Electronic supplementary information for

Potent inhibition of Ca^{2+}-dependent activation of calpain-1 by novel mercaptoacrylates

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All chemicals were purchased from Sigma-Aldrich unless otherwise stated. Anhydrous tetrahydrofuran (THF), diethyl ether, toluene and acetonitrile were obtained from a MBraun SPS800 solvent purification system. Dichloromethane, and triethylamine were distilled from calcium hydride under nitrogen. All other chemicals were of analar quality or better and used as received unless otherwise stated. Reactions were stirred at room temperature in air unless otherwise stated. All glassware was clean and dry before use.

^{1}H and ^{13}C NMR spectra were measured on a Bruker Avance 500 NMR spectrometer, a Bruker Avance DPX400 NMR spectrometer or a Bruker Avance DPX250 NMR spectrometer and are reported as chemical shifts in parts per million downfield from tetramethylsilane, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (to the nearest 0.5 Hz) and assignment, respectively. Assignments are made to the limitations of COSY, DEPT 90/135, gradient HSQC and gradient HMBC spectra. ^{19}F NMR spectra were recorded on a Jeol Eclipse +300 NMR spectrometer and are reported in chemical shift downfield from $CFCl_3$ followed by multiplicity and coupling constant (to the nearest 0.5 Hz) if appropriate. IR spectra were recorded on a Perkin-Elmer 1600 series FTIR spectrometer and samples were prepared as thin films of neat liquid on sodium chloride discs for oils and as KBr disks for solids. Mass spectra were performed by the UK National Mass spectrometry service in Swansea. High performance liquid chromatography was performed on a Dionex Ultimate 3000 HPLC system fitted with a Dionex Acclaim analytic C18 reverse phase HPLC column (3 μm, 120 Å, 4.6 x 150 mm). Melting points are quoted uncorrected.

Enzymatic and Cell Biological Assays

Human blood was donated by healthy volunteers who had given their informed consent. This study was approved by the local Ethics Committee (SMREC ref 10/01) and was undertaken in accordance to their approved guidelines and procedures.

(i) Calpain inhibition enzyme activity

AMC based fluorogenic assay is a standard assay and was performed as given in detail previously[1]

The more specific assay employed a peptide from the calpain-1 substrate α-spectrin, with fluorescein at one terminus internally quenched by DABCYL and the other. (H-K(FAM)-EVYGMMK(DABCYL)-OH).[2] Cleavage by calpain-1 occurs between the Tyr-Gly residues and results in enhanced fluorescence as the quenching effect is relieved. The assays were performed using purified porcine Calpain-1 (CalBiochem) 25nM and fluorogenic calpain-1 substrate, 1 mM (Merck) in an assay buffer consisting of HEPES (10 mM) pH 7.2; DTT (10 mM); EDTA (0.5 mM); bovine serum albumin (0.1%) . The assay was performed using a fluorescent plate reader (BMG Optistar) in an assay volume of 100 μl at a temperature of 37°C, using an excitation band pass filter centred at 490 nm and emission deteced at 520 nm. The compounds to be tested for inhibition were added to the assay mixture before the reaction was initated by the addition of $CaCl_2$ (5 mM). None of the compounds had significant fluorescence at these wavelength and correction for this was unnecessary. The compounds were dissolved in DMSO at 50 mM and diluted into assay buffer to give range of concentrations from 100 nM to 10 mM. In each assay run, the effect of DMSO alone over the concentration used was also measured. Although there was no effect of DMSO at lower concentrations, in some assay runs, DMSO at 0.01%-0.1% produced some inhibitory effect. This DMSO effect (which was only relevant for compounds with poor inhibitory ability) was subtracted before constructing the inhibition curves shown below.

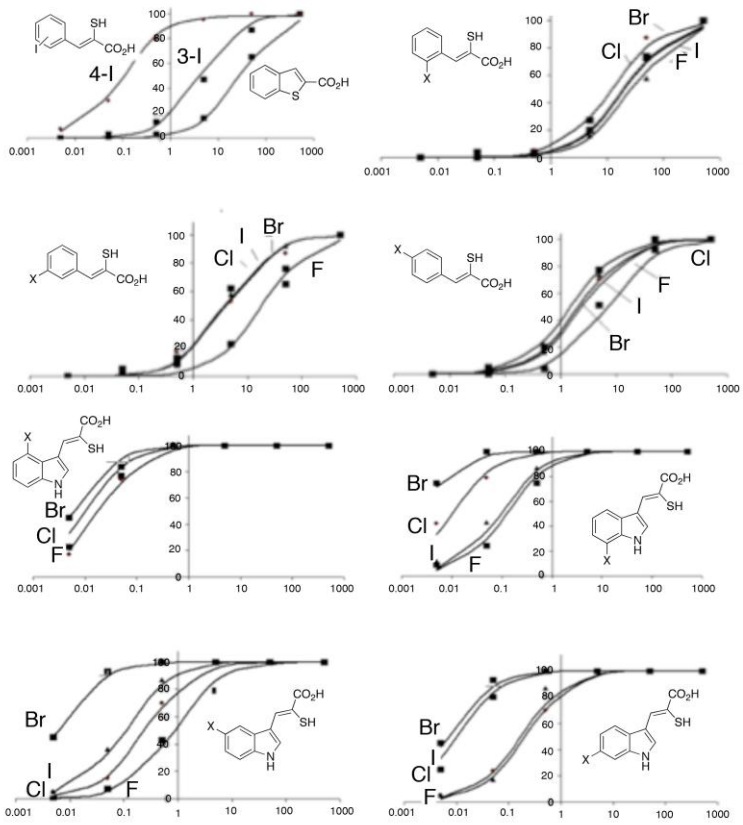


Figure S1. In each of the graphs above the ordinate show the percentage inhibition of calpain-1 (measured using the specific substrate H-K(FAM)-EVYGMMK(DABCYL)-OH) by the compounds indicated in the insert. The data points are means of at least 4 determinations and give the IC_{50} values shown below.

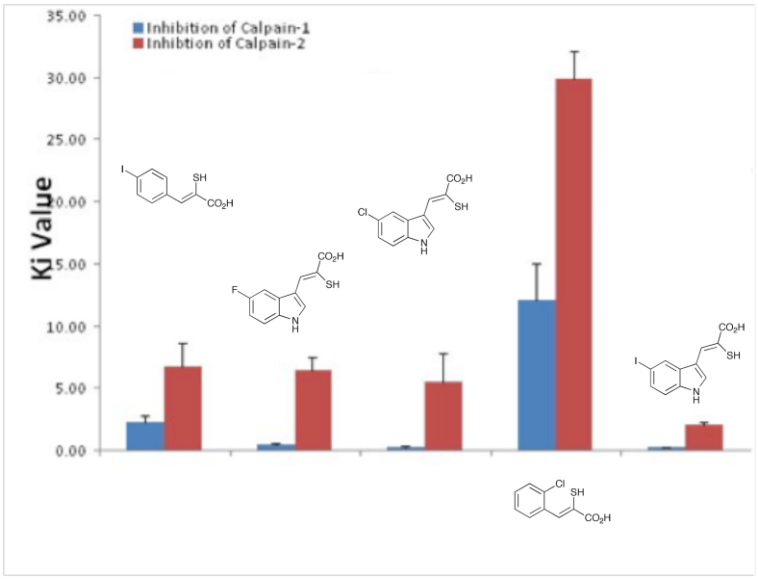


Figure S2. Comparison of IC_{50} values for inhibition of calpain1 and calpain-2 for the compounds shown. In each case there is preferential inhibition of calpain-1. SucLY-AMC which is substrate for both calpain-1 and calpain2 was used in this study.

Phenyl		F	Cl	Br	I
2	mean	21.89925	11.94527	21.03443	29.6046
	sd	8.423165	8.884702	5.221519	21.74467
3	mean	18.99425	4.232	3.9854	4.336
	sd	6.211187	1.836555	1.199259	2.101274
4	mean	6.92125	2.569	1.5458	2.2083
	sd	1.374923	1.409814	0.865214	1.474234
Indole					
4	mean	0.0124	0.016	0.006	
	sd	0.009072	0.010985	0.002517	
5	mean	0.802143	0.2514	0.00625	0.103923
	sd	0.758278	0.213101	0.003304	0.090779
6	mean	0.011667	0.2074	0.007	0.1678
	sd	0.00709	0.103493	0.002121	0.093243
7	mean	0.0124	0.00975	0.00225	0.086286
	sd	0.009072	0.000957	0.0015	0.092097

Table S1. Mean and standard deviation (sd) for at least 4 separate determinations of the IC_{50} value estimated using the calpain-1 specific substrate (H-K(FAM)-EVYGMMK(DABCYL)-OH). Figures are quoted in units of μM.

Spontaneous cell spreading assay

Neutrophils were isolated from human blood as described previously[3] and suspended in HEPES buffered Krebs medium (NaCl 120 mM, KCl, 4.9 mM KH_2PO_4, 1.2 mM $MgSO_4$, 1.2 mM $CaCl_2$, 1.3 mM, HEPES 25 mM and bovine serum albumin, 0.1% adjusted to pH 7.4 with NaOH). The focal plane of convention phase contrast light microscope (Nikon) was set to acquire images at the surface of a clean and untreated glass coverslip held in a heated stage (37°C) on which Krebs medium (100 μl) was placed. Cell suspensions (approx 10^6/ml 100 μl) was added and the cells allowed to sediment onto the glass surface. Once in contact with the glass surface, the cells spontaneously spread. Images were acquired digitally using PTI hardware and ImageMaster software for later analysis. The boundaries of individual cells were defined by contrast enhancement and the 2D area of the cell (footprint) quantified using Image J software (NIH). At least 50 individual cells were analysed in this way over a 3 minute post-contact interval. The inhibitory effect was demonstrated on neutrophils isolated from a least 3 healthy volunteers (as approved by local ethics committee).

In parallel experiments neutrophils were loaded with the Ca^{2+} indicator, fluo4 from its acetoxymethyl ester (fluor4-AM, Invitrogen) as previously described.[4]

Simultaneous bright field and fluorescent images were acquired using a Leica resonant laser scanning confocal microscope (RS2) and the Ca^{2+} signals from within the cells recorded. Although individual cells vary in the magnitude and duration of the "spontaneous" Ca^{2+} signal, clear Ca^{2+} signals were

detected in cells treated with the inhibitors, which subsequently failed to spread fully. An example of the spontaneous Ca^{2+} signals recorded is shown below.

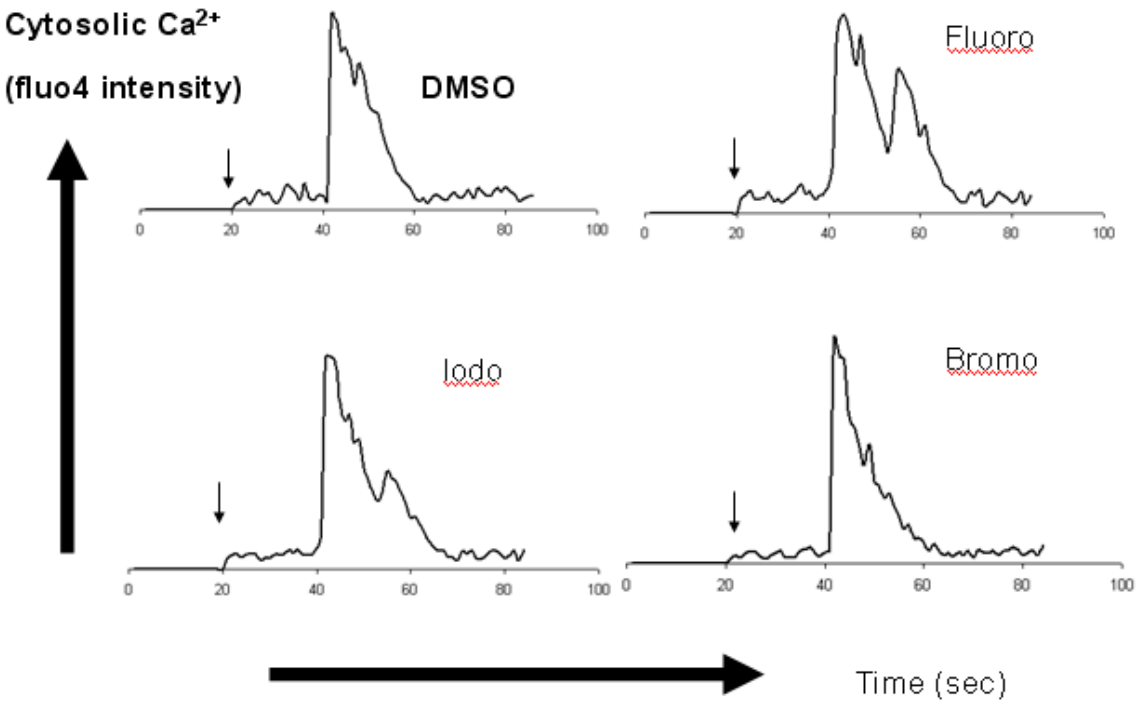
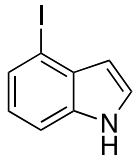


Figure S3.

In each example, the Ca^{2+} signals from single human activated neutrophils were recorded (as fluor4 intensity) following sedimentation onto glass (37°C). The point of contact between the cell and the glass (at the confocal plane) is indicated by the downward arrow. After a short and variable delay (approx 20-100 sec) a transient Ca^{2+} elevation was recorded immediately before the onset of cell spreading. In the examples shown the cells were pre-treated with either DMSO or inhibitors having the halide indicated at position 6 on the indole of the mercaptoacrylate derivative (10 μM).

Synthesis of Calpain inhibitors

4-Iodoindole

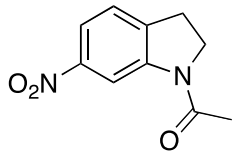


To a suspension of thallium(III)trifluoroacetate (9.13 g, 16.19 mmol) in trifluoroacetic acid (40 cm^3), methyl indole-3-carboxylate (2.0 g, 11.42 mmol) in 2 cm^3 trifluoroacetic acid was added dropwise under argon. The suspension was left to stir for 2 hours at room temperature. The suspension was concentrated under reduced pressure then water (128 cm^3) and potassium iodide (5.7 g, 34.34 cm^3)

were added. This was left to stir for 2 hours. The suspension was extracted with dichloromethane:methanol (95:5, 68 cm^3) and filtered to remove the solid. The organic layer was extracted and washed with aq. Na_2SO_3 (2 × 50 cm^3) and brine (50 cm^3). The organic layer was dried with $MgSO_4$ and concentrated under reduced pressure. The resulting brown oil was passed through a pad of flash silica using hexane:ethyl acetate (1:1) resulting in a crude product which was hydrolysed without further purification.

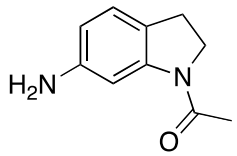
To a solution of the crude material (2.0 g, 6.62 mmol) in methanol (45 cm^3), 40 % aqueous sodium hydroxide solution was added (45 cm^3) and the solution was heated under reflux for 1.5 hour. The solution was cooled to room temperature and concentrated under reduced pressure to remove the methanol. The suspension was extracted with dichloromethane:methanol (95:5, 100 cm^3) and the organic layer was washed with brine (50 cm^3). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The resulting brown oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 3:1) to give the title compound as pale yellow crystals (0.90 g, 33.48 %). mp. 96 - 99 °C. δ_H (400 MHz. $CDCl_3$): 8.36 (1 H, s, NH), 7.56 (1 H, d, J = 7.5, ArCH), 7.39 (1 H, d, J = 8.5, ArCH), 7.29 (1 H, d, J = 2.5, ArCH), 6.96 (1 H, t, J = 7.5, ArCH), 6.52 (1 H, td, J_1 = 2.5, J_2 = 1.0, ArCH). δ_C (100 MHz, $CDCl_3$): 134.73 (ArC), 132.53 (ArC), 129.45 (ArCH), 124.49 (ArCH), 123.36 (ArCH), 111.11 (ArCH), 106.39 (ArCH), 87.49 (ArCI). Mass spectrum: HRMS (EI^+) 242.9544, C_8H_6IN requires 242.9545. υ cm^{-1}: 3400.4, 3101.9, 1733.7, 1623.3, 1605.5, 1558.2, 1500.4, 1483.0, 1474.3, 1424.7, 1411.2, 1330.2, 1268.5, 1175.9, 1138.3, 1094.9, 1067.4, 1042.8, 902.0, 881.8, 799.8, 777.2, 757.9, 745.8, 702.8, 619.0, 562.6, 515.4, 484.5, 437.3.

_N_-Acetyl-6-nitroindoline



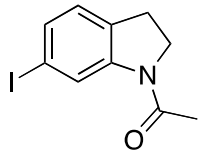
A stirred suspension of 6-nitroindoline (1.0 g, 6.09 mmol) in acetic anhydride (5 cm^3) was heated to 130°C for 15 minutes. The reaction mixture was cooled to room temperature and water was added (20 cm^3). The resulting suspension was heated under reflux for 45 minutes. The reaction mixture was left to cool to room temperature; the precipitate that formed was collected by filtration under reduced pressure and washed with water (20 cm^3). The solid was then air dried under reduced pressure to give the title compound as a yellow solid (1.19 g, 5.77 mmol, 94.7 %). mp. 167 - 169 °C. δ_H (400 MHz, DMSO-d_6): 8.73 (1H, d, J = 2.0, ArCH), 7.87 (1 H, dd, J_1 = 8.5, J_2 = 2.0, ArCH), 7.45 (1 H, d, J = 8.5, ArCH), 4.18 (2 H, t, J = 8.5, CH_2), 3.24 (2 H, t, J = 8.5, CH_2), 2.19 (3H, s, CH_3). δ_C (125 MHz, DMSO-d_6): 170.00 ($COCH_3$), 147.33 (ArC), 144.23 (ArC), 140.87 ($ArCNO_2$), 125.77 (ArCH), 119.11 (ArCH), 110.15 (ArCH), 49.26 (CH_2), 27.96 (CH_2), 24.31 (CH_3). Mass spectrum: HRMS (EI^+) 206.0694, $C_{10}H_{10}N_2O_3$ requires 206.0691, *m/z* (EI^+): 164.0 (100 % $[M\text{-}COCH_3]^+$), 118.1 (80 % $[M\text{-}(COCH_3)(NO_2)]^+$). υ cm^{-1} : 3440.4, 3135.2, 1666.7, 1592.4, 1526.4, 1515.8, 1481.1, 1430.4, 1401.5, 1334.5, 1103.1, 1069.8, 1029.8, 892.9, 813.3, 745.4, 636.4, 565.5, 516.8.

