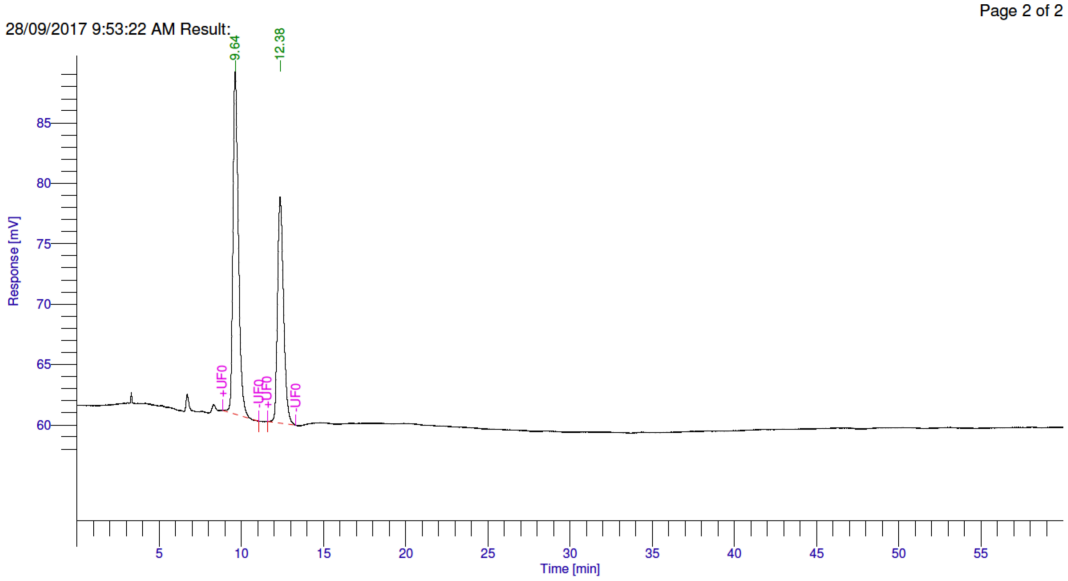


DEFAULT REPORT

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Raw Amount	Adjusted Amount
1		10.898	433620.66	14214.52	50.05	50.05	MM	0.4336	0.4336
2		14.407	432830.27	12522.01	49.95	49.95	MM	0.4328	0.4328
			866450.93	26736.53	100.00	100.00		0.8665	0.8665



15% ee



DEFAULT REPORT

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Raw Amount	Adjusted Amount
1		9.637	643097.93	28393.52	57.26	57.26	MM	0.6431	0.6431
2		12.375	480025.68	18737.70	42.74	42.74	MM	0.4800	0.4800
			1123123.61	47131.22	100.00	100.00		1.1231	1.1231

References

(1) G. Satyanarayana, H. Madhurima, J. Krishna, *Synthesis* 2015, **47**, 1245.
(2) M. A. Schmidt, R. W. Stokes, M. L. Davies, F. Roberts, *J. Org. Chem.* 2017, **82**, 4550.