_N_-Acetyl-6-aminoindoline



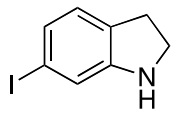
A suspension of *N*-acetyl-6-nitroindoline (1.00 g, 4.86 mmol), 10% Pd/C (0.1 g) in methanol (160 cm^3) was stirred vigorously under an atmosphere of hydrogen for 24 hr. The Pd/C was removed by filtration under reduced pressure through a plug of Celite©. The filtrate was concentrated *in vacuo* to leave the title compound as a white solid (0.68 g, 3.89 mmol, 80.1 %). mp. 172 - 177 °C. δ_H (400 MHz, DMSO-d_6): 7.43 (1 H, d, J = 2.0, ArCH), 6.83 (1 H, d, J = 8.0, ArCH), 6.20 (1 H, dd, J_1 = 8.0, J_2 = 2.0, ArCH), 4.97 (2H, s, NH_2), 3.99 (2 H, t, J = 8.0, CH_2), 2.92 (2 H, t, J = 8.0, CH_2), 2.11 (3 H, s, CH_3). δ_C (62.5 MHz, DMSO-d_6): 168.05 (COCH$_3$), 147.86 (ArC), 143.52 (ArC), 124.51 (ArCH), 118.28 (ArCH), 108.79 (ArCH), 102.59 (ArCNH$_2$), 48.73 (CH_2), 26.50 (CH_2), 24.12 (CH_3). Mass spectrum: HRMS (AP^+) 177.1031, $C_{10}H_{13}N_2O$ requires 177.1028, *m/z* (AP^+): 135.1 (5 % [M-$COCH_3$]$^+$). υ cm^{-1}: 3413.4, 3320.8, 3113.5, 2916.8, 1644.5, 1605.9, 1497.0, 1456.5, 1417.4, 1362.5, 1330.2, 1308.5, 1243.9, 1204.8, 1167.2, 1030.3, 954.6, 876.5, 806.1, 631.6, 550.1.

_N_-Acetyl-6-iodoindoline



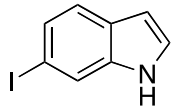
To a solution of *N*-acetyl-6-aminoindoline (0.70 g, 4.04 mmol) in 80% acetic acid (31 cm^3) under argon at 0°C, sodium nitrite (0.32 g, 4.64 mmol) in water (1.4 cm^3) was added and stirred for 15 minutes. Potassium iodide (3.3 g, 19.88 mmol) in water (7.0 cm^3) was added to the reaction mixture which was then stirred for 24 hours at 0 °C. The solution was concentrated *in vacuo* and the black residue was dissolved in ethyl acetate (45 cm^3) and washed with water (3 × 45 ml). The organic layer was separated and dried using anhydrous $MgSO_4$ then filtered and concentrated under reduced pressure. The brown residue was purified using flash chromatography on silica gel (toluene:acetone 20:1) to give light the title compound as yellow crystals. (0.70 g, 2.42 mmol, 59.9 %). mp. 131 - 135 °C. δ_H (400 MHz, $CDCl_3$): 8.55 (1 H, d, J = 2.0, ArCH), 7.30 (1 H, dd, J_1 = 8.0, J_2 = 2.0, ArCH), 6.87 (1 H, d, J = 8.0, ArCH), 4.07 (2 H, t, J = 8.5, CH_2), 3.12 (2 H, t, J = 8.5, CH_2), 2.19 (3 H, s, CH_3). δ_C (125 MHz, $CDCl_3$): 168.87 (COCH$_3$), 144.14 (ArC), 132.55 (ArCH), 130.96 (ArC), 126.09 (ArCH), 125.56 (ArCH), 92.19 (ArCI), 48.98 (CH_2), 28.01 (CH_2), 24.21 (CH_3). Mass spectrum: HRMS (EI^+) 286.9800, $C_{10}H_{13}INO$ requires 287.9807, *m/z* (EI^+): 245.0 (100 % [M-$COCH_3$]$^+$), 117.1 (30 % [M-$COCH_3$+I]$^+$). υ cm^{-1}: 3434.1, 3113.5, 2960.2, 2360.0, 1659.5, 1594.8, 1482.0, 1437.7, 1413.1, 1340.3, 1309.4, 1264.6, 1125.7, 1101.6, 1031.3, 927.1, 882.8, 787.3, 768.0, 624.3, 598.3, 558.3, 508.6, 425.7.

6-Iodoindoline



A 40% aqueous sodium hydroxide solution (12 cm^3) was added to a solution of *N*-acetyl-6-iodoindoline (0.2 g, 0.68 mmol) in methanol (12 cm^3). The reaction mixture was heated to 75°C for 2.5 hours. The cooled reaction mixture was concentrated under reduced pressure. The residue was extracted with ethyl acetate (3 × 30 ml) and the organic layer was dried over anhydrous $MgSO_4$, filtered and then concentrated under reduced pressure. The resulting yellow oil was purified using flash chromatography on silica gel (hexane:ethyl acetate 10:1) to give the title compound as white crystals, (0.11 g, 0.44 mmol, 64.4 %). mp. 93 - 96 °C. δ_H (250 MHz, $CDCl_3$): 6.91 (1 H, dd, J_1 = 7.5, J_2 = 1.5, ArCH), 6.85 (1 H, d, *J* = 1.5, ArCH), 6.74 (1 H, d, *J* = 7.5, ArCH), 3.45 (2 H, t, *J*=8.5, CH_2), 2.89 (2H, t, *J* = 8.5, CH_2). δ_C (100 MHz, $CDCl_3$): 153.41 (ArC), 129.19 (ArC), 127.35 (ArCH), 126.24 (ArCH), 117.97 (ArCH), 91.95 (ArCI), 47.49 (CH_2), 29.36 (CH_2). Mass spectrum: HRMS (EI^+) 244.9707, C_8H_8IN requires 244.9702, *m/z* (EI^+): 85.9456 (65 %), 83.9491 (100 %). υ cm^{-1}: 3378.2, 2931.3, 2864.3, 1590.0, 1488.3, 1474.3, 1438.2, 1321.0, 1309.4, 1250.6, 1239.0, 1160.9, 1048.1, 1021.6, 929.0, 881.8, 845.2, 798.4, 724.6, 699.1, 573.7, 551.5, 513.9, 422.3, 409.3.

6-Iodoindole



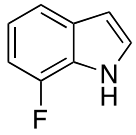
Air was bubbled through a solution of 6-iodoindoline (0.23 g, 0.94 mmol), *N,N'*-bis(salicylidene)ethylenediaminocobalt(II) (0.034 g, 0.10 mmol) in methanol (30 cm^3) for 24 hr. The reaction mixture was concentrated under reduced pressure. The residue was then purified by flash chromatography on silica gel (hexane:ethyl acetate 8:1) solvents system to give the title compound as pale brown crystals, (0.18 g, 0.73 mmol, 77.2 %). mp. 108 - 113 °C. δ_H (400 MHz, $CDCl_3$): 7.96 (H, s, NH), 7.62 (1 H, d, *J* = 1.0, ArCH), 7.31 (2 H, s, ArCH), 7.02 (1 H, t, *J* = 3.0, ArCH), 6.43 (1 H, q, *J* = 1.0, ArCH). δ_C (125 MHz, $CDCl_3$): 137.14 (ArC), 128.67 (ArCH), 127.25 (ArC), 124.66 (ArCH), 122.40 (ArCH), 120.06 (ArCH), 102.90 (ArCH), 85.80 (ArCI). Mass spectrum: HRMS (EI^+) 242.9538, C_8H_6IN requires 242.9545, *m/z* (EI^+): 116.0496 (20 % $[M-I]^+$). υ cm^{-1}: 3853.1, 3823.2, 3412.4, 1624.3, 1598.7, 1494.6, 1451.7, 1440.1, 1394.3, 1333.1, 1311.4, 1232.8, 1201.4, 1089.6, 1042.8, 996.1, 890.0, 878.9, 859.1, 810.0, 758.4, 729.9, 609.4.

General method for the preparation of 7 substituted indoles

7-bromoindole

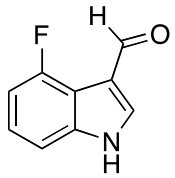
A solution of 1-bromo-2-nitrobenzene (1.0 g, 4.95 mmol) in THF (50 cm^3) under argon was cooled to -40 °C (dry-ice - acetone bath). To this solution was quickly added vinylmagnesium bromide (1 M in THF, 14.76 cm^3, 14.76 mmol). The reaction was left to stir for 20 minutes at -40 °C. The reaction mixture was quenched with aq. NH_4Cl (50 cm^3) then extracted with diethyl ether (2 × 50 cm^3). The pooled organic extracts were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The black oil that resulted was purified using flash chromatography on silica gel (hexane:ethyl acetate 6:1) giving the title compound as an orange solid (0.43 g, 43.8 %). mp. 39 - 41 °C. δ_H (400 MHz. $CDCl_3$): 8.37 (1 H, s, NH), 7.62 (1 H, d, *J* = 8.0, ArCH), 7.29 (1 H, t, *J* = 3.0, ArCH), 7.04 (1 H, t, *J* = 8.0, ArCH), 6.67 (1 H, dt, J_1 = 3.0, J_2 = 1.0, ArCH). δ_C (100 MHz, $CDCl_3$): 134.59 (ArC), 129.00 (ArC), 124.74 (ArCH), 124.34 (ArCH), 121.02 (ArCH), 119.98 (ArCH), 104.67 (ArCBr), 103.86 (ArCH). Mass spectrum: HRMS (EI^+) 194.9686, $C_8H_6{}^{79}BrN$ requires 194.9684, *m/z* (EI^+): 116.0484 (25 % $[M\text{-}Br]^+$), 85.9369 (100 %). υ cm^{-1}: 3400.9, 1901.0, 1613.6, 1560.1, 1483.0, 1428.0, 1408.3, 1329.7, 1282.0, 1214.0, 1190.4, 1135.9, 1094.4, 1065.5, 1032.2, 1032.2, 920.4, 878.4, 817.2.

7-Fluoroindole:



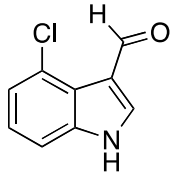
Yield; 14.4 %. mp. 43 - 52 °C. δ_H (400 MHz. $CDCl_3$): 8.17 (1 H, s, NH), 7.31 (1 H, td, J_1 = 8.0, J_2 = 1.0, ArCH), 7.07 (1 H, t, *J* = 3.0, ArCH), 6.92 (1 H, td, J_1 = 8.0, J_2 = 2.5, ArCH), 6.81 (1 H, m, ArCH), 6.49 (1 H, dd, J_1 = 2.5, J_2 = 1.0, ArCH); δ_C (100 MHz, $CDCl_3$): 149.71 (ArCF, d, *J* = 24.0), 131.52 (ArC, d, *J* = 5.0), 124.91 (ArCH, s), 124.27 (ArC, d, *J* = 13.0), 120.06 (ArCH, d, *J* = 6.0), 116.46 (ArCH, d, *J* = 13.0), 106.79 (ArCH, d, *J* = 16.0), 103.35 (ArCH, d, *J* = 2.0). Mass spectrum: HRMS (EI^+) 135.0481, C_8H_6FN requires 135.0484, *m/z* (EI^+): 108.0354 (20 % $[M\text{-}CHNH]^+$), 83.9508 (100 %). υ cm^{-1}: 3631.8, 3390.7, 3111.1, 3071.1, 2956.3, 2923.6, 2689.8, 2627.1, 2516.2, 2361.9, 1895.7, 1823.9, 1726.9, 1640.6, 1610.3, 1579.4, 1521.6, 1489.7, 1443.0, 1415.0, 1342.7, 1286.8, 1235.2, 1214.9, 1160.9, 1106.0, 1066.0, 1046.2, 1023.5, 949.3, 891.9, 878.9, 867.0, 849.0, 841.3.

General method for the preparation of indole-3-carboxaldehydes.



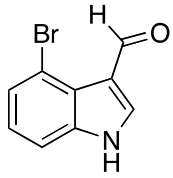
A stirred mixture of 4-fluoroindole (0.50 g, 3.71 mmol) and *N*,*N*-dimethylformamide (1.37 g, 18.78 mmol) was placed in an ice bath until the solution reached 0 °C. Phosphorous oxychloride (0.69 g, 4.50 mmol) was then added dropwise. The mixture was left to stand for 15 minutes at room temperature. The stirred mixture was heated to 40 °C for 1 hr and was then cooled and ice (5 g) was added along with sodium hydroxide solution (2 M, 6 cm^3); the mixture was heated under reflux for 16 hr. After cooling to room temperature; the precipitate that formed was collected by filtration under reduced pressure and washed with water (2 × 10 ml). The solid was air dried under reduced pressure to give the required product as a pink solid (0.59g, 97.8 %). mp. 175 - 181 °C. δ_H (400 MHz, DMSO-d_6): 12.51 (1 H, s, NH), 10.00 (1 H, dd, J_1 = 8.0, J_2 = 3.5, CHO), 8.31 (1 H, d, J = 3.5, ArCH), 7.35 (1 H, t, J = 8.0, ArCH), 7.24 (1 H, td, J_1 = 8.0, J_2 = 5.0, ArCH), 7.01 (1 H, td, J_1 = 8.0, J_2 = 3.0, ArCH). δ_C (125 MHz, DMSO-d_6): 184.07 (CHO), 156.48 (ArCF, d, J = 248.5), 140.21 (ArCH, d, J = 12.0), 136.42 (ArC, s), 124.39 (ArCH, d, J = 8.0), 117.43 (ArC, d, J = 6.0), 113.39 (ArCH, d, J = 21.9), 109.55 (ArCH, d, J = 4.0), 107.71 (ArCH, d, J = 19.0). Mass spectrum: HRMS (EI^+) 162.0434, C_9H_5FNO requires 162.0433, *m/z* (EI^+): 134.0 (30 % $[M\text{-}COH]^+$), 107.0 (25 % $[M\text{-}CHCCOH]^+$). υ cm^{-1}: 3231.2, 2819.4, 2748.1, 1653.7, 1635.3, 1581.3, 1513.4, 1455.0, 1437.7, 1428.0, 1403.4, 1364.9, 1347.0, 1301.2, 1251.6, 1222.7, 1161.9, 1140.2, 1111.3, 1146.7, 1030.3, 849.0, 789.7, 783.0, 764.6, 734.3, 638.3, 618.1, 588.2, 531.3, 519.2.

4-Chloroindole-3-carboxaldehyde:



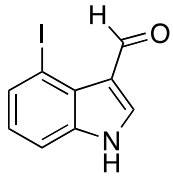
Yield; 80.4 %. mp. 158 - 162 °C. δ_H (400 MHz, DMSO-d_6): 12.59 (1 H, s, NH), 10.50 (1 H, s, CHO), 8.31 (1 H, s, ArCH), 7.53 (1 H, d, J = 8.0, ArCH), 7.30 (1 H, d, J = 8.0, ArCH), 7.23 (1 H, t, J = 8.0, ArCH). δ_C (125 MHz, DMSO-d_6): 185.20 (CHO), 138.75 (ArC), 134.47 (ArCH), 125.03 (ArCCl), 124.01 (ArCH), 123.37 (ArC), 123.05 (ArCH), 118.27 (ArC), 112.45 (ArCH). Mass Spectrum HRMS $[EI^+]$ 179.0138, $C_9H_7{}^{35}ClNO$ requires 179.0138, *m/z* (EI^+): 83.9430 (100 % $[M\text{-}Cl,COH,NHCH]^+$). υ cm^{-1}: 3163.7, 3127.5, 3006.5, 2939.5, 2870.5, 1894.7, 1818.5, 1747.2, 1639.4, 1570.3, 1521.1, 1485.4, 1459.4, 1430.0, 1388.5, 1341.3, 1331.6, 1293.0, 1258.8, 1189.4, 1147.4, 1082.4, 1072.2, 1048.6, 937.7, 872.6, 845.2, 773.8, 729.9, 665.3, 602.6.

4-Bromoindole-3-carboxaldehyde



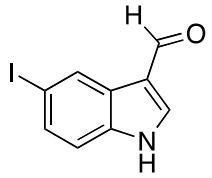
Yield; 93.7 %. mp. 175 - 177 °C. δ_H (400 MHz, DMSO-d_6): 12.59 (1 H, s, NH), 10.69 (1 H, s, CHO), 8.30 (1 H, s, ArCH), 7.58 (1 H, d, *J* = 8.0, ArCH), 7.48 (1H, d, *J*=8.0, ArCH), 7.17 (1 H, t, *J* = 8.0, ArCH). δ_C (125 MHz, DMSO-d_6): 185.03 (CHO), 138.71 (ArC), 134.31 (ArCH), 126.45 (ArCH), 125.16 (ArC), 124.27 (ArCH), 118.29 (ArC), 112.92 (ArCH), 112.75 (ArCBr). Mass Spectrum HRMS [EI^+] 222.9635, $C_9H_7{}^{79}BrNO$ requires 222.9633, *m/z* (EI^+): 83.9487 (100 %). υ cm^{-1}: 3166.1, 3065.3, 2865.3, 1902.0, 1761.7, 1635.8, 1518.2, 1483.0, 1457.0, 1428.5, 1385.6, 1330.6, 1293.5, 1260.7, 1191.3, 1147.9, 1130.1, 1075.1, 1045.2, 913.6, 888.1, 841.3, 773.3, 732.3, 658.6, 608.9.

4-Iodoindole-3-carboxaldehyde



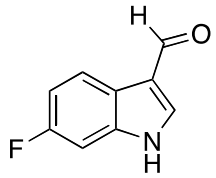
Yield; 91.6 %. mp. 186 - 188 °C. δ_H (400 MHz, DMSO-d_6): 12.50 (1 H, s, NH), 10.95 (1 H, s, CHO), 8.30 (1 H, s, ArCH), 7.73 (1 H, d, *J* = 8.0, ArCH), 7.59 (1 H, d, *J* = 8.0, ArCH), 7.01 (1 H, t, *J* = 8.0, ArCH). δ_C (125 MHz, DMSO-d_6): 184.25 (CHO), 138.29 (ArC), 134.40 (ArCH), 133.29 (ArCH), 128.75 (ArC), 124.59 (ArCH), 118.09 (ArC), 113.41 (ArCH), 83.89 (ArCI). Mass Spectrum HRMS [AP^+] 271.9572, C_9H_7INO requires 271.9572, *m/z* (AP^+): 115.0873 (100 % $[M-I+COH]^+$). υ cm^{-1}: 3155.9, 2929.8, 2863.8, 1767.4, 1628.1, 1515.3, 1480.6, 1456.0, 1424.2, 1383.7, 1337.4, 1292.1, 1259.3, 1191.3, 1147.9, 1125.7, 1068.9, 1040.9, 897.2, 836.0, 799.8, 773.8, 764.2, 734.3, 655.2, 609.9, 600.2, 561.7, 487.9.

5-Iodoindole-3-carboxaldehyde



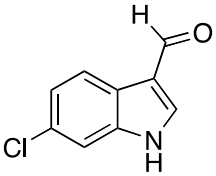
Yield: 95.2 %. mp. 232 - 234 °C. δ_H (400 MHz, DMSO-d_6): 12.29 (1 H, s, NH), 9.92 (1 H, s, CHO), 8.44 (1 H, s, ArCH), 8.30 (1 H, d, *J* = 2.0, ArCH), 7.54 (1 H, d, *J* = 8.5, ArCH), 7.38 (1 H, d, *J* = 8.5, ArCH). δ_C (62.5 MHz, DMSO-d_6): 185.10 (COH), 138.84 (ArC, s), 136.11 (ArC, s), 131.49 (ArCH, s), 129.10 (ArCH, s), 126.17 (ArC, s), 117.12 (ArCH, s), 114.88 (ArCH, s), 86.55 (ArCI, s). Mass spectrum: HRMS (ES^-) 269.9405, C_9H_5INO requires 269.9416. υ cm^{-1}: 2894.6, 1622.8, 1565.9, 1523.0, 1478.7, 1435.3, 1384.2, 1318.1, 1284.4, 1232.3, 1134.4, 1091.0, 1042.3, 877.5, 795.0, 769.9, 748.3, 661.5, 608.4, 562.2.

6-Fluoroindole-3-carboxaldehyde



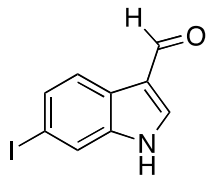
Yield; 76.5 %. mp. 173 - 178 °C.δ_H (400 MHz, DMSO-d_6): 12.19 (1 H, s, NH), 9.92 (1 H, s, CHO), 8.30 (1 H, d, *J* = 2.0, ArCH), 8.08 (1 H, dd, J_1 = 9.0, J_2 = 2.5, ArCH), 7.32 (1 H, dd, J_1 = 9.0, J_2=2.5, ArCH), 7.08 (1 H, td, J_1=9.0, J_2=2.5, ArCH). δ_C (125 MHz, DMSO-d_6): 185.42 (CHO), 160.02 (ArCF, d, *J* = 236.0), 139.54 (ArCH), 137.64 (ArC, d, *J* = 12.5), 122.39 (ArCH, d, *J* = 10.0), 121.28 (ArC), 118.53 (ArC), 110.90 (ArCH, d, *J*=25.0), 99.25 (ArCH, d, *J*=26.5). Mass spectrum: HRMS (EI^+) 162.0431, C_9H_5FNO requires 162.0433, *m/z* (EI^+): 134.0 (45 % $[M\text{-}COH]^+$). υ cm^{-1}: 3868.5, 3852.1, 3819.8, 3800.0, 3748.0, 3743.2, 3674.2, 3445.7, 3130.9, 2812.7, 1626.7, 1594.8, 1532.2, 1505.2, 1448.8, 1389.5, 1335.0, 1283.4, 1230.4, 1149.4, 1117.6, 1082.4, 951.2, 833.1, 812.9, 718.4, 633.5, 620.0, 604.1, 509.6.

6-Chloroindole-3-carboxaldehyde



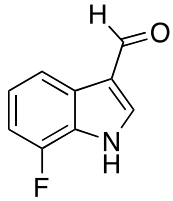
Yield; 96.4 %. mp. 212 - 214 °C. δ_H (400 MHz, DMSO-d_6): 12.23 (1 H, s, NH), 9.94 (1 H, s, COH), 8.40 (1 H, d, *J* = 2.0, ArCH), 8.08 (1 H, d, *J* = 8.0, ArCH), 7.57 (1 H, s, ArCH), 7.24 (1 H, d, *J* = 8.0, ArCH). δ_C (62.5 MHz, DMSO-d_6): 185.06 (CHO), 139.20 (ArCH), 137.49 (ArCH), 127.90 (ArCCl), 122.86 (ArC), 122.41 (ArCH), 122.05 (ArCH), 117.96 (ArC), 112.97 (ArCH). Mass spectrum: HRMS (AP^-) 178.0055, $C_9H_5{}^{35}ClNO$ requires 178.0060, *m/z* (AP^-): 142.0 (30 % $[M\text{-}Cl]^-$). υ cm^{-1}: 3434.1, 3108.2, 3041.9, 2968.9, 2915.4, 2853.2, 1634.4, 1575.6, 1525.4, 1492.2, 1451.7, 1430.9, 1384.6, 1327.8, 1278.6, 1243.4, 1145.0, 1132.0, 1090.1, 1061.1, 906.4, 841.8, 811.4, 752.6, 683.6, 605.5, 504.8.

6-Iodoindole-3-carboxaldehyde



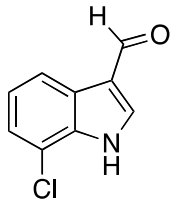
Yield; 94.8 %. mp. 213 - 215 °C. δ_H (400 MHz, DMSO-d_6): 12.19 (1 H, s, NH), 9.93 (1 H, s, CHO), 8.27 (1 H, d, *J*=3.0, ArCH), 7.90 (1 H, d, *J* = 8.5, ArCH), 7.88 (1 H, s, ArCH), 7.51 (1 H, dd, J_1 = 8.5, J_2 = 1.5, ArCH). δ_C (100 MHz, DMSO-d_6): 185.61 (CHO), 139.31 (ArCH), 138.84 (ArC), 131.02 (ArCH), 123.20 (ArCH), 121.45 (ArCH), 123.90 (ArC), 118.44 (ArC), 88.20 (ArCI). Mass Spectrum HRMS [ES^-] 269.9409, C_9H_7INO requires 269.9416. υ cm^{-1}: 3434.6, 2846.9, 1683.6, 1582.3, 1563.0, 1510.0, 1446.4, 1355.2, 1327.8, 1302.7, 1232.8, 1219.3, 1141.7, 1129.6, 1073.7, 1054.4, 847.6, 794.1, 774.8, 725.1, 712.1, 679.3, 661.5.

7-Fluoroindole-3-carboxaldehyde



Yield; 54.1 %. mp. 136 - 142 °C. δ_H (400 MHz, DMSO-d_6): 12.71 (1 H, s, NH), 9.98 (1 H, s, COH), 8.37 (1 H, d, *J* = 3.0, ArCH), 7.91 (1 H, d, *J* = 7.5, ArCH), 7.20 (1 H, dt, J_1 = 7.5, J_2 = 4.5 , ArCH), 7.17 (1 H, dd, J_1 = 11.5, J_2 = 7.5, ArCH). δ_C (125 MHz, DMSO-d_6): 185.67 (CHO), 149.53 (ArCF, d, *J* = 243.5), 139.41 (ArCH), 128.24 (ArC, d, *J* = 5.0), 125.26 (ArC, d, *J* = 12.5), 123.33 (ArCH, d, *J* = 6.0), 119.26 (ArC), 117.43 (ArCH, d, *J* = 4.0), 109.00 (ArCH, d, *J* = 16.0). Mass Spectrum HRMS [EI^+] 163.0431, C_9H_7FNO requires 163.0433, *m/z* (EI^+): 134.0412 (30 % [M-COH]$^+$). υ cm^{-1}: 3744.6, 3675.7, 3629.4, 3117.9, 3035.9, 2877.3, 2362.9, 1617.5, 1529.8, 1499.4, 1467.1, 1400.6, 1344.6, 1282.0, 1229.9, 1179.7, 1151.3, 1133.0, 1044.3, 966.2, 821.5.

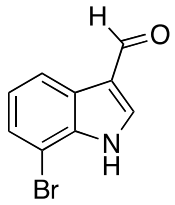
7-Chloroindole-3-carboxaldehyde



Yield; 88.5 %. mp. 177 - 180 °C. δ_H (400 MHz, DMSO-d_6): 12.56 (1 H, s, NH), 9.97 (1 H, s, COH), 8.39 (1 H, d, *J*=3.0, ArCH), 8.06 (1 H, d, *J* = 8.0, ArCH), 7.36 (1 H, d, *J* = 8.0, ArCH), 7.23 (1 H, t, *J* = 8.0, ArCH). δ_C (125 MHz, DMSO-d_6): 185.81 (CHO), 139.61 (ArCH), 134.39 (ArCCl), 126.48 (ArC), 123.79 (ArCH), 123.54 (ArCH), 120.25 (ArCH), 119.34 (ArC), 117.13 (ArC). Mass Spectrum HRMS [EI^+] 179.0134, $C_9H_7{}^{35}ClNO$ requires 179.0138, *m/z* (EI^+): 150.0067 (25 % [M-COH]$^+$) 83.9520 (35 % [M-Cl,COH,NHCH]$^+$). υ cm^{-1}: 3434.6, 3135.2, 3111.1, 3064.8, 3034.9, 2938.5, 2888.8, 2825.2, 2698.4, 2577.9, 1938.1 1642.6, 1621.4, 1526.9, 1499.9, 1453.3, 1390.4, 1340.3,

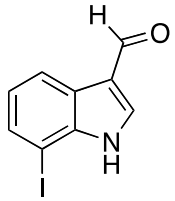
1275.7, 1248.2, 1206.7, 1160.0, 1130.1, 1111.8, 1048.6, 976.8, 890.5, 848.0, 780.1, 740.5, 658.1, 610.36.

7-Bromoindole-3-carboxaldehyde



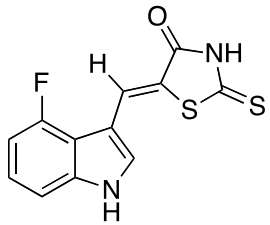
Yield; 81.8 %. mp. 167 - 170 °C. δ_H (400 MHz, DMSO-d_6): 12.40 (1 H, s, NH), 9.97 (1 H, s, CHO), 8.38 (1 H, s, ArCH), 8.11 (1 H, d, J = 8.0, ArCH), 7.50 (1H, dd, J_1=8.0, J_2 = 1.0, ArCH), 7.23 (1H, t, J = 7.8, ArCH). δ_C (125 MHz, DMSO-d_6): 185.93 (CHO), 139.67 (ArCH), 135.92 (ArC), 126.62 (ArCH), 126.23 (ArC), 124.18 (ArCH), 120.72 (ArCH), 119.34 (ArC), 105.30 (ArCBr). Mass Spectrum HRMS [EI$^+$] 221.9552, $C_9H_7{}^{79}BrNO$ requires 221.9554, *m/z* (EI$^+$): 193.9609 (20 % [M-COH]$^+$), 115.0410 (20 % [M-Br+COH]$^+$), 83.9503 (100 % [M-Br,COH,NHCH]$^+$). υ cm^{-1}: 3434.1, 3143.9, 3034.9, 2929.3, 2881.1, 2358.0, 1638.7, 1617.5, 1568.3, 1522.0, 1447.3, 1426.6, 1389.9, 1337.9, 1271.3, 1242.9, 1203.9, 1158.5, 1125.3, 1098.8, 901.6, 879.4, 831.7, 777.7, 740.1, 652.3, 606.0, 561.7, 496.1, 454.2.

7-Iodoindole-3-carboxaldehyde



Yield; 91.5 %. mp. 104 - 109 °C. δ_H (400 MHz, DMSO-d_6): 12.11 (1 H, s, NH), 9.96 (1 H, s, CHO), 8.33 (1 H, d, J = 2.5 ArCH), 8.12 (1 H, d, J = 8.0, ArCH), 7.67 (1 H, d, J = 8.0, ArCH), 7.03 (1H, t, J = 8.0, ArCH). δ_C (125 MHz, DMSO-d_6): 185.98 (CHO), 139.43 (ArCH), 139.25 (ArC), 132.94 (ArCH), 125.19 (ArC), 124.44 (ArCH), 121.24 (ArCH), 119.44 (ArC), 78.04 (ArCI). Mass Spectrum HRMS [EI$^+$] 270.9490, C_9H_6INO requires 270.9494, *m/z* (EI$^+$): 241.9476 (10 % [M-CHO]$^+$), 143.0339 (15 % [M-I]$^+$). υ cm^{-1}: 3433.6, 3063.4, 1638.2, 1610.8, 1558.7, 1522.5, 1488.3, 1442.0, 1384.6, 1331.1, 1277.6, 1237.1, 1204.8, 1149.4, 1127.2, 1092.5, 872.6, 817.2, 773.8, 736.7, 650.4, 608.0, 554.0.

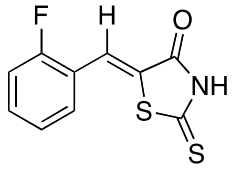
General method for the condensation of aromatic aldehydes with rhodanine.



A suspension of 4-fluoroindole-3-carboxaldehyde (0.40 g, 2.46 mmol), rhodanine (0.33 g, 2.49 mmol) and sodium acetate (0.59 g, 7.21 mmol) in glacial acetic acid (5 cm^3) was heated under reflux for 2 hours. The reaction mixture was then cooled to room temperature and water (15 cm^3) was added to the solution. The precipitate that formed was collected by filtration under reduced pressure and washed with water (2 × 10 cm^3). The solid was air dried under reduced pressure and washed with diethyl ether (5 cm^3) to give the title compound as a dark red solid (0.54 g, 79.3 %). mp. ~340 °C (dec.). δ_H (400 MHz, DMSO-d_6): 13.61 (1 H, s, NH), 12.55 (1 H, s, NH), 7.94 (1 H, s, CH=CS), 7.81 (1 H, d, J_{HH} = 3.5, ArCH), 7.50 (1 H, d, J_{HH} = 8.0, ArCH), 7.22 (1 H, dt, J_{HH} = 8.0, J_{HH} = 5.0, ArCH), 7.00 (1H, ddd, J_{HF}=12.0, J_{HH}=8.0, J_{HH} = 3.5, ArCH). δ_C (125 MHz, DMSO-d_6): 194.63 (CS), 169.08 (CO), 156.49 (ArCF, d, J = 244.5), 138.94 (ArC, d, J = 10.0), 129.89 (ArCH), 125.19 (ArCH, d, J = 5.0), 123.89 (ArCH, d, J = 8.0), 118.95 (ArC), 114.83 (ArC, d, J = 18.0), 109.24 (ArCH, d, J = 4.0), 109.16 (ArC, d, J = 3.0), 106.68 (ArCH, d, J = 19.0). Mass spectrum: HRMS (EI^+) 277.9988, $C_{12}H_7FN_2OS_2$ requires 277.9984, *m/z* (EI^+): 161.1 (30 % $[M\text{-}SCSNHCO]^+$). υ cm^{-1}: 3242.2, 1685.0, 1634.4, 1589.5, 1575.6, 1511.9, 1430.0, 1345.1, 1324.4, 1296.4, 1277.1, 1224.1, 1205.8, 1158.5, 1148.4, 1033.7, 841.8, 808.0, 777.2, 726.6, 690.9, 670.6, 614.2, 597.8, 576.6, 556.4, 495.1, 481.6.

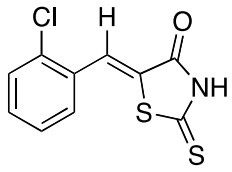
Benzylidene Derivatives

(Z)-5-(2-fluorobenzylidene)-2-thioxothazolidene-4-one



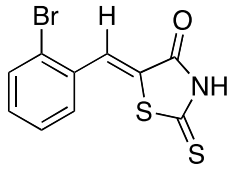
Yield; 91.5 %. mp. 202 - 205 °C. δ_H (400 MHz, DMSO-d_6): 13.93 (1 H, s, NH), 7.58 (1 H, s, CH=CS), 7.55 (1 H, dt, J_{HF} = 7.5, J_{HH}=1.0, ArCH), 7.49 (1 H, dt, J_{HF} = 7.5, J_{HH}=1.0, ArCH), 7.39 (2H, m, ArCH). δ_C (125 MHz, DMSO-d_6): 195.88 (CS), 169.64 (CO), 161.12 (ArCF, d, J = 251.5), 133.50 (ArCH, d, J = 10.0), 129.82 (ArCH), 128.58 (ArC, d, J = 2.5), 126.01 (ArC, d, J = 4.0), 122.77 (ArCH, d, J = 6.5), 121.35 (ArCH, d, J = 11.5), 116.73 (ArCH, d, J = 21.5). δ_F (282 MHz, DMSO-d_6): -114.01. Mass spectrum: HRMS (ES^-) 237.9796, $C_{10}H_5FNOS_2$ requires 237.9797. υ cm^{-1}: 3054.7, 1695.1, 1608.8, 1593.4, 1482.0, 1456.0, 1430.0, 1309.9, 1211.1, 1158.0, 1068.9, 798.9, 751.1, 677.4, 548.7.

(Z)-5-(2-chlorobenzylidene)-2-thioxothazolidene-4-one



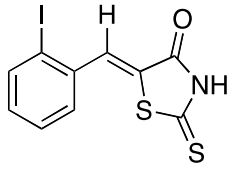
Yield; 22.1 %. mp. 108 - 113 °C. δ_H (400 MHz, DMSO-d_6): 13.96 (1 H, s, NH), 7.75 (1 H, s, CH=CS), 7.64 (1 H, dd, J_1 = 8.5, J_2 = 1.0, ArCH), 7.52 (3H, m, ArCH). δ_C (125 MHz, DMSO-d_6): 195.55 (CS), 169.18 (CO), 134.73 (ArCCl), 132.05 (ArCH), 130.83 (ArC), 130.41 (ArCH), 129.26 (ArCH), 129.11 (ArC), 128.23 (ArCH), 126.02 (ArCH). Mass spectrum: HRMS (EI^+) 254.9586, $C_{10}H_5{}^{35}ClNOS_2$ requires 254.9579, *m/z* (ES^+): 168.0 (50 % $[M\text{-}CSNHCO]^+$). υ cm^{-1}: 3440.9, 3066.7, 2868.6, 1734.7, 1699.0, 1594.6, 1584.7, 1456.5, 1435.7, 1336.0, 1306.5, 1280.5, 1239.5, 1197.6, 1161.9, 1069.8, 1041.4, 805.6, 750.2, 723.7, 701.0, 675.5, 632.5, 532.7, 467.2.

(Z)-5-(2-bromobenzylidene)-2-thioxothazolidene-4-one



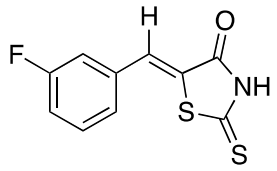
Yield; 92.9 %. mp. 189 - 192 °C. δ_H (500 MHz, DMSO-d_6): 14.00 (1 H, s, NH), 7.88 (1 H, d, J = 8.0, ArCH), 7.63 (1 H, s, CH=CS), 7.61 (1 H, d, J = 7.0 ArCH), 7.49 (1H, t, J_1 = 8.0, J_2 = 7.0, ArCH). δ_C (100 MHz, DMSO-d_6): 196.02 (CS), 169.50 (CO), 134.10 (ArCH), 132.91 (ArC), 132.62 (ArCH), 129.79 (ArCH), 129.53 (ArC), 129.21 (ArCH), 129.18 (ArCH), 126.07 (ArCBr). Mass spectrum: HRMS (AP^-) 297.8987, $C_{10}H_5{}^{79}BrNOS_2$ requires 297.8996, *m/z* (AP^-): 159.0538 (20 % $[M\text{-}Br +CSNH]^-$). υ cm^{-1}: 3093.7, 2848.9, 1732.3, 1605.9, 1452.1, 1429.5, 1277.1, 1233.3, 1196.1, 1065.5, 1002.8, 890.5, 752.6, 724.6, 681.2, 525.5.

(Z)-5-(2-iodobenzylidene)-2-thioxothazolidene-4-one



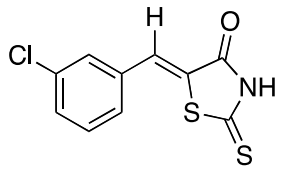
Yield; 70.7 %. mp. 188 - 190 °C. δ_H (500 MHz, MeOD-d_4): 7.75 (1 H, s, CH=CS), 7.65 (1 H, dd, J_1 = 8.0, J_2 = 1.0, ArCH), 7.45 (1 H, dd, J_1 = 8.0, J_2 = 2.0, ArCH), 7.40 (1 H, t, J = 8.0, ArCH), 7.24 (1 H, td, J_1 = 8.0, J_2 = 2.0, ArCH). δ_C (62.5 MHz, THF-d_8): 195.11 (CS), 168.36 (CO), 140.43 (ArCH), 136.90 (ArC), 134.04 (ArCH), 131.32 (ArCH), 129.60 (ArC), 128.83 (ArCH), 128.63 (ArCH), 101.98 (ArCI). Mass spectrum: HRMS (EI^+) 346.8947, $C_{10}H_5INOS_2$ requires 346.8936, *m/z* (EI^+): 159.0119 (25 % $[M\text{-}I +CSNH]^+$), 83.9491 (100 %). υ cm^{-1}: 3142.9, 3051.8, 1694.6, 1589.5, 1455.5, 1428.0, 1311.4, 1281.0, 1230.4, 1198.5, 1068.9, 1014.9, 753.1, 669.2, 651.8, 537.6.

(Z)-5-(3-fluorobenzylidene)-2-thioxothazolidene-4-one



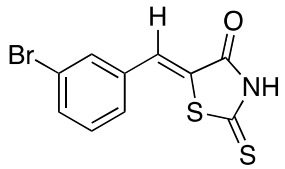
Yield; 68.2 %. mp. 203 - 206 °C. δ_H (400 MHz, DMSO-d_6): 13.91 (1 H, s, NH), 7.63 (1 H, s, CH=CS), 7.58 (1 H, q, *J* = 8.0, ArCH), 7.45 (1 H, dd, J_1 = 10.0, J_2 = 2.0, ArCH), 7.40 (1 H, d, *J* = 8.0 ArCH), 7.33 (1 H, dt, *J* = 8.0, *J* = 2.0, ArCH). δ_C (125 MHz, DMSO-d_6): 195.85 (CS), 169.68 (CO), 162.78 (ArCF, d, *J* = 245.5), 135.88 (ArC, d, *J* = 8.0), 131.93 (ArCH, d, *J* = 8.0), 130.51 (ArCH, d, *J* = 3.0), 127.66 (ArC, s), 126.39 (ArCH, d, *J* = 3.0), 117.90 (ArCH, d, *J* = 21.0), 117.55 (ArCH, d, *J* = 22.0). δ_F (282 MHz, DMSO-d_6): -111.75; Mass spectrum: HRMS (ES^-) 237.9802, $C_{10}H_5FNOS_2$ requires 237.9797. υ cm^{-1}: 3445.7, 3193.5, 2360.0, 1705.3, 1612.2, 1600.6, 1577.0, 1489.7, 1432.9, 1288.2, 1253.5, 1220.7, 952.2, 775.2, 672.1, 529.4.

(Z)-5-(3-chlorobenzylidene)-2-thioxothazolidene-4-one



Yield; 86.2 %. mp. 240 - 242 °C. δ_H (400 MHz, DMSO-d_6): 13.90 (1 H, s, NH), 7.66 (1 H, s, ArCH), 7.61 (1 H, s, CH=CS), 7.55 (1 H, t, *J* = 3.0, ArCH), 7.53 (1 H, d, *J* = 2.0, ArCH), 7.50 (1 H, dd, J_1 = 6.0, J_2 = 2.0, ArCH). δ_C (125 MHz, DMSO-d_6): 195.74 (CS), 169.61 (CO), 135.57 (ArC), 134.49 (ArCCl), 131.63 (ArCH), 130.66 (2ArCH), 130.24 (ArCH), 128.57 (ArCH), 127.78 (ArC). Mass spectrum: HRMS (ES^-) 253.9500, $C_{10}H_5{}^{35}ClNOS_2$ requires 253.9501 *m/z* (ES^-): 238.0 (5 %). υ cm^{-1}: 3111.1, 2848.4, 1717.3 1608.3, 1559.7, 1478.7, 1438.6, 1412.6, 1324.4, 1299.8, 1284.8, 1222.2, 1180.7, 1094.4, 1078.5, 1058.3, 1000.9, 911.2, 895.8, 860.6, 782.0, 739.1, 704.4, 681.2, 630.1, 547.2, 518.3.

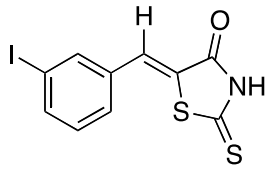
(Z)-5-(3-bromobenzylidene)-2-thioxothazolidene-4-one



Yield; 86.4 %. mp. 250 - 254 °C. δ_H (400 MHz, DMSO-d_6): 13.92 (1 H, s, NH), 7.80 (1 H, s, ArCH), 7.68 (1 H, d, *J* = 8.0, ArCH), 7.61 (1 H, s, CH=CS), 7.48 (1 H, d, *J*=8.0, ArCH), 7.48 (1 H, t, *J*=8.0, ArCH). δ_C (125 MHz, DMSO-d_6): 195.64 (CS), 169.53 (CO), 135.77 (ArC), 133.48 (ArCH), 131.77 (ArCH), 130.13 (ArCH), 128.89 (ArCH), 127.69 (ArC), 122.93 (ArCBr). Mass spectrum: HRMS (ES^-) 297.8999, $C_{10}H_5{}^{79}BrNOS_2$ requires 297.8996, *m/z* (ES^-): 219.2 (28 % $[M-Br]^-$). υ cm^{-1}: 3422.6,

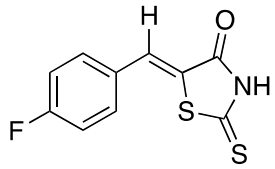
3108.7, 2845.0, 1716.8, 1606.4, 1552.9, 1476.2, 1437.7, 1408.7, 1283.4, 1220.2, 1178.3, 1072.2, 1059.2, 1002.8, 910.2, 881.3, 862.0, 779.6, 737.6, 693.3, 673.0, 627.7, 546.7, 517.8.

(Z)-5-(3-iodobenzylidene)-2-thioxothazolidene-4-one



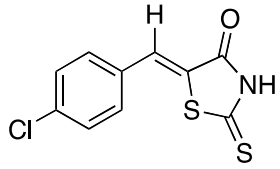
Yield; 74.6 %. mp. 236 - 239 °C. δ_H (400 MHz, DMSO-d_6): 13.90 (1 H, s, NH), 7.96 (1 H, s, ArCH), 7.84 (1 H, d, *J* = 8.0, ArCH), 7.57 (1 H, s, CH=CS) 7.57 (1 H, d, *J* = 8.0, ArCH), 7.32 (1 H, t, *J* = 8.0, ArCH). δ_C (100 MHz, DMSO-d_6): 195.73 (CS), 169.56 (CO), 139.31 (2 ArCH), 135.60 (ArC), 131.67 (ArCH), 130.22 (ArCH), 129.27 (ArCH), 127.27 (ArC), 96.18 (ArCI). Mass spectrum: HRMS (AP^-) 345.8861, $C_{10}H_5INOS_2$ requires 345.8857, *m/z* (AP^-): 219.2 (35 % $[M-I]^-$). υ cm^{-1}: 3396.0, 3147.7, 3055.2, 2847.4, 2349.8, 1690.3, 1600.6, 1563.5, 1550.5, 1472.9, 1437.7, 1404.4, 1310.9, 1280.5, 1230.8, 1193.7, 1179.3, 1099.2, 1066.9, 1013.9, 992.2, 911.2, 885.6, 876.0, 864.9, 805.1, 772.8, 714.0, 685.6, 669.2, 626.8, 546.7, 530.3, 429.1, 414.6.

(Z)-5-(4-fluorobenzylidene)-2-thioxothazolidene-4-one



Yield; 87.6 %. mp. 229 - 231°C.δ_H (400 MHz, DMSO-d_6): 13.86 (1 H, s, NH), 7.66 (3 H, m, ArCH and CH=CS), 7.37 (2 H, t, *J* = 8.5, ArCH). δ_C (125 MHz, DMSO-d_6): 195.45 (CS), 169.26 (CO), 163.01 (ArCF, d, *J* = 251.5), 132.91 (ArCH, d, *J* = 9.0), 130.47 (ArCH), 129.63 (ArC, d, *J* = 4.0), 125.20 (ArCH), 116.58 (2ArCH, d, *J* = 22.0). δ_F (300 MHz, DMSO-d_6): -108.34; Mass spectrum: HRMS (ES^-) 237.9794, $C_{10}H_5FNOS_2$ requires 237.9797. υ cm^{-1}: 3098.1, 1724.1, 1586.7, 1508.1, 1446.8, 1290.6, 1228.4, 1179.3, 1160.9, 1063.6, 921.3, 828.3, 794.1, 748.3, 689.0, 597.3, 549.6, 524.5.

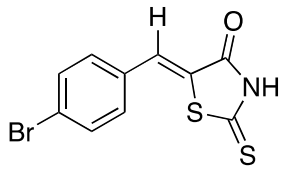
(Z)-5-(4-chlorobenzylidene)-2-thioxothazolidene-4-one



Yield; 76.4 %. mp. 233 - 235 °C. δ_H (400 MHz, DMSO-d_6): 13.90 (1 H, s, NH), 7.61 (1 H, s, CH=CS), 7.58 (4 H, d, *J* = 8.5, ArCH). δ_C (125 MHz, DMSO-d_6): 195.91 (CS), 169.90 (CO), 135.80 (ArCCl), 132.48 (2 ArCH), 132.39 (ArC), 130.54 (ArCH), 129.95 (2 ArCH), 126.92 (ArC). Mass

spectrum: HRMS (ES^-) 253.9509, $C_{10}H_5{}^{35}ClNOS_2$ requires 253.9501. υ cm^{-1}: 3413.9, 3066.7, 2848.8, 1704.8, 1596.3, 1582.3, 1558.2, 1487.3, 1444.9, 1404.4, 1293.0, 1281.5, 1232.3, 1187.5, 1177.3, 1086.7, 1061.6, 1007.6, 917.5, 827.3, 796.9, 756.4, 723.2, 684.1, 572.8, 545.8, 518.8.

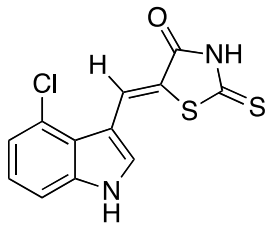
(Z)-5-(4-bromobenzylidene)-2-thioxothazolidene-4-one



Yield; 85.1 %. mp. 243 - 248 °C. δ_H (400 MHz, DMSO-d_6): 13.90 (1 H, s, NH), 7.74 (2 H, d, *J* = 8.5, ArCH), 7.62 (1 H, s, CH=CS), 7.53 (2 H, d, *J* = 8.5, ArCH). δ_C (125 MHz, DMSO-d_6): 195.84 (CS), 169.78 (CO), 132.90 (2 ArCH), 132.69 (ArC), 132.64 (2 ArCH), 130.72 (ArCH), 126.91 (ArCBr), 124.76 (ArC). Mass spectrum: HRMS (ES^-) 297.8991, $C_{10}H_5{}^{79}BrNOS_2$ requires 297.8996. υ cm^{-1}: 3403.3, 3076.9, 2847.9, 1706.2, 1595.8, 1577.5, 1553.9, 1483.5, 1441.5, 1399.1, 1303.6, 1291.6, 1279.1, 1231.3, 1177.8, 1070.8, 1059.2, 1006.7, 918.0, 825.9, 800.8, 750.2, 717.9, 686.1, 665.3, 561.7, 540.0, 516.3.

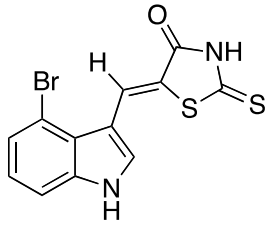
Indole Derivatives

(Z)-5-((4-chloro-1*H*-indol-3-yl)methylene)-2-thioxothiazolidin-4-one



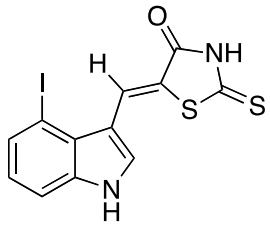
Yield; 86.0 %. mp. ~ 350 °C (dec.). δ_H (400 MHz, DMSO-d_6): 13.62 (1 H, s, NH), 12.63 (1 H, s, NH), 8.52 (1 H, s, C*H*=CS), 7.90 (1 H, d, *J* = 2.5, ArCH), 7.50 (1 H, dd, J_1 = 7.0, J_2 = 2.5, ArCH), 7.24 (2 H, m, 2 x ArCH). δ_C (125 MHz, DMSO-d_6): 195.35 (CS), 169.70 (CO), 138.54 (ArC), 131.63 (ArCH), 125.99 (ArCH), 125.34 (ArCCl), 124.43 (ArCH), 123.03 (ArCH), 122.93 (ArC), 119.10 (ArC), 112.61 (ArCH), 111.24 (ArC). Mass Spectrum HRMS [EI^+] 293.9691, $C_{12}H_7{}^{35}ClN_2OS_2$ requires 293.9688. υ cm^{-1}: 3821.7, 3816.0, 3217.7, 2837.7, 2360.0, 1849.7, 1833.0, 1692.7, 1616.1, 1578.9, 1513.9, 1487.8, 1443.9, 1421.8, 1349.0, 1340.3, 1322.9, 1275.2, 1258.3, 1258.3, 1212.0, 1194.2, 1155.6, 1079.5, 1047.2, 1023.5, 945.4, 936.8, 918.0, 828.3, 801.8, 787.8, 7752, 727.0, 694.7, 648.4, 608.9, 571.3, 540.5, 506.7, 477.3, 455.6, 420.4.

(Z)-5-((4-bromo-1*H*-indol-3-yl)methylene)-2-thioxothiazolidin-4-one



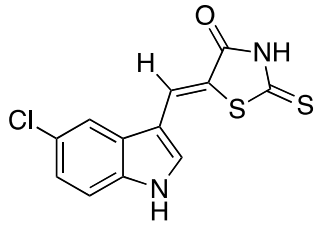
Yield; 35.7 %. mp. ~350 °C (dec.). δ_H (400 MHz, DMSO-d_6): 12.39 (2 H, s, 2 NH), 8.48 (1 H, s, C*H*=CS), 7.75 (1 H, s, ArCH), 7.54 (1 H, d, *J* = 8.0, ArCH), 7.38 (1 H, d, *J* = 8.0, ArCH), 7.13 (1 H, t, *J* = 8.0, ArCH). δ_C (100 MHz, DMSO-d_6): 183.92 (CS), 172.03 (CO), 137.89 (ArC), 129.94 (ArCH), 125.36 (2ArCH), 123.78 (ArCH), 123.72 (ArC), 120.79 (ArC), 112.97 (ArCBr), 112.33 (ArCH), 112.09 (ArC). Mass Spectrum HRMS [EI$^+$] 337.9186, $C_{12}H_7{}^{79}BrN_2OS_2$ requires 337.9183. υ cm^{-1}: 3209.5, 3108.2, 2838.2, 1892.8, 1829.6, 1691.8, 1577.0, 1562.5, 1512.9, 1484.9, 1443.9, 1417.9, 1354.3, 1336.0, 1324.4, 1300.8, 1274.7, 1257.8, 1213.0, 1192.8, 1155.6, 1082.4, 1045.7, 1021.6, 944.0, 914.1, 797.4, 786.3, 772.4, 726.6, 694.2, 642.2, 608.4, 564.6, 534.7, 498.5, 472.5, 453.7, 419.9.

(Z)-5-((4-iodo-1*H*-indol-3-yl)methylene)-2-thioxothiazolidin-4-one



Yield; 53.7 %. mp. ~ 320 °C (dec.). δ_H (400 MHz, DMSO-d_6): 13.66 (1 H, s, NH), 12.53 (1 H, s, NH), 8.94 (1 H, s, C*H*=CS), 7.92 (1 H, d, *J* = 2.0 ArCH), 7.70 (1 H, d, *J* = 7.5, ArCH), 7.58 (1 H, d, *J* = 7.5, ArCH), 7.01 (1 H, t, *J* = 7.5, ArCH). δ_C (100 MHz, DMSO-d_6): 194.23 (CS), 169.73 (CO), 137.79 (ArC), 133.64 (ArCH), 132.15 (ArCH), 126.72 (ArC), 125.30 (ArCH), 125.15 (ArCH), 117.98 (ArC), 113.63 (ArCH), 112.14 (ArC), 85.36 (ArCI). Mass Spectrum HRMS [ES$^-$] 384.8966, $C_{12}H_7IN_2OS_2$ requires 384.8961, *m/z* (ES$^-$): 297.9160 (25 % [M-CONHCS]$^-$). υ cm^{-1}: 3434.1, 3236.9, 3041.2, 2851.7, 1676.8, 1569.8, 1509.5, 1477.2, 1449.2, 1410.2, 1350.9, 1320.0, 1270.4, 1215.9, 1194.2, 1153.2, 1128.2, 1045.2, 1019.7, 877.9, 783.4, 771.9, 736.2, 694.3, 640.7, 608.4.

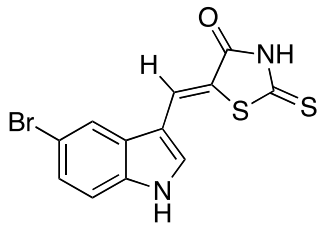
(Z)-5-((5-chloro-1*H*-indol-3-yl)methylene)-2-thioxothiazolidin-4-one



Yield; 79.4 %. mp. ~ 330 °C (dec.). δ_H (500 MHz, DMSO-d_6): 13.57 (1 H, s, NH), 12.40 (1 H, s, NH), 8.06 (1 H, s, CH=CS), 7.95 (1 H, s, ArCH), 7.86 (1 H, s, ArCH), 7.51 (1 H, d, *J* = 8.5, ArCH), 7.26 (1 H, d, *J* = 8.5, ArCH). δ_C (125 MHz, DMSO-d_6): 195.13 (CS), 169.47 (CO), 135.34 (ArC), 131.79

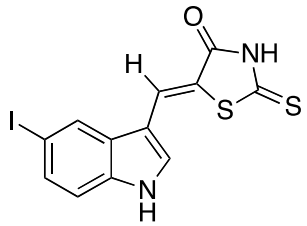
(ArCH), 128.52 (ArC), 126.56 (ArC), 124.66 (ArCH), 123.85 (ArCH), 119.19 (ArC) 118.76 (ArCH), 114.48 (ArCH), 111.16 (ArCCl). Mass spectrum: HRMS (EI^+) 293.9688, $C_{12}H_6{}^{35}ClN_2OS_2$ requires 293.9688, *m/z* (EI^+): 190.0121, 206.9794 (100 % $[M\text{-}CSNHCO]^+$). υ cm^{-1}: 3259.6, 3110.6, 2837.3, 2360.0, 1824.3, 1688.4, 1622.8, 1584.2, 1564.0, 1510.0, 1457.0, 1441.1, 1423.2, 1355.7, 1332.1, 1305.6, 1271.8, 1225.5, 1202.9, 1157.6, 1128.2, 1093.9, 1045.7, 1015.3, 914.6, 895.7, 864.4, 819.6, 797.9, 766.1, 747.8, 729.4, 693.8, 683.2, 609.9, 571.3, 558.8, 531.3, 468.2, 418.5.

(Z)-5-((5-bromo-1*H*-indol-3-yl)methylene)-2-thioxothiazolidin-4-one



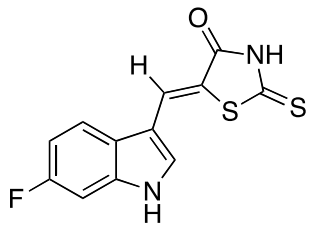
Yield; 86.2 %. mp. decomposed ~ 300 °C. δ_H (400 MHz, DMSO-d_6): 13.60 (1 H, s, NH), 12.44 (1 H, s, NH), 8.23 (1 H, d, *J* = 2.0, ArCH), 7.96 (1 H, s, CH=CS), 7.86 (1 H, d, *J* = 3.0, ArCH), 7.47 (1 H, d, *J* = 8.5, ArCH), 7.38 (1 H, dd, J_1 =8.5, J_2 = 2.0, ArCH). δ_C (100 MHz, DMSO-d_6): 195.17 (CS), 169.57 (CO), 135.57 (ArC), 131.36 (ArCH), 129.11 (ArC), 126.31 (ArCH), 124.90 (ArCH), 121.77 (ArCH), 119.28 (ArCH), 114.92 (ArCBr), 114.55 (ArCH), 111.04 (ArC). Mass spectrum: HRMS (EI^+) 337.9180, $C_{12}H_6{}^{79}BrN_2OS_2$ requires 337.9183. υ cm^{-1}: 3254.8, 3109.2, 3036.9,2849.3, 2725.9, 1868.2, 1810.8, 1678.7, 1616.1, 1580.9, 1565.9, 1511.4, 149.2, 1349.0, 1330.2, 1308.0, 1268.5, 1213.5, 1146.5, 1092.0, 1080.0, 1045.2, 1019.7, 936.7, 908.3, 886.6, 859.1, 803.2, 772.4, 748.2, 723.2, 702.0, 687.5, 668.2, 613.7, 595.4, 570.8, 560.2, 542.9, 528.9, 471.0, 461.4, 461.4, 418.0

(Z)-5-((5-iodo-1*H*-indol-3-yl)methylene)-2-thioxothiazolidin-4-one



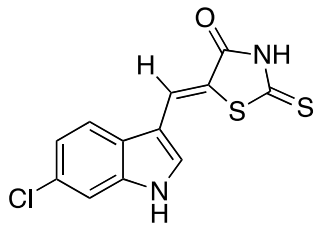
Yield; 74.1 %. mp. ~ 310 °C (dec.). δ_H (500 MHz, DMSO-d_6): 13.56 (1 H, s, NH), 12.38 (1 H, s, NH), 8.37 (1 H, s, CH=CS), 7.94 (1 H, s, ArCH), 7.79 (1 H, s, ArCH), 7.52 (1 H, d, *J* = 8.0, ArCH), 7.34 (1 H, d, *J* = 8.0, ArCH). δ_C (100 MHz, DMSO-d_6): 195.14 (CS), 169.56 (CO), 135.93 (ArC), 134.31 (ArC), 131.77 (ArCH), 130.90 (ArCH), 129.75 (ArC), 127.76 (ArCH), 124.93 (ArCH), 115.27 (ArCH), 110.69 (ArC), 86.13 (ArCI). Mass spectrum: HRMS (EI^+) 385.9038, $C_{12}H_7IN_2OS_2$ requires 385.9045. υ cm^{-1}: 3262.5, 3037.8, 2850.8, 1678.3, 1576.5, 1562.5, 1510.0, 1447.8, 1349.0, 1327.3, 1305.1, 1269.4, 1212.0, 1147.9, 1076.6, 908.3, 879.4, 861.5, 802.7, 769.9, 688.0, 609.9, 590.1, 528.9.

(Z)-5-((6-fluoro-1*H*-indol-3-yl)methylene)-2-thioxothiazolidin-4-one



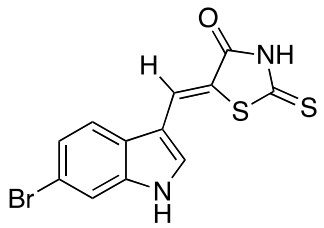
Yield; 69.7 %. mp. ~ 330 °C (dec.). δ_H (400 MHz, DMSO-d_6): 13.57 (1 H, s, NH), 12.30 (1 H, s, NH), 7.94 (1 H, dd J_1 = 8.5, J_2 = 5.5, ArCH), 7.89 (1 H, s, CH=CS), 7.77 (1 H, d, J = 3.0, ArCH), 7.27 (1 H, dd. J_1 = 9.5, J_2 = 2.0, ArCH), 7.41 (1 H, dt, J_1=8.5, J_2 = 2.0, ArCH). δ_C (100 MHz, DMSO-d_6): 194.98 (CS), 169.43 (CO), 160.01 (ArCF, d, J = 236.0), 136.72 (ArC d, J = 12.0), 130.78 (ArC), 124.77 (ArCH), 123.82 (ArC), 120.29 (ArCH, d, J = 10.0), 119.01 (ArCH), 111.32 (ArCH, s), 110.10 (ArCH d, J = 25.0), 98.96 (ArCH, d, J = 26.0). Mass spectrum: HRMS (AP^-) 276.9900, $C_{12}H_6FN_2OS_2$ requires 276.9906, *m/z* (AP^-): 190.0 (54 % [M-CSNHCO]$^-$). υ cm^{-1}: 3446.2, 3214.3, 3107.7, 2851.2, 1811.8, 1678.7, 1626.7, 1599.2, 1573.2, 1516.3, 1497.0, 1448.8, 1438.6, 1419.8, 1357.6, 1340.8, 1301.2, 1190.4, 1146.5, 1107.9, 1072.2, 1052.9, 1019.7, 952.7, 909.3, 854.3, 816.7, 806.6, 733.8, 703.9, 691.4, 614.2, 605.1, 594.5, 571.8, 542.9.

(Z)-5-((6-chloro-1*H*-indol-3-yl)methylene)-2-thioxothiazolidin-4-one



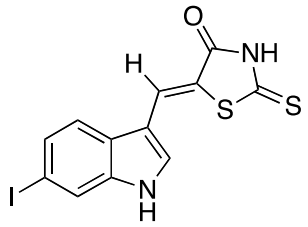
Yield; 84.8 %. mp. ~ 350 °C (dec.). δ_H (400 MHz, DMSO-d_6): 13.59 (1 H, s, NH), 12.35 (1 H, s, NH), 7.94 (1 H, d, J = 8.5, ArCH), 7.88 (1 H, s, CH=CS), 7.82 (1 H, d, J = 2.5, ArCH), 7.53 (1 H, s, ArCH), 7.19 (1 H, d, J = 8.5, ArCH). δ_C (100 MHz, DMSO-d_6): 194.60 (CS), 169.03 (CO), 136.76 (ArCH), 130.66 (ArC), 127.82 (ArCCl), 125.50 (ArCH), 124.17 (ArCH), 121.50 (ArCH), 120.08 (ArC), 118.91 (ArC), 112.09 (ArCH), 110.93 (ArCH). Mass spectrum: HRMS (ES^-) 292.9601, $C_{12}H_6{}^{35}ClN_2OS_2$ requires 292.9610, *m/z* (ES^-): 206.0 (34 % [M-CSNHCO]$^-$). υ cm^{-1}: 3231.6, 3103.9, 2849.3, 2350.3, 1676.8, 1584.7, 1570.3, 1513.4, 1488.3, 1437.2, 1416.5, 1353.3, 1333.1, 1295.5, 1228.0, 1192.8, 1146.5, 1072.2, 1058.3, 1021.1, 931.9, 905.4, 851.9, 798.9, 785.9, 749.7, 735.2, 688.0, 608.9, 594.5, 575.7, 565.0, 538.0, 467.2, 418.5.

(Z)-5-((6-bromo-1*H*-indol-3-yl)methylene)-2-thioxothiazolidin-4-one



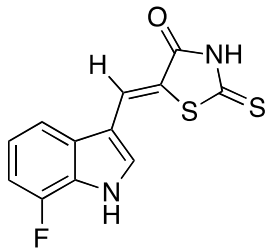
Yield; 71.6 %. mp. ~ 320 °C (dec.). δ_H (400 MHz, DMSO-d_6): 13.59 (1 H, s, NH), 12.34 (1 H, s, NH), 7.91 (2 H, m, ArCH and CH=CS), 7.81 (1 H, d, *J* = 2.5, ArCH), 7.67 (1 H, s, ArCH), 7.31 (1 H, d, *J* = 8.5, ArCH). δ_C (125 MHz, DMSO-d_6): 195.07 (CS), 169.49 (CO), 137.70 (ArC), 131.70 (ArCH), 126.25 (ArC), 124.55 (2ArCH), 120.09 (ArCH), 119.47 (ArC), 116.31 (ArC), 115.53 (ArCH), 111.46 (ArCBr). Mass spectrum: HRMS (ES^-) 336.9098, $C_{12}H_6{}^{79}BrN_2OS_2$ requires 336.9105, *m/z* (ES^-): 249.9298 (70 % $[M\text{-}CSNHCO]^-$). υ cm^{-1}: 3233.1, 3102.4, 2843.0, 1676.8, 1582.8, 1568.8, 1511.9, 1484.0, 1436.2, 1355.2, 1330.6, 1295.0, 1227.5, 1194.7, 1147.4, 1072.2, 1049.1, 1021.1, 931.5, 893.8, 852.4, 797.4, 779.6, 748.2, 687.0, 669.2, 607.5, 587.7, 570.8, 534.2, 466.7, 418.0.

(Z)-5-((6-iodo-1*H*-indol-3-yl)methylene)-2-thioxothiazolidin-4-one



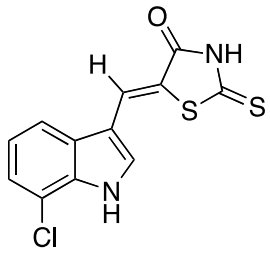
Yield; 69.3 %. mp. ~ 320 °C (dec.). δ_H (400 MHz, DMSO-d_6): 13.59 (1 H, s, NH), 12.32 (1 H, s, NH), 7.88 (1 H, s, CH=CS), 7.85 (1 H, s, ArCH), 7.78 (1 H, d, *J* = 6.5, ArCH), 7.47 (1 H, d, *J* = 8.5, ArCH). δ_C (125 MHz, DMSO-d_6): 194.62 (CS), 169.05 (CO), 137.27 (ArC), 130.27 (ArCH), 129.58 (ArCH), 126.11 (ArC), 124.09 (ArCH), 120.96 (ArCH), 120.70 (ArCH), 118.89 (ArC), 110.97 (ArCH), 87.43 (ArCI). Mass spectrum: HRMS (ES^-) 384.8966, $C_{12}H_6IN_2OS_2$ requires 384.8966, *m/z* (ES^-): 297.9156 (25 % $[M\text{-}CSNHCO]^-$). υ cm^{-1}: 3231.2, 2998.3, 2837.7, 1683.6, 1581.3, 1568.3, 1509.5, 1479.6, 1445.4, 1354.3, 1327.3, 1302.2, 1232.3, 1218.3, 1141.2, 1128.6, 1073.2, 1053.9, 1024.0, 887.1, 847.1, 805.1, 793.6, 775.8, 724.6, 712.1, 678.8, 661.0.

(Z)-5-((7-fluoro-1*H*-indol-3-yl)methylene)-2-thioxothiazolidin-4-one



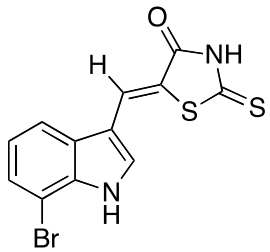
Yield; 54.1 %. mp. ~ 350 °C (dec.). δ_H (400 MHz, DMSO-d_6): 13.59 (1 H, s, NH), 12.82 (1 H, s, NH), 7.90 (1 H, s, CH=CS), 7.80 (1 H, d, *J* = 2.5, ArCH), 7.77 (1 H, d, *J* = 7.5, ArCH), 7.35 (1 H, dt, J_1 = 7.5, J_2 = 5.0, ArCH), 7.21 (1 H, dd, J_1 = 11.5, J_2 = 8.0, ArCH). δ_C (125 MHz, DMSO-d_6): 195.25 (CS), 169.76 (CO), 147.65 (ArCF, d, *J* = 273.5), 130.93 (ArC), 130.71 (ArCH), 124.88 (ArC, d, *J* = 13.0), 124.51 (ArCH), 122.33 (ArCH, d, *J*= 6.0), 120.10 (ArC), 115.21 (ArCH), 112.17 (ArC), 108.67 (ArC, d, *J* = 16.0). Mass Spectrum HRMS [ES^-] 276.9901, $C_{12}H_7FN_2OS_2$ requires 276.9906, *m/z* (ES^-): 190.0099 (100 % [M-CONHCS]$^-$). υ cm^{-1}: 3275.5, 3042.2, 2851.2, 1685.5, 1641.1, 1576.5, 1514.8, 1445.9, 1361.0, 1342.2, 1320.5, 1295.9, 1256.9, 1229.9, 1216.9, 1171.1, 1141.7, 1113.2, 1063.6, 1051.5, 1019.2, 975.8, 910.2, 865.4.

(Z)-5-((7-chloro-1*H*-indol-3-yl)methylene)-2-thioxothiazolidin-4-one



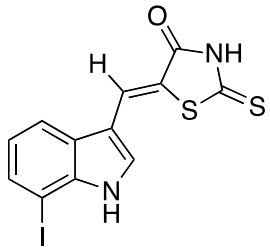
Yield; 63.2 %. mp. ~ 350 °C (dec.). δ_H (400 MHz, DMSO-d_6): 13.64 (1 H, s, NH), 12.70 (1 H, s, NH), 7.94 (1 H, d, *J* = 8.0, ArCH), 7.90 (1 H, s, CH=CS), 7.75 (1 H, d, *J* = 3.0, ArCH), 7.35 (1 H, d, *J* = 8.0, ArCH), 7.21 (1 H, t, *J* = 8.0, ArCH). δ_C (125 MHz, DMSO-d_6): 195.12 (CS), 169.58 (CO), 133.74 (ArC), 130.68 (ArCH), 129.10 (ArCCl), 124.44 (ArCH), 123.33 (ArCH), 122.78 (ArCH), 120.19 (ArC), 118.23 (ArCH), 117.22 (ArC), 112.39 (ArC). Mass Spectrum HRMS [EI^+] 293.9688, $C_{12}H_7{}^{35}ClN_2OS_2$ requires 293.9681, *m/z* (EI^+): 206.9837 (100 % [M-CONHCS]$^+$), 191.0125 (30 % [M-ClCONHCS]$^+$), 163.0167 (50 % [M-CCONHCSS]$^+$). υ cm^{-1}: 3357.9, 3066.7, 2837.7, 1896.7, 1806.97, 1696.6, 1645.0, 1620.9, 1586.7, 1564.5, 1513.9, 1490.2, 1436.7, 1358.6, 1339.3, 1313.8, 1295.5, 1247.2, 1218.8, 1194.2, 1149.4, 1134.4, 1087.2, 1051.0, 1019.7, 899.6, 856.7, 823.9, 785.4, 779.1, 772.8, 734.8, 698.1, 632.1, 609.9.

(Z)-5-((7-bromo-1*H*-indol-3-yl)methylene)-2-thioxothiazolidin-4-one



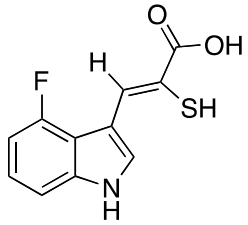
Yield; 90.8 %. mp. ~330 °C (dec.). δ_H (400 MHz, DMSO-d_6): 13.64 (1 H, s, NH), 12.54 (1 H, s, NH), 7.99 (1 H, d, *J* = 7.5, ArCH), 7.90 (1 H, s, CH=CS), 7.72 (1 H, d, *J* = 3.0, ArCH), 7.50 (1 H, d, *J* = 7.5, ArCH), 7.16 (1 H, t, *J* = 7.5, ArCH). δ_C (125 MHz, DMSO-d_6): 195.36 (CS), 168.98 (CO), 134.89 (ArC), 129.96 (ArC), 128.45 (ArCH), 125.79 (ArCH), 123.89 (ArCH), 122.76 (ArCH), 119.73 (ArC), 118.22 (ArCH), 111.78 (ArC), 104.96 (ArBr). Mass Spectrum HRMS [EI^+] 337.9184, $C_{12}H_7{}^{79}BrN_2OS_2$ requires 337.9183. υ cm^{-1}: 3349.8, 3070.1, 2837.6, 1695.1, 1584.2, 1560.6, 1512.9, 1487.8, 1434.5, 1356.7, 1336.0, 1312.8, 1295.0, 1245.3, 1217.8, 1192.4, 1144.6, 1129.6, 1018.2, 882.3, 846.6.

(Z)-5-((7-iodo-1*H*-indol-3-yl)methylene)-2-thioxothiazolidin-4-one



Yield; 78.8 %. mp. ~ 320 °C (dec.). δ_H (250 MHz, DMSO-d_6): 13.63 (1 H, s, NH), 12.24 (1 H, s, NH), 7.97 (1 H, d, *J* = 7.5, ArCH), 7.86 (1 H, s, CH=CS), 7.67 (1 H, d, *J* = 7.5, ArCH), 7.66 (1 H, s, ArCH), 7.01 (1 H, t, *J* = 7.5, ArCH). δ_C (125 MHz, DMSO-d_6): 194.86 (CS), 169.48 (CO), 139.17 (ArC), 132.76 (ArCH), 130.22 (ArCH), 127.67 (ArC), 124.56 (ArCH), 123.43 (ArCH), 119.95 (ArC), 119.10 (ArCH), 112.49 (ArC), 78.08 (ArCI). Mass Spectrum HRMS [ES^-] 384.8966, $C_{12}H_7IN_2OS_2$ requires 384.8967, *m/z* (ES^-): 297.9168 (40 % [M-CONHCS]$^-$). υ cm^{-1}: 3270.2, 3057.1, 2872.9, 1733.7, 1672.0, 1590.5, 1576.0, 1556.8, 1509.5, 1484.4, 1464.7, 1440.6, 1425.6, 1351.4, 1332.1, 1309.0, 1241.0, 1195.7, 1148.9, 1129.1, 1073.2, 1017.3, 876.5, 802.7, 773.3, 738.6, 707.7, 685.6, 629.2, 584.8, 556.8, 530.8.

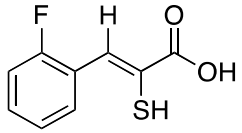
General method for the preparation of α-mercaptoacrylic acids.



To (*E*)-5-((4-fluoro-1*H*-indol-3-yl)methylene)-2-thioxothiazolidin-4-one (0.40 g, 1.44 mmol) was aded 15% aqueous sodium hydroxide solution (4 cm^3). The stirred reaction mixture was heated under reflux under an N_2 atmosphere for 1.5 hr. The reaction mixture was cooled in an ice bath and hydrochloric acid (1 M, 10 cm^3) was added. The precipitate that formed was collected by filtration under reduced pressure and washed with water (2 × 10 cm^3). The solid was air dried under reduced pressure to give the title compound as a light brown coloured solid (0.30 g, 87.2 %). mp. 193 - 196 °C. δ_H (400 MHz, DMSO-d_6): 12.12 (1 H, s, NH), 8.26 (1 H, s, C*H*=CSH), 7.97 (1 H, d, *J* = 2.5, ArCH), 7.33 (1 H, d, *J* = 8.0, ArCH), 7.17 (1 H, dd, J_1 = 5.0, J_2 = 8.0, ArCH), 6.92 (1 H, dt, J_1 =8.0, J_2 = 5.0, ArCH), 5.20 (1 H, s, SH). δ_C (100 MHz, MeOD-d_4): 167.00 (COOH), 157.11 (ArCF, d, *J* = 243.5) 138.86 (ArC, d, *J* = 11.0), 128.64 (ArCH, d, *J* = 4.5), 127.70 (ArCH), 123.60 (ArCH, d, *J* = 8.0), 117.73 (ArC), 115.53 (ArC), 113.47 (ArC), 109.27 (ArCH), 106.15 (ArCH, d, *J* = 20.0). Mass spectrum: HRMS (NSI^-) 236.0190, $C_{11}H_7FNO_2S$ requires 236.0187, *m/z* (NSI^-): 162.0 (30 %). υ cm^{-1}: 3428.8, 2932.7, 2792.4, 2569.7, 1657.0, 1595.8, 1505.2, 1448.8, 1413.1, 1325.3, 1291.6, 1270.9, 1252.5, 1225.5, 1155.2, 1137.8, 1089.6, 1030.3, 901.6, 841.3, 804.2, 775.7, 727.0, 694.2, 648.9, 594.0, 547.7, 519.2, 492.2, 418.5.

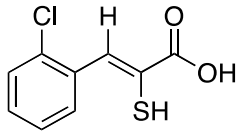
Phenyl Derivatives

(Z)-3-(-2-fluorophenyl)-2-mercaptoacrylic acid



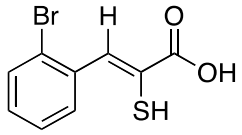
Yield; 91.3 %. mp. 135 - 140 °C. δ_H (400 MHz, MeOD-d_4): 7.91 (2 H, d, *J* = 10.0, ArCH and C*H*=CSH), 7.41 (1 H, q, J_1 = 7.5, J_2 = 6.0, ArCH), 7.29 (1 H, t, J_1 = 8.0, J_2 = 7.5, ArCH), 7.18 (1 H, t, J_1 = 10.0, J_2 = 8.0, ArCH). δ_C (125 MHz, MeOD-d_4): 166.27 (COOH), 160.42 (ArCF, d, *J* = 250.5), 130.46 (ArCH, d, *J* = 8.0), 129.20 (ArCH, d, *J* = 2.0), 126.49 (ArC), 125.42 (ArCH, d, *J* = 7.0), 123.83 (ArCH, d, *J* = 4.0), 123.22 (ArC, d, *J* = 12.0), 115.09 (ArCH, d, *J* = 22.0). Mass spectrum: HRMS (NSI^-) 197.0074, $C_9H_6O_2FS$ requires 197.0078, *m/z* (NSI^-): 133.0119 (10 % $[M-(COOH)(F)]^-$). υ cm^{-1}: 2567.3, 1677.8, 1610.3, 1573.6, 1480.1, 1455.5, 1415.0, 1302.7, 1270.9, 1155.2, 1104.1, 1049.1, 1035.6, 892.9, 846.1, 801.3, 762.7, 721.6, 669.7, 602.2, 540.5, 527.0.

(Z)-3-(-2-chlorophenyl)-2-mercaptoacrylic acid



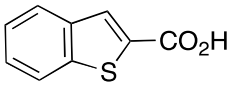
Yield; 63.4 %. mp. 145 - 148 °C. δ_H (400 MHz, MeOD-d_4): 7.96 (1 H, s, C*H*=CSH), 7.83 (1 H, dd, J_1 = 7.5, J_2 = 1.5, ArCH), 7.51 (1 H, dd, J_1 = 7.5, J_2 = 1.5, ArCH), 7.41 (1 H, td, J_1 = 7.5, J_2 = 1.5, ArCH), 7.36 (1 H, td, J_1 = 7.5, J_2 = 1.5, ArCH). δ_C (125 MHz, MeOD-d_4): 166.20 (COOH), 133.80 (ArC), 133.62 (ArCCl), 130.50 (ArCH), 129.74 (ArCH), 129.48 (ArCH), 129.42 (ArCH), 127.09 (ArC), 126.55 (ArCH). Mass spectrum: HRMS (EI^+) 213.9861, $C_9H_7O_2{}^{35}ClS$ requires 213.9855, *m/z* (EI^+): 168.0 (50 %), 85.9 (65 %), 84.0 (100 %). υ cm^{-1}: 3058.55, 2973.21, 2639.11, 2561.97, 1680.66, 1590.02, 1563.50, 1465.63, 1437.67, 1411.64, 1295.45, 1260.25, 1212.52, 1049.09, 1034.62, 887.58, 853.35, 761.26, 743.90, 737.16, 716.91, 686.53, 663.88, 602.16, 534.19, 493.21, 468.62, 418.96.

(Z)-3-(-2-bromophenyl)-2-mercaptoacrylic acid



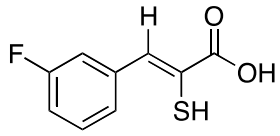
Yield; 84.3 %. mp. 142 - 145 °C. δ_H (400 MHz, MeOD-d_4): 7.89 (1 H, s, C*H*=CSH), 7.77 (1 H, dd, J_1 = 8.0, J_2 = 1.5, ArCH), 7.69 (1 H, dd, J_1 = 8.5, J_2 = 1.5, ArCH), 7.45 (1 H, dt, J_1 = 8.0, J_2 = 1.5, ArCH), 7.27 (1 H, dt, J_1 = 8.0, J_2 = 1.5, ArCH). δ_C (100 MHz, MeOD-d_4) 166.13 (COOH), 135.45 (ArC), 133.00 (ArCH), 132.74 (ArCH), 129.92 (ArCH), 129.59 (ArCH), 127.16 (ArCH), 127.00 (ArC), 123.94 (ArCBr). Mass spectrum: HRMS (EI^+) 257.9344, $C_9H_6{}^{79}BrO_2S$ requires 257.9350, *m/z* (EI^+): 213.9281 (20 % $[M-(COOH)(H)]^+$), 178.0068 (25 % $[M-Br]^+$), 161.0037 (20 % $[M-(Br)(OH)(H)]^+$). υ cm^{-1}: 3445.7, 2828.6, 2649.7, 2570.7, 2548.0, 2360.4, 1683.1, 1600.2, 1560.1, 1463.7, 1434.8, 1416.0, 1318.6, 1289.7, 1264.6, 1212.0, 1047.2, 1028.4, 908.3, 883.2, 850.0, 758.4, 740.5, 733.3, 718.8, 663.4, 600.2, 527.9.

Benzo[*b*]thiophene-2-carboxylic acid



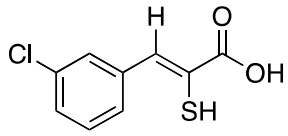
Yield; 72.1 %. mp. 241 - 244 °C. δ_H (400 MHz, MeOD-d_4): 8.07 (1 H, s, C*H*=CSH), 7.94 (2 H, t, J_1 = 7.0, J_2 = 7.0, ArCH), 7.49 (1 H, td, J_1 = 7.0, J_2 = 1.5, ArCH), 7.44 (1 H, dt, J_1 = 7.0, J_2 = 1.5, ArCH). δ_C (125 MHz, MeOD-d_4): 164.37 (COOH), 142.22 (ArC), 138.96 (ArC), 130.18 (ArCH), 126.66 (ArCH), 125.21 (ArCH), 124.32 (ArCH), 122.32 (ArCH), 100.00 (ArC). Mass spectrum: HRMS (NSI^-) 177.0019, $C_9H_5O_2S$ requires 177.0016; υ cm^{-1}: 2817.49, 2578.36, 1666.20, 1593.40, 1557.72, 1521.56, 1460.81, 1439.60, 1415.49, 1338.36, 1318.11, 1306.54, 1276.16, 1253.02, 1184,08, 1162.87, 1155.15, 1136.35, 1079.46, 1051.98, 1011.96, 949.77, 924.70, 886.13, 858.17, 761.74, 750.66, 725.10, 711.60, 584.81, 554.43, 504.29.

(Z)-3-(-3-fluorophenyl)-2-mercaptoacrylic acid



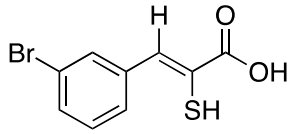
Yield; 68.2 %. mp. 137 - 143 °C. δ_H (400 MHz, MeOD-d_4): 7.77 (1 H, s, C*H*=CSH), 7.45 (3 H, m, ArCH), 7.10 (1 H, m, ArCH). δ_C (100 MHz, MeOD-d_4): 166.40 (COOH), 162.72 (ArCF, d, *J* = 244.5), 137.60 (ArC, d, *J* = 8.1), 132.55 (ArCH), 129.98 (ArCH, d, *J* = 8.0), 125.57 (ArCH, d, *J* = 3.0), 125.52 (ArC, s), 115.58 (ArCH, d, *J* = 22.5), 115.07 (ArCH, d, *J* = 22.0). Mass spectrum: HRMS (ES^-) 197.0077, $C_9H_6O_2FS$ requires 197.0073. υ cm^{-1}: 2567.3, 1677.8, 1610.3, 1573.6, 1480.1, 1455.5, 1415.0, 1302.7, 1270.9, 1155.2, 1104.1, 1049.1, 1035.6, 892.9, 846.1, 801.3, 762.7, 724.6, 669.7, 602.2, 540.5, 527.0.

(Z)-3-(-3-chlorophenyl)-2-mercaptoacrylic acid



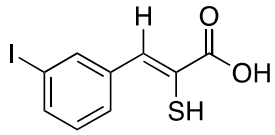
Yield; 79.5 %. mp. 141 - 142 °C. δ_H (400 MHz, MeOD-d_4): 7.75 (1 H, s, C*H*=CSH*)*, 7.68 (1 H, s, ArCH), 7.59 (1 H, d, *J* = 7.5, ArCH), 7.44 (1 H, t, *J* = 8.0, ArCH), 7.37 (1 H, d, *J* = 8.0, ArCH). δ_C (125 MHz, MeOD-d_4): 166.36 (COOH), 137.32 (ArC), 134.17 (ArC), 132.31 (ArCH), 129.71 (ArCH), 128.95 (ArCH), 128.22 (ArCH), 127.74 (ArCH), 125.77 (ArCCl). Mass spectrum: HRMS (ES^-) 212.9769, $C_9H_6O_2{}^{35}ClS$ requires 212.9777, *m/z* (ES^-): 169.0 (60 % $[M-(COOH)(S)]^-$). υ cm^{-1}: 2934.2, 2818.9, 2702.3, 2636.2, 2558.1, 2510.9, 1675.8, 1587.1, 1558.7, 1480.6, 1423.7, 1347.0, 1294.5, 1268.0, 1204.8, 1098.3, 1084.3, 1045.7, 932.4, 903.5, 890.0, 779.6, 748.7, 704.4, 675.9, 658.6, 607.5, 563.6, 495.6, 456.6, 427.6.

(Z)-3-(-3-bromophenyl)-2-mercaptoacrylic acid



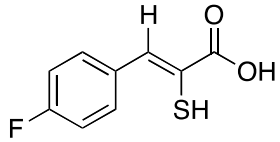
Yield; 74.5 %. mp. 128 - 135 °C. δ_H (500 MHz, MeOD-d_4): 7.84 (1 H, s, ArCH), 7.73 (1 H, s, C*H*=CSH), 7.63 (1 H, d, *J* = 8.0, ArCH), 7.51 (1 H, d, *J* = 8.0, ArCH), 7.37 (1 H, t, *J* = 8.0, ArCH). δ_C (125 MHz, MeOD-d_4): 166.48 (COOH), 137.65 (ArC), 132.05 (ArCH), 131.90 (ArCH), 131.13 (ArCH), 129.92 (ArCH), 128.13 (ArCH), 126.11 (ArC), 122.18 (ArCBr). Mass spectrum: HRMS (ES^-) 256.9270, $C_9H_6O_2{}^{79}BrS$ requires 256.9272, *m/z* (ES^-): 212.9 (30 % $[M-(COOH)(S)]^-$). υ cm^{-1}: 2961.6, 2823.8, 2638.1, 2557.6, 1675.4, 1590.0, 1552.9, 1476.2, 1417.9, 1345.6, 1291.6, 1261.7, 1205.8, 1093.92, 1074.2, 1042.3, 992.7, 905.4, 889.0, 872.6, 779.6, 737.6, 692.8, 675.4, 650.4, 604.1, 555.9, 486.9, 451.3.

(Z)-3-(-3-iodophenyl)-2-mercaptoacrylic acid



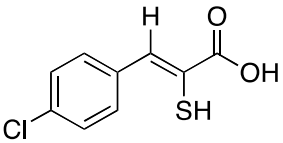
Yield; 68.2 %. mp. 147 - 149 °C. δ_H (500 MHz, MeOD-d_4): 8.02 (1 H, s, ArCH), 7.71 (1 H, d, *J* = 7.0, ArCH), 7.70 (1 H, s, C*H*=CSH), 7.66 (1 H, d, *J* = 8.0, ArCH), 7.22 (1H, t, *J* = 8.0, ArCH). δ_C (125 MHz, MeOD-d_4): 166.36 (COOH), 138.03 (ArCH), 137.53 (ArC), 137.23 (ArCH), 132.20 (ArCH), 129.93 (ArCH), 128.61 (ArCH), 125.59 (ArC), 93.44 (ArCI). Mass spectrum: HRMS (EI^+) 305.9212, $C_9H_6O_2IS$ requires 305.9212, *m/z* (EI^+): 247.0 (40 %), 230.9 (100 %), 202.9 (40 %), 73.0 (95 %). υ cm^{-1}: 2990.6, 2577.9, 1693.7, 1588.1, 1552.4, 1473.4, 1414.5, 1345.6, 1285.8, 1251.1, 1207.7, 1067.4, 1042.3, 989.8, 921.8, 674.0, 644.6, 604.6, 549.1, 488.9, 447.9, 419.0.

(Z)-3-(-4-fluorophenyl)-2-mercaptoacrylic acid:



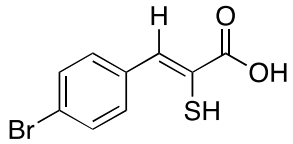
Yield; 87.6 %. mp. 138 - 143 °C. δ_H (400 MHz, MeOD-d_4): 7.79 (1 H, s, C*H*=CSH), 7.72 (2 H, dt, J_1 = 8.5, J_{HF} = 3.5, ArCH), 7.20 (2 H, t, *J* = 8.5, ArCH). δ_C (100 MHz, MeOD-d_4): 167.12 (COOH), 163.57 (ArCF, d, *J* = 250.5), 145.20 (ArCH), 133.12 (ArCH, d, *J* = 8.0), 131.67 (ArCH, d, *J* = 8.0), 127.88 (ArC), 123.48 (ArC), 115.12 (ArCH, d, *J* = 22.0), 114.89 (d, *J* = 22.0, ArCH). Mass spectrum: HRMS (EI^+) 198.0152, $C_9H_6O_2FS$ requires 198.0151, *m/z* (EI^+): 152.0 (50 %), 85.9 (70 %), 84.0 (100 %). υ cm^{-1}: 2822.8, 2577.4, 1667.6, 1596.8, 1580.9, 1505.7, 1421.8, 1307.5, 1298.3, 1264.1, 1233.7, 1165.8, 1105.5, 1039.9, 1014.4, 892.9, 829.2, 798.4, 714.5, 678.3, 621.4, 542.4, 526.0.

(Z)-3-(-4-chlorophenyl)-2-mercaptoacrylic acid



Yield; 58.2 %. mp. 163 – 173 °C. δ_H (400 MHz, MeOD-d_4): 7.77 (1 H, s, C*H*=CSH), 7.66 (2 H, d, *J* = 8.0, ArCH), 7.46 (2 H, dd, J_1 = 6.5, J_2 = 2.0, ArCH). δ_C (125 MHz, DMSO-d_6): 166.52 (COOH), 134.02 (ArC), 132.63 (ArCH), 130.92 (2ArCH), 128.37 (2ArCH), 124.70 (ArCCl). Mass spectrum: HRMS (ES^-) 212.9786, $C_9H_6O_2{}^{35}ClS$ requires 212.9777, *m/z* (ES^-): 169.0 (50 % $[M-(COOH)(S)]^-$), 153.0 (30 %). υ cm^{-1}: 2945.7, 2824.2, 2644.9, 2571.1, 2506.5, 2346.0, 1665.2, 1586.2, 1559.2, 1489.3, 1422.2, 1400.1, 1349.0, 1309.9, 1287.7,123.6, 1207.7, 1115.6, 1092.0, 1037.5, 1013.4, 905.4, 887.1, 845.6, 811.4, 738.1, 702.4, 682.2, 664.8, 623.4, 521.7, 505.3, 446.0.

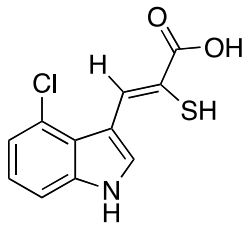
(Z)-3-(-4-bromophenyl)-2-mercaptoacrylic acid



Yield; 81.6 %. mp. 174 – 185 °C. δ_H (400 MHz, MeOD-d_4): 7.75 (1 H, s, C*H*=CSH), 7.60 (4 H, d, *J* = 02.5, ArCH). δ_C (125 MHz, MeOD-d_4): 166.58 (COOH), 134.41 (ArC), 132.62 (ArCH), 131.40 (2ArCH), 131.13 (2 ArCH), 124.97 (ArC), 122.29 (ArCBr). Mass spectrum: HRMS (ES^-) 256.9281, $C_9H_6O_2{}^{79}BrS$ requires 256.9272, *m/z* (ES^-): 212.9 (50 %). υ cm^{-1}: 3445.21, 2951.04, 2823.76, 2638.62, 2587.04, 2558.59, 1674.39, 1580.38, 1557.24, 1485.88, 1418.39, 1395.73, 1342.70, 1308.46, 1288.70, 1270.38, 1206.26, 1181.19, 1115.62, 1077.05, 1037.03, 1009.55, 909.75, 886.61, 850.94, 814.30, 803.21, 768.49, 750.66, 734.75, 699.55, 677.37, 518.76, 499.96, 446.44

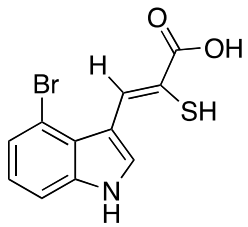
Indole Derivatives

(Z)-3-(4-chloro-1*H*-indol-3-yl)-2-mercaptoacrylic acid



Yield; 80.9 %. mp. 188 - 192 °C. δ_H (400 MHz, DMSO-d_6): 12.17 (1 H, s, NH), 8.81 (1 H, s, C*H*=CSH), 8.06 (1 H, s, ArCH), 7.49 (1 H, m, ArCH), 7.25 (2 H, m, ArCH), 5.20 (1 H, s, SH). δ_C (125 MHz DMSO-d_6): 167.63 (COOH), 139.90 (ArCH), 137.82 (ArCCl), 132.05 (ArCH), 125.03 (ArC), 123.63 (ArCH), 123.54 (ArC), 122.71 (ArCH), 120.71 (ArC), 112.27 (ArCH), 110.85 (ArC). Mass spectrum: HRMS (NSI^-) 251.9892, $C_{11}H_7{}^{35}ClNO_2S$ requires 251.9892. υ cm^{-1}: 3331.9, 3064.8, 2563.9, 1668.6, 1538.3, 1513.4, 1485.4, 1404.9, 1339.8, 1280.5, 1240.5, 1190.8, 1146.0, 1122.4, 1085.2, 1051.5, 1037.5, 938.7, 890.0, 793.1, 776.7, 734.7, 676.9, 570.3, 505.3, 482.1.

(Z)-3-(4-bromo-1*H*-indol-3-yl)-2-mercaptoacrylic acid



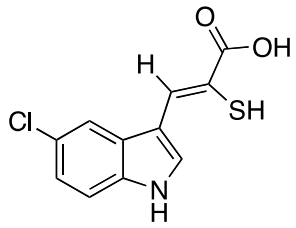
Yield; 70.9 %. mp. 188 - 191 °C. δ_H (400 MHz, DMSO-d_6): 12.22 (1 H, s, NH), 8.94 (1 H, s, C*H*=CSH), 8.05 (1 H, d, *J* = 2.5, ArCH), 7.54 (1 H, d, *J* = 7.5, ArCH), 7.36 (1 H, d, *J* = 7.5, ArCH), 7.12 (1 H, t, *J* = 7.5, ArCH). δ_C (125 MHz DMSO-d_6): 167.69 (COOH), 139.55 (ArCH), 137.80 (ArC), 132.20 (ArCH), 126.10 (ArCH), 124.81 (ArC), 123.97 (ArCH), 120.49 (ArC), 113.11 (ArCH),

112.76 (ArC), 111.13 (ArCBr). Mass spectrum: HRMS (NSI^-) 297.9353, $C_{11}H_7{}^{79}BrNO_2S$ requires 297.9365. υ cm^{-1}: 3403.7, 2559.1, 1661.4, 1579.9, 1558.7, 1509.0, 1481.5, 1403.9, 1335.5, 1281.0, 1238.6, 1188.9, 1142.1, 1080.4, 1048.6, 913.1, 820.6, 774.3, 734.3, 673.0, 607.0, 563.1, 497.1.

5*H*-thiopyrano[4,3,2-*cd*]indole-2-carboxylic acid

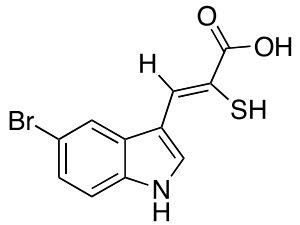
Yield; 68.4 %. mp. ~ 320 °C (dec.). δ_H (400 MHz, DMSO-d_6): 11.14 (1 H, s, NH), 7.44 (1 H, s, C*H*=CS), 7.17 (1 H, d, *J* = 2.5, C=C*H*NH), 6.83 (1 H, t, *J* = 8.0, ArCH), 6.78 (1 H, d, *J* = 8.0, ArCH), 6.43 (1 H, d, *J* = 8.0, ArCH). δ_C (125 MHz DMSO-d_6): 165.21 (COOH), 135.54 (ArC), 128.33 (ArCH), 128.09 (ArC), 125.87 (ArCH), 125.35 (ArC), 122.22 (ArCH), 121.97 (ArC), 112.99 (ArC), 112.30 (ArCH), 108.58 (ArCH). Mass spectrum: HRMS (EI^+) 217.0197, $C_{11}H_7NO_2S$ requires 217.0198. υ cm^{-1}: 3385.9, 2919.2, 2525.8, 2362.9, 1874.0, 1653.2, 1617.0, 1595.3, 1559.7, 1517.2, 1487.3. 1420.8, 1383.7, 1329.7, 1296.9, 1254.5, 1215.9, 1194.2, 1148.9, 1126.2, 1094.4, 1039.9, 1022.1, 948.8, 893.4, 850.0, 825.4, 785.4, 771.4, 733.8, 717.9, 696.7, 629.6, 614.2, 587.2, 554.4, 494.2, 466.2, 419.0.

(Z)-3-(5-chloro-1*H*-indol-3-yl)-2-mercaptoacrylic acid



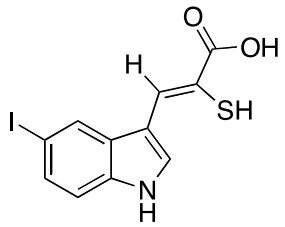
Yield; 97.0 %. δ_H (400 MHz, DMSO-d_6): 12.08 (1 H, s, NH), 8.02 (1 H, s, C*H*=CSH), 8.00 (1 H, d, *J* = 2.0, ArCH), 7.82 (1 H, d, *J* = 2.0, ArCH), 7.51 (1 H, d, *J* = 8.5, ArCH), 7.22 (1 H, dd, J_1 =8.5, J_2=2.0, ArCH) 5.17 (1 H, s, SH). δ_C (100 MHz DMSO-d_6): 167.45 (COOH), 138.26 (ArCH), 134.53 (ArC), 132.07 (ArCH), 129.26 (ArC), 126.09 (ArCCl), 123.03 (ArCH), 121.02 (ArC), 117.86 (ArCH), 114.30 (ArCH), 110.52 (ArC). Mass spectrum: HRMS (NSI^-) 251.9890, $C_{11}H_7{}^{35}ClNO_2S$ requires 251.9892; υ cm^{-1}: 3344.0, 3027.7, 2925.5, 2802.1, 2558.1, 2361.4, 2341.2, 1660.4, 1618.0, 1585.2, 167.8, 1511.0, 1457.9, 1405.8, 1322.9, 1276.6,1258.3, 1225.5, 1139.7,1117.6, 1054.9, 1034.6, 892.9, 852.34, 794.5, 737.5, 740.5, 723.2, 683.6, 656.6, 589.1, 498.5, 475.4, 417.5, 372.2, 354.8, 340.4, 322.1, 313.4.

(Z)-3-(5-bromo-1*H*-indol-3-yl)-2-mercaptoacrylic acid



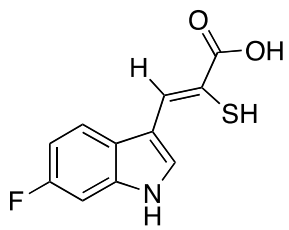
Yield; 89.4 %. mp. 209 - 213 °C. δ_H (400 MHz, DMSO-d_6): 12.05 (1 H, s, NH), 8.05 (1 H, s, C*H*=CSH), 8.03 (1 H, d, *J* = 2.0, ArCH), 8.00 (1 H, d, *J* = 2.0, ArCH), 7.50 (1 H, d, *J* = 9.0, ArCH), 7.37 (1 H, dd, J_1 = 9.0, J_2 = 2.0, ArCH). δ_C (100 MHz DMSO-d_6): 167.05 (COOH), 134.87 (ArC), 129.43 (ArCH), 129.29 (ArC), 125.67 (ArCH), 125.59 (ArC), 121.05 (ArC), 118.01 (ArCH), 114.56 (ArCH), 113.43 (ArC), 111.29 (ArCBr). Mass spectrum: HRMS (NSI^-) 297.9359, $C_{11}H_7{}^{79}BrNO_2S$ requires 297.9365. υ cm^{-1}: 3377.7, 2925.0, 1656.1, 1615.1, 1579.4, 1563.5, 1505.7, 1453.6, 1403.4, 1321.0, 1274.2, 1255.4, 1221.7, 1139.2, 1111.3, 1050.5, 881.3, 793.6, 768.5, 739.6, 718.8, 645.6, 718.8, 645.5, 593.5, 554.0, 496.6, 468.1, 414.1.

(Z)-3-(5-iodo-1*H*-indol-3-yl)-2-mercaptoacrylic acid



Yield; 28.9 %. δ_H (250 MHz, DMSO-d_6): 13.00 (1 H, s, COOH), 12.00 (1 H, s, NH), 8.13 (1 H, s, C*H*=CSH), 8.01 (1 H, s, ArCH), 7.95 (1 H, s, ArCH), 7.49 (1 H, d, *J* = 8.0, ArCH), 7.35 (1 H, d, *J* = 8.0, ArCH). δ_C (100 MHz DMSO-d_6): 167.07 (COOH), 135.23 (ArC), 131.94 (ArCH), 130.98 (ArCH), 130.02 (ArC), 128.87 (ArCH), 127.04 (ArCH), 125.50 (ArC), 114.99 (ArC), 110.95 (ArCH), 84.74 (ArCI). Mass spectrum: HRMS ($APCI^+$) 345.9388, $C_{11}H_9INO_2S$ requires 345.9393. υ cm^{-1}: 3418.2, 2921.2, 2251.5, 1671.0, 1612.2, 1577.0, 1559.2, 1504.7, 1446.8, 1328.7, 1226.0, 1137.3, 1043.8, 878.9, 795.5, 764.6, 699.1, 606.1.

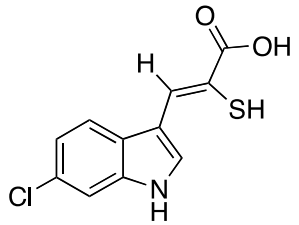
(Z)-3-(6-fluoro-1*H*-indol-3-yl)-2-mercaptoacrylic acid



Yield; 56.2 %. mp. 194 - 196 °C. δ_H (400 MHz, DMSO-d_6): 11.87 (1 H, s, NH), 8.01 (1 H, s, C*H*=CSH), 7.94 (1 H, d, *J* = 2.5, ArCH), 7.76 (1 H, dd, J_1 = 5.5, J_2 = 3.5, ArCH), 7.26 (1 H, dt, J_1 =9.5, J_2 = 2.5, ArCH), 7.00 (1H, td, J_1 = 9.5, J_2 = 2.5, ArCH). δ_C (100 MHz DMSO-d_6): 167.02 (COOH), 159.87 (ArCF, d, *J* = 236.5), 136.05 (ArC, d, *J* = 13.5), 128.76 (ArCH), 125.85 (ArCH), 124.22 (ArC), 119.75 (ArCH, d, *J* = 10.0), 117.80 (ArC), 111.65 (ArC), 109.19 (ArCH, d, *J* = 24.5),

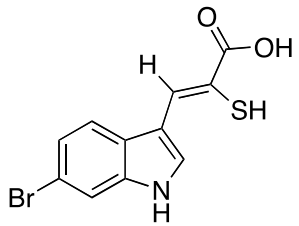
98.58 (ArCH, d, *J* = 25.5). Mass spectrum: HRMS (NSI$^-$) 236.0190, $C_{11}H_7FNO_2S$ requires 236.0187, *m/z* (NSI$^-$). υ cm^{-1}: 3632.8, 3223.9, 1583.3, 1561.6, 1506.1, 1452.1, 1408.8, 1333.5, 1298.8, 1256.4, 1228.4, 1144.1, 1069.8, 907.8, 800.8, 783.4, 725.6, 656.2, 577.6, 491.8.

(Z)-3-(6-chloro-1*H*-indol-3-yl)-2-mercaptoacrylic acid



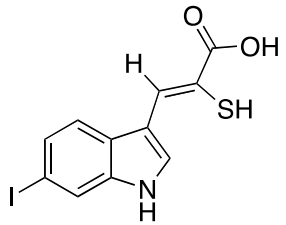
Yield; 51.9 %. mp. 201 - 202 °C. δ_H (400 MHz, DMSO-d_6): 12.93 (1 H, s, COOH), 11.93 (1 H, s, NH), 8.02 (1 H, s, C*H*=CSH), 7.99 (1 H, d, *J* = 2.5, ArCH), 7.78 (1 H, d, *J* = 8.5, ArCH), 7.54 (1 H, t, *J* = 12.5, ArCH), 7.14 (1 H, d, *J* = 8.5, ArCH). δ_C (100 MHz DMSO-d_6): 167.42 (COOH), 138.10 (ArCH), 136.42 (ArC), 131.61 (ArCH), 127.60 (ArCCl), 126.79 (ArC), 121.55 (ArCH), 121.28 (ArC), 119.90 (ArCH), 112.36 (ArCH), 110.82 (ArC). Mass spectrum: HRMS (NSI$^-$) 251.9892, $C_{11}H_7{}^{35}ClNO_2S$ requires 251.9890. υ cm^{-1}: 3632.8, 3223.9, 1583.3, 1561.6, 1506.1, 1452.1, 1408.8, 1333.5, 1298.8, 1256.4, 1228.4, 1144.1, 1069.8, 907.8, 800.8, 783.4, 725.6, 656.2, 577.6, 491.8.

(Z)-3-(6-bromo-1*H*-indol-3-yl)-2-mercaptoacrylic acid



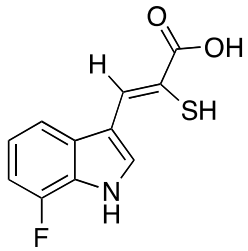
Yield; 77.5 %. mp. 193 – 203 °C. δ_H (400 MHz, DMSO-d_6): 13.11 (1 H, s, COOH), 11.94 (1 H, s, NH), 8.01 (1 H, s, C*H*=CSH), 7.97 (1 H, d, *J* = 2.0, ArCH), 7.73 (1 H, d, *J* = 8.5, ArCH), 7.68 (1 H, d, *J* =1.5, ArCH), 7.27 (1 H, dd, J_1 = 8.5, J_2 = 2.0, ArCH), 5.19 (1 H, s, SH). δ_C (100 MHz DMSO-d_6): 166.99 (COOH), 136.98 (ArC), 129.00 (ArCH), 126.53 (ArC), 125.58 (ArCH), 123.56 (ArCH), 120.43 (ArCH), 118.11 (ArC), 115.65 (ArCBr), 115.10 (ArCH), 111.71 (ArC). Mass spectrum: HRMS (NSI$^-$) 295.9378, $C_{11}H_7{}^{79}BrNO_2S$ requires 295.9386. υ cm^{-1}: 3432.7, 2923.1, 2562.5, 1672.0, 1590.5, 1516.3, 1454.1, 1423.7, 1388.0, 1332.6, 1312.8, 1297.4, 1268.5, 1141.2, 1111.3, 1071.3, 895.8, 851.9, 811.9, 775.2, 726.6, 678.3, 517.3, 419.9

(Z)-3-(6-iodo-1*H*-indol-3-yl)-2-mercaptoacrylic acid



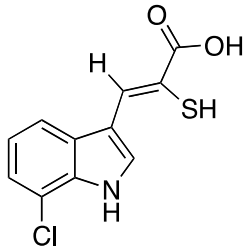
Yield; 66.7 %. mp. 185 - 187 °C. δ_H (400 MHz, DMSO-d_6): 13.02 (1 H, s, COOH), 11.89 (1 H, s, NH), 8.00 (1 H, s, C*H*=CSH), 7.91 (1 H, s, ArCH), 7.85 (1 H, s, ArCH), 7.60 (1 H, d, *J* = 7.5, ArCH), 7.41 (1 H, d, *J* = 7.5, ArCH). δ_C (125 MHz DMSO-d_6): 167.42 (COOH), 138.01 (ArCH), 137.45 (ArC), 131.17 (ArCH), 129.59 (ArCH), 127.42 (ArC), 123.20 (ArC), 121.17 (ArCH), 120.55 (ArCH), 110.87 (ArC), 87.11 (ArCI). Mass spectrum: HRMS (NSI^-) 343.9241, $C_{11}H_7INO_2S$ requires 343.9241. υ cm^{-1}: 3423.5, 2815.6, 2561.5, 1670.1, 1603.5, 1588.6, 1563.5, 1512.9, 1449.7, 1419.4, 1385.1, 1329.7, 1312.8, 1295.5, 1267.0, 1230.8, 1144.6, 1109.8, 1069.8, 1037.0, 901.1, 886.1, 851.9, 808.5, 772.4, 756.0, 742.5, 723.2, 674.0, 635.4, 622.9.

(Z)-3-(7-fluoro-1*H*-indol-3-yl)-2-mercaptoacrylic acid



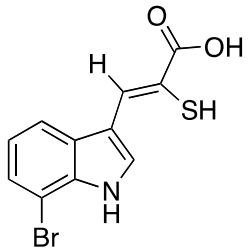
Yield; 77.7 %. mp. 181 - 183 °C. δ_H (400 MHz, DMSO-d_6): 12.38 (1 H, s, NH), 8.03 (1 H, s, C*H*=CSH), 7.95 (1 H, d, *J* = 2.5, ArCH), 7.59 (1 H, d, *J* = 8.0, ArCH), 7.09 (3 H, m, ArCH). δ_C (100 MHz DMSO-d_6): 167.26 (COOH, s), 149.63 (ArCF, d, *J* = 244.5), 138.20 (ArCH), 131.72 (ArC, d, *J* = 5.5), 131.13 (ArCH), 123.75 (ArC, d, *J* = 4.0), 121.75 (ArCH, d, *J* = 6.5), 121.43 (ArC), 114.45 (ArCH), 111.45 (ArC), 107.94 (ArCH, d, *J* = 16.5). Mass spectrum: HRMS (EI^+) 237.0252, $C_{11}H_8FNO_2S$ requires 237.0260. υ cm^{-1}: 3318.4, 3044.1, 2563.4, 1665.7, 1577.0, 1518.2, 1498.4, 1447.3, 1409.2, 1338.4, 1307.5, 1262.2, 1228.9, 1139.2, 1106.0, 1041.9, 975.8, 896.3, 866.4.

(Z)-3-(7-chloro-1*H*-indol-3-yl)-2-mercaptoacrylic acid



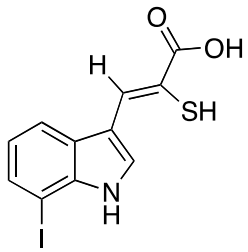
Yield; 81.4 %. mp. 179 - 180 °C. δ_H (400 MHz, DMSO-d_6): 12.24 (1 H, s, NH), 8.01 (1 H, s, C*H*=CSH), 7.93 (1 H, s, ArCH), 7.76 (1 H, d, *J* = 8.0, ArCH), 7.31 (1 H, d, *J* = 8.0, ArCH) 7.18 (1 H, t, *J* = 8.0, ArCH). δ_C (125 MHz DMSO-d_6): 167.64 (COOH), 139.92 (ArCH), 137.82 (ArC), 132.06 (ArCH), 125.03 (ArC), 123.63 (ArCH), 123.54 (ArC), 122.72 (ArCH), 120.70 (ArCCl), 112.27 (ArCH), 110.85 (ArC). Mass spectrum: HRMS (NSI^-) 251.9887, $C_{11}H_7{}^{35}ClNO_2S$ requires 251.9881. υ cm^{-1}: 3344.93, 2810.7, 2567.3, 1669.1, 1623.3, 1596.3, 1569.8, 1518.2, 1491.2, 1435.7, 1422.7, 1405.9, 1338.4, 1306.1, 1265.1, 1243.9, 1200.0, 1155.2, 1119.0, 1090.1, 1042.3, 894.3, 857.7, 780.5, 751.6, 733.8, 718.8, 682.2, 582.4, 540.9, 505.3, 488.4.

(Z)-3-(7-bromo-1*H*-indol-3-yl)-2-mercaptoacrylic acid



Yield; 85.9 %. mp. 165 - 168 °C. δ_H (400 MHz, DMSO-d_6): 12.09 (1 H, s, NH), 8.01 (1 H, s, C*H*=CSH), 7.92 (1 H, d, *J* = 3.0, ArCH), 7.42 (1 H, dd, J_1 = 8.0, J_2 = 3.0, ArCH), 7.10 (1 H, dt, J_1 = 8.0, J_2 = 3.0, ArCH). δ_C (125 MHz DMSO-d_6): 167.26 (COOH), 138.09 (ArCH), 134.48 (ArC), 131.34 (ArCH), 129.74 (ArC), 125.69 (ArCH), 122.66 (ArCH), 121.97 (ArC), 117.97 (ArCH), 111.86 (ArC), 105.29 (ArCBr). Mass spectrum: HRMS (EI^+) 296.9466, $C_{11}H_8{}^{79}BrNO_2S$ requires 296.9459. υ cm^{-1}: 3351.7, 2946.7, 2812.2, 2625.6, 2563.4, 1670.1, 1617.5, 1594.4, 1563.0, 1515.8, 1487.8, 1434.8, 1420.3, 1403.4, 1335.0, 1304.6, 1262.2, 1081.4, 1040.9, 881.3, 847.1, 807.6.

(Z)-3-(7-iodo-1*H*-indol-3-yl)-2-mercaptoacrylic acid



Yield; 81.3 %. mp. 188 - 189 °C. δ_H (400 MHz, DMSO-d_6): 11.78 (1 H, s, NH), 8.24 (1 H, d, *J* = 2.5, ArCH), 8.01 (1 H, s, C*H*=CSH), 7.59 (1 H, d, *J* = 8.0, ArCH), 7.45 (1 H, d, *J* = 8.0, ArCH), 6.80 (1 H, t, *J* = 8.0, ArCH). δ_C (100 MHz DMSO-d_6): 166.94 (COOH), 137.99 (ArCH), 132.02 (ArC), 128.49 (ArCH), 127.93 (ArC), 125.65 (ArCH), 122.61 (ArCH), 118.72 (ArC), 118.59 (ArCH), 112.86 (ArC), 77.96 (ArCI). Mass spectrum: HRMS (NSI^-) 345.9391, $C_{11}H_9INO_2S$ requires 345.9393. υ cm^{-1}: 3384.0, 2920.2, 2571.1, 1679.2, 1588.6, 1555.3, 1514.8, 1481.1, 1419.8, 1396.2, 1331.6, 1303.2, 1260.7, 1239.0, 1197.1, 1143.1, 1112.2, 1072.7, 1039.4, 875.5, 780.5, 752.6, 719.3, 675.9, 605.5, 570.3, 522.6.

Analysis of reversible disulfide formation of mercaptoacrylates

All mercaptoacrylates prepared in this study were observed to change over time as shown below. This change was identified as disulfide formation through the observation that addition of tris(2-carboxyethyl)triphenylphosphine (TCEP, data shown below) or dithiothreitol (DTT, data not shown) caused the compound to revert to its original form. Also loss of the SH resonance (δ_H ~5.20 ppm) was observed by ^{1}H NMR spectroscopy as shown below. Analysis of the kintetics of disulfide formation were determined using a model compound, namely (Z)-3-(1*H*-indol-3-yl)-2-mercaptoacrylic acid, prepared from indole 3-carboxaldehyde exactly as described above.[5] The initial ^{1}H NMR and ^{13}C NMR spectra were acquired immediately and then left for 72 hr and the second set of data was acquired, which demonstrates a movement of proton and carbon resonances and a loss of the sulfhydryl proton.

(Z)-3-(1*H*-indol-3-yl)-2-mercaptoacrylic acid.

δ_H (500 MHz, DMSO-d_6):): 11.87 (1 H, s, NH), 8.06 (1 H, s, C*H*=CSH), 7.94 (1 H, d, *J* = 3.0, ArCH), 7.75 (1 H, d, *J* = 8.0, ArCH), 7.49 (1 H, d, *J* = 8.0, ArCH), 7.22 (1 H, t, *J* = 8.0, ArCH), 7.15 (1 H, t, *J* = 8.0, ArCH) 5.13 (1 H, s, SH). δ_C (125 MHz DMSO-d_6): 167.09 (COOH), 136.15 (ArC), 128.19 (ArCH), 127.53 (ArC), 126.36 (ArCH), 123.02 (ArCH), 120.76 (ArCH), 118.38 (ArCH), 116.92 (ArC), 112.53 (ArCH), 111.56 (ArC).

(2Z,2'Z)-2,2'-disulfanediylbis(3-(1*H*-indol-3-yl)acrylic acid.

δ_H (400 MHz, DMSO-d_6):): 12.01 (1 H, s, NH), 8.46 (1 H, d, *J* = 3.0, ArCH), 8.24 (1 H, s, C*H*=CSH), 7.70 (1 H, d, *J* = 8.0, ArCH), 7.47 (1 H, d, *J* = 8.0, ArCH), 7.20 (1 H, t, *J* = 8.0, ArCH), 7.14 (1 H, t, *J* = 8.0, ArCH). δ_C (125 MHz DMSO-d_6): 167.58 (COOH), 138.72 (ArCH), 136.04 (ArC), 130.71 (ArCH), 128.13 (ArC), 123.06 (ArCH), 121.35 (ArCH), 120.22 (ArC), 118.24 (ArCH), 112.74 (ArCH), 110.79 (ArC).

Analysis of disulfide formation by UV-Vis Spectrophotmetry

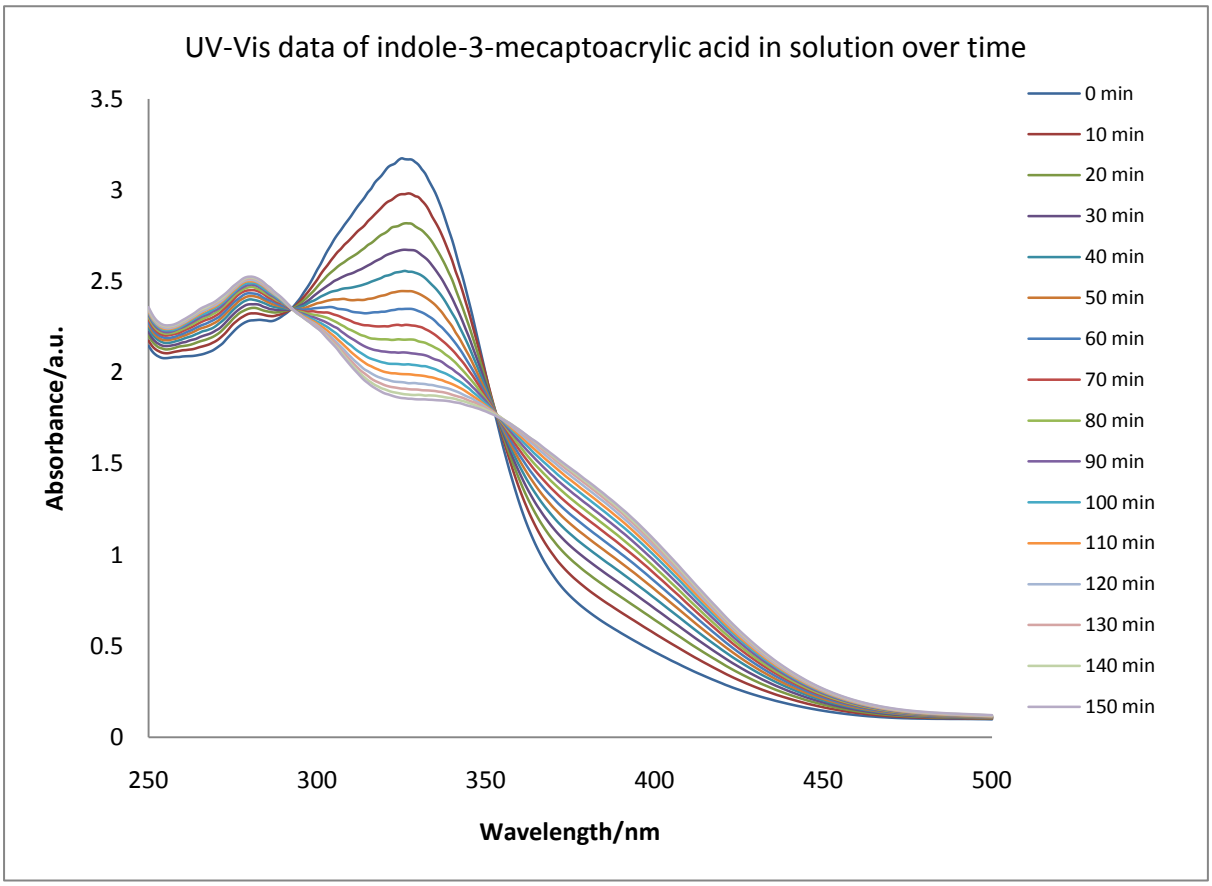


Figure S4. UV-Vis spectra of (Z)-3-(1*H*-indol-3-yl)-2-mercaptoacrylic acid (1mg) in 10 mM phosphate buffer at pH 7.0 (3 cm^3). Spectra were measured every 10 minutes for 3 hr. A clear change in the compound can be observed by the loss of the peak at λ_{max} = 325 nm.

HPLC chromatography

(Z)-3-(1*H*-indol-3-yl)-2-mercaptoacrylic acid (5 mg) was dissolved in 1:1 mixture of acetonitrile and water containing 0.1 % trifluoroacetic acid (pH 4.0, 1 cm^3). This solution (10 mm^3) was injected onto an analytical C18 reverse phase HPLC column and eluted (detecting at 210 nm, flow rate 1 cm^3/min, retention time 23 min) with a linear gradient ranging from 9:1 H_2O:acetonitrile (0.1 % TFA) to 100 % acetonitrile (0.1 % TFA) over 50 min. The solution was left for 24 hr and was then reinjected. The resulting disulfide eluted with a longer retention time of 24.5 min. Following this, a grain (~10 mg) of tris(2-carboxyethyl)phosphine was added and the solution was reinjected (10 mm^3) onto the column at hourly intervals. Within 2 hr the original sulfhydryl peak reappeared returning to a retention time of 23 min.

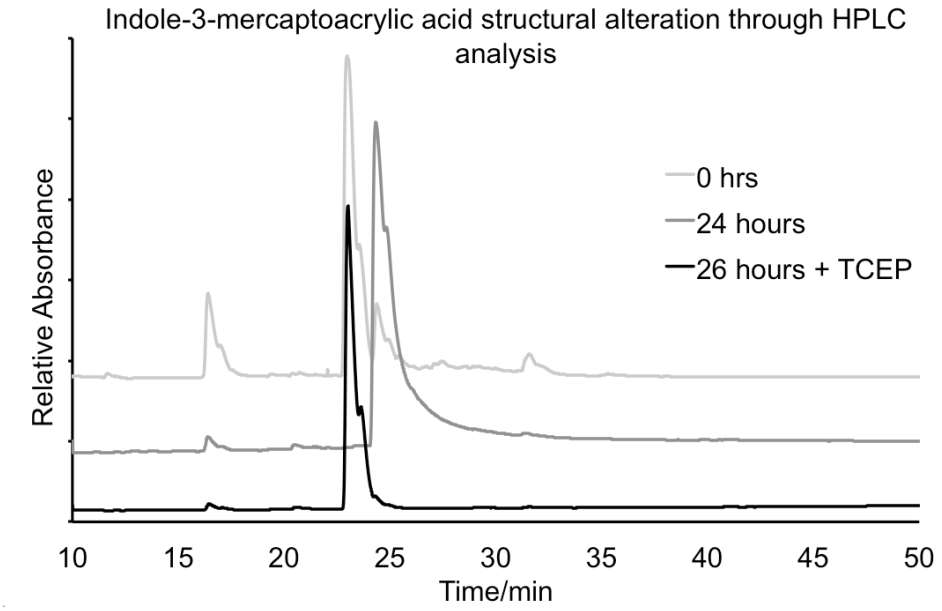


Figure S5. High performance liquid chromatograms (detecting at 210 nm) of reversible disulfide formation from (Z)-3-(1*H*-indol-3-yl)-2-mercaptoacrylic acid through aerial oxidation followed by reduction with TCEP.

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